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## Commentary

# A demographic projection of the contribution of assisted reproductive technologies to world population growth

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### ABSTRACT

Enormous unmet needs for infertility treatment exist because access to assisted reproductive technologies is demographically skewed. Since the first IVF baby in 1978, the number of people conceived by reproductive technology has grown much faster than expected, reaching several million today and rapidly approaching 0.1% of the total world population. As more patients build families, and their children in turn become parents, the number owing their existence to assisted reproductive technologies, either directly or indirectly, will expand tremendously in future decades, but no attempts have been made hitherto to project the magnitude. We have projected growth to the year 2100, along with the fractional contribution to world population. The chief variable driving growth is access to fertility services. If it stagnates at current levels of about 400,000 babies per year, an estimated 157 million assisted reproductive technology-related people will be alive at the end of the century (1.4% of global population), but at an arbitrary upper limit of 30,000 extra births annually there will be 394 million additional people alive (3.5%). As the conquest of infertility continues, assisted reproductive technology-related individuals will quietly make a significant contribution to demographic growth as well as social progress.

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When the first babies were conceived by IVF nearly 40 years ago after a long struggle to develop the technology, it was widely assumed the procedure would remain rare. But in subsequent decades there has been an explosion of fertility services, and what were originally aimed at unblocking Fallopian tubes have been extended to almost every cause of female and male infertility through a family of assisted reproductive technologies (IVF, intracytoplasmic sperm injection [ICSI], frozen embryo replacement, erectile displacement, in-vitro maturation and preimplantation genetic diagnosis/screening). From world reports and taking account of missing information, it was estimated there were 5 million people conceived using assisted reproductive technologies by 2013 [Adamson et al., 2013; IFFS Global Reproductive Health Surveillance, 2016; Sullivan et al., 2013], and from this base we have projected growth to the end of the century.

Involuntary infertility is common and regionally variable [Mascarenhas et al., 2012], but affordability and location are major

barriers to access for treatment. Some poor countries have no assisted reproductive technology clinics, or only one, and across 62 countries where data exist there is a strong correlation between the number of clinics per million and per capita income in US\$ purchasing power parity ( $R^2 = 0.66$ ) [IFFS Global Reproductive Health Surveillance, 2016; World Bank, 2015]. A working party reckoned that IVF/ICSI services for 1500 couples per million inhabitants are required for societal needs [Calhaz-Jorge et al., 2016]. While estimates of need versus provision are imprecise and not strictly congruent, there appears to be a gap across the world of at least an order of magnitude between them, with only three small countries satisfying needs in 2012. Assisted reproductive technology births in Belgium, Slovenia and Denmark represented 4.6%, 4.9% and 6.1% of total natality, respectively [Calhaz-Jorge et al., 2012], far higher than most countries, where there is still vast room for growth.

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At present, assisted reproductive technology services are skewed to high-income Westernized countries where growth has continued more or less linearly or has stabilized in the aftermath of the global financial crisis of 2008 (CDC, 2014; HFEA, 2016). After lagging, services are now rapidly expanding in populous nations like India and China (IFFS Global Reproductive Health Surveillance, 2016), but in places where they are still scarce or absent only privileged people can afford to access them, which often requires crossing national borders. The heterogeneity of fertility services is compounded by the uneven evolution of clinical practices to embrace the care of previously untreatable conditions and for increasing live birth rates. Adding to the challenges of these moving targets for projecting assisted reproductive technology population expansion, there is the problem of gathering reliable data, because only one in three countries currently register data (IFFS Global Reproductive Health Surveillance, 2016). Some relief for the analyst is offered by demographic convergence because the patients who can afford private treatment or live in wealthy countries that mandate insurance or subsidize assisted reproductive technologies tend to have comparable family sizes and start at similar ages, irrespective of cultural differences and geographic spread. Successful treatment is often the start of a family tree as children conceived by assisted reproductive technologies have their own children, and so on. Thus, the demographic impact of reproductive technologies grows substantially over generations because there is no reason to think that the children will in due course have different parental aspirations themselves from the rest of the population, and if they have infertility it can be reversed too.

