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CURRENT OPINION

Unmet Parenthood Goals, Health-Related Quality of Life and Apparent Irrationality: Understanding the Value of Treatments for Infertility

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Abstract

An increasing number of prospective parents are experiencing infertility along with associated negative impacts on mental health and life satisfaction that can extend across a network of individuals and family members. Assistive reproductive technologies (ART) can help prospective parents achieve their parenthood goals but, like any health technology, they must demonstrate acceptable 'value for money' to qualify for public funding. We argue that current approaches to understanding the value of ART, including quality-adjusted life-year (QALY) gains based on changes in health-related quality of life (HRQOL) and, more often, cost per live birth, are too narrow to capture the full impact of unmet parenthood goals and ART. We see a fundamental disconnect between measures of HRQOL and broader measures of wellbeing associated with met and unmet parenthood goals. We also suggest that simple concepts such as 'patient' and 'carer' are of limited applicability in the context of ART, where 'spillovers' extend across a wide network of individuals, and the person receiving treatment is often not the infertile individual. Consideration of individual and societal wellbeing beyond HRQOL is necessary to understand the full range of negative impacts associated with unmet parenthood goals and the corresponding positive impacts of successful ART. We suggest moving towards a wellbeing perspective on value to achieve a fuller understanding of value and promote cross-sector allocative efficiency.

Key Points for Decision Makers

Infertility can impose psychological and broader wellbeing burdens on the individual and their partner and family network, as well as economic losses on society. Assistive reproductive therapies (ART) can help prospective parents achieve parenthood goals and have been shown to have a positive effect on measures of mental health and wellbeing outcomes, but not necessarily in terms of health-related quality of life (HRQOL) as conventionally applied in health technology assessment (HTA).

We highlight empirical evidence that shows achieving parenthood goals worsens HRQOL but improves broader measures of mental health and life satisfaction. The broader wellbeing benefits of ART are not captured under a conventional HRQOL-based HTA, undervaluing the benefit of ART to infertile individuals, their partners and family networks and wider society.

To account for the full value of ART, we argue that a broader conception of value is required and suggest a 'wellbeing-adjusted life year' approach for *all* health technologies to ensure comparability across technologies and to promote allocative efficiency in healthcare.

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1 Introduction

Over recent decades, cultural, socioeconomic, demographic and other trends have led to later childbearing and an increasing number of prospective parents experiencing infertility or subfertility [1–3], defined by the World Health Organization (WHO) as an inability to achieve pregnancy after trying for more than 12 months [4] (for simplicity, we will use the term 'infertility' to refer to the range of experiences [5]). There is evidence that the COVID-19 pandemic could exacerbate this trend, at least in the short term [6].

The negative impacts of infertility on individual health and wellbeing are complex, owing to its distinct social, economic and cultural context. There is evidence that it can have short, intense effects in terms of depression and anxiety and longer-lasting effects on life satisfaction, self-actualisation and fulfilment [7, 8]. Many women, and to a lesser degree, men, report a sense of social stigma associated with involuntary childlessness [9, 10], as well as poorer mental health and social functioning and intense emotional reactions [8]. These effects can extend across family networks, including partners and prospective grandparents, and can include social, political, ethical and philosophical considerations such as the macroeconomic and demographic impacts of reduced fertility, debates over immigration policies in the context of declining fertility and even philosophical debates over the value of new life, including in the context of climate change [11]. Given the scope and complexity of these potential impacts, Brown et al. [12] argue that a biomedical perspective is too narrow a lens for understanding what they call 'involuntary childlessness' or, more broadly, what Gameiro and Finnigan [7] call 'unmet parenthood goals'. The latter term includes individuals who may not be able to have as many children as they desire.

Assistive reproductive technologies (ART), such as in-vitro fertilisation or intracytoplasmic sperm injection, can improve the chances of a live birth and help prospective parents achieve their parenthood goals, avoiding the negative consequences described above. A recent study showed that the public supports public funding for ART [13], but public funding of any medical technology, including ART, requires evidence of good 'value for money'.

