Menopause: diagnosis and management

Consultation on draft scope
Stakeholder comments table updated August 2022

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Stakeholder	Page no.	Line no.	Comments	Developer's response
Astellas Pharma Ltd	General	General	Based on the research recommendations in NG23 and the importance of non-hormonal options, considering that such therapies are in Phase 3, it might be useful to mention other upcoming options for women in menopause who experience hot flashes. Furthermore, such treatment options might be considered especially for women at high risk for whom hormonal treatments might not be appropriate. This comment refers to sections focusing on Vasomotor symptoms (hot flushes and night sweats), "Women with, or at high risk of, breast cancer" and potentially in the sections focusing on Non hormonal treatment options / therapies	Thank you for your comment. Non-hormonal treatments were included in the original guideline network meta-analysis of treatments for short-term menopausal symptoms, and a separate analysis was done for women with a history of breast cancer. The surveillance and scoping process for guideline update did not identify substantive new evidence on these treatments likely to change the existing recommendations, with the exception of cognitive behavioural therapy so we are updating the recommendations on CBT.
Autistic Menopause Study	General	General	Gender inclusive language: we suggest that the scope and documents consider using more gender-neutral language. Calling trans and non-binary people 'women' on the basis that they experience the menopause invalidates their identity and can cause distress [i] . Alternative wording includes "menopausal people", "people who menstruate", "people with wombs".	Thank you for your comment. Careful consideration is given to the language used in the scope and the update of the guideline. NICE also regularly reviews its language guide related to gender-sensitive issues. We aim to use inclusive language by referring to women, non-binary and trans people or at times neutral language by referring to people.
Autistic Menopause Study	003	010 - 016	Consideration should be given to intersectionality – the likelihood that an individual will experience several marginalised identities, e.g. being Black, non-binary, neurodivergent. Intersectionality and marginalised characteristics influence menopausal symptoms and individual understanding and experience of menopause [ii].	Thank you for your comment. We have noted this important point in the Equality Impact Assessment form, for the committee to consider this when reviewing evidence and drafting recommendations.
Autistic Menopause Study	003	015 - 016	Equality considerations: We recommend that **neurodevelopmental conditions associated with 'neurodivergence'** (e.g. ADHD, autism	Thank you for your comment. We have noted this in the Equality Impact Assessment form and the committee will consider your comment when agreeing which subgroups to

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			spectrum conditions) should be recognised here and within the Equality Impact Assessment. Neurodivergence deserves mention because: - Neurodevelopmental conditions may be perceived as disabilities, but can also be perceived as a different neurodevelopmental trajectory that results in a different way of thinking and seeing the world, which may be considered a marginalised identity [iii]. The individual's optimal state of health might look very different to that of a neurotypical person. This sets neurodevelopmental people apart from individuals experiencing different types of disability. - While distinct from other disabilities, neurodevelopmental conditions affect healthcare interactions and health outcomes [iv]. Importantly, the very nature of neurodevelopmental conditions can affect the clarity of communication between individuals and healthcare practitioners – the extent of this may be underappreciated. Importantly, neurodivergent adults experience greater morbidity and mortality [v]. - Studies indicate that being neurodivergent also affects experience of menopause [vi]. - Ageing and changes across the lifespan tend to be overlooked in people with developmental conditions, whereas the above studies show that a person's experience of their neurodivergence changes across the lifespan (with some autistic people experiencing new, severe disabilities during menopause).	include in the evidence reviews when developing the evidence review protocols. Equalities considerations will be taken into account when developing new recommendations.

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			- Neurodivergent adults are at significantly higher risk of mental ill-health and suicidality than neurotypical people [vii]. **The research above suggests that this may be heightened during the menopause.**	
Autistic Menopause Study	007	004	Consideration should be given to individual characteristics that could affect health outcomes, prognosis, and response to treatment options. Being neurodivergent affects response to CBT – professionals must adapt their therapeutic delivery to achieve optimal outcomes [viii]. Being neurodivergent affects responses to pharmacological treatment [ix]. We do not know yet how neurodivergent people respond to pharmacological treatments specifically for menopause, or how to manage these in addition to other medications taken by neurodivergent people.	Thank you for your comment. We have noted this in the Equality Impact Assessment form and the committee will consider your comment when agreeing which subgroups to include in the evidence reviews when developing the evidence review protocols. Equalities considerations will be taken into account when developing new recommendations.
Besins Healthcare (UK) Ltd	008	002	The draft scope has not identified the following issue and question related to "What are the effects of hormone replacement therapy (HRT) for prevention of osteoporosis in postmenopausal women at high risk of future fractures" We feel this group should be included. For menopausal women the risk of fragility fracture is decreased while taking HRT. This benefit: •is maintained during treatment but decreases once treatment stops	Thank you for your comment. HRT taken as a preventative treatment for people with early menopause is within the scope of this update. HRT taken as a preventative treatment (rather than for menopausal symptoms) for other groups at high risk of fractures is outside the scope of this guideline. The team updating the NICE Osteoporosis guideline may consider it for inclusion in the scope of the updated Osteoporosis guideline.

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			•may continue for longer in women who take HRT for longer. Reference: Menopause: diagnosis and management NICE guideline [NG23]	
British Dietetic Association	General	General	We would like to comment that we think there is a significant omission: The subject of weight gain in post-menopausal women should be covered (e.g. https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/menopause-and-weight-gain) . In particular consent and avoidance of accidental harm from 1) weight gaining medication 2) very low calorie diets **1) Weight gaining medications** Polypharmacy and prescribing of a combination of weight gaining medications for post-menopausal women requires further consideration and inclusion. Are women aware, is there informed consent? What Matters to them? Are healthcare professionals confident in discussing the risks of these medications in combination for this population? (Stanford, Fatima Cody MD, MPH, MPA1; Cena, Hellas MD2,3; Biino, Ginevra PhD4; Umoren, Olivia BS5; Jimenez, Monik ScD6; Freeman, Marlene P. MD5; Shadyab, Aladdin H. PhD7; Wild, Robert A. MD, MPH, PhD8; Womack, Catherine R. MD9; Banack, Hailey R. PhD10; Manson, JoAnn E. MD,	Thank you for your comment. Weight gain itself is not included as a key area, instead we are looking at health outcomes that may be associated with increased BMI including cancers, cardiovascular disease and diabetes. These evidence reviews will need to include BMI as a confounding factor. NICE has a suite of guidelines dedicated to the prevention and management of obesity covering issues such as low calorie diets.

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			DrPH6,11 The association between weight-promoting medication use and weight gain in postmenopausal women: findings from the Women's Health Initiative, Menopause: October 2020 - Volume 27 - Issue 10 - p 1117-1125 doi: 10.1097/GME.0000000000001589) **2) Very low calorie diets** Additionally accidental harm, reduced bone density, from very low calorie diets (VLCD) for post menopausal women should be considered. Are these obese post menopausal women given informed choice that the intervention will reduce their bone density? Seimon RV, Wild-Taylor AL, Keating SE, et al. Effect of Weight Loss via Severe vs Moderate Energy Restriction on Lean Mass and Body Composition Among Postmenopausal Women With Obesity: The TEMPO Diet Randomized Clinical Trial. *JAMA Netw Open*. 2019;2(10):e1913733. Published 2019 Oct 2. doi:10.1001/jamanetworkopen.2019.13733 Choksi P, Rothberg A, Kraftson A, et al. Weight loss and bone mineral density in obese adults: a longitudinal analysis of the influence of very low energy diets. Clin Diabetes Endocrinol. 2018;4:14. Published 2018 Jun 19. doi:10.1186/s40842-018-0063-6	

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British Menopause Society	General	General	Review of the balance of benefits and risks with HRT (bone, cardiovascular, breast cancer and total mortality).	Thank you for your comment. The update will focus on the impact of HRT on longer term health outcomes (both risks and benefits), because this is where surveillance has identified important new evidence.
British Menopause Society	General	General	Review of the balance of benefits and risks with HRT (bone, cardiovascular, breast cancer and total mortality) for women who commence HRT under the age 60. Provide guidance regarding starting / re-starting HRT in women above age 60 years to ensure this group are not excluded. This is likely to help guide women to make informed decisions on the balance of benefits and risks of HRT.	Thank you for your comment. The evidence on the benefits and risks of HRT on different overall health outcomes will be reviewed, including cardiovascular disease, breast cancer, and all-cause mortality. The plan is to consider the timing, duration and different age groups when reviewing the evidence on HRT use and its effects on overall health outcomes.
British Menopause Society	General	General	Updating the evidence on risk of menopause, HRT and dementia given the different conclusion in recent reports: -Vinogradova Y, Dening T, Hippisley-Cox J, Taylor L, Moore M, Coupland C. Use of menopausal hormone therapy and risk of dementia: nested case-control studies using QResearch and CPRD databases. BMJ. 2021 Sep 29;374:n2182. doi: 10.1136/bmj.n2182. PMID: 34588168; PMCID: PMC8479814. -Kuh D, Cooper R, Moore A, et al. (2018) Age at menopause and lifetime cognition: findings from a British birth cohort study. Neurology 90: e1673–e1681.	Thank you for your comment and suggestion of studies for review. The evidence on the effect of HRT on dementia will be reviewed as part of the update. Studies for inclusion will depend on the specific criteria outlined in the evidence review protocol which will be developed together with the guideline committee.

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			-Savolainen-Peltonen H, Rahkola-Soisalo P, Hoti F, et al. (2019) Use of postmenopausal hormone therapy and risk of Alzheimer's disease in Finland: nationwide case–control study British Medical Journal 364: l665. -https://pubmed.ncbi.nlm.nih.gov/28274328/	
British Menopause Society	General	General	Reviewing the evidence on the management of women with early menopause (40-45). In most guidance this group (40-45) are overlooked with recommendations covering naturally menopausal women (over 45) and women with POI (under 40). In clinical practice women with early menopause (40–45) are advised in a similar way to women with POI regarding general health implications including bone and cardiovascular health, symptom management, and information on fertility / contraception as required. We would suggest reviewing the evidence on the long-term impact on this group including the references below which show increased risk of osteoporosis and fractures, cardiovascular disease, type 2 diabetes and increase in all-cause mortality in this group.	Thank you for your comment. The scope states that the effects of HRT on overall health outcomes for women, non-binary and trans people aged 40-44 years will be reviewed and guidance updated as needed.
British Menopause Society	General	General	Review evidence on endometrial safety with sequential and continuous combined HRT regimens. Dose of Progesterone/ progestogen, and varying its dose with respect to estrogen dose in this respect to ensure adequate endometrial protection.	Thank you for your comment. We will be reviewing the evidence on endometrial safety in relation to the risks of endometrial cancer. The different HRT regimens and different HRT preparations will be discussed in more detail with the guideline committee members, and the specific details will be agreed on at the protocol development stage.

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British Menopause Society	General	General	CBT: Assess evidence on VMS, Mood, Sleep, Sexual symptoms. There is very limited access to guided CBT in the UK and most patients go down the line of self-help CBT. Assessment of the evidence on self-help CBT would also be useful.	Thank you for your comment. Evidence on cognitive behavioural therapy for managing menopausal symptoms will be reviewed as part of the guideline update. We have revised the wording of the draft review question on CBT not to be specific about which outcomes we will be considering. The outcomes relevant for this review question as well as the different modes of CBT will be discussed and agreed by the guideline committee when developing the evidence review protocol. We recognise the varying or limited access to CBT in the UK in current practice.
British Menopause Society	General	General	Urogenital symptoms: Update on vaginal oestrogens including ultra low dose vaginal oestrogens / Ospemifene / Vaginal DHEA. Evidence on transvaginal laser including: https://jamanetwork.com/journals/jama/article-abstract/2784960	Thank you for your comment. Evidence on the interventions to manage genitourinary symptoms, such as vaginal oestrogens, ospemifene and transvaginal laser therapy will be reviewed. The details about the interventions will be discussed and agreed by the guideline committee at evidence review protocol development stage. The inclusion of relevant studies will depend on the agreed protocol.
British Menopause Society	General	General	HRT in women with breast cancer	Thank you for your comment. This update is focused on areas where surveillance and scoping process for the guideline update has found substantive new evidence which could change the existing recommendations and the issue of HRT in people with breast cancer was not identified in this process. The topic of HRT in people with breast cancer is covered in the NICE early & locally advanced breast cancer guideline (NG101) and familial breast cancer guideline (CG164).
British Menopause Society	General	General	Women with hereditary cancer who undergo risk reducing BSO.	Thank you for your comment. The issue of HRT after risk-reducing surgery for people at increased risk of ovarian cancer

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				is included in the scope of the NICE familial ovarian cancer guideline (NG10225) which is currently being developed.
British Menopause Society	General	General	Review of the evidence on testosterone: indications / preparations / benefits risks. Although there may not be a great deal of shift on evidence about testosterone use, it would be useful to discuss indications for it as at present it should be just libido but there is a lot of pressure from patients to prescribe for other indications.	Thank you for your comment. We acknowledge that testosterone as a treatment for more than HSDD is a contentious area. There is a body of RCT evidence supporting its use for HSDD but evidence on other outcomes such as body composition and musculoskeletal health comes from a small number of study participants. This would prevent us from making evidence based recommendations on testosterone outside of its use for HSDD. The surveillance and scoping process for the guideline update did not identify substantive new evidence likely to change the existing recommendations on testosterone. Therefore, reviewing evidence on testosterone in relation to menopause care was not prioritised. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
British Menopause Society	General	General	Review of the evidence on compounded bioidentical hormones: safety and efficacy.	Thank you for your comment. During the scoping process it has been agreed that the evidence review on efficacy of HRT for symptoms management or short-term safety will not be updated, however, we will be conducting evidence reviews on the overall health outcomes of different HRT formulations (oestrogen alone, or oestrogen combined with progesterone), such as its effect on cardiovascular disease, different cancers and all-cause mortality.

