Genetics inMedicine | CORRESPONDENCE

Response to Ferket et al.

To the Editor:

We thank Ferket and Veenstra[1] for their letter "Economic value of exome sequencing for suspected monogenic disorders" on our paper titled "Long-term economic impacts of exome sequencing for suspected monogenic disorders: diagnosis, management, and reproductive outcomes."[2] We agree that capturing long-term health outcomes and their quality of life impacts using the quality-adjusted life year (QALY) measure is an important step forward in genomic medicine, as is the inclusion of impacts on the proband's relatives, both of which are particularly relevant when seeking public funding.

We agree that sensitivity analysis is important. We did undertake extensive sensitivity analysis on sequencing price, and the timing of onset of symptoms. We did consider undertaking some sensitivity analysis related to the diagnostic rate, which would typically reference a range of diagnostic rates from similar studies. However, we found that there were very few studies similar to our cohort of patients with suspected monogenic conditions who were recruited prospectively in a clinical setting between the ages of 0 and 2 years, as noted in the Introduction. Further, most genomic studies in rare disease do not report health outcomes, but are generally limited to measurement of diagnostic rates and only sometimes include ensuing changes in management. Nonetheless, some variability in the diagnostic rate and medically actionability as indirectly captured in the bootstrapping analysis using sampling with replacement.

The change in QALY outcomes occurred in only a small number of patients, which is typical of contemporary genomic studies in this field given the paucity of effective interventions for rare diseases.[3,4] However, it is important to note that some interventions have such a significant effect of duration and quality of life that cost-effectiveness may be achieved even when few patients exhibit such benefit. Nonetheless, we agree that it is important for further studies to be undertaken to more accurately assess population impacts.

Our analysis did include long-term costs of subsequent treatment. The authors of the letter may have overlooked their inclusion which was briefly described (under the heading, "Cost-effectiveness analysis, model 1: cost and health outcomes in probands only").

The spillover effects for parents including societal costs would have been a valuable addition and we are undertaking further studies where we are including these impacts. In this study, the spillover benefits were limited to capturing quality of life gains for parents due to the birth of subsequent children, which occurred at greater rates in the group where the proband received a diagnosis relevant for reproductive planning (see "Model 3: cost and health outcomes of probands, first degree relatives, and parental reproductive outcomes," second to last paragraph).

DISCLOSURE

The authors declare no conflicts of interest.

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REFERENCES

1. Ferket BS, Veenstra DL. Economic value of exome sequencing for suspected monogenic disorders. Genet Med. 2020. https://doi.org/10.1038/s41436-020-0888-0
2. Schofield D, Rynehart L, Shresthra R, et al. Long-term economic impacts of exome sequencing for suspected monogenic disorders: diagnosis, management, and reproductive outcomes. Genet Med. 2019; 21:2586–2593.
3. Stark Z, Lunke S, Brett GR, et al. Meeting the challenges of implementing rapid genomic testing in acute pediatric care. Genet Med. 2018;20: 1554–1563.
4. Farnaes L, Hildreth A, Sweeney NM, et al. Rapid whole-genome sequencing decreases infant morbidity and cost of hospitalization. NPJ Genom Med. 2018;3:10.

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