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Value-based healthcare delivery through metabolomics-based personalized health platform

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Abstract

Type 2 diabetes is routinely identified in clinical practice by tests that rely on a hyperglycemic index. However, people at risk for developing type 2 diabetes may not present with hyperglycemia. We identified several underlying risks for type 2 diabetes, insulin resistance, and associated co-morbidities, using a liquid chromatography mass spectrometry–based analysis of blood metabolites, in participants with normoglycemia and no clinical symptoms. Personalized lifestyle recommendations, including diet, exercise, and nutritional supplement recommendations, were conveyed to these participants by a web-based platform, and after 100 days of following their recommendations, these participants reported reductions in the health risks associated with type 2 diabetes and associated diseases. Our comprehensive metabolite-based assay can be used for type 2 diabetes risk stratification, and our personalized lifestyle recommendation system could be deployed as a preventative treatment option to improve health outcomes, reduce the incidence of chronic disease, and live healthier lives in an evidence-based way.

Introduction

Recent scientific advances in multi-omics technologies are leading to a growing number of mainstream biomedical applications. Both metabolomics and proteomics are fast becoming emerging "omics" sciences that involve the comprehensive characterization of biological pathways involved in health, disease, and longevity.[1,2] For example, the application of metabolomics has already entered the clinic and is routinely used in newborn screening for errors in metabolism.[1] Metabolomics is increasingly being used in scientific and clinical research to evaluate disease risks, understand underlying pathological mechanisms, identify novel drug targets, and personalize and monitor therapy efficacy in both medications-based and lifestyle interventions.[1]

Type 2 diabetes, also known as adult-onset diabetes, is a form of diabetes characterized by increased blood glucose levels, insulin resistance, and low or lack of the hormone insulin in the blood. Type 2 diabetes symptoms often initiate and progress slowly and the individual may initially not be aware of the implications of the symptoms they are experiencing. Type 2 diabetes can also be classified as a "gateway" chronic disease because it can significantly increase the risk of other chronic disease and long-term health complications including cardiovascular diseases, such as atherosclerosis, coronary artery disease, heart attack, and stroke; eye diseases, including retinopathy and blindness; and kidney diseases, including diabetic nephropathy that may lead to kidney failure.[3] Type 2 diabetes is a global epidemic and ranks among the top leading causes of disease burden with 415 million people suffering from the disease, and this number is expected to rise to 642 million people by 2040.[3,4] Diabetes also significantly affects quality of life as the number of years that people with type 2 diabetes are living has increased by more than one-third over the last few decades due to the increase in age-specific prevalence and population growth and aging.[5] Specifically in North America, more than 100 million adults are currently living with diabetes and about one million new cases of diabetes are diagnosed every year.[5,6]

Type 2 diabetes is also a global economic burden costing about $1.3 trillion or 1.8% of global gross domestic product.[6] The largest costs arise from medical expenditures associated with hospital in-patient care, prescription medications, and diabetes supplies. However, far more reaching economic costs are also indirectly attributed to diabetes, and its associated co-morbidities, such as increased levels of employee absenteeism and reduced productivity at work, referred to as presenteeism, the inability to work as a result of disease-related disability, and lost productive capacity due to disease symptoms.[6] It is determined that one-third of the total

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economic cost of diabetes can be attributed to absenteeism and reduced productivity and disability at work.[7]

Many research studies have verified that type 2 diabetes incidence can be prevented or delayed,[8,9] and lifestyle is a major factor in determining the risk of developing type 2 diabetes but can also be a critical piece to reversing the disease.[8,10,11] In traditional medical practice, people at risk for developing type 2 diabetes can be identified using common clinical measures, such as fasting blood glucose and hemoglobin A_{1c} levels.[12] It is a well-known fact that higher fasting blood glucose levels can predict future type 2 diabetes and individuals with hyperglycemia (high fasting blood glucose levels) have an annual relative risk of developing type 2 diabetes at almost 5%.[13] Because of this, physicians routinely rely on fasting blood glucose and hemoglobin A_{1c} levels to identify patients for increased risk of type 2 diabetes.[14] However, these tests rely on the fact that type 2 diabetes has progressed far enough that the body has lost the ability to maintain normal glucose levels. Since blood glucose is often the final domino to fall in type 2 diabetes, and at this point, the individual body has likely lost the ability to properly maintain proper glucose homeostasis and treatment becomes more of a disease management solution.

