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ORIGINAL ARTICLE

Silences, omissions and oversimplification? The UK debate on mitochondrial donation

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Abstract Drawing on scholarship from ignorance studies, this paper uses the case of the UK debates on mitochondrial donation (2012–2015) to emphasize the importance of deploying an analysis of ignorance that goes beyond medical and safety concerns when scrutinizing debates or campaigns around new reproductive technologies. In contrast to what happened with previous reproductive health treatments or drugs, the potential medical risks of mitochondrial donation were explicitly acknowledged and examined during its public and parliamentary discussions. However, I show, using the concepts of 'acknowledged unknowns' and 'ignored knowns', how the attention drawn to the medical risks contributed to obscuring the assessment of its economic and social impacts by silencing key knowledge regarding the limitations of mitochondrial donation in relation to the potential beneficiaries, the scope of the techniques, their alternatives and their costs. This article therefore calls for more systematic use of an integrated analytical framework of ignorance to be applied in the field of reproductive public policies, paying particular attention not only to the ways that medical risks are addressed, but also to the type of knowledge and disciplines this allows to silence or side-line in the framing and assessment of new biotechnologies.

KEYWORDS: Ignorance studies, Reproductive technologies, Mitochondrial donation, UK biomedical politics, Three-parent baby, Ignored knowns

Introduction

Over the past few years, the field of ignorance studies has expanded progressively to objects and issues of the reproductive domain, opening up stimulating theoretical perspectives and analytical approaches by (re)orienting the focus on what remains silenced or unknown around certain topics, and what knowledge is mobilized. A number of works have emerged, predominantly highlighting the way the medical risks or side-effects of some reproductive practices or treatments have been ignored, dismissed or concealed in order to facilitate their acceptance or dissemination in clinics or society (see the 'Introduction' article in this special

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issue on 'Risk, innovation and ignorance production in the field of reproductive biomedicine'). In line with previous feminist STS works on new reproductive technologies, they have shown, once more, how it is women, their bodies and their offspring that are most exposed to the negative consequences of the ignorance of particular knowledge (Kammen and Oudshoorn, 2002; Tuana, 2006).

Building on this body of work and developing it further, this article seeks to emphasize the importance of deploying an analysis of ignorance, understood in a broad sense as non-knowledge, silences, omissions and concealments, and the dynamic of its production, which goes beyond examining the ways that safety concerns have been handled in debates or campaigns around new reproductive treatments or technologies. The paper draws on my study of reproductive choices in the context of mitochondrial disorders carried out between 2012 and 2016. I use the case of the UK debates on mitochondrial donation, also called 'mitochondrial replacement techniques', to show why it is necessary to integrate the analysis of safety risk assessment into a wider analysis of the different aspects of new technologies or treatments, including their social and economic impacts, which might have been silenced during their public discussions. In contrast to what happened with some previous reproductive health treatments or drugs, such as Primodos, where medical risks and side-effects were concealed or ignored (Olszynko-Gryn et al., 2018), I show, based on the data I collected through various sources (e.g. stakeholder interviews, documentary analysis and observations), that these potential risks, in the case of mitochondrial donation, were explicitly acknowledged and assessed during its public and parliamentary debates. However, key information regarding the targets of the techniques, their impacts, their alternatives and their costs were dismissed, and this contributed to make them appear unique, desirable and necessary. I therefore distinguish and identify the 'acknowledged unknowns' — in this case, the uncertainties associated with specific, recognized medical risks for future offspring — from the 'ignored knowns' of the debates — that is, key issues which were side-lined, omitted or overlooked — in order to show how the attention drawn to these safety risks contributed to obscuring significant limitations of mitochondrial donation. Based on this analysis, I argue that only an integrated analysis of ignorance, looking at the way both the 'acknowledged unknowns' and 'ignored knowns' are articulated together, can provide a sufficiently complex and complete picture of how and why certain types of knowledge surrounding new reproductive treatments are mobilized at the expense of others. This article therefore calls for a more systematic use of such an integrated analytical and theoretical framework of ignorance to be applied in the field of reproductive public policies, paying particular attention not only to the ways that medical risks are addressed, but also to the type of knowledge and disciplines this allows to silence or side-line in the framing and assessment of new biotechnologies.

Context and methods

The UK remains the first and only country to have, since 2015, legalized mitochondrial donation, a high-profile in-vitro fertilization (IVF)-based technique that involves replacing the mitochondria of maternal reproductive cells, including the mitochondrial DNA (mtDNA), which might be passed on to subsequent generations. The aim of mitochondrial donation is to prevent the transmission of maternally inherited mitochondrial disorders, which are caused by mutations of mtDNA situated in the cell's cytoplasm. These disorders can trigger various bodily dysfunctions, such as hearing loss, stroke or neurological problems, and potentially lead to severe or fatal diseases, such as dementia or myopathy. Over the past two decades, several reproductive techniques designated under the umbrella term 'mitochondrial donation' — the two major techniques being maternal spindle transfer and pronuclear transfer — have been developed for transferring the nuclear DNA of an affected embryo into a healthy enucleated donor embryo (Craven et al., 2010). In both cases, if the intervention is successful, the resulting baby will be born with nuclear genes from the intending mother and father, but the unaffected mitochondria, including 37 mitochondrial genes, will come from the egg donor. As these techniques involve the conception of offspring made with the genetic material of three people, they are often dubbed 'three-parent IVF' in the media (Connor, 2014), a particularly questionable trope.

