**The Long-Term Safety of Medically Assisted Reproduction: Ethical Aspects**

**Lucy Frith -** **frith@liverpool.ac.uk** **ORCID 0000-0002-8506-0699**

**Heidi Mertes -** **Heidi.Mertes@ugent.be** **ORCID 0000-0003-3029-2158**

**Nicola Jane Williams -** **n.williams2@lancaster.ac.uk** **ORCID 0000-0002-8400-6279**

**Abstract**

While the central place of safety in medically assisted reproduction (MAR) is self-evident, there are some divergent opinions on which kinds of risks are acceptable. This chapter will consider the following key areas: how the welfare of the future child is to be balanced against the reproductive autonomy of the parents; how we can ensure that safety is not overtaken by other interests; and how to strike the right balance between ensuring safety and ensuring access to medical treatment, et cetera. We will examine some of the ethical principles and debates underlying certain policies, guidelines and common practices in MAR, related to long-term safety.

**Key words**

Welfare of the child

Reproductive autonomy

Ethics

Reproductive rights

Responsibility

Ethical innovation

1. **Introduction**

While the central place of safety in medically assisted reproduction (MAR) is self-evident, there are some divergent opinions on which kinds of risks are admissible for who and when and who gets to decide on the permissibility of risks. Key areas are: how the welfare of the future child is to be balanced against the reproductive autonomy of the parents; how we can ensure that safety is not overtaken by other interests; and how to strike the right balance between ensuring safety and ensuring access to medical treatment, et cetera. In this chapter, we will touch on several of these topics, giving an insight into some of the ethical principles and debates underlying certain policies, guidelines and common practices in MAR, related to long-term safety.

1. **From bench to bedside**

Responsible innovation in MAR ideally proceeds through the steps of preclinical research (in cells, animals and/or embryos), clinical trials and (long-term) follow-up studies, 1,2. While the ethics of preclinical research on animals and of clinical trials on patients are well-rehearsed, issues that are particularly challenging in reproductive medicine are those related to research on human embryos and to long term follow-up of the resulting children. Long term follow-up will be discussed below (see section 4.3 below). Embryo research is controversial due to the instrumentalisation of human creatures who are accorded varying degrees of moral status, based on their inherent value as members of the human species, based on their potential to become a person and/or based on their symbolic value, 3. While many countries allow research on embryos that were created through IVF treatment but will not be transferred to the patient for various reasons, few allow the creation of a human embryo specifically for research purposes, 4. Regulatory limitations on the necessary safety research should however not be seen as an excuse for introducing new treatments without proper risk assessments.

* 1. **The technological imperative**

Requiring 0% risk for the introduction of new reproductive technologies is unattainable and attempting to approximate this zero-risk level would lead to the inaccessibility of many beneficial treatments, which is, given the high burden of disease, morally problematic, 1. This means that difficult weighing efforts are needed to determine when a new treatment is ready for the clinic. One factor that is known to confound sound decision making in this regard, is a phenomenon described as the *technological imperative*. Relying on the typology of the technological imperative in the context of healthcare put forward by Björn Hofmann, 5, we can point to several potential ways in which the technological imperative might plead for a premature introduction of new reproductive technologies. First, the *imperative of possibility and action* appeals to the moral intuition that if we can help patients by means of a novel technology, we should (despite safety concerns), rather than abandoning them (e.g. grant access to uterus transplantation through clinical trials despite considerable risks). Second, the *imperative of demand* refers to the pressure that patients may put on clinicians to receive a certain treatment (e.g. a Turner patient demanding that she receives treatment just as other patients do). As long as we include the considerations above as elements in the weighing of pros and cons, there is no problem. However, once they become *imperatives* and can no longer be put in the balance alongside other considerations, such as safety concerns, an ethical problem arises.

* 1. **Who decides which risks are acceptable?**

In natural reproduction, the reproductive liberty of individuals is only restricted in very exceptional circumstances, for example when people have a severe mental disability or during incarceration. This means that people are free to reproduce, even if they know that by doing so, they risk conceiving a child that will suffer from suboptimal life circumstances (due to physical impairments or contextual factors). Some would argue that reproductive liberty also pleads against any kind of interference in assisted reproduction, both on a governance level and on the level of the hospital or health care workers whose assistance is sought. However, reproductive liberty is generally considered to be a liberty right, not a claim right, meaning that although I am free to reproduce as I wish, I cannot make a claim on others (in terms of practical or financial assistance) to support me in this pursuit. As physicians have sworn an oath not to harm their patients and are co-responsible for the welfare of the children they help conceive, they can therefore legitimately refuse to perform certain procedures on certain patients when – according to their assessment – the risks (for parents and/or child) are unacceptable (See section 3 and section 4 below). Note that informed consent or a waiver of liability signed by a patient in no way removes the moral responsibility a health care professional has for the adverse effects of treatments on their patients and the resulting children. However, reasonable disagreement can exist between different parties involved concerning which risk is – or is not – acceptable.