In the United Kingdom (UK) and many other countries, value in health care is most often considered in terms of cost per quality-adjusted life-year (QALY) gained, based on changes in survival and health-related quality of life (HRQOL). The advantage of this approach is that the same criterion can be applied across different technologies and health conditions. The measurement of the value of ART, however, has been heterogeneous. A review by Goldhaber-Fiebert and Brandeau [14] in 2015 found that some economic evaluations have considered the value of ART in terms of QALYs, but these have been inconsistent in how QALYs are calculated and whose QALYs are included. More often, though, value has been limited to consideration of 'cost per live birth' and broader aspects of the value of ART, including the impacts of involuntary childlessness on health and broader wellbeing, have been neglected [14, 15].

We argue that cost per live birth is too limited to capture the impacts of involuntary childlessness or the value of achieving parenthood goals and that a broader understanding of value is required to assess the value of ART in facilitating parenthood goals. We go on to show that the QALY, with its focus on HRQOL, is still too narrow a concept to capture the full value of achieving parenthood goals. We conclude that a broader approach to understanding the value of ART is necessary to account for the impacts of involuntary childlessness and ART. This includes consideration of elements of value that may not conventionally be seen as 'health-related' and explicit consideration of the wellbeing and economic spillover effects of achieving parenthood goals on partners, family networks and broader society.

2 (Mis)understanding the Value of ART for Unmet Parenthood Goals

The economic and ethical challenges in defining and comparing the value of natural outcomes such as live births, cases prevented, or premature deaths avoided are the primary motivation for adopting a cost-utility approach based on the QALY in evaluating health technologies [15, 16]. However, as others have observed, ART for parenthood goals is not well-suited to a QALY-based cost-utility approach, given the complex impacts and externalities mentioned above [15, 17]. These difficulties can be *further* compounded by considering the value of creating a new life, but this leads to debates outside the scope of this article [18].

Infertility is widely recognised as a medical condition, including by NICE [19]. As Devlin and Parkin [17] have noted, however, ART may be delivered in a healthcare setting, but it is not clear that its principal objective is improved health, at least in the sense normally understood in a cost-utility analysis. In their view, unmet parenthood goals might be more appropriately viewed as a 'social' rather than a 'medical' condition, a view consistent with the breadth of impacts mentioned earlier.

The implication of this view is usefully illustrated by Krol et al. [20]. The authors conducted a time trade-off (TTO) study to understand the utility of involuntary childlessness relative to full health in a general population sample. They developed a vignette that used the EQ-5D, a common measure of HRQOL for QALY calculations, to

describe a health state with no problems on any dimension ('full health') with the additional stipulation of "being infertile with a desire for one or more children". Despite describing 'full health' on the EQ-5D, they estimated TTO utilities in the range of 0.792–0.868, indicating that respondents saw negative impacts associated with involuntary childlessness beyond HRQOL.

The notion of infertility as a social condition, and the recognition that medical conditions can have impacts beyond HRQOL, lead to questions about the appropriate boundary between HRQOL and wellbeing in health technology assessment (HTA). Consistent with most health economists, we use HRQOL to refer to measures of utility based on instruments such as the EQ-5D, SF-6D or HUI. These instruments seek to describe the extent of health problems on dimensions such as—in the case of the EQ-5D—mobility, self-care, usual activities, pain/discomfort and anxiety/depression [21]. Generally, the fewer the problems on any dimension, the greater the HRQOL.

We use wellbeing to describe a broader concept, including but not limited to health. As described by Shah [22], wellbeing encompasses a reflective assessment of one's life (life evaluation), feelings and emotional state at a particular time (affect) and sense of meaning and purpose in life (eudaimonia). Critically, wellbeing does not depend solely on health: 'ill' people can have meaning and purpose, and healthy people can lack the same feelings.

The implications of a distinction between 'HRQOL' and 'wellbeing' in the context of involuntary childlessness are illustrated in Table 1, constructed using the results of a 2017 systematic review [7]. It presents whether being 'successful' (S) or 'unsuccessful' (U) in achieving parenthood goals (with or without treatment) was associated with better outcomes in terms of mental health, life satisfaction, or HRQOL according to the measures used in each study.

