Menopause: identification and management
Consultation on draft guideline - Stakeholder comments table A - L

17/11/2023 – 05/01/2024

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Association of Reflexologists	Guideline	006	016	Lifestyle changes and interventions that can help support health and wellbeing include nutrition, movement, sleep and relaxation. Elevated cortisol increases the likelihood of severe menopausal symptoms, so the introduction of stress-relieving techniques can improve symptoms and overall wellbeing. There is evidence that CAM therapies, in particular Reflexology, can support people through their menopause journey. There have been studies for vasomotor symptoms **https://www.sciencedirect.com/science/article/abs/pii/S1744388116300433?via%3Dihub** Results The mean scores for hot flashes, sweats, and night sweats, were lower in the reflexology group than the control group after the practice; and the difference between the groups was statistically significant ($p < 0.001$). The mean scores for the sub-groups of the MENQOL demonstrated improvements in both groups after the application ($p < 0.001$). As for the sexual domain, there was a significant improvement in the reflexology group ($p < 0.05$), but no improvements were found in the control group ($p > 0.05$). Conclusion	Thank you for your comment. The effectiveness of reflexology was not in the scope of the 2024 guideline update. Evidence for this topic (including the cited references) was therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this. The cited references have been logged with the NICE surveillance team to consider for future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Results showed that reflexology might be effective in decreasing vasomotor problems and increasing quality of life in women in the menopausal period. There is also a study which suggests Reflexology can be beneficial in paitients experiencing depression through menopause. https://www.sciencedirect.com/science/article/abs/pii/S096522991930281X?via%3Dihub Results A total of 121 patients were assessed for eligibility to participate in the study. One-hundred patients met the criteria to participate, and 90 participants—45 participants in each group—completed the study. In the intervention group, the mean scores of depression before, immediately after, and two months after the study were 26.97 ± 4.47 (95% CI = 25.3–28.3), 22.55 ± 5.18 (95% CI = 20.9–24.1), and 21.20 ± 5.74 (95% CI = 19.4–22.9), respectively. In the control group, these scores were 26.15 ± 5.01 (95% CI = 24.6–27.6), 26.22 ± 5.14 (95% CI = 24.7–27.7), and 26.66 ± 3.87 (95%CI = 25.5–27.8), respectively. Using Repeated Measures ANOVA, the comparison of the mean scores of depression in the two groups indicated that the scores were decreased over time. Conclusion The findings indicated that the foot reflexology technique can be effective for reducing women's depression during menopause.	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				However, considering the study's limitations, including a small sample size and no intervention in the control group, more studies are needed to verify the findings. We would strongly recommend that Reflexology is added to this as a signpost for medical professionals to use when offering self-help support to those going through menopause.	
Association of Reflexologists	Guideline	006	024	The inclusion of anxiety and brain fog as an example of effect on mood would be recommended as they are symptoms which are sometimes overlooked or underdiagnosed. The addition of these raises the awareness to medical professionals and will also help the identification of menopause related symptoms and support correct and efficient signposting.	Thank you for your comment. Whilst an update of the list of symptoms and experiences (including anxiety and brain fog) was outside the current scope of the 2024 guideline update and therefore no evidence review was conducted, the NICE surveillance team checks regularly for new evidence for topics within guidelines to see where further work is needed.
Association of Reflexologists	Guideline	007	009	Non-pharmaceutical, for example, CBT and lifestyle activities aimed at reducing stress for improved physical and emotional wellbeing. The inclusion of Reflexology is recommended.	Thank you for your comment. The committee considered this and other feedback and decided that the examples in the bullet points caused confusion. They were often misunderstood as recommendations rather than examples. They were therefore removed. The effectiveness of reflexology was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
Association of Reflexologists	Guideline	011	017	NOTE – a clear differentiation needs to be made between complementary therapies and unregulated preparations:	Thank you for your comment. The effectiveness of reflexology in the management of menopause was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for and not reviewed and discussed

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Explain that other complementary therapies, for example, reflexology, may be beneficial in reducing stress, anxiety and depression and improving menopausal symptoms, sleep and overall wellbeing. To ensure patient safety, therapies regulated by the Complementary and Natural Healthcare Council (CNHC) should be discussed. Reflexology falls under the voluntary regulator Complementary and Natural healthcare Council (CNHC) which the Association of Reflexologists are a Verifying Organisation for. Both the Association of Reflexologists and the CNHC have a high standard for membership and registration alike. We would recommend, if you add reflexology to your review that you specify an AoR member and/or CNHC registrant would be signposted to ensure the appropriate training has been gained by the therapist and insurance is in place. The membership eligibility of the AoR includes that a regulated qualification must have been completed with a high level of face to face training hours and other strict criterion. This ensures, our members, have achieved some of the highest standard of training in the UK.	with the committee. The committee could therefore not comment on this.
Association of Reflexologists	Guideline	014	006	Explain the benefits of relaxation in reducing menopausal symptoms including vasomotor symptoms as chronically elevated cortisol increases the likelihood of severe menopausal symptoms. ***NOTES**:*	Thank you for your comment. The effects of relaxation, reflexology and relationship between levels of cortisol and severity of menopause symptoms was not part of the 2024 guideline update. Evidence for this topic was not searched for, reviewed or discussed with the committee. The committee could therefore not comment on

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Reference *- Cagnacci A, Cannoletta M, Caretto S, Zanin R, Xholli A, Volpe A. Increased cortisol level: a possible link between climacteric symptoms and cardiovascular risk factors. Menopause. 2011 Mar;18(3):273-8. doi: 10.1097/gme.0b013e3181f31947. PMID: 21037488.* Reflexology is effective in reducing vasomotor symptoms and can be used alongside conventional medications, including HRT. ***NOTES:*** ***Reference*** *- Ebru Gozuyesil, Muruvvet Baser. The effect of foot reflexology applied to women aged between 40 and 60 on vasomotor complaints and quality of life, Complementary Therapies in Clinical Practice, Volume 24, 2016, Pages 78-85.* ***Results*** *The mean scores for hot flashes, sweats, and night sweats, were lower in the reflexology group than the control group after the practice; and the difference between the groups was statistically significant (*p < *0.001). The mean scores for the sub-groups of the MENQOL demonstrated improvements in both groups after the application (*p < *0.001). As for the sexual domain, there was a significant improvement in the reflexology group (*p < *0.05), but no improvements were found in the control group (*p > *0.05).*	this. The cited references do not meet inclusion criteria for the 2024 update but were logged with the NICE surveillance team so that they can be considered for a future update.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Association of Reflexologists	Guideline	018	013	Discuss the benefits of relaxation for improved emotional wellbeing. Reflexology has been shown to lower depression scores over time. ***NOTES:*** ***Reference*** *- Mahdavipour F, Rahemi Z, Sadat Z, Ajorpaz NM. The effects of foot reflexology on depression during menopause: A randomized controlled clinical trial. Complement Ther Med. 2019 Dec;47:102195. doi: 10.1016/j.ctim.2019.102195. Epub 2019 Sep 14. PMID: 31780002.* ***Conclusion:*** *The findings indicated that the foot reflexology technique can be effective for reducing women's depression during menopause.*	Thank you for your comment. The effectiveness of reflexology was not in the scope of the 2024 guideline update (and therefore the cited reference was not included because it did not match any of the protocol criteria). Evidence for this topic was therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
Association of Reflexologists	Guideline	019	002	Explain the importance of good sleep hygiene and discuss the benefits of hands-on complementary therapies, such as reflexology. Reflexology has been shown to be effective in improving sleep in menopausal women. ***NOTES:*** ***Reference*** *- Asltoghiri, M., & Ghodsi, Z. (2012). The effects of Reflexology on sleep disorder in menopausal women. Procedia - Social and Behavioral Sciences, 31, 242-246.* ***Conclusion*** *The results showed a significant reduction sleep disorder after intervention*	Thank you for your comment. The effectiveness of good sleep hygiene and reflexology for difficulties with sleep associated with the menopause were not in the scope of the 2024 guideline update. The committee could therefore not comment on these.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				(p < 0.001). Reflexology is effective in improving of sleep disorder *Consider the inclusion of Reflexology for aiding sleep in the guidance. The ASA and CAP allow reflexologists to advertise this as a proven benefit of Reflexology.*	
Association of Reflexologists	Posed Questions (This form)			1. Would it be challenging to implement of any of the draft recommendations? Please say why and for whom. Please include any suggestions that could help users overcome these challenges (for example, existing practical resources or national initiatives. This review, in its current form, would not effect the Association of Reflexologists in terms of implementation as we are not a medical setting – however, it is of interest as we do signpost clients to medical professionals and therapies and sometimes we are the first port of call for people going though menopause. 2. Would implementation of any of the draft recommendations have significant cost implications? Not for the Association of Reflexologists.	**Thank you for this information.**
Astellas Pharma Ltd	Guidance	General	General	Given the pressing need for effective, licensed, treatment options for moderate to severe vasomotor symptoms (VMS) associated with menopause amongst women for whom	Thank you for your comment. Fezolinetant was not part of the scope of this guideline. However, NICE is conducting a Health Technology Appraisal of Fezolinetant. Once completed it will

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				hormone replacement therapy (HRT) is considered unsuitable, it is crucial that the committee considers the now available clinical evidence base for fezolinetant in VMS associated with menopause and that the guideline update paves the way for automatic incorporation of potential positive guidance. In light of these considerations, the guideline development committee should consider inclusion of a placeholder for clinical recommendation for fezolinetant in the current guideline update, subject to the outcome of the ongoing appraisal [ID5071]. Fezolinetant is an innovative oral, first-in-class, non-hormonal therapy designed to specifically target the thermoregulatory pathways that underpin VMS associated with menopause. Fezolinetant 45 mg, indicated for the treatment of moderate to severe VMS associated with menopause, has received regulatory approval from the Medicines and Healthcare products Regulatory Agency (MHRA).[1] A single technology appraisal (STA) submission dossier for fezolinetant is scheduled for submission to NICE in October 2024. This evaluation aims to appraise the cost-effectiveness of fezolinetant for treating vasomotor symptoms associated with menopause [ID5071].[2] At the time of the NICE menopause guideline scoping consultation (08/02/2022 to 08/03/2022), the efficacy and safety results from the pivotal registration trials for fezolinetant 45 mg, encompassing SKYLIGHT	be considered how to cross-reference to the TA in the menopause guideline.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				1™ (NCT04003155)[3], SKYLIGHT 2™ (NCT04003142)[4], and SKYLIGHT 4™ (NCT04003389)[5], were unpublished, as were the results from DAYLIGHT™ (NCT05033886)[6], the trial most relevant to the scope for the ongoing appraisal [ID5071].[2] As a result, the clinical evidence base for fezolinetant was not considered in the ongoing guideline update. However, post-scoping consultation, the efficacy and/or safety results of fezolinetant 45 mg from the phase 3, randomised, double-blind, placebo-controlled SKYLIGHT 1, SKYLIGHT 2 and SKYLIGHT 4 trials have been published in the peer-reviewed literature.[7-9] Topline results from DAYLIGHT have also been presented at the 15th Congress of the European Society of Gynecology in Amsterdam, The Netherlands.[10] In the following sections we present a high-level clinical overview of this evidence for fezolinetant 45 mg: **The outcomes that matter most** Moderate to severe VMS is one of the most common and bothersome symptoms of menopause, which can negatively impact other aspects of health, including sleep, mental health and daily functioning.[11,12] As per the committee discussion in Evidence review A (CBT), all four Phase 3 fezolinetant trials examined the outcomes that matter most to patients, including frequency and severity of moderate to severe VMS, sleep disturbance, quality of life and psychological outcomes. The	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				benefits of fezolinetant 45 mg demonstrated in the above clinical trials will therefore translate to meaningful improvements for women in clinical practice. **The quality of the evidence** SKYLIGHT 1, SKYLIGHT 2 and SKYLIGHT 4 were methodologically robust and well-reported studies that demonstrated the efficacy and/or safety of fezolinetant 45 mg in addressing moderate to severe VMS in postmenopausal women over a 52-week study period. All three trials were sufficiently powered to detect a meaningful treatment effect, owing to their large sample size and collectively provided data on the efficacy and safety of fezolinetant in more than 2,000 women. Likewise, the DAYLIGHT trial was also a robust study, focussing on the efficacy and safety of fezolinetant 45 mg in postmenopausal women with moderate to severe VMS, who were considered unsuitable for HRT i.e., women who cannot take HRT (HRT-contraindicated, HRT-caution and HRT-stoppers) or women who do not wish to take HRT (HRT-averse).The DAYLIGHT trial was conducted over a 24-week, placebo-controlled study period, and included over 450 women considered unsuitable for HRT. **Benefit and harms** The beneficial effects of fezolinetant 45 mg on the frequency and severity of moderate to	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				severe VMS, were observed as early as Week 1, with continued improvement to Week 4 and a sustained benefit throughout the 12-week double-blind period in SKYLIGHT 1 and 2. Across SKYLIGHT 1, 2 and 4, 52-week safety data showed that fezolinetant 45 mg was not associated with an increased risk of endometrial hyperplasia or endometrial malignancy according to pre-specified criteria for endometrial safety. Transvaginal ultrasound did not reveal increased endometrial thickness. Additionally, treatment-emergent adverse events (TEAEs) of fezolinetant 45 mg were comparable with placebo. The clinical evidence base for fezolinetant 45 mg is further supported by preliminary efficacy and safety results from the DAYLIGHT trial.[10] Over the 24-week study period, the results from DAYLIGHT corroborated the positive impact of fezolinetant 45 mg on reducing the frequency and severity of moderate to severe VMS and demonstrated that TEAEs of fezolinetant 45 mg were comparable to placebo, with no safety signals of concern.[10] **VMS and difficulties with sleep** In individual and pooled analyses of the SKYLIGHT 1 and 2 trials, fezolinetant 45 mg met the four co-primary endpoints (the change from baseline in moderate to severe VMS frequency and severity to Weeks 4 and 12). A statistically significant and clinically meaningful (≥2 hot flashes per 24 hours) reduction in	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				moderate to severe VMS frequency at Weeks 4 and 12 was observed for fezolinetant 45 mg versus placebo. Additionally, a statistically significant reduction from baseline in the severity of moderate to severe VMS at Weeks 4 and 12 was observed. The efficacy of fezolinetant 45 mg in alleviating patient-reported sleep disturbance (PROMIS SD SF 8b; key secondary endpoint) was demonstrated in both individual and pooled trials at Week 12, although statistical significance was not achieved in SKYLIGHT 1. Further, DAYLIGHT showed that fezolinetant 45 mg achieved statistically significant reductions in the frequency and severity of moderate to severe VMS and patient-reported sleep disturbance (PROMIS SD SF 8b) at 24 weeks.[10] **Psychological symptoms and health-related quality of life** In individual SKYLIGHT 1 and 2 trials, Menopause-Specific Quality of Life (MENQOL) total score and the vasomotor domain significantly improved from baseline to Weeks 4 and 12 in women treated with fezolinetant 45 mg versus placebo. **Mode of delivery** Fezolinetant 45 mg is administered orally, once daily, with no additional tests or investigations required. The formulation of fezolinetant as an oral tablet offers women a generally easy method of drug administration that minimises treatment	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				burden. Additionally, the limited monitoring requirements are likely to have minimal impact on current National Health Service (NHS) resources in terms of guideline implementation and staffing requirements. **Cost-effectiveness** The clinical development programme for fezolinetant 45 mg has demonstrated the clinical effectiveness of fezolinetant in treating moderate to severe VMS. As such, NICE are conducting an STA to determine the cost-effectiveness of fezolinetant for treating VMS associated with the menopause [ID5071][2], with submission to NICE expected in October 2024. In light of these considerations, the guideline development committee should consider inclusion of a placeholder for clinical recommendation for fezolinetant in the current guideline update, subject to the outcome of the ongoing appraisal [ID5071]. **References** 1. Medicines and Healthcare Products Regulatory Agency (MHRA). Veoza 45 mg film-coated tablets. Summary of Product Characteristics. Available at: https://mhraproducts4853.blob.core.windows.net/docs/b105452ec51f5f4197a8c9f2d2ef29c79710077a [Accessed 15 December 2023] 2. National Institute for Health and Care Excellence (NICE). Fezolinetant for treating vasomotor symptoms associated with the menopause [ID5071]. Available from:	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				https://www.nice.org.uk/guidance/indevelopment/gid-ta11058 [Accessed 5 December 2023] 3. ClinicalTrials.gov. A Study to Find Out if Fezolinetant Helps Reduce Moderate to Severe Hot Flashes in Women Going Through Menopause (Skylight 1). Available from: https://classic.clinicaltrials.gov/ct2/show/NCT04003155 [Accessed 5 December 2023] 4. ClinicalTrials.gov. A Study to Find Out if Fezolinetant Helps Reduce Moderate to Severe Hot Flashes in Women Going Through Menopause - 2 (Skylight 2). Available from: https://classic.clinicaltrials.gov/ct2/show/NCT04003142 [Accessed 5 December 2023] 5. ClinicalTrials.gov. A Study to Find Out How Safe Long-term Treatment With Fezolinetant is in Women With Hot Flashes Going Through Menopause (Skylight 4). Available from: https://classic.clinicaltrials.gov/ct2/show/NCT04003389 [Accessed 5 December 2023] 6. ClinicalTrials.gov. A Study of Fezolinetant to Treat Hot Flashes in Women Going Through Menopause (Daylight). Available from: https://classic.clinicaltrials.gov/ct2/show/NCT05033886 [Accessed 5 December 2023] 7. Lederman S, Shapiro M, Stute P, Lee M, Wang X, Neal-Perry G. Phase 3 study of fezolinetant for treatment of moderate-to-severe vasomotor symptoms associated with menopause [A132]. Obstetrics & Gynecology. 2022;139:39S. 8. Johnson KA, Martin N, Nappi RE, Neal-Perry G, Shapiro M, Stute P, et al.	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Efficacy and safety of fezolinetant in moderate to severe vasomotor symptoms associated with menopause: a phase 3 RCT. The Journal of Clinical Endocrinology & Metabolism. 2023. 9. Neal-Perry G, Cano A, Lederman S, Nappi RE, Santoro N, Wolfman W, et al. Safety of Fezolinetant for Vasomotor Symptoms Associated With Menopause: A Randomized Controlled Trial. Obstet Gynecol. 2023;141(4):737-47. 10. Schaudig K, Wang X, Bouchard C, et al. Efficacy and safety of fezolinetant for the treatment of moderate to severe vasomotor symptoms associated with menopause in women considered unsuitable for hormone therapy: the Phase 3b DAYLIGHT study, 15th Congress of the European Society of Gynecology (ESG), Amsterdam, The Netherlands, November 30, 2023. 11. Blümel JE, Chedraui P, Baron G, et al. A large multinational study of vasomotor symptom prevalence, duration, and impact on quality of life in middle-aged women. Menopause. 2011;18(7):778-785. 12. Todorova L, Bonassi R, Guerrero Carreño FJ, et al. Prevalence and impact of vasomotor symptoms due to menopause among women in Brazil, Canada, Mexico, and Nordic Europe: a cross-sectional survey. Menopause. 2023;30(12):1179-1189.	
Astellas Pharma Ltd	Guideline	General	General	Astellas recognises the timing rationale for why fezolinetant was not included in the scope of this guideline update; however, given its recent marketing authorisation in the UK[1] and imminent NICE STA[2], Astellas expresses	**Thank you for your comment. Fezolinetant was not part of the scope of this guideline. However, NICE is conducting a Health Technology Appraisal of Fezolinetant. Once**

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				concern regarding the absence of fezolinetant in the current guideline update, given the demonstrable efficacy and/or safety of fezolinetant in treating women with VMS, in particular those women with the highest unmet need (women for whom HRT is considered unsuitable).[3-6] Astellas have been informed by UK clinical experts of the significant reliance by NHS prescribers on NICE clinical guidelines, rather than STAs. Recognising the pertinent role these clinical guidelines play in shaping UK general practice, it becomes crucial to ensure that fezolinetant is duly considered in the current guideline update. Astellas have been advised by UK clinical experts that a positive recommendation within the technology appraisal might not be adequate to guarantee equal access to fezolinetant. Therefore, to maintain consistency in treatment access across UK general practice, it is essential to incorporate provisions in the current guideline update anticipating the ongoing STA for fezolinetant. This suggestion is in alignment with NICE's commitment to reducing health inequalities and addressing broader health and social care perspectives. Astellas also acknowledges NICE's strategic objective of integrating technology appraisals into clinical guidelines, presenting a timely opportunity to fulfil this objective in the ongoing guideline update.	**completed it will then be considered how this may be included in the Menopause guideline.**

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				To facilitate this integration, Astellas proposes the inclusion of a placeholder within the clinical guideline for menopause, recognising the ongoing STA for fezolinetant [ID5071].[7] This approach is particularly relevant to the Vasomotor Symptoms recommendations in Section 1.4, focusing on the management of troublesome menopause symptoms in individuals aged 40 or over. An example placeholder could read: "Subject to the ongoing STA [ID5071], offer fezolinetant for moderate to severe vasomotor symptoms associated with the menopause where HRT is unsuitable". By adopting this approach, the guideline maintains its adaptability, ensuring alignment with emerging evidence, and upholding NICE's commitment to providing comprehensive and updated guidance in women's health. **References** 1. Medicines and Healthcare Products Regulatory Agency (MHRA). Veoza 45 mg film-coated tablets. Summary of Product Characteristics. Available at: https://mhraproducts4853.blob.core.windows.net/docs/b105452ec51f5f4197a8c9f2d2ef29c79710077a [Accessed: 15 December 2023] 2. National Institute for Health and Care Excellence (NICE). Fezolinetant for treating vasomotor symptoms associated with the menopause [ID5071]. Available from: https://www.nice.org.uk/guidance/indevelopment/gid-ta11058 [Accessed 5 December 2023]	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				3. Lederman S, Shapiro M, Stute P, Lee M, Wang X, Neal-Perry G. Phase 3 study of fezolinetant for treatment of moderate-to-severe vasomotor symptoms associated with menopause [A132]. Obstetrics & Gynecology. 2022;139:39S. 4. Johnson KA, Martin N, Nappi RE, Neal-Perry G, Shapiro M, Stute P, et al. Efficacy and safety of fezolinetant in moderate to severe vasomotor symptoms associated with menopause: a phase 3 RCT. The Journal of Clinical Endocrinology & Metabolism. 2023. 5. Neal-Perry G, Cano A, Lederman S, Nappi RE, Santoro N, Wolfman W, et al. Safety of Fezolinetant for Vasomotor Symptoms Associated With Menopause: A Randomized Controlled Trial. Obstet Gynecol. 2023;141(4):737-47. 6. Schaudig K, Wang X, Bouchard C, et al. Efficacy and safety of fezolinetant for the treatment of moderate to severe vasomotor symptoms associated with menopause in women considered unsuitable for hormone therapy: the Phase 3b DAYLIGHT study, 15th Congress of the European Society of Gynecology (ESG), Amsterdam, The Netherlands, November 30, 2023. 7. National Institute for Health and Care Excellence (NICE). Fezolinetant for treating vasomotor symptoms associated with the menopause [ID5071]. Available from: https://www.nice.org.uk/guidance/indevelopment/gid-ta11058 [Accessed 5 December 2023]	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy	Evidence Review A Appendix F	195 - end	General	The Gradings of 'serious or very serious', and 'low to very low' quality are applied to most of the study comparisons. This is surprising given that this literature has been reviewed by others e.g. North American Menopause Society, and has provided strong evidence on which to recommend CBT. Most of the 'low' gradings are based on the problem of inability to blind women undergoing psychological treatments, and the use of subjective measures which is normal practice. Can the Grading Table at least mention these shortcomings? Trials that cannot be blinded should not be downgraded in this way – Cochrane reference: Higgins JPT, Savović J, Page MJ, Elbers RG, Sterne JAC. Chapter 8: Assessing risk of bias in a randomized trial. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.4 (updated August 2023). Cochrane, 2023. Available from www.training.cochrane.org/handbook.	Thank you for your comment. The footnotes provided below the GRADE tables aim to explain the process which led to the ratings captured within the GRADE table for each parameter. The risk of bias assessment of subjective outcomes is in line with Cochrane methodology. The difficulty of blinding for trials with psychological treatments was acknowledged in discussions of the evidence and has been made clearer in this review in the quality of the evidence section.
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy	Evidence review A	General		We welcome this guidance and are pleased that NICE is considering this recommendation.	Thank you for your comment in support of this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy	Evidence review A	General		We note that there are claims by some that HRT can prevent dementia and cardiovascular disease and that these claims are not supported. Given the media coverage relating to CBT for 'menopausal symptoms' we strongly support NICE in the importance of upholding the need for evidence based recommendations.	Thank you for your comment in support of this.
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy	Evidence review A	General		Psychologists developed the CBT specifically for vasomotor symptoms (MENOS protocol) British Journal of Health Psychology (2021), 26, 697–708 Editorial: Is cognitive behaviour therapy an effective option for women who have troublesome menopausal symptoms? This has shown in 6 RCTs with over 1000 women to significantly reduce the impact of the symptoms on daily life, i.e. how problematic they are. The evidence gradings (which are standard ROB and ROB2) in the NICE reviews documents do down grade the studies due mainly to non-blinding in psychological interventions (almost impossible) and use of subjective measures. Trials that cannot be blinded should not be downgraded in this way – Cochrane reference: Higgins JPT, Savović J, Page MJ, Elbers RG, Sterne JAC. Chapter 8: Assessing risk of bias in a randomized trial. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for*	Thank you for your comment. The risk of bias assessment of subjective outcomes is in line with Cochrane methodology. The difficulty of blinding for trials with psychological treatments was acknowledged in discussions of the evidence and has been made clearer in this review in the 'the quality of the evidence' section.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Systematic Reviews of Interventions version 6.4 (updated August 2023). Cochrane, 2023. Available from www.training.cochrane.org/handbook.	
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy	Evidence review A	General		It would be helpful to be more specific in describing what is meant by CBT here for example, - the type of CBT i.e CBT for menopausal symptoms. - level of training and experience and supervision required to deliver effective CBT interventions for menopausal symptoms –and whether this is available - The 'intensity' at which the interventions should be delivered – for example, use of CBT-informed approaches at low intensity level - or high intensity CBT psychotherapy - – we note that there is reference to modes of delivery (for example, group and internet- delivered – very few studies looked at face to face individual work even though there may be some additional benefit)? - While we welcome the recommendations for CBT, the availability of appropriately trained and supervised therapists may not meet the demand – which would affect access - Currently waiting times for CBT psychological therapies vary, and can be lengthy – the national curricula for CBT training do not necessarily	Thank you for your comment. The committee considered the wording of the recommendations and have made changes to the wording to provide more information on the type of CBT i.e. for menopausal symptoms - please see the recommendations specific to CBT for more detail. The committee were unable to provide more information regarding the level of training and experience and supervision required to deliver effective CBT interventions as this ranged across studies and considerations around training fall within the remit of professional bodies rather than NICE. The committee were also unable to provide detail on the intensity of the CBT in the recommendation as there was not enough information regarding this. The mode of delivery also ranged across studies, and the committee agreed it was difficult to determine whether a particular mode of delivery was more beneficial than others and available options should be discussed with the person based on preferences and needs. Please see the committee's discussion of the evidence section for more detail on the mode of delivery.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				reference training to work with menopausal symptoms specifically The recommendations could include a training recommendation and cost implications	
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy	Evidence Review A	general	0	Domain 4 Bias is rated as High in many studies due to inability to blind participants as to their knowledge of treatment group (CBT vs Control); this would apply to all studies considered in this evidence review because it is difficult to conceal that they are having CBT and not another control intervention. It is not possible to blind therapists. Trials that cannot be blinded should not be downgraded in this way – Cochrane reference: Higgins JPT, Savović J, Page MJ, Elbers RG, Sterne JAC. Chapter 8: Assessing risk of bias in a randomized trial. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.4 (updated August 2023). Cochrane, 2023. Available from www.training.cochrane.org/handbook.	Thank you for your comment. The risk of bias assessment of subjective outcomes is in line with Cochrane methodology. The difficulty of blinding for trials with psychological treatments was acknowledged in discussions of the evidence and has been made clearer in this review in the 'the quality of the evidence' section.
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy	Evidence Review A	013 - 015	General	Compared to other medical treatments CBT is safe without side effects. Can this be included?	Thank you for your comment. A sentence highlighting safety and lack of side effects was added to 'Other factors the committee took into account' section of the evidence review as suggested.
BABCP – British Association for Behavioural and	Evidence review A	006	007	We are concerned that – in this introduction - CBT is being presented as an alternative to other treatments for menopause symptoms.	Thank you for your comment. The introduction has been amended to present CBT as an option alongside hormone therapy. The quality of the

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy				There is also an implication that this is only suitable for people who are either unable to take hormone replacement therapy or those who choose not to. We are concerned that the recommendations are suggesting that CBT is an equivalent treatment to HRT - CBT does not treat the same symptoms in the same way as HRT - it is it is not an exact alternative, - and suggest that the evidence could be more clearly presented here CBT is also an appropriate treatment alongside others, and can be delivered at the same time as HRT. It can also be appropriate where HRT is not being taken.	evidence is reflected in the wording of recommendations, and this has been revised to ensure clarity about CBT 'as an option: in addition to HRT, for people for whom HRT is contraindicated or for people who prefer not to take HRT'.
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy	Evidence Review A	011	General	CBT Keefer et al study is a pilot study that has 19 participants and does not seem to meet the usual NICE criteria for inclusion.- Should this be included?	Thank you for your comment. The inclusion of trials is not determined by the size of the study population. All trials which fulfil the predefined review protocol criteria are included and where possible meta analysed which increases statistical power.
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for	Evidence Review A	019	001 - 002	It is mentioned that the evidence included pilot studies and secondary analyses of studies which lowered confidence in the findings – ie 'most of the evidence was considered low or very low quality'. Could the analysis be repeated without these studies?	Thank you for your comment. Unless stated in the protocol, all evidence that meets the protocol requirement is assessed together for the relevant interventions and comparisons. This was not a specified sensitivity analyses in the protocol and therefore was not conducted. However, the committee took the quality of the evidence into

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Rational Emotive Behaviour Therapy					account when making their recommendations. They revised the wording to ensure clarity about CBT 'as an option: in addition to HRT, for people for whom HRT is contraindicated or for people who prefer not to take HRT'.
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy	Evidence Review A	021	025 - 030	There is a cross-reference to the guidance on depression – would it be possible to also cross-reference to guidance on anxiety?	Thank you for your comment. For women with menopause-related anxiety CBT was not associated with a significant decrease in levels of anxiety. The committee therefore decided not to comment on this and not to cross-refer to the NICE guideline on generalised anxiety disorder and panic disorder in adults because these guidelines are not specifically related to menopause.
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy	Evidence Review A	103	003	In the study by Hummel et al 2017 women diagnosed with sexual dysfunction following breast cancer treatment are recruited to a trial of CBT for sexual dysfunction. This type of CBT is not the same as CBT for mood or hot flushes. In addition the women in this study are not recruited because they have hot flushes so it is questionable that it should be used to provide evidence for CBT, on the basis of secondary outcomes, for hot flushes and night sweats. We suggest that this study is excluded from the analysis of hot flushes and night sweats.	Thank you for your comment. The protocol developed for this review does not specify the types of CBT or the specific symptoms of menopause for inclusion. On this basis, Hummel 2017 meets the requirement of the protocol. The guideline committee expressed an interest in the population of this trial as people with a personal history of breast cancer was a predefined protocol strata for this review.
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for	Guideline	General		Summary statement We very much welcome the preparation of this guidance and the recommendations to uphold the evidence base in providing interventions where needed for people experiencing menopause symptoms.	Thank you for your comment. The risk of bias of subjective outcomes is in line with Cochrane methodology. Although blinding is difficult in trials looking at psychological treatments, this does not remove bias from the findings. The committee discussed the difficulty of blinding for trials with psychological treatments. The wording describing blinding in quality of the evidence section in

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Rational Emotive Behaviour Therapy				As with previous NICE consultations, we are raising the concern that studies are downgraded due to lack of blinding, where blinding would not be possible. The impact, interpretation and comparison of blinding in non-pharmaceutical trials (eg CBT) as compared (here and elsewhere) to pharmaceutical trials means that there will inherently be a bias in favour of the pharmaceutical. We would like this method of grading to be reviewed, and suggest consideration of what the difference might be if blinding were not taken into account. We also have concerns that the outcomes may be misleading to members of the public due to the way that evidence is reported and graded. Trials that cannot be blinded should not be downgraded in this way – Cochrane reference: Higgins JPT, Savović J, Page MJ, Elbers RG, Sterne JAC. Chapter 8: Assessing risk of bias in a randomized trial. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.4 (updated August 2023). Cochrane, 2023. Available from www.training.cochrane.org/handbook. The guidance should refer to 'CBT for menopause' where this is the approach being described.	Evidence Review A has been made clearer. Thank you for suggesting wording to the recommendations describing the type of CBT that should be recommended. The committee considered this and reviewed the recommendations regarding CBT, which now specify where they related to menopause-specific CBT. The committee noted that there are long waiting times for CBT. Your comment will be considered by NICE where relevant support activity is being planned. Thank you for suggesting that the guidance should address other factors such as delays in identifying or diagnosing symptoms; occupational distress and providing public health information and training for employers. These topics were not in the scope of the 2024 guideline update therefore the committee are unable to comment on them.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				CBT includes a family of evidence-based psychotherapies and approaches to treating many different presenting issues. When the guidance refers to CBT it should state when this is specifically for menopause – where the primary outcome is reduction in severity and impact of menopause symptoms. CBT aimed at these presenting difficulties would then be more clearly distinguished from other CBT approaches such as CBT designed for treating depression and CBT designed for treating anxiety. The guidance could more overtly address other factors which may have impact on wellbeing and health outcomes during the menopause, for example delays in identifying or diagnosing symptoms as mentioned for younger people experiencing symptoms. Occupational distress could also be considered, for example reviewing evidence that people leave jobs due to experiencing menopause symptoms and/or due to lack of understanding and support from employers which may contribute to health care needs not being met. Providing public health information and training for employers and members of the public more generally may contribute to meeting this need, and research recommendations could be made on this. The impact of access to CBT for menopause and other difficulties must be addressed in the impact statement and calculation. It would be challenging to implement this guidance due to availability of appropriately trained, qualified	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				and accredited CBT psychotherapists or registered wellbeing practitioners who could implement CBT-informed approaches for menopause symptoms. Current training in CBT does not require training to work specifically with menopause symptoms. It would be possible to provide such training as a 'top up' option this would have significant cost implications, including the need for experienced and trained clinical supervisors. It could be most appropriate to train existing therapists who work, for example, in NHS Talking Therapies services where long term physical health conditions are addressed. Demand for CBT in general is very high, and waiting times can be lengthy. Decisions about where to provide such services and accessibility would also cost. Note: We would like to acknowledge the contributions of experts in the field of CBT and menopause and members of our organisations who have provided feedback to be included in our response.	
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy	Guideline	general		We are concerned that the included studies that showed 'no important difference in quality of life' in relation to anxiety as a symptom may lead to anxiety symptoms not being addressed appropriately. As CBT is not one discrete therapy, it is important to differentiate between CBT for menopause, - where the primary outcome is reduction in severity and impact of symtoms – and CBT designed for other	Thank you for your comment. The committee added that the CBT approach should be menopause-specific for vasomotor symptoms and sleep problems. However, they decided not to be prescriptive about this for depressive symptoms because the evidence was not restricted to menopause-specific CBT for this and results for this were less certain which meant that the committee drew on their knowledge of

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				difficulties. This would mean that if anxiety is the predominant symptom then CBT for anxiety may be better indicated and this could be clearer in the guidance. However, it is also important to acknowledge that the physiological component of anxiety and vasomotor symptoms of menopause (e.g. palpitations, feeling hot and sweating) overlap significantly, and CBT can help to make sense of both and how they overlap, and prevent further unnecessary psychological distress that can be caused by these symptoms (i.e. the visual nature of the symptoms, catastrophic thinking relating to palpitations). We ask that these guidelines specify 'CBT for menopause' where this is the therapy being described.	effectiveness of CBT in depression (see the rationale section of the guideline for CBT and depressive symptoms). The committee reflected on the wording of the recommendations related to CBT and updated it to make it explicit that this was not recommended as a first line treatment. It is now stated that it is an option (1) in addition to other treatments (including HRT) (2) for people in whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. The recommendation on a discussion about CBT as a treatment option has also been updated to highlight that information about what CBT is (including menopause specific CBT) and to take account of the person's preferences and needs. Having information about the principles of CBT (including menopause-specific CBT) will help people make an informed choice that is right for them. The evidence was uncertain in relation to anxiety associated with the menopause and the committee therefore did not comment on this. Where a diagnosis of depression is suspected the pathway of the NICE guideline on depression in adults should be followed.
BABCP – British Association for Behavioural and Cognitive Psychotherapies AND AREBT Association for Rational Emotive Behaviour Therapy	Guideline	077	016	The Proposal to remove wording to consider CBT to alleviate low mood and anxiety and replace with wording that CBT for menopause targets vasomotor, sleep and/or depressive symptoms – We suggest that it is important that the guideline labels the CBT as specifically for menopause. If primary difficulty is experiencing and managing the menopause symptoms then a	Thank you for your comment. The committee added that the CBT approach should be menopause-specific for vasomotor symptoms and sleep problems. However, they decided not to be prescriptive about this for depressive symptoms because the evidence was not restricted to menopause-specific CBT for this and results for this were less certain which meant that the committee drew on their knowledge of effectiveness of CBT in depression (see the rationale section of the guideline for CBT and

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				menopause specific approach is indicated. If the primary issue is depression and anxiety then the protocol may be different. Patients may disengage if they feel it's suggested that symptoms are 'just mental health'. The key message which we would want people to understand is that CBT is an effective treatment for physical symptoms but the type of CBT is different from CBT for common mental health difficulties. At assessment, anxiety can be considered as both potentially co-morbid and a consequence of menopausal symptoms, as well as pre-morbid in some patients. However anxiety arises in menopause, CBT as an adjuvant therapy for Menopause would be in line with existing evidence and knowledge on psychophysiology and treatment of anxiety and the distress that arises from other medical problems (See other NICE guidelines for medical problems that recommend CBT and psychological interventions for medical problems). Could CBT for anxiety also be cross referenced with other NICE guidance in terms of developing an optimum treatment plan where anxiety is identified- as is suggested for depression – again to ensure that it is clear what the primary outcomes are and to assist with assessment.	depressive symptoms). The committee reflected on the wording of the recommendations related to CBT and updated it to make it explicit that this was not recommended as a first line treatment. It is now stated that it is an option (1) in addition to other treatments (including HRT) (2) for people in whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. The recommendation on a discussion about CBT as a treatment option has also been updated to highlight that information about what CBT is (including menopause specific CBT) and to take account of the person's preferences and needs. Having information about the principles of CBT (including menopause-specific CBT) will help people make an informed choice that is right for them. The evidence was uncertain in relation to anxiety associated with the menopause and the committee therefore did not comment on this. Where a diagnosis of depression is suspected the pathway of the NICE guideline on depression in adults should be followed.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Bayer Plc	Guideline	087 088 089 090 091 092 092 093 093 094 094 095 095 096 097 098		Appendix A, Table 1 Table 2 Table 3 Table 4 Table 5 Table 6 Table 7 Table 8 Table 9 Table 10 Table 11 Table 12 Table 13 Table 14 Table 16 Table 17 The information presented in these tables is complex and likely to be difficult for patients to understand. The tables could be improved by presenting the risk difference in its own row rather than the reader needing to do mental arithmetic. It might increase the understandability of the information in these tables if the risks and benefits could also be presented in terms of NNT (numbers needed to treat) and NNH (numbers needed to harm).	Thank you for your comment. The tables have been reviewed and further introductory information has been added. A narrative version of the tables and a visual representation of the data were also added. Lay member and GP input was also sought to make this more user-friendly to support decision making.
Bayer Plc	Guideline		011	Section 1.4.6	Thank you for your comment. This 2015 recommendation of the guideline was not in the

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				The comment is made that the safety, quality and purity of constituents in unregulated preparations may be unknown. Given that licensed and regulated preparations are available it may be beneficial to add the following statement: *"It is therefore recommended that people are advised to use regulated and/or licensed preparations if available".*	scope of the 2024 guideline update. Evidence for this topic was therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
Bayer Plc	Guideline			Section 1.4.16 The evidence for CBT has been noted as being uncertain in the guideline with efficacy differing according to the underlying symptom(s) i.e. there is relatively strong evidence for CBT in depression/anxiety but the results are mixed in respect of vasomotor symptoms. CBT should only be considered as a standalone treatment if pharmacotherapy therapy is not appropriate. In other instances CBT should only be considered if used in addition to pharmacotherapy. In all circumstances CBT should only be offered in the context of care that is personalised to the individual.	Thank you for your comment. The rationale describes that the results often depended on the measurement that was used and if anything was somewhat stronger for vasomotor symptoms than depressive symptoms associated with menopause (see evidence review A). The committee reflected on the wording of the recommendations related to CBT and updated it to make it explicit that this was not recommended as a first-line treatment. It is now stated that it is an option (1) in addition to other treatments (including HRT) (2) for people in whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. The committee recommended an approach that is tailored to the individual considering the benefits and risks of each treatment in a shared decision-making process.
Bayer Plc	Guideline	General	General	These guidelines are relatively complex and will not be easy for lay people to understand. It is therefore important that patient-friendly materials are developed	Thank you for your comment. Based on the numbers in the appendix of the consultation a discussion aid document has been developed which includes data visualisation as well as a

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					verbal description of what the numbers mean. Descriptions of the underlying concepts and calculation are also provided. This discussion aid has undergone user-testing and was refined based on user feedback.
Bayer Plc	Guideline	General	General	A large number of women will be experiencing menopausal symptoms at the age of 40 years and when risk factors are considered at the NHS Health check. The NHS Health checks represent an important opportunity to consider menopause and its treatment.	Thank you for your comment. The committee agrees that such health checks are a good opportunity to discuss menopause and its treatment. Your comment will be considered by NICE where relevant support activity is being planned.
Bayer Plc	Guideline	006	002 - 009	Individualised treatment is very important and it is good to see recommendations about tailored treatment in several places in the guideline. We anticipate that busy physicians will target their reading of the guideline and 'dip in and out' of various sections according to their need. As a result the message about the importance of individualised care may be missed as it is not included in all sections. It might be of benefit if more sections of the guideline mentioned the importance of individualised care.	Thank you for your comment in support of this. It is not NICE style to repeat recommendations. Once mentioned recommendations would apply throughout.
Besins Healthcare Ltd	Guideline	010	026	We are concerned that patients' expectations are not managed by the omission of providing information about what to expect from	Thank you for your comment. The committee have revised some of the wording in this section, particularly in relation to possible duration of

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				treatment, when to return for a review, the potential need for increasing the dose or moving to a different delivery method if the one they are using does not suit them. Qualitative market research carried out in 2021 provided a key insight that patients are not always optimally managed as they have not been reviewed by a HCP. It can take months to years for a patient to find the correct treatment regime – finding the right HRT can take time with over 50% of women surveyed taking between 6-24 months and 20% of women even longer (Synergy Market Research).	treatment, which now also refers to the guideline section specifying timing and content of reviews. The section on reviews recommends one at 3 months to assess efficacy and tolerability and then annually thereafter, unless there are clinical indications for an earlier review (such as treatment ineffectiveness, side effects or adverse events). It further states that people should be refer to a healthcare professional with expertise in menopause if treatments do not improve their menopause symptoms or they have ongoing side effects. This was recommended to prevent sub-optimal treatment.
Besins Healthcare Ltd	Guideline	010	008 - 010	Is there any evidence on the impact of having no treatment?	Thank you for your comment. The committee agreed to have a person-centred approach to menopause care tailoring the information and plan to each individual. Depending on the severity and impact that any symptoms associated with the menopause may have on the person, having no treatment could be something that someone may prefer. However, this choice is part of a shared decision making process between the person and the healthcare professional. The impact of having no HRT treatment can be found in the tables that include numbers for never users (but it would be unclear whether they would have taken anything else instead).
Besins Healthcare Ltd	Guideline	010	027 - 028	There should be an addition of the need for review and management of symptoms in comparison to baseline and the ability to optimise treatment if needed.	Thank you for your comment. This has been rephrased to read 'discuss the possible duration of treatment at the outset', followed by 'rediscuss the benefits and risks or continuing treatment at every review'. Therefore, it is a general discussion about the potential duration which would then be revisited at review which would usually include symptoms in comparison to

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					baseline and optimising treatment if needed. This also now includes a cross reference to the 'reviewing treatment' section.
Besins Healthcare Ltd	Guideline	011	008	We are concerned that the wording off the CBT recommendation could be misconstrued as CBT being used instead of HRT. We would recommend more inclusive wording such as 'when discussing CBT as a possible treatment, either in addition to HRT or as an alternative for those who cannot or do not wish to use HRT....'	Thank you for your comment. This specific recommendation focuses about information to be given when discussion CBT and what options are available. Further details have been added to this recommendation, such as giving an explanation of what CBT is (including menopause specific CBT) and to take people's preferences and needs into account when making a shared decision about this option. In section 1.5 on symptom management (evidence showed it to be effective in the management of vasomotor symptoms, depressive symptoms and sleep problems) wording has been revised to ensure clarity about CBT 'as an option: in addition to other treatments (including HRT), for people for whom other treatments are contraindicated or for people who prefer not to take HRT'. This clarifies that CBT is not recommended to replace HRT.
Besins Healthcare Ltd	Guideline	011	003	Could prolonged be defined?	Thank you for your comment. The committee reflected on this and the word 'prolonged' has been removed from this recommendation. It has been rephrased to read 'discuss the possible duration of treatment at the outset', followed by 'rediscuss the benefits and risks or continuing treatment at every review'. Therefore, it is a general discussion about the potential duration which would then be revisited at review.
Besins Healthcare Ltd	Guideline	011	006	**[This text was identified as confidential and has been removed]**	Thank you for your comment. This specific recommendation focuses about information to be given when discussion CBT and what options are available. Further details have been added to this recommendation, such as giving an

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					explanation of what CBT is (including menopause specific CBT) and to take people's preferences and needs into account when making a shared decision about this option. In section 1.5 on symptom management (evidence showed it to be effective in the management of vasomotor symptoms, depressive symptoms and sleep problems) wording has been revised to ensure clarity about CBT 'as an option: in addition to other treatments (including HRT), for people for whom other treatments are contraindicated or for people who prefer not to take HRT'. This clarifies that CBT is not recommended to replace HRT.
Besins Healthcare Ltd	Guideline	013	013	Could this please be clarified how/what is off label?	Thank you for your comment. It has now been clarified that the contraindication relates to active or recent arterial thromboembolic disease.
Besins Healthcare Ltd	Guideline	015	005 - 006	We agree with the specified, and would also like to add think it could be improved if the common GU symptoms were added	Thank you for your comment. A definition of genitourinary symptoms associated with the menopause has been added as suggested.
Besins Healthcare Ltd	Guideline	018	011 - 012	We are concerned that this recommendation may be open to interpretation and instead should be aligned to scales.	Thank you for your comment. A definition has now been provided for this.
Besins Healthcare Ltd	Guideline	019	010	This section has no details about titrating the dose or tachyphylaxis and recommend an addition of an explanation of tachyphylaxis, monitoring and optimising the dosing to improve this recommendation.	Thank you for your comment. This recommendation was out of scope of the 2024 guideline update. So, given that a new evidence review was not conducted, the committee could not comment on this.
Besins Healthcare Ltd	Guideline	019	002	We are concerned that the wording off the CBT recommendation could be misconstrued or imply CBT to be used instead of HRT. We would recommend more inclusive wording such as 'when discussing CBT as a possible treatment, either in addition to HRT or as an	Thank you for your comment. Apart from CBT other management options for sleep problems associated with the menopause were not in the scope of the 2024 guideline update. However, the committee acknowledged that there are other options that may be used (including HRT). They

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				alternative for those who cannot or do not wish to use HRT'	have therefore reworded the recommendation to reflect this. It now states that CBT could be used as an option (1) in addition to other treatments (including HRT), or (2) for people for whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. Given the constraints of the scope they could not be more specific than this.
Besins Healthcare Ltd	Guideline	021	013 - 015	Could you please clarify why the referral is to psychology, is this in addition to HRT?	Thank you for your comment. Psychological support is offered where needed is good clinical practice and the committee recognise the benefit it can have on quality of life. This recommendation is in addition to the recommendation for HRT as a treatment option which is in the section on symptom management of the guideline for people over the age of 40.
Besins Healthcare Ltd	Guideline	023		Table 1 We are concerned as this implies all progesterone preparations hold the same/similar risk for breast cancer when there is data to demonstrate the risk differs between MP and synthetic progesterone Evidence: Join statement: https://thebms.org.uk/wp-content/uploads/2020/09/HRT_and_breast_cancer_statement_in_response_to_EMA_PRAC_recommendations_10.9.20.pdf Stute P, Wildt L, Neulen J. The impact of micronized progesterone on breast cancer risk: a systematic review. Climacteric. 2018 Apr;21(2):111-122. **Rapid Response:** **HRT and breast cancer risk - progesterone vs. progestins**	Thank you for your comment. The committee considered the evidence in the review regarding the different progestogenic constituents. They discussed that the number of cases of breast cancer with those using micronised progesterone were few and agreed that this supported a recommendation to highlight that there was insufficient evidence to support any differences in the risk of breast cancer between micronised progesterone and synthetic progesterone. The committee agreed that more evidence was required to make any robust recommendations for micronised progesterone and made a research recommendation. The reference you refer to 'Stute 2018' has been checked and the included studies also checked for inclusion against the protocol. Some of the studies looking at breast cancer incidence and HRT use are not eligible for inclusion in the review because they

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Evidence suggests that there are important differences in breast cancer risks with different progestogens used in combined [oestrogen + progestogen] hormone replacement therapy (HRT) regimens; micronised natural/bio-identical progesterone appears to be a far safer choice than synthetic progestins. A large French study which assessed and compared the association between different HRTs and breast cancer risk, followed up 80,377 women for an average of 8.1 post-menopausal years, and found that compared with HRT never-use, there was no increased risk of breast cancer for oestrogen-progesterone (relative risk 1.00), whereas those using oestrogen plus progestins had a relative risk of 1.16-1.69 (depending on the progestin used). (1) Another French study also found that breast cancer risk differed by type of progestogen among current users of oestrogen-progestogen therapies. No increased risk was apparent among users of oestrogen + micronised natural progesterone for any duration (odds ratio 0.80), whereas among users of combined HRT containing a synthetic progestin, the odds ratio was 1.57-3.35 (depending on the progestin used). (2) A meta-analysis of studies of postmenopausal women using progesterone vs. synthetic progestins in combination with oestrogen found that progesterone-oestrogen was associated with a lower risk of breast cancer compared with synthetic progestins (relative risk 0.67). (3)	do not meet the date limit in the protocol, or the cohorts have already been included in the review. The references noted in the BMJ rapid response have also been checked. Reference (1): This reference includes data from the E3N cohort. Some of the participants of the E3N cohort have been included in the IPD dataset from the CGHFB, which has been included in our review. It was considered that not all participants of the E3N were included in the CGHFB meta-analysis. However, where there are separate publications with overlapping follow-up periods, and no disaggregation of participants, these have not been included, to avoid double counting of participants in the E3N cohort. As per our processes and methods, we do not reanalyse any existing IPD data as NICE does not generally have the same access to the individual participant data, and therefore the data has been used as it has been published. Due to the large size of the IPD data from the CGHFB, this has been prioritised for inclusion in the review. Reference (2): This reference is a case-control study that cannot be included in our review as it does not meet the protocol criteria as information of hormone therapy was collected after the outcome of interest had occurred, which was a reason for exclusion. Reference (3): The references included in this systematic review have been checked for relevance against our protocol. They cannot be included in the review because they do not meet the protocol because either the outcome of interest was known before information on HRT use was collected, or there was an unknown

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Although not mentioned in the main body of the paper, the Lancet meta-analysis found that the relative risk for <5 years use of oestrogen + micronised natural progesterone was 0.91, i.e. 9% lower than for never-users of HRT. (4) [See appendix] 1. Unequal risks for breast cancer associated with different hormone replacement therapies: results from the E3N cohort study. Breast Cancer Res Treat, 2008;107(1):103-11 2. Risk of breast cancer by type of menopausal hormone therapy: a case-control study among post-menopausal women in France. PLoS ONE, 2013; 8(11): e78016. doi:10.1371/journal.pone.0078016 3. Progesterone vs. synthetic progestins and the risk of breast cancer: a systematic review and meta-analysis. Systematic Reviews, 2016; 5:121; DOI 10.1186/s13643-016-0294-5 4. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. Lancet. 2019. www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)31709-X (appendix Figure S15, p. 45) 5. Progesterone, progestins and the breast in menopause treatment. Climacteric, 2018; 24(4): 326-32 https://www.bmj.com/content/367/bmj.l5928/rr-3#:~:text=Rapid%20Response%3A,S15%2C%20p.%2045)	duration as well as unknown recency of HRT use. Some references also included the E3N cohort, some of which have already been included in our review, please see the detailed reasons as described above for reference 1. Reference (4): The Lancet meta-analysis has already been included in the review. Reference (5): This is a non-systematic review of the literature and therefore does not meet our study design criteria set out in the protocol.
Besins Healthcare Ltd	Guideline	037	015	This recommendation will be a challenging change in practice because this is not technically true for all regimes.	Thank you for your comment. This is not a recommendation but a definition of what continuous and sequential HRT refers to.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Oral micronized progesterone can be given day 1-25 in continuous usage, as this is one of the most commonly use progesterones in HRT this guidance may be confusing. Could we please have clarification of continuous and combined.as this is a commonly asked question from HCPs should be reflective of SPCs	Regardless of potential differences in the regimens, it is the case that continuous combined HRT means that oestrogen and progestogen are taken together, daily (to which we 'usually' has been added to indicate that there could be variation in this), whereas in sequential HRT progestogen is not given for all days in the cycle. That is why the term 'usually' is used before half of the month (in the sequential combined definition) to indicate that there may be differences.
Besins Healthcare Ltd	Guideline	047	007 - 008	Due to the way it is written, we are concerned that this point is not elevated to highlight the limitations that affect the quality of evidence suggesting CBT to be an option and may imply that the evidence is strong therefore should be routine treatment	Thank you for your comment. The committee reflected on the wording of the recommendations related to CBT and revised them to ensure clarity about this ' as an option: in addition to other treatments (including HRT), for people for whom other treatments are contraindicated or for people who prefer not to take HRT'. This makes it clear that CBT is not seen as a first line treatment but as an option where this is a preferred choice. As described in the rationale and impact section, the committee considered the quality of the evidence when making recommendations. This is reflected in the wording used which indicates the recommendation strength. The word 'consider' was used for recommendation 1.4.9 as it is a 'weak' recommendation. In 'strong' recommendations for actions that should (or should not) be offered, directive language such as 'offer' is used. For more information on this please see: Developing NICE guidelines: the manual. The committee have also amended the wording of the recommendation to ensure that there is clarity regarding CBT as an option rather than routine treatment.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Besins Healthcare Ltd	Guideline	049	022 - 023	We are concerned that this recommendation may imply that these women's are 'not that important' and feels like a disservice to women	Thank you for your comment. The wording of the recommendation has been revised to make it explicit that this is an option which could be in addition to HRT, for people in whom HRT is contraindicated or for those who prefer not to take HRT. The related rationale has been revised accordingly.
Besins Healthcare Ltd	Guideline	051	020 - 021	We agree with this point but feel it should be raised in the review section of the recommendations	Thank you for your comment. This statement was removed based on other stakeholder comments and a committee discussion.
Besins Healthcare Ltd	Guideline	058	014 - 015	We are concerned that this recommendation may imply that all women do not need a progesterone if they have had a hysterectomy and alienates cases where hysterectomy is due to endometriosis, and for these women who commence HRT, that progesterone may be needed if there is endometrial foci/tissue outside of the uterus.	Thank you for your comment. The committee discussed that choice between oestrogen-only and combined HRT may be different for people with a sub-total hysterectomy. They decided that they could not be prescriptive about the type of HRT to be used for people who have had a sub-total hysterectomy because their condition is clinically complex and they had not reviewed evidence about the effect of HRT on risk of endometrial cancer for this group. They acknowledged that people who were going to have, or had had, a sub-total hysterectomy would be under the care of a specialist who could discuss HRT options tailored to their needs (or a relevant specialist within the MDT). Due to a lack of evidence, no specific recommendation was made for sub-total hysterectomy; however, the term "total" was added before "hysterectomy" in guidance regarding the offer of oestrogen-only HRT to those who have had a hysterectomy. This addition alerts healthcare professionals to consider other factors for patients with a sub-total hysterectomy.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					The committee also noted that some people have a hysterectomy for a condition that may be affected by HRT, such as endometriosis. The committee did not review evidence related to such conditions. They recognised that the decision about the type of HRT that best balances benefits and risks for the person may be affected by that condition (for example endometriosis) or having had a subtotal hysterectomy. For this reason, they added a recommendation highlighting that advice from a healthcare professional with specialist knowledge of that condition may be needed when making this choice. Due to this stakeholder comment and other related comments, this topic has been logged with NICE surveillance so that it can be considered for a possible update to either the Menopause or the Endometriosis guideline in future.
Besins Healthcare Ltd	Guideline	079		Table 3 1.5.5 We are concerned this may imply these patients can only be seen by a WH GP/Menopause specialist and reducing access to treatment	Thank you for your comment. This is the 'update' table and the recommendation referred to is the 2015 recommendation. The committee decided that the healthcare professional with expertise in menopause would be the appropriate specialist to see them because they are defined as people who can advise and support colleagues in managing complex menopause-related needs and risk factors affecting decision making, including complex medical problems that potentially affect use of treatments for menopause symptoms (see terms used in the guideline). Such healthcare professionals are also

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					likely to seek advice from other specialties if there was any doubt on safety.
Bridging the Silos: Autistic Menopause Study	Guideline	006	002-009	*Page 6, section 1.1. Individualised care:* *1.1.1 Tailor your approach to the person at all times when identifying, 4 investigating and managing menopause (based on their changing 5 symptoms).* *Follow recommendations in NICE's guideline on patient 6 experience in adult NHS services. [2015]* *7 1.1.2 For general principles on how to discuss treatment plans with people, 8 including how to communicate risks, benefits and consequences, see 9 NICE's guideline on shared decision making. [2023]* Consultations and treatment plans should be adapted for individual factors, such as neurodivergence and/or the presence of physical or cognitive disabilities, which affect a) menopause symptoms and experience, and/or b) healthcare encounters, the individual's ability to follow recommendations, and the support they need to do so.	Thank you for your comment. It is agreed that consultations and treatment plans should be adapted to each individual, ensuring they are heard and treated with dignity and respect. This includes providing information in the most suitable format to match the individual's ability to follow recommendations and the support they need to do so. Further detail on treating people as individuals is covered in the NICE guideline on patient experience in adult NHS services as well as in the NICE guideline on shared decision-making so this information is not repeated in all other NICE guidelines (which is the reason why they are cross referred to in recommendations 1.1.1 and 1.1.2). There is an emphasis throughout the guideline on tailoring information to the individual, for example it is emphasised that information about benefits and risks needs to be individualised to the person's age, individual circumstances and potential risk factors. There are also recommendations that highlight that a family member or carer can be involved. Making reasonable adjustments as required by the Equality Act 2010 is a statutory requirement and so this would not need to be repeated in each individual NICE guideline. This would include adjustments for people with learning disabilities as well as neurodivergent people. The Equalities Impact Assessment has been reviewed and further points have been included in the section on disabilities to emphasise the person-centred approach that the committee has taken which

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					they felt would positively impact these groups. The NICE guideline on learning disabilities and behaviour that challenges: service design and delivery as well as the NICE guideline on autism spectrum disorder in adults: diagnosis and management contain sections on 'enabling person-centred care and support' and' identifying the correct interventions and monitoring their use' respectively which outline the ways to get people with learning disabilities and neurodivergent people involved in decision making that is tailored to their needs. These apply to all other NICE guidance, so would not need to be repeated in each individual NICE guideline.
Bridging the Silos: Autistic Menopause Study	Guideline	006 007	018-024 001-002	*Page 6, section 1.2 Information and advice* Offer adapted information to meet accessibility issues relating to neurodivergence and/or physical or cognitive disabilities, such as is provided for people for learning disabilities: NHS Inform Scotland EasyRead Menopause leaflet (November-2021) Menopause.pdf (sath.nhs.uk) And consider signposting neurodivergent people to content on the experience of going through menopause as an autistic person or someone with ADHD: Menopause (autism.org.uk) ADHD and the Menopause (berkshirehealthcare.nhs.uk)	Thank you for your comment. It is agreed that people should be assessed in an individualized manner, ensuring they are heard and treated with dignity and respect, including providing information in the most suitable format. Further details on treating people as individuals are covered in the the NICE guideline on patient experience in adult NHS services as well as in the NICE guideline on shared decision-making so this information is not repeated in all other NICE guidelines (which is the reason why they are cross-referred to in recommendations 1.1.1 and 1.1.2). There is an emphasis throughout the guideline on tailoring information to the individual, for example, it is emphasised that information about benefits and risks needs to be individualised to the person's age, individual circumstances and potential risk factors. There are also recommendations that highlight that a family member or carer can be involved. Making reasonable adjustments as required by the

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					Equality Act 2010 is a statutory requirement and so this would not need to be repeated in each individual NICE guideline. This would include adjustments for people with learning disabilities as well as neurodivergent people. The Equalities Impact Assessment has been reviewed and further points have been included in the section on disabilities to emphasise the person-centred approach that the committee has taken which they felt would positively impact these groups. The NICE guideline on learning disabilities and behaviour that challenges: service design and delivery as well as the NICE guideline on autism spectrum disorder in adults: diagnosis and management contain sections on 'enabling person-centred care and support and' identifying the correct interventions and monitoring their use' respectively which outline the ways to get people with learning disabilities and neurodivergent people involved in decision making that is tailored to their needs. These apply to all other NICE guidance, so this would not need to be repeated in each individual NICE guideline. The topic of neurodivergence as well as learning disabilities has been logged with NICE surveillance so they can be considered for future updates.
Bridging the Silos: Autistic Menopause Study	Guideline	038	011	*Recommendations for research.* Neurodivergence and learning disabilities What is the uptake of HRT in populations with lower mortality, including people with learning disabilities, autism and/or ADHD? Is there a relationship between HRT uptake and excess morbidity and mortality in these populations? How should clinical consultations and treatment plans be adapted for	Thank you for your comment. The topic of uptake of HRT in people with learning disabilities, autism and/or ADHD was not in the scope of the 2024 guideline update. In accordance with NICE processes, research recommendations can only be made on topics that are systematically searched for and reviewed. The suggested research recommendation could therefore not be added.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				neurodivergence (autism, ADHD) and/or learning disabilities? What are the healthcare needs of these populations at menopause?	
Bridging the Silos: Autistic Menopause Study	Guideline	049	008-013	*How the recommendations might affect practice. The committee acknowledged that this would be a change to clinical practice. They noted that people would potentially be able to manage their own symptoms after the standard amount of CBT sessions.* Consideration should be given to emerging research evidence suggesting that CBT may need to be adapted for autistic/neurodivergent individuals (Riches S, Hammond N, Bianco M, Fialho C, Acland J. Adapting cognitive behaviour therapy for adults with autism: a lived experience-led consultation with specialist psychological therapists. *The Cognitive Behaviour Therapist*. 2023;16:e13. doi:10.1017/S1754470X23000053).	Thank you for your comment. CBT needs to be accessible and adapted to each individual, making sure that the person is being treated with dignity and respect (which would include tailoring the CBT approach to people with learning disabilities or autism). Further detail on treating people as individuals is covered in the NICE guideline on patient experience in adult NHS services as well as in the NICE guideline on shared decision-making so this information is not repeated in all other NICE guidelines (which is the reason why they are cross referred to in recommendations 1.1.1 and 1.1.2). There is an emphasis throughout the guideline on tailoring information to the individual, for example it is emphasised that information about benefits and risks needs to be individualised to the person's age, individual circumstances and potential risk factors. There are also recommendations that highlight that a family member or carer can be involved. Making reasonable adjustments as required by the Equality Act 2010 is a statutory requirement and so this would not need to be repeated in each individual NICE guideline. This would include adjustments for people with learning disabilities as well as neurodivergent people. The NICE guideline on learning disabilities and behaviour that challenges: service design and delivery as well as the NICE guideline on autism spectrum disorder in adults: diagnosis and management contain sections on 'enabling person-centred care and support' and 'identifying

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					the correct interventions and monitoring their use' respectively which outline the ways to get people with learning disabilities and neurodivergent people involved in decision-making that is tailored to their needs. These apply to all other NICE guidance and so this would not need to be repeated in each individual NICE guideline. The Equalities Impact Assessment has been reviewed and we have included further points in the section on disabilities to emphasise the person-centred approach that the committee has taken which they felt would positively impact these groups.
British Dietetic Association	Evidence review C	General	General	Evidence review C - Cardiovascular disease Nil studies included which investigate diet, exercise and CVD risk in people experiencing menopause. Diet and lifestyle is a key modifiable risk factor and should be included in literature reviews and recommendations for CVD. https://www.bda.uk.com/resource/menopause-diet.html https://www.ahajournals.org/doi/full/10.1161/JAHA.119.013249 https://link.springer.com/article/10.1007/s12020-022-03152-2 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9321164/ Make recommendations for future research on the role of diet and exercise in protecting CVD risk in postmenopausal women	Thank you for your comment. Diet and exercise were not in the scope of the review question for Evidence Review C. Evidence for these topics was not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this. However, in the 'information and support' section of the guideline it is recommended that healthcare professionals should provide information on 'interventions, or changes the person can make to support their health and wellbeing'.
British Dietetic Association	Evidence review D	General	General	Evidence review D – Breast cancer Discussion regarding alcohol intake as a potential contributor to breast cancer (however risk of confounding), however nil reference to	Thank you for your comment. The effectiveness of reducing alcohol intake (or how it may interact with the HRT) on the risk of breast cancer was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for,

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				reducing alcohol intake / in breast cancer recommendations	reviewed or discussed with the committee. The committee could therefore not comment on this.
British Dietetic Association	Guideline			1.4.18 - No mention of isoflavones in natural food form when combined with plant-based diet for alleviation of vasomotor symptoms.	Thank you for your comment. The effectiveness of diet on vasomotor menopause symptoms was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
British Dietetic Association	Guideline		003	Table 1 - no mention of adequate protein combined with physical activity for optimal maintenance of muscle mass.	Thank you for your comment. The effectiveness of adequate protein intake combined with physical activity for optimal maintenance of muscle mass was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
British Dietetic Association	Guideline			No mention of mindfulness as separate technique to CBT	Thank you for your comment. The evidence review was restricted to CBT. Mindfulness was outside the scope of the 2024 guideline update. The committee could therefore not comment on this. However, the NICE surveillance team regularly checks for evidence which may be considered in decisions whether a future update is needed.
British Dietetic Association	Guideline	General		Lack of recognition of risk of resurgence of eating disorder/disordered eating symptoms and behaviours during menopause or development of eating disorder for first time. Consider inclusion within guidelines e.g. screening and referral to specialist services.	Thank you for your comment. The potential impact of menopause on existing or new eating disorder is outside the scope of the guideline. The committee could therefore not comment on this.
British Dietetic Association	Guideline	General	General	Overall lack of reference to the role of diet in managing symptoms and long-term health conditions associated with menopause. Lack of dietary advice with regards to managing	Thank you for your comment. The impact of diet on the management of symptoms associated with the menopause was not in the scope of the 2024 guideline update. Evidence for this topic was

