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THE ECONOMICS OF THE IVF PROGRAMME: A CRITICAL REVIEW

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ABSTRACT

This paper reviews recent literature from an economic viewpoint concerning the costs and benefits of the IVF programme (in-vitro fertilization) in assisting reproduction. The problems with previous studies are highlighted, and suggestions made as to how these problems can be surmounted in future economic evaluation of the programme. The first section of the paper addresses the problem of infertility and the causes of infertility for which IVF has been offered as a treatment. The second section concerns issues of efficacy. Sections three and four detail the costs and benefits of the IVF programme, as they ideally should be presented and as they have been presented in the literature. In the final section of the paper, a suggested framework for economic evaluation is presented.

The Economics of the IVF Programme: A Critical Review

1 Introduction

In-vitro fertilization has become well established in the Australian health care system as a recognized procedure for the alleviation of infertility. There exist a number of IVF treatment centres within every state of Australia.[1] Until recently treatment was only available in the private sector, however a global fee under the medical benefits schedule now covers services utilized in IVF. Most treatment is still undertaken in the private sector. In spite of the acceptability of the procedure, remarkably little research has focused on establishing the efficacy of the treatment administered, particularly in relation to alternative procedures for the treatment of infertility.

Assuming the procedure is efficacious, in addition there are problems in quantifying the costs and benefits of the programme. Studies thus far undertaken in Australia which have taken an economic viewpoint have tended to present the outcome of treatment only in terms of the birth of an infant.[2-3] Unfortunately however, the birth of a liveborn infant occurs in only a small minority of cases, and the most likely outcome of the procedure is the failure to have a child. In order to present an accurate representation of outcomes of treatment, attention should be given to the psychological and health effects experienced by couples who participate in the programme (particularly those who are unsuccessful in achieving conception) as well as the infants. A framework for evaluation is required by which IVF can be compared, firstly with alternative procedures for the treatment of infertility, and secondly with other medical procedures offered within the health care setting which compete for the resources that will be spent on IVF.

Section One: Clinical Background

a) The Problem of Infertility

Although IVF is often presented as treatment for infertility, it is important to note that it can not be defined as treatment in the classical sense, since it does not offer the possibility of cure for infertility. The condition of infertility remains regardless of whether a couple receives

IVF treatment, but what IVF does provide is a means by which conception can occur when it would not otherwise. Infertility itself is defined in a number of ways in the literature. The most commonly accepted definition within medicine is :

> "the inability of a couple to conceive after twelve months of intercourse without contraception".[4]

The World Health Organization extended the time period of the definition to a period of two years.[5] With this latter definition the extent of infertility in Australia is estimated at approximately 10% of the population.

Once the problem has been identified and a couple are admitted to a reproductive technology clinic, they must undergo a number of tests and investigations to ascertain an indication of the cause of infertility. These may include temperature chart tests, an examination of cervical mucus, endocrine assays, semen analysis, ultrasound and urine tests. Background information collected from the patient's GP plus the results of these tests are used to make a clinical decision regarding the most appropriate form of treatment for each couple. IVF was originally developed for patients with tubal damage, in whom surgery was considered inappropriate or where surgery had been unsuccessful.[6] In such cases IVF is a treatment of last resort. However, more recently, successful pregnancies through utilization of IVF have occurred in patients with different types of infertility (see Table 1 for an overview).

b) The Causes of Infertility

The causes of infertility for which IVF is an appropriate treatment option are illustrated in Table 1, (below), together with possible alternative procedures:-

TABLE 1

	Clinical Indication for IVF	Alternative Procedures
1.	Tubal occlusion, distortion	Tubal surgery
2.	Pelvic endometriosis	Surgery ZIFT
3.	Cervical hostility	Artificial insemination by husband
4.	Male infertility	Artificial insemination by donor GIFT
5.	Idiopathic infertility (unexplained infertility)	ZIFT GIFT

The National Perinatal Statistics Unit provides estimates, on an annual basis, of the causes of infertility in couples where pregnancy occurs as a result of In vitro fertilization (IVF) and Gamete intra fallopian transfer (GIFT) programmes within Australia. The primary cause of infertility for which IVF is advanced as treatment is tubal occlusion or distortion (tubal damage). This condition was present in 47% of women becoming pregnant by IVF and in 6% becoming pregnant by GIFT in 1988.[7] By contrast, GIFT pregnancies were highest in the unexplained infertility group. Other causes of infertility for which IVF and GIFT were utilized included male infertility and endometriosis.

1. Tubal Occlusion or Distortion

Where the clinical indication is tubal occlusion or distortion, tubal surgery is often

presented as the most appropriate form of treatment.[6] However, it is important to note that the success of surgery is highly dependant upon the type of procedure performed. Salpingostomy (the opening of the fallopian tube) is the least successful type of tubal surgery. Although the surgeon may be able to open the tube and have it remain open, anatomic and physiologic damage to the remainder of the tube rarely supports the numerous normal reproductive processes necessary to achieve a successful pregnancy. Overall, pregnancy rates following salpingostomy have been reported to range from 10-40%.[7] The most successful primary tubal surgery is correction of mid-tubal occlusion, resulting from previous tubal sterilization. The pregnancy rate ranges from 60-80%.[8] Where there is irreparable tubal damage or after unsuccessful tubal repair, IVF is considered an appropriate alternative to surgery.

2. Pelvic Endometriosis

Where the clinical indication is pelvic endometriosis, reconstructive surgery can be undertaken. However, pregnancy rates following surgery are generally higher in cases of mild rather than severe endometriosis. After unsuccessful surgery or in the case of severe endometriosis, IVF or ZIFT (zygote intra-fallopian transfer) are appropriate treatment options.