* 1. **Excessive risk reduction?**

While most of the ethical concerns in the realm of risks in reproductive medicine are aimed at insufficient risk reduction, too *much* risk reduction may also prove problematic. For example, in the context of preimplantation genetic testing for aneuploidy screening (PGT-A), claims have been made that it would be irresponsible to transfer aneuploid embryos and that therefore all embryos need to be screened. Similarly, some patients only receive treatment after agreeing to take risk-reducing measures, e.g. preconception genetic screening, PGT-M or weight loss, while single, same-sex or ‘older’ patients are completely denied treatment on the alleged basis of concerns over the wellbeing of the future children. What we notice here, is that the – in principle – morally laudable goal of risk reduction might be window dressing for other motives, either commercial (in the case of widespread PGT-A or preconception screening) or ideological (in the case of refusal of treatment for people with certain – mostly non-heteronormative – characteristics). In the context of genetic screening in particular, concerns are voiced regarding the message that such screening and selection requirements send to people with disabilities regarding the differential value of their lives, 6. Thus, while risk reduction is needed to avoid serious risks, it is wise to keep in mind that we take numerous calculated risks on a daily basis in order to obtain the things we value in life. Reproduction, despite all the risk reduction measures we might take, remains an intrinsically risky endeavour.

1. **Recipient Welfare in MAR**

This edited collection has outlined a range of scenarios and possible risks to both those receiving assisted reproductive technologies (which for the purposes of this chapter we will call recipients) and those born from those procedures. In this section we focus on the recipients of treatments, and the ethical issues raised when decisions have to made about who ought to receive fertility treatments and in what circumstances. When deciding who to treat, fertility clinicians have a number of factors to consider. Of overriding concern is, the need to consider the welfare of potential recipients in MAR and the welfare of any future child (which will be explored in section 4). In determining the welfare of potential recipients, it is argued that in the absence of adequate reasons to the contrary clinicians should promote the reproductive rights and respect the autonomy of their patients. In what follows we therefore outline these principles, explore their importance for individual welfare, and consider how these might be balanced against other considerations.

**3.1. The Right To Reproduce**

Questions of access to MAR has been a contentious issue since the development of IVF in the late 1970s. One of the main arguments for not restricting access to MAR is that the infertile have the same right to reproduce as the fertile. This is an area of debate that has been changed radically by the scientific development of MAR, and the right to reproduce free from interference is generally viewed as an important basic human right enshrined in both Article 16 of the United Nations Declaration on Human Rights and Article 12 of the European Convention on Human Rights as the right to marry and found a family. As mentioned above, these articles are usually understood as stipulating what can be called a liberty right or negative right, that is a right not to have one’s reproductive capacities interfered with against one’s will. Thus, an interest in reproduction is generally held to be of significant import, with one of IVF’s pioneer’s Robert Edwards noting: ‘It is impossible to put a price on the benefits to society of producing wanted children raised in a caring environment.’

The development and practice of MAR can therefore provide those who experience infertility with the means to achieve their own reproductive aspirations and exercise their reproductive liberty. John Robertson, 7. has put forward a rights-based argument to support the extended use of MAR. He begins by arguing that the concept of procreative liberty should be given primacy when making policy decisions in this area. Procreative liberty is the freedom to decide whether, when, how, how often, and with whom to reproduce. At first sight, this appears to be a negative right, not to have one’s reproductive capacities interfered with. However, Robertson endorses subsidiary enabling rights to procreation, that is, someone has the right to something if it can be regarded as a prerequisite for procreation. This effectively turns a negative right (not to be interfered with) into a positive right (to have something made available to one). Thus, individuals have a right to access MAR on Robertson’s account, since they enable those who experience infertility to exercise their reproductive rights in the same way as their fertile counterparts.

Robertson’s claim could clearly be problematic. The feminist philosopher Laura Purdy, 8. argues that Robertson adopts a position that blurs the distinction between negative and positive rights. He seems to infer that the strong right not to have one’s reproductive capabilities interfered with implies an equally strong right to reproduce. Embedded in this discussion of reproductive rights is the assumption, made by Robertson, that the issues raised by natural reproduction are akin to those raised by assisted reproduction, although interference in natural reproduction oftentimes implies infringements on the right to physical integrity which are not present when refusing MAR. Christine Overall, 9. a feminist critic of MAR, argues that the issues raised by the two forms of reproduction are fundamentally different, and correspondingly the right to use MAR needs a different burden of proof from the right to be free from reproductive interference.

