Assisted Reproduction Services, Policy Statement 11g:

Summary of the rationale behind departing from NICE guidelines

This paper is based on extractions from the minutes of the Thames Valley Assisted Reproduction policy review meeting held on 24th May 2013 and highlights where the current Thames Valley Assisted Reproduction policy departs from NICE Guidance. The purpose of this review is not to review the evidence or update the policy, but to summarise the rationale behind departing from NICE guidelines.

CCG Governing Bodies considered these recommendations in the context of their budget allocation for assisted reproduction services and the associated opportunity costs. The policy was then implemented across Thames Valley CCGs from November 2013.

The NICE costing template was used to estimate the potential additional cost to Thames Valley CCGs should they implement the NICE guidance in full. The additional costs which would be incurred from year one to year five are shown below. The Committee agreed that as no additional budget was available, these costs would need to be drawn from other existing services should the CCG decide to implement the NICE Fertility Clinical Guideline 2013 (CG156) in full.

	Year 1	Year 2	Year3	Year4	Year5
Total Additional Costs	**2,560,856**	**4,369,889**	**5,274,405**	**4,724,715**	**4,724,715**

Eligibility Criteria:

1. Age:

NICE recommends the following with regard to female age:

1.3.3.1 Use a woman's age as an initial predictor of her overall chance of success through natural conception or with in vitro fertilisation (IVF) **[new 2013]**

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1.10.1.1 Inform women that the chance of a live birth following IVF treatment falls with rising female age. **[2013]**

1.11.1.3 In women aged under 40 years who have not conceived after 2 years of regular unprotected intercourse or 12 cycles of artificial insemination (where 6 or more are by intrauterine insemination), offer 3 full cycles of IVF, with or without ICSI. If the woman reaches the age of 40 during treatment, complete the current full cycle but do not offer further full cycles. **[new 2013]**

1.11.1.4 In women aged 40–42 years who have not conceived after 2 years of regular unprotected intercourse or 12 cycles of artificial insemination (where 6 or more are by

intrauterine insemination), offer 1 full cycle of IVF, with or without ICSI, provided the following 3 criteria are fulfilled:

- they have never previously had IVF treatment
- there is no evidence of low ovarian reserve (see recommendation 1.3.3.2)
- there has been a discussion of the additional implications of IVF and pregnancy at this age.

[new 2013]

A decision was made to depart from NICE guidance and retain the current female age threshold of up to 35 years for access to NHS-funded assisted reproduction treatment. There was consensus that the evidence of clinical effectiveness warranted the inclusion of a female age threshold in the policy. Members considered the evidence provided in NICE's Full Guideline and, in particular, their two graphs (reproduced below) that provide data regarding the change in female fertility with age. Members noted that, although there is no 'step change', the graphs show that conception rates – both natural conception and successful pregnancies associated with IVF – start a marked decline from the age of 35.

The results of the 198 scenarios NICE analysis generated were reviewed for two 'willingness to pay' thresholds: a £20,000 'willingness to pay' for a QALY threshold, and a £30,000 'willingness to pay' for a QALY threshold. NICE based their female age treatment thresholds on a willingness to pay threshold of £30,000. However, at a threshold of £20,000, overall NICE's modelling suggests that a female age of 35 is an appropriate threshold.

Having reviewed the published evidence of clinical and cost effectiveness, the meeting then considered the affordability of potentially extending the female age threshold. Modelling the cost of implementing all NICE's recommendations was estimated to at least double the current spend by the Thames Valley CCGs on assisted reproduction services, which would be unaffordable for the CCGs at the present time.

Figure 5.1 The effect of maternal age on the average rate of pregnancy, calculated on the basis of studies in10 different populations that did not use contraceptives (adapted from Heffner, 2004, based on two reviews by Menken et al, 1986, and Anderson et al, 2000)

