Genetic Risk Prediction for Common Diseases
Methodology and Applications

1. Reclassification of individuals into different risk categories observed in the absence of improvement in discriminative ability means the updated risk prediction model makes different classification errors than the initial model, not fewer errors. (this thesis)

2. When the frequency of the high-risk group in a genetic risk model differs from the frequency of disease, either the sensitivity or the positive predictive value of the genetic test will be high, but not both. (this thesis)

3. Rare genetic variants with strong effects do not improve the discriminative ability of a risk model, but they substantially increase disease risk in carriers of the rare variants. (this thesis)

4. Risks for common diseases predicted for the same individual vary largely between direct-to-consumer genome tests offered by different companies. (this thesis)

5. Because the discriminatory ability varies with characteristics of the study population, genetic risk prediction models should be developed in a representative sample of the population for which genetic testing is envisioned. (this thesis)

6. Accurate risk prediction for common diseases based on genetic information hinges on a deeper understanding of the genome architecture.

7. *Prudens quaestio dimidium scientiae.* – Half of science is asking the right questions. (Roger Bacon, c. 1214 – 1294)

8. Article citation rates determine the journal impact factor, not vice versa. (P.O. Seglen. BMJ. 1997; 314:498-502)

9. Imperfect prediction, despite being imperfect, can be valuable for decision-making purposes. (M. Kattan. J Clin Oncol. 2002;20:885-887)

10. You can't depend on your eyes when your imagination is out of focus. (Mark Twain. A Connecticut Yankee in King Arthur's Court. Webster; New York: 1889)

11. Reaching the summit is only half way.

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