EDITORIAL

Access to ART treatment and gender equality

Infertility is a core component of the growing recognition of sexual and reproductive health as a fundamental human right. It is acknowledged by key international bodies – including the United Nations (UN) and the World Health Organization (WHO) – as a disease that deserves medical care (*United Nations, 2005*; *Zegers-Hochschild et al., 2009*; *WHO, 2012*; *United Nations, 2017*). Infertility is an increasingly prevalent global health issue, conservatively estimated to affect 48 million couples globally (*Mascarenhas et al., 2012*). For couples or individuals, the distress and significant personal suffering caused by not being able to fulfill their wish to have a child, along with its major impact on the quality of life of individuals, should not be underestimated (*Peterson et al., 2014*).

Increasingly efficacious and safe infertility treatments are available, but related financial costs (which patients often have to pay themselves) and burden of treatment are high. Moreover, their effectiveness is largely dependent on the treatment being delivered before the end of a female's reproductive life span (*Broekmans et al., 2009*).

DISPARITIES IN ACCESS TO INFERTILITY CARE

Despite the global growth in ART treatment services, there is enormous variation in access to care (*Deweerdt, 2020*). The latest report from the International Committee for Monitoring Assisted Reproductive Technologies (ICMART) found enormous variation in the number of ART cycles per capita, ranging from less than 30 cycles per million in a number of Asian and African countries to 5218 cycles per million in Israel (*de Mouzon et al., 2020*). Even within geographic regions there is much variation, with the latest report from the European IVF Monitoring Consortium indicating a range of 907 ART cycles per million in Portugal to 3008 cycles per million in Denmark (*Wyns et al., 2020*). ART utilization also varies widely within some developed countries. For example, there is much variation in the uptake of ART services among different states in the USA (*Kawwass et al., 2021*), driven in part by state legislation. Only 19 US states have passed laws requiring insurers to offer coverage for infertility care, many of which do not relate to ART (*CDC, 2020*; *Resolve, 2020*).

In this editorial – as in most public health studies of infertility care – the focus is on ART, necessarily because of a lack of population data on other infertility treatments. Indeed, it has been proposed that ART utilization be used as a global indicator of access to infertility care more generally (*Dyer et al., 2020*).

The most obvious reason for the gross variability in uptake of ART services is the cost of treatment. But this is not the whole story. Reproductive rights, gender equality, socio-cultural norms, and the true cost of not providing affordable infertility care all play important roles.

ECONOMIC AND SOCIO-CULTURAL FACTORS

Financial accessibility to infertility treatment reflects the extent to which patients can afford to pay for treatment, which depends on; the underlying cost of treatment, the level of reimbursement that governments or third-party funders contribute to those costs, and the disposable income of patients. The combination of these factors determines how affordable ART treatment is from a patient's perspective, with reimbursement policies having the greatest impact on affordability (*Chambers et al., 2014*).

There is arguably no other medical treatment that exhibits such varying arrangements for funding by governments and third-parties as ART. In the latest global survey of ART practices and policies undertaken by the International Federation of Fertility Societies (IFFS), fewer than half of the 85 countries that submitted data on the extent of insurance coverage reported any type of financial support for ART treatment, and only 17 offered full reimbursement for ART services (*IFFS 2019*). A number of studies have analysed the relationship between affordability and utilization, concluding unsurprisingly that the greater the affordability of treatment – usually as a result of government or third-party reimbursement – the higher the utilization (*Hamilton and McManus, 2012*; *Chambers et al., 2014*). Not only does affordability drive utilization, but it also incentivizes the way ART is practiced and to health outcomes of mothers and infants. More affordable treatment reduces the incentive to maximise pregnancy rates in the fewest number of cycles possible, and thus encourages safer clinical practice, most notably through single embryo transfer. Such an approach also leads to lower downstream healthcare costs due to fewer complicated pregnancies and suboptimal health outcomes for mothers and offspring (*Boulet et al., 2015*; *Wei et al., 2020*; *van Heesch et al., 2015*).

