Consultation version of evidence tables for 2019 surveillance of menopause

Table 1 Vasomotor and general menopausal symptoms

Reference	Text reference	Study type	Sample size	Number of studies	Duration (months)	Population	Intervention	Comparator	Outcome	Result
Gaudard et al. (2016)	9	SR-C	793	4	–	Women with menopausal symptoms	HRT (oestrogen patch)	Placebo	Hot flushes	Improved with intervention
Gaudard et al. (2016)	9	SR-C	–	3	–	Women with menopausal symptoms	HRT (oestrogen gel)	Placebo	Hot flushes	Improved with intervention
Gaudard et al. (2016)	9	SR-C	356	2	–	Women with menopausal symptoms	HRT (oestrogen, oral)	Placebo	Hot flushes	Improved with intervention
Gaudard et al. (2016)	9	SR-C	–	1	–	Women with menopausal symptoms	HRT (oestrogen topical emulsion)	Placebo	Hot flushes	Improved with intervention
Gaudard et al. (2016)	9	SR-C	458	1	–	Women with menopausal symptoms	HRT (oestrogen intranasal)	Placebo	Hot flushes	Improved with intervention
Santoro et al. (2017)	1	RCT	727	–	48	Postmenopausal women	HRT (conjugated oestrogen plus progestogen)	Placebo	Hot flushes	Improved with intervention
Santoro et al. (2017)	1	RCT	727	–	48	Postmenopausal women	HRT (oestrogen, transdermal)	Placebo	Hot flushes	Improved with intervention
Gaudard et al. (2016)	9	SR-C	–	–	–	Women with menopausal symptoms	HRT (oestrogen, bioidentical oral)	HRT (conjugated equine oestrogen)	Hot flushes	No effect of intervention
Ensrud et al. (2015)	2	RCT	339	–	2	Women with hot flushes	HRT (oestrogen only)	Placebo	Insomnia	Improved with intervention

Santoro et al. (2017)	1	RCT	727	–	48	Postmenopausal women	HRT (conjugated oestrogen plus progestogen)	Placebo	Insomnia	Improved with intervention
Santoro et al. (2017)	1	RCT	727	–	48	Postmenopausal women	HRT (oestrogen, transdermal)	Placebo	Insomnia	Improved with intervention
Yu, C-G; et al. (2016)	3	RCT	100	–	3	Women with menopausal symptoms	HRT (oestrogen)	HRT (progestogen)	Menopause symptoms	Improved with intervention
Santoro et al. (2017)	1	RCT	727	–	48	Postmenopausal women	HRT (conjugated oestrogen plus progestogen)	Placebo	Night sweats	Improved with intervention
Santoro et al. (2017)	1	RCT	727	–	48	Postmenopausal women	HRT (oestrogen, transdermal)	Placebo	Night sweats	Improved with intervention
Caan et al. (2015)	4	RCT	339	–	2	Women with vasomotor symptoms	HRT (oestrogen, low-dose)	Placebo	Quality of life	Improved with intervention
Diem et al. (2018)	5	RCT	302	–	3	Postmenopausal women with vulvovaginal symptoms	HRT (vaginal oestrogen) plus placebo gel	Placebo vaginal tablet and gel	Quality of life (menopause related)	Improved with intervention
Constantine et al. (2019)	6	RCT	726	–	3	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Quality of life (menopause related)	Improved with intervention
Ensrud et al. (2015)	2	RCT	339	–	2	Women with hot flushes	HRT (oestrogen only)	Placebo	Sleep quality	Improved with intervention
Kagan et al. (2018)	7	RCT	1,835	–	3	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Sleep score	Improved with intervention
Formoso et al. (2016)	10	SR-C	1,657	7	–	Women with menopausal symptoms	HRT (tibolone)	Placebo	Vasomotor symptoms	Improved with intervention
Constantine et al. (2019)	6	RCT	726	–	3	Postmenopausal women	Oestrogen plus progestogen (oral capsule)	Placebo	Vasomotor symptoms	Improved with intervention
Paoletti et al. (2015)	8	RCT	100	–	12	Postmenopausal women with vasomotor symptoms	HRT (oestrogen plus progestogen)	Placebo	Vasomotor symptoms	Improved with intervention

Formoso et al. (2016)	10	SR-C	1,336	9	–	Women with menopausal symptoms	HRT (tibolone)	HRT (combined)	Vasomotor symptoms	Worse with intervention

Table 2 Vaginal symptoms

Reference	Text reference	Study type	Sample size	Number of studies	Duration (months)	Population	Intervention	Comparator	Outcome	Result
Lethaby et al. (2016)	18	SR-C	67	1	–	Women with vaginal atrophy after the menopause	HRT (oestrogen ring)	Placebo	Symptoms of vaginal atrophy	Improved with intervention
Lethaby et al. (2016)	18	SR-C	198	2	–	Women with vaginal atrophy after the menopause	HRT (oestrogen cream)	Placebo	Symptoms of vaginal atrophy	Improved with intervention
Lethaby et al. (2016)	18	SR-C	50	1	–	Women with vaginal atrophy after the menopause	HRT (oestrogen cream)	Isoflavone gel	Symptoms of vaginal atrophy	No effect of intervention
Lethaby et al. (2016)	18	SR-C	341	2	–	Women with vaginal atrophy after the menopause	HRT (oestrogen ring)	HRT (oestrogen cream)	Symptoms of vaginal atrophy	No effect of intervention
Lethaby et al. (2016)	18	SR-C	208	2	–	Women with vaginal atrophy after the menopause	HRT (oestrogen tablet)	HRT (oestrogen cream)	Symptoms of vaginal atrophy	No effect of intervention
Lethaby et al. (2016)	18	SR-C	567	3	–	Women with vaginal atrophy after the menopause	HRT (oestrogen ring)	HRT (oestrogen tablet)	Symptoms of vaginal atrophy	No effect of intervention
Lethaby et al. (2016)	18	SR-C	1,638	2	–	Women with vaginal atrophy after the menopause	HRT (oestrogen tablet)	Placebo	Symptoms of vaginal atrophy	No effect of intervention

Constantine et al. (2018)	11	RCT	561	–	3	Postmenopausal women with vulvovaginal atrophy	HRT (oestrogen, intravaginal)	Placebo	Dyspareunia	Improved with intervention
Kroll et al. (2018)	12	RCT	550	–	3	Postmenopausal women with vulvovaginal atrophy	HRT (oestrogen intravaginal)	Placebo	Dyspareunia	Improved with intervention
Taylor et al. (2017)	13	RCT	670	–	48	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Sexual function	Improved with intervention
Mitchell et al. (2018)	14	RCT	302	–	3	Postmenopausal women with moderate to severe vulvovaginal symptoms	HRT (vaginal oestrogen tablet plus placebo gel)	Placebo tablet plus placebo gel	Sexual function	No effect of intervention
Taylor et al. (2017)	13	RCT	670	–	48	Postmenopausal women	HRT (conjugated equine oestrogens plus progestogen)	Placebo	Sexual function	No effect of intervention
Constantine et al. (2017)	15	RCT	764	–	3	Postmenopausal women	HRT (vaginal oestrogen gel capsule)	Placebo	Dyspareunia plus measures of superficial and parabasal cells, and vaginal pH	Improved with intervention
Archer et al. (2018)	16	RCT	576	–	3	Postmenopausal women with vaginal atrophy	HRT (oestrogen vaginal cream)	Placebo	Vaginal dryness	Improved with intervention
Rioux J.E.; et al. (2018)	17	RCT	159	–	6	Women with menopausal symptoms	HRT (oestrogen, intravaginal, 25 mg)	HRT (conjugated equine oestrogen, intravaginal, 1.25 mg)	Vaginal symptoms	No effect of intervention

Table 3 Depression

Reference	Text reference	Study type	Sample size	Number of studies	Population	Intervention	Comparator	Outcome	Result
Gordon et al. (2018)	19	RCT	172	–	Postmenopausal women	HRT (oestrogen, transdermal, plus progestogen, oral)	Placebo	Depression score	Improved with intervention

Gleason et al. (2015)	20	RCT	693	–	Postmenopausal women	HRT (conjugated equine oestrogen, oral, plus progestogen)	Placebo	Depression symptoms	Improved with intervention