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British Menopause Society	General	General	Consider reviewing the economic impact of the menopause.	Thank you for your comment. In line with 'Developing NICE guidelines: the manual' non-comparative costing studies, 'burden of disease' studies and 'cost of illness' studies will usually be excluded from the economic evidence reviews and such analyses would not be undertaken as part of bespoke economic modelling. Economic evidence is most useful for forming recommendations when they consider the cost and outcomes of two competing interventions and committee time and resources will be dedicated to reviewing this evidence.
British Menopause Society	General	General	Highlight is not just an update of the benefits and risks of HRT, but a focus on how those benefits/risks are communicated to patients, particularly in relation/comparison to other risk factors (e.g. obesity, alcohol, etc.) to put them in context in a way that facilitates patient choice.	Thank you for your comment which will be considered when developing the guideline.
British Menopause Society	General	General	To update the NICE Menopause Quality standards to reflect the updated guidance recommendations.	Thank you for your comment. The NICE Quality Standard on menopause will be updated as needed.
Department of Health and Social Care	005	General	Could the scope be expanded to include a review of testosterone as a short-term treatment for menopausal symptoms? The current NICE guideline only has recommendations on testosterone as a second-line treatment for altered sexual function if HRT alone is not effective, however, an evidence review of testosterone as a first-line treatment for altered sexual function and for other menopause symptoms would be of benefit, including an evidence review on long-term benefits and risks of testosterone for menopausal symptoms	Thank you for your comment. We acknowledge that testosterone as a treatment for more than HSDD is a contentious area. There is a body of RCT evidence supporting its use for HSDD but evidence on other outcomes such as body composition and musculoskeletal health comes from a small number of study participants. This would prevent us from making evidence based recommendations on testosterone outside of its use for HSDD. The surveillance and scoping process for the guideline update did not identify substantive new evidence likely to change the existing recommendations on testosterone. Therefore, reviewing evidence on

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				testosterone in relation to menopause care was not prioritised. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
Department of Health and Social Care	005	General	Suggest expanding the scope to include an evidence review of 'starting and stopping HRT'. The draft scope says 'No evidence review: retain recommendations from existing guideline'.	Thank you for your comment. The evidence review underpinning this section focused on discontinuation of HRT and this was not prioritised for update as our surveillance and scoping process did not identify substantive new evidence that would warrant change to the recommendations. However, editorial changes to the retained sections of the existing guideline may be made as needed to reflect current editorial standards and new recommendations made by the committee on topics being updated.
Department of Health and Social Care	005	General	Suggest expanding the scope to include an evidence review of HRT as a preventative treatment especially for CVD and dementia. So for example if a woman has mild symptoms and doesn't feel she needs HRT to relieve her symptoms, could/would HRT still be recommended as a preventive for other health risks like CVD or dementia	Thank you for your comment. The effects (beneficial or harmful) of HRT on cardiovascular disease and dementia will be covered in this update and recommendations will be updated as appropriate. For the early menopause population, the guideline update will review evidence on the effect of HRT whether or not the person has symptoms to see if in this younger group HRT should be recommended regardless of symptoms, however, for the menopausal population 45 years and over, HRT is only recommended when symptomatic and the update won't change that.
Endometriosis UK	001	025	Add after line 25, a new sentence "Induced menopause as a result of surgery or medication, also occurs, sometimes in women younger than the age of natural menopause".	Thank you for your comment. It has been agreed during the scoping process that this guideline will focus on 'permanent' menopause and will therefore cover naturally occurring menopause or surgery-induced menopause but will not cover

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			Induced menopause occurs in several ways: - after surgical removal of the ovaries (bilateral oophorectomy) (1) - from the use of medications to intentionally induce menopause as part of the treatment of certain diseases for example endometriosis (1) - after cancer treatment such as chemotherapy or radiotherapy (2) Induced menopause following oophorectomy is permanent. Induced menopause from the use of medication, for example in women with endometriosis, is temporary (1). Induced menopause in women with endometriosis is often in women younger than the natural age for menopause (1) (1) British Menopause Society Tool for Clinicians (April 2020), "Induced menopause in women with endometriosis" https://thebms.org.uk/wp-content/uploads/2020/04/10-BMS-TfC-Induced-Menopause-in-women-with-endometriosis-APR2020.pdf (2) NHS.UK website "Early menopause", last updated 2 February 2021, https://www.nhs.uk/conditions/early-menopause/	situations where menopause-like symptoms are caused (temporarily) by hormonal treatments. This has now been stated in the scope. We have added about surgery-induced menopause in to the 'Why is this guideline needed' section. A revision has been made to the scope in August 2022 to include menopause and also menopause-like symptoms in people treated for certain cancers, such as breast cancer. These cancers and their treatments may both cause menopause and be associated with menopause-like symptoms and these two possibilities may be indistinguishable. We do not intend to include the menopause-like symptoms that may be associated with treatment of a broader range of conditions. The evidence regarding the efficacy of interventions in such diverse circumstances would likely be complex and varied as the underlying physiological mechanisms are not likely to be uniform.

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Endometriosis UK	003	020 - 021	Change the sentence on lines 20-21 to read: "Women, non-binary and trans people with menopause (including perimenopause, post menopause, and induced menopause)"	Thank you for your comment. We have revised the text in 'Why this guideline is needed' section by adding that sometimes menopause is induced by surgery. The scoping group agreed that temporary menopause-like symptoms caused by hormonal treatments is not within the scope of this guideline and we have clarified this in the scope. Taking the above into account, we did not consider it necessary to include induced menopause as a separate issue in the population definition. A revision has been made to the scope in August 2022 to include menopause and also menopause-like symptoms in people treated for certain cancers, such as breast cancer. These cancers and their treatments may both cause menopause and be associated with menopause-like symptoms and these two possibilities may be indistinguishable. We do not intend to include the menopause-like symptoms that may be associated with treatment of a broader range of conditions. The evidence regarding the efficacy of interventions in such diverse circumstances would likely be complex and varied as the underlying physiological mechanisms are not likely to be uniform.
Endometriosis UK	005	Table	point 1.4 Under "Managing short-term menopausal symptoms" add an additional point: "Women going through induced menopause including temporary induced menopause".	Thank you for your comment. It has been agreed during the scoping process that this guideline will focus on 'permanent' menopause and will therefore cover naturally occurring menopause or surgery-induced menopause but will not cover situations where menopause-like symptoms are caused (temporarily) by hormonal treatments. This has now been

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				stated in the scope. We have added about surgery-induced menopause in to the 'Why is this guideline needed' section. A revision has been made to the scope in August 2022 to include menopause and also menopause-like symptoms in people treated for certain cancers, such as breast cancer. These cancers and their treatments may both cause menopause and be associated with menopause-like symptoms and these two possibilities may be indistinguishable. We do not intend to include the menopause-like symptoms that may be associated with treatment of a broader range of conditions. The evidence regarding the efficacy of interventions in such diverse circumstances would likely be complex and varied as the underlying physiological mechanisms are not likely to be uniform.
Endometriosis UK	006	Table	point 1.5 In the table "Long term benefits and risks of hormone replacement therapy", please add an additional point: "Women going through induced menopause including temporary induced menopause" on the left hand side of the table and on the right hand side please add "Review evidence: new area in guideline". The British Menopause Society Tool for Clinicians "Induced menopause in women with endometriosis" https://thebms.org.uk/wp-content/uploads/2020/04/10-BMS-TfC-Induced-Menopause-in-women-with-endometriosis-APR2020.pdf, states that HRT should be offered to all women	Thank you for your comment. It has been agreed during the scoping process that this guideline will focus on 'permanent' menopause and will therefore cover naturally occurring menopause or surgery-induced menopause but will not cover situations where menopause-like symptoms are caused (temporarily) by hormonal treatments. This has now been stated in the scope. A revision has been made to the scope in August 2022 to include menopause and also menopause-like symptoms in people treated for certain cancers, such as breast cancer. These cancers and their treatments may both cause menopause and be associated with menopause-like

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			with endometriosis going through induced menopause unless contraindicated. The Tool also notes that induced menopause in women with endometriosis is often in women younger than the natural age for menopause.	symptoms and these two possibilities may be indistinguishable. We do not intend to include the menopause-like symptoms that may be associated with treatment of a broader range of conditions. The evidence regarding the efficacy of interventions in such diverse circumstances would likely be complex and varied as the underlying physiological mechanisms are not likely to be uniform.
Endometriosis UK	009	008	Please add an additional question after point 2.7: "2.8 What are the effects of hormone replacement therapy on women going through induced menopause including temporary induced menopause?" The British Menopause Society Tool for Clinicians "Induced menopause in women with endometriosis" https://thebms.org.uk/wp-content/uploads/2020/04/10-BMS-TfC-Induced-Menopa,use-in-women-with-endometriosis-APR2020.pdf, states that HRT should be offered to all women with endometriosis going through induced menopause unless contraindicated.	Thank you for your comment. It has been agreed during the scoping process that this guideline will focus on 'permanent' menopause and will therefore cover naturally occurring menopause or surgery-induced menopause but will not cover situations where menopause-like symptoms are caused (temporarily) by hormonal treatments. This has now been stated in the scope. A revision has been made to the scope in August 2022 to include menopause and also menopause-like symptoms in people treated for certain cancers, such as breast cancer. These cancers and their treatments may both cause menopause and be associated with menopause-like symptoms and these two possibilities may be indistinguishable. We do not intend to include the menopause-like symptoms that may be associated with treatment of a broader range of conditions. The evidence regarding the efficacy of interventions in such diverse circumstances would likely be complex and varied as the underlying physiological mechanisms are not likely to be uniform.

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Endometriosis UK	009	029	Under 3.6 Main Outcomes please add another outcome to the bullet point list: "The impact of induced menopause including temporary induced menopause on younger women" The British Menopause Society Tool for Clinicians "Induced menopause in women with endometriosis" https://thebms.org.uk/wp-content/uploads/2020/04/10-BMS-TfC-Induced-Menopause-in-women-with-endometriosis-APR2020.pdf, notes that induced menopause in women with endometriosis is often in women younger than the natural age for menopause.	Thank you for your comment. It has been agreed during the scoping process that this guideline will focus on 'permanent' menopause and will therefore cover naturally occurring menopause or surgery-induced menopause but will not cover situations where menopause-like symptoms are caused (temporarily) by hormonal treatments. This has now been stated in the scope. A revision has been made to the scope in August 2022 to include menopause and also menopause-like symptoms in people treated for certain cancers, such as breast cancer. These cancers and their treatments may both cause menopause and be associated with menopause-like symptoms and these two possibilities may be indistinguishable. We do not intend to include the menopause-like symptoms that may be associated with treatment of a broader range of conditions. The evidence regarding the efficacy of interventions in such diverse circumstances would likely be complex and varied as the underlying physiological mechanisms are not likely to be uniform.
Faculty of Pharmaceutical Medicine	General	General	Information for specialist services needs to be reinforced through the document.	Thank you for your comment. The guidance will apply to NHS-commissioned services providing menopause care, we have clarified the wording in the scope.
Faculty of Pharmaceutical Medicine	001	013	The guidance covers many aspects of menopause but does not cearly distinguish what is essentially troublesome and pathological. Loss of memory in aging is also a natural process – but extreme loss is pathological and arguably suicidal ideation (mood changes) or 10 plus VMS episodes a day is	Thank you for your comment. Text have been added to clarify that although most people with menopause experience some symptoms, not all will seek treatment. It is troublesome symptoms that impact daily life that will require treatment but the impact of symptoms will vary between individuals.

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Faculty of Pharmaceutical Medicine	001	020	The draft scope and definition of menopause – should include peri-menopause and post-menopause, as some symptoms often do not reverse without treatment. This should be reflected by updated section 1.2 of the guidance and may include the STRAW classification system recognising the changes in symptoms from peri- menopause to post-.	Thank you for your comment. This section of the scope has been amended to refer to perimenopause. The section of diagnosis perimenopause and menopause was not prioritised for update as the surveillance and scoping process did not identify substantive new evidence that would warrant changes to the existing recommendations.
Faculty of Pharmaceutical Medicine	002	012 - 014	Mild, moderate and severe definitions of VMS according to daily number of episodes and Genitourinary Syndrome of Menopause symptoms could be categorised as mild, moderate and severe, so treatments could be guided according to the regulatory label, some of which are classified by severity.	Thank you for your comment. The guideline committee will have the chance to make different treatment recommendations according to the severity of symptoms, if the evidence supports this.
Faculty of Pharmaceutical Medicine	002	005	There is no mention of who may or may not need what kind of treatments – explanation of range of symptoms would be useful and more detailed description of all symptoms.	Thank you for your comment. This section has been revised to say that not everyone experiencing symptoms will seek medical treatment but that treatment is required for those with troublesome symptoms significantly impacting daily life. The detail about which treatments are best for which women is better covered in the guideline itself.
Faculty of Pharmaceutical Medicine	002	010	Benefits including prevention or treatment of osteoporosis and prevention of cardiovascular and other disease arguably should be regulatory and outside of the scope of the document. The evidence needs to be reviewed for each treatment rather than overall assumption for all hormonal menopause interventions.	Thank you for your comment. Prevention and treatment of osteoporosis and prevention of cardiovascular and other disease as such are not within the scope of this guideline. However, the plan is to review the evidence about the effects, both beneficial and harmful of HRT on overall health outcomes. For people with early menopause, this includes reviewing the health effects of HRT use whether or not the person has symptoms. However, for other populations (people

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				45 or over), HRT as preventative treatment for those without symptoms will not be covered. The evidence will be reviewed according to HRT type although the details of these will be determined by the committee at protocol development stage.
Faculty of Pharmaceutical Medicine	004	008 - 010	We do not support the revisions being limited to CBT and HRT on overall health outcomes.	Thank you for your comment. The most important areas where new research has been identified that might change current recommendations have been prioritised for the update. Please see responses to your other comments for further details on the specific issues you have raised.
Faculty of Pharmaceutical Medicine	005	Table	1.2 whilst peri-menopause is defined, no symptoms are discussed, which may be different from menopause itself – these symptoms include menorrhagia and often dysphoria and depression more frequently than in menopause. Patients should be counselled regarding pregnancy. In addition, there are hormonal treatments labelled for menorrhagia and dypsphoria that may be useful in this population and for menorrhagia there is NICE guidance which could be cross-referenced.	Thank you for your comment. Diagnosis of perimenopause based on symptoms is covered in the current guideline NG23 and we will be retaining these recommendations. We will not be including this topic for an evidence review as our surveillance and scoping process did not identify substantive new evidence that would impact existing recommendations, however the recommendations that are being retained may be edited to ensure they meet current editorial standards and reflect practice context. Pregnancy during the menopause is not in the scope of this guideline update, however contraception is referred to in the current guideline NG23 and the recommendation cross refers to NICE accredited guidance Faculty of Sexual and Reproductive Health (FSHR) clinical guideline on Contraception for Women Aged over 40 Years. The plan is to retain this recommendation.
Faculty of Pharmaceutical Medicine	005	Table	Section 1.4 we believe urogenital atrophy should be aligned with Genitourinary Syndrome of Menopause and possibly vulvar vaginal atrophy, as this latter term is still used in labelling for treatment,	Thank you for your comment. The guideline development team will pay careful attention to all the different terms used for urogenital atrophy when designing literature searches to capture any relevant evidence. The guideline committee will

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				agree the most appropriate terms to use when wording the recommendations to be understandable by healthcare professionals and people with menopause.
Faculty of Pharmaceutical Medicine	005	Table	Section 1.4 Whilst isoflavones and black cohosh have well establish use labels there is considerable uncertainty they are effective in VMS, yet the guidance gives little to distinguish from other more effective treatments.	Thank you for your comment. The current guideline NG23 acknowledges the limited evidence and the uncertainty in the evidence for these, which is reflected in the recommendation.
Faculty of Pharmaceutical Medicine	005	Table	Altered sexual function should be separated as dyspareunia from Hypoactive Sexual Desire Disorder (HSDD). Testosterone has been known for some years to be effective for HSDD and whilst Intrinsa testosterone patch demonstrated efficacy over placebo.Treatments for HSDD are available in US but for premenopausal women. The Intrinsa testosterone patch for HSDD was available but limited the indication to women with surgically induced menopause taking concomitant estrogen therapy. Perhaps should be dealt with in separate guidance as is menorrhagia, however.	Thank you for your comment. We are planning not to update this part of the guideline and to retain the existing recommendations. The surveillance and scoping process for guideline update did not identify substantive new evidence likely to change the existing recommendations on testosterone. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
Faculty of Pharmaceutical Medicine	008	011	The risks of hormone replacement therapy should really be related to individual products. There is evidence, particularly for venous thrombosis, that different doses and combinations of oestrogens and progesterones and routes of administration (oral, patch, intravaginal, intrauterine etc) have different impacts on both clinical outcome and well established haematological surrogate markers. This was acknowledged in the Lancet article cited in the 2019 guidance update. The new oestrogen, estetrol (E4), as yet only approved for contraception, but in development for menopause, is a selective foetal oestrogen and has a very different	Thank you for your comment. When reviewing the evidence related to benefits and risks of HRT, different HRT preparations will be considered. The level of detail with regards to the different HRT preparations will be discussed with the guideline committee members at the stage of protocol development.

