Is it time to establish age restrictions in ART?

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Abstract

Providers specializing in reproductive medicine are treating increasing numbers of women pursuing parenthood in their 40s, 50s, and beyond. The rise in later-life parenting can be linked to factors ranging from the advent of assisted reproductive technologies and donor oocytes to the highly publicized pregnancies of older celebrities. We explore the medical and psychosocial implications of this trend for both older parents and their children. We also discuss ethical arguments regarding older parents' access to fertility care, existing professional guidelines, and both public and provider opinions about setting age limits for fertility treatment. Finally, we share preliminary considerations of whether age policies should be established, applied to men as well as women, and standardized or considered on a case-by-case basis.

Keywords Parental age · Age limits · Age restrictions · Ethics · Third-party reproduction

There has been a dramatic increase in women having children in their 40s, 50s, and even 60s [1]. Similarly, while it was once a relatively uncommon occurrence for a man to father a child into his 70s, or even older, this choice is increasingly viewed as reasonable. Thus, advanced-aged parents are becoming more common, and possibly more socially accepted. Simultaneously, concerns for the welfare of children of older aged parents are increasing.

It has been demonstrated that a significant linear relationship exists between advanced maternal age and adverse perinatal outcomes including intrauterine growth restriction, low birth weight, congenital malformations, and perinatal mortality [2]. Further, preliminary research suggests that pregnancy at age 50 years or above is independently associated with adverse perinatal outcomes [3]. However, many of these advanced-age pregnancy risks are managed similarly to high-risk gestations for younger women. Thus, it has been suggested that in carefully considered cases, it may be reasonable to view the prospective pregnancies of advanced-aged women as acceptable high-risk pregnancies as long as appropriate informed consent, screening, and perinatal management are incorporated [4, 5]. While this implies that pregnancy in the sixth decade of life can be managed medically and may lead to a good or reasonable outcome, it risks normalizing the health hazards that exist for pregnancy and childbirth at advanced maternal age. Additionally, the focus on perinatal outcomes does not address the life-long health risks for children born to older parents or the psychosocial impacts of delayed parenting for both parents and their children [6].

Understanding the implications for both parents and children of advanced-age parenting is important in order to provide reproductive health professionals with critical information to guide treatment decisions and to ensure appropriate informed consent.

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Advanced-age parenting as a reasonable prospect

Although a multitude of factors likely contributes to the rise in advanced-age parenting, one commonality is that the prospect is characterized as reasonable. From a medical perspective, this is largely true. While implantation rates and live birth rates decrease with age, healthy babies often are born. Analysis of data regarding donor oocyte IVF cycles from the Society for Reproductive Technology (SART) indicates that implantation and live birth rates for women 45 to 49 years old are 43.3% and 52.7%, respectively, whereas implantation and live birth rates for women ≥ 50 years of age are 40.9% and 48.6%, respectively [7]. Furthermore, while pregnancy at an advanced age confers increased risk to the woman and resultant offspring, the probability is that most pregnancies will result in healthy outcomes for parents and children. Having a child at a later-life stage will likely provide benefits to the older parent, including a sense of meaning, connection, legacy, and future support [8]. These benefits may be particularly salient and meaningful to parents who are closer in proximity to retirement, physical decline, and the end of life.

Media portrayals of later-life parenting are also likely influencing the acceptability of advanced-age parenting. An analysis of mass media depictions of delayed parenting within television series, news reports, and popular magazines suggests that delayed parenting is often presented positively, with little to no attention to risks or poor outcomes [9]. Delayed parenting is described as an option that allows for the attainment of other life goals first and then parenthood later [10].

The media portrayal of advanced-age parenting as increasingly acceptable is likely a welcome reprieve for younger adults who report not being ready to have children. Completing school, establishing career and financial security, finding a suitable partner, and feeling mature enough for parenting are all cited as reasons for postponing parenthood by adults ages 28 to 40 years old [11]. Indeed, it has been suggested that having children late in life is seldom a conscious choice, but rather a consequence of pressures and demands related to education, career, financial security, and relationship stability. It is not the path that is intentionally chosen, but rather the path that remains because of such demands [12].

