

National Institute for Health and Clinical Excellence

Urinary incontinence in women – 1st draft consultation table

5 May – 29 June 2006

Organisation	Version	Section/page	Line no.	Comments	Response
3M Health Care Limited				This organisation was approached but did not respond.	-
Addenbrookes NHS Trust				This organisation was approached but did not respond.	-
Airedale General Hospital - Acute Trust				This organisation was approached but did not respond.	-
Albyn Medical Ltd				This organisation was approached but did not respond.	-
Allergan Limited	Full Version	284	8-10	<p>There are currently 2 preparations of Botulinum Toxin A available in the UK. BOTOX® [Allergan Ltd] and Dysport [Ipsen Ltd]. These have different formulations, molecular structures and manufacturing processes. Most importantly doses are product specific and are lower in Idiopathic detrusor overactivity than in over activity of neurogenic origin. Safety and efficacy also may not be the same for both products.</p> <p>Since all the evidence for Botulinum Toxin A use within the guideline refers solely to BOTOX® [Allergan Ltd] it is our opinion that this should be brought to the attention of the clinician in order to reduce the risk associated with the dosing of different products. We would draw the attention of NICE and clinicians involved in the treatment of female urinary incontinence to the respective SPCs of both products available. In particular we would draw attention to 'Instructions for use / handling in the BOTOX® SPC, where it clearly states that;</p> <p>'The 'unit' by which the potency of preparations of Botox® is measured should be used to calculate dosages of BOTOX® only and is not transferable to other preparations of Botulinum Toxin A'</p>	Thank you for your comments. We have added statements in the text to clarify to which product the evidence in the guideline refers.
Allergan Limited	NICE version	14	1.3.1.4.	As this guideline is likely to be used for several years and the license status of Botulinum Toxin will change to a licensed product. Allergan Ltd would welcome a change to the wording to	The current licensing position for Botulinum toxin A is noted in the document.

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	sion			'Whilst it is unlicensed, Botulinum Toxin A should only be used in women with idiopathic detrusor overactivity in the research environment or when women have not responded to conservative treatments such as lifestyle modifications, behavioural techniques and drug therapy..	
Amdipharm PLC				This organisation was approached but did not respond.	-
American Medical Systems UK		General		Throughout the document, "primary surgery for stress urinary incontinence" is referred to, however we could find no explanation as to it's meaning. In our opinion, synthetic mid-urethral tapes (bottom up, top down, transobturator inside out) are all ideal candidates for the primary surgical procedures for sui.	Thank you for your comments. Definitions for primary and secondary surgery for stress UI added to glossary.
American Medical Systems UK		97	12-14	How much research is really required to prove the efficacy of a procedure, surely lower complication rates & quicker return to normal life are immediate results and do not impact on the longer term.	While there is a high volume of research, most data relate to case series from which neither safe conclusions about efficacy nor comparative complication rates can be drawn.
American Medical Systems UK		381	5-9	The number of deaths associated with bottom up approach exceeds those with the transobturator outside in and top down retropubic approach. To date we have completed over 125,000 top down retropubic procedures and 160,000 outside in transobturator procedures with no major complications.	Noted.
American Medical Systems UK		381	11-14	All the clinical data for Monarc illustrate that peri/immediate complications are significantly lower than with bottom up retropubic approaches (de novo urge, voiding dysfunction, bladder perforations etc). How is it possible to suggest that these safe and effective procedures should be performed under special arrangements only? The clinical community worldwide is adopting the transobturator approach due to it's higher safety profile.	The guideline highlights the likely difference in perforation rates between bottom-up retropubic approaches and transobturator approaches. However, it should be noted that high quality data confirming this fact are limited.
American Medical Systems UK		General		We noticed that 2 key SPARC (top down retropubic approach) papers that were submitted to you for evidence last year, have not been considered. I have reattached them for consideration: <i>Dietz</i> shows similar subjective and objective cure rates between SPARC and TVT along with less post-op voiding difficulties with SPARC. <i>Deval</i> shows high objective cure rates with SPARC and subjective cure rates in line with published TVT rates.	Both were considered. The Dietz paper was excluded because higher evidence level (RCTs) were available for this comparison. Additionally, the TVT cases were also included in a longitudinal case series evaluating TVT outcomes. The Deval paper was included in the first draft.

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American Medical Systems UK		General		<p>Recently we have 3 more papers published and they are attached for further consideration in support of the use of our products in comparison to TVT.</p> <p><i>Morey</i> shows similar efficacy between Monarc and TVT, with Monarc demonstrating significantly fewer voiding difficulties, low de novo urgency and no urethrolisis in comparison to higher results with TVT.</p> <p><i>Hodroff</i> and the authors note some theoretical advantages of SPARC over TVT. Overall success and patient satisfaction were very similar to results obtained with TVT.</p> <p><i>Debodinance</i> showed that the outside in vs inside out TO approaches to be equally safe and both avoid per operative complications often seen with TVT.</p>	<p>The Morey paper was considered and excluded because we undertook our own similar analysis for retropubic vs. transobturator slings.</p> <p>The Hodroff paper was included in the first draft.</p> <p>The Debodinance paper has been reviewed and is included in the guideline.</p>
American Medical Systems UK		General		<p>The American College of Obstetricians and Gynecologists published in June 2005 a practice bulletin regarding the diagnosis and treatment of urinary incontinence. There are many interesting points raised in this guidance and it covers many of the aspects that you are also covering. With particular reference to AMS, it is interesting to note that on page 1541, the top left hand paragraph, it quotes a study (Ref 69) that says “the intermediate and long-term results for suburethral slings suggest that the 10-year continence rate is similar to the 1-year continence rate. In fact, it appears that sling procedures that are effective after 6 months are likely to remain effective for many years”. This is a very valid comment when considering the rapid introduction, early success and clinical efficacy of the transobturator approaches (outside – in) and is supported by the many UK surgeons who are adopting this approach. Bearing in mind the shorter follow-up data available, it is interesting to note that the authors support what many surgeons themselves are experiencing. I have attached this bulletin as support.</p>	<p>Noted - we cannot agree that conclusions about longevity in this report can be extrapolated to all procedures.</p>
Anglesey Local Health Board				<p>This organisation was approached but did not respond.</p>	-
Association for Continence Advice	Full	61	5	<p>The ACA is pleased that OAB syndrome rather than just urge incontinence is included in the guidance.</p>	<p>Thank you for your comments.</p>
Association for Continence Advice	Full	71	6-9	<p>We are unsure of the rationale of only including studies where the majority of population were women.</p>	<p>The guideline scope covered only women.</p>

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Association for Continence Advice	Full	77-78	21-3	Slow release oxybutynin has been shown to have a reduced side effect profile compared to standard therapy, so why not use that as 1 st line.	<p>Thank you for your comments. The GDG has reconsidered the evidence in this area, along with comments from several stakeholders.</p> <p>We note in the evidence statements for antimuscarinic drugs that oxybutynin IR has a poor tolerability profile compared to other antimuscarinic drugs. However an improved tolerability profile does not necessarily translate into improved persistence with therapy. A long term study of oxybutynin ER (Diokno et al 2002) found that discontinuation attributable to adverse effects was 24%, which is similar to that reported for oxybutynin IR.</p> <p>There is evidence from practice that persistence with antimuscarinic therapy is low (Shaya et al 2005).</p> <p>The difference in drug costs is not trivial with non-proprietary oxybutynin being around 10 times cheaper than other antimuscarinic options.</p> <p>The recommendation on antimuscarinic drugs has been revised to include advice on slow release and transdermal formulations of oxybutynin.</p>
Association for Continence Advice	Full	78	all	Should botox therapy be included in this algorithm as well.	Botulinum toxin A is included in the algorithm.
Association for Continence Advice	Full	79	11-14	It is known that many women who think they are performing pelvic floor exercises correctly are found not to be when examined vaginally. Not to suggest this for the 1 st 3 months may lead to a considerable delay in effective treatment and may make the woman lose faith in the treatment. We would recommend strongly that all women (subject to individual differences) should have vaginal assessment by a competent practitioner before	We have considered your comments and reflected on the limited evidence as to whether pelvic floor muscle assessment prior to PFMT improves outcome. Whilst there is not unanimity on this point, it is clearly widespread expert opinion that the determination of

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				commencing pelvic floor exercises.	whether a woman can contract her pelvic floor muscles voluntarily may influence the type of treatment. Hence, the GDG has reconsidered its earlier recommendation, and will advise that pelvic floor muscle assessment should be undertaken before embarking on supervised pelvic floor muscle training for the treatment of UI.
Association for Continence Advice	Full	86	1-3	Although oestrogen is unlikely to cure UI when used in conjunction with PFE or bladder training it can improve symptoms.	Noted. Recommendation regarding intravaginal oestrogen revised.
Association for Continence Advice	Full	254	1-12	A functional inability to reach the toilet should also be a valid reason for catheterisation if all other methods eg female urinals, referral to OT/Physio have failed.	We considered the main indications for catheterisation.
Association for Improvements in Maternity Services (AIMS)				This organisation was approached but did not respond.	-
Association of British Health-Care Industries				This organisation was approached but did not respond.	-
Association of British Neurologists	Full version	61	16	It is regrettable that the decision was taken not to include incontinence caused by neurological disease. Most of the non-surgical measures covered in this document are applicable to neurological patients and they are a group particularly troubled by urinary incontinence. Is there some plan to cover their needs in the future?	Thank you for your comments. We advise you to put forward the suggested topic to NICE via their website.
Association of British Neurologists	Full version	78 89 277	8 4 12	The recommendation that sacral nerve stimulation be used to treat UI due to detrusor overactivity in women who have not responded to conservative treatments is un-realistic. SNS, although not a new technique is very poorly established in the UK and implanting large numbers of stimulators – which would be the result of this recommendation - could not be undertaken without the development of considerable infrastructures to support such an implanting service: estimates of between 30-50% surgical revision rates have been published from centres in Europe and the USA (see p276 line 6). The earlier NICE guidance approved their use for UI (see p271 line 11) rather than recommended widespread	The cost-effectiveness of SNS was not addressed in the draft guideline because it was considered to be a low volume treatment, where the alternatives were also expensive. A cost-consequence analysis of SNS is now included as an additional appendix.

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				usage. Furthermore detrusor botulinum toxin is likely, in the next 3 years, to emerge as the preferred treatment of refractory IDO.	
Association of British Neurologists	Full version	89 286	21 12	I strongly agree with this positive statement about the use of botulinum toxin and suggest that it is specifically added that women be informed about the likelihood of the need to self catheterise following treatment.	Agree. Statement added to recommendations.
Association of British Neurologists	Full version	104	19	I endorse the statements – “No evidence was identified that addressed diagnostic accuracy of neurophysiological testing in relation to non- neurogenic UI. Where history suggests evidence of neurological disease, examination of lower limbs together with sacral sensation and sacral reflexes is required.”	Noted.
Association of British Neurologists		283	21	A PCT from the UK of the use of BoNT-A to treat IDO (including 19 women) has been published in abstract (see attachment) and it is likely that the full paper will be accepted before the final version of this NICE draft is approved.	This study is potentially relevant but unfortunately the full paper was not available in time for the deadline for submitting the final draft guideline to NICE.
Association of British Neurologists		287	4	There is no pharmaceutical source of vanilloids currently available for clinical use.	Noted.
Association of British Neurologists	Full version	General		This is a very thorough and carefully considered review. The GDG are to be congratulated.	Thank you.
Association of the British Pharmaceutical Industry,(ABPI)				This organisation was approached but did not respond.	-
Astellas Pharma Ltd	NICE	Algorithm	OAB ± Urge UI	When adding antimuscarinic drug if partial benefit from bladder training, urgency should also be considered bothersome (as well as frequency), particularly as it is the defining symptom of OAB.	Thank you for your comments. This recommendation has been modified.
Astellas Pharma Ltd	NICE	11	1.2.3.2	As above.	As above.
Astellas Pharma Ltd	Full	85	4	As above.	As above.
Astellas Pharma Ltd	Full	234	1-3	Volume voided results should also be included: <i>Increase in volume voided/micturition:</i> 19.9ml (20%), 38.0ml (28%), 43.2ml (35%), 64.7ml (45%), 14.7ml (14%), 9.7ml (14%) for solifenacin 2.5mg, 5mg, 10mg, 20mg, tolterodine 2mg bd, and	Added. Changes in voided volume are reported in evidence tables but are no longer summarised in the text because the

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				placebo respectively (p<0.005 for solifenacin 5mg, 10mg, 20mg vs placebo).	GDG considers them to be of limited clinical value.
Astellas Pharma Ltd	Full	234	14-16	Between-group differences <u>were</u> reported for urgency, incontinence and volume voided: <i>Reduction in urgency episodes/24hrs: -2.84 (51.4%), -2.90 (52.0%), 1.98 (33.0%) for solifenacin 5mg, 10mg and placebo respectively (p<0.003 for both solifenacin doses vs placebo). Reduction in incontinence episodes/24hrs: -1.63 (60.7%), -1.57 (51.9%), -1.25 (27.9%) for solifenacin 5mg, 10mg and placebo respectively. (p<0.016 for both solifenacin doses vs placebo when baseline included as covariate). Increase in volume voided/micturition: 30.75ml (25.4%), 35.99ml (29.7%), 10.67ml (11.0%) for solifenacin 5mg, 10mg and placebo respectively (p=0.001 for both solifenacin doses vs placebo).</i>	Amended.
Astellas Pharma Ltd	Full	234	20	Statistical comparisons <u>were</u> reported for leakage episodes: <i>Reduction in incontinence episodes/24hrs: -1.42 (59%), -4.45 (47%), -1.14 (59%), -0.76 (29%) for solifenacin 5mg, 10mg, tolterodine 2mg bd and placebo respectively (p<0.008 for both doses of solifenacin vs placebo). Reduction in urge incontinence episodes/24hrs: -1.41 (65%), -1.36 (63%), -0.91 (58%), -0.62 (40%) for solifenacin 5mg, 10mg, tolterodine 2mg bd and placebo respectively (p<0.0028 for both solifenacin doses vs placebo).</i>	Amended.
Astellas Pharma Ltd	Full	235	1	The figures for leakage episodes quoted are for <u>urge</u> incontinence. Overall incontinence episodes are given in the paper as 47 to 61% vs. 59% vs. 28 to 29% .	Amended.
Astellas Pharma Ltd	Full	235	7	1633 out of <u>1802</u> patients who completed the double-blind studies (91%) entered the open-label study and took solifenacin for up to one year. Not 86% as quoted.	Amended.
Astellas Pharma Ltd	Full	245	13-15	The primary outcome of this study was <u>to test for non-inferiority</u> in terms of reduction in micturition frequency (p=0.004). There was no significant difference in the secondary analysis on micturition frequency when tested for superiority. The statement beginning on line 13 is rather misleading and would be more correctly worded in the parenthesis as ... (the primary outcome for non-inferiority was proven) .	Noted. Sentence revised and comment added to evidence table.
Astellas Pharma Ltd	Full	245	19	Patient perception of bladder condition data <u>was</u> reported in the publication in figure 3; solifenacin group -1.51 vs tolterodine group -1.33 (p=0.006).	Amended.

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Astellas Pharma Ltd	Full	745	Ref 388 – patient characteristics	Urinary incontinence or urgency in the inclusion criteria were specified as ≥3 episodes during the 3 day diary period (not ≥1 per 24 hrs as quoted).	Amended.
Astellas Pharma Ltd	Full	746	Ref 388 – patient characteristics	28% of patients had mixed incontinence (not 72% as quoted).	Amended.
Astellas Pharma Ltd	Full	746	Ref 388 – outcome measures	Voided volume is per micturition .	Added.
Astellas Pharma Ltd	Full	746	Ref 388 – effect size	Volume voided figures for solifenacin 5mg (28%), 10mg (35%) and 20mg (45%) should have asterix as p<0.05 vs placebo.	Added.
Astellas Pharma Ltd	Full	746	Ref 389 – number of patients	911 patients were randomised (not 907 as quoted).	907 were randomised and treated as stated.
Astellas Pharma Ltd	Full	746	Ref 389 – patient characteristics	Urinary incontinence or urgency in the inclusion criteria were specified as ≥3 episodes during the 3 day diary period (not ≥1 per 24 hours as quoted).	Amended.
Astellas Pharma Ltd	Full	746	Ref 389 – effect size	Confidence intervals for 10mg solifenacin in frequency/24hrs were -1.7, -0.7 (not -2.8, -1.7 as quoted).	Amended.
Astellas Pharma Ltd	Full	747	Ref 389 – patient characteristics	34% of patients had prior drug therapy for OAB (not 32% as quoted).	Amended.
Astellas Pharma Ltd	Full	747	Ref 389 – patient characteristics	Exclusion criteria for stress incontinence was if stress was the <u>predominant factor</u> .	Added.
Astellas Pharma Ltd	Full	747	Ref 389 – outcome measure	Nocturia episodes are per 24 hrs .	Added.

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Astellas Pharma Ltd	Full	747	Ref 389 – outcome measures	Voided volume is per micturition .	Added.
Astellas Pharma Ltd	Full	747	Ref 389 – effect size	P values for volume voided <u>are</u> quoted in the publication: <i>Increase in volume voided/micturition</i> : 30.8ml (5mg, p=0.0001 vs placebo), 36.0ml (10mg, p=0.0001 vs placebo).	Amended.
Astellas Pharma Ltd	Full	747	Ref 389 – effect size	Statistical significance was reported for leakage episodes: <i>Reduction in incontinence episodes/24hrs</i> : -1.63 (60.7%), -1.57 (51.9%), -1.25 (27.9%) for solifenacin 5mg, 10mg and placebo respectively. (p<0.016 for both solifenacin doses vs placebo when baseline included as covariate). <i>Reduction in urge incontinence episodes/24hrs</i> : -1.30 (62.7%), -1.21 (57.1%), -0.91 (42.5%) for solifenacin 5mg, 10mg and placebo respectively (p<0.042 for both solifenacin doses vs placebo).	Amended.
Astellas Pharma Ltd	Full	747	Ref 390 – number of patients	1033 patients were analysed for efficacy (safety analyses were based on safety population, n=1077).	Noted.
Astellas Pharma Ltd	Full	747-748	Ref 390 – patient characteristics	Urinary incontinence or urgency in the inclusion criteria were specified as ≥3 episodes during the 3 day diary period (not ≥1 per 24 hours as quoted).	Amended.
Astellas Pharma Ltd	Full	748	Ref 390 – patient characteristics	59% of patients had incontinence (not 93% as quoted).	Data from Table 1 of the paper: 70 (7%) had 'no incontinence', 653 had urge UI only (63%), and 309 (30%) had mixed stress and urge UI.
Astellas Pharma Ltd	Full	748	Ref 390 – patient characteristics	47% of patients had urge incontinence (not 63% as quoted).	See above.
Astellas Pharma Ltd	Full	748	Ref 390 – patient characteristics	35% of patients had prior drug treatment for OAB (not 33% as quoted).	Amended.

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Astellas Pharma Ltd	Full	748	Ref 390 – patient characteristics	Exclusion criteria for stress incontinence was if stress was the <u>predominant</u> factor.	Amended.
Astellas Pharma Ltd	Full	748	Ref 390 – effect size	P<0.002 for both solifenacin doses vs placebo in urge incontinence, as reported in the publication.	Amended.
Astellas Pharma Ltd	Full	748	Ref 390 – effect size	P<0.008 for both solifenacin doses vs placebo in total incontinence, as reported in the publication.	Amended.
Astellas Pharma Ltd	Full	748	Ref 390 – outcome measures	Voided volume is per micturition .	Added.
Astellas Pharma Ltd	Full	767	Ref 428 – number of patients	87% of patients were female (not 85% as quoted).	Amended.
Astellas Pharma Ltd	Full	767	Ref 428 - intervention	Superiority efficacy analyses and safety analyses were presented in the publication based on the Full Analysis Set, n=578 for solifenacin patients (not 593 as quoted).	Added.
Astellas Pharma Ltd	Full	767	Ref 428 - comparison	Superiority efficacy analyses and safety analyses were presented in the publication based on the Full Analysis Set, n=599 for tolterodine patients (not 607 as quoted).	Added.
Astellas Pharma Ltd	Full	767	Ref 428 - comparison	Tolterodine comparison was: Tolterodine SR 4mg od for 4 weeks, could request increase in dose for weeks 5-12 (pseudo-increase given).	Noted in comments column.
Astellas Pharma Ltd	Full	767	Ref 428 – effect size	Difference in effect size of 0.21 as quoted for frequency/24hrs relates to the <u>non-inferiority primary analysis</u> . The figure for the secondary analysis of superiority for frequency were not presented in the publication.	Sentence changed.
Astellas Pharma Ltd	Full	767	Ref 428 – outcome measures	Perception of bladder condition is assessed by the <u>patient</u> . This outcome measure should therefore read " Patient perception of bladder condition."	'patient' added.
Astellas Pharma Ltd	Full	767	Ref 428 –	Patient perception of bladder condition data <u>was</u> reported in the publication in figure 3; solifenacin group -1.51 vs tolterodine group	Added.

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			outcome measures	- 1.33 (p=0.006).	
Astellas Pharma Ltd	Full	Evidence tables	Ref 392	This paper is not included in the evidence tables. The paper outlines quality of life improvements from ref 389, 390 and 391.	Relevant data presented in text.
Astra Tech Ltd				This organisation was approached but did not respond.	
Bard Limited	Draft	6	paragraph 2 , line2	Mid-urethral tapes are also made from porcine dermis (e.g Pelvilace) that are not macroporous.	Thank you for your comments. Text revised to exclude biological tapes from this grouping.
Bard Limited	Draft	6	paragraph 2 ,	Surgical injection of Urethral bulking agents are not mention for the treatment of Intrinsic Sphincter Deficiency.	The recommendation made for intramural bulking agents was not considered to be a key priority for implementation, and therefore is not repeated in the section to which you refer in this comment.
Bard Limited	Draft	9	1.1.9.1	Pad tests have been used effectively to measure UI Ref: Dmochowski R et al: Multicenter randomised controlled trial to evaluate Uryx (<i>Changed to Tegress 2005</i>) urethral bulking agent in treating female stress urinary incontinence: comparison of initial and expansion phases of trial: ICS 2004, abstract No 657.	The recommendation refers to their use in the assessment of women with UI. Refer to the full guideline for further information.
Bard Limited	Draft	15	1.3.2.2	Mid-urethral tapes are also made from porcine dermis (e.g Pelvilace) that are not macroporous.	Please refer to response above.
Bard Limited	Draft	15	1.3.2.2	Surgical injection of Urethral bulking agents are not mention for the treatment of Intrinsic Sphincter Deficiency.	The recommendation for intramural bulking agents appears below the recommendation you refer to here.
Bard Limited	Draft	15	1.3.2.3	The following references demonstrate the efficacy of Bard's Uretex retropubic tape for the treatment of SUI. Ref No1: Fendler et Al: Stress Urinary Incontinence Treatment using a specially designed sub-urethral support Uretex. Results at 1 year from a multicenter prospective study ICS 2004, abstract No 723. Ref No2 John B Gebhart: Uretex Urethral Support System for Treatment of Stress Urinary Incontinence :The American Urogynaecological Society & the Society of Gynaecological Surgeons, Abstract 2004	We have systematically searched for trials evaluating Uretex, Tegress, and Uryx on the standard databases as detailed in the method. We found no fully published clinical trial reports for any of these products therefore they were not considered further by the guideline development group. We do not systematically search the grey literature (see method section of the full guideline).

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				<p>Ref No 3: V. Scetbon: Uretex polypropylene urethral support for urodynamic stress incontinence: Issues in Women's Health Vol1 No1 pages 18-21</p> <p>Ref No 4. J-L Pariente: An independent Biomechanical evaluation of commercially available sub urethral slings. Issues in Women's Health Vol. 1 No1 pages 9-12</p> <p>Ref No 5 Giolitto: Stress Urinary Incontinence Treatment using a second generation polypropylene urethral support IUGA 2002.</p>	
Bard Limited	Draft	15	1.3.2.4	<p>Pelvicol (Porcine Dermis) is not macroporous and has been used effectively as a sling.</p> <p>Ref No 1. M. Abdel-Fattah: Pevicoltm Pubovaginal Sling versus Tension –Free vaginal Tape for Treatment of Urodynamics Stress Incontinence: A Prospective Randomized Three –Year Follow –Up Study: European Urology 46 (2004) 629-635</p> <p>Ref No 2 J.W. Barrington: Longitudinal Study of Pelvicol Pubovaginal slings using MRI : Journal of Obstetrics & Gynaecology (August 2004) Vol.24 No 5. 542-546</p> <p>Ref No 3. D. De Ridder. TVT-Erosion: One step partial excision & replacement by Pelvicoltm Implant International Urogynecology Journal & Pelvic Floor Dysfunction 2001 pages 16-17 (ISSN 0937-3462).</p>	<p>The Abdel-Fattah study is included in the guideline.</p> <p>Reference 2 considered the anatomical position of sling and not its effectiveness, therefore it is not eligible. It has not been possible to retrieve the third reference cited from the information given.</p>
Bard Limited	Draft	15	1.3.2.5	<p>Comments do not include Tegress (old trade name Uryx) made from ethylene vinyl alcohol (EVOH). Tegress is indicated for 1st line treatment of SUI caused by Intrinsic Sphincter Deficiency. Repeated injections are not always required and efficacy does not diminish with time.</p> <p>Ref Roger R Dmochowski: Tegresstm Urethral implant Phase III clinical Experience And Product Uniqueness: Reviews in Urology Vol 7. Suppl.1 2005 pages S22-S26.</p>	<p>Please refer to responses above regarding these products.</p>
Bard Limited	Draft	16	1.4.2	<p>Surgeons should receive training from an expert source for the treatment of SUI.</p>	<p>Noted.</p>
Bard Limited	Draft	16	1.4.2.2	<p>Patients would benefit from a patient information booklet describing the advantages & disadvantages of each surgical option.</p>	<p>The provision of information for patients is covered elsewhere in the guideline.</p>

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Bard Limited	Draft	17	1.4.3	For the trans urethral placement of Tegress (bulking agent) surgeons should be trained in the use Cystourethroscope.	The requirement for competence in cystourethroscopy is covered in the section on surgical competence.
Bard Limited	Full	78	15	<p>Pelvicol (Porcine Dermis) is not macroporous and has been used effectively as a sling.</p> <p>Ref No 1. M. Abdel-Fattah: Pevicol™ Pubovaginal Sling versus Tension –Free vaginal Tape for Treatment of Urodynamics Stress Incontinence: A Prospective Randomized Three –Year Follow –Up Study: European Urology 46 (2004) 629-635</p> <p>Ref No 2 J.W. Barrington: Longitudinal Study of Pelvicol Pubovaginal slings using MRI : Journal of Obstetrics & Gynaecology (August 2004) Vol.24 No 5. 542-546</p> <p>Ref No 3. D. De Ridder. TVT-Erosion: One step partial excision & replacement by Pelvicol™ Implant International Urogynecology Journal & Pelvic Floor Dysfunction 2001 pages 16-17 (ISSN 0937-3462).</p>	As above; the Abdel-Fattah study is included in the guideline. Reference 2 considered the anatomical position of sling and not its effectiveness, therefore it is not eligible. It has not been possible to retrieve the third reference cited from the information given.
Bard Limited	Full	291	17	<p>Tegress is injected submuscosal tissues of the mid urethra.</p> <p>Ref: Dmochowski R et al: Multicenter randomised controlled trial to evaluate Uryx (<i>Changed to Tegress 2005</i>) urethral bulking agent in treating female stress urinary incontinence: comparison of initial and expansion phases of trial: ICS 2004, abstract No 657.</p>	We have systematically searched for trials evaluating Uretex, Tegress, and Uryx on the standard databases as detailed in the method. We found no fully published clinical trial reports for any of these products therefore they were not considered further by the Guideline Development Group. We do not systematically search the grey literature (see method section of the full guideline).
Bard Limited	Full	292	4	<p>The following reference compares Contigen with Uryx(Tegress)</p> <p>Ref: Dmochowski R et al: Multicenter randomised controlled trial to evaluate Uryx (<i>Changed to Tegress 2005</i>) urethral bulking agent in treating female stress urinary incontinence: comparison of initial and expansion phases of trial: ICS 2004, abstract No 657.</p>	We have systematically searched for trials evaluating Uretex, Tegress, and Uryx on the standard databases as detailed in the method. We found no fully published clinical trial reports for any of these products therefore they were not considered further by the Guideline Development Group. We do not systematically search the grey literature (see method section of the full

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					guideline).
Bard Limited	Full	328	7	<p>Please consider the following Uretex references as evidence of efficacy</p> <p>Ref No1: Fendler et Al: Stress Urinary Incontinence Treatment using a specially designed sub-urethral support Uretex. Results at 1 year from a multicenter prospective study ICS 2004, abstract No 723.</p> <p>Ref No2 John B Gebhart: Uretex Urethral Support System for Treatment of Stress Urinary Incontinence :The American Urogynaecolgical Society & the Society of Gynaecological Surgeons, Abstract 2004</p> <p>Ref No 3: V. Scetbon: Uretex polypropylene urethral support for urodynamic stress incontinence: Issues in Women's Health Vol1 No1 pages 18-21</p> <p>Ref No 4. J-L Pariente: An independent Biomechanical evaluation of commercially available sub urethral slings. Issues in Women's Health Vol. 1 No1 pages 9-12</p> <p>Ref No 5 Giolitto: Stress Urinary Incontinence Treatment using a second generation polypropylene urethral support IUGA 2002.</p>	Please refer to responses above. Again, we do not systematically search the grey literature, and include only fully published trial reports.
Bard Limited	Full	334	15	Uretex is also available in the suprapubic approach.	Please refer to responses above.
Bard Limited	Full	335	12	<p>2 other references to consider</p> <p>No.1 Green et al: A comparison of the transobturator tape & transabdominal tension free tape procedures for the surgical treatment of SUI ICS 2005 Abstract No 641</p> <p>No 2 De Tayrac: A prospective randomized study comparing TVT and Transobturator suburethral tape (TOT) for the surgical treatment of stress incontinence ICS 2003 Abstract No 344.</p>	Both references are abstracts (we do not systematically search the grey literature, and include only fully published trial reports.). We are aware that reference 2 (De Tayrac) was later published in full but retracted by the authors, and withdrawn from the journal in which it was published because ethical approval was not sought for the study.
Bard Limited	Full	363	2	<p>This paragraph should ideally include the use of Pelvicol as a sling</p> <p>Ref No 1. M. Abdel-Fattah: Pevicoltm Pubovaginal Sling versus Tension –Free vaginal Tape for Treatment of Urodynamics Stress Incontinence: A Prospective Randomized Three –Year Follow –Up</p>	As above; the Abdel-Fattah study is included in the guideline. Reference 2 considered the anatomical position of sling and not its

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>Study: European Urology 46 (2004) 629-635</p> <p>Ref No 2 J.W. Barrington: Longitudinal Study of Pelvic Pubovaginal slings using MRI : Journal of Obstetrics & Gynaecology (August 2004) Vol.24 No 5. 542-546</p> <p>Ref No 3. D. De Ridder. TVT-Erosion: One step partial excision & replacement by Pelvicoltm Implant International Urogynecology Journal & Pelvic Floor Dysfunction 2001 pages 16-17 (ISSN 0937-3462).</p>	effectiveness, therefore it is not eligible. It has not been possible to retrieve the third reference cited from the information given.
Bard Limited	Full	377	1	<p>Tegress Uryx (Tegress) V Contigen study demonstrated Uryx's superior performance</p> <p>Ref: Dmochowski R et al: Multicenter randomised controlled trial to evaluate Uryx (<i>Changed to Tegress 2005</i>) urethral bulking agent in treating female stress urinary incontinence: comparison of initial and expansion phases of trial: ICS 2004, abstract No 657.</p>	Please refer to responses above regarding grey literature.
Bard Limited	Full	377	8	<p>Tegress does not decline with time</p> <p>Ref Roger R Dmochowski: Tegresstm Urethral implant Phase III clinical Experience And Product Uniqueness: Reviews in Urology Vol 7. Suppl.1 2005 pages S22-S26.</p>	Please refer to responses above.
Bard Limited	Full	380	16-17	<p>There is excellent data on the use of Pelvicol as a a sling</p> <p>Ref: Ref No 1. M. Abdel-Fattah: Pevicoltm Pubovaginal Sling versus Tension –Free vaginal Tape for Treatment of Urodynamics Stress Incontinence: A Prospective Randomized Three –Year Follow –Up Study: European Urology 46 (2004) 629-635</p> <p>Ref No 2 J.W. Barrington: Longitudinal Study of Pelvic Pubovaginal slings using MRI : Journal of Obstetrics & Gynaecology (August 2004) Vol.24 No 5. 542-546.</p>	As above; the Abdel-Fattah study is included in the guideline. Reference 2 considered the anatomical position of sling and not its effectiveness, therefore it is not eligible.
Bard Limited	Full	381	6	<p>Description excludes Pelvicol which does not have a macroporous construction.</p>	Noted.
Bard Limited	Full	381	11-14	<p>Description excludes Pelvicol, which has to shown to be an effective treatment for SUI.</p> <p>Ref: Ref No 1. M. Abdel-Fattah: Pevicoltm Pubovaginal Sling versus Tension –Free vaginal Tape for Treatment of Urodynamics Stress Incontinence: A Prospective Randomized Three –Year</p>	As above; the Abdel-Fattah study is included in the guideline. Reference 2 considered the anatomical position of sling and not its effectiveness, therefore it is not eligible.

Organisation	Version	Section/page	Line no.	Comments	Response
				Follow –Up Study: European Urology 46 (2004) 629-635 Ref No 2 J.W. Barrington: Longitudinal Study of Pelvic Pubovaginal slings using MRI : Journal of Obstetrics & Gynaecology (August 2004) Vol.24 No 5. 542-546.	
Bard Limited	Full	382	1-7	Description excludes Tegress (old trade name Uryx) made from ethylene vinyl alcohol (EVOH). Tegress is indicated for 1 st line treatment of SUI caused by Intrinsic Sphincter Deficiency. Repeated injections are not always required and efficacy does not diminish with time. Ref Roger R Dmochowski: Tegress [™] Urethral implant Phase III clinical Experience And Product Uniqueness: Reviews in Urology Vol 7. Suppl.1 2005 pages S22-S26.	Please refer to responses above regarding these products.
Barnet PCT				This organisation was approached but did not respond.	
Barnsley Primary Care Trust				This organisation was approached but did not respond.	
BES Rehab Ltd				This organisation was approached but did not respond.	
Boehringer Ingelheim Ltd				This organisation was approached but did not respond.	
Boston Scientific Limited	Full Version	General		This guideline is very welcome as it will increase awareness of this condition within the NHS and amongst patients which will help to significantly improve the treatment options and experiences for women Boston Scientific offers devices for primary surgical options to treat stress urinary incontinence, described in the draft guideline as Retropubic mid-urethral tape procedures using a 'bottom-up' approach (Advantage [™] and Lynx [™] meshes). Boston Scientific also commercializes slings placed using a transobturator foramen approach, an alternative approach (Obtryx [™]) to the above The list of detailed comments is provided below In summary: We strongly welcome the guideline that mid-urethral tape procedures are preferred to more invasive surgical options. The treatment algorithm should reflect this preference The recommendation and description made on	Thank you for your comments.