Success in achieving parenthood goals was consistently associated with *better* outcomes for mental health and life satisfaction (S>U), whilst HRQOL often showed *poorer* outcomes in the successful group in the short to intermediate term (U>S; highlighted in red). We note that FertiQoL, a fertility-specific instrument that combines elements of life satisfaction and HRQOL, generally shows better outcomes among the successful group across Table 1, but this briefly reverses in the period 3–5 years after ART. Arguably, this is a physically challenging period of parenthood, and we speculate that in this period deficits in HRQOL may outweigh gains in life satisfaction. This is a useful reminder that HRQOL is still an important component of life satisfaction and wellbeing, even if it is not the sole determinant of wellbeing.

Overall, we suggest that the inconsistency between these measures reflects the narrower perspective of HRQOL compared with the other measures. Psychological and life satisfaction measures are more likely to capture aspects of *wellbeing* associated with parenthood goals, such as a sense of purpose, self-actualisation or fulfilment [7, 8]. In contrast, HRQOL appears to be more sensitive to the burdens of early-years parenting, be them physical (sleep deprivation, physical exertion) or emotional (postnatal depression, anxiety associated with caring for a child). Indeed, we speculate that such burdens may be particularly acute among older individuals who have a greater likelihood of infertility [23] and therefore ART. In this context, it is not surprising that HRQOL shows poorer outcomes associated with success in parenthood goals in in the short and intermediate term, whilst the other measures consistently (but not always) show the reverse.

Judging outcomes solely on HRQOL would seem to imply that individuals seeking infertility treatment are behaving irrationally by undertaking treatment that makes them *worse off* in terms of lifetime QALYs. However, the increasing demand we see for fertility services [24, 25], along with evidence of a substantial willingness to pay for improvements in the likelihood of ART success [26], suggests that such 'irrationality' is an artefact of measurement. As suggested by Table 1, it seems more likely that the HRQOL measures that underlie the QALY fail to capture the full value that involuntarily childless individuals (ultimately) derive from ART and achieving parenthood goals. To ensure that this value is appropriately considered in HTA decision making, we suggest that a broader approach to measurement and perspective on value is required.

3 Moving Beyond HRQOL in Valuing ART and Parenthood Goals

As we noted earlier, NICE recognises infertility as a medical condition [19]. However, as implied by Krol et al. [20], the 'symptoms' of this condition are unlikely to manifest on dimensions that NICE considers health related. For individuals with stronger parenthood goals, failing to achieve these goals could conceivably lead to depression or anxiety that would be reflected in HRQOL, but this is likely to be a minority of all individuals with unmet parenthood goals [27]. Limiting concern to those infertile individuals experiencing specific mental distress is arguably analogous to publicly funded cosmetic procedures for the minority of individuals experiencing 'extreme distress' due to their appearance [28]. This, however, frames concern for involuntary childlessness as *the mental distress caused by an inability to become pregnant* rather than the inability to achieve pregnancy per se. Such an interpretation is inconsistent with NICE's guidance around infertility, which describes it solely as an inability to achieve pregnancy after one year of trying, with no reference to mental distress [19].

Table 1 Relative ordering of health/wellbeing according to success/non-success in achieving parenthood goals according to timeframe, wellbeing concept ("what is measured?") *and* instrument ("how measured?")

