Ectopic pregnancy and miscarriage – diagnosis and initial management (update)

Consultation on draft guideline - Stakeholder comments table
19 December 2018 – 24 January 2019

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
British Medical Ultrasound Society	Guideline	General	General	This document was sent out to all experts in our Professional Standards Group and to our associated cohort of experts in the field of early pregnancy and gynaecology. No objections or revisions were sited in any correspondence. Overall agreement with the document on behalf of BMUS.	Thank you for your comment and for consulting with your expert members.
Department of Health & Social Care	Guideline	General	General	Thank you for the opportunity to comment on the above NICE guideline update. I wish to confirm that the Department of Health and Social Care has no substantive comments to make, regarding this consultation.	Thank you for your comment.
International Society of Ultrasound in Obstetrics and Gynecology	Evidence Review B	General	6 Table 2 10 Line 35	Please correct spelling of the author Jurkovic (not Jurcovic) in all tables (e.g. p6 table, p10ln35) and check in case of other misspelling of the name throughout the document	Thank you for your comment. This spelling has been corrected.
International Society of Ultrasound in Obstetrics and Gynecology	Glossary	8	Ectopic Pregnancy definition	We would suggest that the existing definition of ectopic pregnancy (A pregnancy when a fertilised egg implants outside the womb, usually in one of the fallopian tubes (also known as a tubal ectopic pregnancy) is scientifically inaccurate as the embryo implants (not the egg) and ectopic pregnancies can be located in various pelvic sites, not just the fallopian tube. The definition could be Tubal ectopic pregnancy: Implantation of a pregnancy within the fallopian tube OR Ectopic pregnancy: Implantation of a pregnancy outside the uterine cavity	Thank you for your comment. The committee agreed that this definition should be simplified to 'a pregnancy outside the uterus' and we have made this change in the glossary.

International Society of Ultrasound in Obstetrics and Gynecology	Glossary	9	Gestation sac definition	We are concerned that this definition is inaccurate and suggest an amendment to: The term used for the first phase in pregnancy development which is defined by the presence of a fluid filled cavity surrounded by villous tissue. This is the first visible structure of a pregnancy seen with ultrasound scan (prior to the yolk sac or embryo being visible)	Thank you for your comment. The committee agreed that the definition could be improved and have amended it to 'a fluid-filled sac within which the fetus usually develops'.
International Society of Ultrasound in Obstetrics and Gynecology	Glossary	10	Intrauterine pregnancy definition	We would prefer to see a scientifically accurate definition (the current definition does not take account of intrauterine pregnancies without an embryo). We suggest the following: Intrauterine pregnancy: The presence of a gestation sac (with or without embryo or yolk sac) within the uterine cavity	Thank you for your comment. The committee have revised this definition in the glossary as you have suggested to: 'The presence of a gestational sac (with or without yolk sac), embryo or fetus within the uterus'.
International Society of Ultrasound in Obstetrics and Gynecology	Glossary	13	Pregnancy of unknown location definition	The definition used is a lay definition. We feel that for a guideline for professional use that a more careful definition is appropriate. We suggest the following: A term used in the case of a woman with a positive pregnancy test in association with the inability to visualise an intrauterine or ectopic pregnancy with transvaginal ultrasound scan	Thank you for your comment. The committee have revised the definition as you suggest (in the glossary and the guideline) to say: 'When a woman has a positive pregnancy test but no intrauterine or extrauterine pregnancy can be seen with a transvaginal ultrasound scan.'
International Society of Ultrasound in Obstetrics and Gynecology	Guideline	Title	General	The current title 'Ectopic pregnancy and miscarriage…' would suggest the guideline includes nontubal ectopic pregnancies (such as interstitial, cervical, ovarian). We suggest the title should be amended to 'Tubal ectopic pregnancy and miscarriage…' to reflect the content of the guideline which does not make reference to nontubal ectopic pregnancy. The draft guideline has already made this clarification in the contents section (1.4 and 1.6) but not in the main title.	Thank you for your comment. As this guideline has only undergone minor updates we would prefer not to change the guideline title. In addition, future updates may include issues relating to non-tubal ectopic pregnancies and the guideline title would therefore have to be changed again. As you have noticed, we have clarified within the guideline that the sections only relate to tubal ectopic pregnancy.

International Society of Ultrasound in Obstetrics and Gynecology	Guideline	General	General	We would like the guideline committee to take account of the RCOG Diagnosis and Management of Ectopic Pregnancy guideline which we support. For safe clinical care and avoidance of confusion, especially with the large number of guideline documents clinicians are expected to comply with, guidelines should as far as possible be consistent in terminology and recommendations (though we understand that a different review of the evidence may mean that some variation is likely)	Thank you for your comment. The committee were aware of this guideline but NICE guidelines are based on a different methodology and, as you have recognised, this may mean that sometimes recommendations differ between NICE guidelines and other publications.
International Society of Ultrasound in Obstetrics and Gynecology	Guideline			The RCOG 2016 Green Top Guideline 21 (Diagnosis and Management of Ectopic Pregnancy) states 'Systemic methotrexate may be offered to suitable women with a tubal ectopic pregnancy.It should never be given at the first visit, unless the diagnosis of ectopic pregnancy is absolutely clear and a viable intrauterine pregnancy has been excluded. [New 2016]' We feel that the NICE guideline should also include such a patient safety statement, to allow for the occasional false positive diagnosis of ectopic pregnancy with ultrasound and protect such women with intrauterine pregnancies from inadvertently receiving methotrexate which might terminate a wanted pregnancy	Thank you for your comment. The section of the NICE guideline relating to the use of methotrexate was not reviewed but as you have highlighted this as a patient safety issue the committee agreed that it was important not to give methotrexate at the first visit unless the diagnosis of ectopic pregnancy was unequivocal, and they have therefore amended the recommendation to say this.
International Society of Ultrasound in Obstetrics and Gynecology	Guideline	12	4-5	We feel that the addition of the visualisation of the corpus luteum is important in avoiding false positive diagnosis. We also feel that the term 'mass' is misleading and potentially upsetting for a woman if written in a medical report, as in common use it refers to possible tumour/malignancy. We would recommend the wording is amended to: When carrying out a transvaginal ultrasound in early pregnancy always attempt to identify both ovaries and a corpus luteum. Following that, look for these signs indicating there is a tubal ectopic pregnancy:	Thank you for your comment. The committee considered that, as the corpus luteum is within the ovary and not the tube, it was unlikely to be mistaken for a tubal ectopic pregnancy. Therefore whilst they agreed it could be helpful to see an adnexal mass and separate corpus luteum, it was not essential. The committee also discussed the appropriate terminology. They

