NHS

Warwickshire North
Clinical Commissioning Group

Assisted Conception Treatments

Quality & Equality First

VERSION CONTROL

Version:	2.0
Ratified by:	Governing Body
Date ratified:	04 April 2013
Name of originator/author:	Public Health/Commissioning Dept
Name of responsible committee:	Clinical Quality and Governance
Date issued:	03 April 2013
Review date:	01 March 2011 (due for review)

VERSION HISTORY

Date	Version	Comment / Update
22 April 2009	1.0	Version 1 for PCT, 22 April 2009
April 2013	2.0	Version 2.0 amended for CCG and approved on 04 April 2013

Contents

1. Policy Statement

1.1. This Policy describes in detail how the Fertility Services should operate for the people of Warwickshire North. It includes the latest guidance on good practice1 to make sure people receive the most effective forms of treatment.

1.2. This Policy specifically relates to assisted reproduction.

2. Introduction

2.1. Defining Infertility

2.1.1. The United Nations defines reproductive health as 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity in all matters relating to the reproductive system and to its functions and processes'.2 Infertility should, therefore, be considered to be a disease process worthy of investigation and treatment.

2.1.2. Infertility should be defined as failure to conceive after regular unprotected sexual intercourse for 2 years in the absence of known reproductive pathology.1

2.1.3. Infertility can be primary, in couples who have never conceived, or secondary, in couples who have previously conceived.

2.2. Epidemiology

2.2.1. Around 84% of couples in the general population attempting to conceive are successful within 1 year if they do not use contraception and have regular sexual intercourse. After two years this figure rises to 92%. Female fertility declines with age and for women aged 38 only about 77% who have regular unprotected sexual intercourse will get pregnant after 3 years of trying.1

2.2.2. It is estimated that fertility problems (sub-fertility) affect one in seven couples in the UK. A typical primary care trust may therefore expect to see around 230 new consultant referrals (couples) per 250,000 head of population per year. In Warwickshire and Coventry we can expect to see around 762 couples referred for treatment every year as shown in Table 1.

Table 1: Expected Demand for Fertility Related Referral for Treatment

Districts	**Population (All ages)***	**Demand estimate per year** (Number of couples)**
North Warwickshire	62305	57
Nuneaton and Bedworth	120697	111
Rugby	90221	83

Stratford-on-Avon	116074	107
Warwick	132935	122
Warwickshire	**522232**	**480**
Coventry	**306642**	**282**
Grand Total (Coventry & Warwickshire)	**828874**	**762**

* Mid-2006 estimates of resident population (Compendium of Clinical and Health Indicators / NCHOD)

** 230 couples per 250,000 head of population [NICE CG11 (ref 1)]

2.2.3. Whilst the demand for such services has increased the prevalence is thought to be unchanged. The need for fertility services may further increase due to the trend towards delaying having a child and also due to increased public awareness of treatment possibilities. It is likely that there is unexpressed and/or unmet demand, particularly from women with secondary infertility (those who have conceived before but do not necessarily have a child).

2.3. Causes of Infertility

2.3.1. Approximate proportions of principal causes based on studies of couples seeking treatment are given below. A significant proportion of couples will have more than one cause and the distribution varies between primary and secondary infertility:

- Ovulatory failure 27%
- Low sperm count or quality 19%
- Tubal damage 14%
- Endometriosis 5%
- Others 5%
- Unexplained 30%

2.3.2. There is evidence that infertility causes considerable emotional stress, which may affect many areas of couples' lives and can result in social handicap.

2.4. Types of Infertility Treatment

2.4.1. There are three main types of infertility treatment: medical treatment (such as drugs for ovulation induction); surgical treatment (eg laparoscopy for ablation of endometriosis); and assisted reproduction.

2.4.2. Assisted reproduction is a collective name for treatments designed to lead to conception by means other than sexual intercourse. Assisted reproduction techniques include: Intrauterine insemination (IUI), In vitro fertilisation (IVF), Intracytoplasmic sperm injection (ICSI), Donor insemination (DI) and Cryopreservation (sperms, oocytes and/or embryos). Assisted techniques should be only carried out in specialist centres as recommended by the Human Fertilisation and Embryology Authority (HEFA).