Table 4 Other outcomes

Reference	Text reference	Study type	Sample size	Number of studies	Duration (months)	Population	Intervention	Comparator	Outcome	Result
Rioux J.E.; et al. (2018)	17	RCT	159	–	6	Women with menopausal symptoms	HRT (oestrogen, intravaginal)	HRT (conjugated equine oestrogen, intravaginal)	Follicle stimulating hormone level	Improved with intervention
Kingsberg et al. (2017)	3	RCT	764	–	–	Postmenopausal women with vulval and vaginal atrophy	HRT (oestrogen vaginal capsule)	Placebo	Intention to use product again	Improved with intervention
Yu, C-G; et al. (2016)	21	RCT	100	–	3	Women with menopausal symptoms	HRT (oestrogen)	HRT (progestogen)	Luteinising hormone and follicle stimulating hormone levels	Improved with intervention
Rioux J.E.; et al. (2018)	17	RCT	159	–	6	Women with menopausal symptoms	HRT (oestrogen, intravaginal)	HRT (conjugated equine oestrogen, intravaginal)	Oestrogen level	Improved with intervention
Yu, C-G; et al. (2016)	21	RCT	100	–	3	Women with menopausal symptoms	HRT (oestrogen)	HRT (progestogen)	Oestrogen level	Improved with intervention
Rioux J.E.; et al. (2018)	17	RCT	159	–	6	Women with menopausal symptoms	HRT (oestrogen, intravaginal)	HRT (conjugated equine oestrogen, intravaginal)	Patient acceptance	Improved with intervention
Kingsberg et al. (2017)	21	RCT	764	–	–	Postmenopausal women with vulval and vaginal atrophy	HRT (oestrogen vaginal capsule)	Placebo	Satisfaction with treatment	Improved with intervention

Table 5 Adverse events

Reference	Text reference	Study type	Sample size	Number of studies	Duration (months)	Population	Intervention	Comparator	Outcome	Result
Gaudard et al. (2016)	9	SR-C	103	1	–	Women with menopausal symptoms	HRT (oestrogen, oral)	HRT (conjugated equine oestrogen)	Adverse events	No effect of intervention
Gaudard et al. (2016)	9	SR-C	433	3	–	Women with menopausal symptoms	HRT (oestrogen, oral)	Placebo	Adverse events	No effect of intervention
Gaudard et al. (2016)	9	SR-C	200	1	–	Women with menopausal symptoms	HRT (oestrogen topical emulsion)	Placebo	Adverse events	No effect of intervention
Gaudard et al. (2016)	9	SR-C	1,822	9	–	Women with menopausal symptoms	HRT (oestrogen patch)	Placebo	Adverse events	Worse with intervention
Gaudard et al. (2016)	9	SR-C	1,086	3	–	Women with menopausal symptoms	HRT (oestrogen gel)	Placebo	Adverse events	Worse with intervention
Gaudard et al. (2016)	9	SR-C	458	1	–	Women with menopausal symptoms	HRT (oestrogen intranasal)	Placebo	Adverse events	Worse with intervention
Formoso et al. (2016)	10	SR-C	6,438	16	–	Women with menopausal symptoms	HRT (tibolone)	HRT (combined)	Bleeding	Improved with intervention
Formoso et al. (2016)	10	SR-C	7,814	9	–	Women with menopausal symptoms	HRT (tibolone)	Placebo	Bleeding	Worse with intervention
Lethaby et al. (2016)	18	SR-C	151	2	–	Women with vaginal atrophy	HRT (oestrogen tablet)	Placebo	Endometrial thickness	No effect of intervention

						after the menopause				
Lethaby et al. (2016)	18	SR-C	273	2	–	Women with vaginal atrophy after the menopause	HRT (oestrogen ring)	HRT (oestrogen cream)	Endometrial thickness	Worse with intervention
Yu, C-G; et al. (2016)	3	RCT	100	–	3	Women with menopausal symptoms	HRT (oestrogen)	HRT (progestogen)	Adverse events, uterine volume and endometrial thickness	No effect of intervention

Table 6 Non-HRT drug treatments

Reference	Text reference	Study type	Sample size	Number of studies	Duration (months)	Population	Intervention	Comparator	Outcome	Result
Labrie, Fernand; et al. (2015)	22	RCT	482	–	3	Postmenopausal women with vaginal atrophy	Prasterone (dehydroepiandrosterone, intravaginal)	Placebo	Dyspareunia	Improved with intervention
Labrie, Fernand; et al. (2016)	22	RCT	482	–	3	Women with vulvovaginal atrophy	Prasterone (dehydroepiandrosterone, intravaginal)	Placebo	Dyspareunia	Improved with intervention
Labrie, Fernand; et al. (2015)	24	RCT	482	–	3	Postmenopausal women with vaginal atrophy	Prasterone (dehydroepiandrosterone, intravaginal)	Placebo	Lubrication	Improved with intervention
Labrie, Fernand; et al. (2015)	24	RCT	482	–	3	Postmenopausal women with vaginal atrophy	Prasterone (dehydroepiandrosterone, intravaginal)	Placebo	Orgasm	Improved with intervention
Labrie, Fernand; et al. (2015)	24	RCT	482	–	3	Postmenopausal women with vaginal atrophy	Prasterone (dehydroepiandrosterone, intravaginal)	Placebo	Satisfaction	Improved with intervention
Labrie, Fernand; et al. (2015)	24	RCT	482	–	3	Postmenopausal women with vaginal atrophy	Prasterone (dehydroepiandrosterone, intravaginal)	Placebo	Sexual desire	Improved with intervention
Barton, Debra L; et al. (2018)	23	RCT	464	–	3	Postmenopausal women with a history of breast or gynaecological cancer	Prasterone (dehydroepiandrosterone, intravaginal)	Intravaginal moisturiser	Sexual health	Improved with intervention
Labrie, Fernand; et al. (2016)	22	RCT	482	–	3	Women with vulvovaginal atrophy	Prasterone (dehydroepiandrosterone, intravaginal)	Placebo	Vaginal dryness	Improved with intervention
Labrie, Fernand; et al. (2016)	22	RCT	482	–	3	Women with vulvovaginal atrophy	Dehydroepiandrosterone (intravaginal)	Placebo	Parabasal cells	Improved with intervention

Labrie, Fernand; et al. (2016)	22	RCT	482	–	3	Women with vulvovaginal atrophy	Dehydroepiandrosterone (intravaginal)	Placebo	Superficial cells	Improved with intervention
Labrie, Fernand; et al. (2016)	22	RCT	482	–	3	Women with vulvovaginal atrophy	Dehydroepiandrosterone (intravaginal)	Placebo	Vaginal pH	Improved with intervention
Barton, Debra L; et al. (2018)	23	RCT	464	–	3	Postmenopausal women with a history of breast or gynaecological cancer	Dehydroepiandrosterone (intravaginal)	Intravaginal moisturiser	Vaginal dyness of dyspareunia	No effect of intervention
Barton, Debra L; et al. (2018)	23	RCT	464	–	3	Postmenopausal women with a history of breast or gynaecological cancer	Prasterone (dehydroepiandrosterone, intravaginal)	Intravaginal moisturiser	Vaginal dryness or dyspareunia	No effect of intervention
Parandavar, Nehleh; et al. (2018)	28	RCT	240	–	3	Postmenopausal women	Melatonin	Placebo	Low-density lipoprotein cholesterol	No effect of intervention
Li Y.; et al. (2016)	27	RCT	128	–	6	Women with premature ovarian failure	Melatonin	Placebo	Luteinising and follicle stimulating hormone levels	Improved with intervention
Li Y.; et al. (2016)	27	RCT	128	–	6	Women with premature ovarian failure	Melatonin	Placebo	Ovarian hormone secretion	Improved with intervention
Parandavar, Nehleh; et al. (2018)	28	RCT	240	–	3	Postmenopausal women	Melatonin	Placebo	Triglycerides	No effect of intervention
Archer, David F; et al. (2019)	25	RCT	631	–	3	Postmenopausal women with vaginal dryness	Ospemifene	Placebo	Dyspareunia	Improved with intervention
Constantine, G; et al. (2015)	26	RCT	919	–	3	Postmenopausal women with vulvar and vaginal atrophy	Ospemifene	Placebo	Sexual function	Improved with intervention
Archer, David F; et al. (2019)	25	RCT	631	–	3	Postmenopausal women with vaginal dryness	Ospemifene	Placebo	Sexual function	Improved with intervention
Archer, David F; et al. (2019)	25	RCT	631	–	3	Postmenopausal women with vaginal dryness	Ospemifene	Placebo	Vaginal dryness	Improved with intervention

Archer, David F; et al. (2019)	25	RCT	631	–	3	Postmenopausal women with vaginal dryness	Ospemifene	Placebo	Parabasal and superficial cells, vaginal pH, and severity of vaginal dryness	Improved with intervention
Simon, James A; et al. (2016)	29	RCT	148	–		Postmenopausal women	Oxybutynin	Placebo	Vasomotor symptoms	Improved with intervention
Simon, James A; et al. (2016)	29	RCT	148	–	3	Postmenopausal women	Oxybutynin	Placebo	Dry mouth	Worse with intervention
Simon, James A; et al. (2016)	29	RCT	148	–		Postmenopausal women	Oxybutynin	Placebo	Sleep quality	Improved with intervention
Torky H.A.; et al. (2018)	30	RCT	140	–	1	Postmenopausal women with vulvovaginal atrophy	Oxytocin intravaginal gel	Placebo	Dyspareunia	Improved with intervention
Ensrud, Kristine E; et al. (2015)	2	RCT	339	–	2	Women with hot flushes	Venlafaxine	Placebo	Insomnia	Improved with intervention
Caan, Bette; et al. (2015)	4	RCT	339	–	2	Women with vasomotor symptoms	Venlafaxine	Placebo	Quality of life	Improved with intervention
Ensrud, Kristine E; et al. (2015)	2	RCT	339	–	2	Women with hot flushes	Venlafaxine	Placebo	Sleep quality	Improved with intervention

