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ORIGINAL ARTICLE *Infertility*

A cost-effectiveness analysis of *in-vitro* fertilization by maternal age and number of treatment attempts

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BACKGROUND: The increase in use and costs of assisted reproductive therapies including *in-vitro* fertilization (IVF) has led to debate over public funding. A decision analytic model was designed to estimate the incremental cost-effectiveness of IVF by additional treatment programmes and maternal age.

METHODS: Data from the Australian and New Zealand Assisted Reproductive Database were used to estimate incremental effects (live birth and other pregnancy outcomes) and costs for cohorts of women attempting up to three treatment programmes. A treatment programme included one fresh cycle and a variable number of frozen cycles dependent on maternal age.

RESULTS: The incremental cost per live birth ranged from AU$27 373 and AU$31 986 for women aged 30–33 on their first and third programmes to AU$130 951 and AU$187 515 for 42–45-year-old women on their first and second attempts. Overall, these trends were not affected by inclusions of costs associated with ovarian hyperstimulation syndrome or multiple births.

CONCLUSIONS: This study suggests that cost per live birth from IVF increases with maternal age and treatment programme number and indicates that maternal age has the much greater effect. This evidence may help decisionmakers target the use of IVF services conditional on societal willingness to pay for live births and equity considerations.

Key words: cost / cost-effectiveness / assisted reproduction / *in-vitro* fertilization / economic

Introduction

Couples in developed countries are increasingly turning to assisted reproductive technology (ART) to achieve pregnancy and live birth. European registry data from 28 national registers show a 13% increase in the use of ART services from 2002 to 2003 (Andersen *et al.*, 2007), whereas US and Australian data indicate a 6.5 and 16% increase, respectively, during the same period (Centers for Disease Control and Prevention, American Society for Reproductive Medicine, 2004; Australian Government Department of Health and Ageing, 2006). The rise in demand for ART services has resulted in substantial rise in costs to government. In Australia, increased demand, relatively unrestricted access to fertility services and a cap on medical expenses borne by patients saw government expenditure on ART services more than double from $66.3 million to $156.1 in the five-year period from 2000 to 2005 (Australian Government Department of Health and Ageing, 2006).

The increasing financial burden associated with ART services has led to intense debate over the appropriate level of public funding of women with a low chance of success. This debate is fuelled by evidence that the effectiveness of ART may vary substantially according to characteristics of the treated population, in particular by maternal age and also by the number of previous attempts at therapy. The US CDC registry data indicate women aged 43 and above undertaking ART may have only a 2% probability of achieving a successful live birth compared with 16% for women aged 40 and 37% for those aged under 35 (National Center for Chronic Disease Prevention and Health Promotion, 2002). Other studies have shown that the effectiveness of ART across all age groups decreases with each successive attempt at therapy (Allgood, 2003; Vahratian *et al.*, 2003; Centers for Disease Control and Prevention, 2004).

Data limitations have previously restricted the opportunity to examine costs and effects of treatment by both maternal age and the number of attempts at therapy combined, thus there has generally been limited economic evidence available to inform policy decisions (Australian Government Department of Health and Ageing, 2006). Nonetheless, restrictions to public funding for fertility treatment by maternal age and by the number of attempts at therapy already exist in many developed countries (Australian Government Department of Health and Ageing, 2006).

This study was performed as part of a broader assessment of ARTs conducted for a ministerial review (Australian Government Department of Health and Ageing, 2006). The primary objective was to provide decisionmakers with economic evidence to assist decisions about appropriate public funding for ART services. The incremental costs and outcomes of *in-vitro* fertilization (IVF) therapy were estimated by maternal age and the number of treatment attempts (treatment programme number) applying both fresh- and frozen-cycle IVF data. Tabulated registry data on IVF outcomes were provided by the AIHW National Perinatal Statistics Unit, which maintains the Australian New Zealand Assisted Reproduction Database (ANZARD). This database recorded data for 36 483 ART treatment cycles undertaken in 2002 in Australia and New Zealand (19 883 fresh non-donor treatment cycles and 11 370 frozen non-donor cycles), including the success rates for more than 99% of all cycles (Bryant *et al*., 2004). The average maternal age was 35.2 years, and the live birth rate was 18.3% for all fresh, non-donor ART cycles started, and 20.4% per ovarian pick-up (OPU) for fresh IVF (without intracytoplasic sperm injection) non-donor cycles. Of all ART cycles, 94.2% transferred either one or two embryos. Approximately 70% of all deliveries were a BESST (Birth Emphasising a Successful Singleton at Term) outcome, and 22% of infants were born with a low birthweight (<2500 g). It should be noted that the data set used in this analysis was limited to Australian reported IVF data only.