2.5. Scope

2.6. This policy will ensure that all patients across Warwickshire North who require assisted conception are treated according to the CCGs' Commissioning Principles. It consolidates and updates all previous policies.

2.7. This policy applies to Warwickshire North CCG and the principle providers of these services, NHS and private providers, irrespective of where the patient is being treated.

3. Overarching Principles and General Details

3.1. Principles of Care

3.2. The following principles of care should be adhered to:

- Couples concerned about conception should be offered an initial assessment in primary care. GPs will then be the gatekeeper for referral to specialist services.
- Patient management of eligible couples should be in line with an agreed local care pathway. This is based on the NICE clinical practice algorithm3. The pathway identifies the tests and treatments to be undertaken within primary, secondary care and tertiary care. Within the pathway, test results should be passed on and not duplicated. Medical and non-invasive surgical treatments for infertility should be attempted before considering the option of assisted conception.
- Screening for Chlamydia trachomatis should be carried out routinely in primary care as part of infertility work-up. If chlamydial infection is detected both the partners should be notified and treated. Prophylactic antibiotics should be considered before uterine instrumentation if screening has not been carried out.
- Couples should be seen together because both partners are affected by decisions about investigations and treatment.
- Couples should be treated by specialist teams because it is likely to improve the effectiveness and efficiency of treatment.
- Patients should be provided with appropriate and suitable information in a format that patients can understand. This information will be developed by the specialist provider.
- Patients' privacy and dignity should be ensured.
- Patients should be offered counselling prior, during and after assessment or treatment from someone independent of the treatment team – because

fertility problems and the investigation and treatment of infertility can cause psychological stress. This will be provided through the specialist provider.
- Patients should be guided to support from other groups, e.g. fertility support group. This information will be available through the treatment centres.

3.3. Criteria for Treatment Referral

3.3.1. In order to achieve the maximum benefit for the resources available the following treatment referral criteria, as outlined in the NICE guidance, 1 should be used by referring physicians and relates to IVF/ICSI/IUI/OI.

3.3.2. Couples must satisfy all elements of the eligibility criteria to qualify for the treatment.

3.4. Stable Relationship

3.4.1. The couple should have been in their relationship for at least 2 years at the time of referral in keeping with the definition in Section 1.1.

3.4.2. Where there is clear reproductive pathology, infertility of any duration will be considered. This will include couples who cannot achieve full sexual intercourse due to disability.

3.5. Maternal Age

3.5.1. Where the protocol indicates the use of the above named infertility procedures then they will only be offered to women in the age range 23-39 years.

3.5.2. Reason: The decline in normal fertility with age increases markedly from the late 30s and infertility treatment is much less successful in women over 38 years. For IVF, chances of live birth per cycle are: greater than 20% for women aged 23–35 years, 15% for women aged 36–38 years, 10% for women aged 39 years and 6% for women aged 40 years or older. Effectiveness of IVF in women below 23 years is uncertain.

3.6. Exceptions

- In cancer patients, however, it would not be productive to wait until they are 23 to begin treatment. In these cases treatment can commence at an earlier age to enable removal of eggs/sperm prior to starting treatment. Support will still be subject to the other patient criteria being met including that relating to living children.
- Early investigations should be offered where a woman is 35 years or over, or there is a history of predisposing factors (e.g. amenorrhoea, oligomenorrhoea, pelvic inflammatory disease).

3.7. Paternal Age

3.7.1. There is no restriction on the age of the male partner although this issue may be raised under medical suitability or welfare of the child considerations.

3.8. Maternal Weight

3.8.1. Treatment will not be provided for any woman with a Body Mass Index (BMI) <19 kg/m2 or >30 kg/m2 until she is able to attain a reasonable weight through a weight management clinic.