Table 7 Physical and psychological treatments

Reference	Text reference	Study type	Sample size	Number of studies	Duration (months)	Population	Intervention	Comparator	Outcome	Result
Hardy, Claire; et al. (2018)	31	RCT	124	–	2	Women with vasomotor symptoms	CBT, self-help	Wait list control	Hot flushes or night sweats	Improved with intervention
Atema et al. (2019)	32	RCT	254	–	2	Women with a history of breast cancer and	CBT, self-managed	Wait list control	Impact of hot flushes and night sweats	Improved with intervention

						menopausal symptoms				
Atema et al. (2019)	32	RCT	254	–	2	Women with a history of breast cancer and menopausal symptoms	CBT, self-managed	Wait list control	Sleep quality	Improved with intervention
McCurry, Susan M; et al. (2016)	33	RCT	106	–	2	Menopausal women with insomnia	CBT, telephone-based	Menopause education control	Hot flushes	No effect of intervention
McCurry, Susan M; et al. (2016)	33	RCT	106	–	2	Menopausal women with insomnia	CBT, telephone-based	Menopause education control	Insomnia	Improved with intervention
McCurry, Susan M; et al. (2016)	33	RCT	106	–	2	Menopausal women with insomnia	CBT, telephone-based	Menopause education control	Sleep quality	Improved with intervention
Atema et al. (2019)	32	RCT	254	–	2	Women with a history of breast cancer and menopausal symptoms	CBT, therapist-guided	Wait list control	Impact of hot flushes and night sweats	Improved with intervention
Atema et al. (2019)	32	RCT	254	–	2	Women with a history of breast cancer and menopausal symptoms	CBT, therapist-guided	Wait list control	Sleep quality	Improved with intervention
Huang, Alison J; et al. (2015)	34	RCT	123	–	3	Women with vasomotor symptoms	Device-guided slow-paced breathing	Control device	Hot flush frequency	Improved with intervention
Huang, Alison J; et al. (2015)	34	RCT	123	–	3	Women with vasomotor symptoms	Device-guided slow-paced breathing	Control device	Hot flushes	Improved with intervention
Huang, AJ; et al. (2015)	34	RCT	123	–	3	Women with vasomotor symptoms	Device-guided slow-paced breathing	Non-rhythmic music	Hot flushes	No effect of intervention

Daley, A J; et al. (2015)	35	RCT	261	–	6	Women with vasomotor symptoms	Exercise intervention (2 consultations with physical activity facilitator)	Control	Hot flushes or night sweats	No effect of intervention
Daley, A J; et al. (2015)	35	RCT	261	–	6	Women with vasomotor symptoms	Exercise intervention (menopause information DVD and written information to encourage physical activity)	Control	Hot flushes or night sweats	No effect of intervention
Abedi, P; et al. (2015)	36	RCT	106	–	3	Postmenopausal women	Exercise intervention (pedometer-monitored walking)	Unspecified control	Anxiety and insomnia	Improved with intervention
Abedi, P; et al. (2015)	36	RCT	106	–	3	Postmenopausal women	Exercise intervention (pedometer-monitored walking)	Unspecified control	Depression	Improved with intervention
Tadayon, M; et al. (2016)	37	RCT	112	–	3	Postmenopausal women	Exercise intervention (pedometer-monitored walking)	Usual care	Sleep quality	Improved with intervention
Abedi, P; et al. (2015)	36	RCT	106	–	3	Postmenopausal women	Exercise intervention (pedometer-monitored walking)	Unspecified control	Step count increase	Improved with intervention
Gozuyesil, Ebru; Baser, Muruvvet (2016)	38	RCT	120	–	–	Women with vasomotor symptoms	Foot reflexology	Control aromatherapy	Hot flushes, sweats and night sweats	Improved with intervention
Almeida, Osvaldo P; et al. (2016)	39	RCT	351	–	12	Menopausal women	Health coaching	Usual care	Depression symptoms	No effect of intervention

Mirghafourvand, M; et al. (2015)	40	RCT	124	–	2	Women with menopausal symptoms	Self-directed learning	Control (no learning)	Hot flushes	Improved with intervention
Mirghafourvand, M; et al. (2015)	40	RCT	124	–	2	Women with menopausal symptoms	Self-directed learning	Control (no learning)	Menopausal symptoms	Improved with intervention

Table 8 Alternative and complementary medicine

Reference	Text reference	Study type	Sample size	Number of studies	Duration (months)	Population	Intervention	Comparator	Outcome	Result
Heudel P.-E.; et al. (2019)	41	RCT	299	–	1	Women with breast cancer (non-metastatic, localised, ECOG=PS<=1)	Actheane (homeopathic medicine complex)	Placebo	Hot flushes	No effect of intervention
Heudel P.-E.; et al. (2019)	41	RCT	299	–	1	Women with breast cancer and vasomotor symptoms	Actheane (homeopathic medicine complex)	Placebo	Quality of life	No effect of intervention
Steels E.; et al. (2018)	42	RCT	117	–	3	Women with menopausal symptoms	Ayurvedic herbal remedy	Placebo	Vasomotor symptoms	Improved with intervention
Steels E.; et al. (2018)	42	RCT	117	–	3	Women with menopausal symptoms	Ayurvedic herbal remedy	Placebo	Quality of life (menopause related)	Improved with intervention
Farshbaf-Khalili, Azizeh; et al. (2018)	43	RCT	156	–	2	Postmenopausal women	Bitter orange capsule	Placebo	Anxiety	Improved with intervention

Kamalifard M.; et al. (2017)	44	RCT	156	–	2	Women with menopausal symptoms	Bitter orange capsule	Placebo	Depression	Improved with intervention
Kamalifard, Mahin; et al. (2019)	44	RCT	157	–	3	Postmenopausal women	Bitter orange capsule	Placebo	Sleep quality	Improved with intervention
Dastenaei, BM; et al. (2017)	45	RCT	100	–	1	Postmenopausal women	Evening primrose oil	Placebo	Hot flushes	Improved with intervention
Steels, E; et al. (2017)	46	RCT	115	–	3	Women with menopausal symptoms	Fenugreek seed extract	Placebo	Hot flushes	Improved with intervention
Steels, E; et al. (2017)	46	RCT	115	–	3	Women with menopausal symptoms	Fenugreek seed extract	Placebo	Menopausal symptoms	Improved with intervention
Aghamiri, Vida; et al. (2016)	47	RCT	120	–	3	Women with symptoms of menopause	Hop extract	Placebo	Hot flushes	Improved with intervention
Aghamiri, Vida; et al. (2016)	47	RCT	120	–	3	Women with symptoms of menopause	Hop extract	Placebo	Menopausal symptoms	Improved with intervention
Kazemzadeh, Rafat; et al. (2016)	48	RCT	100	–	3	Women with menopausal symptoms	Lavender aromatherapy	Control aromatherapy	Hot flushes	Improved with intervention
Nikjou R.; et al. (2018)	49	RCT	100	–	–	Women with menopausal symptoms	Lavender aromatherapy	Diluted milk control	Menopausal symptoms	Improved with intervention
Farshbaf-Khalili, Azizeh; et al. (2018)	43	RCT	157	–	3	Postmenopausal women	Lavender capsule	Placebo	Anxiety	Improved with intervention
Farshbaf-Khalili, Azizeh; et al. (2018)	43	RCT	157	–	3	Postmenopausal women	Lavender capsule	Bitter orange capsule	Anxiety	No effect of intervention

Kamalifard M.; et al. (2017)	44	RCT	156	–	2	Women with menopausal symptoms	Lavender capsule	Placebo	Depression	Improved with intervention
Kamalifard, Mahin; et al. (2018)	44	RCT	156	–	2	Postmenopausal women	Lavender capsule	Placebo	Sleep quality	Improved with intervention
Sathyapalan, T; et al. (2018)	50	RCT	200	–	6	Women in early menopause	Protein bar with isoflavones	Protein bar without isoflavones	Cardiovascular risk factors	Improved with intervention
Gocan A.; et al. (2018)	51	RCT	180	–	3	Women with hot flushes	Soy germ extract	Placebo	Hot flushes	Improved with intervention
Mitchell, Caroline M; et al. (2018)	14	RCT	302	–	3	Postmenopausal women with moderate to severe vulvovaginal symptoms	Vaginal moisturiser plus placebo vaginal tablet	Placebo tablet plus placebo gel	Sexual function	No effect of intervention