Materials and Methods

A decision analytic model was constructed to estimate incremental effects (live birth and other pregnancy outcomes) and resource use of an additional treatment programme conditional on maternal age and number of previous treatment programmes. Treatment programmes were modelled to commence with ovarian stimulation therapy and comprised one fresh cycle (treatment using fresh embryos) plus a variable number of frozen cycles (treatment using frozen embryos). This is consistent with previous ART decision analytic models (National Collaborating Centre for Women's and Children's Health, 2004). However, unlike such previous analyses, the number of frozen cycles was modelled dependent on maternal age, and pregnancy outcomes were modelled dependent on both maternal age and number of treatment attempts.

Outcomes and associated costs of IVF therapy considered for both fresh and frozen cycles included no pregnancy and clinical pregnancy. The data did not include cycles involving ICSI or GIFT. It was assumed that pregnancies without a live birth (ectopic pregnancy, miscarriage and stillbirth) did not prevent further frozen cycles, nor the commencement of subsequent fresh treatment programmes. IVF therapy was modelled to cease once a successful live birth was achieved or couples discontinued treatment.

Previous studies have indicated that discontinuation rates increase with age (Mardesic *et al*., 1994), the number of new fresh treatment cycles commenced (Schroder *et al*., 2004) and pregnancy (Chambers *et al*., 2005). Discontinuation rates in this study have been modelled dependent on treatment programme and age, calibrated to reflect ANZARD distribution of patients across treatment programmes in 2002. The model structure is depicted in Fig. 1.

Methods for modelling effects

ANZARD 2002 registry data were used to model both fresh- and frozen-cycle clinical pregnancy rates and outcomes by treatment programme number (Table I), with the latter being self-reported by women undergoing therapy. Pregnancies and live births were estimated directly from ANZARD data based on maternal age categories (30–33, 34–37, 38–41 and 42–45 years) and number of previous IVF treatment programmes. Relative rates of miscarriage, ectopic pregnancy and stillbirth were estimated as a proportion of pregnancies not resulting in live birth for each maternal age group based on data for all treatment programmes combined; small cell sizes in ANZARD data prevented direct estimates of these rates by treatment programme and by maternal age.

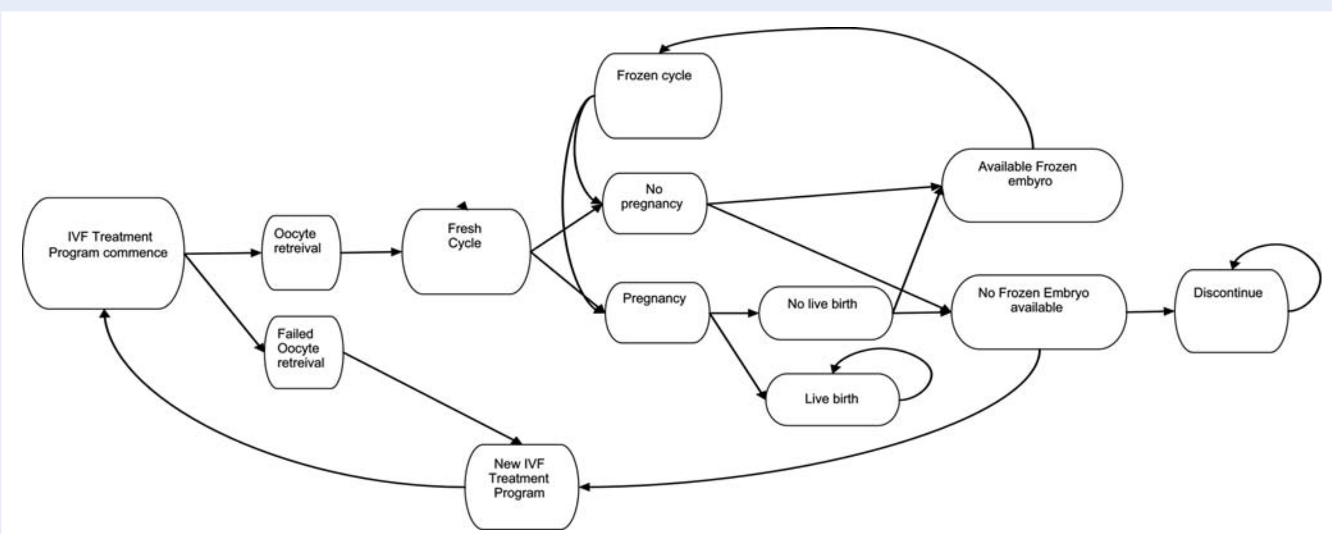

Figure 1 Model structure.

