Risk of Living Longer

Session 4: Biological Clocks

Outstanding Q&A

This document accompanies the webinar recording and slides from the Club Vita and Nationwide event on 18 June 2024, titled *The Risk of Living Longer Series, Session 4: Biological Clocks.* It provides some high-level responses to questions put to the panel that we did not have time for during the event.

1. What do you think about the following case? An individual who, at 40 years old with risk factors falling below the traditional likelihood of Major Acute Coronary Events (MACE - 10yr risk of heart event), presents MedUW data suggesting their biological age is 45 according to the Horvath clock. The insurance company charges a fair premium based on this biological age (age 45), similar to how they would if your ejection fraction was impaired due to MI or CHD, or BP levels or Cholesterol/Triglycerides. When this applicant (i.e. less-informed individual) explains this reasoning to their medical doctor (MD), who is unfamiliar with concepts like Horvath or Lipoprotein(a) or APOB etc., the MD disagrees and requests the case underwriter to provide evidence-based research.

   Peter: There is a reasonable body of evidence that epigenetic age (EA) (especially Horvath's newer GrimAge) correlates with conventional risk factors for cardio vascular disease (CVD), so the scenario may not happen all that often, of if it does, perhaps because the granularity of using epigenetic age is simply greater than conventional underwriting cutoffs. This article points to the relationship between cardiovascular health and GrimAge.
   https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.121.318965

   I think there is less research on the association between epigenetic age and CVD outcomes, likely due to the cost of epigenetics, and the substantial sample sizes and time needed for prospective studies, which make it difficult to study. Case-control studies are plagued by reverse causality - a CVD event may well increase epigenetic age as much as the other way round.

2. What are your thoughts on the ability to Gamify the Horvath (and other) clocks via brief periods of change to techniques temporarily improving the "age", when compared to Traditional Health Questions?

   Peter: This is a good question, on which there is yet, to my knowledge, little research. At Humanity our goal is to use an engaging measure of lifestyle to change behaviour to reduce EA. So in a way this is what we are trying to do, albeit on a sustained rather than temporary basis. But how easy is it, and are the reductions persistent to a degree, even if behaviour relapses? I think we don't really know, but I suspect it is easier (not to say easy) to temporarily lose weight, reduce blood pressure and improve cholesterol score to improve underwriting than to reduce EA. Humanity will be undertaking research on the question though - seeing how much and how quickly and how persistently lifestyle actions reduce biological age. Watch this space!

3. Did the individuals who participated in the metabolic health management pilot program regain weight after the intervention ended?

   John: The study continued for another 6 months, and the participants lost more and improved cardiovascular risk further. What makes this quite different to usual "diets" or weight loss programs, is the quantity is not restricted i.e. hunger does not need to be tolerated. What is critical is reducing carbohydrate to levels that induce a return to insulin sensitivity.

4. Why did the dietary guidance encourage neither the avoidance of fat nor salt?

   John: Evidence on salt is very limited and weak. For a healthy non hypertensive individual there is no evidence to reduce salt. Natural fats do not need to curbed. Any meat eaten should be in its natural state including fat e.g. chicken skin etc. Fat intake when insulin levels are high, and particularly with the backdrop of insulin resistance is almost "mis-metabolized", and even with very little fat intake the body converts much sugar and carb into fat and again the liver mis-metabolizes to create more small dense low-density lipoproteins (LDL), often called the “bad” cholesterol, which reduces when there is insulin sensitivity.

   Anyone interested in learning more about fat should watch these, and read the article below.

   - “Arne Astrup – Evidence on dietary saturated and total fat – Fixing Metabolic Health” on Vimeo (https://vimeo.com/896716543)
   - Fat Fiction - Full Movie - Free (youtube.com) (https://www.youtube.com/watch?v=TUADs-CK7vI&t=63s)
   - Saturated Fats and Health: A Reassessment and Proposal for Food-Based Recommendations: JACC State-of-the-Art Review | Journal of the American College of Cardiology

5. Great session!! lots of valuable information.

   Club Vita: Thanks very much. Don’t forget to sign up to the rest of the series here.