Table 9 Chinese herbal medicine

Reference	Text reference	Study type	Sample size	Number of studies	Duration (months)	Population	Intervention	Comparator	Outcome	Result
Zhu, X; et al. (2016)	52	SR-C	705	7	–	Women with menopausal symptoms	Chinese herbal medicine	Placebo	Adverse events	No effect of intervention
Zhu, X; et al. (2016)	52	SR-C	864	2	–	Women with menopausal symptoms	Chinese herbal medicine	HRT	Adverse events	No effect of intervention
Zhu, X; et al. (2016)	52	SR-C	139	2	–	Women with menopausal symptoms	Chinese herbal medicine	Other drug treatments (such as fluoxetine)	Adverse events	No effect of intervention
Zhu, X; et al. (2016)	52	SR-C	199	2	–	Women with menopausal symptoms	Chinese herbal medicine	Placebo	Hot flushes	No effect of intervention

Jiang D.; et al. (2015)	53	RCT	224	–	3	Women with menopausal symptoms	Chinese herbal medicine	Placebo	Menopausal symptoms	No effect of intervention
Zhu, X; et al. (2016)	52	SR-C	64	1	–	Women with menopausal symptoms	Chinese herbal medicine	Placebo	Night sweats	No effect of intervention
Zhu, X; et al. (2016)	52	SR-C	256	3	–	Women with menopausal symptoms	Chinese herbal medicine	Placebo	Vasomotor symptoms	No effect of intervention
Zhu, X; et al. (2016)	52	SR-C	127	2	–	Women with menopausal symptoms	Chinese herbal medicine	HRT	Vasomotor symptoms	No effect of intervention

Table 10 Acupuncture

Reference	Text reference	Study type	Sample size	Number of studies	Duration (months)	Population	Intervention	Comparator	Outcome	Result
Li, O; Wang, F (2018)	54	RCT	128	–	2	Women with menopausal insomnia	Acupuncture	Alprazolam	Oestrogen levels	Improved with intervention
Avis, Nancy E; et al. (2016)	55	RCT	209	–	6	Women with vasomotor symptoms	Acupuncture	Waitlist control	Vasomotor symptoms	Improved with intervention
Li, O; Wang, F (2018)	54	RCT	128	–	2	Women with menopausal insomnia	Acupuncture	Alprazolam	Sleep quality	Improved with intervention
Li, O; Wang, F (2018)	54	RCT	128	–	2	Women with menopausal insomnia	Acupuncture	Alprazolam	Luteinising hormone and follicle stimulating hormone levels	No effect of intervention
Liu Z.; et al. (2018)	56	RCT	360	–	8	Women with menopausal symptoms	Acupuncture	Sham acupuncture	Hot flushes	Improved with intervention
Liu Z.; et al. (2018)	56	RCT	360	–	8	Women with menopausal symptoms	Acupuncture	Sham acupuncture	Menopausal symptoms	Improved with intervention

Liu Z.; et al. (2018)	56	RCT	360	–	8	Women with menopausal symptoms	Acupuncture	Sham acupuncture	Quality of life (menopause related)	Improved with intervention
Ee, Carolyn; et al. (2016)	57	RCT	327	–	2	Women with vasomotor symptoms	Acupuncture	Sham acupuncture	Hot flushes	No effect of intervention
Lesi, Grazia; et al. (2016)	58	RCT	190	–	3	Women with breast cancer and vasomotor symptoms	Acupuncture plus enhanced self-care	Self-care	Hot flushes	Improved with intervention
Peng, YY; et al. (2018)	59	RCT	100	–	3	Women with menopausal symptoms	Acupuncture therapies (electroacupuncture, plus acupoint injection, plus fire needle treatment)	Control (no intervention)	Menopausal symptoms	Improved with intervention

Table 11 Coronary heart disease

Reference	Text reference	Study type	Sample size	Number of studies	Population	Intervention	Comparator	Outcome	Result
Crandall et al. (2018)	60	Cohort	45,663	–	Postmenopausal women without hysterectomy	HRT (oestrogen, intravaginal)	No HRT	Coronary heart disease	Improved with intervention
Crandall et al. (2019)	60	Cohort	45,664	–	Postmenopausal women with previous hysterectomy	HRT (oestrogen, intravaginal)	No HRT	Coronary heart disease	No effect of intervention
Mikkola et al. (2016)	61	Cohort	195,756	–	Postmenopausal women	HRT (oestrogen, intravaginal, 3–5 year duration)	no HRT	Coronary heart disease (mortality)	Improved with intervention

Table 12 Stroke

Reference	Text reference	Study type	Sample size	Number of studies	Population	Intervention	Comparator	Outcome	Result
Mikkola et al. (2015)	61	Cohort	332 202	–	Postmenopausal women	HRT (stopped more than a year ago)	No HRT	Mortality, stroke	Improved with intervention
Mikkola et al. (2016)	61	Cohort	195,756	–	Postmenopausal women	HRT (oestrogen, intravaginal, 3–5 year duration)	no HRT	Mortality, stroke	Improved with intervention
Mikkola et al. (2015)	61	Cohort	332 202	–	Postmenopausal women	HRT (stopped up to a year ago)	No HRT	Mortality, stroke	Worse with intervention
Mikkola et al. (2015)	61	Cohort	332 202	–	Postmenopausal women	HRT (stopped up to a year ago)	HRT (current use)	Mortality, stroke	Worse with intervention
Carrasquilla et al. (2017)	62	Cohort	88,914	–	Postmenopausal women	HRT (started within 5 years of menopause)	No HRT	Stroke	Improved with intervention
Carrasquilla et al. (2017)	62	Cohort	88,914	–	Postmenopausal women	HRT (conjugated equine oestrogen started later than 5 years after menopause)	No HRT	Stroke	Improved with intervention
Carrasquilla et al. (2017)	62	Cohort	88,914	–	Postmenopausal women	HRT (combined HRT started later than 5 years after menopause)	No HRT	Stroke	Improved with intervention
Lokkegaard et al. (2017)	65	Cohort	980,003	–	Postmenopausal women	HRT (oestrogen, intravaginal)	No HRT	Stroke	Improved with intervention
Lokkegaard et al. (2017)	65	Cohort	980,003	–	Postmenopausal women	HRT (transdermal)	No HRT	Stroke	No effect of intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (combined, continuous)	Placebo	Stroke	Worse with intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (oestrogen only)	Placebo	Stroke	Worse with intervention

Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen only)	Placebo	Stroke	Worse with intervention
Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Stroke	Worse with intervention
Lokkegaard et al. (2017)	65	Cohort	980,003	–	Postmenopausal women	HRT (current use)	No HRT	Stroke	Worse with intervention
Lokkegaard et al. (2017)	65	Cohort	980,003	–	Postmenopausal women	HRT (continuous oestrogen plus progestogen)	No HRT	Stroke	Worse with intervention
Lokkegaard et al. (2017)	65	Cohort	980,003	–	Postmenopausal women	HRT (cyclic oestrogen plus progestogen)	No HRT	Stroke	Worse with intervention
Lokkegaard et al. (2017)	65	Cohort	980,003	–	Postmenopausal women	HRT (oestrogen only)	No HRT	Stroke	Worse with intervention
Chen et al. (2015)	64	Cohort	1,284	–	Postmenopausal women with diabetes	HRT (conjugated equine oestrogen)	No HRT	Stroke (ischaemic)	Improved with intervention
Chang et al. (2019)	63	Cohort	4,982	–	Postmenopausal women	HRT	No HRT	Stroke (ischaemic)	Worse with intervention
Carrasquilla et al. (2017)	62	Cohort	88,914	–	Postmenopausal women	HRT (conjugated equine oestrogen started later than 5 years after menopause)	No HRT	Stroke, haemorrhagic	Improved with intervention
Carrasquilla et al. (2017)	62	Cohort	88,914	–	Postmenopausal women	HRT (started within 5 years of menopause)	No HRT	Stroke, haemorrhagic	No effect of intervention
Carrasquilla et al. (2017)	62	Cohort	88,914	–	Postmenopausal women	HRT (combined HRT started later than 5 years after menopause)	No HRT	Stroke, haemorrhagic	No effect of intervention
Qureshi et al. (2016)	66	Cohort	93,676	–	Postmenopausal women	HRT (oestrogen only, current use)	No HRT	Subarachnoid haemorrhage	No effect of intervention
Qureshi et al. (2016)	66	Cohort	93,676	–	Postmenopausal women	HRT (oestrogen plus progestogen, current use)	No HRT	Subarachnoid haemorrhage	No effect of intervention

Qureshi et al. (2016)	66	Cohort	93,676	–	Postmenopausal women	HRT (current use)	No HRT	Subarachnoid haemorrhage	Worse with intervention