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				cardiovascular risk and osteoporosis risk. No reference to increased calcium requirements post-menopause. No reference to alcohol in the context of cardiovascular disease. Lack of information and advice regarding weight change that many experience during menopause. Also no mention of the association between diet and lifestyle in protecting against long-term health conditions associated with menopause such as CVD, osteoporosis, depression, poor sleep, cancer. Would be great to see signposting to a dietitian to support with making dietary and lifestyle changes.	therefore not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this. The references listed have been checked and none of them meet the criteria set out in the protocols for the evidence reviews that were updated.
British Dietetic Association	Guideline	006 - 008		Section 1.2 lacks information and advice regarding the role of lifestyle/nutrition in managing CV and metabolic risk. Consider reference to PREDICT studies.	Thank you for your comment. The impact of lifestyle and nutrition in relation to menopause and its symptoms or outcomes was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
British Dietetic Association	Guideline	001	013	"The guideline is for women, trans men and non-binary" - Check this is the most appropriate language. ? Those who identify as women.	Thank you for your comment. The guideline's introduction states that the guideline covers women, trans men and non-binary people registered female at birth. For accuracy, some of the recommendations need to list all groups. Elsewhere, the term 'people' is used to be inclusive and concise. This is used with reference to people for whom it has already been identified that their symptoms are associated with menopause.
British Dietetic Association	Guideline	007	025	1.2.7. Provide recommendations on vitamin D3 supplementation	Thank you for your comment. Vitamin D3 supplementation was not in the scope of the 2024 guideline update. Evidence for this topic was

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
British Dietetic Association	Guideline	007	001	1.2.8. Explain to people experiencing menopause that loss of muscle mass is a musculoskeletal consequence in menopause. Muscle mass strength can be maintained through maintaining activities of daily living and meeting protein requirements. Include a link to UK gov recommendations on physical activity levels - https://www.gov.uk/government/publications/physical-activity-guidelines-adults-and-older-adults/physical-activity-for-adults-and-older-adults-19-and-over-text-of-the-infographic Provide details of the importance of returning to/maintaining exercise during and post-menopause + include referral options for those looking to return to exercise	Thank you for your comment. The effectiveness of exercise and diet in the management of symptoms associated with menopause was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this.
British Dietetic Association	Guideline	007	001	1.2.9 Add another recommendation "Give people experiencing menopause advice on protecting cardiovascular health during and post-menopause, and explain the increased risk of CVD. Provide dietary and lifestyle advice including safe alcohol consumption, and refer to local dietitian if the individual would like to discuss further".	Thank you for your comment. This section was not updated so only the wording was revised to be consistent with the current NICE style. The effectiveness of exercise, diet and other lifestyle changes in relation to the management of symptoms associated with the menopause was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this. However, in the 'information and support' section of the guideline it is recommended that healthcare professionals should provide information on 'interventions, or changes the person can make to support their health and wellbeing'.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Dietetic Association	Guideline	008	012 & 024	"1.3.3. *Be aware that people from ethnic minority backgrounds may experience 25 menopause at a younger age compared with people from White 26 backgrounds"* Worthwhile changing the age recommendation in section 1.3.1 in this instance to reflect the average ages of menopause onset for all ethnicities in the UK population. Current recommendation of age 45years is based on white women only. 1.3.3 still does not help healthcare professionals identify menopause in those from ethnic minority backgrounds as it is not specific. Check "ethnic minority background" is still the most appropriate language.	Thank you for your comment. Identification of the menopause was outside the scope of the 2024 guideline update. Recommendation 1.3.3 was a consensus recommendation made in the context of a discussion related to the effect of either taking or not taking HRT in early menopause. Therefore, a full search was not conducted for prevalence of early menopause or average age of menopause in different groups of people. This is why the current wording was used rather than a more active or direct wording with a detailed age or action associated with this information. The committee's aim was to raise awareness about this so that both clinicians and women from minority backgrounds may identify earlier that they may experience signs and symptoms of the menopause and could make shared decisions about available symptom management options. The topics of menopause prevalence has been highlighted to the NICE surveillance team because they look for evidence which inform decisions for future updates.
British Dietetic Association	Guideline	014	010	1.4.18 Provide more helpful information on sources of dietary isoflavones + phytoestrogens to improve vasomotor symptoms. Isoflavones are mentioned however is this only in supplementary form and dietary sources should be recognised Reduction in ultra-processed foods (particularly sausages) and sugar-sweetened beverages, and an increase in vegetables, fruit, legumes, wholegrain carbohydrates, nuts and seeds have been researched to improve vasomotor symptoms as well as mood and sleep.	Thank you for your comment. The effectiveness of sources of dietary isoflavones + phytoestrogens to improve vasomotor symptom was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				https://pubmed.ncbi.nlm.nih.gov/35033227/	
British Dietetic Association	Guideline	018	014	1.4.36 no mention of nutrition or exercise for depression in menopause guideline or NICE guideline on depression in adults. Refer to the SMILES trial, where adoption of a Mediterranean-style diet improved depression scores.	Thank you for your comment. The effectiveness of nutrition or exercise on depressive symptoms related to the menopause were not in the scope of the 2024 guideline update. The committee could therefore not comment on these.
British Dietetic Association	Guideline	018	014	Lack of reference to diet and lifestyle factors to support in depression management during menopause. Need to consider barriers in management of depression as a result of menopause specific symptoms such as poor sleep	Thank you for your comment. The effectiveness of diet and lifestyle factors on depressive symptoms related to the menopause were not in the scope of the 2024 guideline update. The committee could therefore not comment on these. However, in the 'information and support' section of the guideline it is recommended that healthcare professionals should provide information on 'interventions, or changes the person can make to support their health and wellbeing'.
British Dietetic Association	Guideline	019	002	1.4.37 Sleep can be improved through dietary intervention: Ensuring adequate nutrition throughout the day Inclusion of foods rich in Vitamin B12 helps to produce more of the sleep hormone melatonin. Vitamin B6 for improved energy levels and mood. Iodine and iron help the body turn food into energy properly, Vitamin D contributes to sleep hormone production. Inclusion of moderate aerobic exercise has been shown to improve sleep quality in people experiencing menopause. https://www.sciencedirect.com/science/article/abs/pii/S0378512217304838	Thank you for your comment. Apart from CBT other management options for sleep problems associated with the menopause were not in the scope of the 2024 guideline update. However, the committee acknowledged that there are other options that may be used (including HRT). They have therefore reworded the recommendation to reflect this. It now states that CBT could be used as an option (1) in addition to other treatments (including HRT), or (2) for people for whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. Given the constraints of the scope they could not be more specific than this. A recommendation that information should be shared about

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				https://academic.oup.com/nutritionreviews/advance-article/doi/10.1093/nutrit/nuad113/7268827	'interventions, or changes the person can make, to support their health and wellbeing' is included in the section on 'information and support'. Information about diet would fall into the remit of these conversations.
British Dietetic Association	Guideline	019	001	Lack of reference to diet and lifestyle factors to support with sleep problems associated with the menopause	Thank you for your comment. Apart from CBT other management options for sleep problems associated with the menopause were not in the scope of the 2024 guideline update. However, the committee acknowledged that there are other options that may be used (including HRT). They have therefore reworded the recommendation to reflect this. It now states that CBT could be used as an option (1) in addition to other treatments (including HRT), or (2) for people for whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. Given the constraints of the scope they could not be more specific than this. A recommendation that information should be shared about 'interventions, or changes the person can make, to support their health and wellbeing ' is included in the section on 'information and support'. Information about diet and lifestyle factors would fall into the remit of these conversations.
British Dietetic Association	Guideline	021	013	Remove "if needed" from recommendation 1.5.11 as it feels dismissive. Change the wording to "Offer psychological support to people with early menopause (aged 40 to 14 44) who are distressed by their diagnosis or its consequences. Offer a referral to specialist psychology services.	Thank you for your comment. The aim of the recommendation is to allow psychological support to reach the people in need of it most based on symptoms. The concern with making this service accessible to everyone with early menopause is the large resource impact it would have, and limited access for people who are in most need of this support.
British Medical Association	Guideline	General	General	Will there be a clearer summary?	Thank you for your comment. Based on the numbers in the appendix of the consultation a

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					discussion aid document has been developed which includes data visualisation as well as a verbal description of what the numbers mean. Descriptions of the underlying concepts and calculation are also provided. This discussion aid has undergone user-testing and was refined based on user feedback.
British Medical Association	Guideline	General	General	Can all the risks associated with IUS and topical/oral oestrogens be clarified as this seems to have been missed.	Thank you for your comment. There was not always evidence available for all routes of administration of oestrogen-only or combined HRT. The committee acknowledged that this is an important topic and decided to prioritise route of administration for a research recommendation.
British Medical Association	Guideline	General	General	It is disappointing that there is no basic advice about side effects of HRT and how to troubleshoot these, e.g. irregular bleeding, bloating, nausea etc	Thank you for your comment. Basic advice about side effects of HRT was outside the scope of the 2024 guideline update. However the draft guideline contains a recommendation from 2015 related to vaginal bleeding as a common side effect of systemic HRT within the first 3 months of treatment. This was considered to be the most serious side effect and was therefore specifically mentioned. Other less serious side effect can be mentioned during discussions in line with those reported in the BNF or summary of product characteristics as is usual clinical practice.
British Medical Association	Guideline	General	General	In terms of 'how the recommendations might affect practice', we would like NICE to also tell us how long an initiation and first discussion appointment should be, and how long the 3/12 review and annual reviews should be.	Thank you for your comment. It is not within NICE's responsibilities to specify the duration of appointments.
British Medical Association	Guideline	005	Rec 1	Rec 1 (*Healthcare professionals should use their clinical judgement*). They should also be mindful of limits of their expertise and seek advice accordingly. GPs shouldn't be expected to use their clinical judgement if outside of their	Thank you for your comment. The cited text describes the person-centred approach that the guideline is advocating to ensure all people are treated with dignity and respect throughout care. This is not a recommendation but introductory

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				expertise and experience. This should be explicit, especially given there are still a lot of areas requiring further research.	text. This box also includes a link to a webpage 'Making decisions using NICE guidelines' which summarises laws and regulations associated with clinical practice. The committee also made specific recommendations where input from a healthcare professional with expertise in menopause is required (a role which is defined in the 'Terms used in this guideline' section) or input from another speciality (such as oncology). This should ensure that decisions are not made outside the limits of a clinician's expertise.
British Medical Association	Guideline	007	019	Rec 1.2.6 *(Offer support and providing information*) - If including this recommendation, we would suggest that it should be made clear in the guidance that this is the responsibility of the clinician providing the treatment.	Thank you for your comment. The intention was not to be prescriptive about who should have these conversations, for example fertility could be discussed long before the actual treatment and the surgeon may not be the most appropriate clinician to discuss this. Therefore, no change was made to this recommendation.
British Medical Association	Guideline	008	009	(*Referral to a health professional with expertise in menopause*). Whilst colleagues report there are menopause clinics available these are generally in tertiary centres and have very long (12 month) waits. This risks considerably increasing referrals where it could support GPs further in management of menopause.	Thank you for your comment. The definition of 'healthcare professional with expertise in menopause' is not mandating that these professionals are in tertiary centres. They have been defined as professionals with specialist knowledge, skills and training (for example as recognised by the British Menopause Society, the Faculty of Sexual and Reproductive Healthcare or the Royal College of Obstetricians and Gynaecologists) who can advise and support colleagues in managing complex menopause-related needs and risk factors affecting decision making....'. Therefore, this could also be GPs with a special interest in menopause who have undertaken further training. This broader definition would mean a wider pool of such

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					professionals with a positive impact on waiting times.
British Medical Association	Guideline	009	007-012	Rec 1.3.5 (*Consider using a serum follicle-stimulating hormone (FSH) test to confirm 7 menopause only*). This implies that GPs should never request FSH in women over 45.	Thank you for your comment. Identifying perimenopause and menopause was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
British Medical Association	Guideline	009	016-018	Rec 1.3.6 (*Do not use an FSH test to identify menopause in people using combined 16 oestrogen and progestogen contraception or high-dose progestogen*). What is classed as high dose progesterone?	Thank you for your comment. Identifying perimenopause and menopause was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
British Medical Association	Guideline	010	026	Rec 1.4.3 *(If a person chooses to take HRT, discuss the duration of treatment at the outset, taking account of the 27 benefits and risks*). What is the NICE recommendation regarding duration of treatment that should be discussed at the outset? This reads more like a consultation plan than guidance.	Thank you for your comment. This has been rephrased to read 'discuss the possible duration of treatment at the outset', followed by 'rediscuss the benefits and risks or continuing treatment at every review'. Therefore, it is a general discussion about the potential duration which would then be revisited at review.
British Medical Association	Guideline	011	004/5	The tables on the effects 3 of combined HRT on health outcomes and effects of oestrogen-4 only HRT on health outcomes are helpful.	Thank you for your comment in support of this.
British Medical Association	Guideline	012	001-009	Rec 1.4.7 (*Advise people with a history of, or at high risk of, breast cancer that, although there is some evidence that St John's wort may help, there is uncertainty about*). Why does this messaging only apply to people with a history of, or high of, breast cancer?	Thank you for your comment. Whilst this was not part of the 2024 guideline update, the reason for this is that the evidence for St John's wort was in people with a history of breast cancer. Therefore, the previous committee restricted the recommendation to this population.
British Medical Association	Guideline	012	013/14	Rec 1.4.8 (*People who have taken gender-affirming therapy in the past*). Using the term 'professional with expertise in menopause' seems disingenuous as this guidance is not supportive of GPs doing more than basic	Thank you for your comment. The definition of 'healthcare professional with expertise in menopause' is not mandating that these professionals are in tertiary centres. They have been defined as professionals with specialist

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				provision. What is really being suggested is specialist input. It also needs to be clarified who has the responsibility to ensure access to this, given that GPs without such expertise could not.	knowledge, skills and training (for example as recognised by the British Menopause Society, the Faculty of Sexual and Reproductive Healthcare or the Royal College of Obstetricians and Gynaecologists) who can advise and support colleagues in managing complex menopause-related needs and risk factors affecting decision making....'. Therefore, this could also be GPs with a special interest in menopause who have undertaken further training. The committee decided it was important that people who have taken gender affirming hormone therapy in the past would have the opportunity to discuss their symptoms with such a specialist because such decision are complex and would likely depend on a number of factors (for example how long they had taken gender affirming therapy for and how long ago). The committee therefore agreed that such referrals would likely lead to more appropriate care and improved outcomes.
British Medical Association	Guideline	012	021-023	Rec 1.4.10 *(People with type 2 diabetes).* This is too vague. Which co-morbidities are being referred to in association with type 2 that do or don't require specialist advice? Again, this reads more like a consultation plan rather than guidance to support the clinical decision making regarding the risk versus benefit analysis.	Thank you for your comment. Whilst there are some new recommendations in this section, the general topic of comorbidities (including issues relating to type 2 diabetes mellitus) was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this. However, due to this and other feedback some cited references have been passed on to the NICE surveillance team which regularly checks evidence for guideline topics to see whether further updates are needed.
British Medical Association	Guideline	013	002-004	Rec 1.4.11 *(People at increased risk of venous thromboembolism).* Could this guidance link to	Thank you for your comment. The impact of HRT on risk of VTE was not in the scope of the 2024

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				a risk assessment tool to determine who is classified as increased versus high risk of VTE for this purpose?	guideline update. Evidence for this topic was not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this.
British Medical Association	Guideline	013	011-012	Rec 1.4.13 (*For people with a history of coronary heart disease or stroke, ensure that combined or oestrogen-only HRT is discussed with and, if appropriate, initiated by a healthcare professional with expertise in menopause*). This is ambiguous in the way it is written, who does the 'appropriate' refer to?	Thank you for your comment. The wording in this recommendation was reordered so that the 'if appropriate' is after 'initiated'. The committee intended this to mean that it may not always be appropriate to initiate HRT in this group so moving this wording would clarify this.
British Medical Association	Guideline	013	027	It would be helpful to state what current guidance is on 'identifying and managing familial and genetic risk of ovarian cancer', recognising this may change, but it leaves uncertainty in mean time.	Thank you for your comment. The NICE guideline on identifying and managing familial and genetic risk of ovarian cancer has since been published and therefore the cross reference has been updated. This includes a section on HRT after risk-reducing surgery.
British Medical Association	Guideline	014	002-004	Rec 1.4.15 (*Vasomotor symptoms*). Could a link to the benefits and risk be inserted here?	Thank you for your comment. The details of what should be discussed including benefits and risks is recommended in the section entitled 'discussing treatment options'.
British Medical Association	Guideline	015	General	The section on genitourinary symptoms needs to emphasise the symptom of recurrent Urinary Tract Infections as these women need oestrogen treatment.	Thank you for your comment. Urinary tract infection was not in the scope of the 2024 guideline update. However, this is covered in another NICE guideline and a link to the patient decision aid on reducing the chance of recurrent urinary tract infection (UTI) in postmenopausal women in the NICE guideline on urinary tract infection (recurrent) has been added. This includes the use of vaginal oestrogen where appropriate.
British Medical Association	Guideline	015	General	There is no mention of vaginal estring as an alternative for women with no improvement on their genitourinary symptoms.	Thank you for your comment. Whilst this is not specifically mentioned, the recommendation states that there should be a shared decision with the person about whether to use an oestrogen

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					cream, gel, tablet, pessary or ring. Therefore, a ring such as the vaginal estring could be used.
British Medical Association	Guideline	019	006/7	Rec 1.4.38 - If including a recommendation about Testosterone, and if this guidance is advocating initiation and monitoring of testosterone in routine general practice, there needs to be more clarity, as GPs would usually only prescribe under shared care agreements and GPs would usually refer to a specialist for this. We would suggest including further details, such as criteria for use (only low libido, max optimised oestrogen, usually early or abrupt menopause such as surgical), monitoring for this (6-monthly FAI), and the cost implications. There should also be more guidance about risks, benefits, unknowns etc. The BNF states unlicensed and administered on expert advice.	Thank you for your comment. At the time when the scope of the 2024 guideline update was agreed, there was no substantive new evidence that would change the recommendation related to testosterone. It was therefore not included in the update and the committee could not comment on this. However, NICE recognises the importance of this issue and has worked with the NIHR to prioritise funding for research on the matter.
British Medical Association	Guideline	023	003	Table 1 *(Combined HRT).* This table is very helpful, however, we note that there is no information on testosterone despite the recommendation.	Thank you for your comment. At the time when the scope of the 2024 guideline update was agreed, there was no substantive new evidence that would change the recommendation related to testosterone. It was therefore not included in the update and the committee could not comment on this. However, NICE recognises the importance of this issue and has worked with the NIHR to prioritise funding for research on the matter.
British Medical Association	Guideline	035	011-012	It would be helpful to qualify the level of risk of breast cancer for those in early menopause, e.g. Small/moderate increase in relative risk etc.	Thank you for your comment. The recommendations for early menopause have been amended and the statement "Taking HRT increases the risk of breast cancer" has been removed because the evidence was so limited that this statement would cause alarm. That there was only such limited evidence has been used in the justification of the research recommendation

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					for this topic. The recommendation for this section now reads as follows: 'When discussing HRT as a treatment option, explain to people experiencing early menopause, that, for them, the benefits and risks of either taking or not taking HRT are likely to lie between those for people with premature ovarian insufficiency and those for people aged 45 or over'.
British Medical Association	Guideline	051	006	It seems illogical to need specialist advice/referral about increasing topical vaginal oestrogen within the standard therapeutic range. It seems likely this would always be Advice & Guidance and that the recommendation would be to try an increased dose. This risks worsening access for more complex patients.	Thank you for your comment. The related recommendation about increasing the dose has been removed because there was no clear agreement about what would constitute a 'standard therapeutic range' has been removed. However, it has been highlighted that all recommendations refer to treatments within the licensed dosages and a cross reference has been added to sign post to the reviewing treatment options section to ensure that the efficacy and tolerability of treatments are checked. The related rationale section has been updated accordingly.
British Medical Association	Guideline	061	015/16	(*Only women and trans and non-binary people who have had a 15 hysterectomy are eligible to take oestrogen-only HRT*). What about women with Intrauterine System (IUS)/Mirena? In the risk benefit discussion is this classed as combined or oestrogen only for the purpose of risk? This has been taught as the 'safest' option in most menopause courses so needs clarification, and specifically addressing.	Thank you for your comment. The 'terms used in this guideline' section provides a definition of systemic HRT where it is described that progestogen can be taken orally, transdermally as a patch, or be delivered through an intrauterine system. It does not contain oestrogen and therefore is not combined HRT.
British Menopause Society	Evidence Review A	143 - 145	001	The Forest Plots in Figs 6, 8, 10 and 12 show that the Hummel study of sexual dysfunction is out of step compared with the other studies that target VMS, as might be expected as it focuses on a different problem and participants were recruited according to different criteria	Thank you for your comment. The protocol developed for this review is not restricted to specific types of CBT or any specific symptoms associated with the menopause for inclusion. On this basis, Hummel 2017 meets the requirement of the protocol. Where the estimate of effect

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				(sexual problems rather than menopausal symptoms). We suggest that this study is not included in evaluations of VMS outcomes, as VMS were secondary outcomes and it is not clear whether participants had VMS.	varies across studies that have been pooled in the meta-analysis, as with Hummel 2017 in some forest plots, this is explored using the I-squared statistic which is reported under the forest plots. If heterogeneity is serious the result will be downgraded for inconsistency in GRADE. Please see 'supplement 1 methods' for more detail on assessing inconsistency.
British Menopause Society	Evidence Review A Appendix F	195 - end	General	The terms of the Grading Tables and the text refer to 'imprecision' as a particular problem. We take this to mean the variance of the mean scores on the outcome variables which render the CIs to be large. It appears that imprecision is being viewed as a lack of quality of the studies, rather than a result. For example, there is much evidence that Frequency of VMS is highly variable. However, the precision for specific primary outcomes such as VMS interference/bother and sleep are consistent and less variable.	Thank you for your comment. The imprecision ratings given in the GRADE tables (appendix F) refer to the variance of the point estimate per outcome, please see the corresponding footnotes for details on how each imprecision rating was determined. The overall quality of the outcome is determined by taking into consideration the imprecision, as well the other parameters measured in the GRADE table, e.g., risk of bias and inconsistency.
British Menopause Society	Evidence Review A Appendix F	195 - end	General	The terms and concepts used, although with notes at the end of the section, are not easy to follow. The gradings of 'very serious', and 'critical' have been mentioned in the public response to the press release, e.g. on social media, as negating the whole recommendation of the CBT for menopausal symptoms in the draft consultation. Most of the 'serious' gradings are based on the potential bias relating to the nature of the treatment, which is difficult to conceal, and the use of subjective measures which is normal practice. Thus, the Grading Table and the summary texts may be read as overly negative.	Thank you for your comment. The footnotes provided below the GRADE tables aim to explain the process which lead to the ratings captured within the GRADE table for each parameter. Supplement 1 - methods provides additional information on the approaches taken whilst conducting the evidence reviews. The difficulty of blinding for trials with psychological treatments was acknowledged in discussions of the evidence and has been made clearer in the 'quality of the evidence' section.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Menopause Society	Evidence Review A	143 - 179	General	The heterogeneity of outcomes, which contributes to gradings of imprecision appears to be particularly the case for the QOL outcomes (which are typically secondary outcomes which may have less power) as shown in the Forest Plots. The CIs are much smaller when VMS (primary outcomes) are considered as in Figs 94-110; the same applies to the specific sleep outcomes.	Thank you for your comment. This has been added to the 'quality of the evidence' section of the evidence review.
British Menopause Society	Evidence Review A	013 - 015	General	In the summary of evidence almost all the treatment effects and comparisons are described as being on the basis of low or very low-quality evidence. Hence readers may wonder why CBT is recommended. The Forest Plots provide a clearer indication of effectiveness. The Gradings (ROB) are not sensitive to psychological interventions that are difficult to blind, and also the use of PROMS which are the recommended type of outcomes for menopausal symptoms. 'Objective' psychophysiological measures assessed skin conductance (Biolog in Green's and Bahr monitor in Mann's and Ayers' studies) but these are not generally considered reliable for clinical use. Interference/bother/severity are more strongly associated with QOL than frequency of VMS. In this overall summary a nuanced statement could be included that the low-quality evidence in general refers to the issues of blinding participants using CBT and using subjective measures (PROMS which are generally recommended as outcomes), both of which are inevitable.	Thank you for your comment. The quality of the evidence is taken into consideration when formulating recommendations. This is reflected in the wording used which indicated the recommendation strength. The word 'consider' was used for recommendation 1.4.9 as it is a 'weak' recommendation. In 'strong' recommendations for actions that should (or should not) be offered, directive language such as 'offer' is used. For more information on this please see: Developing NICE guidelines: the manual. Recommendations have been revised to ensure clarity about CBT 'as an option: in addition to other treatment (including HRT), for people for whom other treatments are contraindicated or for people who prefer not to take other treatments'. The risk of bias assessments take into consideration whether the intervention was blinded and whether this would affect the bias in patient-reported outcome measures (subjective outcomes). Whether an intervention was difficult to blind does not remove the risk of bias that may affect a subjective or self-reported outcome. However, the risk of bias assessments have been amended to ensure consistency across all the studies. Please see the

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					risk of bias assessments in the Evidence Tables of Appendix D of Evidence Report A. Objective outcomes were assessed in the same way across studies, and the assessments have been reviewed to ensure consistency. The committee did not specify whether some assessments are considered more reliable than others when drafting the protocol criteria, therefore any assessments used have been treated the same in terms of bias assessment. The quality of the evidence section has been amended to provide more details with regard to the reasons the evidence has been downgraded, but for each individual study this information is already provided in the Evidence Tables in Appendix D.
British Menopause Society	Evidence Review A	013 - 015	General	It would be helpful to point out the safety and lack of side effects when using CBT.	Thank you for your comment. A sentence highlighting safety and lack of side effects was added to 'Other factors the committee took into account' section of the evidence review as suggested.
British Menopause Society	Evidence Review A	006	014 - 015	In Table 1 QOL, VMS and sleep are included as outcomes; Sexual dysfunction is not included therefore, given that the one paper on CBT Sexual dysfunction (Hummel et al) evaluates a different type of CBT on a different sample, we suggest removing it from the analysis – in particular that of VMS outcomes which are included as a secondary measure of the Hummel paper.	Thank you for your comment. The protocol developed for this review is not restricted to specific types of CBT or any specific symptoms associated with the menopause for inclusion. On this basis, Hummel 2017 meets the requirement of the protocol. Where the estimate of effect varies across studies that have been pooled in the meta-analysis, as with Hummel 2017 in some forest plots, this is explored using the I-squared statistic which is reported under the forest plots. If heterogeneity is serious the result will be downgraded for inconsistency in GRADE. Please see supplement 1 - methods for more detail on assessing inconsistency.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Menopause Society	Evidence Review A	010	General	The two Green studies are from Canada not the US.	Thank you for your comment. This has been amended accordingly.
British Menopause Society	Evidence Review A	011	General	The Keefer et al study is a pilot study and, with an N of 19, divided between two groups, will inevitably be under-powered so this needs to be considered when reviewing evidence A.	Thank you for your comment. The inclusion of trials is not determined by the size of the study population. All trials which fulfil the predefined review protocol criteria are included and where possible meta analysed which increases statistical power.
British Menopause Society	Evidence Review A	013	015 - 016	This summary paragraph on VMS outcomes for breast cancer patients states that …'very low evidence from one study showing benefit in distress/bother – however, the Mann et al study, and the Fenlon et al studies both showed significant improvements. What was the reason for rating these as 'very low' when both had blind data entry and statistical analysis.	Thank you for your comment. The summary of the evidence paragraph has been corrected to reflect the 2 studies that showed benefit for the vasomotor symptom outcome. The very low-quality rating reflects the risk of bias assessment for the 2 studies which were downgraded for either outcome: reporting bias or missing outcome data bias, as well imprecision due to one of the 95% confidence intervals crossing the minimal importance threshold. See appendix D for the critical appraisal breakdowns and GRADE table 6 for information on the quality assessment.
British Menopause Society	Evidence Review A	018	031 - 032	1.4.9. The evidence around CBT is generally of poor quality. Studies have low numbers and compare with usual treatment outcome – but do not specify what this is.	Thank you for your comment. The evidence review contains a summary table with brief explanations of what the interventions are, the full details of them and the comparisons used are provided in the evidence tables in appendix D. The quality of the evidence is reflected in the wording of recommendations, and this has been revised to ensure clarity about CBT 'as an option: in addition to HRT, for people for whom HRT is contraindicated or for people who prefer not to take HRT'.
British Menopause Society	Evidence Review A	019	001 - 002	It is acknowledged here that the evidence included pilot studies and secondary analyses of studies which lowered confidence in the findings – i.e. 'most of the evidence was	Thank you for your response. Evidence is not necessarily downgraded for being taken from a pilot study or a secondary analysis. Studies included on meeting the protocol requirement

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				considered low or very low quality'. This means that the evidence for CBT may have been unnecessarily downgraded due to the method of analysis.	undergo risk of bias analysis for each outcome extracted. The analysed evidence then undergoes quality assessment taking into consideration risks of bias as well as other factors such as indirectness and imprecision. More information on this is in supplement 1 - methods.
British Menopause Society	Evidence Review A	019	031 - 032	1.4.16 Within the committee's discussion and interpretation of the evidence for CBT for vasomotor symptoms "they agreed that CBT should not be offered routinely" due to the limited, variable and low quality evidence, but rather "considered as a treatment option." The NICE guidelines should reflect these comments throughout the document and it's public messaging and clarify that "CBT should not be offered routinely".	Thank you for your comment. Whether an intervention is a treatment option or should be offered in the first instance is reflected in the words used to formulate recommendations. The recommendation for CBT (1.4.9) uses the word 'consider' indicating a 'weak' recommendation due to the quality of the evidence base (for 'strong' recommendations the word 'offer' would be used). The recommendation has been revised to ensure clarity about CBT 'as an option: in addition to HRT, for people for whom HRT is contraindicated or for people who prefer not to take HRT'. For more information on the wording of recommendations see: Developing NICE guidelines: the manual.
British Menopause Society	Evidence Review A	052	002	Evidence Abdelaziz 2021: Domain 4 Bias is rated as High overall due to inability to blind participants as to their knowledge of treatment group (CBT vs Control); this would apply to all studies considered in this evidence review because it is almost impossible to avoid when using psychological treatments.	Thank you for your comment. The lack of blinding, particularly for subjective outcomes, has been taken into consideration when conducting risk of bias assessments for all trials across the guideline for consistency. However, the difficulty to blind for trials with psychological treatments has been acknowledged and made clearer in the 'quality of the evidence' subsection of the evidence review.
British Menopause Society	Evidence Review A	062	002	Atema 2019: Domain 4. Bias is rated as High overall due to inability to blind participants as to their knowledge of treatment group (CBT vs Control); this would apply to all studies	Thank you for your comment. The lack of blinding, particularly for subjective outcomes, has been taken into consideration when conducting risk of bias assessments for all trials across the guideline for consistency. However, the difficulty

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				considered in this evidence review because it is almost impossible to avoid.	to blind for trials with psychological treatments has been acknowledged and made clearer in the 'quality of the evidence' subsection of the evidence review.
British Menopause Society	Evidence Review A	081	General	Duitjs 2012: Domain 4 Bias rated as high on the basis of measures being subjective – however, this would apply to all the studies. It is acceptable and recommended to use subjective measures of VMS and other menopausal symptoms and QOL.	Thank you for your comment. The lack of blinding, particularly for subjective outcomes, has been taken into consideration when conducting risk of bias assessments for all trials across the guideline for consistency. However, the difficulty to blind for trials with psychological treatments has been acknowledged and made clearer in the 'quality of the evidence' subsection of the evidence review.
British Menopause Society	Evidence Review A	087	General	Fenlon 2020: Domain 4. Bias is rated as high overall due to use of subjective measures (which are Recommended outcomes) and inability to blind participants as to their knowledge of treatment group (CBT vs Control); this would apply to virtually all studies considered in this evidence review because it is almost impossible to avoid. From the Fenlon paper: 'A team from the Clinical Informatics Research Unit at the University of Southampton will develop the trial database. The collected baseline and outcome data and were blind to group allocation.' we suggest that this should be changed to low risk, as has been applied to some of the other studies that have used subjective measures and CBT interventions.	Thank you for your comment. The lack of blinding, particularly for subjective outcomes, has been taken into consideration when conducting risk of bias assessments for all trials across the guideline for consistency. However, the difficulty to blind for trials with psychological treatments has been acknowledged and made clearer in the 'quality of the evidence' subsection of the evidence review.
British Menopause Society	Evidence Review A	092	001	Green 2019: This study is rated as low risk despite facing the same issues as others regarding subjective measures and non-blinding of the participants – factors which have been generally rated as high risk in other	Thank you for your comment. The lack of blinding, particularly for subjective outcomes, has been taken into consideration when conducting risk of bias assessments for all trials across the guideline for consistency. However, the difficulty

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				studies. Consistency is needed so we suggest rating the others as low.	to blind for trials with psychological treatments has been acknowledged and made clearer in the 'quality of the evidence' subsection of the evidence review.
British Menopause Society	Evidence Review A	096	003	Green 2020: This study is rated as low risk despite facing the same issues as others regarding subjective measures and non-blinding of the participants – factors which have been generally rated as high risk in other studies. Suggest rating the others as low for consistency across the guideline	Thank you for your comment. The lack of blinding, particularly for subjective outcomes, has been taken into consideration when conducting risk of bias assessments for all trials across the guideline for consistency. However, the difficulty to blind for trials with psychological treatments has been acknowledged and made clearer in the 'quality of the evidence' subsection of the evidence review.
British Menopause Society	Evidence Review A	102	002	Hardy 2018: Some concerns relating to 'no information about concealment of the allocation sequence'. This is not correct, the paper mentions that randomisation was performed using Microsoft Excel with a ratio of 1:1, and that all data entry and analysis was conducted by a researcher and statistician who were blind to treatment allocation. This study had no face to face or clinician contact so it is hard to see why there were concerns.	Thank you for your comment. The risk of bias rating has been amended and is now noted as low risk. All corresponding GRADE tables have been reassessed and amended where necessary.
British Menopause Society	Evidence Review A	103	003	Hummel 2017: This study includes women diagnosed with sexual dysfunction following breast cancer treatment; CBT for sexual dysfunction is very different from CBT for VMS or CBT for depressive symptoms or sleep experienced during menopause. Sexual dysfunction in this population may not be associated with induced menopause. We suggest that this study is not included together with others as the populations are likely to be different as are the CBT treatments used.	Thank you for your comment. The protocol developed for this review does not specify the types of CBT or the specific symptoms of menopause for inclusion. On this basis, Hummel 2017 meets the requirement of the protocol. The guideline committee expressed an interest in the population of this trial as people with a personal history of breast cancer; this was a predefined protocol strata for this review.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Menopause Society	Evidence Review B2	010	020	This section is entitled benefits and harms but is all about potential harm. There is no recognition of the extreme distress many women with breast cancer feel in relation to their symptoms of urogenital atrophy which is often compounded by the adjuvant therapy. This group of women deserve particular attention and the absence of recognition of the benefits vaginal oestrogens can have in this situation is regrettable. Whilst we accept specific evidence for the efficacy of vaginal oestrogens in women with breast cancer is largely lacking it is surprising the committee have felt the need to be so negative in their conclusions (page 11.5) when the evidence for vaginal oestrogens generally is supportive of its benefits.	Thank you for your comment. The aim of this review is to analyse what the impact of vaginal oestrogen is on incidence (recurrence) of breast cancer for people with a personal history of breast cancer. Therefore, the discussion is focused on the evaluation of this potential risk. Given the data that was consistent with a potential increase or decrease in risk of breast cancer recurrence, the committee decided that non-hormonal options would be the first line and vaginal oestrogen second line option for managing genitourinary symptoms. The reasons for this are highlighted in the discussion section. The committee made changes to the order of recommendations so that considerations of adjuvant treatments are being made early in shared decision making and revised the recommendation related to safety considerations for clarity. This would give this section a more logical flow and greater clarity about safety. The rationale of the guideline and the committee discussion section of the evidence were revised accordingly. A visual summary was produced for the management of genitourinary symptoms to clarify treatment options and facilitate decision making.
British Menopause Society	Evidence Review B2	012	008	Vaginal oestrogens absorbed to a lesser degree than systemic oestrogen. Again this is very negative wording. The implication of that statement is there is still significant absorption which we know is not the case. Repeated studies have shown no increase in plasma oestradiol levels above the postmenopausal range after the first few days of administration.	Thank you for your comment. This was revised in the guideline to highlight that vaginal oestrogen is absorbed locally - a minimal amount is absorbed into the bloodstream (when compared with systemic HRT), but this is unlikely to have a significant effect throughout the body. The committee agreed to highlight this because it means that there is no need to combine low-dose

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				The MHRA concluded the same so it is disappointing this guideline continues to imply there is significant absorption. This is incorrect interpretation of the data.	vaginal oestrogens with systemic progestogen treatment to protect the person against endometrial hyperplasia and cancer. (Conversely, with systemic HRT, progestogen treatment protection is needed for people with a uterus – see evidence review E). In the section on people with a personal history of breast cancer, the committee made changes to the order of recommendations so that considerations of adjuvant treatments are being made early in shared decision making and revised the recommendation related to safety considerations for clarity. This would give this section a more logical flow and greater clarity about safety. The rationale of the guideline and the committee discussion section of the evidence were revised accordingly. A visual summary was produced for the management of genitourinary symptoms to clarify treatment options and facilitate decision making.
British Menopause Society	Evidence Review H	011	036	"moderate quality evidence showed an important benefit for oestrogen-only when compared to placebo or no HRT on all-cause mortality." Is there a particular reason this was not referred to in the recommendations? This is a large sample size from the WHI with long term follow up data that showed clear reduction in risk for women who started HRT at 50-59. OR 0.81; 95% CI: 0.68-0.96 in all cause mortality in women who started oestrogen only HRT age at the age of 50-59.	Thank you for your comment. The evidence shows an isolated risk reduction in the age group 50-59, for oestrogen-only HRT users, however, this is part of a subgroup analysis that did not show a statistically significant difference between the subgroups, and therefore the committee could not conclude that there was a benefit in all-cause mortality that warranted a recommendation. The line you refer to in Evidence Review H has been amended to make it clearer that although there was an isolated benefit, there was not a statistically significant subgroup difference. Thank you for highlighting the Cochrane review by

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				This is further supported by the Cochrane review by Boardman et al 2015 which showed significant reduction in all cause mortality in women who commenced HRT under the age of 60.	Boardman et al 2015. This systematic review was not included in this evidence review because the intervention did not match the pre-specified protocol as combined HRT and oestrogen-only HRT were analysed together. However, the included studies from the systematic reviews were individually checked against the protocol and if they met the criteria in the protocol, they were included separately. Boardman et al 2015 has been added to the excluded studies section of this review, Appendix J. There are discussions about the exclusion of the Boardman et al 2015 and 2 other systematic reviews related to the topic in the 'other considerations relating to cardiovascular disease' in the rationale section of the guideline and also in the 'other considerations the committee took into account' subsection of the 'committee's discussion and interpretation of the evidence' section of evidence review C.
British Menopause Society	Guideline	General	General	We welcome the new NICE draft Menopause guidance, which includes new evidence and has identified several areas of future research requirements and recommendations. It is generally welcomed that the 2015 guideline has been updated to include additional recommendations on GU symptoms and the effects of HRT on health outcomes. However, it is unfortunate that the adverse effects of early menopause on bone, cardiovascular health and cognitive function have not been referred to in the update despite early menopause being part of the update. It was however disappointing that a number of aspects of the 2015 guideline have not been	Thank you for your comment. The 2024 guideline update was a partial update of the 2015 menopause guideline where priority areas identified by the NICE surveillance team were updated. The surveillance of new evidence is an ongoing process and areas that were not updated in this partial update may be updated at a later date. The need to assess the impact of early menopause on health outcomes has been acknowledged and was logged with the NICE surveillance teams for prioritised consideration during future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				updated despite additional efficacy and safety data and meta-analyses becoming available e.g. Diabetes, VTE.	
British Menopause Society	Guideline	General	General	We welcome the inclusiveness of the guideline and we note that the term "women, trans men and non-binary people registered female at birth" is used repeatedly throughout the document. Although correct terminology, we feel this is a cumbersome term and detracts from the message of the recommendations. We would recommend explaining this term at the beginning of the guideline and then using a generic term throughout with only explicit mention where relevant data are discussed?	Thank you for your comment. The guideline's introduction states that the guideline covers women, trans men and non-binary people registered female at birth. For accuracy, some of the recommendations need to list all groups. Elsewhere, the term 'people' is used to be inclusive and concise. This is used where we speak about people for whom it has already been identified that their symptoms are associated with the menopause.
British Menopause Society	Guideline	General	General	The use of the terms "bothersome" and troublesome" menopause symptoms appear repeatedly in the new NICE draft document. These are arbitrary and subjective terms and many clinicians and lay persons feel that they may be considered somewhat paternalistic and patronising to women. We recommend reviewing these terms and considering using more objective terms to describe menopause symptoms, such as moderate/severe, instead of bothersome and troublesome.	Thank you for your comment. Based on this and other feedback the committee reflected on this wording and consequently 'troublesome' has been removed from the guideline. The word 'bothersome' was used in one specific context where a particular measurement scale was used to ask how 'bothered' they were by their symptoms. This was therefore retained it to be consistent with the study's results.
British Menopause Society	Guideline	General	General	We welcome inclusion of the need for research into those with an ethnic minority background but we would also like to see a recommendation for real-world data collection, outside clinical trials, to address the lack of data in groups often under-represented in research trials but who may nonetheless be prescribed treatments such as HRT for menopause—for example, those with diabetes and those with multi-morbidities.	Thank you for your comment. The research recommendations that were made originate from the evidence reviews that were conducted in line with standard NICE processes. These research recommendations do not make restrictions as to what study types ought to be included which could include real-world data (apart from vaginal laser therapy for which randomised controlled trials were deemed the most appropriate study type). Diabetes and multi-morbidities as well as

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					other conditions that may impact on identification or treatment of symptoms associated with the menopause were outside the scope of the current guideline. It was therefore not possible for the committee to comment on this.
British Menopause Society	Guideline	General	General	Whilst CBT is an important intervention and we welcome further evidence highlighting its potential benefits, in our opinion too much emphasis has been placed on it in this guideline, particularly in the original press release. There needs to be consistency between the evidence, the recommendations and the public messaging otherwise there will be (already is) confusion.	Thank you for your comment. The wording of the recommendation has been revised to make it explicit that this is an option which could be in addition to HRT, for people in whom HRT is contraindicated or for those who prefer not to take HRT. The related rationale has been revised accordingly.
British Menopause Society	Guideline	General	General	We are concerned that throughout the guideline there is inconsistency around the interpretation of observational data and RCT data and the relevant weight of each. There appears to be inconsistent weight put on studies with more emphasis on negative findings. The decision-making and reasoning for prioritising RCT data for CVD and observational for breast need to be transparent and explained more clearly. One of the strengths of NICE guidance is looking at the totality of the data and not excluding anything simply because it doesn't suit the argument. We regret that this guideline does not do this. In a number of areas a statistically significant benefit was shown in the analysis but the recommendations appear to refer to 'no increase in risk' rather than acknowledging a benefit. Cardiovascular disease in women	Thank you for your comment. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they agreed that RCT and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				starting HRT under the age of 60 is a stark example where the collective observational evidence presented in the NICE evidence review showed a significant reduction in risk. In addition, the long term RCT data (13 year WHI FU) clearly demonstrated in the NICE analysis a significant reduction in risk in women who commenced oestrogen only HRT at the age of 50-59. For both areas, the recommendations stated 'no increase in risk'.	
British Menopause Society	Guideline	General	General	There are a number of occasions when the recommendations are based on committee opinion. Committee opinion should only be relevant when the data are not clear. The results of the analysis conducted by the NICE team should not be overturned based on the personal views or knowledge of committee members. The recommendations should be based and mainly guided by what was shown in the evidence reviews. If the evidence is inconclusive then this should be reflected in the guideline. Constant changing of recommendations based on personal interpretation of the data is a disservice to patients. It would be more transparent and helpful to state if there is conflicting evidence about the exact degree of harm/benefit for some of these long-term outcomes.	Thank you for your comment. Recommendations were based on evidence reviews which followed rigorous NICE methods and processes, with details outlined in a supplement available on the website (supplement 1 - methods), consistent with the NICE guideline manual. Evidence was systematically reviewed and discussed with a committee consisting of experts and lay people. NICE also commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation).
British Menopause Society	Guideline	General	General	Much of the new data referred to in this guideline is based on the findings of the 2019 Lancet observational meta-analyses. We are surprised that the CGHFBC 2019 data are taken at face value and not subject to further re-analysis by the NICE team as usually happens with NICE guidance. Whilst the	Thank you for your comment. The evidence reviews in this guideline followed rigorous NICE methods and processes, with details outlined in a supplement available on the website (supplement 1 - methods), consistent with the NICE guideline manual. In line with the manual systematic reviews are included when they meet the criteria

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				published analysis was new, the data were not and the limitations and biases inherent within them (largely based on the Million Women Study) are not resolved by reanalysis. Why was it deemed not necessary to apply normal NICE procedure to this paper? We also note that one of the authors of this paper was present on the committee and contributed to the discussions. We question the impartiality in the interpretation of these data and the decision not to re-analyse the CGHFBC 2019 data.	of the review protocol which the Lancet publication did. The Lancet meta-analysis is also an individual patient data (IPD) analysis and NICE would not have the same access to the individual patient data that the epidemiologist had who conducted this work. IPD meta-analyses are also more powerful than taking individual statistics from each study (which would commonly be used in NICE guidelines) because they make use of the overall combined data and can make better adjustments for potential confounding factors. Observational studies have limitations, but they also have particular strength, such as larger data sets, longer follow-up and real-world data. NICE has followed its standard methods and processes in developing the 2024 guideline update, including the way in which we manage conflicts of interest in topic experts and committee members. The details of conflicts of interest and how they have been managed are available in the published register of interests.
British Menopause Society	Guideline	General	General	It is of concern that whilst NICE have an understanding of Conflicts of Interest in relation to the pharmaceutical industry, the same rules are not applied to other interests such as research. Researchers are, naturally, very protective of their work and of course they must defend their work when it is considered as evidence, but this consequently makes it difficult for the group, and readers of this guideline, to make an objective assessment of it unless the researchers concerned are excluded from the discussion.	Thank you for your comment. NICE has followed its standard methods and processes in developing the 2024 guideline update, including the way in which we manage conflicts of interest in topic experts and committee members. The details of conflicts of interest and how they have been managed are available in the published register of interests.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				The NICE guidance on Conflicts of Interest states "All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline." The Lancet paper of 2019 is presented as significant new evidence which had a big impact on the subsequent interpretation of the data and the evidence from MWS, important though it is, dominates several sections of the Guideline which cover cancer. One of the main authors of this paper is on the guideline committee. It is normal practice with NICE and other organisations to exclude someone with significant interest from the relevant discussions but the minutes state that although they did not lead the discussion they were present during the discussions and clearly influenced the committee's decision making.	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Although the statistics within the Lancet paper are complex, NICE has excellent statisticians who would able to give an unbiased view and so it should not have been necessary for one of the principle authors to have been present.	
British Menopause Society	Guideline	General	General	On many occasions throughout the guideline it states that women need to be aware of "these" risks. It is important that the document reflects good clinical practice which is to discuss the benefits and the risks of any proposed treatment such as HRT not just the risks. In the committee discussion (P43 line 5) it states "using an individualised approach with discussions about benefits and risks of treatment options and tailoring information to individual circumstances and potential risk factors". We support this statement which reflects good clinical practice but would like to see this reflected consistently throughout the recommendations.	Thank you for your comment. Recommendations were based on evidence reviews which followed rigorous NICE methods and processes, with details outlined in a supplement available on the website (supplement 1 - methods), consistent with the NICE guideline manual. Evidence was systematically reviewed and discussed with a committee consisting of experts and lay people. NICE also commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation).
British Menopause Society	Guideline	087 - 099	Appendix A - General	**Tables** The actual numbers presented in the Tables are just point estimates and in reality maybe lower or higher, these are simply a guide and readers need to be aware of this. The guideline does not make this clear and we would ask that confidence intervals be included. This is an honest and open approach. If these data were presented in most settings confidence intervals would either be included in the Table or there would be some discussion about them in the accompanying legend. In the previous NICE guideline both RCT and observational risks were included and this was	Thank you for your comment. For the draft guideline, the committee opted for a written format complemented by tables, providing estimates of absolute numbers from a single source rather than from two different study types. This differs from the approach used in the published version of NG23. This decision was made to facilitate conversations between clinicians and individuals, enabling shared decision-making regarding menopause management. The appendix of absolute numbers has been used to produce a discussion aid document including visualisation of the data. This provides details about the type of evidence data originated from, how to interpret the numbers and

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				very helpful in educating and drawing a distinction between uncertainties and certainties. As they stand these tables don't report any uncertainty/sensitivity as part of their point estimates, either as confidence intervals or by showing the range of risks depending on the studies used to inform them. It would be helpful to have 95% confidence intervals included as in the 2015 guidance and separation of risk estimates according to whether data was from observational or randomised studies. Both were useful in explaining the level of uncertainty around some of the risk estimates summarised given that, • Analysis of large patient cohorts (e.g., the CGHFBC and MWS 2019) may provide statistical precision, • Randomised, placebo-controlled evidence is likely more accurate in terms of estimated conferred risk, • Being able to compare the two will aid interpretation of reliability, which can be limited due to biases in observational methodology. Feedback from teaching using the 2015 layout of table content accounting for the above was that this helped in understanding and in explaining the recommendations when counselling women. The way these data are presented now makes it appear that the risks have changed since the	information about uncertainty. It also links to the relevant evidence reviews which contain details of the estimates from different study types as well as the confidence intervals. It also includes links to a separate supplement file which provides the details of each calculation. This discussion aid has undergone user-testing and was refined based on user feedback.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				2015 guideline despite the fact that the evidence itself has not changed (the 2019 Lancet meta-analysis is not "new" data, despite it being published in 2019). It is also difficult in some of the Tables and Figures to know which publications the Figures have come from and this requires clarification.	
British Menopause Society	Guideline	010 - 019	General	1.4 GENERAL– why is there no mention of any other symptoms of the menopause that are common?	Thank you for your comment. Whilst an update of the list of symptoms was outside the current scope of the 2024 guideline update and therefore no evidence review was conducted, the NICE surveillance team checks regularly for new evidence for topics within guidelines to see where further work is needed.
British Menopause Society	Guideline	021 - 029	Table 1	Table 1 Combined HRT: effect on health outcomes Column 3: ''Combined HRT increases the risk of breast cancer mortality compared with not taking HRT''. This is based on the MWS research letter (2019). In itself the inclusion of a research letter as evidence is questionable when so many other relevant papers have been excluded. Under what criteria was this letter deemed to be admissible evidence? It is not a peer-reviewed paper. It is noted that one of the authors of this letter is on the guideline committee. Other studies evaluating breast cancer mortality were not reviewed, including the RCT WHI and Wang T et al 2020 Int J of Cancer, which did not show an increased risk. All of these can be criticised (including the MWS) for	Thank you for your comment. The inclusion of the MWS research letter was deemed appropriate since the MWS has previously published work describing the cohort and methodology, which fits our protocol. The research letter also describes the analysis was adjusted. Given the critical nature of mortality from breast cancer, information from such a source was deemed important and underwent standard quality assessment using GRADE methodology. It was taken into consideration in the critical appraisal of the letter that the publication was not a full publication. Any other papers that have been excluded have all been listed in the excluded studies section (Appendix J) of the evidence report (report D for breast cancer) with a reason for exclusion. NICE has followed its standard methods and processes in developing the 2024 guideline update, including the way in which we manage conflicts of interest in topic experts and

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				lack of control for stage at diagnosis, diagnosis method and treatments used, which influence prognosis. Transparency, honesty and the totality of the data should be the hallmark of a NICE guideline not selective interpretation and inclusion or exclusion of the data to suit a particular viewpoint. Recommending that women are advised that breast cancer mortality is increased could be used out of context on the impact of HRT on overall mortality, which is not increased suggesting this is offset by other mortality benefits (e.g., reduction in colorectal cancer, CVD deaths e.g., Holm M et al BJOG 2019). All-cause mortality is arguably a more useful single measure of major risks and benefit over time. The MWS finding could simply reflect the higher number of diagnoses of breast cancer and not an adverse impact of prognosis and does not provide information to counter this. There should be some context provided if women are to make a fully informed choice. We appreciate colorectal cancer was not one of the outcomes reviewed but there is a statement earlier in the draft that overall mortality is not negatively or positively affected. Why not refer to that here? Column 4: "Combined HRT preparations containing transdermal oestrogen increase the risk of breast cancer less than combined HRT preparations containing oral oestradiol."	committee members. The details of conflicts of interest and how they have been managed are available in the published register of interests. The Women's Health Initiative (WHI) data on mortality was included in this review and is described in the evidence report, please see evidence review D. Wang, T et al, 2020 Int J of Cancer was assessed at full text and was not included in the review as the data on HRT use was collected after the outcome of interest was known. This was one of the criteria set out in the protocol before the review was conducted. The study is also listed in the excluded studies section of the full evidence report D (Appendix J). All the reviews in this guideline were carried out according to NICE methods and processes. The methods as described in Supplement 1 set out the process of how data is included and excluded in the guideline. Pre-specified protocols are drafted and agreed with the guideline committee before the review is carried out. Studies are included and excluded according to the requirements set out in the pre-specified protocol and are not included or excluded based on a particular viewpoint post-hoc. Any risk of bias, or methodological limitations that have not been listed as a reason for exclusion in the protocol, are addressed in the critical appraisal of the studies and reflected in the GRADE quality of the evidence. Interpretation of the evidence is based on a committee discussion of the evidence and details of each discussion can be found in the relevant evidence report (See section 'Committee discussion of the evidence'). The committee reviewed the evidence related to specific-cause

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				This is based on one low quality study (Brusselaers et al 2018). It is also contradicted by the statement about what is said about oestrogen only HRT. The evidence is not conclusive and this statement could be widely misinterpreted. It is far too black and white. Column 5: "It is not known whether preparations containing micronised progesterone or dydrogesterone have a different increased risk for breast cancer compared with preparations containing other progestogens". There are a handful of studies suggesting risk with micronized progesterone or dydrogesterone is elevated to a lesser degree compared with preparations containing synthetic progestogens but we agree more confirmatory clinical evidence is required. However, it shouldn't stop discussion of these studies and the limitations of the CGHFBC results, that were based on very small numbers with longer follow-up. The E3N cohort should at least be acknowledged, it has limitations but so does the CGHFBC. Why has the Fournier 2008 paper not been included but the 2014 paper has? Consistency about interpretation and presentation of the evidence here and across the guideline would be welcome as these messages are very confusing. When the data are not clear, as on this point, a clarifying statement to that effect would be helpful as the reported differences are widely referred to in	mortality, as well as all-cause mortality. They agreed that based on the evidence they would highlight specific-cause mortality as well as all-cause mortality in the recommendation, as it was important to present the available evidence. The evidence reviewed in this guideline did not specifically highlight whether no increase or decrease in overall mortality was offset by other mortality benefits, in addition the 2024 update of this guideline did not cover all outcomes that may be relevant to the use of HRT. The committee considered the evidence for oral and transdermal routes of administration of the oestrogen component of HRT. Since some of the evidence showed a significant difference between the subgroups of oral and transdermal routes of administration in the combined HRT comparison, they had made a recommendation to inform of the reduced risk. However, the committee revisited the evidence, and discussed that since the same difference was not observed in the oestrogen-only comparison, the argument was less robust than previously discussed. Upon reflection the committee agreed to remove this recommendation and an updated detailed discussion of the evidence, and their decision can be found in the committee discussion of the evidence section of Evidence Review D. The committee have reviewed the available evidence on the different progestogenic constituents. Some of the participants of the E3N cohort have been included in the IPD dataset from the CGHFB, which has been included in our review. It has been noted that not all participants of the E3N have been included in the CGHFBC.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				clinical guidance and this concept is commonly considered in clinical practice.	However, where there are separate publications with overlapping follow-up periods, and no disaggregation of participants, these have not been included to avoid double counting of participants in the E3N cohort. As per our processes and methods, we do not reanalyse any existing IPD data and therefore take the data as it has been published. Due to the large size of the IPD data from the CGHFB, this has been prioritised for inclusion in the review. . Fournier 2014 was included as this study had a later follow-up period of the E3N cohort that was not covered by CGHFB. However, since the data from the Fournier 2014 publication did include participants that were in the meta-analysis from CGHFB, the results were analysed separately. The committee considered that the number of cases of breast cancer with those using micronised progesterone were few and agreed that this supported a recommendation to highlight that there was insufficient evidence to support any differences in the risk of breast cancer with micronised progesterone. The committee agreed that more evidence was required to make any robust recommendations for micronised progesterone and made a research recommendation. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
British Menopause Society	Guideline	030 - 034	Table 2	Table 2 Breast Cancer and Oestrogen only HRT Column 2: "Oestrogen-only HRT slightly increases the risk of breast cancer compared to not taking HRT". This statement is completely at odds with the results for CEE in the WHI study. The committee argue that the average age of women (63) and greater proportion who were overweight/obese in the WHI are unrepresentative of the target population for HRT. However, they have opted to disregard that limitation when assessing the CVD data. With regard to age, the WHI subgroup analysis showed no significant risk increase or reduction in the risk of diagnosis. Regarding BMI, the CGHFBC 2019 reported a reduced risk in women with a higher BMI and suggests the large proportion of overweight women in WHI accounts for the findings with CEE. Subgroup analysis by BMI in the WHI shows no increased risk in women with a low or normal BMI range. The WHI report on the effect of being overweight or obese on the risk of breast cancer does not appear to be referred to in this guidance. WHI showed that women who had a body mass index (BMI) of	Thank you for your comment. Due to the differences in RCT and observational study findings, committee revised the recommendation to state that 'there is very little or no increase in breast cancer risk with oestrogen-only HRT' and further details pertaining to duration of use, current and past use and a remaining risk after stopping have been removed. The committee discussed that the RCT evidence from the Women's Health Initiative (WHI) showed results that were not consistent with results from the observational studies. The decision to consider the different population groups between the studies were specific to this outcome since the committee tried to find an explanation for the inconsistent findings. The committee reconsidered the wording of the recommendation and have since updated the wording to describe the direction of evidence from both the RCT and observational studies. As a result, the committee discussion of the evidence section in Evidence Review D has been updated to provide details of the discussion that took place. With regard to subgroup analysis for age at first use, the evidence does not show a statistically significant subgroup difference between the risk of breast

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				over 35 had a significantly increased risk of invasive breast cancer compared with women of normal weight (HR 1.58; 95% CI 1.40–1.79). In addition, obesity was associated with an increase in estrogen receptor-positive and progesterone receptor-positive breast cancers (HR 1.86; 95% CI 1.60–2.17), an increase in advanced diseased (HR 2.12; 95% CI 1.67–2.69). Neuhouser ML et al Overweight, Obesity, and Postmenopausal Invasive Breast Cancer Risk: A Secondary Analysis of the Women's Health Initiative Randomized Clinical Trials. JAMA Oncol. 2015 Aug;1(5):611-21. doi: 10.1001/jamaoncol.2015.1546. PMID: 26182172; PMCID: PMC5070941. The very most than can be concluded from the data is that oestrogen-only HRT *may* increase the risk of breast cancer and the guideline should add that CEE may not increase risk, although we acknowledge that further study is needed. This figure and guideline statement is almost entirely based on the findings of the Lancet meta-analyses. We question why this paper has been given so much weight. We are surprised why the CGHFBC 2019 data are taken at face value and not subject to further re-analysis by the NICE team as usually happens. Whilst the published analysis was new, the data were not and the limitations and biases inherent within them (largely based on the MWS) are not resolved by reanalysis. Why	cancer and the different subgroups for age at first use, therefore the committee were unable to draw any meaningful conclusions. This is discussed in more detail in the committee's discussion of the evidence in Evidence Review D. The subgroup analysis by BMI from the WHI was not included (Neuhouser 2015) as it does not meet our specified criteria in the protocol. The paper referred to in your comment (Neuhouser 2015) is a secondary analysis of the WHI including women from 3 trials, one of these trials does not compare HRT use to no HRT use (the intervention is dietary modifications). They have obtained information on HRT use in the participants, but since approximately 59% of the participants were not randomised to the interventions as specified in our protocol (HRT use or no HRT use) the study has to be treated as observational data. As specified in our protocol, observational studies have to make adjustments for confounders to be included in the review, and the data provided by Neuhouser 2015 on BMI, HRT use and breast cancer incidence has not been adjusted for confounders, therefore we are unable to include it in our review. With regard to the Hazard ratios quoted in your comment, it is also not possible to include these as they are not a comparison between HRT use and no-HRT use, but they compare different BMI ranges to each other. The committee did discuss BMI but did not feel that a separate recommendation was required. The committee considered all the available evidence for oestrogen-only HRT, however because there were inconsistent findings between the RCT data and the CGHFB findings which was informed by

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				was it deemed not necessary to apply normal NICE procedure to this paper. We note that one of the authors of this paper was present on the committee and contributed to the discussions. We question the impartiality in the interpretation of these data and the decision not to re-analyse the CGHFBC 2019 data. Column 3: "There is no difference in the increase of breast cancer risk between transdermal and oral oestrogen." This contradicts the comments in the previous table and is going to cause confusion. Either there is no difference or transdermal is better. Given the limited evidence presented in the previous Table we would favour making no distinction consistently across the board. Column 4: "There is no difference in the increase in breast cancer risk between oestradiol and conjugated equine oestrogen when given at standard therapeutic dosage" This statement completely ignores the data from WHI which was a randomised trial. The committee argue that the average age of women (63) and greater proportion who were overweight/obese in the WHI are unrepresentative of the target population for MHT. The WHI subgroup analysis showed no significant risk increase or reduction in the risk of diagnosis with age. The CGHFBC 2019 reported a reduced risk in women with a higher BMI and suggests large proportion of overweight women in WHI accounts for the findings with CEE. However, subgroup	observational data, they had to consider which data were more relevant to the population in question, as well as other pros and cons of the available data. The committee have since revisited the recommendations and the wording and have changed the wording to 'for oestrogen-only HRT there is little or no increase in the risk of breast cancer compared to not taking HRT'. They agree that this wording includes the conclusions between both RCT and observational data, and since the findings were inconsistent it is necessary to reference both. The CGHFBC 2019 data was taken as is, and not further re-analysed as this data was an individual participant dataset. NICE does not have the same access to the individual participant dataset therefore any other analysis would not have been possible. Normal NICE processes and methods were applied to the study: the study was extracted, critically appraised, and assessed for quality using GRADE methodology. See supplement 1 – methods for detailed methodology, but it is important to note that all included studies are treated with the same process. NICE guideline committee groups do include members with specific interest in topic areas, and correct policy and procedures were also followed regarding this (see declaration of interest register). The committee considered the evidence for oral and transdermal routes of administration of the oestrogen component of HRT. Since some of the evidence showed a significant difference between the subgroups of oral and transdermal routes of administration in the combined HRT comparison, they had made a recommendation to inform of the

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				analysis by BMI in the WHI shows no increased risk in women with a low or normal BMI range. It is perplexing why observational data are being favoured over RCT data. There are also other plausible explanations for a difference between the effect of CEE and E2 e.g., the former has pro-apoptotic properties and the latter anti-apoptotic properties. This is an area that requires further clinical evaluation as there is sufficient uncertainty and to dismiss the WHI results without accounting for this seems inappropriate. A statement that CEE may not increase risk but further evaluation is required would seem a more rational conclusion.	reduced risk. However, the committee revisited the evidence and discussed that since the same difference was not observed in the oestrogen-only comparison, the argument was less robust than previously discussed. Upon reflection the committee agreed to remove this recommendation and an updated detailed discussion of the evidence, and their decision can be found in the committee discussion of the evidence section of Evidence Review D. Regarding column 4, as already mentioned, the committee considered all the evidence included in the review which included RCT evidence and observational evidence. The committee discussed that the population in the WHI had different characteristics to the average population in the observational evidence. They discussed that this could be a reason why the data showed conflicting results. BMI of the women was one of the factors discussed. The reasons for the exclusion of the subgroup analysis of the WHI data by BMI have been provided and therefore the committee cannot make conclusions using this data. The committee agreed that the subgroup analysis by constituent, as reported in the review, showed that both conjugated equine oestrogens and oestradiol had an increased risk of breast cancer. Following changes to the recommendation on overall breast cancer risk with oestrogen-only HRT, which now stands at 'there is little or no increase in the risk of breast cancer', the committee agree that the recommendation 'there is no difference in the increase in breast cancer risk between oestradiol and conjugated equine oestrogen when given at

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					standard therapeutic dosage', is still relevant as it is in line with the data that does show an increased risk. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
British Menopause Society	Guideline	038 - 042	General	We largely agree with the research recommendations but would like to see a recommendation for a health economic analysis of HRT in the UK. We would like to see a research recommendation to study quality of life and long-term health outcomes for the early menopause group as well as POI.	Thank you for your comment. The effectiveness of HRT in early menopause and POI were not in the scope of the 2024 guideline update. In accordance with NICE processes research recommendations can only be made on topics that are systematically searched for and reviewed. The suggested research recommendation could therefore not be added.
British Menopause Society	Guideline	087 - 089	Appendix A - General	We would recommend that the Tables for breast cancer and ovarian cancer should include the findings from both RCT evidence as well as observational evidence with range estimates. These figures are not exact and as presented here, they are misleading. The previous Guideline NG23 presented the figures in this way (Table 3) and this was	Thank you for your comment. For the draft guideline, the committee opted for a written format complemented by tables, providing estimates of absolute numbers from a single source rather than from two different study types. This differs from the approach used in the published version of NG23. This decision was made to facilitate conversations between

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				widely acclaimed by HCPs in the UK and experts around the world as a constructive way to present the data. Indeed these figures were subsequently used in menopause guidance around the world.	clinicians and individuals, enabling shared decision-making regarding Menopause management. The appendix has been used to produce a discussion aid document including visualisation of the data. This provides details about the type of evidence data originated from, how to interpret the numbers and information about uncertainty. It also links to the relevant evidence reviews which contain details of the estimates from different study types (and the relevant sources) as well as the confidence intervals. It also includes links to a separate supplement file which provides the details of each calculation. This discussion aid has undergone user-testing and was refined based on user feedback.
British Menopause Society	Guideline	088 - 090	Appendix A – Tables 2 & 3	-The risk with continuous combined with 5 years and 10 years use for 50-54 appears exactly the same. -With oestrogen only: the risk with 10 years use appears less than the risk with 5 years use. Yet the risk over 20 years is increasing. The figures should be reviewed Why is there no data about deaths from breast cancer?	Thank you for your comment. The committee revisited the data and noted that the risk increased between 5 and 9 years of use and that there was an increase associated with duration of use. They emphasise in the wording that this risk is 'very slightly' increased. The absolute table has been simplified to provide one overall absolute number which is an increase by 1 in 1000 people who take oestrogen-only compared to people who have not taken HRT. The rationale was updated accordingly. The problem with trying to give absolute numbers of mortality from breast cancer due to HRT use is that we cannot give risks by specific patterns of use as we do for incidence. This is because it is recommended that women stop their HRT use as soon as they are diagnosed with breast cancer. This makes it difficult to report on the relationship of a given total duration of use with death from breast

