

**National Institute for Health and Clinical Excellence  
Fertility Update  
Stakeholder Comments**

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<b>Stakeholder Organisation:</b>	British Fertility Society
<b>Name of commentator:</b>	<p>This document represents the British Fertility Society (BFS) response to the National Institute for Health and Clinical Excellence, consultation on the updated Fertility Guidelines.</p> <p>The British Fertility Society is a multi-disciplinary organization representing professionals with an interest in reproductive medicine. The objectives of the society are:</p> <ul style="list-style-type: none"> <li>• To promote high quality practice in the provision of fertility treatment.</li> <li>• To provide a common forum for members of various disciplines having an interest in the science and treatment of infertility.</li> <li>• To promote high quality scientific and clinical research in the causes and treatment of infertility.</li> <li>• To provide professional leadership in the provision and regulation of infertility services.</li> <li>• To promote the increase of NHS funding for and equity of access to fertility treatments.</li> </ul> <p>Therefore the NICE Fertility Guidelines is of interest to BFS members and this document has been prepared by Professor Adam Balen, Chair of the BFS Policy and Practice sub-committee following full consultation with BFS members.</p> <p>It is submitted by the BFS Honorary Secretary whose contact details are:</p> <p>Mrs Alison McTavish, c/o British Fertility Society Secretariat, 22 Apex Court, Woodlands, Bradley Stoke, Bristol, BS32 4JT. Email: <a href="mailto:bfs@bioscientifica.com">bfs@bioscientifica.com</a></p>

Order number	Document	Page Number	Line Number	Comments
1	Full	General		<p>The British Fertility Society welcomes the updated Guidance. We do, however, have certain concerns that relate to the short period of time for the consultation given the size of the document and the complexities of the economic modelling. The funding of fertility therapy is a highly charged political issue. Whilst we appreciate that the NICE Guidance is an attempt to provide an evidence base for the provision of NHS funded fertility treatment, there is still a significant “post code lottery” throughout England, Wales and Northern Ireland. The 2004 recommendations have still not been adopted by the majority of commissioners and so as a general point we are concerned that the new guidance was presented into the public arena with an emphasis on extending the age of provision to 42 (presumably a woman’s 43rd birthday) which was inevitably going to detract from many of the other key areas and yet is not really based on robust evidence. What does “absolute infertility” mean at this age - using a strict definition this would suggest that a woman has to be menopausal or have absent Fallopian tubes. And why then only offer one cycle of treatment when logic would suggest that older women require more treatments and not fewer to provide an equitable chance of success? The BFS feels that such guidance is likely to lead to a reduction in the overall provision for those for whom the treatment is actually going to work.</p>
2	Full	General		<p>Surrogacy is a real issue and it is wrong to exclude it from the review. Women with congenital absence of the uterus and those who have needed a hysterectomy for various reasons (and for a small number for whom pregnancy would be dangerous) have a legitimate right to receive fertility treatment and it is inequitable not to include surrogacy in the review.</p>
3	Full	General		<p>In a number of places AMH is promoted as a marker of the ovarian reserve. This seems appropriate but we are unsure how useful the precise numbers given in the NICE guideline actually are. The guideline group will be aware of the differences in AMH results from the assays currently available and with development of the Gen II assay now</p>

				becoming more widely used these numbers are set to change again. Giving such specific numbers without any discussion as to the assays in which they were derived is therefore potentially misleading and will lead to errors in clinical practice.
4	Full	Research section		The guidelines do not make any recommendations to the use of screening for a methodology for selecting embryos for transfer (PGS) i.e. FISH, CGH array etc. This is a rapidly expanding field where patients could be charged thousands of pounds for a treatment with little evidence base. In addition, there are many adjuvant therapies used in some centres which have not been recommended for use by professional guidelines (Nardo <i>et al.</i> , 2009) The BFS believes this is an opportunity for NICE to recommend that they should only be used in conjunction with a RCT.
5	Full	5		Pathway M Cancer Therapy. It is good to see this clear pathway, which is referred to throughout the document. We think that it should be acknowledged that this is relevant to other diseases other than just cancer where gonadotoxic therapy is used (e.g. some rheumatological conditions, and sickle cell disease where treated with bone marrow transplantation). The application of cryopreservation to other diseases is acknowledged much later in the document (Section 19) but it is rather in the small print and should be highlighted earlier.
6	Full	28		Guidelines 90 - 92. It seems surprising that these 3 guidelines are listed first when they don't address the primary treatment modalities in these patients. Some reordering would be appropriate. Thus recommendations 93 and 94 would seem to be the primary ones.
7	Full	41 45 348 361	11 2 10 5	Typos <i>Prednisoline</i> should read <i>prednisolone</i> .
8	Full	67 - 73	various	The discussion of individual lifestyle choices in males (e.g. alcohol, smoking, recreational drug use) is largely reliant upon univariate analyses. NICE should consider the recent publication by Povey <i>et al.</i> , (2012) as more up to date evidence than the current literature cited.
9	Full	71	34-35	Again, in multivariate analyses many of these occupational risks disappear. A better paper to cite is Cherry <i>et al.</i> , (2008) which looks