3.8.2. Reason: Underweight women often have irregular cycles and may have a reduction in fertility as a result of this ovulatory dysfunction. Restoration of body weight may help to resume ovulation and restore fertility. An increased risk of preterm delivery has been associated with women who are underweight, and ovulation induction in such women has been associated with a higher incidence of babies who were small for gestational age.

3.8.3. Significantly overweight women frequently have ovulatory problems resulting in diminished fertility. For infertile anovulatory women with BMI of over 29 kg/m2, there is evidence that a supervised weight loss programme or a group programme including exercise, dietary advice and support helps to reduce weight, resume ovulation and improve pregnancy rates.1 A BMI of 30 kg/m2 or over was reported to be an independent risk factor for spontaneous abortion in women who were oocyte recipients while an increased risk of miscarriage has been reported in moderately obese women (BMI 25–27.9 kg/m2) undergoing ovulation induction.

3.9. Smoking Status

3.9.1. The expectation is that couples accepted for treatment would be non-smoking. Smokers should initially be referred to the Smoking Cessation Service and should have stopped smoking for at least 4 weeks prior to referral for infertility treatment and continue to refrain from smoking throughout the treatment process.

3.9.2. Reason: Maternal and paternal smoking can adversely affect the success rates of assisted reproduction procedures. Smoking during the antenatal period leads to increased risk of adverse pregnancy outcomes. Minimising exposure to second hand smoke will ensure a healthy start to life to any child/children born as a result of assisted conception.

3.10. Living Children

3.10.1. Treatment will not be funded for those couples where either partner has a living child (under 16 years of age) living with them (including adopted child). Once accepted for treatment, should a pregnancy leading to a live birth occur, the couple will no longer be eligible for NHS funded treatment.

3.10.2. Reason: Resources are limited therefore priority is given to couples with no children. Private treatment is of course available to those couples not eligible for NHS funding.

3.11. Welfare of the Child

3.11.1. In any circumstance where there are known adverse factors that might affect the welfare of the child who might be born, treatment will not be provided. These factors include but are not limited to criminal record of child neglect or abuse. It is the responsibility of the clinician to assure themselves that matters affecting the wellbeing of a future child are considered.

3.11.2. Reason: Legal, under the terms of the Human Fertilisation and Embryology Act and the Code of Practice

3.11.3. According to HFEA guidance6

> *"a woman shall not be provided with treatment services unless account has been taken of the welfare of any child who may be born as a result of the treatment (including the need of that child for a father), and of any other child who may be affected by the birth."*

3.11.4. It is to be noted that Human Fertilisation and Embryology Act 1990 is under review and should the proposed amendments be passed, the treatment centres will no longer be required to take account of the child's need for a father and the above statement will be amended as follows:

"a woman shall not be provided with treatment services unless account has been taken of the welfare of any child who may be born as a result of the treatment (including the need of that child for ***supportive parenting****), and of any other child who may be affected by the birth." (Human Fertilisation and Embryology Bill 2008 [HL], Chapter 37, Section 13, Clause 5).*

3.12. Residency Requirement

3.12.1. The patient should be registered with a Warwickshire North CCG GP.

3.13. Compliance with Treatment

3.13.1. Any couple that is considered to be unlikely to be able to accept or comply with the demands of adhering to a treatment plan should ideally not be referred unless it is specifically for support/acceptance counselling.

3.13.2. Reason: Social - most techniques require a high degree of commitment and motivation to complete the treatment regime.

3.14. Previous Sterilisation

3.14.1. NHS funded fertility treatment will not be available if infertility is the result of a sterilisation procedure in either partner.

3.14.2. Reason: Resources are limited therefore priority is given to individuals with greatest need. Patients undergoing sterilisation receive counselling and all the consequences are explained to them at the time.

3.15. Previous Assisted Conception Treatment

3.15.1. Any couple who has had one previous completed cycle (i.e. including embryo implantation) of stimulated IVF/ICSI funded by the NHS or had three or more privately funded cycles will not be eligible for further NHS funding.

3.15.2. Any couple, who has had 3 attempts at intrauterine insemination (IUI), will not be eligible for any further IUI attempts. See Section 2.3.4.