While many prospective parents may not have intended to have their children later in life, they may find solace in the idea that children of older parents enjoy benefits that their peers with younger parents do not. Specifically, it is asserted that with age comes maturity, wisdom, patience, life experience, financial resources, strong marital or co-parenting relationships, and emotional readiness for parenting that may translate into advantages for children of older parents [13, 14]. Research suggests some age-related increase in positive parenting; however, the benefits appear to plateau once the parent reaches age 30 to 40 [13]. In other words, parents in their 30s

are likely providing a more positive parenting experience than parents in their teens, but the same cannot be said when comparing parents in their 50s with parents in their 30s.

Finally, and importantly, a prominent argument in support of parenting at an advanced age is the principle of procreative liberty or, restated, the right to reproduce without interference or limitation. Robertson argued that “procreative liberty deserves primacy because it is an important aspect of self-determination and well-being” [15]. Robertson asserted that “reproductive choices have such a major impact on a person’s life—on one’s body, and one’s sense of meaning—that we are committed to assigning discretion over them to the individuals directly involved, unless great harm to others from the choice would ensue.” As applied to the issue of advanced-age parenting, the argument would be that older potential parents enjoy the same rights as younger potential parents and that the value of reproduction does not differ across age groups. The open question that remains with this argument is what constitutes “great harm”?

Concerns regarding delayed parenting

There are many known potential harms to the children of older parents that vary in terms of seriousness, probability, and proximity. A thorough discussion of the risks to children born to older parents is beyond the scope of this discussion, but a brief summary may be helpful. Researchers define “older age” variably, but in this review, we will focus on maternal age ≥ 45 years and paternal age ≥ 45 years. In a cautionary note, it is important to recognize that, to date, there is no research that directly examines physiological and psychological health outcomes for ART-conceived children born to older parents and it can be argued that outcomes may differ from children resulting from spontaneous pregnancies, particularly in terms of the strength of motivation for parenting. Studies of ART-conceived children of older parents may help to illuminate outcomes more clearly. However, the method of conception is unlikely to substantially alter the physical and psychological outcomes, and thus, we believe it is both valid and appropriate to discuss similar data regarding children born naturally to older age parents.

Children born to older parents are at increased risk for autistic spectrum disorders and pervasive developmental disorders [16, 17]. More specifically, children born to fathers 35 to 49 years of age are more likely to be diagnosed with autism [16, 17]. A recent review suggests a 21% increased risk of autism in children with each additional decade of paternal age [18]. The same review suggests an 18% increased risk of autism for each additional decade of maternal age [18]. Additional data suggest that children born to mothers 35 years old or more are at increased risk for Asperger’s syndrome and children born to mothers 40 years of age or more are at

increased risk for pervasive developmental disorder [17]. Schizophrenia may also be more common amongst children of older parents. Research suggests that children of fathers age 35 and older have higher risks of schizophrenia (pooled estimate 1.33; 95% CI, 1.25–1.42) [18] whereas, after adjustments for paternal age, male children of mothers aged > 45 demonstrate an increased risk of schizophrenia (increased relative risk 1.86; 95% CI, 1.12–3.10) [19]. Furthermore, children born to older fathers are at increased risk for depression and anxiety, whereas children born to older mothers are at increased risk for hyperkinetic disorders [20, 21]. The studies just cited regarding increased risks associated with maternal age do not discuss the method of conception, particularly the possible use of donor oocytes. Thus, it is not possible to specify whether it is the age of the oocyte versus the age of the woman carrying the pregnancy that is associated with the increased risks for children. However, the authors suggest that the higher risks for maternal hypertension, pre-eclampsia, and placental pathology associated with advanced maternal age can lead to fetal hypoxia which, in turn, has been associated with downstream health risks for children [17]. In terms of the increased risks associated with advanced paternal age, it has been speculated that higher rates of de novo mutations and/or epigenetic modifications may be causal [17].

There are also concerns regarding possible shortened longevity for the children of older parents. German genealogical data for births between 1650 and 1927 suggest that daughters of mothers ≥ 40 years were likely to live nearly 9 years less and sons 5 years less than those whose mothers were 20–29 years of age [22]. Similarly, Danish data on births between 1980 and 1996 revealed that children of fathers ≥ 45 years of age were more likely to die in infancy and more likely to die by age 18 [23]. Animal studies also suggest older mothers and fathers produce shorter lived offspring [24]. Finally, an analysis of approximately 43,000 women in the US-based Sister Study suggests that daughters of older mothers are more likely to be childless [25], although this finding remains to be replicated and more closely examined to clarify the extent to which the childlessness may be intentional.