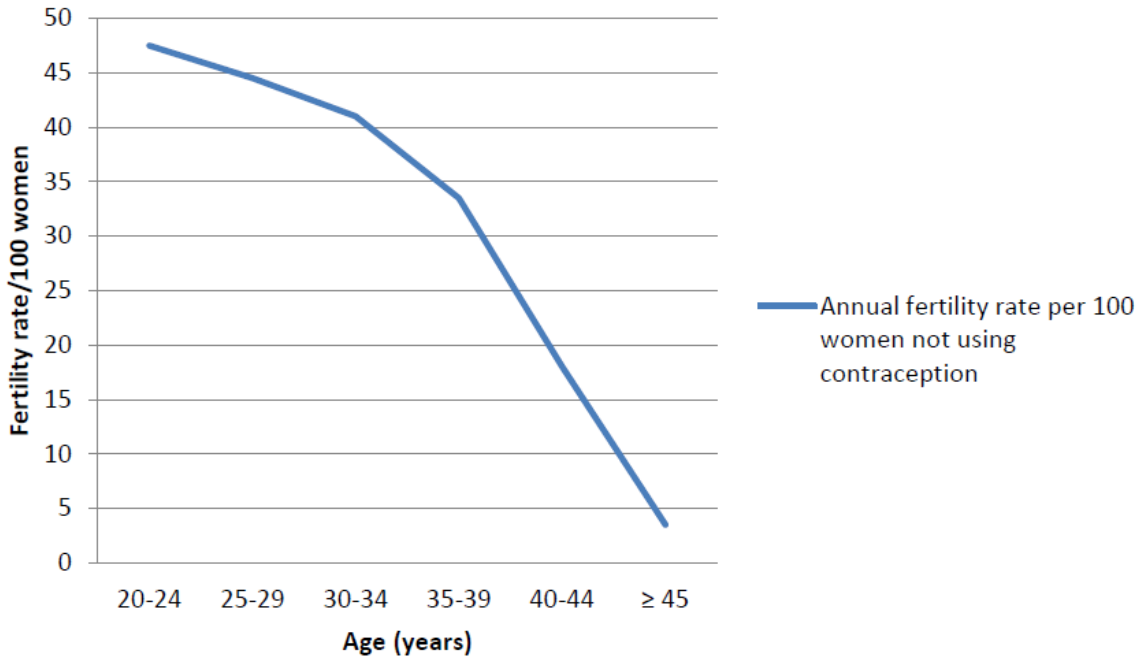
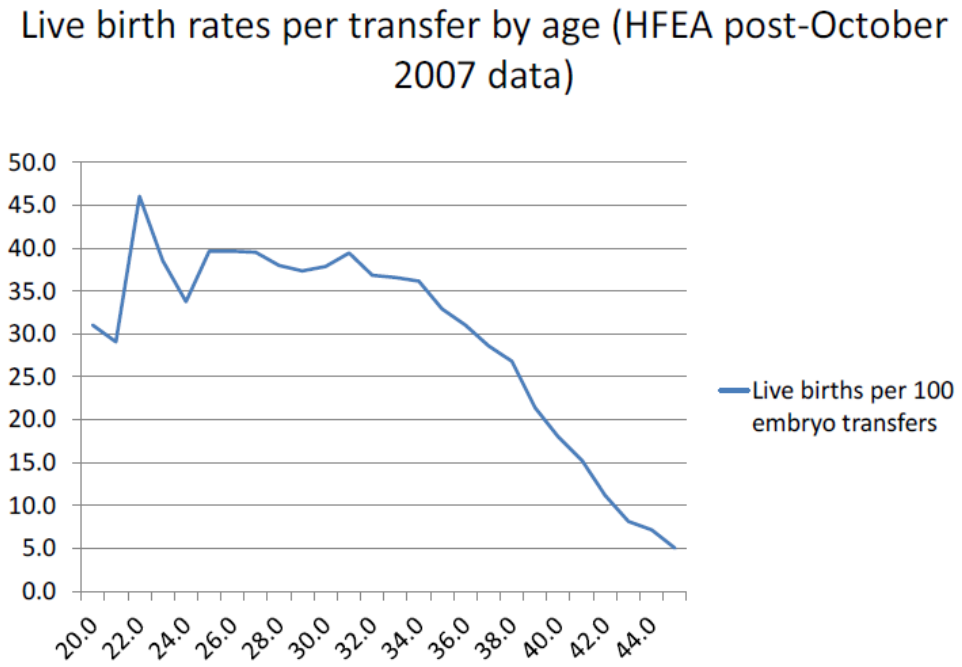


Table 5.1 Cumulative probability of conceiving a clinical pregnancy by number of menstrual cycles in women in four different age categories attempting to conceive (assuming vaginal intercourse occurs twice per week) (adapted from Dunson et al., 2004)

Age (years)	Pregnant after 1 year (12 cycles) (%)	Pregnant after 2 years (24 cycles) (%)
19–26	92	98
27–29	87	95
30–34	86	94
35–39	82	90

Figure 6.1 IVF success in terms of live births per 100 embryo transfers (vertical axis) according to age of woman (horizontal axis) based on 52,996 embryo transfers using the woman's own eggs undertaken in the UK between 1 October 2007 and 30 June 2009 (HFEA, personal communication; [note: small numbers of women below age 24 years in the HFEA database])



The meeting then discussed whether it was appropriate to retain the current age threshold in the context of the new age discrimination legislation. It was noted that all NHS assisted reproduction policies have some female age limits in place and thus all potentially amount to age discrimination. It follows that any suggestion that a female age limit on access to IVF is discriminatory would result in challenge to all IVF policies, including NICE's recommendations. Further, such an approach would ignore the clinical evidence and would require CCGs to fund treatment that was not likely to be clinically and/or cost effective. There is published clinical evidence to support the meeting's recommendation that the woman's age of 35 years or greater is a proxy for the reduced clinical and cost effectiveness of IVF treatment.

It was therefore agreed to recommend retention of the current female age threshold of up to 35 years for access to NHS-funded assisted reproduction treatment.

'Offer an earlier referral for specialist consultation to discuss the options for attempting conception, further assessment and appropriate treatment where the woman is aged 36 years or over' was not considered by the meeting because no extension to the current upper female age threshold of 35 years is being recommended.

