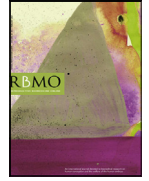




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## COMMENTARY



# Assisted reproductive technology, justice and autonomy in an era of COVID-19

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## ABSTRACT

Fertility services were significantly curtailed or suspended as an initial response to the coronavirus (COVID-19) pandemic earlier this year, following guidance from European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) as well as a General Direction (GD0014) issued by the Human Fertilisation and Embryo Authority (HFEA). It is difficult to argue with triage of medical care and resources in the face of anticipated overwhelming demand, but this situation resulted in considerable distress, as shown by a change.org petition opposing ASRM recommendations, which has gathered over 21,000 signatures to date. Although halting assisted reproductive technology (ART) as the pandemic unfolded was ethical because public health goals superseded individual patient autonomy, the fertility sector now faces a greater challenge balancing ethical considerations in an era characterized by the ongoing threat of COVID-19. This article discusses justice and autonomy in the context of ART, potential conflicts and resolutions.

## JUSTICE AND COVID-19 PANDEMIC

Healthcare provision considers four main areas when evaluating justice; fair decisions, competing needs, equal distribution of limited resources, and rights and legal obligations (including upholding laws and human rights, as well as potential conflicts with established legislation). Assisted reproductive technology (ART) already creates ethical dilemmas because treatment is not equally available to all people. But the unprecedented situation of the coronavirus (COVID-19) pandemic clearly presented an extraordinary demand on healthcare resources and an immediate need to restructure health provision with a suspension of all but absolutely essential and urgent treatment, including

ART. Many fertility specialists, certainly in the UK, retrained and upskilled to provide frontline obstetric care and gynaecology cancer diagnostic services, while nursing, scientific and laboratory staff were redeployed to a variety of clinical settings to serve the greater good. In the face of imminent threat, it is hard to argue against utilizing transferrable skills of fertility clinic personnel to maintain the delivery of essential and unscheduled healthcare.

Distributive justice encompasses the concept that the burden and benefit of treatment should be distributed equally among all groups in society and that medical decisions are fair. Reproduction is an essential human right that exists regardless of race, gender or sexual orientation. One objection to the suspension of fertility services

was that of perceived discrimination, because LGBTQ individuals and those with infertility were denied the possibility to procreate. However, this objection overlooks an important distinction between negative rights (the right *from* something) and positive rights (the right *to* something). In medicine, negative rights are almost universal. For example, people can refuse lifesaving treatment. COVID-19 is a notable exception, as people can be quarantined against their wishes. Nonetheless, negative rights unrelated to the safety of others are maintained during the pandemic, including the choice to reproduce by heterosexual intercourse. Positive rights, in contrast, are limited in medicine. For example, a patient may ask for a certain medication or to be scheduled first on the day of surgery, but there is usually no ethical obligation to do so. The pandemic

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situation undeniably warranted a prioritization of public health, and justice therefore prevailed over autonomy. Although it is regrettable that this disproportionately affected individuals with infertility and LGBTQ individuals, the response has not been, and should not be, to 'level the playing field' by not allowing reproduction during a pandemic, but rather to strive to minimize health inequalities, to resume fertility services when safe and feasible to do so and to protect ART services against future disruption.

Embedded within pandemic responses, there has been a seismic shift in the organization and delivery of clinical care. Similar to other sectors, technology has provided a major evolution in communication. Critics have highlighted risks to privacy and confidentiality, exclusion of vulnerable patients due to a lack of resource, limited access or inability to use it, as well as the obvious limitations of electronic interactions in terms of physical examination (*Chaet et al., 2017*). Nonetheless, telemedicine has been an invaluable mechanism for consultations, shared decision making, counselling and patient support and will continue to be key to risk mitigation and ongoing provision of fertility services in pandemic times. It also represents an opportunity to reduce the carbon footprint of ART, which should be embraced for the sake of the next generation that we are part of creating.

Infertility is a disease. Intuitively, therefore, medical treatment of infertility is warranted. And while there is a need to mitigate risk, minimize the spread of COVID-19 and preserve local healthcare resources to address the pandemic, there is also a need to recognize that ART is time sensitive, because female age is the single most important factor determining success. There is clearly a distinction between treatment that cannot be postponed even for a few days (such as a laparotomy for peritonitis), and treatment that is time sensitive but not a medical emergency (such as IVF). However, the description of ART as 'elective' in ASRM guidelines attracted significant criticism (*ASRM, 2020*). Elective procedures are defined as those 'planned or undertaken by choice and without urgency', usually based on risk of disease harm, specifically morbidity and mortality, and generally without consideration of psychological

effects. Yet a diagnosis of infertility can be extraordinarily distressing. Given that anxiety, depression and stress have been reported to be widespread during the pandemic and heightened by quarantine measures, it might be argued that extreme distress is unlikely to be a phenomenon restricted to those undertaking fertility treatment. However, significant negative effects have been documented following the suspension of fertility services. In a survey of 518 patients where 50% of respondents had a cycle cancelled due to the COVID-19 pandemic, 85% of those affected found it to be moderately to extremely upsetting and 22% rated it to be equivalent to the loss of a child (*Turocy et al., 2020*). For this reason, we must advocate to avoid this situation again, although clinics may need to reduce activity in response to pandemic spikes or waves, staff absence or pressure on aligned services.

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### AUTONOMY AND COVID-19 PANDEMIC

Autonomy requires patient decision making to be free of coercion and fully informed. Patients must understand all the risks and benefits of a procedure, including the likelihood of success, yet our own knowledge of the implications of COVID-19 infection during pregnancy remains limited. And because infertility is highly emotive, it is likely that patients will want to go ahead with treatment 'come what may'.