Children of older parents are more likely than their peers to be in a caregiving role for their parents before reaching adulthood. Children serving as caregivers are at increased risk for depression, anxiety, eating disorders, substance abuse, and behavioral problems [21, 26]. Further, they can have difficulty emancipating from the home and tend to delay advanced education, dating, and marriage [21]. Children of older parents can be anxious regarding their parents' health and risk of death and report fear of parental death [27]. They report an emotional struggle watching parental decline, illness, or pain, as well as fear of finding their parent dead [21].

It has been noted that these above-listed risks for children of older parents have not been well studied and thus require caution as a basis for implementation of age

policies [28]. What is far more clear is the increased likelihood that children of older parents will experience the death of a parent while still in childhood or early adulthood, a loss consistently rated by children as the worst of feared personal events, more so than going blind [29]. Actuarial data suggest that fathers who are 50 years old when their child is born have a nearly 14% chance of dying by the time their child is 15 years old and a 22% chance of dying by the time their child is 20 years old. Similarly, mothers who are 50 years of age at the time of their child's birth have a roughly 9% chance of dying by the time their child is 15 and a nearly 15% chance of dying by the time their child is 20 years old [30]. Bereaved children are at increased risk for emotional/behavioral problems, psychiatric disorders, social withdrawal, lower self-esteem, and lower achievement [31]. In addition, children who lose a parent between the ages of 5–17 years are at risk for shortened life span [32].

It is also important to note that there may be unforeseen concerns for advanced age parents themselves. A large population-based prospective study of nulliparous women examined women's evaluation of the quality of their life using the Satisfaction With Life Scale (SWL) at 17 weeks' gestation, 30 weeks' gestation, 6 months' postpartum, and 3 years' postpartum. Women in the very advanced-age group (defined as ≥ 38 years of age) consistently had the lowest SWL scores, with the most pronounced differences evident at 3 years after birth [33]. SWL scores for this group were also significantly lower relative to their same aged peers in the general population, suggesting that the lower scores are not simply attributable to age. Similarly, a curvilinear relationship has been found between age at first birth and rates of depression in women. Women who had their first child at the age of 30 years had the lowest rates of depression whereas rates of depression increased in progressively younger and older mothers, with the highest rates of depression found in mothers ≤ 15 and ≥ 45 years of age [34]. Lastly, research suggests that it is not until they are actually rearing their children that parents who have their children at or beyond the age of 40 begin to experience worry about the impact of delayed parenting on their child. Specifically, these older parents report concern about how their advanced age may affect their child and the possibility that they may die before their child has reached sufficient psychological maturity to cope with that experience [35]. Two-thirds of these later-life mothers and fathers concluded that the optimal age for becoming a parent is in one's early to mid-30s and 90% recommended that individuals should pursue parenthood before age 40.

While there are clear risks for both parent and child in advanced-age reproduction, the question that remains is whether the risk of children serving as caregivers or parental death, as well as other potential hazards, is serious enough to support an age limit on assisted reproduction.

What guides might there be?

In a discussion of provider autonomy, ethicist John Robertson wrote that “Providers faced with patients who pose a risk of having children with less favorable physical, social, or psychological situations, may not wish to treat them. Precisely because fertility services could produce a child, physicians may reasonably view themselves as having a moral responsibility for causing the existence of the resulting child and choose not to help bring about such an outcome” [36]. Similarly, ASRM Ethics Guidelines on child-rearing ability affirm that “The wellbeing of offspring is an overriding ethical concern that should be considered in determining whether to provide infertility services” and “Physicians may take the welfare of resulting children into account in deciding whether to provide services” [37]. While these ethical principles and guidelines may help direct decision-making, in practice, it is difficult for physicians to know precisely where the boundaries for responsible and ethical care lie. Concerns for the child are often more hypothetical than based upon real-life experience, making it difficult to know precisely when and where to implement restrictions. In a somewhat contrasting view, ethicist John Harris rejected the argument for restricting access to reproductive technologies based upon potential harm to the resulting child by asserting that the concerns raised are seldom of sufficient seriousness, probability, or proximity to justify a constraint on reproductive liberty [38].