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					cancer because this will be necessarily truncated in those who get breast cancer but not in those who do not. For this reason, we cannot calculate absolute numbers but can only look at the relationship of use of HRT with subsequent breast cancer mortality in women with no prior breast cancer diagnosis at the time of reporting their HRT use which is the evidence we are reporting in evidence review D.
British Menopause Society	Guideline	095 - 096	Appendix A - Table 14	This Table has not been changed form 2015 guideline which is fine but it shows clearly the benefit of including confidence intervals with the data and we would recommend all the Tables are presented in this way.	Thank you for your comment. The appendix has been used to produce a discussion aid document to make it more user friendly to support decision-making.. This discussion aid has undergone user-testing and was refined based on user feedback. Parts of the osteoporosis tables were incorrect in the 2015 guideline and have been updated to rectify this. It still shows that HRT improves fracture risk, but the RCT and observational data now align. Further changes have been made for consistency with the other tables. All confidence intervals are available in the evidence reports.
British Menopause Society	Guideline	097 - 098	Appendix A - Table 16	Number of breast cancer cases over a 5-year period per 1,000 people who never used HRT. This should clearly state the control group are women with early menopause who have a significantly lower risk of breast cancer (not age matched premenstrual women). As stated previously the breast cancer argument for early menopause makes no biological sense and the data in the table on p96 adds to this confusion and should be explained appropriately.	Thank you for your comment. The statement related to an increased risk for breast cancer in the early menopause group was removed because it was the only evidence identified for the comparison specified in the protocol (people in early menopause taking HRT versus people in early menopause not taking HRT). The committee decided that having only this one piece of information could be detrimental to decision-making and used it in the rationale underpinning a related research recommendation. The topics of prevalence of early menopause, impact of early menopause on specific health outcomes and management of early menopause, whilst not part

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					of the 2024 guideline update, have been logged with the NICE surveillance team (together with key publications as cited by stakeholders) to be considered for future updates.
British Menopause Society	Guideline	098 - 099	Appendix A - Table 17	Table 17 showed that women aged 40 who took HRT for 10 years had a similar risk of breast cancer to women who did not take HRT. The recommendations should clearly reflect these findings.	Thank you for your comment. The comparison addressed in the related evidence review is women with early menopause taking HRT versus women in early menopause not taking HRT. Whether or not women in early menopause have a lower risk of breast cancer to start with was not the focus of the question posed. In table 17 (related to oestrogen-only HRT) differences are statistically significant even if in one of them the difference is too small to show up as a difference per 1000. The committee reflected on this and decided that the limited evidence identified (only evidence for breast cancer incidence) was a reason for a research recommendation in this area and removed the reference to this from the recommendation. Topics related to early menopause that were mentioned as important by stakeholders and were not addressed in the 2024 guideline update were logged with surveillance so that they could be considered for future updates.
British Menopause Society	Guideline	006	003	We welcome the support for individualised care	Thank you for your comment in support of this.
British Menopause Society	Guideline	008	001	1.2.8 The word "exercise" is missing	Thank you for your comment. This recommendation has not been updated in 2024 and is in its original wording. Therefore, the word 'exercise' has not been added to it.
British Menopause Society	Guideline	008	015	1.3.1. suggest saying as well as rather than and changes in their menstrual cycle to make it clearer this is a pre-requisite of peri-menopause	Thank you for your comment. Defining perimenopause was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					with the committee. The committee could therefore not comment on this.
British Menopause Society	Guideline	008	024	1.3.3. we would suggest saying *some ethnic groups* rather than ethnic minority background as there is a large heterogeneity amongst ethnic minority backgrounds.	Thank you for your comment. The word 'some' has been added as suggested.
British Menopause Society	Guideline	010	012	1.4.2 we welcome this focus on balanced discussion with the patient. This should be reflected consistently throughout the document.	Thank you for your comment. The committee agreed that a person-centred approach is of critical importance. To facilitate this, the data in the appendix have been used to produce a discussion aid document including visual presentation to aid decision making. This discussion aid has undergone user-testing and was refined based on user feedback. It is not NICE style to repeat recommendations in every section. Once mentioned recommendations would apply to throughout.
British Menopause Society	Guideline	010	027	1.4.3. The duration of HRT cannot be discussed at the outset because the exact HRT regimen may not have been determined and side-effects and beneficial effects need to be assessed which is usually done at the first review. It would be preferable to say "after the first review".	Thank you for your comment. This has been rephrased to read 'discuss the possible duration of treatment at the outset', followed by 'rediscuss the benefits and risks or continuing treatment at every review'.
British Menopause Society	Guideline	010 011	012 - 028 001 - 005	1.4.3 We agree that the potential risks must be discussed at the outset but this should be balanced with the benefits in this section as stated in 1.4.1.and 1.4.2. It is important that the document reflects good clinical practice which is to discuss the benefits and the risks of any proposed treatment such as HRT not just the risks. In the committee discussion (P43 line 5) it states "using an individualised approach with discussions about benefits and risks of	Thank you for your comment. The committee agreed that this has to be a person-centred approach and in recommendation 1.4.2 state: 'tailor the information about benefits and risks to the person's age, individual circumstances and potential risk factors.' It is in the sections about what and how options should be discussed and is therefore an overarching recommendation. It is not NICE style to repeat recommendations or

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				treatment options and tailoring information to individual circumstances and potential risk factors". We support this statement which reflects good clinical practice but would like to see this reflected consistently throughout the recommendations.	rationales for recommendations throughout documents.
British Menopause Society	Guideline	011	001	1.4.3 There is no arbitrary age cut off or time limit for HRT use. The word "prolonged" sounds judgmental. It would be better to say 'explain that the risks may increase with duration of HRT use'. In the committee discussion (page 43 line 22) it states "it is impossible to recommend one specific duration of use because this would depend on several factors, including the reason for starting HRT and a person's health history, age and symptoms." We support this statement which reflects good clinical practice. The term "prolonged use" implies longer than advised which as the committee acknowledges is not something that can be generalised at the outset.	Thank you for your comment. The committee reflected on this and the word 'prolonged' has been removed from this recommendation. It has been rephrased to read 'discuss the possible duration of treatment at the outset', followed by 'rediscuss the benefits and risks or continuing treatment at every review'. Therefore, it is a general discussion about the potential duration which would then be revisited at each review (and a link to the relevant section on reviews has been added).
British Menopause Society	Guideline	011	007 - 014	1.4.4. Whilst CBT is an important intervention in our opinion too much emphasis has been placed on it in this guideline, particularly in the original press release. The committee discussion concluded (page 44, line 1) "the committee also agreed that evidence showed that CBT could be an option for some people". This is a reasonable conclusion from the data yet the recommendations and headline press release were not consistent with this message implying it should be a firstline therapy for most if not all menopausal women. As is argued elsewhere	Thank you for your comment. The committee has revised the wording to ensure clarity about CBT 'as an option: in addition to HRT, for people for whom HRT is contraindicated or for people who prefer not to take HRT'. In relation to resourcing the committee acknowledged in the impact section of the guideline that there are long waiting times for CBT. They also noted that people currently trained in providing this kind of therapy may not be familiar with menopause-specific CBT and training on this may incur costs and increase waiting times in the short term. However, online and group CBT may be easier and less costly to

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				this is actually doing CBT a disservice as inappropriate and ineffective use will lead to it being misunderstood and abandoned when in reality it is a good option for some women. The wording throughout the document and in particular in the recommendations and any press releases need to accurately reflect this. 1.4.4. CBT is also very under-resourced and expensive – has there been a health economic appraisal?	adapt to menopause-specific CBT. There are also resources available to train people in providing menopause-specific CBT (and could also inform the adaptation of online CBT), which could facilitate implementation. Your comment will be considered by NICE where relevant support activity is being planned. The results of the evidence review varied according to the different measurement scales used and the committee also took into account based on expertise its effectiveness related to depressive symptoms outside the context of menopause and therefore made a recommendation to use it as an option.
British Menopause Society	Guideline	012	015	1.4.9. CBT for people who have taken gender-affirming therapy in the past. The draft guidelines and evidence reviews present no published evidence for the use of CBT in a transgender population. Given the limited weak evidence presented for other populations, it is difficult to see the rationale for this specific recommendation. The committee provide an explanation that it is not risky. However, any treatment intervention used where it is not likely to be efficacious can have negative consequences. If CBT is not an appropriate or efficacious treatment there would be the issue of wasted resources (for the health service and also for the individual themselves in time, energy or finances) but also the possibility of negative outcomes including frustration and sense of failure in engaging in ineffective treatment. There is evidence that engaging in unsuccessful treatments can lead to worsening of symptoms (such as sleep). Transgender and gender non-conforming adults are highly	Thank you for your comment. The wording of the recommendation has been revised to make it explicit that CBT is an option which could be in addition to other treatments, for people in whom other treatments are contraindicated or for those who prefer not to take other treatments. The guideline recommends a person-centred approach where discussions are tailored to the individual and their preference or risk factors. CBT is recommended for all other populations in this guideline and denying trans men or non-binary people registered female at birth who have taken gender-affirming hormone therapy in the past access to this as an option is an equality issue. It is also recommended that it should be ensured that trans men or non-binary people registered female at birth who have taken gender-affirming hormone therapy in the past and have symptoms associated with the menopause can discuss these with a healthcare professional with expertise in menopause. This would ensure that all options are explored. The recommendation

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				marginalised, stigmatised and victimised and may present with complex mental health issues in addition to menopause symptoms. The limited evidence base for use of CBT in this population suggests that adaptations may need to be made to CBT to include a trauma informed and transgender affirming to ensure it is efficacious and culturally sensitive. Perhaps it is reasonable to include "consider CBT" for this population but we feel a cautionary comment needs to be made as to lack of evidence, and consideration of specifically adapted CBT is desirable.	related to discussions about CBT in another section of the guideline has been updated to include that the person's preferences and needs should be taken into account. If the person's preferences and needs may mean that CBT is not suitable for them then this can be discussed during the shared decision making process. The lack of direct evidence is highlighted in the related rationale section. Making reasonable adjustments is part of the Equality Act 2010 and does not have to be repeated in all NICE guidelines.
British Menopause Society	Guideline	012	015	1.4.9. This recommendation is not consistent with the text on p47, lines 4-8 which states "not all the evidence on vasomotor symptoms showed that CBT was beneficial. Most of the benefits were seen in reducing how much women were bothered by the symptoms….CBT should be an option rather than a routine treatment for all." The recommendation should be adjusted to reflect that.	Thank you for your comment. The wording has been revised to ensure clarity about CBT as an option which could be in addition to other treatments, for people in whom other treatments are contraindicated or for those who prefer not to take other treatments.
British Menopause Society	Guideline	012	015	1.4.9. There should be acknowledgement that CBT is not suitable for all.	Thank you for your comment. The wording of the recommendation has been revised to make it explicit that this is an option which could be in addition to other treatments, for people in whom other treatments are contraindicated or for those who prefer not to take other treatments. The guideline recommends a person-centred approach where discussions are tailored to the individual and their preference or risk factors. The recommendation related to discussions about CBT has been updated to include that the person's preferences and needs should be taken

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					into account. If the person's preferences and needs may mean that CBT is not suitable for them then this can be discussed during the shared decision making process.
British Menopause Society	Guideline	012	015	1.4.9. Whilst recommending CBT, the draft guidance has completely overlooked the evidence for hypnosis in treating menopausal hot flushes. Clinical hypnosis is recognised as a valid therapy by the Royal College of Psychiatrists, whose patient information webpage states that it "has been shown to help menopausal symptoms." (https://www.rcpsych.ac.uk/mental-health/treatments-and-wellbeing/hypnosis-and-hypnotherapy). The North American Menopause Society has recommended hypnosis for vasomotor symptoms of menopause based on level 1 ("good and consistent") evidence since 2015 and once again in their latest update (2023). An RCT of hypnosis, a large, clinically significant mean reduction of 70% to 80% in objectively (physiologically measured) hot flushes was observed, which is comparable to hormone replacement therapy but without its potential adverse effects. In addition, in further analysis of both studies hypnosis had important effects on anxiety and has also shown promise for other troublesome menopausal symptoms such as sleep quality and sexual function. A further large NIH-funded multicentre RCT of Clinical Hypnosis for menopausal hot flashes is currently being conducted in the USA. This study examines the mechanisms of effects (heart rate	Thank you for your comment. Hypnosis was not part of the scope of the 2024 guideline update. Therefore, the committee could not comment on this. However, because of this and other stakeholder comments this has been logged with the NICE surveillance team which regularly checks for evidence in topics included in guideline so that this can be considered for future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				variability, saliva cortisol) and remote/digital delivery of the intervention. Enrolment is complete, with 232 post-menopausal women and breast cancer survivors randomized to either Hypnotherapy or a Sham Hypnotherapy intervention. Results should be available by March 2024 or sooner and could be included for analysis, should NICE decide to assess Clinical Hypnosis. References: Elkins GR et al Menopause 2013;20:1097 doi.org/10.1097%2FGME.0b013e31826ce3ed Elkins GR et al Randomized trial of a hypnosis intervention for the treatment of hot flashes among breast cancer survivors. Journal of Clinical Oncology. 2008;26(31):5022–5026.The 2023 North American Menopause Society nonhormone therapy position statement Menopause 2023;30(6):573-90. In summary, by overlooking hypnosis, NICE is unwittingly denying women knowledge of, and potentially access to, an evidence-based, safe and effective non-hormonal treatment other than CBT.	
British Menopause Society	Guideline	012	019	Taking comorbidities into account - it would be helpful to have an additional clause to the effect of 'Be aware that patients taking levothyroxine to treat hypothyroidism may require an increase in their dose after commencing oral HRT. Re-test thyroid function after starting tablet-combined HRT.'	Thank you for your comment. Whilst there are some new recommendations in this section, the general topic of comorbidities (including issues relating to hypothyroidism) was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this. The issue of thyroid function has been logged with the NICE sureveillance team for considerations in future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Menopause Society	Guideline	012	021	1.4.10 It is a missed opportunity that this has not been updated. There is still a lot of caution about prescribing HRT in women with Diabetes. A stronger recommendation that there is no reason why women with Diabetes cannot have HRT if indicated and co-morbidities considered would be welcome. Women with type 2 diabetes mellitus are a group for whom there is a dearth of data on menopause treatment outcomes, in particular risks and benefits of HRT. We would like to see a recommendation for inclusion of the need to collect real-world data in women with type 2 diabetes as they are usually excluded from clinical trials of menopause treatments. WHI showed that continuous combined CEE and MPA resulted in statistically significant reduction in the incidence of type 2 diabetes (HR 0.81; 95% CI: 0.70-0.94). CEE alone also resulted in a significant reduction in type 2 diabetes (HR 0.86; 95% CI: 0.76-0.98). Also a meta-analysis of RCTs by Sapeter et al with pooled results from 107 trials and showed that HRT reduced new-onset diabetes [relative risk 0.7 (CI, 0.6-0.9)] in women without diabetes abdominal fat [-6.8% (CI, -11.8 to -1.9%)] and HOMA-IR [-12.9% (CI, -17.1 to -8.6%)]. In women with diabetes, HRT reduced fasting glucose [-11.5% (CI, -18.0 to -5.1%)] and HOMA-IR [-35.8% (CI, -51.7 to -19.8%)]. Manson JE et al. Menopausal hormone therapy and health outcomes during the intervention and extended post stopping	Thank you for your comment. Whilst there are some new recommendations in this section, the general topic of comorbidities (including issues relating to type 2 diabetes mellitus) was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this. Therefore, the cited references did not meet inclusion criteria for any protocols. However, these have been passed on to the NICE surveillance team which regularly checks evidence for guideline topics to see whether further updates are needed.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				phases of the Women's Health Initiative randomized trials. JAMA. 2013 Oct 2;310(13):1353-68. doi: 10.1001/jama.2013.278040. PMID: 24084921; PMCID: PMC3963523. Salpeter SR et al Meta-analysis: effect of hormone-replacement therapy on components of the metabolic syndrome in postmenopausal women. Diabetes Obes Metab. 2006 Sep;8(5):538-54. doi: 10.1111/j.1463-1326.2005.00545.x. PMID: 16918589.	
British Menopause Society	Guideline	013	002	1.4.11 We recognise this is not being updated but based on the evidence we would recommend this is updated to say transdermal is first line in women at increased risk of VTE which is in keeping with current practice. There was no update on the absence of risk of VTE with transdermal HRT – the data all point to no increase in risk whereas the guideline refers to a greater risk with oral versus transdermal, but this implies that there is still may be some risk with transdermal. In addition, several studies have now shown that the risk is significantly influenced by the type of progestogen in HRT with natural progesterone and dydrogesterone appearing to be lower risk – this should be indicated in the guideline. Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases. BMJ. 2019 Jan 9;364:k4810.	Thank you for your comment. The impact of HRT on risk of VTE was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this. The cited references have been passed on to the NICE surveillance team to consider for a future update.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Canonico M, Oger E, Plu-Bureau G, Conard J, Meyer G, Lévesque H, Trillot N, Barrellier MT, Wahl D, Emmerich J, Scarabin PY; Estrogen and Thromboembolism Risk (ESTHER) Study Group. Hormone therapy and venous thromboembolism among postmenopausal women: impact of the route of estrogen administration and progestogens: the ESTHER study. Circulation. 2007 Feb 20;115(7):840-5. Graham S, Archer DF, Simon JA, Ohleth KM, Bernick B. Review of menopausal hormone therapy with estradiol and progesterone versus other estrogens and progestins. Gynecol Endocrinol. 2022 Nov;38(11):891-910.	
British Menopause Society	Guideline	013	005	1.4.12 We recognise this is not being updated but referral to a haematologist will not change management when there is good quality observational data indicating transdermal HRT does not affect risk of VTE. Unnecessary referral wastes patient's time and NHS resources. If referral is needed this could be to a menopause specialist or a haematologist.	Thank you for your comment. The impact of HRT on risk of VTE was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this. Some stakeholders have provided a list of related references and this has been passed on to the NICE surveillance team to consider for a future update.
British Menopause Society	Guideline	013	027	1.4.14 People at high familial risk of ovarian cancer: whilst NICE is right to draw attention to its own guideline, this is not yet published and there are national and international recommendations already out there which could be referenced. Vermeulen RFM et al Climacteric 2019:22:352-60, Manley K et al Post Repro Health 2023;29:42-52	Thank you for your comment. The NICE guideline on identifying and managing familial and genetic risk of ovarian cancer has since been published and therefore the cross reference has been updated. This includes a section on HRT after risk-reducing surgery.
British Menopause Society	Guideline	014	002	1.4.15 states HRT should be offered to people with troublesome vasomotor symptoms whereas 1.4.16 recommends that CBT should	Thank you for your comment. The wording has been revised to ensure clarity about CBT 'as an option: in addition to HRT, for people for whom

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				be considered, which is not as strong a recommendation despite its prominence in the guideline and official press release. There needs to be consistency between the evidence, the recommendations and the public messaging otherwise there will be (already is) confusion.	HRT is contraindicated or for people who prefer not to take HRT'.
British Menopause Society	Guideline	014	005	1.4.16 Consider CBT for troublesome vasomotor symptoms. The majority of the studies compared the specific CBT (for menopause symptoms or insomnia) and compared these to "no treatment" for the control group. This means it is not possible to say whether it was the specific CBT intervention that was responsible for any improvements seen. For instance there may have been therapeutic benefits of clinician contact, menopause education, psychoeducation or other factors. In fact in the referenced Kalmbach - RCT targeting insomnia CBT for insomnia (CBT-I) was compared with separate component treatments (the second group had sleep restriction therapy and the third group had sleep hygiene.) All 3 groups saw improvements in hot flush self reporting at 6 months - suggesting that it was not the CBT itself that led to improvements. The uncertainty of the data should be reflected in the strength of the recommendations and public messaging.	Thank you for your comment. The protocol stated that studies would be grouped together depending on the intervention and comparator. The committee listed a number of comparators, and 'no treatment' was a separate comparator to 'treatment as usual' therefore the studies were analysed separately depending on the comparison groups. Studies where the comparator had no intervention, or there was minimal intervention that was considered to have none, or very little therapeutic effects were classified as 'no treatment'. The committee considered this evidence separately to studies where the comparator arm had some components of an intervention similar to what might be expected in the real-world, and this was classified as 'treatment as usual'. Kalmbach 2019 was a 3-armed trial, as you mention in your comment, however 1 of the arms (sleep restriction) was not included in the evidence review as the intervention did not match those listed in the protocol. The comparator arm included in the review was 'sleep hygiene' and this was classified under 'treatment as usual'. The committee recognised these aspects and considered them when discussing the evidence. The committee recognised that there was wide variability among the studies in terms of the CBT

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					intervention arms and the 'treatment as usual' arms. Due to the variability, and therefore uncertainty as to the specific features of the CBT that contributes to the benefits seen in the evidence, the committee were unable to be too prescriptive in the recommendations. The committee also considered the quality of the evidence and this is reflected in the wording used which indicates the recommendation strength. The word 'consider' was used for recommendation 1.4.9 as it is a 'weak' recommendation. In 'strong' recommendations for actions that should (or should not) be offered, directive language such as 'offer' is used. For more information on this please see: Developing NICE guidelines: the manual. The recommendation was also updated to make it explicit that CBT is an option which can be added to other treatments, where other treatments are contraindicated or where people prefer not to have other treatments.
British Menopause Society	Guideline	014	005	1.4.16 Consider CBT for troublesome vasomotor symptoms. The evidence presented for this recommendation is weak. Of the 17 CBT studies, 13 of these looked at vasomotor symptoms. 5 out of these studies looked only at a population of women who had menopausal vasomotor symptoms following breast cancer. There are many reasons why this population may respond to CBT differently to a non-breast cancer population (including the nature and severity of vasomotor symptoms, other associated symptoms and experience of cancer treatment journey). The results of these studies should not be	Thank you for your comment. The committee were interested in the effectiveness of CBT in those with symptoms associated with the menopause in both populations with and without a history of breast cancer. The committee were particularly interested in those with a history of breast cancer as CBT may offer an alternative treatment if other treatments such as HRT are contraindicated in this population. The committee recognised at the start of the review that the effectiveness of the intervention may differ between these two populations, and specified in the protocol for the review that the data should be analysed separately where this was possible. The

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				extrapolated to a non-breast cancer population which will make up a majority of individuals for whom these guidelines will be in use for. This leaves 8 small studies all of which utilised a specially adapted form of CBT targeted directly at menopause symptoms (sometimes referred to as "CBT-Meno ") or CBT targeted specifically at insomnia "CBT-I". This distinction is not mentioned in the draft guidelines. It is important to accurately describe the intervention utilised in the studies reference. Using the term "CBT " is likely to be confusing and could end up with individuals referred for general CBT (which is most commonly used for depression and anxiety within NHS talking therapies services). There were no studies included in the evidence briefing that utilised this more general CBT. Therefore, we request that the recommendation should be adjusted to specify CBT targeted to menopause symptoms (or insomnia).	data was analysed separately where possible, and as the evidence showed a benefit of CBT in both those with and without a personal history of breast cancer, the committee made the recommendation for all. The committee have reconsidered the wording of the recommendations and have made amendments to specify that the CBT is an option to manage either vasomotor symptoms, depressive symptoms or difficulties with sleep as an addition to other treatments, where other treatments are contraindicated or when a person prefers not to have other treatments.
British Menopause Society	Guideline	015	001	The term "Genito-urinary symptoms" or "Genito-urinary symptoms of the menopause" or "genito urinary menopause symptoms" has been introduced in this guideline and is used variably. It is not a term that is used in the mainstream literature. It is not clear what this is referring to. The previous guideline referred to symptoms of uro-genital atrophy and it is not clear why this has been changed. It is entirely separate entity form Genito-urinary *syndrome* of the menopause which is a term now used in some of the literature to reflect a syndrome of	Thank you for your comment. The guideline has now included a definition of genitourinary symptoms associated with the menopause which consists of vulvovaginal dryness, pain with sex, vulvovaginal discomfort or irritation, and discomfort or pain when urinating. This is consistent with the terminology used in evidence reviews B1 and B2.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				symptoms. However, this term is North American and not universally accepted. Correct and consistent terminology is important in a national guideline. "Genito-urinary symptoms" is a potentially useful term but if the committee wish to introduce this term, it should be clearly explained in the glossary with supporting standardised and validated evidence for the change in terminology. We would recommend using the term "genitourinary symptoms associated with the menopause" as used in Evidence Review B2 consistently across the document otherwise there will be significant confusion about what is being discussed.	
British Menopause Society	Guideline	015	014	1.4.20 "some oestrogen is absorbed but, compared with systemic HRT, the amount is small " This statement is confusing and may cause alarm for both patients and GPs and raise concern that progestogens maybe required for endometrial protection. The amount of oestrogen absorbed with the widely used ultra-low doses of vaginal estrogen is not clinically significant (not just "small"). After a small spike in oestradiol levels in the first few days of treatment the levels fall to normal postmenopausal levels. The MHRA has reviewed all the data and approved vaginal oestrogen 10mcg for over-the-counter use. We recommend re-phrasing to: "the amount absorbed is not clinically significant effect and has no stimulatory effect on the endometrium"	Thank you for your comment. This bullet point was reworded to say vaginal oestrogen is absorbed locally - a minimal amount is absorbed into the bloodstream (when compared with systemic HRT), but this is unlikely to have a significant effect throughout the body. It is then described in the rationale section that 'the committee agreed to highlight this because it means that there is no need to combine low-dose vaginal oestrogens with systemic progestogen treatment to protect the person against endometrial hyperplasia and cancer'.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Menopause Society	Guideline	015	016	1.4.20 It is good clinical practice to encourage reporting of any vaginal bleeding post-menopause not just on vaginal oestrogen. This statement is unnecessary and following on from the previous statement will again cause confusion and alarm.	Thank you for your comment. On reflection, the committee decided to remove this statement in the context of vaginal oestrogen.
British Menopause Society	Guideline	015	019	1.4.21 please clarify this statement "increasing the dose within the standard therapeutic range". Does this mean increasing the dose off label? The standard doses are often insufficient to fully alleviate symptoms as the doses have been reduced by the manufacturers (e.g. vaginal tablets now 10mcg but were 25mcg) so it is common clinical practice to recommend more frequent use than twice weekly.	Thank you for your comment. This recommendation has been removed.
British Menopause Society	Guideline	015	023	1.4.22 The terminology here is confusing. Vaginal oestrogens are a treatment for the symptoms of an overactive bladder such as urinary urgency and frequency.	Thank you for your comment. This recommendation is creating a link between this guideline and a recommendation to 'offer intravaginal oestrogens to treat overactive bladder symptoms in postmenopausal women with vaginal atrophy' in NICE's guideline on managing urinary incontinence and pelvic organ prolapse which is relevant in the context of genitourinary symptoms associated with the menopause and overactive bladder symptoms.
British Menopause Society	Guideline	015	026	1.4.23 Vaginal moisturisers do not improve urinary symptoms. This statement is misleading due to the adoption of the term genito-urinary symptoms.	Thank you for your comment. The term genitourinary symptoms has now been defined and the committee agreed that moisturisers and lubricants may be useful for all of the listed comments.
British Menopause Society	Guideline	016	001	1.4.24 Prasterone does not improve urinary symptoms. This statement is misleading due to the adoption of the term genito-urinary symptoms.	Thank you for your comment. A definition of genitourinary symptoms associated with the menopause has been added to the terms used in the guideline section. The NMA found that

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					prasterone was effective for those symptoms but not cost effective as a first line treatment option. It was therefore only recommended if vaginal oestrogen, moisturisers or lubricants have been ineffective or are not tolerated.
British Menopause Society	Guideline	016	005	1.4.25 Personal preference for an oral preparation should also be an indication for the use of Ospemifene. Some women are resistant or uncomfortable with inserting treatments vaginally.	Thank you for your comment. The analysis of the clinical and cost effectiveness evidence showed that the wider recommendation for ospemifene would not be value for money. The committee therefore only recommended this where local use was not practical.
British Menopause Society	Guideline	016	004	1.4.25 Ospemifene does not improve urinary symptoms. This statement is misleading due to the adoption of the term genito-urinary symptoms	Thank you for your comment. A definition of genitourinary symptoms associated with the menopause has been added to the terms used in the guideline section. The NMA found that this was effective for those symptoms but not cost effective as a first or second line treatment. It was therefore only recommended if locally applied treatments are impractical, for example, because of disability.
British Menopause Society	Guideline	016	011	1.4.26 It would be helpful to emphasise the importance of ensuring a physiological pH and osmolality in choosing a vaginal moisturiser. Edwards D, Panay N. Treating vulvovaginal atrophy/genitourinary syndrome of menopause: how important is vaginal lubricant and moisturizer composition? Climacteric. 2016 Apr;19(2):151-61.	Thank you for your comment. The pH level and osmolarity of moisturisers and lubricants was not in the scope of this review question. This means that different levels of pH and osmolarity were not compared with each other to investigate the impact on genitourinary outcomes associated with the menopause. The article by Panay was not included because it did not meet protocol criteria (it was a narrative review). The committee could therefore not comment on this.
British Menopause Society	Guideline	016	019	1.4.28 This statement is confusing. Vaginal oestrogens appear to be effective in this group but the use of Aromatase inhibitors is generally considered a contra-indication to vaginal oestrogens. It is not clear why this has been	Thank you for your comment. The recommendation related to uncertainty about the effectiveness of vaginal oestrogen in people with a history of breast cancer has been deleted. The safety of vaginal oestrogens in those who are

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				changed. We accept there are limited data on their efficacy in this situation but the main concern here is safety. In women treated with AIs, serum E2 ≥ 0.5 pg/mL is associated with a 2-fold increase in the risk of recurrence (Ingle JN et al Clin Cancer Res. 2020 Jun 15;26(12):2986-2996). We would recommend a stronger statement regarding the use of vaginal oestrogen in women using an aromatase inhibitor. Conversely the consensus is that vaginal oestrogens can be used with tamoxifen if indicated.	taking aromatase inhibitors is considered in a later recommendation (1.4.30) which has now been moved up in the order of recommendations to give it greater emphasis. The committee agreed that this was important and therefore they have made a recommendation that this should be discussed with an oncologist specialist, so that any alternative treatment options, if appropriate, can be considered and the correct support provided to someone on adjuvant treatment who is seeking management for genitourinary symptoms. Thank you for highlighting the study by Ingle et al 2020. This reference has been checked for inclusion but it does not meet the criteria set out in the review protocol for review B2 on genitourinary symptoms and breast cancer, therefore cannot be used to support any recommendations.
British Menopause Society	Guideline	017	003	1.4.29 This section is unduly negative and may deter women being prescribed vaginal oestrogens when appropriate. The data, such as they are, are reassuring and this should be stated. It is appropriate to acknowledge that the data are limited but no study has suggested an increased risk of recurrence. A recent UK meta-analysis in JAMA Oncol (McVicker L et al doi:10.1001/jamaoncol.2023.4508) showed no evidence of increased early breast cancer mortality in patients using vaginal oestrogens. Although we recognise that this publication was after the relevant discussion, nevertheless it provides further important information from a large UK cohort that is consistent with existing data and should provide further reassurance.	Thank you for your comment. The committee considered the data available and concluded that there was uncertainty regarding the risks of breast cancer recurrence which is reflected in the recommendations. The reference linked in the comment is not a meta-analysis but a cohort study. This study would not have met the criteria specified in the protocol for the review question related to vaginal oestrogens as breast cancer recurrence was not reported and mortality was not one of the outcomes listed in the protocol. The committee made changes to the order of recommendations so that considerations of adjuvant treatments are being made early in shared decision making. They also revised the recommendation related to safety considerations

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					for clarity. This would give this section a more logical flow and greater clarity about safety. The rationale of the guideline and the committee discussion section of the evidence were revised accordingly. A visual summary was produces for the management of genitourinary symptoms to clarify treatment options and facilitate decision making.
British Menopause Society	Guideline	017	011	1.4.29 Again, the statement about vaginal oestrogen being absorbed is misleading. The amount of vaginal oestrogen that is absorbed is very small and all the pharmacokinetic data show that this is only in first few days of administration. After that oestradiol levels are within the post-menopausal range	Thank you for your comment. This bullet point was reworded to say that vaginal oestrogen is absorbed locally - a minimal amount is absorbed into the bloodstream (when compared with systemic HRT), but this is unlikely to have a significant effect throughout the body. Recommendations relating to discussions of factors affecting safety have been revised for clarity highlighting when it is likely to be safer to use vaginal oestrogen for people with a personal history of breast cancer.
British Menopause Society	Guideline	018	003	1.4.32 add in "or any other vaginal treatments such as Prasterone or Ospemifene.	Thank you for your comment. In this section vaginal oestrogen is first line treatment, prasterone is second line and ospemifene should only be used if locally applied treatments are impractical. Therefore, adding that these treatments can be used in combination with non-hormonal moisturisers or lubricants to recommendation 1.4.2 would be confusing because it would mix up treatment pathways. It would also not be in keeping with the message related to ospemifene because non-hormonal moisturisers or lubricants would be locally applied treatments which would in this case also be impractical to use. This has, therefore been added to the recommendation directly related to

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					prasterone to make people aware that this could also be used in combination with non-hormonal moisturisers or lubricants.
British Menopause Society	Guideline	018	006	1.4.33 reference NICE guideline IPG967	Thank you for your comment. A reference to IPG967 has been added.
British Menopause Society	Guideline	019	002	1.4.37 This recommendation is an oversimplification of the literature. The committee acknowledged that it is difficult to define sleep difficulties associated with the menopause and that the research is heterogeneous. However, no attempt has been made to signpost clinicians to appropriate guidelines and tools for assessment and diagnosis of sleep disorders which become more prevalent at the time of the menopause. 8 studies were mentioned as looking at sleep in Table 2. However, one of these made no mention of sleep measures or outcomes within the abstract (Ayers) and for one (Cheng 2020) the reference appeared to be a trial comparing the side effects of excessive sleepiness between different treatments - which does not appear to answer the question in hand. Of the remaining 6 studies reporting on sleep symptoms following CBT, 2 were in a breast cancer population and 4 were in the general population. All of these used either CBT designed specifically for insomnia (CBT-I) or CBT targeted directly at menopause symptoms. It is likely a majority of individuals experiencing sleep problems at the time of menopause will meet the diagnostic criteria for insomnia disorder (DSM-V). Although CBT is a well evidenced treatment for insomnia it is vital to highlight that it is not "CBT" per se which	Thank you for your comment. The assessment and diagnosis of sleep disorders related to menopause was not in the scope of the 2024 guideline update. The committee could therefore not comment on this. The references listed within the links cited have been checked and none of them meet the criteria set out in the protocols for the evidence reviews that were updated.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				has known efficacy for insomnia disorder and sleep symptoms in the menopause. It is specifically adapted CBT called CBT for Insomnia (CBT-I). This is a very different treatment from the general CBT which is offered as part of the UK talking therapy programme, and this distinction should be made for readers of these guidelines. This distinction is made clear and CBT-I is referenced as the first line treatment for insomnia in the NICE CKS and also in international guidelines including American guidelines and recently updated European guidelines https://esrs.eu/guidelines/ We would ask that the NICE guidelines refer to these sleep guidelines in a similar way that it refers to the NICE depression guidelines. This will ensure that clinicians are prompted to use an evidence based diagnostic framework to manage sleep disorders (which should be recommended whether experiencing menopause or not.) Within these referenced guidelines clinicians are prompted to consider other sleep disorders such as sleep apnoea and restless legs syndrome in addition to (the most common disorder) insomnia. This is important as the incidence of these disorders increase after menopause.	
British Menopause Society	Guideline	019	002	1.4.37 It is not clear why only CBT is considered for sleep difficulties given that HRT can also be of benefit by alleviating night sweats (and possibly having a direct effect on the hypothalamic sleep centre). HRT should	Thank you for your comment. Apart from CBT other management options for sleep problems associated with the menopause were not in the scope of the 2024 guideline update. However, the committee acknowledged that there are other options that may be used (including HRT). They

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				also be considered if sleep problems occur in conjunction with other menopausal symptoms.	have therefore reworded the recommendation to reflect this. It now states that CBT could be used as an option (1) in addition to other treatments (including HRT), or (2) for people for whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. Given the constraints of the scope they could not be more specific than this.
British Menopause Society	Guideline	019	006	1.4.38 Whilst we recognise that the use of Testosterone was outside the scope of this guideline it is disappointing that no additional recommendation about Testosterone has been made in light of Global consensus paper and recent meta-analyses. It would be helpful to mention that there is no evidence for the use of Testosterone to improve cognitive function, mood or other symptoms and to give clearer advice around off license prescribing of Testosterone.	Thank you for your comment. At the time when the scope of the 2024 guideline update was agreed, there was no substantive new evidence that would change the recommendation related to testosterone. It was therefore not included in the update and the committee could not comment on this. However, NICE recognises the importance of this issue and has worked with the NIHR to prioritise funding for research on the matter.
British Menopause Society	Guideline	019	006	1.4.38 It would be helpful to highlight the need for further research into the potential non-sexual health benefits of Testosterone as a research priority	Thank you for your comment. At the time when the scope of the 2024 guideline update was agreed, there was no substantive new evidence that would change the recommendation related to testosterone. It was therefore not included in the update and the committee could not comment on this. However, NICE recognises the importance of this issue and has worked with the NIHR to prioritise funding for research on the matter.
British Menopause Society	Guideline	019	013 - 015	1.5.1 This recommendation is too simplistic. There is no mention of women who have had a subtotal hysterectomy or hysterectomy for severe endometriosis when progestogens would usually be prescribed with oestrogen.	Thank you for your comment. The committee discussed that choice between oestrogen-only and combined HRT may be different for people with a sub-total hysterectomy. They decided that they could not be prescriptive about the type of HRT to be used for people who have had a sub-total hysterectomy because their condition is

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					clinically complex and they had not reviewed evidence about the effect of HRT on risk of endometrial cancer for this group. They acknowledged that people who were going to have, or had had, a sub-total hysterectomy would be under the care of a specialist who could discuss HRT options tailored to their needs (or a relevant specialist within the MDT). Due to a lack of evidence, no specific recommendation was made for sub-total hysterectomy; however, the term "total" was added before "hysterectomy" in guidance regarding the offer of oestrogen-only HRT to those who have had a hysterectomy. This addition alerts healthcare professionals to consider other factors for patients with a sub-total hysterectomy. The committee also noted that some people have a hysterectomy for a condition that may be affected by HRT, such as endometriosis. The committee did not review evidence related to such conditions. They recognised that the decision about the type of HRT that best balances benefits and risks for the person may be affected by that condition (for example endometriosis) or having had a subtotal hysterectomy. For this reason, they added a recommendation highlighting that advice from a healthcare professional with specialist knowledge of that condition may be needed when making this choice. Due to this stakeholder comment and other related comments, this topic has been logged

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					with NICE surveillance so that it can be considered for a possible update to either the Menopause or the Endometriosis guideline in future.
British Menopause Society	Guideline	019	016	The term "lowest effective dosage" needs further explanation. In our opinion it should state "the appropriate individualised dosage" which balances full effectiveness for individual treatment goals with the risk of possible adverse effects. This is an individualised decision. We would also welcome a comment to say that initial prescribing should be within the licensed dosages. We feel that careful wording is need here as on the one hand there is a tendency amongst some practitioners to be reluctant to prescribe an effective dose and on the other hand there are some who are advocating and prescribing doses of HRT well above the recommended doses from the outset.	Thank you for your comment. The committee recommended the lowest effective dosage which would be reviewed in 3 months to assess efficacy and tolerability and annually thereafter (as highlighted in a different recommendation on reviewing treatments). The suggested wording of 'appropriate individualised dosage' would be difficult to use because it would require a lot of additional explanation of what it would entail with the same outcome that it would be reviewed and potentially adjusted if necessary. All dosages would be within licensed ranges and a statement has now been added to emphasise this.
British Menopause Society	Guideline	019	017	1.5.3. The committee should be aware that Guidelines for the management of bleeding on HRT are currently being developed by the BMS, BSGE, BGCS, RCOG in conjunction with GIRFT and NHS England Cancer task force. This is in response to an increasing clinical problem and the overwhelming of many fast-track clinics by abnormal bleeding on HRT. It is hoped the guidelines will be published in the first quarter of 2024. We therefore request that if the committee publish the final NICE guidance after the publication of this bleeding on HRT guidance, that the new guidance is signposted in the NICE guideline.	Thank you for your comment. NICE reviewed the published guideline and noted that it conflicts with the NICE guideline of suspected cancer: recognition and referral. Therefore, it would be currently difficult to signpost to the guidelines for the management of bleeding on HRT published by the BMS, BSGE, BGCS, RCOG in conjunction with GIRFT and NHS England Cancer task force. It was therefore decided to remove the current cross reference to the conflicting NICE guideline and this topic was logged with the NICE surveillance team.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Menopause Society	Guideline	021	013 - 015	1.5.11 We agree that psychological support should be offered to people with early menopause but they should also be offered referral to a specialist menopause service as would be recommended for women with POI. These women are also at short term quality of life risks and long term health risks if not adequately managed.	Thank you for comment. The origin of this recommendation is the topic of early menopause for which one question was included in the 2024 guideline update and the aim of the recommendation is to allow psychological support to reach the people in need of it most based on symptoms. Whether or not psychological support is needed for everyone in menopause (apart from CBT) was not part of the scope of the 2024 guideline update. The committee were also concerned of the large resource impact recommending referral to a menopause specialist would have, bearing in mind the already very long waiting times for access. They discussed this could potentially make it even harder for people in particular need of this service to gain access. In light of this, the committee agreed to not recommend referrals to menopause specialists.
British Menopause Society	Guideline	021	021 - 022	1.6.1 This recommendation does not adequately reflect the data, particularly for oestrogen only HRT. There is a large body of evidence (e.g. Salpeter, the WHI RCT and Cochrane) that all-cause mortality is reduced by hormone therapy if commenced before the age of 60 and yet this beneficial effect is not reflected in the updated guideline. It is not clear why the guideline committee have ignored this evidence. These and several other studies have been excluded form the analysis on the grounds that they did not report separate results for combined and oestrogen only HRT. However some similarly designed studies in other disease areas are included reflecting inconsistency in the way these criteria have been applied. These studies were	Thank you for your comment. The reference to Salpeter 2006 in your comment is a report for coronary heart disease events and not for all-cause mortality. However, there are 2 systematic reviews listed in the excluded studies section of Evidence Review H that might be relevant to your comment, and so will be referred to in this response. Boardman 2015 and Salpeter (2004 and 2009) are systematic reviews that were assessed for inclusion but were not included as a systematic review because they did not separate results by combined and oestrogen-only HRT. This was criteria set out in the pre-specified protocol and cannot be changed. The committee therefore cannot comment on the conclusions these systematic reviews reached. The individual studies included in these systematic reviews were

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				all published in high quality peer-reviewed journals and there results are very pertinent to the discussion. Their exclusion, on whatever grounds, is a significant weakness in this NICE Guideline. Salpeter RS et al Journal of general internal medicine 2006;21(4):363-6 Boardman HM, et al Hormone therapy for preventing cardiovascular disease in post-menopausal women. Cochrane Database Syst Rev. 2015 Mar 10;2015(3):CD002229. Manson JE, et al for WHI Investigators. Menopausal Estrogen-Alone Therapy and Health Outcomes in Women With and Without Bilateral Oophorectomy: A Randomized Trial. Ann Intern Med. 2019 Sep 17;171(6):406-414.	checked against the protocol criteria, and where relevant they were included in the review. WHI results have been included in this evidence review. The evidence in Evidence Review H shows an isolated risk reduction in the age group 50-59, for oestrogen-only HRT users, however this is part of a subgroup analysis that did not show a statistically significant difference between the subgroups, and therefore the committee could not conclude that there was a benefit in all-cause mortality that warranted a recommendation. The related rationale sections of the guideline have been updated to make it explicit why some widely cited systematic reviews could not be included. The evidence reviews in this guideline followed rigorous NICE methods and processes, with details outlined in a supplement available on the website (Supporting document 1 - Methods), consistent with the NICE guideline manual. With regard to inconsistency over the exclusion criteria across reviews, the NICE processes have been followed, and that each review question follows the criteria set out in the protocol for that particular review. Some review protocols are not identical to others, see the specifics of each protocol in Appendix A of the Evidence Reviews. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
British Menopause Society	Guideline	035	002 - 016	1.6.4 This whole section is misleading and does not reflect the data. The evidence review on early menopause (Page 74, lines 10-11) states: "Whether early menopause affects long-term health is uncertain". There is no reference to why HRT is considered in women with early menopause in the first instance i.e. the significantly increased risk of CVD and osteoporosis in women with early menopause due to oestrogen deficiency and no reference to HRT being considered in clinical practice in this situation to counter that effect. The reference to the evidence of adverse effect of oestrogen deficiency in this group being uncertain is inaccurate and does not appear to acknowledge the large observational evidence (references below) that shows an increase. There is increased risk for CVD, cardiovascular mortality, osteoporosis and related fractures as well as all-cause mortality reported in large observational reviews and meta-analyses. Whilst evidence from controlled studies to demonstrate this is lacking, this is a very similar limitation to the evidence for POI which NICE acknowledged in 2015 and despite this made recommendations to offer HRT to women with POI following the same logic).	Thank you for your comment. The aim of the evidence review carried out was assessing whether either taking HRT or not taking HRT for people with early menopause impacts on various health outcomes. The review did not assess early menopause as a risk factor for health outcomes and therefore could not include the suggested references. Whilst the cited references did not match the review protocol, the need to assess the consequences of early menopause on health outcomes has been acknowledged and will be passed onto the NICE surveillance teams, including the provided references, for prioritised consideration during future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Muka T, Oliver-Williams C, Kunutsor S, Laven JS et al., Association of age at onset of menopause and time since onset of menopause with cardiovascular outcomes, intermediate vascular traits, and all-cause mortality: a systematic review and meta-analysis, JAMA Cardiol. 1 (2016) 767–776. Zhu D, Chung HF, Dobson AJ, et al. Age at natural menopause and risk of incident cardiovascular disease: a pooled analysis of individual patient data. Lancet Public Health 2019;4:e553–e564. Anagnostis P, Siolos P, Gkekas NK et al., Association between age at menopause and fracture risk: a systematic review and meta-analysis, Endocrine 63 (2019) 213–224. Gallagher JC. Effect of early menopause on bone mineral density and fractures. Menopause. 2007 May-Jun;14(3 Pt 2):567-71. doi: 10.1097/gme.0b013e31804c793d. PMID: 17476146. Hao W, Fu C, Dong C, Zhou C, Sun H, Xie Z, Zhu D. Age at menopause and all-cause and cause-specific dementia: a prospective analysis of the UK Biobank cohort. Hum Reprod. 2023 Sep 5;38(9):1746-1754. doi: 10.1093/humrep/dead130. PMID: 37344154; PMCID: PMC10663050. The interpretation of this evidence in guidelines globally is to offer HRT in this group until the natural age of the menopause. Indeed, in the review of evidence the Guideline committee acknowledge this (page 74 16-17) but this is	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				not reflected in the recommendation. If adopted as it stands, this will make the NICE guideline an outlier. This raises serious questions about the NICE methodology and makes it less likely the guideline will be used.	
British Menopause Society	Guideline	035	004	1.6.4 It should be made clear that lack of evidence does not mean lack of benefit. This is a continuum of risk and the data can be extrapolated from POI (Guideline page 74;16-17) and age should be taken into consideration when assessing potential adverse effects of menopause to highlight that this population is also at risk. The guideline recommendations do not reflect this. It is very unlikely that any RCTs will randomise women with early menopause to placebo given the large observational evidence of adverse effects. Indeed one such proposed study was denied ethics approval on the grounds it would be unethical to randomise women with early menopause to placebo. Recent RCTs including an ongoing multi-centre national RCT are comparing two types of hormonal preparations rather than hormones to placebo. For both topics - early menopause and POI - there is large observational evidence showing an increased risk of osteoporosis and related fractures, cardiovascular disease, cardiovascular mortality, type 2 diabetes and increase in all-cause mortality. For both topics, however, we acknowledge that there is lack of objective evidence assessing the effect of hormone replacement on these outcomes but this is unlikely to ever be realized. POI and	Thank you for your comment. The aim of the evidence review carried out was assessing the impact of HRT on people with early menopause and the development of various health outcomes. The need to assess the impact of early menopause on health outcomes has been acknowledged and has been logged with the NICE surveillance teams for prioritised consideration during future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				early menopause represent a continuum of risk that should be recognised and reflected firmly in the guideline.	
British Menopause Society	Guideline	035	010	The evaluation of the impact of HRT on women with early menopause is limited to one analysis of observational data (CGHFBC 2019 meta-analysis) pertaining to breast cancer yet the findings appear to be applied to an array of outcomes not addressed in the one included paper of evidence (all-cause mortality and developing: venous thromboembolism, cardiovascular disease, type 2 diabetes, endometrial cancer, ovarian cancer, osteoporosis, dementia and loss of muscle mass and strength). It does not appear that the impact of the variables listed here in brackets have been examined. If there was evidence that HRT use put women with early menopause at greater risk of breast cancer than their normally ovulating counterparts then there would be a basis for advice cautioning against HRT for this age group. As this evidence is lacking, and in the context of the overwhelming evidence of adverse cardiometabolic, bone and cognitive effects with early menopause, as well as the impact on quality of life, then advocating against HRT in this age group is associated with a high probability of causing harm. POI and early menopause should be regarded as a risk continuum with many of the bone, cardiovascular and dementia / Parkinson's data applying both to POI and women < 45 years of age.	Thank you for your comment. The committee agreed the appropriate comparator for this evidence review would be people in early menopause not taking HRT/placebo. People not in early menopause were outside the scope of the review protocol. The recommendation was based on evidence from the CGHFBC 2019 meta-analysis subgroup which matched the review protocol. Given that early menopause as a risk factor for health outcomes was not the topic under review, the committee reconsidered stating breast cancer risk alone in the recommendation as it would provide a skewed interpretation of the potential health risks. Therefore, the statement "Taking HRT increases the risk of breast cancer" has now been removed from the recommendation. The recommendation for this section now reads as follows: 'When discussing HRT as a treatment option, explain to people experiencing early menopause, that, for them, the benefits and risks of either taking or not taking HRT are likely to lie between those for people with premature ovarian insufficiency and those for people aged 45 or over'. The need to review evidence for the management of early menopause, including the use of HRT, has been acknowledged and will be passed onto the NICE surveillance teams for prioritised consideration during future updates. Other areas that will be flagged to the NICE surveillance team are the prevalence of early menopause, highlighting particular susceptible subgroups, and the impact

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				The "norm" for women younger than 45 is to be premenopausal. In the CGHFBC meta-analysis HRT users younger than 45 years were compared with postmenopausal women younger than 45 years not using HRT, whereas in terms of breast cancer risk, the clinically meaningful comparator would be age-matched premenopausal women. As the authors of the CGHFBC 2019 paper have previously reported, women who become postmenopausal before the age of 45 years have a 30% lower risk of breast cancer compared with women who remain premenopausal until the age of 45 years. In the 2019 paper the authors report that young postmenopausal women who use HRT have an increase in breast cancer risk compared with young postmenopausal women who are not using HRT but fail to acknowledge that for women with early menopause. In reality HRT may not even restore their breast cancer risk to what it would have been if they had not gone through an early menopause. This extremely important point should be acknowledged as menopause before the age of 45 years is associated with epigenetic ageing, a greater risk of premature death from all causes, including premature death from cardiovascular disease, as well as substantially greater risk of osteoporosis and fragility fracture in later life. Early menopause has been shown to be associated with an increased risk of CVD/ death from CVD, stroke and osteoporosis related fractures. By ignoring all these data and	of early menopause on health outcomes e.g. symptoms associated with the menopause, mental health, specific cancer (e.g. breast, ovarian, endometrial), cardiovascular disease and fragility fractures.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				focusing on a flawed analysis the recommendation is risking significant harm to a cohort of women and impact on their quality of life. Data from the Women's Health Initiative showed that women who had undergone bilateral oophorectomy before age 45 and who were also younger than 60 years at the time of random assignment had a significant reduction in all cause mortality with a cumulative oestrogen-associated HR for all-cause mortality of 0.60 (CI, 0.38 to 0.95).	
British Menopause Society	Guideline	035	010	1.6.4. People in early menopause. "Taking HRT increases the risk of breast cancer." This statement is inappropriate, too strong and not supported by the data in this age group. The way this is presented in isolation and without added context is misleading and will cause considerable confusion and alarm and in our opinion this could cause long term harm to thousands of women if they stop taking HRT as a consequence of this statement. The reality is we do not know what the risk is in this age group. This statement is based on the 2019 CGHFBC meta-analysis which reported an increase in the risk of a breast cancer diagnosis in this cohort of women if they use HRT, but the control group consists of those with an early menopause not using HRT. This was not an unexpected finding as women with an early menopause have a lower risk of breast cancer. We believe that this analysis is profoundly flawed in that the effects of MHT for women who go through early menopause must be seen in the context of what is "normal" for women of this age. There is no evidence that	Thank you for your comment. The committee agreed the appropriate comparator for this evidence review would be people in early menopause not taking HRT/placebo. People not in early menopause were outside the scope of the review protocol. The recommendation was based on evidence from the CGHFBC 2019 meta-analysis subgroup which matched the review protocol. Most of the available evidence in the literature is based on HRT formulations that were previously used and may not currently be common practice, however the committee agreed this would still be useful in the absence of other evidence. The committee have subsequently made a research recommendation focussing on the risk of progesterones more commonly prescribed, as they recognised more evidence on newer HRT formulations were required. The committee agreed it would be beneficial to provide information to people in early menopause on the impact HRT can have for health outcome specific to them. Given that early menopause as a risk factor for health outcomes was not the topic under review, highlighting breast cancer risk

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				the risk for breast cancer in women with early menopause taking HRT is increased when compared to age matched control who have normally functioning ovaries and are not taking HRT. Currently there is international agreement from all major international menopause societies (including the BMS) that years of HRT exposure is counted from the age of 50. This assumes that add-back HRT will delay the effect of the menopause on breast cancer risk and was indirectly supported by the 1997 CGHFBC re-analysis, which reported: a) Postmenopausal women have a lower risk of breast cancer than premenopausal women of the same age and parity and b) The increased risk of breast cancer diagnosis per year with current/recent MHT exposure (2.3%) is like that associated with each year the menopause is delayed (2.8%). The new draft recommendation should not refute this as no analysis was undertaken using a control group of normally cycling women to compare with those taking MHT who had an early menopause (Supporting information 19). We would recommend adjusting the statement to say "may increase the risk of breast cancer compared to women with early menopause not taking HRT" which more accurately reflects the data. We also note that the CGHFBC paper which was used as primary data to inform the advice does not inform us of the impact of current	alone would provide a skewed interpretation of the potential health risks. Therefore, the statement "Taking HRT increases the risk of breast cancer" has now been removed from the recommendation. The recommendation for this section now reads as follows: 'When discussing HRT as a treatment option, explain to people experiencing early menopause, that, for them, the benefits and risks of either taking or not taking HRT are likely to lie between those for people with premature ovarian insufficiency and those for people aged 45 or over'. NICE has followed its standard methods and processes in developing the 2024 guideline update, including the way in which conflicts of interest in topic experts and committee members are managed. The details of declarations of interest and how they have been managed are available in the published register of interests.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				recommended HRT prescribing practices on breast cancer risk for women at any age. The median year of diagnosis of breast cancer cases from North America (25% of the included data) was 1999, and for the European studies, 2007, with one as early as 1981. With an average use of 10 years of HRT in current users at diagnosis, and 7 years in past users, much of the exposure to HRT preceded the first publication of the Women's Health Initiative study, after which prescribing practices changed substantially. Consequently, virtually all of the included information pertains to HRT formulations and doses known to have adverse breast effects that are no longer recommended or used. This needs to be acknowledged. Yet again we note that one of the authors of the CGHFBC 2019 paper was present on the committee and participated in the discussions. We therefore have to question the impartiality in the interpretation of these data and the undue weight they have been given.	
British Menopause Society	Guideline	037	008	Genito-urinary symptoms of the menopause – as per previous comments. If this term is going to be used, its meaning and the validation for its use (which is not in the mainstream literature) should be explained in the *Terms used in this guideline* section.	Thank you for your comment. A definition of the relevant symptoms has been added.
British Menopause Society	Guideline	038	005	Systemic HRT: This paragraph should be at the beginning of the section, not after continuous combined and sequential.	Thank you for your comment. The 'Terms used in this guideline' section is in alphabetical order.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Menopause Society	Guideline	041	010	We would welcome a recommendation for further research into the potential non-sexual health benefits of Testosterone.	Thank for your comment. The surveillance and scoping process for the 2024 guideline update did not identify substantive new evidence likely to change the existing recommendations on testosterone. Therefore, reviewing evidence on testosterone in relation to menopause care was not prioritised. However, NICE discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and they prioritised funding for urgent research in this area.
British Menopause Society	Guideline	041	021	Consider changing IUS to IUD to keep with the recent terminology update	Thank you for your comment. This is referring to a research recommendation that remains active from the 2015 guideline. Currently the NHS uses both IUS and IUD on their website. IUS was also considered by the committee to be still commonly and interchangeably used. They therefore decided not to change this.
British Menopause Society	Guideline	046	002 - 016	As per comments on recommendation 1.4.13 we would like to see a stronger statement in support of the use of transdermal HRT in this context.	Thank you for your comment. This particular recommendation is related to people with a history of coronary heart disease and stroke. The committee agreed that decisions about HRT in this context are complex, depending on individual risk levels and that therefore advice needs to be tailored to each individual. They agreed that this could best be achieved by a healthcare professional with expertise in menopause. Transdermal was not mentioned in this section because tailoring to the individual may not result in an offer for HRT depending on personal risk factors. If it was recommended for all then the risks featuring in table 1 and 2 would apply that highlight transdermal as the preferred option related to risk of stroke.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Menopause Society	Guideline	048	013	"The committee acknowledged that there may be other options to manage difficulties with sleep associated with the menopause" There is no mention of HRT. HRT should also be considered if sleep problems occur in conjunction with other menopausal symptoms	Thank you for your comment. Apart from CBT other management options for sleep problems associated with the menopause were not in the scope of the 2024 guideline update. However, the committee acknowledged that there are other options that may be used (including HRT). They have therefore reworded the recommendation to reflect this. It now states that CBT could be used as an option (1) in addition to other treatments (including HRT), or (2) for people for whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. Given the constraints of the scope they could not be more specific than this.
British Menopause Society	Guideline	049	014	"Currently, the usual treatment for vasomotor symptoms associated with the menopause is HRT" This is a gross oversimplification of current practice. Currently many women do not have specific treatment, use over the counter remedies or are recommended lifestyle measure as per the guidance of many professional bodies, including the BMS. Only a proportion of women have access to treatment and CBT is already offered as an option to be considered as per BMS guidelines. We welcome the greater emphasis on CBT being offered but the emphasis on it should be in line with the quality of the data supporting it and recognising the other options such as hypnosis. It should also state that HRT remains the most proven effective therapy for those that need it. Whilst the call for greater access to CBT is welcome the infrastructure is not there to support it. This should be recognised as the	Thank you for your comment. The statement has been reworded to indicate that it is currently the recommended treatment for vasomotor symptoms because this is still the case in the guideline. The committee reflected on the wording of the recommendations related to CBT and updated it to make it explicit that this was not recommended as a first line treatment. It is now stated that it is an option (1) in addition to other treatments (including HRT) (2) for people in whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. It is NICE style to use the wording 'consider' indicating a recommendation where there is some uncertainty about the evidence. The rationale then describes the uncertainties and why the committee, on balance, concluded that CBT could be an option. Taking into account current pressures on services, your comment will be considered by NICE where relevant support activity is being planned. Hypnosis was not part of

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				guideline will potentially be a powerful tool for change.	the scope of this update but because of this comment and cited references in other comments this has been logged with the NICE surveillance team so that it may be considered in future updates.
British Menopause Society	Guideline	051	009	"The committee also decided that it was important to discuss with the person that, with vaginal oestrogen, some oestrogen is absorbed into the bloodstream, but generally much less than with systemic HRT " This statement again implies there is significant absorption yet the guideline goes on to say "there is no need to combine low-dose vaginal oestrogens with systemic progestogen treatment to protect the person against endometrial hyperplasia and cancer ". This is correct so the initial statement should be much clearer that any absorption is minimal, not "generally much less". The appropriate use of wording is crucial in making sure the guideline does not give mixed messages.	Thank you for your comment. This bullet point was reworded to say that absorption is minimal and not clinically significant. It is then described in the rationale section that 'the committee agreed to highlight this because it means that there is no need to combine low-dose vaginal oestrogens with systemic progestogen treatment to protect the person against endometrial hyperplasia and cancer'.
British Menopause Society	Guideline	051	017	"The committee also highlighted, based on experience, that vaginal bleeding can occur when vaginal oestrogen is started." Where is the evidence for this? If it's common then why encourage them to "see the GP so that other causes for the bleeding can be ruled out". This makes no clinical sense. Far better to reiterate than vaginal bleeding per se in postmenopausal patients should be looked into, not just with vaginal oestrogens.	Thank you for your comment. On reflection, the committee decided to remove this statement in the context of vaginal oestrogen.
British Menopause Society	Guideline	051	029	"The committee was aware that overactive bladder can co-occur with genitourinary menopause symptoms". This is not correct use of terminology. Overactive bladder is a	Thank you for your comment. This was revised accordingly.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				condition. It should state that the "symptoms of overactive bladder " can co-occur with genito-urinary symptoms.	
British Menopause Society	Guideline	052	029	"For example, people with physical or intellectual disabilities may find it difficult to use vaginal oestrogens". This is an oversimplification. There are many women who choose not to use vaginal preparations, e.g. for cultural reasons or discomfort, and these women should have the option of using an effective oral therapy. We would favour the wording saying "when oral therapy is preferred" rather than restrict it to "in specific circumstances".	Thank you for your comment. The committee considered the comment but thought the clinical and cost effectiveness evidence was not strong enough to make this available to all women who prefer this as an option.
British Menopause Society	Guideline	053	012	The committee acknowledged the evidence was sparse. Whilst we recognise that the recent large UK meta-analysis was published after the discussion date, the results are so pertinent to this discussion that we feel it should be acknowledged here. McVicker L et al JAMA Oncol 2023. doi:10.1001/jamaoncol.2023.4508)	Thank you for your comment. The cited UK meta-analysis includes women with a current diagnosis of breast cancer and excluded women with a previous diagnosis of any cancer. Therefore, this study does not fit the inclusion criteria for the review that your comment refers to - see the review protocol in appendix A of evidence review B2 genitourinary symptoms and breast cancer recurrence, as the review is focused on the risk of breast cancer recurrence in those with a personal history of breast cancer (or otherwise high risk).
British Menopause Society	Guideline	054	021 - 022	"increasing the risk of breast cancer recurrence would be worse than treating menopausal symptoms slightly less effectively." This point is confusing: what is meant by treating symptoms slightly less effectively? In the previous lines it has already been stated (correctly) that vaginal oestrogens should only be used when symptoms continue to negatively impact on quality of life. Vaginal oestrogens are effective so why say "slightly less effectively". This	Thank you for your comment. To address this, the bullet point has been revised and is now referring to 'any potential increased risk of breast cancer' and the word 'slightly' has been removed.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				implies they don't make much difference which is contrary to the evidence and clinical experience. This negatively framed terminology undermines the important point being made, that there is a potential risk of a recurrence that we cannot be sure about. Equally the symptoms can be debilitating and the patient should be given the correct information about pros and cons to decide for herself.	
British Menopause Society	Guideline	055	003	"Genitourinary symptoms vary depending on hormone receptor status and type of adjuvant treatment." Consider re-phrasing. Adjuvant therapy may have an effect on the symptoms but not the receptor status itself. There is no evidence that women with ER +ve disease have any better or worse symptoms than women with ER-ve. It's the effect of the adjuvant therapy.	Thank you for your comment. The committee agreed with this and 'depending on hormone receptor status' was removed from this bullet.
British Menopause Society	Guideline	058	014	It should be acknowledged that there are clinical situations where progestogen is indicated after a hysterectomy such as sub-total hysterectomy, previous severe endometriosis etc.	Thank you for your comment. The committee discussed that choice between oestrogen-only and combined HRT may be different for people with a sub-total hysterectomy. They decided that they could not be prescriptive about the type of HRT to be used for people who have had a sub-total hysterectomy because their condition is clinically complex and they had not reviewed evidence about the effect of HRT on risk of endometrial cancer for this group. They acknowledged that people who were going to have, or had had, a sub-total hysterectomy would be under the care of a specialist who could discuss HRT options tailored to their needs (or a relevant specialist within the MDT). Due to a lack of evidence, no specific recommendation was

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					made for sub-total hysterectomy; however, the term "total" was added before "hysterectomy" in guidance regarding the offer of oestrogen-only HRT to those who have had a hysterectomy. This addition alerts healthcare professionals to consider other factors for patients with a sub-total hysterectomy. The committee also noted that some people have a hysterectomy for a condition that may be affected by HRT, such as endometriosis. The committee did not review evidence related to such conditions. They recognised that the decision about the type of HRT that best balances benefits and risks for the person may be affected by that condition (for example endometriosis) or having had a subtotal hysterectomy. For this reason, they added a recommendation highlighting that advice from a healthcare professional with specialist knowledge of that condition may be needed when making this choice. Due to this stakeholder comment and other related comments, this topic has been logged with NICE surveillance so that it can be considered for a possible update to either the Menopause or the Endometriosis guideline in future.
British Menopause Society	Guideline	058	016	The term "smallest effective dosage" needs further explanation. In our opinion it should state "the appropriate individualised dosage" which balances full effectiveness for individual treatment goals with the risk of possible	Thank you for your comment. The committee recommended the lowest effective dosage which would be reviewed in 3 months to assess efficacy and tolerability and annually thereafter (as highlighted in a different recommendation on