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			pharmacological profile to E2. Grouping all products together will be very confusing for both prescriber and user.	
Faculty of Pharmaceutical Medicine	008	011	With regard to benefits – again these will also not apply to all hormonal treatments and routes of administration. Treatment should be separated from prevention with regard to benefit. Whilst there is some evidence for treatment for osteoporosis this is unlikely to be carried into the label of newer products, even those with hormonal basis for treatment. Prevention is difficult to demonstrate compared to risk and as with lipid lowering drugs should be demonstrated with interventional studies rather than the epidemiological data used for risk. A review of benefits is welcomed, but the implication that all treatments result in this should be avoided.	Thank you for your comment. We will be reviewing the evidence related to benefits and risks of HRT on particular overall health outcomes, considering the different HRT preparations. The level of detail with regards to the different HRT preparations will be discussed with the guideline committee when developing the protocols for the individual reviews. HRT as a preventative treatment for people with early menopause is within the scope of this update as we will review the evidence on the beneficial and harmful impact of HRT on overall health outcomes whether or not the person has symptoms in this younger age group. However, for other populations (people 45 or over), HRT as preventative treatment for those without symptoms will not be covered.
Faculty of Pharmaceutical Medicine	008	011	There is evidence from epidemiological and registry studies that hormonal replacement therapy has a benefit against progression in COVID to death, but no interventional studies have shown this.	Thank you for your comment. In relation to HRT, the focus of the update is on issues where there is substantive new evidence which could impact the existing recommendations, or which could help decision making on whether or not to take HRT for those considering it. After careful consideration, COVID was not prioritised as an outcome for the use of HRT in the update of the guideline.
Faculty of Pharmaceutical Medicine	009	011	Main long term outcomes – are very varied in terms of how robust the evidence might need to be collect and how 'long term' is defined. Some outcomes have been studied using scoring systems longitudinally, but many benefit outcomes will be difficult to separate individual treatments. Risks should be studied in conjunction with the big safety databases.	Thank you for your comment. For each review question the committee will agree a review protocol defining how and when outcomes should be measured and the appropriate research study designs.

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Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit	General	General	Testosterone: indications, effectiveness for these, safety, monitoring. Use alone without HRT. Use after breast cancer. Again, no guidance and hugely variable practice	Thank you for your comment. The surveillance and scoping process for the guideline update did not identify substantive new evidence likely to change the existing recommendations on testosterone. Therefore, reviewing evidence on testosterone in relation to menopause care was not prioritised. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit	General	General	use of definitions – nothing in intro uses the word climacteric which is what is being described here. Traditionally medically menopause refers to the last period	Thank you for your comment. The word 'climacteric' is less often used and not necessarily known to wider audiences so we have not used it in the scope. However, we have revised the 'Why this guideline is needed' section to include explanation of the perimenopause or menopause transition to highlight the gradual process that leads to menses stopping.
Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit	General	General	Contraception and fertility do not appear to be included, particularly important with premature ovarian failure but in view of relatively high proportion of TOP in women >40, important.	Thank you for your comment. This topic was not prioritised for update because there is a NICE-accredited Faculty of Sexual and Reproductive Health (FSHR) clinical guideline on Contraception for Women Aged over 40 Years which the current guideline NG23 refers to. The plan is to retain this recommendation.
Faculty of Sexual and Reproductive Healthcare Clinical	General	General	Spelling of oestrogen – this should now be estrogen	Thank you for your comment. NICE uses 'oestrogen' as the spelling.

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Effectiveness Unit				
Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit	General	General	As the issue of Menopause is enormously topical at present, I hope there will be very clear information on 'complementary/alternative' therapies. I note this is mentioned but it is an area where there is huge misinformation and where products are sold to women when most vulnerable and the evidence is totally missing.	Thank you for your comment. Complementary therapies and lifestyle advice were included in the original guideline network meta-analysis of treatments for short-term menopausal symptoms. The surveillance and scoping process for the guideline update did not identify substantive new evidence on these interventions likely to change the existing recommendations.
Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit	General	General	suggest something on Testosterone use- there has been a statement on its use Global Consensus Position Statement on the Use of Testosterone Therapy for Women (imsociety.org)	Thank you for your comment. The global consensus position statement on the use of testosterone is consistent with the existing recommendations in NG23 - in that there is a body of RCT evidence supporting its use for HSDD but as yet insufficient evidence on other outcomes. The global consensus position statement has a wider scope than NG23 and also makes recommendations on measurement of testosterone, female sexual dysfunction and endogenous androgen levels - areas not covered in NG23. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
Faculty of Sexual and Reproductive Healthcare Clinical	General	General	would also like an emphasis on the affect of cancer (radio and chemo) treatment on menopause symptoms and management	Thank you for your comment. Treatment related morbidity due to chemotherapy or radiotherapy would be more appropriately covered in the guidelines for the primary cancers - for example breast cancer or ovarian cancer. This is because their effects on menopause symptoms and management must be balanced with their benefits in terms of overall and disease free survival.

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Effectiveness Unit				It may be possible to look at subgroups of people previously treated with chemo or radiotherapy in our review of CBT - if the guideline committee thinks this is appropriate. A revision has been made to the scope in August 2022 to include menopause and also menopause-like symptoms in people treated for certain cancers, such as breast cancer. These cancers and their treatments may both cause menopause and be associated with menopause-like symptoms and these two possibilities may be indistinguishable. We do not intend to include the menopause-like symptoms that may be associated with treatment of a broader range of conditions. The evidence regarding the efficacy of interventions in such diverse circumstances would likely be complex and varied as the underlying physiological mechanisms are not likely to be uniform.
Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit	General	General	Use of testosterone and Oestrogen implants	Thank you for your comment. We are not planning on updating the section of guideline NG23 covering hormonal treatments for short-term symptoms because the surveillance and scoping process for the guideline update did not identify substantive new evidence likely to change the existing recommendations on hormonal treatments. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
Faculty of Sexual and	General	General	Perhaps a guideline on time to treatment/management so that commissioners are shaken up a bit	Thank you for your comment. We are not entirely sure what is meant by this comment but it is possible that new

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Reproductive Healthcare Clinical Effectiveness Unit				recommendations related to the topics being updated may touch upon the timing of treatment, although this is not specifically being reviewed.
Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit	General	General	Management of Bleeding on HRT	Thank you for your comment. This update is focused on areas where surveillance and scoping process has found substantive new evidence which could change the existing recommendations and the issue of management of bleeding on HRT was not identified in this process.
Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit	005	Table	Section 1.4 in addition to the section re women with, or at high risk of breast cancer, there should be a section on women with established cardiovascular disease and women with thrombophilia/personal history of VTE (risk associated with HRT use by the general population as covered in section 1.5/2.7 may not apply to these groups and practice is hugely variable).	Thank you for your comment. We are not proposing to update the evidence review on hormonal treatments - we plan to review new evidence about CBT in people with or at high risk of breast cancer. The guideline committee will have the chance to look for evidence in subgroups of people with established cardiovascular disease or people with thrombophilia/personal history of VTE if they agree it is appropriate.
Foundry Healthcare Lewes	005	001	Altered sexual function I was involved in the draft scope consultation. There was a repeated request from the clinicians involved (from both primary and secondary care) for the position on testosterone	Thank you for your comment. The existing guideline NG23 only recommends testosterone for "menopausal women with low sexual desire if HRT alone is not effective". There is a body of RCT evidence supporting its use in this context but

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			for women to be expanded and clarified. This does not seem to have made it into the draft scope.	evidence on other outcomes such as body composition and musculoskeletal health comes from a small number of study participants. This would prevent us from making evidence based recommendations on testosterone outside of its use for HSDD. The surveillance and scoping process for the guideline update did not identify substantive new evidence likely to change the existing recommendations for altered sexual function. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
Hywel Dda University Health Board	General	General	like an emphasis on the affect of cancer (radio and chemo) treatment on menopause symptoms and management	Thank you for your comment. Treatment related morbidity due to chemotherapy or radiotherapy would be more appropriately covered in the guidelines for the primary cancers - for example breast cancer or ovarian cancer. Effects on menopause symptoms and management must be balanced with benefits in terms of overall and disease free survival. It may be possible to look at subgroups of people previously treated with chemo or radiotherapy in our review of CBT - if the guideline committee thinks this is appropriate.
Hywel Dda University Health Board	General	General	would agree something on contraception use in the >40 years	Thank you for your comment. This topic was not prioritised for update because there is a NICE-accredited Faculty of Sexual and Reproductive Health (FSHR) clinical guideline on Contraception for Women Aged over 40 Years which the current guideline NG23 refers to. The plan is to retain this recommendation.

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Hywel Dda University Health Board	General	General	Perhaps a guideline on time to treatment/management so	Thank you for your comment. We are not entirely sure what is meant by this comment but it is possible that new recommendations related to the topics being updated may touch upon the timing of treatment, although this is not specifically being reviewed.
Hywel Dda University Health Board	008	004	Include management of bleeding on HRT	Thank you for your comment. This update is focused on areas where surveillance and scoping process has found substantive new evidence which could change the existing recommendations and the issue of management of bleeding on HRT was not identified in this process.
Hywel Dda University Health Board	008	011	Comments on Testosterone use, stetment on its use: Global Consensus Position Statement on the Use of Testosterone Therapy for Women (imsociety.org)	Thank you for your comment. The global consensus position statement on the use of testosterone is consistent with the existing recommendations in NG23 - in that there is a body of RCT evidence supporting its use for HSDD but insufficient evidence on other outcomes. The global consensus position statement has a wider scope than NG23 and also makes recommendations on measurement of testosterone, female sexual dysfunction and endogenous androgen levels - areas not covered in NG23. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
Hywel Dda University Health Board	008	011	Use of Testosterone and Oestrogen implants	Thank you for your comment. We are not planning on updating the section of guideline NG23 covering hormonal treatments for short-term symptoms because the surveillance and scoping process for guideline update did not identify substantive new evidence likely to change the existing recommendations. NICE

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				has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
Institute and Faculty of Actuaries	008	024 - 027	In 2016, the Institute and Faculty of Actuaries (IFoA) commissioned a five-year research programme to develop methodology to use big data to better understand the impact of certain conditions and interventions on life expectancy. The research team at the University of East Anglia included Aviva which oversaw the robustness of the research methodology, along with a Steering Group of actuaries, who are experts in analyzing risk. The research into HRT was the first of its kind to look at the impact of HRT on overall life expectancy using UK primary care data. It followed 105,199 healthy women aged 46 to 65 years at first HRT prescription over up to 32 years with an average follow-up of 13 years, and compared their outcomes with 224,643 non-users of the same age and GP practice. The research adjusted for type 2 diabetes, hypertension and its treatments, coronary heart disease and oophorectomy/hysterectomy status, as well as body mass index, smoking and deprivation status. The research found that oestrogen-only therapy does not impact the risk of death from all causes, while taking combined HRT is associated with an average 9% reduction in death from all causes.	Thank you for your comment. We plan to review the evidence in this area and have included a draft review question on this subject "What are the effects of hormone replacement therapy for menopausal symptoms on all-cause mortality?"

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			The main limitation of using observational data is that there may be some differences between women using HRT and non-users that were not accounted for. Randomised trials are better at accounting for all differences between groups, and interestingly the data from aggregated trials found a reduced risk of breast cancer in HRT users. The main strengths of this study are the long period of follow-up over up to 32 years with all-cause mortality as the key outcome, and the use of a large primary healthcare database that enabled HRT users to be matched with controls with information on co-existing illnesses and sociodemographic factors. "The effect of hormone replacement therapy on the survival of UK women: a retrospective cohort study 1984−2017" was published in the BJOG https://obgyn.onlinelibrary.wiley.com/doi/10.1111/1471-0528.17008	
Lobular Breast Cancer UK	007	006 - 007	At Lobular Breast Cancer UK, we feel that extra support and help is needed for individuals who experience an extreme and rapid menopause, as a consequence of taking tamoxifen or aromatase inhibitors for the treatment of oestrogen-positive breast cancers. Currently, little/ no treatment and support is given, despite these individuals being in active treatment under a breast care team. There is a missed opportunity for referral to menopause specialists and clear help and guidance for these individuals, with evidence-based therapy for those who are struggling psychologically to cope with rapid menopause after the trauma of a breast cancer diagnosis. We believe that	Thank you for your comment. This update will not look at help and support for people with breast cancer experiencing menopausal symptoms, as this would be more appropriately covered in a breast cancer guideline. However our review of the evidence on CBT may allow the recommendation in the early breast cancer guideline and familial breast cancer guideline to be updated.

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			this intervention would increase adherence to medication, and therefore reduce the possibility of breast cancer recurrence.	
Lobular Breast Cancer UK	007	006 - 007	1.12.12 As part of a multi-disciplinary approach to treatment, pharmacological therapies such as antidepressants should be considered for all individuals with breast cancer provided there is an evidence base for their safety. In the current breast cancer guidelines, there are no recommendations for antidepressants in those who are on tamoxifen. Need clear guidance on antidepressants as a consequence of early and rapid menopause regardless of the type of hormone suppressants.	Thank you for your comment. This update will not look at all different treatments for menopausal symptoms in people with breast cancer. However our review of the evidence on CBT may allow the recommendation in the early breast cancer guideline to be updated.
Lobular Breast Cancer UK	007	006 - 007	1.12.13 In the current breast cancer guidelines the evidence on soy having a negative (as opposed to positive) effect is not well evidenced and needs to be updated. This is problematic for people who consume soy for health or ethical reasons. Research on the other products in this section needs to have an evidence base and be updated. For example, can women with hormone-positive breast cancer use vaginal creams or other methods to mitigate vaginal atrophy (Lubián López DM. Management of genitourinary syndrome of menopause in breast cancer survivors: An update. *World J Clin Oncol* 2022; 13(2): 71-100 [DOI: 10.5306/wjco.v13.i2.71])	Thank you for your comment. This update will not look at all different treatments for menopausal symptoms in people with breast cancer. However our review of the evidence on CBT may allow the recommendation in the early breast cancer guideline to be updated.
Lobular Breast Cancer UK	007	006 - 007	1.12.11 In the current guidelines, only counselling is suggested but this may not be the best method of psychological intervention, compared to therapies such as acceptance and	Thank you for your comment. Evidence on cognitive behavioural therapy for managing menopausal symptoms will be reviewed as part of the guideline update.

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			commitment therapy (ACT) and other cognitive behavioural therapies which have a growing evidence base.	
Lobular Breast Cancer UK	008	008 - 010	The draft scope currently does not mention women with a breast cancer diagnosis who are receiving oestrogen suppression. Can these local treatments be used in women with a breast cancer diagnosis?	Thank you for your comment. The evidence review can look at subgroups of people (such as those receiving oestrogen suppression treatment) if the guideline committee agrees it is appropriate. The best evidence for effectiveness will come from randomised trials, however, which may well exclude those people receiving oestrogen suppression.
Lobular Breast Cancer UK	008	014 - 015	This recommendation should also look at subtypes of breast cancer that have been more strongly linked to HRT use. For example, lobular breast cancer has been more strongly associated with the use of HRT. Need to look at the type of HRT and the relative risk of breast cancer, and women need to be be informed of that risk when they are given HRT.	Thank you for your comment. These additional details about the subtypes of breast cancer and the type of HRT are typically included in the review protocol, as appropriate, which will be agreed by the guideline committee.
Lobular Breast Cancer UK	009	012	Can sexual dysfunction and problems be included? Also weight gain as a possible contributor to diabetes and cardiovascular disease?	Thank you for your comment. The main outcomes list provides outcomes for the committee to consider when developing review protocols, but may be expanded during protocol development based on the committee's expertise. When looking at evidence of the impact of HRT on long term health outcomes, BMI is an important confounder which will need to be accounted for in the analysis.
Menopause Exchange	General	General	1.3.1 There could be more information on self-help lifestyle changes and complementary therapies. Self-help measures are a cost saving intervention.	Thank you for your comment. Complementary therapies and lifestyle advice were included in the original guideline network meta-analysis of treatments for short-term menopausal symptoms. The surveillance and scoping process for guideline update did not identify substantive new evidence on these interventions likely to change the existing recommendations.