				an adnexal ~~mass~~ swelling, moving separate to the ovary1, comprising a gestational sac containing a yolk sac, or an adnexal ~~mass~~ swelling, moving separate to the ovary1, comprising a gestational sac and an embryo/fetal pole (with or without fetal heartbeat).	considered that the structure visualised was more accurately described as a "mass", rather than a "swelling", as it was comprised of a variety of tissues, not just fluid. Furthermore, the terminology 'mass' was well understood in this context, including by the lay members on the committee.
International Society of Ultrasound in Obstetrics and Gynecology	Guideline	12	10-16	We suggest that the term mass is removed and replaced with 'swelling' and other minor revisions to wording as follows: When carrying out a transvaginal ultrasound in early pregnancy, look for these signs indicating a high probability of a tubal ectopic pregnancy: a complex, inhomogeneous adnexal swelling, moving separate to the ovary1, or an adnexal swelling with an empty gestational sac, moving separate to the ovary1 (also called a 'tubal ~~ring' or 'bagel sign'2~~). In these cases it is essential to identify a corpus luteum separate to the swelling to minimise the risk of false positive diagnosis	Thank you for your comment. The committee discussed the appropriate terminology. They considered that the structure visualised was more accurately described as a "mass", rather than a "swelling", as it was comprised of a variety of tissues, not just fluid. The committee also considered that, as the corpus luteum is within the ovary and not the tube, it was unlikely to be mistaken for a tubal ectopic pregnancy. Therefore whilst they agreed it could be helpful to see an adnexal mass and separate corpus luteum, it was not essential. However, the committee did amend the description of the tubal ring, and changed the terminology to 'previously described as'.
International Society of Ultrasound in Obstetrics and Gynecology	Guideline	13	12-14	We would ask for an improvement of the wording to emphasise the importance of more than one corpus luteum (ovulation) to identify women at higher risk of heterotopic pregnancy and suggest: When scanning women during early pregnancy, scan the adnexa as well as the uterus, even if there is an intrauterine	Thank you for your comment. The committee considered that that it was not always possible to accurately identify the corpus luteum. Therefore the recommendation is worded to emphasise the importance of being vigilant for heterotopic pregnancy in all

				pregnancy, to confirm there is no coexisting ectopic pregnancy. This is particularly important in women with more than one corpus luteum in the ovaries.	women, not just those in women more than one corpus luteum is identified.
International Society of Ultrasound in Obstetrics and Gynecology	Guideline	19	12	We would suggest that the upper cut off level for expectant management for hCG is 1500IU/L and would therefore recommend that the wording is changed to be in line with the 2016 RCOG Green Top Guideline: have a serum hCG level of ~~1,000~~ 1500 IU/L or less, and	Thank you for your comment. The evidence for this review suggested that expectant management was effective and safe with an hCG level less than 1,000 IU/L and should be offered to this population of women, but the committee agreed that there was uncertainty over what should be offered to women with an hCG above 1,000 and below 1,500 IU/L, so a separate 'consider' recommendation has been added for this population of women.
International Society of Ultrasound in Obstetrics and Gynecology	Guideline	19	14-15	The timing of hCG is highly variable (in published studies and clinical practice) and therefore we recommend that in order to avoid the impression that blood tests need to be specifically timed, and to minimise unnecessary out of hours visits, the wording is less prescriptive and is changed to: For women with an ectopic pregnancy being managed expectantly, repeat hCG levels after ~~48 hours~~ two to three days:	Thank you for your comment. The recommendation has been changed to state 'on day 2' as this allows some flexibility.
International Society of Ultrasound in Obstetrics and Gynecology	Guideline	19	16-17	We do not believe that a 15% drop in hCG for expectant management of ectopic as a marker of success has any scientific basis (it is likely that this may have arisen from an extrapolation from studies on methotrexate management or a misunderstanding of the protocol in the Jurkovic 2017 RCT). We recommend the Guideline wording is changed to: If the level drops ~~by 15% or more~~, repeat ~~weekly~~ between two and seven days depending of clinical judgement until a negative result (<20 IU/L) is obtained, or	Thank you for your comment. The 15% change compared to prior value is well-documented in several studies (Silva 2015, Van Mello 2012) as an indication of an hCG level that is changing in a specific direction and not just subject to random fluctuation, and therefore we have retained the 15% as a guide.

				if hCG levels plateau or rise, review the woman's clinical condition to help decide the further management plan.	
International Society of Ultrasound in Obstetrics and Gynecology	Guideline	24-25	Key Recommendations for research	We appreciate that this section is not being updated on this occasion but would like to be sure that the NICE Guideline committee is aware that recommendations 1 and 3 have been carried out, under national research funding, and are due for imminent publication: PRISM: ISRCTN14163439 : PRISM: Progesterone in spontaneous miscarriage VESPA: ISRCTN10728897 : Organisation of Early Pregnancy Units and its effects on quality of care	Thank you for your comment. We have passed these studies onto the NICE surveillance team for consideration in future updates of this guideline.
International Society of Ultrasound in Obstetrics and Gynecology	Guideline	28	6	Typo: Incidence	Thank you for your comment. This typo has been corrected.
International Society of Ultrasound in Obstetrics and Gynecology	guideline (and Evidence Review A)	12 (and Evidence review p 11)	15-16 (and Evidence review ln27)	We feel that the term 'bagel', whilst used in some previous publications, is an inappropriate term, referring to food, and may cause offence if used in medical reports. We would prefer that all references to 'bagel' are removed from the evidence review and guideline as the terms 'empty gestation sac' and 'tubal ring' are sufficient.	Thank you for your comment. The committee were aware that the term bagel may still be widely used but had fallen out of favour, so amended the recommendation to say that the relevant features were 'sometimes described as…' to indicate that it was not current terminology.
International Society of Ultrasound in Obstetrics and Gynecology	guideline (and Evidence Review A)	12 (and Evidence review p 11)	15-16 (and Evidence review ln27)	We feel that the term 'bagel', whilst used in some previous publications, is an inappropriate term, referring to food, and may cause offence if used in medical reports. We would prefer that all references to 'bagel' are removed from the evidence review and guideline as the terms 'empty gestation sac' and 'tubal ring' are sufficient.	Thank you for your comment. The committee were aware that the term bagel may still be widely used but had fallen out of favour, so amended the recommendation to say that the relevant features were 'sometimes described as…' to indicate that it was not current terminology.

