Use of frozen semen to avoid human immunodeficiency virus type 1 transmission by donor insemination: a cost-effectiveness analysis

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of fresh versus frozen semen in donor insemination was examined.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of women whose husbands were azoospermic. The women were nulliparous, had regular cycles, and had no history of sexually transmitted diseases, pelvic surgery or endometriosis.

Setting
The setting was a hospital or fertilisation centre. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness and resource use data were derived from studies published from 1977 to 2000. The costs were estimated from studies published between 1995 and 1998. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was derived from a review of completed studies and some assumptions.

Modelling
A decision modelling approach, based on a Markov process with monthly cycles, was used to evaluate the benefits and costs of fresh versus frozen semen in donor insemination procedures. The model considered a hypothetical cohort of 80,000 nulliparous women aged 30 years, whose partners were azoospermic. The women agreed to receive a series of no more than 12 intrauterine inseminations, but refused adoption and assisted reproductive technology. The model included 27 finite and mutually exclusive Markov states. The time horizon of the model was lifetime.

Outcomes assessed in the review
The outcomes estimated from the literature were the probabilities of the following:

dearth during pregnancy;
drop-out per cycle;
HIV infection in one fresh semen cycle, in one cycle with infected donor, and among potential donors;
HIV window period among potential donors;
HIV vertical transmission to foetus;
pregnancy after one fresh insemination;
pregnancy loss;
relative fecundity (frozen/fresh) and relative infecundity (window/not-window); and
the sensitivity and specificity of ELISA.

Qualify of life factors and duration for HIV Phase 2 to 5 were estimated. Vital statistics data were also use to estimate survival.

Study designs and other criteria for inclusion in the review
The primary estimates were derived from randomised clinical trials and observational studies.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
The evidence was obtained from approximately 18 primary studies.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not reported.

Results of the review
The following probabilities were estimated:
0.0001 (range: 0 - 0.1) for death during pregnancy;
0.091 (range: 0 - 0.5) for drop-out per cycle;
4.7 x 10^-7 (range: 0 - 0.02) for HIV infection in one fresh semen cycle;
0.005 (range: 0 - 0.5) for HIV infection in one cycle with infected donor;
0.0005 (range: 0 - 0.05) for HIV infection among potential donors;
9.141 x 10^{-5} (range: 0 - 0.9141) for HIV window period among potential donors;
0.083 (range: 0 - 0.25) for HIV vertical transmission to foetus;
0.103 (range: 0 - 0.5) for pregnancy after one fresh insemination;
0.18 (range: 0 - 0.5) for pregnancy loss;
0.62 (range: 0.1 - 2) for relative fecundity (frozen/fresh);
0.995 (range: 0.1 - 1) for the sensitivity of ELISA and 0.995 (range: 0.1 - 1) for the specificity of ELISA.

Quality of life factors for HIV phases were 0.63 for Phase 2, 0.51 for Phase 3, and 0.21 for Phases 4 and 5.
The duration of HIV phases was 9 years for Phase 2, 4 years for Phase 3, 1 year for Phase 4 and 2 years for Phase 5.

Methods used to derive estimates of effectiveness
The authors made some assumptions that were used in the decision model.

Estimates of effectiveness and key assumptions
The following assumptions were made:
there was only one live birth per woman;
pregnancy did not occur by any means other than donor insemination;
the probability of pregnancy for HIV-1 infected women was the same as that for uninfected women;
women learn of their HIV-1 status at the end of the last insemination, after dropping out, or between the second and third month of pregnancy;
pregnancy losses and the few pregnancy-related deaths take place between the second and third month;
the probability of relative infecundity (window/not-window) was 10 (range: 0 - 200);
the utility values were 0.9 for insemination treatment, 0.7 for drop-out state, 0.8 for pregnancy loss, 0.95 for childless state and 0.8 for infected child.

Measure of benefits used in the economic analysis
The summary benefit measure used was the quality-adjusted life-years (QALYs). The estimated QALYs were derived from the decision model and an annual discount rate of 3% was applied. The utility values were derived from the general public. Other model outputs, such as the number of live births and the numbers of infected women and infected newborns, were considered.

Direct costs
An annual discount rate of 3% was used since the lifetime costs were estimated. The unit costs were reported only for a few items. Generally, the quantities of resources used were not presented separately from the costs, which were not broken down. The health services included in the economic evaluation were insemination with fresh or frozen semen, lifetime medical care, lifetime HIV treatment for a child, litigation for one HIV infection, and pregnancy loss.
treatment. The cost/resource boundary of the study was unclear. The resource use data came from the review of the literature, from which the probability values used in the decision model were derived. The costs were mainly estimated from studies published between 1995 and 1998, and were then presented in 2000 values.

