(Mis-)understanding COVID-19 and digit ratio: Methodological and statistical issues in Manning and Fink (2020)

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WORD COUNT: 498

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Open practices statement:
The code and data used to create the analyses and figure in this comment are available from the Open Science Framework: osf.io/p8k43
In their study, Manning and Fink (1; henceforth M&F); report positive associations between the relative lengths of the index and ring fingers (2D:4D)—an intended proxy for prenatal exposure to testosterone—and two national COVID-19 outcomes: case fatality rate (CFR) and the percentage of male deaths (%MD). Whilst we encourage the production of science that can aid international responses to COVID-19, there are significant methodological and analytic concerns with M&F’s paper that lead it to be uninformative in the current climate.

First, while M&F assume that 2D:4D functions as a proxy of prenatal testosterone, it should be noted that scholars have repeatedly pointed to the lack of evidence for this relationship (2–4) and 2D:4D findings across different contexts have failed to replicate (5).

Second, M&F set out to test the hypothesis that prenatal testosterone levels are associated with COVID-19 mortality risk. To test this, M&F examine data on national average 2D:4D and national COVID-19 outcomes. These variables in this study are sampled from separate populations and do not give insight into the proposed individual-level mechanism in M&F’s discussion. Crucially, associations that hold at one level of analysis (e.g., nations), do not necessarily hold at another level of analysis – here specifically at the individual level (6).

Third, in their use of national aggregates for analysis, the number of cases for analysis are far from the claimed 103482 men and 83366 women. Rather, most of their analyses are based on 41 cases and, in the central finding for %MD, only 16 cases. Simulation studies show that such small samples yield highly volatile and unreliable correlation coefficients (7).

Even when casting aside these methodological issues, a closer look at the data reveals different results to M&F’s findings. National COVID-19 data is continuously updated and provides an opportunity to test the robustness of M&F’s results. M&F only examined data from one time point (which appears to be from April 8, not April 21 as reported in the paper).
Analyzing the most recent data from Global Health 50/50 (May 20), with a larger set of countries (31 instead of 16 countries), we find no significant association between male 2D:4D and %MD (left hand: $r = -0.32, p = 0.079$; right hand: $r = -0.20, p = 0.283$; see Figure 1).

Figure 1. Left: Data from M&F, April 8th male death percentage. Right: Male death percentage from May 20th and M&F digit data.

In sum, the reported study is ill-suited to test M&F’s hypothesis and there is little to learn about the role of testosterone in the current pandemic in this paper. Further, analyses of updated COVID-19 data question the reliability of M&F’s claims. There is an urgent need for high quality science during this pandemic, and any results that might inform medical
decisions surrounding the COVID-19 pandemic should be subject to, and withstand, close scrutiny. We show that M&F’s results do not, and in fact their study cannot, advance our understanding of COVID-19 and its relationship to male or female health outcomes.
Conflict of Interests: None declared.

References

2. Hollier LP, Keelan JA, Jamnadass ESL, Maybery MT, Hickey M, Whitehouse AJO. Adult digit ratio (2D:4D) is not related to umbilical cord androgen or estrogen concentrations, their ratios or net bioactivity. Early Hum Dev. 2015 Feb 1;91(2):111–7.