				specifically at occupational risks in a population of UK men.
10	Full	69	8	There's a huge amount published on obesity and reproductive health since 2004. The BFS appreciate this topic isn't being revised, but feel it would be helpful to add some more recent references that fit with the guidance and also strengthen it: The RCOG Scientific Study Group: <i>Obesity and Reproductive Health</i> . And the BFS Guidelines: Balen <i>et al.</i> , (2007).
11	Full	74	6	<b>34</b> Please mention that a higher dose of folic acid (5mg) may be more effective for obese women.
12	Full	75	13	<p>Whilst we recognise that lesbian couples may embark upon 'do-it-yourself methods' including home insemination we feel there should be a stronger statement by NICE discouraging this practice. We should not condone this "treatment" as it is unregulated and uses unscreened, fresh sperm. There is almost an inference here that NICE is suggestion that DIY Methods should be undertaken prior to NHS funded treatment NHS. Greater clarity is required in the wording here.</p> <p>Lesbian couples may receive NHS funding for treatment straight away if other infertility factors are identified (e.g. anovulation). Given that it is recognised that DI for lesbian couples has excellent outcomes we believe that it would be simpler, more straightforward and justifiable to avoid confusion and offer a set number of cycles of treatment at the outset after appropriate investigation, rather than expect lesbian couples to either home-inseminate or pay for 6 cycles of DI before having access to NHS care.</p>
13	Full	78	8	Section 6.2 comments on the relevance of physical examination findings, but as this is perhaps the most cost-effective intervention then it should recommend examination of male genitalia in cases of male factor infertility, to emphasize the importance of this intervention.
14	Full	81		Diagnostic semen analysis: Recommendation 44. The threshold of 58% vitality is of little or no use and in direct conflict with the threshold of 32 progressive motility. A man may have plenty of progressive sperm (e.g. 40%) but insufficient vitality (e.g. 50%). There is no practical value in testing vitality unless there is low motility (ABA, 2012). A figure of <5% is

				suggested.
15	Full	81		<p>There should be emphasis that the WHO reference ranges are only valid if WHO recommended methods for semen analysis are used.</p> <p>It would be appropriate also to have some mention that sperm concentration is a better predictor of fertility than motility or morphology and that there is also debate as to whether concentration or total sperm number is the more appropriate parameter. The text also appears to be written from the point of view that spermatogenesis is either normal or abnormal while of course it is shades of grey and indeed recognition of this is the basis for the current WHO guidelines based upon 95% confidence intervals rather than distinct diagnostic categories (Cooper <i>et al.</i>, 2010).</p>
16	Full	81		<p>There is no mention of best practice in the extraction of sperm from urine. The Liverpool solution is the only properly documented and (partially) validated method for retrieving sperm after the adjustment of urine pH and osmolarity (Aust <i>et al.</i>, 2008).</p>
17	Full	100		<p>Recommendation 56. The timing of gonadotrophin assessment should be commented on as measurement outside the early follicular phase will at times detect spontaneous ovulation and these results are frequently misinterpreted.</p>
18	Full	101	1	<p>Whilst the following may not have been included in the review it is wrong not to have done so if there is evidence to support a change in practice. This is one of the great limitations of a selective review of a rapidly changing field.</p> <p>The prevalence of disorders of thyroid dysfunction in women of reproductive years is approximately 5%, which is high enough to warrant a simple assessment of thyroid function – especially if one considers the potential implications for the developing fetus. (Stratford <i>et al.</i>, 2000).</p> <p>The use of Chlamydia screening – indication / methods / male and female / should be mentioned. This informs the method of tubal patency assessment. It is mentioned briefly below but needs expansion. The BFS recently published guidance on this topic see Akande <i>et al.</i>, (2010).</p>