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				<p>transobturator slings does not reflect the evidence available on safety and efficacy of this approach. Available evidence shows similar efficacy for retropubic and transobturator approach and an excellent safety profile for transobturator slings. Given the similarity of this evidence the level of recommendation should be the same and the choice of approach left to clinician preference.</p> <p>In summary it seems that the most important aspect of the guideline might be included in the <i>Urinary incontinence: NICE guideline draft</i> when it is stated that '<i>Women with urinary incontinence should have the opportunity to make informed decisions</i>'. Unfortunately the social stigma associated with this disease can discourage women to look for available treatments. Successful programmes to increase patient's awareness of the condition should to be designed.</p>	
Boston Scientific Limited	Full Version	P. 78	14 to 18	<p>It is extremely welcome to see that retropubic mid-urethral tape procedures are the preferred surgical option, and that open colposuspension and autologous rectus fascial sling procedures are only recommended as alternative surgical treatment.</p> <p>Mid-urethral (MU) tape procedures, the minimally-invasive option is favoured and more invasive surgery is only an alternative option. It is reflected by the number of procedures performed annually in the English NHS [see graph Page 288]. Numbers of MU slings and colposuspension have had an inverse curve. The minimally invasive option is better for the patient as the hospital stay and time to recovery is shorter. It is a better option for the NHS as the procedure time and the need for a hospital bed is shorter. It is also a better option for the economy as a whole as return to normal activities is quicker.</p>	Noted.
Boston Scientific Limited	Full Version	P. 90	19 to 22	<p>Boston Scientific strongly welcomes this statement that the only material recommended for slings are macroporous (type 1) polypropylene meshes. To reinforce this, page 91, Lines 1-3, it is stated that "<i>Slings using materials other than macroporous (type 1) construction (made of polyester, polytetrafluoroethylene, silicone) are not recommended for the treatment of stress UI</i>".</p> <p>It is therefore felt that a contradiction exists between these 2 statements. If mid-urethral slings using other material than macroporous (type 1) polypropylene meshes are not</p>	This section has been revised, including a change to the recommendation on transobturator tapes.

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				<p>recommended for treatment of stress UI, caution should be used in using them, even within an audit/research environment.</p> <p>This line of recommendation [page 90, lines 19-22] is confusing as 2 different aspects are mixed: approach type and material/design. It is felt that:</p> <ul style="list-style-type: none"> - recommendations about <u>approach</u> (retropubic 'top-down' or a transobturator foramen approach) and recommendations about <u>types of material</u> should be separated and not combined - the comment on transobturator foramen approach should be amended to reflect clinical evidence available showing that retropubic and transobturator ('outside-in') approaches have been shown to have similar efficacy, and that the transobturator approach was introduced to address some of the potential complications of the retropubic placement. <p><i>(See relevant comment of P.335, line 12 to P.336, line 2).</i></p>	
Boston Scientific Limited	Full Version	P.94	14 to 17	<p>Boston Scientific would like to let the Committee know that the company is currently running a web-based registry on mid-urethral tapes (mostly using the transobturator approach). It is a worldwide registry that should collect 12 month outcomes from 1800 to 2000 cases. Any centers using Boston Scientific tapes can submit data. Enrollement should be completed in November 2006 and the first 3 month results should be available in the first quarter of 2007.</p>	Noted.
Boston Scientific Limited	Full Version	P.91	1 to 3	<p>Boston Scientific strongly welcomes this statement that the mid-urethral slings recommended are macroporous (type 1) polypropylene meshes, and that Slings using materials other than macroporous (type 1) construction (made of polyester, polytetrafluoroethylene, silicone) are not recommended for the treatment of stress UI.</p> <p>As underlined in the draft consultation document, data is not available to show they have similar efficacy. Moreover slings employing other material than macroporous (type 1) polypropylene meshes appear to have higher rates of erosion and infection.</p>	Noted.
Boston Scientific Limited	Full Version	P.332	4 to 6	<p>This is a critical aspect of this procedure. As commented earlier, the minimal invasiveness of this procedure, compared to open colposuspension makes it an ideal treatment for the patient, the NHS, and the overall economy.</p>	Noted.

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				<p>The rapid increase in the number of mid-urethral tape procedure (since 98-99) has coincided with a decline in the number of colposuspension procedures [see graph page 288]. The number of beddays avoided is immense.</p> <ul style="list-style-type: none"> In 1998-99, there were 212 tape procedures episodes recorded and 5477 colposuspensions. In 2004-05, there were 7290 tape procedures and 757 colposuspensions As the latest median figure for length of stay is 2 days for TVT and 6 days for colposuspension In 6 years, the number of saved beddays was 14164 At the same time, the number of women treated has increased by 41% <p>These figures show the extremely positive impact on the system capacity brought by minimally invasive alternatives.</p> <p>The Payment by Results regime is also favorable to procedures reducing length of stay. As the tariff is a fixed price, daycases of interventions with a short hospital stay will drive the costs down and allow hospitals to break-even or even make surpluses compared to payment.</p> <p>No difference in terms of length of stay and return to normal activities should exist between different approaches (retropubic and transobturator). But two comparative trials (1,2) report a shorter procedure time with the transobturator approach (8minutes vs 32 minutes, 23.5 minutes vs 46 minutes)</p> <p><i>Ref (1): Fischer A, Fink T, Zachmann S et al. Comparison of Retropubic and Outside-In Transobturator Sling Systems for the Cure of Female Genuine Stress Urinary Incontinence. Eur Urol 2005;48(5):799-804</i></p> <p><i>Ref (2): Ansquer Y, Marcollet A, Yazbeck C. The Suburethral Sling for Female Stress Urinary Incontinence: A Retropubic or Obturator Approach? J Am Assoc Gynecol Laparosc 2004, 11(3):353-358).</i></p>	
Boston Scientific Limited	Full Version	P.335	12 to 18	<p><u>Efficacy: retropubic vs transobturator approach</u></p> <p>The 2 cohort studies comparing TVT and transobturator approach used in the Full draft guideline both have a follow-up of at least 12</p>	The Ansquer paper was considered and excluded because it is not a direct comparison of one tape vs. another, or of different methods of introducing the

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				<p>months. They found no significant difference between TVT and TOT in cure, improvement and satisfaction rates (<i>ref 716 and 717</i>).</p> <p>Another retrospective cohort analysis was found in the literature. Ansquer and colleagues (2) reported results for 25 patients who underwent surgery with the retropubic approach and 24 with the obturator approach. They found that one month after surgery, continence results did not differ significantly between the two groups (cure rate of 80% for TVT and 83% for TOT, $p = .30$). Those initial results were unchanged at last follow-up (mean follow-up was 13.7 ± 3 months for the retropubic approach group and 7.2 ± 2 months for the obturator approach group).</p> <p><i>Ref (2): Ansquer Y, Marcollet A, Yazbeck C. The Suburethral Slings for Female Stress Urinary Incontinence: A Retropubic or Obturator Approach? J Am Assoc Gynecol Laparosc 2004, 11(3):353–358</i></p>	<p>same tape; it compares the retropubic approach to a sling (using TVT) vs. the obturator approach using any tape (TVT, IVS, prolene mesh, mersuture mesh, uratape).</p>
Boston Scientific Limited	Full Version	P.33 5 & P.33 6	20 to 23 & 1 to 2	<p>Safety profile: retropubic vs transobturator approach</p> <p>Overall complications following mid-urethral tape procedures are relatively uncommon. Death due to the procedure has never been reported.</p> <p>Haemorrhage is quoted as a common complication in both groups. Mellier <i>et al</i> (<i>ref 716 of full draft guideline</i>) reported a rate of 10% (n=8) for TVT and 2% (n=2) for TOT (p=ns). The additional reference mentioned above (Ansquer <i>et al</i>) reported rates of 0% for TVT and 4% (n=1) for TOT (p=ns). However it is important to note that blood losses in all those cases were inferior to 200mL therefore was not severe and did not require any blood transfusion.</p> <p>A distinction between severe and non-severe haemorrhage should be made.</p> <p>The rest of the complications listed differ between the 2 techniques. Especially bladder injuries are more common in the retropubic approach than the transobturator approach. This can be explained by the approach itself. Slings placed using the retropubic approach enter the retropubic space, whereas it is not the case with the transobturator approach. In fact, the transobturator approach was designed to reduce, or even</p>	<p>We note your comments.</p> <p>The bladder injury rate with retropubic and transobturator approaches is considered in the text.</p>

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				<p>eliminate the complications related to the penetration of the retropubic space.</p> <p>To make sure that the bladder is not injured, cystoscopy is compulsory during a procedure using a retropubic approach. On the contrary cystoscopy is not routinely performed during a transobturator procedure, as bladder injuries are not to be expected. This is what IPAC overview document has underlined as the 2 approaches main difference. In the 3 trials, the rates of bladder perforations ranged from 4.5% to 10% in the TVT cohorts and from 0% to 0.5% in the TOT cohorts</p> <p>[see additional information on bladder injuries in the next comment].</p>	
Boston Scientific Limited	Full Version	P.352	10 to 14	<p>Efficacy: Transobturator case series</p> <p>Boston Scientific welcomes the extensive review of the literature undertaken by the National Collaborating Centre for Women's and Children's Health. A cure rate ranging from 55% to 92% is reported. However it is unclear how the minimum value was obtained. All the abstracts of the papers mentioned (<i>references 829 to 838 of full draft guideline</i>) were reviewed and the 55% cure rate was not found.</p> <p>Moreover the IPAC overview reported that the proportion of patients satisfied with the outcome of surgery ranged from 78% to 92%. For the case series with a minimum 12 month follow-up (<i>ref 836, 838 of full draft guideline</i>), the percentage of patients with complete resolution of incontinence ranged from 80% to 92%.</p> <p>A clearer indication on the origin of the 55% cure rate would be useful as it does not reflect our understanding of the procedure efficacy. Also, considering the cure rate median figure (91%), 55% looks as an outlier that might be misleading.</p>	<p>Naidu 2005 reported that 55% were completely dry; see evidence tables.</p> <p>The median quoted in the full guideline is 81%. Median values are used consistently throughout the surgery section.</p>
Boston Scientific Limited	Full Version	P.352	15 to 21	<p>Safety Profile: Transobturator case series</p> <p>These excellent efficacy results are supported by an excellent safety profile of the trans-obturator approach. Transobturator foramen procedures use tape similar to the tension-free vaginal tape, but different techniques are used to insert it. The main difference between this procedure and the insertion of a tension free vaginal tape is that the retropubic space is not entered and cystoscopy is not routinely required (as bladder injuries are not to</p>	Noted.

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				<p>be expected). The tape is placed between the two obturator foramina, from outside to inside. This was done in order to reduce or even eliminate the complications related to the penetration of the retropubic space, mainly bladder perforations. This theoretical advantage has so far been demonstrated in the literature as the bladder perforation rate across 8 case series was 0.5% (median – range: 0 to 1%) [page 352, line 17]</p> <p>Overall evidence so far supports the use of the transobturator approach as it shows similar efficacy results and excellent safety profile.</p>	
Boston Scientific Limited	Full Version	P.353	9 to 12	<p>The transobturator 'inside-out' is a variation of the transobturator technique recently described by de Leval <i>et al</i> (ref 828 of full draft guideline). Little research has been carried out on this technique. Some studies on the anatomy of this region suggest that the 'inside-out' procedure should be used with caution. This caution is due to the fact that in the 'inside-out' version of the transobturator approach, the procedure carries more risk of having a 'blind track'. In 2005, Delmas (3) underlined the importance of introducing the needle "outside-in", as <i>introduction in the opposite direction may transfix the pudendal pedicle with damage to the nerve and vascular branches of the obturator pedicle</i>. He also found that the anatomical safety of the transobturator approach (described above) "<i>is further improved by the fact that introduction of the needle from the thigh to the vagina [outside-in] allows direct visual or digital control over almost the entire course.</i>"</p> <p>In 2004, Delmas and Costa had already described a potential 'blind track' with the inside-out and the danger of a more exposed pedicle. (4)</p> <p>In terms of patient outcomes, these findings from the anatomy could explain the high rate of post-op pain and discomfort (16%) reported in the initial series of de Leval <i>et al</i>. (ref 829 of the full draft guideline)</p> <p>Results from a registry in France recently reported (5) were consistent with these results. Investigators found that 148 patients had abnormal pain up to 3 months after the procedure, which represents 14.9% of the total population included in the registry (N=994).</p>	Noted.

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				<p>Ref (3): Delmas V. Anatomical Risks of Transobturator Suburethral Tape in The Treatment of Female Stress Urinary Incontinence. European Urology 2005; 48: 793–798.</p> <p>Ref (4): Costa P and Delmas V. Trans-obturator-tape procedure – ‘inside out or outside in’: current concepts and evidence base. Current Opinion in Urology 2004, 14:313–315</p> <p>Ref (5): Collinet P, <u>Costa P</u>, Ciofu C, Cosson M, Deval B, Grise P, Haab F, Jacquetin B. French Gynecological meeting « Le Choix des Armes » Marseille, 11 March, 2006.</p>	
Bradford Teaching Hospitals NHS Foundation Trust				This organisation was approached but did not respond.	-
Britannia Pharmaceuticals Limited				This organisation was approached but did not respond.	-
British Association for Behavioural & Cognitive Psychotherapies (BABCP)				This organisation was approached but did not respond.	-
British Association for Counselling and Psychotherapy (BACP)				This organisation was approached but did not respond.	-
British Association of Paediatric Surgeons				This organisation was approached but did not respond.	
British Association of Urological Surgeons	Full	51	4	Incontinence surgery has been linked to those surgeons who are trained to do prolapse surgery – in present format this will exclude most urologists in a stroke. We would therefore recommend that this to be reworded along the lines of incontinence surgery be	Thank you for your comments. Having reconsidered this point, the GDG remains of the view that surgery for UI should only be undertaken by surgeons

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(BAUS)				performed by appropriately trained urological surgeons with w subspecialist interest in female urology or urogynaecologists.	with appropriate training in the assessment and treatment of both UI and prolapse. We acknowledge however, that the development of female urology and urogynaecology has meant that many surgeons now function within the context of a multidisciplinary team, the members of which possess the relevant training and expertise. We have modified the recommendation in this area to reflect your comments.
British Association of Urological Surgeons (BAUS)	Full	61	6	The remit of the document – we feel that a chance has been missed to improve continence services as a whole in that men and children have been actively excluded, and also patients with neurological disease	Noted.
British Association of Urological Surgeons (BAUS)	Full and NICE	general		Both are too long and convoluted and will be very difficult to use and be adapted by general practitioners.	Noted. Please see the Quick reference Guide on the NICE website
British Association of Urological Surgeons (BAUS)	Full	227 227 241 250	8 22 21 5	The use of anticholinergics – a high proportion of the membership are unhappy regarding the recommendation to use oxybutynin as the first line drug in the treatment of OAB. Whilst they obviously accept that it is the cheapest option, it has the highest side effect profile. In the current era of treating symptoms and quality of life, they feel that other anticholinergics with much lesser side effect profiles should be allowed to be used as first line treatment.	The GDG has reconsidered the evidence in this area, along with comments from several stakeholders. We note in the evidence statements for antimuscarinic drugs that oxybutynin IR has a poor tolerability profile compared with other antimuscarinic drugs. However an improved tolerability profile does not necessarily translate into improved persistence with therapy. A long term study of oxybutynin ER (Diokno et al 2002) found that discontinuation attributable to adverse effects was 24%, which is similar to that reported for oxybutynin IR. A transdermal formulation of oxybutynin has been developed to further improve the tolerability profile but no studies have reported on long term tolerability

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					<p>and persistence.</p> <p>There is evidence from practice that persistence with antimuscarinic therapy is low (Shaya et al 2005).</p> <p>The difference in drug costs is not trivial with non-proprietary oxybutynin being around 10 times cheaper than other antimuscarinic options.</p>
British Association of Urological Surgeons (BAUS)	Full	general		Dipstick haematuria – we feel that although this is mentioned several times in the document, we felt that the potential seriousness of this finding needs to be highlighted more authoritatively, and that onward referral to a urology department which deals with investigation for urothelial malignancy should be highlighted as mandatory	Recommendations regarding referral based on haematuria are taken directly from the NICE 'Referral guidelines on suspected cancer' (2005). It is the GDG's view that we cannot be more specific than this. The NICE definition for urgent referrals has been added.
British Association of Urological Surgeons (BAUS)	Full and NICE	11 136 137 138	3	Urodynamics: many of the members were unhappy with the position of urodynamics assigned by NICE in the algorithm for the investigation and treatment of (urodynamic) stress incontinence, in that in the algorithm it appears that urodynamics are only indicated AFTER failed primary surgery. As a group we would feel more comfortable with them being placed within the algorithm PRIOR to primary surgery. We would agree that they should be performed prior to surgical intervention for detrusor overactivity.	The GDG has considered the many comments received regarding the use of urodynamic testing prior to primary surgery for stress UI. We reflected further on the evidence and current practice. We maintain the view that urodynamics investigation is not essential in every woman prior to primary surgery for stress UI, and therefore is not <u>routinely</u> recommended. However, we acknowledge the weight of expert opinion that it is of value in specific circumstances; we have included recommendations as to those circumstances in the guidance.
British Association of Urological Surgeons (BAUS)	Full	109 110		Pelvic floor examination: at no point in the document is there a recommendation made for routine pelvic floor examination, either as part of the initial assessment at outpatient level, or prior to the initiation of pelvic floor exercises. We feel this should be made mandatory. One of the main reasons for the failure of PFE's as a first line treatment in women is a woman's inability to either (i) contract her pelvic floor at all, or (ii) partially or incorrectly contract her pelvic floor, and for these reasons we feel that pelvic floor	We have considered your comments and reflected on the limited evidence as to whether pelvic floor muscle assessment prior to PFMT improves outcome. Whilst there is not unanimity on this point, it is clearly widespread expert opinion that the determination of whether a woman can contract her

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				muscle examination should be mandatory, so that PFE education will be more effective. Furthermore in terms of PFMT as the first line treatment for SUI/MUI we would agree with it being the sole treatment for the former, but would prefer a recommendation for PFMT and an anticholinergics for mixed urinary incontinence.	pelvic floor muscles voluntarily may influence the type of treatment. Hence, the GDG has reconsidered its earlier recommendation, and will advise that pelvic floor muscle assessment should be undertaken before embarking on supervised pelvic floor muscle training for the treatment of UI.
British Association of Urological Surgeons (BAUS)	Full	78 89 227	8 4 12	The role of sacral nerve stimulation in the treatment of urge urinary incontinence, following the failure of anticholinergic therapy. SNS is a highly expensive treatment available in a limited number of centres. A number of members wished for a recommendation for intravesical botox, which will probably supersede SNS within the next 3 years, given either as part of a trial or prospective audit. It is cheaper and there is data emerging in the literature to support its use. It would require the development of a highly expensive infrastructure to support the widespread use of SNS.	The cost-effectiveness of SNS was not addressed in the draft guideline because it was to be considered a low volume treatment, where the alternatives were also expensive. A cost-consequence analysis of SNS is now included as an additional appendix. The GDG has also reflected on the research recommendation previously made for botulinum toxin and made it a priority research recommendation.
British Association of Urological Surgeons (BAUS)	Full	250	5	The use of anticholinergic therapy in the treatment of urgency and urgency incontinence. It is completely agreed that this should be a first line treatment for storage symptoms, however there was major disagreement with the recommendation of proprietary oxybutinin as the first line drug. Whilst its efficacy cannot be denied, it has the worst side effects profile of all anticholinergic agents, and many members wishes for the recommendation of a sustained release anticholinergic as the first line drug treatment, which would have far greater patient compliance, and would thus cut out the need for repeated outpatient consultation, thus cutting back on follow up consultations.	Please refer to response above regarding antimuscarinic therapy. Additionally, the recommendation on antimuscarinic drugs has been revised to include advice on slow release and transdermal formulations of oxybutynin. Furthermore, good prescribing practice requires that patients be reviewed when starting on new pharmacological treatment and therefore the costs of switching from a poorly tolerated drug are, at least partly, subsumed within this review process.
British Association of Urological Surgeons (BAUS)	Full	302 302	5 11	Operative considerations: (i) artificial urinary sphincters. The NICE guidelines in this document indicate that it should only be considered when other treatments have failed. There are a number of excellent large numbered long-term follow up series published in the scientific literature	We agree with the points made, although most data regarding the artificial urinary sphincter relate to its use in men or in men and women with neurogenic bladders. We have added a statement explaining this to the text.

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				which have shown excellent results for the AUS used as a primary treatment for type 3 urodynamic stress incontinence, and feel that the AUS should be recommended as a primary treatment, therefore, for type 3 USI. Furthermore there is also good evidence in the literature that in more complex cases of type 3 USI, when the AUS is used as a secondary or even tertiary procedure that there is an increased risk of cuff erosion.	The recommendation has also been modified.
British Association of Urological Surgeons (BAUS)	Full	89 286	21 12	We strongly agree with this positive statement about the use of Botulinum toxin and suggest that it is specifically added that women be informed about the likelihood of the need to self catheterise following treatment.	Agree. Statement added to recommendations.
British Association of Urological Surgeons (BAUS)	Full	general		A huge undertaking, very comprehensive as expected, but big opportunity missed to review male, children and neurogenic incontinence.	Noted.
British Dietetic Association				This organisation was approached but did not respond.	-
British Geriatrics Society				This organisation was approached but did not respond.	-
British Healthcare Trades Association				This organisation was approached but did not respond.	-
British Menopause Society				This organisation was approached but did not respond.	-
British National Formulary (BNF)				This organisation was approached but did not respond.	-
British Psychological Society, The				This organisation was approached but did not respond.	-
British Society of				This organisation was approached but did not respond.	-

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Urogynaecologists					
Cancer Services Collaborative 'Improvement Partnership' (CSCIP)				This organisation was approached but did not respond.	-
Central Liverpool PCT				This organisation was approached but did not respond.	-
Chartered Society of Physiotherapy				This organisation was approached but did not respond.	-
CIS'ters				This organisation was approached but did not respond.	-
City Hospitals Sunderland NHS Trust				This organisation was approached but did not respond.	-
Clinimed Limited	Full Version	86	18-22	<p>An appropriate anaesthetic, antiseptic lubricating gel from a single use container should be used prior to catheter insertion as it will produce an effective and protective lubricant film on the urethra. This will help to prevent microlesions which may lead to strictures, will also reduce the danger of via falsa and lowers the risk of infection.</p> <p>References Doherty, W. (1999) Instillagel: an anaesthetic antiseptic gel for use in catheterisation. British Journal of Nursing 8: 2, 109-112</p> <p>Kambal, C., Chance, J., Cope, S. et al. (2004) Catheter-associated UTI's in patients after major gynaecological surgery: audit. Professional Nurse 19: 9, 515-518</p> <p>National Institute for Clinical Excellence - Guideline. (2003) Infection Control – Prevention of healthcare associated infection in primary and community care. London: NICE</p> <p>Stewart, E. (2006) Development of catheter care guidelines for Guy's and St Thomas'. British Journal of Nursing 15:8, 420-425</p>	Thank you for your comments. However, the GDG considered when to use catheterisation as being included within its brief, but not the methods of catheterisation.

Organisation	Version	Section/page	Line no.	Comments	Response
				Woodward, S. (2005) Use of lubricant in female urethral catheterisation. British Journal of Nursing 14:19, 1022-1023	
Colchester Primary Care Trust				This organisation was approached but did not respond.	-
College of Occupational Therapists (Functional continence special interest group – PromoCon, Manchester)	NICE & Full	General		A very positive document which encompasses a holistic and sensitive approach to urinary incontinence in women.	Thank you for your comments.
College of Occupational Therapists (Functional continence special interest group – PromoCon, Manchester)	NICE & Full	General		Very pleasing to see that conservative management is so strongly recommended as a priority first line treatment. Might be nice to see occupational therapy mentioned specifically as a health care profession that may be involved in the assessment / identification of environmental issues impacting on continence, ie functional problems associated with another medical condition that leads to problems with dressing/ undressing in time, mobility, rising from bed/ chair etc.	Service configuration and models of healthcare delivery are outside the scope of this guideline. However, occupational therapists are mentioned within the introduction, in the list of healthcare professionals who are involved in the care of women with UI or OAB.
College of Occupational Therapists (Functional continence special interest group – PromoCon, Manchester)	NICE	Pg 7	1.1.1	Assessment: what about those women who struggle with functional incontinence but who initially present or are referred with symptoms of stress, urge or mixed UI?	Assessment of mobility and the environment are considered under general assessment in the full guideline.
College of Occupational Therapists	NICE	Pg7	1.1.1 - 13	Assessment: There is no mention of the need to assess the home environment, levels of social support available, psychological factors, functional ability etc in the NICE version but	The NICE version of the guideline lists only recommendations; the evidence base and further detailed consideration

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(Functional continence special interest group – PromoCon, Manchester)				some of this is covered in the full version.	are given in the full version. We have modified the text of the full guideline to include assessment of the home environment etc (within general assessment).
College of Occupational Therapists (Functional continence special interest group – PromoCon, Manchester)	Full	Pg 107	6	Mobility assessment is something that is not just for the elderly population, should be included in assessment for all – in particular clients identified p104 in the general history section with specific disorders or neurological system etc.	Noted; 'in the elderly' deleted.
College of Occupational Therapists (Functional continence special interest group – PromoCon, Manchester)	Full	107	1-9	Assessment of functional ability should also be included in the assessment section of both the Full version and the NICE summary.	Added to general assessment in the full version.
College of Occupational Therapists (Functional continence special interest group – PromoCon, Manchester)	Full	Pg 114	1.1.4	Urine testing – very pleased to see that type of 'dipstick' most relevant has been recommended (ie leucocyte and nitrite sensitive) as this is a common problem in many secondary care settings (financial reasons).	Noted.

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College of Occupational Therapists (Functional continence special interest group – PromoCon, Manchester)	NI CE	Pg 9	1.1.9	Pad testing: pleasing to see that this is not recommended. Still being carried out too often.	Noted.
College of Occupational Therapists (Functional continence special interest group – PromoCon, Manchester)	NI CE	Pg10	1.2	Conservative treatment: no mention of functional issues again. Many options available for women whose stress, urge or mixed UI is being compounded by environmental, barriers, psychological or physical dysfunction. The use of assistive technology, alternative solutions to inaccessible toilets or where the woman 'cannot make it to the toilet in time', adapted clothing, etc should all be included. These can be used in isolation as a management strategy or as support mechanisms during treatments. Appropriate and sensitive referral to OT would identify functional problems earlier in the process and may reduce the need for medication / surgery therefore saving a lot of time and money.	A recommendation regarding the use of urinals and toileting aids has been added to the section on non-therapeutic interventions. Service configuration and models of healthcare delivery are outside the scope of this guideline.
Coloplast Limited				This organisation was approached but did not respond.	
Commission for Social Care Inspection				This organisation was approached but did not respond.	
Connecting for Health				This organisation was approached but did not respond.	-
Continence Foundation	NI CE	3		In seeking to produce concise definitions of the forms of urinary incontinence, some of the true complexity of the condition is lost, e.g. there is no reference here to nocturia. Also, the most recent ICS term is "urgency incontinence" not "urge incontinence". We understand that the change was made to ensure clarity in the international context, and while NICE guidance is only issued for this country, it will be consulted by people from elsewhere.	Thank you for your comments. We understand that the term 'urgency incontinence' has been advocated by the International consultation on incontinence although is not current ICS terminology. As you indicate guidance is for use within the NHS although we are aware that NICE guidance is used internationally, our terminology and recommendations aim to reflect current

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					UK practice.
Continence Foundation	Full	General		The full version of the Guideline seems to be written for statisticians – no concession is made to people from other backgrounds. Everyone we have spoken to who has ploughed through the full version has said they were unable to read large sections at a time – this includes lecturers and consultants. For a more readable Guideline document see, for instance, the one on Dementia also currently out for consultation.	We appreciate the effort taken by stakeholders to read the whole guideline.
Continence Foundation	Full	p.40	Glossary	Add the acronym POP to the text about pelvic organ prolapse, since this is used often in the text.	We have now added abbreviations to the glossary as well as the list of abbreviations.
Continence Foundation	Full		Glossary	Explanations needed for PPV and NPV.	Added.
Continence Foundation	Full	General		Where the term “ continence advisor ” is used, it would be better to substitute “ continence nurse specialist ” to clarify the status of these nurses. Where a continence nurse specialist is noted as being equivalent to a Senior 1 grade physiotherapist (e.g. p.451), the salaries may be similar, but surely the oncosts are not the same for nurse specialists who work in primary care and those physiotherapists who are hospital-based, especially since self-referral is possible to continence nurse specialists. Where referral to a physiotherapist comes via a consultant, there will be a consultation cost to add. It should also be noted that some specialist physiotherapists work in primary care, which would change the costings.	‘continence nurse specialist’ used. The costings need to be interpreted in the light of the caveat given in Appendix E; “Considerable heterogeneity exists within many of the conservative treatments for UI. As far as possible the cost estimates presented here are based on ‘standard’ or ‘typical’ treatment (as informed by expert opinion on the GDG) but in practice such a standard may not exist. Therefore, the actual costs of particular conservative treatments will vary according to the actual practice followed.” The consultation cost can probably be considered a “sunk cost” and would therefore not be relevant to any treatment path/decision.
Continence Foundation	Both			Information for patients & carers. Provision of information is briefly mentioned in the short version, p.4, but the details of support organisations are only in the full version, p.158. These ought to appear in the short version since very few people (including professionals) will read the full one. It would be useful	NICE will produce a version of the guideline for people who use NHS services, which will include details of support organisations .

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				to give postal & telephone details, not just the websites.	
Continence Foundation	Full	159	6	“Information provided must be designed for use by patients with their clinicians”: while that is an essential strand of information, it is just as important to produce information that patients (and the public) can understand without input from a professional.	Please see above comment.
Continence Foundation	Full	77	11-13	Since the evidence (Appendix C) against the use of multi-channel cystometry before primary surgery is only Grade D, it would be more appropriate to recommend that surgeons continue their current practice pending the outcome of further research.	The GDG has considered the many comments received regarding the use of urodynamic testing prior to primary surgery for stress UI. We reflected further on the evidence and current practice. We maintain the view that urodynamics investigation is not essential in every woman prior to primary surgery for stress UI, and therefore is not <u>routinely</u> recommended. However, we acknowledge the weight of expert opinion that it is of value in specific circumstances; we have included recommendations as to those circumstances in the guidance.
Continence Foundation	Full	81	9-18	The wording concerning possible referral needs to take account of the fact that some continence nurse specialists are quite capable of dealing with, “associated faecal incontinence” and the consequences of “pelvic radiation therapy”. (Also see comments from the GDG for faecal incontinence.) And all should be able to provide initial treatment for “symptoms of voiding difficulty”.	The GDG has discussed your comment. We feel that the wording of the recommendation reflects your concern, in that we recommend consideration rather than mandatory referral to a specialist service.
Continence Foundation	Full	87	15-17	“Indwelling catheters ... may be associated with a lower rate of symptomatic urinary tract infection”. Professor [X], a recognised expert regarding catheters, states that there is no evidence for this in long-term catheterisation, only some evidence for short-term.	Amended.
Continence Foundation	Full	93, & 387, 389		We welcome the recommendation that surgeons should work within the context of an integrated continence service. The reference to the 2000 DH Good practice document only occurs on p.387. It should be on the other pages as well (and also in the short version), since many readers will not sufficiently understand the concept.	The DH 2000 document is listed under ‘other relevant documents’ in the introduction section of the full guideline.
Continence Foundation	Full	105		Faecal incontinence with UI doesn’t only suggest neurological or cognitive impairment, but possible obstetric trauma (regardless of the extent of nerve damage).	‘Anatomical damage’ added.

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Continence Foundation	Full	107	2-9	General assessment. Life-style factors assessed should not only be those that might impact negatively on continence status, but also the sort of life the woman wishes to lead, e.g. types of exercise and the nature of her career, since the desire to continue with these can influence treatment choices.	We believe that this is already covered in the general assessment section.
Continence Foundation	Full	115	4-15	There appears to be a recommendation concerning when <u>not</u> to commence antibiotic treatment, but I cannot find the opposite: when antibiotics should be given. This may be a matter of common sense, but needs to be stated. There is also a question about whether antibiotics should be started while awaiting culture results. This section also omits the need to look for bacterial sensitivity as part of the urine culture.	This section has been revised to reflect your concerns. Microbiologist opinion has been sought regarding culture, and antibiotic use. An explanation for the recommendations is given in the full guideline.
Continence Foundation	Full	120	3	Note re the recommendation for urgent referral of women over 50 with microscopic haematuria: there is a new HTA just published, a systematic review of diagnostic tests and algorithms used in the investigation of haematuria – it has not been possible to find time to read this.	As indicated, this recommendation is taken from the NICE 'Referral guidelines for suspected cancer' (2005). The systematic review you note concluded that there are insufficient data to derive an evidence-based algorithm of the diagnostic pathway for haematuria.
Continence Foundation	Full	79	11-14	The recommendation not to assess PFM contraction flies in the face of common sense: see below about standard practice. The following comments come from [X], a physiotherapist who commands international respect: <ul style="list-style-type: none"> a) it establishes that the woman is ABLE to voluntarily contract her PFM's. A small proportion of patients cannot. So for these, time is saved which would be wasted, and <u>from the start</u> additional assistance eg. biofeedback/electrical stimulation, can be introduced as recommended in 1.2.2.6 to facilitate voluntary contraction. b) it enables the physiotherapist or continence advisor to grade the PFM contraction using the widely used modified Oxford Scale which in turn gives a starting point against which to judge improvement, and even more importantly informs planning of the exercise training program i.e (put very simply) a very weak muscle cannot do much at any one time while a stronger muscle will benefit from greater challenges in terms of length of holds, numbers of repetitions and the position in which contractions are performed. This is what the rehabilitation of muscle is all 	We have considered your comments and reflected on the limited evidence as to whether pelvic floor muscle assessment prior to PFMT improves outcome. Whilst there is not unanimity on this point, it is clearly widespread expert opinion that the determination of whether a woman can contract her pelvic floor muscles voluntarily may influence the type of treatment. Hence, the GDG has reconsidered its earlier recommendation, and will advise that pelvic floor muscle assessment should be undertaken before embarking on supervised pelvic floor muscle training for the treatment of UI.