2. Body Mass Index:

Despite the significant body of clinical evidence, NICE does not recommend restricting access to infertility services on the basis of over- or underweight in men or women (although the meeting noted that NHS England's policy for IVF associated with preimplantation genetic diagnosis does include a female weight criterion).

The meeting felt there was sufficient clinical evidence to recommend the inclusion of a criterion regarding female weight and, further, accepted the specialists' argument that weight management should be integral to the primary care fertility pathway. The latter was agreed because female overweight and underweight management at an early stage could improve the chance of natural conception, particularly for couples with unexplained infertility.

3. Smoking:

The meeting considered the evidence that smoking by the male and female partner, and passive smoking, may affect a couple's fertility, and noted that, whilst NICE makes recommendations regarding the provision of *information* about the effects of smoking on fertility, the guideline does not recommend restricting access to assisted reproduction services on the basis of the smoking status.

The meeting noted the lack of congruence between the recommendations in the NICE guideline for *Fertility*, and the advice in NICE *Antenatal Care* guidelines and NICE public health guidelines *Quitting smoking in pregnancy and following childbirth*. These two guidelines make specific recommendations regarding assessment of smoking status and interventions for smoking cessation for the female partner during and after pregnancy.

The meeting discussed the clinical evidence, the different advice in NICE's guidelines, and the importance of the public health/NHS message regarding the adverse health effects of smoking in general, not just in the context of achieving pregnancy. As a result of those discussions, it was agreed to recommend retention of the current policy point on the grounds of

- clinical evidence of impairment of fertility in smokers, and the health impacts of smoking on babies and children
- congruence with the recommendations regarding smoking in pregnancy and after childbirth in NICE clinical guideline *Antenatal care* (No. 62, 2010) and NICE public health guidance *Quitting smoking in pregnancy and following childbirth* (No. 26, 2010).

Treatments funded for eligible patients:

1. Number of cycles:

The NICE guideline recommends that three cycles of IVF/ICSI cycles should be provided by the NHS, and that the outcome of previous cycle(s) of IVF/ICSI treatment should be taken into account when assessing the likely effectiveness and safety of subsequent IVF/ICSI treatment.

Currently, one full fresh cycle of IVF/ICSI is funded for eligible patients. In reviewing the number of cycles that might be recommended, the meeting considered the affordability of two options: providing two full, fresh cycles; and providing one full fresh cycle and a second frozen-thawed cycle. It was estimated that funding a second fresh cycle under the current criteria would increase current spend by 65-70%; funding a second frozen cycle would cost considerably less, but nevertheless could increase spend by 30%. The meeting discussed the likelihood that additional resources would be available to fund either of these options. Members felt that, if additional funds were available, these should be used to extend the female age eligibility criterion so that more couples could access NHS-funded services rather than provide additional cycles. It was agreed, therefore, to recommend retention of the current policy point of funding one cycle in order to allow as many couples as possible one opportunity to have NHS-funded treatment. Thus, any previous NHS-funded fresh cycle of IVF/ICSI treatment should be an exclusion criterion.

2. Storage (cryopreservation) of surplus embryos

The meeting noted the evidence provided by NICE on the effectiveness of frozen embryo transfer, and NICE's recommendations that support the cryopreservation of good quality supernumerary embryos retrieved from a fresh cycle for use in subsequent NHS-funded IVF cycles.

The fertility specialists at the meeting advised that 20-30% of fresh IVF cycles result in good quality embryos, and there was discussion of the benefits to couples of cryopreservation of these which would increase the number of potential embryo replacement cycles whilst avoiding the need to repeat some interventions, eg, the need for the female partner to undergo further stimulated 'fresh' cycles.

Members therefore agreed, - on patient safety grounds, and because advances in cryopreservation technology have facilitated improved success rates from frozen-thawed cycles - that a recommendation should be made to continue to fund the cryopreservation of good quality, surplus embryos that result from a NHS-funded fresh cycle for three years, for use in subsequent self-funded cycles. The meeting also recommended the removal of the criterion regarding NHS-funded storage to an upper female age limit of 40 years as this point is effectively encompassed in the three-year storage period.

Preservation in relation to medical treatment is considered separately to this policy.

Thames Valley Priorities Committee review, January 2015

In January 2015 the Thames Valley Priorities Committee (TVPC) undertook a review of the Assisted Conception policy. The purpose of this review was to document the rationale behind departing from NICE guidelines, the TVPC did not to review the evidence or update the policy.

The TVPC considered the NICE Clinical Guideline for Fertility (CG156, 2013) and its Ethical Framework. Although it supports the principles and objectives expressed in the CG, the TVPC acknowledges that local CCGs are duty-bound not to exceed their annual financial allocations. The opportunity costs of investing resources in additional IVF services mean that full adoption of this

guideline could not be achieved without disinvesting from the treatments available to other NHS patients. Given these constraints the TVPC has considered the Clinical Guideline for Fertility and recommended retention of local guidelines on Fertility care, agreed in 2013, in order to promote the best interests of the community of patients as a whole.