3. Cervical Hostility

Cervical hostility refers to infection or swelling located at the neck of the womb in the female. Artificial insemination by the husband is the procedure most commonly used in this case. However where artificial insemination is considered inappropriate or has failed, IVF may be offered as an alternative procedure.

4. Male Infertility

Male infertility is a broad heading which includes several male reproductive system problems, which may be presenting in isolation or as confounding factors. Oligozoospermia is the scarcity of sperm in the semen. Azoospermia is the absence of sperm in the semen. Other problems include high viscosity of semen and low sperm mobility. Treatments for male infertility are fewer than for female infertility. Several different hormonal and other therapies have been used to treat male

infertility. More recently, most male factor infertility problems are being managed by artificial insemination or by utilization of assisted reproductive technology programmes.

5. Idiopathic Infertility

Where infertility is diagnosed as unexplained, assisted reproductive technology programmes, in particular IVF, GIFT or ZIFT may be used as a treatment of last resort.

(c) Assisted Reproductive Technology Programmes

It is important to recognize that GIFT and ZIFT are both variants of IVF. The clinical procedures adopted are very similar in each of these techniques. Each procedure is outlined in more detail below:

1. In-vitro Fertilization

Once admitted to the IVF programme, a couple must begin a treatment cycle. The cycle begins at the commencement of menstruation in the female. The use of clomid and pergonal drugs in the early stages of the menstrual cycle is common, as these drugs facilitate the growth of more follicles than the usual one so that more eggs can be collected from the female. Under the IVF programme the eggs of the female are removed by the process of laparoscopy approximately mid-way through the menstrual cycle. A small tube is inserted below the navel into mature ovarian follicles, or alternatively by ultrasound-guided probe through the back of the vaginal wall into the follicles. In both cases, the eggs are collected from the follicles by a very fine aspiration needle. Following this procedure the eggs are incubated. Sperm is required 2-4 hours after egg collection. The sperm is washed, prepared for insemination, placed with eggs and then incubated for a period of between 16 and 20 hours. If fertilization has occurred, the embryos are placed in a fresh tube of growth medium and returned to the incubator for 24 hours. At the end of this period, the embryos are transferred, via a very fine catheter, through the vagina into the uterus.

2. Gamete Intrafallopian Transfer (GIFT)

GIFT as a procedure is very similar to IVF. However GIFT is restricted to those women whose fallopian tubes are still intact. The same cycle is followed until the point at which The eggs of the female are collected by laparoscopy. Once collected, the eggs are placed in a small volume of transport media together with the sperm of the male and then directly transferred into the fallopian tubes where fertilization takes place. Fertilization thus takes place within the body of the female, whereas with IVF and ZIFT (see next section) fertilization takes place outside the body of the female.

3. Zygote Intrafallopian Transfer (ZIFT)

ZIFT is another variation of IVF. The egg is fertilized in the laboratory in the same manner as for IVF and exactly the same procedures are followed, except that the fertilized egg is transferred to the mother's fallopian tubes (instead of the uterus) the day after fertilization.

4. Artificial Insemination

This procedure can be of two types. Donor insemination occurs when the woman is injected with donor semen into the vagina, and is used when the husband has little or no spermatozoa in his semen. In the second case artificial insemination utilizes the semen of the husband and is used in cases where the wife's cervical mucus prevents the passage of semen through the cervix into the uterus.

Section Two: Problems of Efficacy

It is possible that the efficacy of IVF may differ according to the cause of infertility. A study undertaken in the U.S.[9] based on observational data of the IVF procedure in one hospital found that success was highly dependant upon the utilization of good quality semen. The procedure was much less effective when utilized due to male infertility where the primary cause was low quality semen. A recent study undertaken in the Netherlands of the costs and effects of IVF noted that the average success rate (defined as the birth of a live born infant) was significantly reduced in the case of male factor infertility compared to all other causes, being 5.9% for male factor infertility versus 11% for all other causes.[10]

In addition, there is evidence that natural pregnancy occurs quite frequently independently of treatment for some couples on reproductive technology programmes. In a study of 1214 couples registered as infertile at an infertility clinic in the U.S. the proportion of treatment independent pregnancies, after a period of two to seven year follow up, was 38% overall.[11] Analysis of those couples who experienced treatment independent pregnancy revealed that in 96% of cases the original diagnosis was cervical factors or idiopathic infertility. The results of this study suggest that the utilization of reproductive technology programmes for couples with unexplained causes of infertility is probably not the most effective option. Greater effort should be channelled into the area of prevention of infertility in the first instance.

Although this study is not a substitute for a properly designed clinical trial as a method for treatment evaluation, it does provide interesting results which clearly need to be investigated through the use of randomized control trials of IVF versus alternative treatments for infertility. As yet, there is no published evidence of such trials having been undertaken.

When considering the success rate of IVF, it is important to note that success itself can and is defined in a number of ways in the literature. Often the success rate of IVF is defined as the number of biochemical pregnancies relating to a treatment cycle. Studies reported in this manner suggest comparatively high success rates of 33 - 55%.[12] However, the risk of spontaneous abortion, ectopic pregnancy and fetal death following biochemical pregnancy make these results misleading. Measurement of success is better measured in terms of the number of live birth pregnancies as a percentage of the number of treatment cycles,

since this is ultimately what IVF seeks to achieve. Defined in these terms success rates are far more modest. There were 9,191 IVF treatment cycles carried out in Australia and New Zealand in 1988, and of these only 8.1% resulted in pregnancy in which there was a live born infant.[7] This low success rate is important in assessing the cost effectiveness of IVF. Looked at from one perspective, the effectiveness of a given expenditure is significantly reduced because of the low success rate. From another perspective, the low success rate increases the cost of a successful pregnancy. Consequently, variation in the success rate could be critical to overall cost effectiveness.