Table I Model inputs

Variable[a]	Treatment programme	Maternal age			
		30–33	34–37	38–41	42–45
Fresh-cycle pregnancy rates (actual ANZARD data)	1	0.32	0.28	0.20	0.07
	2	0.28	0.28	0.20	0.09
	3	0.25	0.28	0.20	–
Fresh-cycle live birth rates as a proportion of pregnancies (actual ANZARD data)	1	0.81	0.78	0.67	0.72
	2	0.77	0.78	0.67	0.31
	3	0.76	0.78	0.67	–
Frozen cycles undertaken per treatment programme[b]	All	0.77	0.65	0.48	0.27
Frozen-cycle pregnancy rates[c]	All	0.22	0.21	0.16	0.12
Frozen-cycle live birth rates[c]	All	0.80	0.73	0.67	0.54
Discontinuation rates[d]	1	0.20	0.25	0.25	0.30
	2	0.30	0.40	0.40	0.50
	3	0.40	0.45	0.45	0.50
OHSS[e]	All	0.018	0.012	0.007	0.001
Proportion of singleton births	All	0.78	0.83	0.86	0.87
Proportion of twin births	All	0.21	0.17	0.14	0.12
Proportion of HOMs	All	0.01	0.01	0.01	0.01
Proportion of low-birthweight babies single, twin and HOMs		Single	Twin	HOMs	
<1 kg	All	0.01	0.04	0.23	
1–1.5 kg	All	0.01	0.05	0.26	
1.5–2 kg	All	0.02	0.13	0.31	
2–2.5 kg	All	0.04	0.27	0.12	
>2.5 kg	All	0.92	0.52	0.07	

[a]Model inputs based on ANZARD 2002 unpublished registry data provided for the purposes of the Independent Review of ART (Ref DOHA 2006) by the Australian Institute of Health and Welfare National Perinatal Statistics Unit.
[b]Estimated from a simulation model based on the number of frozen embryos available and transferred by age. Cross-calibrated with ANZARD data. Reported rates represent the average across all treatment programmes.
[c]In the absence of data from ANZARD, frozen-cycle outcomes were assumed to be independent of the treatment programme number but dependent on maternal age.
[d]Discontinuation was assumed to occur at the end of a treatment programme (both fresh and frozen cycles).
[e]ANZARD data suggested that 1.1% of women suffered OHSS. Expert opinion was used to estimate OHSS rates by maternal age group.

Frozen cycles within a treatment programme were modelled as ceasing when all viable frozen embryos were used or a live birth was achieved. Age and cycle data were not tracked by individual women, which precluded direct analysis of the number of frozen cycles undertaken per fresh cycle. The proportion of frozen cycles undertaken in each treatment programme was therefore modelled using ANZARD 2002 data on the number of frozen embryos available and successfully transferred by maternal age. The modelled rates were cross-validated against the ratio of fresh to frozen cycles undertaken in 2002.

Statistical methods

ANZARD 2002 data were used to model the odds of a live birth for women undertaking IVF by maternal age and number of treatment programmes. The economic model compared age groups 34–37, 38–41 and 42–45 against the youngest age group (30–33) and by treatment programme in the youngest and oldest cohorts. Statistical analyses were undertaken to estimate the strength of the effect by maternal age and treatment programme number.

Cost and cost-effectiveness methods

Expected costs associated with IVF therapy and pregnancy outcomes were based on existing treatment patterns and resource use in Australia (Table II). Costs are in Australian 2005 dollars and include direct costs of treatment based on expected average clinic fees (Australian Government Department of Health and Ageing, 2006). In the base case analysis, costs were consequently modelled from a limited societal perspective and incorporated Australian Commonwealth Medicare fees plus patient born gap payments. A short time horizon was assumed, consequently no discounting was applied. Estimated costs and effects were used to calculate incremental costs and effects and the incremental cost-effectiveness ratio for each additional treatment programme by maternal age.

A probabilistic sensitivity analysis was performed to model the effect of joint parameter uncertainty on the incremental cost-effectiveness ratios. Beta distributions were applied to probabilities for pregnancy and live birth rates and gamma distributions to cost estimates, and a dirichelet distribution was used to model the proportion of live births resulting in stillbirth, miscarriage or ectopic pregnancy. Direct costs of IVF treatment or adverse events were assumed to fall within 10% of estimated figures in sensitivity analyses.

One-way sensitivity analyses were also conducted on model parameters to test the effect on the incremental cost per live birth of varying one parameter at a time. In the first sensitivity analysis, a government rather than societal perspective was taken, with costs included restricted to direct government-incurred costs. A second sensitivity analysis was undertaken to consider the impact of including costs of ovarian hyperstimulation syndrome (OHSS). OHSS costs could not be appropriately applied in the base case analysis, as it was not possible to include both the effects and costs of