International Society of Ultrasound in Obstetrics and Gynecology	Guideline and Glossary	General (and Glossary 9)	General	We are concerned that the appropriate medical terms should be used as far as possible and would suggest that the term fetus is replaced with embryo (or use embryo/fetus) throughout the guideline in order that scientific accuracy is maintained. (The term fetus refers to a baby after eight weeks gestation when embryogenesis is complete. The majority of scenarios in the guideline refer to early first trimester and hence embryo is more accurate). The term 'fetal pole' is outdated and has no scientific meaning and should be replaced with embryo throughout the documents.	Thank you for your comment. The committee agreed that the correct medical terms should be used, but that the terms used in clinical practice when carrying out, reporting and discussing ultrasound findings were 'fetus' and 'fetal pole' and therefore they would prefer to continue with these terms.
International Society of Ultrasound in Obstetrics and Gynecology	Guideline and Glossary	General	General and p23 Ln5	It would be helpful if the terms used are consistent across the glossary and guideline. For example 'Expectant management' is defined in the glossary (p9) as 'A management approach, also called "wait and watch" whereby no medical or surgical treatment is administered, with the aim of seeing whether the condition will resolve naturally' which we feel is a comprehensive definition. It is then described slightly differently in the draft guideline definitions (p23,Ln5) as 'A management approach in which treatment is not administered, with the aim of seeing whether the condition will resolve naturally'	Thank you for your comment. We have amended the definition used in the guideline so it is the same as the one used in the glossary.
IPULA Group	Guideline	13-15	1.4.23-1.4.32	Adjuncts such as the M4 model (initial hCG, hCG 48 hour / hCG 0 hour) and the M6 model (progesterone, initial hCG and hCG 48 hour / hCG 0 hour) use values mentioned above in a logistic regression manner to risk stratify PUL. It is standardised, easy to use methodology and can give management guidance - instead of calculating the hCG ratio in isolation for each case (the hCG ratio is essentially what the guideline describes). The hCG ratio in itself is less sensitive than either the M4 and M6 model for identifying ectopic pregnancy and overall is a worse triage tool. See Diagnostic protocols for the management of pregnancy of unknown location: a systematic review and meta-analysis.	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest. However, thank you for highlighting the published article, which has been sent to the NICE surveillance team for consideration in future updates to this guideline.

				Bobdiwala S, Saso S, Verbakel JY, Al-Memar M, Van Calster B, Timmerman D, Bourne T. BJOG. 2019 Jan;126(2):190-198. doi: 10.1111/1471-0528.15442. Epub 2018 Sep 20. Review.	
IPULA Group	Guideline	4	12	Delete 'some'	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	4	14	'should also be trained'	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	4	17	'should also be trained'	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	5	20-21	Not possible to always provide the healthcare professional of choice for the woman. Clinicians usually rotate in an Early Pregnancy Unit as well as being on a full on call rota	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	5	24	North West Thames not 7 days a week for EPU. Few are safely. Should be '5-7 days/up to 7 days a week'	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.

IPULA Group	Guideline	5	29	Patients attend with symptoms other than pain and/or bleeding in early pregnancy	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	6	1	Should be 'serum biomarkers, for example, hCG or progesterone'	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	6	13	Replace A&E with Emergency Department (ED), add UCC (Urgent Care Centre)	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	6	24	Point must be added – any symptomatic woman with a positive pregnancy test must be considered an ectopic pregnancy until proven otherwise	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest. However, as the committee agreed that this may be a patient safety issue they discussed the comment, but noted that the guideline makes it clear in recommendations 1.3.7 to 1.3.9 that women with pain and bleeding should be assessed in an early pregnancy assessment service, and so the concern you have raised is already covered.
IPULA Group	Guideline	6	25-26	Directly to Emergency Department but ensure local Early Pregnancy Unit as well as gynaecology specialists are	Thank you for your comment. This section of the guideline was not

				informed immediately in order to plan for necessary investigations and management	included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	7	4, 8	Delete line 4 and line 8	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	7	5	Unilateral or central	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	7	6-7	Switch lines 6 and 7	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	7	10	e.g. Diarrhoea	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	7	19, 23	Delete line 19 and 23	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.

IPULA Group	Guideline	7	25	Delete peritoneal signs – they have all been discussed already	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	8	1	Add below line 1 – tachypnoeia :RR>20	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	8	1.3.5	Should be moved to 1.3.2	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	8	1.3.8 18-21	The possibility of ectopic pregnancy should always be considered, whether risk factors are present or not	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	8	1.3.9	Key referral points already mentioned in point 1.3.7, with modifications above	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	8	4	Delete ‘think about’ and replace with ‘offer’	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were

					unable to make the change you suggest.
IPULA Group	Guideline	8	15-17	Replace with all points of 1.3.4	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	9	1.3.10	Can get bleeding <6/40 and no pain in women who then are diagnosed with an ectopic pregnancy. If Pregnancy of Unknown Location (PUL), should be managed as per PUL protocol. To advise otherwise is dangerous as an ectopic is not excluded and an intra uterine pregnancy has never been visualised. If a woman is bleeding, with a positive pregnancy test, USS will confirm PUL as a classification and the PUL protocol must then be followed. Presuming non viable intra uterine pregnancy or failed pregnancy of unknown location is not safe	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed but as you have suggested this may be a patient safety issue the committee reviewed this comment and agreed that bleeding at less than 6 weeks was most likely to be due to an early pregnancy loss and that nothing would be seen by scanning at this early stage. However, the committee did agree that this recommendation would be improved by moving the third bullet to the top and by adding that this recommendation should only apply to women who had no risk factors for ectopic pregnancy.
IPULA Group	Guideline	9	1.3.11	Should already be referred. Line 12-13 questionable re requirement. The fact a woman has re-presented/been re-admitted is a prognostic factor in itself	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	9	1.4.1	Not ‘offer’ but ‘all’ (line 20), ‘should have’ (line 22) and ‘to attempt to’ (line 22)	Thank you for your comment. This section of the guideline was not included in the update and no evidence

					was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	9	1.4.2	Line 27 – add 'or if a pregnancy is not seen on trans vaginal ultrasound'	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	10	3	Add 'including fact that ectopic pregnancy may be missed'	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	10	21-22	As mentioned above, this is not necessary, and can prolong the waiting time unnecessarily for women and lead to complications of miscarriage that could be avoided	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	10	26-27	CRL <7mm use PUV guidance – repeat scan after 7 days minimum, not 14 days	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	10	1.4.4	CRL 7mm or greater with no FH or MSD ≥25mm with no contents within, at first scan **is** accurate for diagnosis of miscarriage. Need two competent scanners to confirm diagnosis but can be diagnosed with one ultrasound scan. Any other findings = PUV (pregnancy of unknown location)	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.