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				adverse effects. This is an individualised decision. We would also welcome a comment to say that initial prescribing should be within the licensed dosages. We feel that careful wording is need here as on the one hand there is a tendency amongst some practitioners to be reluctant to prescribe an effective dose and on the other hand there are some who are advocating and prescribing doses of HRT well above the recommended doses from the outset. In the same paragraph the term smallest effective dose (line 15) and lowest effective dose (line 18) are used. There needs to be standardisation of terminology. We would favour lowest.	reviewing treatments). The suggested wording of 'appropriate individualised dosage' would be difficult to use because it would require a lot of additional explanation of what it would entail with the same outcome that it would be reviewed and potentially adjusted if necessary. All dosages would be within licensed ranges and a statement has now been added to emphasise this.
British Menopause Society	Guideline	058	022 - 025	Stopping HRT. The phrase "that HRT could potentially lead to cancer progression or risk of recurrence" is misplaced here. We agree this is relevant after a diagnosis of breast cancer but this sentence is part of the general topic of stopping HRT and doesn't refer to breast cancer specifically. It should be moved to later in the section. Some general advice about stopping HRT should precede the issue about stopping after a diagnosis of breast cancer.	Thank you for your comment. This has been rephrased to clarify that a history of breast cancer is a contraindication to HRT.
British Menopause Society	Guideline	060	016	"Evidence showed that there was no overall effect on life expectancy" If this is the committee's conclusion why then does this not feature more prominently in the recommendations and guideline? It should be a prominent message in the recommendations as it offsets some of the very negative messaging in the draft guideline.	Thank you for your comment. This was already part of the first recommendation in this section to give it prominence. However, this has now also been added to tables 1 and 2 to emphasise this point in the context of other health outcomes.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Menopause Society	Guideline	060	022	Why is there no clear mention of benefits to give balance here? This would normally be included in the discussion and the guideline elsewhere emphasises the importance of discussing benefits and risks together.	Thank you for your comment. This has been revised accordingly.
British Menopause Society	Guideline	061	002 - 005	"Most of the evidence was from a meta-analysis of individual patient data from observational studies, but there was also evidence from randomised controlled trials (RCTs)." There is no rational explanation as to why the observational meta-analyses data was given more prominence than the large RCT. The recommendations on breast cancer almost totally overlook the large RCT evidence for HRT and breast cancer and rely heavily on a large meta-analysis of previous published research. Much of the evidence reviewed has not changed in any major way in direction or conclusions compared to that reviewed within NG23. Some of the figures may have changed slightly based on the new analysis but not in any significant way, yet the approach to reviewing the evidence appears to be very different and based almost entirely on the observational evidence instead of the totality of the evidence (both observational and RCT). The Lancet meta-analysis had 40% of its entire sample size from the Million Women Study, an observational study with significant methodological limitations and very high loss to follow up that have been highlighted in many peer reviewed published commentaries and reviews. Whilst the meta-analysis would have	Thank you for your comment. In accordance with NICE methodology for reasons of transparency and reproducibility, studies are included and excluded from reviews on the basis of criteria set out in a pre-specified protocol agreed with the committee before a review has been started. When evidence has met the review protocol criteria it is included in the review and the committee consider this evidence when making recommendations. Agreed protocols are also published on the PROSPERO website before the analysis of data commences). The committee discuss the evidence available in the review and use this evidence to support their recommendations. The committee must take into account the quality of the evidence, as well as the applicability to current practice when considering how best to make recommendations that are supported by the evidence. Randomised controlled trials are often considered to be the gold standard in terms of study design, however the clinical question will determine which study design is the most appropriate. Factors such as sample size, follow-up periods, and incidence of the outcome of interest in the population, may mean that observational studies provide information that RCT studies cannot. The committee discussed and considered the pros and cons of all study designs that were included in each review. As the pros and cons differ

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				included very detailed and robust analyses, this does not take away the significant limitations in the methodology of the study/studies included. Again we note that one of the authors of this study was on the guideline committee and present for these discussions.	depending on the outcome of interest, the discussions are different across reviews and outcomes, and reasons for using some evidence over others will be specific to the review. The committee used the evidence from both RCT and observational data when making recommendations on the risk of breast cancer following HRT use. Since the evidence from RCT and observational studies were consistent for the comparison of combined HRT versus either no HRT or placebo, the recommendations made were supported by both data. However, for the comparison oestrogen-only HRT versus either no HRT or placebo, the RCT and observational data were inconsistent. To make a recommendation the committee discussed the specific characteristics of the different data and used the data they agreed was most relevant to the target population. The full details are discussed in the committee discussion of the evidence report section of evidence report D. The committee have since reconsidered the wording of the recommendations and have agreed that the data from both RCT and observational studies should be represented in the wording of the recommendations relevant to oestrogen-only HRT use, and the recommendation now reads 'there is little or no increase in the risk of breast cancer..' The committee discussion of the evidence section in evidence report D has also been updated to reflect the further discussion that took place. The evidence reviewed within NG23 has not changed in that no new RCT data have been published since the publication of NG23, however

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					the publication of the IPD data (referenced as CGHFB 2019 in evidence review D) warranted a review of the evidence. The approach to reviewing is in line with the NICE methodology, and the interpretation of the evidence is based on committee discussion. One of the reasons the 2015 guideline required updating was that the Lancet analysis was a contributing factor for the pharmacovigilance risk assessments by the MHRA and the EMA, concerning the impact of HRT on the risk of breast cancer. NICE is required to follow regulatory guidance from MHRA in its guidance and as such the additional information on breast cancer does change the balance of risks and benefits from that in the original 2015 guideline. With regard to the inclusion of the Million Women Study in the Lancet meta-analysis by the collaborative group in hormonal factors of the breast (CGHFB), it is correct that this study was a major contributor to the Lancet meta-analysis. However, there was consistency in the main findings across the numerous studies therefore any analysis excluding the Million Women Study would not have materially altered the conclusions. There are indeed limitations with any observational studies, and these have been considered in the evidence reviews, and by the committee in discussions and interpretation of the evidence for recommendations. However, the committee agree that the Lancet meta-analysis by CGHFB is a valuable source of evidence and can inform recommendations. With regard to the presence of one of the authors of the Lancet

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					meta-analysis on the committee and at the discussions of the evidence, please be assured that we have followed NICE policy and process concerning the inclusion of committee members with special interest in topic areas. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
British Menopause Society	Guideline	062	005	"The committee noted that the RCT evidence was consistent with the observational data" This is not a correct interpretation of the data. The RCT evidence did **not** report an increase risk of breast cancer with less than one year of HRT use. That finding of the MWS is implausible and highlights one of the many significant limitations of the observational evidence. These limitations should be acknowledged. We also wish to highlight that one of the limitations of the MWS was that there was a significantly higher incidence of	Thank you for your comment. The statement refers to an overall increase in the risk of breast cancer following combined HRT use and does not specify that the data was consistent at less than one year of use. The committee discussed that the direction of effect from both the observational and RCT evidence was the same. This is discussed in more detail in the committee's discussion of the evidence section in Evidence Review D. The MWS, due to its sample size is a large contributor to the Lancet 2019 meta-analysis (references CGHFBC 2019 in Evidence

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				breast cancer in the HRT group at 4 months from the start of the study which is likely to explain the increase noted with less than one year of use. This is biologically implausible and highlights how concerned we are as to the additional weight this study has been given. Again we note that one of the authors of this study was on the guideline committee and present for these discussions.	Review D). The committee discussed that all observational studies are subject to bias. They discussed that randomised controlled trials are considered to be the gold standard in terms of study design, but that observational studies could provide useful information. As is the case for the observational studies in Evidence Review D, the observational data provides a larger sample size which increases the power to detect rare outcomes such as breast cancer, and also more information on different durations of use with long follow-up periods. NICE has followed its standard methods and processes in developing the 2024 guideline update, including the way in which we manage conflicts of interest in topic experts and committee members. The details of conflicts of interest and how they have been managed are available in the published register of interests. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. All sections that previously stated that RCT evidence is consistent with observational data have been revised to include a

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					separate section on the findings from RCTs to clarify explicitly what the findings of each study type were.
British Menopause Society	Guideline	062	008	The breast cancer mortality recommendations appears to be entirely based on a single, one page research letter with 4 authors from the MWS group that has not been published as a full manuscript and published separately from the Lancet meta-analysis. This was not authored by the collaborative group who published the meta-analysis. The letter included very limited detail. It appears that this entire important recommendation has been based on this letter and overlooked the WHI RCT findings on the topic particularly with oestrogen only intake or to acknowledge the limitations of this recommendation being based on a research letter that included very little detail. We would like to know the decision making in including a non-peer reviewed research letter as admissible evidence strong enough to make a recommendation about mortality, yet other studies and RCT data is given less weight. It is noted again that one of the authors of this letter is on the guideline committee. There are a number of aspects of breast cancer risk with HRT that the guideline has not addressed which is rather concerning. The primary focus has been on the collaborative group on hormonal factors in breast meta-analysis of prospective cohort studies, and the published correspondence related to follow up data from the Million Women Study, referring	Thank you of your comment. The inclusion of the MWS research letter was deemed appropriate since the MWS has previously published work describing the cohort and methodology, which fits our pre-specified protocol. The research letter also describes the analysis was adjusted. Given the critical nature of mortality from breast cancer, information from such a source was deemed important and underwent quality assessment using GRADE methodology. The team has however taken into consideration that the publication was not a full publication in the critical appraisal of the letter. The committee considered a number of things when discussing the use of the letter to support their recommendation. They discussed the difference in sample size between the observational and RCT evidence for mortality, and they also discussed that an increase in mortality was in line with the evidence relating to an increased incidence of breast cancer. The committee's discussion of the evidence section in Evidence Review D has been updated to provide more detail on the discussion the committee had on mortality. NICE has followed its standard methods and processes in developing the 2024 guideline update, including the way in which we manage conflicts of interest in topic experts and committee members. The details of conflicts of interest and how they have been managed are available in the published register of interests. The results from the WHI study (Chlebowski 2020) were and are included in Evidence Review

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				to breast cancer mortality. However there is RCT evidence from the WHI that there is a reduction in risk of breast cancer incidence and mortality with conjugated estrogens alone. Chlebowski RT, Anderson GL, Aragaki AK et al Association of Menopausal Hormone Therapy With Breast Cancer Incidence and Mortality During Long-term Follow-up of the Women's Health Initiative Randomized Clinical Trials. JAMA. 2020 Jul 28;324(4):369-380. One of the arguments used for not including the RCT data was that the characteristics of the RCT population e.g. on obesity differed from the observational data yet the impact of HRT is less in women who are overweight than in lean women. This is an important observation from MWS itself as the incidence of obesity in the UK has increased since the participants in MWS were recruited, making the figures from this study less valuable. In fact, it makes the findings from WHI more relevant as the incidence of obesity in the US in 1980 is similar to the UK in 2020! This fact is not acknowledged anywhere in the Guideline. It could equally be argued that it is not possible to control for all variables in an observed population e.g. data from the Million Women Study were derived from a breast screened population that may have been at higher risk of breast cancer because of where the population was recruited. This just highlights the uncertainty of the data and the mistake of making such specific and dogmatic recommendations about risk and mortality.	D for breast cancer incidence and mortality and now has also been included in the same forest plot. The hazard ratio from Chlebowski for those on combined HRT in this publication is HR = 1.35 [0.94 to 1.95], whilst not statistically significant, is in the direction of increased risk and in line with the findings from the observational study. The committee noted that the findings for oestrogen-only HRT from RCT and observational studies go into the opposite direction. The decision to consider the different population groups between the studies were specific to this outcome since the committee tried to find an explanation for the findings. The committee reconsidered the wording of the recommendation and have since updated the wording to describe the direction of evidence from both the RCT and observational studies and uncertainties associated where results differ. As a result, the committee discussion of the evidence section in Evidence Review D has been updated to provide details of the discussion that took place. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). This review agree that the Beral letter is a linked report to a study that is already included, and so is appropriate to include, in the same way that it is appropriate to contact study authors for supplementary information. They suggested to add further details about this (such as it not being peer reviewed) in the GRADE quality assessment

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				These will cause unnecessary fear and confusion.	and main body of the text which has since been implemented. They also highlighted that in the consultation version 'there is a strong focus in places on statistical significance, and conflating this with clinical significance, which can suggest that RCT and observational evidence conflicts when in fact effects are in the same direction, but one achieves statistical significance and the other does not' and reflected on the Chlebowski hazard ratio in this context.
British Menopause Society	Guideline	062	011	"They decided that people should be aware of these risks so that they can make an informed choice." This seems like a major weakness in the NICE methodology which seems to have been 'dumbed down' from a much stricter methodology in the previous guidance. There is no discussion about the weight of evidence here.	Thank you for your comment. The rationale sections relate to individual risks and the evidence related to them. If 'weight of the evidence' refers to the relationship between these different risks, then this would be an individual shared decision between the healthcare professional and the person weighing up the different risks depending on their own background risk. The absolute numbers in the appendix were reviewed and used to produce a discussion aid document with visualisation of the data and verbal description aimed to facilitate shared decision making. This discussion aid has undergone user-testing and was refined based on user feedback.
British Menopause Society	Guideline	062	013	The committee noted that the evidence showed that there was a smaller increase associated with taking transdermal oestrogen rather than oral oestradiol" Brusselers et al 2018 showed no overall difference between transdermal and oral. A similar effect was also noted in the Lancet meta analysis and other registry reports. If this conclusion applies to combined it should apply	Thank you for your comment. The committee considered the evidence for oral and transdermal routes of administration of the oestrogen component of HRT. Since some of the evidence showed a significant difference between the subgroups of oral and transdermal routes of administration in the combined HRT comparison, they had made a recommendation to inform people that the increase was smaller with transdermal than oral. This now also includes a

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				to oestrogen only. We suggest the data are too inconclusive to be able to make this statement.	study by Vinogradova (2020) which include data on transdermal versus oral HRT but did not provide greater clarity on this matter. The committee considered this and the Brusseler 2018 evidence and discussed that since the same difference was not observed in the oestrogen-only comparison, the argument was less robust than previously discussed. Upon reflection the committee agreed to remove this recommendation and the rationale section revised accordingly as well and a detailed discussion of the evidence and their decision was updated and can be found in the committee discussion of the evidence section of Evidence Review D. The committee also decided that more evidence is needed to clarify this and prioritised this for a research recommendation.
British Menopause Society	Guideline	062	028	"For current users of oestrogen-only HRT the risk of breast cancer was higher in those who had been taking HRT for at least 1 year" As discussed above this is implausible and different to the breast cancer findings reported in the WHI RCT 50-79 (where also no difference was noted in the risk of breast cancer between 50-59 / 60-69 / 70-79 groups). This is a major flaw in the Lancet meta-analysis and highlights why it is scientifically wrong to give this paper so much prominence. Given that the data are so unconvincing it is inappropriate and dangerous to make such a dogmatic statement.	Thank you for your comment. The analysis of HRT and breast cancer risk in the Million Women Study (which is included in this analysis) excluded all women with any record of breast cancer prior to recruitment. Obviously there will be some participants with undiagnosed/pre-clinical breast cancer at the start of follow-up but this is likely to be true of all observational studies (and probably some trials). Whilst it may have been the case that cancers diagnosed very soon after recruitment were present to some degree at recruitment, this does not invalidate the comparisons between HRT users and non-users in terms of subsequent breast cancer risk. All women who entered the study reported on HRT use prior to coming for screening (and hence before they had any knowledge of any abnormalities) and all women who were recruited

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					had a routine screen at entry and so would have had the same opportunity of getting any pre-existing disease diagnosed. Thus, the observation of an increased risk of breast cancer in HRT users– even in a relatively short period after recruitment– should be robust and is likely to reflect an association between HRT and increased risk.
British Menopause Society	Guideline	063	007	"The committee agreed that it is important that people are aware of these facts so that they can make an informed decision." This heavy and alarmist tone is not used with other recommendations. Given this "finding" was different to the RCT findings and had previously been acknowledged in NG23, such wording comes across as too negative. The language, if applied, should apply to all areas of the evidence assessed and not only to breast cancer.	Thank you for your comment. The conclusion and wording in this section has been reviewed and revised to highlight greater uncertainty because of the differences between results from different study types. The sentence referred to was removed.
British Menopause Society	Guideline	063	012	"The committee noted that the population of the RCT studies differed from that of the observational studies in that the average age at starting HRT use was higher in the RCT (63 years, with an age 14 range of 50 to 79 years old) than in the observational studies (50 years)" The WHI RCT included 50-79 and reported no difference in breast cancer risk between 50-59 / 60-69 / 70-79 groups. It is not clear why the Vinogradova paper was overlooked. This reports on 98,611 women aged 50-79 with a primary diagnosis of breast cancer between 1998 and 2018, matched by age, general practice, and index date to 457	Thank you for your comment. The committee considered the evidence from both RCT and observational data. The RCT data, which included the Women's Health Initiative (WHI), and observational data were consistent for the comparison combined oestrogen and progesterone versus no HRT or placebo, and both showed an increased risk in breast cancer. The committee discussed that the RCT evidence from the WHI showed conflicting results to the observational studies, for the comparison of oestrogen-only HRT versus placebo or no HRT. The decision to consider the different population groups between the studies were specific to this outcome since the committee tried to find an explanation for the inconsistent findings. The

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				498 female controls. The importance of this work is that it addresses the contemporary use of HRT as opposed to the Collaborative Group on Hormonal Factors in Breast 2019 paper which primarily pertains to doses and formulations no longer prescribed today. Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of breast cancer: nested case-control studies using the QResearch and CPRD databases. BMJ 2020; **371**: m3873	committee reconsidered the wording of the recommendation and have since updated the wording to describe the direction of evidence from both the RCT and observational studies. As a result, the committee discussion of the evidence section in Evidence Review D has been updated to provide details of the discussion that took place. The Vinogradova 2020 study does meet the criteria for inclusion in this review. Note that some of the cohort in this publication (from the CPRD database) was already included in the review, therefore only data from the QResearch cohort have been included. The relevant sections of the review were updated with data from the study that fits our protocol. Subgroup analyses, where available, were included addressing the risk of breast cancer in the different oestrogenic constituents and progestogenic constituents where newer formulations showing an increase in risk of breast cancer in line with other constituents. The committee have seen the available data and have made recommendations based on this data. In particular, the committee discussed that there are progestogenic constituents that are more commonly used in practice today, however agreed there was insufficient evidence to make a recommendation. The committee agreed that more evidence was required to make any robust recommendations for micronised progesterone and made a research recommendation.
British Menopause Society	Guideline	063	024	"The committee decided that they would put more weight on the observational evidence to support their recommendations, as this was more reflective of the target population"	Thank you for your comment. In accordance with NICE methodology for reasons of transparency and reproducibility, studies are included and excluded from reviews on the basis of criteria set

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Such an admission is concerning and goes against the very ethos of what NICE stands for. It has resulted in a very large well controlled randomised study findings being overlooked in favour of observational data with well known methodological flaws. The totality of the evidence should be reflected in the recommendations as was done in NG23. Given that there is conflicting observational and RCT data statements such as this demonstrate a potential bias within the committee." We note that one of the authors of the observational data was on the guideline committee.	out in a pre-specified protocol agreed with the committee before a review has been started. When evidence has met the review protocol criteria it is included in the review and the committee consider this evidence when making recommendations. Agreed protocols are also published on the PROSPERO website before the analysis of data commences). The committee discuss the evidence available in the review and use this evidence to support their recommendations. The committee considered the evidence from both RCT and observational data. The RCT data, which included the Women's Health Initiative (WHI), and observational data were consistent for the comparison combined oestrogen and progesterone versus no HRT or placebo, and both showed an increased risk in breast cancer. The committee discussed that the RCT evidence from the WHI showed conflicting results to the observational studies, for the comparison of oestrogen-only HRT versus placebo or no HRT. The decision to consider the different population groups between the studies were specific to this outcome since the committee tried to find an explanation for the inconsistent findings. The committee discussed that all observational studies are subject to bias. They discussed that randomised controlled trials are considered to be the gold standard in terms of study design, but that observational studies also provide useful information. As is the case for the observational studies in Evidence Review D, the observational data provides a larger sample size which increases the power to detect rare outcomes such as breast cancer, and also more

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					information on different durations of use with long follow-up periods. The committee reconsidered the wording of the recommendation and have since updated the wording to describe the direction of evidence from both the RCT and observational studies. As a result, the committee discussion of the evidence section in Evidence Review D has been updated to provide details of the discussion that took place. NICE has followed its standard methods and processes in developing the 2024 guideline update, including the way in which we manage conflicts of interest in topic experts and committee members. The details of conflicts of interest and how they have been managed are available in the published register of interests. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Menopause Society	Guideline	063	029	"transdermal or oral routes of administration." This contradicts the earlier reference to a lower risk for transdermal. Transdermal with combined is often referring to the route of oestradiol administration and it is likely to be a similar effect with transdermal and oral for both groups from a plausibility point of view. Transdermal oestrogen is often given with oral progestogens and therefore if there is an effect related to transdermal intake you would expect to see it with both (oestrogen and combined HRT). We suggest making no distinction between oral and transdermal as the evidence is inconsistent and preferencing one over the other will cause unnecessary alarm and a change in prescribing habits.	Thank you for your comment. The committee considered the evidence for oral and transdermal routes of administration of the oestrogen component of HRT. Since some of the evidence showed a significant difference between the subgroups of oral and transdermal routes of administration in the combined HRT comparison, they had made a recommendation to inform people that the increase was smaller with transdermal than oral. This now also includes a study by Vinogradova (2020) which include data on transdermal versus oral HRT but did not provide greater clarity on this matter. The committee considered this and the Brusseler 2018 evidence and discussed that since the same difference was not observed in the oestrogen-only comparison, the argument was less robust than previously discussed. Upon reflection the committee agreed to remove this recommendation and the rationale section revised accordingly as well and a detailed discussion of the evidence and their decision was updated and can be found in the committee discussion of the evidence section of Evidence Review D. The committee also decided that more evidence is needed to clarify this and prioritised this for a research recommendation.
British Menopause Society	Guideline	064	004	The advice is not informed by new data but relies on reinterpretation of the data that informed NICE 2015 (the 2020 WHI paper does not provide evidence that departs from the 2013 analyses). What is different is the interpretation of the data that seems to reflect a different lens of looking at the data rather than new data itself. NICE guidelines should	Thank you for your comment. The approach taken by the 2015 guideline was different to the 2024 criteria because all evidence was split by whether combined or oestrogen-only HRT was used. In NICE methodology all evidence meeting criteria of a pre-specified review protocol is systematically reviews. These protocols are agreed with the committee and quality assured

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				reflect the totality of the data not committee opinion on how best to interpret the data.	internally before searches begin to avoid bias (see supplement 1 - methods). This evidence is then discussed with the committee. However, the conclusion and wording in this section has been reviewed and revised to reflect the uncertainty because of the differences between results from different study types (between RCT and observational studies).
British Menopause Society	Guideline	064	013	"The committee discussed the evidence from randomised controlled trials (RCTs) and 13 observational studies. They noted that the evidence from RCTs was uncertain" This does not acknowledge that the WHI reported on the risk of endometrial cancer with continuous combined HRT in a very large sample size and reported long term follow up data. Why is that not included here? The data around endometrial cancer have been so clear for many years that it has not been feasible to do a placebo controlled randomised trial on this subject for decades. These statements rather overlook this.	Thank you for your comment. The recommendation has been revised to refer to a decrease in endometrial cancer with continuous combined HRT and the wording of the rationale has been revised to describe the findings from the WHI RCT.
British Menopause Society	Guideline	065	005	The guideline could give some direction here and advise switching from sequential HRT after 5 years or as soon as practical. In reality most women tend not to stay on sequential very long as they don't want bleeding.	Thank you for your comment. The committee reflected on the wording related to continuous combined HRT and agreed to change it from 'does not increase' to 'decreases' the risk of endometrial cancer to make this message stronger and clearer. This may mean that people would potentially choose continuous from the outset given that there is a potential for a 'slight increase' in endometrial cancer risk with sequential combined HRT. The committee did not want to be prescriptive about how and when to switch from one to another.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Menopause Society	Guideline	066	011	The evidence for the potential risk of ovarian cancer is derived from the observational meta-analysis and does not consider the long term WHI RCT long term follow up data. The WHI RCT showed no difference in the risk of ovarian cancer with HRT. This does not appear to have been considered in the recommendations or mentioned in the discussion. The figures presented in the Tables (page 92) and in figures 2,13,16,19 and 21 do not support an ongoing increase as referred to in the recommendations. Why did the committee consider the RCT data (no increased risk) and the observational data (very small increased risk at 10 years) and then conclude that HRT increases the risk of ovarian cancer at all? The most that can be said is that there is uncertainty about whether long term use may increase the risk. We are concerned about a potential conflict of interest in this section. A co-author on the observational meta analysis on which these ovarian cancer recommendations were based, was on the guideline committee and does not appear to have been excluded from the discussion. We would like a transparent explanation as to why the committee decided to overlook the WHI RCT ovarian cancer data and base their recommendations entirely on the observational meta analysis of which this member was an author.	Thank you for your comment. There was data from 1 RCT that showed more people diagnosed with ovarian cancer in the combined HRT group than in the placebo group at approximately 6-year follow-up. However, the difference did not reach statistical significance because the number of diagnosed cases in both arms was very small (overall 32 people with a diagnosis of ovarian cancer). This made the finding less robust because of lack of statistical power. The observational studies have both sufficient numbers overall as well as numbers of people diagnosed with ovarian cancer (there were 2273 people with diagnosed with ovarian cancer in one study alone). The observational studies showed an increased risk of ovarian cancer with combined HRT. The committee agreed that, although the risk was increased overall, the risk was small in absolute terms, especially with the low baseline risk of ovarian cancer. In relation to the duration of use in combined HRT, the subgroup analysis by duration of use was not significant and this was therefore removed from the recommendation. The rationale section of the guideline as well as the committee discussion of the evidence review subsection of evidence review F have been updated with the RCT findings accordingly. For oestrogen-only HRT only observational studies were identified. Subgroup analysis for the impact of oestrogen-only HRT on ovarian cancer in relation to duration of use was statistically significant and therefore the reference to duration of use was retained. NICE has followed its standard methods and processes in developing the 2024 guideline

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Collaborative Group On Epidemiological Studies Of Ovarian Cancer; Beral V, Gaitskell K, Hermon C, Moser K, Reeves G, Peto R. Menopausal hormone use and ovarian cancer risk: individual participant meta-analysis of 52 epidemiological studies. Lancet. 2015 May 9;385(9980):1835-42. doi: 10.1016/S0140-6736(14)61687-1. Epub 2015 Feb 13. PMID: 25684585; PMCID: PMC4427760.	update, including the way in which we manage conflicts of interest in topic experts and committee members. The details of conflicts of interest and how they have been managed are available in the published register of interests.
British Menopause Society	Guideline	066	015	oestrogen-only HRT very slightly increases the risk of ovarian cancer after 5 years of use and this risk increases with duration of use" The Table shows no increase in risk at 5 years and a slight increase at 10. It cannot be extrapolated that the risk goes up at 5 years, it should say 10.	Thank you for your comment. For oestrogen-only HRT a significant risk increase was identified from the evidence (5 to 9 years of use) - see evidence review F (figure 21). The tables of absolute numbers were checked, and this amounted to an increase of 1 in 1000 women which whilst significant is small.
British Menopause Society	Guideline	066	016	"the risk of ovarian cancer increases with duration of use". What was this evidence based on? The observational data show no increase with up to 5 years and a very small increase with 10 years use but no further ongoing data to support such a statement. The RCT data show no increase in risk.	Thank you for your comment. The related statement in table 1 on combined HRT about duration of use was removed because the duration of use subgroup analysis did not reach significance. However, there was a significant duration of use subgroup difference for ovarian cancer, so the statement remained in this group. The rationale sections were revised accordingly.
British Menopause Society	Guideline	067	006	One of the strengths of NICE guidance is looking at the totality of the data and not excluding anything simply because it doesn't suit the argument. We regret that this guideline does not do this . The data are conclusive and show a clear and statistically significant reduction in the risk of cardiovascular disease yet this is not recognised or made reference to in the recommendation.	Thank you for your comment. In accordance with NICE methodology for reasons of transparency and reproducibility, studies are included and excluded from reviews on the basis of criteria set out in a pre-specified protocol agreed with the committee before a review has been started. When evidence has met the review protocol criteria it is included in the review and the committee consider this evidence when making recommendations. Agreed protocols are also published on the PROSPERO website before the

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					analysis of data commences). The committee discuss and consider all the evidence available in the review and use this evidence to support their recommendations. The committee discussed that there was evidence from RCT studies and observational studies, which were not always consistent with each other in their findings. The committee discussed the concerns with residual confounding in the observational studies and some of the concerns regarding the population in the RCT evidence. The committee also discussed the data from the subgroup analysis, which also showed inconsistent findings across the evidence. The committee consider all of these factors in their discussion and decision to not make a recommendation informing people that there is a reduction in the risk of cardiovascular disease, following the use of HRT. The committee's discussion of the evidence section in Evidence Review C has been updated to reflect a more detailed discussion of the committee's decision. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). With regards to the conclusion related to coronary heart disease the independent review concluded 'If considering each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular benefits, which have been noted in the stakeholder comments. However, we agree with

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					the committee's interpretation of the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
British Menopause Society	Guideline	067	022	"In contrast to this, the committee noted that observational evidence consistently showed an overall decrease in coronary heart disease risk in current users of either oestrogen-only or combined HRT." However despite this very clear and consistent finding in the presented evidence this is not referred to in the recommendations. This should be included in the recommendations based on the evidence presented. It is not clear why on this occasion observational data which show a benefit are overlooked when the committee has chosen to prioritise observational data for negative impacts such as breast cancer. This highlights significant methodological inconsistencies in	Thank you for your comment. The committee considered all of the evidence that met the protocol criteria which was included in the review. The committee considered each outcome separately and the discussions for each outcome can be found in the committee's discussion of the evidence section of the evidence report for the relevant review. The committee discussed the evidence related to breast cancer separately from the evidence related to cardiovascular disease, as the outcomes in these reviews are difference. The committee noted that whilst confounding is a potential source of bias in all observational studies, the likely impact of confounding on any given association will vary depending on the strength of the association of potential

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				the way the data have been interpreted and imply a bias within the committee.	confounders with both HRT and the outcome of interest. Therefore, the committee's discussions around confounders are specific to each review and the outcomes in that review. The committee discussed that the scope for residual confounding of associations of HRT with cardiovascular disease due to inadequate adjustment for confounding factors is likely to be considerably greater than it is for associations of HRT with other conditions such as breast cancer. The committee have chosen to prioritise observational study evidence for some outcomes over others based on the specific concerns of each outcome. The committee's discussion of the evidence in Evidence Review C has been updated to provide more detail on how the committee made recommendations. There is also further detail on residual confounders in the committee's discussion of the evidence section in Evidence Review C. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). With regards to the conclusion related to coronary heart disease the independent review concluded 'If considering each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular benefits, which have been noted in the stakeholder comments. However, we agree with the committee's interpretation of the evidence, based on the limited power in these analyses to

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
British Menopause Society	Guideline	067	013 - 021	Long term FU from the WHI RCT showed that there was a reduced risk of coronary heart disease for women starting oestrogen only HRT aged 50 to 59. Manson et al 2013 showed significant reduction in coronary heart disease including MI OR 0.67 95% CI 0.46-0.98 with oestrogen only HRT in women aged 50-59. This was presented in the NICE analysis yet is not reflected in the recommendations. Why not? This finding is consistent with the Cochrane review (Boardman et al) and the observational evidence (above). This should be reflected in the recommendations. Doctors and their patients need to know that if they start HRT at the time of the menopause, this is likely to be associated with CVD benefit. This is not saying that HRT should be used for primary	Thank you for your comment. The result mentioned in your comment refers to a result in Evidence Review C for the comparison oestrogen-only versus placebo, outcome coronary heart disease (including MI) in current and past users (unknown recency) with 5-9 years duration of HRT use at 13 years cumulative follow-up, for the age at first use 50-59, which is part of a subgroup analysis that also includes results for age at first use 60-69 and 70-79. The data shows that there is a statistically significant difference in the individual subgroup 50-59 (RR 0.67 (0.46 to 0.98)), but no statistically significant differences for 60-69 (RR 1.01 (0.83 to 1.22) or 70-79 (RR 0.98 (0.79 to 1.23)). However, it is misleading to conclude that there is a difference in effect in different subgroups, because the test for subgroup differences was not statistically

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				prevention, simply that all should be aware. This finding was also consistent with the findings from the Cochrane review by Boardman et al and the review of the observational evidence above.	significant p=0.17 (please see forest plot figure 77 in Appendix E of Evidence Review C). Therefore, it is misleading to conclude that the reduced effect shown is specific to the age group 50-59. This methodology is in line with the NICE methods and processes and the Cochrane Handbook. As a result, the committee are unable to make a recommendation highlighting any reduced risk in coronary heart disease based on this result. This is further discussed in the committee's discussion of the evidence section in Evidence Review C which has been updated. The Cochrane review (Boardman et al) was assessed for inclusion but was excluded due to the data not being presented separately for combined HRT and oestrogen-only HRT, as specified in the protocol criteria of the review. The included studies in Boardman et al were individually assessed and included where they met the protocol criteria. Boardman et al is listed in the excluded studies section of Evidence Review C. The related rationale section of the guideline has been updated to explain the reason for the exclusion of this review to clarify this matter. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). With regards to the conclusion related to coronary heart disease the independent review concluded 'If considering each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					benefits, which have been noted in the stakeholder comments. However, we agree with the committee's interpretation of the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
British Menopause Society	Guideline	067	020	"and an increased risk for combined cardiac events in current users taking continuous combined HRT for 1 to 4 years." This was from the Wisdom study in which the total number of events was very low (single digit) and the average age of women much older. With these limitations no meaningful conclusions can be made from this study.	Thank you for your comment. The committee did discuss the limitations with regard to the WISDOM study, and this is noted in the committee's discussion of the evidence section in Evidence Review C. The committee agreed that they would be cautious with results from the WISDOM study and the reasons are discussed in the committee's discussion of the evidence in Evidence Review C.
British Menopause Society	Guideline	067	025 - 028	"The committee agreed that it is unclear how much the observational findings may have been influenced by residual confounding factors such as sociodemographic, smoking,	Thank you for your comment. Residual confounding is a concern across all observational studies. Residual confounding is the bias that remains even after controlling or adjusting for confounders that are known, and can be caused

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				prior morbidities or other factors which may be related to HRT use and cardiovascular risk". This is an assumption and not based on any information of exclusion or lack of it in these studies. These studies adjusted for confounders (further supported by the fact that these same studies noted an increased risk of stroke with oral oestrogen intake). This limitation applies in equal measures to all observational evidence reviews including breast cancer and dementia. There needs to be a consistent approach to interpreting the evidence for all aspects reviewed.	by unknown confounders, therefore even though the studies adjusted for confounders some concern may remain. The approach to analysing evidence was consistent across all reviews in terms of methodological processes, however not all outcomes can be interpreted consistently as they will be affected and influenced by difference factors. The committee noted that whilst confounding is a potential source of bias in all observational studies, the likely impact of confounding on any given association will vary depending on the strength of the association of potential confounders with both HRT and the outcome of interest. The guideline rationale section has been revised to focus on similarities and differences between study types. Residual confounding was discussed so it remains in the discussion in this section, but it has been revised to clarify that this was only one of many factors that were considered. The committee's discussion of the evidence in Evidence Review C has been updated to provide more detail on this matter. With regard to stroke outcomes, the committee discussed that since the RCT evidence, of which there is no concern regarding residual confounders, was in line with the observational evidence, they were able to support a recommendation to advise people of the increased risk of stroke with oestrogen-only HRT. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					conclusions reached by the committee (with changes made post consultation). With regards to the conclusion related to coronary heart disease the independent review concluded 'If considering each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular benefits, which have been noted in the stakeholder comments. However, we agree with the committee's interpretation of the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
British Menopause Society	Guideline	068	004	"Based on the committee's knowledge" Conclusions should be based on the body of evidence reviewed. Committee opinion should only be relevant when the data are not clear. In this context the data are conclusive and show a clear and statistically significant reduction in the risk of cardiovascular disease from the	Thank you for your comment. The committee discuss and consider all the evidence available in the review and use this evidence to support their recommendations. The evidence in Evidence Review C consists of data from RCT and observational studies. The committee discussed that the findings between the RCTs and

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				analysis conducted by the NICE team, this should not be overturned based on the personal views or knowledge of committee members. The recommendations should be based and mainly guided by what was shown in the evidence reviews. The inclusion of observational data is important in measuring uncommon events and this is true with cardiovascular episodes in women between ages 50-59. In general, observational studies are subject to bias, which is why they are GRADED lower than RCTs, although it appears there have been modifications to the application of GRADE system in this Guideline for reasons that are not entirely clear. It seems that the assessment of bias, which is subjective in itself, is used as justification. The studies adjusted for confounders. This limitation applies in equal measures to all observational evidence reviews including breast cancer and dementia. There needs to be a consistent approach to interpreting the evidence for all systematic reviews undertaken. Where there are data available, the 'Committee' knowledge is considerably less important than the evidence available. The available data show a clear and statistically significant reduction in the risk of cardiovascular disease. The recommendations should be based on the evidence reviews not on committee opinion.	observational studies were inconsistent, with RCT evidence showing no increase or decrease in the risk of cardiovascular disease outcomes, and some of the observational evidence showing a reduction. The committee also discussed the data from the subgroup analyses, which also showed inconsistent findings across the evidence. The committee discussed the limitations across all of the evidence and raised concerns regarding residual confounding in the observational studies and some concerns regarding the population in the RCT evidence. Considering the limitations of the evidence, they agreed that the evidence did not support a recommendation that there is a reduction in the risk of cardiovascular disease following HRT use. The decisions made regarding recommendations are supported by the evidence in Evidence Review C and are not based on personal views of committee members. Where the evidence presented in the reviews are not consistent, or are not conclusive, the committee members may use their knowledge to discuss possible reasons for inconsistency. The committee's discussion of the evidence section in Evidence Review C has been updated to reflect a more detailed discussion of the committee's decision with regard to recommendations for cardiovascular disease risk. The GRADE system has not been modified for this guideline. In general, observational studies are graded lower than RCTs in the GRADE quality assessment, however there are exceptions to this and some observational studies, when assessed with specific critical appraisal tools, start off with the same level of quality as RCTs; they then follow

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					the same process for rating each domain as all the evidence. The GRADE domain risk of bias is assessed at study level for each outcome using a critical appraisal tool appropriate to each study design. Where confounders are an issue, they are addressed in the critical appraisal, which is reflected in the GRADE risk of bias parameter and in turn contributes to the overall quality rating. Residual confounding is a bias that remains even after controlling or adjusting for confounders and can be as a result of unknown confounders. It is a potential source of bias in all observational studies, and although the committee refer to the GRADE rating, there may still be residual confounding from unknown factors, or factors that are difficult to adjust for which are discussed and taken into consideration. A consistent approach to analysing the evidence was taken across all reviews, however interpretation can depend on the outcome of interest. The committee discussed that the likely impact of confounding on any given association will vary depending on the strength of the association of potential confounders with both HRT and the outcome of interest. Therefore, the committee's discussions around confounders are specific to each review and the outcomes in that review. The committee discussed that the scope for residual confounding of associations of HRT with cardiovascular disease due to inadequate adjustment for confounding factors is likely to be considerably greater than it is for associations of HRT with other conditions such as breast cancer. NICE commissioned an independent review of the breast cancer and cardiovascular evidence

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					reviews and these checks support the conclusions reached by the committee (with changes made post consultation). With regards to the conclusion related to coronary heart disease the independent review concluded 'If considering each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular benefits, which have been noted in the stakeholder comments. However, we agree with the committee's interpretation of the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly
British Menopause Society	Guideline	068	010	'For this reason, the scope for residual confounding of associations of HRT with cardiovascular disease is likely to be much greater than it is for associations of HRT with other health outcomes'	Thank you for your comment. Residual confounding is a concern across all observational studies. Residual confounding is the bias that remains even after controlling or adjusting for confounders that are known, and can be caused by unknown confounders, therefore even though

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				This is contradicted by the fact that the same studies showed a significant increase in the risk of stroke with oral intake of oestrogen (and a reduction in CVD) which does not support an issue with significant confounders being not adjusted for. The reference to these limitations appears to be based on an assumption rather than specified omissions noted in the published peer reviewed papers.	the studies adjusted for confounders some concern may remain. The approach to analysing evidence was consistent across all reviews in terms of methodological processes, however not all outcomes can be interpreted consistently as they will be affected and influenced by difference factors. The committee noted that whilst confounding is a potential source of bias in all observational studies, the likely impact of confounding on any given association will vary depending on the strength of the association of potential confounders with both HRT and the outcome of interest. The guideline rationale section has been revised to focus on similarities and differences between study types. Residual confounding was discussed so it remains in the discussion in this section, but it has been revised to clarify that this was only one of many factors that were considered. The committee's discussion of the evidence in Evidence Review C has also been updated to provide more detail on this matter. With regard to stroke outcomes, the committee discussed that since the RCT evidence, of which there is no concern regarding residual confounders, was in line with the observational evidence, they were able to support a recommendation to advise people of the increased risk of stroke with oestrogen-only HRT. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					changes made post consultation). With regards to the conclusion related to coronary heart disease the independent review concluded 'If considering each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular benefits, which have been noted in the stakeholder comments. However, we agree with the committee's interpretation of the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
British Menopause Society	Guideline	068	014	"HRT with cardiovascular diseases should give relatively more weight to RCT evidence, particularly where the findings from observational studies and RCTs are qualitatively different" We agree but this limitation equally applies to all topics where observational evidence is	Thank you for your comment. The lines you quote in your comment are relevant to this issue of residual confounding. The committee recognised that whilst confounding is a potential source of bias in all observational studies, the likely impact of confounding on any given association will vary depending on the strength of the association of potential confounders with both HRT and the

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				reviewed including breast cancer. The committee appear to prefer to use observational data for breast cancer risks and for cardiovascular outcomes they prefer to use RCT data. Although they give an explanation (opinion) for this inconsistent approach, it could and should be open to debate. The committee has not considered the data from estrogen only WHI and the DOPS trial in formulating the recommendations regarding the reduction in risk of CV disease in younger women using certain types of HRT. The lack of discussion about the potential differential metabolic impacts of HRT regimens containing progesterone/dydrogesterone rather than androgenic progestogens on cardiometabolic risk is concerning and not even mentioned from a future research perspective.	outcome of interest. Therefore, the committee's discussions around confounders are specific to each review and the outcomes in that review. The DOPS study (referenced Schierbeck 2012 in Evidence Review C) was not included in the review as it did not distinguish between oestrogen-only HRT and combined HRT, which was criteria set out in the pre-specified protocol. The data in Evidence Review C was stratified by age at first use of HRT where possible. The committee discussed the subgroup analysis from the RCT data and since there were no statistically significant subgroup differences, they could not conclude that there was a reduced incidence of heart disease related events when HRT was used at a particular age. The committee also considered the observational study evidence, which was also stratified by age at first use where possible. They discussed that evidence from one study supported a reduced risk in coronary heart disease which was specific to a younger age group, however this pattern was not reflected in another observational study which also presented subgroup data. Since there were inconsistent results between the observational studies as well as inconsistencies between observational and RCT evidence, and no statistically significant subgroup differences in the RCT evidence, the committee could not reach the conclusion that there was a reduced risk of coronary heart disease depending on the age at first use of HR. The related rationale section of the guideline has been updated to explain this in more detail. This committee's discussion section in Evidence Review C has also been revised accordingly. The

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					committee did not specify metabolic impacts of HRT in the pre-specified protocol, therefore the evidence base (including the impact of different regimens containing progesterone or dydrogesterone) was not searched for these outcomes. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). With regards to the conclusion related to coronary heart disease the independent review concluded 'If considering each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular benefits, which have been noted in the stakeholder comments. However, we agree with the committee's interpretation of the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
British Menopause Society	Guideline	068	022	"The evidence showed that, for people with no history of coronary heart disease, there was no increase in mortality from cardiovascular disease from taking HRT and the committee agreed that it was important for people to know this to make an informed choice" Yet there is clear evidence of reduced mortality in the under 60s that is not referred to. The Cochrane review (Boardman et al 2015) showed a significant reduction in CVD and CVD mortality in women who commenced HRT under the age of 60. This review was not included. Given the large sample size from RCTs, this is surprising and the findings should be discussed here. No evidence is presented as to why NICE methodology is preferable to Cochrane. The recommendations should be on the body of evidence not committee opinion particularly when the evidence differs from committee opinion. This and other studies (WHI, Schierbeck, PEPI and ELITE) have demonstrated cardiovascular benefit for women starting HRT below the age of 60 years. Given the large body of evidence on this topic it is concerning how conservative the guideline is regarding the possibility of cardiovascular benefit with HRT. Schierbeck LL, Rejnmark L, Tofteng CL, Stilgren L, Eiken P, Mosekilde L, Køber L,	Thank you for your comment. The evidence in Evidence Review C does not support a reduced mortality from cardiovascular disease following HRT use in those under 60. If considering each forest plot individually, there were subgroups where observational evidence suggests that HRT appears to be associated with cardiovascular benefits. However, the committee's interpretation was that the benefit when starting under 60 was not supported by the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects. To address the limited power a research recommendation has now been included. The Boardman et al 2015 review was assessed for inclusion but was excluded due to the data not being presented separately for combined HRT and oestrogen-only HRT, as specified in the protocol criteria of the review. The included studies in Boardman et al were individually assessed and included where they met the protocol criteria. Boardman et al is listed in the excluded studies section of Evidence Review C. NICE methodology is in line with Cochrane methodology, however where Cochrane reviews do not fit the criteria set out in the pre-specified protocols they cannot be included in the review. The related rationale section of the guideline has been updated to explain the reason for the exclusion of this review to clarify this matter.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Jensen JE. Effect of hormone replacement therapy on cardiovascular events in recently postmenopausal women: randomised trial. BMJ. 2012 Oct 9;345:e6409. Hodis HN, Mack WJ, Henderson VW, Shoupe D, Budoff MJ, Hwang-Levine J, Li Y, Feng M, Dustin L, Kono N, Stanczyk FZ, Selzer RH, Azen SP; ELITE Research Group. Vascular Effects of Early versus Late Postmenopausal Treatment with Estradiol. N Engl J Med. 2016 Mar 31;374(13):1221-31.	In relation to the cited RCTs, data from the WHI have been included in the review and data were stratified by age at first use. Analysis showed that the test for subgroup difference was not statistically significant between the age groups for age at first use of HRT, therefore the committee did not conclude that there was a cardiovascular benefit based on this evidence. The data from PEPI trial (referenced Anonymous 1995 in Evidence Review C) was included in the review where the outcomes matched those set out in the protocol, however there was no stratification by age at first use. Schierbeck 2012 was not included in the review as the data was not separated by type of HRT (combined HRT and oestrogen-only HRT), which was one of the criteria specified in the protocol. The ELITE study was not included in the review as it did not report any outcomes that matched those specified in the review protocol. The reasons for exclusion for these studies have been listed in the excluded studies section in Evidence Review C. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). With regards to the conclusion related to coronary heart disease the independent review concluded 'If considering each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular benefits, which have been noted in the stakeholder comments. However, we agree with

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					the committee's interpretation of the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
British Menopause Society	Guideline	070	024 - 025	"How the recommendations might affect practice. It is usual practice to inform people of the risks associated with a treatment option." As above there should be consistent emphasis throughout the document for both benefits and risks.	Thank you for your comment. This has been revised to say that 'it is current practice that benefits and risks are discussed with people when treatment options are considered'.
British Menopause Society	Guideline	071	001	"It is unclear whether it is current practice to use HRT for the specific purpose of primary or secondary coronary heart disease prevention in current practice." This is incorrect. National and international guidance from BMS, IMS and others do not recommend HRT for the sole benefit of primary prevention of cardiovascular disease. We welcome consistency but please be factually correct. The fact that some individual	Thank you for your comment. This statement is not about the practices recommended by professional bodies but current practice out there. Some stakeholders have indicated that they do think it is and should be used for this purpose. The committee therefore believed that 'unclear' is appropriate terminology in this context.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				practitioners advocate this does not mean it is normal current practice.	
British Menopause Society	Guideline	072	016	**"**However, the committee reached a majority decision. Taking all evidence into account, they decided the evidence pointed towards a possible increased risk in dementia incidence, particularly with results showing increased risk when started at a later age. They agreed it was important that people considering HRT for troublesome menopause symptoms should be made aware of the potential risk, so that they could make an informed decision" The recommendation presented by NICE refers to an increase in risk in women who *first start HRT at the age of 65 and above* (The WHIMS study). The wording above needs to be amended to reflect this to avoid any public misunderstanding. The current wording may be viewed as misleading as the recommendation does not apply to women who start HRT under the age of 65. It is concerning that in discussing the limitations of the WHIMS trial the committee regarded the age group of the trial (65 years or over) as only "slightly different from typical users of HRT" (Page 73 Line 8)…there is clearly considerable difference in these age cohorts. We would like further clarification as to why the committee decide to focus on the Danish and WHIMS trials in making their recommendations. After all, they accepted that the population in WHIMS did not represent a	Thank you for your comment. The wording in the guideline ' Taking all evidence into account, they decided the evidence pointed towards a possible increased risk in dementia incidence, particularly with results showing increased risk when started at a later age' has been removed and now only refers to an initiation of HRT after the age of 65 as in the RCT findings. The word 'slightly' was also removed in the phrase 'slightly different from a typical user of HRT' in relation to starting HRT after the age of 65. The committee did not focus on the observational Danish study to inform recommendations. The committee noted that the results from the observational Danish study were in line with the findings from the RCT data (WHIMS), however they agreed that both the observational Danish study and the observational UK study had limitations. The committee discussed that the observational data were inconsistent, and since the studies did not adjust for all the relevant confounders, the committee could not decide in which direction there may have been bias. Therefore, the committee used the RCT data to inform their recommendations. See the related rationale section of the guideline and the committee's discussion of the evidence section of Evidence Review G for more detail. Thank you for highlighting Nerattini et al 2023. This systematic review was not included in Evidence Review G, as it was published after the cut-off date. Some of the studies in this systematic review do not meet our protocol criteria which specifies that data on HRT should

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				typical HRT using population in most countries and in the breast cancer data one of the arguments for not using the RCT data was that it did not represent a typical HRT population. There needs to be consistency and transparency in the way data are treated. As far as the Danish trial is concerned this only showed association with HRT and could not prove causation. This population could have been at increased risk of cognitive problems anyway. Also, the types of HRT used in this trial have largely been superseded by the more natural types of hormone therapy, particularly with transdermal estradiol and micronized progesterone which are less pro thrombotic and more metabolically favourable. It appears that NICE has placed much more emphasis on a smaller Danish study and overlooked the much larger UK general Practice CPRD study by Vinogradova et al 2021. This was a much larger UK study included a total of 118,501 women diagnosed with dementia and 497,416 female controls. The latter study was from a UK population and the full data were presented with more detailed presentation of the adjustments and did not show an overall increase in the risk of dementia. Is there any particular reason that NICE placed more weight on the smaller Danish study and appear to have overlooked conclusions from the Vinogradova paper?	be separated into oestrogen-only and combined HRT, therefore this systematic review would not have been included as a whole. The individual studies were also checked against our protocol criteria, and of the ones that met the protocol criteria were already included in the review. Most of the studies included in the Nerattini systematic review that do not meet the protocol criteria have already been listed in our excluded studies list in appendix I of Evidence Review G.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				In addition, a significant limitation of the Danish study, was that the HRT user group in the study had significantly higher prevalence (compared to the control group) of lower level education, lower household income, and were more likely to live alone and to have hypertension, diabetes, and thyroid disease – all risk factors for dementia. This recent systematic review should be included in the data analysis. Nerattini M, Jett S, Andy C et al (2023) Systematic review and meta-analysis of the effects of menopause hormone therapy on risk of Alzheimer's disease and dementia. Front. Aging Neurosci. 15:1260427.	
British Menopause Society	Guideline	073	018	We welcome the statement that HRT should not be used to prevent dementia.	Thank you for your comment in support of this.
British Menopause Society	Guideline	074	017	"The committee considered the possibility that, like premature ovarian insufficiency, early menopause may either increase or decrease the baseline risk of some health outcomes" It is concerning that no background reference is made to the large observational evidence of adverse effect of early menopause on bone, cardiovascular and cognitive health. Whilst this may not have been part of the scope of the guidance at least some reference to this effect should be included here. There is large observational evidence that shows an adverse effect on bone (including osteoporosis and fractures), cardiovascular disease and cognitive function in both these	Thank you for your comment. The aim of the evidence review carried out for the 2024 guideline update was assessing the impact of either taking HRT or not taking HRT on people with early menopause and the development of various health outcomes. The need to assess the impact of early menopause on health outcome has been acknowledged and will be passed onto the NICE surveillance teams for prioritised consideration during future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				groups. This should be referred to in this section. Whilst the guideline is restricted by the scope, HCPs should be guided by the totality of the evidence. When NICE refers to '*early menopause being somewhere in between POI and menopause at and above* the age of 45', this is implying (but not mentioning) the adverse effects that POI and early menopause have on bone, cardiovascular health and cognitive function in women. We believe this should be clearly mentioned to help guide healthcare professionals as well as the lay public.	
British Menopause Society	Guideline	075	003	"Evidence showed an increased risk of breast cancer for people with early menopause who used HRT compared to those not using HRT. The committee decided that it was important to explain this to people" This should be the same tone as other sections and should clearly state compared to women with early menopause not taking HRT who have a lower risk of breast cancer (not to age matched premenopausal controls).	Thank you for your comment. This sentence has been removed.
British Menopause Society	Guideline	083	001	Table Column 2 - "Replaced by the following statements in tables 1 and 2: Combined HRT may increase risk of dementia if started over the age of 60" This is inaccurate: the recommendation (based on WHIMS) states over 65. WHIMS did not include women under 65. This needs to be	Thank you for your comment. This has been corrected.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				amended. Further the recommendation states *might* not *may*.	
British Menopause Society	Guideline	094	Appendix A – Tables 10 & 11	These contain inaccurate information and can be potentially misleading. The original WHI groups at randomisation were 50-59, 60-69 and 70-79. It would be relevant to state that no significant increase was noted in any of these groups. Only at post hoc analysis and when looked in a different way (not the original protocol allocations) a difference was noted in the more than 20 years group ***but not*** in the 10-20 years group. This needs emphasising. In clinical practice some women may start HRT 10 years after the menopause and they should be reassured that HRT is unlikely to increase their risk of CVD. It is very unlikely that women will start HRT (any preparation, and certainly not oral CEE 0.625 mg) for the first time >20 years after the menopause but if they do they should be aware of the increased risks. What are the figures on CVD risk with HRT tables based on? The observational evidence reviewed showed a very clear and consistent reduction in risk (Figures 46 and 73). Table 46 clearly shows a reduction. If these are based on RCT evidence, it should clearly state the WHI cohort included a very wide age range 50-79 years old which would not apply to most users who are likely start HRT around the age of 50. The data would be better presented by age as per WHI.	Thank you for your comment. For the draft guideline, the committee opted for a verbal format complemented by tables, providing estimates of absolute numbers from a single source rather than from two different study types. This differs from the approach used in the published version of NG23. This decision was made to facilitate conversations between clinicians and individuals, enabling shared decision-making regarding Menopause management. The appendix has been used to produce a discussion aid document including visualisation of the data. This provides details about the type of evidence data originated from, how to interpret the numbers and information about uncertainty. It also links to the relevant evidence reviews which contain details of the estimates from different study types (and the relevant sources) as well as the confidence intervals. It also includes links to a separate supplement file which provides the details of each calculation. This discussion aid has undergone user-testing and was refined based on user feedback.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Menopause Society	Guideline	095	Appendix A - Table 12	Dementia. What is the objective of including this Table? In clinical practice hardly anyone starts HRT for the first time at the age of 65 or above. Including these figures here may come across as the risk of dementia with HRT use for all users. The vast majority of users would have started before 65 and these figures would therefore not apply to them.	Thank you for your comment. This statement is underpinned by RCT data of women who initiated HRT use after the age of 65. This study showed an increased risk and therefore the committee decided that it was important to highlight this. Data for ages younger than 65 were inconclusive because there were studies that were inconsistent with each other (one showing and increased risk and the other showing no difference). The committee therefore decided not to comment on dementia risk for people initiating HRT use before the age of 65 because no clear conclusions could be reached.
British Menopause Society	Implementation	General	General	CBT for menopausal symptoms is being implemented by training health professions (BMS have biannual courses which are typically over-subscribed), use of a published manual for health professionals to use Group CBT, self-help books, and on-line resources. Breast cancer nurses and counsellors have been trained and are running groups and some IAPT services are using on-line CBT. Training IAPT health professionals in CBT for menopause within their training for LTC (long term conditions) might be one option to increase access. More education is needed so that the public understand that CBT can help people manage physical symptoms, such as VMS, as well as anxiety and depressive symptoms. In this context CBT can give people more choice and therefore increase equity to treatments for those who do not want to have, or have medical reasons that contraindicate HRT.	Thank you for your comment in support of this. Your comment will be considered by NICE where relevant support activity is being planned.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
British Thyroid Foundation	Guideline	008	General	The NICE guideline on thyroid disease: assessment and management states in section 1.2.5 ' Be aware that in menopausal women symptoms of thyroid dysfunction may be mistaken for menopause.' We are concerned that there is currently no reference to thyroid disease in section 1.3 'Identifying perimenopause and menopause' and that thyroid dysfunction may be missed in individuals presenting with menopause-like symptoms. We would like a clause added to the effect: 'consider testing for thyroid dysfunction where peri/menopause has been ruled out but individuals are presenting with 'menopause-like' symptoms.	Thank you for your comment. Identifying perimenopause and menopause was not in the scope of the 2024 guideline update. Evidence for this topic (including the potential impact of thyroid disease) was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this. The issue of thyroid function tests have been logged with the NICE surveillance team for consideration for future updates.
British Thyroid Foundation	Guideline	010	001	We find the term 'troublesome' when referring to symptoms unhelpful. The term is a little dismissive of patients, suggesting there's an element of them overplaying them. 'Problematic' or 'unmanageable' would seem more appropriate ways to describe these symptoms.	Thank you for your comment. Based on this and other feedback the committee reflected on this wording and consequently 'troublesome' has been removed from the guideline.
British Thyroid Foundation	Guideline	012	019	We would like to see a clause added in the section 'taking comorbidities into account' for people with primary hypothyroidism being treated with levothyroxine to the effect: 'Be aware that individuals taking levothyroxine to treat hypothyroidism may require an increase in their dose after starting oral HRT. Re-test thyroid function after starting tablet-combined HRT.'	Thank you for your comment. Whilst there are some new recommendations in this section, the general topic of comorbidities (including issues relating to hypothyroidism) was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
British Thyroid Foundation	Guideline	012	019	It would also be helpful to include information in this section about individuals being treated with levothyroxine to treat primary hypothyroidism possibly requiring a change in	Thank you for your comment. Whilst there are some new recommendations in this section, the general topic of comorbidities (including issues relating to hypothyroidism) was not in the scope

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				dose during menopause transition due to changes to oestrogen levels, bone density and/or weight. Regular thyroid monitoring (usually annually unless otherwise indicated) will show whether a change in dose is needed	of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this. The topic of thyroid function tests has been logged with the NICE surveillance team to be considered for future updates.
British Thyroid Foundation	Guideline	035	General	'Managing premature ovarian insufficiency' It would be helpful to have a reference to the association between POI and autoimmune hypothyroidism here (Thyroid problems can occur in 14-27% of women with POI). We suggest 'There is an association between premature ovarian insufficiency and autoimmune hypothyroidism. Consider testing for thyroid peroxidase antibodies (TPOAb) and screening for thyroid-stimulating hormone (TSH) levels at presentation.'	Thank you for your comment. The association of POI and hypothyroidism was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this.
BSCAH (British Society of Clinical and Academic Hypnosis)	Guideline	005	001	GID-NG10241 Submission to NICE (GID -NG1024) re-menopause guidance on behalf of BSCAH (British Society of Clinical and Academic Hypnosis) Dear NICE colleagues We are writing on behalf of the British Society of Clinical and Academic Hypnosis (BSCAH). We believe it is important that NICE considers the following evidence which shows that clinical hypnosis is an important non-hormonal option for treatment of women suffering from vasomotor and other symptoms of the menopause.	Thank you for your comment. The effectiveness of hypnosis was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this. The cited references have been logged with the NICE surveillance team for future consideration.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Clinical Hypnosis is: the integration, by a qualified clinician, of hypnotic techniques with other established treatments for a given condition. Hypnotic techniques include: hypnotic induction; deep relaxation; and suggestions for alterations in perceptions and experiences, which are often delivered by way of individualised imagery. The evidence for use of clinical hypnosis in postmenopausal symptoms are considered below: Hot flashes, sleep disturbance and anxiety. In clinical practice, these symptoms are usually treated together since they are closely related to each other, particularly in the lived experience of the women themselves. <u>Evidence for clinical Hypnosis in management of hot flashes in post-menopausal women</u> 3 papers containing relevant evidence: In 2013, a single blind RCT was performed (1). 187 postmenopausal women who reported a minimum of 50 hot flashes a week at baseline underwent structured–attention control intervention. One arm of this trial had the addition of clinical hypnosis to the attention control. The women in this arm reported significantly lower hot flash frequency and scores (in addition to this subjective improvement, physiologically monitored hot flashes also proved to be reduced to a clinically significant level). It was shown in a follow-up analysis (2) that these positive effects were not related to the	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				women's expectations about the likely positive effect of the hypnosis intervention. In a separate study on 60 women who had had treatment for breast cancer resulting in hot flashes (3), hypnosis was found to be significantly better in reducing hot flashes than no treatment. Improvements included frequency of hot flashes and average severity. <u>Evidence for clinical hypnosis in the management of sleep disturbance in post–menopausal women</u> A self-hypnosis program was found to improve sleep quality in a randomised controlled trial of 90 menopausal women (4). This trial involved either 5 in-person sessions; 3 in-person sessions; 5 phone calls including self-hypnosis; or 3 phone calls including self-hypnosis. Sleep quality, and sleep duration, were improved in all groups. In the trial mentioned above (3), female breast cancer survivors who underwent the hypnosis intervention were found to have significant improvements in sleep in addition to the improvement in hot flashes. <u>Evidence for clinical hypnosis in the management of anxiety in postmenopausal women</u> The positive effect of clinical hypnosis on anxiety in breast cancer survivors with hot flashes was shown in a study (5), which was a reanalysis of the data collected in the	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				previously mentioned paper (3). This shows that the anxiety scores in the intervention group reduced significantly compared to the control group. The North American Menopause Society (6) has recommended hypnosis since the first publication in 2015. The 2023 update continues this, basing this on level 1 evidence – with the recommendation stating that there is "good and consistent scientific evidence". We very much hope that NICE will assess the evidence mentioned above before finalising the updated guidelines. Women with troublesome menopausal symptoms deserve a choice in evidence based non-hormonal treatments for their condition. Thank you very much for your consideration. Yours faithfully Dr Gillian M Smith MB, BCh, BAO, MRCPsych. Honorary Secretary BSCAH (British Society of Clinical and Academic Hypnosis) Dr. Cathryn Woodward Clinical Oncology Consultant West Suffolk and Cambridge University Hospitals MB, ChB, MRCP, FRCR, Dipl. Hypnosis and Stress Management Dr. Jane Boissiere MB. ChB. President BSCAH	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Dr. Jane Reid General Practitioner with Specialism in Sexual and Reproductive Medicine (retired) 1. Elkins GR, Fisher WI, Johnson AK, Carpenter JS, Keith TZ. Clinical hypnosis in the treatment of postmenopausal hot flashes: a randomized controlled trial. Menopause. 2013 Mar;20(3):291-8. doi: 10.1097/gme.0b013e31826ce3ed. PMID: 23435026; PMCID: PMC3556367. 2. Sliwinski JR, Elkins GR. Hypnotherapy to reduce hot flashes: examination of response expectancies as a mediator of outcomes. J Evid Based Complementary Altern Med 2017;22:652-659. doi: 10. 1177/2156587217708523 3. Elkins G, Marcus J, Stearns V, Perfect M, Rajab MH, Ruud C, Palamara L, Keith T. Randomized trial of a hypnosis intervention for treatment of hot flashes among breast cancer survivors. J Clin Oncol. 2008 Nov 1;26(31):5022-6. doi: 10.1200/JCO.2008.16.6389. Epub	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				2008 Sep 22. PMID: 18809612; PMCID: PMC2652097. 4. Roberts RL, Rhodes JR, Elkins GR. Effect of Hypnosis on Anxiety: Results from a Randomized Controlled Trial with Women in Postmenopause. J Clin Psychol Med Settings. 2021 Dec;28(4):868-881. doi: 10.1007/s10880-021-09810-3. Epub 2021 Aug 17. PMID: 34403019. 5. Johnson AJ, Marcus J, Hickman K, Barton D, Elkins G. Anxiety Reduction Among Breast-Cancer Survivors Receiving Hypnotic Relaxation Therapy for Hot Flashes. Int J Clin Exp Hypn. 2016 Oct-Dec;64(4):377-90. doi: 10.1080/00207144.2016.1209042. PMID: 27585723; PMCID: PMC5373901. 6. "The 2023 Nonhormone Therapy Position Statement of The North American Menopause Society" Advisory Panel. The 2023 nonhormone therapy position statement of The North American Menopause Society. Menopause. 2023 Jun 1;30(6):573-590. doi: 10.1097/GME.0000000000002200. PMID: 37252752.	
BSCAH (British Society of Clinical	Guideline	011	006	GID-NG10241 Submission to NICE (GID -NG1024) re-menopause guidance on behalf of BSCAH	Thank you for your comment. The effectiveness of hypnosis was not in the scope of the 2024 guideline update. Evidence for this topic was

