**Letter: Regulation to reality: COVID-19 and IVF activity**

Sir,

As COVID-19 has spread worldwide, governments, regulators and professional bodies have implemented a wide range of measures to mitigate overwhelming healthcare resources, including travel restrictions and cessation of fertility treatments. These measures have had multiple implications for infertile couples, including delays in time sensitive treatment and unequitable access to cross-border reproductive care within Europe. Sequential ESHRE statements from 19 March 2020 through to 2 April increased in severity, initially recommending avoidance of pregnancy and culminating in a recommendation to not commence treatment, with subsequent reversal incorporating a framework that would allow treatment to recommence on 23 April 2020 (Vermeulen *et al.* 2020). This guidance underpinned the advice of many national professional bodies and influenced national governance restrictions across Europe (see e.g. the UK Human Fertilisation and Embryology Authority (HFEA) General Direction 14, 23 March 2020). A notable difference between the UK and other jurisdictions, however, is that whilst ESHRE (like ASRM) established a working group to monitor and advise on the impact of coronavirus, the HFEA relied on guidance from professional bodies in the UK, albeit reinforced by the threat of regulatory action in the event of non-compliance with that guidance. This professional guidance therefore took on great potential significance in the UK.

Understanding the temporal implications of this relatively short period of only 3 weeks to complete cessation of treatment (except for urgent fertility preservation) is essential as further similar recommendations may be considered as COVID-19 rates continue to escalate across Europe. Figure 1 shows the impact on cycle activity from 1 January 2020 to 30 June 2020 on a group of 19 private clinics across six European countries (Austria, Denmark, Germany, Netherlands, Poland and the United Kingdom) as compared to the preceding six months 1 July to 31 December 2019. Overall, the

median duration where no oocyte retrievals performed was 51 days (interquartile 26 to 56 days, range 26 to 79 days), with an associated median decrease in ovarian stimulation cycles started of -26% (interquartile -39% to -24%, range -52% to -3%) over the 6 months. There was evidence of national variation in closure reflecting the different interpretations of professional guidance. The observed reduction in overall stimulation cycle activity, despite accounting for a period of catchup of two months, highlights the discordance between relatively short periods of recommended cessation of treatments (11.5% of the time period analysed) and the disproportionate impact on overall ART treatment. We acknowledge that individual national policies may have influenced the duration of discontinuation of ART treatment further. Notably, within the UK which exhibited the longest closure, with enforcement by the statutory regulator, the HFEA, cessation of treatment services was required by 15 April 2020 and resumption of licenced activities only allowed the week of the 11 May 2020, a total period of 4 weeks (and only following HFEA approval). However, as shown in Figure 1, the overall effect on UK clinics both in terms of closure and cycle numbers was far greater, further highlighting the discordance between apparently short-term measures and the clinical reality. As the unabated increases in COVID-19 continue globally, the adoption of comprehensive risk mitigation strategies to protect staff and patients while ensuring the continuity of ART provision are critical (Nelson *et al.* 2020). The timing of imposition and easing of future mitigation strategies may include further reconsideration of short-term temporary cessation of ART treatments (ESHRE 2020). Our data would suggest that the magnitude of impact may far exceed initial expectations and careful consideration of the long-term harm of time sensitive procedures are required (Smith *et al.* 2020).

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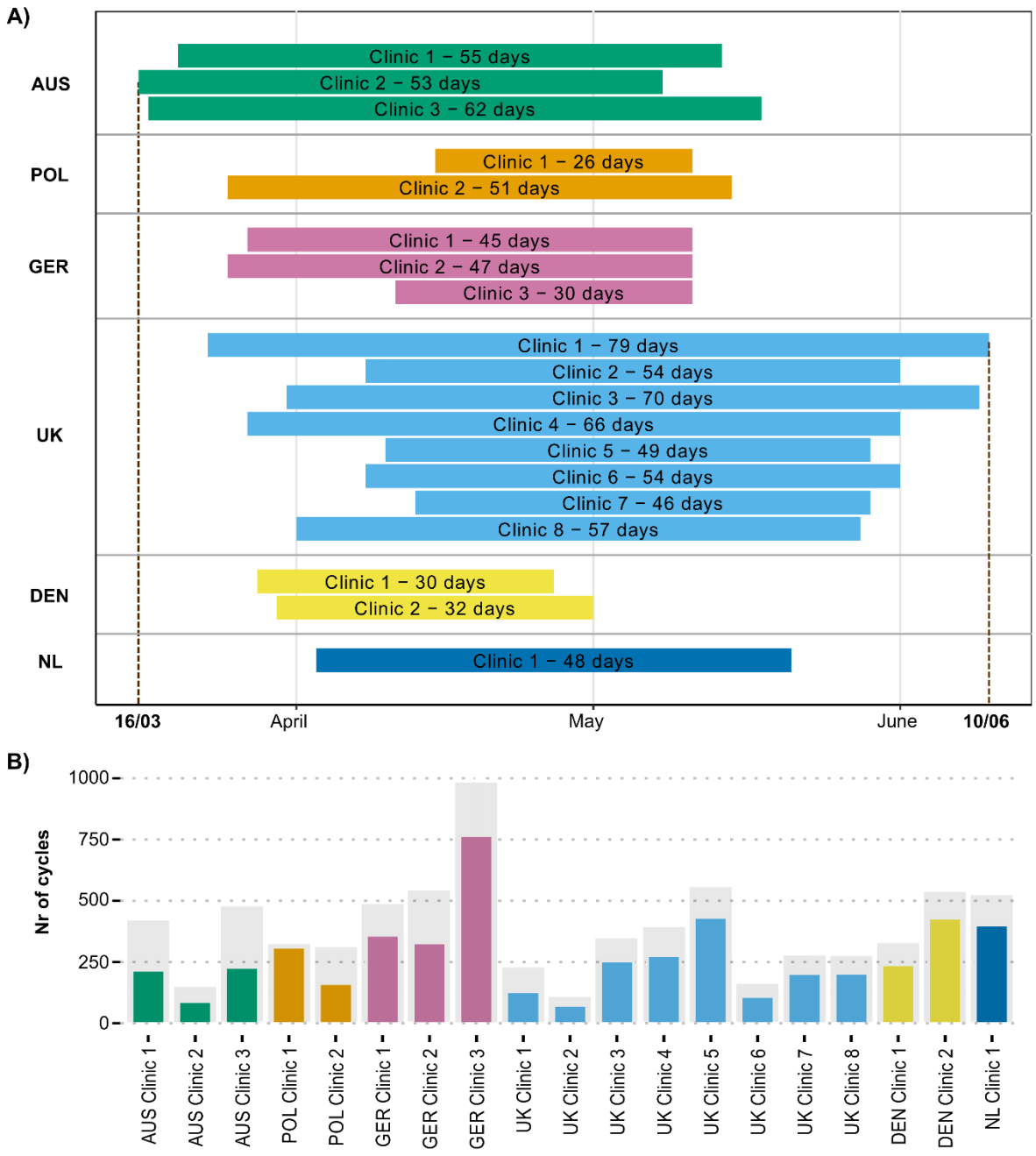


**Figure 1: Effect of recommendation of cessation of ART treatment on clinical activity on 19 clinics across six European countries.**

Panel A shows the time between the first and last oocyte retrievals, and the overall time for which no oocyte retrievals were undertaken.

Panel B shows the number of ovarian stimulation cycles undertaken in the preceding 6 months (1 July to 31 December 2019) in each clinic (grey bars), as compared to the number of cycles undertaken in the six months (1 January to 30 June 2020)(coloured bars).

**References**

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