Section Three: Costs and Benefits

Since the IVF programme is now firmly established, the basic question is not whether to employ the IVF procedure, but rather when to employ it, when to employ alternative procedures, how often to use it, under what clinical conditions and in what specific circumstances. To answer these questions requires a full economic analysis of the costs and benefits of IVF. This, in turn, requires a substantial amount of clinical information. Ideally an economic evaluation of this procedure should take place in conjunction with or following the results of randomized control trials to determine the efficacy of the procedure. Although it is often difficult to ascertain the marginal or incremental costs of the intervention and the marginal benefits expected, estimates of these figures are of interest since there is no other basis for determining the optimal level of service provision of IVF and expanding or contracting the use of IVF to this optimal level.

(a) Costs

In order to evaluate the IVF programme from an economic perspective, it is important to consider <u>all</u> costs and benefits. Cost in economic terms means more than just monetary expenditures. Economists employ the concept of an opportunity cost; the true cost of a programme arises from the fact that resources are scarce, and utilization of resources by that programme means that the opportunity to use them in another activity is foregone. The economic costs can be categorized into two groupings, direct and indirect costs:[13]

1. Direct Costs

These include all of the costs of running the programme from a societal perspective. This includes both medical and non-medical components, i.e.the cost to the individual institution concerned and the cost to the individual patients involved.

A cost effectiveness study of the IVF programme should include the following direct costs:-

a) Costs of the medications.

b) Costs of diagnostic tests; laboratory tests, ultrasound, pathology and urine tests.
c) Costs of all consumables utilized during the procedure.
d) Staffing costs; nursing care, physician services, para-medical services.
e) Overhead costs; heating, power, lighting, laundry, linen, cleaning services, clerical staff and administration for the infertility unit.
f) Capital costs; costs of the buildings and equipment utilized in order to administer treatment.
g) Patient transportation to and from the hospital.
h) Time taken off work to receive treatment.

Direct costs can be subdivided into fixed and variable costs. Variable costs are dependent upon the volume of services rendered, whereas fixed costs do not alter as a result of changes in service volume. Examples of variable costs include the costs of medications and consumables utilized. Capital costs and overheads represent fixed costs; they must be incurred regardless of the extent of service provision.

2. In-direct costs

These include the following:

a) The monetary value of the changes in productivity that a patient experiences as a result of treatment.

b) The intangible costs of the psychologically harmful effects of participation in the programme, e.g. pain, grief and suffering of the patient and the family.

In the case of the IVF programme, it is important to note that the direct costs of producing a liveborn infant include not only the cost of that particular treatment cycle but also the cost of the failures. A study recently commissioned by the Australian Government noted this.[14] Given that the cost per treatment cycle was estimated at $4000 and only about 10% of treatment cycles are successful, then the true cost of a liveborn infant is in fact $40,000. In addition, observation suggests that many IVF babies are born prematurely and are of low birth weight.[3] As such it is likely that further demands on the health care system will arise e.g. neo-natal

intensive care.

The indirect costs of treatment can be quite substantial. If the mother of a child conceived by IVF decides to withdraw from the labour market in order to care for the child, this represents a cost not only to the family involved but to society.[15] Child care can be distinguished from almost every other household activity with regard to the inflexibility of its organization. Child care cannot be flexibly organized since the existence of dependant children makes continuous care or supervision necessary. Child care competes directly with time in paid activity - normally the two cannot be undertaken simultaneously. There is some controversy within the economics discipline as to how such a cost should be calculated. From the point of view of society, the most appropriate measure is what could be earned in paid employment, or the opportunity cost of the activity. However from the family's point of view, the importance lies in the cost of replacing those services through the use of a child minder or the services of a creche. These costs may well be fundamentally different from the cost of lost employment. The correct approach depends on the viewpoint for the analysis. Given that the societal perspective is taken, then the opportunity cost approach represents the correct form of analysis.

The intangible costs of the IVF programme are more difficult to quantify. A number of studies have been undertaken which address the psychological effects experienced as a result of involvement in the programme.[16,22] In a recent study undertaken in Canada it was noted that both males and females exhibited a significant increase in anxiety levels after failed treatment; particularly noticeable was the extent to which anxiety was generally higher for childless women compared to those women in the programme who had previously born a child.[16] As a result of this study, the authors suggested that childless women on the IVF programme may well benefit from some form of anxiety management training to manage the stress of IVF, but also to assist in coping with treatment failure. The indications are, therefore, that the treatment imposes stress on couples involved and especially on the women receiving treatment and this represents a cost of the procedure.

(b) Benefits

The economic benefits of a health care programme can be categorized into three groupings:[13]

1. Direct Benefits

Are the savings in health care costs since the programme makes people healthier and, as such, means that they will use fewer health care resources in the future.

2. Indirect Benefits

a) These are the gains to society which accrue from the birth of an individual who would not otherwise have been born.

b) The reduction in pain, grief and suffering of the patient and family due to the improved health outcome i.e. quality of life.

The direct benefits of the programme are not likely to be substantial, since physical health is largely unaffected as a result of involvement in the programme. However, since IVF is often portrayed as a treatment of last resort, there is some evidence to suggest that demands on infertility services will be reduced after withdrawal from the programme regardless of the outcome achieved.[11] However, in contrast, the indirect and intangible benefits of the IVF programme are likely to be quite substantial. Success results in the birth of a healthy and productive individual who would not otherwise have been born. In addition, there may be psychological benefits accruing to those couples who do succeed on the programme. For those couples who do not succeed there is often a feeling of having done everything that they could to conceive a child. It is possible that in some instances this makes a state of childlessness easier to bear.[16]

Ideally both costs and benefits should be measured in units which enable comparison of IVF with other treatments and procedures in health care. Current practice suggests two methods of evaluation which may be employed as a framework in this instance, cost-benefit and cost-utility analysis:-

(c) Cost-benefit Analysis

Cost-benefit analysis may be defined as an economic analysis of any programme or technology in which all real costs and benefits of that programme are expressed in

monetary terms. Therefore, the results of a cost-benefit analysis are presented in terms of a net benefit (where this is defined as benefit minus cost) for each treatment. This is important, because the net benefits of one treatment may be compared with the net benefits of another, even though the treatment may be vastly different and have entirely different clinical outcomes.