Table 13 Venous thromboembolism

Reference	Text reference	Study type	Sample size	Number of studies	Population	Intervention	Comparator	Outcome	Result
Formoso et al. (2016)	10	SR-C	4529	4	Women with menopausal symptoms	HRT (tibolone)	HRT (combined)	Venous thromboembolism	No effect of intervention
Formoso et al. (2016)	10	SR-C	9,176	–	Women with menopausal symptoms	HRT (tibolone)	Placebo	Venous thromboembolism	No effect of intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (combined, continuous)	Placebo	Venous thromboembolism	Worse with intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women with cardiovascular disease	HRT (combined, continuous)	Placebo	Venous thromboembolism	Worse with intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (oestrogen only)	Placebo	Venous thromboembolism	Worse with intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (oestrogen only)	Placebo	Venous thromboembolism	Worse with intervention
Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen only)	Placebo	Venous thromboembolism	Worse with intervention
Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Venous thromboembolism	Worse with intervention
Chang et al. (2019)	63	Cohort	4,982	–	Postmenopausal women	HRT	No HRT	Venous thromboembolism	Worse with intervention

Lee et al. (2015)	70	Cohort	924,557	–	Postmenopausal women	HRT	No HRT	Venous thromboembolism	Worse with intervention

Table 14 Diabetes

Reference	Text reference	Study type	Sample size	Number of studies	Population	Intervention	Comparator	Outcome	Result
Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen only)	Placebo	Diabetes	Improved with intervention
Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Diabetes	Improved with intervention

Table 15 Other cardiovascular outcomes

Reference	Text reference	Study type	Sample size	Number of studies	Population	Intervention	Comparator	Outcome	Result
Chang et al. (2019)	63	Cohort	4,982	–	Postmenopausal women	HRT	No HRT	Acute coronary syndrome	Worse with intervention
Dinger, J; et al. (2016)	72	Cohort	30,597	–	Postmenopausal women	HRT (oestrogen plus progestogen, drospirenone)	HRT (oestrogen plus non-drospirenone progestogen)	Arterial thromboembolic events	Improved with intervention
Paoletti et al. (2016)	8	RCT	101	–	Postmenopausal women with vasomotor symptoms	HRT (oestrogen plus progestogen)	Placebo	Blood pressure	Improved with intervention
Formoso et al. (2016)	10	SR-C	8,401	4	Women with menopausal symptoms	HRT (tibolone)	Placebo	Cardiovascular events	No effect of intervention

Formoso et al. (2016)	10	SR-C	3,794	2	Women with menopausal symptoms	HRT (tibolone)	HRT (combined)	Cardiovascular events	No effect of intervention
Huang et al. (2018)	71	RCT	2,763	–	Postmenopausal women with congestive heart disease who did not have hot flushes at baseline	HRT (conjugated equine oestrogens plus progestogen)	Placebo	Cardiovascular events	No effect of intervention
Huang et al. (2018)	71	RCT	2,763	–	Postmenopausal women with congestive heart disease who had hot flushes at baseline	HRT (conjugated equine oestrogens plus progestogen)	Placebo	Cardiovascular events	Worse with intervention
Simon et al. (2016)	29	Cohort	–	–	Women with menopausal symptoms	HRT (oestrogen, transdermal)	HRT (oestrogen, oral)	Cardiovascular events	No effect of intervention
Formoso et al. (2016)	10	SR-C	7,930	4	Women with menopausal symptoms	HRT (tibolone)	Placebo	Cerebrovascular events	No effect of intervention
Formoso et al. (2016)	10	SR-C	4,562	4	Women with menopausal symptoms	HRT (tibolone)	HRT (combined)	Cerebrovascular events	No effect of intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (oestrogen only)	Placebo	Coronary event	No effect of intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (combined, continuous)	Placebo	Coronary event	Worse with intervention
Swica et al. (2018)	73	RCT	27,347	–	Postmenopausal women without history of hysterectomy who did not have hypertension at baseline	HRT (conjugated equine oestrogens plus progestogen)	Placebo	Hypertension (diagnosis)	Worse with intervention
Swica et al. (2018)	73	RCT	27,347	–	Postmenopausal women with history of hysterectomy who did not have hypertension at baseline	HRT (conjugated equine oestrogens)	Placebo	Hypertension (diagnosis)	Worse with intervention

Ki et al. (2016)	74	Cohort	2,232	–	Postmenopausal women	HRT	No HRT	Low-density lipoprotein	Improved with intervention
Mikkola, Tomi S; et al. (2015)	67	Cohort	332 202	–	Postmenopausal women	HRT (stopped up to a year ago)	HRT (current use)	Mortality, cardiac	Worse with intervention
Chen et al. (2017)	75	Cohort	13,715	–	Postmenopausal women	HRT (started 3 or more years ago)	No HRT	Mortality, cardiovascular	Improved with intervention
Chen et al. (2017)	75	Cohort	13,715	–	Postmenopausal women	HRT (started after hysterectomy or oophorectomy, in past 3 years)	No HRT	Mortality, cardiovascular	Improved with intervention
Chen et al. (2017)	75	Cohort	13,715	–	Postmenopausal women	HRT (started after hysterectomy or oophorectomy, more than 3 years ago)	No HRT	Mortality, cardiovascular	Improved with intervention
Holm et al. (2019)	76	Cohort	29,243	–	Women aged 50–64 years	HRT (after 5 years of follow-up)	No HRT	Mortality, cardiovascular	Improved with intervention
Mikkola et al. (2015)	67	Cohort	332 202	–	Postmenopausal women	HRT (stopped more than a year ago)	No HRT	Mortality, cardiovascular	Improved with intervention
Manson et al. (2017)	77	RCT	27,347	–	Postmenopausal women	HRT (conjugated equine oestrogen alone or with progestogen)	Placebo	Mortality, cardiovascular	No effect of intervention
Chen et al. (2017)	75	Cohort	13,715	–	Postmenopausal women	HRT (started in past 3 years)	No HRT	Mortality, cardiovascular	No effect of intervention
Chen et al. (2017)	75	Cohort	13,715	–	Postmenopausal women	HRT (started after natural menopause)	No HRT	Mortality, cardiovascular	No effect of intervention
Mikkola et al. (2015)	67	Cohort	332 202	–	Postmenopausal women	HRT (stopped up to a year ago)	No HRT	Mortality, cardiovascular	Worse with intervention
Ki et al. (2016)	74	Cohort	2,232	–	Postmenopausal women	HRT	No HRT	Non-high-density lipoprotein	Improved with intervention

Ki et al. (2016)	74	Cohort	2,232	–	Postmenopausal women	HRT	No HRT	Total cholesterol to high-density lipoprotein ratio	Improved with intervention
Ki et al. (2016)	74	Cohort	2,232	–	Postmenopausal women	HRT	No HRT	Triglycerides	Improved with intervention

Table 16 Long-term HRT breast cancer outcomes

Reference		Study type	Sample size	Number of studies	Duration (months)	Population	Intervention	Comparator	Outcome	Result
Marjoribanks et al. (2017)	68	SR-C	–	–	84	Postmenopausal women	HRT (oestrogen only)	Placebo	Cancer, breast	Improved with intervention
Formoso et al. (2016)	10	SR-C	5,500	4	–	Women with menopausal symptoms and no history of breast cancer	HRT (tibolone)	Placebo	Cancer, breast	No effect of intervention
Formoso et al. (2016)	10	SR-C	4,835	5	–	Women with menopausal symptoms	HRT (tibolone)	HRT (combined)	Cancer, breast	No effect of intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	67	Postmenopausal women	HRT (combined, continuous)	Placebo	Cancer, breast	Worse with intervention
Formoso et al. (2016)	10	SR-C	3,165	2	–	Women with menopausal symptoms and a history of breast cancer	HRT (tibolone)	Placebo	Cancer, breast	Worse with intervention
Gartlehner et al. (2017)	69	SR	40,058	18	–	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Cancer, breast (invasive)	Worse with intervention
Chlebowski et al. (2016)	87	RCT	27,344	–	–	Postmenopausal women	HRT (oestrogen only)	No HRT	Cancer, breast	Improved with intervention
Chlebowski et al. (2017)	87	RCT	1,616	–	86	Postmenopausal women with more than 80% African ancestry who have had hysterectomy	HRT	Placebo	Cancer, breast	Improved with intervention