3.15.3. Reason: Most patients who respond to assisted conception techniques can be expected to do so quite quickly.

3.16. Chronic Viral Infections

3.16.1. People who are known to have chronic viral infections (e.g. HIV, Hepatitis B or Hepatitis C) should be referred to centres that have appropriate expertise and facilities to provide investigation and treatment if they meet all other criteria.

3.17. Access to services for People not in Partnerships

3.17.1. NHS funding will not be available for access to insemination facilities for fertile women who are not in a partnership.

4. Assisted Conception Procedures and Specific Criteria

4.1. Provider of Services

4.1.1. The preferred providers of tertiary assisted conception services will be the Centre for Reproductive Medicine (CRM), University Hospitals Coventry and Warwickshire and Midlands Fertility Services Aldridge.

4.2. Intra-uterine Insemination (IUI)

4.2.1. The CCG has agreed that approved providers will offer appropriate women up to 3 cycles of stimulated IUI rather than moving to 6 cycles of unstimulated IUI as recommended by NICE.

4.2.2. Reason: Evidence suggests that outcome i.e., pregnancy and live birth rate is higher in couples who receive stimulated IUI as opposed to those couples who receive unstimulated IUI.7,8,9

4.2.3. Providers will provide annual audit data summarising pregnancy rates per cycle of IUI and multiple pregnancy rates. The continuation of this variance in respect of IUI will be reviewed annually by the CCG on the basis of the received audit data and phased introduction of additional cycles will be undertaken based on financial position.

4.3. In-vitro Fertilisation (IVF)/Intracytoplasmic Sperm Injection (ICSI):

4.3.1. Due to resource constraints, Warwickshire North CCG are currently unable to prioritise further investment in IVF/ICSI. The policy will, therefore, remain as in 2005/06, which is:

- Only One fresh cycle of IVF or ICSI will be funded (including drug costs) per couple together with up to two associated frozen cycles (including drug costs where necessary).
- Funding will include the costs of cryopreservation/freezing of embryos for one year. It is expected that the associated frozen cycles funded under this policy would be completed during this time period. (Frozen embryo transfer can be undertaken after a gap of 2-3 months if a previous attempt has not resulted in pregnancy. So it is anticipated that 2 frozen cycles can be concluded within a year of cryopreservation).
- Providers should adhere to the HFEA Code of Practice, including the "Multiple Births Minimisation Strategy" dated 30 September 2008..
- An IVF/ICSI cycle for which NHS funding is provided includes the following:
    - Counselling
    - Super Ovulation
    - Ultrasound Scans
    - Blood tests
    - Retrieval of ova (eggs)
    - Fertilisation with sperm
    - Embryo transfer

4.3.2. The appropriate drugs are included and provided by the service providers, and GPs are advised that they should not prescribe drugs for patients in any circumstances.

- The CCG expect a patient to undertake the NHS Cycle within 12 months of being accepted on to the assisted fertility programme.

4.3.3. NICE Guidance states that CCGs should move towards offering 3 cycles and so the current policy will be reviewed on an annual basis and phased introduction of additional cycles will be undertaken based on the financial position.

4.4. Donor Sperm and Eggs

- Donor sperm will only be funded if it is included within the NHS treatment cycle.
- Donor eggs will be funded for managing fertility problems associated with the following conditions:
    - premature ovarian failure
    - gonadal dysgenesis including Turner syndrome
    - bilateral oophorectomy
    - ovarian failure following chemotherapy or radiotherapy
- Egg donation has also been advocated in certain cases of repeated failure of IVF but as the CCG are funding only 1 cycle of IVF at the moment, the condition of repeated failure cannot be satisfied. As a result egg donation will not be funded for managing fertility problems associated with repeated failure of IVF.

4.5. Frozen Semen Storage

- The CCG support frozen semen storage for patients with a cancer related condition and where a treatment of the condition could render the patient sterile.
- The CCG will fund up to 5 years of storage.
- The use of NHS facilities is preferred although storage in private sector is supported as appropriate subject to the provider being on the approved HFEA list of preferred providers.