Organisation	Version	Section/page	Line no.	Comments	Response
				about!!	
Continence Foundation	Full	196	1-3	The GDG believes they should give guidance on the number of contractions needed. This is in spite of their statement that “there is no clear evidence on optimum training regimens”. Surely the reason there is no clear evidence is that standard practice is to create an individual programme, after a physical examination to assess the current ability of each woman to contract her pelvic floor. The individual programme will recommend what the nurse or physiotherapist judges to be reasonable to start with and then a gradual increase. There are very many studies into the problems of non-compliance with PFME. Any programme which starts a woman on a level of PFM exercise that she is unable to achieve will result in demoralisation and failure to seek further treatment. It would seem logical only to make a recommendation for the maximum number of contractions to build up to.	The GDG has discussed your comment. We feel that the recommendation made is appropriate and the reasons are explained in the text.
Continence Foundation	Full	196	13	“Where pelvic floor muscle training is successful exercises should be continued.” This seems to imply indefinite continuation of the same exercise regime. There needs to be a sensible recognition that women do not continue exercises indefinitely at a high level of intensity. Maintenance programmes of exercises need to be at a lower level than the programme needed to build up tone initially.	This recommendation has been modified to reflect your concerns.
Continence Foundation	Full	198	22	“Supervised “ bladder training is recommended partly on the basis of a study that took place with in-patients. The term “supervised” needs to be clarified, since training that involved a hospital stay would be prohibitively expensive.	‘supervised’ deleted.
Continence Foundation	Full	213	21-23	Shouldn’t the contraindications for desmopressin form part of the recommendation?	It is assumed that prescribers will use the summary of product characteristics for information on contraindications.
Continence Foundation	Full	214-220		Duloxetine. What has in effect happened with this guideline is a Technology Appraisal of duloxetine, but without some of the elements that would have formed part of a TA: there was, for instance, no opportunity for patient groups to present oral evidence about patient experience, and duloxetine was evaluated against pelvic floor muscle exercise, but not its effectiveness per se. There was a suggestion in 2003 that duloxetine might be the subject of a TA (the Director of the Foundation was asked for her view on the proposal but not informed why it did not proceed.) What we have here is a recommendation that duloxetine should not be offered as “first line” treatment, but no evidence about its use at	The statement ‘when used second-line to PFMT, duloxetine dominates standard treatment’ is taken from the Das Gupta 2006 paper (cost-effectiveness analysis of duloxetine) - we have modified this section to make it clear. However that result was based on a model which had factored in waiting times. The reason we did not want to include waiting times in our model is given in the section ‘cost-effectiveness

Organisation	Version	Section/page	Line no.	Comments	Response
				a later stage in a treatment pathway, either in conjunction with PFME or for women for whom PFME has failed, or they have been unable to maintain compliance. On p. 218, ll 18-19, it is stated “When used second-line to PFMT, duloxetine dominates standard treatment” but that is not reflected in the recommendations. We also note that the recommendation here is not in line with the SIGN Guidelines or those of the 2005 ICI.	of duloxetine’. A second model has now been included in the guideline to address its possible use as a second-line treatment. We share your concern that our recommendations do not concord with the SIGN guidance, but feel that our recommendations are appropriate to the currently available clinical and economic evidence.
Continence Foundation	Full	249	11	Darifenacin. Evidence concerning the effectiveness of darifenacin is presented but there is no recommendation regarding its use. Presumably this is because darifenacin is not actually available in the UK although Novartis has an EU licence. However, most readers cannot be expected to know that.	We have now given advice regarding darifenacin.
Continence Foundation	Full	250	5-6	There is no doubt that “non-proprietary” oxybutynin is cheaper than the SR preparations and other medications for OAB, but the evidence collected shows what is well known: it is poorly tolerated – dry mouth figures in the cited publications go as high as 93%. Patients calling the Continence Foundation’s Helpline report giving up the attempt to access any treatment at all for many years because of their unpleasant experience of the various side-effects of oxybutynin when no alternatives were available. If this recommendation stands, GPs will be forced by their PCTs to start patients on a treatment that most will find intolerable.	<p>The GDG has reconsidered the evidence in this area, along with comments from several stakeholders. We note in the evidence statements for antimuscarinic drugs that oxybutynin IR has a poor tolerability profile compared to other antimuscarinic drugs. However an improved tolerability profile does not necessarily translate into improved persistence with therapy. A long term study of oxybutynin ER (Diokno et al 2002) found that discontinuation attributable to adverse effects was 24%, which is similar to that reported for oxybutynin IR. A transdermal formulation of oxybutynin has been developed to further improve the tolerability profile but no studies have reported on long term tolerability and persistence.</p> <p>There is evidence from practice that persistence with antimuscarinic therapy is low (Shaya et al 2005).</p> <p>The difference in drug costs is not trivial</p>

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					<p>with non-proprietary oxybutynin being around 10 times cheaper than other antimuscarinic options. Furthermore, good prescribing practice requires that patients be reviewed when starting on new pharmacological treatment and therefore the costs of switching from a poorly tolerated drug are, at least partly, subsumed within this review process.</p> <p>We believe that the guideline recommendations make a clear point that alternative antimuscarinic drugs are available. We have made further recommendations regarding alternative drug formulations.</p>
Continence Foundation	Full	255	12 etc	<p>The only evidence presented regarding absorbent products compares pads and pants as a 'treatment' option compared to an intervention to reduce incontinence, and concludes that pads and pants are ineffective as treatment. This is very misleading. Clearly pads and pants are not a treatment for incontinence and it is rather spurious to use evidence from a study where pads and pants have been used as the control to show this. Perhaps the point that the document wishes to make is that pads and pants should not be used INSTEAD OF treatment i.e. in place of assessment and consideration of treatment options. This section should contain evidence from the body of literature that indicates that different designs of absorbents products (e.g. menstrual pads versus disposable incontinence pads) are more or less effective. This evidence is reviewed in the recent WHO Incontinence book (3rd international consultation) volume 1, pages 160-169. We do agree with the main evidence statement and recommendations, but feel that it is important to provide guidance to clinicians regarding appropriate selection of products for women and this is currently not covered by the document..</p>	<p>The guideline question regarding absorbent products concerned circumstances of use and not effectiveness of individual products.</p>
Continence Foundation	Full	381	11	<p>There is a danger that the recommendation about transobturator procedures will be overtaken by changes in surgical practice based on the wish of surgeons to achieve the best outcomes. We note that the Interventional Procedures section of NICE has just</p>	<p>Noted. Statements and guidance revised. Although the final IPAC guidance is not available at the time of going to press, we believe that they will</p>

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				started its third round of consultation on the topic, and with each version the evidence has become more positive.	concord with the recommendations made in this guideline.
Continence Foundation	Full	395 & 398		If a majority of surgeons recommend at least 10 of any procedure annually to ensure competence, it is inappropriate to then give a let out for those performing less than 5 of any procedure. If the GDG think 20 operations is the correct level, they should stick to it, for the sake of patient safety – this is supported by surgeons we have spoken to.	The GDG recommendation is clear - that 20 cases per year for each primary procedure is recommended as the minimum annual workload. Workloads will however vary from year to year, and some flexibility around the 'cut-off' figure was thought appropriate, particularly in recommending a figure at which special clinical governance arrangements should be invoked.
Continence Foundation	Full	408		The surgical questions should have included one about the appropriate forms of surgery for stress incontinence for women who intend to have more children: since none of the tape procedures is suitable for these women, asking this question might have modified the conclusions about the place for bulking agents.	We have incorporated a statement to the recommendation regarding counselling about surgical procedures.
Continence Foundation	Algorithm			The line on the top far right of the diagram goes back to the woman herself. I presume it is meant to go to other services since it starts from a box about referral.	This line indicates that women may re-enter the urinary incontinence pathway following treatment or investigation for other symptoms identified during the initial assessment.
Conwy & Denbighshire NHS Trust				This organisation was approached but did not respond.	-
Co-operative Pharmacy Association				This organisation was approached but did not respond.	-
Croydon Primary Care Trust				This organisation was approached but did not respond.	-
Department of Health	Full	267	10-12	We believe that there are implications for antenatal care in the recommendation that “Pelvic floor muscle training [PFMT] should be offered to women in their first pregnancy as a preventative strategy for UI”. Would it be possible for this recommendation to be drawn to the attention of the Group up-dating the Antenatal Care guideline because it would be useful to have greater detail on how and where the PFMT should take place and the resource (i.e. staffing) implications.	Thank you for your comments. Information passed on to our colleagues.

Organisation	Version	Section/page	Line no.	Comments	Response
Department of Health Sciences				This organisation was approached but did not respond.	-
Diagnostic Ultrasound (UK) Ltd				This organisation was approached but did not respond.	-
Dudley Group of Hospitals NHS Trust				This organisation was approached but did not respond.	-
Eli Lilly and Company Ltd	Full/NICE & algorithm	general		<ul style="list-style-type: none"> • Good practice would indicate that conservative treatment, including medication, should precede surgical interventions. (This is supported by the NICE guidance on TVT which recommends that surgery is considered when conservative management has failed. [NICE Guidance on the use of TVT for stress incontinence, 2003]). • The sections on overactive bladder (OAB) in the UI guideline and the OAB arm of the algorithm capture the use of medication as a conservative therapy. • The effectiveness of duloxetine for the treatment of women with stress UI is not fully and appropriately reflected in the UI guideline. The guideline recommends that duloxetine should not be used first line, but then fails to recommend where and how it should be used. • Since duloxetine is the only licensed pharmacological treatment for women with moderate to severe stress UI and as clarity is regarded as one of the 'key features' of good clinical guidelines (NICE Guideline Development Process, 2004 & AGREE 2001 [item 15]), both the guideline and the algorithm should expand on this conservative treatment further and provide clear and unequivocal advice on the use of duloxetine in the second line position, as evident in other recently produced guidelines/advice (see below). This will aid implementation and avoid confusion for healthcare professionals and patients alike. 	Thank you for your comments. We have included a model of duloxetine as a second line treatment in the guideline. Please see responses to specific points below.
Eli Lilly and Company Ltd		general		<ul style="list-style-type: none"> • Clinical and cost effectiveness data supports the use of duloxetine as a second line conservative treatment option with or without PFMT, following the failure of PFMT alone (Full Guideline p218 line 18-19 & Das Gupta <i>et al.</i> JME 2006; 9: 1-25). We think this should be made explicit in both the guideline and algorithm. 	Another model has now been included in the guideline to compare the cost-effectiveness of duloxetine versus surgery as a second line treatment for stress incontinence in women who have failed PFMT as first line. Although we

Organisation	Version	Section/page	Line no.	Comments	Response
				<ul style="list-style-type: none"> ○ Duloxetine should be added to the conservative management box of the NICE algorithm indicating the use of duloxetine with or without PFMT (in patients who have failed on PFMT alone). <p>PFMT → duloxetine + PFMT / duloxetine alone → surgery</p>	conclude that surgery is more cost-effective than duloxetine, we do now say that duloxetine can be considered where women prefer pharmacological to surgical alternatives. We believe that this patient choice is also justifiable on health economics grounds as duloxetine is considerably cheaper than surgery and therefore its use would not necessarily impose opportunity costs on the NHS.
Eli Lilly and Company Ltd		general		PFMT is effective in around half to two-thirds of patients with stress UI, yet only a small percentage of patients are referred to secondary care (Martin 2003) with even fewer receiving surgery (Wagg 2005, Papanicolaou 2005). Therefore other conservative treatment options should be considered to address the needs of patients who fail on PFMT.	Noted.
Eli Lilly and Company Ltd		general		Further conservative treatment options, including medication, should also be considered for patients with stress UI who are referred for surgery but either do not want or are not appropriate for surgery, and for patients who still leak after surgery.	Noted.
Eli Lilly and Company Ltd	NICE	1.2.4.2		<p>Other recently published guidelines/advice also considered the evidence base and produced specific and practical guidance on the use of duloxetine in the treatment of stress UI:</p> <p>The 3rd International Consultation on Incontinence (ICI) (Abrams et al 2005) stated that for the 'initial management of UI in women' conservative treatment may be augmented with appropriate drug therapy, antimuscarinics with OAB and dual serotonin noradrenaline reuptake inhibitors with SUI. This was also represented pictorially in their algorithm (extract below):</p>	<p>Noted.</p> <p>We share your concern that our recommendations do not concord with the SIGN guidance, but feel that our recommendations are appropriate to the currently available clinical and economic evidence.</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>Both the Scottish Medicines Consortium (SMC) and Scottish Intercollegiate Guidelines Network (SIGN) have accepted duloxetine for use as part of an overall management strategy for SUI in addition to PFMT. This indicates that the SMC regarded duloxetine as cost-effective in its appropriate setting.</p>	
Eli Lilly and Company Ltd	Full	218	3	<p>In the contents of the UI guideline there is a reference to 'optimal sequencing' of conservative therapies. In the cost-effectiveness section on duloxetine (page 218) the document states 'we considered the cost-effectiveness of duloxetine in order to inform recommendations about the sequencing of conservative therapies, something which could potentially have a large impact on clinical practice.'</p> <p>The decision analytic model used to assess the cost-effectiveness of duloxetine (appendix F) does not include any form of sequencing in conservative therapies and therefore over-simplifies the decision problem facing a primary care physician. It merely compares efficacy of PFMT vs duloxetine first line and concludes that duloxetine is not recommended first line. However Das Gupta et al (2006) found the 2nd line positioning of</p>	Noted; as above, recommendation made regarding second-line use of duloxetine.

Organisation	Version	Section/page	Line no.	Comments	Response
				duloxetine to be more cost effective than first line use.	
Eli Lilly and Company Ltd	Full Appendix F	468		<p>The cost-effectiveness model is poorly designed. In particular (see above), the model is designed to assess the cost-effectiveness of duloxetine only as first line treatment. It does not consider the use of duloxetine as a treatment option between PFMT and surgery. Even if the model was designed for the appropriate population, there are the following problems:</p> <ul style="list-style-type: none"> The model tree shown on page 468 is incorrect and does not match the probability parameter table on page 470 (the probability of discontinuing duloxetine between 12 and 52 weeks in the baseline analysis is 0.32, not 0.00) An unrealistic assumption is made that 75% of patients who fail PFMT continue and receive an average reduction in episodes of 27.5%. This appears to be a very high reduction for those deemed to have failed therapy, and leads to a relatively high gain in QALYs for these patients. Another unrealistic assumption is made that all patients who discontinue between 12 and 52 weeks do so as a result of adverse events. This does not match the clinical evidence, which shows that most adverse events occur within the first 12 weeks. This assumption leads to a lower gain in QALYs for these patients (due to the disutility associated with adverse events). 	<p>First bullet point: The observation is correct and we have amended the tree appropriately.</p> <p>Second bullet point: This assumption was adopted from Das Gupta 2006; this same assumption was included in your own submission to the guideline developers - 'those who were unsuccessfully treated with PFMT and continued with a PFE routine were assumed to experience an IEF reduction of 28% (mid-point between 55 and 0% reductions)'.</p> <p>Third bullet point: In the model using baseline data 'most adverse events' do occur within the first 12 weeks – 26% v $(0.32 \times 0.74 = 23.7\%)$</p> <p>Undoubtedly the assumption that all patients who discontinue between 12-52 weeks are due to adverse events is a simplifying one. However, there is an underlying economic rationale for it – that is, that those who discontinue must perceive that the costs (including adverse events) of continuing exceed the benefits (reduction in IEF). For an individual this can be because the adverse event is important and/or the</p>

Organisation	Version	Section/page	Line no.	Comments	Response
					<p>efficacy is limited. The assumption is just a mechanism to ensure that the benefits are cancelled out which seems to make sense given the decision to discontinue.</p> <p>The assumption also should not be considered in isolation. In particular the model also assumes that all patients who continue with duloxetine have no side effects. However, economic theory would predict that patients would continue as long as the benefits exceeded the 'cost'. Therefore, it would be expected that some patients who continue with duloxetine would nevertheless have some adverse effects (disutility). Therefore, this assumption leads to a higher QALY gain for these patients as it doesn't include any disutility associated with adverse event.</p> <p>It seems reasonable to suppose that these simplifying assumptions approximately balance out and therefore we think they can be justified.</p> <p>There is probably one other simplifying assumption that needs to be mentioned here. We've assumed that patients would continue with duloxetine so long as utility > disutility (this seems reasonable in terms of what economics predicts for rational behaviour. However, when patients discontinue I've assumed utility = disutility (i.e. net QALY gain = 0). It's inevitable that for some patients the reason for stopping is more like utility < disutility. We've no</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<ul style="list-style-type: none"> <li data-bbox="651 432 1440 611">• An analysis of the model pathways shows that the patients who fail PFMT but continue therapy receive a higher QALY gain than those who discontinue duloxetine between 12 and 52 weeks. This is driven by the assumption that all duloxetine discontinuation between 12 and 52 weeks is due to adverse events. <li data-bbox="651 834 1440 986">• 50% of patients in each arm achieve a full QALY payoff. However, only 12.5% of PFMT patients receive a zero payoff, compared to 26% of duloxetine patients. This, in combination with the previous point, is the key driver of the lower QALY gain with duloxetine. <li data-bbox="651 1145 1440 1329">• If a lower proportion of failed PFMT patients did not continue, and 0% of duloxetine patients discontinuing between 12 and 52 weeks did so due to adverse events, duloxetine would generate more QALYs than PFMT. In particular, if the analysis is conducted in the second line setting, fewer PFMT patients would continue after failure. <li data-bbox="651 1393 1440 1450">• There is a very rigid definition of “Success” or “Failure” in the PFMT arm of the model. The outcomes vary depending upon 	<p data-bbox="1467 217 1944 395">way of estimating this but we think it is clear that this assumption represents a lower bound estimate for the QALY disutility associated with adverse events. Using a lower bound estimate is a bias in favour of duloxetine.</p> <p data-bbox="1467 432 1944 794">Fourth bullet point: This is a continuation of points made above. QALY gain of those who fail PFMT but continue = Reduction in IEF if PFMT fail/continue x QALY gain if continue = 0.275×0.063 QALY gain of those who discontinue duloxetine (12 - 52 weeks) = Reduction in IEF if duloxetine works x QALY gain if continue x $(32/52) = 0.55 \times 0.063 \times 32/52$</p> <p data-bbox="1467 834 1944 1106">Fifth bullet point: Again this is a continuation of above points. The 12.5% of PFMT patients receiving a zero payoff comes from Das Gupta (2006). The 26% from duloxetine comes from their data on discontinuation in first 12 weeks and my assumption for stopping that utility = disutility</p> <p data-bbox="1467 1145 1944 1353">Sixth bullet point: The proportion of PFMT patients who did not continue has been taken from Das Gupta (2006). The explanation of the assumption about patients who discontinue duloxetine between 12 and 52 weeks is made above.</p> <p data-bbox="1467 1393 1944 1450">Seventh bullet point: Again, taken from Das Gupta (2006).</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>the definition of treatment success used.</p> <ul style="list-style-type: none"> The model is not a Markov model, which removes any element of time spent in various states of health from the analysis. It is important to incorporate time because treatment success and failure have different quality of life impacts in the longer term – the time spent in each of these health states will be a key driver of differences in health outcomes between duloxetine and PFMT. In addition, the exclusion of surgery from the model is problematic. It is always important to delay negative events – this is why discounting is used in economic models. <p>Hence, this model has several serious flaws which reduce its ability to assist decision makers.</p>	<p>Eighth bullet point: Markov models are suitable for diseases where events can occur repeatedly over time (e.g cancer recurrence). They therefore can model patients' movement into different health states over a period of time.</p> <p>Markov models would make a negligible difference to the conclusions of the model, unless waiting times for surgery/physio were factored in. The reasons why we did not want to include waiting times in our model were given in the guideline text.</p> <p>Ninth bullet point: Discounting is used to account for the differential timing of costs and effects, reflecting "time preference" – i.e. people prefer to receive goods and services sooner rather than later.</p> <p>We don't think that it is necessary to include surgery, in effect a comparison of the cost-effectiveness of treatment pathways rather than a comparison of the cost-effectiveness of the treatments.</p>
Eli Lilly and Company Ltd	NI CE			<p>The guideline should clearly state at the outset that the most predominant symptom should be treated in patients with mixed UI (as in the algorithm). Sections 1.2.2.1, 1.2.3.1 and 1.2.4.4 suggest treatments for mixed UI without clearly stating this.</p>	Statement added to recommendation, incorporating your suggestion.
Eli Lilly and Company Ltd	NI CE			<p>References</p> <p>AGREE 2001 Appraisal of Guidelines research and Evaluation Instrument. London: Healthcare Evaluation Unit at St George's Hospital Medical School. http://www.agreecollaboration.org</p>	Noted.

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>Abrams <i>et al.</i> Recommendations of the International Scientific Committee. Incontinence. Third International Consultation on Incontinence. Edition 2005.</p> <p>Das Gupta <i>et al.</i> An Evaluation of the cost-effectiveness of duloxetine as a treatment for women with moderate to severe stress urinary incontinence. Journal of Medical Economics 2006; 9: 1-25</p> <p>Martin ML, Bushnell DM, Das Gupta RJ, Assassa P, Shaw C. Treatments received for stress urinary incontinence (SUI) symptoms by patients seeking help within a UK primary care setting. Poster presented at the International Society For Pharmacoeconomic Research, European Congress, Barcelona. November 2003</p> <p>NICE. Guidance on the use of tension free vaginal tape (Gynecare TVT) for stress incontinence. Technology Appraisal Guidance No.56. London: NICE, February 2003</p> <p>NICE. The Guideline Development Process. An overview for stakeholders, the public and the NHS. London:NICE, February 2004</p> <p>Papanicolaou S, Pons M, Hampel C <i>et al.</i> Medical resource utilisation and cost of care for women seeking treatment for urinary incontinence in an outpatient setting. Examples from three countries participating in the PURE study. Maturitas 2005; 52 Supplement 2:S35-S47.</p> <p>Wagg AS, et al. Secondary care treatment patterns in the UK for women with urinary incontinence. BJU 2005; 96: 839-842</p>	
English Community Care Association				This organisation was approached but did not respond.	-
Faculty of Public Health				This organisation was approached but did not respond.	-

Organisation	Version	Section/page	Line no.	Comments	Response
Ferring Pharmaceuticals Limited	Full	PAGE 85	10-16	<p>Whilst we welcome the inclusion of desmopressin in the guideline we feel it is necessary to reinforce that desmopressin is not licensed for the treatment of urinary incontinence or for the treatment of nocturia in the UK.</p> <p>Ferring did apply to the MHRA to add nocturia to the license for desmopressin. The CSM was unable to approve the application to include the treatment of nocturia associated with nocturnal polyuria in patients up to 65 years of age.</p> <p>In the pivotal trials, the majority of the patients who were included were over 65 years of age and this group of older patients were found to be more susceptible to developing hyponatraemia. Although the application was limited to patients up to 65 years of age, it was assumed that older patients would receive treatment. For example, patients who had been successfully treated up to the age of 65 may naturally wish to continue treatment.</p> <p>The diagnosis and selection of a suitable patient population who would derive a significant benefit from treatment with desmopressin was also considered to be difficult because of the need to establish that the symptom of nocturia was caused by an excessive nocturnal urine production.</p> <p>In summary, although the application was for an indication up to the age of 65 years, the committee considered that the potential risk of side effects in the elderly outweighed the benefit of treating younger patients, up to 65 years of age.</p> <p>Ferring are investigating what the specific risk factors for hyponatraemia are in nocturia patients in the hope that a better defined patient population may improve the risk:benefit of the use of desmopressin in this indication.</p> <p>In some other countries, such as Ireland, the product is approved for this use.</p> <p>In Ireland, Nordurine Tablets are indicated for the symptomatic treatment of nocturia in adults up to 65 years only, associated with nocturnal polyuria, i.e. nocturnal urine production exceeding</p>	<p>Thank you for your comments. We feel that the guideline already makes it clear that desmopressin is not licensed for the treatment of nocturia in the UK for the population considered in this guideline.</p>

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				bladder capacity. But in the UK the product remains unlicensed for the treatment of nocturia.	
Ferring Pharmaceuticals Limited	Full	Page 211-214	211 line 5 through to page 214 line 3	See comment above	See response above.
Ferring Pharmaceuticals Limited	Full	Page 213	6-7	The Hyponatraemia figure given in this line is a combination of male and female. In this long term follow up 14 of 117 women – a rate of just under 12%. The rest of the highlighted events from this trial are for the female patients only, the male figures have not been included. It might be useful to be consistent in using the only the female figures only.	Thank you for this suggestion which we have adopted.
Ferring Pharmaceuticals Limited	Full	212	13-22	Daytime use of desmopressin for urinary incontinence is not a licensed indication. Patients must limit fluid intake to a minimum from 1 hour before taking desmopressin to at least 8 hours after taking desmopressin. This is to avoid potential fluid overload - a potentially serious problem. By using desmopressin during the day it could be difficult to adhere to this important fluid limit.	Agreed. We do not recommend its use for UI.
Fibroid Network Charity				This organisation was approached but did not respond.	-
Galen Limited	Full	86	5-10	It may be worth considering the CNS side-effects of the antimuscarinics which are reported commonly against tertiary amines. Trospium has demonstrated low lipophilicity and therefore negligible penetration of the blood-brain barrier and no known effect on cognitive function. In comparison, antimuscarinics most commonly prescribed (eg. oxybutynin and tolterodine) are tertiary amines, which are lipophilic and have the potential to cross the blood-brain barrier more easily. CNS side effects reported on the Summary of Product Characteristics are very rare for trospium and are reported as frequently as “common” for all tertiary antimuscarinics. Trospium only lists two CNS side effects – headache and dizziness, both reported as very rare.	Thank you for your comments. Other than headache, CNS effects were not reported in trospium studies included in this guideline. We do not know of comparative studies of antimuscarinic drugs focusing on CNS effects in women with UI or OAB. Prescribers should consult the relevant SPCs in making prescribing decisions for individual patients.
Galen Limited	Full	86	5-10	Within Urinary Incontinence the majority of sufferers are elderly. The lack of effect on cognitive function of trospium when compared with the existing antimuscarinics is an important benefit in light of the National Service Framework (NSF) for Older People 2001. Within the NSF the prevention of falls has been identified	Noted.

Organisation	Version	Section/page	Line no.	Comments	Response
				as a key area for review and action and cognitive impairment has been identified as one of the intrinsic factors contributing to falls.	
Galen Limited	Full	86	5-10	<p>Metabolism by the cytochrome P450 (CYP450) system is an important step in the activation or elimination of a large number of drugs, including oxybutynin, tolterodine, and solifenacin, raising the possibility of clinically relevant and potentially serious drug interactions. Trospium is largely excreted unchanged by the kidneys and has no clinically significant influence on the metabolic activities of the cytochrome P450 enzymes in the liver. Therefore, no metabolic drug interactions are expected.</p> <p>In elderly patients, the majority of urge sufferers, such interactions are of particular relevance given the potential for declining activity of certain members of the CYP450 family combined with decreased hepatic blood flow, which can reduce first-pass metabolism. As 51% of patients aged over 65 receive >4 concurrent repeats it would be prudent to consider adverse events due to polypharmacy when prescribing to the elderly. The prevention of adverse reactions has been highlighted in the NSF for Older People and therefore Regurin offers a suitable alternative for patients on polypharmacy. Indeed, many adverse reactions, which are implicated in 5-17% of hospital admissions, could be prevented.</p>	<p>As above.</p> <p>Prescribers should consult the relevant SPCs in making prescribing decisions for individual patients.</p>
Galen Limited	Algorithm	1	Table (OAB +/- Urge UI)	<p>As urge is predominantly seen in the over 65s it may be prudent to consider age-specific issues in line with the National Service Framework (NSF) for Older People 2001. Metabolism by the cytochrome P450 (CYP450) system (trospium has no clinically significant influence on the metabolic activities of the cytochrome P450 enzymes in the liver) unlike oxybutynin, tolterodine, and solifenacin.</p> <p>Also when considering the elderly CNS effects are important to consider. Trospium, unlike oxybutynin, has been found not to impair cognitive function (this may be advantageous when we consider that the majority of urge sufferers will be elderly and, in general, not prone to complain about their medication). A recent study has shown that across all age groups studied, trospium does not increase daytime sleepiness or affect alertness (effect comparable to placebo) as measured by the validated Stanford Sleepiness Scale. In particular, the lack of effect on cognitive function when compared with the existing antimuscarinics is an</p>	<p>We have made reference to data in older patients where relevant throughout the text on antimuscarinic drugs.</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				important benefit in light of the National Service Framework (NSF) for Older People 2001.	
Galen Limited	NICE	12	1.2.4.4	It may be worth considering the CNS side-effects of the antimuscarinics which are reported commonly against tertiary amines. Trospium has demonstrated low lipophilicity and therefore negligible penetration of the blood-brain barrier and no known effect on cognitive function. In comparison, antimuscarinics most commonly prescribed (eg. oxybutynin and tolterodine) are tertiary amines, which are lipophilic and have the potential to cross the blood-brain barrier more easily. CNS side effects reported on the Summary of Product Characteristics are very rare for trospium and are reported as frequently as "common" for all tertiary antimuscarinics.	Other than headache, CNS effects were not reported in trospium studies included in this guideline. Prescribers should consult the relevant SPCs in making prescribing decisions for individual patients.
Gloucestershire Hospitals NHS Trust				This organisation was approached but did not respond.	-
Good Hope Hospitals NHS Trust	FULL & NICE	GENERAL		This is a very welcome report and on the whole is useful pragmatic and well balanced. Sometimes however no evidence for can also mean no evidence available at all although anecdotal experience suggests a useful role.	Thank you for your comments.
Good Hope Hospitals NHS Trust	FULL	147	2-7	Whilst urodynamics investigations may be overperformed and not strictly necessary in cases of clinically pure stress incontinence, many women have a very mixed picture of symptoms and signs especially with increasing age. Also the consequences of performing any sort of incontinence surgery on women with marginal, incomplete or poor voiding can be devastating for the patient and surgeon. Could I suggest that : 1) Free Flow studies should be performed on all women before this type of surgery. Its simple, cheap, non invasive and quick and highlights a group where extreme care is needed. 2) Women with a very mixed or confusing clinical picture should undergo basic cystometry prior to assessing suitability for surgery	The GDG has considered the many comments received regarding the use of urodynamic testing prior to primary surgery for stress UI. We reflected further on the evidence and current practice. We maintain the view that urodynamics investigation is not essential in every woman prior to primary surgery for stress UI, and therefore is not <u>routinely</u> recommended. However, we acknowledge the weight of expert opinion that it is of value in specific circumstances; we have included recommendations as to those circumstances in the guidance.
Good Hope Hospitals NHS Trust	NICE	9	Sect 1/1/10/1	Conclusion as above	-

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Good Hope Hospitals NHS Trust	FULL	227	5-6	I would agree that intra vaginal oestrogens have not been shown to have any value in the treatment of incontinence. As you point out however they can be effective in the treatment of other OAB symptoms such as urge, nocturia, and frequency in the post menopausal age group, and are simple and safe when combined with life style changes. As many women have a mix of symptoms and causation without one overall cure, could you add into the conclusion in both documents "but may be useful in treating other symptoms of the OAB (urge, frequency and nocturia) in the post menopausal age group."	Noted. Recommendation regarding intravaginal oestrogen revised.
Good Hope Hospitals NHS Trust	NICE	12	Sec1/2/4/3	Conclusion as above	
Good Hope Hospitals NHS Trust	FULL	379	9-19	Both of these and the subsequent NICE comments refer to TOT / TVTOs. There has been evidence for sometime that should have been acted upon by any surgeon interested in this field that tapes other than macroporous type 1 meshes should not be used (IVS, Mentor etc). Erosions and rejection are always higher. Similarly the top down approaches are rarely used in the UK. The Trans Obturator approach however has become widely used and the initial NICE guidance was largely positive resulting in further expansion of the technique. Withdrawing this because of ethical problems with one paper did not change the evidence or usage which as recent NICE comments (March 2006) show is growing rapidly and will continue to do so. Having now performed over 1100 TVTs over 9 years and 350 TOTs / TVTOs over 2-3 years using a type 1 mesh the results and lack of complications which we have audited are identical to date. Ease of use and teaching, quicker recovery, increased day cases and less equipment are some positive points in favour of the TOT. The basic problem with these procedures relates to tape material and surgeon experience/ technique. Given a suitable type 1 mesh (TVTO, Monarch) and an experienced surgeon this technique has a definite future. I was encouraged by the recent NICE comments (March 2006) and await the final report with interest. To place Obturator techniques as a group (which are rapidly growing in popularity for good reason and which NICE are seriously assessing) with outmoded meshes and little used techniques (top down, adjustable etc) which are on their way out is	We have separated and revised the recommendations to which you refer.

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				perhaps a little unfair.	
Good Hope Hospitals NHS Trust	NICE	15	Sect 1/3/2/3	Could the comments re other meshes and top down techniques be separate from the obturator comments with reference given to further advice expected soon from NICE.	Please refer to response above; recommendations have been separated.
Guys & St Thomas NHS Trust				This organisation was approached but did not respond.	-
Hampshire Partnership NHS Trust				This organisation was approached but did not respond.	-
Health Protection Agency				This organisation was approached but did not respond.	-
Healthcare Commission				This organisation was approached but did not respond.	-
Heart of England NHS Foundation Trust	Full version	77	11	Needs to be a caveat here. Cystometry is very helpful in someone with an unclear history, continuous passive leakage, etc.	Thank you for your comments. The GDG has considered the many comments received regarding the use of urodynamic testing prior to primary surgery for stress UI. We reflected further on the evidence and current practice. We maintain the view that urodynamics investigation is not essential in every woman prior to primary surgery for stress UI, and therefore is not <u>routinely</u> recommended. However, we acknowledge the weight of expert opinion that it is of value in specific circumstances; we have included recommendations as to those circumstances in the guidance.
Heart of England NHS Foundation Trust	Full version	79	12	How can you determine whether a patient is able to perform a pelvic floor muscle contraction without any form of assessment, inspection or digital examination? Without this, the patient may well be wasting her time. When on review after a period of months she is found not to be able to contract her pelvic floor muscle, there is the risk of disillusionment with physiotherapy.	We have considered your comments and reflected on the limited evidence as to whether pelvic floor muscle assessment prior to PFMT improves outcome. Whilst there is not unanimity on this point, it is clearly widespread expert opinion that the determination of whether a woman can contract her

Organisation	Version	Section/page	Line no.	Comments	Response
					pelvic floor muscles voluntarily may influence the type of treatment. Hence, the GDG has reconsidered its earlier recommendation, and will advise that pelvic floor muscle assessment should be undertaken before embarking on supervised pelvic floor muscle training for the treatment of UI.
Heart of England NHS Foundation Trust	Full version	General		Is there a place for UPPs before secondary surgery?	Please see above.
Heart of England NHS Foundation Trust	Full version	90	22	What is meant by "special arrangements for consent"?	'Special' indicates over and above the norm. We refer to clinical governance and audit.
Heart of England NHS Foundation Trust	Full version	91	20	Is it worth adding 'urethral buttressing' to this list?	This procedure was not identified as being one to consider within the guideline, therefore there are no recommendations regarding its use.
Heart of England NHS Foundation Trust		General		If cystometry is not to be performed routinely before primary surgery for stress UI, the surgery should be performed by a surgeon who has had training in urodynamics. Otherwise there is the danger that we shall have surgeons being able to perform the surgery without being able to appreciate the significance of flow rates, voiding pressures, residuals, quality of investigations, etc.	The recommendations regarding urodynamics have in fact been modified. It should be noted however that the specialist training programmes referred to in the guideline incorporate training to a high level in urodynamics.
Help the Hospices				This organisation was approached but did not respond.	-
Herefordshire Primary Care Trust				This organisation was approached but did not respond.	-
Hertfordshire Partnership NHS Trust				This organisation was approached but did not respond.	-
Hollister Ltd				This organisation was approached but did not respond.	-
Hospital Infection Society				This organisation was approached but did not respond.	-

Organisation	Version	Section/page	Line no.	Comments	Response
Incontact (Action on Incontinence)	Full	General		<p><i>The costings and their assumptions</i> describe a Senior 1 Physio working in a Hospital setting. The paper does not reflect changes in direction with patients being seen in Primary Care rather than Secondary Care linked to the White Paper, Shifting the Balance, Liberating the Talents, Independent Nurse Prescribing and Delivering a Patient led NHS. The Guidelines also seem to miss the whole function of Good Practice Guidelines in Continence Services and Integrated teams with treatment being delivered mainly in primary care. The guideline reads that physio's are the main deliverers of care whilst this is not the truth. This could sway commissioners; PCT's and GP's in their decision-making and their suggestions would greatly change the face of bladder care provision.</p> <p>We recommend that all these assumptions for pelvic floor exercises, bladder re-training, electrical stimulation and biofeedback be made for both Primary Care as first line and Hospital settings second line.</p> <p>We would suggest, as the majority of Nurse Specialists provide this in Primary Care, that it does not just describe a physio but Specialist Physio/Nurse or Consultant Nurse/Therapist with the relevant training and expertise to be decided at a local level.</p> <p>We would like to see the term Continence Advisor changed to Continence Nurse Specialist.</p> <p>The guidelines describe a Senior 1 Physio. This should read Band 6/7 Specialist Nurse/Physio with the relevant accredited training and expertise.</p> <p>Particular equipment is described. Trusts will use these descriptions to dictate what equipment is purchased. You should not specify particular equipment by name, and if you do, you should describe all the available equipment. We suggest you should use an average figure for a stimulator or biofeedback machine without specifying a particular product.</p> <p>Another suggestion could be costing for the full package delivered in Primary Care by both the specialists and the consultants</p>	<p>Thank you for your comments.</p> <p>Good practice in continence services (Department of Health) is referred to in the introduction and in the competence section.</p> <p>The <i>raison d'être</i> of Appendix E was to compare the cost-effectiveness of different treatments, and not the cost-effectiveness of different settings. Nor is it the function of a clinical guideline to give PCTs the cost implications of recommendations, although NICE do a cost impact analysis of the guideline as a supplementary piece of work.</p> <p>The costings need to be interpreted in the light of the caveat given in Appendix E: "Considerable heterogeneity exists within many of the conservative treatments for UI. As far as possible the cost estimates presented here are based on 'standard' or 'typical' treatment (as informed by expert opinion on the GDG) but in practice such a standard may not exist. Therefore, the actual costs of particular conservative treatments will vary according to the actual practice followed."</p> <p>The consultation cost can probably be considered a "sunk cost" and would therefore not be relevant to any treatment path/decision.</p> <p>The title 'continence nurse specialist'</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>(Nursing or Therapy). This costing to include prescribing and prescribing follow up.</p> <p>There should be a further costing on how much this would be if patients were referred directly to Hospital Therapists/Nurses - due to the cost of Tariffs.</p> <p>There should be a further costing, as a comparison, for the full package if a patient is referred directly to a Hospital Medical Consultant, i.e. Urologist, Uro-Gynaecologist, Geriatrician, Gynaecologist with a specialist interest. PCT's need to know all the costing implications in these days of Choose and Book, Payment by Results and GP Commissioning.</p>	has now been used instead of continence advisor.
Incontact (Action on Incontinence)	NICE	4		All patients have a right to confidentiality, and not " <i>unless specifically excluded by the woman, carers and relatives should have the opportunity to be involved in decisions about the woman's care and treatment</i> " A woman should be asked if she agrees to carers and/or relatives being involved of her care and treatment. A woman may not want her condition disclosed to relatives due to fear of embarrassment or rejection. Patients' individual wishes, cultural and faith needs must be respected. The normal rules of consent to any treatment should apply.	Usual arrangements for consent apply. The sentence to which you refer has been deleted.
Incontact (Action on Incontinence)	NICE & Full	General 106	13-14	It should be made clear which treatments are suitable for women who may continue child bearing.	We have incorporated a statement to the recommendation regarding counselling about surgical procedures.
Incontact (Action on Incontinence)	NICE and Full	5, 9, 20 77	11	Assessment & Investigation – MC cystometry, ambulatory UD/ videourodynamics. While understanding the reasons for the GDG view and the need for cost-effective use of resources, it is important that women undergoing an anaesthetic and surgery are made fully aware of expected outcome based on accurate diagnosis. Results of videourodynamics may influence decisions on the type of surgery for SUI. Other patients may be disappointed with outcome due to continuing incontinence due to having mixed incontinence not being identified by not undergoing ambulatory urodynamics, and other tests only suggesting SUI. Evidence used to make decisions on various treatments in the guideline has often been based on studies which positive outcome has been at least partly measured by use of some form of urodynamics. More research in to what affects the accuracy of these useful diagnostic	The GDG has considered the many comments received regarding the use of urodynamic testing prior to primary surgery for stress UI. We reflected further on the evidence and current practice. We maintain the view that urodynamics investigation is not essential in every woman prior to primary surgery for stress UI, and therefore is not <u>routinely</u> recommended. However, we acknowledge the weight of expert opinion that it is of value in specific circumstances; we have included recommendations as to those