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Menopause Inclusion Collective	General	General	Some studies cite differences between heterosexual and lesbian women's experience of menopause (Hyde et al., 2011; Winterich 2003) and the problematic nature of heteronormative sexuality in menopause (Lazar et al,. 2019) . There is no mention of lesbian/queer women's identity as needing updating or developing on p2, 'sexual orientation' section of the Equality Impact Assessment. Although only anecdotal evidence, most gay & queer women in peri / menopause / postmenopausal age range have a slew of stories of our sexuality being ignored or dismissed as 'hetero-lite' by health professionals, so I honestly cannot imagine that we're not also experiencing the same silencing or ignoring in regard to menopausal issues.	Thank you for your comment. We have noted this in the Equality Impact Assessment form and the committee will consider your comment when agreeing which subgroups to include in the evidence reviews when developing the evidence review protocols. Equalities considerations will be taken into account when developing new recommendations.
Menopause Inclusion Collective	General	General	Including trans-masculine people might be even more inclusive.	Thank you for your comment. Trans-masculine people will be included in the guideline. We will give careful consideration to the language used in the guideline in order to be inclusive.
Menopause Inclusion Collective	General	General	Regarding trans men and hormones, it is more complex than is stated in the Equality Impact Assessment. Taking supplemental testosterone may largely prevent menopause but the person may still experience Genitourinary Symptoms of Menopause and benefit from vaginal oestrogen. The medical profession can help a lot of these processes by not signing up to the absolute binary gendering of hormones, and helping trans masculine patients to understand that a small amount of a hormone will not feminise them. Greater	Thank you for your comment. We recognise this as an important issue. When reviewing the evidence and drafting recommendations on the topics included within the scope of the guideline update, the committee will consider how equalities considerations relating to non-binary and trans people could be taken into account to improve clinical care on menopause. Hormonal treatments for non-binary and trans people as part of medical transition healthcare per se is not within the remit of this guideline, although the committee will consider referring to the World Professional Association for

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			understanding of gender dysphoria would be extremely helpful here. More generally, clinics need to make their offerings (wording, graphics) more gender neutral, and/or more inclusive of all patients, in recognition of the fact that menopause happens to people. Also educate staff about respecting changed names and pronouns. LGBTQ+ people report poor experiences in this: https://www.tandfonline.com/doi/full/10.1080/14681994.2021.1881770	Transgender Health (WPATH) Standard of Care, which is currently being updated. Some of the issues you raise, such as more appropriate and inclusive communication and respecting people's changed names and pronouns apply beyond menopause care and may be something that NICE guidance that relate to people's experience of health and social care services (e.g. Patient experience in adult NHS services) could consider in future updates. We have flagged this with the surveillance team at NICE.
Menopause Inclusion Collective	General	General	Where 'Sex'is referred to there needs to be more recognition of the needs of Intersex patients.	Thank you for your comment. We have noted this in the Equality Impact Assessment form and the committee will consider this when developing the evidence review protocols and recommendations on the topics covered in the scope.
Menopause Inclusion Collective	General	General	Assumptions about someone's sexual preferences and orientation cause frustration, along with the idea that all people in menopause have a husband and are having, or wish to be having, penis-in-vagina sex.	Thank you for your comment. We have noted this in the Equality Impact Assessment form. Your comment raises an important point about LGBTQ+ awareness among health care professionals. Assumptions about people's sexual preferences and orientation applies beyond menopause care and may be something that NICE guidance that relate to people's experience of health and social care services (e.g. Patient experience in adult NHS services) could consider in future updates. We have flagged this with the surveillance team at NICE.
Menopause Inclusion Collective	General	General	The Equality Impact Assessment could include reference to the religious beliefs and cultural values in relation to menopause. Not all religious and cultural groups have the same approach or attitude toward the menopause, this may impact the patients willingness and ease of disclosure of troublesome symptoms.	Thank you for your comment. We have noted this in the Equality Impact Assessment form.

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Menopause Inclusion Collective	002	015	Current Practice - This may be beyond the scope of this document but it would be good if policy makers recognised that for a trans patient, changes in hormones may induce a 'menopause-like' effect. i.e a trans man having oestrogen levels reduced via testosterone or oestrogen blockers, or a trans woman having testosterone levels reduced via oestrogen or testosterone blockers; and if they have to stop taking oestrogen for any reason. There may be a debate over whether this is a menopause or like a menopause, however the effects can be significant and it feels important to decide on their legal (and medical) weight in terms of impact on quality of life and how this can be recognised.	Thank you for your comment. We recognise the importance of this issue, however, it has been agreed during the scoping process that this guideline will not cover situations where menopause-like symptoms are caused by hormonal treatments. This has now been stated in the scope.
Menopause Inclusion Collective	004	017	Hormones - there needs to far greater understanding, and willingness to understand, the complexities of hormones when a person is both trans or non-binary and in menopause, whether 'natural' menopause, or menopause due to removal of ovaries for any reason (gender affirmation or premenstrual dysphoric disorder or anything else) and there needs to be a far clearer pathway through this.	Thank you for your comment. When reviewing the evidence and drafting recommendations on the topics included within the scope of the guideline update, the committee will consider how equalities considerations for non-binary and trans people could be taken into account to improve clinical care. Hormonal treatments as part of medical transition healthcare for non-binary and trans people per se is not within the remit of this guideline, although the committee will consider referring to the World Professional Association for Transgender Health (WPATH) Standard of Care, which is currently being updated.
Menopause Inclusion Collective	005	Table	1.1 Doctors need to be trained in trans and non-binary awareness. As above there needs to be a far clearer pathway between menopause services and gender services. Doctors need to understand the needs of, say, an assigned female at birth non-binary patient in their late 40s who is microdosing testosterone,	Thank you for your comment. We recognise this as an important issue. When reviewing the evidence and drafting recommendations on the topics included within the scope of the guideline update, the committee will consider how equalities considerations relating to non-binary and trans people could be taken into account to improve clinical care on

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			but who is also in need of hormone replacement therapy for menopause, There is currently great confusion and patients left with no help because of being passed around, and General Practitioners fearing, and not understanding, gender affirmative treatments and therefore not wanting to engage with trans and non-binary patients.	menopause. Hormonal treatments as part of medical transition healthcare for non-binary and trans people per se is not within the remit of this guideline, although the committee will consider referring to the World Professional Association for Transgender Health (WPATH) Standard of Care, which is currently being updated. The issue around trans and non-binary awareness applies beyond menopause care and may be something that NICE guidance that relate to people's experience of health and social care services (e.g. Patient experience in adult NHS services) could consider in future updates. We have flagged this with the surveillance team at NICE.
Menopause Inclusion Collective	005	Table	1.2 There needs to be more acknowledgement of the fact that so many are reporting being in perimenopause much younger than has previously been assumed. People are being told by doctors that they 'cannot' be in peri, despite presenting many side effects, in their early 40s and late 30s. More research is needed, and much more respect and acceptance of patients' lived experiences.	Thank you for your comment. The 'Why the guideline is needed' section acknowledges that for some people menopause transition starts earlier than others and includes prevalence estimates for early menopause (40-44 years) and premature ovarian insufficiency (under 40 years). In relation to people's lived experience, NICE is committed to involving patient groups and service users in their work, including during consultation of the draft guideline products. Importantly, all guideline committees include lay members who are usually people with lived experience of the condition/topic at hand.
Menopause Inclusion Collective	005	Table	1.4 'Altered sexual function' I am glad to see this phrase here rather than 'sexual dysfunction'. It is a failure of sex education that pushes this notion, particularly when applied to people Assumed Female at Birth.	Thank you for your comment, we agree that altered sexual function is a better phrase.

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Menopause Inclusion Collective	007	006 - 008	Re. refresh of 1.12.12 (SSRIs for hot-flushes). SSRIs are commonly prescribed for depression and the equation of depression and menopause in people experiencing menopause is debated (see Bryant et al., 2012; Judd et al., 2012; Lock and Kaufert 2001; Vesco et al., 2007). However, what is not debated is the exacerbation of physiological experience when under psychological duress - given the psychological impact of breast cancer diagnosis and treatment, especially when it is accompanied by medical/surgical menopause (particularly compounded in those under 'usual' menopause age) – it seems limited to merely offer SSRIs as in 1.12.12 without also taking into account the psycho-socio-cultural elements that contribute to vasomotor symptomology and/or the non-medical alternatives for the same symptomology (Balabanovic et al., 2013; Diel et al., 2019; Mann et al., 2011; Stefanopolou & Hunter, 2014). Again, limiting the understanding of menopause merely to the biomedical fails to address other elements that can be usefully engaged in a wider sphere – eg, talking therapies/IAPT/exercise.	Thank you for your comment. This update will not look at all different treatments for menopausal symptoms in people with breast cancer. However our review of the evidence on CBT may allow the recommendation in the early breast cancer guideline to be updated.
Menopause Inclusion Collective	009	014 - 029	Urge NICE to look further than the purely biomedical HRT response to outcomes listed on page 9. A large number of studies on lifestyle, diet and exercise (Astbury-Ward, 2003; Ayers et al., 2011; Brown et al., 2015; Bryant et al., 2012; Driel et al., 2019; Hoga et al., 2015; Palacios et al., 2010) point to any number of psycho-socio-cultural approaches to menopause experiences that can also alleviate symptomology, increase quality of life, combat osteoporosis/loss of muscle	Thank you for your comment. Non-pharmaceutical treatments were included in the original guideline network meta-analysis of treatments for short-term menopausal symptoms including: acupuncture, lifestyle advice, relaxation therapies (including yoga), psychological therapies and cognitive behavioural therapy. The surveillance and scoping process for the guideline update did not identify substantive new evidence on these treatments likely to change the existing

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			mass and strength – given there will always be people for whom hormone treatment is contraindicated and/or who do not wish to make use of hormone treatment, a range of possibilities in the guidelines is vital.	recommendations, with the exception of cognitive behavioural therapy so we are updating the recommendations on CBT.
Newson Health Limited	General	General	Needs more details about other health preventative effects of HRT	Thank you for your comment. Evidence related to benefits and risks of HRT on particular overall health outcomes will be reviewed. Evidence on HRT as a preventative treatment will be considered for people with early menopause as we will be reviewing evidence on the benefits and harms of HRT in this younger population whether or not they have symptoms. However, for other populations (people 45 or over), HRT as preventative treatment for those without symptoms will not be covered.
Newson Health Limited	002	006	**Common symptoms currently only mentions vasomotor symptoms and vaginal dryness.** The wide range of potential Menopausal symptoms should be mentioned here, rather than just highlighting 2 common ones. Around 25% of perimenopausal and menopausal women do not have vasomotor symptoms.	Thank you for your comment. This section has been revised by adding "changes to sleep and mood" as examples of signs and symptoms of the menopause.
Newson Health Limited	002	008	**It is difficult to differentiate between Menopausal symptoms and the natural ageing process**.CRG to confirm accuracy of this statement. I do not think it is that difficult if women are asked to monitor symptoms every 3 months then it is easier to determine a change	Thank you for your comment. Research in this area can be difficult and the scope merely acknowledges that changes related to ageing may overlap with changes relate to menopause. We are not proposing to cover diagnosis of perimenopause or menopause in this update as surveillance did not identify evidence that would warrant changing the existing recommendations.

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Newson Health Limited	002	012	**There may be significant personal and societal costs for those experiencing 12 troublesome symptoms.** There are significant personal and societal costs. Modelling done by the NHSE Menopause programme have confirmed this.	Thank you for your comment. We recognise that there can be significant personal costs for some women, non-binary or trans people experiencing menopause, but not all. We also recognise that there can be a significant impact on wider society. We have revised the text.
Newson Health Limited	003	015	**Considerations of inequality should be extended** to include vulnerable groups who are known to have issues accessing primary care (e.g. for diagnosis, prescriptions) such as those with no fixed address; women living in closed institutions e.g. prisons, residential care facilities; and also where women are disproportionately affected e.g. those living with domestic abuse; carers; lone parents.	Thank you for your comment. We have noted this important point in the Equality Impact Assessment form, for the committee to consider this when reviewing evidence and drafting recommendations.
Newson Health Limited	003	025	**Related conditions requiring specific consideration:** Do women suffering from early on set or other non cancer comorbidities require specific consideration as well. This does not make clinical sense	Thank you for your comment. The groups requiring specific consideration have now been removed from the scope. The committee will consider which subgroups to include in the evidence review for specific topics.
Newson Health Limited	004	005	**Guidelines will '*apply to all settings where NHS care is commissioned*'**. Does this include mental health services and/or dental services, for example? If not, this needs to be explicitly stated. And, if so, then an explicit link to these services made in the guidance document.	Thank you for your comment. The guidance will apply to NHS-commissioned services providing menopause care, we have clarified the wording in the scope.
Newson Health Limited	004	010	**Suggest widen scope to include Testosterone** as a treatment for more than HSDD. Review and referal	Thank you for your comment. We acknowledge that testosterone as a treatment for more than HSDD is a contentious area. There is a body of RCT evidence supporting its use for HSDD but evidence on other outcomes such as body composition and musculoskeletal health comes from a small number of study participants. This would prevent us from

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				making evidence based recommendations on testosterone outside of its use for HSDD. The surveillance and scoping process for the guideline update did not identify substantive new evidence likely to change the existing recommendations on testosterone. Therefore, reviewing evidence on testosterone in relation to menopause care was not prioritised. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
Newson Health Limited	005	Table	1.2 **'Diagnosis of perimenopause and menopause':** this is apparently out of scope. However, there is significant debate about which are definitive symptoms (e.g. changing periods) and needs to be defined. The scope of the review should be altered to reflect this.	Thank you for your comment. The existing recommendations about diagnosis of perimenopause and menopause will not be updated. This is because the NICE surveillance and scoping process has not identified substantive new evidence that would change these existing recommendations.
Newson Health Limited	005	Table	**More symptoms should be listed here. Also should state "associated with the perimenopuase and menopause"**	Thank you for your comment. The short term menopausal symptoms listed here are taken from the existing menopause guideline NG23. The update of treatments for short term symptoms will focus on CBT and treatments for genitourinary symptoms associated with the menopause because this is where surveillance has identified important new evidence.
Newson Health Limited	005	Table	**There is no evidence to support the use of clonidine so this should be deleted**	Thank you for your comment. The current guideline NG23 refers to clonidine in two recommendations: 1.3.3 is about providing information about types of treatments and clonidine given as an example of non-hormonal treatment. Recommendation 1.4.3 states that clonidine should not be routinely offered as first-line treatment for vasomotor

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				symptoms alone. Neither are recommending the use of clonidine, nor are we aware of evidence that would warrant changes in these recommendations. However, the existing recommendations to be retained may be subject to editorial changes which will be considered during the development of the update guidance.
Newson Health Limited	005	Table	**Title is "Managing short-term menopausal symptoms" – "short-term" should be deleted as many women experience symptoms for several years or decades**	Thank you for your comment. The table reflects the sections in the current guideline NG23. NG23 defines short-term outcomes as up to 5 years. When updating the guideline, editorial changes to section headings and recommendation wording will be considered, as needed.
Newson Health Limited	005	Table	**Need to add progesterone to progestogen. Oestrogen alone to women without a uterus is not always the correct management (eg patients with severe endometriosis who have had a hysterectomy)**	Thank you for your comment. The committee will consider evidence on the effect of different HRT types on general health outcomes and update the recommendations as needed.
Newson Health Limited	005	Table	**Evidence for isoflavones or black cohosh is very limited**	Thank you for your comment. The current guideline NG23 acknowledges the limited evidence and the uncertainty in the evidence for these, which is reflected in the recommendation.
Newson Health Limited	005	Table	**Need to add prasterone as an alternative to vaginal oestrogen**	Thank you for your comment. The scope for the guideline update includes a review question on the effect of, for example, prasterone, for managing genitourinary symptoms associated with the menopause so the evidence on prasterone will be reviewed.
Newson Health Limited	005	Table	**Women with a high risk of breast cancer should be in a different section to women with breast cancer**	Thank you for your comment. The guideline committee will have the chance to make different recommendations for people with breast cancer and for those at high risk of breast cancer if the evidence supports this.