In order to undertake a cost-benefit analysis of the IVF programme, therefore, it is necessary to convert the costs and benefits of treatment into monetary values. Data on direct hospital costs are already available in dollar values and thus easily estimatable. However, the psychological costs (sometimes perceived as negative benefits) of participation in the programme are not easy to quantify, neither are the direct benefits of the programme. One approach utilized by economists in this type of situation is the "willingness to pay" approach.

The direct hospital costs of provision of a service would be calculated in the first instance. Individuals would then be asked how much they would be willing to pay in order to receive treatment. The costs of participation in the programme would be traded off with the positive benefits associated with the probability of having a child. The value that individuals place on the provision of the service is thus ascertained in monetary terms.

(d) Cost Utility Analysis

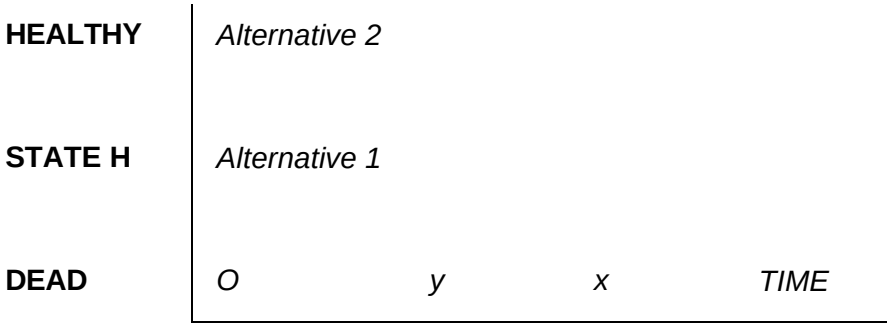
In cost utility analysis, no attempt is made to measure the benefits of treatment in monetary terms. Instead, outcomes are measured in terms of quality of life. More specifically, an attempt is made to adjust the number of years gained through an intervention in accordance with their quality. This is exactly what economists are seeking to do when they evaluate QALYs (quality adjusted life years).

There are a number of methods which can be utilized in order to elicit quality of life values. In the literature, it is quite common to see states of health rated on an interval scale. This is based on a score of one for a year of life in good health, a discounted figure for years of life in less than good health, to a figure of zero for death. Individuals are then asked to rate the likely outcomes of a procedure according to this scale. The benefits of a procedure can then be estimated according to the number of QALYs generated.

Another method of eliciting people's preferences between different states of health is to utilize the time trade off technique.[13] The subject whose values are being sought is asked to make a trade off between the chronic health condition for a period of x years and good health for a shorter period, y years. The period of good health is varied until the individual is indifferent between the two states. At the point of indifference the valuation (h) of the chronic health condition is calculated as h=y/z. These trade offs are illustrated in tabular form below. Such measures could then be used in economic appraisal to express the benefits of the interventions in terms equivalent to years of life gained in full health.

FIGURE 1

Time Trade Off for a Chronic Health State Preferred to Death



Section Four: The Literature from an Economic Viewpoint

Most of the studies undertaken on the IVF programme from an economic viewpoint have been concerned mainly to elicit estimates of the costs of the programme. Benefits have focused mainly on clinical issues.[2,3,10] Pure outcome studies on the benefits of neonatal intensive care, and on infertility services more generally have been undertaken however, which provide an indication of the techniques which could be utilized to measure the benefits of treatment from a wider socio-economic perspective.

(a) Outcome Studies

As highlighted earlier in the paper, one possible approach to measuring the benefits of the IVF programme, is to use the willingness to pay approach. This type of analysis was undertaken recently by Maureen Dalton at St James' University Hospital, Leeds, U.K.[17] In a questionnaire survey of the general public and patients attending an infertility clinic, people were asked what they would be prepared to pay in terms of financial loss in order to have a child.

When the probability of having a child was 100%, the percentage of a year's income individuals were prepared to give up was the same in both groups (see Table 2 overleaf). However, when the probability of having a child was reduced to only 50% predictably, the general population group was more risk averse than the infertility population group, giving up 29% of a year's income as opposed to 34%. However, this difference is not substantial and emphasizes the importance that the general public place on the possibility of having a child.

Her findings refute the suggestion that infertility programmes such as IVF deserve a low priority in competition for resources. Indeed one can argue that her results suggest the high value that the general public and infertile people place on having a child and that this exceeds the value of a few extra years gained at the end of life. The percentage of income both groups would be prepared to pay to have a child with either 100% or 50% success is higher than the percentage of income they would be prepared to pay to have five extra years at the end of life. This result is important, since it suggests the possibility that resources should be re-directed towards assisted reproduction programmes.

Unfortunately, however, Dalton's analysis remains incomplete, since no attempt was made to couple the perceived benefits of treatment with the direct hospital costs involved. A more complete analysis would require this type of comparison.

TABLE 2

Trade Off Values in Infertility

	General Population (n = 32)	Infertility Population (n = 16)
% of a year's post-tax income people prepared to pay to have a child with:		
100% success	38	38
50% success	29	34
Years off end of life to be pregnant once?	12.0	11.6
% year's post-tax income to gain 5 years at end of life	18	31
% risk of death to have one child	20	35

(ref. Dalton, M. and Lilford, R., "Benefits of IVF", letter to the editor, The Lancet, Dec. 1989).