Organisation	Version	Section/page	Line no.	Comments	Response
				tools is needed. Is ambulatory UD better at identifying abnormal detrussor activity?	circumstances in the guidance. A statement regarding ambulatory UD and DO is made in the full guideline.
Incontact (Action on Incontinence)	NI CE	6 15		For women not suitable for general or spinal anaesthesia, and for women who may desire to child bear subsequently, intramural bulking agents should be mentioned as a surgical option for SUI	Please refer to the revised recommendation regarding counselling before surgery.
Incontact (Action on Incontinence)	NI CE	7	1.1.4.1	The general expert opinion is that you should treat leucocytes and nitrites etc if the patient has symptoms of frequency and urgency, as these are symptoms of a UTI (but can be interpreted as OAB dry). If you send MSU's on everyone then the labs will be inundated. Also did you know that labs also dipstick samples? We would suggest that you re-look at this whole section and get a microbiologists point of view, as there was no microbiologist on the group.	The recommendations have revised reflecting your concerns, and microbiologist opinion sought regarding culture, and antibiotic use. An explanation for the recommendations is given in the full guideline.
Incontact (Action on Incontinence)	NI CE Full Full	7 & 11-12 109 79 84 111	16-12 17 8	Pelvic floor assessment. The cost of carrying out digital pelvic floor muscle contraction is minimal when carried out as part of the initial examination. It may help identify undiagnosed neurological disease and allow other women to identify the correct muscles. Allowing a patient to waste 3 months unable to carry out PFME correctly is not good care. How do you identify the patients for biofeedback/electrical stimulation?	We have considered your comments and reflected on the limited evidence as to whether pelvic floor muscle assessment prior to PFMT improves outcome. Whilst there is not unanimity on this point, it is clearly widespread expert opinion that the determination of whether a woman can contract her pelvic floor muscles voluntarily may influence the type of treatment. Hence, the GDG has reconsidered its earlier recommendation, and will advise that pelvic floor muscle assessment should be undertaken before embarking on supervised pelvic floor muscle training for the treatment of UI.
Incontact (Action on Incontinence)	NI CE	8	1151	Please describe voiding dysfunction. We would suggest that as well as dribbling and feelings of incomplete voiding they also include frequency and urgency and continual leakage and nocturia. In routine everyday practice you can find residual urines in a lot of women who do not have the cardinal voiding dysfunction signs.	Voiding dysfunction added to glossary.
Incontact (Action on Incontinence)	NI CE Full	8 111	21	If giving advice on UTI, advice should also be given on finding protein, blood and glucose. (basic information given in Full version)	See below regarding protein, blood glucose. The NICE definition for urgent referrals

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		79-81 120 101	80 1 6	Referral – Urgent if this is to rule out cancer it should be stated. Further indications for referral should include all women with haematuria not associated with UTI, and outside of menstrual bleed. Women with recurrent or persisting UTI. Non inclusion suggests they do not need further investigations.	has been added. Recommendations regarding referral based on haematuria are taken directly from the NICE 'Referral guidelines on suspected cancer' (2005). It is the GDG's view that we cannot be more specific than this. We believe that recurrent UTI are covered within the referral criterion 'symptoms of voiding difficulty'.
Incontact (Action on Incontinence)	NICE	8	1161	This will concern some urologists, who do not want to see everyone with microscopic haematuria, as they do not have the staff to deal with the numbers coming through and the dipsticks are notoriously oversensitive. The guideline group need to decide what level of microscopic haematuria should be referred...i.e. 2 plus etc?	Recommendations regarding referral based on haematuria are taken directly from the NICE 'Referral guidelines on suspected cancer' (2005). It is the GDG's view that we cannot be more specific than this.
Incontact (Action on Incontinence)	NICE	9	1162	Associated faecal incontinence - we have been advised that the faecal incontinence guidelines will not be saying this, indeed they will be saying the opposite. Specialist Nurse/Therapists in Primary Care are quite qualified to deal with faecal incontinence. Symptoms of voiding problems. Specialist nurses in Primary Care will usually teach ISC, review and then refer on. Should be assessed by specialist Primary Care Services and then referred if assessed as necessary.	The GDG has discussed your comment. We feel that the wording of the recommendation reflects your concern, in that we recommend consideration rather than mandatory referral to a specialist service.
Incontact (Action on Incontinence)	NICE	10	1221	PFE assessment - have you reviewed Morkved and Bo (1997)? In clinical practice all practitioners will tell you that you cannot teach pfe's without first assessing the pelvic floor. If you teach without assessing how do you know if the woman can do a contraction? If you verbally teach and they can't do a contraction successfully, you are then setting them up to fail and to stop doing them and never come back because they feel guilty. If they are then seen by a physio or nurse for one to one therapy they have then lost all confidence in pelvic floor exercises and it is even harder to get them to believe that they do work. All patients must have a PV, do the research later. This part of the guidance is misinformed.	Please see response above regarding change to the recommendations on pelvic floor muscle assessment.
Incontact (Action on Incontinence)	NICE	11	1225	There is no recommendation of whether electrical stimulation should be used in OAB dry or wet? Can you please rectify this pls?	We have added an evidence statement and recommendation regarding electrical stimulation for OAB.

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Incontact (Action on Incontience)	NI CE	11	1241	In the drugs section you do not mention Frusemide for nocturia/nocturnal polyuria, which is a sign of OAB dry. This omission must be rectified.	We identified one study on furosemide which was excluded as it only enrolled men. Sentence to that effect added to text.
			1243	In line with this you exclude topical HRT for UI but don't mention its use on OAB dry when a post menopausal women has signs of frequency and urgency and uro-genital atrophy...although the group recognise in their script that there is evidence to support its use. This must be added (1.2.4.3).	Noted. Recommendation regarding intravaginal oestrogen revised.
			1244	Concerns have been raised over the use of Oxbutynin Hydrochloride. We agree it is cost effective but patients dislike it (due to its side effects) and don't always continue taking it, many do not come back to get another alternative prescription. The guideline mentions the drugs to use if Oxybutynin Hydrochloride fails. You have missed out Oxybutynin ER (Lyrinel) and this must be added.	We note in the evidence statements for antimuscarinic drugs that oxybutynin IR has a poor tolerability profile compared to other antimuscarinic drugs. However an improved tolerability profile does not necessarily translate into improved persistence with therapy. A long term study of oxybutynin ER (Diokno et al 2002) found that discontinuation attributable to adverse effects was 24%, which is similar to that reported for oxybutynin IR. A transdermal formulation of oxybutynin has been developed to further improve the tolerability profile but no studies have reported on long term tolerability and persistence.
			1245	They also say that Propiverine does not decrease UI but can improve frequency, which is a part of OAB. Since these guidelines are also for OAB dry and wet. Propiverine must also be included as a second line drug.	There is evidence from practice that persistence with antimuscarinic therapy is low (Shaya et al 2005). The difference in drug costs is not trivial with non-proprietary oxybutynin being around 10 times cheaper than other antimuscarinic options. The recommendation on antimuscarinic drugs has been revised to include advice on slow release and transdermal formulations of oxybutynin.
					Propoverine: we believe that this is

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					covered in the recommendation that states 'propiverine should be considered as an option to treat frequency' etc.
Incontact (Action on Incontinence)	NI CE	13	1255	The pad guidelines are excellent and will really help practice.	Thank you.
Incontact (Action on Incontinence)	NI CE Full	13 86	16	Non Interventional therapies – These should aim at maintaining the woman's dignity and enable her and her relatives to continue normal activities of daily living. The patient should be involved in the choice of all products whether catheters /pads or aids. A patient's needs must be regularly reviewed.	Noted.
Incontact (Action on Incontinence)	Full			There is a need to add use of hand held urinals, toileting aids/commodos. Many women with mobility/dexterity difficulties e.g. caused by arthritis have UI due to not being able to reach a toilet. These patients may not need absorbent products or catheters.	We have now included these products and made a recommendation regarding their use.
Incontact (Action on Incontinence)	Full NI CE	88 255 13	1 1	Absorbent Products: it is vital that those patients who require them are provided with them in quantities appropriate to the individually continence needs. Arbitrary ceilings are inappropriate. The supply of pads should not depend on the patient being able to collect them. Women may end up with an indwelling catheter and/ or admitted to a care home as a result of pad rationing and a carer unable to cope. Those on low incomes cannot afford to buy extra.	Noted.
Incontact (Action on Incontinence)		general		Patients and carers should have access to counselling services and be given details of support organisations by their health care professional to help with both long and short term coping strategies.	NICE will produce a version of the guideline for people who use NHS services which will include details of support organisations.
Incontact (Action on Incontinence)	NI CE Full	16 384	1421 1	Incontact welcomes "Competence of surgeons performing operative procedures for urinary incontinence in women". When discussing surgeons experience can you please stipulate that they must also have a record of attending one national and one international conference in the area annually so as to keep up to date with research and practice. We would also like to suggest that all Gynaecologists must have met the requirements and competencies set out in the Uro-gynaecologists sub-speciality training.	Whilst continuing professional development is of relevance to the development and maintenance of surgical skill, and surgeons must of course conform to the standards of good medical practice and good surgical practice (GMC and RCS), the detail of CPD requirements is an issue for the appropriate Royal Colleges and specialist societies.

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		17 General	147	<p>The idea of recommending one surgeon with overall responsibility linked to Integrated services is excellent.</p> <p>It is vital that all women with UI have access to healthcare professionals trained in continence care at all stages of assessment or treatment, and where needed on going care.</p>	<p>At present, the term 'subspecialty training' implies different things in urology (2 years of training following 'core' training) and gynaecology (3 years following training to year 4 SpR level). It is certainly impractical, and probably inappropriate to suggest that all gynaecologists undertaking surgery for incontinence should undergo 3 years additional training. The GDG does however recommend that those undertaking surgery should have appropriate training in the assessment and management of UI and prolapse, or should work within the context of a multidisciplinary team with this training and expertise. We also indicate that existing surgeons should be able to demonstrate that their training, experience and current practice equates to the standards laid out for newly trained surgeons.</p> <p>We note your comments regarding other healthcare professionals. However, the competence of health professionals other than surgeons is outwith the scope of the guideline.</p>
Incontact (Action on Incontinence)	Full version	64	11	<p>National Service Framework for Older People (DH 2001) needs adding to the list as it has a major importance on Integrated continence care (pg 38) in Good Practice in Continence Care for all patients. The 2005 RCP audit on integrated continence services should also be considered.</p> <p>SIGN Urinary Incontinence Guidelines 2004 (updated 2005).</p>	<p>The NSF for Older People has been added to the list of other relevant documents.</p> <p>We have not listed the SIGN guideline because of differences in the scope of the guidelines.</p>
Incontact (Action on Incontinence)	Full version	59	9	<p>Costs to patient does not take account of the financial cost of absorbent products (many women buy their own, or have to supplement those rationed by PCTs) laundry and associated short life of clothing, linen and floor coverings. A patient with moderate/severe incontinence may spend in excess of £30/week</p>	<p>Sentence added.</p>

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				on pads.	
Janssen-Cilag Ltd	Full	77 78 250	21-22 1-3 4-9	<p>The Drug Recommendation Fails to Adequately Incorporate Extended-Release Oxybutynin in the Treatment Pathways</p> <p>In several parts of the document, including the summary of recommendations, non-proprietary immediate-release (IR) oxybutynin is recommended as the first line drug treatment for women with overactive bladder (OAB). Other products such as tolterodine and trospium are specifically recommended as possible second line treatment options. However this guidance fails to adequately consider use of oxybutynin extended release (ER) as a treatment option.</p> <p>The failure to include oxybutynin ER as a treatment option is important because there is robust clinical and economic evidence demonstrating that oxybutynin ER is a valuable treatment option for patients with OAB. This fact is acknowledged in section 4.4.4, but these findings are not captured in the summary of recommendations or the summary of section 4.4.4. Specifically:</p> <ul style="list-style-type: none"> • Oxybutynin ER has similar efficacy, but a superior tolerability profile, to oxybutynin IR (Barkin <i>et al</i>, 2004; Birns <i>et al</i>, 2000; Versi, 2000; Anderson <i>et al</i>, 1999). This is important because side effects are an important treatment limiting factor with oxybutynin IR. Clinical trials demonstrate that oxybutynin ER provides the efficacy of oxybutynin with the benefits of lower rates of treatment limiting adverse events. • Evidence suggests oxybutynin ER improves the quality of life of patients with improved treatment compliance due the once daily dosing and improved tolerability (Diokno <i>et al</i>, 2002; Tuttle & Antoci, 2000). • Oxybutynin ER is more effective than tolterodine ER (Diokno <i>et al</i>, 2003) in terms of the following: <ul style="list-style-type: none"> ○ A significantly higher percentage of patients reported total dryness when taking oxybutynin ER compared to tolterodine ER ○ Oxybutynin ER was significantly more effective than tolterodine ER in reducing micturition frequency • Oxybutynin ER is more effective than tolterodine IR (Appell <i>et</i> 	<p>Thank you for your comments. We note in the evidence statements for antimuscarinic drugs that oxybutynin IR has a poor tolerability profile compared to other antimuscarinic drugs. However an improved tolerability profile does not necessarily translate into improved persistence with therapy. A long term study of oxybutynin ER (Diokno et al 2002) found that discontinuation attributable to adverse effects was 24%, which is similar to that reported for oxybutynin IR. A transdermal formulation of oxybutynin has been developed to further improve the tolerability profile but no studies have reported on long term tolerability and persistence.</p> <p>There is evidence from practice that persistence with antimuscarinic therapy is low (Shaya et al 2005).</p> <p>The difference in drug costs is not trivial with non-proprietary oxybutynin being around 10 times cheaper than other antimuscarinic options. The recommendation on antimuscarinic drugs has been revised to include advice on slow release and transdermal formulations of oxybutynin. Furthermore, good prescribing practice requires that patients be reviewed when starting on new pharmacological treatment and therefore the costs of switching from a poorly tolerated drug are, at least partly, subsumed within this review process.</p>

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				<p><i>al, 2001</i>). At the end of the study (adjusting for baseline) patients taking oxybutynin ER, compared to tolterodine IR, experienced:</p> <ul style="list-style-type: none"> ○ Significantly less weekly urge incontinence episodes (p=0.03) ○ Significantly less total incontinence episodes (p=0.02) ○ Significantly lower micturition frequency (p=0.02) <ul style="list-style-type: none"> • Oxybutynin ER has a similar tolerability profile to tolterodine IR and ER (Appell <i>et al</i>, 2001; Diokno <i>et al</i>, 2003). • Oxybutynin ER is cheaper than both preparations of tolterodine. <p>Based on the available evidence, oxybutynin ER should be included as a first-line treatment option, alongside oxybutynin IR prior to use of the other products such as tolterodine.</p>	The outcomes listed from the Appell 2001 study are discussed in the guideline text.
Janssen-Cilag Ltd	Full	77/78 247 248 249 250	21-22/1-3 15-23 1-23 2-8 4-9	<p><u>The guidance fails to consider the cost-effectiveness evidence</u></p> <p>In the economic evidence section of 4.4.4 the conclusion is that oxybutynin ER is a cost-effective treatment, economically dominating oxybutynin IR and both formulations of tolterodine. However, this evidence fails to be considered in the drug recommendations where oxybutynin ER has been excluded.</p> <p>The key points for consideration are that:</p> <ul style="list-style-type: none"> • The evidence provides a strong argument on cost-effectiveness grounds for oxybutynin ER to be offered as a first line treatment alongside non-proprietary oxybutynin IR and ahead of other treatments such as tolterodine (Getsios <i>et al</i>, 2004(a); Getsios <i>et al</i>, 2004(b); Guest <i>et al</i>, 2004; Arikian <i>et al</i>, 2000). • Oxybutynin ER is either equivalent or superior in terms of efficacy compared to tolterodine (Appell <i>et al</i>, 2001; Diokno <i>et al</i>, 2003). • Oxybutynin ER is significantly cheaper than other branded products such as tolterodine and solifenacin. • Overall, oxybutynin ER: <ul style="list-style-type: none"> ○ <i>'dominated standard tolterodine, being at least as</i> 	<p>The 'conclusion' that oxybutynin ER is cost-effective is that of the studies, not necessarily this guideline.</p> <p>The strength of the argument made in the first bullet is questionable. In a 2005 review of economic evaluations of pharmacological management of overactive bladder Getsios <i>et al</i>. commented:</p> <p>"While there has been a fair amount of economic research on treatment for OAB, the economic implications of these treatments have not been established definitively....</p> <p>...the comparison among the IR and long acting formulations of oxybutynin and tolterodine have been inconclusive, with conflicting results. These differences result almost entirely from the sources of data used to estimate</p>

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				<p><i>cheap and more efficacious'</i> (lines 6-7; <ul style="list-style-type: none"> ○ <i>'dominated standard oxybutynin in addition to ER tolterodine'</i> (lines 7-8; Guest <i>et al</i>, 2004; Arikian <i>et al</i>, 2000) <p>We strongly suggest that the cost-effectiveness evidence substantiates the use of oxybutynin ER as a first line treatment option alongside IR and we recommend this should be incorporated into the overall drug recommendation.</p> </p>	<p>effectiveness and rates of discontinuation, and the selection of these data may be influenced by the funding sources for the economic analyses...</p> <p>...The limited head-to-head clinical studies suggest that differences among the drugs in terms of effectiveness are small. No reliable data are available on the relative long-term performance of these drugs in real-world settings, and this is likely to be a key determinant of cost-effectiveness, given the similarities in short-term effectiveness...</p> <p>...many of the economic modelling efforts have relied on rates of treatment discontinuation reported in clinical trials, sometimes without accounting for the large differences in rates of premature discontinuation reported in trials compared with actual practice..</p> <p>....To date, however, reliable data on the relative performance of available pharmacological agents in actual practice are lacking."</p>
Janssen-Cilag Ltd	Full	231/2		<p>The summary of evidence reports the results of the placebo-controlled trials conducted for oxybutynin IR, but fails to include the available evidence for oxybutynin ER. A separate section has been included for tolterodine ER on page 237.</p> <ul style="list-style-type: none"> • A double-blind, placebo-controlled trial has been conducted to assess the efficacy and safety of oxybutynin ER and IR (Schmidt, 1998). This showed that over a six-week study period oxybutynin ER had a significantly greater mean reduction in number of weekly urge urinary incontinence episodes than placebo (92% vs 45% respectively, p<0.001). • A significantly higher percentage of patients achieved 	<p>We did not systematically search for, nor include grey literature in this guideline. The Schmidt paper you refer to here is a poster from 1998.</p>

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				<p>continence when taking oxybutynin ER compared to placebo (50% vs 13%, p=0.003).</p> <p>We therefore recommend that a section is included reporting the efficacy benefits of oxybutynin ER in a placebo-controlled trial setting for consistency.</p>	
Janssen-Cilag Ltd	Full	240	2,10,17	<p>The evidence reported refers to oxybutynin but does not make it clear that this relates to oxybutynin IR and not ER.</p> <ul style="list-style-type: none"> It is important to clarify that oxybutynin IR and oxybutynin ER are different formulations and the outcomes may vary when using the different treatments. <p>We recommend that it should be made clear which preparation of oxybutynin the evidence refers to and this should be reflected in section headings.</p>	We have clarified which preparation of oxybutynin was used in studies.
Janssen-Cilag Ltd	Full	244	20-22	<p>The results reported indicate there were no significant differences found between oxybutynin ER and tolterodine ER. However, even though oxybutynin ER and tolterodine ER were found not to be significantly different in terms of the primary outcome measure, episodes of urge urinary incontinence, the evidence fails to show that when compared to tolterodine ER, oxybutynin ER was found to be significantly better on the secondary outcome measures, reduction in micturition frequency and percentage of patients achieving total dryness.</p> <p>Although oxybutynin ER is similar to tolterodine ER on some efficacy measurements, it is significantly better on others. The following highlights the key results from the OPERA study (Diokno <i>et al</i>, 2003) that have been excluded:</p> <ul style="list-style-type: none"> A significantly higher percentage of patients taking oxybutynin ER reported total dryness compared to tolterodine ER (23% versus 16.8% respectively, p=0.03). The trial reported that oxybutynin ER was significantly more effective than tolterodine ER in reducing micturition frequency (p=0.003). <p>We recommend this evidence be included in this section to provide a balanced summary of the results from this clinical trial</p>	<p>There were no significant differences in <i>changes in</i> leakage episodes– this has been clarified in the text.</p> <p>Percentage reporting total dryness added to evidence table.</p>

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				comparing oxybutynin ER and tolterodine ER.	
Janssen-Cilag Ltd	Full	244	22-23	<p>This section reports evidence from the OPERA study (Diokno <i>et al</i>, 2003) including two other studies, stating that dry mouth occurred significantly more often in oxybutynin ER patients compared to tolterodine ER patients. This fails to acknowledge the non-significant difference in the percentage of patients experiencing moderate to severe dry mouth (results from the OPERA study: 7.4% (oxybutynin ER) versus 5% (tolterodine ER), ns).</p> <p>The level of severity of dry mouth is a likely indicator for discontinuation of treatment. Those patients experiencing moderate to severe dry mouth are more likely to discontinue. This is supported by the definitions of level of severity of dry mouth used in the OPERA study:</p> <ul style="list-style-type: none"> • Those patients classified as having moderate to severe dry mouth experience a significant change to their daily activities as well as the possible to likely need for an intervention. • Whereas mild dry mouth is classified as not requiring intervention and not significantly changing daily activities. <p>We recommend this result is included in the evaluation of the tolerability results from the OPERA trial to provide a balanced summary of the evidence when comparing oxybutynin ER and tolterodine ER.</p>	Data given in evidence tables.
Janssen-Cilag Ltd	Full	246	2-8	<p>This evidence compares transdermal and oral oxybutynin. But it fails to clarify this is a comparison against oxybutynin IR and not ER.</p> <ul style="list-style-type: none"> • Currently there is no available evidence comparing transdermal oxybutynin with oxybutynin ER. <p>We propose that it be made clear this evidence relates to oxybutynin IR and not ER in both the title and the main body of the text.</p>	Preparation of oxybutynin clarified in the text.
Janssen-Cilag Ltd	Full	246 247	11-23 1-7	<p>The evidence reported is based on four double-blinded RCTs comparing oxybutynin ER with IR. However one other RCT comparing oxybutynin ER with IR has not been included in the</p>	We did not systematically search for, nor include grey literature in this guideline. The Schmidt paper you refer

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>evidence (Schmidt, 1998).</p> <p>This trial provides additional evidence showing the following:</p> <ul style="list-style-type: none"> The mean reduction in weekly urge urinary incontinence episodes was 92% for oxybutynin ER and 72% for oxybutynin IR. The percentage of patients achieving continence after six weeks was 50% for oxybutynin ER compared to 28% for oxybutynin IR. Oxybutynin ER was significantly higher than placebo for both efficacy measurements. Significantly less patients reporting dry mouth in the oxybutynin ER group compared to IR (p=0.05). <p>We recommend the results from this trial should be included in the overall evaluation of the comparison between the two preparations of oxybutynin.</p>	to here is a poster from 1998
Janssen-Cilag Ltd	Full	247	1-3	<p>It is stated that two studies (Barkin <i>et al</i>, 2004 and Birns <i>et al</i>, 2000) reported no significant differences in efficacy or adverse effects between ER and IR. The Barkin <i>et al</i> (2000) paper also reports patient's views on the tolerability of the two treatments and this has not been included.</p> <p>Barkin <i>et al</i> (2000) reports the following:</p> <ul style="list-style-type: none"> A significantly greater number of patients rated their medication more tolerable when taking oxybutynin ER than those taking oxybutynin IR (p<0.02) This result suggests that patients taking oxybutynin ER may have improved compliance due to its once daily formulation and less moderate to severe dry mouth. <p>We propose this evidence on patient's views on tolerability of oxybutynin ER should be included to provide an overall evaluation of oxybutynin ER in comparison to oxybutynin IR.</p>	Comment added to evidence table.
Janssen-Cilag Ltd	Full	247	3-4	<p>This reports the incidence of dry mouth to be significantly lower in patients taking oxybutynin ER compared to IR (68% versus 87% respectively, p=0.04). Whilst this is correct, the significant difference in the percentage of patients reporting moderate to</p>	<p>'Significantly' added to text.</p> <p>We have not focused on severity of dry mouth – while we acknowledge such</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>severe dry mouth between oxybutynin ER and IR has been ignored.</p> <p>Although overall tolerability is important, patients experiencing moderate to severe dry mouth are more likely to discontinue treatment, therefore this is extremely important to also consider this sub-group when assessing tolerability. The results from Anderson <i>et al</i> (1999) report the following:</p> <ul style="list-style-type: none"> Patients taking oxybutynin ER experienced significantly less moderate to severe dry mouth than patients taking IR (25% versus 46% respectively, p=0.03). <p>We recommend this analysis be incorporated into the comparison between the tolerability of the two preparations of oxybutynin to provide an overall and balanced view of tolerability.</p>	<p>data exist in clinical trials, such data would only be useful if it predicts withdrawal from therapy in clinical practice. As stated above, evidence from practice suggests that persistence with all antimuscarinic therapy is low.</p>
Janssen-Cilag Ltd	Full	247	4-7	<p>The evidence summarised here reports the overall rates of dry mouth of 47.7% and 59.1% for oxybutynin ER and IR respectively. This difference is based on Versi <i>et al</i> (2000), and was found not to be significantly different (p=0.09). In addition, the evidence appears to summarise, in lines 5 –7, the cumulative percentage of patients reporting any dry mouth. This is reported to be significantly lower in the oxybutynin ER group versus the IR group (p=0.003). However, the summary of evidence does not include the incidence of first reported moderate to severe dry mouth.</p> <p>As mentioned previously, the severity of the dry mouth is a likely predictor for discontinuation of treatment and therefore should be the focus in terms of assessing tolerability. Important points requiring consideration are as follows:</p> <ul style="list-style-type: none"> This paper is primarily investigating the difference in the incidence of dry mouth between the two treatments. The incidence of first reported moderate to severe dry mouth is significantly different between oxybutynin ER and oxybutynin IR (p=0.007). <p>We propose the evidence based on this paper is expanded to include the significant differences in the first reported incidence of moderate to severe dry mouth between the two preparations of</p>	<p>Please refer to responses above.</p>

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				oxybutynin.	
Janssen-Cilag Ltd	Full	244 246 247	7-15 10-23 1-7	<p>The tolerability comparison between tolterodine IR and oxybutynin ER and oxybutynin ER and IR fails to include evidence from a randomised, double blind, crossover study comparing oxybutynin ER, tolterodine IR and oxybutynin IR (Chancellor <i>et al</i>, 2001).</p> <p>The evidence from this study should be incorporated for the following reasons:</p> <ul style="list-style-type: none"> • All three treatments had not been studied in a controlled setting before • This is the first study to evaluate dry mouth as measured by saliva output • Oxybutynin ER was significantly associated with greater saliva output compared to oxybutynin IR ($p < 0.01$) • The overall result found that oxybutynin ER and tolterodine were found to be similar with respect to dry mouth but were associated with less dry mouth than oxybutynin IR. <p>We recommend this evidence is incorporated to support the differences between oxybutynin ER and IR along with the similarity between oxybutynin ER and tolterodine IR</p>	This study was excluded because it was conducted in healthy volunteers and only evaluated single doses of treatment; it does not meet the inclusion criteria for consideration of effectiveness of these treatments in women with UI or OAB.
Janssen-Cilag Ltd	Full	247	9-13	<p>The results summarised are based on a long-term open label study of oxybutynin ER (Diokno <i>et al</i>, 2003). They relate to the Individual Incontinence Impact Questionnaire, which shows there was significantly less impact on lifestyle and sleep at one year compared to baseline ($p < 0.001$). Whilst these results are important further evidence on quality of life based on the General Health and Bother Scale have not been included.</p> <p>Quality of life is an important issue in patients with OAB and there is evidence suggesting that OAB affects emotional and physical well-being ultimately having a profound impact on quality of life which may lead to a limitation of activities, negative self-image and feelings of loss of control (Diokno <i>et al</i>, 2002). Key points are as follows:</p> <ul style="list-style-type: none"> • Significant improvements on the General Health and Bother Scale were found in patients taking oxybutynin ER at 3, 9 and 	We considered condition-specific quality of life scales in preference to generic scales. Quality of life data are reported in the text of the full guideline.

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>12 months (p<0.001).</p> <ul style="list-style-type: none"> 93% of patients would recommend oxybutynin ER to others. These results are based on a large study involving over 1,000 patients and provides substantial evidence that oxybutynin ER is a well tolerated, efficacious product which improves the quality of life of patients with OAB. <p>We recommend this more detailed analysis of the impact on quality of life should be included in the evaluation of this paper due to the potential impact of OAB on sufferers.</p>	
Janssen-Cilag Ltd	Full	247	12-13	<p>Further to the above, other important quality of life data appear to have been omitted.</p> <ul style="list-style-type: none"> Tuttle & Antoci (2000) showed that patients experienced significantly less bothersomeness of OAB when taking oxybutynin ER over one year. 65.9% of the under 65s, 61.2% of 65-74 year olds and 54.8% of 75+ years rated oxybutynin ER as a treatment which worked well, very well or excellently at 6 months. <p>We recommend this evidence should be incorporated in the overall evaluation of the impact on quality of life in patients taking oxybutynin ER.</p>	We did not systematically search for, nor include grey literature in this guideline. The Tuttle paper you refer to here is an abstract.
Janssen-Cilag Ltd	Full	249 250	22-23 1	<p>It is stated that dry mouth is more likely with oral oxybutynin than tolterodine, trospium or transdermal oxybutynin. This fails to make it clear that oral oxybutynin refers to the IR preparation and not ER.</p> <ul style="list-style-type: none"> There is evidence to suggest that oxybutynin IR causes more dry mouth than trospium and transdermal oxybutynin, however there is no evidence comparing oxybutynin ER with these two products. There is evidence comparing oxybutynin ER and tolterodine. <ul style="list-style-type: none"> The incidence of dry mouth was found to be similar between the two treatments (Appell et al, 2001) The percentage of patients experiencing any dry mouth was higher in patients taking oxybutynin ER group compared to tolterodine ER but the percentage experiencing moderate to severe dry 	We have clarified which preparation of oxybutynin (and other antimuscarinic drugs) studies evaluated in the text.

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>mouth was not significantly different between the two treatments.</p> <p>We recommend this evidence is summarised in two clear sentences. The first comparing oxybutynin IR with tolterodine, trospium and transdermal oxybutynin and the second comparing oxybutynin ER with both preparations of tolterodine.</p>	
Janssen-Cilag Ltd	Full	250 77 78	4-9 21-22 1-3	<p>The guidance states <i>'Treatment with non-proprietary oxybutynin should be offered as first-line antimuscarinic drug treatment to women with OAB or mixed UI. If oxybutynin is not well tolerated, solifenacin, tolterodine or trospium may be considered as alternatives'</i>. This fails to include oxybutynin ER as a treatment option.</p> <p>Oxybutynin ER should be included as a treatment option because of the following:</p> <ul style="list-style-type: none"> • There is a clear cost-effectiveness argument suggesting oxybutynin ER should be a first line treatment as it dominates oxybutynin IR and tolterodine. • Even when assuming all products have equivalent efficacy oxybutynin ER should feature as the first second line choice after oxybutynin IR before tolterodine and the other branded products due to its lower cost. • This overall drug treatment guidance should reflect the clinical and economic benefits of taking oxybutynin ER over IR and other products such as tolterodine. <p>We recommend the guidance be changed to the following:</p> <p><i>'Treatment with oxybutynin IR or oxybutynin ER should be offered as first-line antimuscarinic drug treatments to women with OAB or mixed UI. If oxybutynin is not well tolerated, solifenacin, tolterodine or trospium may be considered as alternatives'</i>.</p>	We have revised this recommendation to include advice on oxybutynin ER.
Janssen-Cilag Ltd	NICE	12	Section 1.2.4.4	As above	Recommendation has been revised.
Janssen-Cilag Ltd	Treatment			<p>As above</p> <p>Oxybutynin ER is not mentioned in the OAB ± Urge UI box.</p> <ul style="list-style-type: none"> • There is clear cost-effective evidence showing that oxybutynin 	Recommendation has been revised.

Organisation	Version	Section/page	Line no.	Comments	Response
	algorithm			ER dominates both oxybutynin IR and tolterodine. Oxybutynin ER should be specifically mentioned as a treatment option	
Janssen-Cilag Ltd	Evidence tables	765/6		The evidence from the Diokno <i>et al</i> (2003) study does not include the significantly higher percentage of patients achieving total dryness of 23% for oxybutynin ER compared to 16.8% for tolterodine ER ($p=0.03$). <ul style="list-style-type: none"> It is important to report that oxybutynin ER is significantly better than tolterodine ER in the percentage of patients achieving total dryness. <p>We recommend this result should be included in the evidence tables to provide an overall comparison between the two treatments.</p>	This information has been added to the evidence tables.
Janssen-Cilag Ltd				References Anderson R, <i>et al</i> . Once daily controlled versus immediate release oxybutynin chloride for urge incontinence. <i>Journal of Urology</i> 1999; 161:1809-1812 Appell RA <i>et al</i> . Prospective randomized controlled trial of extended release oxybutynin chloride and tolterodine tartrate in the treatment of overactive bladder: Results of the OBJECT study. <i>Mayo Clin Proc</i> 2001; 76: 358-363 Arikian SR <i>et al</i> . A pharmacoeconomic evaluation of two new products for the treatment of overactive bladder. <i>Managed Care Interface</i> 2000; 13:(2)88-94. Barkin J <i>et al</i> . A randomised, double-blind, parallel-group comparison of controlled and immediate release oxybutynin chloride in urge urinary incontinence. <i>Clin Ther</i> 2004 26(7): 1026-1036 Birns J <i>et al</i> . A randomised controlled trial comparing the efficacy of controlled-release oxybutynin tablets (10mg once daily) with conventional oxybutynin tablets (5mg twice daily) in patients	Noted.