Chlebowski et al. (2016)	87	RCT	27,344	–	–	Postmenopausal women	HRT (oestrogen plus progestogen)	No HRT	Cancer, breast	Worse with intervention
Liu et al. (2016)	81	Cohort	22,929	–	–	Postmenopausal women	HRT (4-year duration)	No HRT	Cancer, breast	Improved with intervention
Liu et al. (2016)	81	Cohort	22,929	–	–	Postmenopausal women	HRT (8-year duration)	No HRT	Cancer, breast	Improved with intervention
Suhrke and Zahl (2015)	85	Cohort	449,717	–	60	Postmenopausal women	HRT (oestrogen only, at least 1-year duration)	No HRT	Cancer, breast	No effect of intervention
Ettinger et al. (2019)	79	Cohort	455	–	–	Postmenopausal women	HRT (long-term use)	No HRT use	Cancer, breast	No effect of intervention
Jones et al. (2016)	86	Cohort	58,148	–	65	Postmenopausal women	HRT (oestrogen only)	No HRT	Cancer, breast	No effect of intervention
Suhrke and Zahl (2015)	85	Cohort	449,717	–	60	Postmenopausal women	HRT (oestrogen plus progestogen, at least 1-year duration)	No HRT	Cancer, breast	Worse with intervention
Suhrke and Zahl (2015)	85	Cohort	449,717	–	60	Postmenopausal women	HRT (tibolone, at least 1-year duration)	No HRT	Cancer, breast	Worse with intervention
Brusselaers et al. (2018)	78	Cohort	1,160,351	–	–	Postmenopausal women	HRT (oestrogen only, current use)	No HRT	Cancer, breast	Worse with intervention
Brusselaers et al. (2018)	78	Cohort	1,160,351	–	–	Postmenopausal women	HRT (oestrogen plus progestogen, current use)	No HRT	Cancer, breast	Worse with intervention
Ettinger et al. (2018)	79	Cohort	454	–	–	Postmenopausal women	HRT (long-term use)	No HRT use	Cancer, breast	Worse with intervention
Jones et al. (2016)	86	Cohort	58,148	–	65	Postmenopausal women	HRT (oestrogen plus progestogen, current use)	No HRT	Cancer, breast	Worse with intervention
Holm et al. (2018)	80	Cohort	29,152	–	–	Postmenopausal women	HRT	No HRT	Cancer, breast	Worse with intervention
Siegelmann-Danieli et al. (2018)	83	Cohort	40,678	–	–	Perimenopausal women	HRT (progestogen, intrauterine)	Control	Cancer, breast (invasive)	Worse with intervention

Obi et al. (2016)	82	Cohort	3,321	–	–	Postmenopausal women diagnosed with breast cancer	HRT (current use at breast cancer diagnosis)	No current HRT use at time of breast cancer diagnosis	Cancer, breast (mortality)	Improved with intervention
Obi et al. (2016)	82	Cohort	3,321	–	–	Postmenopausal women diagnosed with breast cancer (low grade)	HRT (current use at breast cancer diagnosis)	No current HRT use at time of breast cancer diagnosis	Cancer, breast (mortality)	Improved with intervention
Holm et al. (2019)	76	Cohort	29,243	–	–	Women aged 50–64 years	HRT (after 15 years of follow-up)	No HRT	Cancer, breast (mortality)	Worse with intervention
Obi et al. (2016)	82	Cohort	3,321	–	–	Postmenopausal women diagnosed with breast cancer	HRT (current use at breast cancer diagnosis)	No current HRT use at time of breast cancer diagnosis	Cancer, breast (recurrence)	Improved with intervention
Simin et al. (2017)	84	Cohort	290,186	–	–	Women aged 40 years or older	HRT	No HRT	Cancer, breast, endometrial or ovarian	Worse with intervention

Table 17 Long-term HRT other cancer outcomes

Reference	Text reference	Study type	Sample size	Number of studies	Duration (months)	Population	Intervention	Comparator	Outcome	Result
Blanks et al. (2015)	88	Cohort	899,166	–	–	Postmenopausal women	HRT (ever use)	No HRT	Cancer, adenoma (detected by bowel cancer screen)	Improved with intervention
Edey et al. (2018)	102	SR-C	1,236	1	36	Women who previously had endometrial cancer	HRT	Placebo	Cancer, any	No effect of intervention
Holm et al. (2018)	80	Cohort	29,152	–	–	Postmenopausal women	HRT	No HRT	Cancer, any	Worse with intervention
Simin et al. (2017)	84	Cohort	290,186	–	–	Women aged 40 years or older	HRT	No HRT	Cancer, any	Worse with intervention

Simin et al. (2017)	84	Cohort	290,186	–	–	Women aged 40 years or older	HRT (oestrogen only)	No HRT	Cancer, any	Worse with intervention
Simin et al. (2017)	84	Cohort	290,186	–	–	Women aged 40 years or older	HRT (oestrogen plus progestogen)	No HRT	Cancer, any	Worse with intervention
Simin et al. (2017)	84	Cohort	290,186	–	–	Women aged 70 years or older	HRT (oestrogen plus progestogen)	No HRT	Cancer, any	Worse with intervention
Manson et al. (2017)	77	RCT	27,347	–	67–86	Postmenopausal women	HRT (conjugated equine oestrogen alone or with progestogen)	Placebo	Cancer, any (mortality)	Worse with intervention
Morch et al. (2016)	96	Cohort	1,006,219	–	–	Menopausal women	HRT (oestrogen only)	No HRT	Cancer, colon	Improved with intervention
Morch et al. (2016)	96	Cohort	1,006,219	–	–	Menopausal women	HRT (oestrogen plus progestogen)	No HRT	Cancer, colon	Improved with intervention
Simin et al. (2017)	84	Cohort	290,186	–	–	Women aged 40 years or older	HRT	No HRT	Cancer, colon	Improved with intervention
Gartlehner et al. (2017)	69	SR	40,058	18	–	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Cancer, colorectal	Improved with intervention
Blanks et al. (2015)	88	Cohort	899,166	–	–	Postmenopausal women	HRT (ever use)	No HRT	Cancer, colorectal	Improved with intervention
Botteri, Edoardo; et al. (2017b)	90	Cohort	466,822	–	–	Postmenopausal women	HRT (current use)	HRT (past use)	Cancer, colorectal	Improved with intervention
Holm et al. (2018)	80	Cohort	29,152	–	–	Postmenopausal women	HRT	No HRT	Cancer, colorectal	Improved with intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	–	Postmenopausal women	HRT	Placebo	Cancer, colorectal	No effect of intervention
Botteri et al. (2017b)	90	Cohort	466,822	–	–	Postmenopausal women	HRT (oestrogen only, current use)	No HRT	Cancer, colorectal	No effect of intervention

Botteri et al. (2017b)	90	Cohort	466,822	–	–	Postmenopausal women	HRT (oestrogen plus progestogen, current use)	No HRT	Cancer, colorectal	No effect of intervention
Botteri, Edoardo; et al. (2017b)	90	Cohort	466,822	–	–	Postmenopausal women	HRT (current use)	HRT (past use)	Cancer, colorectal (metastatic)	Improved with intervention
Holm et al. (2019)	76	Cohort	29,243	–	–	Women aged 50–64 years	HRT (after 15 years of follow-up)	No HRT	Cancer, colorectal (mortality)	Improved with intervention
Chlebowski et al. (2016)	102	RCT	16,608	–	67	Postmenopausal women	HRT (conjugated equine oestrogen plus progestogen)	Placebo	Cancer, endometrial	Improved with intervention
Formoso et al. (2016)	10	SR-C	8,504	9	–	Women with menopausal symptoms	HRT (tibolone)	Placebo	Cancer, endometrial	No effect of intervention
Formoso et al. (2016)	10	SR-C	3,689	5	–	Women with menopausal symptoms	HRT (tibolone)	HRT (combined)	Cancer, endometrial	No effect of intervention
Holm et al. (2018)	80	Cohort	29,152	–	–	Postmenopausal women	HRT	No HRT	Cancer, endometrial	Worse with intervention
Lokkegaard and Morch (2018)	98	Cohort	900,000	–	–	Postmenopausal women	HRT (tibolone)	No HRT	Cancer, endometrial	Worse with intervention
Chlebowski et al. (2016)	102	RCT	16,608	–	67	Postmenopausal women	HRT (conjugated equine oestrogen plus progestogen)	Placebo	Cancer, endometrial (mortality)	No effect of intervention
Kilander et al. (2019)	97	Cohort	1,160,351	–	–	Postmenopausal women	HRT	No HRT use	Cancer, extra-hepatic bile duct	No effect of intervention
Kilander et al. (2019)	97	Cohort	1,160,351	–	–	Postmenopausal women	HRT	No HRT use	Cancer, gallbladder	Improved with intervention
Kilander et al. (2019)	97	Cohort	1,160,351	–	–	Postmenopausal women	HRT	No HRT use	Cancer, gallbladder	No effect of intervention
Brusselaers et al. (2017)	94	Cohort	1,160,352	–	–	Postmenopausal women	HRT (ever use)	No HRT	Cancer, gastric adenocarcinoma	Improved with intervention
Simin et al. (2017)	84	Cohort	290,186	–	–	Women aged 40 years or older	HRT	No HRT	Cancer, gastrointestinal cancer	Improved with intervention

