Reply: Benefit of genome-wide prenatal cfDNA testing requires further investigation through a case–control study

We agree with Bekker *et al*. that further research is needed to define the benefits *vs* harms of genome-wide cell-free DNA (GW-cfDNA) testing of maternal blood. We believe that the best approach to answer this question is through a case–control study in which no action is taken on positive results other than for trisomies 21, 18 and 13. We strongly disagree that it is ethically acceptable to 'test and learn' through an implementation study such as TRIDENT-2[1] that is partly funded by the pregnant women themselves and in which neither the women nor their doctors know what is the purpose of testing and what is the clinical significance of most of the positive results other than those for the major trisomies. Although in The Netherlands a major effort has been made to optimize pre-test patient

counseling, the value of such counseling is questionable in the absence of data on the clinical significance of findings detected by GW-cfDNA testing.

The situation in Belgium is more worrying. cfDNA screening is nearly fully funded by the government and genetic laboratories carry out GW-cfDNA testing as an 'opt-out' test without proper pre-test counseling; if the pregnant woman does not tick the box stating that she does not want to be informed about relevant chromosomal abnormalities other than trisomies 21, 18 and 13, a GW-cfDNA test is conducted[2]. The Belgian medical deontological code insists on patients being correctly informed about any diagnostic or therapeutic measure they are offered[3]. However, a recent survey showed that 20% of women who underwent cfDNA testing were not aware that this included screening for trisomy 21[4].

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References

1. van der Meij KRM, Sistermans EA, Macville MVE, Stevens SJC, Bax CJ, Bekker MN, Bilardo CM, Boon EMJ, Boter M, Diderich KEM, *et al*. TRIDENT-2: National Implementation of Genome-Wide Non-Invasive Prenatal Testing as a First-Tier Screening Test in the Netherlands. *Am J Hum Genet* 2019; **105**: 1091–1101.
2. Centrum voor Medische Genetica. http://www.brusselsgenetics.be/default.aspx.
3. Belgian Advisory Committee on Bioethics. Opinion no. 66 of 9 May 2016 on the ethical challenges posed by non-invasive prenatal testing (NIPT) for trisomies 21, 13 and 18. www.health.belgium.be/bioeth.
4. Abousleiman C, Lismonde A, Jani JC. Concerns following rapid implementation of first-line screening for aneuploidy by cell-free DNA analysis in the Belgian healthcare system. *Ultrasound Obstet Gynecol* 2019; **53**: 847–848.