

Reply: More details on microbiome profile and IVF, would allow readers to judge for themselves

Sir,

We thank Gruteke *et al.* (2021) for their suggestions and requests regarding our recent publication (Koedooder *et al.*, 2019a). We would like to elaborate on our study and on the points raised.

Concerning their first suggestion, to provide a supplementary table listing presence of the four risk elements and outcome in all the 34 individuals classified as 'unfavourable microbiome profile', we would like to respond that due to patent developments this additional information cannot yet be made public. This has already been made known to Dr Gruteke in an earlier conversation before we received this letter to the editor.

Regarding their second request to clarify the role of the different *Gardnerella* subtypes, we can answer that the *Gardnerella* with IS-pro (or IS) type I seemed to play an important role and was found in 17 of the 34 women with an unfavourable profile.

Their final issue concerning the presence of *Atopobium vaginae*, which is part of the bacterial vaginosis qPCR, but not part of the unfavourable profile of the ReceptIVFity test. In our study, we found that the presence of *A. vaginae* was not an independent predictor of pregnancy outcome. Instead, it was co-correlated with the presence of other species. To maximize generalizability of the predictive algorithm, we included only the most predictive species and left out co-correlating species that did not add to predictive accuracy.

Finally, we would like to conclude with the opinion that the results of different analysis methods (e.g. qPCR and IS-pro) are difficult to compare head on. More information about this can be read in our review (Koedooder *et al.*, 2019b) and our latest paper concerning this issue (to be published *BMC Microbiology* April 2021).

Conflict of interest

The authors would like to state a number of competing interests. The author A.E.B. is co-founder of InBiome B.V. and co-inventor of the IS-pro technology. The authors R.K. and J.D.d.J. report that they are an employee at ARTPred B.V. J.S.E.L. reports consultancy fees from Titus Health Care and is co-inventor of the patent 'Method and kit for prediction success of *in vitro* fertilization' (US-9896733-B2) which is

assigned to ARTPred B.V. The author S.S. declares that there is no conflict of interest.

J.D.d.J. and A.E.B. have obtained patents 'Microbial population analysis' (9506109) and 'Microbial population analysis' (20170159108), both licenced to ARTPred B.V. J.D.d.J. and A.E.B. report co-inventorship on patent applications 'Method and kit for predicting the outcome of an assisted reproductive technology procedure' (392EPP0) and patent 'Method and kit for altering the outcome of an assisted reproductive technology procedure' by ARTPred.

References

- Gruteke P, van den Boogaard N, van de Laar T. More details on microbiome profile and IVF, would allow readers to judge for themselves. *Hum Reprod* 2021;doi:10.1093/humrep/deab102.
- Koedooder R, Singer M, Schoenmakers S, Savelkoul PHM, Morre SA, de Jonge JD, Poort L, Cuypers WJSS, Beckers NGM, Broekmans FJM *et al.* The vaginal microbiome as a predictor for outcome of *in vitro* fertilization with or without intracytoplasmic sperm injection: a prospective study. *Hum Reprod* 2019a;**34**:1042–1054.
- Koedooder R, Mackens S, Budding A, Fares D, Blockeel C, Laven J, Schoenmakers S. Identification and evaluation of the microbiome in the female and male reproductive tracts. *Hum Reprod Update* 2019b;**25**:298–325.
- R. Koedooder^{1,*}, S. Schoenmakers², J.D. de Jonge³, A.E. Budding⁴ and J.S.E. Laven¹
- ¹Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Erasmus University Medical Center, Rotterdam, The Netherlands
- ²Division Obstetrics, Department of Obstetrics and Gynecology, Erasmus University Medical Center, Rotterdam, The Netherlands
- ³ARTPred B.V., Oude Meer, The Netherlands
- ⁴inBiome, Amsterdam, The Netherlands

*Correspondence address. Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Erasmus University Medical Center, Wytemaweg 80, 3015 CN Rotterdam, The Netherlands. E-mail: r.koedooder@erasmusmc.nl

 <https://orcid.org/0000-0002-0233-6312>

doi:10.1093/humrep/deab103