Timeframe	What is measured?			How measured?	Sex	Source
	Mental health	Life satisfaction	HRQOL	Instrument		
Immediately after treatment, up to 1 year	S > U			STAI	F	[45]
	S > U			BDI	F	[45]
			U > *S*	EQ-5D index	F & M	[46]
		S > U		FertiQol	F & M	[46]
1–2 years after ART		S > U		LSS	F	[47]
			U > *S*	EQ-5D index	F & M	[46]
		S–U		FertiQol	F & M	[46]
3–5 years after ART		S > U		LSS	F	[47]
		S > U		SWLS	F	[48]
	S–U			GHQ-12	F	[48]
	S > U			BDI	F	[45]
	S > U			STAI	F	[45]
	S > U			RSES	F	[49]
		S > U		Item—LS	F	[49]
	S > U			BSI	F	[49]
		S > U		PGWB	Couples	[50]
	S > U			CCEI	Couples	[51]
		S > U		QOL	Couples	[51]
			U > *S*	EQ-5D index	F & M	[46]
		U > *S*		FertiQol	F & M	[46]
6–10 years after ART		S–U		LSS	F	[47]
	S > U			RSES	F	[49]
		S > U		Item—LS	F	[49]
	S > U			BSI	F	[49]
			S–U	EQ-5D index	F & M	[46]
		S > U		FertiQol	F & M	[46]
>10 years after ART	S > U			SF-36 (MHI-5)	F	[52]
		S–U		LSS	F	[47]
	S > U			Item—Self-esteem	Couples	[53]
			S–U	Item—Qol	Couples	[53]
	S > U			RSES	F	[49]
		S > U		Item—LS	F	[49]
	S > U			BSI	F	[49]
	S > U			HSCL-90	F	[54]
			S–U	EQ-5D index	F & M	[46]
		S–U		FertiQol	F & M	[46]

S = successful in achieving parental goals (have parental goals and have children—natural or via ART); U = unsuccessful in achieving parental goals (have parental goals and don't have children). < worse than; > better than;–similar to

ART Assistive reproductive technologies, *BDI* Beck Depression Inventory, *BSI* Brief Symptom Inventory, *CCEI* Crown-Crisp Experiential Index, *F* Females, *FertiQol* Fertility Quality of Life instrument, *GHQ-12* General Health Questionnaire, *HRQOL* health-related quality of life, *HSCL-90* Hopkins Symptom Checklist 90 items, *Item-LS* Item-self-esteem, *Item Qol* single-item questions about subjective life satisfaction, self-esteem and quality of life, respectively, *LSS* Life Satisfaction Scale, *M* males, *MHI-5* five-item Mental Health Inventory [part of the SF-36], *PGWB* psychological general wellbeing, *QOL* quality of life scales [a wellbeing measure], *RSES* Rosenberg Self-Esteem Scale, *SF-36* 36-item Short-Form Health Survey Questionnaire, *STAI* State and Trait Anxiety Inventory, *SWLS* Satisfaction with Life Scale

This narrow HRQOL perspective on the harms of involuntary childlessness is exacerbated by a parallel neglect of its broader impacts. First, the impact of not achieving parenthood goals also falls upon the partners of infertile individuals and other family members. Most HTA guidelines, however, focus on the HRQOL of the 'patient'—the person receiving treatment—even when this may not be the infertile individual. In most cases of male infertility, it is still typically the woman that receives treatment. Furthermore, guidelines do not address how the impacts of unmet parenthood goals should be aggregated across the network of affected individuals. Specifically, consideration of spillovers in HTA is typically limited to informal carers, which does not seem an appropriate conceptualisation of the network of individuals, including partners and prospective grandparents, who share the direct and indirect burdens. Given the broad (and often interrelated) impacts of involuntary childlessness, any estimates focusing solely on the person receiving treatment will underestimate broader spillover benefits [29].

Further, governments are increasingly considering access to fertility treatment as an element in their 'population policy mix' as part of broader macroeconomic objectives that are not considered in NICE's direct-payer perspective [30, 31]. Another helpful analogy may be substance abuse prevention programmes. Although there are meaningful direct HRQOL benefits to treating a person with substance abuse, a 'health-focused' evaluation would neglect important spillovers, including the wellbeing of family members and potential victims of abuse or crime, costs of crime and incarceration and societal productivity [32]. Similarly, the COVID-19 pandemic has demonstrated that the value of treatments—in this case, vaccines—can extend beyond individual HRQOL to include macroeconomic effects and enabling 'life goals' over and above 'improved health' [33].