4.6. Frozen Egg/Frozen Embryo Storage

- Warwickshire North CCG support frozen embryo storage for patients with a cancer related condition and those cancer patients who satisfy the IVF Policy criteria at the time of application.
- The CCG will provide a maximum of 5 years storage for cancer patients.
- It is the responsibility of provider to ensure consent obtained from both individuals before providing storage.
- Cryopreservation of oocytes (eggs) is not supported as there is limited evidence to support the effectiveness of this procedure.
- The CCG needs to consider that Human Fertilisation and Embryology Act 1990 is under review and should the proposed amendments be passed, the statutory storage period for embryos will increase from five to ten years.

4.7. Other Procedures

- NICE does not recommend assisted reproduction procedures like Gamete intrafallopian transfer (GIFT) or Zygote intrafallopian transfer (ZIFT) and these will not be funded by the CCG.
- Assisted hatching has not been shown to improve pregnancy rates and is not recommended by NICE. As a result, it will not be funded by the CCGs.
- Preimplantation Genetic Diagnosis (PGD): Is an intervention that can help couples at risk of an inherited disorder to avoid the birth of an affected child. There is relatively little specific evidence about the long-term safety of the procedure with no guarantee of success in achieving a pregnancy.10,11 Furthermore, PGD is not a method for treating infertility (although it does employ IVF techniques to create embryos but that is for extracting one or two cells from each embryo to test for the specific genetic abnormality, and identify unaffected embryos for transfer to the womb). Each case requesting funding for PGD will, therefore, be considered individually.

4.8. Reversal of Male and Female Sterilisation

4.8.1. Reversal of female or male sterilisation eg vasectomy or tubal ligation or treatment to bypass the sterilisation is not routinely available for NHS funding.

4.8.2. Reason: Resources are limited therefore priority is given to individuals with greatest need. Patients undergoing sterilisation receive counseling, sign a consent form and the procedure and consequences are explained to them at the time. On this basis patients cannot, therefore, expect the NHS to fund reversal of sterilisations in the normal course.

4.8.3. The CCG will only consider funding a reversal of sterilisation in exceptional circumstances.

4.8.4. It is important to note that reversal of sterilisation is an issue in its own right and is not linked to IVF.

4.9. Exceptional Circumstances

4.9.1. As in all cases, where a patient does not meet the policy criteria but where they, or their clinician, feel that there are exceptional circumstances in their case that would warrant access to funded treatment, they, or their clinician, may request consideration through CCGs' Individual Cases Panels.

5. Scheme of Delegation

5.1. It is the responsibility of the current providers of services to implement and instigate the Policy.

5.2. It is the responsibility of the Commissioning Advisory Group (CAG) to review the policy as appropriate and upon the stipulated review date.

6. Development and Consultation Process

6.1. The following individuals/groups have been involved in the development of this policy, or are key stakeholders:

Name of Individual/Group	Representing
Commissioning Advisory Group	Acute Providers Mental Health Trust Warwickshire PCT Coventry Teaching PCT GP Representative Patient Representative
PCT PECs as part of ratification	Executive Directors Non-Execs PEC GPs

7. Policy Implementation Plan

ACCOUNTABLE DIRECTOR: Paul Maubach

Issues identified/Action to be taken		Timescale
Co-ordination of implementation How will the implementation plan be co-ordinated and by whom?	Co-ordinated through CAG members who have been involved in development and will communicate back to their relevant organisation.	Immediately post ratification
Engaging staff Who is affected directly or indirectly by the policy? Are the most influential staff involved in the implementation? How will the policy be communicated to staff?	Particularly acute organisations that carry out the procedures. General practice. Communicated via CAG members. GPs notified of policy – by AM/PB. Other relevant NHS and non-NHS providers notified of the policy – by AM/PB. Policy placed on PCT websites.	1 month post ratification
Involving service users and carers Is there a need to provide information to service users and carers regarding this policy? Are there service users, carers, representatives or local organisations who could contribute to the implementation?	Patient representative on CAG. Patients have access to PCT websites, and under freedom of information requests.	
Communicating What are the key messages to communicate to the different stakeholders? How and to whom will these messages be communicated?	The PCTs will fund specific IVF procedures, where specific criteria are met. In exceptional cases the Individual Case Panel can consider patients who do not fall into the category if supported by their clinician.	
Training What are the training needs related to this policy? Are people available with the skills to	Nothing specific. Individual acute providers should inform their relevant staff.	

deliver the training?		