IPULA Group	Guideline	11	1	14 days here not 7 days	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	11	1.4.11	Miscarriage diagnosed with most accuracy and certainty with trans vaginal ultrasound	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	11	1.4.16	This is a dangerous point. If it is the woman's first scan you cannot say it is a complete miscarriage as there has never been evidence of an intra uterine pregnancy. It must be classified as a pregnancy of unknown location and therefore go through the PUL protocol	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed but as you have suggested this may be a patient safety issue the committee reviewed this comment and revised the recommendation to state that this could be a pregnancy of unknown location, as you suggest.
IPULA Group	Guideline	11	3	If MSD has doubled, a yolk sac seen or CRL seen <7mm	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	11	6	Confirm with second opinion re miscarriage	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.

IPULA Group	Guideline	11	7-8	Again, as mentioned above, this is not necessary, and can prolong the waiting time unnecessarily for women and lead to complications of miscarriage that could be avoided	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	12	17-19	Look at other scan features, if patient is symptomatic during scan, hCG levels are useful for PUL risk stratification and assisting the management of ectopic pregnancy, but has no role in diagnosis if an ectopic pregnancy seen on ultrasound	Thank you for your comment. The committee agreed that other scan features should be taken into consideration and have mentioned this in their recommendation, but that as the features listed in this recommendation only suggest a high probability of an ectopic pregnancy, then hCG levels may need to be taken into account when making the diagnosis as well.
IPULA Group	Guideline	12	1.4.19	Empty uterus and no pregnancy seen outside the uterus = PUL. It is far more likely that fluid in the cavity is an early gestation sac (see Doubilet et al) – the so called "pseudosac" is discredited and is not a marker of ectopic pregnancy. Intra-cavity fluid in the absence of any other features and not thought to be a gestations sac is a PUL. Not enough here to diagnose an ectopic pregnancy. **Cannot** use these features with hCG levels to make a diagnosis of ectopic pregnancy	Thank you for your comment. This recommendation suggests that these features indicate a 'possible' ectopic pregnancy and we are not suggesting that they are diagnostic on their own, or in conjunction with hCG levels. The committee recognised that these may also be features of a pregnancy of unknown location (PUL) and so have cross-referred to the recommendations on identifying a PUL.
IPULA Group	Guideline	13	1.4.20	Should be transvaginal ultrasound, free fluid alone not diagnostic, neither is hCG. Patient condition most important if ectopic pregnancy not seen	Thank you for your comment. The committee agreed that free fluid alone and hCG are not diagnostic and have stated in the recommendation that the women's clinical presentation should be considered. The committee were aware that free fluid may be seen on either

					transabdominal or transvaginal scans and so have left both in the recommendation.
IPULA Group	Guideline	13	1.4.21	Can try and identify number of corpus lutei also	Thank you for your comment. The committee considered that, whilst it may be helpful to visualise the number of corpus lutei, it was not essential as part of the ultrasound features to identify a tubal ectopic pregnancy and so did not add this to the recommendations.
IPULA Group	Guideline	13	1.4.22	2 professionals should confirm diagnosis	Thank you for your comment. The committee did not think it was necessary or practical to recommend that a diagnosis always required 2 professionals.
IPULA Group	Guideline	14	20	7 days later only	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	14	20-22	Earlier scan only indicated if symptomatic change	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	14	1.4.26	Can also be used in risk stratification (see below)	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.

IPULA Group	Guideline	14	1.4.27	+/- 8 hours (around the 48 hour mark) – useful for risk stratification and to advise on further management	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	15	1.4.32	Progesterone can be used for failed pregnancy of unknown location classification (especially in modelling when Progesterone <2nmol/L)	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest. However, your comment has been passed to the NICE surveillance team for consideration in future updates to this guideline.
IPULA Group	Guideline	16	1.5.3	Sometimes not appropriate to do so e.g. if CRL >30mm or MSD > 50mm then surgical management advised due to complication risk otherwise	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest. However, your comment has been passed to the NICE surveillance team for consideration in future updates to this guideline.
IPULA Group	Guideline	16	1.5.6	Would tend to offer routine a follow up scan for all expectant management	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	16	1.5.7	Should be 'during/after'	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were

					unable to make the change you suggest.
IPULA Group	Guideline	17	1.5.12	E.g. to have PV misoprostol given in the EPU as opposed to self-administration	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	17	1.5.9	Barnhart 2018 NEJM paper 10.1056/NEJMoa1715726 on Mifepristone + Misoprostol vs Misoprostol alone	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest. However, this article has been forwarded to the NICE surveillance team for consideration in future updates to the guideline.
IPULA Group	Guideline	18	1.5.16	Offer all a follow up scan for all medical management	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	19	1.6.3	hCG level must be falling. Ectopic pregnancies <35mm can still rupture	Thank you for your comment. The committee agreed that ectopic pregnancies less than 35 mm could still rupture but to continue with expectant management the hCG levels would need to fall, otherwise the management plan would be reviewed (as specified in recommendation 1.6.5)
IPULA Group	Guideline	19	1.6.5	Mental health complications high with a diagnosis of ectopic pregnancy, no matter what management used	Thank you for your comment. The committee were aware that mental health conditions may be associated

					with a diagnosis of ectopic pregnancy. Further information on support and counselling services is covered in section 1.1 of the guideline.
IPULA Group	Guideline	20	1-4	Difficult to add to guideline without evidence	Thank you for your comment. The committee were aware that questions about time to resolution and future fertility were often asked by women so although there was no evidence found for these outcomes, they based these recommendations on their clinical experience, so that women were more likely to receive consistent advice on these topics.
IPULA Group	Guideline	22	1.6.14	May not be safe to do so, even with infertility as a risk factor	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed but as you have mentioned this may be a patient safety issue the committee discussed this comment. The committee noted that this was a 'consider' recommendation and so salpingotomy would only be considered as an alternative to salpingectomy in women when it was safe to do so.
IPULA Group	Guideline	22	1.6.16	Also, for women with IVF, >1 egg transfer with no previous evidence of where other pregnancy/pregnancies may be	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	22	1.7.1	250-500IU in some units	Thank you for your comment. This section of the guideline was not