Stakeholder	Document	Page No	Line No	Comments	Developer's response
and Academic Hypnosis)				(British Society of Clinical and Academic Hypnosis) Dear NICE colleagues We are writing on behalf of the British Society of Clinical and Academic Hypnosis (BSCAH). We believe it is important that NICE considers the following evidence which shows that clinical hypnosis is an important non-hormonal option for treatment of women suffering from vasomotor and other symptoms of the menopause. Clinical Hypnosis is: the integration, by a qualified clinician, of hypnotic techniques with other established treatments for a given condition. Hypnotic techniques include: hypnotic induction; deep relaxation; and suggestions for alterations in perceptions and experiences, which are often delivered by way of individualised imagery. The evidence for use of clinical hypnosis in postmenopausal symptoms are considered below: Hot flashes, sleep disturbance and anxiety. In clinical practice, these symptoms are usually treated together since they are closely related to each other, particularly in the lived experience of the women themselves. <u>Evidence for clinical Hypnosis in management of hot flashes in post-menopausal women</u> 3 papers containing relevant evidence:	therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				In 2013, a single blind RCT was performed (1). 187 postmenopausal women who reported a minimum of 50 hot flashes a week at baseline underwent structured–attention control intervention. One arm of this trial had the addition of clinical hypnosis to the attention control. The women in this arm reported significantly lower hot flash frequency and scores (in addition to this subjective improvement, physiologically monitored hot flashes also proved to be reduced to a clinically significant level). It was shown in a follow-up analysis (2) that these positive effects were not related to the women's expectations about the likely positive effect of the hypnosis intervention. In a separate study on 60 women who had had treatment for breast cancer resulting in hot flashes (3), hypnosis was found to be significantly better in reducing hot flashes than no treatment. Improvements included frequency of hot flashes and average severity. <u>Evidence for clinical hypnosis in the management of sleep disturbance in post–menopausal women</u> A self-hypnosis program was found to improve sleep quality in a randomised controlled trial of 90 menopausal women (4). This trial involved either 5 in-person sessions; 3 in-person sessions; 5 phone calls including self-hypnosis; or 3 phone calls including self-	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
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Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Yours faithfully Dr Gillian M Smith MB, BCh, BAO, MRCPsych. Honorary Secretary BSCAH (British Society of Clinical and Academic Hypnosis) Dr. Cathryn Woodward Clinical Oncology Consultant West Suffolk and Cambridge University Hospitals MB, ChB, MRCP, FRCR, Dipl. Hypnosis and Stress Management Dr. Jane Boissiere MB. ChB. President BSCAH Dr. Jane Reid General Practitioner with Specialism in Sexual and Reproductive Medicine (retired) 1. Elkins GR, Fisher WI, Johnson AK, Carpenter JS, Keith TZ. Clinical hypnosis in the treatment of postmenopausal hot flashes: a randomized controlled trial. Menopause. 2013 Mar;20(3):291-8. doi: 10.1097/gme.0b013e31826ce3ed. PMID: 23435026; PMCID: PMC3556367. 2. Sliwinski JR, Elkins GR. Hypnotherapy to reduce hot flashes: examination of	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				response expectancies as a mediator of outcomes. J Evid Based Complementary Altern Med 2017;22:652-659. doi: 10.1177/2156587217708523 3. Elkins G, Marcus J, Stearns V, Perfect M, Rajab MH, Ruud C, Palamara L, Keith T. Randomized trial of a hypnosis intervention for treatment of hot flashes among breast cancer survivors. J Clin Oncol. 2008 Nov 1;26(31):5022-6. doi: 10.1200/JCO.2008.16.6389. Epub 2008 Sep 22. PMID: 18809612; PMCID: PMC2652097. 4. Roberts RL, Rhodes JR, Elkins GR. Effect of Hypnosis on Anxiety: Results from a Randomized Controlled Trial with Women in Postmenopause. J Clin Psychol Med Settings. 2021 Dec;28(4):868-881. doi: 10.1007/s10880-021-09810-3. Epub 2021 Aug 17. PMID: 34403019. 5. Johnson AJ, Marcus J, Hickman K, Barton D, Elkins G. Anxiety Reduction Among Breast-Cancer Survivors Receiving Hypnotic Relaxation Therapy for Hot Flashes. Int J Clin Exp Hypn. 2016 Oct-Dec;64(4):377-90. doi: 10.1080/00207144.2016.1209042. PMID: 27585723; PMCID: PMC5373901.	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				6. "The 2023 Nonhormone Therapy Position Statement of The North American Menopause Society" Advisory Panel. The 2023 nonhormone therapy position statement of The North American Menopause Society. Menopause. 2023 Jun 1;30(6):573-590. doi: 10.1097/GME.0000000000002200. PMID: 37252752.	
Claire Mellon & Associates	Evidence review C	General	General	Tables 1 and 2 state that neither oestrogen-only nor combined HRT increase the risk of coronary heart disease (CHD), and combined HRT does not increase CV mortality. The committee's opinion is informed by the results of 30 RCTs and 11 observational studies. The cardiovascular benefits of HRT have been comprehensively summarised in the following article: Hodis HN, Mack WJ. Menopausal Hormone Replacement Therapy and Reduction of All-Cause Mortality and Cardiovascular Disease: It Is About Time and Timing. Cancer J. 2022 May-Jun 01;28(3):208-223. doi: 10.1097/PPO.0000000000000591. PMID: 35594469; PMCID: PMC9178928. In summary: 1. Observational studies that have assessed outcomes in younger (30-55 years) healthier women, with	Thank you for your comment. The review by Hodis and Mack 2022 has been checked and as it does not fit the study design criteria set out in the protocol it cannot be included directly in Evidence Review C (cardiovascular disease). The RCT data in Evidence review C is also stratified by age at first use. The evidence shows an isolated risk reduction in younger women however, this is part of a subgroup analysis that did not show a statistically significant difference between the subgroups, and therefore the committee could not conclude that there was a difference in the risk of coronary heart disease depending on age at first use. Further details have been added to the committee's discussion of the evidence section in Evidence Review C, including the subgroup analysis discussion of the observational data, to clarify this point. The DOPS study (referenced Schierbeck 2012 in Evidence Review C) was not included in our review as it did not distinguish between oestrogen-only HRT and combined HRT, which was criteria set out in the pre-specified protocol.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				menopausal symptoms, who initiated HRT within 2 years of the menopause and used it for 10-40 years, have consistently demonstrated a 30-50% reduction in CHD. 2. Randomised controlled trials that have assessed outcomes in older women (>63 years), with CV risk factors but without menopausal symptoms, who initiated HRT more than 10 years after the menopause and used it for less than 7 years, have demonstrated a null effect across all ages. BUT when stratified by age, risk reductions have been observed in younger women who initiated HRT within 10 years of the menopause – because **timing is key**. 3. The only RCT to assess CV outcomes in younger women like those included in observational studies is the DOPS trial. In DOPS, CVD incidence was 52% lower in women who used oestradiol +/- NET for 10 years. 4. The ELITE study is the only RCT specifically designed to test the timing hypothesis. It demonstrated significantly reduced progression of atherosclerosis in healthy postmenopausal women who initiated oestradiol +/- vaginal progesterone within 6 years of the menopause (median 3.5 years, mean age 55.4 years), but not when initiated more than 10 years later (median 14.3 years, mean age 65.4 years).	The ELITE study (referenced Karim 2022 in Evidence Review C) was not included in our review as it did not report on the outcomes listed in the pre-specified protocol. Progression of atherosclerosis was not an outcome listed in the review protocol therefore the committee cannot comment on the results of this outcome. Both the DOPS and ELITE study publications have been listed in the excluded studies section of Evidence Review C. The WHI 18 years cumulative follow-up results you mention (CEE alone HR 0.81, 0.32-2.04; CEE+MPA 0.77, 0.33-1.79) are not statistically significant so it cannot be concluded that there is a reduced CV risk. They are however in line with the committee's recommendation that HRT use does not increase the risk of coronary heart disease. The committee considered and discussed both the RCT and observational studies. They discussed that although there were limitations to the RCT evidence, they were more concerned with the potential for residual confounding from the observational studies. They discussed that although there are concerns with residual confounding with all observational studies, it was a particular concern for cardiovascular outcomes since factors such as sociodemographic status, smoking, prior morbidities, may be related to both HRT use and cardiovascular risk. This is further discussed in the committee's discussion of the evidence section in Evidence Review C. Thank you for highlighting the Salpeter and the Cochrane (Boardman et al) meta-analyses, which have been listed in the excluded studies section of Evidence Review C. The term non-relevant was

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				5. Over 18 years of cumulative follow up, the WHI reported no association between HRT and CV risk, but a trend for reduced CV risk was observed in younger women that was most evident during the intervention phase (CEE alone HR 0.81, 0.32-2.04; CEE+MPA 0.77, 0.33-1.79). It is concerning that the committee have decided to give more weight to the RCT evidence (Draft guideline – p68) given that, as outlined above, women included in RCTs are not representative of the target population (older, CV risk factors, established CVD, shorter duration of therapy). The RCT data should be included, but the observational study data is more generalisable and should also be considered. Furthermore, as outlined by Hodis and Mack, the results of the DOPS and ELITE trials are of particular interest because they are the only RCTs that have included younger, healthier women, and the ELITE trial was designed to test the timing hypothesis. However, neither trial has been included in the evidence review. Hodis and Mack have also presented data from two meta-analyses: 1. Salpeter et al (n=30 RCTs) demonstrated that HRT initiated close to menopause significantly reduced	used to describe studies that did not meet the criteria set out in the protocol. The systematic review Salpeter and the Cochrane (Boardman et al) included some studies that did not meet the protocol criteria for this review and therefore the systematic review could not be included as a whole. However, the included studies from the systematic reviews were individually checked against the protocol and if they did meet the criteria in the protocol, they were included separately. The wording of the reason for exclusion was reviewed and revised in all instances to provide a clearer explanation. NICE processes and methods describe that reviews are conducted according to the protocol criteria set out before the review was conducted. This is to ensure transparency and reproducibility. Therefore, any post-hoc analysis not listed in the protocol cannot be undertaken. Women using both HRT regimens may be adequately represented in the Cochrane meta-analysis as you describe, however the protocol for this review states that the data must be separated by HRT regimen, that is data for oestrogen-only HRT preparations must be separate from the data from combined HRT preparations. The committee are unable to comment on any data or evidence that were not included in our review if they did not meet the protocol criteria. The WHI RCT has been included in the review and the results have been discussed with the committee. The discussion can be viewed in the committee's discussion of the evidence section in Evidence Review C. As you have not provided a reference to the meta-analysis by Kim et al, it is not

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				CHD by 32% and all-cause mortality by 39%. 2. A Cochrane systematic review and meta-analysis (Boardman et al, n= 19 RCTs) demonstrated that HRT initiated close to menopause significantly reduced CHD by 52% and all-cause mortality by 30% compared with placebo. Neither the Salpeter MA nor the Cochrane MA have been included in the NICE evidence review, the former on the grounds that 'it included non-relevant studies', and the latter on the grounds that it 'did not report outcomes separately for participants receiving combined HRT or oestrogen-only HRT'. NICE have not specified which studies they consider 'non-relevant', or why. Regarding the Cochrane MA, it is true that the authors haven't stratified the data according to HRT regimen, and this information would be interesting and helpful. However, approximately 7000 of 40,410 participants used oestrogen alone, 14,000 women were treated with combined HRT, and the remainder were randomised to placebo. As such, women using both HRT regimens are adequately represented, and the significant reduction in CHD and all-cause mortality in HRT users should not be dismissed just because we don't yet have MA-level data that enables us to compare the two regimens. The WHI – by far and away the largest RCT with the longest	possible to make a comment on whether the specific review you refer to was considered. However, a systematic review by Kim et al 2020 was considered for inclusion and is listed in the excluded studies section in Evidence Review C. Since there were studies in the review that did not fit the criteria specified in the protocol the results of this meta-analysis were not included in our review but the included studies list was checked for any relevant studies. The test for subgroup differences in the observational data for transdermal and oral routes of administration did not show a statistically significant result. The data was also stratified by oestrogenic and progestogenic constituents where possible, as well as by age at first use. However, the committee did not reach a conclusion that the data showed a difference in risk with any of the particular subgroups. The committee agree that more personalised advice when counselling women considering HRT would be beneficial, but the available data did not allow specific recommendations to support this type of counselling. The committee discussed the evidence that was included in this review and agreed that whilst they agreed that HRT does not increase the risk of coronary heart disease, they could not recommend the use of HRT for the prevention of cardiovascular disease. In addition, the review question for this review does not ask the question related to cardiovascular disease prevention, and therefore the committee are unable to make further comment or conclusions regarding this (see the committee's discussion of the evidence section of evidence review C for

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				post-intervention follow up – reported a trend towards benefit for both CEE-alone and CEE+MPA, and the findings of the Cochrane review were consistent with the earlier MA conducted by Salpeter et al. The benefit is likely to have been underestimated because (1) many women in RCTs are likely to have had subclinical CVD, or established CVD (secondary prevention trials), and HRT prevents/ slows the development of atherosclerosis but does not treat existing disease, and (2) women in clinical trials mainly received oral oestrogen with or without a synthetic progestin, but transdermal oestrogen and body-identical progesterone have superior cardioprotective effects. In a recent meta-analysis Kim et al pooled data from 26 RCTs and found no association between HRT and cardiovascular death but a significantly lower risk in women who initiated HRT early (SE 0.26, 0.11-0.64) - although this was based on a single RCT (DOPS). In subgroup analysis no association was observed with regimen, but the authors only compared oestrogen-only with combined regimens and were unable to compare different types (synthetic vs body-identical hormones). Of note, meta-analysis of observational study data revealed a lower risk in transdermal vs oral users. RCTs are needed to explore CV outcomes in women who initiate body-identical hormone replacement therapy during the menopause	more detail on the discussion regarding the use of HRT of cardiovascular prevention). NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				transition, and a MA that stratifies benefit in younger women according to HRT regimen and type would enable clinicians to offer more personalised advice when counselling women considering HRT. CHD is the second most common cause of death in women in the UK. When combined with stroke, CVD is the leading cause of female death (1 in 6 women in the UK die from CVD, compared with 1 in 27 women who die from breast cancer). The United States Preventive Services Task Force doesn't currently recommend that HRT should be used to prevent chronic disease other than osteoporosis (JAMA. 2022;328(17):1740-1746. doi:10.1001/jama.2022.18625). Many menopause specialists do not agree with this view because there is accumulating and compelling high-quality evidence that HRT has multiple long-term mental and physical health benefits when initiated in midlife (Glynne S, Newson L, Reisel D. Hormone Therapy for the Prevention of Chronic Conditions in Postmenopausal Persons. JAMA. 2023;329(11):940–941. doi:10.1001/jama.2023.0180). It is essential that both clinicians and women have access to balanced information about both the risks and benefits of HRT, including the impact of type and timing, to facilitate effective shared decision making and enable women to make informed treatment choices, in line with the NICE shared decision-making guideline (CG197).	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Claire Mellon & Associates	Evidence review D	General	General	Tables 1 and 2 state that there is a duration dependent increase in breast cancer risk associated with both combined and oestrogen-only HRT. This conclusion is based largely on a meta-analysis of 24 prospective, observational studies published in the Lancet in 2019. The largest observational study included in the meta-analysis is the widely criticised Million Women Study (MWS), which contributed 40% of the pooled data. The MWS has many flaws, but the major ones include: 1. Women were recruited from a breast cancer screening clinic. Women attending for screening are not representative of women in the general population; they are more likely to be breast aware, have enhanced anxiety about breast cancer risk (for example due to a positive family history), and be diagnosed with breast cancer (surveillance bias). Selection bias is likely to account for the higher incidence of breast cancer in the study cohort at baseline compared with the general population and may account for the higher incidence of breast cancer	Thank you for your comment. The Million Women Study (MWS) was a large contributor to the data in the Lancet 2019 meta-analysis (referenced as CGHFBC 2019 in Evidence Review D). However, CGHFBC 2019 describes that there was large consistency across the main findings between the MWS and the other included studies, therefore any exclusions would not have altered conclusions. It is correct that observational studies are subject to more bias than randomised controlled trials (RCTs) however, this is likely to be true of all observational studies. With regard to the point made on tumours already present at the start of the MWS, the analysis of the MWS excluded women who had a record of breast cancer before recruitment. All the women who were recruited had a routine screening at entry into the study, therefore any pre-existing disease could have been detected at this stage. There may have been some women who were recruited who had undiagnosed, or pre-clinical breast cancer but this would also be an issue for other observational studies, and also some RCTs. You raise concerns regarding the inclusion of retrospective studies, namely the CPRD, into the CGHFBC 2019 meta-analysis of prospective studies. The CPRD is a database, and the data from this dataset was included in the CGHFBC 2019 meta-analysis. The authors define the studies as prospective if the information on hormonal therapy use was recorded before the diagnosis of breast cancer was known. Therefore, any recall bias, which would be the concern with retrospective studies, was not an issue with these

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				during the study interval in the HRT group. 2. Women attending a breast cancer screening are more likely to use HRT – a source of confounding bias. 3. The average time from enrolment to breast cancer diagnosis was 1.2 years, and the mean time from study enrolment to breast cancer death was only 1.7 years. Given that breast cancer takes 5 to 15 years to develop it is very likely that the tumours were already present at the start of the study and were not related to HRT use (biologically implausible). 4. Further, the small increase in breast cancer risk was only identified in current users, but not past users - even if past use had exceeded 15 years (biologically implausible). The second largest observational study included in the meta-analysis is not actually a prospective study. The CPRD study was a retrospective case-control study. Retrospective studies are even more prone to bias and confounding than prospective studies. Electronic health records may be incomplete (missing data, mis-coded data etc), and women presenting with breast lumps/	studies. The committee discussed that all observational studies are subject to bias by confounders. They specified in the protocol that studies would only be included if they made adjustments for confounders. Whilst they did not list all the confounders that needed to be adjusted for, they discussed whether studies had made appropriate adjustments when discussing the evidence. The committee also discussed the issue regarding residual confounding, which is a bias that remains due to not adjusting for unknown confounders or factors that are difficult to adjust for. The committee discussed that the likely impact of confounding on any given association will vary depending on the strength of the association of potential confounders with both HRT and the outcome of interest. They discussed that for breast cancer, residual confounding was less of a concern than might be for outcomes related to cardiovascular disease for example. This is discussed in more detail in the committee's discussion of the evidence section of Evidence Review D. Other limitations to observational studies you describe are limitations subject to all observational studies and not specific to the CGHFBC 2019 meta-analysis. The committee discussed the pros and cons of the different study designs and considered that observational studies are subject to bias, such as the biases you mention in your comment (surveillance bias, selection bias, confounding bias). They also discussed that observational studies can be useful, in that they can include large sample sizes and so are powered to detect rare outcomes, such as breast cancer or

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				concerns/ risk factors for breast cancer are more likely to be asked about a history of HRT use and/or have data regarding HRT use recorded (information or measurement bias). It is not clear why this study has been included in a meta-analysis of prospective studies, but it has contributed approximately 30% of the pooled data. Observational study data cannot give detailed information about HRT type, route, cross-over, or adherence. Further, observational study data cannot be used to prove a causal relationship between an exposure (HRT) and an outcome (breast cancer) because it is not possible to fully adjust for confounding factors – only those that are known and measured can be adjusted for, which vary from study to study. It is particularly difficult to avoid bias in studies when the period of exposure (HRT use) overlaps with the period of risk (breast cancer incidence). The finding that breast cancer risk was only elevated in lean HRT users, but not in obese women using HRT, confirms that the data is likely to be flawed because obesity is a well-recognised risk factor for breast cancer. All the factors listed above may account for the small increase in breast cancer incidence in HRT users including women using oestrogen-only HRT in observational studies. The WHI randomised controlled trial reported a 23% lower incidence of breast cancer and 40% reduced risk of breast cancer death in women	mortality. Observational studies often have longer follow-up periods than RCTs. The committee also discussed that RCTs can be limited if the results are not generalisable to the population specified in the review question. They discussed that this is one of the limitations of the WHI findings because the mean age of women in the trial was 63, which is post-menopausal. They discussed that the observational data in this review was more generalisable to menopausal women as the mean age across the data was 50, therefore more reflective of the population in the review protocol. The committee's discussion of the evidence section also describes the discussion the committee had regarding obesity and the findings in the evidence regarding this topic, in relation to breast cancer. The concerns raised in your comment regarding the population included in the RCT evidence have been considered by the committee. RCT data has not been excluded from Evidence Review, however, given the inconsistency in the findings between RCT and observational data, the committee discussed the limitations of all the evidence and made recommendations considering these limitations. The committee reconsidered the wording of the recommendation relevant to the risk of breast cancer following oestrogen-only HRT, to now reflect the data from both the RCT and observational evidence. The details of the discussion have been updated and can be found in the committee's discussion of the evidence section in Evidence Review D. The evidence review does consider data from the E3N. Some of the participants of the E3N cohort have been

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				using oestrogen-only HRT (CEE), and a small increase in risk in combined HRT users (CEE+MPA, nominal HR 1.26, 95% CI 1.00-1.59), but no increased risk of breast cancer death after 20 years of follow up. In a recent review, Bluming et al question whether the increased incidence in CEE+MPA users was true; the small increase in risk failed to reach statistical significance after per protocol adjustment for confounders (adjusted HR 1.26, 95% CI 0.83-1.92), and a lower than expected incidence of breast cancer in the placebo group may have accounted for the apparent increase in risk in the combined HRT group (Bluming, Hodis and Langer, Menopause, 2023). If HRT causes breast cancer, a higher incidence might have been expected in the HRT arm of the WHI because the women were older (average age 63) and had cardiovascular risk factors (e.g., 70% were overweight or obese, half the women were past or current smokers), which are also associated with an increased risk of breast cancer - the 'common soil' hypothesis. An absolute increase in breast cancer incidence will be greater if a hazard ratio x1.26 is applied to a higher background incidence. However, an additional 0.8 cases per 1000 women using HRT per year is a 'rare' adverse event, and casts further doubt as to whether the original claims of the WHI investigators were valid. In the CGHFBC paper, the authors included a meta-analysis of RCT evidence and found that when the WHI data was excluded from the	included in the IPD dataset from the CGHFBC, which has been included in our review. The team has considered that not all participants of the E3N have been included in the CGHFBC 2019 meta-analysis. However, where there are separate publications with overlapping follow-up periods and no disaggregation of participants, those have not been included to avoid double counting of participants in the E3N cohort. As per our processes and methods, we do not reanalyse any existing IPD data as NICE does not generally have the same access to the individual participant data, and therefore the data has been used as it has been published. Due to the large size of the IPD data from the CGHFBC, this was prioritised for inclusion in the review. Fournier 2014 was included as this study had a later follow-up period of the E3N cohort that was not covered by CGHFBC. However, since the data from the Fournier 2014 publication did include participants that were in the meta-analysis from CGHFBC, the results were analysed separately. The committee considered that the number of cases of breast cancer with those using micronised progesterone were few, and agreed that this supported a recommendation to highlight that there was insufficient evidence to support any differences in the risk of breast cancer with micronised progesterone. The committee agreed that more evidence was required to make any robust recommendations for micronised progesterone and made a research recommendation. The reference you refer to 'Stute 2018' has been checked and the included studies also checked for inclusion against the protocol. Some of the

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				meta-analysis, there was no statistically significant increase in breast cancer risk in combined HRT users (RR 1.14, 95% CI 0.78-1.65). None of the RCT data (neither the WHI study nor the CGHFBC RCT meta-analysis) has been used to inform Evidence Review D. Finally, the CGHFBC Lancet meta-analysis failed to emphasise that the increase in breast cancer risk was observed only in women using synthetic progestins. Only 49 of 108,647 incident cases of breast cancer occurred in women using body-identical micronised progesterone (MP) – too few to infer an association – hence women using MP were excluded from the main analysis. The CGHFBC authors have included the MP data in the supplementary material and reported a 2.05-fold increased risk of breast cancer in women who used MP for 5-14 years, based on just 38 cases. This is the data that NICE have used to inform their opinion that "there is insufficient evidence to suggest that micronised progesterone is associated with a lower risk of breast cancer versus synthetic progestogens". NICE has failed to consider data from the E3N cohort study, which demonstrated no increased risk of breast cancer in women who used MP for up to 5 years. In 2018, a systematic review confirmed that short-term MP use is not associated with an increased risk of breast cancer (Stute P, Wildt L, Neulen J, Climacteric, 2018), but this data has also been excluded from the NICE evidence review.	studies looking at breast cancer incidence and HRT use are not eligible for inclusion in the review because they do not meet the date limit in the protocol, or the cohorts have already been included in the review. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added to the forest plots alongside each other where possible so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				In summary, it is concerning that NICE has relied so heavily on the results of the CGHFBC meta-analysis given that it is based on observational study data - mainly the MWS and a retrospective case control study which together account for more than two thirds of the pooled data. Indeed, the MWS has been referenced twice - both directly (it is one of the 6 reviewed studies) and indirectly (via its inclusion in the meta-analysis). Observational studies can only demonstrate association, not causation. The RCT data is not perfect and may not be wholly generalisable to the target population (neither is the MWS study because women were recruited from a breast cancer screening clinic), but it is of higher quality than the observational study data and should not be excluded from the evidence review. It is also essential that the progesterone data should be included in the review because the available evidence consistently demonstrates that MP is not associated with an increased breast cancer risk when used for up to 5 years. Long-term use may or may not be associated with an increase in risk; in the E3N study breast cancer risk was increased in women who used MP for more than 5 years, but 57% of women in the E3N also used a progestin (Fournier et al, 2014). More research is needed to assess breast cancer outcomes in long-term MP users.	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Claire Mellon & Associates	Evidence review G	General	General	Tables 1 and 2 state that combined HRT may increase the risk of dementia if started over the age of 65 (an additional 9 cases per 1000 women per 4 years when HRT is initiated over the age of 65), and oestrogen-only HRT is unlikely to increase the risk of dementia. To reach this conclusion the committee has reviewed 7 studies. The experts have acknowledged that the observational data is limited and conflicting and have focussed their review mainly on the recent Danish retrospective case control study published by Pourhadi et al in the BMJ, and the WHIMS study. The WHIMS study reported an increased risk of dementia in women who initiated combined HRT aged > 65 years (40 of 2229 cases in the hormone therapy group vs 21 of 2303 cases in the placebo group, HR 2.05, 95% CI 1.21-3.48). 50% of the women were aged over 70 years when they started HRT; 18% were over 75 years. The increase in risk began to emerge a year after randomisation. It is implausible that HRT taken for less than a year can cause dementia. Women in the WHI/WHIMS had multiple risk factors for cardiovascular disease (and therefore dementia) - 70% were overweight, around 50% were smokers, 35% had hypertension - and it is likely that these women would have developed dementia irrespective of treatment allocation because dementia is common in elderly women, and they were already at high	Thank you for your comment. Since the WHIMS is an RCT, any other risk factors present as you mention (cardiovascular disease, overweight, smoking, hypertension) would be an issue in both groups, HRT users and non-users. Therefore, any increase in the risk of dementia due to factors other than HRT use would also be present in the control group. A difference of 19 cases was seen in the WHIMS study, which is an RCT. Any reference to confounding in Evidence Review G would only apply to observational studies as randomised controlled trials are not subject to bias for confounding. Randomisation of participants into the experimental and control arms would mean the prevalence of the factors you have listed are balanced between the two groups. The baseline differences from the WHIMS study are balanced, therefore there are no concerns that the randomisation was inadequate. The committee discussed that the population from the WHI/WHIMS study were an older group and that women usually initiate HRT at a much younger age. Therefore, they agreed that it was important the recommendation was specific to the age group of the population in the WHIMS study and specified that the risk might be increased if HRT was started after 65 years old. The committee have not made a recommendation advising of the risk of dementia if HRT is started at 50 years old, as they were not comfortable that the evidence base supported a recommendation. This is discussed in the committee's discussion of the evidence section in Evidence Review G. Cognitive function was not an outcome in the pre-specified protocol, therefore the committee

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				risk. The authors failed to adjust for the high number of confounding variables, including factors known to specifically increase dementia risk such as family history and ApoE4 status, and acknowledged that the wide confidence interval may therefore exclude 1 by chance alone. This may account for the higher incidence of dementia in the HRT group, especially as the difference between the two groups was small (just 19 cases). Older women > 65 years with probable subclinical cardiovascular disease and/or neuropathology are not representative of the target population. Most women initiate HRT during or soon after the menopause transition when the risk benefit profile is very different. In the WHIMS-Y study no adverse effect on cognitive function was observed in women who initiated CEE +/- MPA aged 50 to 55 years. Further, Manson and colleagues found that there was no increased risk of dementia death in women in the WHI who used CEE +/- MPA for 5-7 years after 18 years of cumulative follow up (suggesting that the 'risk' is negligible). Pourhadi et al reported a duration-dependent increase in dementia risk in HRT users in a retrospective case-control study. As discussed above, observational studies cannot prove causality, they can only demonstrate association. Risk factors for dementia were not evenly distributed between the two groups (cases had lower education, lower income, and	cannot make any reference or conclusions regarding this outcome. Thank you for providing references to editorials describing the issues pertaining to confounding. The committee discussed that confounding in observational studies can lead to bias in the results. They also discussed the confounders in Pourhadi 2023 and Vinogradova 2021. Since the data were conflicting, they agreed that confounding may have led to bias, but they were unable to comment in which direction there may have been bias. As a result of this, the committee decided to base their recommendations on the evidence from the WHIMS study, which is an RCT and not subject to bias. This discussion is recorded in the committee's discussion of the evidence section in Evidence Review G. Thank you for highlighting Nerattini et al 2023. This systematic review was not included in Evidence Review G as it was published after the cut-off date. Some of the studies in this systematic review do not meet our protocol criteria which specifies that data on HRT should be separated into oestrogen-only and combined HRT, therefore this systematic review would not have been included as a whole. The individual studies were also checked against our protocol criteria, and of the ones that met the protocol criteria, these have already been included in the review. Most of the studies that do not meet the protocol criteria have already been listed in our excluded studies list in the Evidence Review.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				were more likely to be hypertensive, diabetic and/or have thyroid disease). The differences were small, but the combined effect may have confounded the results. Further possible sources of confounding were discussed in a linked Editorial written by Kantarci and Manson (BMJ 2023;381:p1404). In summary: 1. HRT use is a confounding variable. For example, oestrogen deficiency causes vasomotor symptoms, insomnia, and weight gain, and is associated with adverse metabolic effects (dyslipidaemia, insulin resistance, hypertension), which all increase CV and dementia risk. Women experiencing menopausal symptoms are also more likely to use HRT. 2. HRT users seek more frequent medical attention and are likely to be diagnosed with dementia earlier than women not using HRT/ infrequent attenders. 3. Following the publication of the WHIMS study in 2003, women and their clinicians may have been more vigilant for symptoms of cognitive decline in HRT users. Multiple sources of confounding and bias may account for the small increase in dementia risk observed in women who used HRT for less than a year (biologically implausible), and the inconsistent findings in relation to HRT and risk of Alzheimer's disease (AD); AD risk was	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				not increased in women who used HRT for < 1 yr or 4-8 years, but it was increased in women who used HRT for 1-4 years of > 12 years. Kantarci and Manson conclude that 'the observed associations could be artefactual and should not be used to infer a causal relationship between hormone therapy and dementia risk', and 'these findings cannot inform shared decision making about use of hormone therapy for menopausal symptoms'. Almost all of the data pertaining to dementia risk relates to women using oral oestrogen with or without a synthetic progestin (In the WHIMS study all women received CEE + MPA; in the Pourhadi study 100% of women used oral oestrogen and 90% used a synthetic progestin). Unlike transdermal oestradiol, oral oestrogen is associated with proinflammatory changes and deleterious effects on blood pressure, blood lipids, and coagulation factors. Unlike body-identical progesterone, progestins increase oestrogen-associated risk of thrombosis and counteract oestrogens beneficial cardiometabolic effects. Only two observational studies have stratified dementia risk by HRT type. In a UK-based case-control study Vinogradova and colleagues reported an association between long-term HRT use (> 5 years) and Alzheimer's dementia, but not for women using dydrogesterone (a 'body-similar' progestogen), or for women using oestrogen alone. Similarly, in a retrospective claims-based analysis Kim et al reported a reduced risk of neurodegenerative diseases including	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				dementia and AD in HRT users (RR 0.42, 0.40-0.43). The greatest risk reductions were observed in women using transdermal 17β-oestradiol, especially when combined with progesterone (RR 0.19, 0.15-0.23). Both studies were observational and retrospective, and therefore flawed, but their findings are consistent with experimental data demonstrating anti-inflammatory and neuroprotective effects of sex steroid hormones, as well as biomarker and neuroimaging studies that have mapped changes in brain structure and function across the menopause transition in association with falling levels of oestrogen (such as the work of Lisa Mosconi and her colleagues in the States). In October a systematic review and meta-analysis was published in Frontiers in Ageing and Neuroscience (Nerattini et al, 2023). The authors pooled data from 6 RCTs (> 40,000 participants) and 45 observational studies (6 million women; 768,866 cases and 5.5 million controls) and reported a 32% lower risk of dementia in women who started oestrogen-only therapy in midlife (RR 0.685, 95% CI 0.513-0.915). Combined HRT was also associated with a 23% lower risk, but the trend failed to reach statistical significance (RR 0.775, 95% CI 0.474-1.266). In keeping with previous reports, oestrogen-only therapy had a neutral effect when started more than 10 years after the menopause, and later use of combined HRT was associated with a non-	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				significant increase in risk that was largely linked to the use of synthetic progestins. To date, the meta-analysis published by Nerattini et al is the most comprehensive, in-depth analysis of dementia outcomes in HRT users. Its findings are biologically plausible and consistent with the timing hypothesis (see above). However, it has not been included in the NICE evidence review. Women can be informed that there may be a potential risk, but women should also be advised that there is potential benefit and overall, the evidence suggests that HRT may decrease – or at least not increase – the risk of dementia when initiated in mid-life. The risk is likely to be lower in women who use body-identical hormones. Alzheimer's disease is the leading cause of death in females in the UK, women are twice as likely to develop AD as men, and currently there is no cure. Advising clinicians 'not to offer HRT for dementia prevention' (draft guideline, page 22) because there may be a small increase in risk in older women who use synthetic hormones fails to consider the best available evidence or the needs and preferences of the individual. Women, especially those with non-modifiable risk factors such as the ApoE4 mutation, need balanced information about both the risks and benefits to enable them to make an informed treatment choice.	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Further research that includes perimenopausal women and focuses on outcomes in women using 17β-oestradiol and progesterone initiated close to menopause is urgently needed.	
Claire Mellon & Associates	Evidence Review H	General	General	NICE have stated that overall, taking either oestrogen-only or combined HRT is unlikely to increase or decrease life expectancy. It is true that evidence has consistently demonstrated a neutral effect on all-cause mortality among all women who use HRT (mainly oral oestrogen and synthetic progestins). However, studies that have enrolled younger women initiating HRT closer to menopause have overall demonstrated benefit. To examine the effect of combined HRT on all-cause mortality in younger women (aged 50-59), NICE has pooled data from 4 RCTs and reported a hazard ratio of 0.96 (0.82-1.12) (Fig 4). Two of the included RCTs were very small; Nachtigall et al reported a HR of 0.41 (0.10-1.63) based on 3 deaths among 84 women randomised to HRT vs 7 deaths among 84 women assigned to placebo, and Komulainen et al reported 2 deaths among 115 HRT users vs 1 death among 115 controls (HR 1.97, 0.18-21.92). Given the low event rates, it is arguable whether these studies should be included in a MA of just 4 RCTs. In the much larger WHI trial, all-cause mortality was reduced in women aged 50-59 years treated with CEE+MPA for 5.6 years (HR 0.67, 0.43-	Thank you for your comment. Regarding the inclusion of low events in the meta-analysis of 4 RCTs to show the effect of combined HRT use on all-cause mortality, in those starting HRT at 50-59 (as shown in figure 4); studies were not excluded based on a number of events. The studies included in this review were included or excluded based on the pre-specified criteria set out in the review protocol which can be found in Appendix A of Evidence Review H. Therefore, the studies you specify cannot be excluded for the reason you provide. The meta-analysis takes into account the sample size of the study and this impacts the weighting that each study has on the overall combined effect estimate. The forest plots in Appendix E show the weighting of the studies for each meta-analysis. The studies you referenced, Nachtigall and Komulainen, each have a weighting of 1.3% and 0.4%, respectively, for the meta-analysis relevant for the subgroup 50-59 in combined HRT users and therefore already contribute very little to the overall combined effect estimate. The WHI trial result you highlight, HR 0.67 (0.43 to 1.04) is not statistically significant therefore the conclusion that all-cause mortality is reduced cannot be made. This point also stands for other non-significant results you have listed in your comment. The committee did not make recommendations on trends in the data. The hazard ratios relating to all-cause mortality across

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				1.04). The benefit persisted but was not statistically significant in the postintervention phase, presumably because benefits associated with HRT diminish if treatment is discontinued. NICE have used the hazard ratio relating to all-cause mortality across 18-years of cumulative follow up (HR 0.97, 0.83-1.13), but women received HRT for less than a third of this time. Data pertaining to oestrogen only therapy is similarly limited. Event rates were generally low, and the benefits of oestrogen diminish over time after treatment completion (women in the WHI were treated with CEE-alone for 7.2 years but mortality data includes the 10.8-year postintervention phase). The finding of a null effect in younger women is inconsistent with the results of the DOPS study - the only RCT to assess outcomes in women who initiated HRT close to menopause. In DOPS, all-cause mortality was reduced by 43% in women who used combined HRT for 10 years. The finding of a null effect in younger women is inconsistent with the results of a 2004 meta-analysis of 30 RCTs that reported a 39% lower risk of death in younger women using HRT (OR 0.61, 0.39-0.95, Salpeter et al, 2004). Because RCT evidence in younger women is limited, the authors published an updated MA in 2009. The results of 19 RCTs were pooled with 8 prospective observational studies and	18-years of cumulative follow-up were included in this review, as a longer follow-up period for the outcome of mortality is preferred as it allows time for the events to occur. It would be inappropriate to exclude the interventional period as this would be cherry-picking the data. The DOPS study (referenced Schierbeck 2012 in Evidence Review H) was not included in our review as it did not distinguish between oestrogen-only HRT and combined HRT, which were criteria set out in the pre-specified protocol. Thank you for highlighting the Salpeter 2004 and 2009 systematic reviews that are excluded from the review. The systematic reviews were excluded as per the reasons provided in Appendix J, individual studies were checked for relevance, and where they met the review protocol criteria, they were included in the review. The inclusion of systematic reviews in Evidence Review H was for the sole purpose of aiding with data extraction and risk of bias assessment. The individual RCT data was re-analysed in Evidence Review H. This has been outlined in the effectiveness evidence section of Evidence Report H. You note that other systematic reviews pooled RCT and observational data together. This approach was not taken in Evidence Review H as the study design inclusion criteria set out in the protocol limited this review to RCT studies only, therefore the committee are unable to comment on any analysis including observational evidence. For clarification, the reason for the committee limiting the study designs to RCT evidence only has now been added to Evidence Report H (see the effectiveness evidence section, included studies).

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				the results confirmed a 28% reduction in mortality in young HRT users. Both the 2004 and 2009 MA have been excluded from Evidence Review H on the grounds that more recent systematic review evidence is available (Nudy et al, 2019, and Kim et al, 2020). However, only 7 of 31 RCTs included in the former, and 8 of 26 RCTs included in the latter, were published after 2004, and the results of later analyses may underestimate benefit – this is discussed further below. The finding of a null effect in younger women is inconsistent with the results of a Cochrane review published in 2015. Boardman et al reviewed 19 RCTs published between 1979 and 2012 and reported a 30% reduction in all-cause mortality in younger women starting HRT within 10 years of the menopause (RR 0.70, 0.52-0.95). Their finding is consistent with the risk reduction reported by Salpeter et al. No reason has been given for excluding the Cochrane review from Evidence Review H. The finding of a null effect in younger women is inconsistent with the MA published by Nudy et al that was included in Evidence Review H. Nudy et al pooled data from 31 RCTs and reported a null effect overall, but reduced mortality in younger women with a mean age of 54.5 years: 2.2% in the HRT group vs 3.2% in the control group, OR 0.72 (0.57-0.91). The authors concluded that HRT may have beneficial effects on mortality (and CVD events) in younger menopausal women.	Thank you for highlighting the Boardman 2015 Cochrane review. The data from this systematic review could not be directly used as the analysis did not separate oestrogen-only HRT users from combined HRT users, as was the criteria set out in the review protocol. The Boardman 2015 review was not initially in the excluded studies section of Evidence Review H as the primary focus was on cardiovascular disease (it has already been listed in the review focused on cardiovascular disease, Evidence Review C). However, it has now been added to the excluded studies section of Evidence Review H for clarity. All the individual RCTs included in the review were checked for relevance, and the relevant studies were included in the review. With regard to the point made for a beneficial effect of HRT on mortality in younger women, you mention data from observational studies and as mentioned above this study design was excluded from this review. You also mention that the data in this review includes a post-intervention period from the WHI, and this could be a reason why the benefits of HRT on mortality are not seen. Again, as mentioned above the longer follow-up periods are preferred for mortality to allow for the outcome to take place. The data presented in this review does not support a beneficial effect of HRT on mortality in younger women.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				The only analysis that has reported a null effect in younger women is the MA published by Kim et al in 2020. However, a non-significant trend for lower mortality was observed in younger women (SE 0.78, 95% CI 0.57-1.07 when started early vs 1.00, 95% CI 0.96-1.04 when started later). A separate analysis of prospective observational study data confirmed benefit in younger but not older women (SE 0.68, 0.51-0.92 vs SE 0.94, 0.73-1.21 respectively). In contrast to earlier meta-analyses, which included data from the intervention phase of the WHI, Kim et al – like NICE - have cited a more recent analysis and included data from 18 years of cumulative follow-up (Manson et al, 2017). It is possible that the summary estimate based on 4 RCTs failed to reach significance because benefit in the WHI was diluted in the postintervention phase, when women no longer received HRT. It is concerning that NICE has based its opinion mainly on RCT data that is likely to underestimate benefit in younger women (because WHI data, which dominates the analysis, includes a 12-year postintervention phase when women randomised to HRT didn't receive HRT), and has failed to emphasise the importance of type and timing. Most of the women enrolled in RCTs were older with risk factors for chronic disease and/or established CVD, and mainly used oral oestrogen with or without a progestin. RCT data that specifically	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				evaluates outcomes in younger women using HRT is limited, but overall suggests benefit. Observational studies have enrolled younger, relatively healthier women who are more representative of the target population and have consistently demonstrated benefit. Data obtained in observational studies should not be excluded from an evidence review aimed largely at younger women, for whom relevant RCT data is lacking.	
Claire Mellon & Associates	Guideline	011	007	To my knowledge there have been no head-to-head trials comparing HRT with CBT. CBT is relatively expensive, time-consuming, and not widely available because the NHS has limited resources. Many women, especially those from ethnic minority groups, are likely to have difficulty accessing CBT. Further, unlike HRT, the benefits of CBT are limited to vasomotor and mood symptoms, and CBT does not reduce the risk of chronic diseases such as osteoporosis, diabetes, cardiovascular disease, and dementia (please refer to my comments below). Menopause guidelines agree that HRT is the most effective treatment for symptoms due to hormone deficiency and has long-term health benefits. It is therefore likely to be the most cost-effective option in the long-term. CBT can be a useful treatment option for some women, especially those who choose not to have HRT, or can't have it because the risks outweigh the benefits. But when making a	Thank you for your comment. The committee has revised the wording to ensure clarity about CBT 'as an option: in addition to other treatments (including HRT), for people for whom other treatments are contraindicated or for people who prefer not to take HRT'. Your comment will be considered by NICE where relevant support activity is being planned. The 2015 recommendation to offer HRT for vasomotor symptoms has not changed and the guideline is advocating a person-centred approach tailoring the information about benefits and risks of HRT 'to the person's age, individual circumstances and potential risk factors'. The effects of HRT on specific health outcomes is the topic of section 1.6.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				treatment decision, women should be aware that HRT using body-identical hormones is the gold-standard treatment for menopausal symptoms.	
Diabetes UK	Guideline	012	019 - 021	Although section 1.4.10 is highlighted in grey, the final scope document states there will be updates to the existing recommendations as needed. We know that the menopause can affect diabetes. A fall in the levels of hormones including oestrogen and progesterone during menopause has an effect on blood sugar levels which makes managing diabetes more difficult. We would recommend that type 1 diabetes is also included within this guideline to improve the support for people living with diabetes who are experiencing the menopause. Workshops conducted by Diabetes UK highlighted that people living with diabetes are not receiving the support they need to manage this change in their condition. Greater awareness of the effects the menopause has on diabetes is needed, particularly for the health care professionals supporting these patients. We would therefore recommend that there is direct reference to NG17 into the recommended reference to type 1 diabetes, and direct reference to NG28 in section 1.4.10 on type 2 diabetes. In addition, it should be highlighted that continuous glucose monitoring	Thank you for your comment. Whilst there are some new recommendations in this section, the general topic of comorbidities (including issues relating to type 2 diabetes mellitus) was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this. However, due to this and other feedback the cited references have been passed on to the NICE surveillance team which regularly checks evidence for guideline topics to see whether further updates are needed.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				and/or hybrid closed loop systems can be used to help manage these symptoms. Direct reference to this guideline in both NG17 and NG28 would also improve awareness and support further.	
Dr Louise Oliver Therapeutic Life Coaching	Guideline	014	005 - 006	The Icelandic sleep apnoea cohort study (4) showed nocturnal sweating can be related to OSA and can resolve with treatment. The conclusion of the study was: 'The prevalence of frequent nocturnal sweating was threefold higher in untreated OSA patients than in the general population and decreased to general population levels with successful positive airways pressure (PAP) therapy. Practitioners should consider the possibility of OSA in their patients who complain of nocturnal sweating' I therefore believe the NICE menopause guideline in the section discussing vasomotor symptoms should: - highlight the increase in sleep disordered breathing as women transition through to post-menopause and is associated with nocturnal sweating. - provide a link to NICE guideline NG202. - highlight OSAHS initial assessment questionnaires may not be accurate in women.	Thank you for your comment. The impact of other conditions on symptoms of the menopause is outside the scope of the 2024 guideline update. Evidence for this topic was not searched for, reviewed or discussed with the committee (this meant that the cited reference could not be included). The committee could therefore not comment on this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				(4) Arnardottir ES, Janson C, Bjornsdottir E, et al Nocturnal sweating—a common symptom of obstructive sleep apnoea: the Icelandic sleep apnoea cohort BMJ Open 2013;3:e002795. doi: 10.1136/bmjopen-2013-002795	
Dr Louise Oliver Therapeutic Life Coaching	Guideline	019	002 - 003	Studies have shown a steep rise in sleep disordered breathing as women transition from perimenopause to post menopause. A meta-analysis (1) states: 'Studies have shown that 47 to 67% of postmenopausal women have (obstructive sleep apnoea) OSA [54, 55]……..Dancey et al. reported the prevalence of apnea among women based on menopausal stages to be 47% in postmenopause, yet with a lower prevalence of 21% at the premenopause stage [33]. The study by Heinzer reported the prevalence of OSA at the postmenopause stage as 23%, and 9% at the premenopause stage, showing the higher prevalence of this disorder during postmenopause [56].' Women with sleep disordered breathing are less likely to report snoring or witnessed gaps in breathing (apnoea) but are more likely to complain of daytime fatigue, lack of energy, insomnia, morning headaches, mood disturbance and nightmares compared to men (2)	Thank you for your comment. The outcome sleep disordered breathing for women in transition from perimenopause to postmenopause was not in the scope of the 2024 guideline update. The committee could therefore not comment on this. The references listed have been checked and none of them meet the criteria set out in the protocols for the evidence reviews that were updated.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				The NICE guideline NG202 'Obstructive sleep apnoea/hypopnoea syndrome (OSAHS) and obesity hypoventilation syndrome in over 16s' states on page 7 – 8: 'Take a sleep history and assess people for OSAHS if they have 2 or more of the following features: (1) snoring (2) witnessed apnoeas (3) unrefreshing sleep (4) waking headaches (5) unexplained excessive sleepiness, tiredness, or fatigue (6) nocturia (waking from sleep to urinate) (7) choking during sleep (8) sleep fragmentation or insomnia (9) cognitive dysfunction or memory impairment.' On page 56 of the NICE guideline NG202 it states 'Sensitivity is a priority for questionnaires used for initial assessment. The committee had some concerns about its accuracy in people with less common presentations and in women'. Furthermore, on page 98 it states 'OSAHS is a common, but frequently unrecognised cause of serious disability that has important health and social consequences…. These conditions can have a profound impact on people's lives, causing excessive sleepiness or sleep disturbance that affects social activities, work performance, the ability to drive safely and quality of life.	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Undiagnosed, these conditions are closely associated with serious health problems, including hypertension, diabetes, stroke, and heart disease, and can shorten life expectancy. High numbers of the population are affected by these conditions, and they are often undiagnosed'. In the JAMA 'Risk factors for OSA in adults' linking evidence and experience article (3) it stated: 'Comparison of the male to female ratio in OSA patient populations (8:1) and in undiagnosed OSA from populations studies (2:1) indicate that women with OSA are less likely to be evaluated and diagnosed. Furthermore, some data show poorer survival in female OSA patients, suggesting that OSA in women may be diagnosed late in the course of the disease or may not be aggressively treated.' This matches my clinical experience that women generally do not volunteer that they are snoring or have pauses in breathing whilst asleep unless they are specifically asked about their breathing pattern during asleep. I therefore believe the NICE menopause guideline in the section discussing sleep should: - highlight the increase in sleep disordered breathing as	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				women transition through to post-menopause. - include the recommendation to 'take a sleep history and assess people for OSAHS if they have 2 or more of the following features…' - provide a link to NICE guideline NG202. - highlight OSAHS initial assessment questionnaires may not be accurate in women. (1) Salari N, Hasheminezhad R, Hosseinian-Far A, Rasoulpoor S, Assefi M, Nankali S, Nankali A, Mohammadi M. Global prevalence of sleep disorders during menopause: a meta-analysis. Sleep Breath. 2023 Oct;27(5):1883-1897. doi: 10.1007/s11325-023-02793-5. Epub 2023 Mar 9. PMID: 36892796; PMCID: PMC9996569. (2) Saaresranta T, Anttalainen U, Polo O. Sleep disordered breathing: is it different for females? ERJ Open Res. 2015 Nov 3;1(2):00063-2015. doi: 10.1183/23120541.00063-2015. PMID: 27730159; PMCID: PMC5005124. (3) Young T, Skatrud J, Peppard PE. Risk factors for obstructive sleep apnea in adults. JAMA. 2004 Apr 28;291(16):2013-6. doi: 10.1001/jama.291.16.2013. PMID: 15113821.	
Epilepsy Action	Equality impact assessment	001		Section 2.1	Thank you for your comment. People with epilepsy are not excluded from this guideline. The

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				People with epilepsy are usually classed as disabled. This guideline excludes this group of people who are likely to be doubly impacted in terms of osteoporosis risk; quality of life if symptoms of menopause are not treated e.g. lack of sleep, stress etc can be an epilepsy seizure trigger.	committee agrees that people need to be heard and treated with dignity and respect, for example by taking their individual risk factors or triggers into account. Further details on treating people as individuals is covered in the NICE guideline on patient experience in adult NHS services as well as in the NICE guideline on shared decision-making so this information is not repeated in all other NICE guidelines (they are cross referred to in recommendations 1.1.1 and 1.1.2). Due to this and other stakeholder comments, the recommendation relating to experiencing menopause at an earlier age has been updated to say that people with lifelong medical conditions may also experience menopause at an earlier age. Another recommendation related to discussions about CBT has also been revised to include that peoples' preferences and needs should be taken into account. There is an emphasis throughout the guideline on tailoring information to the individual, for example it is emphasised that information about benefits and risks needs to be individualised to the person's age, individual circumstances and potential risk factors. There are also recommendations that highlight that a family member or carer can be involved. Making reasonable adjustments as required by the Equality Act 2010 is a statutory requirement and so this would not need to be repeated in each individual NICE guideline. This would include adjustments for people with disabilities such as people with epilepsy. The Equalities Impact Assessment has been reviewed and further

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					points have been included in the section on disabilities to emphasise the person-centred approach that the committee has taken which they felt would positively impact these groups.
Epilepsy Action	Guideline			***1. Would it be challenging to implement of any of the draft recommendations? Please say why and for whom. Please include any suggestions that could help users overcome these challenges (for example, existing practical resources or national initiatives.*** The recommendations feature CBT quite heavily, mental health services are already overstretched, are there plans to increase practitioners in this area with an expertise in menopause, will consideration be given to waiting times and the impact this would have on people affected by the menopause and their quality of life. We know from our service users that there is a lack of awareness and knowledge amongst health professionals around the menopause and prescribing HRT, for fear of how it will impact on the epilepsy and interact with anti-seizure medications which then leads to people with epilepsy not receiving treatment for their menopause symptoms. A clear pathway is needed, and a programme of work to support delivery of the guidelines effectively with investment in training for health professionals not only in menopause but in epilepsy awareness and prescribing HRT.	Thank you for your comment. Your comment will be considered by NICE where relevant support activity is being planned. People with epilepsy are not excluded from this guideline and HRT is recommended for vasomotor symptoms. The potential relationship between epilepsy and menopause and how medication may interact with other treatments was outside the scope of the 2024 guideline update. The guideline recommends a person-centred approach to treatment where information and management plans are tailored to each individual and their specific risk factors. The Equality Impact Assessment form has been reviewed and the section on disabilities has been updated to emphasise this approach which the committee decided would have a positive impact on this population (including people with epilepsy).

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Epilepsy Action	Guideline			***2. Would implementation of any of the draft recommendations have significant cost implications?*** Having CBT available nationally for people affected by the menopause will be costly if it is to be delivered in a timely manner, especially given the challenges on mental health services currently. A national training programme for health professionals (GP's etc) could be costly, however if more understand epilepsy this could reduce the revolving door situation of people affected by epilepsy not being treated effectively for menopause symptoms and therefore reducing the burden on the health service longer term	Thank you for your comment. The committee and the previous economic evidence both highlighted that making CBT more widely available would lead to an increase in costs even when downstream costs were included although considered cost-effective. The team has added a sentence to the 'Cost-effectiveness and resource use' section of the guideline to reflect this. Training is outside of the scope of NICE guidelines and is the responsibility of academic institutions or Royal Colleges so the committee is unable to make recommendations in that area. Your comment will be considered by NICE where relevant support activity is being planned. The potential relationship between epilepsy and menopause was outside the scope of the 2024 guideline update and therefore the cost-effectiveness of treatment options related to this was not discussed. The guideline recommends a person-centred approach to treatment where management plans are tailored to each individual and their specific risk factors. The Equality Impact Assessment form has been reviewed and the section on disabilities has been updated to emphasise this approach which the committee decided would have a positive impact on this population (including people with epilepsy).
Epilepsy Action	Guideline	General	General	People with epilepsy are at higher risk of osteoporosis due to their epilepsy and the side effects of anti-seizure medication (ASM), if they are also at risk of poor bone health due to early menopause, this is a significant factor that adds weight to considering epilepsy and HRT on an individual basis.	Thank you for your comment. The impact of epilepsy or related medication on osteoporosis and its relationship with HRT treatment was not in the scope of the 2024 guideline update. The committee could therefore not comment on this. There is an osteoporosis guideline update in

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Hophing, L., Kyriakopoulos, P. and Bui, E. (2022) 'Chapter Seven - Sex and gender differences in epilepsy', in E. Moro et al. (eds) *International Review of Neurobiology*. Academic Press (Sex and Gender Differences in Neurological Disease), pp. 235–276. Available at: https://doi.org/10.1016/bs.irn.2022.06.012.	development so the cited reference has been passed on to this guideline for consideration.
Epilepsy Action	Guideline	General	General	Symptoms of perimenopause may also be missed if healthcare professionals are not looking for them earlier in people with epilepsy - the symptoms can easily be confused with symptoms of epilepsy and side effects of ASMs.	Thank you for your comment. Identifying or diagnosing the menopause and the symptoms of the menopause were not in the scope of the 2024 guideline update. This means that evidence for these topics was not searched for or systematically reviewed. The committee could therefore not comment on the relationship between epilepsy and symptoms of the perimenopause.
Epilepsy Action	Guideline	General	General	A key focus for NHS and people with more than one condition is shared decision making more. An individual should be informed and supported to manage the risks and benefits of treatments that consider the whole person. As the guidelines do not mention epilepsy, there is a lack of a clear pathway for those affected	Thank you for your comment. People with epilepsy are not excluded from this guideline, and need to be heard and treated with dignity and respect, for example by taking their individual risk factors or triggers into account. Further detail on treating people as individuals is covered in the NICE guideline on patient experience in adult NHS services as well as in the NICE guideline on shared decision-making so this information is not repeated in all other NICE guidelines (they are cross referred to in recommendations 1.1.1 and 1.1.2). There is an emphasis throughout the guideline on tailoring information to the individual, for example it is emphasised that information about benefits and risks needs to be

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					individualised to the person's age, individual circumstances and potential risk factors. There are also recommendations that highlight that a family member or carer can be involved. Making reasonable adjustments as required by the Equality Act 2010 is a statutory requirement and so this would not need to be repeated in each individual NICE guideline. This would include adjustments for people with disabilities such as people with epilepsy. The Equalities Impact Assessment has been reviewed and we have included further points in the section on disabilities to emphasise the person-centred approach that the committee has taken which they felt would positively impact these groups. The absolute numbers in the appendix were reviewed and used to produce a discussion aid document with visualisation of the data and verbal description aimed to facilitate shared decision-making between the person and the healthcare professional (including for people with epilepsy). This discussion aid has undergone user-testing and was refined based on user feedback.
Epilepsy Action	Guideline	General	General	Whilst the guideline acknowledges that research is lacking, we would suggest menopause and epilepsy does need to be a priority due to the impact of anti-seizure medication and some of the common symptoms of the menopause can have on seizures i.e. lack of sleep, memory issues etc Would healthcare professionals such as GP's benefit from a menopause and epilepsy toolkit to help with training and prescribing Epilepsy Action would be happy to support in the	Thank you for your comment. Identifying or diagnosing the menopause and the symptoms of the menopause, (as well as menopause as a potential trigger for seizures) were not in the scope of the 2024 guideline update. This means that evidence for these topics was not searched for or systematically reviewed. The committee could therefore not comment on the impact of anti-seizure medication and the impact of menopause symptoms on seizures.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				development of this with appropriate clinical input	
Epilepsy Action	Guideline	006	017	This should also refer to the impact of underlying medical conditions e.g epilepsy and associated medications e.g. anti seizure medication	Thank you for your comment. People with epilepsy are not excluded from this guideline. It is agreed that people need to be heard and treated with dignity and respect, for example, by considering their medication needs. Further details on treating people as individuals are covered in the the NICE guideline on patient experience in adult NHS services as well as in the NICE guideline on shared decision-making so this information is not repeated in all other NICE guidelines (they are cross-referred to in recommendations 1.1.1 and 1.1.2). There is an emphasis throughout the guideline on tailoring information to the individual, for example, it is emphasised that information about benefits and risks needs to be individualised to the person's age, individual circumstances and potential risk factors. There are also recommendations that highlight that a family member or carer can be involved. Making reasonable adjustments as required by the Equality Act 2010 is a statutory requirement and so this would not need to be repeated in each individual NICE guideline. This would include adjustments for people with disabilities such as people with epilepsy. The Equalities Impact Assessment has been reviewed and further points have been included in the section on disabilities to emphasise the person-centred approach that the committee has taken which they felt would positively impact these groups. The NICE guideline on learning disabilities and behaviour that challenges: service design and delivery as well as the NICE guideline

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					on autism spectrum disorder in adults: diagnosis and management contain sections on 'enabling person-centred care and support' and 'identifying the correct interventions and monitoring their use' respectively which outline the ways to get people with learning disabilities and neurodivergent people involved in decision making that is tailored to their needs. These apply to all other NICE guidance so this would not need to be repeated in each individual NICE guideline.
Epilepsy Action	Guideline	008 042	024 019	(1.3.3) This should also refer people with epilepsy.	Thank you for your comment. The committee made this recommendation related to time of menopause and potential differences by ethnic background based on their knowledge and experience. Prevalence of early menopause (including in different subgroups of people, for example with disabilities) was neither part of the original guideline nor part of the scope of the 2024 update. The committee agreed that knowledge of this could impact practice and have logged this with the NICE surveillance team so that relevant information can be identified which could inform future updates.
Epilepsy Action	Guideline	009	014 - 015	"Premature ovarian failure, characterized by undergoing menopause before 40 years (Burger et al., 2007), has been described in women with epilepsy with a higher incidence seen in women with a history of catamenial epilepsy (Klein, Serje, & Pezzullo, 2001). A correlation between higher seizure frequency and earlier age at onset of menopause has also been described (Harden et al., 2003). This is thought to be related to dysfunction of the hypothalamic-pituitary axis described in the previous section leading to poor maturation	Thank you for your comment. The committee made this recommendation related to time of menopause and potential differences by ethnic background based on their knowledge and experience. They reflected on this and decided based on consensus to add that people with lifelong medical conditions may also experience menopause at a younger age to this recommendation. However, the committee has also logged prevalence of menopause (including in different subgroups of people, for example with

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				and early loss of follicles (Harden & Pennell, 2013)."	epilepsy) with the NICE surveillance team so that this could be considered for future updates.
Epilepsy Action	Guideline	010	017	(1.4.2) Needs more clarity on if there are greater benefits of using transdermal over oral for people with epilepsy, especially if they are taking enzyme-inducing medicines. This is not covered in the 'effect on health outcomes' section.	Thank you for your comment. There was limited data on transdermal or oral HRT and the evidence did not divide this by pre-existing conditions such as epilepsy. The committee were therefore not able to comment on this.
Epilepsy Action	Guideline	012	019	We would suggest epilepsy should be included and associated comorbidities	Thank you for your comment. This is not a comprehensive section on any comorbidity that could be related to menopause because possibilities and combinations could be very high. There was no review question related to this section, but recommendations originated from discussions of the effects of HRT on specific health outcomes. It therefore covers these health outcomes only. The committee also felt that some issues related to epilepsy mentioned elsewhere, such as osteoporosis and menopause as a potential seizure trigger would be more relevant for an osteoporosis or epilepsy guideline rather than the menopause guideline. This and the related comments have been forwarded to the NICE surveillance team so that evidence can be considered for future updates.
Epilepsy Action	Guideline	029		Table 1 We would suggest epilepsy should be included due to the complexity of drug management aligned to the NICE guidelines	Thank you for your comment. This table summarises the effects of HRT on the listed health outcomes rather than other health outcomes that may mediate these effects, for example in relation to the medication that are used to treat them. This was not something that was considered in the 2024 guideline update. The committee could therefore not comment on this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Epilepsy Action	Guideline	034		Table 2 We would suggest epilepsy should be included due to the complexity of drug management aligned to the NICE guidelines	Thank you for your comment. This table summarises the effects of HRT on the listed health outcomes rather than other health outcomes that may mediate these effects, for example in relation to the medication that are used to treat them. This was not something that was considered in the 2024 guideline update. The committee could therefore not comment on this.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Evidence review A	General		Overwhelmingly the evidence suggests that CBT is not superior to TAU, or very low-quality evidence. This needs to be highlighted to otherwise it may be seen as misleading.	Thank you for your comment. The committee reflected on the wording of the recommendations related to CBT and revised them to ensure clarity about this 'as an option: in addition to other treatments (including HRT), for people for whom other treatments are contraindicated or for people who prefer not to take HRT'. This makes it clear that CBT is not seen as a first line treatment but as an option where this is a preferred choice. Discussions of the evidence base that lead to CBT recommendations as a treatment option has been captured in 'The committee's discussion and interpretation of the evidence' section of the evidence review in the 'the quality of the evidence' section. The rationale for recommending CBT as a treatment option has been made clearer in the guideline (see the rationale section for CBT and vasomotor symptoms, depressive symptoms and sleep problems).
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	006	019	The use of the word 'troublesome' here and elsewhere in the document. We feel that the language used in the guideline is subjective, and minimises women's experiences and is not truly representative of the women we see in clinic asking for HRT. Suggest more appropriate and reflective language of the	Thank you for your comment. Based on this and other feedback the committee reflected on this wording and consequently 'troublesome' has been removed from the guideline. NICE recognises and takes seriously the debilitating symptoms and the considerable concern and how these symptoms impact daily activities that

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				severity of symptoms experienced by women. There is no clear definition of what counts as "troublesome", and it is also valid to seek treatment to prevent e.g. GSM worsening.	people report. Whilst an update of the list of symptoms and experiences was outside the current scope of the 2024 guideline update (and therefore no evidence review was conducted), the NICE surveillance team checks regularly for new evidence for topics within guidelines to see where further work is needed. Apart from the removal of the word 'troublesome' the committee decided that without further evidence they could not comment on this.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	008	015	For many women, the earliest symptoms of perimenopause are of mood change. These symptoms overlap with, and tend to be worse in, women who have PMS/PMDD. This can be a reason to initiate HRT.	Thank you for your comment. Whilst an update of the list of symptoms and experiences (for the purposes of diagnosis and appropriate treatment) was outside the current scope of the 2024 guideline update and therefore no evidence review was conducted, the NICE surveillance team checks regularly for new evidence for topics within guidelines to see where further work is needed.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	009	017	FSH can be taken in those on high-dose progestogen at the time of their repeat injection, as per FSRH guidance (https://www.fsrh.org/documents/fsrh-guidance-contraception-for-women-aged-over-40-years-2017/)	Thank you for your comment. Identifying perimenopause and menopause was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee (and the cited reference did therefore not meet inclusion criteria). The committee could therefore not comment on this. However, we have logged this issue with the NICE surveillance team for consideration for future updates.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	010	027	Misleading sentence. There are no arbitrary limits or cut offs to use of HRT. As per BMS Menopause Practice Standards review should be annual and duration of HRT use tailored to individual need. (https://thebms.org.uk/wp-	Thank you for your comment. This has been rephrased to read 'discuss the possible duration of treatment at the outset', followed by 'rediscuss the benefits and risks or continuing treatment at every review'. This does not suggest arbitrary limits or cut offs.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				content/uploads/2022/12/BMS-Menopause-Practice-Standards-DEC2022-A.pdf)	
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	011	007	CBT. Patients/Public may have unrealistic views/expectations on being able to access CBT, especially in person, if they feel it is being recommended through NICE. CBT is not widely available and training very limited. HRT is more widely available, is safe and effective for most women, and from this guideline appears to be demoted to a second-line treatment option after CBT. We would support women being given choice over which treatment to try first, or whether to use both treatments in combination.	Thank you for your comment. The committee acknowledged in the impact section of the guideline that there are long waiting times for CBT. They also noted that people currently trained in providing this kind of therapy may not be familiar with menopause-specific CBT and training on this may incur costs and increase waiting times in the short term. However, online and group CBT may be easier and less costly to adapt to menopause-specific CBT. There are also resources available to train people in providing menopause-specific CBT (and could also inform the adaptation of online CBT), which could facilitate implementation. Your comment will be considered by NICE where relevant support activity is being planned. The section referred to in the comment is related to discussing CBT treatment rather than the symptoms for which it is recommended which are addressed in section 1.5 on symptom management. The wording in relation to discussing CBT treatment has been revised to ensure that information is provided about what CBT is (including menopause-specific CBT) and that preferences and needs should be taken into account. In section 1.5 on symptom management (evidence showed it to be effective in the management of vasomotor symptoms, depressive symptoms and sleep problems) wording has been revised to ensure clarity about CBT 'as an option: in addition to other treatments (including HRT), for people for whom other treatments are contraindicated or for people who prefer not to take HRT'.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	015	026	Non-hormonal vaginal moisturisers and lubricants can/**should** be used alongside topical vaginal oestrogen preparations- and not instead of – as this statement appears to indicate. This could be confusing.	Thank you for your comment. This recommendation was specifically related to people in whom vaginal oestrogen preparations are contraindicated or for people who would prefer not to use vaginal oestrogen. However, on reflection it was recognised that the order of recommendations could have led to confusion. The recommendation stating that vaginal oestrogen and non-hormonal moisturisers or lubricants can be used alone or in combination has therefore been moved up to a position before this recommendation to clarify this point.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	015	005	The use of the word "troublesome" here suggests women or AFAB individuals need wait until a certain level of symptoms occur before seeking help and starting treatment. As changes in the genitourinary tract are expected after menopause, and associated with changes in urinary function, sexual function and pelvic organ prolapse. We also know we see more lichen sclerosus, and other vulval dermatoses, in women with low oestrogen. The wording intimates that treatment should be withheld until a certain threshold is met, rather than encouraging practitioners to consider the role of vaginal oestrogen in all low risk women and enquiring actively about their wishes regarding sexual function, and responding quickly to early changes in continence, recurrent UTI, sexual function and so on.Treating proactively is also likely to have economic benefits due to the evidence supporting the role of vaginal oestrogen in prevention of recurrent UTI, improving continence and vaginal microbiome.	Thank you for your comment. The word 'troublesome' has been removed from the guideline. This clarifies that treatment should not be withheld until a threshold is reached. The committee recommended vaginal oestrogen for people with no history of breast cancer for genitourinary symptoms associated with the menopause.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	015	018	Vagifem was previously licenced at 25mcg estradiol dose and it is common to find women need a higher than licenced dose when using the newer, 10mcg products. Estring releases 7.5mcg estradiol daily. We find women commonly need higher doses of the newer 10mcg estradiol products and would like to see the guidelines reflect this and not seek referral routinely as the system is unlikely to be able to service this level of referral for this common issue.	Thank you for your comment. The committee reflected on this and decided that there was generally no clear consensus about the standard therapeutic range in relation to vaginal oestrogen. The committee therefore decided to remove this recommendation. The guideline contains recommendations about reviewing treatment and recommends that treatment for symptoms associated with the menopause should be reviewed at 3 months to assess efficacy and tolerability and annually thereafter, unless there are clinical indications for an earlier review (such as treatment ineffectiveness, side effects or adverse events). It is also recommended to 'refer people to a healthcare professional with expertise in menopause if treatments do not improve their menopause symptoms or they have ongoing side effects.' This means that if symptoms are not resolved after vaginal oestrogen is prescribed treatment is reviewed and other differential diagnoses could be considered.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	016	004	The guideline suggests considering ospemifene as an oral treatment option for troublesome genitourinary menopause symptoms, if locally applied treatments are impractical, for example, because of disability. It would be useful to also include other indications e.g. not tolerated, or for example phobia for vaginal insertion.	Thank you for your comment. The committee decided that the cost effectiveness evidence was not strong enough to make a wider recommendation. Additional discussion has been added to 'The committee's discussion and interpretation of the evidence' section to discuss this in more detail.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	016	011	The guideline suggests only commencing these safe, useful measures for GSM related to breast cancer if symptoms are "troublesome". Again, we know that this is a very common sequelae to breast cancer (and other cancer-induced menopause e.g. after	Thank you for your comment. The word 'troublesome' has been removed to clarify that non-hormonal moisturisers or lubricants are offered to all people with a personal history of breast cancer and genitourinary symptoms associated with the menopause. It is