Aside from the consideration of cost to patients, socio-cultural values affect the level of acceptability of ART treatment and also strongly predict utilization (*Präg and Mills, 2017*). In addition, access to ART treatment has been repeatedly shown to be lower in minority groups and women of colour, even after accounting for socioeconomic and country factors (*Amstrong and Plowden, 2012*).

REUCING COST AND COMPLEXITY

The isolated focus on optimising pregnancy rates per cycle has given rise to extremely complex, expensive, and sometimes hazardous approaches in ART treatment, including highly personalized stimulation protocol and preimplantation screening techniques. Furthermore, the use of often unproven adjunct therapies,

so called 'add-ons', adds to patient costs and treatment complexity. At times add-ons expose patients to unnecessary health risks and create tensions between paying more for treatment and perceived treatment benefits. These developments have driven ART out of reach for many, even in resource-rich countries, and added to the burden of treatment, adverse health outcomes and complications. Such approaches may be questioned in general, but certainly do not help solve the problem of global inequality of access to ART care in countries where resources, geographic remoteness and patient needs may be distinctly different (*Macklon and Fauser, 2020*). The reporting in IVF registries of pregnancy rates per cycle as the most important treatment outcome – driving the way ART is practiced – should also be reconsidered (*Fauser, 2019*).

In addition to single embryo transfer, examples of how to dramatically simplify IVF treatment include mild ovarian stimulation (*Nargund and Fauser, 2020*), home telemonitoring of ovarian response (*Gerris and Fauser, 2020*), the introduction of mobile ART laboratories, simplified devices for in-vitro/in-vivo fertilisation and embryo culture, and circumventing the need for sophisticated and expensive laboratory equipment, particularly in low resource settings (e.g. The Walking Egg initiative: https://thewalkingegg.com/the-project), or fully automated fertilization and embryo culture systems. All such recent developments significantly reduce complexity of treatment, cost, and patient discomfort, and therefore could dramatically improve access to ART care.

REDUCED FERTILITY RATES AND THE ROLE OF INFERTILITY

Fertility rates in many developed countries have been falling significantly over the past few decades compounded by the trend to later childbearing. The worldwide fertility rate (number of children born per woman) has halved over the last 50 years and at present the fertility rate is well below the replacement level of 2.1 in most developed and developing countries. The economic and social consequences of low fertility and an ageing population are a priority for an increasing number of countries.

The recognition of the role that access to infertility treatment may play in a policy response promoting population growth warrants further consideration and evaluation (*Faddy et al., 2018*). Few studies have investigated the role that infertility treatments play in population management. While it is tempting to believe that access to ART may increase fertility rates, it may also have the reverse effect as individuals delay childbearing in the belief that ART treatment represents a foolproof insurance against age-related reduced fecundity (*Habbema et al., 2009*; *Thévenon and Gauthier, 2011*).

GENDER EQUALITY AND HEALTH

But how do economic and socio-cultural factors interact to influence ART utilization, and are they independent? An increasing understanding of how gender norms create pathways to gender-based health inequities provides new insights. Clear evidence exists of how restrictive gender norms, values and expectations perpetuate health inequalities across the lifecourse and across generations for men and women. In recognition of the fundamental role that gender equality plays in health, it is an explicit goal of the 2030 Agenda for Sustainable Development (*Heise et al., 2019*; *Kennedy et al., 2020*).

More wealthy countries – those with higher gross domestic product (GDP) and human development indices (HDI) – have more ART clinics and higher utilization levels per capita. Importantly, such countries also tend to have much higher gender equality. In fact, a measure of a country's wealth is highly correlated with its level of gender equality (*United Nations, 2019*). Gender equality is itself highly intrinsic to human development, with gender inequality responsible for a startling 56% loss in measures of global human development (*United Nations, 2010*).

Gender inequality is particularly relevant for a highly gendered problem such as infertility, which largely remains a social and medical burden for women. Paradoxically, women in the poorest countries suffer the highest rates of infertility, have the poorest access to reproductive health care (including infertility care), and suffer the greatest social burden. The level of reproductive health in a country is a clear signal of a woman's status in society (*United Nations, 2017*). Further, regional data reveal that reproductive health is the largest contributor to gender equality around the world, even greater than empowerment of women and economic independence (*United Nations, 2010*).