Resources Have the financial impacts of any changes been established? Is it possible to set up processes to re-invest any savings? Are other resources required to enable the implementation of the policy eg increased staffing, new documentation?	Negative resource implications should be eliminated, as there is more standardisation. Investment to remain unchanged.	
Securing and sustaining change Have the likely barriers to change and realistic ways to overcome them been identified? Who needs to change and how do you plan to approach them? Have arrangements been made with service managers to enable staff to attend briefing and training sessions? Are arrangements in place to ensure the induction of new staff reflects the policy?	Clear communication from commissioners on CAG to ensure that the policy is well known and adhered to following ratification. Internal communication should take place by providers.	Immediate following ratification by PEC.
Evaluating What are the main changes in practice that should be seen from the policy? How might these changes be evaluated? How will lessons learnt from the implementation of this policy be fed back into the organisation?	Clarification of what PCTs will and will not support	
Other considerations		

8. Equality Impact Analysis

Equality and Diversity Implications

The purpose of this policy is to implement NICE guidance to enable access for all who meet the criteria. The policy does not discriminate against individuals because of their background, culture, religion, gender or disability.

Age cohorts set out in the policy are in line with national requirements based upon clinical effectiveness information.

Please note: where the term 'other diverse groups' is referred to below, this covers gender, disability, sexual orientation, religion/belief and age.					
Dept/Service Area	Medicines Management	Section		Person Responsible for the assessment	Amin Mitha
Name of the policy to be assessed		Infertility Services		Is this a new or existing policy?	Revision of several policies
In what areas are there any concerns that the policy could have an adverse/differential impact? AGE, GENDER, SEXUAL ORIENTATION				Date of the assessment	28.7.08

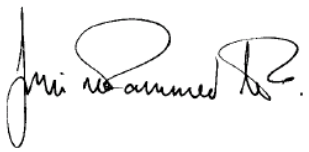
		Explain/Evidence
1	What is the aim/objective/purpose of the policy/service?	To ensure that there is consistent treatment for patients, whose condition/heath would benefit from fertility treatment.
2	What are the expected outcomes of the policy? What are we trying to achieve?	As above

		Explain/Evidence
3	Are there any groups who might be expected to benefit from the intended outcomes but who do not?	Yes The policy is to ensure that the procedures are available to those who might give the most favourable outcome based on clinical evidence, therefore this may benefit certain groups more than others. This includes being part of a stable couples, maternal age, weight etc.
4	How does/will the policy meet needs, particularly with regard to race, gender disability?	Treatment is available to the total population of both PCTs subject to fulfilment of the criteria requirements stipulated in the policy
5	Are there any obvious barriers to accessing the service? e.g. language, physical access?	N/A
6	How does the policy fit in with the PCT's wider objectives?	Aligned to PCT's commissioning objectives to provide clinically and cost effective care.
7	Explain why there are concerns that this policy could be affecting different groups in different ways, or could be having an adverse/negative impact on particular groups	See above. But a requirement to make the policy effective and most appropriate care offered.
8	What existing data is there in-house/externally to support this? Is there a need to collect primary data or any additional data to assist in the determination about the level of adverse impact?	See introduction of policy.
9	If the policy is indirectly discriminatory could it still be justifiable under legislation?	Yes, as based on clinical effectiveness.
10	Is there any evidence of unmet needs that can affect different groups?	Unmet needs can be addressed through the individual cases procedure if appropriate.
11	What advice/information is available from experts or interest groups?	Expert Consultant, GP and Commissioning advice sought as part of policy development, so any variations are applicable to patient need
12	Please explain in detail the views/evidence that they have been able to provide.	See references