A study undertaken in Canada highlights the possibility of eliciting QALY values as a method of measuring the benefits of IVF.[18] The study was actually a cost-effectiveness analysis of neonatal services for low weight infants, but the method of measurement has since been applied to the IVF programme.

A classification of health states was developed to measure the health of survivors according to their physical function, role function, social and emotional function and health problems. This classification was then given to a random sample of Canadian parents who were asked to assign a utility value to each health state ranging from one (for perfect health) to zero (for death). In fact some chronic dysfunctional states in children were considered as worse than death and hence given a negative score. These utilities were then used to adjust life years gained for quality, e.g. a life year in a state judged to be 0.75 on the utility scale would represent 0.75 quality adjusted life years. The benefits of neo-natal intensive care were then evaluated according to

the number of QALY's that were generated.

It was discovered that the costs of neo-natal intensive care were higher for infants of very low birth weight (500-999g) as compared to those of moderately low birth weight (1000-1499g). Consequently the cost per QALY was higher in the first group at $9,100 Canadian, than in the second group ($900 Canadian). If a similar type of methodology is applied to the IVF programme, where the benefit of treatment is assumed to accrue to the liveborn infants conceived as a result, the benefits are likely to be quite substantial, since the number of life years gained is large and it is probable that the quality of those life years will be good.

A recent discussion paper provided an estimate of the number of QALY's which will accrue to an IVF baby.[19] It is assumed that they will live for 50 years on average, and in a state of reasonably good health. This estimate was then multiplied by the total number of IVF babies conceived within Australia from 1980-1984. According to these calculations, the IVF programme yielded a total of 30,900 QALY's over this four year period. This information was then coupled with the cost estimates of IVF over the same period reported by Bartels (see section B below), to provide an estimate of the cost per QALY of $1036. If we compare this figure with other health care programmes evaluated on this basis, antepartum anti-D therapy costs $1220 per life year gained, neonatal intensive care for infants weighing between 1 and 1.5kg, $4500, thyroid screening $6300, coronary artery by-pass grafting $36,300 and hospital haemodialysis, $54,000. Presented in this manner the author noted that IVF would seem to provide good value for money.

(b) Economic Assessment Studies

A number of economic assessment studies of the IVF programme have provided evidence which suggests that the cost of treatment under IVF is directly related, not only to the level of service provision provided, but also to the organization of the administration of the service. That is, the evidence suggests that X- inefficiency may be an important factor in determining cost. The term "X-inefficiency" was initially developed by Leibenstein to draw attention to the potential importance of internal organizational relationships and behavioural relationships within the unit as influences on its technical performance and hence on the costs of running the unit itself. [20]

A recent study undertaken in the Netherlands of the diffusion of IVF concluded that the monetary costs of providing IVF treatment were highly dependant upon the level and type of service provision offered.[10] The sample utilized for the Netherlands study was the 1462 couples registering for the IVF procedure between August 1986 and June 1988 in five separate hospitals.

It was found that the costs of the IVF treatment varied according to the following:

a) the treatment protocol (medication and frequency of monitoring)
b) the task division between academic and other personnel
c) the organization of the IVF unit
d) the size of the programme, and
e) the assumptions made concerning the level of physicians' fees.

For most of these factors, a sensitivity analysis was employed and two alternative situations were calculated: one providing a low estimate and another a high estimate. In addition the author highlighted the existence of economies of scale in the level of service provision offered in the Netherlands. As illustrated in Table 3, overleaf, for 375 started treatments annually, the average costs per started IVF treatment were between NLG 2100 and 2700 (where NLG 1 = US$ 0.5). For 750 started treatments annually this figure decreased to NLG 2000 - 2400. For 1250 started treatments the figure was NLG 2000 - 2400. However, it was noted that these savings could be differentiated with regard to patient groups, hospitals, number of treatments per couple and size of the IVF programme. A figure of NLG 2500 was assessed as providing the best estimate of an average treatment cost. Benefits were presented purely in terms of a clinical assessment, i.e. the number of live born babies as a percentage of the number of treatment cycles. No attempt was made to measure the benefits of treatment in a form which would enable comparison of this procedure with others. Defined in these terms, a 10% success rate was observed,which is in agreement with international experience.

Another study of IVF undertaken in the UK highlighted the differences in costs of treatment which arise because of differences in the extent and type of treatment administered.[21] The study aimed to provide information on the demand for IVF, costs and likely outcome of service provision, in order to assist the Trent Regional

Health Authority in deliberations about the funding of IVF. Information was obtained from three hospitals concerning the running costs of their IVF units. The hospitals were based in the north of England.

TABLE 3

Treatment Costs per Ongoing Pregnancy, Differentiated

The average costs per reached ongoing pregnancy were NLG 25000, but differentiated to several subgroups, the costs per reached ongoing pregnancy (in NLG) were:

Patient groups		
	only tubal pathology	22,000
	male factor	43,000
	one ovary (two ovaries)	33,000 (22,000)
	woman > 35 years (< 35)	36,000 (21,000)
	infertility period > 5 years	30,000
	primary infertility	27,000
	(secondary)	(20,000)
Maximum number of treatments		
	1	20,000
	3	23,000
	6	27,000
IVF-center	best	17,000
	worst	48,000
Annual number of IVF treatments per center		
	375	26,000 to 33,000
	500	23,000 to 30,000
	750	21,000 to 27,000
	1250	20,000 to 24,000

(ref. Haan, G. "The Effects and Costs of IVF", Institute of Medical Technology Assessment, 1990).