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				gynae cancer) and many women suffer in silence. A proactive approach would be to recommend women are made aware of the prevalence of GSM in their cohort, and are given simple advice about vaginal moisturisers and emollients including considering their routine use. There is evidence to support the benefit of this, and also of massage/gentle vibration.	recommended in the section on 'information and support' that information should be shared about common symptoms (including genitourinary symptoms) to raise awareness about this. No evidence was identified about massage / vibration that met the inclusion criteria of the protocol and therefore the committee could not comment on this.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	016	019	Agree we have no RCT to support the use of vaginal oestrogen in this group of women, and probably never will. However, we have increasing amounts of observational data, and 'expert advice' to support its use. **We strongly feel that this guideline could go further to assure and support the use of topical vaginal oestrogen in this group who have significant morbidity and psychological/physical and relational impact due to GSM.** Cold S et al. Systemic or vaginal hormone therapy after early breast cancer: A Danish observational cohort study. *J Natl Cancer Inst* 2022 Jul 20; [e-pub]. (https://doi.org/10.1093/jnci/djac112. opens in new tab) and Cathcart-Rake EJ and Ruddy KJ. Vaginal estrogen therapy for the genitourinary symptoms of menopause: Caution or reassurance? *J Natl Cancer Inst* 2022 Jul 20; [e-pub]. (https://doi.org/10.1093/jnci/djac113. opens in new tab)	Thank you for your comment. This review does include observational studies, and the study by Cold et al you mention has been included in the study. The committee discussed the evidence and agreed that due to the limitations of the evidence they had to be cautious with recommendations. A detailed discussion can be found in the committee discussion of the evidence section in Evidence Review B2. The committee made changes to the order of recommendations so that considerations of adjuvant treatments are being made early in shared decision making. They also revised the recommendation related to safety considerations for clarity. This would give this section a more logical flow and greater clarity about safety. The rationale of the guideline and the committee discussion section of the evidence were revised accordingly. A visual summary was produces for the management of genitourinary symptoms to clarify treatment options and facilitate decision making. Thank you for highlighting the publication by Ruddy 2022. This paper does not meet the study

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					design criteria listed in the protocol for review B2 and cannot be included in the review, therefore the committee are unable to comment on it.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	018	003	Agree with this sentence, that moisturisers and lubricants can be used alongside topical vaginal oestrogens. This sentence is not in line however with the sentence p15 line 26 which implies they are to be used instead of.	Thank you for your comment. This recommendation was specifically related to people in whom vaginal oestrogen preparations are contraindicated or for people who would prefer not to use vaginal oestrogen. However, on reflection it was recognised that the order of recommendations could have led to confusion. The recommendation stating that vaginal oestrogen and non-hormonal moisturisers or lubricants can be used alone or in combination has therefore been moved up to a position before this recommendation to clarify this point.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	018	009	Use of language that could be stigmatised or alienating for women such as 'depressive/depression'. Many women will consider they have low mood or mood disturbance, and again this is a range of experiences, but may object to being labelled as 'depressed' which may lead to an anti-depressant being prescribed over HRT. (Depressive symptoms vs clinical depression). We feel the NICE guideline should move away from language, which alienates women or leads to misdiagnosis or incorrect treatment. We also feel the guidance should recognise the prevalence of mood change in women with a pre-existing diagnosis of premenstrual disorders or of previous post natal depression. The RCOG green top guidelines and NAPS guidelines show the benefit of using HRT in managing mood disturbance.	Thank you for your comment. The effectiveness of HRT in the management of depressive symptoms associated with the menopause was not in the scope of the 2024 guideline update. This means that a search for evidence was not conducted and the committee did not discuss the evidence related to this. The committee could therefore not comment on this. The committee has added a definition of depressive symptoms that is in line with the NICE guideline on the management of depression in adults. They reflected on language and agreed that language related to mental rather than physical health is considered to be more negative however not using the relevant words would make them more rather than less stigmatising / alienating in the longer term.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	019	002	We feel sleep disturbance is slightly more complex than appears in this guideline and very common. It should be thoroughly assessed, with sleep diaries for example and diagnosis made where appropriate using DSM V. Although CBT can help in some cases/type of sleep problems, HRT is also important where main issue is night sweats which are impacting sleep. We feel there is a larger body of evidence around diagnosis, management and treatment of sleep disturbances, beyond CBT, which should be considered and included. The guideline does not directly suggest considering HRT for this indication, which, combined with the limited access to CBT in the UK, may limit the access of many women to useful treatments for this debilitating symptom.	Thank you for your comment. Apart from CBT other management options for sleep problems associated with the menopause were not in the scope of the 2024 guideline update. However, the committee acknowledged that there are other options that may be used (including HRT). They have therefore reworded the recommendation to reflect this. It now states that CBT could be used as an option (1) in addition to other treatments (including HRT), or (2) for people for whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. Given the constraints of the scope they could not be more specific than this.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	019	005	The section on altered sexual function is reductive and does not suggest any other approaches to this common issue beyond testosterone. There should be reference to a biopsychosocial assessment of the cause of sexual problems, and discuss the fact that loss of libido is commonly present where there is a loss of arousal, difficulty or inability to climax, dyspareunia or recurrent intercourse-related UTI, all of which are common changes in sexual function associated with menopause. There is no reference to the role of vaginal oestrogen, moisturisers and lubricants (and the need to discuss these measures proactively with menopausal individuals) as effective and safe options to improve sexual function. There is also no reference to commonly co-	Thank you for your comment. The section on altered sexual function associated with the menopause was not in the scope of the 2024 guideline update. Therefore, an evidence review was not conducted. The committee could therefore not comment on these.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				prescribed drugs, such as SSRIs and SNRIs, that are known to have negative impacts on sexual function.	
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	019	015	We feel there needs to be reference to where hysterectomy where endometriosis is diagnosed, or where the individual may have had a subtotal hysterectomy. In this case a combination oestrogen and progestogen are recommended (BMS)	Thank you for your comment. The committee discussed that choice between oestrogen-only and combined HRT may be different for people with a sub-total hysterectomy. They decided that they could not be prescriptive about the type of HRT to be used for people who have had a sub-total hysterectomy because their condition is clinically complex, and they had not reviewed evidence about the effect of HRT on risk of endometrial cancer for this group. They acknowledged that people who were going to have, or had had, a sub-total hysterectomy would be under the care of a specialist who could discuss HRT options tailored to their needs (or a relevant specialist within the MDT). Due to a lack of evidence, no specific recommendation was made for sub-total hysterectomy; however, the term "total" was added before "hysterectomy" in guidance regarding the offer of oestrogen-only HRT to those who have had a hysterectomy. This addition alerts healthcare professionals to consider other factors for patients with a sub-total hysterectomy. The committee also noted that some people have a hysterectomy for a condition that may be affected by HRT, such as endometriosis. The committee did not review evidence related to such conditions. They recognised that the decision about the type of HRT that best balances benefits and risks for

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					the person may be affected by that condition (for example endometriosis) or having had a subtotal hysterectomy. For this reason, they added a recommendation highlighting that advice from a healthcare professional with specialist knowledge of that condition may be needed when making this choice. Due to this stakeholder comment and other related comments, this topic has been logged with NICE surveillance so that it can be considered for a possible update to either the Menopause or the Endometriosis guideline in future.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	021	022	What is the evidence for this statement ? Hormone replacement therapy and longevity - PubMed (nih.gov)	Thank you for your comment. See evidence in evidence review H on all-cause mortality. Full details on the studies included for this review, and the committee's discussion of the evidence which led to the recommendations can be found in appendix D of evidence review H.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	022	017	**We strongly disagree with this statement** and believe there is an increasing body of evidence to show HRT reduces incidence of heart disease related events when used at the right time . Including the timing hypothesis Hormone replacement therapy and the association with coronary heart disease and overall mortality: clinical application of the timing hypothesis - PubMed (nih.gov) and Menopausal Hormone Replacement Therapy and Reduction of All-... : The Cancer Journal (lww.com)	Thank you for your comment. The reference you provide is a narrative review, which is not included as an eligible study design in the protocol for Evidence Review C. However, the data in Evidence Review C was stratified by age at first use, and time since menopause at first use of HRT where possible. The committee discussed the subgroup analysis from the RCT data for age at first use and the time since menopause at first use, and since there were no statistically significant subgroup differences, they could not conclude that there was a reduced incidence of heart disease related events when HRT was used at a particular age, or a specific time period following the start of menopause. The committee

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					also considered the observational study evidence, which was also stratified by the same subgroups where possible. They discussed that evidence from one study supported a reduced risk in coronary heart disease which was specific to a younger age group, however this pattern was not reflected in another observational study which also presented subgroup data. Since there were inconsistent results between the observational studies, and no statistically significant subgroup differences in the RCT evidence, the committee could not reach the conclusion that there was a reduced risk of coronary heart disease depending on the age at first use, or the time since menopause when HRT was first used. This is discussed in more detail in the committee's discussion of the evidence section in Evidence Review C. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly. NICE commissioned an independent review of the breast cancer and cardiovascular

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	074	007	The guideline refers to the importance of HRT for bone protection in premature menopause but does not make recommendations for its use in other age groups. We feel this is lacking from the guideline considering the morbidity and mortality attributed to fractures in women and cost to the NHS, and that the evidence supports the use of HRT as a treatment option, including the Royal Osteoporosis Society	Thank you for your comment. The aim of the evidence review carried out was assessing the impact of either taking HRT or not taking HRT on people with early menopause and the development of various health outcomes. The need to assess the impact of early menopause on health outcomes, including osteoporosis and fragility fractures, and the treatment to prevent such health outcomes has been acknowledged and will be passed onto the NICE surveillance teams for prioritised consideration during future updates.
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline	087		Appendix A There is no QALY data for HRT which is incredibly important when discussing risks and benefits	Thank you for your comment. For the topics that were updated the outcomes related to incidence of specific health conditions and condition specific mortality or all-cause mortality. They were not effectiveness / intervention reviews where quality of life data would be an outcome. Therefore, QALY data is not presented in the appendix.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Faculty of Sexual and Reproductive Health – Menopause Guardian	Guideline and Evidence review A	012	009	Agree that there needs to be equitable access to all groups, but needs to be highlighted that there is no evidence to support the use of CBT for people taking gender-affirming therapy? Again this could be seen as misleading recommendation when evidence is lacking	Thank you for your comment. The cited section refers to people who have taken gender affirming hormone therapy in the past. People who are currently taking gender affirming hormone therapy are not in the scope of the guideline due to the side effects of that therapy that can mirror menopause symptoms. The committee thought that people who have taken gender affirming hormone therapy should have the same option to have CBT than other people and the recommendation was revised in line of the wording changes elsewhere clarifying that is an option (1) in addition to other treatments (including HRT) (2) for people in whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. This was identified as an issue in the equality impact assessment and the committee considered this as part of the discussions in line with NICE methodology related to equality considerations.
FemISA	Guideline		006	1.1.1 As well as symptoms the approach should be to fully inform the woman or person experiencing menopause and take their wishes and aspirations into account. The choice should be made by the patient, not the GP or gynaecologist.	Thank you for your comment. This 2015 recommendation was not part of the 2024 guideline update. However, the recommendation emphasises the need for a tailored approach in accordance with the stakeholder's comment.
FemISA	Guideline		006	1.2.2 A number of important and debilitating symptoms are missing – • Night sweats leading to sleep disturbance and sleeplessness • Brain Fog – memory loss and cognitive impairment	Thank you for your comment. NICE takes the reports of the debilitating symptoms, the considerable concern it causes and the impact that symptoms associated with the menopause have seriously. Whilst an update of the list of symptoms was outside the scope of the 2024 guideline update (and therefore no evidence review was conducted), the NICE surveillance

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				• Mood swings – sudden rage which can result is disturbing behaviour for no or little reason • Loss of bone density • Los of libido – although mentioned this is very often ignored and rarely treated. This is sexually discriminatory as men's loss of libido is treated more seriously and more frequently. Hair loss or thinning which can be distressing	team checks regularly for new evidence for topics within guidelines to see where further work is needed.
FemISA	Guideline		011	CBT 1.4.4 It must be explained that the decision of which treatment lies with the woman or person experiencing menopause symptoms not the GP or gynaecologists or even the ICB. CBT is not a replacement for effective treatment of symptoms and is not 'instead of' effective medicines etc It can be 'as well as' other effective treatments if the patient thinks it is appropriate for them. The onset/length of time to achieve symptom relief must be discussed realistically with the patient. CBT/ Talking therapies have a very long waiting time, whereas relief using HRT will be relatively quick. Patient may have to wait well over 6 months or a year to get a CBT appointment and then any positive effects will take some time. CBT may help patients to cope with some symptoms, but will not relieve symptoms which do not have a psychological base – sweats, mood swings – sudden rage, loss of bone	Thank you for your comment. The guideline advocates a person-centred approach tailoring it 'to the person at all times when identifying, discussing, investigating and managing menopause and adapt the approach if symptoms change over time'. The committee has revised the wording to ensure clarity about CBT 'as an option: in addition to HRT, for people for whom HRT is contraindicated or for people who prefer not to take HRT'. Your comment will be considered by NICE where relevant support activity is being planned.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				density, brain fog – memory loss and cognitive enhancement, loss of libido. No amount of counselling will help stop night sweats, bone loss or brain fog. The danger of recommending CBT is that it reinforces the very negative myth that menopause problems do not exist, that it is all in women's minds and that they are being hysterical.	
FemISA	Guideline		014	1.4.15 CBT will not be able to resolve vasomotor symptoms which are due to the decline in hormones. CBT should not be offered as an effective alternative to HRT. If patient prefers not to have HRT or think CBT would be a useful additional treatment, they should be referred for it ,but the delay will be quantified. When would they realistically be able to start CBT? How long would it take to have any effect?	Thank you for your comment. The committee reflected on the wording of the recommendations related to CBT and updated it to make it explicit that this was not recommended as a first-line treatment. It is now stated that it is an option (1) in addition to other treatments (including HRT) (2) for people in whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. Your comment will be considered by NICE where relevant support activity is being planned.
FemISA	Guideline		018	Depressive symptoms 1.4.34 No treatment is offered for mood swings, sudden rage. No treatment is offered for 'brain fog' – memory loss and cognitive impairment. These are both very debilitating for women and those suffering menopausal symptoms but are ignored.	Thank you for your comment. NICE is taking reports of debilitating symptoms seriously and whilst this was not part of the scope of the 2024 guideline update, the surveillance team regularly checks guidelines for topics to be considered for update. Effectiveness for treatment of these symptoms was not within the scope of the 2024 guideline update.
FemISA	Guideline		018	Sleep 1.4.37	Thank you for your comment. The committee reflected on the wording of the recommendations related to CBT and sleep problems. The

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				HRT is very effective at controlling night sweats and sleep disturbance with very swift positive results for patients. HRT must be included as an effective treatment option. CBT will not stop night sweats.	recommendation was updated to emphasise that it is an option (1) in addition to other treatments (including HRT) (2) for people in whom other treatments are contraindicated or (3) for people who prefer not to have other treatments.
FemISA	Guideline		018	Altered sexual function 1.4.38 Loss of libido is common and very often ignored. This is disgraceful discrimination against women, showing lack of equality in the NHS for women. In men this is taken much more seriously and treatment more frequently. If a woman complains about loss of libido this should be taken seriously and she should be offered referral and effective treatment such as testosterone.	Thank you for your comment. The management of loss of libido was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this. At the time when the scope of the guideline update was agreed, there was no substantive new evidence that would change the recommendation related to testosterone. However, NICE recognises the importance of this issue and has worked with the NIHR to prioritise funding for research on the matter.
FemISA	Guideline		022	HRT for dementia Prevention 1.6.3 The evidence on the role of HRT in dementia prevention and treatment for 'brain fog' is mixed and conflicting and one cannot draw a conclusion at this time. More evidence is needed. Certainly, women who remain on HRT are noticeably more alert, brighter, more engaged, have better memory retention and cognition.	Thank you for your comment. The committee used the evidence included in Evidence Review G to inform the recommendations on the risk of HRT and dementia risk. The protocol related to evidence review G did not specify alertness, brightness, engagement, memory retention, or cognition as the outcomes that would be analysed. The committee are therefore unable to comment on the impact of HRT use on these outcomes.
FemISA	Guideline	General	001	2 Recommendations Under the NHS constitution women (and men) must be fully informed of all their treatment options with all the pros and cons, side effects, adverse effects efficacy etc and make a choice that suits them – "No decision about me	Thank you for your comment. The guideline recommends when discussing hormonal, non-hormonal or non-pharmaceutical management options with people with menopause-associated symptoms, the benefits and risks associated with each of these options should be explained. It is

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				without me". Women have been particularly badly served especially with gynaecological conditions often given no information about all their treatment options and no choice. This is contrary to the requirement under the NHS constitution is too often ignored.	also recommended that the information about benefits and risks should be tailored to the person's age, individual circumstances and potential risk factors when making treatment choices. This person-centred approach was recommended to facilitate conversations between clinicians and individuals, enabling shared decision-making regarding menopause management. This approach reflects the information that is in the NHS constitution.
FemISA	Guideline	General		Patient Benefit Assessment – does this draft guidance help menopausal women and other menopausal people? If CBT and other treatments are offered to women as alternative or additional choices and menopausal symptoms are taken more seriously these draft guidelines could be beneficial to patients. However, recommending CBT over HRT or other treatments for non-psychological symptoms is not acceptable. CBT will not stop night sweats, 'Brain Fog' which is not addressed at all. The onset of symptom relief is also not addressed at all. HRT offers swift relief from symptoms. There is a very long NHS waiting list for CBT 6 months? 1 year? longer? before any treatment starts. Any benefit will also take some time. This is a very important consideration for patients experiencing debilitating and problematic menopausal	Thank you for your comment. The CBT recommendations were based on RCT evidence some of which was high quality. However, the committee reflected on the wording of the recommendations and updated it to make it explicit that this was not recommended as a first line treatment. It is now stated that it is an option (1) in addition to other treatments (including HRT) (2) for people in whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. In relation to access to CBT. Your comment will be considered by NICE where relevant support activity is being planned.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				symptoms which will have significant effects on their lives.	
FTWW: Fair Treatment for the Women of Wales	Guideline	General	General	We are concerned at the overall tenor of the guidance, which seems to make some rather sweeping generalisations and assumptions about the menopause experience. We feel that those who have an early medical or surgical menopause are not adequately considered within the guidance. For example, comments early on in the document, such as, 'approaching the age of menopause' and 'normal life transition', exclude a significant number of women for whom these statements would not apply, specifically those who experience an artificially induced menopause at an early age, whether through chemical or surgical interventions, or as a result of premature ovarian insufficiency (POI). We would suggest that the guidance makes clear that it is inclusive of these individuals, so as not to perpetuate stereotypes about the nature of menopause, and ensure both patients and clinicians are better informed and able to identify and manage instances where the menopause experience is not 'typical'. Our concern that the guidance is not sufficiently inclusive is compounded by the adjective, 'troublesome' used throughout to describe symptoms. We believe that this fails to capture the spectrum of impact experienced by individuals, with some suffering symptoms	Thank you for your comment. The committee reviewed wording related to the menopause that may exclude people with early medical or surgical menopause. In the recommendation that mentions 'approaching the age of menopause' the word 'age' was removed to be more inclusive and 'can also happen earlier because of surgery or medical treatment, an inherited condition, or an unknown cause' has been added to clarify this point. In the phrase 'normal life transition' the word 'normal' has been removed. The wording 'troublesome' has been removed throughout. In relation to other experiences NICE takes the reports of the debilitating symptoms, the considerable concern they cause, and the impact menopause has seriously. Whilst an update of the list of symptoms and experiences (including cognitive symptoms) was outside the current scope of the 2024 guideline update and therefore no evidence review was conducted. The topic of symptoms and experience of the menopause has been logged with NICE surveillance team which checks regularly for new evidence for topics within guidelines to see where further work is needed. The topic of identification and diagnosis of menopause was not in the scope of the 2024 guideline update. The committee could therefore

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				of such severity that their wellbeing and lives are irrevocably harmed. There is much evidence to show that women with severe and unmanaged symptoms of menopause leave employment and suffer relationship breakdown. Data also reveals that the age-specific rate of suicide amongst females in the UK is highest amongst those aged 45-54 years https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/suicidesintheunitedkingdom/2022registrations and there are widespread reports of this being at least partially linked to hormone fluctuations associated with menopause: https://www.theguardian.com/society/2023/jan/12/not-just-hot-flushes-how-menopause-can-destroy-mental-health . We would advise revisiting the use of 'troublesome', which implies irritation / annoyance to something which more accurately captures the breadth of experiences, up to and including, severely life-affecting. Whilst it is understandable that the guidance should cite changes in menstrual cycle as a key identifier of the menopausal transition, we would like to see more emphasis placed on the experiences of women whose menstrual cycles are historically erratic, who are using LARC to manage menstruation-related symptoms, or who have been hysterectomised. Another problem with centering changes to the menstrual cycle is that many women have	not comment on identification related menstrual changes and conditions related to menstruation. The NICE surveillance team checks regularly for new evidence for topics within guidelines to see where further work is needed. In relation to CBT the committee have revised the recommendation and referred to 'management' rather than 'treatment' in relation to this. They have also made changes to the recommendation to make it explicit that in the case of vasomotor symptoms CBT has been recommended as an option (1) in addition to HRT (2) for people for whom HRT is contraindicated or (3) for those who prefer not to take HRT. This also makes it clear that it is not considered as a first line option to replace HRT. The evidence that was searched for was only restricted to CBT rather than other psychological therapies which means that the committee could not comment on ' mindfulness or Acceptance and Commitment Therapy (ACT)'. It is already stated in the guideline that information should be shared with the person on lifestyle changes and interventions that can support health and wellbeing. With regards to healthcare professional with expertise in menopause, the committee recommended input from these only in very specific circumstance, for example when combined or oestrogen-only HRT could be a treatment option for someone with a history of coronary heart disease or stroke. The committee also provided a definition of 'healthcare professional with expertise in menopause' which

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				historically 'normalised' experiences of heavy and / or erratic bleeding, so may delay help-seeking for this reason. Given the panoply of symptoms associated with menopause and the potential for women not to be aware of changes to their menstrual cycle, we would like to see the guidance emphasise more the need for awareness of a range of symptoms which might indicate menopause transition and the role that better / more accessible information and symptom tracking might play in expediting attribution and treatment. We were particularly concerned at the prioritisation of CBT (Cognitive Behavioural Therapy) throughout the guidance, not least the reference to it as a 'treatment' for menopausal symptoms. We spoke to a clinical psychologist in our evidence-gathering for this response, who made clear that CBT *might*, in some patients, prove helpful in the acquisition of skills to better cope with the impact of a physiological symptom but that this does not constitute a 'treatment' for that symptom. CBT could be offered as a therapy to manage symptoms, **in addition to** a formal / ongoing treatment plan which should, under normal circumstances, include the offer of HRT. We are of the opinion that by referring to CBT as a treatment and positioning it as such in the guidance, the result will be to confuse patients (particularly those who believe that HRT is not	is more inclusive than consultants in specialist setting. This could include GPs who have received training by a recognised by a professional body. Your comment will be considered by NICE where relevant support activity is being planned. Recommendations about training are outside the scope of NICE guidelines because this is the responsibility of professional bodies. Based on the numbers in the appendix of the consultation version of the guideline (with tables of absolute numbers) a discussion aid document has been developed which includes data visualisation as well as a verbal description of what the numbers mean and where they come from. This uses lay language was produced to facilitate conversations between clinicians and individuals, enabling shared decision-making regarding Menopause management. This discussion aid has undergone user-testing and was refined based on user feedback.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				safe). The guidance should emphasise the need for informed choice, based on accurate research. As it stands, we are unsure how far any recommendation to offer CBT to anyone struggling with menopause-related symptoms is evidence-based, particularly with regards to those who are in premature menopause. It would appear that the RCTs discussed in the Evidence Review have all been carried out with females of an age where menopause would be naturally expected to occur (the average age of participants is 56) so it is uncertain whether CBT would have any benefit for patients in medical, surgical or premature menopause. Without robust and inclusive studies to ascertain efficacy, we do not believe NICE should recommending CBT as a first-line option for patients going through the menopause transition under these circumstances, and should reconsider wording so that it is not described as a 'treatment'. CBT (if/when available) might be considered only when challenging symptoms continue and are not / cannot be treated with HRT alone. Indeed, CBT has historically been available for depressive symptoms (outside of menopause) and patients will usually be offered pharmaceutical interventions (SSRIs) alongside because they tend to put patients in a more stable state to benefit from a psychological / talking therapy, much like analgesia for pain ahead of undertaking physiotherapy or exercise. We would like to see the guidance focus more on CBT as a tool	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				to 'complement' the offer of pharmaceutical treatment (HRT) rather than a first-line intervention in its own right. Of course, this then begs the question, 'why CBT over other lifestyle adjustments or psychological therapeutic approaches, such as mindfulness or Acceptance and Commitment Therapy (ACT)'? We believe that people should be given accurate, well researched advice, and HRT should always be offered as the first choice to support the alleviation of menopausal symptoms and declining hormones being experienced. We need more research on brain and vital organ function as our hormones decline. By offering CBT as a first choice 'treatment', there is the potential for long term health span to be significantly and adversely affected. In summary, we would strongly urge the Committee to review the use of the word 'treatment' in conjunction with CBT in menopause management and, instead, posit it as a complementary therapy or tool which may be beneficial for some patients in developing coping mechanisms in their menopause journey, as part of a holistic care plan, and where it is based on informed patient choice. Other possible ramifications of including CBT as a first-line 'treatment' for menopause symptoms in the guidance include:	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				• An inference that physiological symptoms affecting women during the menopause transition might be 'psychological' in origin, perpetuating stereotypes about the female psyche. • Prolonging delays in patients seeking or accessing HRT, ultimately worsening patient experience and prognosis and costing the NHS more in the longer-term. • An increase in waiting times for community mental health services, negatively impacting patients who have a confirmed mental health diagnosis and need to access talking therapies as part of their psychiatric treatment plan. • Exacerbation of health inequalities; patients on long waiting lists for NICE recommended CBT for menopause may feel they have no option but to take out loans or credit cards to pay for it. • An increased risk of harm, with patients accessing unregulated CBT. We note that the guidance makes clear concerns about unregulated complementary therapies and would advise that the same degree of caution is applied to unregulated CBT. We talk about this in more detail in our comments on page 45 of the guidance. We have some concerns about a possible over-reliance on menopause specialists	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				throughout the guideline, given that not all UK regions are currently offering such a service. Whilst this remains an issue, we fear the result may be some patients not being offered the opportunity to discuss, or be prescribed, HRT (or other interventions) appropriate to their circumstances and needs. We also question how far a reliance on menopause specialists (usually in tertiary settings) potentially disincentivises the acquisition of learning in primary care where, ideally, most people should be able to benefit from prompt identification and management of menopause symptoms. This does not negate the need for menopause specialists, but it does have implications for practice in primary care. We would like to see the Committee make a recommendation regarding the need for menopause to be prioritised in medical training and continuing professional development for healthcare professionals in primary care settings, not least as 'normalising' menopause awareness, identification, and treatment within primary care would echo the guidance's description of menopause as a 'normal life transition / event'. This would also help to reduce increasing delays and bottlenecks in accessing specialist services which should, in reality, be reserved for the management of more complex patients or those for whom symptoms are particularly severe / challenging / not responding to usual HRT types and dosage.	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				We would also like to see the Guidance offer some narrative around the role of community pharmacy in providing HRT to patients where a diagnosis of menopause has already been made and prescription written. We note a widespread reluctance on the part of pharmacists to offer repeat prescriptions or offer alternative forms of HRT when there are shortages, without the explicit say-so of a clinician, requiring patients to make repeated appointments with the GP (or consultant, where applicable). This is not only creating unnecessary bottlenecks in primary care, it also results in delays, fragmented care, and disruptions to symptom management for patients. In terms of the structure of the guidance and language used, we would ask that, where possible, plain language is used, particularly where communicating risk. As the majority of prescribing will (or should) take place in primary care rather than specialist clinics, we would suggest that expecting general practitioners to refer to a multitude of additional tables and links in a 10-minute appointment is likely not feasible and might result in poorer patient experience and outcomes. Making information about risk as accessible as possible would help both clinician and patient engage in shared decision-making.	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
FTWW: Fair Treatment for the Women of Wales	Guideline	008	024	We are pleased to see efforts on the part of the Committee to include people from ethnic minority backgrounds, who may experience menopause at a younger age than white people. This should be better factored-into the introduction to the guidance (page 6 onwards) where there is reference to 'approaching the age of menopause'. We would also ask that more consideration be given to disabled people, for example, women with Down syndrome. Evidence shows that they will tend to go through menopause at a slightly younger age, with the median age of menopause in women with Down syndrome reported to be 46 (https://onlinelibrary.wiley.com/doi/10.1111/j.1365-2788.2001.00286.x). The median age of menopause in white women without Down syndrome from industrialized countries is reported to be between the ages of 50-52. The median age at the onset of perimenopause in those same women was reported to be 47.5, with (as the NICE guidance makes clear) some variation by race and ethnicity. Public Health England's briefing paper 'Health Inequalities: Menopause' notes a UK study where women with learning disabilities had similar experiences of menopausal symptoms to other women but that they had poorer understanding of menopause and menstruation (Willis DS, Wishart JG, and Muir WJ. Menopausal experiences of women with intellectual disabilities. Journal of Applied	Thank you for your comment. The committee made this recommendation related to time of menopause and potential differences by ethnic background based on their knowledge and experience. It was not a specific research question that was part of the scope of the 2024 guideline update. They reflected on this and decided based on consensus to add that people with lifelong medical conditions may also experience menopause at a younger age to this recommendation. The Equalities Impact Assessment has been reviewed and further points have been included in the section on disabilities to emphasise the person-centred approach that the committee has taken which they felt would positively impact these groups. Making reasonable adjustments as required by the Equality Act 2010 is a statutory requirement and so this would not need to be repeated in each individual NICE guideline. The 2024 update focused on the effects of HRT compared to not HRT on the incidence of specific health outcomes. The effects of HRT or impact of menopause on symptoms of another condition, such as endometriosis or epilepsy, is a different questions and potentially quite a complex relationship between the 2. Potentially an argument could be made that this would be better covered in the endometriosis or epilepsies NICE guidelines. However, it was out of scope for the 2024 menopause guideline update. The committee has also logged the raised topics (including in prevalence of menopause at a younger age, for example people with disabilities and experience / impact of menopause on people

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Research in Intellectual Disabilities, 2011. 24(1): p. 74-85). Level of knowledge about the menopause has been found to be generally low in women with learning disabilities (McCarthy M. Going through the menopause: perceptions and experiences of women with intellectual disability. Journal of Intellectual & Developmental Disability, 2002. 27(4): p. 281-295). Carers report being poorly trained and resourced to help women understand the menopause and, as a result, may miss symptoms of the menopause and have difficulty in disentangling physical and psychological problems stemming from menopausal changes from changes in behaviours due to other causes (Willis DS, Wishart JG and Muir WJ. Carer knowledge and experiences with menopause in women with intellectual disabilities. Journal of Policy and Practice in Intellectual Disabilities, 2010. 7(1): p. 42-48). We would ask the Committee, in any development of guidance pertaining to disabled people, that they reference the Equality Act 2010 which makes clear that 'disability' can also include those living with long-term health conditions. We note that Diabetes Type 2 is included in the guidance, but would ask that, given the prevalence of conditions like epilepsy, asthma, and endometriosis, and the impact of female sex hormones on associated symptoms, patients	with learning disabilities or other long-term health conditions and their carers) with the NICE surveillance team, including the cited references, so that this could be considered for future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				affected be similarly referenced as amongst those who may need additional support during / beyond the menopause transition. The PHE briefing points out that epilepsy is common in people with learning disabilities (Robertson J and others. Prevalence of epilepsy among people with intellectual disabilities: A systematic review. Seizure: European Journal of Epilepsy, 2015. 29: p. 46-6) and women with catamenial epilepsy (where seizure frequency is related to the menstrual cycle) might experience an increase in seizure frequency in perimenopause and decrease after menopause (Røste LS and others. Does menopause affect the epilepsy? Seizure, 2008. 17(2): p. 172-175). Asthma and Lung UK's 2022 report, 'Asthma is Worse for Women' cites research demonstrating how 'female hormones can also trigger asthma symptoms during perimenopause' (https://www.asthmaandlung.org.uk/sites/default/files/2023-02/asthma-is-worse-for-women-report-1.pdf). Endometriosis patients may find themselves in early medical or surgical menopause in attempts to manage symptoms of their condition. HRT may then need to be carefully managed by care providers to ensure long-term health is protected whilst avoiding exacerbation of endometriosis symptoms. It is likely that these patients will be considered	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				'complex', so advice should be sought from a menopause specialist / clinic and / or a referral initiated. Whilst it may not be reasonable to expect primary care physicians to be cognisant of the specific details of the correlation between various long-term health conditions and menopause-related hormone fluctuations, we would nevertheless urge the Committee to highlight the need for a more general awareness of the potential intersectional impacts of menopause on disabled people / people living with a wide range of pre-existing multi-morbidities.	
FTWW: Fair Treatment for the Women of Wales	Guideline	009	013	We query why patients in medical and / or surgical menopause are not included in the recommendation that psychological support be offered. It is our understanding that these patients are more likely to struggle with sudden onset of menopausal symptoms (including those relating to their mental health) and be at a relatively young age, with these interventions regularly offered to patients with gynaecological disease. Loss of fertility may be a particular issue facing this cohort, an experience well-established as having considerable impact on psychological wellbeing. We would urge the Committee to amend this recommendation to make clear that it equally applies to patients in medical and / or surgical menopause.	Thank you for your comment. This is not an independent recommendation but is part of the previous recommendation that refers directly to these age groups. The formatting was updated to clarify this. It is recommended that people experiencing menopause as a result of medical or surgical treatment have the opportunity to have discussions with a healthcare professional with expertise in fertility and a healthcare professional with expertise in menopause. Such medical or surgical treatments would also be discussed with a condition specific healthcare professional. Any of these specialist could refer to psychological services if needed on a case by case basis but the committee thought that this may not apply equally to everyone in this situation so they decided not to include this in the recommendation.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
FTWW: Fair Treatment for the Women of Wales	Guideline	014	005	Suggesting CBT for troublesome vasomotor symptoms associated with the menopause needs far more explanation, given that vasomotor symptoms are physiological in origin and not a psychological disturbance. It is vital that NICE makes clear that CBT in these instances is purely a tool to help (some) patients possibly cope better with the impact of a symptom on their lives, not a way to treat or resolve the underlying hormonal cause of that symptom.	Thank you for your comment. The wording has been revised to ensure clarity about CBT 'as an option: in addition to HRT, for people for whom HRT is contraindicated or for people who prefer not to take HRT'.
FTWW: Fair Treatment for the Women of Wales	Guideline	015	006 - 007	We feel more clarity is needed around the recommendation to only continue treatment for as long as is required to relieve symptoms, given that symptoms might return upon cessation of treatment. This approach seems to run the risk of fragmented care, repeated appointments, and uncertainty regarding decision-making – is duration of treatment based upon patient reporting and preference, or stipulations made by the clinician?	Thank you for your comment. The recommendation was reworded to say 'for as long as it is needed'. This does not set a limit and it is described in the 'reviewing treatment' section that the 'efficacy and tolerability' should be reviewed at 3 months and then annually thereafter unless there are clinical indications for an earlier review (such as treatment ineffectiveness, side effects or adverse events). It is also stated in another recommendation 'explain that symptoms may return when HRT is stopped and discuss the option of restarting treatment if necessary'. Therefore, vaginal oestrogen can be taken as long as is needed and if symptoms return after stopping, they could restart treatment if they wanted to. The committee agreed that this would be reassuring and would not result in fragmented care, repeated appointments, and uncertainty regarding decision-making.
FTWW: Fair Treatment for the Women of Wales	Guideline	015	022	We wondered whether the Committee has considered or might consider referencing here the possible role of pelvic physiotherapy	Thank you for your comment. Incontinence and prolapse are covered in NICE's guideline on managing urinary incontinence and pelvic organ

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				(sometimes known as 'women's health physiotherapy') with regard to expanding the range of tools available to patients in managing symptoms linked to continence and prolapse as an adjunct to HRT / vaginal oestrogen.	prolapse (which includes pelvic physiotherapy) in women to which a cross reference has been made. Pelvic physiotherapy was not in the scope of the 2024 guideline update. That means that an evidence review was not conducted. The committee could therefore not comment on this.
FTWW: Fair Treatment for the Women of Wales	Guideline	018	010	We advise changing 'consider' to 'discuss', as 'consider' implies that it is the clinician who chooses what options are to be discussed, and reduces patient autonomy.	Thank you for your comment. In NICE style the wording 'consider' reflects the strength of a recommendation. When there is a closer balance between benefits and harms as in CBT (for instance when evidence is rated lower), the word 'consider' is used to reflect that the recommendation is 'weak' - for further information related to the wording of recommendations, see 'Making decisions using NICE guideline'..
FTWW: Fair Treatment for the Women of Wales	Guideline	018	012	We advise changing 'consider' to 'discuss', as 'consider' implies that it is the clinician who chooses what options are to be discussed, and reduces patient autonomy. A recommendation to 'discuss' is particularly important here, given that the efficacy of CBT for depressive symptoms associated with menopause is tenuous, as NICE delineates in Evidence Review 'A'. It is important to share this context with patients so that they can make an informed decision. However, lack of evidence to support the offer of CBT is not made clear within the guidance itself, including this recommendation. Given that the majority of readers will look only to the main body of the document for advice, we would strongly advise the Committee to highlight the limited evidence	Thank you for your comment. In NICE style the wording 'consider' reflects the strength of a recommendation. When there is a closer balance between benefits and harms as in CBT (for instance when evidence is rated lower), the word 'consider' is used to reflect that the recommendation is 'weak' - for further information related to the wording of recommendations, see the section on decision making of the NICE guideline manual. Social prescribing was not part of the 2024 guideline update and was therefore not included in the evidence review. The committee could therefore not comment on this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				to support this recommendation and adjust the wording accordingly. Furthermore, alongside HRT, there may be other therapeutic approaches and lifestyle changes which would be just as beneficial as CBT in supporting patients with depressive symptoms associated with menopause. We recommend including a reference to 'social prescribing' in this section, as there may well be a range of activities and groups available in the locality or online which could be beneficial to patients' mental health and wellbeing.	
FTWW: Fair Treatment for the Women of Wales	Guideline	019	002	We advise changing 'consider' to 'discuss', as 'consider' implies that it is the clinician who chooses what options are to be discussed, and reduces patient autonomy. A recommendation to 'discuss' is particularly important here, given that the efficacy of CBT for difficulties with sleep associated with menopause is tenuous, as NICE delineates in Evidence Review 'A'. It is important to share this context with patients so that they can make an informed decision. However, lack of evidence to support the offer of CBT is not made clear within the guidance itself, including this recommendation. Given that the majority of readers will look only to the main body of the document for advice, we would strongly advise the Committee highlight the limited evidence to support this recommendation and adjust the wording accordingly.	Thank you for your comment. The committee considered the quality of the evidence when formulating recommendations. This is reflected in the wording used which indicates the recommendation strength. The word 'consider' was used for recommendation 1.4.9 as it is a 'weak' recommendation. In 'strong' recommendations for actions that should (or should not) be offered, directive language such as 'offer' is used. For more information on this please see: Developing NICE guidelines: the manual. The committee has revised the wording to ensure clarity about CBT 'as an option: in addition to other treatments (including HRT), for people for whom other treatments are contraindicated or for people who prefer not to have other treatments'. This has been done to clarify that CBT is an option rather than a first line treatment.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Furthermore, alongside HRT, there may be other therapeutic approaches and lifestyle changes which would be just as beneficial as CBT in supporting patients with difficulties with sleep associated with menopause. We recommend including a reference to 'social prescribing' in this section, as there may well be a range of activities and groups available in the locality or online which could be beneficial to patients in managing difficulties with sleep associated with menopause.	
FTWW: Fair Treatment for the Women of Wales	Guideline	019	016	In establishing the 'lowest effective dosage', we wonder if the guidance should make some reference to the increasingly reported difficulties regarding absorbency for some people using topical HRT preparations, such as Oestrogel, and how this might require higher than anticipated doses to be effective alongside monitoring of hormone levels. It may be that this issue forms a recommendation for further research.	Thank you for your comment. The committee recommended the lowest effective dosage which would be reviewed in 3 months to assess efficacy and tolerability and annually thereafter (as highlighted in a different recommendation on reviewing treatments). All dosages would be within licensed ranges and a statement has now been added to emphasise this. Specific monitoring of hormone levels was outside the scope of the current guideline.
FTWW: Fair Treatment for the Women of Wales	Guideline	020	004	We would suggest that the section on 'Stopping HRT' advises clinicians to establish patients' reasons for stopping treatment, to ensure properly informed decision-making.	Thank you for your comment. Whilst this recommendation was not part of the 2024 guideline update the committee have included a recommendation that stating that in discussions with people about HRT should include the likelihood of symptoms returning when HRT is stopped and, the possibility option of restarting treatment if necessary. The committee decided that they could not comment further because an evidence review on the topic of stopping HRT was not conducted.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
FTWW: Fair Treatment for the Women of Wales	Guideline	021	013	We would ask that the Committee extend the recommendation to 'offer psychological support' to any patient in peri-/menopause who is experiencing distressing symptoms, including those who with premature ovarian insufficiency, in medical and / or surgical menopause. We would also suggest that this section of the guidance flag up the increased chance of psychological distress / symptoms in patients who have a history of hormone-mediated mental health conditions, such as premenstrual exacerbation (PME) premenstrual dysphoric disorder (PMDD), or perinatal / postnatal depression or psychosis, as it may be that those individuals require a referral back to their community mental health team or consultant, (alongside HRT).	Thank you for your comment. The origin of this recommendation is the topic of early menopause for which one question was included in the 2024 guideline update and the aim of the recommendation is to allow psychological support to reach the people in need of it most based on symptoms. Whether or not psychological support is needed for everyone in menopause (apart from CBT) was not part of the scope of the 2024 guideline update. The concern with making this service accessible to everyone with early menopause is also the potential for large resource impact it would have, and limited access for people who are in most need of this support. Since the evidence review did not focus on people with premenstrual exacerbation, premenstrual dysphoric disorder, perinatal / postnatal depression or psychosis, it is not possible for the committee to make a specific recommendation on these populations.
FTWW: Fair Treatment for the Women of Wales	Guideline	021	016	We would ask that this section of the guidance references the need for clinicians to keep abreast of latest research on the effect of hormone replacement on health outcomes, and a willingness to discuss enrolment on associated clinical trials / participation in research projects with patients.	Thank you for your comment. Issues such as training and being up to date with research and trials was not in the scope of the 2024 guideline update. The committee could therefore not comment on this.
FTWW: Fair Treatment for the Women of Wales	Guideline	021	021 - 022	We assume that the comment here regarding HRT as unlikely to have an effect on life expectancy does not include those with a hormone sensitivity which might lead to an exacerbation of symptoms of an underlying mental and / or physical health condition. We wonder whether the Committee may wish to	Thank you for your comment. The committee noted that high-quality evidence showed no difference in mortality with either oestrogen-only or combined HRT compared to not taking HRT. They decided that this is an important message given that there are increased risks for some specific health outcomes highlighted in tables 1

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				add a line here to remind readers to be aware of potential differences in those patients (whilst also recognising that Page 22, Line 1 does advise weighing up individual risks and benefits).	and 2. The guideline advocates a person-centred approach that takes into account the person's age, individual circumstances and potential risk factors (which could include a history of hormone sensitivity).
FTWW: Fair Treatment for the Women of Wales	Guideline	023	003	We would like to see Table 1 extended to include other long-term health conditions which are relatively common in women and might be impacted by menopause symptoms and Combined HRT. We would particularly welcome the inclusion of endometriosis, given its similar prevalence to Diabetes Type 2 and because (medical and / or surgical) menopause is still regularly offered as a treatment for the condition, albeit not always appropriately. Some narrative around the potential impacts of HRT on symptoms of hormone-mediated conditions like endometriosis and PMDD would be welcomed here so that these patients are provided with the more specialist expertise they might need to optimise treatment. We would also ask the Committee to consider referencing the potential impact of HRT in patients with epilepsy and who are taking anti-seizure medication. Given that there is some uncertainty on the part of clinicians managing these patients, it might be prudent for this section of the guidance to summarise any recommendations regarding menopause and HRT from the NICE Guidance on the Diagnosis and Treatment of Epilepsy.	Thank you for your comment. Tables 1 and 2 focus on the effects of HRT compared to not HRT on the incidence of specific health outcomes. The effects of HRT on symptoms of another condition is a different questions and potentially quite a complex relationship between the 2. The same would apply to PMDD. Potentially an argument could be made that this would better sit in the guidelines of the particular condition or in the section of 'Taking medical history into account before offering treatment for menopause associated symptoms' rather than in tables. However, it was out of scope for the 2024 guideline. These topics have been logged with the NICE surveillance team so that they can be considered for future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
FTWW: Fair Treatment for the Women of Wales	Guideline	030	002	We would like to see Table 2 extended to include other long-term health conditions which are relatively common in women and might be impacted by menopause symptoms and Oestrogen-only HRT. We would particularly welcome the inclusion of endometriosis, given its similar prevalence to Diabetes Type 2 and because (medical and / or surgical) menopause is still regularly offered as a treatment for the condition, albeit not always appropriately. Some narrative around the potential impacts of HRT on symptoms of hormone-mediated conditions like endometriosis and PMDD would be welcomed here so that these patients are provided with the more specialist expertise they might need to optimise treatment. We would also ask the Committee to consider referencing the potential impact of HRT in patients with epilepsy and who are taking anti-seizure medication. Given that there is some uncertainty on the part of clinicians managing these patients, it might be prudent for this section of the guidance to summarise any recommendations regarding menopause and HRT from the NICE Guidance on the Diagnosis and Treatment of Epilepsy.	Thank you for your comment. Other health outcomes apart from those listed (such as endometriosis or epilepsy) were not part of the 2024 guideline update. Evidence for these topics was therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this. However, people who experience menopause as a result of surgical or medical intervention are included in the population of the guideline and there is a specific recommendation related to this (see the section on 'any comorbidity the treatment of which is likely to result in menopause').
FTWW: Fair Treatment for the Women of Wales	Guideline	037	016	We would suggest that the guidance elaborates further on the role of the menopause specialist to make clear that they should be consulted early on in support of	Thank you for your comment. The section referred to in the comment is the definition of a healthcare professional with expertise in menopause. It is not a recommendation. There

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				those patients whose menopause is as a result of medical and or surgical intervention, not least as symptom management may be more complicated for those patients.	are some specific recommendations related to menopause as a result of medical and or surgical interventions including having the opportunity to discuss fertility and menopause with healthcare professionals with expertise in these specialities both before and after they have their treatment.
FTWW: Fair Treatment for the Women of Wales	Guideline	041	010	We would ask the Committee to extend its recommendations for research to include: • Menopause, HRT, and health outcomes in disabled women, including those with learning disabilities, or who are neurodivergent. • The impact and use of HRT in patients with a history of long-term 'menstrual health' conditions such as endometriosis, PMDD, and PCOS (note that there are justifiable reasons for not referring to these conditions as 'menstrual health'-related). • The impact of menopause and HRT on mental health, including where there is a pre-existing mental health diagnosis or history of hormone-mediated mental health condition. • How far absorbency rates of topical HRT in individual patients might impact treatment optimisation and how this might be measured and ameliorated. • An assessment of the role of CBT for patients in premature, medical, or surgical menopause. • The use of testosterone as part of an HRT regimen, where loss of libido is not a concern. We note the	Thank you for your comment. The NICE research recommendation process is restricted to areas covered in the 2024 guideline update for which gaps have been identified. These are specific to each protocol the details of which can be found in appendix A of each evidence report. The committee decided to highlight equality groups (which would include people with physical disabilities or mental health conditions) as specific populations where further research is encouraged in the research recommendations that were made for the guideline (see the full details of the research recommendations in appendix K of evidence reviews B1, B2, C, D, E and I). HRT in people with a history of long-term 'menstrual health' conditions was not in the scope of the evidence reviews. The committee decided that there are specialist services related to these conditions and that they would have links with other relevant specialties. The decisions around HRT would be complex because of the nature of these conditions and therefore the committee felt that people with these conditions are better served by their individual services. Whilst the committee commented on absorbency of topical oestrogen in the guideline, they agreed it was minimal and therefore it would not be feasible to compare different rates. At the time when the scope of the 2024 guideline update was agreed,

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				recommendation regarding testosterone as an option only for reduced sexual desire remains unchanged from 2015 Guidance, but would urge the Committee to make reference to the growing number of observational studies and patient testimonies which evidence the role of testosterone in improving mood, confidence, motivation, and cognition. It may be that Page 19 / Line 5 recommends clinicians keep abreast of new and emerging studies / clinical trials and seek to enrol patients where appropriate. • The use of vaginal oestrogens in people who carry genetic variants that increase the risk of breast cancer. • Further analysis of the interface between peri-/menopause and Long Covid, as posited in The Lancet: (https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00228-3/fulltext).	there was no substantive new evidence that would change the recommendation related to testosterone. However, NICE recognises the importance of this issue and has worked with the NIHR to prioritise funding for research on the matter. The committee recognises the importance of continuous professional development but decided that singling out one individual topic for a statement related to keeping abreast of research would cause confusion because this would be expected for every topic within the guideline. The committee prioritised the use vaginal oestrogen for people at high familial or genetic risk of breast cancer for a research recommendation (see research recommendation 4). The interface between peri-/menopause and Long Covid was not part of the scope of this update. The committee could therefore not make a research recommendation related to this.
FTWW: Fair Treatment for the Women of Wales	Guideline	042	008	We would ask that this section be expanded to include references to early onset of menopause in some disabled people, particularly those with Down syndrome or other genetic and / or chromosomal disorders. We would also suggest that the challenges of communicating, identifying, and optimally treating perimenopause and menopause symptoms in patients with learning disabilities	Thank you for your comment. Prevalence of menopause (including in different age groups and different populations, such as people with disabilities) was neither part of the original guideline nor part of the 2024 guideline update. The committee reflected on this and decided based on consensus to add that people with lifelong medical conditions may also experience menopause at a younger age to this recommendation. The committee agreed that

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				or neurodevelopmental differences be included here, so that clinicians are aware of these potential barriers to help-seeking and treatment and can act to address them. This might lead to a change in clinical practice, such as the inclusion of menstrual health and menopause in annual health checks for people with learning disabilities where they are not included currently.	knowledge of this could impact practice and have logged this with the NICE surveillance team so that relevant information (including the references highlighted) can be identified which could inform future updates. People need to be assessed in an individualised way, making sure that the person is heard and being treated with dignity and respect (which would include for example tailoring communication, identification and optimal treatment of perimenopause and menopause). Further detail on treating people as individuals is covered in the NICE guideline on patient experience in adult NHS services as well as in the NICE guideline on shared decision-making so this information is not repeated in all other NICE guidelines (they are cross referred to in recommendations 1.1.1 and 1.1.2). There is an emphasis throughout the guideline on tailoring information to the individual, for example it is emphasised that information about benefits and risks needs to be individualised to the person's age, individual circumstances and potential risk factors. There are also recommendations that highlight that a family member or carer can be involved. Making reasonable adjustments as required by the Equality Act 2010 is a statutory requirement and so this would not need to be repeated in each individual NICE guideline. This would include adjustments for people with learning disabilities as well as neurodivergent people. The Equalities Impact Assessment has been reviewed and we have included further points in the section on disabilities to emphasise the person-centred approach that the committee

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					has taken which they felt would positively impact these groups.
FTWW: Fair Treatment for the Women of Wales	Guideline	044	004	We would dispute the reference to CBT as 'effective' in guidance on managing menopause where the evidence reviewed by the Committee contradicts this. In fact, the Committee indicates that there is little to support the offer of CBT, even merely as an option for menopause symptom management.	Thank you for your comment. This sentence referred to the ways CBT was provided (group or individual). There was effectiveness that was shown in either, but 1 way of providing it was not more so than another. Therefore, the committee decided that this should be discussed, and that CBT should be considered as an option to provide a wider choice of treatments. As stated in other sections this could be in addition to other treatments (including HRT), for people in whom other treatments are contraindicated or those who prefer not to have other treatments.
FTWW: Fair Treatment for the Women of Wales	Guideline	045	007	We would query the Committee's reference to CBT as an intervention without risk, particularly where patients might seek out unregulated practitioners / services as a result of its being a NICE recommendation without adequate NHS provision to support delivery. There is also evidence to suggest that CBT can pose risk for patients with a history of trauma and / or previous mental health diagnoses. It is vital that CBT is not suggested as a universal panacea but that history-taking be a key element of individualised care pathways for management of menopause (or any other physical health issue) because state of mind and circumstances can impact on patient response to psychological / talking therapies. We note instances where approaches like CBT and GET (Graded Exercise Therapy) are being	Thank you for your comment. The committee reflected on the wording of the recommendations related to CBT and revised them to ensure clarity about this ' as an option: in addition to other treatments (including HRT), for people for whom other treatments are contraindicated or for people who prefer not to take HRT'. This makes it clear that CBT is not seen as a 'universal panacea' but as an option where this is a preferred choice. The first recommendation of the guideline emphasises a person centred approach by tailoring it 'to the person at all times when identifying, discussing, investigating and managing menopause, and adapt the approach if symptoms change over time'. The committee decided that such a tailored approach used by trained professionals is likely to be safe because it would consider the individual person's circumstances and history to come to a shared decision. The recommendation on a discussion about CBT as a treatment option has also been updated to highlight that information

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				removed from clinical guidance due to patients' reporting of harm, side effects, and negative reactions caused, including: • Psychologising a physical health issue / set of symptoms, with implications for self-belief and that of patient's wider circle. • Perpetuating a culture of 'victim-blaming' where patients are held responsible for the onset of symptoms and a perceived inability to cope with them, alongside being described as 'resistant' to treatment, where these approaches prove ineffective. • Unwanted effects, such as deterioration, new symptoms, distress, strain on relationships, and stigma • More serious adverse effects, such as suicidality, relationship breakdown, negativity from family and friends, withdrawal, shame, guilt, intense crying and emotional disturbance during CBT sessions (https://link.springer.com/article/10.1007/s10608-018-9904-y).	about what CBT is (including menopause specific CBT) and to take account of the person's preferences and needs. This change was made to clarify that this may not be an option suitable for all or may need to be adapted to the person's needs (for instance for people with learning disabilities). This should make it less likely that there would be harms or side effects from the treatment. Your comment will be considered by NICE where relevant support activity is being planned. In relation to psychologising physical symptoms, the committee considered a systematic review of evidence from randomised controlled trials which showed CBT to be effective using some measurements for vasomotor symptoms, depressive symptoms and sleep problems. They therefore agreed to make this available to people who may benefit from this and having this as an 'option' widens people's treatment choices. To further ensure that people's treatment choices are effective and not cause harm the committee recommended that each treatment for symptoms associated with the menopause is reviewed at 3 months to assess efficacy and tolerability and annually thereafter, unless there are clinical indications for an earlier review (such as treatment ineffectiveness, side effects or adverse events).
FTWW: Fair Treatment for the Women of Wales	Guideline	047	003	We are concerned at the choice of wording here, particularly 'bothered by', which can indicate both a physical and emotional reaction to stimulus.	Thank you for your comment. The wording 'bother' was used to be consistent with the evidence because this was measured by a questionnaire that asked about 'distress and bother'. The wording has been revised to clarify this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Given that CBT might be beneficial only in helping the patient better cope emotionally with a symptom, rather than resolving its physiological cause, we would ask the Committee to reconsider its wording here to be more specific and clarify the precise role of CBT, not as a treatment but as a possible self-management tool for some patients.	
FTWW: Fair Treatment for the Women of Wales	Guideline	049	008 - 013	We would emphasise here that the 'standard amount of CBT sessions' assumes that they are available and accessible for all patients in every area. We are concerned at the inference that CBT's role in possibly helping some patients self-manage symptoms could trump the provision of HRT. This seems akin to comparing apples with oranges, given that HRT should always be first-line treatment for symptoms and improved health outcomes, such as prevention of osteoporosis. In the vast majority of cases, CBT should really only be offered as an adjunct to HRT, not an alternative. We would question the comment that offering CBT might 'benefit' the NHS, unless sessions are undertaken privately. CMHT services are under immense pressure, with waiting lists for CBT and other talking therapies extending into years. It is without question that patient wellbeing and prognosis is being severely impacted as a result, with longer-term cost implications to the NHS and the public purse more widely.	Thank you for your comment. The wording has been revised to ensure clarity about CBT 'as an option: in addition to other treatments, for people for whom other treatments are contraindicated or for people who prefer not to have other treatments'. Any mention of this being cost saving for the NHS has been removed. The committee acknowledged in the impact section of the guideline that there are long waiting times for CBT. They also noted that people currently trained in providing this kind of therapy may not be familiar with menopause-specific CBT and training on this may incur costs and increase waiting times in the short term. However, online and group CBT may be easier and less costly to adapt to menopause-specific CBT. There are also resources available to train people in providing menopause-specific CBT (and could also inform the adaptation of online CBT), which could facilitate implementation. Your comment will be considered by NICE where relevant support activity is being planned.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				We would also suggest that the potential harms to some patients arising from CBT (both NHS and unregulated) may cause additional health-related problems for those patients, in addition to the possibility of unresolved physiological symptoms. This has additional cost implications for the NHS and public purse. In sum, we are not convinced that the economic argument for suggesting CBT as a benefit to the NHS has been fully considered.	
FTWW: Fair Treatment for the Women of Wales	Guideline	055	022	Given lack of evidence preventing the Committee making a recommendation here, we would suggest it is added to the recommendations for further research.	Thank you for your comment. This has now been revised to clarify that this group of people was already included in research recommendation 5 (which related to people with a personal history of breast cancer or people at high familial or genetic risk of breast cancer).
FTWW: Fair Treatment for the Women of Wales	Guideline	056	023	We would welcome more information about the different types of moisturisers and lubricants available and which ones are most efficacious / with fewest side-effects, given the likelihood of patients purchasing their own.	Thank you for your comment. A comparison of different types of moisturisers and lubricants based on individual constituents was outside the scope of this review question. The committee could therefore not comment on this.
FTWW: Fair Treatment for the Women of Wales	Guideline	059	001	We would suggest that the Committee considers including the option of signposting to third sector and peer support here for help in coping with the emotional impact of menopause.	Thank you for your comment. The committee agreed that support should be provided but this was based on consensus rather than an evidence review of what the most effective interventions for support are. They therefore did not want to be too prescriptive about where and how this support should be provided.
FTWW: Fair Treatment for the Women of Wales	Guideline	067	008 - 010	We are uncertain of meaning here and query whether there is a typographical error.	Thank you for your comment. The wording has been changed to 'in women post menopause who have a history of cardiovascular disease' to clarify this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
FTWW: Fair Treatment for the Women of Wales	Guideline	076	001 -002	We would ask the Committee to extend this section to include people for whom menopause occurs as a result of medical suppression of ovarian function (using GnRH analogues in the treatment of endometriosis or PMDD, for example) and where that function does not return to baseline post-treatment, and patients whose ovaries cease to function after hysterectomy (removal of uterus).	Thank you for your comment. The need to consider evidence for the people that are more likely to develop early menopause has been acknowledged. The committee have highlighted the following subgroups to the NICE surveillance team for incorporation into future menopause guideline updates when considering early menopause; spontaneous versus iatrogenic, people with disabilities (physical or mental, people with rare illnesses or underlying conditions), ethnic minorities, specific disorders (for example, diabetes), medical menopause for example due to medical suppression of ovarian function (e.g., using GnRH analogues in the treatment of endometriosis or PMDD), people on chemotherapy/radiotherapy and surgical (hysterectomy, oophorectomy).
FTWW: Fair Treatment for the Women of Wales	Guideline	084	Table 1.4.7	Given the number of patients experiencing mental health-related symptoms as a consequence of their menopause transition who are still being offered SSRIs as a first-line treatment over and above HRT, we would suggest that this recommendation not be stood down at this time but amended to make clear that SSRIs are not advised in these instances. We do not believe that all physicians in primary care or mental health services are (as yet) sufficiently able to identify where mental health issues are exacerbated or caused by hormone fluctuations, including peri-/menopause, so would urge the Committee to make this as clear as possible within the Menopause Guidance and not rely on physicians cross referring to the Depression Guidance. We are	Thank you for your comment. The recommendation is inconsistent with the NICE guideline on depression in adults: treatment and management. Effectiveness of SSRI for depressive symptoms associated with the management was not part of the scope of the 2024 guideline update which means that neither evidence in favour or against its use was identified. The committee could therefore not comment on this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				concerned that failure to be explicit regarding SSRIs in the Menopause Guidance will inadvertently lead to the possibility of more, not fewer, instances of their being prescribed inappropriately.	
FTWW: Fair Treatment for the Women of Wales	Guideline	086	001	We would reiterate here concerns about the sweeping definition of menopause as a 'a normal part of life (not a condition)' for those whose menopause is as a result of medical or surgical intervention, or POI. We are of the opinion that excluding these instances from the description both underplays the significant physical and psychological consequences of early and induced menopause, and undermines the commitment to 'patient-centredness'.	Thank you for your comment. This section has been reworded to make it inclusive for people whose menopause is as a result of medical or surgical intervention or POI.
HealthSense UK	Evidence review G and LETR	General	General	We do not understand how a signal about causing an important harm (when it is more unusual to find such signals than benefits from RCTs), i.e. the increased risk of Alzheimer's disease in women taking combined hormone treatment, was interpreted and dismissed in favour of observational studies with all their confounders. The committee seems to have been irrational at this point. The LETR discussion noted that the "committee used the RCT evidence to address the discordance between the observational studies, to reach a majority decision that the evidence suggested an increased risk in dementia, in combined HRT users when HRT was started after the age of 65. They agreed it	Thank you for your comment. The committee discussed the RCT evidence and the observational evidence that was included in Evidence Review G. The committee agree that the observational studies' findings were inconsistent and that this was likely due to them not making all the necessary adjustments for confounders and based their recommendation on the RCT evidence. Advising women of the increased risk of dementia if HRT was started after the age of 65 years this would be in line with the evidence and would help guide women into making an informed choice with regard to risks following the use of HRT. The draft includes a recommendation not to offer combined or oestrogen-only HRT for dementia prevention.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				was important to highlight in the recommendations that the increased risk of dementia with HRT use might be related to the age at starting of 65 years or older. They agreed that women who are considering HRT use for troublesome menopause symptoms associated with the menopause should be made aware of the potential risk and given all the relevant information necessary so that they can make an informed decision". Surely, on the basis of the evidence, there is enough evidence for some kind of "Do not offer" recommendation: "Do not offer ovarian hormones for prophylaxis for dementia" OR "Do not offer ovarian hormones for prophylaxis after age 65" OR "Do not offer ovarian hormones after age 65 for any reason" OR "Do not start ovarian hormones after age 65" AND "Inform women who are considering combined oestrogen/progestagen treatment for symptomatic relief of the potential increased risk of Alzheimer's dementia" .	
HealthSense UK	Guideline	General	General	Testosterone was not covered in the scope as at the time it was not available as there was no licensed product. Some GDG members (including Dr Haitham Hamoda) encourage the use of testosterone as a 'choice' (ie not because its evidence based – e.g. here https://www.theguardian.com/society/2023/apr/	Thank you for your comment. At the time when the scope of the 2024 guideline update was agreed, there was no substantive new evidence that would change the recommendation related to testosterone. However, NICE recognises the importance of this issue and has worked with the NIHR to prioritise funding for research on the matter.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				03/first-testosterone-patch-for-menopausal-women-to-begin-clinical-trials-this-year) and presumably offers testosterone in his practice. Testosterone MUST be put on surveillance for an early review as it is an increasingly prescribed drug.	
HealthSense UK	Guideline	General	General	Missing advice re oestrogen dosage The guideline does not offer any indications or contraindications to high dose oestrogen? Anecdotally, many doctors are offering increasingly high doses of oestrogen in the private sector, maybe failing to recognise the distinction between mood disorders, dependence and the menopause itself, and thus muddling the indication (for symptom relief vs prophylaxis) and mislabelling dependence (what used to be called 'tachyphylaxis'. Many charities and private providers quote NICE about offering 'HRT' for low mood. E.g https://www.themenopausecharity.org/2021/05/10/mood-changes-in-the-menopause-and-effective-treatments/ or dismiss risks with high doses https://www.newsonhealth.co.uk/why-are-some-patients-prescribed-higher-doses-of-oestrogen-than-others/ saying things like "absence of evidence does not mean proof of harm" when (a) there is consistent evidence of harms without benefit for prophylaxis and (b) dependence has been raised as a risk, with some evidence of its existence.	Thank you for your comment. The committee acknowledged and discussed concerns related to increasingly high doses. They decided to remove statements related to 'standard therapeutic range' or 'standard therapeutic dosage' from specific recommendations where this was mentioned because they felt that this was open to misinterpretation. To prevent HRT being prescribed outside licensed ranges the committee added a statement emphasising that the benefits and risks of HRT described in this guideline only cover the use of HRT within the licensed dosages. There is also further information about prescribing medicines in the link provided at the beginning of the guideline 'Making decisions using NICE guidelines' emphasising that it is expected, when we recommend medicines that healthcare professionals will prescribe or advise their use within the terms of their UK marketing authorisations, as described in manufacturers' summaries of product characteristics (SPCs). This therefore does not have to be repeated within every NICE guideline.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
HealthSense UK	Guideline	011	007	Para 1.4.4 We were, as usual, impressed by the amount of work and detail that NICE put in. We were dismayed by the abreaction to the recommendation about CBT. We hope NICE feels able to hold fast about that, as it's the 'context' in which women experience symptoms that counts. Menopause is a natural transition in hormones, a kind of 'withdrawal' itself. Thus the impact of symptoms varies, not just biologically, but for individuals depending on their circumstances. Maybe this can be explained more in the final document or at the launch. CBT helps because of the context.	Thank you for your comment in support of this.
HealthSense UK	Guideline	019	008	Section 1.5 It is a basic pharmacokinetic principle to use a drug at the smallest effective dose, for the shortest time, for a clear indication. The risks of the longer term complications that ovarian hormone supplementation can cause will be greater if it is used at higher dose, for unclear indications and for excessively long periods. Therefore a discussion about reviewing symptoms and the need for hormone treatment, with a plan to continue, stop, or consider tapering medication, should occur with the first prescription and at least yearly (or maybe after 2-5 years if that is a more appropriate timescale). Did anyone consider the evidence about dependence on female sex hormones when considering harms? If not, why not? Please see the 1992 article in the Lancet by Bewley & Bewley (a gynaecologist and addiction	Thank you for your comment. The guideline contains a recommendation on reviewing treatments. It is recommended that healthcare professionals review each treatment for symptoms associated with menopause: at 3 months to assess efficacy and tolerability /annually thereafter, unless there are clinical indications for an earlier review (such as treatment ineffectiveness, side effects or adverse events). The references you have provided have been checked but as they do not meet the criteria for any of the evidence reviews updated in this guideline update the committee are unable to comment on them.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				psychiatrist) https://pubmed.ncbi.nlm.nih.gov/1346294/. Implants are not used in the UK (although they are in other parts of the world, partly because of this and subsequent papers inc O'Leary et al. "Are high levels of oestradiol after implants associated with dependence?" https://pubmed.ncbi.nlm.nih.gov/10492109/. However, the lessons of the past seem to have been forgotten. Oestrogen is a mood changing drug, so it is not entirely surprising that some women will become dependent, a rare and late-to-be-recognised complication. If there is no evidence about stopping (except that women say their symptoms return, sometimes with a vengeance), then this should be a research recommendation. It would be positively cruel to stop a drug that causes dependence abruptly, as is advised in the breast cancer section.	
HealthSense UK	Guideline	021	016	Section 1.6 The GDG did not seem to get to grips with the fact that there was no evidence on the risk:benefit calculus for prevention of chronic disorders, illness or death, maybe partly because of the loose use of language throughout and not distinguishing the indications enough. By discussing each disease (e.g. cancer, heart disease, dementia etc) separately, an overall	Thank you for your comment. The scope of the 2024 consisted predominantly of an assessment of the impact of HRT on some specific health outcomes. This means that the comparisons were people taking HRT for menopause symptoms versus people who are not taking HRT for their symptoms. When the evidence was systematically reviewed and the committee discussed the results several risks were identified and some health outcomes did not show an increased risk with HRT or with certain routes of