Preliminary professional and public views on age limit policy

Despite guidance provided by ASRM and the advice to practitioners to establish clear policies, clinicians struggle with the complex task of considering and setting age cutoffs. For example, a recent qualitative study of attitudes, process, and decisions regarding age cutoffs provides some insight into how ART providers grapple with this issue [39]. While this study was limited to 27 clinicians, and thus may not be representative of the views of the diverse membership of ASRM, the interviewees discussed concerns related to age limits for women using donor eggs ranging from 47 through 55 years. There was recognition that, with respect to oocyte donation, there is no firm upper age limit for women. However, clinicians cited concerns regarding the health of the baby, the life expectancy of the parents, and whether there would be a parent to raise the child into adulthood. On the other hand, age limits for men tended to be considered only in relation to the age of the female partner. This is reflected in the creation of a metric related to combined ages of prospective parents (e.g., not exceeding 90 total years). There was an over-arching theme of discomfort with the challenge of age and age policy as indicated by the quote

“We’re often very unsure of what decision to make, so we do the best we can.” To this end, many practitioners indicated that they were making age limit decisions based on personal feelings and beliefs as well as on perceptions of public opinion, noting further that public opinions are fueled by unrealistic information presented in the media.

The public’s view on age limits for fertility care suggests support for age limits [40]. In a survey study, a nationally representative sample of 1427 adults was given age groupings to select from when answering the question of what age limit should be placed on women for carrying a pregnancy (i.e., including the possibility of donor eggs). A majority, 67%, felt there should be age limits for women receiving fertility care. Forty-six percent of respondents chose the 45–54 age group as an upper limit and an additional 24% chose the 55–64 age group for an upper limit. Fifty-seven percent supported age limits for men in reproductive care, with 24% feeling that the oldest age a man should become a father was 45–54 years and 33% feeling the oldest age should be 55–64. Interestingly, only male respondents were likely to support age limits for women, but not for men.

In 2018, we led an ASRM Pre-Congress course attended by physicians, mental health professionals, nurses, practice managers, and attorneys on the pursuit of parenthood at advanced age. As part of that course, we divided attendees into nine working groups and asked them to consider whether clinics should implement an age policy, how an age policy would be applied to women and to men, and whether it should be a firm policy or a case-by case review. One group declined to answer the specific questions and chose instead to discuss the issues broadly. The remaining eight groups felt that clinics should develop a policy or a guideline regarding age limits for care. The eight groups were split as to whether policy should be firm or viewed as a guideline only. Five groups advocated for age restrictions to be the same for men and women, two groups advocated for combined age policies, and one did not address the question. Of the five working groups that suggested specific age limits, one group listed 50 years for both men and women, one group 55 for men and women, one group indicated that one partner needed to be 50 and healthy, one group was undecided between 50 and 55, and one group was undecided between 52 and 55 years.

Considering preliminary information surveyed from the public, as well as from members of the ASRM, it seems that both the professional and the lay public are interested in openly discussing age limits for providing fertility care. Importantly, this dialog should occur with equal consideration for age limits for men and women, given the known health risks incurred by children of older aged parents of both sexes. We acknowledge that with the growing number of patients of advanced reproductive age entering fertility treatment, consensus, and policy development will not be easily accomplished.

Final thoughts

Advanced-age parenting is increasing, and it is a self-perpetuating issue; the more older patients that seek treatment, the more people feel that it is reasonable to seek treatment, especially in an age where sensational births are widely celebrated as positive events in the media. The discomfort that some professionals feel regarding their role in assisting both men and women of advanced reproductive age will likely increase as they personally encounter cases that result in social, psychological, and/or medical welfare concerns in children resulting from their care. Clinicians may also struggle with concerns regarding the adequacy of informed consent with this patient group, given the fact that the risks are complex and that older prospective parents are often focused on achieving pregnancy rather than family functioning and child adjustment across decades.

Will our field choose to address this complicated issue before we feel overwhelmed with concern and discomfort or will we continue to view age restrictions as unjust and off-limits? We believe that a robust discussion of this issue is long overdue.

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