While these assumptions helped to simplify our analysis, the present era of global insecurity and demographic transition (i.e. ageing) makes it harder to confidently project trends in world population or the assisted reproductive technology subpopulation. Only modest and guarded claims are acceptable because even small differences in fertility can lead to significant over- or undershooting of estimates after a few decades. Our projections are at best 'ballpark' and couched in a range of growth levels. They extend from 2014 to 2100 and involve five factors conservatively estimated from authoritative sources. We rounded numbers as an acknowledgement of numerical imprecision, but when more precise information is available the methodology can update forecasts.

The factors for our calculations were 5 million assisted reproductive technology babies by 2013 with 400,000 births in that year (Adamson et al., 2013; Sullivan et al., 2013), which were corroborated from a survey of treatment cycles assuming an average live birth rate of 15–20% (IVF Worldwide, 2017). The assisted reproductive technology subpopulation was projected to the year 2100 for four levels of increase: from conservative values of zero and 10,000 to more speculative 20,000 or 30,000 additional births per year. An annual increase of 10,000 is a rough figure for countries where assisted reproductive technology is widely available, considering recent UK and US data (CDC, 2014; HFEA, 2016). Growth will never be evenly distributed, of course, but regional discontinuities from different phases of clinical development (from lag to rapid to plateau) are smoothed by the thousands of clinics already in existence. We chose a conservative linear increase instead of an exponential rise because services are likely to be constrained by the pace at which new clinics are built and staffed. The methodology required making a choice for the ages of assisted reproductive technology individuals born up to the starting year; these were taken to be distributed about a mean of 10 years but skewed towards lower ages because, although no reliable estimates exist, most growth will have occurred in the last quarter of the

four decades since IVF began. Patients undergoing fertility treatment tend to have babies at slightly older ages than their peers with natural fertility, but we chose 30 years for the average age of parenting (not just the first). The average number of children per family was set at 1.8 after adjusting for parental survival to age 30 and allowing for some individuals having no children. As infant mortality falls and average lifespans lengthen almost everywhere, a mortality rate of around 1% up to 30 years of age has a trivial impact on the results (Office for National Statistics, 2013–15).

The **Supplementary Material** shows how we estimated numbers of individuals who owe their lives either directly or indirectly to assisted reproductive technologies, and cumulative annual estimates are plotted in **Figure 1**. The **Supplementary Material** also gives the number of these individuals who would still be alive by a given year.

If no further growth in fertility services occurs this century, we calculate 167 million assisted reproductive technology-related people will have been born by 2100, and 157 million will still be alive that year – representing 1.4% of humanity based on the median estimate of 11.2 billion in the world (United Nations, 2015). But according to present trends, services will continue to grow robustly and the number of births is likely to be much higher. If the average annual increase is 10,000 or 20,000 births the numbers of people alive that year will rise to 236 or 315 million, respectively. At 30,000 more births per year, 394 million people will be alive and represent over 3% of humanity. Only a minority will have been directly conceived by assisted reproductive technologies: 40 million (24%) at the zero growth level or 155 million (38%) at the upper level of 30,000 births.

These striking projections offer numbers for the first time instead of what was previously only guesswork. The fraction of assisted reproductive technology-related individuals could eventually approach one in ten in countries where service needs are saturated, and by the end of the century their total number is likely to exceed the size of the current population in Russia, and possibly even the USA.

Although demographic projections have been surprisingly accurate in the past, there are more pitfalls in our era of economic and social insecurity, where fertility rates are also in flux. The fraction of assisted reproductive technology-related people will be underestimated if world population growth slows more than expected or if prosperity grows and is distributed more equitably. Africa is a special case as the most under-served continent with the greatest potential for growing fertility services if economic conditions improve, because it has a young age profile and a widespread social stigma associated with childlessness. There is less sympathy for infertile people in countries with the highest natural fertility (even if in decline) because contraception is regarded as a priority, but more affordable assisted reproductive technology protocols might one day offer access for millions of additional patients in developing countries (Van Blerkom et al., 2014).

Despite many cautions and qualifications, we can still be confident in predicting that, barring a global humanitarian or economic catastrophe, hundreds of millions of people will be alive later in the century whose existence will have depended one way or another on reproductive technologies.

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