As a result, it is by no means clear that good arguments can be provided to support the claims by scholars like Robertson that there is a positive right to reproduce (and accordingly that the infertile should have the means made available for them to reproduce or what the practical implications of such a right would be in terms of funding etc). It is not generally recognized that just because the means are available to achieve some end, people have a right to those means. In terms of providing the basis for access to MAR, these arguments based on a conception of the positive right to reproduce have not had the significant practical effects that their proponents might have hoped. Most healthcare systems have limits on whether, when, and for whom MAR will be funded as part of socialised or insurance based medical care.

**3.2. Reproductive choice and Liberty**

Another key principle to consider when discussing the risks that recipients of MAR ought to be permitted to shoulder is that of reproductive choice. MAR is often considered to broaden the range of *meaningful* reproductive options that are available to prospective reproducers. Any extension of choice is frequently portrayed as desirable, and this is often also claimed of reproductive choices. Appeals to the importance of reproductive choice have underpinned many arguments provided in favour of innovation in MAR. Advocates of reproductive autonomy (e.g. Savulescu, 10.Harris) endorse the pre-eminence of parental choice in most circumstances. The central claim of this view is that personal reproductive decisions should be free from interference unless they will cause *serious harm to others* 12. As will be discussed below (in section 4), it is unclear how concerns regarding the welfare of *future* persons should be weighed against reproductive liberty.

This view has significant philosophical pedigree with many philosophers and jurists holding that individual freedom is the appropriate baseline assumption when discussing the permissibility of the acts and choices of moral agents.Mill, for example, held that “in practical matters, the burden of proof is supposed to be with those who are against liberty.” (Mill, 1869) 13. Locke held similarly that man is naturally in “a State of perfect Freedom to order their actions...as they see fit… without asking leave or depending upon the Will of any other Man” (Locke, 1689) 14 and that this should place limits on the liberty limiting abilities of the state, whose goal should be seen to preserve and protect natural liberties and property. More recent expression is also found in the work of Stanley Benn who suggests that “The burden of justification falls on the interferer, not on the person interfered with” 15 and Rawls who argues that in a just society “there is a general presumption against imposing legal and other restrictions on conduct without a sufficient reason.” (Rawls, 2001) 16.

This argument is sometimes reinforced by claims that reproductive choices are “integral to a person’s sense of being” 17. and any restrictions therefore require even more robust justification than less important choices 7. There is a belief that the more important the choice, the stronger the case for restricting it has to be. Hence, as reproductive choice is very important – the desire for a child is perceived by many as a fundamental need – allowing people to exercise it is a good in itself and this good *outweighs the production of a certain level of harm* such as in cases where treatment is provided to women who have serious background medical conditions.

**3.3. Balancing Principles and Rights**

While respecting individuals’ free choices to reproduce may, at first blush (prima facie), seem a good rule of thumb, attention to competing considerations may lead to different conclusions.

Balancing harms and benefits of treatments need to be considered at a number of levels and it is important to think about what types of harm are relevant here. While clinicians may be concerned about harms experienced by the patients in front of them, there could be wider societal harms caused by the use and provision of MAR. For example, while some feminists have argued that MAR technologies and techniques extend women’s procreative choices, by offering additional choices, others argue that desires to avail oneself of assisted reproductive technologies and techniques are in some sense, inauthentic, as the harms of infertility are the result of problematic societal pressures and norms. Thus, the very existence of MAR can constrain and influence choices, and their provision can reinforce and validate such pressures and norms, causing expressive harm. Here, what are presented as new options can quickly become seen as the standard of care that women have to actively refuse. Thus, some have claimed that the availability of such technologies has imposed upon reproducers a *forced choice* to either pursue or refuse to pursue new technological options 18, with childlessness no longer seen as an acceptable option unless women have tried to conceive by using MAR.