Finally, the very concept of infertility as a disease is complicated by same-sex couples or single individuals who will never be able to achieve parenthood without assistance despite the absence of any objective health condition. Here, questions over access to fertility treatment move into the realm of human rights [34] rather than cost per health outcome gained. In this regard, Brown et al. [12] suggest "that recognition of subfertility as a disease is likely to be a poor guide as to who might benefit from ART". They note that not all unmet parenthood goals are linked to specific biomedical 'dysfunctions' and suggest that similar harms can occur whether these unfulfilled goals are due to biomedical factors or social context. In this view, societal concerns for unmet parenthood goals should be based on harms and not (biomedical) origins. This implies moving beyond a narrow focus on specific health problems and towards a broader understanding of individual and societal harms and wellbeing.

4 The Wellbeing Way Forward?

Together, these challenges give ART some of the characteristics of a public health intervention. This characterisation is supported by a recent willingness-to-pay study conducted across eight countries, including the United Kingdom, that demonstrated public willingness to contribute to nationally funded fertility programmes based, in part, on support for the view that a desire for children is a basic human right [13].

We do not suggest that HTA of ART is inappropriate. Rather, echoing previous arguments [15, 17], we suggest that the evaluation of ART and other technologies with similarly broad impacts must consider individual and societal wellbeing, not just aggregate health, as well as macroeconomic policy and human rights. This will require fundamentally rethinking how the benefits of ART are conceptualised and measured.

This could take the form of a comparison of the costs and benefits of ART in monetary terms within a willingness-to-pay (WTP) or cost-benefit framework, as recently suggested by Keller and Chambers [35]. We agree with their identification of the shortcomings of a conventional QALY approach in the context of infertility and ART, particularly the impact of infertility beyond the conventional dimensions of HRQOL. However, as they note, price signals in healthcare are often distorted by health insurance and WTP is unavoidably constrained by ability to pay [35]. A WTP approach to valuing fertility would give greater weight to the parenthood goals of those with the greatest ability to pay. We believe such an approach is out of step with current approaches to HTA and is unlikely to be adopted by publicly-funded systems.

A more practical and less ethically fraught solution is to move towards some version of a 'wellbeing-adjusted life-year' to value not just fertility treatments but *all* health technologies. Such an approach would capture broader elements of wellbeing whilst simultaneously maintaining comparability between HTAs and facilitating cross-sector allocative efficiency [36–38]. This will require methodological development but arguably work on the EQ Health and Wellbeing (EQ-HWB) [39, 40] and ICECAP [41–43] measures already represent moves in this direction.

There should also be more explicit guidance for when and how spillover benefits should be considered in economic evaluations [29, 44]. This includes understanding when concepts such as 'patient' and 'carer' may not be sufficient in considering the full impacts of a condition or its treatment. We have noted that the person with the 'biomedical dysfunction' may not be the person receiving fertility treatment (e.g., women treated for male factor infertility), and in some cases, there may be no dysfunction at all (e.g., same-sex couples).

Likewise, involuntary childlessness impacts a network of individuals beyond the person receiving treatment, making it difficult to identify a single 'patient'. Similar conceptual challenges can exist in settings such as obstetrics, sexual health, mental health and public health. A wellbeing approach, rather than a narrow health-focused approach, can sidestep these identification challenges by focusing on harms and benefits rather than health gains. This may begin to break down silos between health-related and non-health-related wellbeing and promote greater allocative efficiency across all public spending [38].

We recognise that many of these are not novel recommendations. Similar arguments were made by Devlin and Parkin [17] 20 years ago, and Goldhaber-Fiebert and Brandeau [14] highlighted inconsistencies in ART evaluations almost 8 years ago. More recently, Luyten et al. [15] have discussed other challenges that ART presents to conventional HTA, including the appropriate scope and perspective on costs and benefits and the appropriate time horizon for the analysis. We go further, however, by illustrating our conceptual arguments with empirical evidence that demonstrates how an understanding of value based on HRQOL would lead to different conclusions around the value of ART than value based on broader considerations of wellbeing. We hope that this combination of conceptual and empirical arguments will spur methodological developments that promote consideration of the full range of impacts of unmet parenthood goals and how the value of ART—and similar technologies with multifaceted impacts—can be understood within HTA.

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Declarations

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