The possibility of legalizing the clinical use of mitochondrial donation attracted increased attention in 2012 when Nuffield Council on Bioethics published a report on this topic (Nuffield Council on Bioethics, 2012), followed by a public consultation launched by the Human Fertilisation and Embryology Authority (HFEA, 2013) — the body that regulates application of reproductive technologies and embryo research in the UK. The techniques were mentioned and discussed regularly in the media and the public sphere up until 2015, when they were debated within the Houses of Parliament. Over these debates, mitochondrial donation generated high expectations from patient support groups and part of the UK scientific community, including the Wellcome Trust, and was subject to many claims regarding its potential to meet patients' needs and promote UK biomedical scientific advances (Dimond and Stephens, 2018a). In the media, some framed it as the 'only hope' for at-risk women who wanted a genetically-related offspring unaffected by mitochondrial disorders, while others suggested a more sinister framing by emphasizing its 'unnaturalness' and using the terms 'designer babies' or 'three-parent babies' (Herbrand and Dimond, 2018; Ravitsky et al., 2015).

Due to its pioneering role in developing and finally authorizing mitochondrial donation under strict conditions, the UK is regularly presented and praised as a model to follow when developing, debating and regulating these techniques (ISSCR, 2015). For instance, in December 2015, at a well-attended public conference, Sally Cheshire, the Chair of HFEA at that time, attributed the adoption of the law to particular features of the UK: its specialized scientific expertise; its regulatory system; the existence of HFEA; and the capacity of HFEA to engage with the public through consultation exercises (Herbrand, 2016). These institutions and modes of regulation have certainly helped guarantee the basis for good research and safe therapeutic treatments, as well as facilitating public acceptance of mitochondrial donation in the UK. However, they alone may not have been sufficient to convince Members of Parliament

to pass the regulations without a number of more strategic actions by the advocates of the techniques.

Previous work from social scientists has shown that a number of elements contributed to easing and accelerating the legalization of mitochondrial donation, particularly the active engagement of patients with the media and politicians, the development of a powerful alliance in favour of the techniques supported by the Wellcome Trust — a major UK research funder — and the framing of the debates on the techniques as one of 'religion versus science' (Dimond and Stephens, 2018a). Moreover, the campaign in favour of the techniques was characterized by the mobilization of an emotionally-driven rhetoric of hope (Herbrand and Dimond, 2018), inaccurate and exaggerated claims regarding the purpose of this reproductive intervention by assimilating it to a 'treatment' (Rulli, 2016), the use of a number of specific labels and metaphors euphemizing the presentation of the techniques (Baylis, 2017), and the deliberate minimization of both the role of mitochondrial donors (Haimes and Taylor, 2015) and the significance of mitochondria (Chan, 2015; Turkmendag, 2017). Some authors also pointed out a number of issues that were distorted or neglected during the debates (Haimes and Taylor, 2017; Herbrand, 2017).

By drawing on scholarship from ignorance studies (Gross and McGoey, 2015; Proctor and Schiebinger, 2008), this article seeks to pursue these critical analytical efforts and discuss how the legalization of mitochondrial donation was facilitated by both the mobilization and the ignorance of particular knowledge, which contributed to overlooking or downplaying information about potentially controversial issues during the mitochondrial donation public and policy debates. Analyses using the conceptual tools of ignorance studies show how ignorance and the cultivation of strategic unknowns can be harnessed as a resource to obscure or conceal knowledge, and ultimately used as a source of power (Gross and McGoey, 2015). As a number of authors have shown (Callon et al., 2009), when undergoing democratic debates on new and controversial technologies which, by definition, are still surrounded by many uncertainties and risks, it appears crucial to analyse critically which knowledge and non-knowledge have been provided, by whom and to which audience, as these directly shape the framing of the debates and the assessment of the technologies. This is particularly important when the information comes from institutional actors, such as Nuffield Council on Bioethics and HFEA, and is presented as the official knowledge available in the field. Revisiting the UK debates on mitochondrial donation through the lens of ignorance production therefore allows an examination of the way the silences and omissions around certain aspects of the techniques have worked in favour of its advocates by significantly amplifying its potential in the public eye. Furthermore, this particular case offers new insights into the way safety risks can be used strategically to divert attention from other potentially controversial issues in debates on emerging reproductive treatments.

Silences and omissions are, of course, not entirely and necessarily attributable to one type of actor, and opponents of the techniques also deployed a number of strategies to depict mitochondrial donation in a negative light, using a rhetoric of fear, misleading comparisons and simplistic tropes (e.g. the 'three-parent baby' or the 'designer baby'). However, these silences and omissions mostly served, in the case of the debates on mitochondrial donation, the interests of the proponents of the techniques. They are thus prioritized in this analysis, particularly as the advocates of mitochondrial donation played a key role in influencing the debates, notably by initially selecting the issues to be addressed in the public debates that were to come (Dimond and Stephens, 2018a).