It is argued that women are particularly susceptible to essentialist and pronatalist social pressures and norms surrounding reproduction and womanhood. Pronatalism is an attitude or policy that encourages reproduction and promotes the role of parenthood. Pronatalism particularly affects women who are encouraged to become mothers. In a patriarchal society true femininity is often equated with childbearing, and motherhood is thereby regarded as a necessary aspect of womanhood with women considered essentially or naturally mothers. The way in which society pressures women to have children and the focus on genetic relationships can be said to be socially determined ways of constructing our reproductive relationships. It could be argued that we do not have to respond to such pressure to reproduce, and it is important to give women the freedom to choose to remain child free and have that choice be equally valued and respected 19. The wider social implications of the use of MAR and its potential to forward or set-back attempts to drive social change thus needs to be considered when weighing up their associated harms and benefits.

That our choices are both constrained and constructed by our social, economic, and political situations, however, is increasingly acknowledged and accepted in new theories of autonomy such as relational autonomy questioning the western interpretation of autonomy as excessively individualistic 20, and depending on “an asocial, abstract conception of individuals” 21. These consider the person in their wider context, and these kind of theories of autonomy might be more useful in deciding how decisions should be made and determining who should make them. Dove et al define relational autonomy as: ‘a conception of autonomy that places the individual in a socially embedded network of others.’ (22) It is often argued that people usually make important decisions by discussing them with people they are close to. Therefore, the notion of the individual as ideally atomistic and self-sufficient may be a misnomer in medical practice in general and particularly unhelpful in considering MAR. MAR has as its focus, the creation of families and is therefore never solely about the risks to one person.

**3.4 Professional responsibility**

Healthcare professionals have a responsibility to act in the interests of the individuals’ who are presenting for treatment as well as any future offspring. Reasons for overriding the reproductive autonomy of a potential recipient, might be that to treat them may result in undue harm to them, i.e. a women with cardiac problems for whom pregnancy would put an undue strain on them; or what is asked for is not legally allowed in the country where treatment is being offered, i.e. sex-selection for social reasons is currently forbidden in the UK (Human Fertilisation and Embryology Act 1990: Schedule 2, 1ZB(1)); or payment or reimbursement systems will not pay for the treatment, i.e. in the UK limits are placed on the number of IVF cycles people can receive on the National Health Service 23. Therefore, it is often not in the fertility clinician’s power to be able to give the recipient exactly what they want for reasons that may be regulatory or financial in nature or related to the particular patient. While physicians may be constrained by the context in which they practice, as medical professionals, they also have to weight their own duties to do no harm and promote beneficence for their patients. Therefore, in certain situations, it is not ethically desirable to accede to whatever the patient requests, but to act to further the patient’s best interests and in line with professional codes that recognise such responsibilities. Often through discussion and counselling, recipients can see how certain actions, such as continuing IVF cycles when there is little chance of success, are not in their interests, and they can be supported to make the best decision in the circumstances for themselves and one that the medical team can also work with.

In order for physicians to adequately discharge these duties in this complex area, recipients need to be provided with the relevant information on all aspects of their treatment. Counselling is recommended to enable recipients to both understand the medical implications of the treatment, but also the psycho-social aspects of forming a family in this way. MAR is much more than a form of medical treatment, and is most appropriately seen as an exercise in family formation, and this should be born in mind when appraising recipients of the risks and benefits of MAR, and ensuring that recipients receive the necessary support to make sufficiently informed decisions for themselves and their future family, and if relevant, the implications of using donated reproductive material (i.e. gametes/embryos) 24. Even then, if conception does not take place, the feeling of failure and the stress, strain and costly medical treatment can all take their toll 25.

In sum, while it is often argued that fertility clinicians should aim to respect their patient’s autonomy, often this is not possible, societal harms have to be weighed against individual benefit, potential harms to the individual have be weighed and sometimes patients need to be counselled and supported to act in their own best interests.

1. **The Welfare and Interests of Children Produced through MAR**

Unlike many other arenas in medicine where safety concerns have as their primary focus the welfare of those who receive treatment, reproductive medicine differs in that its primary function is *the creation of an additional party*: a child. Thus, discussion of safety concerns in MAR are complicated by the need to consider - not only the safety of a procedure or intervention for the individuals and/or couples who seek them and how this should be balanced against a desire to respect the autonomy of prospective reproducers – but also the welfare of the children that may be produced through MAR who do not and cannot consent to the risks involved in treatment. Indeed, in cases where interventions affect the germline (such as mitochondrial replacement therapy, and gene editing) safety concerns extend to children who may be born *many generation*s into the future, leading to an even more pressing need to carefully consider the risks and burdens such treatments may impose on parties other than the intended parents over both the short and long-term.