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>whose symptoms were stabilised on 5mg twice daily of oxybutynin. <i>BJU International</i> (2000), 85, 793-798</p> <p>Chancellor M <i>et al.</i> A comparison of the effects on saliva output of oxybutynin chloride and tolterodine tartrate. <i>Clin Ther</i> 2001 23(5):753-760</p> <p>Diokno A <i>et al.</i> Prospective randomised double-blind study of the efficacy and tolerability of the extended-release formulations of oxybutynin and tolterodine for overactive bladder: results of the OPERA trial. <i>Mayo Clin Proc</i> 2003; 78:687-695</p> <p>Diokno A <i>et al.</i> Long-term safety of extended release oxybutynin chloride in a community dwelling population of participants with overactive bladder: A one year study. <i>J Urol & Neph</i> 2002 34; 43-49</p> <p>Getsios D <i>et al.</i> Oxybutynin extended release and tolterodine immediate release: A health economic comparison. <i>Clinical Drug Investigation</i> 2004; 24:(2)81-8. (a)</p> <p>Getsios D <i>et al.</i> Canadian economic comparison of extended release oxybutynin and immediate-release tolterodine in the treatment of overactive bladder. <i>Clin. Ther.</i> 2004; 26:(3)431-8. (b)</p> <p>Guest JF <i>et al.</i> Cost effectiveness of controlled-release oxybutynin compared with immediate-release oxybutynin and tolterodine in the treatment of overactive bladder in the UK, France and Austria. <i>Clinical Drug Investigation</i> 2004; 24:(6)305-21.</p> <p>Schmidt RA. <i>Efficacy of controlled-release once-a-day oxybutynin chloride for urge urinary incontinence. Study C-95-031, 28th ICS meeting, Jerusalem 1998</i></p> <p>Tuttle J and Antoci J. <i>Controlled-release oxybutynin for overactive bladder in an elderly population. J Am Geriatr Soc, 2000; 48(8): S49 (abstract number P155)</i></p> <p>Versi E <i>et al.</i> Dry mouth with conventional and controlled-release oxybutynin in urinary incontinence. <i>Obst & Gyn</i> 95(5): 718-721</p>	

Organisation	Version	Section/page	Line no.	Comments	Response
Johnson & Johnson Medical	Both	General		<p><u>An introduction to our comments:</u></p> <p><i>We are providing feedback on the section 'Surgery for Stress Urinary Incontinence' within the draft guidance:</i></p>	
Johnson & Johnson Medical	Full	378 379	13-23 1-19	<p>The section concludes all mid urethral slings using “bottom up” retropubic approach and a “macroporous (type 1) mesh” are safe and effective. We believe this statement to be flawed as it assumes evidence on all type 1 slings is inter-changeable. (<i>Slack et al 2004¹</i>) (<i>Weinberger & Ostergard, 1995²</i>)</p> <p>By definition, any monofilament polypropylene mesh is Type 1, according to Amid’s classification system (<i>Amid, 1997³</i>). However, there is no evidence that one type of polypropylene mesh will perform the same as any other, due to key differences in the biomechanical properties which are determined by the type of polymer, nature of fibres, weight and porosity (<i>Ward & Hilton, 2002⁴</i>). In addition to the biomechanical properties, insertion method and placement determine the clinical outcome (<i>Slack et al 2004¹</i>)</p> <p>As noted in the evidence table supporting the Full Guidance, efficacy of differing meshes vary greatly. The safety and efficacy of Gynecare TVT (the only device considered in the Technology Appraisal no 56), has not been reproduced in clinical studies by any other type of polypropylene mesh and there is no convincing evidence of equivalence. Evidence from good quality randomized studies supporting the long-term efficacy and safety of Gynecare TVT™ are not therefore indicative of all “macroporous, type 1 mesh” and are not transferable. (<i>Siegel et al, 2005⁵</i>) (<i>Yildirim et al, 2004⁶</i>). This is supported by previous guidance published by the Royal College of Obstetricians and Gynaecologists (RCOG-2003) which states: “<i>There is a need for long-term results for this procedure. It must be emphasised that newer slings based on similar technology to Gynecare TVT, but using different materials, do not have the some evidence base and should be subjected to RCT’s</i>”</p>	<p>Thank you for your comments. We have classified tapes into distinct groups as far as possible, using characteristics known or strongly suspected to influence outcome.</p> <p>The Ward & Hilton paper is a clinical RCT of TVT and colposuspension, it does not look at the effect of tape characteristics. The Slack paper is an abstract, and not identified as a peer-reviewed publication; we have not searched ‘grey literature’.</p>
Johnson & Johnson Medical	NICE	15	1.3.2.2	The recommendation inappropriately assumes that the evidence available for Gynecare TVT™ can be applied to all devices. Since the quality of evidence is variable and length of follow up is	We have indicated in the text that the abbreviation TVT refers to Gynecare TVT™.

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>inadequate for many type 1 meshes, we suggest that your recommendation make reference to the desired evidence that should be available for such devices, such as evidence with long-term outcome data showing efficacy of >80%. This is considered appropriate as many of these devices have now been available for a number of years, and therefore evidence supporting the longer term durability of these devices (rather than simply 12 month efficacy data) should now be expected, considering the length of time patients can expect to live with such implants.</p> <p>We consider that the recommendation be revised to reflect the evidence base available, and suggest an alternative recommendation 1.3.2.2 of:</p> <p>“Retropubic mid-urethral tape procedures using a "bottom up" approach with macroporous (type 1) polypropylene mesh, are recommended as treatment options where conservative management has failed. The selection of an appropriate tape should consider the properties of the mesh utilised and be supported by RCT evidence of efficacy and long term outcome data demonstrating maintained efficacy rates in excess of 80% after at least 5 years follow-up.”</p>	
Johnson & Johnson Medical	Full	334	12	<p>We would like to draw your attention to evidence that has not been considered in the draft Clinical Guideline, and which has emerged since the publication of this draft Clinical Guideline and the last version of the NICE Interventional Procedure Guideline on “Transobturator foramen procedures for Stress Urinary Incontinence”.- references 7 – 14 below.</p> <p>The evidence refers to the inside-out approach using the Gynecare TVT-O device. In particular, the evidence from the randomized study by Liapis et al⁷ concludes that efficacy of the Gynecare TVT-O inside-out procedure is equivalent to that of Gynecare TVT after a minimum follow-up of 12 months, thus demonstrating the equivalence in outcomes between the ‘inside-out’ approach and the current clinical standard of care.</p>	The Liapis study you refer to (reference 7 in your list) has been reviewed and is now included in the guideline. Other publications listed are either abstracts or not yet available as full publications.
Johnson & Johnson Medical	NICE	15	1.3.2.3	We recognize the need for long-term clinical evidence for surgical procedures using the trans-obturator approach. We also note that this recommendation is consistent with the proposed Interventional Procedure Guideline on “Transobturator Foramen Procedures for	Noted.

Organisation	Version	Section/page	Line no.	Comments	Response
				Stress Urinary Incontinence”.	
Johnson & Johnson Medical	Both	General		<p>Potential ‘generic use’ of trademark terminology.</p> <p>We request that the terms “TVT” and “Tension Free Vaginal tape” when referring to our specific product, are used in the proper trademark form, ie Gynecare TVT™. Please note this is the only marketed sub urethral sling that uses the terms “Tension Free Vaginal Tape” in its product description. TVT is recognised as Gynecare TVT™ and we would prefer that NICE make this distinction in their discussion of the evidence as the RCT evidence pertaining to Gynecare TVT™ and subsequent follow up data are not transferable between implants for the reasons stated above. This issue was discussed and agreed with the Institute in 2003 before the publication of NICE Guidance no. 56. At that time, it was agreed that references to Gynecare’s product would be quoted as ‘Gynecare TVT’, and that generic references to the class would be quoted as ‘suburethral slings’. We see no reason for this to change in the clinical guideline.</p> <p>The use of Gynecare TVT should not be contentious, as other device trademarks are used in the document, such as page 334 where the brand name SPARC is referred to and page 353 where SAFYRE is used. Other instances can be found throughout this section of the full guidance.</p>	Where relevant we have used TVT to indicate where this specific brand was used in studies. We have added a statement to the text that TVT refers to Gynecare TVT™.
Johnson & Johnson Medical				<p>References</p> <ol style="list-style-type: none"> 1 Slack MC et al (2004) Suburethral slings – are all mesh types the same? In: Abstracts of the 34th Meeting of the ICS; August 23-27. Paris, France Abstract 682 2 Weinberger MW, Ostergard DR. Long-term clinical and urodynamic evaluation of the polytetrafluoroethylene suburethral sling for treatment of genuine stress incontinence. <i>Obstet Gynecol</i> 1995;86:92–96. 3 Amid PK. Classification of biomaterials and their related complications in abdominal wall hernia surgery. <i>Hernia</i> 1997;1:15–21. 4 Ward KL, Hilton P. Prospective multicentre randomised trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence. <i>BMJ</i> 2002; 325: 	Noted.

Organisation	Version	Section/page	Line no.	Comments	Response
			5	67-70 Siegel AL; Kim M; Goldstein M; Levey S; Ilbeigi P (2005) High incidence of vaginal mesh extrusion using the intravaginal slingplasty sling. J Urol 174(4 Pt 1):1308-11	
			6	Yildirim A, Basok Ek, Gulpinar T, Gurbuz C, Zemheri E, Tokuc R (2005) Tissue Reactions Of 5 Sling Materials And Tissue Material Detachment Strength Of 4 Synthetic Mesh Materials In A Rabbit Model The Journal Of Urology November (Vol. 174, Issue 5, Pages 2037-2040)	
Johnson & Johnson Medical				New evidence on 'inside-out' obturator approach	Please refer to comments above.
			7	Liapis A, Bakas P, Giner M, Creatsas G. Tension-Free Vaginal Tape versus Tension-Free Vaginal Tape Obturator in Women with Stress Urinary Incontinence. Gynecol Obstet Invest 2006; 62:160–164	
			8	De Leval J, Waltregny D. New Surgical Technique for Treatment of Stress Urinary Incontinence TVT-Obturator: New Developments and Results. Surgical Technology International 2005;14:212-21.	
			9	Waltregny D, Reul O, Mathantu B, Gaspar Y, Bonnet P, de Leval J. Inside-out transobturator vaginal tape (TVT-O): results of a prospective study after a minimum follow-up time of 1 year. Presented at International Continence Society, 2005.	
			10	Neuman M. TVT and TVT-Obturator: Comparison of two operative procedures. Eur J Obstet Gynecol Reprod Biol. 2006 Apr 16 [E-publication]	
			11	Raders JL, Lucente VR, Murphy M. Transobturator TVT (TVT-O) "inside-out" suburethral sling for the treatment of stress urinary incontinence (SUI): early clinical experience. IUGA 2005.	
			12	Cordeiro A, Sabbo MJ, Costa M, Martins P, Moniz L. Transobturator suburethral tape in female stress urinary incontinence: comparison of results with outside-in and inside-out procedures. IUGA 2005	
			13	Ryu K, Shin J, Du J, Choo M, Lee K. Randomized trial of tension-free vaginal tape (TVT) vs. Tension-free Vaginal Tape Obturator (TVT-O) in the surgical treatment of stress urinary incontinence: comparison of operation related morbidity. Abstract EAU 2005.	

Organisation	Version	Section/page	Line no.	Comments	Response
			14	Lim JL, Quinlan DJ. Safety of a new Transobturator suburethral synthetic sling (TVT-O) procedure during the training Phase J Obstet Gynaecol Can 2006;28(3):214–217	
King George's Hospital NHS Trust				This organisation was approached but did not respond.	-
Kingston Primary Care Trust				This organisation was approached but did not respond.	-
Knowsley Primary Care Trust				This organisation was approached but did not respond.	-
Leeds Teaching Hospitals NHS Trust				This organisation was approached but did not respond.	-
Liverpool Women's Hospital NHS Trust				This organisation was approached but did not respond.	-
Long Term Medical Conditions Alliance				This organisation was approached but did not respond.	-
Luton and Dunstable Hospital NHS Trust				This organisation was approached but did not respond.	-
Maternity Health Links				This organisation was approached but did not respond.	-
Medicines and Healthcare Products Regulatory Agency (MHRA)				This organisation was approached but did not respond.	-
Medtronic Europe Sarl				This organisation was approached but did not respond.	-

Organisation	Version	Section/page	Line no.	Comments	Response
Medtronic Limited				Overall Medtronic consider the guideline to be a good representation of the management of urinary incontinence. We have only two comments related to the treatment algorithm.	Thank you for your comments.
Medtronic Limited				1. Where primary surgery options are considered for stress urinary incontinence we believe ACT should be included. Medtronic submitted data to the institute on this which appears to have not been fully considered. ACT is CE marked for use in the UK, is minimally invasive and clinically effective. On this basis we believe it should be included in the treatment algorithm.	As stated in the full guideline ACT was not considered because NICE IPAC guidance exists which states that the procedure should not be undertaken without special arrangements for consent and for audit and research. This approach was also explained in the method section of the guideline.
Medtronic Limited				2. In principle, Medtronic do not disagree with Botox being included in the guideline despite it not being licensed for use for this indication in the UK. We do however strongly believe that the clause currently included that it should only be used in the context of clinical research should remain in the guideline.	Noted.
Mid Staffordshire General Hospitals NHS Trust				This organisation was approached but did not respond.	-
Multiple Sclerosis Society	Full	General		PLEASE can abbreviations be written out in full – there are many abbreviations within this document, many of which are quite specialised making it more difficult for non- urological specialists to read easily.	Thank you for your suggestion. The list of abbreviations is given at the beginning of the document.
Multiple Sclerosis Society	Full	56	2	Do these prevalence figures refer to the general population, an elderly population etc.? Prevalence within some sectors of the population will be much higher and will differ widely between different sectors of the population	Figures are given for severe incontinence in women over and under 65 years of age.
Multiple Sclerosis Society	Full	58	2	This would read easier if colour ways of the two figures corresponded i.e. so that same colour is used to represent the same thing in both	This is not possible because the figures refer to different aspects of incontinence.
Multiple Sclerosis Society	Full	59	1	Whilst not included within this guidance it is important to highlight the fact that neurological conditions such as MS pre dispose to urinary incontinence, this may be a presenting symptom of MS	Sentence added.
Multiple Sclerosis Society	Full	99	2	Some mention of undiagnosed neurological conditions such as MS should be made as urinary Incontinence may be a presenting problem	This is covered under general history within the assessment section.
Multiple	Full	107	5	Key relationships should be defined; potential problems with	Sentence added in history section.

Organisation	Version	Section/page	Line no.	Comments	Response
Sclerosis Society				sexual function should be raised and addressed via referral to ... - this subject needs to be flagged up as something to be raised with patients	
Multiple Sclerosis Society	NICE	4		It needs to be made clear early within the guidance that this doesn't refer to Neurological conditions	This is covered in section 2 of the NICE version.
Multiple Sclerosis Society	NICE	General		Please no abbreviations – particularly in this version	Only universally accepted abbreviations are used in the NICE version.
National Childbirth Trust				This organisation was approached but did not respond.	-
National Council for Disabled People, Black, Minority and Ethnic Community (Equalities)				This organisation was approached but did not respond.	-
National Patient Safety Agency				This organisation was approached but did not respond.	-
National Public Health Service - Wales				This organisation was approached but did not respond.	-
Newcastle PCT				This organisation was approached but did not respond.	-
Newcastle Upon Tyne Hospitals NHS Trust				This organisation was approached but did not respond.	-
Newham Primary Care Trust				This organisation was approached but did not respond.	-
NHS Direct				This organisation was approached but did not respond.	-
NHS Health and Social Care Information				This organisation was approached but did not respond.	-

Organisation	Version	Section/page	Line no.	Comments	Response
Centre					
NHS Quality Improvement Scotland				This organisation was approached but did not respond.	-
Norgine Ltd				This organisation was approached but did not respond.	-
North Essex Mental Health Partnership				This organisation was approached but did not respond.	-
North Tees and Hartlepool NHS Trust				This organisation was approached but did not respond.	-
North Tyneside Primary Care Trust				This organisation was approached but did not respond.	-
Northumberland Care Trust				This organisation was approached but did not respond.	-
Northwest London Hospitals NHS Trust				This organisation was approached but did not respond.	-
Nottingham City Hospital				This organisation was approached but did not respond.	-
Nottingham City PCT	Full	77	2.2	It is recommended that first line treatment for OAB is oxybutinin. This is often not tolerated by patients due to Adverse drug reactions and has been associated with causing an increase in cognitive dysfunction in older people.	Thank you for your comments. The GDG has reconsidered the evidence in this area, along with comments from several stakeholders. We note in the evidence statements for antimuscarinic drugs that oxybutynin IR has a poor tolerability profile compared to other antimuscarinic drugs. However an improved tolerability profile does not necessarily translate into improved persistence with therapy. A long term study of oxybutynin ER (Diokno et al 2002) found that discontinuation attributable to adverse effects was 24%, which is similar to that reported for oxybutynin IR. A transdermal

Organisation	Version	Section/page	Line no.	Comments	Response
					<p>formulation of oxybutynin has been developed to further improve the tolerability profile but no studies have reported on long term tolerability and persistence.</p> <p>There is evidence from practice that persistence with antimuscarinic therapy is low (Shaya et al 2005).</p> <p>The difference in drug costs is not trivial with non-proprietary oxybutynin being around 10 times cheaper than other antimuscarinic options. The recommendation on antimuscarinic drugs has been revised to include advice on slow release and transdermal formulations of oxybutynin.</p>
Nottingham City PCT	Full	79	3.3	It is a shame that Digital vaginal examination is not recommended as part of the assessment.	This recommendation has been revised (see below for further information).
Nottingham City PCT	Full	79	44.3	Intravaginal oestrogens do not seem to have evidence of efficacy, but in practise reduce Stress urinary incontinence and mixed incontinence.	The recommendation regarding intravaginal oestrogens has been revised.
Nottingham City PCT	Full	84	8	Guideline state that a minimum eight pelvic floor contractions should be performed but this should be based on patient ability also.	We feel that the recommendation made is appropriate and the reasons are explained in the text.
Nottingham City PCT	Full	105	2	Bowel history. The guideline states that women with faecal incontinence may require referral for management of this problem. As coexisting bladder and bowel symptoms are common it is very likely that the treating practitioner can manage both symptoms and only require referral with inadequate outcome from initial assessment and treatment.	The GDG has discussed your comment. We feel that the wording of the recommendation reflects your concern, in that we recommend consideration rather than mandatory referral to a specialist service.
Nottingham City PCT				Most continence practitioners are very capable of assessing and treating faecal incontinence.	Noted.
Nottingham City PCT	Full	109	14	Pelvic floor assessment is essential to check correct technique and is not just an indicator of outcome. There is some evidence to show that verbal instruction is insufficient in 49% of patients to assure correct technique and could be detrimental in 25%. (Bump 1991).	We have considered your comments and reflected on the limited evidence as to whether pelvic floor muscle assessment prior to PFMT improves outcome. Whilst there is not unanimity on this point, it is clearly widespread

Organisation	Version	Section/page	Line no.	Comments	Response
					expert opinion that the determination of whether a woman can contract her pelvic floor muscles voluntarily may influence the type of treatment. Hence, the GDG has reconsidered its earlier recommendation, and will advise that pelvic floor muscle assessment should be undertaken before embarking on supervised pelvic floor muscle training for the treatment of UI.
Nottingham City PCT				It is essential to determine at initial assessment those patients that require biofeedback and/ or electrical stimulation or other treatment to activate the pelvic floor. This should be done at first visit so not to waste 3 months of both patient and practitioner time in assuming technique is correct for 3 months as is suggested in the guideline. The best way of establishing this is digital assessment of the pelvic floor. All patients should receive this assessment.	We have revised the recommendation regarding pelvic floor muscle assessment.
Nottingham City PCT	Full	111	2	States that digital assessment of the pelvic floor is not necessary prior to pelvic floor training.	We have revised the recommendation regarding pelvic floor muscle assessment.
Nottingham City PCT	Full	111	8	States that digital assessment of the pelvic floor may determine whether a patient can contract their pelvic floor and therefore direct further treatment.	We have revised the recommendation regarding pelvic floor muscle assessment.
Nottingham City PCT				The above points appear to contradict one another.	We have revised the recommendation regarding pelvic floor muscle assessment.
Nottingham City PCT	Full	196	11	The CSP Clinical guidelines for the management of stress urinary incontinence (2001) recommend that pelvic floor muscle training should be continued for 15-20 weeks after correct technique is established. this is based on muscle training principles and maximum muscle hypertrophy. Is the 3 months stated in the guideline long enough to give maximum benefit from pelvic floor training? Could it lead to inappropriately early referral for surgical review?	Your comments have been considered by the GDG, which is satisfied with a 3 month trial.
Nottingham City PCT	Full	197	2	There is no mention of the use of electrical stimulation for the treatment of OAB in the guideline.	We have added an evidence statement and recommendation regarding electrical stimulation for OAB.
Nottingham City PCT	Full	398	18	The recommendation that there should be a nominated clinical lead for continence surgery and that this lead should work within	Noted.

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				an integrated continence service is to be applauded. A great recommendation.	
Nottingham City PCT	Full	Appendix E	447 onwards	<i>Costing first line conservative treatments</i> The costings for pelvic floor muscle training are based on a physiotherapist in secondary care, as there is an increasing shift of these services into primary care the costings for a practitioner in primary care would be a useful comparison. This is in conflict with the recommendations made in the Good Practice in Continence services and integrated continence service goals.	The 'conflict' presumes there is an implicit preference for secondary care because of how labour costs were calculated. The labour cost is illustrative and there is no implicit preference for services delivered in any setting
Nottingham City PCT				The guidance states a senior I physiotherapist. This should read band 6/7 physiotherapist/ practitioner.	As above; the labour cost is illustrative and there is no implicit preference for services delivered in any setting.
Nottingham City PCT	Full	General		It is a shame the emphasis appears to be so secondary care based. This guideline should be in accordance with other publications notably Good Practice in Continence services. This seems a missed opportunity.	Good practice in continence services is cited under other relevant documents.
Novartis Pharmaceuticals UK Ltd	Full	77-8	21-3	Darifenacin should be included as an alternative to treatment with non-proprietary oxybutynin.	Thank you for your comments. Recommendation made regarding darifenacin.
Novartis Pharmaceuticals UK Ltd	Full	250	5-8	Darifenacin should be included as an alternative to treatment with non-proprietary oxybutynin.	Recommendation made regarding darifenacin.
Novartis Pharmaceuticals UK Ltd	Full	228-229	10-10	As described in section 1.7, the literature search strategy targeted the identification of relevant published evidence to inform the guideline development process and answer the clinical questions reproduced in Appendix B. It includes evidence published and included in the databases used in the search until 17 March 2006. Appendix B states that the effectiveness of conservative techniques for the treatment of UI or OAB in women include aspects such as benefits and unwanted effects. Therefore, Novartis believe that additional relevant publications supporting the efficacy and safety of darifenacin that were not identified in the literature search should be included as clinical evidence for the preparation of the guidelines. These publications demonstrate: - that darifenacin was efficacious in the treatment of symptoms of OAB, well tolerated, and associated with an incidence of nervous and cardiovascular system adverse events comparable to placebo, including in the older patient; ^{1,2}	Thank you for your suggestions. Please refer to comments below regarding the studies you cite.

Organisation	Version	Section/page	Line no.	Comments	Response
				<ul style="list-style-type: none"> - that the safety and efficacy profiles, including in older patients, were sustained in the long-term treatment of OAB with darifenacin, as demonstrated in a two-year open-label extension study;^{3,4,5} - that darifenacin has efficacy comparable to oxybutynin IR in both urodynamic and clinical endpoints while associated with a lower impact on the secretion of saliva and lower incidence of dry mouth;^{6,7} - that darifenacin was shown not to cause cognitive impairment in healthy younger and older subjects against placebo in three published studies, including one with oxybutynin SR as comparator;^{8,9,10} - that darifenacin in doses up to 75 mg does not cause prolongation of the QTc interval compared to placebo.¹¹ 	
Novartis Pharmaceuticals UK Ltd				<p>SUPPORTING REFERENCES:</p> <ol style="list-style-type: none"> 1. Chapple C, Steers W, Norton P, Millard R, Kralidis G, Glavind K, Abrams P. A pooled analysis of three phase III studies to investigate the efficacy, tolerability and safety of darifenacin, a muscarinic M3 selective receptor antagonist, in the treatment of overactive bladder. <i>BJU Int.</i> 2005;95:993-1001. 2. Foote J, Glavind K, Kralidis G, Wyndaele JJ. Treatment of overactive bladder in the older patient: pooled analysis of three phase III studies of darifenacin, an M3 selective receptor antagonist. <i>Eur Urol.</i> 2005;48:471-7. 3. Steers W, Dwyer P, Gittelman M, Lheritier K, Kawakami F. Long-term tolerability and safety of darifenacin demonstrated in a 2-year extension study in patients with overactive bladder. Presented as a non-discussion poster at the meeting of the International Continence Society, Montreal, Canada. 28 August to 2 September 2005:A141 http://www.continet.org/publications/2005/PDF/0141.PDF 4. Steers W, Dwyer P, Gittelman M, Lheritier K, Kawakami F. Efficacy of darifenacin in a 2-year long-term extension study in patients with overactive bladder. Presented as a non-discussion poster at the meeting of the International Continence Society, Montreal, Canada. 28 August to 2 	<p>References 1, 2, were reviewed and excluded because the source of original trial data was not referenced.</p> <p>References 3, 4, 5 are abstracts. We did not systematically search for, nor include grey literature.</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>September 2005:A149 http://www.continet.org/publications/2005/PDF/0149.PDF</p> <p>5. Haab F, Hill S, Lheritier K, Kawakami FT, Gittelman M. Long-term treatment of overactive bladder with darifenacin in older patients: analysis of responder rates in a 2-year, open-label extension study. Poster presented at the 21st European Association of Urology Annual Congress, 2006, Paris, France. <i>European Urol Suppl</i> 2006;5:117. Abstract 378.</p> <p>6. Chapple CR, Abrams P. Comparison of darifenacin and oxybutynin in patients with overactive bladder: assessment of ambulatory urodynamics and impact on salivary flow. <i>Eur Urol</i>. 2005;48:102-9.</p> <p>7. Zinner N, Tuttle J, Marks L. Efficacy and tolerability of darifenacin, a muscarinic M3 selective receptor antagonist (M3 SRA), compared with oxybutynin in the treatment of patients with overactive bladder. <i>World J Urol</i>. 2005;23:248-52.</p> <p>8. Kay GG, Wesnes KA. Pharmacodynamic effects of darifenacin, a muscarinic M selective receptor antagonist for the treatment of overactive bladder, in healthy volunteers. <i>BJU Int</i>. 2005;96:1055-62.</p> <p>9. Lipton RB, Kolodner K, Wesnes K. Assessment of cognitive function of the elderly population: effects of darifenacin. <i>J Urol</i>. 2005;173:493-8.</p> <p>10. Kay G, Crook T, Reveda L, Lima R, Ebinger U, Arguinzoniz M, Steel M. Differential Effects of the Antimuscarinic Agents Darifenacin and Oxybutynin ER on Memory in Older Subjects. <i>Eur Urol</i>. 2006 Apr 19; [Epub ahead of print]</p> <p>11. Serra DB, Afrime MB, Bedigian MP, Greig G, Milosavljev S, Skerjanec A, Wang Y. QT and QTc interval with standard and suprathreshold doses of darifenacin, a muscarinic M3 selective receptor antagonist for the treatment of overactive bladder. <i>J Clin Pharmacol</i>. 2005;45:1038-47.</p>	<p>Reference 6 was excluded because the duration of the study was 7 days only which was considered too short to evaluate effectiveness.</p> <p>Reference 7 was also excluded because of the short duration of the study (2 weeks).</p> <p>References 8 to 10 are not eligible because the population does not have UI or OAB.</p> <p>Reference 11; this is not eligible because it reviewed 7 days treatment in healthy volunteers.</p>
Novartis Pharmaceuticals UK Ltd	NI CE	5	3 rd para	Darifenacin should be included as an alternative to treatment with non-proprietary oxybutynin.	Recommendation made regarding darifenacin.

Organisation	Version	Section/page	Line no.	Comments	Response
Novartis Pharmaceuticals UK Ltd	NICE	12	1.2.4.4	Darifenacin should be included as an alternative to treatment with non-proprietary oxybutynin.	Recommendation made regarding darifenacin.
Novartis Pharmaceuticals UK Ltd	Algorithm	1	OAB +/- urge UI	Darifenacin should be included as an alternative to treatment with non-proprietary oxybutynin.	Recommendation made regarding darifenacin.
Novo Nordisk Limited	NICE version	12	1.2.4.3	"Intravaginal oestrogen preparations and systemic hormone replacement therapy are not recommended for the treatment of UI" despite the fact that a significant improvement in incontinence symptoms have been shown in a number of RCTs (see below for specific comments). Whilst intravaginal oestrogen preparations are an off-licence indication, the success of such treatments suggests consideration should be given to their usage. These products are non-invasive, low-cost, low-risk and improve patient quality of life.	Thank you for your comments. The recommendation regarding intravaginal oestrogens has been revised.
Novo Nordisk Limited	Full version	221	20-23	An RCT of intravaginal oestrogen: "...reported significantly greater subjective improvement of incontinence with intravaginal estradiol compared to placebo at six months (68% vs 16%, n=88) ³⁴⁶ "	The recommendation regarding intravaginal oestrogens has been revised.
Novo Nordisk Limited	Full version	222	8-10	The results of one RCT comparing two intravaginal preparations: "Responder rates across all outcomes ranged from 51% to 61% and cure rates from 27 to 44% (n=251) ³⁵¹ [EL=1+]"	The recommendation regarding intravaginal oestrogens has been revised.
Novo Nordisk Limited	Full version	222	14-15	A placebo controlled RCT of intravaginal oestrogen: "The prevalence of UI and frequency/nocturia fell to a greater extent with an intravaginal estradiol tablet than with placebo at 1 year (UI prevalence 18% vs 10%; frequency/nocturia 38% vs 10%) ³⁵⁴ "	The recommendation regarding intravaginal oestrogens has been revised.
Novo Nordisk Limited	Full version	222	19-22	Another placebo controlled RCT of intravaginal oestrogen: "Significantly more women who had urological symptoms (41% to 53%) reported improvement in symptoms (frequency, dysuria, urge or stress UI) with intravaginal 17-beta-estradiol vs placebo after 3 months treatment (63% vs 32%, n=164) ³⁵⁸ "	The recommendation regarding intravaginal oestrogens has been revised.
Oxfordshire Mental Healthcare NHS Trust				This organisation was approached but did not respond.	-
Parkinson's Disease Society				This organisation was approached but did not respond.	-

Organisation	Version	Section/page	Line no.	Comments	Response
Pembrokeshire and Derwen NHS Trust				This organisation was approached but did not respond.	-
PERIGON (formerly The NHS Modernisation Agency)				This organisation was approached but did not respond.	-
Peterborough & Stamford NHS Hospitals Trust				This organisation was approached but did not respond.	-
Pfizer Limited	Full version	General		<p>We welcome the development of a national guideline on urinary incontinence and OAB, as this is a positive step in raising awareness of these debilitating and embarrassing conditions. Patients are often hesitant to approach or access medical help to treat symptoms, and in some cases, sufferers can take up to several years to seek medical help.</p> <p>A patients' perception of their bladder condition is highly individual to that patient. As such, it is important to uncover what the patient thinks and their goals for therapy before selecting the most appropriate treatment. As it stands this guideline fails to adequately reflect that all types of treatment, conservative, behavioural and drug therapy have an equal part to play in tailoring treatment to the individual.</p>	Thank you for your comments.
Pfizer Limited	Full version	General		<p>Evidence supporting antimuscarinic drug therapy has been inconsistently and inappropriately interpreted within the guideline. This leads to a recommendation for non-proprietary oxybutynin to be prescribed first line in women with OAB and mixed UI as it is the cheapest. We believe this recommendation to be detrimental to long term patient care and not in the best interests of women suffering with this condition.</p> <p>Physicians are in the best position to discuss individual patient needs and tailor treatments to optimise patient care. Issues such as tolerability, compliance, quality of life, and long term benefits are important attributes that differ between available antimuscarinics and formulations. These differences are clinically and economically meaningful and should not be ignored to enforce all women to try a potentially inferior treatment option. Furthermore the choice of antimuscarinic drug therapy in combination with physical or behavioural interventions should be</p>	<p>Thank you for your comments. The GDG has reconsidered the evidence in this area, along with comments from several stakeholders.</p> <p>We note in the evidence statements for antimuscarinic drugs that oxybutynin IR has a poor tolerability profile compared to other antimuscarinic drugs. However an improved tolerability profile does not necessarily translate into improved persistence with therapy. A long term study of oxybutynin ER (Diokno et al 2002) found that discontinuation attributable to adverse effects was 24%, which is similar to that reported for oxybutynin IR. A transdermal</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>evidence based. By recommending non-proprietary oxybutynin as first line treatment, all recommendations that state the use of antimuscarinic therapy become statements for oxybutynin regardless of whether or not the evidence base included oxybutynin. It is unreasonable to make recommendations based on the totality of evidence for antimuscarinics and then restrict to first line oxybutynin treatment across all recommendations.</p> <p>We emphasise that all antimuscarinics that are shown to be effective and cost-effective should be recommended treatment options. A full economic assessment is required if differentiation between antimuscarinics and formulations is to be meaningful.</p>	<p>formulation of oxybutynin has been developed to further improve the tolerability profile but no studies have reported on long term tolerability and persistence.</p> <p>There is evidence from practice that persistence with antimuscarinic therapy is low (Shaya et al 2005).</p> <p>The difference in drug costs is not trivial with non-proprietary oxybutynin being around 10 times cheaper than other antimuscarinic options. The recommendation on antimuscarinic drugs has been revised to include advice on slow release and transdermal formulations of oxybutynin. Furthermore, good prescribing practice requires that patients be reviewed when starting on new pharmacological treatment and therefore the costs of switching from a poorly tolerated drug are, at least partly, subsumed within this review process.</p>
Pfizer Limited	Full version	121	11-16	<p>“ • ICI-Q, BFULTS, SUIQQ, for combined evaluation of symptoms and QOL impact of UI • I-QOL, SEAPI-QMM, KHQ, IIQ, IIQ-7, UISS, and CONTILIFE for evaluation of QOL impact of UI • QAB-Q, UDI, UDI-6, ISI, BFLUTS for combined evaluation of symptoms and QOL impact of OAB”</p> <p>The listed instruments have been validated within differing subsets of UI, it may be more valuable to demonstrate which instruments are appropriate for use within SUI, MUI and OAB populations as these areas are also the remit of the guideline. Within the evidence presented only the OABq has been validated to show a QOL impact of OAB. The other instruments listed were validated within UI populations only.</p>	<p>The GDG has discussed your comments in relation to OABq. We believe that the reasons for not recommending OABq are clear in the text, and do not believe that a change in the recommendation is warranted.</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				OABq should be recommended as it is the only tool validated for an OAB population.	
Pfizer Limited	Full version	124	Table 6	<p>The table provides the evidence for why the OABq has been excluded from recommendation of use. This decision has little scientific rationale. The evidence for the OABq showed all items of the questionnaire to be highly correlated when assessed via Spearman' Rank – the scores range between 0.8 and 0.94 and are comparable to the correlation scores presented for other tools subsequently recommended for use.</p> <p>The rationale for excluding the OABq appears to be based upon the fact the symptom bother scores measured within this tool fell between test and retest. Although the change was shown to be significant (p=0.01) the clinical relevance of this change is unclear. It has been hypothesised that symptom bother is likely to vary depending upon activities e.g. the frequent need to urinate may be more bothersome when travelling than when at home all day. In addition the complexity of symptoms associated with OAB could mean that symptom bother appropriately changes over time.</p> <p>The OABq is a valid tool with high correlation and should be recommended for use in an OAB population.</p>	The GDG has discussed your comments in relation to OABq. We believe that the reasons for not recommending OABq are clear in the text, and do not believe that a change in the recommendation is warranted.
Pfizer Limited	Full version	126	9-11	<p>"The following incontinence-specific quality of life scales are recommended when therapies are being evaluated: ICIQ, BFLUTS, I-QOL, SUIQQ, UISS, SEAPI-QMM, ISI and KHQ."</p> <p>Clarification is requested as to why the GDG chose to reduce the list of tools regarded by the ICI to be Grade A. The three tools (UDI, IIQ and OABq) not listed are all considered to be highly recommended in terms of their validity, reliability and responsiveness. As it stands this recommendation conflicts with ICI's professional assessment of these tools.</p>	The GDG has discussed your comments in relation to OABq. We believe that the reasons for not recommending OABq are clear in the text, and do not believe that a change in the recommendation is warranted.
Pfizer Limited	Full version	172	16-17	<p>"Four enrolled women with stress UI, and one included women with stress or mixed UI"²²⁴</p> <p>The identified study (ref 224) by Burns et al only included 12 women with mixed UI out of 135 women randomised (8.9%). The objective of the study was clearly stated as an evaluation of treatments for sphincteric incompetence. No results or conclusions were provided specifically for women with mixed UI.</p>	The proportion of women with mixed UI in the included studies is detailed in the evidence tables and included in the text of the full guideline where relevant.