Table II Costs of fresh-cycle IVF treatment

	MBS item no.[a]	MBS fee (100%) ($)	Quantity	Estimated clinic fee ($)[b]	Resource use ($)[c]
Fresh-cycle (failed oocyte pick-up) total cost					5541
Fresh-cycle (with embryo transfer) total cost					7179
Planning and management	13 209	74	1	620	
Stimulated IVF treatment (including all examinations, treatment counselling, pathology)	13 200	1730	1	3301	
Oocyte pick-up	13 212	315	1	312	
Anaesthetist (oocyte pick-up) 16-20 min	23 021	34		420	
Oocyte pick-up hospital day bed charge	NA		1	335	
Oocyte pick-up theatre fees	NA		1	310	
Preparation of semen	13 221	45	1	119	
Transfer of embryos	13 215	99	1	142	
Pharmaceutical[d]				1620	
Frozen-cycle total cost					2279
Planning and management	13 209	74	1	620	
Preparation and transfer of frozen embryos	13 218	742	1	1184	
Embryo freezing (per batch)			1	175	
Embryo storage (1 year)			1	300	
IVF treatment programme outcome	AN-DRG[e]				
Miscarriage termination or reduction	O40Z				1545
Live birth (vaginal delivery single)	O60D				3323
Ectopic pregnancy	O03Z				3574
Stillbirth (vaginal delivery with complications)	O60B				4145
Sensitivity analyses					
Neonatal care <750 g	P61Z				113 461
Neonatal care 705 g–1 kg	P62Z				85 338
Assumed 50% <750 g; 50% 750 g–1 kg					
Neonatal care 1–1.25 kg	P63Z				35 690
Neonatal care 1.25–1.5 kg	P64Z				26 081
Assumed 50% 1–1.25 kg; 50% 1.25–1.5 kg					
Neonatal care 1.5–2 kg	P65B				18 687
Neonatal care 2–2.5 kg	P66B				12 227
Live birth (Caesarean section)	O01B				8105
Single birth 50% Caesarean birth					
Twins 75% Caesarean birth					
HOMs 95% Caesarean birth					
Treatment of OHSS	X63A				5012

[a]MBS—Medicare Benefits Schedule fee taken from the 2005 schedule.
[b]Estimated clinic fee provided by the Australian Commonwealth Department of Health and Ageing (Australian Government Department of Health and Ageing, 2006).
[c]Direct costs of treatment estimated in Australian 2005 dollars.
[d]Estimated pharmaceutical costs from the Australian Government Department of Health and Ageing (2006).
[e]AN-DRG denotes Australian National Diagnostic Related Groups. Costs of miscarriage, live birth, ectopic pregnancy and stillbirth sourced from AN-DRG 2003/2004 and indexed to 2005 (Australian Government Department of Health and Ageing, 2007).

OHSS given the incremental cost-effectiveness ratio measure (cost per live birth) excluded maternal outcomes. Event rates for OHSS were modelled from ANZARD 2002 data (rate for all ages), which suggested 1.1% of women suffered OHSS (Bryant *et al.*, 2004). Younger women have a higher propensity towards developing OHSS than older women (Whelan and Vlahos, 2000), and rates were consequently adjusted to reflect this on the basis of expert opinion (Table I).

A final sensitivity analysis was undertaken to extend the model to include potential estimates of neonatal costs and outcomes resulting from multiple births. Published ANZARD data were used to estimate rates of twin and higher order multiple births and the proportion of low weight babies by maternal age (Bryant *et al.*, 2004) (Table I), and Australian National Diagnostic Related Group (AN-DRG) costs per inpatient episode by birthweight were subsequently applied. However, while neonates of low birthweight (<2.5 kg) were modelled as incurring additional inpatient expenses in this sensitivity analysis, it should be noted that only the initial inpatient episode was included for each low-birthweight baby. Additional modelled costs for low-birthweight babies therefore do not allow for costs beyond inpatient separation and consequently may be conservative estimates of additional treatment costs to society. Costs for delivery and neonatal care were estimated for each infant delivered and were consequently multiplied for twin births or higher order multiples (HOMs). In this analysis, it was assumed that 50% of single births, 75% of twin births and 95% of HOMs were by Caesarean section and the remainder were vaginal births based on ANZARD 2002 data. ANZARD neonatal death rates to 28 days were used to model effects and the outcome was considered to be one live birth delivery under the assumption that the desired outcome was a single live birth (or BESST) outcome.

Results

The odds of a live birth decreased with increasing maternal age group ($P < 0.0001$). A similar analysis across all age groups by treatment programme showed significant evidence of a decrease in the odds of live birth as the number of treatment programmes increased after controlling for maternal age ($P = 0.038$). However the reduced odds of a live birth by increasing number of treatment programmes was only evident in the youngest and oldest age groups (Table I). The expected incremental cost, effects and incremental cost-effectiveness (incremental cost per additional live birth) are reported by maternal age and by treatment programme number in each age group. These results are presented in Table III and graphically on the incremental cost-effectiveness plane (Fig. 2). The incremental cost per live birth for women aged 30–33 increased from AU$27 373 for the first treatment programme to AU$30 098 for a second programme and AU$31 986 for a third programme. In comparison, the incremental cost per live birth for women aged 42–45 increased from AU$130 951 for the first treatment programme to AU$187 515 for a second treatment programme.