As noted by Robertson 26, in respect of child welfare, MAR therefore has the following ethical structure:

“The use of [MAR] may enable an infertile person or one who carries genes for serious disease to reproduce, but in doing so they risk having a child with diminished welfare. The degree, certainty, and kind of risk vary, as does the motivation for seeking reproductive assistance and the person’s other options for reproducing. But they all pose a risk that the child will experience physical, psychological, or social limitations that ordinarily do not occur without the use of MAR.” (p. 8)

Yet, how risky is *too* *risky*? How should we calculate and weigh such risks in the face of uncertainty? And, to what lengths ought practitioners and policymakers go in service of the aim of protecting the welfare of children born through MAR? In this section we explore questions of *child welfare arising from safety concerns in MAR* such as the risks to the physical welfare of offspring posed by modifying, selecting, and manipulating gametes and embryos, and from interventions such as IVF and ICSI.

**4.1 Welfare Standards and Non-Identity Problems**

As explained by Pennings et al (2007) 27 there are different positions on determining acceptable risks to offspring which can be identified as falling somewhere on a spectrum from accounts providing very minimal welfare requirements sitting at one end and accounts providing extremely strong welfare requirements sitting at the other. In this section we will explore standards from both ends of the spectrum (the so-called ‘maximal’ and ‘minimal’ welfare standards) and a more moderate position known as the ‘reasonable welfare standard’.

According to the maximal welfare standard, medically assisted reproduction should not be provided “when it is indicated that the life conditions of the future child will not be optimal.” (Pennings, 2007: 2586) 27 On this view, no risks of harm to children produced through MAR should be considered acceptable, which would, given that no fertility treatment is risk free, preclude provision in all cases. Setting such a high bar when it comes to MAR, however, is problematic, as those able to reproduce without assistance are not generally considered to be blameworthy when they (inevitably) bring children into the world in sub-optimal conditions. Thus, it is often considered unfair or unreasonable to set the bar for responsible reproduction so high in one reproductive context but not others. At the other end of the scale is the ‘wrongful life’ or ‘minimal welfare’ standard. This view suggests that MAR should be permitted so long as it does not result in the births of children whose lives have been variously described in the ethics literature surrounding assisted reproduction as “less than worth living” (Steinbock) 28, “intractably miserable” (Rakowski) 29 “dominated by pain and suffering” (Bennett) 30, and “worse than no life at all” (Brock) 31. Given that the majority of individuals with even the most painful and life-limiting diseases and disabilities consider their own lives to be worth living, requirements regarding safety and risk to children produced through MAR would, on this view, be incredibly permissive, with little requirement to even attempt to reduce any risks.

Given concerns regarding excessiveness and unfairness on the maximal standard, some have suggested that rather than maximising child welfare or failing to account for it in all but the most significant cases, we should instead aim for sufficiency, accepting some risks in MAR, but requiring that they are both: reduced in so far as possible; and fall below an acceptable or ‘reasonable’ threshold for harm. Yet, how should we determine what risks are acceptable or reasonable? Some suggest that natural conception should be used as the benchmark for acceptable levels of risk such that treatments and techniques which impose risks on offspring that are *greater* than those imposed by natural reproduction ought to be forbidden. Yet this threshold seems arbitrary and seems to make an unjustified leap from a descriptive statement about the world to a claim about how things ought to be. Others therefore suggest a more principled limit, suggesting that responsible reproductive policies (and reproducers) should make decisions regarding acceptable and unacceptable levels of risk to offspring on the basis of whether the children produced are likely to have “at least a *normal opportunity* for the good life” (Purdy)8, or “the abilities and opportunities to realise those dimensions and goals that in general make a life valuable” (Pennings et al) 27.

However, while: it seems self-evident that the welfare of children produced by MAR should be of paramount importance to physicians, researchers, and prospective parents – many nations world-wide have incorporated child-welfare requirements into legislation and policy governing assisted reproduction (26; Human Fertilisation and Embryology Act, 1990)[[1]](#footnote-1), and so too do many professional bodies[[2]](#footnote-2) – philosophically the matter is a little more complex. This is the result of a paradox known in philosophy as ‘the non-identity problem’ (Parfit) 32 which arises in situations where the only means we have of protecting some individual (or group of individuals) from some particular (and negative) event or occurrence is to prevent their existence. Where this is the case, unless that individual’s life is so bad that is fails to meet the ‘wrongful life’ or ‘minimal welfare’ standard discussed previously, they cannot be considered harmed. For, even if their existence is marked by suffering, this is a condition of their very existence: it is unavoidable. They could not exist in any other state and their existence is, on balance, a benefit to them. In the context of MAR, many decisions to provide or not to provide treatments alter the timing and manner of conception and thus fall prey to the non-identity problem such as the use of fertility drugs, pre-implantation genetic diagnosis followed by embryo selection, gamete donor selection decisions, *and* potentially, mitochondrial replacement therapy. Such cases force us to reconsider the ultimate ‘goals’ of child welfare requirements in MAR. Candidates include: impersonal considerations such as a commitment to reducing levels of suffering and limited opportunity in the world regardless of who experiences it (33, 32); and public health goals to reduce the overall burden of disease and disability within a given society (Williams) 34.