					included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	22	1.7.2	Anti D can be given for medical management also	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
IPULA Group	Guideline	25	General	Mife-Miso trial running	Thank you for your comment and for informing us of this trial. We have passed this information onto the NICE surveillance team for consideration in future updates of this guideline.
King's College Hospital	Guideline	1.4.18		The use of the word 'complex' is concerning in that it is a term often associated with ovarian pathology and suspected malignancy. Could you consider defining what the word 'complex' means in this context or consider removal. We would suggest the term 'solid' as a preference for the diagnosis of ectopic pregnancy.	Thank you for your comment. The committee agreed that 'complex' was a widely used and understood term used to describe ectopic pregnancies, and that 'solid' was not the correct term as the adnexal mass is not always solid.
King's College Hospital	Guideline	1.4.19		Would read better as 'indirect' signs of a possible ectopic pregnancy. We would suggest removing 'empty uterus' . This is because the uterus may appear or be empty for many other reasons – too early, too difficult or too late. An intrauterine pregnancy does not exclude a coexisting ectopic. We feel it should also make it clear that you cannot make the diagnosis of an ectopic pregnancy on these ultrasound features.	Thank you for your comment. The committee considered that these were direct signs, but that they only indicated the possibility of an ectopic pregnancy. The committee agreed that an empty uterus may be (or appear to be) empty for a variety of reasons but that the recommendation did not suggest this was a sole feature upon which a diagnosis of ectopic pregnancy could be made.

King's College Hospital	Guideline	1.4.20		We would suggest: 'look for a moderate to large amount of echogenic fluid in the peritoneal cavity i.e haematoperitoneum or blood clots. Anechoic (clear) fluid does not suggest an ectopic pregnancy and is seen very commonly with early intrauterine pregnancies.	Thank you for your comment. The committee considered that 'a moderate to large amount of free fluid' was not commonly seen with an intrauterine pregnancy, therefore should still raise suspicion of an ectopic pregnancy. However they agreed that it was useful to add more detail about the type of fluid so have included the detail about haemoperitoneum in the recommendation.
King's College Hospital	Guideline	1.4.21		Suggest 'when scanning *symptomatic* women in early pregnancy'. Practitioners scanning asymptomatic women, for example in termination of pregnancy services, should not be expected to screen the adnexae for a coexisting ectopic or ovarian pathology. We believe that they need to be able to accurately identify an intrauterine pregnancy and date it, but no more.	Thank you for your comment. The committee were concerned that if the word symptomatic was added, this may lead to ectopic pregnancies being missed in women with heterotopic pregnancies.
King's College Hospital	Guideline	1.6.17		We feel that a pregnancy test should only be needed if the histology was negative, and in which case, two weeks would be more appropriate. It's not clear what is the purpose of the pregnancy test is. Is it in case the pregnancy was missed at surgery?	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to comment on the appropriateness of the timing of this pregnancy test or make the changes you suggest.
King's College Hospital	Guideline	1.6.3		We would suggest that this level should be increased to 1500IU/l to reduce the risk of inadvertent use of methotrexate in an IUP and this is in line with published research in expectant management, which would be the alternative. Offering methotrexate as a first line with low hCG increases the risk of inadvertent use in an IUP. If NICE are to continue to recommend using methotrexate with low hCG then we would recommend that this should only be	Thank you for your comment. This recommendation relates to expectant management and so will not lead to inadvertent use of methotrexate in an intrauterine pregnancy. We have added a further recommendation to highlight that expectant management could be

				after a repeat hCG after 48 hours, with a repeat ultrasound if the hCG is rising to try and exclude an intrauterine pregnancy.	considered for women with hCG levels of above 1000 and below 1500IU/L
King's College Hospital	Guideline	1.6.6	12	Is there a typo here with the cut off of <1500 for MTX? Shouldn't it be 5000? We are concerned that this may imply that MTX can be given on a single hCG level. We feel that the decision to use MTX should be based on a second hCG and scan 48 hrs later in the presence of a lower hCGs, This will also mean that if the hCG is falling, expectant management could be adopted.	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to comment on the appropriateness of the cut-off level, or make the changes you suggest. However, please note that recommendation 1.6.9 highlights that MTX could be offered to women with an hCG level of between 1500 and 5000 (as an alternative to surgery)
King's College Hospital	Guideline	1.6.8		This suggests that <1500 can have expectant management, but based on the recommendations preceding this it makes it unclear what the management should be for women with hcg between 1000-1500?	Thank you for your comment. The committee agreed that, as the new recommendations suggest expectant management for women with an hCG less than 1000, it was now unclear what options should be offered to women with an hCG above 1000 and below 1500. Therefore, the committee added an additional recommendation that expectant management could be considered in this group.
Royal College of Midwives	Documentation	General	General	RCM supports the proposed changes to the guideline update and has no further comments.	Thank you for your comment.
Royal College of Nursing	General	General	Genera	The Royal College of Nursing (RCN) welcomes proposals to update the NICE Ectopic and miscarriage: diagnosis and initial management guideline.	Thank you for your comment and for inviting your members to comment.

				The RCN invited members who care for pregnant women to review and comment on the draft guidance on its behalf. The comments reflect the views of our reviewers.	
Royal College of Nursing	Guideline	General	General	The guideline appears sound and most comprehensive.	Thank you for your comment.
Royal College of Nursing	Guideline	General	General	Good to see highlighted in the document that 'women are to be given time' and dealt with by sensitive trained specialists. The reality is that early pregnancy assessment units are on the increase and serious cases are routed directly to Emergency Departments so treatment is timely.	Thank you for your comment.
Royal College of Nursing	Guideline	33 - 35	Table	The tables are really helpful for the practitioner with limited time. Flow charts could be helpful as practitioners generally find them useful.	Thank you for your comment. This table is to explain what changes have been made to recommendations where a full evidence review has not been undertaken, and why.
Royal College of Obstetricians and Gynaecologiests	Guideline	12	4, 10	I'm not clear what the difference is in these two recommednatoins. Both are stating look for an adnexal mass separate from the ovary.	Thank you for your comment. The first recommendation relates to definitive features of an ectopic pregnancy (i.e. presence of a yolk sac or fetal pole within the adnexal mass). The second recommendation identifies features which are highly suspicious for ectopic, but not definitive, i.e. a complex mass or empty gestational sac
Royal College of Obstetricians and Gynaecologiests	Guideline	12	17-19	This recommendation is really soft and from a clinical perspective doesn't do much to aid the clinician in diagnpstic decision making. What other ultrasound features would you look for and what would that mean in terms of management? What HCG level ? What features in the clinical presentation?	Thank you for your comment. The recommendations in this section provide detail on the ultrasound features, and then further interpretation of the clinical features and hCG levels and the effects this would have on the management are covered in more detail in section 1.6 of the guideline.