Sensitivity analyses

The probabilistic sensitivity analyses (Table III) indicate greatest uncertainty in the incremental cost-effectiveness ratios for the 42–45 age group, although the incremental cost per live birth remained substantially higher for the 42–45 age group than for younger age groups even at the lower bound confidence interval for the first treatment programme (incremental cost AU$93 030–AU$195,935). The wider confidence intervals in the 42–45 age group reflect the smaller number of women and fewer live birth events in this age category.

Results of one-way sensitivity analyses are depicted graphically in the Tornado diagram (Fig. 3). This figure shows the effect of varying one model assumption at a time on the incremental cost per live birth for women aged 42–45, treatment programme one while keeping other parameters equivalent to the base case. Each bar represents changes in a single assumption; a wider bar indicates that the incremental cost per live birth was more sensitive to a change in that parameter. Applying government perspective costs reduced the incremental costs per live birth across all age groups by more than one-third (Table IV). The results of other one-way analyses showed that the incremental cost per live birth was most sensitive to variations in fresh-cycle pregnancy and live birth rates within specified confidence limits. The incremental cost per live birth ranged between AU$100 180 and AU$190 056 for the upper and lower confidence intervals for fresh-cycle pregnancy in women aged 42–45.

The inclusion of post-natal costs of multiple births in the alternative modelled analysis increased the overall incremental cost per live birth across all age groups. Analyses suggested that the relative increase in the incremental cost per live birth would be greatest in the younger age groups due to the greater propensity towards live births (and hence multiple births). The incremental cost per live birth was estimated to be approximately 1.7 times higher than base case values for the 30–33 age group, but 1.1 times higher for 42–45 year olds. However, overall there was little effect on the general trend of a higher incremental cost per live birth in the older age groups and successive treatment programme numbers (Tables I and V). The inclusion of costs for OHSS had little impact on ICER estimates; the incremental cost per live birth increased from AU$27 373 to AU$27 753 for women aged 30–33 and from AU$130 951 to AU$130 959 for women aged 42–45, for the first treatment programme.

Discussion

The data from our evaluation are designed to help decisionmakers balance evidence on incremental costs, effects and cost-effectiveness of IVF by the number of treatment programmes as well as by age.

Table III Base case analysis: incremental cost per live birth by maternal age and treatment programme based on Australian Commonwealth Government Medicare-incurred costs plus patient born gap payments

Incremental cost per live birth	Maternal age			
	30–33	34–37	38–41	42–45>
Treatment programme 1 versus 0	$27 373 ($25 787–$29 181)	$32 564 ($30 708–$34 692)	$51 635 ($47 195–£56 816)	$130 951 ($93 030–$195 935)
Treatment programme 2 versus 1	$30 098 ($27 535–$32 785)	$32 564 ($30 708–$34 692)	$51 635 ($47 195–£56 816)	$187 515 ($117 925–$326 867)
Treatment programme 3 versus 2	$31 986 ($28 156–$36 521)	$32 564 ($30 708–$34 692)	$51 635 ($47 195–£56 816)	

95% confidence interval in brackets estimated from probabilistic sensitivity analysis.