**4.2 Weighing Risks To Offspring**

In cases of MAR which do not fall prey to the non-identity problem, or where child welfare goals are motivated by impersonal and public health goals, attention should also be directed to questions of whether and when certain risks associated with MAR should be considered to fall within the remit of safety considerations, and how such risks should be weighted.

With respect to the former question, ought, for example, the social harms that may befall children, conceived through gamete donation, mitochondrial replacement, surrogacy arrangements, and gene editing, be counted as safety risks alongside the physical risks of such technologies? Such concerns, after-all, may be considered to arise primarily as a result of discrimination and/or prevailing norms and attitudes regarding the importance of genetic and gestational ties for parenthood, which may be reduced through altering the social context rather than restricting the use of MAR. A clear example where social solutions to the suffering of MAR conceived children may be deemed more appropriate can be found in cases where children born outside of heteronormative family structures experience discrimination as a result of the manner of their conception. A slightly more complicated case is that of the interests of donor conceived children who may claim that they are ‘harmed’ where they are unable to access identifying information regarding their donors or by the very knowledge that they are donor conceived (Cohen 35, Wilkinson) 36. For, while in some cases, risks and welfare concerns resulting from donor anonymity may clearly be related to considerations regarding safety such as a lack of knowledge regarding propensity to genetic disease, in others these decrements are *primarily* caused by social norms and attitudes which privilege genetic ties between families and lead donor conceived offspring to place significant value on cultivating relationships with their donors and donor siblings. Indeed, given increasing acceptance of the social nature of many of the harms associated with disability, it may also be found that the physical risks associated with the use of MAR to children, may be significantly reduced in their intensity through attending to the social context in which disability arises (Beaudry) 37 and this too may affect calculations regarding risk.

Once we have determined which risks count within the remit of safety considerations, questions then move to focus on how we should weigh such risks given difficulties in both forecasting the long-term risks of MAR and their incidence, the catastrophic nature of some of those risks which may affect the germline, *and* in obtaining data through the long-term follow up studies of children born through MAR. Ought, we, as in other contexts, calculate the acceptability of risks by straightforwardly using expected value analysis: combining data we have regarding the probability of their occurrence with their disvalue. Ought we only to take into account *known* harms and risks, using a narrow evidence-based methodology (Read & O’Riordan) 38? Or, given the inevitability of uncertainty in this context and attendant difficulties in establishing causal connections between our activities and outcomes, ought we to take a more risk averse approach by implementing a precautionary approach which assigns greater disvalue to small and/or uncertain risks of significant harm/damage than standard approaches to risk management (Manson)39? One thing is certain, however we choose to weigh risks, proper attention to safety concerns in MAR, as in all areas of medicine, requires robust pre-clinical research on offspring risks prior to application in humans, and long-term and wide-ranging follow-up of children born through MAR in order to track both foreseen and unforeseen outcomes, and improve technologies and techniques.

**4.3 Long Term Follow-up of MAR Conceived Children**

While proper attention to the long-term safety risks of MAR for children born requires research exploring outcomes for such children, difficulties in obtaining data over the long-term are significant, and careful attention should be paid, as in all research contexts involving children, to principles relating to the best interests of the children involved, necessity, harm minimisation, and informed consent. For patients and children regular attendance at clinical appointments, for example, can impose significant physical, psychological and financial costs. As a result it is generally considered that attention should be directed to the question of compensation for research involvement, follow-up studies should involve only minimal risks to children, be performed only when the results of research are considered to be in the best interests of the child or children generally such as where the information collected over time is liable to impact the direction of treatment in the future, and where parties to the research are made aware of its purpose and appropriate consent/assent is provided by the parents and child and/or the child once they have reached majority (Medical Research Council) 40.