I begin by examining how safety concerns were addressed in the debates on mitochondrial donation held at both the Houses of Parliament and at a number of public events organized by the Wellcome Trust, HFEA and the Progress Educational Trust — a charity whose mission is to educate and debate the responsible application of reproductive and genetic science — as well as the discussions on this topic that appeared in the media between 2012 and 2015. Next, I discuss some issues that were dismissed or ignored due to key information and knowledge being absent from these public and parliamentary debates, and examine the processes whereby these omissions happened, examining how they were introduced and maintained. Following this, I question the extent to which these omissions were deliberate, suggesting that they may have been part of the wider efforts deployed by the advocates of the techniques to present the potential of mitochondrial donation in a wholly positive light. I then explore the various impacts of these omissions and the use of strategic unknowns in the debate on mitochondrial donation, and conclude by stressing the importance of examining the silences and omissions beyond, and in relation to, safety issues when analysing reproductive policy debates.

This analysis is drawn from a qualitative study of reproductive choices in the context of mitochondrial disorders carried out between 2012 and 2016 (Herbrand, 2017; Herbrand and Dimond, 2018). This consisted of in-depth interviews with 28 women affected by mitochondrial disorders and 12 scoping interviews undertaken with key stakeholders, such as genetic counsellors, clinicians and support group representatives (for which ethical approval was granted by De Montfort University and the London NRES Committee), as well as an analysis of a range of UK public documents on mitochondrial donation circulated between 2012 and 2015 in the UK, including all the official briefs and statements, the policy and parliamentary reports and transcripts, the information documents provided by the key actors, the debates, and a large sample of the media and scientific releases published on this topic. These documents were systematically collected and analysed using thematic analysis. I also attended numerous public and policy debates and events surrounding mitochondrial donation that took place over that period, such as the public discussion events at the Houses of Parliament, the Progress Educational Trust public debates and academic conferences. This enabled me to gain a detailed and in-depth understanding of the topic from the perspective of various actors, and to identify key omissions and inaccuracies in the debates by cross-checking the different sources of information. The data presented here are primarily based on the stakeholder interviews, the documentary and media analysis, and the debate observation.

The risks taken or 'acknowledged unknowns'

Before delving into the omissions in the debates, it is important to examine how the safety issues around mitochondrial donation were addressed. Indeed, as mentioned earlier, a number of new reproductive health treatments and technologies have been criticized retrospectively because of the way their clinical applications, or the campaigns or debates sustaining them, minimized, dismissed or obscured some of their possible medical risks and side-effects. In the case of mitochondrial donation, however, it is interesting to observe that the potential risks posed by the technology to the welfare and health of future offspring were an important source of concern in the UK debates, and were eventually, as I show below, acknowledged as part of the uncertainties and risks surrounding any new medical treatment. I therefore refer to these issues as the 'acknowledged unknowns' or 'not yet knowns' of the debates (i.e. the uncertainties surrounding both the medical and psychosocial implications for the future offspring born from mitochondrial donation techniques), which were openly discussed and acknowledged.

Three main issues regarding the risks for future offspring marked these debates: the potential side-effects caused by the co-existence of two different types of mitochondria within the embryo's cytoplasm, including the possible carry-over of pathogenic mtDNA; the possible defects caused by mismatching the nuclear and mitochondrial genomes, such as metabolic dysfunction and epigenetics effects; and the social and psychological consequences of having been conceived using genetic material from three people. The majority of discussions around these issues happened between 2012 and 2015 during the public debates preceding the vote on the draft regulation, through press releases, scientific publications, policy reports and communications at public events, where a number of experts and policy makers intervened. The safety risks were assessed on various occasions by independent key experts and institutions, including an expert panel commissioned by HFEA (2014). They were also outlined briefly in the report by Nuffield Council on Bioethics (2012), which also included the possible impacts of the techniques on the health and identity of children conceived through mitochondrial donation. It is worth noting that both opponents and proponents of the legalization of the techniques also played a key role in focusing the attention on these safety issues; the former by using these issues as a way to challenge and contest the techniques (Morrow, 2014), and the latter in their efforts to mobilize expertise and evidence in order to minimize the risks involved. Safety concerns were mentioned less often during the parliamentary debates; other issues prevailed during these discussions, such as the suffering experienced by the families or the 'slippery slope' towards designer babies (Dimond and Stephens, 2018a; Herbrand, 2017).

Overall, it seems fair to contend that these safety issues were taken seriously given the time, the expertise and the publications mobilized during the debates. It nonetheless remains difficult to establish with certainty whether the safety risks needed to be investigated further, and whether their potential impacts were given enough attention. At the time of the public debates, some scientists and politicians claimed that clinical applications of mitochondrial donation should not take place before more evidence was gathered from preclinical trials (Hansard, 2015: 105). However, on this point it appears that 'in comparison with ICSI [intracytoplasmic sperm injection] and PGT [preimplantation genetic testing], preclinical research on MRT [mitochondrial replacement techniques] was more extensive and more structured' (Jans et al., 2020: 4), as findings from preclinical studies conducted in embryo and animal models in the USA and the UK were available and examined by the HFEA review panel. Ultimately, these questions partly depend on scientific standards, ethical choices and whether judgements are sufficiently pluralistic. Ethical and technical evaluations are often entangled, and even the assessments and the deliberations of the HFEA advisory panel, which aimed to examine scientific and technical issues alone, encompassed some ethical judgement (Lewens, 2019).