Simin et al. (2017)	84	Cohort	290,186	–	–	Women aged 40 years or older	HRT	No HRT	Cancer, liver	Improved with intervention
Chlebowski et al. (2016)	99	RCT	16,608	–	168	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Cancer, lung	No effect of intervention
Chlebowski et al. (2016)	99	RCT	16,608	–	168	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Cancer, lung (mortality)	No effect of intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	12–48	Postmenopausal women	HRT (combined, continuous)	Placebo	Cancer, lung (mortality)	Worse with intervention
Botteri et al. (2017a)	89	Cohort	684,969	–	57	Postmenopausal women	HRT (oestrogen plus progestogen)	no HRT	Cancer, melanoma	No effect of intervention
Botteri et al. (2017a)	89	Cohort	684,969	–	57	Postmenopausal women	HRT (oestrogen only)	No HRT	Cancer, melanoma	Worse with intervention
Botteri et al. (2017a)	89	Cohort	684,969	–	57	Postmenopausal women	HRT (oestrogen only, oral)	No HRT	Cancer, melanoma	Worse with intervention
Botteri et al. (2017a)	89	Cohort	684,969	–	57	Postmenopausal women	HRT (oestrogen only, intravaginal)	No HRT	Cancer, melanoma	Worse with intervention
Cervenka et al. (2019)	95	Cohort	98,995	–	–	Postmenopausal women	HRT (ever use)	No HRT use	Cancer, melanoma	Worse with intervention
Cervenka et al. (2019)	95	Cohort	98,995	–	–	Postmenopausal women	HRT (past use)	No HRT use	Cancer, melanoma	Worse with intervention
Cervenka I.; et al. (2019)	95	Cohort	98,995	–	–	Postmenopausal women	HRT (starting within 6 months of menopause)	HRT (starting 2 or more years after menopause)	Cancer, melanoma	Worse with intervention
Kato et al. (2016)	101	RCT	16,654	–	67	Postmenopausal women	HRT (conjugated equine oestrogen)	Placebo	Cancer, non-Hodgkin's lymphoma	No effect of intervention
Kato et al. (2016)	101	RCT	16,654	–	67	Postmenopausal women	HRT (conjugated equine oestrogen alone or with progestogen)	Placebo	Cancer, non-Hodgkin's lymphoma	No effect of intervention

Kato et al. (2016)	101	RCT	16,654	–	67	Postmenopausal women	HRT (conjugated equine oestrogen plus progestogen)	Placebo	Cancer, non-Hodgkin's lymphoma	No effect of intervention
Brusselaers et al. (2017)	94	Cohort	1,160,351	–	–	Postmenopausal women	HRT (ever use)	No HRT	Cancer, oesophageal	Improved with intervention
Simin et al. (2017)	84	Cohort	290,186	–	–	Women aged 40 years or older	HRT	No HRT	Cancer, oesophageal	Improved with intervention
Brusselaers et al. (2017)	94	Cohort	1,160,354	–	–	Postmenopausal women younger than 60 years	HRT (ever use)	No HRT	Cancer, oesophageal (adenocarcinoma)	Improved with intervention
Brusselaers et al. (2017)	94	Cohort	1,160,353	–	–	Postmenopausal women	HRT (ever use)	No HRT	Cancer, oesophageal (squamous cell)	Improved with intervention
Collaborative Group On Epidemiological Studies Of Ovarian Cancer et al. (2015)	96	Cohort	12,110	–	–	Postmenopausal women	HRT (current use but less than 5-year duration)	No HRT	Cancer, ovarian	Worse with intervention
Holm et al. (2018)	80	Cohort	29,152	–	–	Postmenopausal women	HRT	No HRT	Cancer, ovarian	Worse with intervention
Lokkegaard and Morch (2018)	98	Cohort	900,000	–	–	Postmenopausal women	HRT (tibolone)	No HRT	Cancer, ovarian	Worse with intervention
Lokkegaard and Morch (2018)	98	Cohort	900,000	–	–	Postmenopausal women	HRT (tibolone)	No HRT	Cancer, ovarian (serous)	Worse with intervention
Collaborative Group On Epidemiological Studies Of Ovarian Cancer et al. (2015)	96	Cohort	12,110	–	–	Postmenopausal women	HRT (current use but less than 5-year duration)	No HRT	Cancer, ovarian (endometrioid)	Worse with intervention
Collaborative Group On Epidemiological Studies Of Ovarian Cancer et al. (2015)	96	Cohort	12,110	–	–	Postmenopausal women	HRT (current use but less than 5-year duration)	No HRT	Cancer, ovarian (serous or endometrioid)	Worse with intervention
Collaborative Group On Epidemiological Studies Of Ovarian Cancer et al. (2015)	96	Cohort	12,110	–	–	Postmenopausal women	HRT (current use but less than 5-year duration)	No HRT	Cancer, ovarian (serous)	Worse with intervention

Eeles et al. (2015)	100	RCT	150	–	60	Women with epithelial ovarian cancer	HRT	No HRT	Cancer, ovarian, (recurrence-free survival)	Improved with intervention
Eeles et al. (2015)	100	RCT	150	–	60	Women with epithelial ovarian cancer	HRT	No HRT	Cancer, ovarian, (survival)	Improved with intervention
Sadr-Azodi et al. (2017)	89	Cohort	1,160,351	–	–	Postmenopausal women	HRT (ever use)	No HRT	Cancer, pancreatic	Improved with intervention
Sadr-Azodi et al. (2017)	89	Cohort	1,160,351	–	–	Postmenopausal women	HRT (1–2 year duration)	No HRT	Cancer, pancreatic	Improved with intervention
Sadr-Azodi et al. (2017)	89	Cohort	1,160,351	–	–	Postmenopausal women	HRT (more than 3-year duration)	No HRT	Cancer, pancreatic	Improved with intervention
Morch et al. (2016)	88	Cohort	1,006,219	–	–	Menopausal women	HRT (oestrogen only)	No HRT	Cancer, rectal	Improved with intervention
Morch et al. (2016)	88	Cohort	1,006,219	–	–	Menopausal women	HRT (oestrogen plus progestogen)	No HRT	Cancer, rectal	Improved with intervention
Zamora-Ros et al. (2015)	90	Cohort	345,157	–	–	Postmenopausal women who had natural menopause (not surgical)	HRT (use at baseline)	No HRT use at baseline	Cancer, thyroid	No effect of intervention
Zamora-Ros et al. (2015)	90	Cohort	345,157	–	–	Postmenopausal women	HRT (use at baseline)	No HRT use at baseline	Cancer, thyroid	Worse with intervention

Table 18 Osteoporosis

Reference	Text reference	Study type	Sample size	Number of studies	Population	Intervention	Comparator	Outcome	Result
Kuh et al. (2016)	104	Cohort	848	–	Postmenopausal women	HRT	No HRT	Bone mineral density	Improved with intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (combined, continuous)	Placebo	Fracture	Improved with intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (oestrogen only)	Placebo	Fracture	Improved with intervention

Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen only)	Placebo	Fracture	Improved with intervention
Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Fracture	Improved with intervention
Watts et al. (2017)	106	RCT	15,187	–	Women with hysterectomy	HRT (conjugated equine oestrogen)	Placebo	Fracture	Improved with intervention
Watts et al. (2017)	106	RCT	15,187	–	Women with menopausal symptoms	HRT (oestrogen plus progestogen)	Placebo	Fracture	No effect of intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (oestrogen only)	Placebo	Fracture (clinical)	Improved with intervention
Saarelainen et al. (2016)	105	Cohort	5,119	–	Postmenopausal women	HRT (10 year duration)	No HRT	Fracture, wrist	Improved with intervention
Saarelainen et al. (2016)	105	Cohort	5,119	–	Postmenopausal women	HRT (15 year duration)	No HRT	Fracture, wrist	Improved with intervention

Table 19 Dementia

Reference	Text reference	Study type	Sample size	Number of studies	Population	Intervention	Comparator	Outcome	Result
Imtiaz et al. (2017)	107	Cohort	8,195	–	Postmenopausal women	HRT (long-term use)	No HRT	Alzheimer's disease	Improved with intervention
Imtiaz et al. (2017)	107	Cohort	8,195	–	Postmenopausal women	HRT	No HRT	Alzheimer's disease	No effect of intervention
Espeland et al. (2017)	108	RCT	4,256	–	Women with menopausal symptoms aged 50–54 years	HRT (conjugated equine oestrogens, plus progestogen for women without hysterectomy)	Placebo	Cognitive function	No effect of intervention
Espeland et al. (2017)	108	RCT	4,256	–	Women with menopausal symptoms aged 65–79 years	HRT (conjugated equine oestrogens, plus progestogen for women without hysterectomy)	Placebo	Cognitive function	Worse with intervention