However, these tests are unreliable for a many people who present with normal fasting glucose and hemoglobin A_{1c} levels. Often, these individuals may have relevant health concerns, such as increased weight, increased abdominal fat, high blood pressure, improper diet and bad eating habits, and lack of physical activity, while maintaining a normal level of fasting glucose during routine clinical tests. In these cases, often the medical advice is to "eat better and exercise more," which is a blanket advice that leaves these individuals underserved and without proper guidance to address their nutritional and exercise gaps. As expected, it is often the case that these individuals, while they may attempt to eat better and exercise more, ultimately fail at addressing these challenges and give up, only to go through the same cycle of medical advice at their next yearly checkup. These individuals may be unaware of their hidden risks associated with potentially developing type 2 diabetes if their current lifestyle trends remain unchanged. Furthermore, studies have proved that even in the presence of normal fasting glucose and hemoglobin A_{1c} levels, there is a significant population at risk of developing type 2 diabetes within a decade if left unchecked.[13-15] For instance, 10% of adults of European descent with completely normal fasting glucose and normal hemoglobin A_{1c} levels develop type 2 diabetes over a 5- to 10-year period.[13-16] And the incidence rate is even higher in adults from other ethnic backgrounds. For example, adults with an Asian Indian background and normal glucose and hemoglobin A_{1c} levels have almost a 20% incidence rate of type 2 diabetes within a 10-year span.[17] Therefore, traditional medical techniques fail to account for individuals who are at risk of developing type 2 diabetes and also do not account for the fact that individuals are very unique, with unique biochemical makeups and diverse lifestyles. Additionally, a one size fits all approach of traditional medicine without proper nutritional and exercise guidance does not work for most people.

As healthcare costs, life expectancy, and population of older adults continue to rise every year, our current healthcare delivery model is overburdened and becoming exponentially more costly.[18] There is a growing shift toward value-based healthcare and increasing health literacy that is being promoted by health decision-makers and stakeholders worldwide.[19-21] Value-based healthcare is a healthcare delivery model in which health practitioners are rewarded based on patient health outcomes. This is different from the current model, which is a fee-for-service model, where health providers are paid based on volume of healthcare delivery. Key attributes of a value-based healthcare model include adopting evidence-based care standards and protocols that represent the best outcomes for patients, lowering costs while increasing quality of healthcare delivery to patients, and streamlining clinic/hospital operational processes to create better patient care experiences through guidance and support systems.

Many studies in the last decade have identified metabolites in blood that are associated with the development of future type 2 diabetes in individuals with normal fasting glucose levels. These predictive plasma metabolites are often better predictors of type 2 diabetes risk than the conventional clinical measures used by most physicians, as these metabolites are intricately linked with earliest changes in the relevant biological pathways involved in insulin resistance and type 2 diabetes development. These metabolites include alterations in lipid oxidation, amino acid, and sugar metabolism.[22-29] The organ sites of these biological pathways include the liver, heart, and muscles, which are prime targets for nutrition and exercise interventions for organ protection and prevention of disease. Recent studies have used these metabolites in blood as a means of developing statistical models to predict the risk of type 2 diabetes.[30] We take this concept even further by not only analyzing these blood metabolite indicators of disease but also integrate each individual's unique characteristics and medical history to develop personalized molecular signature profiles, which enable us to compute their risk of developing disease, including type 2 diabetes even when they have normal fasting glucose and hemoglobin A_{1c} levels and are deemed not to be at risk by physicians. We can leverage these personalized molecular signature profiles as training datasets for our machine learning efforts to automate and enhance the identification of individuals at risk for type 2 diabetes development. We have also developed a comprehensive curated database around dietary, exercise, and nutritional supplement recommendations based on metabolomics that we can link to each individual's molecular signatures to recommend personalized lifestyle interventions to potentially mitigate disease risk.

We believe the future of medicine requires a more proactive personalized and value-based approach leveraging the advantages of multi-omics and AI technologies to detect early indicators of disease, divert disease development before symptoms manifest, and help patients improve their health outcomes and live healthier lives in an evidence-based way.[1,2,31]