However, some commentators have also argued that the aforementioned risks were, at times, presented in an optimistic manner and relativized in a way that is to some extent questionable (Haimes and Taylor, 2017). For instance, the report by Nuffield Council of Bioethics stated, in regard to the questions regarding the offspring's future wellbeing and sense of identity, that the answers were yet unknown, but 'in societies where gamete donation, surrogacy and adoption are established and largely accepted it seems unlikely that any greater problems would result for children born after the donation of mitochondria' (Nuffield Council on Bioethics, 2012: 77). This implies that these different forms of family making can be compared, as they involve the intervention of a third party. However, in mitochondrial donation, the genetic contribution of a third party happens at the cellular level, with DNA materials from three different people combined together to create a new embryo. It is therefore difficult to predict whether it will or will not create new issues in terms of personal identity and parental connection. Another example of the normalization of the risks was offered by Professor Mary Herbert, a researcher working on mitochondrial donation, in her response to Nuffield Council on Bioethics' call for evidence. She explained that 'while the findings of ongoing research into PNT/MST [pronuclear transfer/maternal spindle transfer] will help to inform patients considering these treatments, obviously it will not be possible to gather information on live births until the techniques are offered in clinical treatment. Thus, an element of risk will remain. This is analogous to the situation for other techniques in assisted conception and indeed in many other areas of medical practice. In this respect, there is therefore no new ethical dilemma' (Nuffield Council on Bioethics, 2012: 66). As illustrated by this quotation, safety risks relative to mitochondrial donation are presented not only as part of any experimental medical procedures and thus 'unavoidable', but also as similar to those raised by other IVF-based procedures; however, mitochondrial donation involves an extra layer of complexity and risk by transferring the nuclear material between eggs or embryos. In a similar way to discourses around other previous high-profile techniques (O'Riordan and Haran, 2009), the novel and controversial features of mitochondrial donation are downplayed by depicting it as an extension of existing IVF practices,

showing how IVF operates as a core technology for normalizing novel technology (Throsby, 2004).

While the extent to which the safety risks should be investigated can be perceived differently, it does not mean that these issues were ignored or hidden during the public and policy debates on mitochondrial donation. On the contrary, these concerns, I contend, were made visible and addressed in a serious manner. If the risks did not appear sufficient to abandon the legalization of the techniques, they nonetheless prompted the Members of Parliament to adopt a 'cautious approach' (Jans et al., 2020), in which clinical applications of mitochondrial donation were authorized provided that further experiments were conducted and under a number of strict conditions recommended by HFEA. This approach illustrates a willingness to act in spite of some areas of 'well-defined ignorance' or 'non-knowledge', defined by Gross and McGoey as 'the possibility of becoming knowledgeable about the specifics of one's own ignorance' (Gross and McGoey, 2015: 4). In the case of mitochondrial donation, the areas of non-knowledge were investigated, discussed and taken into consideration in order to manage the risks as well as possible, based on the scientific and medical information collected and provided to the Members of Parliament by HFEA, the Department of Health, the Progress Educational Trust and patient support groups. This is why I refer to them as the 'acknowledged unknowns' of the debates, which are destined to evolve through political investment and knowledge production work. The parliamentary decision reflects a willingness to support innovation and accept some risks, as long as the benefits of the innovation appear to overcome the potential harms, and the risks are minimized through safety measures.

The omissions or 'ignored knowns'

As a number of scholars have highlighted, focusing on a few specific issues often draws attention away from broader or more controversial ones (O'Riordan and Haran, 2009; Parry, 2003). From the perspective of ignorance studies, it is especially interesting to examine how particular knowledge has been put forward while other knowledge has been ignored. In the case of mitochondrial donation, one can observe that while the risks related to the welfare of future offspring born from mitochondrial donation were acknowledged and discussed at length during the debates, some key scientific, medical, social and financial information affecting the impact of the technologies was rarely mentioned, including the heterogeneous profiles of the future users, limited access to the techniques, existing reproductive alternatives, and the costs involved.

The beneficiaries of the techniques: a partial view of women's profiles

During the public debates in the UK, media releases and official briefs from HFEA, the Department of Health and the Wellcome Trust usually depicted mitochondrial donation as a technology that would allow 'women at risk' to have a non-affected biological child. While the functioning of mitochondrial donation and mitochondrial disorders were often described briefly, there was little explanation of who might be 'at risk', and very few details of the potential users of the technique were provided. They were usually referred to as 'patients', 'women carrying maternal disorders' or 'women with mitochondrial disorders'; however, these broad descriptions did not provide a sense of the number and characteristics of women who could potentially benefit from the techniques. Only partial information was provided about the medical conditions and family situations of these women. The women featured in the media were usually healthy women with seriously ill children, or women who had lost a child and were desperate to have another one. People affected by mitochondrial disorders were therefore predominantly represented as a homogenous group, sharing a common experience of suffering and loss due to the severe illness of their child. It is important to note, however, that mitochondrial disease is a complex condition, highly variable, and is late-onset for many people. The representation of mitochondrial disease as only affecting seriously ill children does not reflect the experiences of many of those who are currently living with the disease as adults (Herbrand and Dimond, 2018).

In this respect, there was almost no mention of women of reproductive age who were affected by the disorders themselves, and had started developing mild to severe symptoms that were likely to worsen in future. Yet, as I observed during my research interviews, several participants already affected by the disorder were willing to use these techniques to have a child; for some single women, this also required the use of a sperm donor. Interestingly, in situations where the potential future mother may be ill, the implications in terms of childbearing were usually absent from the media and public debates.