The three units' running costs were calculated (see Table 4). A number of assumptions were made in the determination of these costs. With regard to staffing levels, in the early stages of setting up an IVF unit it was observed that the consultant is likely to be involved almost full-time, but once the clinic is established

the consultant generally provides managerial supervision and a limited clinical input, which probably accounts for three or four sessions each week. Therefore only one third of the consultant's time was costed. The cost for utilization of hospital facilities was based on half the average costs of an overnight stay per cycle. Most units attempt to keep inpatient stay to a minimum, but even when no inpatient stay has occurred the patient still has the use of the facilities and general services of the hospital. The cost components calculated were staffing levels, drugs and consumables, inpatient stay, annual equivalent cost of buildings, and the annual equivalent cost of equipment.

TABLE 4

Running Costs of an IVF Unit

Number of couples	440	300	330
Number of Cycles	1320	900	1000
Staff (Inc. Consultant)	£229,611	£175,481	£160,626
Drugs & consumables	£149,292	£111,618	£111,300
Inpatient stays	69,960	47,700	53,000
Annual equivalent cost of building	£16,000	£16,000	£16,000
Annual equivalent cost of equipment	£7,793	£7,793	£7,793
TOTAL	**£472,656**	**£358,592**	**£348,719**
Average Annual Cost = £439,739 to treat approximately 400 couples			

(ref. Page H. "Economic Appraisal of IVF" Journal of the Royal Society of Medicine, Feb. 1989)

As illustrated in Table 4, the average annual cost in 1989 was estimated at £439,739 to treat approximately 400 couples, or £366 per cycle of treatment. Again, no attempt was made to measure benefits in this study. They were presented in terms of the number of liveborn pregnancies as a percentage of the number of treatment cycles. Presented in this way results indicated a 10% success rate.

The studies of IVF undertaken in Australia from an economic viewpoint have mainly been concerned with establishing the overall cost of treatment, and in particular the Government contribution. Dita Bartels, in her study of the extent of government

financing of the IVF program in Australia during the first five years of the technology's operation (1980-84), utilized information collected by the Commonwealth Department of Health concerning the Medicare rebate schedules.[2] The costs of an IVF treatment cycle were ascertained through the charging system of Medicare. In addition to listing the various procedures involved in an IVF treatment cycle, the costs of each procedure and the direct government contribution to it were calculated. The typical costs associated with the pre-laparoscopy stage of IVF were totalled and then added to the typical costs of IVF treatment from laparoscopy to assessment of pregnancy. On this basis the total cost of a treatment cycle was estimated at $3738, of which the direct contribution of government was $2665. Note that, unlike the Netherlands study, no attempt was made to cost on the basis of differences in treatment scenario, organizational size or structure. Instead an average scenario of IVF treatment was used and the results were presented in terms of the number of hormonally defined pregnancies relating to the number of treatment cycles.

From information collected at Monash Medical Centre, Bartels concluded that 1775 treatment cycles gave rise to 229 hormonally defined pregnancies, yielding a ratio of 7.75 to 1 for the average number of treatment cycles per hormonally defined pregnancy. During the period 1980 -1984 there were 909 hormonally defined pregnancies recorded. But success at Monash Medical Centre is generally higher than at other centres, so to take account of this it was assumed that about twice as many treatment cycles per hormonally defined pregnancy were required at other centres. This would lead to around 12,000 treatment cycles performed in Australia in the five year period 1980-84. This implies a cost of $2665 x 12,000 or a figure of $31.98 million for the direct government expenditure on IVF treatment in Australia during 1980 -1984. By combining this estimate with information on the number of live birth pregnancies achieved over the same period, Bartels estimated that direct Government expenditure was $64,500 per live birth on average.

Gail Batman's discussion paper on IVF estimated the total cost for the provision of IVF in Australia in one year, 1987.[14] The estimates were obtained from information collected in Commonwealth Government statistics. In a similar exercise to that previously undertaken by Bartels, the cost of an average treatment cycle was estimated and was found to be $3574. This figure was then multiplied by the number of treatment cycles undertaken in that year to obtain an estimate of total

expenditure of $30 million in 1987, with Commonwealth Government outlays being approximately $17 million. If this estimate is divided by the number of live birth pregnancies relating to IVF in the same year (National Perinatal Statistics Unit), this averages out at a total cost of $33,000 per birth with Commonwealth Government contributions totalling $18,500. This estimate of Government expenditure per live birth is considerably lower than that quoted three years earlier by Bartels. However, Batman's estimate of the extent of Government financing as a percentage of total expenditure was lower than that claimed by Bartels (government contribution of 56% as opposed to 71%).

In spite of this difference, Batman's evidence indicated that the costs of providing IVF treatment in Australia had lowered quite considerably in the period 1984-1987 compared to in earlier years.

The Western Australian Government commissioned a study to monitor and evaluate the practice of IVF and related procedures such as GIFT in Western Australia.[3] Item numbers, rebate types, frequency and costs associated with treatment were all recorded for a 10% sample of all IVF and GIFT treatment cycles undertaken in Western Australia between January 1983 and December 1986. Cost calculations were split into two components: retrospective costs (costs up to delivery) and prospective costs (costs from delivery to discharge from the hospital of birth). Following the actual treatment cycle, additional costs were assigned if required, e.g. a failed pregnancy requiring further treatment. Average costs associated with normal delivery, early admission of mothers, caesarian section and special care were also assigned at a later date.

By 1986, the mean cost of an IVF treatment cycle was $3,893. By far the greatest contribution to the weighted treatment cycle cost for IVF came from the most likely outcome, failure of a woman to become pregnant. Government contributions to these total costs were estimated and at approximately 50% overall were considered as quite considerable. The mean prospective costs were estimated at $3,750. The authors pointed out that the true cost of a pregnancy must include not only the cost of a successful treatment cycle, but also the cost of all failed treatment cycles. Given a 10% success rate then the true costs of one IVF live birth include the cost of one treatment cycle divided by the probability of success plus the mean prospective costs of delivery. Calculated in this manner, the costs of one IVF live

birth were $42,927. The benefits of the IVF programme were presented in terms of the number of live births as a percentage of the number of treatment cycles.