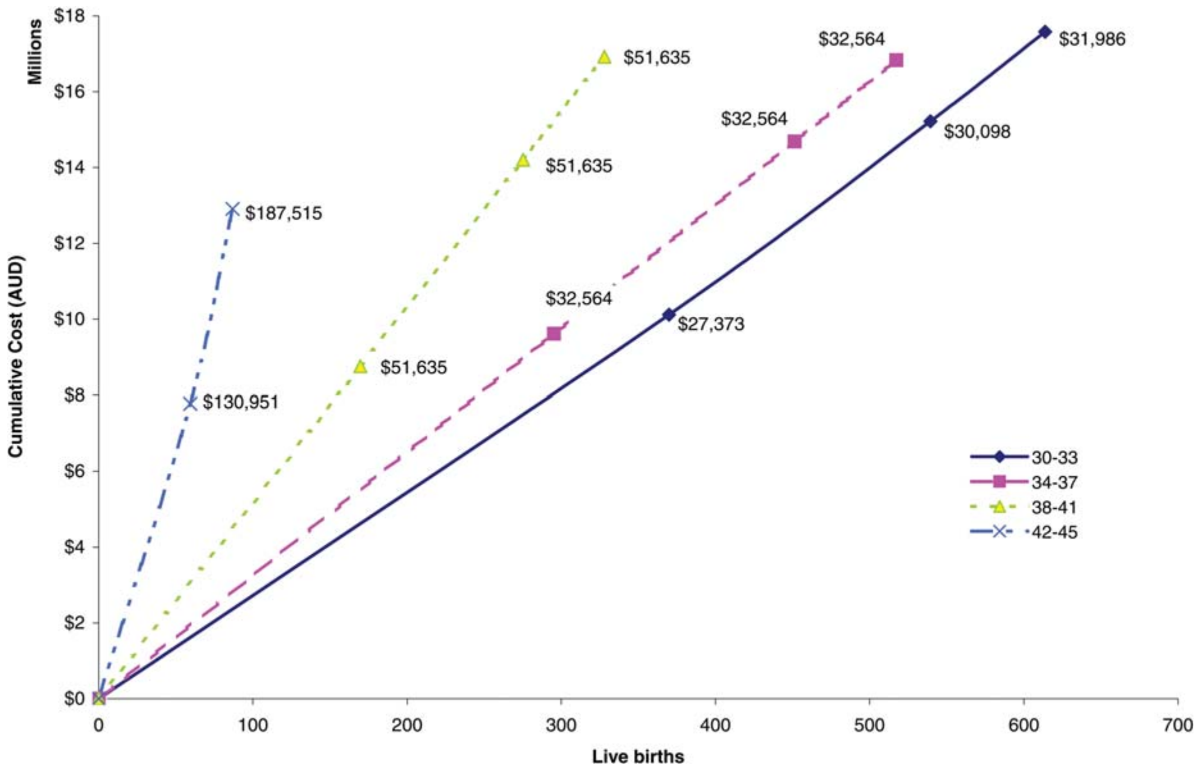

Figure 2 Cumulative costs and live births per 1000 women commencing IVF and incremental cost per live birth by maternal age and treatment programme.

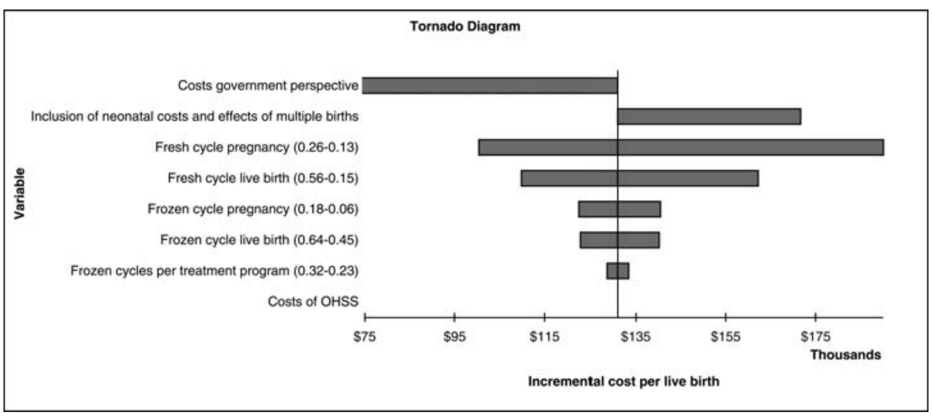

Figure 3 One-way sensitivity analyses (maternal age 42–45, first treatment programme).

This study suggests that the incremental cost per live birth increases both with maternal age and sometimes with the number of additional treatment programmes (IVF attempts from ovarian stimulation cycle, with fresh and frozen embryos). However, the number of previous attempts at IVF appears to have a smaller impact on the incremental cost per live birth than maternal age. The incremental cost per live birth increased moderately by each additional treatment attempt for women aged 30–33, with approximately $4500 per live birth difference between the first and third treatment programmes. This may suggest that there is little economic evidence to restrict funding to less than three programmes (fresh plus frozen cycles) in younger women, subject to the decisionmakers' willingness to pay for a live birth threshold. The additive effects of age and treatment programme combined to magnify differences in cost-effectiveness with later treatment programmes for women aged 42–45. In this age category, the difference in the cost per live birth between the first and third attempts was more substantial, with an increase of approximately AU$56 000 from the first to the second attempt (Table III).

Table IV Results of sensitivity analysis: incremental cost per live birth by maternal age and treatment programme (Australian Commonwealth Government Medicare-incurred costs only)

Incremental cost per live birth	Maternal age			
	30–33	34–37	38–41	42–45
Treatment programme 1 versus 0	$16 028	$18 931	$29 506	$73 401
Treatment programme 2 versus 1	$17 428	$18 931	$29 506	$105 109
Treatment programme 3 versus 2	$18 308	$18 931	$29 506	

Table V Results of sensitivity analysis including costs and effects of multiple births based on Australian Commonwealth Government Medicare-incurred costs plus patient born gap payments

Incremental cost per live birth	Societal perspective			
	30–33	34–37	38–41	42–45
Treatment programme 1 versus 0	$51 285	$52 726	$73 848	$171 651
Treatment programme 2 versus 1	$55 312	$52 726	$73 848	$242 484
Treatment programme 3 versus 2	$57 881	$52 726	$73 848	

A simple sensitivity analysis which took into account neonatal costs for one inpatient episode confirmed that the incremental cost per live birth would be higher across all age groups with the inclusion of the costs and effects of multiple births and given a preference for a BESST outcome. The increase in the incremental cost per live birth is proportionally greater in the younger age groups given the inclusion of costs and effects of multiple births due to their higher propensity for live births, although the overall trend of a high cost-effectiveness ratio in older women and successive treatment programme numbers remained. Further research into the costs-effectiveness of IVF treatment including neonatal costs and outcomes is required.