The explanation for this limited representation of 'at-risk women' in the public eye might be that women who were mildly or severely affected by mitochondrial disorders were more reluctant, or found it more difficult, to appear in the media due to their health conditions, compared with the asymptomatic women who were at risk of transmitting the disorders. People interviewed in the media were also often referred by a particular patient support group, the Lily Foundation, which was mainly composed of families who had lost a child or were living with an ill child. Whether unfortunate or not, these omissions regarding the range of women affected by mitochondrial disorders led to a distorted representation of the potential beneficiaries of the technique. This resulted in an obscuring of the experiences and needs of the women directly affected by the disorders, who had to make complex reproductive decisions while taking their health condition and personal circumstances into consideration (Baylis, 2017; Herbrand, 2017).

The scope of the techniques: obscuring their limits

Another important element minimized during the debates was the — intrinsic or imposed — limits of the technologies, which considerably impacted the number of individuals who could access them and use them successfully. The media and parliamentary reports regularly made reference to 'the families affected by mitochondrial disorders' and 'the women who could benefit from the techniques' without clearly differentiating them, which tended to assimilate

these two groups. However, these groups are very distinct in terms of access to mitochondrial donation, and only a small proportion of the families affected by mitochondrial disorders will be able to benefit from the techniques. There were a number of constraining medical and legal factors limiting their access and successful applications.

First, the use of mitochondrial donation depends on the transmission mode of the mutation, as the techniques can only prevent the transmission of disorders caused by mitochondrial DNA mutations (i.e. when the mutation is situated in the mitochondria outside the nucleus) and not those caused by nuclear defects (i.e. when the mutation is situated in the cell nucleus). In this respect, it is important to emphasize that most maternally inherited mitochondrial disorders only develop in adulthood (e.g. Melas or MERRF syndromes), whereas mitochondrial disorders that severely affect babies and children are caused, in approximately 80% of cases, by nuclear defects that are inherited from both parents (HFEA, 2014: 12). This means that most families who have a child affected by a mitochondrial disorder and wish to have another child will not be able to use the new techniques. However, these have tended to be the families portrayed in the media as the future beneficiaries of the techniques (McVeigh and Sample, 2014).

This key genetic distinction, and the fact that most families whose children were affected by mitochondrial disorders could not use the new techniques, were rarely explained in the public debates and in the reports by HFEA, the Department of Health and Nuffield Council on Bioethics. When these issues were mentioned, the reports stated that mitochondrial disorders could be caused by both types of mutations, but did not indicate the proportions or characteristics of the respective groups affected, or what it meant for the beneficiaries of the techniques. For instance, the HFEA document reporting patients' views from a focus group including six patients affected directly or indirectly by the disorders was written in a way that was rather confusing, if not misleading. While a brief description of the participants' backgrounds was provided, it was not specified whether or not they or their relatives could use the techniques, implying this was *a fortiori* the case, even when they were not suitable for them (HFEA, 2013: 8).

During an interview with an HFEA representative, I was told that these genetic differences and their consequences were too complex and thus needed to be simplified in order to push the legislation through. It seems, however, that this oversimplification was not just a matter of facilitating the public's general understanding of the issue. I myself observed how some confusions were also introduced and maintained throughout the parliamentary debates. For instance, some patients whose children were affected by nuclear defects stated during a debate in Parliament that if 'they could, they would use the technology', which they could not as it was not suitable for them from a medical point of view. However, this was understood by the audience as meaning that they would use the technique if they could legally access it, contributing to reinforce a collective misrepresentation. As I have mentioned elsewhere (Herbrand, 2017), it was also striking to observe, during the parliamentary debates, that most Members of Parliament did not seem to be aware of this crucial distinction. In a debate that mobilized so many medical and scientific experts, it is rather concerning that this distinction was never clarified or picked up by anyone, not even by the opponents to the techniques.

It is important to highlight here that the problem was not the scientific literacy of different publics and their engagements, but rather the ways that particular information, including scientific knowledge, was selected and framed in the debates. While it was, of course, expected for the information provided by the HFEA consultation and the media briefs to be limited in order to keep people engaged in the issues, this information was partial and mainly focused on the energy dysfunctions, the severe disorders, and the functioning of mitochondrial donation. The limited scope of the techniques and the issues at stake could have been explained more clearly by providing a more precise estimate of the number and profiles of the patients who were expected to actually benefit from the techniques.

Besides its medicotechnical limits, the use of mitochondrial donation was also restricted significantly by the 2015 UK law, which imposed specific medical criteria under which the technologies could be accessed. It required the existence of a high probability of both (i) transmission of faulty mtDNA from the mother's eggs; and (ii) development of a serious mitochondrial disease in the future offspring (HFEA, 2015). In practice, such criteria are complex and difficult to assess, as the intending mother has to be aware that she is a carrier and to have her mutation identified. This means that she first needs to obtain a genetic diagnosis, which is not always possible for various reasons (Herbrand, 2017), particularly in the case of asymptomatic women. These women usually discover that they can transmit the condition only after giving birth to an affected child. Furthermore, there is considerable uncertainty surrounding the evolution of the disease for an individual offspring, as siblings carrying the same mutation can develop the disorder to varying degrees. It is therefore difficult to predict if, when and to what extent a future child might develop some symptoms.