Royal College of Obstetricians and Gynaecologiests	Guideline	13	12-14	Think this should be the first recommendation	Thank you for your comment. The committee agreed that this recommendation was about identifying the very rare occurrence of a heterotopic pregnancy in a women in whom an ectopic pregnancy had been seen or was suspected, and not a general recommendation about ultrasound scanning for all women and so it was not appropriate to move it to the beginning of the section. However, the committee amended the wording of the recommendation to clarify that it was the uterus and adnexae should be scanned
Royal College of Obstetricians and Gynaecologiests	Guideline	19	8-13	It would be important to stress that expectant management is only an option if the woman has support at home and access to healthcare services in an emergency. Section 1.6.8 (methotrexate therapy) has appropriate wording ('Advise women who choose methotrexate that their chance of needing further intervention is increased and they may need to be urgently admitted if their condition deteriorates').	Thank you for your comment. The committee agreed, based on their clinical experience, that this wording should be added to the expectant management section as well, and have added it.
Royal College of Obstetricians and Gynaecologiests	Guideline	19	11	'tubal ectopic pregnancy on transvaginal ultrasound scan measuring less than 35 mm with no visible heartbeat..'. Consider being more specific with regards to what exactly is 'measuring less than 35mm', i.e. mean gestational sac diameter?? in a live tubal ectopic, or the ectopic 'mass' ?? etc., as this could potentially cause confusion.	Thank you for your comment. The committee agreed that the 35mm measurement referred to the mass seen on ultrasound and defined as an ectopic pregnancy, and that this would be determined by the professional conducting the ultrasound.
Royal College of Obstetricians and	Guideline	19	17	'repeat weekly until a negative result (<20 IU/L) is obtained' Please consider that some biochemistry labs use <1IU/L, others <5IU/L etc. as their cut-off for 'negative' hCG. Therefore the definition of 'negative' hCG as specifically	Thank you for your comment. The levels of <1 IU/L and <5 IU/L are both below 20 IU/L so labs that report these levels will not prevent professionals from confirming a level of <20 IU/L.

Gynaecologiests				<20IU/L may not be applicable to some early pregnancy unit settings across the UK.	
Society and College of Radiographers	Guideline	General	General	Would it be helpful to mention the National Bereavement Care Pathway, as this relates to miscarriage and ectopic pregnancy. http://www.nbcpathway.org.uk/file/aw_5844_nbcp_miscarriage_pathway.pdf	Thank you for your comment. The committee considered this suggestion but were aware that this pathway was currently only in a pilot stage and therefore did not think it was appropriate to add this link until it is finalised.
Society and College of Radiographers	Guideline	6	4	There is a move from patient groups to use the term 'delivering difficult news' or 'unexpected findings' rather than 'breaking bad news'	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
The Ectopic Pregnancy Trust	Evidence Review B	General	6 Table 2 10 Line 35	Please correct spelling of the author Jurkovic (not Jurcovic) in all tables (e.g. p6 table, p10ln35) and check in case of other misspelling of the name throughout the document	Thank you for your comment. This spelling has been corrected.
The Ectopic Pregnancy Trust	Glossary	9	Gestation sac definition	We are concerned that this definition is inaccurate and suggest an amendment to: The term used for the first phase in pregnancy development which is defined by the presence of a fluid filled cavity surrounded by villous tissue. This is the first visible structure of a pregnancy seen with ultrasound scan (prior to the yolk sac or embryo being visible)	Thank you for your comment. The committee agreed that the definition could be improved and have amended it to 'a fluid-filled sac within which the fetus usually develops'
The Ectopic Pregnancy Trust	Glossary	10	Intrauterine pregnancy definition	We would prefer to see a scientifically accurate definition (the current definition does not take account of intrauterine pregnancies without an embryo). We suggest the following: Intrauterine pregnancy: The presence of a gestation sac (with or without embryo or yolk sac) within the uterine cavity	Thank you for your comment. The committee have revised this definition in the glossary as you have suggested to: 'The presence of a gestational sac (with or without yolk sac), embryo or fetus within the uterus'.
The Ectopic Pregnancy Trust	Glossary	13	Pregnancy of unknow	The definition used is a lay definition. We feel that for a guideline for professional use that a more careful definition is appropriate. We suggest the following:	Thank you for your comment. The committee have revised the definition as you suggest (in the glossary and the

			n location definitio n	A term used in the case of a woman with a positive pregnancy test in association with the inability to visualise an intrauterine or ectopic pregnancy with transvaginal ultrasound scan	guideline) to say: 'When a woman has a positive pregnancy test but no intrauterine or extrauterine pregnancy can be seen with a transvaginal ultrasound scan.'
The Ectopic Pregnancy Trust	Guideline	Title	General	The current title 'Ectopic pregnancy and miscarriage…' would suggest the guideline includes nontubal ectopic pregnancies (such as interstitial, cervical, ovarian). We suggest the title should be amended to 'Tubal ectopic pregnancy and miscarriage…' to reflect the content of the guideline, given it does not make reference to nontubal ectopic pregnancy. The draft guideline has already made this clarification in the contents section (1.4 and 1.6) but not in the main title.	Thank you for your comment. As this guideline has only undergone minor updates we would prefer not to change the guideline title. In addition, future updates may include issues relating to non-tubal ectopic pregnancies and the guideline title would therefore have to be changed again. As you have noticed, we have clarified within the guideline that the sections only relate to tubal ectopic pregnancy.
The Ectopic Pregnancy Trust	Guideline	General	General	We would like the guideline committee to take account of the RCOG Diagnosis and Management of Ectopic Pregnancy guideline, which we support. For safe clinical care and avoidance of confusion, especially with the large number of guideline documents clinicians are expected to comply with, guidelines should, as far as possible, be consistent in terminology and recommendations (though we understand that a different review of the evidence may mean that some variation is likely).	Thank you for your comment. The committee were aware of this guideline but NICE guidelines are developed using a different methodology and, as you have recognised, this may mean that sometimes recommendations differ between NICE guidelines and other publications.
The Ectopic Pregnancy Trust	Guideline	General		The RCOG 2016 Green Top Guideline 21 (Diagnosis and Management of Ectopic Pregnancy) states 'Systemic methotrexate may be offered to suitable women with a tubal ectopic pregnancy. It should never be given at the first visit, unless the diagnosis of ectopic pregnancy is absolutely clear and a viable intrauterine pregnancy has been excluded. [New 2016]'	Thank you for your comment. The section of the NICE guideline relating to the use of methotrexate was not reviewed but as you have highlighted this as a patient safety issue the committee agreed that it was important not to give methotrexate at the first visit unless the diagnosis of ectopic pregnancy was unequivocal, and they