Methods

Metabolomics quantification

Unlike genomics, in which a single instrument is often sufficient to perform the necessary analysis and interpretation of results, metabolomics requires a broad array of instrumentation and software packages for analysis. However, over the last decade, three experimental techniques have emerged as the primary workhorses that allow accurate and reproducible metabolomics quantification robust enough for clinical use: nuclear magnetic resonance spectroscopy, gas chromatography mass spectrometry, and Liquid Chromatography Mass Spectrometry (LCMS). Each technique provides broad coverage of many classes of organic compounds, including lipids, amino acids, sugars, biogenic amines, and organic acids. However, given the need for quick, accurate, and reproducible absolute quantification in clinical environments, a recent emerging trend in metabolomics has been heightened emphasis on quantification and automation, which serve not only to increase data throughput but also increase reliability and reproducibility.[32] Furthermore, these parameters are critical for eventual clinical test adoption and regulatory approval. This push toward automation and clinical adoption is now well underway specifically with LCMS-based multi-omics analysis.[2,33] We analyzed the metabolomics of our study population using standard LC-MS-based techniques already developed and published in many scientific publications.[1,34,35]

Study population and study design

We analyzed a total study population of 40 healthy participants who self-reported with no diagnosed diseases and no apparent clinical symptoms at the time of testing. The study population consisted of an almost equal group of males and females (55% female vs 45% male) and an age range of 28-65 years old. We collected and analyzed blood samples from the participants at time point 1, also referred to as baseline. The sample collection was done after an 8-hour fast and 24-hour no vigorous physical activity. The blood samples were analyzed by LC-MS-based metabolomics techniques, and health reports were delivered to all participants by a web-based reporting platform. Their health reports included a number of lifestyle recommendations based on analysis of their metabolite biomarker levels and health risks of various diseases (based on statistical computations of metabolites associated with risks of disease which we used to create individual molecular signatures of disease). Lifestyle recommendations, which we also refer to as an action plan, include personalized diet, exercise, and nutritional supplement recommendations that take into account not only each participant's metabolite levels but also their dietary preferences, food allergies, and any exercise limitations (such as injury). All participants were given 100 days (approximately 3 months) to follow their personalized action plans before a subsequent blood sample collection, and analysis was performed (time point 2) using the same procedure (8-hour fast and 24-hour no vigorous exercise) and analytical methods. Similar to the initial test, all health reports were delivered to all participants by a web-based reporting platform. We compared the health risks and metabolite biomarker levels from both of their reports and assessed whether our personalized lifestyle recommendations had an impact on the participants' health risks.

Results

Most participants have normal fasting glucose levels

We analyzed fasting blood glucose concentrations in our study population of healthy volunteers using LCMS-based metabolomics analysis. We found that the majority of the participants have normal fasting blood glucose levels, with concentrations within the normal physiological ranges of 4,000-6,000 μM, while a small number of individuals had slightly low levels, below 4,000 μM. However, these low levels were not below the threshold to be categorized as hypoglycemic, which is fasting glucose levels below 3,900 μM in the blood. Therefore, these individuals would not be classified as "at risk" for diabetes under the conventional clinical tests that rely on the hyperglycemic index.

Study cohort with normal fasting blood glucose has elevated health risks

Of our study population of healthy volunteers, a small cohort of 28 individuals with normal fasting blood glucose levels were found to have increased risk of insulin resistance and type 2 diabetes, as determined by our metabolomics analysis and personalized molecular signature profiles (Figure 1). Within this cohort, seven individuals were determined to have a high risk of type 2 diabetes, as determined by our metabolite signature profiles (Figure 1). Furthermore, our analysis revealed that these individuals also had risks in a number of other well-known diabetes-related co-morbidities including Alzheimer disease, metabolic syndrome, liver and kidney disease, and cardiovascular diseases, such as atherosclerosis, heart attack, and hypertension. It becomes very clear that insulin resistance and type 2 diabetes have the potential for a combined detrimental impact on the cardiovascular system, liver, brain, and kidneys.

Health intelligence reporting platform for health risks and health insights

We have developed a web-based health reporting platform that displays each participant's health risks colour coded by three risk stratifications: normal risk (in green), moderate risk (in yellow), and high risk (in red). Each participant receives a web-based health report where their health conditions are colour coded and ranked in descending order from high to moderate to normal risk. The same colour-coding is used for each metabolite biomarker where green represents metabolite levels within normal physiological range, yellow for metabolite levels slightly above or below normal range, and red for