These legal criteria, while they provide an ethical justification based on what seems at first to be robust medical criteria, appear to be quite vague and confusing in practice. They might provide clinicians with some leeway to make decisions on a case-by-case basis, but they will nonetheless exclude a number of women affected by less severe forms of the disease from accessing mitochondrial donation (e.g. those with hearing or sight loss). What thus emerges from these different legal and ethical restrictions is that only a very narrow pool of women will be in a position to access the techniques: those of reproductive age willing to use high-profile reproductive technologies (Herbrand, 2017), who not only carry a severe form of the mitochondrial disorder and are aware of it, but whose mutation load is particularly high, meaning that they are unable to use PGT. At the same time, these women should not themselves be too severely affected by the disorder, as this could compromise their ability to take care of a child, as suggested in a short section of the report by Nuffield Council on Bioethics (2012: 71). This profile appears much more complex and restricted than what was shown in the media and, possibly, expected by patients. While access to the technology may have been restricted intentionally, by medical and legal conditions, to a few individuals in the first instance because of its experimental nature, this was not reflected in the public and par-

liamentary debates. Rather, the research team in Newcastle working on mitochondrial donation published a paper in 2015 estimating that mitochondrial donation could enable 'about 150 births a year if all women opted for the procedure' (Gorman et al., 2015). The following day, BBC News announced that nearly 2,500 women in the UK would benefit from mitochondrial donation (Gallager, 2015), creating high expectations and false hopes. Although the conditions for accessing mitochondrial donation might have been relaxed at a later stage, it is very unlikely that the number of users of the technology would have met the announced figures. This seems to be confirmed by the fact that the birth of a baby conceived from mitochondrial donation is yet to be reported in the UK.

Overall, these silences and omissions regarding the limitations of mitochondrial donation helped to exaggerate the impact of the techniques by presenting them as having the potential to help any women at risk of transmitting a mitochondrial mutation, for any type of mitochondrial disease, whereas in reality this will only be possible in very specific cases. It will certainly not eradicate mitochondrial disorders at a population level, as was frequently announced in the media and in Parliament (Herbrand, 2017). Moreover, the focus on the more serious forms of mitochondrial diseases during the debates contributed to the experience and needs of adult patients with milder symptoms being ignored and dismissed, particularly with respect to reproduction and parenting.

The existing alternatives: overlooking other reproductive options

Another element that did not attract much attention during the mitochondrial donation debates was the existence and availability of alternative reproductive options to mitochondrial donation. Most of the time, mitochondrial donation was presented as a straightforward solution and the preferred, if not only, option for women at risk of transmitting an mtDNA mutation to have children. However, this meant biologically related children, rather than unaffected ones. The emphasis was placed on the supposed 'need' for women carrying faulty mutations to have their own biologically related child, thus participating in the 'medicalisation of a social preference' (Rulli, 2016: 5). As Baylis explains, 'all too often, claims about a ''need'' for human nuclear genome transfer to satisfy a ''need'' for genetically-related children are asserted as though uncontroversial, when they should be interrogated' (Baylis, 2017: 13). By setting up biological parenting as an ultimate and unquestionable goal, the debate reinforced the normative — and thus culturally determined — injunctions to have biologically related children, dismissing or ignoring safer, cheaper well-established routes to achieving parenthood such as gamete donation or adoption, as well as the option of remaining childfree. These possibilities, if they were mentioned at all, were usually just listed briefly without detail, or characterized by their shortcomings and depicted in a negative light.

Interestingly, although the existing techniques of prenatal diagnosis (PND) and PGT can also help women to have biologically related and non-affected children by checking whether their embryos or fetuses are affected, these options were rarely discussed during the debates. PND has the disadvantage that it might lead to a selective abortion if the fetus is affected, and PGT may not be effective for the minority of women whose eggs have a very high level of mutated mitochondria. However, these techniques have been tested and proven useful for a number of patients. They are also cheaper and much simpler than mitochondrial donation. Contrary to what was claimed during the debates by the proponents of the techniques, mitochondrial donation was thus not necessarily the only option for women at risk to have a non-affected and biologically related child. For these reasons, both techniques deserve more attention and further explanation, not only to put the costs and benefits of mitochondrial donation into perspective but also in an effort to provide better public understanding of existing reproductive options and, ultimately, to widen their access and applications. Presenting mitochondrial donation as the only way to prevent the transmission of these disorders was misleading and inaccurate, especially as mitochondrial donation is only accessible by a limited number of women, as described above.

The efficiency of the technology: omitting the costs and resources involved

Surprisingly, the financial and human resources involved in the development and application of mitochondrial donation were rarely mentioned during the debates. The treatment cost only appeared in an annex of the consultative document on draft regulations published by the Department of Health, stating that 'we estimate each cycle of mitochondrial donation should cost in the region of £20,000' (Department of Health, 2014: 38). As a successful conception was expected to require four cycles [according to the 23% IVF success rate reported by HFEA (2018)], the estimated cost of successful mitochondrial donation treatment would amount to £80,000.