The comparison of IVF with alternative procedures for the treatment of infertility has been considered in some cases e.g. in the Western Australian study IVF was compared with GIFT as a procedure.[3] Because of the relatively higher success rates of GIFT, (approximately a 25% success rate), the total cost of each GIFT new born was roughly half that of IVF - $21,635. The study concluded with the recommendation to the Commonwealth Government of the need for randomized control trials to determine the true effectiveness of IVF. Also called for were long term follow up studies of the children born under the IVF programme and the participants.

In the study undertaken in the Netherlands by Ger Haan, IVF was compared with tubal surgery as a treatment option.[10] Treatment costs for tubal surgery are between NLG 5000 - 7000, and additional health care costs are NLG 5500 - 7000. The success rate in terms of the birth of a live born infant is 30%. On average three IVF episodes are needed to reach an on going pregnancy chance of 30% . The average costs per on going pregnancy for the treatment possibility three IVF episodes are about 7,500 which is approximately equal to that of one tubal reconstruction operation. It must be noted, however, that between patient groups there are great differences in results, both for IVF and for tubal surgery. As suggested earlier in this paper, according to the diagnosis of infertility some patient groups are better off with IVF and others with tubal surgery. Therefore, it is not satisfactory to consider tubal surgery and IVF as direct substitutes in the treatment of infertility for all patient groups. The study authors conceded that this was the case in fact. On the basis of the findings of this study, the Health Insurance Executive Board recommended that reimbursement to patients for the cost of entering an IVF programme should occur. It is interesting to note, however, that an initial discussion of the financing of the IVF programme eventually turned into a general discussion of fertility treatments and the level of financial provision which should be given to this whole area vis-a-vis other unrelated procedures in health care eg cardiology, paediatrics, etc.

Summary of the Literature Reviewed from an Economic Viewpoint

AUTHOR/S	TYPE OF STUDY	DATA SOURCE AND SIZE
Haan G. (1990)	Cost-effectiveness study of IVF	All couples registering for IVF from August 1986 until June 1988 in five major Dutch Hospitals. Sample consisted of 1462 couples and a total of 3092 treatment cycles.
Page H. (1989)	Economic Appraisal of IVF	Survey of two Regional Health Authorities. Sample consisted of 400 couples treated over a period of one year. Average of 3 treatment cycles per couple was assumed.
Bartels D. (1987)	Economic Appraisal of IVF	Survey of medicare rebates offered in the period 1980-1984 for IVF treatment. Expenditures are calculated in 1987 prices based on information supplied by the Commonwealth Department of Health.
Webb S.M. Holman C.D.J. (1990)	Demographic, clinical and economic assessment of IVF	All couples who began IVF treatment in Western Australia between January 1983 and June 1987. In total 1,240 couples were surveyed. A total of 2,982 treatment cycles were commenced in this period.
Batman G. (1987)	Economic Appraisal of IVF	Commonwealth Government statistics of expenditure on IVF Australia wide in 1987. Also information on IVF birth rates supplied by the National Perinatal Statistics Unit.

AUTHOR/S	METHOD	RESULTS	COMMENTS
Haan. G (1990)	The calculations of the real costs of IVF were differentiated according to the size and scale of the operation. Data utilized for costings was provided by the financial departments of the hospitals.	For an IVF programme of 375 started treatments annually, average costs per started IVF treatment are between NLG 2600 and 3300 (NLG 1 = US $0.50). The costs of an expanded programme are lower (1). The success rate of treatment was 10%.	1. The authors concentrated on the actual costs of treatment. Capital costs were excluded from the analysis. An interesting observation was the finding that the costs of treatment were variable according to the organizational structure and the diagnosis of infertility. Range was NLG 22,000 for tubal pathology to NLG 43,000 for male factor infertility.
Page H. (1989)	The costs of adding IVF to three centres already offering specialist infertility services in the UK were calculated.	The average annual cost of IVF was calculated by adding together the estimated running costs of the three units, which totalled _439,739 per annum (1).	1. Capital costs were included in the analysis in the form of the annual equivalent cost of buildings.
Bartels D. (1987)	The costs of an average treatment cycle are calculated from information supplied by Monash Medical Centre. The government contribution to this figure was calculated and then multiplied by the number of treatment cycles undertaken in the period to provide an estimate of total Government expenditure.	The costs of a typical treatment cycle in 1987 prices was $3,738 of which the Government contribution was $2,665. The total direct Government contribution to IVF expenditure in the period 1980-84 was approx. $32 million (1).	1. Bartels' estimates are low because she does not take account of government expenditure over and above the direct costs of treatment cycles, nor the expenditure of the government in regard to the pregnancy and live birth complications frequently associated with IVF treatments.