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Newson Health Limited	005	Table	**'Review and Referral': a review of this is apparently out of scope.** However, if psychological support e.g. CBT is in scope, then depending on conclusions, this may affect the referral process so it is unclear how these two objectives are aligned?	Thank you for your comment. Depending on the evidence review on CBT, and the committee's conclusions around it, editorial changes to the 'Review and referral' section of the existing guideline may be made as needed to reflect any new recommendations.
Newson Health Limited	005	Table	Need to state that lower risk of cardiovascular disease when started within 10 years of the menopause (Cochrane data)	Thank you for your comment. Evidence on the benefits and risks of HRT on cardiovascular disease will be reviewed as part of the guideline update and recommendations will be updated as appropriate.
Newson Health Limited	005	Table	Women taking HRT have lower risk of type 2 diabetes	Thank you for your comment. The surveillance and scoping processes did not identify substantive new evidence on the effect of HRT on type 2 diabetes that would likely change the existing recommendations on this issue for people taking HRT for menopausal symptoms. However, evidence on the effect of HRT for women, non-binary and trans people with early menopause whether they have symptoms or not will be considered on various overall health outcomes, including type 2 diabetes, will be reviewed in the update.
Newson Health Limited	005	Table	Breast cancer section needs rewriting with new evidence from WHI	Thank you for your comment. New evidence on the effect of HRT on breast cancer will be reviewed and the guidance on it will be updated as needed.
Newson Health Limited	008	001	These key issues and draft questions may need widening dependant on CRG feedback on scope of consultation (as assessed above).	Thank you for your comment. Stakeholder comments on the draft scope have been considered and revisions made to the scope based on them, however, the update of the guideline will focus on key areas where substantive new evidence has emerged that might warrant changes to existing recommendations.

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Newson Health Limited	009	016	**Low mood (not clinical depression)** is the extent of the planned assessment on Mental health concerns. This may not be sufficent as previously clinical colleagues have confirmed the severity of some womens mental health symptoms.	Thank you for your comment. Please note that we have listed anxiety and sleep disturbance as outcomes. The main outcomes list provides outcomes for the committee to consider when developing review protocols, but may be expanded during protocol development based on the committee's expertise. It should be noted that the NICE guideline CG90 on Depression in adults and its imminent update (expected to be published in June 2022) will be applicable to people with clinical depression during the menopause.
NHSEI	General	General	Facts and figures on page 2 suggest that symptoms may vary between different ethnic background but planned updated guideline does not cover implications of proposed guidelines for ethinic and diverse population.	Thank you for your comment. We have noted this in the Equality Impact Assessment form and the committee will consider your comment when agreeing which subgroups to include in the evidence reviews when developing the evidence review protocols. Equalities considerations will be taken into account when developing new recommendations.
NHSEI	002	006	**Common symptoms currently only mentions vasomotor symptoms and vaginal dryness.** The wide range of potential Menopausal symptoms should be mentioned here, rather than just highlighting 2 common ones. Around 25% of perimenopausal and menopausal women do not have vasomotor symptoms.	Thank you for your comment. This section has been revised by adding "changes to sleep and mood" as examples of signs and symptoms of the menopause.
NHSEI	002	006	**Common symptoms currently only mentions vasomotor symptoms and vaginal dryness.** The wide range of potential Menopausal symptoms should be mentioned here, rather than just highlighting 2 common ones. Around 25% of perimenopausal and menopausal women do not have vasomotor symptoms.	Thank you for your comment. This section has been revised by adding "changes to sleep and mood" as examples of signs and symptoms of the menopause.

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NHSEI	002	012	**There may be significant personal and societal costs for those experiencing 12 troublesome symptoms.** There are significant personal and societal costs. Modelling done by the NHSE Menopause programme have confirmed this.	Thank you for your comment. We recognise that there can be significant personal costs for some women, non-binary or trans people experiencing menopause, but not all. We also recognise that there can be a significant impact on wider society. We have revised the text.
NHSEI	002	012	**There may be significant personal and societal costs for those experiencing 12 troublesome symptoms.** There are significant personal and societal costs. Modelling done by the NHSE Menopause programme have confirmed this.	Thank you for your comment. We recognise that there can be significant personal costs for some women, non-binary or trans people experiencing menopause, but not all. We also recognise that there can be a significant impact on wider society. We have revised the text
NHSEI	003	023 - 025	The scope of the review should include specific considerations of women, non-binary and trans people who have **any cancer**, not just (familial) breast cancer.	Thank you for your comment. Other cancers are not excluded and the section of the scope you are referring to has been revised. It no longer highlights people who have breast cancer or who have familial risk of breast cancer specifically. Instead, when developing the evidence review protocols the committee will consider which specific subpopulations might be of interest for stratified analyses.
NHSEI	003	023 - 025	The scope of the review should include specific considderations of women, non-binary and trans people who have **any cancer**, not just (familial) breast cancer.	Thank you for your comment. Other cancers are not excluded and the section of the scope you are referring to has been revised. It no longer highlights people who have breast cancer or who have familial risk of breast cancer specifically. Instead, when developing the evidence review protocols the committee will consider which specific subpopulations might be of interest for stratified analyses.
NHSEI	003	015	**Considerations of inequality should be extended** to include vulnerable groups who are known to have issues accessing primary care (e.g. for diagnosis, prescriptions) such as those	Thank you for your comment. Wee have noted this important point in the Equality Impact Assessment form, for the

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			with no fixed address; women living in closed institutions e.g. prisons, residential care facilities; and also where women are disproportionately affected e.g. those living with domestic abuse; carers; lone parents.	committee to consider this when reviewing evidence and drafting recommendations.
NHSEI	003	015	**Considerations of inequality should be extended** to include vulnerable groups who are known to have issues accessing primary care (e.g. for diagnosis, prescriptions) such as those with no fixed address; women living in closed institutions e.g. prisons, residential care facilities; and also where women are disproportionately affected e.g. those living with domestic abuse; carers; lone parents.	Thank you for your comment. We have noted this important point in the Equality Impact Assessment form, for the committee to consider this when reviewing evidence and drafting recommendations.
NHSEI	004	001	(1.4) **Review and referral** should be within the scope of the consultation due to changes in trends around how long people are receiving HRT. This topic must be considered in the context of multiple different settings, such as [insert relevant example].	Thank you for your comment. This topic was not prioritised for an update because our surveillance and scoping process did not identify substantive new evidence specific to the review question underpinning this section. However, editorial changes to the 'Review and referral' section of the existing guideline may be made as needed to reflect current editorial standards and new recommendations made by the committee on topics being updated.
NHSEI	004	001	(1.4) **Starting and Stopping HRT** should also be reviewed as trends around how long people stay on HRT have changed.	Thank you for your comment. The evidence review underpinning this section focused on discontinuation of HRT and this was not prioritised for update as our surveillance and scoping process did not identify substantive new evidence that would warrant change to the recommendations. However, editorial changes to the retained sections of the existing guideline may be made as needed to reflect current editorial

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				standards and new recommendations made by the committee on topics being updated.
NHSEI	004	001	(1.4) NICE discusses **CBT** in respect of psychological and vasomotor symptoms but it doesn't currently include reference of it **as a treatment for poor sleep**. There is growing evidence of its use in this area and the scope of this review should be extended to include this.	Thank you for your comment. We have revised the wording of the draft review question on CBT not to be specific about which outcomes we will be considered. The outcomes relevant for this review question will be discussed and agreed by the guideline committee when developing the evidence review protocol
NHSEI	004	001	(1.5) **Cardiovascular disease: E**nsure that all people and not just Trans and non-binary patients are reviewed with respect to this comorbidity. This may be the intent but the wording is not clear. (*This comment also applies to Type 2 Diabetes and Osteoperosis included in this section 1.5*). Ther term '*with early menopause (40-45)*' is used. This review should include the data for all women and not just those with early menopause. It's assumed that the breast cancer and other cancer data are being reviewed for all women so the osteoporosis, cardiovascular diabetes etc data should be too.	Thank you for your comment. The evidence review on the effect of HRT on cardiovascular disease will be updated, no population is specified in relation to this topic but will include women, non-binary and trans people with menopause 40 years and above. This review is updated because there is a need to further review the evidence on the outcome of cardiovascular disease to address the needs of people with menopausal symptoms who are over 60 and considering hormone replacement therapy. Furthermore, there is a need to review evidence for this and other outcomes, such as venous thromboembolism, diabetes and osteoporosis even when there are no menopausal symptoms because the current guideline NG23 only addresses those with symptoms.
NHSEI	004	002	Proposal suggests women, non-binary and trans people with premature ovarian insufficiency will not be covered in the update, however, bottom three rows of the table on page 6 suggest that evidence related to premature ovarian insufficiency will be retained.	Thank you for your comment. New evidence in relation POI will not be reviewed and thus the guidance on POI will not be updated but will be retained from the current guideline NG23. This is because no substantive new evidence was identified in the surveillance and scoping process for this topic.

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NHSEI	004	005	**Guidelines will '*apply to all settings where NHS care is commissioned*'**. Does this include mental health services and/or dental services, for example? If not, this needs to be explicitly stated. And, if so, then an explicit link to these services should be made in the guidance document to make clear the role of each.	Thank you for your comment. The guidance will apply to NHS-commissioned services providing menopause care, we have clarified the wording in the scope.
NHSEI	004	005	**Guidelines will '*apply to all settings where NHS care is commissioned*'**. Does this include mental health services and/or dental services, for example? If not, this needs to be explicitly stated. And, if so, then an explicit link to these services should be made in the guidance document to make clear the role of each. Community Pharmacy should also be explicity included.	Thank you for your comment. The guidance will apply to NHS-commissioned services providing menopause care, we have clarified the wording in the scope.
NHSEI	004	010	**The scope should be widened to include Testosterone** as a treatment for more than HSDD. There is growing use of Testosterone as a treatment to aid women with a number of menopausal symptoms and a Testosterone product designed for female use is currently in the process of being licensed by the MHRA. The use of testosterone has also been touted from some clinicians due to its ability to prevent some osteoperosis issue in later life.	Thank you for your comment. We acknowledge that testosterone as a treatment for more than HSDD is a contentious area. There is a body of RCT evidence supporting its use for HSDD but evidence on other outcomes such as body composition and musculoskeletal health comes from a small number of study participants. This would prevent us from making evidence based recommendations on testosterone outside of its use for HSDD. The surveillance and scoping process for the guideline update did not identify substantive new evidence likely to change the existing recommendations on testosterone. Therefore, reviewing evidence on testosterone in relation to menopause care was not prioritised. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National

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				Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
NHSEI	004	010	**The scope should be widened to include Testosterone** as a treatment for more than HSDD. There is growing use of Testosterone as a treatment to aid women with a number of menopausal symptoms and a Testosterone product designed for female use is currently in the process of being licensed by the MHRA. The use of testosterone has also been touted from some clinicians due to its ability to prevent some osteoperosis issue in later life.	Thank you for your comment. We acknowledge that testosterone as a treatment for more than HSDD is a contentious area. There is a body of RCT evidence supporting its use for HSDD but evidence on other outcomes such as body composition and musculoskeletal health comes from a small number of study participants. This would prevent us from making evidence based recommendations on testosterone outside of its use for HSDD. The surveillance and scoping process for the guideline update did not identify substantive new evidence likely to change the existing recommendations on testosterone. Therefore, reviewing evidence on testosterone in relation to menopause care was not prioritised. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
NHSEI	005	Table	**1.4 Review and referral** should be within the scope of the consultation due to changes in trends around how long people are receiving HRT. This topic must be considered in the context of multiple different settings, such as [insert relevant example].	Thank you for your comment. This topic was not prioritised for an update because the surveillance and scoping process did not identify substantive new evidence specific to the review question underpinning this section. However, editorial changes to the 'Review and referral' section of the existing guideline may be made as needed to reflect current editorial standards and new recommendations made by the committee on topics being updated.
NHSEI	005	Table	**1.4 Starting and Stopping HRT** should also be reviewed as trends around how long people stay on HRT have changed.	Thank you for your comment. The evidence review underpinning this section focused on discontinuation of HRT

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				and this was not prioritised for update as our surveillance and scoping process did not identify substantive new evidence that would warrant change to the recommendations. However, editorial changes to the retained sections of the existing guideline may be made as needed to reflect current editorial standards and new recommendations made by the committee on topics being updated.
NHSEI	005	Table	1.4 NICE discusses **CBT** in respect of psychological and vasomotor symptoms but it doesn't currently include reference of it **as a treatment for poor sleep**. There is growing evidence of its use in this area and the scope of this review should be extended to include this.	Thank you for your comment. We have revised the wording of the draft review question on CBT not to be specific about which outcomes we will be considered. The outcomes relevant for this review question will be discussed and agreed by the guideline committee when developing the evidence review protocol.
NHSEI	005	Table	**1.5 Cardiovascular disease:** Ensure that all people and not just Trans and non-binary patients are reviewed with respect to this comorbidity. This may be the intent but the wording is not clear. (*This comment also applies to Type 2 Diabetes and Osteoperosis included in this section 1.5*). Ther term '*with early menopause (40-45)*' is used. This review should include the data for all women and not just those with early menopause. It's assumed that the breast cancer and other cancer data are being reviewed for all women so the osteoporosis, cardiovascular diabetes etc data should be too.	Thank you for your comment. The evidence review on the effect of HRT on cardiovascular disease will be updated, no population is specified in relation to this topic but will include women, non-binary and trans people with menopause 40 years and above. This review is updated because there is a need to further review the evidence on the outcome of cardiovascular disease to address the needs of people with menopausal symptoms who are over 60 and considering hormone replacement therapy. Furthermore, there is a need to review evidence for this and other outcomes, such as venous thromboembolism, diabetes and osteoporosis, in relation to women, non-binary and trans people aged 40-44 years (i.e. early menopause) even if there are no have menopausal symptoms because the current guideline NG23 only addresses those with symptoms.