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>It appears that this is the only evidence supporting the benefit of pelvic floor exercises for women with mixed UI.</p> <p>The proportion of women with mixed UI should be clearly stated.</p>	
Pfizer Limited	Full version	174	10-12	<p>“At 5 years in women with stress, mixed or urge UI (those with stress or mixed undergoing PFMT) 69% reported improvement compared with pre-treatment”²²⁷</p> <p>From the study by Largo-Janssen (ref 227) the treatment for women with mixed UI was PFMT initially followed by bladder training. Women with mixed UI only represented 18% (20/110) of the original 3 month trial.</p> <p>Only the results for stress UI are relevant to this section of the guideline.</p> <p>The statement should be clarified and PFMT referenced to stress UI only.</p>	The proportion of women with mixed UI in the included studies is detailed in the evidence tables and included in the text of the full guideline where relevant.
Pfizer Limited	Full	193	2-3	<p>“Daily PFMT is an effective treatment for stress or mixed UI compared with no treatment over the short-term”</p> <p>No evidence has been provided for the effectiveness of PFMT for mixed UI. Only one study included women with mixed UI treated with PFMT (ref 224). This study was designed specifically for sphincteric incompetence and no results were provided or would be meaningful for the 12 women (8.9%) with mixed UI.</p> <p>The evidence statement should be restricted to stress UI only or clarified that no data was available specifically for mixed UI.</p>	The proportion of women with mixed UI in the included studies is detailed in the evidence tables and included in the text of the full guideline where relevant.
Pfizer Limited	Full version	193	14-16	<p>“There is no additional benefit from the use of PFMT in patients undergoing treatment with tolterodine for OAB, and more side effects associated with the use of antimuscarinic drug therapy”</p> <p>This statement appears to be based on the clinical trial by Millard (ref 239) and provides evidence grade EL=1++. However, the trial was designed as tolterodine plus PFMT versus tolterodine alone; therefore, the side effects within this trial were comparable between the arms (9.7% vs 9.1% respectively).</p> <p>If the statement is referring to more side effects with tolterodine therapy versus PFMT, no evidence has been presented for this comparison.</p>	The paragraph summarising this study has been revised, and the statement regarding side effects deleted.

Organisation	Version	Section/page	Line no.	Comments	Response
				The reference to “more side effects” should be clarified with an appropriate grade of evidence.	
Pfizer Limited	Full version	196	11-12	<p>“A trial of supervised pelvic floor muscle training of at least 3 months’ duration should be offered to women with stress of mixed UI as first-line treatment. [A]”</p> <p>There is no specific evidence provided for the effectiveness of PFMT for mixed UI.</p> <p>The recommendation should be restricted to stress UI based on the grade [A] evidence base evaluated.</p>	The proportion of women with mixed UI in the included studies is detailed in the evidence tables and included in the text of the full guideline where relevant.
Pfizer Limited	Full version	196	11-12	<p>“A trial of supervised pelvic floor muscle training of at least 3 months’ duration should be offered to women with stress or mixed UI as first-line treatment. [A]”</p> <p>There is no indication for the appropriate trial duration of treatment, particularly for mixed UI. The only study with any women with mixed UI included had a treatment period of 8 weeks.</p> <p>The 3 month trial period is based upon the GDG opinion from the clinical trials of stress UI and therefore should be restricted to stress UI and graded accordingly.</p>	We have considered your comments and are satisfied that the reasons for our recommendation are detailed in both the physical therapies and the optimal sequence sections.
Pfizer Limited	Full	197	6	<p>“Research recommendations for physical therapies”</p> <p>There is clear need for evidence of the effectiveness and cost-effectiveness of physical therapies versus drug therapy or in combination with drug therapy. No evidence has been provided as to whether drug therapy plus physical therapies is better than physical therapy alone.</p>	See section 4.4.1
Pfizer Limited	Full version	209	11-14	<p>“Bladder training had a similar subjective cure rate to oxybutynin after a 6-week programme, but side effects and relapse rates were lower with bladder training.”</p> <p>It appears that this statement is based on evidence from Colombo et al (ref 300). It should be clarified that this study provides evidence for bladder training versus oxybutynin for women with urge UI only and should not be applied to all UI.</p>	Clarified.
Pfizer Limited	Full	209	14-17	“The combination of antimuscarinic drugs and bladder training programmes may result in greater reduction in frequency of	

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>micturition, but has not been shown to lead to further improvements in incontinence.”</p> <p>The only trial identified for antimuscarinic drugs in combination with bladder training versus bladder training alone was an oxybutynin trial (ref 302). This one trial did not show any further improvements in incontinence.</p> <p>There is an absence of any evidence for tolterodine in combination with bladder training versus bladder training alone – therefore there is no evidence of the absence of any improvements in incontinence for tolterodine <i>versus bladder training alone</i>.</p> <p>The statement should be clarified to specifically state that oxybutynin has evidence of combination therapy that has not been shown to lead to further improvements versus bladder training alone. This is not true for tolterodine or other antimuscarinic drugs.</p>	<p>We have clarified that the evidence relates to oxybutynin and tolterodine.</p>
Pfizer Limited	Full version	209	14-17	<p>“The combination of antimuscarinic drugs and bladder training programmes may result in greater reduction in frequency of micturition, but has not been shown to lead to further improvements in incontinence.”</p> <p>The quoted trial by Mattiasson et al (ref 305) for tolterodine does not address the question as to whether combination therapy is better than bladder training alone. This trial shows that combination therapy with tolterodine is in fact better than tolterodine alone. It is therefore feasible to assume that combination therapy with tolterodine versus bladder training alone would indeed improve incontinence outcomes other than frequency of micturition.</p> <p>Such a trial is ongoing and until evidence is available it should not be assumed that combination therapy only improves frequency of micturition versus bladder training alone.</p> <p>The evidence statement should be revised to recognise that the use of combination therapy with tolterodine has not been compared to bladder training alone, but has shown benefits versus tolterodine alone.</p> <p>The GDG should consider that combination therapy with tolterodine may lead to further improvements in incontinence versus bladder training alone. Which we would endorse.</p>	<p>The GDG has based its decisions on the best available evidence. We cannot speculate on the results of ongoing or future clinical trials.</p>

Organisation	Version	Section/page	Line no.	Comments	Response
Pfizer Limited	Full version	210	10-11	<p>“Bladder training is less costly than most antimuscarinic drug treatment and is not associated with adverse effects”</p> <p>No economic analysis has been conducted or provided to support the recommendation that bladder training is less costly than most antimuscarinic drug treatment. All costs would need to be taken into consideration, not simply drug acquisition costs.</p> <p>There is a need to recommend further evidence on the cost-effectiveness of the combined roles and positioning of physical, behavioural, drug, and other therapies.</p>	<p>Where no evidence of greater efficacy exists between treatments (e.g. bladder training and antimuscarinic drug therapy), the cheapest option is the most cost effective.</p> <p>We have a research recommendation that reflects your comment.</p>
Pfizer Limited	Full version	210	17-19	<p>“Where women achieve partial benefit from bladder training programmes, the combination of an antimuscarinic agent with bladder training may be considered where frequency is a bothersome symptom.[A]”</p> <p>No definition is provided for “partial benefit”. It is unclear why combination therapy should not be recommended for all women as the grade A evidence suggests incremental benefit above bladder training alone and above drug treatment alone for all women.</p> <p>The recommendation should not be restricted to women who achieve “partial” benefit, but should be available for all women.</p>	<p>This recommendation has been reworded to reflect your comments.</p>
Pfizer Limited	Full version	210	17-19	<p>“Where women achieve partial benefit from bladder training programmes, the combination of an antimuscarinic agent with bladder training may be considered where frequency is a bothersome symptom.[A]”</p> <p>As noted above, combination therapy with tolterodine or oxybutynin have both been shown to reduce frequency of micturition; however, whilst oxybutynin was versus bladder training alone, tolterodine was versus bladder training in combination with tolterodine. These evidence bases therefore address different questions and cannot be judged comparable.</p> <p>Whilst combination therapy with tolterodine is better than tolterodine alone with regards to frequency of micturition; it is realistic to expect that versus bladder training alone, tolterodine combination therapy would improve other aspects of UI not just frequency.</p>	<p>This recommendation has been reworded to reflect your comments.</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				A lower grade recommendation for combination therapy to improve all aspects of UI, not just frequency, should be considered by the GDG.	
Pfizer Limited	Full version	231	7-10	<p>“The studies showed greater benefit in efficacy outcomes with oxybutynin and tolterodine compared with placebo. Reductions in frequency of 15-21% were seen with oxybutynin and tolterodine compared with 10 to 11% with placebo”</p> <p>This evidence is misleading and inappropriate. Of all four trials quoted for oxybutynin versus placebo, three do not have a significant ($p > 0.05$) reduction in frequency versus placebo (refs 380-382), and the remainder (ref 383) is inconclusive with the 95% confidence interval for the median difference for oxybutynin versus placebo touching zero (-1.1, 0). In comparison all four studies show significant reductions in frequency for tolterodine versus placebo.</p> <p>The text should be amended to accurately reflect the lack of evidence supporting oxybutynin for reduction in frequency versus placebo from these studies.</p>	The variable statistical significance of results across the studies has been noted in the text.
Pfizer Limited	Full version	236	17-18	<p>“Following completion of these 3 studies patients were offered continued treatment with tolterodine 2mg bd for a further 12 months.”</p> <p>Long term evidence of treatment benefit with tolterodine is important to take into consideration when considering the optimal treatment choice for individual patients. There is no indication that this evidence for tolterodine has been taken into consideration when forming the recommendation for non proprietary oxybutynin. There is no long term evidence included for standard formulations of oxybutynin in the guideline.</p> <p>Evidence of long term benefits of antimuscarinic therapy should be used within the evidence statements and recommendations.</p>	Noted.
Pfizer Limited	Full version	237-238	19-8	<p>“Tolterodine slow release”</p> <p>The study by Van Kerrebroeck et al (ref 398) provides direct evidence comparing different formulations of tolterodine. The paragraph of text in the guideline fails to acknowledge that the ER formulation was 18% more effective than the IR formulation</p>	<p>Paragraph added under ‘different formulations of the same drug compared’.</p> <p>We note that the 18% reduction quoted is a relative risk reduction.</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>($p < 0.05$). This is important as it provides strong evidence for differences between formulations and highlights this as an important consideration.</p> <p>Evidence supporting the comparison of tolterodine ER versus IR should be included and consideration given when formulating recommendations.</p>	
Pfizer Limited	Full version	238	2 and 21	<p>QOL evidence for tolterodine.</p> <p>Significant improvements in QOL using the recommended KHQ are evident with tolterodine ER. There is no indication that QOL evidence for tolterodine has been taken into consideration when forming the recommendation for non proprietary oxybutynin. There is no QOL evidence from recommended tools included for oxybutynin in the guideline.</p> <p>Evidence of QOL benefits of antimuscarinic therapy should be used within the evidence statements and recommendations.</p>	Quality of life evidence has been described in the text and is noted in the evidence statement.
Pfizer Limited	Full version	246	1	<p>“Different formulations of the same drug compared”</p> <p>This section omits the direct evidence comparing tolterodine ER with tolterodine IR from the study by Van Kerrebroeck et al (ref 398). The ER formulation was 18% more effective than the IR formulation ($p < 0.05$). This is important as it provides strong evidence for differences between formulations and highlights this as an important consideration.</p> <p>Evidence supporting the comparison of tolterodine ER versus IR should be included and consideration given when formulating recommendations.</p>	<p>Paragraph added under ‘different formulations of the same drug compared’.</p> <p>We note that the 18% reduction quoted is a relative risk reduction.</p>
Pfizer Limited	Full version	249	2	<p>“Where treatments are of equivalent efficacy, the cheapest treatment will be the most cost-effective. Since we did not find consistent evidence of greater efficacy of one antimuscarinic over another, a cost minimisation analysis has been adopted in this guideline.”</p> <p>The simplistic method used within this evaluation fails to consider the other direct costs and consequences of this condition which have been documented to be part of the overall cost burden of UI. These other direct costs may include <i>diagnostic</i> (physician visits,</p>	<p>Please see above.</p> <p>We accept that there are limitations to a cost minimisation approach. However, we nevertheless believe that the approach was justified for the following reasons:</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>lab test, urodynamic evaluations); <i>treatment costs</i> (e.g. surgery, behavioural therapy); and <i>consequence costs</i> (e.g. management of comorbid events, management of drug side effects, premature nursing home admissions. Lengthened hospital stay).</p> <p>Efficacy does not always equate with effectiveness, therefore the cheapest drug is not always the most cost-effective. The therapies may be equally efficacious at reducing the symptoms of this condition but their long term use may result in differences in the side effects, and tolerability. Such differences can lead to increases in the costs of treatment, for example the management of side effects could lead to more visits, switches in treatment, patient loss or reduced persistence.</p> <p>Cost minimisation should be used when it is reasonable to assume that medical benefit is equivalent. The lack of data supporting great efficacy of one therapy over the others does not prevent a thorough cost-effectiveness analysis of these therapies. Efficacy is not the only way to differentiate these treatments other ways could include examining the: quality of life impact; number of successfully treated patients; patient perception of improvements in symptoms; persistency and reductions in withdrawal from treatment; controlled time; and incontinence free time. In this instance, by only conducting a cost minimisation analysis these important differences have been ignored.</p> <p>Cost minimisation has been inappropriately applied and economic evaluation in this case should not only consider direct drug acquisition costs. A full economic analysis should be undertaken in order to support differential recommendations between drug classes and formulations.</p>	<p>i. the “drug acquisition cost” of non-proprietary oxybutynin is substantially less than the alternatives</p> <p>ii. clinical data suggest that differences in effectiveness are very small</p> <p>iii. there are some data to suggest that in a real world setting, persistence may not differ substantially, in which case “downstream” savings from better tolerability would not be realised</p> <p>iv. in the absence of evidence of “downstream cost savings” and evidence of similar effectiveness then it seems questionable that other treatments can be considered as “cost-effective” for the appropriate incremental analysis.</p>
Pfizer Limited	Full version	249	5-8	<p>“The costs (See Appendix E) were based on a typical dose, as determined by the GDC, taken for 12 months and using prices published in BNF 50. Based on this, non-proprietary oxybutynin is the most cost-effective”</p> <p>This approach to cost-minimisation assumes that only drug costs are important within the overall cost of this condition. The cost of treatment should include other direct costs such as those highlighted by Hu 2000: <i>diagnostic</i> (physician visits, lab test,</p>	<p>All economic evaluation is partial equilibrium analysis and there are clearly value judgements around this. However, we consider that a comparison of the incremental costs and effects of conservative treatment could potentially improve efficiency, without factoring all possible treatment</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>urodynamic evaluations); <i>treatment costs</i> (e.g. surgery, behavioural therapy); and <i>consequence costs</i> (e.g. management of comorbid events, management of drug side effects, premature nursing home admissions, lengthened hospital stay).</p> <p>It is misleading to assume that patients will have 12 months of treatment, published persistency rates for each treatment shows this is unlikely. In addition patients tend to take treatment breaks too, so calculating yearly costs is inappropriate. Therefore it may be more appropriate to consider the cost per successfully treated patient, in this instance non-proprietary oxybutynin is not most cost-effective (Chapple, 2001).</p> <p>The tolerability of a product will affect the costs of an individual treatment as this could lead to a treatment switch or an add on therapy. It is inferred later in this guideline (page 250 lines 6-8) that Oxybutynin may not be tolerated by all patients and therefore a switch to another therapy should be considered. This would mean that the costs associated with oxybutynin treatment would be increased however this is not accounted for in the current approach to modelling the therapy options. Potentially it would be cheaper to get treatment right the first time and reduce costs by reducing the need to switch therapies.</p> <p>In the absence of a thorough economic analysis of all therapies it is inappropriate to make a strong recommendation suggesting one therapy is more cost-effective, all therapies should be recommended for treatment to allow clinicians to tailor treatment to patient's symptoms and goals, which in turn enable patient choice and maximise individual patient benefit.</p>	<p>sequelae into the analysis.</p> <p>The yearly costs give some indication of the variation in costs of drug therapy when compared on a like for like basis. Clearly, in practice there will be further variation caused by treatment breaks, persistence etc.</p> <p>Without the citation for Chapple 2001 it has not been possible to identify and review this paper.</p> <p>See earlier responses re antimuscarinics, in particular actual practice data, as opposed to trial data, suggesting that significant switching is an issue for all antimuscarinics if judged by discontinuation.</p> <p>See paragraph above on partial equilibrium analysis.</p>
Pfizer Limited	Full version	249	11-13	<p>"Treatment with darifenacin, oxybutynin, solifenacin, tolterodine, and trospium in women with OAB is associated with improvements in frequency, leakage episodes, and quality of life. [EL=1+]"</p> <p>Quality of life data from the recommended validated questionnaires has not been identified within the guideline for darifenacin, oxybutynin, or trospium. Further the evidence base supporting quality of life has not been fully compared between treatment options to ascertain whether any differences exist.</p>	<p>The tools used are specified in the text summarising the relevant studies.</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				The evidence statement for quality of life should be clearly linked to the treatments with evidence of benefit.	
Pfizer Limited	Full version	249	22	<p>“Antimuscarinic side effects are common with all antimuscarinic drugs”</p> <p>It has been shown that side effects, and in particular dry mouth, can be reduced with new formulations. The tolerability of different formulations should be considered within the evidence statements and recommendations.</p>	There is evidence from practice that persistence with antimuscarinic therapy is low (Shaya et al 2005).
Pfizer Limited	Full version	250	6-7	<p>“Treatment with non-proprietary oxybutynin should be offered as first-line antimuscarinic drug treatment to women with OAB or mixed UI. If oxybutynin is not well tolerated, solifenacin, tolterodine, or trospium may be considered as alternatives. Women should be counselled regarding the side effects of antimuscarinic drugs. [A]”</p> <p>It is acknowledged within the guideline that UI is an embarrassing problem to many women and there are often barriers to presentation. Women may take up to 10 years before seeking help. They may be too embarrassed to seek advice, may not wish to bother their General Practitioner, may believe UI to be a normal consequence of the ageing process, or not appreciate that treatments are available. Under these circumstances it is perverse to offer these women a treatment that is well recognised to have the highest incidence of dry mouth and likely not to be well tolerated. Such a negative first experience of drug treatment could significantly impede the long term management and benefits of appropriate treatment tailored to an individual’s needs.</p> <p>We request that the recommendation is revised to enable an appropriate choice of all available treatments through discussions between patients and physicians to optimise individual patient care.</p>	<p>We note in the evidence statements for antimuscarinic drugs that oxybutynin IR has a poor tolerability profile compared to other antimuscarinic drugs. However an improved tolerability profile does not necessarily translate into improved persistence with therapy. A long term study of oxybutynin ER (Diokno et al 2002) found that discontinuation attributable to adverse effects was 24%, which is similar to that reported for oxybutynin IR. A transdermal formulation of oxybutynin has been developed to further improve the tolerability profile but no studies have reported on long term tolerability and persistence.</p> <p>There is evidence from practice that persistence with antimuscarinic therapy is low (Shaya et al 2005).</p> <p>The difference in drug costs is not trivial with non-proprietary oxybutynin being around 10 times cheaper than other antimuscarinic options. Furthermore, good prescribing practice requires that patients be reviewed when starting on new pharmacological treatment and therefore the costs of</p>

Organisation	Version	Section/page	Line no.	Comments	Response
					switching from a poorly tolerated drug are, at least partly, subsumed within this review process.
Pfizer Limited	Full version	250	6-7	<p>“Treatment with non-proprietary oxybutynin should be offered as first-line antimuscarinic drug treatment to women with OAB or mixed UI. If oxybutynin is not well tolerated, solifenacin, tolterodine, or trospium may be considered as alternatives. Women should be counselled regarding the side effects of antimuscarinic drugs. [A]”</p> <p>It appears the rationale for recommending non-proprietary oxybutynin is purely based on drug acquisition cost. A full economic assessment has not been carried out. Any cost savings from the reduced drug acquisition costs may be short sighted when the cost consequences of patients switching due to poor tolerability with oxybutynin, patient counselling, and patient compliance or drop out are taken into consideration. Further, other antimuscarinics and other formulations have been shown to be cost-effective treatment options and therefore should be recommended to optimise patient choice, flexibility and optimal care.</p> <p>We request recommendation is given for all effective and cost-effective treatment options and the choice of antimuscarinic and formulation is not restricted based on an incomplete and inaccurate assessment of cost minimisation.</p>	Please refer to all our responses above.
Pfizer Limited	Full version	250	16-18	<p>“There is a need for a comparison of the cost-effectiveness of drug therapy compared with other conservative therapy as first-line treatment for women with OAB or mixed UI”</p> <p>In addition there is a clear need for evidence of the cost-effectiveness of the newer drug therapies within the stated populations and the SUI population.</p>	Noted.
Princess Alexandra Hospital NHS - Trust				This organisation was approached but did not respond.	-
PromoCon (Disabled				This organisation was approached but did not respond.	-

Organisation	Version	Section/page	Line no.	Comments	Response
Living)					
Q-Med (UK) Ltd				This organisation was approached but did not respond.	-
Queen Victoria Hospital NHS Foundation Trust				This organisation was approached but did not respond.	-
RCM Consultant Midwives Forum				This organisation was approached but did not respond.	-
Regional Public Health Group - London				This organisation was approached but did not respond.	-
Rotherham General Hospitals NHS Trust				This organisation was approached but did not respond.	-
Rotherham Primary Care Trust				This organisation was approached but did not respond.	-
Royal College of General Practitioners	Full			<p>I consider this to be definitely one of the better guidelines NICE has produced. Although even the concise guideline is fairly lengthy, there are wide ranges of treatment modalities discussed, which reflects the very different underlying pathologies which cause the different forms of urinary incontinence.</p> <p>Overall, I would suggest that these recommendations do very much reflect best practice. I applaud the emphasis on both pelvic floor exercise (both preventive in pregnancy and for management in those with existing symptoms) and of bladder retraining for patients with OAB incontinence. The algorithm is, despite its complexity, both unequivocal and practical, and offers an appropriate combination of lifestyle, surgical and medical options. I approve of the stratification of medications, although I would like to see more clarity on where the members feel that duloxetine, the only drug licensed for the management of SUI, could be usefully instigated. Their only recommendation is that it should not be used first line (and that patients should be counseled about the side</p>	<p>Thank you for your comments.</p> <p>Duloxetine: another model has now been included in the guideline to compare the cost-effectiveness of duloxetine versus surgery as a second line treatment for stress incontinence in women who have failed PFMT as first line. Although we conclude that surgery is more cost-effective than duloxetine, we do now say that duloxetine can be considered where women prefer pharmacological to surgical alternatives. We believe that this patient choice is also justifiable on health economics grounds as duloxetine is considerably</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>effects).</p> <p>The only other negative comment I have to make about the guideline itself is that in the complete guideline, the initial estimates for prevalence are laughably low. This misconception is corrected later in the same section, but I do feel that given that the International Continence Society estimates its prevalence at 4 million women in the UK alone (Ref Hunskar S et al. Prevalence of Stress Urinary Incontinence in women in four European countries. Proceedings of the International Continence Society 32nd Meeting, August 2002, Heidelberg. Abstract 257. pg 166),</p> <p>I would be unhappy to think that this positioning of the much lower prevalence figures at the start of the introductory paragraph might be misleading.</p> <p>Otherwise, the big question mark is, as ever, over availability of the services and treatment options recommended. They are mostly behavioural rather than drug related - as is entirely appropriate for this condition - but my own extensive experience, and discussion with colleagues across the country, confirms that such service provision is extremely patchy. Urinary incontinence is, to say the least, not high on the average PBC group's agenda, and I would be extremely sad to see such a useful document rendered effectively useless by lack of implementation. I would urge the RCGP to be vocal in its support of resources to be set aside for allied healthcare professional services for this important and debilitating condition</p>	<p>cheaper than surgery and therefore its use would not necessarily impose opportunity costs on the NHS.</p> <p>The section describing prevalence has been revised, including data from the Leicestershire MRC Incontinence study.</p>
Royal College of General Practitioners	Full			<p>Patients should be involved in decision making. There should be more community led facilities. Many surgical procedures are rather heavy-handed. Full implication of surgical procedures should be known to patients.</p>	<p>Thank you for comments. We agree with the sentiments but feel this has been covered in the recommendations.</p>
Royal College of General Practitioners Wales				<p>This organisation was approached but did not respond.</p>	-
Royal College of Midwives				<p>This organisation was approached but did not respond.</p>	-

Organisation	Version	Section/page	Line no.	Comments	Response
Royal College of Nursing	NICE	8	1.1.5.1	Recommends the use of bladder scan to check for residual urine.	Noted.
Royal College of Nursing	NICE	9	1.1.13.1	States that routine ultrasound should not be carried out - does this include bladder scanning for residual urine?	This recommendation has been clarified reflecting your concern.
Royal College of Nursing				The above points appear to conflict each other.	This recommendation has been clarified reflecting your concern.
Royal College of Nursing	NICE	General		It seems to have a very specialist focus which may do little for improving the assessment and management of typical incontinence in older people, as it makes no reference to continence as a result of functional issues, either physical or cognitive. This seems a missed opportunity.	We believe that this is covered under general assessment.
Royal College of Nursing	Full	Appendix E	Page 441 onwards	<p><i>Costing for first line conservative treatments for urinary incontinence</i></p> <p>1) The costing and their assumptions describe a Senior 1 Physio working in a Hospital setting. The document does not reflect changes in direction with patients being seen in Primary Care rather than Secondary Care linked to the White Paper, Shifting the Balance, Liberating the Talents, Independent Nurse Prescribing and Delivering a Patient led NHS. The Guidelines also seem to miss the whole function of Good Practice Guidelines in Continence Services and Integrated teams with treatment being delivered mainly in primary care.</p> <p>Also think the draft guidance seems to suggest that physiotherapists are the main deliverers of care, whilst this is pertinently not the truth. This could sway commissioners, PCTs and GPs in their decision making and their suggestions would greatly change the face of bladder care provision.</p> <p>a) We would like to suggest that all these assumptions for pelvic floor exercises, bladder re-training, electrical stimulation and biofeedback are made for both Primary Care as first line and Hospital settings as second line.</p> <p>b) Would also suggest, as the majority of Nurse Specialists provide this in Primary Care that the guidance does not just describe a physiotherapist but include Specialist Physiotherapist / Nurse or Consultant Nurse/Therapist with the relevant training and expertise to be decided at a</p>	<p>The <i>raison d'être</i> of Appendix E was to compare the cost-effectiveness of different treatments, and not the cost-effectiveness of different settings. Nor is it the function of a clinical guideline to give PCTs the cost implications of recommendations, although NICE do a cost impact analysis of the guideline as a supplementary piece of work.</p> <p>The costings need to be interpreted in the light of the caveat given in Appendix E: "Considerable heterogeneity exists within many of the conservative treatments for UI. As far as possible the cost estimates presented here are based on 'standard' or 'typical' treatment (as informed by expert opinion on the GDG) but in practice such a standard may not exist. Therefore, the actual costs of particular conservative treatments will vary according to the actual practice followed."</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>local level.</p> <p>c) Would like to see the term Continence Advisor changed to Continence Nurse Specialist.</p> <p>d) The guidance describes a Senior 1 Physiotherapist - this should read Band 6/7 Specialist Nurse/Physiotherapist with the relevant accredited training and expertise.</p> <p>e) Also the guidance describes particular equipment. Trusts will use these descriptions to dictate what equipment is purchased. The guidance should not specify particular equipment by name....and if they do, should describe all the available equipment. Suggest they should just use an average figure for a stimulator or biofeedback machine without specifying a particular product.</p> <p>f) Another suggestion could be costing for the full package delivered in Primary Care by both the specialists and the consultants (Nursing or Therapy). This costing to include prescribing and prescribing follow up.</p> <p>g) There should be a further costing on how much this would be if patients are referred directly to Hospital Therapists/Nurses...due to the cost of Tariffs.</p> <p>h) There should be a further costing, as a comparison, for the full package if a patient is referred directly to a Hospital Medical Consultant, i.e. Urologist, Uro-Gynaecologist, Geriatrician, Gynaecologist with a specialist interest.</p> <p>a. PCTs need to know all the costing implications in these days of Choose and Book, Payment by Results and GP Commissioning.</p>	<p>The consultation cost can probably be considered a “sunk cost” and would therefore not be relevant to any treatment path/decision.</p> <p>c) The title ‘continence nurse specialist’ has now been used instead of continence advisor.</p> <p>f) to h) a cost impact report will be generated by NICE at the time of publication of the guideline; please refer to these.</p>
Royal College of Nursing	Full	2.1 & 4.4.4	21 6	2) Concerned over the medication advice. Agree that Oxbutynin Hydrochloride is cheap, but patients dislike it and do not continue taking it and then do not go back to get another	The GDG has reconsidered the evidence in this area, along with comments from several stakeholders.

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>prescription!</p> <p>Suggest that this drug is not recommended due to its side effects.</p>	<p>We note in the evidence statements for antimuscarinic drugs that oxybutynin IR has a poor tolerability profile compared to other antimuscarinic drugs. However an improved tolerability profile does not necessarily translate into improved persistence with therapy. A long term study of oxybutynin ER (Diokno et al 2002) found that discontinuation attributable to adverse effects was 24%, which is similar to that reported for oxybutynin IR. A transdermal formulation of oxybutynin has been developed to further improve the tolerability profile but no studies have reported on long term tolerability and persistence.</p> <p>There is evidence from practice that persistence with antimuscarinic therapy is low (Shaya et al 2005).</p> <p>The difference in drug costs is not trivial with non-proprietary oxybutynin being around 10 times cheaper than other antimuscarinic options. Furthermore, good prescribing practice requires that patients be reviewed when starting on new pharmacological treatment and therefore the costs of switching from a poorly tolerated drug are, at least partly, subsumed within this review process.</p>
Royal College of Nursing	Full	2.1 & 4.4.4	21 6	3) The guidance mentions the drugs to use if Oxybutynin Hydrochloride fails. It has missed out Oxybutynin ER (Lyrinel) and this should be added.	The recommendation on antimuscarinic drugs has been revised to include advice on slow release and transdermal formulations of oxybutynin.
Royal College of Nursing	Full	Page 249	17	<p><i>Evidence statements from antimuscarinic drugs</i></p> <p>(ii) The draft guidance also states that Propiverine does not</p>	We believe that this is covered in the recommendation for propiverine.

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				decrease UI but can improve frequency which is a part of OAB. Since these guidelines are also for OAB dry and wet. Propiverine must also be included as a second line drug.	
Royal College of Nursing	Full & NICE	4.4.3 page 221		4) In line with this the guidance excludes topical HRT for UI but does not mention its use on OAB dry when a post menopausal women has signs of frequency and urgency and uro-genital atrophy...although they do recognise in their script that there is evidence to support its use. This must be added (1.2.4.3)	Noted. Recommendation regarding intravaginal oestrogen revised.
Royal College of Nursing	NICE	1.1.4.1		1.1.4.1....the general expert opinion is that one should treat leucocytes and nitrites etc if the patient has symptoms of frequency and urgency as these are symptoms of a UTI (but can be interpreted as OAB dry). If one sends MSUs on everyone then the labs will be inundated. It should also be noted that labs also dipstick samples. Would suggest a review of this whole section, particularly from a Microbiologists point of view...	The recommendations have revised, and microbiologist opinion sought regarding culture, and antibiotic use. An explanation for the recommendations is given in the full guideline.
Royal College of Nursing	NICE	1.1.5.1		6) 1.1.5.1.. A description of voiding dysfunction would be appropriate here. Suggest that as well as dribbling and feelings of incomplete voiding the guidance should also include frequency and urgency and continual leakage and nocturia. In routine everyday practice one can find residual urines in a lot of women who do not have the cardinal voiding dysfunction signs.	Voiding dysfunction added to the glossary. The GDG considers that the lack of evidence for what constitutes a clinically significant residual volume in women with UI precludes making a recommendation other than in women who have signs or symptoms suggestive of voiding dysfunction.
Royal College of Nursing				7) 1.1.6.1...and haematuria. This will worry a lot of urologists who do not want to see everyone with microscopic haematuria as they do not have the staff to deal with the numbers coming through as the dip sticks are notoriously oversensitive. The guideline development group needs to decide what level of microscopic haematuria should be referred...i.e. 2 plus etc?	Recommendations regarding referral based on haematuria are taken directly from the NICE 'Referral guidelines on suspected cancer' (2005). It is the GDG's view that we cannot be more specific than this.
Royal College of Nursing	NICE	1.1.6.2		8) 1.1.6.2...Associated faecal incontinence should be included. (Specialist Nurse/Therapists in Primary Care are quite qualified to deal with Faecal Incontinence).	The GDG has discussed your comment. We feel that the wording of the recommendation reflects your concern, in that we recommend consideration rather than mandatory referral to a specialist service.