Importantly, the crucial party to follow-up, the resulting child, cannot be asked for a long-term commitment at the onset of treatment (Jans) 2. Moreover, long term follow-up, and especially cross-generational follow-up is also challenging as it requires studies that continue over several years and decades, which are difficult to fund. These limitations lead to a situation in which it is oftentimes incorrect to label a treatment as ‘established’, although it has surpassed the early experimental phase. For this reason, it was suggested that a third, intermediate label should be introduced, ‘innovative treatment’, to better clarify to the patient that there is continuum from experimental to established treatment and that uncertainties oftentimes remain even when treatments no longer have the ‘experimental’ label (Provoost) 41. In order to gather sufficient data to be able to re-categorise innovative treatments as established treatments, those collecting, collating and analysing such data must ensure long-term sources of funding are available to support follow-up studies and establish long term risks.

**5 Conclusion**

* When judging whether long term risks in MAR are justified, different aspects need to be balanced against one another.
* Discussions regarding the right to reproduce and liberty grant individuals’ significant autonomy with respect to reproductive decision making.
* The physician’s responsibility to reduce harm to both recipients and offspring cast doubt on the paramount nature of individual autonomy in the context of reproduction, as do worries regarding problematic social pressures and norms.
* Worries regarding child welfare are also particularly difficult to weigh in this context given both the implications of the non-identity problem and difficulties in long term follow-up of MAR conceived children.
* Our reproductive choices do not occur in a vacuum, as such the wider social implications of MAR must also be considered and principles of responsible innovation be adhered to, both in the clinic and in research contexts.