Despite the high cost of this treatment, at the time of the debates, there was a lack of discussion of who would fund the access to mitochondrial donation, how much it might cost the National Health Service (NHS), and, if it were not publicly funded, how widespread its use would be, given issues of affordability. First, it is worth mentioning that even if mitochondrial donation were publicly funded, this would not mean that patients would actually be able to benefit from NHS funding, as current criteria to access NHS funding for reproductive treatments are quite restrictive. A comparison with PGT, an existing treatment that also offers a possible avenue to conceiving an unaffected child (see above), is helpful here. In my study, although several couples met the medical criteria for PGT, they were not eligible for NHS funding because they did not meet the 'social' eligibility criteria, such as not already having a healthy child from a current or previous relationship. They therefore had to forego the option of PGT as they could not afford private treatment (Herbrand, 2017). If current commonly applied criteria for NHS funding for PGT were to be applied to eligibility for mitochondrial donation, it would similarly prevent some women accessing NHS-funded treatment. PGT typically costs £7000—13,000 per cycle. If women are unable

to afford PGT, private treatment using mitochondrial donation, costing around £20,000 per cycle, will also be out of their reach. Issues about the restricted public funding of reproductive technologies in the UK and existing inequalities in access to treatment were never raised during the debates.

In addition, there was no mention in the debates of the many other considerable costs involved in the development and implementation of mitochondrial donation, such as the costs required to train specialized teams, put the adequate infrastructures and administrative regimes in place, conduct follow-up studies, and collect a large number of eggs for research and future treatments (Haimes and Taylor, 2015). The financial and administrative means necessary to recruit and compensate egg donors (£750 per cycle), especially in the context of the current shortage of egg donors, were also absent from the debates. Although these costs were partly funded by the Wellcome Trust — initially via an investment of £4.4 m in 2012 and then a £6.3 m fund in 2016 (Newcastle University, 2016) - it is unclear why there was no proper assessment of the cost-effectiveness of developing mitochondrial donation techniques and offering them in a context of limited healthcare resources. The financial impact of mitochondrial donation for individuals or the NHS may not have been the most pressing or relevant issue in the parliamentary debate, but it remains an important element of any public health policy and must be assessed in relation to the common good and the needs of the many (Baylis, 2017). It would therefore have been useful, in particular, to discuss and consider the costs of implementing mitochondrial donation in the UK against the costs of treating children and adults who have mitochondrial diseases, often over many years. It was only two years after the parliamentary debates, when the £8 m NHS funding in mitochondrial donation clinical trial was announced, that it was indicated that 'the lifetime treatment cost for a patient with serious mitochondrial disease is around £1.3 m' (NHS, 2016).

Intentional ignorance: to what extent?

By analysing the information drawn from interviews with key experts and from the key documents circulated or published during the UK public and parliamentary debates, I have identified a number of central elements regarding mitochondrial donation that were ignored or dismissed: the heterogeneous profiles of the potential users; limited access to the techniques; existing reproductive alternatives; and the costs involved. These elements were reliant on existing medico-scientific knowledge and socio-economic data, which could have been made available, explained and mobilized during the discussions on mitochondrial donation. All these elements were potentially significant for the public understanding of patients' needs and the impacts of these technologies. Omitting them left policy makers and society with an incomplete picture of what clinical applications of mitochondrial donation implied and who the potential beneficiaries would be.

It is difficult, however, to determine whether these elements were just unfortunate omissions and misunderstandings resulting from a lack of time or effort, or whether they were intentionally generated and maintained in the debates, possibly for strategic reasons. While some Members of Parliament might not have been aware of all the scientific information and of its consequences, I have shown in the analysis above that some key actors in the debates, including scientific experts, clinicians and representatives of patient support groups and the Wellcome Trust, did know about these important omissions and confusions, but did not take the time or the opportunity to clarify or discuss them. Other analyses of the debates tend to suggest that these 'ignored knowns' were part of a wider set of strategic actions deployed by the advocates of the technologies.

Dimond and Stephens, in particular, have shown how proponents of the legalization of mitochondrial donation included a number of key people and groups, e.g. scientists and clinicians specializing in mitochondrial disorders, patient support groups and the Wellcome Trust, who prepared and organized a campaign in favour of the techniques from 2010, in parallel to the scientific developments (Dimond and Stephens, 2018a: 29). This core group was supported by other established personalities and organizations, some of whom had already played a key role in previous UK debates around the 2008 HFEA Act. For instance, the Science Media Centre, a UK independent press office, drew on the experience they had acquired through orchestrating the campaign in the human admixed embryos debate to engage scientists and media professionals in the mitochondrial donation debate (Dimond and Stephens, 2018b: 35). Together, this 'working group looked to gather information, predict potential challenges to legalisation, and gain insight into the voting intentions of parliamentarians' (Dimond and Stephens, 2018b: 30). In the same vein, a number of commentators have emphasized how rhetorical and persuasion strategies were discussed and agreed on by these advocates in order to embellish the role of the techniques (Rulli, 2016) and to minimize the role of the egg donors and the significance of mitochondria, while banning terminologies that would describe the techniques in a negative or suspicious way (Chan, 2015; Haimes and Taylor, 2015).

