A Response to ‘Why Realistic Test Scenarios in Translational Research Remain Hypothetical’

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We appreciate the thoughtful commentary offered by Dr. Janssens [1] and are in full agreement that the discovery of genetic susceptibility markers for common health conditions has posed many challenges. We also agree with Dr. Janssens that we do not know if these advances can be used to improve public health. Nonetheless, Dr. Janssens raised several issues that we believe would benefit from further discussion.

For the purposes of clarity, we would like to restate the overall objectives of our report [2]. Our aim was neither to put forth our schema for marker selection as an exemplar, nor to imply that others should adopt this particular prototype multiplex genetic test. Rather, we were most interested in presenting a model that would generate discussion about what factors should be considered when designing a genetic test for translational research. Actively addressing this question is important to the field because translational research that returns genetic information will always have to develop a transparent process for designing a genetic test that is appropriate to the aims of a study.

Concern has been expressed on a number of fronts that providing personalized health behavior recommendations based upon genetic susceptibility tests would be premature. We agree with this assessment. Although health behavior recommendations known to decrease

disease risk in the general population are well-established, there currently is insufficient evidence to support tailoring health advice to individual genotypes. In the absence of such specific information, the logic adopted by the Multiplex Initiative is that it would be most appropriate to recommend the same prevention measures to all participants, regardless of genotype. Importantly, we chose prevention measures shown to decrease risk for the health condition in the general population that are currently recommended for use in medical practice in the United States. This provides useful health information to all study participants and tests whether personal genotype information alters individual responses to generic prevention recommendations. As Dr. Janssens notes, our study did not offer criteria for selecting effective interventions based on genotype. We believe that it would have been premature for us to develop criteria, given the near absence of relevant data supporting tailored recommendations. However, we agree that establishing selection criteria will become necessary as the evidence base for variant-specific prevention measures evolves.

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Given the speed at which genetic research is evolving, any genetic susceptibility test designed for research purposes is unlikely to fully reflect the predictive capacity of future tests. For this reason, early research using prototype tests cannot provide the last word on whether genetic susceptibility tests will have a public health benefit. While Dr. Janssens describes such research as ‘hypothetical’, we believe that using empirical methods to explore the implications of testing is a considerable improvement over speculation. Having real data, even if based upon an early prototype of future tests, should give us valuable insight into the effectiveness and applications of genomic susceptibility testing.

We expect future tests that assess risk for common health conditions will use carefully selected genomic, proteomic, transcriptional, environmental, behavioral, family health history, and other types of information in

combination to provide the most accurate risk estimate possible. One could argue that we should wait until we have the technical ability to carry out such a test to determine whether it has a net positive public health impact. However, we believe that the best method of bringing this vision into fruition is for iterative translational research to occur in-step with advances in risk estimation technology.

References

- 1 Janssens ACJW: Why realistic test scenarios in translational genomics research remain hypothetical. *Public Health Genomics* DOI: 10.1159/000236062.
- 2 Wade CH, McBride CM, Kardia SLR, Brody LC: Considerations for designing a prototype genetic test for use in translational research. *Public Health Genomics* DOI: 10.1159/000236061.