19	Full	105	5	<b>63</b> The guidelines only recommend the viruses to be screened. The HFEA have recently stated that patients should be screened for HBV by serological testing for HBsAg and anti-HBc. If this does not occur it will be a breach of compliance. Therefore this should be included and a reference to standards which should be followed included as a minimum.
20	Full	121	4	<b>66 and 67</b> Advising on unprotected sex where the male partner is positive may cause anxiety and be met with reluctance. The document states the evidence was low in quality which may not be robust enough to base a guideline on. On some samples where a positive result was still found after washing the couple were given the choice whether to proceed. Patient choice is not possible if intercourse is the only line of treatment. It stated that it could be considered if the patient is anxious but their chance of conception may not be lower with IUI than natural conception. We believe that poorly designed studies have influenced the conclusion that sperm washing produces a poorer pregnancy rate compared with natural intercourse and that a well designed RCT would need to be carried out to help determine this.
21	Full	123	14	Reference should be made to Akande <i>et al.</i> , (2010). Also, no reference is made to Chlamydia screening in the male, yet we know that men who have the infection have reduced semen quality (Al-Mously <i>et al.</i> , 2009) and that sperm function can be compromised (Eley <i>et al.</i> , 2005). Strategies for screening males in a fertility context have been proposed (Eley and Pacey, 2011).
22	Full	125	1	Surely donor insemination is the <b>only</b> option for such couples.
23	Full	128	24	Can the Cochrane review by Showell <i>et al.</i> , (2011) be better incorporated into the section on antioxidants as it would seem to be more robust than the current literature cited and is lost as a footnote.
24	Full	130	18	With regard to surgical treatment of varicoceles. more recent evidence should have been discussed including an RCT (Abdel-Mequid <i>et al.</i> , 2011) and a meta-analysis (Baazeem <i>et al.</i> , 2011). The impact of treatment on sperm quality should be discussed specifically, even if the conclusions remain unchanged. The European Association of Urologists has recently

				published updated guidelines on Male Infertility (Jungwirth <i>et al.</i> , 2012), which discusses these topics in detail. They discuss MicroTESE, which is not mentioned in the NICE guidelines and the guidelines have a good overview of male genetics. They recommend varicocele treatment in the context of infertility in certain instances, which is a view contrary to NICE. They also state the importance of including the need for male patients with subfertility to be examined.
25	Full	132	11	The comment on anxiolytics is not backed up by evidence and is not cited in the referenced article. If the point is to consider the minority of men who have a psychological cause for their ED, then other psychological treatments (i.e. sexual counselling) should be mentioned. Anxiolytic drugs can cause erectile and ejaculatory dysfunction and are not considered a treatment for straightforward erectile dysfunction. It might be better just to remove the entire reference to anxiolytics.
26	Full	133	28,	Kallmann is miss spelt should have 2 n's.
27	Full	134	16	There is frequent recommendation of the use of pulsatile GnRH. The guideline group will know that this is unlicensed, and appropriate expertise is rare. Furthermore the current formulation of GnRH used for this therapy makes it extremely expensive. While it is clear that this is an extremely effective therapy in women (and also in men as mentioned in the relevant section), in the right hands, it would appear appropriate to mention these caveats rather than the straightforward across the board recommendation as presently phrased.
28	Full	135	22	This section seems to be omitting a clear statement on the efficacy and safety of clomiphene alone as first line therapy in anovulatory women.
29	Full	169	1	It would be helpful to give specific guidance on the number of allowable follicles in Ovulation Induction. For example BFS and ESHRE suggest "no more than a total of 2 follicles greater than 14mm in diameter, with at least one of 17mm" (The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group 2008). In order to reduce multiple pregnancy rates.
30	Full	170	26	The BFS suggests that an additional comment should be added to this paragraph to indicate that women who have a body mass index of more than 29, and who are not