				We feel that the NICE guideline should also include such a patient safety statement, to allow for the occasional false positive diagnosis of ectopic pregnancy with ultrasound and protect such women with intrauterine pregnancies from inadvertently receiving methotrexate which might terminate a wanted pregnancy	have therefore amended the recommendation to say this.
The Ectopic Pregnancy Trust	Guideline	6	24	We feel that it is important to add the point that any symptomatic woman who has had a positive pregnancy test must be considered ectopic until proven otherwise.	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest. However, as the committee agreed that this may be a patient safety issue they discussed the comment, but noted that the guideline makes it clear in recommendations 1.3.7 to 1.3.9 that women with pain and bleeding should be assessed in an early pregnancy assessment service, and so the concern you have raised is already covered.
The Ectopic Pregnancy Trust	Guideline	8	4	We feel that it is important to ALWAYS offer a pregnancy test if a woman is symptomatic of ectopic pregnancy and of child bearing age.	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
The Ectopic Pregnancy Trust	Guideline	10	3	Add that it should also be explained specifically that an ectopic pregnancy may be missed using transabdominal ultrasound only.	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.

The Ectopic Pregnancy Trust	Guideline	12	4-5	We feel that the addition of the visualisation of the corpus luteum is important in avoiding false positive diagnosis. We also feel that the term 'mass' is misleading and potentially upsetting for a woman if written in a medical report as, in common use, it refers to possible tumour/malignancy. We would recommend the wording is amended to: When carrying out a transvaginal ultrasound in early pregnancy always attempt to identify both ovaries and a corpus luteum. Following that, look for these signs indicating there is a tubal ectopic pregnancy: an adnexal ~~mass~~ swelling, moving separate to the ovary1, comprising a gestational sac containing a yolk sac, or an adnexal ~~mass~~ swelling, moving separate to the ovary1, comprising a gestational sac and an embryo/fetal pole (with or without fetal heartbeat).	Thank you for your comment. The committee considered that, as the corpus luteum is within the ovary and not the tube, it was unlikely to be mistaken for a tubal ectopic pregnancy. Therefore whilst they agreed it could be helpful to see an adnexal mass and separate corpus luteum, it was not essential. The committee also discussed the appropriate terminology. They considered that the structure visualised was more accurately described as a "mass", rather than a "swelling", as it was comprised of a variety of tissues, not just fluid. Furthermore, the terminology 'mass' was well understood in this context, including by the lay members on the committee.
The Ectopic Pregnancy Trust	Guideline	12	10-16	We suggest that the term mass is removed and replaced with 'swelling' and other minor revisions to wording as follows: When carrying out a transvaginal ultrasound in early pregnancy, look for these signs indicating a high probability of a tubal ectopic pregnancy: a complex, inhomogeneous adnexal swelling, moving separate to the ovary1, or an adnexal swelling with an empty gestational sac, moving separate to the ovary1 (also called a 'tubal ring'~~ or 'bagel sign'2~~). In these cases, it is essential to identify a corpus luteum separate to the swelling to minimise the risk of false positive diagnosis.	Thank you for your comment. The committee discussed the appropriate terminology. They considered that the structure visualised was more accurately described as a "mass", rather than a "swelling", as it was comprised of a variety of tissues, not just fluid. The committee also considered that, as the corpus luteum is within the ovary and not the tube, it was unlikely to be mistaken for a tubal ectopic pregnancy. Therefore whilst they agreed it could be helpful to see an adnexal mass and separate corpus luteum, it was not

				We feel that the term 'bagel', whilst used in some previous publications, is an inappropriate term, referring to food, and may cause offence if used in medical reports. We would prefer that all references to 'bagel' are removed from the evidence review and guideline as the terms 'empty gestation sac' and 'tubal ring' are sufficient.	essential. However, the committee did amend the description of the tubal ring, and changed the terminology to 'previously described as'.
The Ectopic Pregnancy Trust	Guideline	13	12-14	We would ask for an improvement of the wording to emphasise the importance of more than one corpus luteum (ovulation) to identify women at higher risk of heterotopic pregnancy and suggest: When scanning women during early pregnancy, scan the adnexa as well as the uterus, even if there is an intrauterine pregnancy, to confirm there is no coexisting ectopic pregnancy. This is particularly important in women with more than one corpus luteum in the ovaries.	Thank you for your comment. The committee considered that that it was not always possible to accurately identify the corpus luteum. Therefore the recommendation is worded to emphasise the importance of being vigilant for heterotopic pregnancy in all women, not just those in women more than one corpus luteum is identified.
The Ectopic Pregnancy Trust	Guideline	13	20	We would suggest that waiting 14 days is too long both for physical health and for the mental health of the woman who is worried about the risk. Guideline should read 7 days later only.	Thank you for your comment. We believe this relates to page 14, line 20. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
The Ectopic Pregnancy Trust	Guideline	16	11-13	It is not appropriate to offer medical management if the CRL >30mm or MSD >50mm. In this instance, surgical management is recommended.	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest. However, your comment has been passed to the NICE surveillance team for consideration in future updates to this guideline.