**Statistical analysis of costs**
The costs were treated deterministically in the base-case.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way sensitivity analyses were conducted on all model inputs to address the issue of variability in the data. Two alternative scenarios were considered. The first considered all child-related benefits and costs. The second addressed physicians' concerns about medicolegal liability.

**Estimated benefits used in the economic analysis**
In the whole cohort of 80,000 women, the number of live births was 35,145 with fresh semen and 26,264 with frozen semen. The difference was 8,881.

The number of infected women was 0.19443 with fresh semen and 0.00003 with frozen semen. The difference was 0.019440.

The number of infected newborns was 0.0047928 with fresh semen and 0.0000006 with frozen semen. The difference was 0.0047922.

The discounted QALYs per woman were 21.06 with fresh semen and 20.97 with frozen semen. The difference was 0.09.

**Cost results**
The mean, lifetime total direct health care costs per woman were $52,781 with fresh semen and $54,676 with frozen semen. The difference was $1,896.

**Synthesis of costs and benefits**
An incremental cost-effectiveness ratio (ICER) was calculated to combine the costs and benefits of the interventions under examination.

Under base-case conditions, it was not necessary to calculate the ICER since the strategy based on fresh semen was more effective and less costly than that based on frozen semen.

The one-way sensitivity analysis showed that only two variables had a significant impact on the results of the analysis. For the choice of the preferred strategy to change, the cost of insemination with frozen semen should be less than 83% of the cost using fresh semen, or the relative fecundity of insemination with frozen semen would need to be equal to that of insemination with fresh semen.

The option of fresh semen remained the preferred strategy in the two-way sensitivity analysis.
In the scenario that considered all child-related benefits and costs, the ICER of fresh semen over frozen semen was $711 per QALY.

In the scenario where medicolegal costs were added, these costs would have to exceed $92 million to eliminate the absolute dominance of fresh over frozen semen and to make frozen semen the preferred option.

**Authors' conclusions**
The exclusive use of frozen semen to prevent the transmission of human immunodeficiency virus 1 (HIV-1) by donor insemination was not cost-effective. The guidelines should be revised to include the possibility of informed recipients using fresh semen.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was clear. Frozen and fresh semen represented the two available strategies for donor insemination. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness was based on data coming from the literature and some assumptions. A formal review of the literature was not conducted. The authors reported the design of the primary studies, but not the methods used to combine the primary estimates. Details of the study samples were also not provided. The validity of the primary estimates was not discussed. The authors conducted several sensitivity analyses, in which all the model inputs were varied, to deal with the issue of uncertainty in the estimates used in the analysis. The authors discussed the choice of some probability values from among the published studies.

**Validity of estimate of measure of benefit**
The choice of QALYs as the summary benefit measure was appropriate for detecting the impact of the interventions on the individual's health. The source of the utility values was reported. Discounting was applied, as recommended in a guideline for economic evaluation. QALYs represent a benefit measure that can be compared with the benefits of other health care interventions.

**Validity of estimate of costs**
The authors stated that a societal perspective was adopted, but the indirect costs were not considered in the analysis. Therefore, the cost/resource boundary of the study was unclear since some costs are usually borne by infertile couples. There was limited information on the unit costs and the quantities of resources used, and the costs were presented as macro-categories. This reduces the possibility of replicating the study in other settings. The sources of the economic data were provided. The cost estimates were not treated stochastically but reasonable variations were explored in the sensitivity analysis. The price year was reported, which would facilitate reflation exercises in other settings. Discounting was appropriately performed. The authors noted that additional savings could be achieved by avoiding multiple pregnancies with their associated risk of premature delivery.

**Other issues**
The authors did not compare their findings with those from other studies. They also did not explicitly address the issue of the generalisability of the study results to other settings. However, the external validity of the analysis was enhanced by the extensive sensitivity analyses that were conducted on both the effectiveness and cost sides of the study. The authors noted some limitations to their analysis, which were mainly related to the use of published data.

**Implications of the study**
The study results suggested that decision-makers should consider cost-effectiveness issues among all factors affecting the decision to allow the use of fresh semen in donor insemination.
Source of funding
None stated.

Bibliographic details

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Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
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