				<p>ovulating, should be informed that losing weight is likely to increase their chance of conception <b>and this should be considered as part of their fertility treatment and not as a "barrier" to treatment.</b> This is in line with The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (2008).</p>
31	Full	170	14	<p><b>94</b> It is wrong to present metformin as a first line therapy for anovulatory PCOS. This flies in the face of all international consensus groups (ESHRE, ASRM, RCOG, BFS, WHO). Metformin only has a first line role for those with IGT or Type 2 DM. Can NICE really explain how metformin induces ovulation or justify its use as first line therapy?</p> <p>Metformin is not appropriate as first line therapy for anovulatory PCOS and should be used only in those with CC resistance (combined with CC) or those with IGT/Type 2DM (this was agreed in ESHRE/ASRM Consensus (The RotterdamESHRE/ASRM-sponsored PCOS consensus workshop group, 2004; The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2008), the 2010 RCOG Scientific Group on PCOS (Balen <i>et al.</i>, 2010) and the Cochrane Database (Tang <i>et al.</i>, 2012).</p>
32		170	25	<p><b>96</b> No evidence is presented for limiting clomiphene treatment to 6 months, This seems to derive entirely from the duration of the licence of this therapy. This also seems at odds with the lengthy discussion and justification of 12 cycles of donor insemination for women who require that therapy. There is also no mention of the management of women who are not clomiphene resistant but who do not conceive on clomiphene therapy despite have regular ovulation.</p>
33	Full	171	12	<p><b>99</b> "...dopamine agonists such as bromocriptine <i>or cabergoline...</i>" The addition of cabergoline is based on the text that appears later in the document, giving numbers indicating that cabergoline may be even more effective than bromocriptine.</p> <p>In the full discussion of this it would be appropriate to mention current guidelines on echocardiography to assess mitral valve fibrosis in patients taking bromocriptine.</p> <p>The manufacturer's view is that cabergoline</p>

				<p>should be stopped a month before conception and therefore it cannot be used in women attempting to conceive. This seems to be accepted without question despite the finding that it is associated with improved pregnancy rates as well as a rather better side effect profile. This seems to be without any analysis of whether cabergoline does indeed carry a risk of teratogenicity and the guideline group will be aware that it has been widely used for many years in women at the time of conception without apparent clinical risk.</p>
34	Full	189	12	<p><b>110</b> This may be controversial in many centres that offer IUI as a first line less invasive treatment. The NHS currently supports the use of IUI for the groups which are now being recommended to move directly to IVF. Some BFS members are concerned on the evidence being based on low quality trials and whilst the guidelines specify use of clomifene citrate, letrozole or anastrozole there are no studies comparing the use of gonadotrophins. The studies are also several years old and better well designed stimulation regimens for IUI using gonadotrophins now exist.</p>
35	Full	189	9-22	<p>It is clear that fertility declines with age and the graphical representations clearly show this, yet the statements in the document seem to bracket all women up to the age of 40 within the same spectrum of potential chance of success, which we find misleading. The BFS believes that the age groups should be separated and that women in their late 30's warrant earlier investigation and treatment.</p> <p>The age limit for offering 2 years of expectant management could be stated more clearly. Is it really as high as 40 years? On page 189 (lines 21-22 in particular), the document refers to good figures, 80% and 90% chances of conception after 1 and 2 years expectant management, respectively and merges all age groups together as one group. However, many women over the age of 37 would benefit from a more proactive approach to their management and delaying a further year is likely to reduce the chance for many to have a live birth. The decline in fertility is a continuum and not quite as simply stated in the document.</p>
36	Full	192	L15	<p>The evidence which compares stimulated IUI with expectant management (EM) is</p>