The UN Developmental Program has developed the Gender Inequality Index (GII) to measure progress of countries and inform global policy on the goal of gender equality (*United Nations, 2010*). The components of the GII are reproductive health, empowerment, and labour market participation. When the GII is plotted against ART utilization for all countries reporting to ICMART, the relationship between them is clear – as gender equality increases so does ART utilization (**FIGURE 1**). The intersecting pathways and mechanisms that give rise to the high correlation between gender equality and ART utilization, and the directions of the causation, are complex. For example, a country's wealth and human development clearly play a role in increasing ART access, and conversely, making ART accessible and affordable increases gender equality by providing opportunities for women to fulfill their life goals and for the problem of infertility to be shared by couples (e.g. increasing diagnosis and education while reducing stigmatization) (*Inhorn and Patrizio, 2015*).

Unfortunately, the focus of global efforts over recent decades to prevent unintended pregnancy (through support for contraception) has over-shadowed the parallel need to support those suffering from infertility (*Inhorn and Patrizio, 2015*; *(UNFPA), U.N.P.F. 2019*). For example, the WHO has failed to develop updates of infertility guidelines for decades despite the high demand, and infertility care is not specifically included in the landmark UN International Conference on Population and Development (ICPD) beyond 2014 Program of Action (*United Nations 2014*). All aspects of sexual and reproductive health should be considered holistically from both a policy and translation perspective, starting from early adolescence and continuing through the childbearing years. Pleasingly, the WHO and UN have recently included infertility care under the definitions of sexual and reproductive health and rights (*WHO, 2012*; *United Nations, 2019*; *Gipson et al., 2020*). No longer should infertility be a forgotten goal of the global sexual and reproductive health agenda. Furthermore, policies that focus on social determinates that allow girls and women

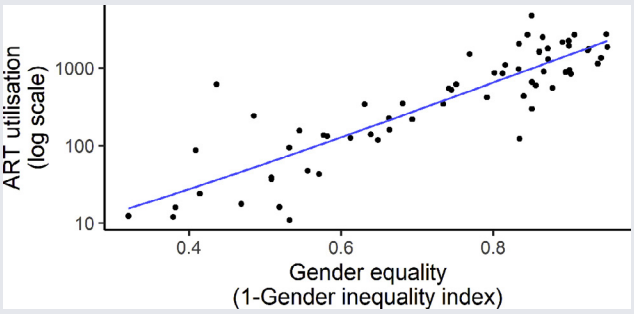

FIGURE 1 Relationship between assisted reproductive technology utilization (cycles per million population) and the degree of gender equality in countries reporting to the United Nation's Development Programme Gender Inequality Index (GII). Each black dot represents a country. Utilization from the International Committee for Monitoring Assisted Reproductive Technologies (ICMART) 2012 World Registry.

to access to sexual and reproductive healthcare through their lifecourse will, as a consequence, improve access to infertility care (*Kennedy et al., 2020*).

PROPOSED NEXT STEPS

Effecting national policies that remove gender inequalities is a lofty aspiration, but for those of those of us who want to see more equal access to ART treatment there is much we can do. As healthcare professionals who look after patients, and researchers who focus on improving the efficacy and safety of treatment, we need to broaden our focus to consider universal goals at a local and global level that will ultimately make a difference to those suffering from infertility. We need to:

- Champion sexual and reproductive rights for all women and girls.
- Elevate infertility as a disease which should be taken seriously and deserves to be including in public and third-party funding arrangements.
- Promote infertility care as a core component of sexual and reproductive health.
- Make ART more accessible and affordable worldwide.

Gender equality is the underlying right that enforces these goals, and thus a natural consequence of striving for these goals will be more equitable access to infertility care for all.

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G.M. Chambers
E-mail address: g.chambers@unsw.edu.au
Director, National Perinatal Epidemiology and Statistics Unit (NPESU), University of New South Wales, Sydney

Bart C.J.M. Fauser
Chief Editor, *RBMO*
E-mail address: b.c.fauser@umcutrecht.nl