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Royal College of Nursing	NI CE	1.1.6. 2		9) 1.1.6.2 ...Symptoms of voiding difficulty. Once again as commented earlier, Specialist nurses in Primary Care will usually teach ISC, review and then refer on.	See above; referral should be considered, but is not mandatory.
Royal College of Nursing	NI CE	1.1.6. 2		10) 1.1.6.2...Should be assessed by specialist Primary Care Services and then referred if assessed as necessary.	See above; referral should be considered, but is not mandatory.
Royal College of Nursing	NI CE	1.2.2		<p>11) Pelvic assessment.... In clinical practice...practitioners consider that one cannot teach pelvic floor exercises (PFE) without first assessing the pelvic floor. If one teaches PFE without assessment how would one know if the woman can do a contraction? (Morkved and Bo (1997) refers)</p> <p>If one verbally teaches a patient and they do not work, then these women are being set up to fail and could stop doing the exercises and would never come back because they feel guilty. If they are then seen by a physiotherapist or nurse for one-to-one therapy, it is usually found that they have lost confidence in pelvic floor exercises and it is harder to get them to believe that they do work.</p> <p>It is recommended that all patients must have a pelvic floor assessment. This part of the guidance needs to be reviewed from the physiotherapist's perspective and not driven by the medic's perspective.</p>	We have considered your comments and reflected on the limited evidence as to whether pelvic floor muscle assessment prior to PFMT improves outcome. Whilst there is not unanimity on this point, it is clearly widespread expert opinion that the determination of whether a woman can contract her pelvic floor muscles voluntarily may influence the type of treatment. Hence, the GDG has reconsidered its earlier recommendation, and will advise that pelvic floor muscle assessment should be undertaken before embarking on supervised pelvic floor muscle training for the treatment of UI.
Royal College of Nursing	NI CE	1.2.2. 5		(iii) There is no recommendation as to whether or not electrical stimulation should be used in OAB dry or wet. This needs to be stated.	We have added an evidence statement and recommendation regarding electrical stimulation for OAB.
Royal College of Nursing	NI CE	1.2.4		12) In the drugs section the guidance does not mention Frusemide for nocturia/nocturnal polyuria which is a sign of OAB dry. This omission should be rectified.	We did not find evidence evaluating the use of furosemide for nocturia in women. A sentence has been added to that effect.
Royal College of Nursing	NI CE	1.2.5. 5		13) The pad guidelines are brilliant and will really help practice.	Thank you.
Royal College of Nursing	NI CE	1.4		14) When discussing surgeons' experience can the guidance stipulate that they must also have a record of continuous professional development i.e. by attending at least one national and one international conference in the area annually so as to keep up to date with research and practice?	While continuing professional development is of relevance to the development and maintenance of surgical skill, and surgeons must of course conform to the standards of good medical practice and good surgical practice (GMC and RCS), the

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					detail of CPD requirements is an issue for the appropriate Royal Colleges and specialist societies.
Royal College of Nursing	NICE	1.4		15) We would also like to suggest that all Gynaecologists must have met the requirements and competencies set out in the Uro-gynaecologists sub-speciality training.	At present, the term 'subspecialty training' implies different things in urology (2 years of training following 'core' training) and gynaecology (3 years following training to year 4 SpR level). It is certainly impractical, and probably inappropriate to suggest that all gynaecologists undertaking surgery for incontinence should undergo 3 years additional training. The GDG do however recommend that those undertaking surgery should have appropriate training in the assessment and management of UI and prolapse, or should work within the context of a multidisciplinary team with this training and expertise. We also indicate that existing surgeons should be able to demonstrate that their training, experience and current practice equates to the standards laid out for newly trained surgeons.
Royal College of Nursing	NICE	1.4.7		(iv) The idea of recommending one surgeon with overall responsibility linked to Integrated services is welcomed.	Noted.
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology	Full version	78	5	If supervised pelvic floor muscle training is recommended during pregnancy how is this to be funded? It should be noted that the long-term follow-up results no longer show a protective effect (Glazener et al BMJ 2005). This has been confirmed in another (eight year) follow-up, which will be presented at IUGA this year.	Thank you for your comments. NICE clinical guidelines do not provide guidance on who should deliver care. Implementation tools will be generated by NICE at the time of publication of the guideline; please refer to these. The Glazener study you refer to is included in the guideline.
Royal College of Obstetricians and		79,80	18,22	A definition of 'Specialist' would be helpful should this be a Gynaecologist, Urogynaecologist or Urologist?	Added to glossary: a specialist is any health care professional who has received appropriate training to be able

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Gynaecologists and British Society of Urogynaecology					to provide the particular range of specialist services they undertake and who works within the context of an integrated, multidisciplinary continence team. Particular service profiles will differ from one place to another.
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		81	2	Patients with haematuria should be referred to a Urology Specialist.	Recommendations regarding referral based on haematuria are taken directly from the NICE Referral guidelines on suspected cancer (2005). It is the GDG's view that we cannot be more specific than this.
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		81	9	Concomitant symptomatic prolapse would be a further indication for referral in women with UI	We have stated this in the recommendations.
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		81	20	<p>In a recent systematic review it has been suggested that the IIQ or I-QOL with or without UDI be used in trials of incontinence treatments (<i>Ross S, Soroka, D et al. Incontinence – Specific Quality of Life Measures used in Trials of Treatments for Female Urinary Incontinence: A Systematic Review. Int Urogynaecol J (2006) 17: 272-285</i>).</p> <p>This Paper might have been published after the draft was completed. Consideration should be given to including IIQ and UDI.</p> <p>In addition the e-PAQ (<i>Radley S C, Jones G L, Tanguy E A et al. Computer Interviewing in Urogynaecology: Concept, development and psychometric testing of an Electronic Pelvic Floor Assessment Questionnaire (e-PAQ) in Primary and Secondary Care. BJOG 2006; 113: 231-8</i>) has been fully validated and includes questions on all pelvic floor symptoms including urinary incontinence, bowel dysfunction, prolapse and sexual dysfunction. Has this been considered?</p>	<p>We are aware of the Ross review, and note that the authors' reason for recommending UDI and IIQ is that they are the most commonly used questionnaires. The GDG has reflected on this recommendation and decided that this evidence (opinion) is not sufficient to change it.</p> <p>We have not considered e-PAQ; only ICI Grade A questionnaires as stated.</p>

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Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		95	7	The two Stakeholder Groups (BSUG and RCOG) felt that research should be performed prior to any change in clinical practice, particularly where the recommended change is based on expert opinion and/or poor quality data (see under general comments).	The GDG has considered the many comments received regarding the use of urodynamic testing prior to primary surgery for stress UI. We reflected further on the evidence and current practice. We maintain the view that urodynamics investigation is not essential in every woman prior to primary surgery for stress UI, and therefore is not <u>routinely</u> recommended. However, we acknowledge the weight of expert opinion that it is of value in specific circumstances; we have included recommendations as to those circumstances in the guidance.
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		111	13	It isn't clear from this recommendation how pelvic floor training (PFMT) can be commenced without assessment of the patient's ability to perform a pelvic floor contraction. The evidence suggests that many patients are unaware how to do this (<i>e.g. Bump RC et al. AJOG 1991, Chiarelli P. Aust J Physiotherapy 1999, Bo K. Acta Obstet Gynecol Scand 1998</i>). Despite lack of evidence that assessing pelvic floor contraction has any effect on outcome of treatment, it seems logical to know if pelvic floor training is being done correctly. This is alluded to in Line 7. Women with Oxford score 4/5 and those with 1/2 are unlikely to benefit from PFMT either because there is no 'room for improvement' (in 4-5's) or that they cannot contract (in 1-2's). Assessment will allow these women to be 'fast-tracked' to other treatments thus saving resource for women most likely to benefit.	We have considered your comments and reflected on the limited evidence as to whether pelvic floor muscle assessment prior to PFMT improves outcome. Whilst there is not unanimity on this point, it is clearly widespread expert opinion that the determination of whether a woman can contract her pelvic floor muscles voluntarily may influence the type of treatment. Hence, the GDG has reconsidered its earlier recommendation, and will advise that pelvic floor muscle assessment should be undertaken before embarking on supervised pelvic floor muscle training for the treatment of UI.
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		120	3	It is recommended that a distinction be made between haematuria on dipstick and MSU. Persistent blood on dipstick should not be ignored in the absence of haematuria on MSU. It is recommended that this be highlighted.	Definition of haematuria added to glossary (in addition to the footnote in the first draft).

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Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		134	10	While pad testing might not effect outcome nonetheless incorporating it with a dye test (e.g. Pyridium or Methylene Blue) might help to identify incontinence where this cannot be demonstrated clinically.	Noted.
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		135	3.11 (General Comments)	<ul style="list-style-type: none"> • These Stakeholder Groups felt that the absence of evidence in relation to pre-operative urodynamics affecting surgical outcome, did not constitute 'evidence of absence'. It is agreed that further research is required and this ought to be performed prior to recommending changes in clinical practice. The Stakeholders would support a recommendation from NICE to the HTA that further research into the value of urodynamics be supported. BSUG would be willing to carry out such a study following which clinical recommendations can be made. • It is of concern that undertaking invasive treatments without a definitive diagnosis is setting a potentially dangerous precedent. One study not reviewed has shown that the predictive value of stress symptom alone was not high enough to serve as the basis for surgical management (<i>Weidner A C, Myers E R, Visco A G et al AJOG 2001; 184: 20-7</i>). • There is a concern that without a diagnosis, surgical rates for 'presumed' stress incontinence might increase further. Higher rates of UI surgery are already performed in the UK compared with other European Countries (Hunskaar et al BJU Int 2004; 93:324-30). • Much of the evidence is 'expert opinion' and further advice/opinions should be sought. The opinion of these Stakeholders is that urodynamics safeguards many patients from inappropriate surgery. • While we agree that urodynamics may be unnecessary in patients with a single symptom of stress incontinence, a normal frequency/ volume chart and no post void residual, the majority of patients (as shown in the epidemiology section) do not have 	<p>Urodynamics recommendation revised as stated above.</p> <p>The Weidner paper you refer to was included in the first draft (reference 56).</p> <p>Urodynamics recommendation revised as stated above.</p> <p>Noted.</p> <p>Noted.</p>

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>'pure' stress incontinence but mixed symptoms. Where this is due to urodynamic stress incontinence and detrusor overactivity, the outcome might be unsatisfactory. For example, the WHO/ICI (2002) have stated that <i>“there is level 3 evidence that women who have pre-operative detrusor overactivity are likely to have a less favourable outcome from surgery”</i>.</p> <ul style="list-style-type: none"> • The recommendation is not in keeping with that of the International Consultation on Incontinence Expert Group who have suggested in their 3rd report (Page 1608) that <i>“if initial management has been given an adequate trial then interventional therapy may be desirable. Prior to the intervention, urodynamic testing is highly recommended, because it is used to diagnose the type of incontinence and therefore inform the management plan. Within the urodynamic investigation urethral function testing by urethral pressure profile or leak point pressure is optional”</i>. • There is a risk that international consensus will be lost if NICE recommend that pre-operative urodynamics is not required for patients in the UK. • The economic analysis is based on the assumption that 80% of patients will have 'pure' stress incontinence. As mentioned this is not supported by epidemiological evidence which suggests a figure of 30-50%. The difference is likely to have an affect on the outcome of the analysis. Has this been performed by a health economist? • There is a risk that should the recommendation be implemented, some NHS Trusts might withdraw funding for all urodynamics. • Detailed audit of the long-term effects of the recommendation will be required along with appropriate funding to perform the audit. 	<p>Noted.</p> <p>All health economic input into the guideline was undertaken by a health economist on the GDG. The 80% is the posterior probability after a basic office evaluation which includes detailed history and physical examination, urinalysis, a provocative stress test, and measurement of residual urine. It must be remembered that these figures are not intended as estimates of prevalence of symptoms or of urodynamic abnormalities in the whole population. A sensitivity analysis on this assumption was included as part of the economic analysis (see Appendix</p>

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					D).
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		137	5	<p><i>Reference 119 is quoted. However, this was a retrospective study using different operations and concomitant procedures. It was interesting to note that post-operative voiding difficulty was more common in those without pre-operative urodynamics (in the group operated on by Urologists).</i></p> <p>In addition a low pre-operative flow rate and abdominal straining during voiding have been shown to be associated with voiding difficulty after colposuspension (Bombieri L et al BJOG 2002;109: 402-412). The inconsistent predictive value of pre-operative urodynamics in other studies might be due to methodological differences and definitions e.g. the use of arbitrary voiding pressures.</p>	The poor quality of reference 119 is reflected in the evidence level it has been given (2-). The Bombieri study has been reviewed and included in the section on prognostic value of pre-operative urodynamic testing. We believe that the limitations and poor quality of evidence in this section is covered in the text.
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		147	13	The GDG felt that urodynamics was indicated in cases of failed surgery. This seems illogical. If the GDG assumes that urodynamics are not indicated for primary surgery, then why should it be any different for secondary surgery?	The GDG recognised the inconsistency here, but felt able to recommend urodynamics prior to secondary surgery on the grounds that the primary procedure may have adversely affected anatomy or function of the lower urinary tract. Having reconsidered our recommendation relating to urodynamic investigation prior to primary surgery, in recognition of current practice and expert opinion, this comment is addressed.
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		147	13	For completeness the urethral electrical conductance test (UEC) and the urethral retro-resistance pressure (URP) tests should be included.	These tests have not been included as they were not considered to be relevant to current clinical practice.
Royal College of Obstetricians and Gynaecologists and British Society of		250	4	<ul style="list-style-type: none"> The antimuscarinic side-effects of Oxybutynin are well documented. Kelleher et al (1997) reported low compliance and persistency with immediate-release Oxybutynin. Only 18% of women continued medication beyond six months. OAB is a life-long condition and might require long-term therapy. The poor side-effect profile of IR Oxybutynin can lead to poor 	The GDG has reconsidered the evidence in this area, along with comments from several stakeholders. We note in the evidence statements for antimuscarinic drugs that oxybutynin IR has a poor tolerability profile compared

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Urogynaecology				<p>compliance and persistency. As a result patients might not be prepared to try other anticholinergics. This is despite evidence of reduced side-effects with e.g. slow-release preparations.</p> <ul style="list-style-type: none"> • Cognitive impairment in the elderly needs to be addressed. The M1 effects are important and the studies have not focused on the already cognitively impaired who would be at greater risk from generic IR Oxybutynin. • The economic arguments used are selective with bias in favour of the cheapest option in all cases. Data exists regarding a more thorough approach. An economic model was developed to assess the comparative cost effectiveness of Tolterodine ER, Tolterodine IR and Oxybutynin IR. The categories of costs included incontinence pads, physician visits, laboratory test/diagnosis and associated co-morbidities. Results included patients who are treated with success and those who are not. Clearly exclusion of the latter from the analysis will steer results towards the cheapest option. In this case the results in terms of cost in successfully treated patients with Tolterodine ER = £1,052, Oxybutynin = £4092. (Kelleher C, Cardozo et al. A Medium Term Analysis of the Subjective Efficacy of Treatment for Women with Detrusor Instability and Low Bladder Compliance. BJOG 1997; 104: 988 Bentkover J D, Chapple C et al. US Cost-offset Economic Model for Overactive Bladder for the European Market Place. Value in Health 2000; 3:361). 	<p>to other antimuscarinic drugs. However an improved tolerability profile does not necessarily translate into improved persistence with therapy. A long term study of oxybutynin ER (Diokno et al 2002) found that discontinuation attributable to adverse effects was 24%, which is similar to that reported for oxybutynin IR. A transdermal formulation of oxybutynin has been developed to further improve the tolerability profile but no studies have reported on long term tolerability and persistence.</p> <p>There is evidence from practice that persistence with antimuscarinic therapy is low (Shaya et al 2005).</p> <p>The difference in drug costs is not trivial with non-proprietary oxybutynin being around 10 times cheaper than other antimuscarinic options. The recommendation on antimuscarinic drugs has been revised to include advice on slow release and transdermal formulations of oxybutynin.</p> <p>Furthermore, good prescribing practice requires that patients be reviewed when starting on new pharmacological treatment and therefore the costs of switching from a poorly tolerated drug are, at least partly, subsumed within this review process.</p> <p>We found no evidence on cognitive function in the population of this guideline.</p>

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					The model referred to is only described in an abstract, providing insufficient detail for appraisal.
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		280	9	With regards the complications of clam cystoplasty, carcinoma of the ileal patch should be mentioned. In addition there are no quality of life data presented on the effects of clam cystoplasty.	We recognise that malignant transformation has been sporadically reported but is not common. However we agree this is an important issue and is reflected in our revised recommendation for lifetime follow up. There are no quality of life data on Clam Cystoplasty other than satisfaction rates.
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		78 91 Review Pages 308-311	17	<p>The Guideline refers to the fact that open colposuspension is an alternative to TVT. It also states that laparoscopic colposuspension is not recommended as a routine procedure (recommendation D (GPP)).</p> <p>Studies are included where a 'standard' laparoscopic colposuspension (i.e. with at least two sutures each side) was not performed. In addition, one of the apparent randomised studies (Su et al. Reference No 621), was not properly randomised as patient choice was allowed. In addition in the laparoscopic arm a single suture on each side was allowed and is referred to in the review of the literature; this results in a higher failure rate (Person et al. Reference 623).</p> <p>The MRC Study (Reference 622) has now been accepted for publication in the BJOG (along with another RCT). The data in the abstract fail to show that laparoscopic colposuspension is inferior. The conclusion with regards laparoscopic colposuspension should read that it is a reasonable alternative to open colposuspension when it is carried out in a similar manner by surgeons experienced in performing the procedure.</p>	<p>The quasi randomisation used in the Su study is reflected in the grading of evidence given (EL=1-); studies with a ' grading are not used as a basis for recommendations (see method).</p> <p>A pre-publication copy of the MRC study has been obtained and is considered within the guideline.</p> <p>The recommendation has been modified to reflect your comment about surgeons experience.</p>
Royal College of Obstetricians and Gynaecologists and British Society of Urogynaecology		396	9	A consensus view has been agreed by the GDG that to maintain competence a surgical workload of 20 cases per procedure per annum was an appropriate volume based on the survey of UK consultants (Reference 919). It is of note that a majority of 'general gynaecologists' felt that 10-20 procedures per annum was sufficient to maintain competence while accredited urogynaecologists/sub-specialists and gynaecologists with a	It was felt that an absolute figure was more appropriate than a range, in this context. The figure chosen (being included in the ranges suggested by gynaecologists, urologists, and subspecialty trained urogynaecologists) was deemed to be the most

Organisation	Version	Section/page	Line no.	Comments	Response
y				<p>special interest in urogynaecology felt that 20-50 procedures per annum was a more appropriate number. Why has the GDG chosen the suggestion by general gynaecologists rather than those with subspecialty training or special interest?</p> <p>These Stakeholder Groups felt that 20 cases of primary surgery per year were possibly adequate provided urethral injectables and Botox were not regarded as major procedures. However, would 20 cases of one procedure e.g. TVT be acceptable for competence in SUI surgery? Would this include the ability to deal with peri-operative complications e.g. bleeding in the retropubic space? Competence in operating in this space is necessary. For primary and secondary surgery 20 major cases per year was felt to be inadequate. It is, however, clarified on Page 398, Line 12, that 20 cases per primary procedure per year is recommended. There should be a clear recommendation on how many cases of secondary and repeat surgery should be performed to maintain competence.</p> <p>General Comments: While these Stakeholders wish to thank and congratulate the Group for the excellent review and presentation, we feel that the following recommendations need further discussion:</p> <p>(1) <u>the recommendation that pre-operative urodynamics is not necessary in patients with 'pure' stress urinary incontinence (SUI).</u> While this might be appropriate for the small number of patients who have 'pure' SUI, the recommendation might result in patients with mixed or urge symptoms undergoing surgery for 'presumed pure' SUI. To identify whether patients have pure stress or mixed symptoms requires detailed history taking. There is a concern that surgery will be performed in patients with detrusor overactivity, which is undiagnosed. The WHO/ICI (2002) has stated that "there is level 3 evidence that women who have pre-operative detrusor overactivity are likely to have a less favourable outcome from surgery".</p> <p>For surgery in patients with intractable urge incontinence e.g. Botox, SNRS and cystoplasty, demonstration of detrusor</p>	<p>appropriate.</p> <p>It is recognised in the guideline that BAUS-SFRU and BSUG are currently developing training schemes and structured assessment methods specific for those undertaking continence surgery. It is also recommended that operative competence of surgeons undertaking surgical procedures to treat UI or OAB in women should be formally assessed by trainers through a structured process. We look to these specialist societies for detailed advice on the content of training. The figure of 20 refers to each primary procedure and should apply as much to urethral bulking agents as to sling procedures. Given that complications of these procedures are rare, it is doubtful that even a much higher number of cases would ensure a high level of competence to deal with complications.</p> <p>We agree that a recommendation for primary vs. secondary surgery would be helpful, we have not found either evidence nor published opinion on this issue.</p> <p>Please see responses above to your 'general comments'.</p>

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				<p>overactivity and an assessment of voiding function would be considered important; a diagnosis is necessary before surgical intervention.</p> <p>If the recommendation is upheld careful auditing of changes to clinical practice is required with funding made available to undertake this work.</p> <p>The predictive value of pre-operative urodynamics for post-operative voiding difficulty needs further assessment.</p> <p>(2) <u>IR Oxybutinin</u> There is concern about the use of immediate-release Oxybutynin and whether this is truly cost effective as the side effects are bothersome and compliance is poor. In such patients, further treatments are likely to be viewed 'with suspicion', thus affecting compliance and outcome. The cognitive effects in elderly patients need careful consideration.</p> <p>(3) <u>Surgical Competence</u> While 20 major cases for primary surgery seems acceptable for 'competence' this was not felt to be as suitable for secondary procedures. Competence in more than one procedure is recommended.</p> <p>(4) <u>Research Recommendations</u> Finally, recommendations are made for research following those for changing clinical practice. This was felt to be inappropriate and 'the wrong way around'. Once the research data are available only then should changes to clinical practice take place.</p>	(3) Whilst we agree that such a recommendation would be helpful, we have not found either evidence nor published opinion on this issue. We feel that the requirement for surgeons to be functioning within the context of a multidisciplinary team provides appropriate safeguards here.
Royal College of Physicians of London				This organisation was approached but did not respond.	-
Royal College of Psychiatrists				This organisation was approached but did not respond.	-
Royal National Orthopaedic Hospital NHS Trust				This organisation was approached but did not respond.	-

Organisation	Version	Section/page	Line no.	Comments	Response
Schwarz Pharma				This organisation was approached but did not respond.	-
Scottish Intercollegiate Guidelines Network (SIGN)				This organisation was approached but did not respond.	-
Sheffield Children's Hospital NHS Trust				This organisation was approached but did not respond.	-
Sheffield South West Primary Care Trust				This organisation was approached but did not respond.	-
Sheffield Teaching Hospitals NHS Trust	NI CE	Page 9	1.1.7.1	<p>Paragraph refers to symptom scoring and quality of life assessment. We would want ePAQ [Electronic Pelvic Floor questionnaire] to be included in the recommendations</p> <p>This has been developed in Sheffield by my colleague [X]. It allows the patient to complete a symptom based questionnaire in a number of domains including those of urinary, bowel, sexual function and vaginal lump and looks at the impact upon quality of life. Furthermore it is innovative in being electronic and has applications in the community setting as well as in hospitals It has been fully validated and I append a list of relevant publications.</p>	Thank you for your comments. We have not considered e-PAQ; only ICI Grade A questionnaires as stated.
Sheffield Teaching Hospitals NHS Trust	NI CE	Page 3		<p>Introduction</p> <p>I think they should use a proper definition of urgency here in other words "a compelling desire to void" rather than saying "urgent need to urinate" and they use urge incontinence when it should be urgency incontinence due to the compelling desire to void which is difficult to defer. The definition of overactive bladder is not also the same as the ICS one it states the complaints of urgency and frequency and this needs to be clarified.</p>	Amended - ICS definitions used for urgency and OAB.
Sheffield Teaching Hospitals NHS Trust	NI CE	Page 5		<p>Key priorities for implementation - assessment and investigation</p> <p>Whilst there is a limited evidence base that urodynamics alters outcome it is contentious to state that cystometry or video</p>	The GDG has considered the many comments received regarding the use of urodynamic testing prior to primary surgery for stress UI. We reflected further on the evidence and current

Organisation	Version	Section/page	Line no.	Comments	Response
				<p>urodynamics is not recommended prior to non-invasive treatments or primary surgery for stress incontinence.</p> <p>The use of non-preparatory oxybutynin is all very well but this drug is poorly tolerated and whilst cheap and effective many patients are not prepared to take this and it is therefore difficult to understand why this should be first line treatment - although other drugs are recommended as second line treatment as stated in the consultation report.</p>	<p>practice. We maintain the view that urodynamics investigation is not essential in every woman prior to primary surgery for stress UI, and therefore is not <u>routinely</u> recommended. However, we acknowledge the weight of expert opinion that it is of value in specific circumstances; we have included recommendations as to those circumstances in the guidance.</p> <p>The GDG has reconsidered the evidence regarding antimuscarinics, along with comments from several stakeholders.</p> <p>We note in the evidence statements for antimuscarinic drugs that oxybutynin IR has a poor tolerability profile compared to other antimuscarinic drugs. However an improved tolerability profile does not necessarily translate into improved persistence with therapy. A long term study of oxybutynin ER (Diokno et al 2002) found that discontinuation attributable to adverse effects was 24%, which is similar to that reported for oxybutynin IR. A transdermal formulation of oxybutynin has been developed to further improve the tolerability profile but no studies have reported on long term tolerability and persistence.</p> <p>There is evidence from practice that persistence with antimuscarinic therapy is low (Shaya et al 2005).</p> <p>The difference in drug costs is not trivial with non-proprietary oxybutynin being around 10 times cheaper than other</p>

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					antimuscarinic options. The recommendation on antimuscarinic drugs has been revised to include advice on slow release and transdermal formulations of oxybutynin.
Sheffield Teaching Hospitals NHS Trust	NI CE	Page 6		Surgical Management Certainly sacral nerve stimulation can be effective but it is highly expensive with significant recurrent costs and carries with it approximately a 30% cure rate, 30% improved and 30% failed.	Noted. A cost-consequences analysis has been added in an Appendix.
Sheffield Teaching Hospitals NHS Trust	NI CE	Page 6		Efficacy based on PNE The common retro pubic mis urethral tape procedures are certainly supported by the evidence base but clearly now there has been a change in practice towards the transobrotator tape procedure. This comment as it stands at present will out date this consultation before it has even been published.	Noted. However, recommendations are based on the evidence and not on changes in practice.
Sheffield Teaching Hospitals NHS Trust	NI CE	Page 7	1.1.2	Assessment and Investigation Pelvic Floor Assessment It is contentious to suggest that assessment of the pelvic floor contraction is not required in the assessment of women with UI but only in those who do not benefit from pelvic muscle training.	We have considered your comments and reflected on the limited evidence as to whether pelvic floor muscle assessment prior to PFMT improves outcome. Whilst there is not unanimity on this point, it is clearly widespread expert opinion that the determination of whether a woman can contract her pelvic floor muscles voluntarily may influence the type of treatment. Hence, the GDG has reconsidered its earlier recommendation, and will advise that pelvic floor muscle assessment should be undertaken before embarking on supervised pelvic floor muscle training for the treatment of UI.
Sheffield Teaching Hospitals NHS Trust	NI CE			Drug Therapies EEDAP is mentioned but there should be a qualifying comment to state that this should be used with caution with monitoring of sodium levels in the elderly, being especially important after instigating therapy.	It is assumed that practitioners will consult the summary of product characteristics for desmopressin for prescribing information and guidance.

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		Page 12	1.2.4.5	It is not clear why propriverine is singled out in this fashion which is at variance to the ICI committee recommendations after all its side effect profile and efficacy seem to be equivalent to Oxybutynin even though there is only data up to 30 days.	We believe that the reason for this recommendation for propiverine is set out clearly in the relevant evidence statement in the full guideline.
		Page 14	1.3.1.1	Once again sacral nerve stimulation is recommended as first line therapy after failure of conservative treatment and the implication here is that it should pre-date augmentation cycstoplasty.	Please refer to responses above regarding sacral nerve stimulation.
		Page 15	1.3.2.3	The comments here about the trans-obturator approach whilst very reasonable in view of the lack of evidence about the trans obturator approach but by the fact that there is now a change in fashion towards this procedure the expert opinion is that there are many aspects of the trans obturator approach which make it preferable to the retro-pubic sling procedure.	The recommendation regarding transobturator procedures has been revised.
		Page 16	1.4.1	I fully agree with the comments about the competence of surgeons.	Competence: It is recognised in the guideline that BAUS-SFRU and BSUG are currently developing training schemes and structured assessment methods specific for those undertaking continence surgery. It is also recommended that operative competence of surgeons undertaking surgical procedures to treat UI or OAB in women should be formally assessed by trainers through a structured process. We look to these specialist societies for detailed advice on the content of training.
		Page 17	1.4.4	This is excellent but how is the committee suggesting that competence should be assessed - what is the structured process you had in mind?	
		Page 18	2		
				The term OAB syndrome is used - this should be OAB symptom complex. It is not clear if it is a syndrome but more a term which encompasses storage symptoms affecting the lower urinary tract.	
Society and College of Radiographers				This organisation was approached but did not respond.	-
South Birmingham				This organisation was approached but did not respond.	-

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Primary Care Trust					
South East Sheffield Primary Care Trust				This organisation was approached but did not respond.	-
South Essex Partnership NHS Trust				This organisation was approached but did not respond.	-
South West Kent & Maidstone Weald Primary Care Trusts		Page 7		how do manufacturing companies become stakeholder organisations and why?	Thank you for your comments. Detailed information on who can register as a stakeholder for the guidelines can be found on the NICE website - http://www.nice.org.uk/page.aspx?o=stakeholderregistration
South West Kent & Maidstone Weald Primary Care Trusts		Page 56	reference 3, line 4-6	reports prevalence on men and women – why when guideline is for women?	Not all studies distinguish between prevalence for men and women - some give only an overall figure. We have given the breakdown for men and women where possible.
South West Kent & Maidstone Weald Primary Care Trusts		Page 58	line 10-12	Statistics quoted on <u>all</u> population per PCT, NOT just women – only women would be more appropriate.	Please refer to above response.
South West Kent & Maidstone Weald Primary Care Trusts		Page 61		<p>AIM of guideline should be at start of full guideline, NOT waiting until page 61, even before the glossary.</p> <p>WHY are symptoms of voiding dysfunction not listed with stress, urge and mixed. Although the cause is often neurological which is covered in another guideline, a female can experience symptoms including UI when the bladder is not emptied fully even experiencing overflow UI – should it not be mentioned here and then refer the user to the alternative guideline if the suspected cause is neurological?</p> <p>I think that surgery including competence required by surgeons should be in another NICE guideline as it makes the full version</p>	<p>Readers are advised to use the contents page to direct them to specific sections they wish to read.</p> <p>The focus of the guideline is on stress UI, mixed UI, and OAB (wet or dry).</p> <p>Competence of surgeons is addressed</p>

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				too long; - again could the user not be referred to an alternative guideline for the specifics regarding surgery?	as required by the remit for this guideline.
South West Kent & Maidstone Weald Primary Care Trusts		Page 77	2.1, line 4	- categorisation into type of incontinence cannot always be made at initial clinical assessment, depending on who is undertaking the assessment. Indeed shouldn't this section start with WHO should be doing the clinical assessment, particularly as so much time is spent describing the research, recommendations and treatments? Also should include the competence of the assessor.	The healthcare professional providing initial assessment will vary depending on geographical service provision. NICE guidelines do not advise on who should deliver care.
South West Kent & Maidstone Weald Primary Care Trusts			2.1, line 7	- could an example of a bladder diary be included as an appendix?	We believe that including one example would be too prescriptive.
South West Kent & Maidstone Weald Primary Care Trusts			2.1, line 11	- If non-invasive treatments are unsuccessful, may need to consider cystometry to obtain an accurate diagnosis. I am surprised at the recommendation not to perform urodynamics before primary surgery for stress incontinence.	The GDG has considered the many comments received regarding the use of urodynamic testing prior to primary surgery for stress UI. We reflected further on the evidence and current practice. We maintain the view that urodynamics investigation is not essential in every woman prior to primary surgery for stress UI, and therefore is not <u>routinely</u> recommended. However, we acknowledge the weight of expert opinion that it is of value in specific circumstances; we have included recommendations as to those circumstances in the guidance.
South West Kent & Maidstone Weald Primary Care Trusts			Line 15	supervised by whom - ?expert.	Please refer to response above regarding delivery of care.
South West Kent & Maidstone Weald Primary Care Trusts			Line 18	Supervised bladder training – how long for and by whom?	Recommendation revised, reflecting your comments.

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South West Kent & Maidstone Weald Primary Care Trusts			Page 78, line 5	Why ONLY first pregnancy – may not have been taught in first pregnancy or not well.	The supporting evidence is for women in their first pregnancy.
South West Kent & Maidstone Weald Primary Care Trusts			Line 8 – sacral nerve stimulation	seems a fairly drastic recommendation - ? Botox first or other intravesical instillations – never seen this recommended routinely, particularly as there are few centres that perform this.	Please see below.
South West Kent & Maidstone Weald Primary Care Trusts			Line 20	– surgery – what is appropriate training?	The details are given in Chapter 6 of the full version of the guideline.
South West Kent & Maidstone Weald Primary Care Trusts			Page 79, 3.2	again should guideline not recommend who should do this (particularly as guideline comments on surgeons' training elsewhere). Again can't always categorise type of UI immediately, and what about voiding problems?	Please refer to response above re service delivery. The majority of UI can be classified according to symptom profile and this will expedite the immediate treatment.
South West Kent & Maidstone Weald Primary Care Trusts			3.3, line 12	I don't agree with this – why is it not required?	The evidence behind all recommendations is detailed in chapters 3 to 6. Chapter 2 which you refer to here lists the recommendations only.
South West Kent & Maidstone Weald Primary Care Trusts			3.4	who is the specialist?	Due to geographical differences in service configuration it is not possible to state to which service or healthcare professional women should be referred. The GDG has amended the recommendation to say 'specialist service'.
South West Kent & Maidstone Weald Primary Care Trusts			3.6, line 14 –	why are symptoms of voiding dysfunction ONLY first mentioned here and shouldn't they be described here?	Voiding dysfunction has been added to the glossary.
South West Kent & Maidstone			Line 21 –	who is the specialist?	See above.

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Weald Primary Care Trusts					
South West Kent & Maidstone Weald Primary Care Trusts			Page 81, line 9 –	what about recurrent UTI's without Haematuria – the cause should be sought via investigations	The GDG has considered your suggestion and believe that recurrent UTI is covered under the referral criterion of symptoms of voiding difficulty.
South West Kent & Maidstone Weald Primary Care Trusts			3.11, line 11 –	urodynamics should be performed prior to surgery for SUI.	The recommendations for urodynamics have been revised.
South West Kent & Maidstone Weald Primary Care Trusts			Page 83, 4.1 –	<p>Not enough included re lifestyle interventions.</p> <p>Which reference supports this profound statement re caffeine – some recent thinking is that caffeine is OK and that fizzy drinks are the culprit.</p> <p>Very poor limited advice – need to mention toileting habits, constipation / straining, distraction therapy.</p>	Please refer to above responses regarding where to find the evidence in the guideline.
South West Kent & Maidstone Weald Primary Care Trusts			Line 13	fluid intake modification – not specific enough	The GDG considers that there is no evidence on which to base a specific recommendaiton regarding quantity of fluid.
South West Kent & Maidstone Weald Primary Care Trusts			Line 16	weight loss – HOW? Most female sufferers will not exercise due to the presence of the UI!	Noted.
South West Kent & Maidstone Weald Primary Care Trusts			Page 84	Pelvic floor muscle training does help with OAB in deferring the first urge to void.	Most evidence for PFMT relates to its use for stress or mixed UI, as noted in the evidence statements.
South West Kent & Maidstone Weald Primary Care Trusts			Line 8	Where does this come from – must have a reference.	The evidence behind all recommendations is detailed in chapters 3 to 6. Chapter 2 which you refer to here lists the recommendations only.

Organisation	Version	Section/page	Line no.	Comments	Response
South West Kent & Maidstone Weald Primary Care Trusts			Line 11 – why not?	Sometimes need biofeedback to motivate sufferer to continue with PFME's.	We believe that the recommendation regarding biofeedback reflects this.
South West Kent & Maidstone Weald Primary Care Trusts			Page 85, line 2	PFME's may be offered before medication	Agreed.
South West Kent & Maidstone Weald Primary Care Trusts			4.41 –	Desmopressin – I don't agree with this – not routinely used. Desmopressin (as the guideline also states) is not marketed for non- neurogenic UI, therefore should not be included here.	Desmopressin was considered in this guideline because the guideline development group believed it to be an important question.
South West Kent & Maidstone Weald Primary Care Trusts			4.42	Advised not recommended (need to say WHY), therefore why go on with comment re counselling.	This recommendation has been revised.
South West Kent & Maidstone Weald Primary Care Trusts			Page 86, 4.4	Why are antimuscarinic drugs only 4 th in list, as they are generally used before the first 3 – could give the reader that the first 3 should be considered first.	The section has been reorganised to have drugs for OAB first followed by those for stress UI, reflecting the sequence in the surgery section.
South West Kent & Maidstone Weald Primary Care Trusts			Page 87, line 1	Intermittent self catheterisation should be first choice for catheter treatment.	Noted.
South West Kent & Maidstone Weald Primary Care Trusts			4.5	Indications for catheterisation – skin wounds etc – catheterisation should be SHORT TERM (with frequent reviews) until same are healed NOT long-term.	The importance of careful consideration of the need for catheterisation is highlighted in the recommendations.
South West Kent & Maidstone Weald Primary Care Trusts			Line 15	Should supra-pubic indwelling catheters be the first choice for long term – where is the reference that supports line 16 statement – need to mention more difficult insertion.	The evidence behind all recommendations is detailed in chapters 3 to 6. Chapter 2 which you refer to here lists the recommendations only.

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South West Kent & Maidstone Weald Primary Care Trusts			Page 88, 4.5.2	more should be said on absorbent products – disposable, reusable. If provided by health, lady must have continence assessment first, as mentioned earlier in guideline to ensure that treatments have been attempted, monitored and reviewed. Products are expensive, sophisticated and easily abused – need measures in place to prevent this - reviews etc and evidence of treatment plans.	We believe that the recommendation will alleviate some of your concerns.
South West Kent & Maidstone Weald Primary Care Trusts			4.5.3 -	such as	Again, refer to corresponding section describing the evidence.
South West Kent & Maidstone Weald Primary Care Trusts			4.6, line 18/19 –	what is reference for supportive evidence.	The evidence behind all recommendations is detailed in chapters 3 to 6. Chapter 2 which you refer to here lists the recommendations only.
South West Kent & Maidstone Weald Primary Care Trusts			4.7 –	NOT just 1 st pregnancy – comments on page 75, line 5	The supporting evidence is for women in their first pregnancy.
South West Kent & Maidstone Weald Primary Care Trusts			Page 89 –	surgical management – 5.1 – where has this recommendation come from? I don't think this should feature here.	Refer to chapter 5.
South West Kent & Maidstone Weald Primary Care Trusts			Line 21 –	need to note route of administration. Also what about warning re complications particularly urine retention and need to have further injections?	Route of administration added to recommendation.
South West Kent & Maidstone Weald Primary Care Trusts			Page 92 –	Should competence of surgeons be included in this guidance – could there be another guideline – “surgical options for UI in women?”	Competence of surgeons is addressed as required by the remit for this guideline.
South West Kent & Maidstone			Page 94 –	who is going to assess this and audit, and who decided on number of cases – REFERENCE.	This is explained in Chapter 6.