The Ectopic Pregnancy Trust	Guideline	16	22-25	It is likely, women's mental health would improve if offered a routine follow up scan.	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
The Ectopic Pregnancy Trust	Guideline	18	5-9	It is likely, women's mental health would improve if offered a routine follow up scan.	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
The Ectopic Pregnancy Trust	Guideline	19	14-19	Our medical advisors know of instances where hCG levels fall and the rise again. We would like to see the expectant protocol FU with 4 and 7 days after the initial fall rather than going straight to weekly FU.	Thank you for your comment. The recommendation has been revised to include follow-up at 4 and 7 days as you suggest,
The Ectopic Pregnancy Trust	Guideline	19	14-15	The timing of hCG is highly variable (in published studies and clinical practice) and therefore we recommend that in order to avoid the impression that blood tests need to be specifically timed, and to minimise unnecessary out of hours visits, the wording is less prescriptive and is changed to: For women with an ectopic pregnancy being managed expectantly, repeat hCG levels after 48 hours, +/- 8 hours:	Thank you for your comment. The recommendation has been changed to state 'on day 2' as this allows some flexibility.
The Ectopic Pregnancy Trust	Guideline	19	16-17	We do not believe that a 15% drop in hCG for expectant management of ectopic as a marker of success has any scientific basis (it is likely that this may have arisen from an extrapolation from studies on methotrexate management or a misunderstanding of the protocol in the Jurkovic 2017 RCT). We recommend the Guideline wording is changed to: If the level drops ~~by 15% or more~~, repeat ~~weekly~~ between two and seven days depending of clinical judgement until a negative result (<20 IU/L) is obtained, or	Thank you for your comment. The 15% change compared to prior value is well-documented in several studies (Silva 2015, Van Mello 2012) as an indication of an hCG level that is changing in a specific direction and not just subject to random fluctuation, and therefore we have retained the 15% as a guide.

				if hCG levels plateau or rise, review the woman's clinical condition to help decide the further management plan.	
The Ectopic Pregnancy Trust	Guideline	19	12	We would suggest that the upper cut off level for expectant management for hCG is 1500IU/L and would therefore recommend that the wording is changed to be in line with the 2016 RCOG Green Top Guideline. It is also REALLY important to be clear on hCG dynamics. hCG levels must be clearly falling and it must be clear that ectopic pregnancies <35mm can still rupture.	Thank you for your comment. The evidence for this review suggested that expectant management was effective and safe with an hCG level less than 1,000 IU/L and should be offered to this population of women, but the committee agreed that there was uncertainty over what should be offered to women with an hCG between 1,000 and 1,500 IU/L, so a separate 'consider' recommendation has been added for this population of women. The recommendations on the measurement and changes in hCG levels have also been clarified. The committee agreed that ectopic pregnancies less than 35 mm could still rupture but to continue with expectant management the hCG levels would need to fall, otherwise the management plan would be reviewed (as specified in recommendation 1.6.5).
The Ectopic Pregnancy Trust	Guideline	22	9-11	Would be useful to add a line that repeats the same hCG guidance for women with IVF, >1 egg transfer with no previous evidence of where other pregnancies may be.	Thank you for your comment. This section of the guideline was not included in the update and no evidence was reviewed so the committee were unable to make the change you suggest.
The Ectopic Pregnancy Trust	Guideline	24-25	Key Recommendations for	We appreciate that this section is not being updated on this occasion but would like to be sure that the NICE Guideline committee is aware that recommendations 1 and 3 have	Thank you for your comment. We have passed these studies onto the NICE surveillance team for consideration in future updates of this guideline.

			research	been carried out, under national research funding, and are due for imminent publication: PRISM: ISRCTN14163439 : PRISM: Progesterone in spontaneous miscarriage VESPA: ISRCTN10728897 : Organisation of Early Pregnancy Units and its effects on quality of care GEM3 and MIFE-MISO important trials are also running	
The Ectopic Pregnancy Trust	Guideline	28	6	Typo: Incidence	Thank you for your comment. This typo has been corrected.
The Ectopic Pregnancy Trust	guideline (and Evidence Review A)	12 (and Evidence review p 11)	15-16 (and Evidence review ln27)	We feel that the term 'bagel', whilst used in some previous publications, is an inappropriate term, referring to food, and may cause offence if used in medical reports. We would prefer that all references to 'bagel' are removed from the evidence review and guideline as the terms 'empty gestation sac' and 'tubal ring' are sufficient.	Thank you for your comment. The committee were aware that the term bagel may still be widely used but had fallen out of favour, so amended the recommendation to say that the relevant features were 'sometimes described as…' to indicate that it was not current terminology.
The Ectopic Pregnancy Trust	Guideline and Glossary	General (and Glossary 9)	General	We are concerned that the appropriate medical terms should be used as far as possible and would suggest that the term fetus is replaced with embryo (or use embryo/fetus) throughout the guideline in order that scientific accuracy is maintained. (The term fetus refers to a baby after 10 weeks gestation when embryogenesis is complete. The majority of scenarios in the guideline refer to early first trimester and hence embryo is more accurate). The term 'fetal pole' is outdated and has no scientific meaning and should be replaced with embryo throughout the documents.	Thank you for your comment. The committee agreed that the correct medical terms should be used, but that the terms used in clinical practice when carrying out, reporting and discussing ultrasound findings were 'fetus' and 'fetal pole' and therefore they would prefer to continue with these terms.
The Ectopic Pregnancy Trust	Guideline and Glossary	General	General and p23 Ln5	It would be helpful if the terms used are consistent across the glossary and guideline. For example, 'Expectant management' is defined in the glossary (p9) as 'A management approach, also called "wait and watch" whereby no medical or surgical treatment is administered,	Thank you for your comment. We have amended the definition used in the guideline so it is the same as the one used in the glossary.

				with the aim of seeing whether the condition will resolve naturally' which we feel is a comprehensive definition. It is then described slightly differently in the draft guideline definitions (p23, Ln5) as 'A management approach in which treatment is not administered, with the aim of seeing whether the condition will resolve naturally'	
The Miscarriage Association	Guideline	General	General	With regard to helping users overcome any challenges, it may be helpful to reference the National Bereavement Care Pathway, especially the guidance on miscarriage, ectopic pregnancy and molar pregnancy, as a national initiative that supports best practice. The main website is http://www.nbcpathway.org.uk/pathways/ and the specific pathway and full guidance can be found at http://www.nbcpathway.org.uk/file/aw_5844_nbcp_miscarriage_pathway.pdf and http://www.nbcpathway.org.uk/file/aw_5844_nbcp_miscarriage_full_guidance.pdf respectively.	Thank you for your comment. The committee considered this suggestion but were aware that this pathway was currently only in a pilot stage and therefore did not think it was appropriate to add this link until it is finalised.

**None of the stakeholders who comments on this clinical guideline have declared any links to the tobacco industry.*