Nonetheless, millions have been infected with SARS-CoV-2, and COVID-19 appears to be less severe in adults of reproductive age, although men appear to be more vulnerable than women. Data show an undeniable age gradient in terms of both disease severity, as well as risk of death. A large Italian study of 1591 COVID-19 patients requiring intensive care reported a median age of 63 years, with only 13% of patients younger than 51 years (*Grasselli et al., 2020*). Similar data have been reported from China. It is also telling that, thus far, there are only limited reports of affected pregnancies, and overall maternal and neonatal morbidity and mortality appears to be low. UK Intensive Care National Audit and Research Centre (ICNARC) data consistently show that intensive care unit (ICU) admissions of pregnant or postnatal women critically ill with COVID-19 have comprised less than 1% of ICU admissions and

represent comparable numbers to those of matched patients with seasonal viral pneumonia. Similarly, UK hospital admissions with confirmed SARS-CoV-2 infection in pregnancy are reported as low (4.9 per 1000 maternities; 95% CI 4.5–5.4 per 1000). Most pregnant women admitted to hospital with COVID-19 infection have been in the late second or third trimester, supporting guidance for social distancing measures in later pregnancy. Most had good outcomes, and transmission of COVID-19 to infants was uncommon (only 12/265 [5%] infants tested positive for SARS-CoV-2 RNA, 50% of them within the first 12 h after birth) (*Knight et al., 2020*).

However, it must be acknowledged that there remains limited experience of severe maternal COVID-19 infection globally, and there are conflicting reports regarding increased risk during the third trimester of pregnancy and a potential sequela of preterm delivery. Certainly, COVID-19 with associated respiratory compromise in late pregnancy creates a complex clinical scenario. And similar to data concerning non-maternity populations, a notably high proportion of women (56%) from black and minority ethnic groups have required admission with antenatal SARS-CoV-2 infection, revealing justice concerns and health disparities at the intersection of COVID-19 and maternal health (*Knight et al., 2020*). The risks of acquiring COVID-19 in the first trimester are also not known and will not be known for some time. However, while high rates of miscarriage are reported for other severe coronavirus-related infections, there appears to be no increased risk specifically related to COVID-19 (*Yan et al., 2020*), although numbers are small. Notably, there has been no public health advice to avoid natural conception and pregnancy, so, one would argue, there is no compelling reason to avoid ART either.

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### PANDEMIC PRESENT AND FUTURE

While stopping of fertility treatments happened very quickly, resumption of fertility services has been more complex and necessarily cautious, not least due to the need to test new ways of working and minimize risk of infection. Working at less than capacity has been, or still is, a reality for many clinics, and many patients have therefore experienced further delays

due to treatment backlog. While one study recently demonstrated that minor delays in treatment do not appear to adversely affect patients with diminished ovarian reserve (Romanski *et al.*, 2020), it is almost inevitable that delays in treatment will negatively impact ART outcomes for older women, particularly those aged over 40 years. Which patients and what treatments to prioritize, and for how long, is ethically conflicted, although a prioritization strategy based on prognosis has been suggested (Alvigi *et al.*, 2020) and is likely to be fairer than other rationing methods (random lottery, first come first served). Fertility clinics must also be prepared to address the psychological distress that patients may suffer due to treatment delays by proactively recommending resources and/or counselling support.

One argument supporting the suspension of ART was to reduce pressure on healthcare systems by avoiding sedation and complications associated with oocyte retrieval, ovarian hyperstimulation syndrome (OHSS) and early pregnancy problems. Yet complications directly relating to oocyte retrieval are negligible. Bleeding and infection are the problems most commonly encountered; however, reported rates are 0.2% and 0.04% respectively, and the majority of these complications can be managed conservatively (Levi-Setti *et al.*, 2018). Anaesthetic-related issues, such as hypotension, pulmonary oedema and malignant hyperthermia, are also reported, but extremely rarely (Levi-Setti *et al.*, 2018). Significant OHSS complications are also increasingly rare, although notoriously under-reported, but certainly represent a very small burden on medical services. ART solely using antagonist cycles with agonist trigger and a freeze-all strategy potentially removes the immediate risk of OHSS, early pregnancy complications and multiple pregnancy, and therefore any immediate collateral burden on healthcare. But there is a more complex ethical dilemma when considering the justice of this approach, as it does not increase the live birth rate in normo-responders and may increase the risk of later pregnancy complications including hypertensive disorders and pre-eclampsia following subsequent frozen embryo transfer (FET) (Roque *et al.*, 2019). It is also worth reiterating that studies comparing fresh embryo transfer and FET consistently demonstrate an association between

FET and increased risk of large for gestational age (LGA) (Orvieto *et al.*, 2020). Macrosomic and LGA births have a notably higher risk of fetal hypoxia, stillbirth, shoulder dystocia, perineal trauma, operative delivery including Caesarean section, postpartum haemorrhage and neonatal metabolic disturbances at birth.

## CONCLUSION

Living and operating in a society where COVID-19 exists is a reality for everyone. COVID-19 will remain a factor to be managed in our lives and ART practices for the foreseeable future. Even with the benefit of hindsight, many professionals support the previous suspension of fertility treatment, yet most are resolved to avoid the same situation again. The new normal has been a unique opportunity to rethink and reinvent healthcare delivery for the benefit of all, to introduce sustainable changes in working practices, reduce unnecessary travel and build resilience against further surges in COVID-19. But we must also be sure to incorporate ethical considerations, and uphold patient autonomy and the balance of justice.

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