We have used data from a population-based register (ANZARD) which captured >99% of ART cycles in Australia and New Zealand in 2002 (Bryant *et al*., 2004). These data are acknowledged as providing the highest quality of epidemiological data available (Tyldesley *et al*., 2001). Nonetheless, it is recognized that there are limitations inherent to the 2002 ANZARD data collection and the subsequent analysis, which should be considered during the interpretation of results. In particular, it is noted that the number of treatment attempts reflects less reliable data than maternal age. While it has been assumed for this analysis that the number of previous attempts at therapy has been reported by fresh OPU, this definition may not have been strictly adhered to in the 2002 data collection given self-reported outcomes. It is also noted that frozen cycles undertaken were not tracked by individual women, which prevented direct estimation of the number of frozen cycles undertaken per fresh cycle. Analyses were consequently based on a simulation using ANZARD 2002 data, and while model validation exercises indicated that our estimates were consistent with the overall ratio for frozen and fresh cycles undertaken in 2002, it is acknowledged that this parameter is not based on direct evidence. Data limitations also restricted analysis to IVF treatment for up to three programmes and to specified age groups which may or may not represent appropriate ranges for decisionmakers. Furthermore, results are reported for IVF outcomes which may not generalize to ICSI or GIFT treatment, which constituted 58% of cycles in 2002 in Australia (Bryant *et al*., 2004). Finally, it should be acknowledged that maternal life and quality of life have not been taken into account in this model due to the live birth outcome measure employed.

Results of this study are consistent with cost-effectiveness trends previously reported. A US study, which reviewed fresh-cycle ART data on 1238 women aged 26–42, indicated that the cost per live birth rose above US$100 000 birth if the live birth rate fell below 10% (Henne *et al*., 2008). The high cost per live birth was also reflected in our analysis for women aged 42–45 in whom the expected live birth rate was 4%. A UK model which estimated the cost per live birth by the number of previous attempts using data from the Oxford Fertility Unit for up to three treatment cycles in maternal age groups younger than 39 and 39 years and older also showed a trend towards increasing cost per live birth (National Collaborating Centre for Women's and Children's Health, 2004). The incremental cost per live birth for first, second and third rounds of treatment was estimated as £11 694, £11 548 and £12 758 for women younger than 39 years, and £27 611, £28 938, £12 835 for women 39 years and older (the latter figure was noted as unreliable due to a small sample size). The propensity towards increasing cost by increasing number of treatment attempts has also been demonstrated in our results.

This analysis is more extensive than previous ART cost-effectiveness analyses. The decision analytic model populated by these data enables decisionmakers to consider the potential cost per live birth across maternal age and treatment programme with a greater level of differentiation between age groups, the incorporation of potential adverse events and frozen embryo cycles using larger data set than previous studies by treatment cycle. This analysis extends a previously published Australian maternal age-specific cost–outcome study of ART (Chambers *et al*., 2007) which did not explore cost-effectiveness by different treatment cycle numbers because the completeness of the relevant data item had not been verified in early ANZARD data collections. To our knowledge, this represents the first study to incorporate the potential effects (live birth and pregnancy outcomes) of both maternal age and number of IVF attempts, applying both fresh- and frozen-cycle IVF treatment data.

Our study has demonstrated that there is a high cost per live birth for older women, and this cost increases by additional IVF programme attempts. However, it should be recognized that despite this apparently high incremental cost per live birth, public funding of fertility treatment for older women may still be consistent with economic arguments. First, our analyses include only the costs and effects of pregnancy to the point of a successful live birth and do not include infant lifetime costs and effects. While the cost per live birth for older women appears high relative to thresholds used for other generic ratio statistics such as the incremental cost per life-year saved, this comparison may not be appropriate given the outcome of a live birth is conceptually different from a life saved. The decision-maker's willingness to pay per additional birth may differ from that per additional life-year saved conditional on societal preference and equity considerations. It is notable that Australia currently supports a policy to encourage population growth, which includes a baby bonus payment to couples with newborn infants. Unrestricted funding of fertility services may therefore be consistent with a high value per live birth. A high incremental cost per live birth may also be considered acceptable in older age groups if the potential population of interest is comparatively small compared with younger cohorts. In Australia, only 9% of women starting IVF in 2002 were aged 42–45 (Bryant *et al*., 2004), which means that the total financial impact of IVF for this age group would be expected to be substantially lower than for younger women.