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NHSEI	005	Table	**1.2 'Diagnosis of perimenopause and menopause':** this is apparently out of scope. However, there is significant debate about which are definitive symptoms (e.g. changing periods) and needs to be defined. The scope of the review should be altered to reflect this.	Thank you for your comment. The existing recommendations about diagnosis of perimenopause and menopause will not be updated. This is because the surveillance and scoping process has not identified substantive new evidence that would change these existing recommendations.
NHSEI	005	Table	**1.4 'Review and Referral': a review of this is apparently out of scope.** However, if psychological support e.g. CBT is in scope, then depending on conclusions, this may affect the referral process so it is unclear how these two objectives are aligned?	Thank you for your comment. Depending on the evidence review on CBT, and the committee's conclusions around it, editorial changes to the 'Review and referral' section of the existing guideline may be made as needed to reflect any new recommendations.
NHSEI	005	Table	1.2 **'Diagnosis of perimenopause and menopause':** this is apparently out of scope. However, there is significant debate about which are definitive symptoms (e.g. changing periods) and needs to be defined. The scope of the review should be altered to reflect this.	Thank you for your comment. The existing recommendations about diagnosis of perimenopause and menopause will not be updated. This is because the NICE surveillance and scoping process has not identified substantive new evidence that would change these existing recommendations.
NHSEI	005	Table	1.4 **'Review and Referral': a review of this is apparently out of scope.** However, if psychological support e.g. CBT is in scope, then depending on conclusions, this may affect the referral process so it is unclear how these two objectives are aligned?	Thank you for your comment. Depending on the evidence review on CBT, and the committee's conclusions around it, editorial changes to the 'Review and referral' section of the existing guideline may be made as needed to reflect any new recommendations.
NHSEI	005	001	Proposed outline for the guidelines does not include considerations about family planning for perimenopausal women.	Thank you for your comment. This topic was not prioritised for update because there is a NICE-accredited Faculty of Sexual and Reproductive Health (FSHR) clinical guideline on Contraception for Women Aged over 40 Years which the

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				current guideline NG23 refers to. The plan is to retain this recommendation.
NHSEI	005	001	Proposed outline for the guidelines does not suggest covering monitoring for HRT once it is started and possible considerations about stopping it.	Thank you for your comment. Our surveillance and scoping process did not identify substantive new evidence that would change recommendations in the sections 'Review and referral' and 'Starting and stopping HRT'. However, editorial changes to the these sections of the existing guideline may be made as needed to reflect current editorial standards and new recommendations made by the committee on topics being updated.
NHSEI	008	024 - 026	**It is unclear if the guidelines cover early menopause** too (as suggested on page 8) or not (as suggested on page 4). If not currently in scope, we strongly recommend early menopause is explicitly and completely included.	Thank you for your comment. Early menopause is defined as menopause transition starting between 40-44 years, whilst for under 40s this is referred to as premature ovarian insufficiency. The scope states that early menopause (40-44 years) is covered in the update but premature ovarian insufficiency (under 40 years) is not covered in the update but current guidance is retained.
NHSEI	008	024 - 026	**It is unclear if the guidelines cover early menopause** too (as suggested on page 8) or not (as suggested on page 4). If not currently in scope, we strongly recommend early menopause is explicitly and completely included.	Thank you for your comment. Early menopause is defined as menopause transition starting between 40-44 years, whilst for under 40s this is referred to as premature ovarian insufficiency. The scope states that early menopause (40-44 years) is covered in the update but premature ovarian insufficiency (under 40 years) is not covered in the update but current guidance is retained.
NHSEI	009	016	**Low mood (not clinical depression)** is the extent of the planned assessment on Mental health concerns. This may not	Thank you for your comment. Please note that we have listed anxiety and sleep disturbance as outcomes. The main outcomes list provides outcomes for the committee to consider

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			be sufficent as previously clinical colleagues have confirmed the severity of some womens mental health symptoms.	when developing review protocols, but may be expanded during protocol development based on the committee's expertise. It should be noted that the NICE guideline CG90 on Depression in adults and its imminent update (expected to be published in June 2022) will be applicable to people with clinical depression during the menopause.
NHSEI	009	016	**Low mood (not clinical depression)** is the extent of the planned assessment on Mental health concerns. This may not be sufficent as previously clinical colleagues have confirmed the severity of some womens mental health symptoms.	Thank you for your comment. Please note that we have listed anxiety and sleep disturbance as outcomes. The main outcomes list provides outcomes for the committee to consider when developing review protocols, but may be expanded during protocol development based on the committee's expertise. It should be noted that the NICE guideline CG90 on Depression in adults and its imminent update (expected to be published in June 2022) will be applicable to people with clinical depression during the menopause.
Pelvic Obstetric and Gynaecological Physiotherapy	General	General	Osteoporosis update Updated guidelines for osteoporosis, will the LIFTMOR trial be considered? Watson, S., Weeks, B., Weis, L., Harding, A., Horan, S. and Beck, B., 2019. High-Intensity Resistance and Impact Training Improves Bone Mineral Density and Physical Function in Postmenopausal Women With Osteopenia and Osteoporosis: The LIFTMOR Randomized Controlled Trial. Journal of Bone and Mineral Research, 34(3), pp.572-572. https://pubmed.ncbi.nlm.nih.gov/28975661/	Thank you for your comment. The evidence review for the guideline update will look at the association between HRT use and the incidence of osteoporosis or other related outcomes in the early menopause population, rather than interventions to improve bone strength - which are outside the scope of this guideline update.
Pelvic Obstetric and	General	General	Loss of lean muscle mass	Thank you for your comment. Non-pharmaceutical treatments were included in the original guideline network meta-analysis

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Gynaecological Physiotherapy			Can the following publications be considered: Berin, E., Hammar, M., Lindblom, H., Lindh-Åstrand, L., Rubér, M., & Spetz Holm, A. C. (2019). Resistance training for hot flushes in postmenopausal women: A randomised controlled trial. Maturitas, 126(May), 55–60. de Oliveira Júnior, G. N., de Sousa, J. de F. R., Carneiro, M. A. da S., Martins, F. M., Santagnello, S. B., & Orsatti, F. L. (2020). Resistance training-induced improvement in exercise tolerance is not dependent on muscle mass gain in post-menopausal women. European Journal of Sport Science, 0(0), 1–19. Helms, E., Cronin, J., Storey, A. and Zourdos, M., 2016. Application of the Repetitions in Reserve-Based Rating of Perceived Exertion Scale for Resistance Training. Strength & Conditioning Journal, 38(4), pp.42-49. Khalafi, M., Malandish, A., & Rosenkranz, S. K. (2021). The impact of exercise training on inflammatory markers in postmenopausal women: A systemic review and meta-analysis. Experimental Gerontology, 150(December 2020), 111398.	of treatments for short-term menopausal symptoms including: acupuncture, lifestyle advice, relaxation therapies (including yoga), psychological therapies and cognitive behavioural therapy. The surveillance and scoping process for guideline update did not identify substantive new evidence on these treatments likely to change the existing recommendations, with the exception of cognitive behavioural therapy so we are updating the recommendations on CBT.

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			Nunes, P. R. P., Oliveira, A. A., Martins, F. M., Souza, A. P., & Orsatti, F. L. (2017). Effect of resistance training volume on walking speed performance in postmenopausal women: A randomized controlled trial. Experimental Gerontology, 97(August), 80–88. Thomas, E., Gentile, A., Lakicevic, N., Moro, T., Bellafiore, M., Paoli, A., Drid, P., Palma, A., & Bianco, A. (2021). The effect of resistance training programs on lean body mass in postmenopausal and elderly women: a meta-analysis of observational studies. Aging Clinical and Experimental Research Woods, R., Hess, R., Biddington, C., & Federico, M. (2020). Association of lean body mass to menopausal symptoms: The Study of Women's Health Across the Nation. Women's Midlife Health, 6(1), 1–7.	
Pelvic Obstetric and Gynaecological Physiotherapy	002	006	As the signs and symptoms are much more broad than vaginal dryness can this be broadened? Basu, M., 2020. Assessment of the urogynaecology patient in primary care and when to refer. Post Reproductive Health, 26(2), pp.57-62.	Thank you for your comment. This section has been revised by adding "changes to sleep and mood" as examples of signs and symptoms of the menopause.

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			Briggs, P. and Hapangama, D., 2021. Urogenital atrophy: The 'unknown factors' challenging current practice. Post Reproductive Health, 27(2), pp.109-120. df	
Pelvic Obstetric and Gynaecological Physiotherapy	010	015	Pelvic floor muscle training to be considered a valid option for treating uro-genital atrophy Mercier J, Morin M, Zaki D, Reichetzer B, Lemieux MC, Khalifé S, Dumoulin C. Pelvic floor muscle training as a treatment for genitourinary syndrome of menopause: A single-arm feasibility study. Maturitas. 2019;125:57-62. https://pubmed.ncbi.nlm.nih.gov/31133219/ https://www.imsociety.org/2021/03/15/pelvic-floor-muscle-training-as-a-treatment-for-genitourinary-syndrome-of-menopause/	Thank you for your comment. The guideline committee will have the opportunity to include pelvic floor muscle training as an intervention in the evidence review for urogenital atrophy if considered a priority when developing the evidence review protocol. NICE guideline NG210 recommends to "encourage women of all ages to do pelvic floor muscle training", so it could be considered part of standard care against which other interventions could be compared.
Royal College of General Practitioners	General	General	We would like to request more information included in the scope of this guideline around the length of an HRT prescription and the safety factors involved. The current NICE guidance does not specify what length of HRT prescription should or could be given out or the safety implications of different durations of prescriptions, and only mentions that medication reviews can be every 12 months. However the DHSC is currently advocating for 12 month prescriptions of HRT to be offered to women across the country, which is not covered in the BNF, and so we would like to request a look at the evidence regarding the safety of prescribing 12 month HRT cycles.	Thank you for your comment. The plan is that the evidence review on the effect of HRT on longer-term health outcomes will include consideration for the duration of HRT use, however, we are not planning to review evidence on the length of HRT prescription. The surveillance and scoping process did not identify substantive new evidence on this issue that would warrant an evidence review.
Royal College of	General	General	We would like to request further information to be included in the scope of this guideline regarding the use and prescription	Thank you for your comment. We acknowledge that testosterone as a treatment for more than HSDD is a

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General Practitioners			of testosterone for women going through the menopause. Current guidelines state that testosterone can be considered for a reduced libido if symptoms persist post oestrogen/progesterone replacement. However, clinicians are being encouranged to prescribe this now for other reasons too. We would like to know the following: ar there other indiciations for testosterone for women going through the menopause? What duration of testosterone treatment should be used? What testing is required to determine optomisation of testosterone replacement? Is there any evidence to support its use in all post/perimenopausal women?	contentious area. There is a body of RCT evidence supporting its use for HSDD but evidence on other outcomes such as body composition and musculoskeletal health comes from a small number of study participants. This would prevent us from making evidence based recommendations on testosterone outside of its use for HSDD. The surveillance and scoping process for guideline update did not identify substantive new evidence likely to change the existing recommendations on testosterone. Therefore, reviewing evidence on testosterone in relation to menopause care was not prioritised. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
Royal College of Nursing	General	General	The scope review should aim to balance the guidance around benefits and risks	Thank you for your comment. The evidence on the benefits and risks of hormone replacement therapy on specific overall health outcomes will be reviewed and the committee will make careful considerations around weighing the benefits and harms of HRT.
Royal College of Nursing	General	General	review of evidence and revised guidance around diagnostic testing for women presenting with peri menopausal symptoms between 40 - 44	Thank you for your comment. The existing recommendations about diagnosis of perimenopause and menopause will not be updated. This is because the NICE surveillance and scoping process did not identify substantive new evidence that would change the existing recommendations.
Royal College of Nursing	General	General	review of evidence and revised guidance on starting HRT for women over 60 and around assessing the individual risk for continuing or stopping HRT beyond 60	Thank you for your comment. The evidence reviews on the overall health outcomes associated with HRT will aim to look at the impact of HRT in relation to age. Depending on the

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				available evidence, the committee will consider making recommendations around the use of HRT in people over 60.
Royal College of Nursing	General	General	Clearer guidance on use of hrt with perimeno women age 40-45 who have normal fsh/lh levels	Thank you for your comment. The scope states that the effects of HRT on overall health outcomes for women, non-binary and trans people aged 40-44 years will be reviewed and guidance updated as needed.
Royal College of Nursing	General	General	Clearer guidance on explaining /managing risks of use of hrt with breast cancer survivors	Thank you for your comment. Recommendations related HRT for people with breast cancer or with a history of breast cancer is covered by another NICE guideline NG101 and therefore will not be covered in the update of the menopause guideline (NG23).
Royal College of Nursing	General	General	Initiating hrt with people who are beyond 10 years from lmp	Thank you for your comment. The plan is to consider the timing, duration and different age groups when reviewing the evidence on HRT use and its effects on overall health outcomes.
Royal College of Nursing	General	General	Clear indication of indications for specialist referral	Thank you for your comment. Depending on the evidence reviews conducted and the committee's conclusions around them, editorial changes to the 'Review and referral' section of the existing guideline may be made as needed to reflect any new recommendations.
Royal College of Nursing	002	005	Mood changes are not included?	Thank you for your comment. The text has been revised to add "changes to sleep and mood" as examples of signs and symptoms of menopause.
Royal College of Nursing	003	023	Why are other forms of cancer excluded, especially those which are hormone dependant and women with endometrisois	Thank you for your comment. Other cancers are not excluded and the section of the scope you are referring to has been revised. It no longer highlights people who have breast cancer or who have familial risk of breast cancer specifically. Instead,

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				when developing the evidence review protocols the committee will consider which specific subpopulations might be of interest for stratified analyses.
Royal College of Nursing	003	024	Why are other forms of cancer excluded, especially those which are hormone dependant and women with endometrisois RCN	Thank you for your comment. Other cancers are not excluded and people with endometriosis are not excluded (although it has been clarified that temporary menopause-like symptoms caused by hormonal treatments are not covered in this guideline, which may apply to people with endometriosis). The section of the scope you are referring to has been revised. It no longer highlights people who have breast cancer or who have familial risk of breast cancer specifically. Instead, when developing the evidence review protocols the committee will consider which specific subpopulations might be of interest for stratified analyses. A revision has been made to the scope in August 2022 to include menopause and also menopause-like symptoms in people treated for certain cancers, such as breast cancer. These cancers and their treatments may both cause menopause and be associated with menopause-like symptoms and these two possibilities may be indistinguishable. We do not intend to include the menopause-like symptoms that may be associated with treatment of a broader range of conditions. The evidence regarding the efficacy of interventions in such diverse circumstances would likely be complex and varied as the underlying physiological mechanisms are not likely to be uniform.

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Royal College of Nursing	005	Table	Altered sexual function No review of testosterone products and stronger advice around prescribing?	Thank you for your comment. We are planning not to update this part of the guideline and to retain the existing recommendations. The surveillance and scoping process for the guideline update did not identify substantive new evidence likely to change the existing recommendations on testosterone. NICE has discussed the need for research in relation to testosterone use for menopausal symptoms with the National Institute for Health and Care Research (NIHR) and have asked them to fund urgent research in this area.
Royal College of Nursing	005	Table	Complementary therapies and unregulated preparations There have been more studies and a review is needed to help inform women of the beniftis	Thank you for your comment. Complementary therapies and unregulated preparations were included in the original guideline network meta-analysis of treatments for short-term menopausal symptoms, and there was some evidence of effectiveness for example with St John's wort. The surveillance and scoping process for the guideline update did not identify substantive new evidence likely to change the existing recommendations on complementary therapies and unregulated preparations. Therefore, this topic area was not prioritised in the guideline update.
Royal College of Obstetricians and Gynaecologists	General	General	The RCOG language guidance states "However, we recognise it is not only women who use services for their gynaecological health and reproductive wellbeing. We must therefore ensure our language is appropriate, inclusive and sensitive to the needs of individuals whose gender identity does not align with the sex they were assigned at birth. This may include transgender or trans men, and non-binary people. We do not use terms such as 'transsexual', 'transgendered', or 'transwomen/transmen.'"	Thank you for your comment. Careful consideration is given to the language used in the scope and the update of the guideline. NICE also regularly reviews its own language guide.

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Royal College of Obstetricians and Gynaecologists	005	Table	1.2 The definition of menopause used in the guideline deserved close attention. If the definition is the cessation of a previous physiological state (repeated menstruation), then this implies that firstly the definition of menstruation is needed, either within the guideline or referred from elsewhere (e.g. FIGO parameters). The impacts of the definition used in effect define the population who would be considered as having 'post menopausal bleeding'. It would also be helpful in defining what 'peri menopause' is and whether there is overlap between this and a post menopausal state. I had inferred that these were mutually exclusive states, but this may not be the case. I wonder if the definition related to the underlying physiology of the activity of the hypothalamic-pituitary-ovarian axis would be better for these three possibly overlapping state of pre menopause, peri menopause and post menopause. This would circumvent some of the ambiguity with iatrogenic causes of menopause. Would this section include any data or advice as to at what age, if any, a menopause would be considered to be late, in a analgous way to POI referring to menopause being 'early'. Would this section include how to make the diagnosis of menopause 1. Clinical symptoms/signs only 2. In women with	Thank you for your comment. The existing guideline covers the definition of perimenopause and menopause, including the diagnosis of menopause. We will be retaining those recommendations, and have not included the diagnosis or the definition of menopause as a topics for an evidence review as the surveillance and scoping process did not identify substantive new evidence that would impact the current recommendations; however, recommendations in areas that are being retained from the existing guideline may be edited to ensure that they meet current editorial standards, and reflect practice context. We have however amended the scope to mention perimenopause in the Why this guideline is needed section.