References

1. Dondorp, W., & de Wert, G. (2011). Innovative reproductive technologies: risks and responsibilities. Human Reproduction, 26(7), 1604-1608.
2. Jans et al. 2020. V. Jans, W. Dondorp, S. Mastenbroek, H. Mertes, G. Pennings, H. Smeets, G. de Wert, “Between innovation and precaution: how did offspring safety considerations play a role in strategies of introducing new reproductive techniques?”, *Human Reproduction Open*. 2 (2020). pp. 1-9.
3. ESHRE Task Force on Ethics and Law. (2011) “The moral status of the pre-implantation embryo” *Human Reproduction* 16(5), pp 1046–1048, <https://doi.org/10.1093/humrep/16.5.1046>
4. H. Mertes. 2012. “Understanding the ethical concerns that have shaped European regulation of human embryonic stem cell research” *Proceeding of the Belgian Royal Academies of Medicine* 1, pp.127-139.
5. Hofmann, B. (2002). Is there a technological imperative in health care?. International journal of technology assessment in health care, 18(3), 675-689.
6. Parens, E., & Asch, A. (2003). Disability rights critique of prenatal genetic testing: reflections and recommendations. Mental retardation and developmental disabilities research reviews, 9(1), 40-47.
7. J. A. Robertson, 1994. *Children of Choice: Freedom and the New Reproductive Technologies*. Princeton: Princeton University Press).
8. L. M. Purdy. 1989. “Genetic Diseases: Can having children be immoral?” in *Ethical Issues in Modern Medicine*, ed. John Arras and Nancy K Rhoden 3rd ed. California: Mayfield publishing company. Pp. 311-317.
9. Overall, C (1993) Human Reproduction: Principles, Practices, Policies, Oxford University Press, Toronto.
10. Savulescu, J (1999) Sex selection: the case for. Medical Journal of Australia 171, 373-375.
11. Harris, J (2004) On Cloning: Thinking in Action. London, Routledge.
12. Feinberg, J (1973) Social Philosophy. Prentice Hall, Engelwood Cliffs, NJ.
13. J. S. Mill. 1869. *The Subjection of Women*. London: Longmans, Green, Reader and Dyer.
14. J. Locke. 1689. “The Second Treatise of Government', in P. Laslett (ed.), *Two Treatises of Government* Cambridge: Cambridge University Press, 1960.
15. S. I. Benn. 1988. *A Theory of Freedom*. Cambridge: Cambridge University Press.
16. J. Rawls. 2001. *Justice as Fairness: A Restatement*. Cambridge, Massachusetts: Belknap Press.
17. Jackson, E (2007) Rethinking the pre-conception welfare principle. In Horsey, K. and Biggs, H. (eds) Human Fertilisation and Embryology: Reproducing Regulation. Routledge-Cavendish, London.
18. S. Franklin, 1998. 'Making Miracles: Scientific Progress and the Facts of Life', in S. Franklin and H. Ragone (eds.), *Reproducing Reproduction*. Philadelphia: University of Pennsylvania Press. pp. 102-117.
19. Mertes, H. (2017). The role of anticipated decision regret and the patient's best interest in sterilisation and medically assisted reproduction. Journal of medical ethics, 43(5), 314-318.
20. Mackenzie C and Stoljar N (eds) (2000) Relational Autonomy: Feminist Perspectives on Autonomy, Agency, and the Social Self. Oxford: Oxford University Press.
21. Donchin A. (2001) Understanding autonomy relationally: toward a reconfiguration of bioethical principles. J Med Philos 2001; 26: 365–386.
22. Dove, E. et al (2017) Beyond individualism: Is there a place for relational autonomy in clinical practice and research? Clinical Ethics, 12(3) 150–165.
23. National Health Service. 2021. ‘Availability: IVF’. Available at: <https://www.nhs.uk/conditions/ivf/availability/> [accessed 13 July 2021].
24. M. Crawshaw, et al on behalf of the British Infertility Counselling Association (2021): Counselling challenges associated with donor conception and surrogacy treatments – time for debate, Human Fertility, DOI: 10.1080/14647273.2021.1950850
25. J. Daniluk, 2002. “If We Had It to Do Over Again . . .”: Couples’ Reflections on Their Experiences of Infertility Treatments. The Family Journal: Counseling and therapy for couples and families, Vol. 9 No. 2, April 2001 122-133.
26. J. A. Robertson. 2004. “Procreative Liberty and Harm to Offspring in Assisted Conception” *American Journal of Law and Medicine* 30: 7-40.
27. G. Pennings, G. de Wert, F. Shenfield, J. Cohen, B. Tarlatzis & P. Devroey. 2007. “ESHRE Task Force on Ethics and Law 13: the welfare of the child in medically assisted reproduction.” *Human Reproduction* 22(10), pp. 2585-2588.
28. B. Steinbock. 2009. “Wrongful life and procreative decisions”. *In Harming future persons: Ethics,genetics and the non-identity problem*, ed. M. A. Roberts and D. T. Wasserman, London: Springer, pp. 155–178.
29. E. Rakowski. 2002. Who should pay for bad genes? *California Law Review* 90(5): 1345–1414.
30. R. Bennett. 2009. “The fallacy of the principle of procreative beneficence”. *Bioethics* 23(5), pp. 265–273.
31. D. W. Brock. 1995. “The non-identity problem and genetic harms: The case of wrongful handicaps.” *Bioethics* 9: 269–275.
32. D. Parfit. 1984. *Reasons and Persons*. Oxford: Clarendon Press.
33. A. Buchanan, D. W. Brock, N. Daniels & D. Wikler. 2000. *From Chance To Choice: Genetics and Justice.*  New York: Cambridge University Press.
34. N. J. Williams. 2017. “Harms to ‘others’ and the Selection Against Disability View” *Journal of Medicine and Philosophy*. 42 (2): 154-183.
35. I. G. Cohen. 2011. “Prohibiting Anonymous Sperm Donation and the Child Welfare Error.” *Hastings Centre Report*. 41(5): 13-14.
36. S. Wilkinson. 2016. “Gamete donor motives, payment, and child welfare.” In S. Golombok, R. Scott, J. B. Appleby, M. Richards, & S. Wilkinson. *Regulating Reproductive Donation*. Cambridge: Cambridge University Press, pp. 232-258.
37. J. S. Beaudry. 2016. “Beyond (Models of) Disability?”  *Journal of Medicine and Philosophy*. 41(2): 210-28.
38. R. Read & T. O’Riordan. 2017. “The Precautionary Principle Under Fire.” *Environment: Science and Policy For Sustainable Develipment*. 59(5): 4-15.
39. N. A. Manson. 2002. “Formulating the precautionary principle” *Environmental Ethics*. 24(3): 263-274.
40. Medical Research Council. 2004. *MRC Ethics Guide:**Medical research involving children*. Available online at: <https://mrc.ukri.org/documents/pdf/medical-research-involving-children/> [accessed 04 July 2021]
41. V. Provoost, K. Tilleman, A D'Angelo, P. De Sutter, G. de Wert, W. Nelen, G. Pennings, F. Shenfield, W. Dondorp. 2014. Beyond the dichotomy: a tool for distinguishing between experimental, innovative and established treatment, *Human Reproduction*, 29 (3), pp. 413-417.
1. In the UK, for example, it is held that in matters affecting the interests of children their welfare is to be considered of paramount importance, and that in the context of assisted reproduction practices and procedures which pose *significant risks of physical and/or psychological harm* to children will be prohibited (Human Fertilisation and Embryology Act, 1990, s. 13(5)). [↑](#footnote-ref-1)
2. For example, ESHRE’s Ethics and Law Taskforce claims that “Technology and research must always be subordinate to the welfare of the future offspring…the interests of future offspring must prevail on the development and progress of science.” (Pennings et al, 2007, p.2587). [↑](#footnote-ref-2)