Finally, it is acknowledged that there may be potential longer term repercussions of restrictions by age or the number of treatment attempts on ART usage not taken into account in this analysis. Couples facing restricted access later, for example, may elect to have more embryos transferred per cycle earlier, leading to higher costs and potentially poorer outcomes due to multiple births.

Conclusion

This study provides very strong evidence of a progressive decrease in the odds of a live birth with increasing maternal age and some evidence of a progressive decrease in the odds of a live birth with increasing treatment programme number. The lower chance of success by maternal age has a greater effect on the cost per live birth than treatment programme number, although the additive effects of age and treatment programme combine to magnify differences in cost-effectiveness in later treatment programmes in older women. This evidence may aid decisionmakers target the use of IVF services conditional on societal willingness to pay for additional live births alongside equity and other considerations.

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References

Allgood P. Successive attempts at in vitro fertilisation. In: Bazian Ltd (ed.), Wessex Institute for Health Research and Development, University of Southampton, UK, 2003.

Andersen AN, Goossens V, Gianaroli L, Felberbaum R, de Mouzon J, Nygren KG. Assisted reproductive technology in Europe, 2003. Results generated from European registers by ESHRE. *Hum Reprod* 2007;**22**:1513–1525.

Australian Government Department of Health and Ageing. Report of the independent review of assisted reproductive technologies. http://www.health.gov.au/internet/ministers/publishing.nsf/Content/health-mediarel-yr2006-ta-abb156.htm?OpenDocument&yr=2006&mth=11(2006, date last accessed).

Australian Government Department of Health and Ageing. *National Hospital Cost Data Collection. Round 8*. http://www.health.gov.au/internet/main/publishing.nsf/Content/health-casemix-data-collections-about_NHCDC (2007, date last accessed).

Bryant J, Sullivan E, Dean J. *Assisted Reproductive Technology in Australia and New Zealand 2002*. Sydney: Australian Institute of Health and Welfare National Perinatal Statistics Unit, 2004.

Centers for Disease Control and Prevention, American Society for Reproductive Medicine, and Society for Assisted Reproductive Technology. *2002 Assisted Reproductive Technology Success Rates*. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention, 2004.

Chambers GM, Ho TM, Sullivan EA. Assisted reproductive technology treatment costs of a live birth: an age-stratified cost-outcome study of treatment in Australia. *Med J Aust* 2005; rapid online publication 19 December, 1–4.

Chambers GM, Chapman MG, Grayson N, Shanahan M, Sullivan EA. Babies born after ART treatment cost more than non-ART babies: a cost analysis of inpatient birth-admission costs of singleton and multiple gestation pregnancies. *Hum Reprod* 2007;**22**:3108–3115.

Henne MB, Stegmann BJ, Neithardt AB, Catherino WH, Armstrong AY, Kao TC, Segars JH. The combined effect of age and basal follicle-stimulating hormone on the cost of a live birth at assisted reproductive technology. *Fertil Steril* 2008;**89**:104–110.

Mardesic T, Muller P, Zetova L, Mikova M. Factors affecting the results of in vitro fertilization - I. The effect of age. [Czech]. *Ceska Gynekol* 1994; **59**:259–261.

National Center for Chronic Disease Prevention and Health Promotion, ASRM, SART. *Assisted Reproductive Technology Success Rates, 2002. National Summary and Fertility Clinic Reports*. Atlanta, GA: Centers for Disease Control and Prevention, Division of Reproductive Health, 2002.

National Collaborating Centre for Women's and Children's Health. *Fertility: Assessment and Treatment for People with Fertility Problems*. London: National Institute for Clinical Effectiveness, Royal College of Obstetrics and Gynaecologists Press, 2004.

Schroder AK, Katalinic A, Diedrich K, Ludwig M. Cumulative pregnancy rates and drop-out rates in a German IVF programme: 4102 cycles in 2130 patients. *Reprod Biomed Online* 2004;**8**:600–606.

Tyldesley S, Boyd C, Schulze K, Walker H, Mackillop WJ. Estimating the need for radiotherapy for lung cancer: an evidence-based, epidemiologic approach. *International Journal of Radiation Oncology Biology Physics* 2001; **49**:973–985.

Vahratian A, Schieve LA, Reynolds MA, Jeng G. Live-birth rates and multiple-birth risk of assisted reproductive technology pregnancies conceived using thawed embryos, USA 1999–2000. *Hum Reprod* 2003;**18**:1442–1448.

Whelan JG III, Vlahos NF. The ovarian hyperstimulation syndrome. *Fertil Steril* 2000;**73**:883–896.

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