Gleason et al. (2015)	20	RCT	693	–	Postmenopausal women	HRT (conjugated equine oestrogen, oral, plus progestogen)	Placebo	Cognitive outcomes	No effect of intervention
Gleason et al. (2015)	20	RCT	693	–	Postmenopausal women	HRT (oestrogen, transdermal)	Placebo	Cognitive outcomes	No effect of intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (combined, continuous)	Placebo	Dementia	Worse with intervention
Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Dementia (probable)	Worse with intervention
Espeland et al. (2017)	108	RCT	4,256	–	Women with menopausal symptoms aged 65–79 years	HRT (conjugated equine oestrogens, plus progestogen for women without hysterectomy)	Placebo	Executive function	Worse with intervention
Henderson et al. (2016)	110	RCT	567	–	Postmenopausal women	HRT (oestrogen, oral, plus progestogen in women without hysterectomy)	Placebo	Memory, verbal	No effect of intervention
Espeland et al. (2017)	108	RCT	4,256	–	Women with menopausal symptoms aged 65–79 years	HRT (conjugated equine oestrogens, plus progestogen for women without hysterectomy)	Placebo	Memory, working	Worse with intervention
Espeland et al. (2015)	109	RCT	1,402	–	Postmenopausal women without diabetes	HRT (conjugated equine oestrogen plus progestogen)	Placebo	Total brain volume	No effect of intervention
Espeland et al. (2015)	109	RCT	1,402	–	Postmenopausal women with diabetes	HRT (conjugated equine oestrogen plus progestogen)	Placebo	Total brain volume	Worse with intervention

Table 20 Mortality

Reference	Text reference	Study type	Sample size	Number of studies	Population	Intervention	Comparator	Outcome	Result
Chen et al. (2017)	75	Cohort	13,715	–	Postmenopausal women	HRT (started 3 or more years ago)	No HRT	Mortality	Improved with intervention
Chen et al. (2017)	75	Cohort	13,715	–	Postmenopausal women	HRT (started in past 3 years)	No HRT	Mortality	Improved with intervention
Chen et al. (2017)	75	Cohort	13,715	–	Postmenopausal women	HRT (started after hysterectomy or oophorectomy, in past 3 years)	No HRT	Mortality	Improved with intervention
Chen et al. (2017)	75	Cohort	13,715	–	Postmenopausal women	HRT (started after hysterectomy or oophorectomy, more than 3 years ago)	No HRT	Mortality	Improved with intervention
Paganini-Hill et al. (2018)	111	Cohort	8,801	–	Postmenopausal women	HRT	No HRT use	Mortality	Improved with intervention
Formoso et al. (2016)	10	SR-C	8,242	4	Women with menopausal symptoms	HRT (tibolone)	Placebo	Mortality	No effect of intervention
Manson et al. (2017)	77	RCT	27,347	–	Postmenopausal women	HRT (conjugated equine oestrogen alone or with progestogen)	Placebo	Mortality	No effect of intervention
Manson et al. (2017)	77	RCT	27,347	–	Postmenopausal women	HRT (conjugated equine oestrogen)	Placebo	Mortality	No effect of intervention
Manson et al. (2017)	77	RCT	27,347	–	Postmenopausal women	HRT (conjugated equine oestrogen plus progestogen)	Placebo	Mortality	No effect of intervention
Chen et al. (2017)	75	Cohort	13,715	–	Postmenopausal women	HRT (started after natural menopause)	No HRT	Mortality	No effect of intervention

Holm et al. (2019)	76	Cohort	29,243	–	Women aged 50–64 years	HRT	No HRT	Mortality	No effect of intervention
Obi et al. (2016)	82	Cohort	3,321	–	Postmenopausal women diagnosed with breast cancer	HRT (current use at breast cancer diagnosis)	No current HRT use at time of breast cancer diagnosis	Mortality (all cause)	Improved with intervention
Obi et al. (2016)	82	Cohort	3,321	–	Postmenopausal women diagnosed with breast cancer	HRT (current use at breast cancer diagnosis)	No current HRT use at time of breast cancer diagnosis	Mortality (not breast cancer related)	Improved with intervention

Table 21 Other long-term risks associated with HRT

Reference	Text reference	Study type	Sample size	Number of studies	Population	Intervention	Comparator	Outcome	Result
Kattah et al. (2018)	119	SR	–	12	Postmenopausal women	HRT	No HRT	Albuminuria	Improved with intervention
Kattah et al. (2018)	119	Cohort	2,217	–	Postmenopausal women	HRT	No HRT	Albuminuria	Improved with intervention
Gleason et al. (2015)	20	RCT	693	–	Postmenopausal women	HRT (conjugated equine oestrogen, oral, plus progestogen)	Placebo	Anxiety	Improved with intervention
Al-Rousan et al. (2018)	117	Cohort	16,053	–	Postmenopausal women with hysterectomy	HRT (conjugated equine oestrogen)	Placebo	Carpal tunnel syndrome	Improved with intervention
Al-Rousan et al. (2018)	117	Cohort	16,053	–	Postmenopausal women without hysterectomy	HRT (conjugated equine oestrogen plus progestogen)	Placebo	Carpal tunnel syndrome	Improved with intervention
Staller et al. (2017)	116	Cohort	55,828	–	Postmenopausal women	HRT (past use)	No HRT	Faecal incontinence	Worse with intervention
Staller et al. (2017)	116	Cohort	55,828	–	Postmenopausal women	HRT (current use)	No HRT	Faecal incontinence	Worse with intervention
Sommer et al. (2015)	115	Cohort	610,604	–	Postmenopausal women (without hysterectomy or history of fibroids)	HRT	No HRT	Fibroids	Worse with intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (combined, continuous)	Placebo	Gallbladder disease	Worse with intervention
Marjoribanks et al. (2017)	68	SR-C	–	–	Postmenopausal women	HRT (oestrogen only)	Placebo	Gallbladder disease	Worse with intervention
Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen only)	Placebo	Gallbladder disease	Worse with intervention
Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Gallbladder disease	Worse with intervention
Kilander et al. (2019)	97	Cohort	1,160,351	–	Postmenopausal women	HRT	No HRT use	Gallstone disease	Worse with intervention

Crandall, Carolyn J; et al. (2017)	122	Cohort	45,112	–	Postmenopausal women	HRT (conjugated equine oestrogen, less than 0.625 mg/day, plus progestogen)	HRT (conjugated equine oestrogen, 0.625 mg/day, plus progestogen)	Global index event (coronary heart disease, breast cancer, stroke, pulmonary embolism, hip fracture, colorectal cancer, endometrial cancer, or death)	Improved with intervention
Crandall, Carolyn J; et al. (2017)	122	Cohort	45,112	–	Postmenopausal women	HRT (conjugated equine oestrogen, 0.625 mg/day, plus progestogen for at least 5 years)	HRT (conjugated equine oestrogen, 0.625 mg/day, plus progestogen for less than 5 years)	Global index event (coronary heart disease, breast cancer, stroke, pulmonary embolism, hip fracture, colorectal cancer, endometrial cancer, or death)	Worse with intervention
Curhan et al. (2017)	114	Cohort	80,972	–	Postmenopausal women	HRT (5 to 10 year duration of oestrogen-only or oestrogen plus progestogen)	No HRT	Hearing loss	Worse with intervention
Curhan et al. (2018)	114	Cohort	80,973	–	Postmenopausal women	HRT (more than 10 year duration of oestrogen-only or oestrogen plus progestogen)	No HRT	Hearing loss	Worse with intervention
Vajaranant et al. (2016)	121	RCT	1,668	–	Postmenopausal women	HRT (conjugated equine oestrogen in women with hysterectomy)	Placebo	Intraocular pressure	Improved with intervention
Vajaranant et al. (2016)	121	RCT	2,679	–	Postmenopausal women	HRT (oestrogen plus progestogen in women without hysterectomy)	Placebo	Intraocular pressure	No effect of intervention
Chlebowski et al. (2018)	113	RCT	10,739	–	Postmenopausal women with hysterectomy	HRT (conjugated equine oestrogens)	Placebo	Joint pain (frequency)	Improved with intervention
Chlebowski et al. (2018)	113	RCT	10,739	–	Postmenopausal women with hysterectomy	HRT (conjugated equine oestrogens)	Placebo	Joint swelling (frequency)	Worse with intervention

Triebner et al. (2019)	120	Cohort	658	–	Postmenopausal women	HRT (6–10 years of use)	No HRT	Lung function (FEV1)	Improved with intervention
Triebner et al. (2019)	120	Cohort	658	–	Postmenopausal women	HRT (more than 10 years of use)	No HRT	Lung function (FEV1)	Improved with intervention
Bengtsson et al. (2017)	112	Cohort	237,130	–	Postmenopausal women	HRT (use for 8 years or more)	No HRT or less than 8 years of HRT	Rheumatoid arthritis (seropositive)	Worse with intervention
Chen et al. (2019)	118	Cohort	13,112	–	Postmenopausal women	HRT	No HRT use	Sudden sensorineural hearing loss	No effect of intervention
Chen et al. (2018)	118	Cohort	55,680	–	Postmenopausal women	HRT	No HRT	Tinnitus	Improved with intervention
Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen only)	Placebo	Urinary incontinence	Worse with intervention
Gartlehner et al. (2017)	69	SR	40,058	18	Postmenopausal women	HRT (oestrogen plus progestogen)	Placebo	Urinary incontinence	Worse with intervention

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