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			previous surgery (hysterectomy/ablation) 3. Women with IUS During the reduced access to benign gynae operating with covid-19 some women who may have been listed for surgery have been treated with GnRH for fibroids/heavy bleeding etc. Would the above definition/other data be able to suggest a likely age as to when the majority of women could stop GnRH and reasonably expect to be in the natural menopause?	
Royal College of Obstetricians and Gynaecologists	005	Table	1.4 I am unclear if there are planned to be any recommendation about HRT in women who have endometriosis (in situ) or previous surgery for endometriosis where there was felt to be complete excision of the lesions. There is variation in practice between the use of combined and estrogen only HRT for this group.	Thank you for your comment. Hormonal treatments for endometriosis are covered in NICE guideline NG73 and will not be covered in this update.
Royal College of Obstetricians and Gynaecologists	006	Table	Ovarian Cancer: The Risk of Malignancy Index is commonly used and recommended for the triage of ovarian masses is used for menstruating and non mentstruating women , between malignant and non malignant. A woman who had a low risk RMI score will, as the calculation stands currently, have her score triple if she is considered to be in the menopause. I wonder if the risk of menopause intervention on the womans risk of ovarian cancer will be discussed but also the how women with ovarian masses, or symptoms of ovarian cancer after might be investigation in light of them becoming menopausal.	Thank you for your comment. The investigation of ovarian masses is outside the scope of the guideline and covered elsewhere (for example CG122 and NG12).

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Royal College of Obstetricians and Gynaecologists	006	Table	1.6 Need to add 'and non-binary' alongside trans people to section on equality considerations, for consistency.	Thank you for your comment, this was an omission. The text has been revised.
Royal Pharmaceutical Society	General	General	Could you include a recommendation or guidance on the duration of use of HRT? The British Menopause Society & Women's Health Concern 2020 recommendations on hormone replacement therapy in menopausal women states; duration of its use should be made on an individualised basis after discussing the benefits and risks with each patient. Arbitrary limits should not be placed on the duration of usage of HRT. (reference; Hamoda H, Panay N, Pedder H, Arya R, Savvas M. The British Menopause Society & Women's Health Concern 2020 recommendations on hormone replacement therapy in menopausal women. Post Reprod Health. 2020 Dec;26(4):181-209. doi: 10.1177/2053369120957514. Epub 2020 Oct 12. PMID: 33045914.)	Thank you for your comment. The plan is that the evidence review on the effect of HRT on longer-term health outcomes will include consideration for the duration of HRT use.
Royal Pharmaceutical Society	008	012 - 013	Will you include a review of the evidence on the risks of late starting of HRT (>10 years post menopause) on developing cardiovascular disease, and provide recommendations or guidance on this. The MHRA drug safety update Dec 2014 Hormone replacement therapy:updated advice states there is	Thank you for your comment. The plan is that the evidence review on the effect of HRT on cardiovascular disease will include consideration for the timing, duration and different age groups.

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			an increased risk (https://www.gov.uk/drug-safety-update/hormone-replacementtherapy-updated-advice), however The British Menopause Society & Women's Health Concern 2020 recommendations on hormone replacement therapy in menopausal women states; "Cochrane data-analysis as well as the long-term follow-up data from the Women's Health Initiative (WHI) showed no increase in cardiovascular events, cardiovascular mortality or allcause mortality in women who initiated HRT more than 10 years after the menopause." (reference; Hamoda H, Panay N, Pedder H, Arya R, Savvas M. The British Menopause Society & Women's Health Concern 2020 recommendations on hormone replacement therapy in menopausal women. Post Reprod Health. 2020 Dec;26(4):181-209. doi: 10.1177/2053369120957514. Epub 2020 Oct 12. PMID: 33045914.)	
Society of Occupational Medicine	General	General	Appointment of members to menopause guideline committee: The Society of Occupational Medicine (SOM) is the professional body for occupational health (OH), whose membership includes 1,800+ doctors, nurses, physiotherapists, occupational therapists etc. OH professionals contribute the health of the nation through their evidenced based knowledge on the workplace as a wider determinant of health; and use expert skills to give the best health outcomes for the businesses and employees they serve. OH professionals work with employers to discharge their duty of	Thank you for your comment. The committee membership constituency was agreed based on the draft key areas in the scope. We recognise the importance of occupational health clinician in menopause care in general, however, it was not prioritised as a role to be included in the committee membership because of the nature of the clinical review questions that are covered by the update. The recommendations in NICE guideline NG23 Workplace health: management practices will be applicable to people with menopause.

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			care, to help them understand, accommodate, and normalise the symptoms of challenging menopause transitions. It's long established that the menopause transition is a workplace issue affecting a large portion of the workforce, not just concerning an employer's legal responsibility but also contributing operational problems of performance, sick absence presenteeism and attrition. However, on looking at the supporting information for applicants we noted there is no advisory role for which an OH Clinician could apply. We feel it is important that menopause and managing health at work are considered at the planning stages. We request consideration of an additional advisory role on your committee for an Occupational Health Clinician. To highlight the type of expertise we could propose our vice chair of the Diversity and Inclusion Task Force at the SOM, is a qualified nurse, health and wellbeing specialist with Menopause Specialist Skills certificate, Cognitive Behaviour Therapy for Menopause Symptoms certificate and has undertaken further study on living beyond cancer and returning to work; all awarded by the British Menopause Society. She sits on the European Menopause and Andropause Task Force who recently published a global statement on introducing menopause education into health care professional's curriculum. Emma also consults with the Faculty of Occupational Medicine's 2022 menopause guidance update for all OH professionals. I am	

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			convinced her experience with menopause and health in the workplace would be if benefit when looking at the guidelines. OH is an essential service and, in relation to menopause care, the link between primary care, gynaecologist, GP and the workplace. OH is in a unique position to be able to introduce, health education, risk reduction behaviours and self-management strategies to all employees to improve physical and mental health during the menopause transition. However, not all employees have access to OH so including key consideration into guidance such as this is vital for clinician, employee and manager's education. I appreciate any process for such a role would be an open application for any OH Clinician. The SOM could assist with advertising this request for applicants given the tight deadline.	
Turner Syndrome Support Society	General	General	I am pleased to see that you are reviewing cardiovascular risk please also look at the benefits	Thank you for your comment and support for the guideline update.
UK Clinical Pharmacy Association	General	General	UKCPA welcomes the updating of the NICE NG23 Menopause Guidance to ensure that patients are being provided updated evidence based care. Pharmacists have been key in helping women with issues around HRT shortages over the last few years and are a trusted source for advice.	Thank you for your comment and support for this guideline update. We recognise the important role that pharmacists have and a pharmacist has been recruited to the guideline committee.
UK Clinical Pharmacy Association	002	004	Symptoms …average duration of 7 years but can continue for as long as 12 years (SWAN study analysis]	Thank you for your comment. The duration varies considerably between individuals and subpopulations (based on e.g. ethnic background or age at start of perimenopause) and it would be

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				difficult to say a maximum duration. We have revised the text to be more accurate and state the median duration is 7 years, this indicates some experience it longer and some shorter. We have also noted that duration may vary between ethnic groups.
UK Clinical Pharmacy Association	002	006	The other menopause symptoms [in addition to hot flushes and vaginal dryness] should be stated here to give readers a complete picture of all the menopausal symptoms that a woman can struggle with. Low moods and anxiety, and sleep issues are well documented menopausal symptoms.	Thank you for your comment. This section has been revised by adding "changes to sleep and mood" as examples of signs and symptoms of the menopause.
UK Clinical Pharmacy Association	002	009	Delete 'some' from 'Some studies' – Good quality studies have shown that loss of estrogen during the menopause can affect bone and cardiovascular health	Thank you for your comment. The wording 'some studies' is used because the previous sentence states that it can be difficult to differentiate between the effects of ageing and menopause.
UK Clinical Pharmacy Association	002	012	There are significant personal and societal costs – this is the reason why the NHSE is looking at workforce menopause support programs.	Thank you for your comment. We recognise that there can be significant personal costs for some women, non-binary or trans people experiencing menopause, but not all. We also recognise that there can be a significant impact on wider society. We have revised the text.
UK Clinical Pharmacy Association	004	002	Consider adding in the statement that current medical consensus is use of HRT to age of natural menpause with POI.	Thank you for your comment. Guidance in relation POI will not be updated but will be retained from the current guideline NG23. This is because no substantive new evidence was identified in the surveillance and scoping process for this topic.
UK Clinical Pharmacy Association	005	Table	Section 1.4 Consider reviewing evidence base for treatments such as Gabapentin and Oxybutynin, under evaluation for menopause symptom control. Non licensed, emerging treatment options?	Thank you for your comment. Non-hormonal pharmacological treatments were included in the original NG23 menopause guideline. Gabapentin was included in the network meta-analysis of treatments for short-term symptoms in NG23 and

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			NB: A new non hormonal therapy currently being evaluated - NK3 antagonists. Reference: Modi M, Dhillo WS. Neuroendocrinology 2019;109:242-248	surveillance has identified no additional evidence on Gabapentin which would change the existing recommendations. Oxybutynin was not included in NG23, however we are only aware of 2 relatively small RCTs of oxybutynin for menopausal symptoms and adding these trials to the existing main network meta-analysis of treatments for short-term symptoms is very unlikely to change the existing recommendations. These trials used different dosages and could not be combined together in meta-analysis due to different side effect rates, which would increase uncertainty about effectiveness. The non-hormonal treatments are particularly relevant for people with a history of breast cancer, however the 2 oxybutynin trials were not limited to people with a history of breast cancer and could not be included in a network meta-analysis of treatments for people with a history of breast cancer (as done in NG23). NK3 antagonists are not yet a stage of development where they could be included in a clinical guideline. Based on the above considerations, reviewing evidence on these treatments were not prioritised in the update.
UK Clinical Pharmacy Association	007	023	It may be helpful when considering economic aspects, to review the table from reference Menopause International 2011;17:137-141, which looks at the efficacy for fracture reduction and monthly costs of treatments for osteoporosis. HRT is considered as a treatment option. Please note that the costs for the injectable options, Zoledronate and Teriparatide will be lower now that we have generic formulations available.	Thank you for your comment and for providing this reference. Economic evidence on topics covered in the scope will be searched, reviewed and presented to the committee before forming recommendations. The committee will also agree on areas for bespoke economic analysis where there may be a resource impact but there is a paucity of recent, applicable and high-quality economic evidence identified. This may include

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				areas where key inputs into previous economic analyses, such as drug prices, have significantly changed.
UK Clinical Pharmacy Association	008	011	This is an important section and will help health professionals provide an improved risk benefit evaluation individualised to their patients. This is a question that often comes up in pharmacist led medication reviews.	Thank you for your comment and support for this topic area being updated.
UK Clinical Pharmacy Association	009	007 - 008	If the update work indicates that there is any benefit for use of HRT for dementia or loss of muscle mass or strength, then the duration of HRT use needs to be explicitly reviewed.	Thank you for your comment. The plan is that the duration of HRT use will be considered when reviewing the evidence on the effects of HRT.
University of East Anglia	008	024 - 027	We feel that it is important that this update of the guidance includes the effects of hormone replacement therapy for menopausal symptoms on all-cause mortality. HRT can make some causes of death more likely and others less likely. All-cause mortality is a useful summary measure for women and their doctors because it combines information on rare and common causes of death with differing effect sizes and directions. We have recently published the results of a long term large cohort study on HRT and all cause mortality: https://obgyn.onlinelibrary.wiley.com/doi/full/10.1111/1471-0528.17008	Thank you for your comment. We agree and have included a draft review question on this subject "What are the effects of hormone replacement therapy for menopausal symptoms on all-cause mortality?"
University of Essex	001	011	Please use perimenopause along with menopause. It is not until p3 – line 20 that this is mentioned. There needs to be recognition that this transition phase of change prepares the body/women for menopause. The guidance should alert women and practitioners that this is very much an important stage and prepares the woman for menopause and this is usually the longest and can be most uncomfortable phase.	Thank you for your comment. Mention of perimenopause or menopause transition has now been added to the beginning of the section on "Why the guideline is needed".

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			Recognition of this is required as the effects on individuals do vary with each person, and requires recognition on the impact of physical and mental health.	
University of Essex	001	022	Please could "sometimes longer" be classified. At the British Menopause Society there was agreement amongst clinicians this can last beyond age 60 with hot flushes continuing in older women (Parsons 2021).	Thank you for your comment. The wording has been revised and now refers to the duration varying between people but typically lasting for a few years.
University of Essex	002	006	While vasomotor symptoms are common and seen very much in clinical evidence/primary research other primary research from disciplines such occupational health are finding fatigue and troubling sleeping leading the menopause symptoms. Around 60% of menopausal women have difficulty concentrating (Pausivity #KnowYourMenopause)	Thank you for your comment. This section has been revised by adding "changes to sleep and mood" as examples of signs and symptoms of the menopause.
University of Essex	002	008	If menopause is a natural part of ageing then there needs to be more recognition about it. Current studies Cronin (2021) and key writers such asGriffith et al (2016) and Hardy et al (2018) have recognised these symptoms in occupational health. Current work by Pausitivity #KnowYourMenopause campaign surveyed more then 850 peri-post menopauseal women and asked them how much they knew about the menopause. Hot flushes, night sweats and irregular periods are the most known symptoms. Hwowever the main symptoms women first saw their GP with were anxiety, depression and sleep problems, And these were thee symptoms that led to a diagnosis for menpause but leading to 57% waiting more than 12 months for a diagnosis.	Thank you for your comment. This section has been revised by adding "changes to sleep and mood" as examples of signs and symptoms of the menopause.

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University of Essex	002	012	There are significant societal costs and also large economic costs as this group of women are the fastest and largest growing employed group and will impact different workplaces globally eg health care professional groups and teaching where a largest percentage are women.	Thank you for your comment. We recognise that there can be significant impact on the wider society as well as personal costs for some women, non-binary or trans people experiencing menopause. We have revised the text.
University of Essex	002	016	Does everyone need medical treatment? No and many women do not want medical intervention but do need help and advise to understand the problems and what to do to better undertsnd their bodies and prepare for this (Cronin 2021).	Thank you for your comment. We agree, the population defined in the scope is women, non-binary and trans people with menopause, regardless of their need for medical treatment.
University of Essex	002	022	There is still a lot of work required on talking on of the benefits of HRT. The BMS (2021) annual conference brought this up and still not great confidence even amongst practitioners. So a lot of education and support is required for medical staff, GPs and specialists, and nurses to provide this information to the public and strengthen confidence.	Thank you for your comment. In the guideline update, evidence on the effects of HRT, whether beneficial or harmful, will be looked at in relation to various overall outcomes, such as cardiovascular disease, dementia, breast, endometrial and ovarian cancer.
University of Essex	003	018	Who is the focus? There is no real mention of managing the symptoms at work. Perimenopause and menopause is affecting a large amount of the workplace, with women forming a significant part of the workforce and the biggest growing group which will have an impact on health care. Globally, 657 million women worldwide are aged 45-59, placing them into peri-menopause and menopause (Rees et al 2021). Approximately 47% of these women are employed and may experience symptoms that impact working life (Rees el al 2021). Rees M, Bitzer J, Cano A, et al. Global consensus recommendations on menopause in the workplace: A	Thank you for your comment. When developing the evidence review protocols, the committee may consider impact on work as an outcome of interest. The section of scope 'Why this guideline is needed' has been revised and the potential impact of menopause on working life is highlighted.