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				picture has been lost (i.e. 'not seeing the wood for the trees' and thus 'cherry picking' where there were gaps or discrepancies in smaller groupings of studies). This inappropriate aggregation of evidence regarding long term use as prophylaxis needed to be emphasised, but wasn't. The GDG should be reconvened and challenged to look at the data for female sex hormone therapy as prophylaxis. We suggest that the recommendation should say "Do not offer ovarian hormones for the prevention of disease to women without bothersome symptoms"; this would be much more helpful and clearer for the general public and practitioners alike.	administration or regimens. It was not the case that the evidence showed that HRT could or should be taken as a treatment to prevent diseases. However, the message that HRT is offered for vasomotor symptoms has not been changed and remains as it is in the 2015 guideline. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the methodology used and the conclusions reached by the committee (with changes made post consultation). Tables 1 and 2 have been designed so that people can look at the results for different health outcomes in one place whereas the 2015 version had those all arranged in separate sections. The language and tone have been reviewed and revised for clarity and to present a more neutral tone. NICE has also produced a discussion aid document which includes data visualisation for the health outcomes mentioned which can be used by lay people and healthcare professionals in the shared decision-making context when making treatment choices. This discussion aid has undergone user-testing and was refined based on user feedback.
HealthSense UK	Register of Interests	General	General	Dr Haitham Hamoda & register of interests Did Dr Hamoda declare all his interests at the outset when he was appointed, and were these fully explored at interview? We note Mr Hamoda's comment on Register of Interests "I have provided comments and interviews to press, radio and TV regarding	Thank you for your comment. NICE has followed its standard methods and processes in developing the 2024 guideline update, including the way in which we manage conflicts of interest in topic experts and committee members. The details of conflicts of interest and how they have been managed are available in the published register of interests. A NICE committee is appointed to reach conclusions by consensus

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				menopause matters. These have not included any reference to the NICE guidance update" Does Mr Hamoda really represent NICEs view when he says NICE supports testosterone? eg here https://twitter.com/hamoda_h25/status/1382451023323758595?lang=bg Regarding micronized progesterone, Mr Hamoda is an author of a 2022 RCT that must have been ongoing, in press or found in the review https://pubmed.ncbi.nlm.nih.gov/35486948/. This trial does not appear in the Register of Interests. This would normally enough to exclude an expert from discussions. This should have been declared as he must have been aware of it at appointment, and certainly by the end of the GDG. It is a serious conflict of interest that might have meant he was not appointed, or at least he would be recused for part of the GDG. The extremely long list of many newspaper articles suggests that at some stage details were recognised as important, but not this RCT? This put him in a very powerful position to argue inside the GDG, and failure to declare it by the end is unacceptable as NICE cannot decide retrospectively on how to manage the COI. Does this threaten the whole guideline or just the micronized progesterone recommendations which should be removed?	rather than representing individual opinions. The committee was appointed to represent a balance of views (and it would not be a conflict if a media comment is about a topic that is outside the scope of the 2024 update). The cited reference would not have been included in any evidence review because it is restricted to comparing different types of progestogen rather than comparing HRT to no HRT. The topic of testosterone refers to a recommendation that was not in the scope of the 2024 update and was therefore retained. When it comes to micronised progesterone the committee decided to opt for a research recommendation because they concluded that there is insufficient evidence to conclude that one type of progestogen is better than another.
Hyperparathyroid UK Action4Change	Guideline	General	General	Many menopausal symptoms are also associated with primary hyperparathyroidism. We believe this should be noted as primary	Thank you for your comment. The 2024 guideline did not update the sections on identification of the menopause including menopause symptoms. The

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				hyperparathyroidism is often misdiagnosed as menopause with potentially devastating consequences to women's health • vasomotor symptoms (hot flushes and sweats) • effects on mood (for example, depressive symptoms) • insomnia • depression • anxiety • muscular fatigue and aches • general fatigue • brain fog • frequent urination • musculoskeletal symptoms (for example, joint and muscle pain) • sexual difficulties (for example, low sexual desire). Some are listed in your guideline for primary hyperparathyroidism; https://www.nice.org.uk/guidance/ng132/chapter/recommendations#chronic-non-differentiated-symptoms	committee could therefore not comment on this. NICE surveillance regularly checks for evidence that can be considered for future updates.
Hyperparathyroid UK Action4Change	Guideline	General	General	At several points during this guideline you reference [2015]. The guideline for primary hyperparathyroidism was published on 23 May 2019, so we would recommend the guideline committee should read the PHPT guideline published 4 years after the 2015 guideline you refer to, as it makes logical sense to ensure your advice isn't outdated. https://www.nice.org.uk/guidance/ng132/chapter/recommendations	Thank you for your comment. Recommendations tagged with [2015] are those that were not prioritised for an update and were not consulted on. The committee could therefore not comment on the impact that the NICE guideline on hyperparathyroidism (primary) would have on these recommendations. The issue of albumin-adjusted serum calcium, PTH level and Vitamin D tests to rule out primary hyperparathyroidism has

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					been logged with the NICE surveillance team for consideration for future updates.
Hyperparathyroid UK Action4Change	Guideline	General	General	We strongly recommend to include in this guideline that hormone replacement therapy (HRT) can reduce serum calcium which often leads to a delayed or missed diagnosis of Primary Hyperparathyroidism (PHPT) by keeping calcium within range, which is why the recommendation to rule out PHPT first is vitally important by testing calcium, PTH, vitamin D, magnesium and 24-hour urinary calcium.	Thank you for your comment. The identification of menopause, including potential tests to carry out was not part of the 2024 guideline update. The committee could therefore not comment on this. The issue of albumin-adjusted serum calcium, PTH level and Vitamin D tests to rule out primary hyperparathyroidism has been logged with the NICE surveillance team for consideration for future updates.
Hyperparathyroid UK Action4Change	Guideline	General	General	We strongly advise including a link to NG132 which is imperative for bone health. https://www.nice.org.uk/guidance/ng132/chapter/recommendations#diagnostic-testing-in-primary-care	Thank you for your comment. Osteoporosis and fracture risk was not part of the 2024 guideline update. The committee could therefore not comment on this. NICE surveillance regularly checks for evidence that can be considered for future updates.
Hyperparathyroid UK Action4Change	Guideline	General	General	Whether a serum follicle-stimulating hormone test (FSH) does or does not indicate perimenopause or menopause, we would strenuously recommend including serum tests for calcium, PTH, vitamin D, magnesium and 24-hour urinary calcium in all patients where perimenopause or menopause is suspected to rule out primary hyperparathyroidism or be aware that the patient may have both menopause and primary hyperparathyroidism, before recommending HRT which can reduce serum calcium, often leading to a delayed or missed diagnosis of Primary Hyperparathyroidism (PHPT) by keeping calcium within range, which is why we strongly recommend to rule out PHPT first which is vitally important.	Thank you for your comment. The identification of menopause, including potential tests to carry out was not part of the 2024 guideline update. The committee could therefore not comment on this. The issue of albumin-adjusted serum calcium, PTH level and Vitamin D tests to rule out primary hyperparathyroidism has been logged with the NICE surveillance team for consideration for future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Also, before recommending CBT. A patient needs to know what they are dealing with before commencing CBT.	
Hyperparathyroid UK Action4Change	Guideline	010	008	1.4.1 We recommend after 'When discussing treatment options with people who have troublesome menopause symptoms', inserting; 'It is important to rule out primary hyperparathyroidism before we recommend lifestyle changes and interventions that can support health and wellbeing recommended in [2015]. The guideline for management of Primary Hyperparathyroidism was published [2019].' https://www.nice.org.uk/guidance/ng132/chapter/recommendations	Thank you for your comment. Identification of the perimenopause (including differential diagnoses) was outside the scope of the 2024 guideline update. The NICE surveillance team regularly checks for evidence for guideline topics to inform future updates and the issue of albumin-adjusted serum calcium, PTH level and Vitamin D tests to rule out primary hyperparathyroidism has been logged with them so that it could be taken into account when decisions about updates are made.
Hyperparathyroid UK Action4Change	Guideline	010	008	1.4.1 We recommend all patients with menopause symptoms of all ages should have primary hyperparathyroidism tested/ruled out primarily, as symptoms are often similar. Many patients have a prolonged delay in diagnosis of primary hyperparathyroidism as a result of their symptoms being wrongly assigned to menopause.	Thank you for your comment. Identifying perimenopause and menopause (including issues relating to hyperparathyroidism) was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
Hyperparathyroid UK Action4Change	Guideline	010	008	We recommend including a brief description of primary hyperparathyroidism, the similarity in some symptoms and why it should first be excluded before menopause is determined, regardless of age. Blood tests we advise to rule out primary hyperparathyroidism are calcium, Parathyroid hormone (tested in	Thank you for your comment. Identifying perimenopause and menopause (including issues relating to hyperparathyroidism) was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				EDTA), vitamin D, magnesium and a 24-hour urinary calcium excretion.	
Hyperparathyroid UK Action4Change	Guideline	010	013	We recommend inserting after 'troublesome menopause symptoms', 'only when primary hyperparathyroidism has been ruled out,'	Thank you for your comment. Issues related to hyperparathyroidism were not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
Hyperparathyroid UK Action4Change	Guideline	013	010 - 012	'For people with a history of coronary heart disease or stroke, ensure that combined or oestrogen-only HRT is discussed with and, if appropriate, initiated' We recommend including information here regarding increased risks of cardiovascular disease associated with elevated parathyroid hormone and low vitamin D which should both be ruled out with serum tests. Increased risks include ischemic stroke, and sudden cardiac death. Excess PTH (as seen in primary and secondary hyperparathyroidism) is associated with a higher incidence of hypertension, left ventricular hypertrophy, heart failure, cardiac arrhythmias, and valvular calcific disease, which may contribute to higher cardiac morbidity and mortality. Parathyroid hormone (PTH) and 25-dihydroxyvitamin D levels together can make important contributions to determination of stroke risk. PTH levels were elevated in studies of patients with acute ischemic cerebrovascular events. We strongly advise primary hyperparathyroidism be ruled out even in patients without a history of coronary heart	Thank you for your comment. Whilst the impact of HRT on the risk of cardiovascular disease was part of the scope of the 2024 guideline update, looking at comorbidities was not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				disease or stroke due to the prevalence of PHPT patients who are misdiagnosed with menopause.	
Hyperparathyroid UK Action4Change	Guideline	018	010	1.4.34 Depressive symptoms 'Consider HRT to alleviate mild depressive symptoms with onset in association with other menopause symptoms.' We recommend ruling out primary hyperparathyroidism first by testing Calcium, PTH, vitamin D, magnesium and 24-hour urinary calcium, as a cause of depressive symptoms before initiating HRT. https://www.nice.org.uk/guidance/ng132/chapter/recommendations#chronic-non-differentiated-symptoms includes 'fatigue, mild confusion, bone, muscle or joint pain, anxiety, depression, irritability, low mood, apathy, insomnia, frequent urination…'	Thank you for your comment. The effectiveness of HRT in the management of depressive symptoms associated with the menopause (as well as looking at subgroups that may have an impact on this) was not in the scope of the 2024 guideline update. This means that a search for evidence was not conducted and the committee did not discuss the evidence related to this. The committee could therefore not comment on this. The reference provided has been checked, and did not meet the criteria set out in the protocols for the evidence reviews that were updated.
Hyperparathyroid UK Action4Change	Guideline	018	012	1.4.35 'Consider CBT for depressive symptoms associated with the menopause' CBT will be of no use if depression is caused by PHPT rather than menopause. In our experience menopause has often been cited as a cause of depressive moods and anxiety, then patients find out years later from looking back at their medical records finding elevated calcium, that the real reason was there all along, but missed because healthcare	Thank you for your comment. The effectiveness of HRT in the management of depressive symptoms associated with the menopause (as well as looking at subgroups that may have an impact on this) was not in the scope of the 2024 guideline update. This means that a search for evidence was not conducted and the committee did not discuss the evidence related to this. The committee could therefore not comment on this. The reference provided has been checked and

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				professionals blamed the menopause and didn't look any further for causes.	did not meet the criteria set out in the protocols for the evidence reviews that were updated.
Hyperparathyroid UK Action4Change	Guideline	018	014 - 018	1.4.36 'For people experiencing menopause who are suspected to have, or are diagnosed, with depression, We would advise including 'once Primary Hyperparathyroidism has been excluded as a cause.' https://www.nice.org.uk/guidance/ng132/chapter/recommendations#chronic-non-differentiated-symptoms	Thank you for your comment. The effectiveness of HRT in the management of depressive symptoms associated with the menopause (as well as looking at subgroups that may have an impact on this) was not in the scope of the 2024 guideline update. This means that a search for evidence was not conducted and the committee did not discuss the evidence related to this. The committee could therefore not comment on this. The reference provided has been checked, and did not meet the criteria set out in the protocols for the evidence reviews that were updated.
Hyperparathyroid UK Action4Change	Guideline	019	002	1.4.37 We recommend ruling out primary hyperparathyroidism first by testing Calcium, PTH, vitamin D, magnesium and 24-hour urinary calcium, as a cause of 'difficulties with sleep (such as night time awakening)'. We have extensive patient feedback of relief after treatment for PHPT, even from menopausal patients.	Thank you for your comment. The topic of sleep was only considered as an outcome related to cognitive behavioural therapy; hyperparathyroidism was not part of the related review protocol on the effectiveness of CBT on difficulties with sleep. The committee could therefore not comment on this.
Hyperparathyroid UK Action4Change	Guideline	021	013	1.5.11 Offer psychological support to people with early menopause (aged 40 to 14 44) who are distressed by their diagnosis or its consequences. If needed, refer them to specialist psychology services. [2023] We recommend adding 'once primary hyperparathyroidism has been excluded as a cause of their distress/anxiety	Thank you for your comment. People with hyperparathyroidism were not included as a population subgroup of interest for this evidence review, thus no evidence for this population was assessed. The committee therefore cannot comment on this. However, The issue of albumin-adjusted serum calcium, PTH level and Vitamin D tests to rule out primary hyperparathyroidism in the identification of menopause has been logged with the NICE surveillance team.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Hyperparathyroid UK Action4Change	Guideline	021	021 - 022	'explain that, overall, taking either oestrogen-only or combined HRT is unlikely to increase or decrease life expectancy', We recommend adding 'however, it is worth ruling out primary hyperparathyroidism as a cause of the troublesome symptoms, as treatment can improve decreased life expectancy	Thank you for your comment. The committee noted that high-quality evidence showed no difference in mortality with either oestrogen-only or combined HRT compared to not taking HRT. They decided that this is an important message given that there are increased risks for some specific health outcomes highlighted in tables 1 and 2. The guideline advocates a person-centred approach that takes into account the person's age, individual circumstances and potential risk factors (which could include primary hyperparathyroidism). Identifying menopause and ruling out hyperthyroidism in relation to this was not part of the scope of the 2024 update. However, the issue of albumin-adjusted serum calcium, PTH level and Vitamin D tests to rule out primary hyperparathyroidism has been logged with the NICE surveillance team for consideration in relation to future updates.
Hyperparathyroid UK Action4Change	Guideline	022	021	1.6.3 'Do not offer HRT for the purpose of dementia prevention.' We recommend ruling out Primary hyperparathyroidism which can mimic menopause symptoms and is often mistaken for menopause and can also cause rapidly progressive dementia which is reversible with treatment (parathyroidectomy).	Thank you for your comment. The topic of comorbidities that may impact on recognition of dementia and identification of the menopause was outside the scope of the 2024 guideline update. Therefore, evidence reviews were not conducted for this topic. The committee could therefore not comment on this.
Hyperparathyroid UK Action4Change	Guideline	026	001	Dementia 'Combined HRT might increase the risk of dementia if started over the age of 65.' We strongly advise primary hyperparathyroidism and increased risks of rapidly progressive dementia be mentioned here, as a person who stops HRT suspecting it	Thank you for your comment. The guideline advocates a person-centred approach that takes into account the person's age, individual circumstances and potential risk factors (which could include primary hyperparathyroidism). Identifying menopause and ruling out

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				to be the cause of dementia, might have an entirely different cause that is missed, yet treatment can reverse the dementia. There are many medical studies about this available.	hyperthyroidism in relation to this was not part of the scope of the 2024 guideline update neither was the relationship between HRT, hyperparathyroidism and dementia. However, The issue of albumin-adjusted serum calcium, PTH level and Vitamin D tests to rule out primary hyperparathyroidism has been logged with the NICE surveillance team for consideration in relation to future updates.
Hyperparathyroid UK Action4Change	Guideline	026	-	Osteoporosis. We agree that HRT decreases the risk of fragility fracture. Menopausal patients with primary hyperparathyroidism however will still experience bone loss whilst cortical wrist bone density is not preserved. We recommend Dexa bone density scans to include the non-dominant forearm for patients with multiple symptoms, suspected of menopause and/or primary hyperparathyroidism. In many cases we see people benefit from improvement of cortical bone thickness of the distal radius as well as reversal of osteoporosis after surgical treatment for primary hyperparathyroidism.	Thank you for your comment. Osteoporosis is a topic that was not in the scope of the 2024 guideline update. This means that searches and evidence reviews were not conducted and discussed with the committee. The committee could therefore not comment on this.
Hyperparathyroid UK Action4Change	Guideline	027	001	Whilst risks of stroke in women under 60 may be very low but increased with HRT, a Swedish Study in June 2022, concluded that risks of heart or attack or stroke with primary hyperparathyroidism increased by 51%. We appreciate ages were not noted, and this study was not conducted in the UK, but we believe the cost of blood tests calcium, PTH, vitamin D, magnesium, and a 24-hour urinary calcium	Thank you for your comment. Identification of perimenopause and menopause' was not a topic that was updated in 2024. This would include symptoms that may overlap with other conditions. Having not reviewed the evidence, the committee could not comment on this. The issue of albumin-adjusted serum calcium, PTH level and Vitamin D tests to rule out primary hyperparathyroidism has

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				test are worthwhile to rule out increased risks of stroke in patients who may have primary hyperparathyroidism misdiagnosed as menopause, especially due to increased stroke risk whilst prescribed HRT. In a study conducted by us in 2023, we were advised by 100 NHS Trusts that during 2019-2022, there were 328,017 strokes recorded.	been logged with the NICE surveillance team for consideration for future updates.
Hyperparathyroid UK Action4Change	Guideline	042	021 - 025	Whilst your recommendations will raise awareness of healthcare professionals about the possibility that people from some ethnic minority groups experience menopause at a younger age, we hope that our recommendations to rule out or test for PHPT will also raise awareness that some younger people of any ethnic group with symptoms of menopause at a younger age might actually have a different reason for those symptoms which is curable, or that they may have both menopause and PHPT together. We are now seeing numerous people as young as thirteen diagnosed with primary hyperparathyroidism.	Thank you for your comment. A comprehensive analysis of populations and conditions related to menopause (including primary hyperparathyroidism) as well as general identification of the menopause and menopause symptoms were all topics that were outside the scope of the current guideline. The committee could therefore not comment on this. The issue of albumin-adjusted serum calcium, PTH level and Vitamin D tests to rule out primary hyperparathyroidism has been logged with the NICE surveillance team for consideration for future updates.
Hyperparathyroid UK Action4Change	Guideline	046	002	Taking comorbidities into account. We entirely agree that different risk factors mean that people have different baseline levels of risk and that decisions on hormone replacement therapy (HRT) use for menopause symptoms would need to be tailored to the person and their particular risk	Thank you for your comment. The general topic of comorbidities that may be related to menopause is outside the scope of the guideline. The recommendations in these sections originated from discussions of the specific health outcomes discussed in section 1.6. The committee could therefore not comment on this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				factors and risk levels, which is the precise reason we recommend to include that primary hyperparathyroidism must be a comorbidity considered in this guideline due to similarities in many symptoms, and increased risks of cardiovascular disease and strokes, bone loss https://www.nice.org.uk/guidance/ng132/chapter/recommendations	
Hyperparathyroid UK Action4Change	Guideline	046	015 - 016	'This recommendation to discuss this with a healthcare professional with expertise in menopause will standardise practice.' The health care professional with expertise in menopause, should be the same healthcare professional with expertise in primary hyperparathyroidism. Yet rarely are the two looked at together. We recommend inclusion of information about primary hyperparathyroidism might standardise practice into looking for and distinguishing between them both or recognise that symptoms could be caused by both comorbidities rather than one or the other. We feel there is an opportunity within this guideline to benefit patients with your assistance, to change that.	Thank you for your comment. The definition of 'healthcare professional with expertise in menopause' notes that these professionals can advise and support colleagues in managing complex menopause-related needs and risk factors affecting decision making, including complex medical problems that potentially affect use of treatments for menopause symptoms. The committee agreed that primary hyperparathyroidism would fall into such a 'complex medical problem' category. The issue of albumin-adjusted serum calcium, PTH level and Vitamin D tests to rule out primary hyperparathyroidism has been logged with the NICE surveillance team for consideration for future updates.
Hyperparathyroid UK Action4Change	Guideline	047	007 - 015	CBT therapy will not be of any use if sleep disturbance is caused by primary hyperparathyroidism, insomnia and the need to urinate often during the night, rather than menopause. Symptoms of PHPT; 'insomnia, frequent urination' included in;	Thank you for your comment. The recommendations related to CBT refer to symptoms associated with the menopause. Identifying the menopause is in a separate section which did not feature in the 2024 guideline update. However, once it is established that the symptoms are associated with the menopause the evidence showed that CBT was

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				https://www.nice.org.uk/guidance/ng132/chapter/recommendations#chronic-non-differentiated-symptoms In our experience menopause has been cited as a cause of many symptoms, then a patient finds out years later from looking at their medical records, that they had elevated calcium and that the real reason was there all along but missed because healthcare professionals blamed the menopause and didn't look any further for causes.	associated with some benefit and should therefore be an option to be considered. The issue of albumin-adjusted serum calcium, PTH level and Vitamin D tests to rule out primary hyperparathyroidism has been logged with the NICE surveillance team for consideration for future updates.
Hyperparathyroid UK Action4Change	Guideline	049	008 - 013	'The committee acknowledged that this would be a change to clinical practice. They noted that people would potentially be able to manage their own symptoms after the standard amount of CBT sessions. This would benefit the NHS because people may not need other treatments which would require regular reviews and ongoing prescriptions, such as hormone replacement therapy (HRT).' We found this paragraph astonishing and in complete contrast to the preceding 48 pages. It appears to suggest that CBT sessions will eliminate the need for HRT, to benefit the NHS, saving them time and money. We would assume the committee have neither endured menopause or taken it seriously.	Thank you for your comment. The wording of the recommendation has been revised to ensure clarity about CBT 'as an option: in addition to other treatments, for people for whom other treatments are contraindicated or for people who prefer not to have other treatments'. Any mention of this being cost saving for the NHS or leading to fewer prescriptions has been removed (the paragraph referred to was deleted).

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				This one paragraph rather makes a mockery of this whole guideline and reads like an obscure attempt at playing devil's advocate. It may as well advise menopausal women that their symptoms are, 'all in their heads', to go away and chomp on the bit until it's over, and stop bothering doctors (for some that's up to twenty years).	
Hyperparathyroid UK Action4Change	Guideline	049	008 - 013	The following symptoms are taken from the NHS page for menopause; https://www.nhs.uk/conditions/menopause/symptoms/ Mental Health symptoms of menopause and perimenopause include; • changes to your mood, like low mood, anxiety, mood swings and low self-esteem • problems with memory or concentration (brain fog) Common physical symptoms of menopause and perimenopause include: • hot flushes, when you have sudden feelings of hot or cold in your face, neck and chest which can make you dizzy • difficulty sleeping, which may be a result of night sweats and make you feel tired and irritable during the day • palpitations, when your heartbeats suddenly become more noticeable	Thank you for your comment. The wording of the recommendation has been revised to ensure clarity about CBT 'as an option: in addition to other treatments, for people for whom other treatments are contraindicated or for people who prefer not to have other treatments'. The identification of menopause including updating the list of symptoms in the guideline was out of scope of the 2024 guideline update. The committee could therefore not comment on the extend of the impact of CBT on all of these. The paragraph referring to potential cost savings has been removed.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				• headaches and migraines that are worse than usual • muscle aches and joint pains • changed body shape and weight gain • skin changes including dry and itchy skin • reduced sex drive • vaginal dryness and pain, itching or discomfort during sex • recurrent urinary tract infections (UTIs) The role of CBT for menopausal women is to support them and help them understand the changes to their bodies and mental health, and to cope mentally with the transgression to post menopause. CBT is not going to help with physical symptoms. HRT should not be refused to these women to benefit the NHS by saving them from regular reviews and ongoing prescriptions. We recommend this paragraph to be removed entirely due to its offensive nature to all menopausal women.	
Hywel Dda University Health Board- Specialist Menopause Clinic	Evidence review A	General	General	Overwhelmingly the evidence suggests that CBT is not superior to TAU, or very low-quality evidence. This needs to be highlighted to otherwise it may be seen as misleading.	Thank you for your comment. Discussions of the evidence base that led to CBT recommendations as a treatment option have been captured in 'The committee's discussion and interpretation of the evidence' section of the evidence review. The rationale for recommending CBT as a treatment option has been made clearer in the guideline. The committee reflected on the wording of the recommendations related to CBT and revised them to ensure clarity about this ' as an option: in addition to other treatments (including HRT), for people for whom other treatments are contraindicated or for people who prefer not to

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					take HRT'. This makes it clear that CBT is not seen as a first line treatment but as an option where this is a preferred choice.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	General	General	Appendix A There is no QALY data for HRT which is incredibly important when discussing risks and benefits	Thank you for your comment. Analysis of quality-of-life data in relation to systemic HRT was not part of the scope of the 2024 guideline update. Therefore, QALYS could not be included in the appendix.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	006	019	The use of the word 'troublesome' here and elsewhere in the document. We feel that the language used in the guideline minimises women's experiences and is not truly representative of the women we see in clinic asking for HRT. Suggest more appropriate and reflective language of the severity of symptoms experienced by women	Thank you for your comment. Based on this and other feedback the committee reflected on this wording and consequently 'troublesome' has been removed from the guideline. NICE takes the reports of the debilitating symptoms, the considerable concern it causes and the impact that symptoms associated with the menopause have seriously. Whilst an update of the list of symptoms and experiences was outside the current scope of the 2024 guideline update (and therefore no evidence review was conducted), the NICE surveillance team checks regularly for new evidence for topics within guidelines to see where further work is needed. Apart from the removal of the word 'troublesome' the committee decided that without further evidence they could not comment on this.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	009	017	FSH can be taken in those on high-dose progestogen at the time of their repeat injection, as per FSRH guidance (https://www.fsrh.org/documents/fsrh-guidance-contraception-for-women-aged-over-40-years-2017/)	Thank you for your comment. Identifying perimenopause and menopause was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee (and the cited reference did therefore not meet inclusion criteria). The committee could therefore not comment on this.
Hywel Dda University Health	Guideline	010	027	Misleading sentence. There are no arbitrary limits or cut offs to use of HRT. As per BMS	Thank you for your comment. This has been rephrased to read 'discuss the possible duration

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Board- Specialist Menopause Clinic				Menopause Practice Standards review should be annual and duration of HRT use tailored to individual need. (https://thebms.org.uk/wp-content/uploads/2022/12/BMS-Menopause-Practice-Standards-DEC2022-A.pdf)	of treatment at the outset', followed by 'rediscuss the benefits and risks or continuing treatment at every review'. This does not suggest arbitrary limits or cut offs.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	011	007	CBT. Patients/Public may have unrealistic views/expectations on being able to access CBT, especially in person, if they feel it is being recommended through NICE. CBT is not widely available and training very limited. HRT is more widely available, is safe and effective for most women, and from this guideline appears to be demoted to a second-line treatment option after CBT.	Thank you for your comment. Taking into account current pressures on services, your comment will be considered by NICE where relevant support activity is being planned.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	015	026	Non-hormonal vaginal moisturisers and lubricants can/should be used alongside topical vaginal oestrogen preparations- and not instead of – as this statement appears to indicate. This could be confusing.	Thank you for your comment. This recommendation was specifically related to people in whom vaginal oestrogen preparations are contraindicated or for people who would prefer not to use vaginal oestrogen. However, on reflection it was recognised that the order of recommendations could have led to confusion. The recommendation stating that vaginal oestrogen and non-hormonal moisturisers or lubricants can be used alone or in combination has therefore been moved up to a position before this recommendation to clarify this point.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	016	019	Agree we have no RCT to support the use of vaginal oestrogen in this group of women, and probably never will. However, we have increasing amounts of observational data, and 'expert advice' to support its use. We feel that this guideline could go further to assure and support the use of topical vaginal oestrogen in this group. Cold S et al. Systemic or vaginal hormone therapy after early breast cancer: A	Thank you for your comment. Observational studies were considered for inclusion in Review B2, which is the evidence review related to genitourinary symptoms and breast cancer recurrence. Cold 2022 was included in this review. The committee made changes to the order of recommendations so that considerations of adjuvant treatments are being made early in shared decision making. They also revised the

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Danish observational cohort study. *J Natl Cancer Inst* 2022 Jul 20; [e-pub]. (https://doi.org/10.1093/jnci/djac112. opens in new tab) and Cathcart-Rake EJ and Ruddy KJ. Vaginal estrogen therapy for the genitourinary symptoms of menopause: Caution or reassurance? *J Natl Cancer Inst* 2022 Jul 20; [e-pub]. (https://doi.org/10.1093/jnci/djac113. opens in new tab)	recommendation related to safety considerations for clarity. This would give this section a more logical flow and greater clarity about safety. The rationale of the guideline and the committee discussion section of the evidence were revised accordingly. A visual summary was produces for the management of genitourinary symptoms to clarify treatment options and facilitate decision making.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	018	003	Agree with this sentence, that moisturisers and lubricants can be used alongside topical vaginal oestrogens. This sentence is not in line however with the sentence p15 line 26 which implies they are to be used instead of.	Thank you for your comment. This recommendation was specifically related to people in whom vaginal oestrogen preparations are contraindicated or for people who would prefer not to use vaginal oestrogen. However, on reflection it was recognised that the order of recommendations could have led to confusion. The recommendation stating that vaginal oestrogen and non-hormonal moisturisers or lubricants can be used alone or in combination has therefore been moved up to a position before this recommendation to clarify this point.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	018	009	Use of language that could be stigmatised or alienating for women such as 'depressive/depression'. Many women will consider they have low mood or mood disturbance, and again this is a range of experiences, but may object to being labelled as 'depressed' which may lead to an anti-depressant being prescribed over HRT. (Depressive symptoms vs clinical depression). We feel the NICE guideline should move away from language, which alienates women or leads to misdiagnosis or incorrect treatment.	Thank you for your comment. The committee decided that 'low mood' or 'mood disturbance' is difficult to define by a clinician or a person seeking advice. There were also a variety of measures used in the associated literature to measure such symptoms. They therefore agreed that a definition would be helpful and have added this. Depressed mood is one of the symptoms. The terminology 'depressive symptoms' has been used to differentiate it from a diagnosis of depression. The committee reflected on this and noted that it was important to provide clarity about these symptoms which are all related to feelings

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					of depression so that these types of symptoms can be openly discussed rather than giving them different labels that cannot be clearly defined.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	019	002	We feel sleep disturbance is slightly more complex than appears in this guideline and very common. It should be thoroughly assessed, with sleep diaries for example and diagnosis made where appropriate using DSM V. Although CBT can help in some cases/type of sleep problems, HRT is also important where main issue is night sweats which are impacting sleep. We feel there is a larger body of evidence around diagnosis, management and treatment of sleep disturbances, beyond CBT, which should be considered and included.	Thank you for your comment. Apart from CBT other management options for sleep problems associated with the menopause were not in the scope of the 2024 guideline update. However, the committee acknowledged that there are other options that may be used (including HRT). They have therefore reworded the recommendation to reflect this. It now states that CBT could be used as an option (1) in addition to other treatments (including HRT), or (2) for people for whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. Given the constraints of the scope they could not be more specific than this.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	019	015	We feel there needs to be reference to where hysterectomy where endometriosis is diagnosed. In this case a combination oestrogen and progestogen are recommended (BMS)	Thank you for your comment. The committee discussed that choice between oestrogen-only and combined HRT may be different for people with a sub-total hysterectomy. They decided that they could not be prescriptive about the type of HRT to be used for people who have had a sub-total hysterectomy because their condition is clinically complex and they had not reviewed evidence about the effect of HRT on risk of endometrial cancer for this group. They acknowledged that people who were going to have, or had had, a sub-total hysterectomy would be under the care of a specialist who could discuss HRT options tailored to their needs (or a relevant specialist within the MDT). Due to a lack of evidence, no specific recommendation was made for sub-total hysterectomy; however, the term "total" was added before "hysterectomy" in

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					guidance regarding the offer of oestrogen-only HRT to those who have had a hysterectomy. This addition alerts healthcare professionals to consider other factors for patients with a sub-total hysterectomy. The committee also noted that some people have a hysterectomy for a condition that may be affected by HRT, such as endometriosis. The committee did not review evidence related to such conditions. Therefore, they recognised that the decision about the type of HRT that best balances benefits and risks for the person may be affected by that condition (for example endometriosis) or having had a subtotal hysterectomy. For this reason, they added a recommendation highlighting that advice from a healthcare professional with specialist knowledge of that condition may be needed when making this choice. Due to this stakeholder comment and other related comments, this topic has been logged with NICE surveillance so that it can be considered for a possible update to either the Menopause or the Endometriosis guideline in future.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	021	022	What is the evidence for this statement ? Hormone replacement therapy and longevity - PubMed (nih.gov)	Thank you for your comment. Please see the evidence in Evidence Report H on all-cause mortality. Full details on the studies included for this review, and the committee's discussion of the evidence which led to the recommendations can be found in the related rationale section of the guideline and in evidence review H.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	022	017	We strongly disagree with this statement and believe there is an increasing body of evidence to show HRT reduces incidence of heart disease related events when used at the right time . Including the timing hypothesis Hormone replacement therapy and the association with coronary heart disease and overall mortality: clinical application of the timing hypothesis - PubMed (nih.gov) and Menopausal Hormone Replacement Therapy and Reduction of All-... : The Cancer Journal (lww.com)	Thank you for your comment. The cited reference is a narrative review, which is not included as an eligible study design in the protocol for Evidence Review C. However, the data in Evidence Review C was stratified by age at first use, and time since menopause at first use of HRT where possible. The committee discussed the subgroup analysis from the RCT data for age at first use and the time since menopause at first use, and since there were no statistically significant subgroup differences, they could not conclude that there was a reduced incidence of heart disease related events when HRT was used at a particular age, or a specific time period following the start of menopause. The committee also considered the observational study evidence, which was also stratified by the same subgroups where possible. They discussed that evidence from one study supported a reduced risk in coronary heart disease which was specific to a younger age group, however this pattern was not reflected in another observational study which also presented subgroup data. Since there were inconsistent results between the observational studies, and no statistically significant subgroup differences in the RCT evidence, the committee could not reach the conclusion that there was a reduced risk of coronary heart disease depending on the age at first use, or the time since menopause when HRT was first used. The rationale section of the guideline and the 'committee's interpretation of the evidence section' of evidence review C have been updated to make this clearer. NICE commissioned an independent review of the breast cancer and cardiovascular evidence

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline	074	007	The guideline refers to the importance of HRT for bone protection in premature menopause but does not make recommendations for its use in other age groups. We feel this is lacking from the guideline considering the morbidity and mortality attributed to fractures in women and cost to the NHS, and that the evidence supports the use of HRT as a treatment option, including the Royal Osteoporosis Society	Thank you for your comment. The aim of the evidence review carried out was assessing the impact of either taking HRT or not taking HRT on people with early menopause and the development of various health outcomes. The need to assess the impact of early menopause on health outcomes, including osteoporosis and fragility fractures, and the treatment to prevent such health outcomes has been acknowledged and will be passed onto the NICE surveillance teams for prioritised consideration during future updates.
Hywel Dda University Health Board- Specialist Menopause Clinic	Guideline and Evidence review A	012	009	Agree that there needs to be equitable access to all groups, but needs to be highlighted that there is no evidence to support the use of CBT for people taking gender-affirming therapy? Again this could be seen as misleading recommendation when evidence is lacking	Thank you for your comment. The cited section refers to people who have taken gender affirming hormone therapy in the past. People who are currently taking gender affirming hormone therapy are not in the scope of the guideline due to the side effects of that therapy that can mirror menopause symptoms. The committee thought that people who have taken gender affirming

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					hormone therapy should have the same option to have CBT than other people and the recommendation was revised in line of the wording changes elsewhere clarifying that is an option (1) in addition to other treatments (including HRT) (2) for people in whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. This was identified as an issue in the equality impact assessment and the committee considered this as part of the discussions in line with NICE methodology related to equality considerations.
Imperial College Healthcare NHS Trust	Guideline	General	General	I have submitted my comments on behalf of the British and International Menopause Societies in order to reduce duplication.	Thank you.
International Menopause Society				**1.4.20** Vaginal bleeding should be reported as per guidance for any post-menopausal bleeding	Thank you for your comment. On reflection, the committee decided to remove this statement.
International Menopause Society	Evidence Review I/Appendix K	063	018	It is welcomed that there is a research recommendation for this age group to study quality of life and long-term health outcomes. POI and early menopause should be regarded as a risk continuum with many of the bone, cardiovascular and dementia / Parkinson's data applying both to POI and women less than 45 years of age.	Thank you for your comment. The recommendation and rationale in the guideline document have been revised taking into consideration the overlapping risks of POI to the early menopause population. The recommendation for this section now reads as follows: 'When discussing HRT as a treatment option, explain to people experiencing early menopause, that, for them, the benefits and risks of either taking or not taking HRT are likely to lie between those for people with premature ovarian insufficiency and those for people aged 45 or over'. The need to assess the impact of early menopause on health outcomes has been acknowledged and have been passed onto the NICE surveillance teams for prioritised consideration during future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
International Menopause Society	Guideline	General	General	Why is the term hormone replacement therapy (HRT) still being used. This is no longer the norm in several countries as this is not replacement therapy but therapy to alleviate menopause symptoms, help GSM and protect against osteoporosis. Would it not be better to use menopause hormone therapy (MHT) as IMS and EMAS have been doing for a while?	Thank you for your comment. The committee were aware of the shift in terminology within the professional and scientific communities. However, it was decided not to update the wording in 2024 guideline update because it is currently in the UK context more readily understood by lay people.
International Menopause Society	Guideline	General	General	Why is the spelling of oestrogen still with an "o" when international nomenclature has changed this to estrogen?	Thank you. This has been agreed within NICE and the 'oe' version is still the more commonly used one in the UK for oestradiol. So, we have left this as is.
International Menopause Society	Guideline	General	General	It is welcomed that the updated draft includes additional recommendations on GU symptoms, the effects of HRT on health outcomes and the effects of early menopause.	Thank you for your comment in support of this.
International Menopause Society	Guideline	General	General	The guideline recommends that HRT should be "offered" to people with troublesome vasomotor symptoms **(1.4.15)** and recommends that CBT should be "considered" **(1.4.16)** which is a weaker recommendation. It is therefore surprising how prominently CBT appears both in the guideline and in the press release.	Thank you for your comment. The committee reflected on the wording of the recommendations and updated it to make it explicit that this was not recommended as a first line treatment. It is now stated that it is an option (1) in addition to other treatments (including HRT) (2) for people in whom other treatments are contraindicated or (3) for people who prefer not to have other treatments.
International Menopause Society	Guideline	General	General	In discussion with some international colleagues at conferences, it is their impression from the publicity that NICE now	Thank you for your comment. The committee reflected on the wording of the recommendations and updated it to make it explicit that this was not recommended as a first line treatment. It is now stated that it is an option (1) in addition to other

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				favours CBT over HRT for managing troublesome vasomotor symptoms.	treatments (including HRT) (2) for people in whom other treatments are contraindicated or (3) for people who prefer not to have other treatments.
International Menopause Society	Guideline	General	General	It is disappointing that a number of aspects of the 2015 guideline have not been updated despite there now being additional data on efficacy and safety of HRT from studies and meta-analyses – these will be outlined in the subsequent responses.	Thank you for your comment. The NICE surveillance team regularly checks for evidence for topics in guidelines to be considered for future updates.
International Menopause Society	Guideline	General	General	**POI:** The ESHRE 2015 POI guideline is currently being updated in a partnership of ESHRE, IMS, Monash and ASRM so it was appropriate that it was omitted from the NICE guideline update. However, can we please ensure that the updated NICE guideline contains a link to the new POI guideline when it is published?	Thank you for your comment. POI was not part of the scope of the 2024 guideline update and the ESHRE guideline has not yet been published. A cross reference cannot be added because it is uncertain what the guideline will say.
International Menopause Society	Guideline	021/022	021/016	Tables 1 and 2 **1.6.1/1.6.2** We ask the committee to consider rewording or adding to these recommendations, given that high-quality evidence exists for reduction of cardiovascular and all-cause mortality with HRT. Whilst these are not primary indications for use of HRT, the evidence for these potential benefits as well as risks should be included in a comprehensive counselling process.	Thank you for your comment. The committee discussed the evidence in Evidence Review C relevant to cardiovascular mortality following the use of HRT. They concluded that the evidence did not show a reduction in cardiovascular mortality, nor did it show an increase in cardiovascular mortality. They used this evidence to inform their recommendations. Please see the committee's discussion of the evidence section in Evidence Review C for more details. The committee discussed the evidence in Evidence Review H relevant to all-cause mortality. They discussed that overall, the evidence did not show a reduction or an increase in all-cause mortality for combined HRT or oestrogen-only HRT. The data was stratified by age at first use. They

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				There are a number of studies and meta-analyses in peer reviewed journals which have demonstrated a reduction in cardiovascular and all-cause mortality. Some of the relevant publications are shown below. Salpeter RS et al Journal of general internal medicine 2006;21(4):363-6 Schierbeck LL, Rejnmark L, Tofteng CL, Stilgren L, Eiken P, Mosekilde L, Køber L, Jensen JE. Effect of hormone replacement therapy on cardiovascular events in recently postmenopausal women: randomised trial. BMJ. 2012 Oct 9;345:e6409. Boardman HM, Hartley L, Eisinga A, Main C, Roqué i Figuls M, Bonfill Cosp X, Gabriel Sanchez R, Knight B. Hormone therapy for preventing cardiovascular disease in post-menopausal women. Cochrane Database Syst Rev. 2015 Mar 10;2015(3):CD002229. Manson JE, Aragaki AK, Bassuk SS et al for WHI Investigators. Menopausal Estrogen-Alone Therapy and Health Outcomes in Women With and Without Bilateral Oophorectomy: A Randomized Trial. Ann Intern Med. 2019 Sep 17;171(6):406-414.	discussed that for combined-HRT use, there were no differences in the risk of all-cause mortality depending on the age at first use. They also discussed the evidence for oestrogen-only HRT. They noted that the evidence showed an isolated risk reduction in younger women, however this was part of a subgroup analysis that did not show a statistically significant difference between the subgroups, and therefore the committee did not conclude that there was a difference in the risk of all-cause mortality depending on age at first use. Please see the committee's discussion of the evidence section in Evidence Review H for more details. The Salpeter et al, and the systematic review by Boardman et al. Both included some studies that did not meet the protocol criteria for the relevant reviews and therefore the systematic review could not be included as a whole. However, the included studies from the systematic reviews were individually checked against the protocols and if they did meet the criteria in the protocols then they were included separately. The rationale section of the guideline has been updated to clarify this. The highlighting study by Manson 2019 is one of the publications from the WHI and did meet inclusion criteria. The data from the WHI were included in Evidence Review C and Evidence Review H.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
International Menopause Society	Guideline	011	006	**1.4.4** CBT to manage menopause symptoms - is there level 1 evidence for this?	Thank you for your comment. The committee reflected on the wording of the CBT recommendations in light of the evidence quality and updated it to make it explicit that this was not recommended as a first line treatment. It is now stated that it is an option (1) in addition to other treatments (including HRT) (2) for people in whom other treatments are contraindicated or (3) for people who prefer not to have other treatments.
International Menopause Society	Guideline	011	016	**1.4.5/6** I think this paragraph is too brief and there should be further information describing unregulated compounded hormone therapy and the safety, efficacy, quality and purity risks of these hormones.	Thank you for your comment. Complementary therapies and unregulated preparations were not a topic that was part of the 2024 guideline update. The committee could therefore not add details to this given that evidence was not reviewed.
International Menopause Society	Guideline	013	010	**1.4.13** There does not seem to be enough information on the possible risks, and also there is no discussion of what medications the patient is presently taking or the age of the patient. This type of patient should be exposed to a multidisciplinary team of a cardiologist and a menopause expert	Thank you for your comment. For people with a history of coronary heart disease or stroke, the committee agreed that different risk factors mean that people have different baseline levels of risk (this could include any relevant medication). They concluded that decisions on HRT use for menopause symptoms would need to be tailored to the person and their particular risk factors and risk levels. The committee decided that the healthcare professional with expertise in menopause would be the appropriate specialist to see them because they are defined as people who can advise and support colleagues in managing complex menopause-related needs and risk factors affecting decision making, including complex medical problems that potentially affect use of treatments for menopause symptoms (see terms used in the guideline). Such healthcare professionals are also

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					likely to seek advice from other specialties if there was any doubt on safety.
International Menopause Society	Guideline	014	005	**1.4.16** In addition to CBT, should hypnosis not also be considered by NICE as a non-hormonal way of dealing with vasomotor symptoms? There is evidence for effectiveness, and it is included in the NAMS (now The Menopause Society) position statement (shown below). Elkins GR et al Randomized trial of a hypnosis intervention for the treatment of hot flashes among breast cancer survivors. Journal of Clinical Oncology. 2008;26(31):5022–5026. The 2023 North American Menopause Society Non-Hormone therapy position statement Menopause 2023;30(6):573-90. An NIH-funded multicentre RCT of Clinical Hypnosis for menopausal hot flashes is also being conducted in the USA.	Thank you for your comment. Hypnosis was not part of the scope of the 2024 guideline update. Therefore, the committee could not comment on this. The cited references do not fit inclusion criteria for this update but were logged with the NICE surveillance team so that they can be considered for a future update.
International Menopause Society	Guideline	015	001	Clarification of terminology required here "Genitourinary symptoms / Genitourinary menopause symptoms etc – suggest that the terminology used synergises with the current indications for use of vaginal products otherwise there could be concern regarding off label use of these products	Thank you for your comment. The document was reviewed for consistency and is now referring to 'genitourinary symptoms associated with the menopause' throughout. A definition of these symptom has also now been added to the 'terms used in this guideline' section which corresponds to the current indications.
International Menopause Society	Guideline	015	014	**1.4.20** The amount of estrogen absorbed with ultra-low doses of regulated vaginal estrogen should be regarded as not clinically significant (not just "small")	Thank you for your comment. This bullet point was reworded to say that vaginal oestrogen is absorbed locally - a minimal amount is absorbed into the bloodstream (when compared with systemic HRT), but this is unlikely to have a

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					significant effect throughout the body. It is then described in the rationale section that 'the committee agreed to highlight this because it means that there is no need to combine low-dose vaginal oestrogens with systemic progestogen treatment to protect the person against endometrial hyperplasia and cancer'.
International Menopause Society	Guideline	015	014	**1.4.20** Symptoms commonly return when treatment is stopped (might be a better term than "often")	Thank you for your comment. Within NICE style 'commonly' is considered less plain English than 'often'. Therefore, 'often' has been retained.
International Menopause Society	Guideline	015	018	**1.4.21** Increasing the dose "within the standard therapeutic range" is commonly insufficient to fully alleviate symptoms – guidance should be given as to what to do under these circumstances	Thank you for your comment. The committee decided to remove this recommendation because they could not be more specific about dosage. The guideline contains recommendations about reviewing treatment and recommends that treatment for symptoms associated with the menopause should be reviewed at 3 months to assess efficacy and tolerability and annually thereafter, unless there are clinical indications for an earlier review (such as treatment ineffectiveness, side effects or adverse events). It is also recommended to 'refer people to a healthcare professional with expertise in menopause if treatments do not improve their menopause symptoms or they have ongoing side effects.' This means that if symptoms are not resolved after vaginal oestrogen is prescribed treatment is reviewed and other differential diagnoses could be considered. It has now also been highlighted in the guideline that 'the benefits and risks of HRT described in this guideline only cover the use of HRT within the licensed dosages. Making decisions using NICE guidelines has information about prescribing medicines'.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
International Menopause Society	Guideline	015	026	**1.4.23** The section on non-hormonal vaginal moisturisers and lubricants does not appear to be specific enough, as some silicone-based products may cause irritation, as do scented products	Thank you for your comment. A comparison of different types of moisturisers and lubricants based on individual constituents was outside the scope of this review question. The committee could therefore not comment on this.
International Menopause Society	Guideline	016	001	**1.4.24** Is there a reason why prasterone cannot be considered as a first line option alongside vaginal estrogen for VVA symptoms? **1.4.25** Why are women unable to choose ospemifene if they cannot/or do not choose to use vaginal preparations for VVA symptoms?	Thank you for your comment. Recommendations were based on the clinical and cost effectiveness evidence which highlighted the locally applied oestrogens as the most cost-effective treatment and thus was recommended first line. Prasterone and ospemifine were not the most cost or clinically effective options so were only recommended in selected circumstances.
International Menopause Society	Guideline	016	019	**1.4.28** Key issue is concern about safety of vaginal estrogen in women with breast cancer, particularly when using AIs (not just the efficacy)	Thank you for your comment. The recommendation about potential uncertainty related to efficacy of vaginal oestrogen for people with a personal history of breast cancer has been removed.
International Menopause Society	Guideline	018	010	**1.4.34** The evidence favours estrogen-only therapy to alleviate mild depressive symptoms. There is not enough good quality evidence regarding combined HRT. Certain progestogens may exacerbate depressive symptoms (Maki PM, et al and the Board of Trustees for The North American Menopause Society (NAMS) and the Women and Mood Disorders Task Force of the National Network of Depression Centers. Guidelines for the evaluation and treatment of perimenopausal depression: summary and	Thank you for your comment. The evidence related to HRT's and other treatments' effectiveness in the management of depressive symptoms associated with the menopause was not part of the 2014 guideline update. Therefore, the cited reference was not included because it did not meet inclusion criteria for any protocol. The decision to amend the wording was made to avoid an overlap with the NICE guideline on depression in adults. A definition of depressive symptoms has now also been provided. The NICE surveillance team checks topics in guidelines regularly which can then be considered for potential future update.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				recommendations. Menopause. 2018 Oct;25(10):1069-1085)	
International Menopause Society	Guideline	019	002	**1.4.37** NB: Cognitive Behavioral Therapy for Insomnia (CBT-I) is a multi-component treatment for insomnia that targets difficulties with initiating and/or maintaining sleep (Walker J, et al, Cognitive Behavioral Therapy for Insomnia (CBT-I): A Primer. Klin Spec Psihol. 2022;11(2):123-137)	Thank you for your comment. The evidence was for all kinds of CBT, not restricted to CBT-I. The committee therefore decided to keep this recommendation broad relating to all relevant types of CBT. However, the committee acknowledged that there are other options that may be used (including HRT). They have therefore reworded the recommendation to reflect this. It now states that CBT could be used as an option (1) in addition to other treatments (including HRT), or (2) for people for whom other treatments are contraindicated or (3) for people who prefer not to have other treatments.
International Menopause Society	Guideline	019	002	**1.4.37** Since HRT is helpful in alleviating hot flushes and night sweats, HRT may help with sleep disturbances related to waking up at night. Ref: The 2022 Hormone Therapy Position Statement of The North American Menopause Society. *Menopause.* 2022;29(7):767-794.	Thank you for your comment. Apart from CBT other management options for sleep problems associated with the menopause were not in the scope of the 2024 guideline update. However, the committee acknowledged that there are other options that may be used (including HRT). They have therefore reworded the recommendation to reflect this. It now states that CBT could be used as an option (1) in addition to other treatments (including HRT), or (2) for people for whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. Given the constraints of the scope they could not be more specific than this.
International Menopause Society	Guideline	019	005	**1.4.38** This should be more comprehensive. It is disappointing that it was not considered to update this part of the guideline, particularly given the huge	Thank for your comment. The surveillance and scoping process for the 2024 guideline update did not identify substantive new evidence likely to change the existing recommendations on testosterone. Therefore, reviewing evidence on testosterone in relation to menopause care was

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				amount of recent interest in testosterone therapy. A strong guideline regarding the evidence-based benefits and risks of testosterone would have been very helpful, particularly given the key meta-analyses and consensus statements since the 2015 guideline and the confusion about the non-sexual effects of testosterone. Islam RM, Bell RJ, Green S, Page MJ, Davis SR. Safety and efficacy of testosterone for women: a systematic review and meta-analysis of randomised controlled trial data. Lancet Diabetes Endocrinol. 2019 Oct;7(10):754-766. doi: 10.1016/S2213-8587(19)30189-5. Epub 2019 Jul 25. Davis SR, Baber R, Panay N, Bitzer J, Cerdas Perez S, Islam RM, Kaunitz AM, Kingsberg SA, Lambrinoudaki I, Liu J, Parish SJ, Pinkerton J, Rymer J, Simon JA, Vignozzi L, Wierman ME. Global Consensus Position Statement on the Use of Testosterone Therapy for Women. Climacteric. 2019 Oct;22(5):429-434.	not prioritised. However, NICE discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and they prioritised funding for urgent research in this area.
International Menopause Society	Guideline	019	016	**1.5.2** "Lowest effective dose" It would be helpful if the terms "individualised" or "personalised" were also used in this	Thank you for your comment. The committee recommended the lowest effective dosage which would be reviewed in 3 months to assess efficacy

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				sentence to indicate that "one dose/type" of HRT does not suit all.	and tolerability and annually thereafter (as highlighted in a different recommendation on reviewing treatments). The suggested wording of 'appropriate individualised dosage' would be difficult to use because it would require a lot of additional explanation of what it would entail with the same outcome that it would be reviewed and potentially adjusted if necessary. All dosages would be within licensed ranges and a statement has now been added to emphasise this.
International Menopause Society	Guideline	021	013	**1.5.11** "Offer psychological support to people with early menopause …." Agree…. but women with early menopause should also be assessed in a specialist menopause service (at least initially) in order to optimise their chances of a good quality of life and long-term health.	Thank you for your comment. Organisation of services was outside the scope of the current guideline.
International Menopause Society	Guideline	021	021	**1.6.1** …explain that, overall, taking either oestrogen-only or combined HRT is unlikely to increase or decrease life expectancy." Is this blanket statement correct or necessary?	Thank you for your comment. Overall, most of the evidence did not show any significant differences in all-cause mortality. There was an isolated risk reduction in the age group 50-59, for oestrogen-only HRT users, however this is part of a subgroup analysis that did not show a statistically significant difference between the subgroups, and therefore the committee could not conclude that there was a benefit in all-cause mortality that warranted a recommendation. Evidence Review H has been amended to make it clearer that although there was an isolated benefit, there was not a statistically significant subgroup difference. The committee thought it was an important finding and decided that it was necessary to highlight this since it would be a reassuring message to people in the context of some risks related to some specific health outcomes.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
International Menopause Society	Guideline	015 & 016	026 & 011	**1.4.23/1.4.26** The aim should be to replicate the natural vaginal environment – worth mentioning pH and osmolality which should be similar to physiological levels e.g. Edwards D, Panay N. Treating vulvovaginal atrophy/genitourinary syndrome of menopause: how important is vaginal lubricant and moisturizer composition? Climacteric. 2016 Apr;19(2):151-61. Potter N, Panay N. Vaginal lubricants and moisturizers: a review into use, efficacy, and safety. Climacteric. 2021 Feb;24(1):19-24.	Thank you for your comment. The pH level and osmolarity of moisturisers and lubricants was not in the scope of this review question. This means that different levels of pH and osmolarity were not compared with each other to investigate the impact on genitourinary outcomes associated with the menopause. The article by Panay was not included because it did not meet protocol criteria (it was a narrative review). The committee could therefore not comment on this.
International Menopause Society	Guideline	035	004	**1.6.4** The evaluation of the impact of MHT on women with early menopause is limited to one analysis of observational data pertaining to breast cancer yet the findings appear to be applied to an array of outcomes not addressed in the one included paper of evidence (all-cause mortality and developing: venous thromboembolism, cardiovascular disease, type 2 diabetes, endometrial cancer, ovarian cancer, osteoporosis, dementia and loss of muscle mass and strength?). It does not appear that any of the variables listed here in brackets have been examined.	Thank you for your comment. The only evidence that matched the protocol requirements for this review was from a meta-analysis subgroup related to breast cancer. The committee acknowledge the lack of evidence on the other health outcomes and have developed a research recommendation to address this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
International Menopause Society	Guideline	035	010	**1.6.4** The main concern in the early menopause section is the conclusion from the evidence that women with early menopause who take HRT have an increased risk of breast cancer compared to women with early menopause who do not take HRT. Although true, this is misleading and potentially frightening for consumers. Previous work showed that women with early menopause who do not take HRT have a lower risk of breast cancer compared to women without early menopause (Collaborative Group on Hormonal Factors in Breast C. Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. Lancet Oncol. 2012;13(11):1141-51). The investigators have not used an appropriate comparison group- they should have compared women with early menopause who take HRT versus age matched women without early menopause to get an accurate view of the risks of HRT in this setting. **NB:** This concern is shared by a number of IMS board members.	Thank you for your comment. The committee decided the appropriate comparator for this evidence review would be people in early menopause not taking HRT/placebo. People not in early menopause were outside the scope of the review protocol. The committee agreed that although it would be beneficial to provide information to people in early menopause on the impact HRT can have for health outcome specific to them, early menopause as a risk factor for health outcomes was not the topic under review. Thus, highlighting breast cancer risk alone would provide a skewed interpretation of the potential health risks and therefore the statement "Taking HRT increases the risk of breast cancer" has now been removed from the recommendation.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
International Menopause Society	Guideline	035	010	**1.6.4** I believe that use of this analysis to advise women about MHT is profoundly flawed in that the effects of MHT for women who go through early menopause (before the age of 45 years) must be seen in the context of what is "normal" for women of this age. My greatest concern is this advice is likely to cause a large number of women harm and impair their quality of life. IF there was evidence that MHT use put women with early menopause at greater risk of breast cancer than their normally ovulating counterparts then there would be a basis for advice cautioning against MHT for this age group. As this evidence is lacking, and in the context of the overwhelming evidence of cardiometabolic and bone protection of MHT for women with early menopause, and improving quality of life, then advocating against MHT in this age group is associated with a high probability of causing harm. The "norm" for women younger than 45 is to be premenopausal. In this study MHT users younger than 45 years were	Thank you for your comment. The committee decided the appropriate comparator for this evidence review would be people in early menopause not taking HRT/placebo. People not in early menopause were outside the scope of the review protocol. The committee agreed that although it would be beneficial to provide information to people in early menopause on the impact HRT can have for health outcome specific to them, early menopause as a risk factor for health outcomes was not the topic under review. Thus, highlighting breast cancer risk alone would provide a skewed interpretation of the potential health risks and therefore the statement "Taking HRT increases the risk of breast cancer" has now been removed from the recommendation. The need to assess the impact of early menopause on health outcomes has been acknowledged and was passed onto the NICE surveillance teams for prioritised consideration during future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				compared with postmenopausal women younger than 45 years not using MHT, whereas in terms of breast cancer risk, *the clinically meaningful comparator would be age-matched premenopausal women.*	
International Menopause Society	Guideline	023 & 030	Tables 1 & 2	**VTE:** There was no update on the absence of risk of VTE with transdermal HRT The data all point to no increase in risk, but the guideline still refers to a greater risk with oral versus transdermal, but this implies that there is still some risk with transdermal HRT. "The risk of VTE associated with HRT is greater for oral than transdermal preparations."	Thank you for your comment. The impact of HRT on risk of VTE was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this. Some stakeholders have provided a list of related references, and this has been passed on to the NICE surveillance team to consider for a future update.
International Menopause Society	Guideline	023 & 030	Tables 1 & 2	**VTE:** Several studies have now shown that the risk is significantly influenced by the type of progestogen in HRT with micronised progesterone, dydrogesterone and other less androgenic progestogens demonstrating lower risk – this should be indicated in the updated guideline. Canonico M, Oger E, Plu-Bureau G, Conard J, Meyer G, Lévesque H, Trillot N, Barrellier MT, Wahl D, Emmerich J, Scarabin PY; Estrogen and Thromboembolism Risk (ESTHER) Study Group. Hormone therapy and venous	Thank you for your comment. The impact of HRT on risk of VTE was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this. The list of related references has been passed on to the NICE surveillance team to consider for a future update.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				thromboembolism among postmenopausal women: impact of the route of estrogen administration and progestogens: the ESTHER study. Circulation. 2007 Feb 20;115(7):840-5. Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases. BMJ. 2019 Jan 9;364:k4810. Graham S, Archer DF, Simon JA, Ohleth KM, Bernick B. Review of menopausal hormone therapy with estradiol and progesterone versus other estrogens and progestins. Gynecol Endocrinol. 2022 Nov;38(11):891-910.	
International Menopause Society	Guideline	066	008	Ovarian Cancer: Once again, the data from WHI have not been given sufficient prominence regarding the issue of ovarian cancer. The long-term follow-up data from WHI did not demonstrate an increased incidence of ovarian cancer. Instead, the committee decided to give the observational data greater prominence, even though the increased risk was described as "small in absolute terms".	Thank you for your comment. There was data from 1 RCT that showed more people diagnosed with ovarian cancer in the combined HRT group than in the placebo group at approximately 6-year follow-up. However, the difference did not reach statistical significance because the number of diagnosed cases in both arms was very small (overall 32 people with a diagnosis of ovarian cancer). This made the finding less robust because of lack of statistical power. The observational studies have both sufficient numbers overall as well as numbers of people diagnosed with ovarian cancer (there were 2273

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Given the uncertainty of the data, is it still the committee's opinion that there is sufficient concern to warrant routine counselling re the potential risk of ovarian cancer in low-risk individuals deciding about HRT usage?	people with diagnosed with ovarian cancer in one study alone). The observational studies showed an increased risk of ovarian cancer with combined HRT. The committee agreed that, although the risk was increased overall, the risk was small in absolute terms, especially with the low baseline risk of ovarian cancer. In relation to the duration of use in combined HRT, the subgroup analysis by duration of use was not significant and this was therefore removed from the recommendation. The rationale section of the guideline as well as the committee discussion of the evidence review subsection of evidence review F have been updated with the RCT findings accordingly. For oestrogen-only HRT only observational studies were identified. Subgroup analysis for the impact of oestrogen-only HRT on ovarian cancer in relation to duration of use was statistically significant and therefore the reference to duration of use was retained. NICE has followed its standard methods and processes in developing the 2024 guideline update, including the way in which we manage conflicts of interest in topic experts and committee members. The details of conflicts of interest and how they have been managed are available in the published register of interests.
International Menopause Society	Guideline	067	001	(inc. 1.6.2 / Tables 1 and 2) The recommendation on cardiovascular disease and the explanations given below could be criticised for not informing healthcare providers and the public that there may be cardiovascular benefit with	"Thank you for your comment. With regard to the improved cardiovascular mortality, the committee discussed the evidence in Evidence Review C relevant to cardiovascular mortality following the use of HRT. They concluded that the evidence did not show a reduction in cardiovascular mortality, nor did it show an increase in cardiovascular mortality. They used this evidence

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				HRT, even though this would not be a primary indication for its usage. "Given that the majority of the RCT and observational evidence both showed that the risk of coronary heart disease was not increased, the committee agreed that this conclusion should be shared with people to allow them to make an informed decision." "The evidence showed that, for people with no history of coronary heart disease, there was no increase in mortality from cardiovascular disease from taking HRT and the committee agreed that it was important for people to know this to make an informed choice". This is despite various studies demonstrating improved cardiovascular morbidity and mortality for women starting HRT below the age of 60 years e.g. WHI/Boardman/Schierbeck (references previously provided) and other studies such as PEPI[1] and ELITE[2] showing benefit for cardiovascular risk markers. 1.The Writing Group for the PEPI Trial. Effects of estrogen or estrogen/progestin regimens on heart disease risk factors in postmenopausal women. The Postmenopausal Estrogen/Progestin Interventions (PEPI) Trial. JAMA. 1995 Jan 18;273(3):199-208.	to inform their recommendations. The committee also specified in the protocol that, where data allowed, the evidence would be stratified by different ages at first use of HRT. The committee discussed the subgroup analysis from the RCT data for age at first use of HRT and the risk of coronary heart disease, and since there were no statistically significant subgroup differences, they could not conclude that there was a reduced risk of cardiovascular morbidity when HRT was used at a particular age. The committee also considered the observational study evidence, which was also stratified by age at first use where possible. They discussed that evidence from one study supported a reduced risk in coronary heart disease which was specific to a younger age group, however this pattern was not reflected in another observational study which also presented subgroup data. Since there were inconsistent results between the observational studies, and no statistically significant subgroup differences in the RCT evidence, the committee could not reach the conclusion that there was a reduced risk of coronary heart disease depending on the age at first use of HRT. This is discussed in more detail in the committee's discussion of the evidence section in Evidence Review C. Cardiovascular risk markers were not outcomes listed in the pre-specified protocol, therefore the cited evidence on cardiovascular markers from PEPI and ELITE cannot be included in the review. Randomised controlled trials are often considered to be the gold standard in terms of study design, however the clinical question will determine which study design is the most appropriate. Factors such as

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				2.Hodis HN, Mack WJ, Henderson for ELITE Research Group. Vascular Effects of Early versus Late Postmenopausal Treatment with Estradiol. N Engl J Med. 2016 Mar 31;374(13):1221-31. There is methodological inconsistency and therefore data interpretation in the guideline formulation, which is based on committee opinion rather than the typical NICE statistical analyses, with greater weight given to RCT data for cardiovascular issues, and greater weight for observational data for breast cancer. Although an explanation (view) is provided for this inconsistent approach, the inconsistency could be open to external debate and criticism. "On this basis, the committee decided that assessment of the evidence for the association of HRT with cardiovascular diseases should give relatively more weight to RCT evidence, particularly where the findings from observational studies and RCTs are qualitatively different." The absence of discussion about the potential differential metabolic impacts of HRT regimens containing progesterone / dydrogesterone rather than androgenic progestogens on cardiometabolic risk is	sample size, follow-up periods, and incidence of the outcome of interest in the population, may mean that observational studies provide information that RCT studies cannot. The committee discussed and considered the pros and cons of all study designs that were included in each review. As the pros and cons differ depending on the outcome of interest, the discussions are different across reviews and outcomes, and reasons for using some evidence over others may be specific to the outcome. Where the findings from observational studies and RCTs were qualitatively different in the evidence reviews, the committee carefully considered what factors could be affecting the results. The discussions were specific to each outcome, as the factors would vary according to the outcome. The committee recognised that whilst confounding is a potential source of bias in all observational studies, the likely impact of confounding on any given association will vary depending on the strength of the association of potential confounders with both HRT and the outcome of interest. The guideline rationale section has been revised to focus on similarities and differences between study types. Residual confounding was discussed so it remains in the discussion in this section, but it has been revised to clarify that this was only one of many factors that were considered. The committee's discussion of the evidence in Evidence Review C has also been updated to provide more detail on this matter. Please see the related rationale sections of the guideline as well as the committee's discussion sections in Evidence

