**GENETIC PREDISPOSITION IMPACTS CLINICAL CHANGES IN A NUTRITION AND LIFESTYLE COACHING PROGRAM.** **Niha Zubair PhD, Arivale, Inc., Seattle, WA 98104, USA, Matthew P. Conomos PhD, Arivale, Inc., Seattle, WA 98104, USA, Andrew T. Magis PhD, Arivale, Inc., Seattle, WA 98104, USA, Jennifer C. Lovejoy PhD, Arivale, Inc., Seattle, WA 98104, USA and Institute for Systems Biology, 401 Terry Ave N, Seattle, WA 98109, USA**

**Background:**

A unique set of dietary, lifestyle, environmental, and genetic factors contribute to an individual's risk for common chronic conditions, suggesting a systems based approach is essential for prevention.1 Intervention studies have generally found nutrition and lifestyle coaching to improve clinical outcomes related to these conditions. 2,3 However, to our knowledge, the impact of genetic predisposition on the clinical response to coaching has not been studied. Objectives: To address these gaps, we developed a systems-based approach, "Scientific Wellness"®, which combines multi-omic data with personalized nutrition and lifestyle coaching. 4 Here we report: 1) the impact of a Scientific Wellness program on clinical markers related to nutrition, insulin resistance, heart health, and inflammation, and 2) the effect of genetic predisposition on these clinical changes.

**Methods**:

Longitudinal clinical and anthropometric data from 2531 participants (enrolled between 2015-2018) in a commercial program were analyzed. Generalized linear mixed models were used to estimate average changes in clinical markers after 6 and 12 months. Selected genetic markers were tested for association with baseline measurements. 5-11 Linear mixed models were used to identify interaction effects of these genetic markers on longitudinal changes.

**Results**: There were significant and sustained improvements in clinical markers. Notably, several clinical markers, including omega-3 index, vitamin-D, triglycerides, gamma-glutamyl transpeptidase, hemoglobin A1c (HbA1c), waist circumference, and weight, had significant improvements in the entire population as well as in each baseline strata. For example, the adjusted average increase of omega 3-index at 12 months was 1.30% (95% CI: 1.14, 1.45) in the entire cohort and 1.53% (1.34, 1.71) among participants with low baseline omega 3-index levels. In terms of insulin resistance markers, the adjusted average decrease of HbA1c at 12 months was 0.20% (0.22, 0.18) in the entire cohort and 0.26% (0.30, 0.23) among participants with elevated baseline HbA1c; these improvements are akin to those observed in landmark clinical trials, such as the Diabetes Prevention Program.12 Genetic markers were significantly associated with changes in corresponding clinical markers. For example, the G allele of rs174537 was additively associated with higher baseline levels of both arachidonic acid and EPA among participants in the program. Interestingly, having more copies of the G allele was associated with a greater increase of arachidonic acid through the course of the program (0.3 % by wt. for GT

vs TT , and 0.6 % by wt. for GG vs. TT), but no difference in change of EPA.
**Conclusions**:

These results from this Scientific Wellness program demonstrate not only significant clinical improvements in participants with out of range biomarkers at baseline, but also many significant improvements in the overall population, presumably related to sustained engagement and dietary and lifestyle changes. Furthermore, for the first time, we report that genetic predisposition for health-related markers impacts clinical responses to personalized nutrition and lifestyle coaching.

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