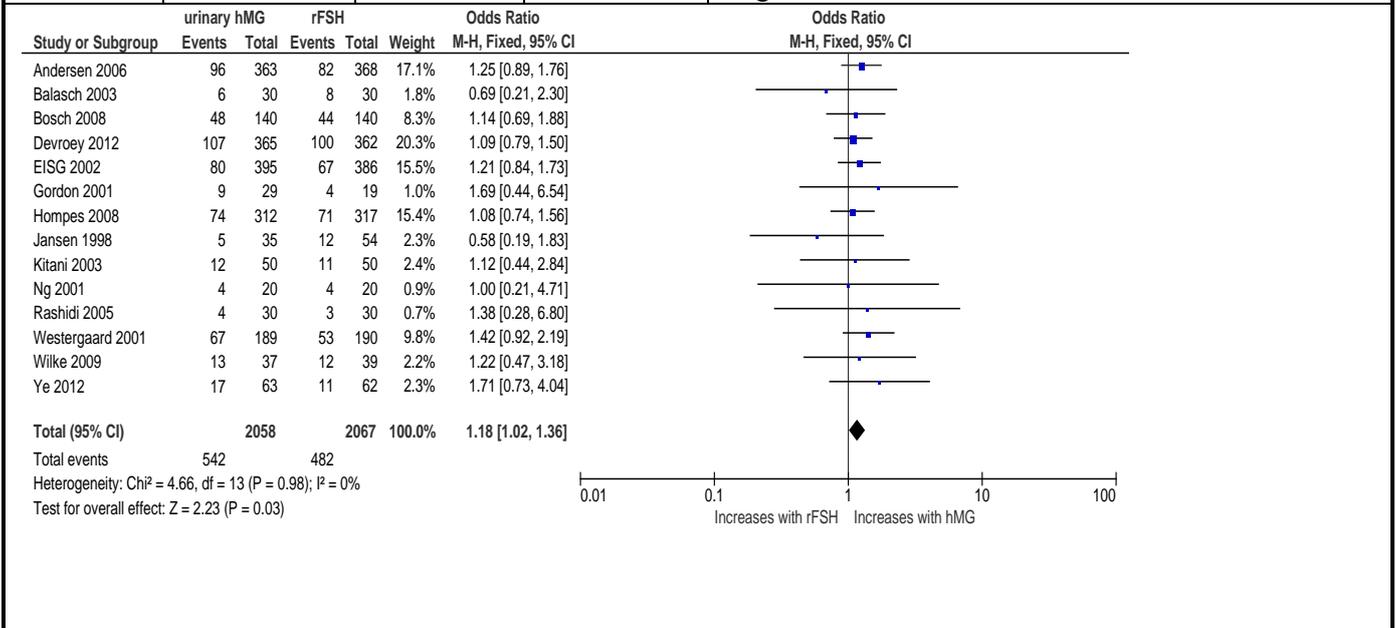
		199	6	<p>extremely thin and does not truly represent IUI in its best light. Indeed the guidance reads:</p> <p><i>“IUI with ovarian stimulation versus expectant management (evidence profile 12.2)</i></p> <p><i>The evidence quality was very low due to limitations in the study design and wide confidence intervals. P199 L6”</i></p> <p>The guidelines recommend that IUI (w ovulation induction) should no longer be used as first treatment for UNEXPLAINED INFERTILITY in favour of expectant management (EM). The major flaw in this assessment is that:</p> <ol style="list-style-type: none"> <li>1. Only 2 papers were used to arrive at these conclusions – indeed the guidance suggests that quality evidence is either low or very low;</li> <li>2. One paper Tummon <i>et al.</i>, 1997 actually suggests that IUI is effective with an LBR of 11% in endometriosis patients;</li> <li>3. The main paper used was: Steures <i>et al.</i>, 2006 which showed EM to be as effective as IUI in 253 couples. However: <ol style="list-style-type: none"> <li>a. The IUI pregnancy rate was pitiful at only 6.5% with an incredible miscarriage rate of 33% and an ongoing PR 4%. In contrast, BFS members have reported they have pregnancy rates of (approx.) 16% PR and 14% LBR. This suggests that this isolated paper ‘selected’ was operating a ‘less than’ effective service and should not be used for comparative purposes;</li> <li>b. Within the Steures paper the patients with multifollicular growth the PR is only 5%, whereas BFS members reported that they have achieving a LBR of 23%;</li> <li>c. Some patients were shown to have tubal infertility;</li> <li>d. Basically the study is weak with a poor quality treatment service and should not be cited to influence national policy.</li> </ol> </li> </ol> <p>Goverde <i>et al.</i>, 2000 in the Lancet demonstrated using an RCT that IUI was more cost-effective than IVF in the treatment</p>
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				<p>of unexplained infertility.</p> <p>There is no economic evaluation or accurate costing for IUI with stimulation within the papers cited, which appear to have been carefully selected to portray IUI as ineffective.</p> <p>There is no similar comparison to show the effectiveness of IVF treatment vs EM for unexplained infertility.</p>
37	Full	204	4	<p><b>115</b> Whilst it is clear when not to use IUI and clear when un-stimulated IUI should be used it is not clear when stimulated IUI could be used. Studies are classified as low quality and are contradictory, some studies showed a statistical difference with gonadotrophin stimulation but this is not represented in the recommendations.</p>
38	Full	284	2	<p>In the review by Coomarasamy <i>et al.</i>, (2008) and in the updated Cochrane review by Van Wely <i>et al.</i>, (2011) there was a statistically significant but 'small' increase in live birth/ongoing pregnancy in favour of hMG.</p> <p>Although a small effect size (3% in the updated review), there is good evidence that patients regard this as an important difference (the patient preference work was an international study, with a focus on America and Australia, and showed that patients regard a 3% difference in live birth as important, and would rank this as a key factor when deciding on clinics).</p> <p>In the NICE review it appears that the figures have been rounded off, giving a non-significant result.</p> <p>However, the true figures show significantly less live births occurred with rFSH when compared with hMG/HP-hMG (<b>OR 0.84; [95% CI: 0.72–0.99]</b>; p=0.04; 11 trials; n=3197)  <a href="http://dx.doi.org/10.1002/14651858.CD005354.pub2">http://dx.doi.org/10.1002/14651858.CD005354.pub2</a></p> <p>What is also important about this evidence is its consistency across the study. There was virtually no evidence of heterogeneity (p-value 0.96, highly non-significant for heterogeneity; and I-squared statistics of 0%, indicating the absence of heterogeneity).</p> <p>It is therefore not surprising that Cochrane</p>