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			European Menopause and Andropause Society (EMAS) position statement. *Maturitas* 2021; 151: 55-62. DOI: 10.1016/j.maturitas.2021.06.006.	
University of Essex	003	020	More work is needed to explain and educate the effect on different groups and aceptance around this.	Thank you for your comment which will be considered when developing the guideline.
University of Essex	004	005	All settings – this should be applied to all settings and the information freely available. There should be no restriction to information.	Thank you for your comment. NICE guidance can be used by non-NHS settings including private practice but the remit of NICE clinical guidance is to give guidance to NHS-commissioned services.
University of Essex	004	011	It would be interesting to see how CBT helps with the symptoms, but there could be a place to explore the digital interventions to alleviate the discomfort associated with menopause. Many women do not want to take anything e.g. HRT tablets and consequently manage on for years. In a scoping review Cronin et al (2021) found little evidence looking at digital interventions for women experiencing menopause. Cronin C, Hungerford C and Wilson RL. Using digital health technologies to manage the psychosocial symptoms of menopause in the workplace: A narrative literature review. *Issues in Mental Health Nursing* 2021; 42: 541-548. DOI: 10.1080/01612840.2020.1827101.	Thank you for your comment. The guideline update will review evidence on the effectiveness of CBT in managing menopausal symptoms. The details of this evidence review will be agreed by the guideline committee, but may include different modes of delivering CBT, including digital interventions. Otherwise, the surveillance and scoping processes have not identified evidence on digital interventions that would warrant an evidence review on this topic and therefore it has not been prioritised.
University of Essex	004	023	The proposed guidelines looks comprehensive however I note the heavy focus on physical sysmptoms and there needs to be some investigative work around anxiety, depression, brain fog and fatigue which makes a lot of the symptoms seem much	Thank you for your comment. We have added "changes to sleep and mood" to the Key facts and figures section as examples of signs and symptoms of the menopause, and we have included anxiety, low mood and sleep disturbance in our

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			worse. A physical symptoms that also needs more attention is heavy periods described as "flooding". This seems to have been ignored. Maybe this might related to some of the key issues raised in 3.5 of the report.	list of main outcomes. This update is focused on areas where surveillance has found new evidence which could change the existing recommendations and the issue of heavy periods was not identified in this process. NICE has a separate guideline on heavy menstrual bleeding, NG88.
Viatris	General	General	In addition to your comments below, we would like to hear your views on the below question: 1.Are there any cost saving interventions or examples of innovative approaches that should be considered for inclusion in this guideline? Viatris suggest that NICE committee consider highlighting the increased need for individualised care of menopausal women, specifically with regard to use of hormone replacement therapy (HRT). The appropriate use of oral and transdermal HRT could be a cost saving intervention; oral therapy is less expensive and may be the preferred choice for women without an increased risk of venous thromboembolism and otherwise suitable for oral HRT. There is a place for both oral and transdermal options and when individualised to the right patients, could provide both cost effective symptom relief and improved quality of life. The attitudes and knowledge of HRT has been evolving through the years. HRT is now widely accepted as having benefits both for bone and cardiovascular health: the International Menopause Society believe it can be considered as "first-line" therapy to prevent fractures in women aged 50-60 years. Similarly oestrogen therapy has shown strong and	Thank you for your comment. The evidence on the benefits and risks of HRT on different overall health outcomes will be reviewed, including cardiovascular disease, and bone health for early menopausal population. The cost effectiveness of the interventions will be considered together with the clinical effect. The level of detail around the different types and formulations of HRT will be considered by the committee during protocol development for each of the review questions.

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			consistent evidence that it may be cardioprotective if started around the time of the menopause (or the "window of opportunity"). With this in mind, HRT for the appropriate woman, can be considered to confer benefits not just for immediate symptom control, but also as a health prevention strategy to reduce morbidity and mortality associated with osteoporosis and cardiovascular disease.	
Viatris	005	Table	1.4: Vasomotor symptoms (hot flushes and night sweats) HRT is widely recognised to be the most effective therapy for the relief of vasomotor symptoms, achieving up to 80-90% symptom reduction, compared to 50-60% with alternative therapies. Viatris would like to suggest if this can be emphasised in the new guideline. Reference: RCOG: Alternatives to HRT for the Management of Symptoms of the Menopause (Scientific Impact Paper No. 6) 2010. Available at: https://www.rcog.org.uk/en/guidelines-research-services/guidelines/sip6/	Thank you for your comment. The effectiveness of HRT for vasomotor symptoms will not be covered in this update and the existing recommendations will stand because the surveillance and scoping process did not identify substantive new evidence that would impact existing recommendations. Instead the update will focus on the impact of HRT on longer term health outcomes, because this is where surveillance has identified important new evidence.
Viatris	005	Table	**1.5 Long-term benefits and risks of hormone replacement therapy:** Viatris welcome the NICE Clinical Guideline on Menopause and welcome NICE views that women need to know the available HRT treatment options, their benefits and risks. With this in mind Viatris is concerned that the Guidance is limited	Thank you for your comment. The evidence on the risks and benefits of HRT associated with breast cancer among other outcomes will be reviewed and recommendations updated as needed. The evidence reviews will consider different HRT preparations, however the level of detail with regards to HRT preparations will be agreed during the evidence review protocol development stage with the guideline committee.

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			with respect to highlighting the different forms of progestogen in HRT preparations as these differ markedly with respect to their risk profiles. Not all HRT preparations are the same, for example dydrogesterone, compared to other progestogens has no binding affinity for oestrogenic, androgenic or glucocorticoid receptors (as per selective receptor binding activity below). Also studies have shown marked differences amongst HRT preparations in their associated risk of breast cancer and VTE. Viatris agree that it is key that information on all available treatment options should be provided, this should also include differences between HRT preparations particularly progestogen risks. Viatris is concerned that this lack of awareness from healthcare professionals, may result in women being ill-informed of the differences amongst HRT preparations. <u>Receptor binding table</u>	

Progestogen	Progestogenic	Estrogenic	Androgenic	Anti-androgenic	Glucocorticoid	Anti-mineralocorticoid
Dydrogesterone	+	–	–	±	–	±
Progesterone	+	–	–	±	+	+
MPA*	+	–	±	–	+	–
Norethisterone	+	+	+	–	–	–

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			+ Effective; ± Weakly effective; – Not effective *Table reproduced from Maturitas, 46 (S1), Schindler AE, Campagnoli C, Druckman R, Huber J, Pasqualini JR, Schweppe KW, Thijssen JHH. Classification and pharmacology of progestins. 7–16. Copyright (2003), with permission from Elsevier.*	
Viatris	005	Table	**1.5 Long-term benefits and risks of hormone replacement therapy:** **Venous thromboembolism** Viatris would like to highlight that the risk of VTE is not only associated with mode of delivery but also oestrogen dose and type of progestogen used. Low dose oestrogen is associated with a lower risk of VTE whilst oral preparations containing the pregnane derivatives such as Dydrogesterone appear to have an acceptable thrombotic risk profile. <u>Oestrogen Dose</u> The Vinogradova 2019 case-control study analysed the risk of VTE with different types of HRT. This large study included 80 396 women with VTE matched to 391 494 controls and concluded that higher doses of oral oestrogen used resulted in higher risks of VTE.[1]	Thank you for your comment. The evidence on the risks and benefits of HRT associated with VTE among other outcomes will be reviewed among population with early menopause (40-44 years). This is a population that based on stakeholder feedback is not sufficiently covered in the current guideline. Otherwise, the surveillance and scoping process have not identified new evidence that would warrant change to recommendations around HRT and VTE among the wider population. The review for early menopausal population will consider different HRT preparations, however the level of detail with regards to HRT preparations will be agreed during the evidence review protocol development stage with the guideline committee.

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			Type of progestogen in combined oral HRT The same Vinogradova 2019 study demonstrated that with regards to VTE risk, combined oral preparations containing dydrogesterone conferred the lowest risk of VTE: *"compared with no exposure, conjugated equine oestrogen with medroxyprogesterone acetate had the highest risk (2.10, 1.92 to 2.31), and estradiol with dydrogesterone had the lowest risk (1.18, 0.98 to 1.42)."*[1] The favourable profile of dydrogesterone is echoed in the ESTHER study which was a multicentre case-control study investigating the impact of route of oestrogen administration and progestogen on the risk of venous thromboembolism (VTE) among postmenopausal women (aged 45–70 years) receiving HRT. The study included 271 consecutive cases with a first documented episode of idiopathic VTE matched with 610 controls. The study found no statistically significant association of VTE with micronized progesterone or pregnane derivatives (which included dydrogesterone, medrogestone, chlormadinone acetate, cyproterone acetate, and MPA). (OR, 0.7; 95% CI, 0.3 to 1.9 and OR, 0.9; 95% CI, 0.4 to 2.3, respectively) Norpregnane derivatives (either nomegestrol acetate or promegestone) were however, associated with an approximately 4-fold increased risk of VTE vs. no use. (OR, 3.9; 95% CI, 1.5 to 10.0).	

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			The results suggest that norpregnane derivatives may be thrombogenic, whereas micronized progesterone and pregnane derivatives (e.g. Dydrogesterone) appear to have an acceptable thrombotic risk profile.[2] References: 1. Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases. BMJ. 2019 Jan 9;364:k4810 2. Canonico M et al, Estrogen and Thromboembolism Risk (ESTHER) Study Group. Hormone therapy and venous thromboembolism among postmenopausal women: impact of the route of estrogen administration and progestogens: the ESTHER study. Circulation. 2007 Feb 20;115(7):840-5.	
Viatris	005	Table	**1.5 Long-term benefits and risks of hormone replacement therapy:** Viatris would like to highlight that the type of progestogen in combined HRT may influence effects on lipid profiles and insulin sensitivity. These effects may be particularly relevant for women who are overweight and those with diabetes, prediabetes.	Thank you for your comment. When reviewing evidence on the effect of HRT on overall health outcomes, different HRT preparations will be considered, however the level of detail around this will be determined by the guideline committee at the evidence review protocol development stage.

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			Combined HRT with oestradiol + dydrogesterone may have metabolic advantages over other combinations in terms of insulin resistance and lipid profiles.[1-3] Oestrogen increases HDL (high density lipoprotein), but this beneficial effect is blunted by addition of androgenic progestogens: medroxyprogesterone acetate and norethisterone acetate.[1-3] This blunting effect is not seen with dydrogesterone.[1-3] Oestrogen reduces insulin resistance, but the beneficial effect of the oestrogen on insulin sensitivity may be blunted by the addition of a progestogen[3,4] dydrogesterone has a neutral effect on glucose metabolism, and may be better considered to be used in women with insulin resistance or diabetes[3] References: 1. Godsland, et al. Effects of postmenopausal hormone replacement therapy on lipid, lipoprotein and apolipoprotein(a) concentrations: analysis of studies published from 1974-2000. *Fertil Steril*. 2001; 75(5): 898–915. 2. Stevenson J et al. 1 and 2 mg 17beta-estradiol combined with sequential dydrogesterone have similar effects on the serum lipid profile of postmenopausal women. *Climacteric*, 2005 Dec; 8(4): 352–9.	

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			3. Stevenson JC et al. Progestogens as a component of menopausal hormone therapy: the right molecule makes the difference. *Drugs Context*. 2020 Dec 2; 9: 2020-10-1. 4. Lindheim SR et al. A possible bimodal effect of estrogen on insulin sensitivity in postmenopausal women and the attenuating effect of added progestin. *Fertil Sieril.* 1993; 60: 664–667.	
Viatris	005	Table	**1.5 Long-term benefits and risks of hormone replacement therapy:** **Breast Cancer** Breast cancer is the most common cancer in women and affects 1 in every 7 over their lifetime. It is known that HRT can increase the risk of breast cancer and this can cause significant worry and anxiety amongst women considering HRT. However, the risks of breast cancer should be put into perspective with other risk factors for breast cancer including lifestyle choices (smoking, obesity, alcohol consumption). The possible increased risk of breast cancer associated with HRT is small and estimated at less than 0.1% per annum, which is similar to, or lower than the increased risks associated with common lifestyle factors such as reduced physical activity, obesity and alcohol consumption.[1] Additionally the impact HRT may have on the risk of breast cancer is an individualised	Thank you for your comment. When reviewing evidence on the effect of HRT on breast cancer, confounding factors (e.g. smoking and BMI) as well as different HRT preparations will be considered. However the level of detail around these will be determined by the guideline committee at the evidence review protocol development stage.

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			consideration and the overall health and background risk of each woman may affect the risk benefit profile of using HRT. Furthermore, although oestrogen alone and oestrogen with progestogen HRT in combination can be associated with an increased risk of breast cancer, it is important to highlight that there are different classes of progestogens available and these differentially impact on the risk of breast cancer. Both the British and International Menopause Societies recognise that micronized progesterone or dydrogesterone used with oestradiol may be associated with a better risk profile for breast cancer than other synthetic progestogens.[1,2] We note that the Lancet 2019 meta-analysis on breast cancer risk is referred to by the NICE guideline[3], however, this meta-analysis contains data only from epidemiological data. If this meta-analysis is to be included within the NICE guideline, then Viatris would like to suggest other key cohort and case-control studies on breast cancer risks with HRT to be considered: In particular, the recent Vinogradova 2020 study provides large scale, UK relevant, homogenous data to allow "real-world" insights into the breast cancer risk associated with exposure to the commonly prescribed formulations over the past 20 years.[4] Individualisation is therefore key to treating women with HRT and consideration should be given to the progestogen	

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			component of HRT as an independent differentiating factor for the risk of breast cancer. Including guidance on the importance of the progestogen component of HRT within the NICE guideline, may better inform healthcare professionals on the differences in risk, thereby ensuring that women are afforded an informed choice in their treatment. References: 1. Baber RJ et al; IMS Writing Group. 2016 IMS Recommendations on women's midlife health and menopause hormone therapy. Climacteric. 2016 Apr;19(2):109-50. 2. Hamoda H et al, The British Menopause Society & Women's Health Concern 2020 recommendations on hormone replacement therapy in menopausal women. Post Reproductive Health. 2020;26(4):181-209. 3. Collaborative Group on Hormonal Factors in Breast Cancer. Type and timing of menopausal hormone therapy and breast cancer risk: Individual participant meta-analysis of the worldwide epidemiological evidence. The Lancet. 2019;394(10204):1159–68 4. Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of breast cancer: nested case-control studies using the QResearch and CPRD databases. BMJ. 2020 Oct 28;371:m3873	

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[i] Goldberg et al., 2019, The Counseling Psychologist
[ii] E.g. Nowakowski et al., 2016, Journal of Racial and Ethnic Health Disparities; Riach & Jack, 2021, International Journal of Environmental Research and Public Health
[iii] Bottema-Beutel et al., 2021, Autism in Adulthood
[iv] For a sample of literature, see Bradshaw et al., 2021, Australian Journal of General Practice; Doherty et al., 2022, BMJ
[v] Cashin et al., 2018, Journal of Intellectual Disabilities; Hirvikoski et al., 2016, British Journal of Psychiatry
[vi] Moseley et al., 2020, Autism; Moseley et al., 2021, British Journal of Health Psychology; Groenman et al., Autism, 2021; Karavidas et al., 2021, Journal of Autism and Neurodevelopmental Disorders
[vii] Cassidy et al., 2022, British Journal of Psychiatry; Septier et al., 2019, Neuroscience & Biobehavioural Reviews
[viii] See, for e.g., Cooper et al., 2018, Research in Autism Spectrum Disorders
[ix] See Howes et al., 2019, Journal of Pharmacology