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Weald Primary Care Trusts					
South West Kent & Maidstone Weald Primary Care Trusts			Page 99, 3.1, introduction	which health care professional and do they have the competence to do an initial assessment, and what will it consist of? Not every health care professional will have this ability – what about training?	The healthcare professional providing initial assessment will vary depending on geographical service provision. All healthcare professionals work within their own levels of competence. The scope of the guideline does not include training. NICE guidelines do not advise on who should deliver care.
South West Kent & Maidstone Weald Primary Care Trusts			Page 104, line 12	not done as part of initial assessment	Noted. This paragraph has been moved, and the history & physical examination section revised to reflect the order in which a history and assessment would usually be taken.
South West Kent & Maidstone Weald Primary Care Trusts			Page 105, line 3	Constipation can also contribute to frequency and urgency, and voiding dysfunction. Where is reference?	We have considered your comments and are satisfied with the statement that is used in the guideline.
South West Kent & Maidstone Weald Primary Care Trusts			Page 106, line 12	do we have no interest in obstetric/gynae history?	Additional statements made in this section.
South West Kent & Maidstone Weald Primary Care Trusts			Line 16	who does this and when?	NICE guidelines do not advise on who should deliver care.
South West Kent & Maidstone Weald Primary Care Trusts			Page 109	can't always categorise – depends on knowledge and experience of those doing assessment – no recommendations on who and how.	Noted.
South West Kent & Maidstone Weald Primary Care Trusts			Page 111, line 1	I find this hard to believe! Surely if examination shows woman can't contract pelvic floor muscles, then treatment / management may well be different.	We have considered your comments and reflected on the limited evidence as to whether pelvic floor muscle assessment prior to PFMT improves outcome. Whilst there is not unanimity

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					on this point, it is clearly widespread expert opinion that the determination of whether a woman can contract her pelvic floor muscles voluntarily may influence the type of treatment. Hence, the GDG has reconsidered its earlier recommendation, and will advise that pelvic floor muscle assessment should be undertaken before embarking on supervised pelvic floor muscle training for the treatment of UI.
South West Kent & Maidstone Weald Primary Care Trusts			Page 118	What are signs/symptoms of voiding dysfunction?	Voiding dysfunction added to glossary.
South West Kent & Maidstone Weald Primary Care Trusts			Page 121	what about recurrent UTI's and/or positive bladder scan?	Please refer to evidence statements for this section.
South West Kent & Maidstone Weald Primary Care Trusts			Page 130	Bladder diaries= motivator for women when improvements seen.	Noted. This is discussed under 'does the use of bladder diaries affect outcomes?'
South West Kent & Maidstone Weald Primary Care Trusts			Page 160-161	bowel habit - ?any recommendations.	We considered that there was insufficient evidence on which to base a recommendation.
South West Kent & Maidstone Weald Primary Care Trusts			Page 165	Reducing fluid from what to what – excessive to normal or normal to little? – need to state this as the reader can't research all references.	The GDG considers that there is no evidence on which to base a specific recommendation regarding quantity of fluid.
South West Kent & Maidstone Weald Primary			4.1.5 – Smoking	did the study analyse smoking only or with coughing – there was no mention of this – therefore is the suggestion that nicotine is the problem?	The GDG has reconsidered the evidence regarding smoking and UI and concluded that there are no data to support smoking cessation specifically

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Care Trusts					in women with this condition. Therefore the recommendation has been deleted.
South West Kent & Maidstone Weald Primary Care Trusts			Page 168, 4.1.7, - Exercise.	I can't see relevance of this study on past USA Olympians – what relevance on normal population?	The study illustrates the lack of appropriate evidence to address the question of whether modifying exercise habit affects UI, and therefore supports the research recommendation made in the lifestyle section.
South West Kent & Maidstone Weald Primary Care Trusts			Line 16-20, - type of exercise	- ?incidence and amount of UI before - ?monthly, weekly, little amount	Further details of all studies are given in the accompanying evidence tables.
South West Kent & Maidstone Weald Primary Care Trusts			4.2 etc –	almost makes one wonder if physical therapies could be a small guideline on its own.	Noted.
South West Kent & Maidstone Weald Primary Care Trusts			Page 200, line 21	– why study terodiline when no longer available.	There are few RCTs comparing bladder training with antimuscarinic drugs, therefore this was considered to be useful.
South West Kent & Maidstone Weald Primary Care Trusts			Page 213	I was very surprised at this recommendation re Desmopressin for nocturia particularly in light of problems with elderly – not licensed for non-neurogenic UI so why recommend this for these women?	The GDG considered this an important question to ask.
South West Kent & Maidstone Weald Primary Care Trusts			Page 227/228	Flavoxate / tricyclic anti-depressants – surprised that evaluation of these studies was included when not commonly used.	The guideline development group believed it to be important to consider these drugs.
South West Kent & Maidstone Weald Primary Care Trusts			Page 251 – containm ent.	Consensus statements and narrative statements – using these as a basis for recommendations could be questioned.	Evidence level 4 is considered where there is no evidence of higher level (refer to method).
South West Kent &			Page 253, line	if overflow incontinence can be contained by pads, and renal function is not compromised, why should a catheter be used?	Please refer to above response regarding catheters.

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Maidstone Weald Primary Care Trusts			9		
South West Kent & Maidstone Weald Primary Care Trusts			Page 254, line 5	short term catheter and review NOT long-term.	Noted.
South West Kent & Maidstone Weald Primary Care Trusts			Line 10-12	indwelling supra pubic catheter associated with leakage via urethra.	Noted.
South West Kent & Maidstone Weald Primary Care Trusts			Page 270/271 –	should sacral nerve stimulation be included in the guideline for neurological incontinence?	We have searched the literature on SNS for women with idiopathic DO and the recommendations are based on that.
South West Kent & Maidstone Weald Primary Care Trusts			Page 272, line 19 –	how many women?	Please refer to the evidence tables for data.
South West Kent & Maidstone Weald Primary Care Trusts			Page 274, line 9 –	33%= high adverse events.	Noted and agreed.
South West Kent & Maidstone Weald Primary Care Trusts			Page 276 –	Recommendation – in other sections, mention is made of costs and economies of provision – WHY none for sacral nerve stimulation. This treatment is very specialised and more expensive with longer waits.	The cost-effectiveness of SNS was not addressed in the draft guideline because it was to be considered a low volume treatment, where the alternatives were also expensive. A cost-consequence analysis of SNS is now included as an additional appendix.
South West Kent & Maidstone Weald Primary Care Trusts			Line 16 –	who can do preliminary peripheral nerve evaluation?	NICE guidelines do not advise on who should deliver care. Nevertheless we recognise that these will only be done in the specialised units who provide this service.

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South West Kent & Maidstone Weald Primary Care Trusts			Page 286 –	Recommendations – as complication can be retention, how come ISC not mentioned as preparation for Botox? What about counselling re period of benefit – 3-12months.	Statement regarding need to self-catheterisation added to recommendations.
South West Kent & Maidstone Weald Primary Care Trusts			Page 287 – as before -?	separate guideline for surgery. I can't comment on this section, as I am not knowledgeable enough.	Noted.
South West Kent & Maidstone Weald Primary Care Trusts	NICE			I would ask that if people are only accessing the short guideline should bold statements be specifically referenced – this would be my criticism of some of the other guidelines for example multiple sclerosis.	The standard NICE template does not incorporate references.
Spinal Injuries Association				This organisation was approached but did not respond.	-
Staffordshire Moorlans Primary Care Trust				This organisation was approached but did not respond.	-
Stockport PCT				This organisation was approached but did not respond.	-
Stroke Association, The				This organisation was approached but did not respond.	-
Tameside and Glossop Acute Services NHS Trust				This organisation was approached but did not respond.	-
The Chartered Society of Physiotherapy	NICE version	General		It is not clear at whom the document is aimed. Urinary incontinence is treated by professionals from several disciplines, each with their particular remit and at a variety of levels of care. Physiotherapists aim to work in a co-operative way, and this means that each knows where their role begins and ends. The guideline is not completely clear about what applies to whom, for example, 'referral to a specialist' (page 8) presumably applies to GPs, whereas 'the use of multi-channel cystometry. . . is not recommended' can only apply to specialists. It would be clearer if the guideline specified which recommendations apply to which	Thank you for your comments. The guideline is primarily of relevance to healthcare professionals in the NHS in England and Wales; please refer to section 1.4. Due to geographical differences in service configuration it is not possible to state which service or healthcare professional women should be referred

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				level and specialism within the service. This is particularly important for physiotherapists: please see below.	to.
The Chartered Society of Physiotherapy	NICE version	7	1.1.2.1.	If this guidance is aimed at GPs then we would agree that routine digital assessment of the pelvic floor is probably inappropriate. However, physiotherapists do not generally treat any muscle group without first assessing it to establish its baseline performance from which progress can be measured, and to determine the optimum exercise programme. In the case of the pelvic floor this is particularly important because nerve damage is a common cause of pelvic floor muscle dysfunction. Where there is sensory or motor loss the woman may be unable to initiate a pelvic floor contraction; in this case a simple instruction to contract the pelvic floor will be useless. Therefore for physiotherapy practice, digital assessment may well be routine. Thus the recommendation that digital assessment for all professionals is not indicated in not appropriate. The professional groups to whom it applies should be specified. It would not be appropriate for NICE to define what is, or isn't, part of routine physiotherapy UI assessment. This guideline also appears to be in conflict with the CSP's <i>Clinical guidelines for the physiotherapy management of females aged 16-65 with stress urinary incontinence</i> . NICE is invited to review this document, which we can provide for you on request, and see if the 2 documents can be reconciled.	We have considered your comments and reflected on the limited evidence as to whether pelvic floor muscle assessment prior to PFMT improves outcome. Whilst there is not unanimity on this point, it is clearly widespread expert opinion that the determination of whether a woman can contract her pelvic floor muscles voluntarily may influence the type of treatment. Hence, the GDG has reconsidered its earlier recommendation, and will advise that pelvic floor muscle assessment should be undertaken before embarking on supervised pelvic floor muscle training for the treatment of UI.
The Chartered Society of Physiotherapy	NICE version	11	1.2.2.6.	The purpose of electrical stimulation for the pelvic floor is to initiate a pelvic floor contraction in a muscle which is either extremely weak or inactive. It may indeed aid compliance and motivation but this is not its primary purpose and should not be stated as if it is.	The recommendation reflects the GDG's view of the appropriate use of electrical stimulation.
The Chartered Society of Physiotherapy	Full	79	11	Who does this imply – GPs? Although there is no evidence to suggest that women with different PFM strengths have different outcomes with physiotherapy, common sense would suggest that it is not effective to send patients with very strong well co-ordinated pelvic floor muscles for treatment. These should be discovered by GP/consultant by vaginal assessment.	Recommendation regarding pelvic floor muscle assessment revised.
The Chartered Society of Physiotherapy		79 and 111	14 and 16	The patient is often seen first in primary care, and is not always examined. Physiotherapists treating UI may work in either primary or secondary care. However, if the primary care professional is not a physiotherapist, and UI is suspected or diagnosed, then women should be referred to a specialist physiotherapist (either in primary or secondary care depending on how local services are organised)	See above. Vaginal examination is described in the guideline text (physical examination).

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				sooner rather than later, rather than just assumed to have failed treatment in primary care. They should be informed about physiotherapy when assessed by the primary care nurse, and have the option of physiotherapy as first line treatment, or if there is no subjective improvement after one month. Then a vaginal examination is essential.	
The Chartered Society of Physiotherapy				Vaginal examination provides valuable information gained from observation/digital assessment which contributes to an effective management plan.	See above.
The Chartered Society of Physiotherapy		83		There is no description of reducing constipation under lifestyle interventions, although this is recognised on page 105	There is no evidence in relation to modifying bowel habit and its effects on UI /OAB.
The Chartered Society of Physiotherapy		96	5	Pelvic floor muscle.	'muscle' added.
The Chartered Society of Physiotherapy		111	16	<p>Physiotherapists are the experts in muscle re education. Our core training focuses on muscle assessment, muscle training programmes and rehabilitation .We are trained to do this -and it makes us unique within recognised AHP groups</p> <p>Any muscle training physiotherapy programme, for striated voluntary muscles must be preceded by muscle assessment i.e. by observation, palpation and evaluation of muscle function. It is only then that a specific programme of rehabilitation can be carried out.</p> <p>Physiotherapists would perform this for any muscle or muscle group - and pelvic floor muscles are no different.</p> <p>Many women are unsure if they are performing a pelvic floor muscle contraction correctly (and many do not)and therefore a vaginal examination is key to establishing this at the outset of treatment.</p>	Recommendation regarding pelvic floor muscle assessment revised.
The Chartered Society of Physiotherapy				<p>General health education in the form of pelvic floor muscle exercises in a group setting such as Antenatal classes, primary care or group sessions prior to individual assessment is acceptable without a vaginal examination as this is <i>information</i> given as <i>advice</i> and not treatment.</p> <p>Treatment must be specific and should be based on the findings of a vaginal examination (subject to patient consent) not just 'considered'</p> <p>'Experts' in the field refer to digital examination as being integral to</p>	Recommendation regarding pelvic floor muscle assessment revised.

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				<p>effective treatment (Bump, Bo, Sampsel, Wilson, Department of Health 1997). If women are taught PFME verbally and are doing them incorrectly and failing to improve then either a) it may be considered that conservative therapy was ineffective and the patient referred on for more invasive treatment or b) the patient will be disillusioned with PFME, and less compliant with subsequent physiotherapy.</p> <p>It is recommended that the health professional performing the vaginal examination should be appropriately trained in muscle assessment and vaginal examination prior to prescribing an effective exercise programme, which is tailored to the individual needs of the woman. Physiotherapists are specialists in this field and as the acknowledged experts work across both primary and secondary care aiming towards an integrated service.</p>	
The Chartered Society of Physiotherapy				Patient choice and woman-centred care. Treatment and care should take into account the woman's individual needs and preferences: many women <u>ask</u> and most women <u>expect</u> to be examined to confirm correct performance of the contraction.	Recommendation regarding pelvic floor muscle assessment revised.
The Chartered Society of Physiotherapy				Patient self-efficacy.	It is not clear what your comment refers to, therefore we are unable to respond.
The Chartered Society of Physiotherapy		173	2	PFMT training (duplication).	'training' deleted.
The Chartered Society of Physiotherapy	All			bladder instillations of oxybutynin for DO/OABS not fully discussed.	We considered all relevant evidence identified. This consisted of only 1 study regarding intravesical oxybutynin.
The Chartered Society of Physiotherapy				No mention of ES for DO/OABS	We have added an evidence statement and recommendation regarding electrical stimulation for OAB.
The Chartered Society of Physiotherapy	General			The numbering system in the NICE version appears to be different to that in the full guideline? If this is the case, how do we cross-refer the one to the other? The CSP is delighted that antenatal pelvic floor exercises are recommended but cannot find where the evidence is in the full version.	<p>The NICE version contains the recommendations only.</p> <p>See Chapter 4, Preventive use of conservative therapies for a summary of evidence regarding preventive use of PFMT.</p>
The David Lewis Centre				This organisation was approached but did not respond.	-

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The North West London Hospitals NHS Trust				This organisation was approached but did not respond.	-
The Robert Jones & Agnes Hunt Orthopaedic & District Hospital NHS Trust				This organisation was approached but did not respond.	-
The Royal Society of - Medicine				This organisation was approached but did not respond.	-
-The Royal West Sussex Trust				This organisation was approached but did not respond.	-
The Survivors Trust				This organisation was approached but did not respond.	-
Tissue Viability Nurses Association				This organisation was approached but did not respond.	-
Tissue Viability Society (UK)	NI CE	4	5	? if a need for beliefs to be added.	Thank you for your comments. We believe this is covered in the preceding paragraph regarding culturally sensitive information.
Tissue Viability Society (UK)	NI CE	13	7	Change pressure sore to pressure ulcer.	Changed as suggested.
Tissue Viability Society (UK)	NI CE	16	1.4.1	What is appropriate? Interpretation.	This is explained in Chapter 6 of the full guideline.
Tissue Viability Society (UK)	NI CE	16	1.4.2.2	To add written consent.	Unchanged.
Tissue Viability Society (UK)	NI CE	17	1.4.3	Total agreement.	Thank you.
Tissue Viability Society (UK)	NI CE	17	1.4.8	Total agreement.	Thank you.
Tissue Viability Society (UK)	NI CE	18	1.4.9	Total agreement.	Thank you.
Tissue Viability Society (UK)	NI CE	19		Cost to trust to implement interesting information.	Noted.

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		246		<p>women (92% women) with DO, all of whom had urge UI and were currently responding to oral oxybutynin (n=76). No significant differences were identified in efficacy (leakage episodes, cure, bladder volume) between treatment groups. Significantly more patients reported dry mouth with oral oxybutynin (39 vs. 82%)."</p> <p>SMC Decision Advice For your further information, the SMC Decision Advice Document, oxybutynin 3.9mg/24h transdermal patch Kentera) No. (190/05) stated:</p> <p>"Transdermal oxybutynin appears to have similar efficacy to oral antimuscarinics and a lower rate of anticholinergic adverse events. However, patients have the additional effect of application site reactions, which in some patients lead to treatment discontinuation. Transdermal oxybutynin has a lower total cost than oral tolterodine, but a higher total cost than oral oxybutynin."</p> <p>Conclusion In light of this data it would seem reasonable to allow the inclusion of the oxybutynin transdermal patch (Kentera) as a treatment option available to clinicians for patients who have received benefit from, but are experiencing unacceptable side effects with oral oxybutynin.</p>	
UK Specialised Services Public Health Network				This organisation was approached but did not respond.	-
University College London Hospitals NHS Trust	NICE' s draft guideline on urinary incontinence	Line 17, page 78 and line 17 page 91 and review pages 308 to 311	Line 17, page 78 and line 17 page 91 and review pages 308 to 311	<p>The Nice guideline refers to the fact that open colposuspension is an alternative to TVT (line 17, page 78 and line 16, page 90). It also states that laparoscopic colposuspension is not recommended as a routine procedure (recommendation D (GPP) (line 17, page 91). The data are reviewed (pages 308 to 311).</p> <p>The studies quoted include many studies that they confirm did not perform standard laparoscopic colposuspension with at least 2 sutures each side. In addition one of the apparent randomised studies examined (Su et al Ref 621), was nor properly randomised as patient choice was allowed. In addition in the laparoscopic arm a single suture each side was allowed and as referred to in the review of the literature this results in a higher failure rate (Person</p>	<p>Thank you for your comments.</p> <p>The quasi randomisation used in the Su study is reflected in the grading of evidence given (EL=1-); studies with a ' - ' grading are not used as a basis for recommendations (see method).</p>

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	online	sections 308 to 311		<p>et al ref 623).</p> <p>The MRC study (ref 622) has now been accepted for publication in the BJOG. The data as in the abstract fails to show that the laparoscopic colposuspension is inferior. It is probably unethical to use large amounts of research money and NHS time and to enrol patients in a study to merely ignore a multicentre study of this nature. The primary author would be happy to provide any data which may help the committee.</p> <p>The conclusion with regards laparoscopic colposuspension should read that it a reasonable alternative to open colposuspension when it is carried out in a similar manner by those surgeons experienced in performing it. This is what the data shows and as personal experience is not an appropriate reason to condemn it.</p>	<p>A pre-publication copy of the MRC study has been obtained, and is considered within the guideline.</p> <p>Recommendation modified to reflect your comment about surgeons experience.</p>
University College London Hospitals NHS Trust	NICE's draft guideline on urinary incontinence	Appendix c (page 417)	Appendix c (page 417)	<p>More than 50% of women who have a history of pure stress UI also have a positive finding of pure stress UI on multichannel cystometry.</p> <p>This would appear to be far short of the 100% certainty that one would wish to have for an accurate diagnosis before embarking on an operation, which does have an associated mortality and significant morbidity. We would be one of the few specialties who are not striving to make a diagnosis prior to surgery.</p>	Agreed. This section has been revised, with further interpretation of the data. The data relate to women undergoing assessment for UI, not necessarily those who are to undergo surgery for stress UI.
University College London Hospitals NHS Trust	NICE's draft guideline on	Page 136 (line 19)	Page 136 (line 19)	<p>The randomised study compared PFMT or bladder training versus PFMT + bladder training to confirm that UDS was not necessary. There was no difference in outcome. Not an enormous surprise!</p> <p>The Black study can hardly be used as evidence to reject urodynamics. It aimed to demonstrate the need for competent surgeons.</p> <p>The summary states that there is little evidence for the need for</p>	<p>We agree that the evidence in relation to urodynamics affecting outcome is poor; however reporting the evidence as it is supports the need for research in this area.</p> <p>The GDG has considered the many comments received regarding the use of urodynamic testing prior to primary</p>

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	urinary incontinence			<p>UDS prior to surgery for primary surgery but admits that the data are poor. It also states that the data for secondary surgery is even poorer.</p> <p>Hence if we are to reject urodynamics prior to primary surgery we should also abandon it prior to secondary surgery and merely guess the diagnoses for all.</p> <p>You cannot abandon the test when there is a statement stating that research needs to be carried out looking at the need. We can only abandon it when data exists to confirm that standard practice should be altered.</p>	<p>surgery for stress UI. We reflected further on the evidence and current practice. We maintain the view that urodynamics investigation is not essential in every woman prior to primary surgery for stress UI, and therefore is not <u>routinely</u> recommended. However, we acknowledge the weight of expert opinion that it is of value in specific circumstances; we have included recommendations as to those circumstances in the guidance.</p>
University of Leicester Department of Health Science	Full	general		<p>Service organisation has not been covered in the guideline; we consider this of major importance for service providers and commissioners. The way in which services are configured has a huge impact on quality of care, effectiveness and cost. Evidence on effective service configuration would strengthen the guideline. A paper which could be included under this heading would be <i>Williams KS, R P Assassa, N J Cooper, D A Turner, C Shaw, C W McGrother, KR Abrams, C Mayne, C Jagger, R Matthews, M Clarke, and the Leicestershire MRC Incontinence Study Team. Clinical and cost-effectiveness of a new nurse-led continence service. A Randomised Controlled Trial. British Journal of General Practice September 2005; 55:696-703.</i> There is also extensive information on service configuration in the Health Care Needs Assessment chapter on Incontinence, reference <i>McGrother C, Donaldson M, Wagg A, Matharu G, Williams KS, Watson J, Wasame J, Assassa RP. Health Care Needs Assessment: The epidemiologically based needs assessment reviews.2004</i> http://hcna.radcliffe-oxford.com/contframe.htm.</p> <p>Within the area of service configuration, methods of improving access to services should be considered, barriers to access identified and strategies to overcome barriers to help seeking identified.</p> <p><i>Shaw C. A framework for the study of coping, illness behaviour and outcomes. Journal of Advanced Nursing 1999;29(5):1246-1255.</i></p> <p><i>Shaw C, Tansey R, Jackson C, Hyde C, Allan R and the Leics MRC Incontinence study team. Barriers to help seeking in people</i></p>	<p>Thank you for your comments. Service configuration and models of healthcare delivery are outside the scope of this guideline.</p>

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				<i>with urinary problems. Family Practice 2001;18(1):48-52.</i>	
University of Leicester Department of Health Science	Full	General		Health care requirement (i.e. those actually wanting help with professionally defined health care need) is the recognised Public Health indicator on which to base the provision of services. This has been estimated by the Leicestershire MRC Incontinence study at 20.4% in people aged 40 and over, representing 5 million people in the UK. In women aged 40 and over, 23.4% were affected, increasing from 20.5% at age 40-49 up to 35.6% at age 80 and over. <i>McGrother CW, Donaldson MMK, Shaw C, Matthews RJ, Hayward TA, Dallosso HM, et al. Storage Symptoms of the Bladder: Prevalence, Incidence and Need for Services in the UK. BJU International 2004;93(6):763-769.</i>	This information has been incorporated into the text.
University of Leicester Department of Health Science	Full	general		Whilst the area of surgeon's competence is covered, there is no mention of other care providers education and training (including GPs, nurses, physiotherapists etc). In order for services to be delivered effectively, primacy needs to be given to practitioners education and training. The evidence on educational preparation of practitioners in urinary incontinence should be included. Evidence on education is provided in the HCNA chapter (details above) and from the International Consultation on Incontinence chapter, <i>Newman DK, Denis L, Gruenwald I, Ee CH, Millard R, Roberts R, Sampelle C, Williams K. Continence promotion: Prevention, Education and Organisation. In: Incontinence Abrams P, Cardozo L, Khoury S, Wein A. 2005.</i> Details of the evaluation of a specific continence module for nurses have also been published: <i>Williams K, Assassa RP, Smith N, Shaw C, Carter E and the Leicestershire MRC Incontinence Study Team (1999). Educational preparation for specialist practice in continence care: A model for the future. British Journal of Nursing ;8:18:1198-1207</i>	Competence of health professionals other than surgeons is outside the scope of this guideline.
University of Leicester Department of Health Science	Full	9	7	Stakeholder organisations. Only the first line of our address is given, Department of Health Sciences, this does not indicate that we are from the University of Leicester.	'University of Leicester' added.
University of Leicester Department of Health Science	Full	39		Definition of overactive bladder (OAB) in glossary: this does not conform to the ICS standardisation of terminology although on page 54 line 10 you refer to the ICS 2002 publication (ref 1) as the source of your definitions. The ICS OAB definition is "urgency, with or without urge incontinence, usually with frequency and	Amended.

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				nocturia” By this definition, neither frequency nor nocturia is a prerequisite for the condition although urgency is, wet or dry.	
University of Leicester Department of Health Science	Full	56	3-6	The estimates quoted for men and women could be replaced with more specific estimates for women, as follows: The Leicestershire MRC Incontinence study found that while 34.2% of women reported UI at times, only 3.5% experienced symptoms that were profound (daily wet/soaked); 11.8% severe (weekly damp/wet); 7.3% moderate (monthly/damp); 11.1% minimal (yearly /less than damp); <i>McGrother CW, Donaldson MMK, Shaw C, Matthews RJ, Hayward TA, Dallosso HM, et al. Storage Symptoms of the Bladder: Prevalence, Incidence and Need for Services in the UK. BJU International 2004;93(6):763-769.</i>	Suggested figures and reference incorporated.
University of Leicester Department of Health Science	Full	58	8	The Leicestershire MRC Incontinence study found an overall prevalence of OAB in women aged 40 and over of 21.4% (pure 7.7%; mixed 12.7%) and an incidence rate of 9.9% per annum (i.e. pure 5.4%; mixed 4.5%). <i>McGrother CW, Donaldson MM, Hayward TA, Matthews R, Dallosso HM, Hyde C, et al. Urinary storage disorder and comorbidities: a prospective population cohort study in middle-aged and older women. Age and Ageing 2005;35:16-24.</i>	Reference added.
University of Leicester Department of Health Science	Full	59	1	The term risk factor is not defined. I suggest this is primarily an epidemiological term for which the definition suggested by Last is: “.an aspect of personal behaviour or lifestyle, an environmental exposure or an inborn or inherited characteristic which, on the basis of epidemiological evidence, is known to be associated with health related conditions...” <i>A Dictionary of Epidemiology, Fourth Edition - Edited by John M. Last, Robert A. Spasoff, and Susan S. Harris. Oxford University Press, New York, New York</i>	Noted.
University of Leicester Department of Health Science	Full	59	6	A review of prospective studies identified the following consistent predictive factors: cystitis; pregnancy; parity; obesity. <i>McGrother C, Donaldson M, Wagg A, Matharu G, Williams K, Watson J, et al. Continence: The epidemiologically based needs assessment reviews. 2004 http://hcna.radcliffe-oxford.com/contframe.htm Last accessed 29 June 2006.</i>	Noted.
University of Leicester Department of	Full	60	3	The year 2001 (ref 17) was the year of publication but the costings referred to 1995. Wagner and Hu 1998 is another widely cited paper using 1995 costings.	Amended in text.

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Health Science				<i>Wagner T, Hu T. Economic costs of urinary incontinence in 1995. Urology 1998;51(3):355-360.</i>	
University of Leicester Department of Health Science	Full	60	10	Other literature which is relevant here: <i>The Continence Foundation. Making the case for investment in an integrated continence service: a source book for continence services. London: 2001</i> <i>Turner DA, Shaw C, McGrother CW, Dallosso HM, Cooper N and the MRC Incontinence Team. The Cost of Clinically Significant Urinary Storage Symptoms for Community Dwelling Adults in the Uk. BJU International 2004;93(9):1246-1252.</i>	Data from Turner publication added.
University of Leicester Department of Health Science	Full	60	22	Ref 19 refers to OAB, but there are also 2 US studies which refer to SUI: <i>Ramsey, S., Wagner, T. & Bavendam, T. Estimated costs of treating stress urinary incontinence in elderly women according to the AHCPR clinical practice guidelines. The American Journal of Managed Care 1996, 11(2), 147-154.</i> <i>Birbaum HG, Leong SA, Oster EF, Kinchen K, Sun P. Cost of Stress Urinary Incontinence - a Claims Data Analysis. Pharmacoeconomics 2004;22(2):95-105.</i>	Noted.
University of Leicester Department of Health Science	Full	101	10	We published a study looking at the relationship between symptoms reported in a postal questionnaire and urodynamic diagnosis. Our paper is unique as it is the only study of which we are aware to have looked at symptoms from a general population in the community rather than a group of patients referred to secondary care. Some of this community group went on to have urodynamic investigation. Despite the latter being a select group, the distribution of symptoms between the baseline population and those undergoing cystometry was very similar. We used multivariate analysis to identify which symptoms and which level of severity of those symptoms was associated with which urodynamic diagnosis. We also present sensitivities, specificities, PPVs and NPVs of our models. <i>Matharu G, Donaldson MM, McGrother CW, Matthews RJatLMIST. Relationship between urinary symptoms reported in a postal questionnaire and urodynamic diagnosis. NeuroUrol Urodyn 2005;24(2):100-5.</i>	This study was excluded because of an interval of at least 8 weeks between reporting symptoms and undertaking urodynamic assessment, during which women were included in a RCT evaluating a nurse-led continence service. Inappropriate to compare diagnoses after such an intervention as the initial diagnosis may have changed after intervention.
University of Leicester	Full	104	11	One of the major problems within primary care is the identification of women with abnormal symptoms who would benefit from further	Noted; this is outside the guideline scope.

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Department of Health Science				assessment. Specific thresholds for abnormality have been suggested – based on evidence from population surveys. <i>McGrother CW, Donaldson MMK, Shaw C, Matthews RJ, Hayward TA, Dallosso HM, et al. Storage Symptoms of the Bladder: Prevalence, Incidence and Need for Services in the UK. BJU International 2004;93(6):763-769.</i>	
University of Leicester Department of Health Science	Full	107	9	It is important to be aware that poor physical and mental health often precede or accompany the onset of incontinence. <i>McGrother CW, Donaldson MM, Hayward TA, Matthews R, Dallosso HM, Hyde C, et al. Urinary storage disorder and comorbidities: a prospective population cohort study in middle-aged and older women. Age and Ageing 2005;35:16-24.</i>	Noted; statement added regarding mental health.
University of Leicester Department of Health Science	Full	126		On page 100, line 20, the importance of assessing storage symptoms is emphasised. A well validated questionnaire for storage symptoms which includes incontinence is published by <i>Shaw C, Matthews RJ, Perry S, Assassa RP, Williams K, McGrother C, Dallosso H, Jagger C, Mayne C, Clarke M, and the Leicestershire MRC Incontinence Study Team. Validity and reliability of an interviewer-administered questionnaire to measure the severity of lower urinary tract symptoms of storage abnormality: the Leicestershire Urinary Symptom Questionnaire. BJU International, 2002, 90, 205-215.</i> This tool is validated to assess the outcome of all storage symptoms, there is also a related storage symptom impact questionnaire, <i>Shaw C, Matthews RJ, Perry SI, Williams K, Spiers N, Assassa RP, McGrother CW, Dallosso H, Jagger C, Mayne C, Clarke M, and the Leicestershire MRC Incontinence Study Team. Validity and reliability of a questionnaire to measure the impact of lower urinary tract symptoms on quality of life: the Leicester Impact Scale. Neurourology and Urodynamics, 2004;23(3):229-236.</i>	Noted.
University of Leicester Department of Health Science	Full	161	7	Bowel urgency has been shown to be independently predictive for the onset of OAB (relative risk 2.2) <i>McGrother CW, Donaldson MM, Hayward TA, Matthews R, Dallosso HM, Hyde C, et al. Urinary storage disorder and comorbidities: a prospective population cohort study in middle-aged and older women. Age and Ageing 2005;35:16-24.</i>	Added to summary of data.
University of Leicester Department of Health Science	Full	162	4	Add zinc following vitamin B12.	Added to summary of data.

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University of Leicester Department of Health Science	Full	164	2	There is one prospective study that found no independent link between caffeine intake and the onset of OAB or SUI (<i>see ref 184</i>).	It is noted that tea and coffee intake was only considered within univariate analysis - comment added to evidence table.
University of Leicester Department of Health Science	Full	173		A paper currently in press may offer further evidence for future updates. <i>Williams KS, Assassa RP, McGrother CW et al. Randomised Controlled trial of the effectiveness of pelvic floor therapies for Urodynamic Stress Incontinence (USI) and Mixed incontinence. Accepted by British Journal of Urology International, 2006.</i>	Noted.
University of Leicester Department of Health Science	Full	267	20	Studies of the natural history of progression of severity of symptoms are used to indicate the optimum window for preventive action. One population study has suggested such intervention should begin before age 60. <i>Donaldson MMK, Thompson JR, Matthews RJ, Dallosso HM, McGrother CW. The natural history of overactive bladder and stress urinary incontinence in older women in the community; a three year prospective cohort study. Accepted by Neurourology & Urodynamics 2006.</i>	Noted.
University Hospital Birmingham NHS Trust				This organisation was approached but did not respond.	-
Vale of Aylesbury Primary Care Trust				This organisation was approached but did not respond.	-
Welsh Assembly Government	general	general		Thank you for giving the Welsh Assembly Government the opportunity to comment on the above appraisal determination. We are content with the technical detail of the evidence supporting the provisional recommendations and have no further comments to make at this stage.	Thank you.
West of Cornwall PCT	NICE	9	1.1.10.1	draft consultation says 'no urodynamics needed before primary surgery', we would like clarification please	The evidence and rationale for all recommendations is given in the full guideline. The GDG has considered the many comments received regarding the use of urodynamic testing prior to primary surgery for stress UI. We reflected further on the evidence and current

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					practice. We maintain the view that urodynamics investigation is not essential in every woman prior to primary surgery for stress UI, and therefore is not <u>routinely</u> recommended. However, we acknowledge the weight of expert opinion that it is of value in specific circumstances; we have included recommendations as to those circumstances in the guidance.
West of Cornwall PCT	"	7	1.1.2.1	Routine PF digital assessment is not required – we are concerned about this as some women cannot recruit the correct muscle.	We have considered your comments and reflected on the limited evidence as to whether pelvic floor muscle assessment prior to PFMT improves outcome. Whilst there is not unanimity on this point, it is clearly widespread expert opinion that the determination of whether a woman can contract her pelvic floor muscles voluntarily may influence the type of treatment. Hence, the GDG has reconsidered its earlier recommendation, and will advise that pelvic floor muscle assessment should be undertaken before embarking on supervised pelvic floor muscle training for the treatment of UI.
West of Cornwall PCT	"	7	1.1.3.1	Would women with prolapse be referred to a physio or a surgeon. We feel physio should be the first line for mild to moderate prolapse.	Due to geographical differences in service configuration it is not possible to state which service or healthcare professional women should be referred to. The GDG has amended the recommendation to say 'specialist service'.
West Sussex Health & Social Care NHS Trust				This organisation was approached but did not respond.	-
Whipps Cross University Hospital NHS				This organisation was approached but did not respond.	-

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Trust					
Wirral Hospital NHS Trust				This organisation was approached but did not respond.	-
Women's Health Concern				This organisation was approached but did not respond.	-