		Explain/Evidence
13	Taking into account the views of these groups/experts and the available evidence, please clearly state the risks associated with the policy, weighed against the benefits of the policy.	If not clear there is a risk of inconsistency for some patients, and/or inappropriate procedures being undertaken which are not clinically effective for a particular patient group.
14	Is there anything you can do now, based upon the evidence available, to a) Remove or minimise the adverse/differential impact? b) Address any unmet needs?	N/A – considered as part of the policy.
15	What plans do you have for further consultation with the different groups?	NA
16	What monitoring arrangements will you put in place to monitor the future impact of this Policy, especially in relation to race, gender and disability?	Will be reviewed as part of planned policy review.
As a result of the PIA, is a Full Impact Assessment (FIA) necessary? (FIA required if PIA identifies the need for: policy rewrite requiring MDT input and consultation)		No
Date by which FIA to be completed:		

Signed by Amin Mitha

Date: 12.02.2009



Reference Documents and Bibliography

1. Fertility: assessment and treatment for people with fertility problems. National Institute for Clinical Excellence Clinical Guideline 11, February 2004.
2. International Conference on Population and Development – Cairo 1994; Programme of Action, para 7.2.
3. Clinical practice algorithm: Fertility Assessment and treatment for people with fertility problems. NICE, February 2004.
4. Zorn B, Auger J, Velikonja V, Kolbezen M, Meden-Vrtovec H. Psychological factors in male partners of infertile couples: relationship with semen quality and early miscarriage. Int J Androl. 2007 Jul 25. [Epub ahead of print]
5. Clarke RN, Klock SC, Geoghegan A, Travassos DE. Relationship between psychological stress and semen quality among in-vitro fertilization patients. Hum Reprod. 1999; 14: 753-8.
6. Human Fertilisation and Embryology Act 1990, Chapter 37, Section 13, Clause 5.
7. Goverde AJ, McDonnell J, Vermeiden JP, Schats R, Rutten FF, Schoemaker J. Intrauterine insemination or in-vitro fertilisation in idiopathic subfertility and male subfertility: a randomised trial and cost-effectiveness analysis. Lancet 2000; 355: 13–8.
8. Guzick DS, Carson SA, Coutifaris C, Overstreet JW, Factor-Litvak P, Steinkampf MP, Hill JA, Mastroianni L, Buster JE, Nakajima ST, Vogel DL, Canfield RE. Efficacy of superovulation and intrauterine insemination in the treatment of infertility. National Cooperative Reproductive Medicine Network. N Engl J Med 1999; 340: 177–83.
9. Hendin BN, Falcone T, Hallak J, Goldberg J, Thomas AJ Jr, Nelson DR, Agarwal A. Effect of clinical and semen characteristics on efficacy of ovulatory stimulation in patients undergoing intrauterine insemination. J Assist Reprod Genet. 2000; 17: 189-93.
10. Human Genetics Commission (January 2006) '4. Preimplantation genetic diagnosis' (pp. 44-53) in Making Babies: reproductive decisions and genetic technologies. [Available from: http://www.hgc.gov.uk/UploadDocs/DocPub/Document/Making%20Babies%20Report%20-%20final%20pdf.pdf].

11. Soini S, Ibarreta D, Anastasiadou V, Aymé S, Braga S, Cornel M, Coviello DA, Evers-Kiebooms G, Geraedts J, Gianaroli L, Harper J, Kosztolanyi G, Lundin K, Rodrigues-Cerezo E, Sermon K, Sequeiros J, Tranebjaerg L, Kaariainen H. The interface between assisted reproductive technologies and genetics: technical, social, ethical and legal issues. Eur J Hum Genet. 2006; 14: 588–645. Available online in full text from: [http://www.nature.com/ejhg/journal/v14/n5/full/5201598a.html or http://www.nature.com/ejhg/journal/v14/n5/pdf/5201598a.pdf].