GRADE-ed this evidence as +++, but NICE has given it a very low grade.

Furthermore, three randomised trials have been published since the Cochrane Review, which all confirm the increase in livebirth with hp-HMG.

The forest plot of the updated meta-analysis is given below:



39	Full	313	14	<p><b>141</b> The BFS believe that clinical presentation should be taken into account especially now day 5 embryo transfers are being carried out. Clinical assessment, a full blood count and urea and electrolyte assessment would confirm the patient's suitability for transfer if carried out periodically after egg collection and the morning of embryo transfer. There is recent evidence that triggering antagonist cycles with agonists (Humaidan <i>et al.</i>, 2011) plus low dose hCG or the use of cabergoline reduces risk. The meta analysis 2010 (Yousef <i>et al.</i>, 2010) concluded that dopamine agonist used as a preventative treatment leads to significantly lower OHSS in high risk patients without compromising pregnancies. This guideline is too rigid.</p> <p>The issue with the use of GnRH agonist trigger in antagonist cycles is more complex as it relates to luteal phase issues and if embryos are cryopreserved (as many would do if there is risk of OHSS) and transferred in a subsequent FERC cycle then the pregnancy rates appear to be satisfactory.</p>
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40	Full	325	1	No comment is made on the quality of
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				retrieved sperm between the various techniques. There is some evidence that the quality and quantity of retrieved sperm is higher in MESA than PESA (The Practice Committee of the ASRM, 2008) and therefore male patients may need fewer interventions with this approach.
41	Full	325	16	Failure rates of recovery. The differences in sperm recovery between TESE techniques in non-obstructive azoospermia should be discussed (single site v multi site v microTESE) numerous references including review by Pantke <i>et al.</i> , (2008).
42	Full	346	15	<b>159</b> Whilst the BFS are fully supportive of reducing multiple pregnancy rates this should be in line with the HFEA target which will be 10% from Oct 2012. It is inappropriate to state all patients under 37 should have single embryo transfer in their first cycle. This will compromise some patients' chance of success. NICE should follow the professional guidance (Cutting <i>et al.</i> , 2008) and allow flexibility as long as the HFEA targets are met.  Whilst IVFPredict can be used as guidance to give the chance of success there are still many variables which need to be taken into account which can make the figure inaccurate. In a study, introducing an eSET policy across the board in women under the age of 38, irrespective of embryo quality, resulted in a halving of live birth rates compared to DET (Van Montfoort <i>et al.</i> , 2006). Age of the woman, the first cycle of treatment, the number of embryos available for selection, embryo quality, and the stage at which the embryos are transferred are all factors that appear to influence the chance of a multiple pregnancy if more than one embryo is replaced. Of these, embryo quality and age are the most influential (Gerris, 2005). The BFS therefore feels it is inappropriate to have a blanket policy.
43	Full	347	8	<b>161</b> In certain cases women over 40 years old it may be appropriate to consider replacing 3 embryos.
44	Full	366	31	The team have completely misinterpreted the referenced article (1020) that states (correctly) that only AZFc carriers have the potential for spermatogenesis. The remainder (AZFa, AZFb and combinations involving these two) have no proven capacity for sperm production and therefore have a fertilization,