While it seems reasonable to conclude that there were some strategic ignorance strategies deployed during the debates, it is unclear why the opponents did not pick up on these silences to challenge the potential of mitochondrial donation. One possible explanation could be that they included a number of smaller and very disparate groups who did not make natural allies and thus did not adequately mobilize when opposing the legislation. These included religious groups, secular groups positioned against human genetic interventions, and some scientists. In addition, the lack of scientific expertise among their ranks might explain their limited engagement regarding the various scientific and clinical aspects of the disorders (Dimond and Stephens, 2018b: 56). This might also account for their focus on raising safety concerns and emphasizing the risks of 'slippery slopes', instead of examining the actual scope and limitations of the techniques more closely.

Silences and unknowns around mitochondrial donation: the implications

This analysis of the omissions and strategic unknowns in the debates on mitochondrial donation, besides contributing to

a better understanding of the impacts and limitations of these technologies, has proven useful in providing important insights regarding the way they were framed and debated in the UK. It offers a novel perspective on the way particular knowledge, especially scientific and medical knowledge, was mobilized, side-lined or ignored in order to serve specific interests, completing previous analyses that focused on the more tangible elements such as the discursive strategies, the arguments and the interactions between actors that marked the debates.

I have shown that while the dismissal of the safety risks of new treatments has often been denounced in the domain of reproductive health, these risks were not only put to the fore in the debates on mitochondrial donation, but also played a key role in the way that these debates and the technologies were framed. Interestingly, both the advocates and the opponents of the techniques participated in emphasizing safety concerns. A direct consequence of this was discussion, at length, of a number of issues of which the impacts and side-effects for embryos and future offspring were uncertain. In light of what I refer to as the 'acknowledged unknowns', the Members of Parliament then decided to adopt a cautious approach, allowing clinical use of the techniques under strict conditions and in specific cases, while minimizing the possible safety risks. This cautious approach has contributed to providing legitimacy and credibility for the public and an international audience.

However, it is also important to emphasize that this focus on safety issues drew attention away from sensitive and significant topics, such as the reproductive and broader needs of adult patients affected by the disease, the potential to improve access to other reproductive options, and the ethical questions raised by the increasing demand for egg/mitochondrial donors, such as compensation, commodification (of their bodies), and social and legal recognition. It also avoided addressing health access and inequalities in the UK context. As I explained, these ignored knowns therefore helped to magnify the scope and desirability of the techniques by exaggerating their potential and silencing their shortcomings and limitations. Ultimately, they facilitated public acceptance of mitochondrial donation and its legalization, making the UK appear to be a pioneer in this medical and scientific field as well as a moral leader on germline therapies.

Conclusion

When analysing debates where there are particular political, ethical, social and political stakes at play, it appears crucial to identify if, and how, some issues and information have been strategically ignored or dismissed to serve the interests of particular stakeholders. This is important as it not only allows us to recognise — and possibly act upon — the detrimental consequences these omissions might have on the potential beneficiaries of the treatments under discussion, but also to anticipate, monitor and possibly reduce similar omissions in future debates through an enhanced understanding of the strategies deployed in debates on new biomedical innovations. In this respect, ignorance studies offer conceptual tools and analytical frameworks that prove especially useful, as illustrated in this article, to provide another layer of understanding of the framing of the debate by focusing on the use of knowledge and non-knowledge around particular issues.

This article therefore calls for a more systematic use of ignorance studies to be applied in the field of reproductive policies, paying particular attention to the type of information, knowledge and disciplines silenced in the framing and assessment of new treatments and technologies under discussion. While existing analysis of ignorance in the field of reproduction has mainly focused on the dismissal of medical risks and its consequences for women's health, this analysis shows that, beyond ensuring that this type of risk has been assessed thoroughly and properly, it is also important to analyse how it may have been handled in strategic ways at the expense of other issues, such as social and economic impacts. Increased attention to safety concerns may be used as a placeholder for more fundamental ethical or religious concerns, and used strategically to oppose technological innovations, but may also divert, intentionally or not, attention away from other key issues or sources of information that should be taken into consideration in the public evaluation of emerging reproductive treatments. It therefore appears crucial to conduct an integrated analysis of ignorance, looking at the tensions between the 'acknowledged unknowns' and 'ignored knowns' and the ways they may be articulated strategically, in order to provide a sufficiently complex and complete picture of the interests and issues at stake in debates on new reproductive treatments.

Furthermore, this analysis highlights the importance, in debates on controversial emerging biotechnologies, of careful consideration of the full range of their impacts. In parliamentary debates surrounding the legalization of new biotechnologies, one would indeed expect that the social, political and economic conditions of these technologies, both positive and negative, would be assessed in a balanced and neutral manner, and discussed thoroughly, in order to determine the extent to which the benefits of the technologies outweigh their shortcomings and risks. As Magnus explained, 'a value-based assessment of whether the degree of risk is worth the potential benefit of an action involves weighing many factors, including economic and public benefits, against risks' (Magnus, 2008: 252). The assessment of the risks and efficacy should, of course, be a starting point, but the examination of the impacts of new treatments or techniques should not stop there. An appreciation of a wider range of issues, including the social, political and economic aspects of their application, is needed for a full assessment of the relevance and implications of such technologies. In future debates, it would therefore seem advisable, in light of these observations, for the institutional actors in charge of providing the official knowledge for the debates to consult a wider range of international experts and to mobilize knowledge from a broader range of disciplines, such as health economics or social science, in order to ensure, as far as possible, that a wider range of perspectives are addressed and weighed while assessing novel biomedical innovations.

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