AUTHOR/S	METHOD	RESULTS	COMMENTS
Webb S.M./ Holman C.D.J. (1990)	A 10% sample of treatment cycles was followed up and the costs associated with each were calculated. Additional costs following the actual treatment costs were assigned later. The outcomes of all treatment cycles were recorded and the likelihood of a treatment cycle resulting in a live birth was estimated.	By 1986, the mean cost of each IVF treatment cycle was $3,893. The average cost of a liveborn infant requiring neo-natal care was much higher at $12,886.	Valuable information which would have enabled a more complete evaluation was not forthcoming because the project leaders were thwarted by a lack of cooperation from some clinicians in the area. In spite of these problems the study remains the most comprehensive so far undertaken within Australia.
Batman G (1987)	From Commonwealth Government statistics, information relating to the number of treatment cycles carried out in Australia in 1987 was obtained. From Hospital statistics an estimate was made of the cost of a typical IVF treatment cycle and hence of the total cost of IVF in 1987.	The results suggest that the total expenditure on IVF in 1987 was $30 million. An estimate of Government expenditure per livebirth of $18,500 was substantially lower than Bartels estimate of $64,500 (1).	1. Batman utilized a figure of 56% of total expenditure coming from Government sources as opposed to an estimate of 71% from Bartels. Despite this possible under-representation of the Government contribution, the results still suggest a lowering of the costs of IVF over time.

Problems of Analysis from an Economic Viewpoint

The economic assessment studies of IVF so far undertaken have differed in terms of the viewpoint of the analysis, and the method of cost calculations employed. To a large extent the different results for the costs of IVF cited above depend upon the viewpoint of the analysis taken. By contrast, the benefits of IVF treatment are almost always presented in the same format, the number of live births as a percentage of the total number of treatment cycles. This figure remains remarkably consistent between studies at approximately 8 - 10%. The economic appraisals so far undertaken can be criticized because they offer only partial evaluation. Results are presented in terms of the actual resource costs of IVF per

liveborn infant. Presented in this way the results offer little scope for the comparison of IVF with other treatments and procedures competing for health care dollars, in terms of value for money.

If we accept the World Health Organization's definition of health as 'a state of complete physical and mental well being' then it must be accepted that there are two sides to health improvement, physical health improvement and psychological health improvement.[5] For women who participate in the programme, the outcome is predominantly a psychological effect.[17] It is necessarily related to success (or otherwise) in the programme - where success is defined in terms of a liveborn baby and its health. However, it is a distinct outcome in itself and should therefore be treated as such for the purposes of evaluation.

Section Five: Suggested Framework for Evaluation of the IVF Programme

It appears that no one in Australia (or indeed overseas) has attempted to undertake a comprehensive cost-benefit analysis of the IVF programme to date. A correct evaluation should consider all costs (both direct and indirect) and all benefits of treatment, according to the criteria established earlier in this paper.

Currently a large research effort is focusing on the desirability of QALYs as a guiding mechanism for resource allocation decisions within health care. Unfortunately, there are some obvious problems in using QALYs to evaluate the IVF programme, as it presents us with some difficult questions which are not easily answered. In particular, there are two main issues:-

1. Do we value the maintenance of an existing life in the same way as we value the creation of a new life? The answer might well be no, and then the question becomes how can we make meaningful comparisons using cost per QALY data of IVF with, for example, kidney transplantation which improves the length and quality of life of an existing individual?

   The willingness to pay approach can be utilized to gain values from a sample of the general population as to the relative importance of the provision of IVF versus other more conventional heallth care programmes. This would also be the case if QALY measures were utilized using utility values elicited from the general population, where the benefits of IVF were assumed only to accrue to the couples who go through the IVF programme, rather than the live born infants conceived.

2. In theory all benefits of IVF treatment must be included in any economic evaluation. However,in practice this has not been the case. Both the willingness to pay and Dalton's analysis quantify only the benefits to parents of the provision of treatment, whereas the studies measuring the quality adjusted life years of children measure benefits to children. Each set of studies ignores the other benefit. It can be argued that each set of benefits is probably independant and therefore should be treated as such for the purposes of an evaluation.

I propose that a study should be initiated which enables two types of analyses to take place simultaneously. The first approach is to calculate the cost per quality adjusted life year, where the benefit is assumed to accrue to the child. The second approach is to calculate the cost per quality adjusted life year, where the benefits are assumed to accrue to the couples involved in receiving treatment. A comparison of results, depending upon the perspective taken for the analysis, would then be possible.

The outcome of interest for the couples involved is primarily a psychological effect (either positive or negative) and not a physical health effect as such.[17] This is not to deny that involvement in the programme does not have some uncomfortable physical health side effects. However, what we are interested in primarily is health outcome, and I would suggest that the psychological outcomes of treatment are likely to be the predominant ones in this instance. Herein lies a problem for researchers, since the traditional health status scales, e.g. the Rosser Index, are inappropriate for the evaluation of IVF, as they are not sensitive to the psychological effects of treatment. In addition, they do not include such factors as marriage satisfaction, sexual functioning or reproductive ability. One possibility might be to develop programme specific descriptions of outcome states following treatment. These profiles could be built up from information presented in the literature, and/or by questioning a representative sample of couples who have been through the IVF programme about their outcome experiences. A random sample of the general population would then be asked to value each of the possible outcome states on an interval scale. These values could then be elicited to obtain QALY measures. As discusssed earlier in the paper, another favoured approach to eliciting QALY valuations concerning the health state scenario is the time trade off technique. Individuals would be asked to trade off different outcome states following treatment. In addition, one could gain an indication of the value individuals place on the provision of assisted reproduction programmes such as IVF by obtaining preferences between long term childlessness and other chronic states of ill health.

Conclusion

A cost-utility analysis of the IVF programme would provide useful information, which is currently not available, concerning the importance that individuals place on infertility and its treatment. More specifically, individual preferences for expenditure on IVF versus other more conventional procedures in health care could be assessed. A two pronged analysis, which measures the benefits of the procedure in relation to a) the couples involved and b) the live born infants, should also reveal useful information concerning the effect of the procedure on the majority of couples for whom IVF is not successful, and enable an interesting comparison of results relating to the perspective taken for the analysis. In addition, the utilization of a common unit of measurement (the QALY) will allow IVF to be evaluated in cost per QALY terms, thus providing a basis for inter-programme comparisons with other procedures in health care.

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