				implantation and Ibr of zero. This conflicts with the comment written in the review, which should be amended. Men with genotypes containing AZFa and b should not be offered surgical sperm-retrieval and this should be the conclusion.
45	Full	367	20	<b>177</b> The BFS do not agree that couples should be informed that ICSI improves fertilisation rates compared to IVF alone. This would encourage all patients to have ICSI which is clearly inappropriate given the associated risk of birth defects (ref). If this recommendation stays then it should be clear that this is only when ICSI is clinically relevant and ICSI should not be used for men with normal semen parameters unless otherwise clinically indicated i.e. low fertilisation in a previous cycle. This statement will be taken by some to mean that ICSI should be used in all cases of IVF. This is misleading and should be removed.
46	Full	369		Donor Insemination: The reference still used today to define the rate of male infertility at 25% (Hull <i>et al.</i> , 1985) is almost 30 years out of date. The data is based on WHO reference ranges of the time: sperm concentration 20 millions per ml, 50% progression and 50% normal forms which do not compare well with the recently revised reference range of 2010.
47	Full	370	11	<b>180</b> This guideline could be misleading in that it could imply the use of ICSI with donor sperm as opposed to partner sperm which we assume is the intent. This is important because it could lead sperm banks to relax their donor recruitment criteria for donor selection and accept men with poor quality sperm as donors. The ABA, ACE, BAS, BFS and RCOG (2008) donor screening guidelines specifically outline that donor should not be selected on this basis and that ICSI should not be used with donor sperm, except in cases of known donation where it might be unavoidable.
48	Full	391	34	<b>203</b> It is very controversial to recommend that vitrification should replace slow rate freezing. There is no robust evidence to state that vitrification results in better outcomes especially as there are very few long term follow up studies of children. Initial studies are promising (Noyes <i>et al.</i> , 2009) but the numbers are too small to reach conclusions.  The problem with the studies is that although

there is increased survival rates this does not necessarily translate into more clinical pregnancies (Borini *et al.*, 2006) and there is no data yet on the cumulative pregnancy rates with vitrification. Data in oocyte cryopreservation studies which show improved survival, fertilisation and pregnancy rates are often incomplete and do not take into account the number of embryos transferred, the number of oocytes thawed and the degree of embryo selection. Furthermore much of the evidence comes from a few clinic most of which have been involved in the development of vitrification (e.g. Kuwayama *et al.*, 2007; Cobo *et al.*, 2011; Rienzi *et al.*, 2010; Nagy *et al.*, 2009)

The meta analysis (Kolibianakis, 2009) collated all evidence available from RCTs but whilst survival increased there were no differences in pregnancy rates. The strength of the evidence is also questionable as the method of randomisation is not always clear.

There is very little data on vitrifying cleavage stage embryos and most are not randomised studies. Evidence is conflicting; Raju *et al.*, (2005) found vitrification improved survival, implantation rates and pregnancy rates but the method of randomisation was unclear and the sample size was very small. Li (2007) saw no difference in post thaw survival rates.

Vitrification uses much higher concentrations of cryoprotectants which may have safety implications and therefore as with all new technology we should be cautious. The cost effectiveness also needs assessing. There are many different methods available and the variety of solutions and carriers need further evaluation. The problems with using open and closed systems needs addressing.

The BFS agree with the GDG that evidence is strong in favour for the use of vitrification but disagree that it should be a recommendation. It is too early to conclude if the efficiency of vitrification can be concluded and there are issues with the methodology which need to be resolved.

New freezing protocols are emerging which may improve survival rates with slow

				<p>freezing. Edgar and Gook (2012) reported similar implantation rates with fresh and frozen embryos after freezing.</p> <p>Properly conducted randomised control trials should be carried out before recommending one method over another. It is not enough to build on early studies and we should only use good evidence. From the best practice meeting held by ACE in 2011 (Brison <i>et al.</i>, 2012) it was clear that no one defined method is producing consistently good results, some centres had concerns and were not achieving the published survival rates and some centres are getting better results with slow freezing. There is a strong feeling that there is a learning curve when implementing vitrification.</p> <p>Further data needs to become available before this is made a recommendation.</p>
49	Full	390	37	<p><b>204</b> Patients considering whether to have oocytes or embryos frozen should be informed of the legalities of having to have partner consent to use frozen embryos in the future and the benefits of having oocytes frozen if consent is withdrawn. This is an important point in the counselling process in pre chemotherapy treatment</p>

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**Closing date: 5pm on 3 July 2012**

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