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				also concerning and should be included at least as a research recommendation.	Review C and Evidence Review D for a detailed discussion around the decisions the committee made regarding which evidence they gave more weight to and the reasons why. The committee did not specify metabolic impacts of HRT in the pre-specified protocol; therefore, the evidence base was not searched for these outcomes. A research recommendation cannot be made in this area as it was not identified that there is a lack of research in the topic. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). With regards to the conclusion related to coronary heart disease the independent review concluded 'If considering each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular benefits, which have been noted in the stakeholder comments. However, we agree with the committee's interpretation of the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly."
International Menopause Society	Guideline	071	005	Dementia: There should be discussion of brain fog/cognitive issues in the section on dementia (or in the section on symptom management). It is one of the most commonly associated symptoms of the menopause transition and one of the issues most frequently mentioned/questioned by healthcare providers and the public. (Maki PM, Jaff NG. Brain fog in menopause: a health-care professional's guide for decision-making and counselling on cognition. Climacteric. 2022 Dec;25(6):570-578.)	Thank you for your comment. The question posed was the effect on dementia for people taking HRT compared to people not taking HRT. The symptoms and signs of menopause was not part of the 2024 guideline update. Therefore, recommendations on this could not be made. For this reason, the cited reference did not meet inclusion criteria. The NICE surveillance team regularly checks topics in guidelines to assess whether an update is needed. The related reference has been logged with this team.
International Menopause Society	Guideline	071	005	Dementia: Can the committee please provide further clarification as to why they decided to focus on the WHIMS and Danish trials in making their recommendations on dementia? For instance, it is notable that they accepted that the population in WHIMS did	Thank you for your comment. The committee noted that the results from the observational Danish study were in line with the findings from the RCT data (WHIMS), however they agreed that both the observational Danish study and the observational UK study had limitations. The committee discussed that the observational data were inconsistent, and since the studies did not adjust for all the relevant confounders, the committee could not underpin in which direction

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				not represent a typical HRT using population in most countries. The Danish trial showed an association with dementia but did not prove causation; the types of hormone therapy used were less metabolically favourable than those used more recently and the population treated with HRT could have been at higher risk of dementia to begin with. We agree that whilst uncertainty exists more research is required, and HRT should not be recommended for primary or secondary prevention of dementia.	there may have been bias. Therefore, the committee used the RCT data to inform their recommendations. See the rationale section of the guideline and committee's discussion of the evidence section of evidence review G for more detail. The committee noted that the population in the WHIMS did not represent a typical HRT using population with an age of initiation of HRT of 65 or over, therefore they agreed that they would specify this as the age of women that the recommendation referred to.
International Menopause Society	Guideline	073	008	Dementia: It is concerning that in discussing the limitations of the WHIMS trial the committee regarded the age group of the trial (65 years or over) as only "slightly different from typical users of HRT" - there is clearly considerable difference in these age cohorts!	Thank you for your comment. The word 'slightly' has been removed.
International Menopause Society	Guideline	061 & 062	019 & 024	There is some cherry picking of the data. For combined HRT it is stated that because RCT and observational data agreed, there was a sound conclusion of an association between combined HRT and breast cancer.	Thank you for your comment. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				The conclusions for estrogen only are driven primarily by observational data which were allowed to override the RCT data; it is claimed that this is justified because the observational data included more women at a closer age to menopause. However, all the flaws in observational data were not taken into account and neither were the known limitations of observational analyses which generally overestimate an effect due to bias. This could be challenged as not an objective opinion regarding the data to hand, but a highly subjective opinion. In addition to this, there is a potential conflict of interest due to a committee member, who had been a key member of the observational study research group, being included in these discussions.	independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly. One of the changes made post consultation relate to the effects of oestrogen-only HRT on incidence of breast cancer. Given the differences between RCT and observational evidence the committee decided to revise the statement to say that there is little or no increase in breast cancer risk with oestrogen-only HRT. NICE has followed its standard methods and processes in developing the 2024 guideline update, including the way in which we manage conflicts of interest in topic experts and committee members. The details of conflicts of interest and how they have been managed are available in the published register of interests.
International Menopause Society	Guideline	061 & 062	019 & 024	There are a number of aspects of breast cancer risk with HRT that the guideline has not addressed which is rather concerning. The primary focus has been on the collaborative group on hormonal factors in breast meta-analysis of prospective cohort studies, and the published correspondence related to follow up data from the Million	"Thank you of your comment. The inclusion of the MWS research letter was deemed appropriate since the MWS has previously published work describing the cohort and methodology, which fits our pre-specified protocol. The research letter also describes the analysis was adjusted. Given the critical nature of mortality from breast cancer, information from such a source was deemed important and underwent quality assessment

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Women Study, referring to breast cancer mortality. The involvement of one of the collaborative group investigators in the committee discussions on breast cancer risks is also of concern. One of the arguments used for not including the RCT data was that the characteristics of the RCT population e.g. on obesity, differed from the observational data but one could also argue that it is not possible to control for all variables in an observed population e.g. data from the Million Women Study were derived from a breast screened population that may have been at higher risk of breast cancer because of where the population was recruited. Evidence from the WHI RCT that there is a reduction in risk of breast cancer incidence and mortality with conjugated estrogens alone should have been given due consideration as per the original guideline from 2015, particularly taking into account the increase in overweight and obesity in the target population over the last decade. Chlebowski RT, Anderson GL, Aragaki AK et al Association of Menopausal Hormone Therapy With Breast Cancer Incidence and Mortality During Long-term Follow-up of the Women's Health Initiative Randomized	using GRADE methodology. It was however taken into consideration that the publication was not a full publication in the critical appraisal of the letter. The committee considered a number of things when discussing the use of the letter to support their recommendation. They discussed the difference in sample size between the observational and RCT evidence for mortality, and they also discussed that an increase in mortality was in line with the evidence relating to an increased incidence of breast cancer. The committee's discussion of the evidence section in Evidence Review D has been updated to provide more detail on the discussion the committee had on mortality. NICE has followed its standard methods and processes in developing the 2024 guideline update, including the way in which we manage conflicts of interest in topic experts and committee members. The details of conflicts of interest and how they have been managed are available in the published register of interests. Thank you for raising the WHI study (Chlebowski 2020). The results from the WHI publications have been included in Evidence Review D for breast cancer incidence and mortality and now has also been included in the same forest plot. The hazard ratio from Chlebowski for those on combined HRT in this publication is HR = 1.35 [0.94 to 1.95], which is in the direction of increased risk and in line with the findings from the observational study. The committee noted that the findings for oestrogen-only HRT from RCT and observational studies go into the opposite direction. The decision to consider the different population groups between the studies

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Clinical Trials. JAMA. 2020 Jul 28;324(4):369-380.	were specific to this outcome since the committee tried to find an explanation for the findings. The committee reconsidered the wording of the recommendation and have since updated the wording to describe the direction of evidence from both the RCT and observational studies and uncertainties associated where results differ. As a result, the rationale section in the guideline and the committee discussion of the evidence in Evidence Review D has been updated to provide details of this. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). They noted that in the consultation version 'there is a strong focus in places on statistical significance, and conflating this with clinical significance, which can suggest that RCT and observational evidence conflicts when in fact effects are in the same direction, but one achieves statistical significance and the other does not' and reflected on the Chlebowski hazard ratio in this context. It was also highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					have been revised to implement these changes accordingly."
International Menopause Society	Guideline / Table 1	061 / 023	019 / 003	Table 1: it states… "It is not known whether preparations containing micronised progesterone or dydrogesterone have a different increased risk for breast cancer compared with preparations containing other progestogens." Evidence from the E3N, and other studies that micronized progesterone and dydrogesterone combinations with estrogen have a lower risk of breast cancer compared to HRT combinations with more androgenic progestogens. Fournier A, Berrino F, Clavel-Chapelon F. Unequal risks for breast cancer associated with different hormone replacement therapies: results from the E3N cohort study. Breast Cancer Res Treat. 2008 Jan;107(1):103-11. Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of breast cancer: nested case-control studies using the QResearch and CPRD databases. BMJ. 2020 Oct 28;371:m3873. It concerns me that the evidence which has been used to formulate the breast outcome	Thank you for your comment. Some of the participants of the E3N cohort have been included in the IPD dataset from the CGHFB, which has been included in our review. It was considered that not all participants of the E3N have been included in the CGHFBC. However, where there are separate publications with overlapping follow-up periods, and no disaggregation of participants, we have not included these to avoid double counting of participants in the E3N cohort. As per our processes and methods, we do not reanalyse any existing IPD data as NICE does not generally have the same access to the individual participant data, and therefore the data has been used as it has been published. Due to the large size of the IPD data from the CGHFB, we have prioritised this for inclusion in the review. Fournier 2014 was included as this study had a later follow-up period of the E3N cohort that was not covered by CGHFB. However, since the data from the Fournier 2014 publication did include participants that were in the meta-analysis from CGHFB, the results were analysed separately. The committee considered that the number of cases of breast cancer with those using micronised progesterone were few and agreed that this supported a recommendation to highlight that there was insufficient evidence to support any differences in the risk of breast cancer with micronised progesterone. The committee agreed that more evidence was required to make any robust recommendations for micronised progesterone and made a research recommendation. The

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				recommendations has not sufficiently considered these data.	QResearch data from the Venogradova (2020) publication has now been included the CPRD data is already part of the IPD meta-analysis. However, this does not provide further clarity about types of progestogens. This is why a research recommendation was made for this topic.
International Menopause Society	Guideline/Appendix A	035/097	010/012	**1.6.4 & Appendix A, Tables 16/17** As the authors of the Collaborative Group on Hormonal Factors in Breast 2019 paper[1] (the one paper used to inform this advice) have previously reported, women who become postmenopausal before the age of 45 years have a 30% lower risk of breast cancer compared with women who remain premenopausal until the age of 45 years [2]. In the 2019 paper the authors report that young postmenopausal women who use MHT have an increase in breast cancer risk compared with young postmenopausal women who are not using MHT. But what they fail to acknowledge is that for women with early menopause, MHT may not even restore their breast cancer risk to what it would have been if they had not gone through an early menopause. This is extremely important as menopause before the age of 45 years is associated with epigenetic ageing[3], a greater risk of premature death from all causes, including premature death from cardiovascular	Thank you for your comment. The committee decided the appropriate comparator for this evidence review would be people in early menopause not taking HRT/placebo. People not in early menopause were outside the scope of the review protocol. The committee agreed that although it would be beneficial to provide information to people in early menopause on the impact HRT can have for health outcome specific to them, early menopause as a risk factor for health outcomes was not the topic under review. Thus, highlighting breast cancer risk alone would provide a skewed interpretation of the potential health risks and therefore the statement "Taking HRT increases the risk of breast cancer" has now been removed from the recommendation. The need to assess the impact of early menopause on health outcomes has been acknowledged and was passed onto the NICE surveillance teams for prioritised consideration during future updates.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				disease [4], as well as substantially greater risk of osteoporosis and fragility fracture in later life[5]. MHT has been shown to ameliorate the increased risks of CVD/ death from CVD, stroke and prevent fracture[5,6]. Therefore early/premature menopause is a relative hormone deficiency state, and in these young women, MHT is a hormone restorative therapy. Further evidence to support the benefit of MHT is from the Women's Health initiative. Women who had undergone bilateral oophorectomy before age 45 and who were also younger than 60 years at the time of random assignment had a cumulative oestrogen-associated HR for all-cause mortality of 0.60 (CI, 0.38 to 0.95)[7].	
International Menopause Society	Guideline/Appendix A	035/097	010/012	1. CGoHFiB. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. Lancet 2019; 394: 1159-68. 2. CGoHFiB. Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				epidemiological studies. Lancet Oncol 2012; 13(11): 1141-51. 3. Levine ME, Lu AT, Chen BH, et al. Menopause accelerates biological aging. Proc Natl Acad Sci U S A 2016; 113(33): 9327-32. 4. Muka T, Oliver-Williams C, Kunutsor S, et al. Association of Age at Onset of Menopause and Time Since Onset of Menopause With Cardiovascular Outcomes, Intermediate Vascular Traits, and All-Cause Mortality: A Systematic Review and Meta-analysis. JAMA Cardiol 2016; 1(7): 767-76. 5. Adwan L, Zawia NH. Epigenetics: A novel therapeutic approach for the treatment of Alzheimer's disease. Pharmacology & Ther. 2013.139(1):41-50. 6. Boardman HM, Hartley L, Eisinga A, et al. Hormone therapy for preventing cardiovascular disease in post-menopausal women. Cochrane Database Syst Rev 2015; (3): CD002229. 7. Manson JE, Aragaki AK, Bassuk SS, et al. Menopausal Estrogen-Alone Therapy and Health Outcomes in Women With and Without Bilateral Oophorectomy: A Randomized Trial. Ann Intern Med 2019; 171(6):406-414.	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				8. Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal Hormone Therapy and Health Outcomes During the Intervention and Extended Post stopping Phases of the Women's Health Initiative Randomized Trials. JAMA 2013; 310(13): 1353-68. 9. Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of breast cancer: nested case-control studies using the QResearch and CPRD databases. BMJ 2020; 371: m3873.	
International Menopause Society	Guideline/Appendix A	035/097	010/012	The considerable healthcare benefits of HRT in women with early (including iatrogenic) menopause, where HRT is not contraindicated, should be discussed in greater detail by the guideline to put any possible risks into perspective; this is an area of great concern to IMS and other society board members. Further relevant references indicating the risks of early menopause include: Rocca W, Bower J, Maraganore D, et al. Increased risk of cognitive impairment or dementia in women who underwent oophorectomy before menopause. Neurology. 2007;69(11):1074–1083. Georgakis M, Petridou E. Long-term risk of cognitive impairment and dementia	Thank you for your comment. The committee decided the appropriate comparator for this evidence review would be people in early menopause not taking HRT/placebo. People not in early menopause were outside the scope of the review protocol. The cited references therefore did not meet inclusion criteria for this topic. The committee agreed that although it would be beneficial to provide information to people in early menopause on the impact HRT can have for health outcome specific to them, early menopause as a risk factor for health outcomes was not the topic under review. Thus, highlighting breast cancer risk alone would provide a skewed interpretation of the potential health risks and therefore the statement "Taking HRT increases the risk of breast cancer" has now been removed from the recommendation. The need to assess the impact of early menopause on health outcomes has been acknowledged and the cited

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				following bilateral oophorectomy in premenopausal women - time to rethink policies? JAMA Netw Open. 2021; 4(11):e2133016.	references were passed onto the NICE surveillance teams for prioritised consideration during future updates.
International Menopause Society	Guideline/Evidence Review D	060	026	1.6.1 / Tables 1 & 2 / Evidence D It is extremely important to note that the paper[1] used as primary data to inform the advice does not inform us of the impact of current recommended MHT prescribing practices on breast cancer risk for women at any age. The median year of diagnosis of breast cancer cases from North America (25% of the included data) was 1999, and for the European studies, 2007, with one as early as 1981. With an average use of 10 years of MHT in current users at diagnosis, and 7 years in past users, much of the exposure to MHT preceded the first publication of the Women's Health Initiative study, after which prescribing practices changed substantially. Consequently, virtually all of the included information pertains to MHT formulations and doses known to have adverse breast effects that are no longer recommended. 1.CGoHFiB. Type and timing of menopausal hormone therapy and breast	Thank you for your comment. One of the reasons the 2015 guideline required updating was the pharmacovigilance risk assessments by the MHRA and the EMA, concerning the impact of HRT on the risk of breast cancer. NICE is required to consider the impact of regulatory guidance from MHRA in its guidance and as such the additional information on breast cancer was important to summarise. All evidence that matches the criteria of a pre-specified review protocol is systematically analysed, summarised and discussed. Whether older routes and types are less effective or risky can only be concluded if all the relevant evidence is systematically analysed. There was insufficient evidence to recommend one type of progestogen over another and a research recommendation was made so that future research may clarify this issue. There were some findings related to route of administration that the committee described in Tables 1 & 2.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. Lancet 2019; 394: 1159-68.	
International Menopause Society	Guideline/Evidence Review D	060	026	1.6.1 The advice is not informed by new data but relies on reinterpretation of data that informed NICE 2015 (the 2020 WHI paper does not provide evidence that departs from the 2013 analyses). So, this is an interpretation that seems to reflect a different lens as opposed to new data. Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal Hormone Therapy and Health Outcomes During the Intervention and Extended Post stopping Phases of the Women's Health Initiative Randomized Trials. JAMA 2013; 310(13): 1353-68.	Thank you for your comment. One of the reasons the 2015 guideline required updating was the pharmacovigilance risk assessments by the MHRA and the EMA, concerning the impact of HRT on the risk of breast cancer. NICE is required to consider the impact of regulatory guidance from MHRA in its guidance and as such the additional information on breast cancer was important to summarise. This was partly related to the Lancet Individual Patient Meta-Analysis which was published post 2015 and has been included in the current review. Therefore, whilst not including different data, individual patient data meta-analysis is a powerfully different analysis of the data then what is possible from extracting data from individual studies. Therefore, the interpretation can be different.
International Menopause Society	Guideline/Evidence Review D	060	026	Has the Vinogradova paper been overlooked? (it has not even been "excluded") This reports on 98 611 women aged 50-79 with a primary diagnosis of breast cancer between 1998 and 2018, matched by age, general practice, and index date to 457 498 female controls. The importance of this work is that it addresses the contemporary use of HRT as opposed to the Collaborative Group on Hormonal Factors in Breast 2019 paper which primarily pertains to doses and formulations little prescribed today.	Thank you for your comment. The Vinogradova 2020, has been checked against inclusion criteria and has now been added. Note that some of the cohort in this publication (from the CPRD database) was already included in the review, therefore only data from the QResearch cohort have been included. This study has been assessed and it does meet the criteria for inclusion in this review, therefore we have updated the relevant sections of the review with data from the study that fits our protocol.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of breast cancer: nested case-control studies using the QResearch and CPRD databases. BMJ 2020; 371: m3873.	
International Menopause Society	Guideline/Evidence Review E	064	008	1.6.1 / Tables 1 and 2 Evidence E "The committee discussed the evidence, which suggested that sequential combined HRT may increase the incidence of endometrial cancer. The committee agreed that the constituent and dose of the combined HRT affects the risk of endometrial cancer (including duration of use, doses and days of progestogen per cycle & higher oestrogen dose). " What seems to be missing here is whether the sequential combined HRT is delivered as a single therapy (e.g., a single tablet/ patch containing an estrogen phase and then a combined estrogen and progestogen phase) or whether the user is required to use a continuous estrogen and then take an additional progestogen tablet. My understanding is that the former is not associated with an increased endometrial cancer risk, but when the user is required to add an extra tablet for several days a month there is a greater likelihood of insufficient progestational effect.	Thank you for your comment. No evidence was identified that looked at differences between sequential combined HRT is delivered as a single therapy (e.g., a single tablet/ patch containing an estrogen phase and then a combined estrogen and progestogen phase) or preparations where the user is required to use a continuous estrogen and then take an additional progestogen tablet. The committee therefore decided not to comment on this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				This may need to be added as part of the advice.	
Leeds and York Partnership NHS Foundation Trust	Evidence review A	General	General	We are concerned that this recommendation may imply that CBT will eliminate, rather than help to manage the psychological impact of some of the many symptoms experienced. It may then be considered as an alternative to HRT rather than an addition to it, or as a sole treatment for those for whom HRT is contraindicated. As a mental health Trust we are concerned that this recommendation may provide a further barrier to accessing HRT for those with existing mental health issues or serious mental illness. In this group of individuals symptoms may already be diagnostically overshadowed by their mental illness and not considered as peri/menopausal symptoms[1]. Individuals with serious mental illness already experience health inequalities and on average, die 15 to 20 years earlier than the general population[2]. Additionally, they are 3.3 times more likely to die from heart disease[2]. The protective cardiovascular effects of oestrogen have been well documented[3] [4] and there should be a focus on ensuring those with SMI having equal access to HRT. [1] Berhman, S. & Crockett, C. 2023. Severe mental illness and the perimenopause. *BJPsych Bulletin.* 2023: 1-7. [Online]. [Accessed 18 December 2023]. Available from: https://www.cambridge.org/core/journals/bjpsych-bulletin/article/severe-mental-illness-and-the-	Thank you for your comment. The committee reflected on the wording of the recommendations related to CBT and revised them to ensure clarity about this ' as an option: in addition to other treatments (including HRT), for people for whom other treatments are contraindicated or for people who prefer not to take HRT'. This makes it clear that CBT is not seen as a first line treatment but as an option where this is a preferred choice. The cardioprotective effects of HRT was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this. The references listed have been reviewed, and none of them meet the criteria outlined in the updated evidence review protocols..

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				perimenopause/8D072AACBCD3C7888C173B36635C08C3 [2] Public Health England. 2018. Severe mental illness and serious mental illness (SMI) and physical health inequalities: briefing. [Online]. London: Public Health England. [Accessed 4 January 2024]. Available from:https://www.gov.uk/government/publications/severe-mental-illness-smi-physical-health-inequalities/severe-mental-illness-and-physical-health-inequalities-briefing [3] Kannel, W. B. et al. 1978. Menopause and risk of cardiovascular disease: the Framingham Study. *Annals of Internal Medicine.* Oct; **85**(4):447-52. [4] Mikkola TS, Tuomikoski P, Lyytinen H, Korhonen P, Hoti F, Vattulainen P, Gissler M, Ylikorkala O. Estradiol-based postmenopausal hormone therapy and risk of cardiovascular and all-cause mortality. Menopause. 2015 Sep;22(9):976-83. [Online]. [Accessed 4 January 2024]. Available from: https://pubmed.ncbi.nlm.nih.gov/25803671/	
Leeds and York Partnership NHS Foundation Trust	Guideline	010 011	001, 008, 013 007	1.4 We are concerned that the use of the word 'troublesome' to describe menopausal symptoms diminishes the extent of distress they can cause. Suicide rates are highest in females in the age group 45-55[1]. The usual occurrence of menopause in the UK is between these ages, with the average age being 51[2], suggesting that many of these women will have been peri/menopausal at the time of ending their	Thank you for your comment. Based on this and other feedback the committee reflected on this wording and consequently 'troublesome' has been removed from the guideline. NICE takes the reports of the debilitating symptoms, the considerable concern it causes and the impact menopause has seriously. Whilst an update of the list of symptoms and experiences (including statistics related to suicide) was outside the current scope of the 2024 update and therefore no evidence review was conducted, the NICE

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				lives. Further research is needed into peri/menopause and suicide, particularly for those with existing mental illness. [1] House of Commons Library. 2022. Suicide Statistics. (HC 07749 2022). [Online]. London: The Stationery Office. [Accessed 4 January 2024]. Available from: https://commonslibrary.parliament.uk/research-briefings/cbp-7749/ [2] British Menopause Society. 2022. Tool for Clinicians. [Online]. London: British Menopause Society [Accessed 4 January 2024]. Available from: https://thebms.org.uk/wp-content/uploads/2023/08/17-BMS-TfC-What-is-the-menopause-AUGUST2023-A.pdf	surveillance team checks regularly for new evidence for topics within guidelines to see where further work is needed. Apart from the removal of the word 'troublesome' the committee decided that without further evidence they could not comment on this.
Liverpool Women's Hospital	Guideline	All		Appendix A Further clarity is needed in the tables to include confidence intervals and publication source.	Thank you for your comment. For the draft guideline, the committee opted for a verbal format complemented by tables, providing estimates of absolute numbers from a single source rather than from two different study types. This differs from the approach used in the published version of NG23. This decision was made to facilitate conversations between clinicians and individuals, enabling shared decision-making regarding menopause management. All sources and confidence intervals are presented in the evidence reviews which also presents absolute numbers from RCT and observational studies separately. Based on the numbers in the appendix of the consultation a discussion aid document has been developed which includes data visualisation as well as a verbal description

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					of what the numbers mean. Descriptions of the underlying concepts and calculation are also provided. It has been made easy to navigate from the relevant section of the discussion aid to the evidence reviews where the complete set of information is available. This discussion aid has undergone user-testing and was refined based on user feedback.
Liverpool Women's Hospital	Guideline	General	General	We welcome the additional recommendations on genitourinary symptoms and treatment options. It would be helpful to understand the process of evaluation for different types of data: RCT vs observational study evidence. Conflict of Interest Policy. Call for transparency for both pharma collaboration and researcher involvement. The term bothersome is demeaning and should be replaced with mild, moderate and severe symptoms. The reference to psychological support is welcomed as this is an essential aspect of management and should be offered in all specialist menopause clinics. There should be further reference to the importance of prescribing standard doses of HRT stressing the potential risks of endometrial cancer from prescribing high doses of oestrogen without sufficient progestogen for endometrial protection.	Thank you for comment in support of the additional recommendations on genitourinary symptoms and treatment options. With regards to RCT and observational studies NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they agreed that RCT and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly. NICE has followed its standard methods and processes in developing the 2024 guideline update, including the way in which we manage conflicts of interest in topic experts and committee members. The details of conflicts of interest and how they have been managed are available in the published register of interests.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Due to the increase in requests for Testosterone treatment in the menopause, this should be discussed in the guideline.	The term troublesome has been removed throughout. We retained a discussion on bothersome in one of the rationale sections because some of the evidence measured how much the symptoms bothered the person (using a questionnaire that measured 'distress or bother'). Thank you also for your comment in support of the reference to psychological support. Where this would be provided was outside the scope of the 2024 guideline update, but your comment will be considered by NICE where relevant support activity is being planned. A statement was added to the guideline emphasising that the benefits and risks of HRT described in this guideline only cover the use of HRT within the licensed dosages. At the time when the scope of the 2024 guideline update was agreed, there was no substantive new evidence that would change the recommendation related to testosterone. However, NICE recognises the importance of this issue and has worked with the NIHR to prioritise funding for research on the matter.
Liverpool Women's Hospital	Guideline	038 - 042		There should be a recommendation to study quality of life and long-term health outcomes for women with POI and early menopause.	Thank you for your comment. A review of the quality of life and long-term health outcomes for women with POI was not in the scope of the 2024 guideline update. In accordance with NICE processes research recommendations can only be made on topics that are systematically searched for and reviewed. The suggested research recommendation in relation to POI could therefore not be added. Whilst early menopause was within scope, it was only in the context of specific health outcomes for people with early menopause who take HRT compared to those in early menopause who do not take HRT. The

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					committee discussed that this was a very narrow question which does not fully address the need of this population. During discussions and considerations of this and other stakeholder feedback the committee suggested that future guideline updates should include additional questions on early menopause with one focusing on 'health consequences of early menopause'. These have been passed on to the NICE surveillance team to consider for future inclusion.
Liverpool Women's Hospital	Guideline	088 - 090		Appendix A Further clarity is required in relation to breast cancer risk and mortality.	Thank you for your comment. The problem with trying to give absolute numbers of mortality from breast cancer due to HRT use is that we cannot give risks by specific patterns of use as we do for incidence. This is because it is recommended that women stop their HRT use as soon as they are diagnosed with breast cancer. This makes it difficult to report on the relationship of a given total duration of use with death from breast cancer because this will be necessarily truncated in those who get breast cancer but not in those who do not. For this reason, we cannot calculate absolute numbers but can only look at the relationship of use of HRT with subsequent breast cancer mortality in women with no prior breast cancer diagnosis at the time of reporting their HRT use which is the evidence we are reporting in evidence review D.
Liverpool Women's Hospital	Guideline	006	003	1.1 LWH welcome support for individualised care, to include a focus on lifestyle interventions including diet & exercise. The importance of dedicated psychological support could also be added here.	Thank you for your comment. The impact of diet and exercise was not in the scope of the 2024 guideline update. Evidence for this topic was therefore not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this. However, in the 'information and support' section of the

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					guideline it is recommended that healthcare professionals should provide information on 'interventions, or changes the person can make to support their health and wellbeing'.
Liverpool Women's Hospital	Guideline	010	027	1.4.3. Ongoing management should be based on the outcome of the initial review, ideally at 12 weeks. This can be facilitated via patient initiated follow up (PIFU). Ongoing treatment should be based on an individualised risk assessment.	Thank you for your comment. This has been rephrased to read 'discuss the possible duration of treatment at the outset', followed by 'rediscuss the benefits and risks or continuing treatment at every review'. This does not suggest arbitrary limits or cut offs.
Liverpool Women's Hospital	Guideline	011	General	1.4.4. CBT is an important intervention, but too much emphasis was placed on it in this guideline, particularly in the original press release. 1.4.4. Has a health economic appraisal of CBT to manage menopausal symptoms been undertaken?	Thank you for your comment. The wording has been revised to ensure clarity about CBT 'as an option: in addition to HRT, for people for whom HRT is contraindicated or for people who prefer not to take HRT'. A bespoke economic evaluation was not undertaken for this question but two previous economic evaluations were identified by the search of the evidence and considered by the committee. How this evidence was used to inform recommendations is recorded in the evidence review for the topic. The wording used reflect the strength of the evidence around the recommendation. In 'strong' recommendations for actions that should (or should not) be offered, directive language such as 'offer' is used, as it is used for example in the recommendation related to HRT for vasomotor symptoms. If the evidence is less clear the word 'consider' is used to reflect that the evidence around the recommendation is weaker.
Liverpool Women's Hospital	Guideline	012	013	1.4.8. The term "troublesome" does not reflect the impact of potential symptoms on QoL.	Thank you for your comment. Based on this and other feedback the committee reflected on this wording and consequently 'troublesome' has been removed from the guideline.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Liverpool Women's Hospital	Guideline	012	General	1.4.9. Hypnosis is another valuable treatment option.	Thank you for your comment. Hypnosis was not part of the scope of the 2024 update. Therefore, the committee could not comment on this. However, because of this and other stakeholder comments this has been logged with the NICE surveillance team which regularly checks for evidence in topics included in guideline so that this can be considered for future updates.
Liverpool Women's Hospital	Guideline	012	019	Women taking levothyroxine to treat hypothyroidism may require an increase in the dose of levothyroxine after commencing oral HRT. Repeat thyroid function tests should be done after starting oral HRT.	Thank you for your comment. Whilst there are some new recommendations in this section, the general topic of comorbidities (including issues relating to hypothyroidism) was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this.
Liverpool Women's Hospital	Guideline	012	010	Consideration of specifically adapted CBT is desirable.	Thank you for your comment. It has been added that this should be menopause-specific CBT.
Liverpool Women's Hospital	Guideline	012	021	Caution remains in relation to prescribing HRT in women with Diabetes. There is no reason why women with Diabetes cannot have HRT if indicated. Women with type 2 diabetes mellitus are a group for whom there is a dearth of data on menopause treatment outcomes, in particular risks and benefits of HRT. There is a need to collect real-world data in women with type 2 diabetes as they are usually excluded from clinical trials.	Thank you for your comment. Whilst there are some new recommendations in this section, the general topic of comorbidities (including issues relating to type 2 diabetes mellitus) was not in the scope of the 2024 guideline update. Evidence for this topic was not searched for and not reviewed and discussed with the committee. The committee could therefore not comment on this. However, due to this and other feedback some cited references have been passed on to the NICE surveillance team which regularly checks evidence for guideline topics to see whether further updates are needed.
Liverpool Women's Hospital	Guideline	013	002	1.4.11 Transdermal oestrogen is the first line treatment option in women at increased risk of VTE.	Thank you for your comment. The impact of HRT on risk of VTE was not in the scope of the 2024 guideline update. Evidence for this topic was

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					therefore not searched for, reviewed or discussed with the committee. The committee could therefore not comment on this. Some stakeholders have provided a list of related references and this has been passed on to the NICE surveillance team to consider for a future update.
Liverpool Women's Hospital	Guideline	013	010	1.4.13 Transdermal HRT recommended.	Thank you for your comment. The committee noted that in people with a history of cardiovascular disease taking either combined HRT (continuous and sequential) or oestrogen-only HRT, the RCT evidence did not suggest any difference in coronary heart disease risk and cardiac event composite scores, when compared to placebo. Observational evidence did not include people with a history of cardiovascular disease. The committee discussed how the evidence suggested that a history of coronary heart disease may not be a contraindication to combined or oestrogen-only HRT. However, they felt that for this group of people the use of HRT should be discussed with and initiated, if appropriate, by a healthcare professional with expertise in menopause. This would ensure that people with a history of coronary heart disease who commence HRT are advised in an individualised way that relates to their specific history of coronary heart disease. For details see the 'committee's discussion and interpretation of the evidence' section of evidence review C.
Liverpool Women's Hospital	Guideline	014	005	Too much emphasis has been placed on CBT, particularly in the press release This is a potential alterative treatment option for women in whom HRT is contraindicated or for those	Thank you for your comment. The wording of the recommendation has been revised to make it explicit that CBT is an option which could be in addition to HRT, for people in whom HRT is

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				who prefer to avoid hormonal treatment options. A risk vs benefit evaluation is important for all women is relation to managing menopausal symptoms.	contraindicated or for those who prefer not to take HRT.
Liverpool Women's Hospital	Guideline	015	001	There is a need for terminology relating to lack of oestrogen adversely affecting urogenital tissue quality.	Thank you for your comment. The committee were unclear about what this terminology would be. So they did not comment on it.
Liverpool Women's Hospital	Guideline	016	004	Ospemiphene can also be considered if other topical treatments have not been effective.	Thank you for your comment. The committee decided that the cost effectiveness evidence did not support a wider recommendation. Additional text has been added to 'The committee's discussion and interpretation of the evidence' to discuss this in more detail.
Liverpool Women's Hospital	Guideline	017	001	Use of Aromatase inhibitors is generally considered a contra-indication to vaginal oestrogens. The consensus is that vaginal oestrogens can be used with tamoxifen if indicated.	Thank you for your comment. The cited section has been reordered with the recommendation related to aromatase inhibitors (referred in the comment to as 1.4.30) moving up in the order to make this more explicit from the start. This would then place the other recommendations within this context.
Liverpool Women's Hospital	Guideline	019	002	HRT can be of benefit by possibly having a direct effect on the hypothalamic sleep centre in addition to reducing night sweats, which can disrupt sleep. HRT should be considered if sleep problems occur in conjunction with other menopausal symptoms.	Thank you for your comment. Apart from CBT other management options for sleep problems associated with the menopause were not in the scope of the 2024 guideline update. However, the committee acknowledged that there are other options that may be used (including HRT). They have therefore reworded the recommendation to reflect this. It now states that CBT could be used as an option (1) in addition to other treatments (including HRT), or (2) for people for whom other treatments are contraindicated or (3) for people who prefer not to have other treatments. Given

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					the constraints of the scope they could not be more specific than this.
Liverpool Women's Hospital	Guideline	019	006	Whilst it is recognised that the use of testosterone is outside the scope of this guideline, it is disappointing that no additional recommendation about testosterone has been made in light of the global consensus paper and recent meta-analyses. It would be helpful to mention that the only indication for use of testosterone in women is low libido. There is currently no evidence for the use of testosterone to improve cognitive function, mood or other symptoms.	Thank you for your comment. At the time when the scope of the 2024 guideline update was agreed, there was no substantive new evidence that would change the recommendation related to testosterone. It was therefore not included in the update and the committee could not comment on this. However, NICE recognises the importance of this issue and has worked with the NIHR to prioritise funding for research on the matter.
Liverpool Women's Hospital	Guideline	019	017	1.5.3. Guidelines for the management of bleeding on HRT are currently being developed by the BMS, BSGE, BGCS & RCOG in conjunction with GIRFT and NHS England Cancer task force in response to an increase in women with abnormal bleeding on HRT presenting to rapid access clinics.	Thank you for your comment. NICE reviewed the published guideline and noted that it conflicts with the NICE guideline of suspected cancer: recognition and referral. Therefore, it would be currently difficult to signpost to the guidelines for the management of bleeding on HRT are published by the BMS, BSGE, BGCS, RCOG in conjunction with GIRFT and NHS England Cancer task force. It was therefore decided to remove the current cross reference to the conflicting NICE guideline and this topic was logged with the NICE surveillance team.
Liverpool Women's Hospital	Guideline	021	013 - 015	Women with early menopause should be offered referral to a specialist menopause service as would be recommended for women with POI.	Thank you for comment. The origin of this recommendation is the topic of early menopause for which one question was included in the 2024 guideline update and the aim of the recommendation is to allow psychological support to reach the people in need of it most based on symptoms. General service organisation was not part of the scope of the 2024 guideline update. The committee were also concerned of the large

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					resource impact recommending referral to a menopause specialist would have, bearing in mind the already very long waiting times for access. They discussed this could potentially make it even harder for people in particular need of this service to gain access. In light of this, the committee agreed to not recommend referrals to menopause specialists.
Liverpool Women's Hospital	Guideline	023	003	Table 1 Combined HRT: effect on health outcomes Column 3: ''Combined HRT increases the risk of breast cancer mortality compared with not taking HRT''. This statement is not consistent with available RCT long term follow up clinical trial data. Consideration of all-cause mortality would have more relevance for women considering use of HRT and is referenced earlier in the draft guideline. Column 4: "Combined HRT preparations containing transdermal oestrogen increase the risk of breast cancer less than combined HRT preparations containing oral oestradiol." This is a double negative statement which could be misinterpreted and should be reviewed. Column 5: Available evidence is not consistently represented, potentially leading to confusion. Table 2 Breast Cancer and Oestrogen only HRT Column 2: "Oestrogen-only HRT slightly increases the risk of breast cancer compared to not taking HRT" This statement completely contrasts with the results of the WHI study, a long term RCT vs the MWS, an observational	Thank you for your comment. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly. In table 1 in relation to combined HRT and the risk of breast cancer mortality (column 3), Both RCT and observational evidence showed that mortality from breast cancer was slightly higher in women who have taken combined HRT than in those who have not taken HRT. As in all other rationale and evidence reviews have been updated to include both the RCT and observational study evidence has now been included in the discussion. The hazard ratio

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				study. A high BMI is a significant risk factor for breast cancer and as such should be highlighted. Column 3: "There is no difference in the increase of breast cancer risk between transdermal and oral oestrogen" State the evidence or remove. There needs to be a consistent approach across this document as a whole. Column 4: "There is no difference in the increase in breast cancer risk between oestradiol and conjugated equine oestrogen when given at standard therapeutic dosage" Would the committee consider a more balanced statement Eg. CEE may not increase risk, but further evaluation is required.	from Chlebowski for those on combined HRT in this publication is HR = 1.35 [0.94 to 1.95], which is in the direction of increased risk and in line with the findings from the observational study (rather than the two study types disagreeing with each other). Based on results from both studies they concluded that there is an increase in breast cancer incidence and agreed that this should be explained to people. However, they also emphasised that the difference in risk is very small between those who have taken HRT and those who have not and that it should be thought about within the wider context, in that there is no overall change in life expectancy with HRT (and all-cause mortality has now been added to tables 1 and 2). For transdermal compared to oral combined HRT (column 4) the committee noted that one study showed the difference that was highlighted but the same pattern did not feature in oestrogen-only and that this isolated difference in one study was not sufficient to confidently conclude this. The committee therefore the statement was removed, and they added a new research recommendation to the guideline to see whether further research would clarify this pattern. The evidence for different types of progestogens (in column 5) mostly showed an increase (both in RCT and observational studies) but the committee thought that further research may change lead to different conclusions. This is why they concluded that the evidence was insufficient and made a research recommendation. In table 2 in relation to risk of breast cancer (column 2) the committee reflected on the difference in results between RCT and

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					observational data and revised the conclusion to say that there was 'there is very little or no increase in breast cancer risk with oestrogen-only HRT'. There was evidence of that transdermal was not different to oral (column 3). However, this evidence was limited and removed the statement but added a research recommendation to gather more evidence related to this. In relation to oestradiol and conjugated equine oestrogen (column 4) the evidence showed an increased risk in both but no difference between these increases therefore highlighting that CEE may not increase risk would be incorrect.
Liverpool Women's Hospital	Guideline	035	010	POI and early menopause should be regarded as a risk continuum in relation to bone, cardiovascular, dementia and Parkinson's data. Menopause before the age of 45 years is associated with a greater risk of premature death from all causes, including cardiovascular disease, as well as a substantially greater risk of osteoporosis and fragility fracture in later life. It is important that women in this cohort have the correct information on which to base decision making in relation to use of HRT.	Thank you for your comment. The aim of the evidence review carried out was assessing the impact of either taking or not taking HRT on people with early menopause and the development of various health outcomes. The need to assess the consequences of early menopause on health outcomes has been acknowledged and has been logged with the NICE surveillance teams for prioritised consideration during future updates.
Liverpool Women's Hospital	Guideline	035	010	Women with early menopause. "Taking HRT increases the risk of breast cancer." – this is misleading. Years of HRT exposure is counted from the age of 50. No analysis has been undertaken using a control group of normally cycling women compared with women with early menopause taking HRT.	Thank you for your comment. The section on early menopause has been revised and only the message to explain to people experiencing early menopause that, for them, the benefits and risks of either taking or not taking HRT are likely to lie between those for people with premature ovarian insufficiency and those for people aged 45 or over has been retained from the consultation version. In accordance with the systematic review protocol only evidence on breast cancer was identified but

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					it was decided that this highlighted that further research is necessary to clarify the benefits and risks. The committee also noted that the focus of this topic was too narrow to cover early menopause adequately and suggested several topics that based on stakeholder feedback which were logged with the NICE surveillance team for future consideration in an update. This also includes the topic of the impact of early menopause itself on various health outcomes and what the best options are to manage potential negative impact. However, this was not part of the 2024 guideline update and so the committee could not comment on this.
Liverpool Women's Hospital	Guideline	037	008	Genito-urinary symptoms of the menopause - If this term is going to be used, there should be an explanation of what it means.	Thank you for your comment. A definition of the genitourinary symptoms has been added.
Liverpool Women's Hospital	Guideline	041	001	There is a need for real-world data for women with diabetes and those with multi-morbidities.	Thank you for your comment. How to manage menopause symptoms in people with diabetes and multi-morbidities was not in the scope of the 2024 guideline update. In accordance with NICE processes research recommendations can only be made on topics that are systematically searched for and reviewed. The suggested research recommendation could therefore not be added.
Liverpool Women's Hospital	Guideline	041	010	Further research is needed in relation to testosterone therapy for women.	Thank for your comment. The surveillance and scoping process for the 2024 guideline update did not identify substantive new evidence likely to change the existing recommendations on testosterone. Therefore, reviewing evidence on testosterone in relation to menopause care was not prioritised. However, NICE discussed the need for research in relation to testosterone use

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and they prioritised funding for urgent research in this area.
Liverpool Women's Hospital	Guideline	061		The Million Women Study, is an observational study with significant methodological limitations and a very high loss to follow up rate. This needs to be taken into account when making recommendations.	Thank you for your comment. The Million Women Study (MWS) was a large contributor to the to the data in the Lancet 2019 meta-analysis that was included in Evidence Review D (referenced as CGHFBC 2019 in Evidence Review D). It is correct that there are limitations to the Million Women Study, as is the case with all observational studies. The limitations relevant to observational studies have been considered and discussed with the committee. The committee also discussed that observational studies can be useful, in that they can include large sample sizes and so are powered to detect rare outcomes, such as breast cancer or mortality, and have long follow-up periods. More detail on the discussion can be found in the committee's discussion of the evidence section in Evidence Review D.
Liverpool Women's Hospital	Guideline	062	005	The committee noted that "the RCT evidence was consistent with the observational data" This does not reflect the results in relation to the data.	Thank you for your comment. This section has been revised into sections describing the RCT and observational data in detail. This will provide greater clarity about where the data is consistent and where there may be differences.
Liverpool Women's Hospital	Guideline	062	008	LWH requests clarification on the weighting of evidence. There needs to be clarity in relation to obesity as a potential risk factor for breast cancer.	Thank you for your comment. In relation to the 'weighing' of the evidence, if this refers to RCT and observational evidence we have updated the section to provide more detail on each to give them equal weight. Obesity is mentioned at the beginning of the section as a factor that increases the risk of breast cancer and the guideline provides a link to another NICE guideline that lists these risk factors (the NICE guideline on early

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					and locally advanced breast cancer: diagnosis and management).
Liverpool Women's Hospital	Guideline	062	011	A clear explanation of the methodology used in grading research is required.	Thank you for your comment. The methods (including grading) are described in a separate supplement (see supplement 1 - methods). Details of the individual gradings of each outcome are provided in the GRADE tables of each evidence report. This would be appendix F of evidence review D.
Liverpool Women's Hospital	Guideline	062	013	There is no appreciable difference in breast cancer risk between oral and transdermal HRT.	Thank you for your comment. The committee considered the evidence for oral and transdermal routes of administration of the oestrogen component of HRT. Since some of the evidence showed a significant difference between the subgroups of oral and transdermal routes of administration in the combined HRT comparison, they had made a recommendation to inform of the reduced risk. This now also includes a study by Vinogradova (2020) which include data on transdermal versus oral HRT but did not provide greater clarity on this matter. The committee considered this and the Brusseler 2018 evidence and discussed that since the same difference was not observed in the oestrogen-only comparison, the argument was less robust than previously discussed. Upon reflection the committee agreed to remove this recommendation and the rationale section revised accordingly as well and a detailed discussion of the evidence and their decision was updated and can be found in the committee discussion of the evidence section of Evidence Review D. The committee also decided that more evidence is needed to clarify this and prioritised this for a research recommendation.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Liverpool Women's Hospital	Guideline	063	004	The committee decided that they would put more weight on the observational evidence to support their recommendations. The committee is biased and this should be challenged formally. Why was this paper reflecting current day practice not reviewed to inform the updated guideline? Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of breast cancer: nested case-control studies using the QResearch and CPRD databases. Bmj 2020; 371.	Thank you for your comment. The committee considered the evidence from both RCT and observational data. The RCT data, which included the Women's Health Initiative (WHI), and observational data were consistent for the comparison combined oestrogen and progesterone versus no HRT or placebo, and both showed an increased risk in breast cancer. The committee discussed that the RCT evidence from the WHI showed conflicting results to the observational studies, for the comparison of oestrogen-only HRT versus placebo or no HRT. The decision to consider the different population groups between the studies were specific to this outcome since the committee tried to find an explanation for the inconsistent findings. The committee reconsidered the wording of the recommendation and have since updated the wording to describe the direction of evidence from both the RCT and observational studies. As a result, the committee discussion of the evidence section in Evidence Review D has been updated to provide details of the discussion that took place. The Vinogradova 2020 study does meet the criteria for inclusion in this review. Note that some of the cohort in this publication (from the CPRD database) was already included in the review, therefore only data from the QResearch cohort have been included. The relevant sections of the review were updated with data from the study that fits our protocol.
Liverpool Women's Hospital	Guideline	063	024	"The committee decided that they would put more weight on the observational evidence to support their recommendations, as this was more reflective of the target population" It is	Thank you for your comment. The committee considered the evidence from both RCT and observational data. The RCT data, which included the Women's Health Initiative (WHI), and

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				important to include all of the evidence when making recommendations.	observational data were consistent for the comparison combined oestrogen and progesterone versus no HRT or placebo, and both showed an increased risk in breast cancer. The committee discussed that the RCT evidence from the WHI showed conflicting results to the observational studies, for the comparison of oestrogen-only HRT versus placebo or no HRT. The decision to consider the different population groups between the studies were specific to this outcome since the committee tried to find an explanation for the inconsistent findings. The committee reconsidered the wording of the recommendation and have since updated the wording to describe the direction of evidence from both the RCT and observational studies. As a result, the committee discussion of the evidence section in Evidence Review D has been updated to provide details of the discussion that took place.
Liverpool Women's Hospital	Guideline	064	012	"The committee discussed the evidence from randomised controlled trials (RCTs) and 13 observational studies. They noted that the evidence from RCTs was uncertain". However, the WHI study reported on rates of endometrial cancer and provided important long term follow up data.	Thank you for your comment. The recommendation has been revised to refer to a decrease in endometrial cancer with continuous combined HRT and the wording of the rationale has been revised to describe the findings from the WHI RCT.
Liverpool Women's Hospital	Guideline	066	011	The evidence for the potential risk of ovarian cancer does not consider the WHI RCT long term follow up data (no difference in risk of ovarian cancer in women using HRT).	Thank you for your comment. The RCT (with a follow-up of 5.6 years) had higher numbers of women with ovarian cancer in the HRT group compared to the no HRT group, but this was not statistically different. It was discussed that this was most likely due to the low number of people diagnosed with ovarian cancer (overall 32). The

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					observational studies had both a larger population as well as more people diagnosed with ovarian cancer (over 2000 people diagnosed with ovarian cancer) therefore higher statistical power to find differences. The committee therefore concluded that there was an increased risk with combined HRT but that this was a 'very slight increase' overall given the low baseline risk. The rationale has been amended accordingly.
Liverpool Women's Hospital	Guideline	066	015	Oestrogen-only HRT very slightly increases the risk of ovarian cancer after 10 years of use. This needs further evidence-based clarification.	Thank you for your comment. For oestrogen-only HRT a significant risk increase was identified from the evidence (5 to 9 years of use) - see evidence review F (figure 21). The tables of absolute numbers were checked, and this amounted to an increase of 1 in 1000 women which whilst significant is small.
Liverpool Women's Hospital	Guideline	067	006	The information provided on cardiovascular risk is not supported by current evidence, which shows a clear and statistically significant reduction in the risk of cardiovascular disease.	Thank you for your comment. The evidence in Evidence Review C consists of data from RCT and observational studies. There were some similarities and some differences between study types, with RCT evidence showing no increase or decrease in the risk of cardiovascular disease outcomes, and some of the observational evidence showing a reduction. The committee also discussed the data from the subgroup analyses, which showed some inconsistent findings across the evidence. The committee discussed the limitations across all of the evidence and raised concerns regarding residual confounding in the observational studies and some concerns regarding the population in the RCT evidence. Considering the limitations of the evidence, they agreed that the evidence did not support a recommendation that there is a reduction in the risk of cardiovascular disease

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					following HRT use. The committee's discussion of the evidence section in Evidence Review C has been updated to reflect a more detailed discussion of the committee's decision with regard to recommendations for cardiovascular disease risk. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). With regards to the conclusion related to coronary heart disease the independent review concluded 'If considering each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular benefits, which have been noted in the stakeholder comments. However, we agree with the committee's interpretation of the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
Liverpool Women's Hospital	Guideline	067	022	The information relating to a reduction in cardiovascular risk associated with use of HRT should be clearly demonstrated in the evidence based recommendations.	Thank you for your comment. The evidence in Evidence Review C consists of data from RCT and observational studies. There were some similarities and some differences between study types, with RCT evidence showing no increase or decrease in the risk of cardiovascular disease outcomes, and some of the observational evidence showing a reduction. The committee also discussed the data from the subgroup analyses, which showed some inconsistent findings across the evidence. The committee discussed the limitations across all of the evidence and raised concerns regarding residual confounding in the observational studies and some concerns regarding the population in the RCT evidence. Considering the limitations of the evidence, they agreed that the evidence did not support a recommendation that there is a reduction in the risk of cardiovascular disease following HRT use. The committee's discussion of the evidence section in Evidence Review C has been updated to reflect a more detailed discussion of the committee's decision with regard to recommendations for cardiovascular disease risk. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). With regards to the conclusion related to coronary heart disease

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					the independent review concluded 'If considering each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular benefits, which have been noted in the stakeholder comments. However, we agree with the committee's interpretation of the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
Liverpool Women's Hospital	Guideline	067	013 - 021	A reduced risk of coronary heart disease for women starting oestrogen only HRT aged 50 to 59 (Cochrane review Boardman et al) is not reflected in the recommendations.	Thank you for your comment. There is evidence in Evidence Review C, for oestrogen-only HRT use when the age at first use is 50-59, which is part of a subgroup analysis that also includes results for age at first use 60-69 and 70-79. The data shows that there is a statistically significant difference in the individual subgroup 50-59 (RR 0.67 (0.46 to 0.98)), but no statistically significant differences for 60-69 (RR 1.01 (0.83 to 1.22) or 70-79 (RR 0.98 (0.79 to 1.23)). However, it is

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					misleading to conclude that there is a difference in effect in different subgroups, because the test for subgroup differences was not statistically significant p=0.17 (please see forest plot figure 77 in Appendix E of Evidence Review C). Therefore, it is misleading to conclude that the reduced effect shown is specific to the age group 50-59. This methodology is in line with the NICE methods and processes and the Cochrane Handbook. As a result, the committee are unable to make a recommendation highlighting any reduced risk in coronary heart disease based on this result. This is further discussed in the committee's discussion of the evidence section in Evidence Review C which has been updated. The Cochrane review (Boardman et al) was assessed for inclusion but was excluded due to the data not being presented separately for combined HRT and oestrogen-only HRT, as specified in the protocol criteria of the review. The included studies in Boardman et al were individually assessed and included where they met the protocol criteria. Boardman et al is listed in the excluded studies section of Evidence Review C. The related rationale section of the guideline has been updated to explain the reason for the exclusion of this review to clarify this matter. NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). With regards to the conclusion related to coronary heart disease the independent review concluded 'If considering

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular benefits, which have been noted in the stakeholder comments. However, we agree with the committee's interpretation of the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
Liverpool Women's Hospital	Guideline	067	025 - 028	Has the GRADE system been modified for this guideline – if so why?	Thank you for your comment. The standard GRADE methodology has been used which has not been modified for this guideline (see supplement 1 - methods). The lines referred to (lines 25-28 on page 67), describes committees concerns regarding residual confounding. The GRADE domain risk of bias is assessed at study level for each outcome using a critical appraisal tool appropriate to each study design. Where confounders are an issue, they are addressed in the critical appraisal, which is reflected in the

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					GRADE risk of bias parameter and in turn contributes to the overall quality rating. Residual confounding is a bias that remains even after controlling or adjusting for confounders and can be as a result of unknown confounders. It is a potential source of bias in all observational studies, and although the committee refer to the GRADE rating, there may still be residual confounding from unknown factors, or factors that are difficult to adjust for which are discussed and taken into consideration. However, the guideline rationale section has been revised to focus on similarities and differences between study types. Residual confounding was discussed so it remains in the discussion in this section, but it has been revised to clarify that this was only one of many factors that were considered. The committee's discussion of the evidence in Evidence Review C has also been updated to provide more detail on this matter.
Liverpool Women's Hospital	Guideline	068	021	Why is the preference for NICE methodology vs Cochrane? RCT data should have a higher weighting. The guideline is excessively conservative in relation to potential CV benefit with HRT in otherwise healthy menopausal women.	Thank you for your comment. NICE methodology is in line with Cochrane methodology, however where Cochrane reviews do not fit the criteria set out in the pre-specified protocols they cannot be included in the review. The committee considered the evidence on cardiovascular outcomes related to the use of HRT, and this can be found in Evidence Review C. They discussed the limitations across the RCT evidence and observational evidence and agreed that the evidence did not support a cardiovascular benefit in those taking HRT. The rationale section of the guideline as well as the committee's discussion section in Evidence Review C have been revised to provide more detail on this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					NICE commissioned an independent review of the breast cancer and cardiovascular evidence reviews and these checks support the conclusions reached by the committee (with changes made post consultation). With regards to the conclusion related to coronary heart disease the independent review concluded 'If considering each forest plot individually, there were subgroups where evidence suggests that HRT appears to be associated with cardiovascular benefits, which have been noted in the stakeholder comments. However, we agree with the committee's interpretation of the evidence, based on the limited power in these analyses to detect subgroup differences, and lack of interpretable trends of effects.' To address the issue of 'limited power' highlighted in this independent review a research recommendation was made to increase the evidence base. However, they highlighted that RCT, and observational study evidence should be discussed separately and given equal prominence throughout. The independent review also recommended that evidence from both study types should be added into the forest plots alongside each other where possible, so that a visual comparison of findings is easier. RCT and observational evidence is still analysed separately in accordance with NICE methodology. These and other evidence reviews have been revised to implement these changes accordingly.
Liverpool Women's Hospital	Guideline	069	001	"should be explained to anyone considering HRT"	Thank you for your comment. This sentence has to be interpreted in the context of the preceding sentence which highlights the overall very low

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Pros and Cons should be presented to women without bias.	baseline risk for stroke in this age group. Given such a low baseline risk it is fair to say that the increase may also be small even if different. The committee therefore thought that this is an appropriate statement to make.
Liverpool Women's Hospital	Guideline	070		There is a significant all-cause mortality risk reduction in women starting HRT below the age of 60. This should be highlighted to facilitate patient counselling.	Thank you for your comment. The committee discussed the evidence in Evidence Review H relevant to all-cause mortality. They discussed that overall, the evidence did not show a reduction in mortality, nor did it show an increase in all-cause mortality. The data was stratified by age at first use. They discussed that for combined-HRT use, there were no differences in the risk of all-cause mortality. They also discussed the subgroup data for oestrogen-only HRT. They noted that the evidence shows an isolated risk reduction in younger women, however this was part of a subgroup analysis that did not show a statistically significant difference between the subgroups, and therefore the committee did not conclude that there was a difference in the risk of all-cause mortality. The rationale has been revised to provide a more detailed discussion of these analyses. The committee's discussion of the of Evidence Review H was updated accordingly.
Liverpool Women's Hospital	Guideline	072	016	''the evidence pointed towards a possible increased risk in dementia incidence, particularly with results showing increased risk when started at a later age. They agreed it was important that people considering HRT for troublesome menopause symptoms should be made aware of the potential risk, so that they could make an informed decision''	Thank you for your comment. The section has been revised to clarify that this only applies to people who initiate HRT aged 65 or older.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				The recommendation presented by NICE refer to an increase in risk in women who first start HRT at the age of 65 and above (The WHIMS study).	
Liverpool Women's Hospital	Guideline	073	018	HRT should not be used to prevent dementia.	Thank you for your comment in support of this.
Liverpool Women's Hospital	Guideline	074	016	"The committee considered the possibility that, like premature ovarian insufficiency, early menopause may either increase or decrease the baseline risk of some health outcomes" It is concerning that no background reference is made to the large observational evidence of adverse effect of early menopause on bone, cardiovascular and cognitive health. Whilst this may not have been part of the scope of the guidance at least some reference to this effect should be included here. There is large observational evidence that shows an adverse effect on bone (including osteoporosis and fractures), cardiovascular disease and cognitive function in both these groups (POI and early menopause). This should be referred to in this section.	Thank you for your comment. The aim of the evidence review carried out was assessing the impact of either taking HRT or not taking HRT on people with early menopause and the development of various health outcomes. The need to assess the impact of early menopause on health outcome has been acknowledged and will be passed onto the NICE surveillance teams for prioritised consideration during future updates.
Liverpool Women's Hospital	Guideline	094		Appendix A Osteoporosis – this is important.	Thank you for your comment. Parts of the osteoporosis tables were incorrect in the 2015 guideline and have been updated to rectify this. It still shows that HRT improves fracture risk, but the RCT and observational data now align.
Liverpool Women's Hospital	Guideline	098	004	Appendix A Table 17 showed that women aged 40 who took HRT for 10 years had a similar risk of breast cancer to women who did not take HRT.	Thank you for your comment. The comparison addressed in the related evidence review is women with early menopause taking HRT versus women in early menopause not taking HRT. Whether or not women in early menopause have

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				The recommendations should clearly reflect these findings.	a lower risk of breast cancer to start with was not the focus of the question posed. In table 17 (related to oestrogen-only HRT) differences are statistically significant even if in one of them the difference is too small to show up as a difference per 1000. The committee reflected on this and decided that the limited evidence identified (only evidence for breast cancer incidence) was a reason for a research recommendation in this area and removed the reference to this from the recommendation. Topics related to early menopause that were mentioned as important by stakeholders and were not addressed in the 2024 guideline update were logged with surveillance so that they could be considered for future updates.
Llais Cymru.	Guideline	General	General	Llais Cymru is concerned primarily with the patient experience. Quality of care from the patient's perspective, ease of access and informed consent are the issues we will focus on in this response. In a recent series of Safe Space events for women experiencing menopause we heard the following suggestions, comments and concerns; • Lack of general awareness in the wider population about perimenopause/menopause – our respondents suggest that this is an issue that should be taught at school as part of health awareness learning, as well as part of a wider education and information programme more generally. Such a programme could not only help women to	Thank you for your comment. NICE is aware of the significant impact from the stakeholder responses of people's experiences. Raising awareness of perimenopause / menopause was not part of the scope of the 2024 guideline update. The committee could therefore not comment on this. The NICE surveillance team regularly checks for evidence related to topics in guidelines (including information and support needs) to identify where further update work should be considered.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				prepare for menopause but also help others better understand and support women living through it. This can only be achieved if there is a good awareness and knowledge of the issues • The need for Well-Woman Clinics for those women approaching menopause – symptoms of brain fog, muscular pain and mental health issues such as depression and anxiety can be prepared for and mitigated. Presently they come as a shock for many women who are aware of some of the more commonly understood aspects such as hot flushes. Not all women suffer severe symptoms and many just need support and advice to cope well with the condition • Paucity of knowledge and experience in Primary Care about diagnosis and treatment of menopause • Knowledge of HRT use appears to be limited and out of date in some Primary Care settings • Menopause affects all the female population at some point in their lives and has a knock-on effect in the home and the workplace. Yet it is not treated as a public health issue in the same way as, say, diabetes or heart disease.	
Llais Cymru.	Guideline	General	General	Access to Services Access to specialist menopause services has historically been inequitable across Wales. As a result, we have heard from some women that they turned to private medical care. Lots of	Thank you for your comment. The guideline describes only in a limited number of cases referral to a healthcare professional with expertise in menopause and the definition of this allows this to be a GP with a special interest in menopause.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				women told us that they had to fight to get the treatment they were now receiving. Many felt that they had to go private to get a diagnosis and informed and effective advice on medication and care. The All Party Parliamentary Group on Menopause also reported that women felt driven to access private care for menopause and peri-menopause; "*When it comes to treatment, the APPG's central concern is that women face a postcode lottery on whether they can access the right treatment from their GP. While some are fortunate to be able to seek private treatment, this is not the reality for the majority of women. Complementary therapies and alternative treatments such as herbal remedies may be helpful for some, but they cannot treat symptoms the way HRT can, and again, come at cost. Put together, this creates a stark socio-economic divide between those that are able to seek treatment via their own means, and those that are not. It is these women who risk suffering the most, with further knock-on impacts on their working lives and financial situations*".	The majority of recommendations are aimed at any healthcare professional who may encounter someone with symptoms associated with the menopause. This could be in primary care. The guideline recommends a person-centred approach tailoring discussions about treatment choices to the person's age, personal circumstances and potential risk factors. The committee reflected on the numerical information in the appendix of the consultation version of the guideline and decided that more information and some visual presentation of the data would help in making treatment choices. The absolute numbers in the appendix were reviewed and used to produce a discussion aid document with visualisation of the data and verbal description aimed to facilitate shared decision-making. This discussion aid has undergone user-testing and was refined based on user feedback.
Llais Cymru.	Guideline	005	General	Recommendations "*People have the right to be involved in discussions and make informed decisions about their care*". Llais strongly supports the principle that informed consent is at the heart of good healthcare	Thank you for your comment in support of this.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Llais Cymru.	Guideline	006	011	Recommendations - 1.2.1 In our recent Safe Space events on Menopause, women who attended concurred with this point, telling us that there is a lack of general awareness in the wider population about perimenopause/menopause.	Thank you for your comment in support of this.
Llais Cymru.	Guideline	045	029 & 030	Equality of Access "*The committee agreed that access to a healthcare professional with expertise in menopause and access to CBT is a matter of equality and inclusivity".* This approach is welcomed. All of those we spoke to agreed that they had received very little support from their own GP. One woman told us; "…it feels that the patient has to drive and steer everything. I got treatment and tests only because I asked for them. It is all reactive not preventative.". Another told us: "I went back to the GP and asked for some information or advice about the Menopause. She printed off some pages from the internet and handed them to me to take home. I went home and wept"	Thank you for your comment in support of this.
Llais Cymru.	Guideline	047	010 & General	Depressive Symptoms Almost all the women attending our Safe Space events told us that "the change" was something that had not been discussed openly in their families. As a result, few women were	Thank you for your comment and sharing these experiences. The committee reflected on the wording of the recommendations related to CBT and revised them to ensure clarity about this ' as an option: in addition to other treatments

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				aware of the symptoms beyond hot flushes. Many were unaware that they were in perimenopause and, for some, the symptoms were distressing and led them to believe that they were suffering a range of conditions such as cancer, early onset dementia or serious mental illness. "I had physical and mental health symptoms. I expected to have hot flushes and dryness, but I didn't expect it to change my mental health". Worryingly, some of those seeking help were prescribed anti-depressants, rather than menopause-specific medication; "I had a telephone conversation with my GP and told them the emotional side of it all. I have a feeling of doom, hot flushes, have vivid dreams and wake up feeling as if I've been in a war zone. It's now affecting my life; I feel physically and emotionally exhausted. I told the GP I'm not depressed, I'm Menopausal. The GP prescribed something to help with that, I googled the prescription when I went home, it was Prozac, despite what I'd said to her."	(including HRT), for people for whom other treatments are contraindicated or for people who prefer not to take HRT'. This makes it clear that CBT is optional. The recommendation on a discussion about CBT as a treatment option has also been updated to highlight that information about what CBT is (including menopause specific CBT) and to take account of the person's preferences and needs. This change was made to clarify that this may not be an option suitable for all or may need to be adapted to the person's needs (for instance for people with learning disabilities). In relation to physical symptoms being addressed by CBT, the committee considered a systematic review of evidence from randomised controlled trials which showed CBT to be effective using some measurements for vasomotor symptoms, depressive symptoms and sleep problems. They therefore agreed to make this available to people who may benefit from this and having this as an 'option' widens people's treatment choices.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				CBT is, potentially, a very helpful tool in treatment of menopause. However, it needs to be used sensitively and as a part of a combined approach to care, if patients are not to be given the impression that their practitioner believes it is "all in their heads". Many women reported that they were already experiencing such attitudes from partners and family members and found it distressing.	
Llais Cymru.	Guideline	060	026	Cancer - Breast Patients expect realism, consistency and clarity of advice on the risk of breast and other cancers from the use of HRT. We have heard from some women who had been told by their GP that they should not consider HRT because of the high risk of cancer – **this advice was reported to us as being given before the GP had taken a history or considered individual circumstances with the patient**.	Thank you for your comment. In NICE methodology all evidence (meeting pre-specified protocols that are agreed with the committee and separately quality assured before the data is searched for), is systematically reviewed and presented to the committee who have drawn conclusions from it. In the consultation absolute numbers per 1000 people for each health conditions are presented for people who have taken HRT compared to people who have never taken HRT for symptoms of menopause. Based on the numbers in this appendix a discussion aid document has been developed which includes data visualisation as well as a verbal description of what the numbers mean. For clarity and consistency, this discussion aid document can be used in shared decision-making between the person and the healthcare professional to facilitate making treatment choices. This discussion aid has undergone user-testing and was refined based on user feedback.