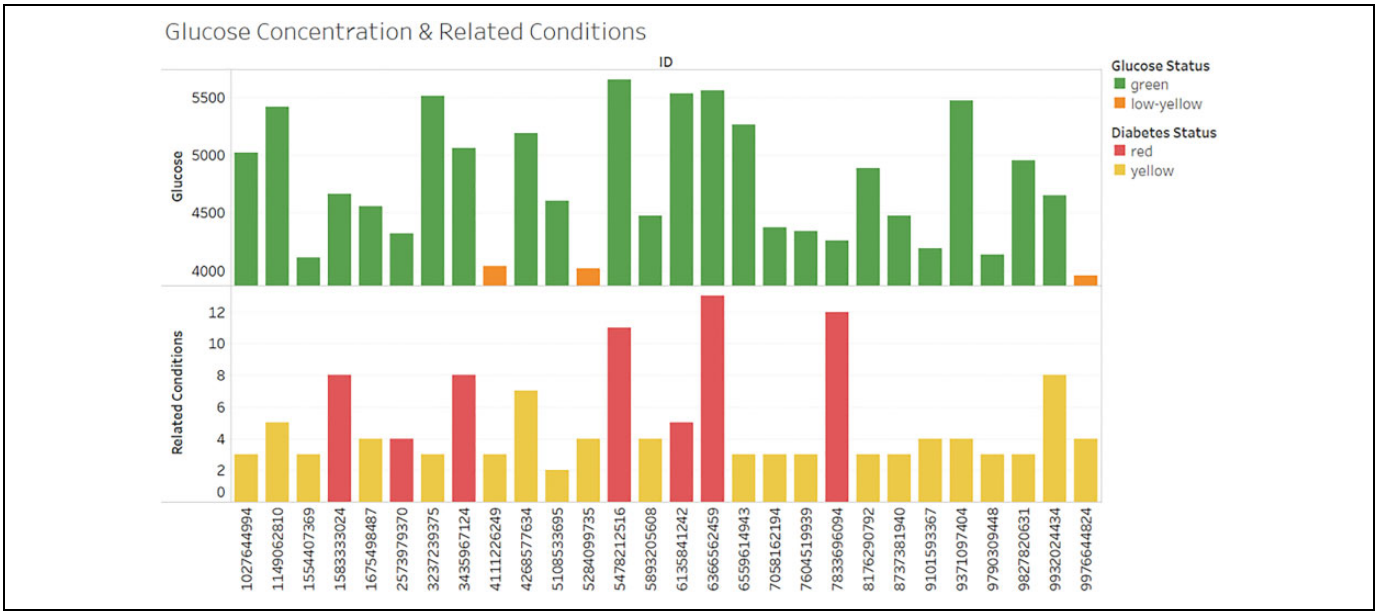

Figure 1. Subset of individuals in our study cohort had a number of health risk conditions despite having normal fasting blood glucose levels (top). This chart displays the fasting blood glucose levels of the individuals in our study cohort (bottom). The height represents the number of related health risk conditions, and the colours represent the risk for developing type 2 diabetes, specifically red for high risk and yellow for moderate risk, as determined by our metabolomics analysis and personalized signature profiles.

metabolite levels above or below normal range. For example, the metabolite glucose would be reported in green if it is within its normal physiological range (4,000-6,000 μM), in yellow if its slight above this normal range, and in red if above 7,000 μM (hyperglycemia) or below 3,900 μM (hypoglycemia).

Our health intelligence reporting platform also allows users to explore and pinpoint the different metabolite biomarkers that are outside of their normal ranges and contributing to their elevated risks of disease (Figure 2). This tool also allows users to explore their diverse network of metabolite biomarkers and how they are linked to their various health risks. This also allows users to understand that perturbations in the levels of one biomarker may have a multitude of effects when it comes to disease risk. Our health Intelligence platform can also group these metabolite biomarkers according to their biological functional role. For example, biomarkers associated with inflammation or involved in immune health can be grouped and analyzed together in our platform. This can give early insights into each participants' health status that may not have yet manifested as health risks or clinical symptoms that could be measured by conventional medical tests.

Health intelligence platform action plan

Our health intelligence platform outputs personalized lifestyle recommendations, based on data analysis of a participant's metabolite biomarker levels and health risks of various diseases (based on statistical computations of metabolites associated with risks of disease which we used to create individual molecular signatures of disease). Lifestyle recommendations, referred to as an action plan, include each participants' personalized diet, exercise, and nutritional supplement recommendations that take into account not only each participants' metabolite levels but also their dietary preferences, food allergies, and any exercise limitations. This action plan is also delivered to them by our web-based and mobile app platforms. A representative action plan displayed on a mobile app is outlined in Figure 3. Both the web and mobile app platforms allow users to quickly retrieve their personalized diet and exercise recommendations, such as "to consume one serving of beans, chickpeas, or lentils two times weekly" and "15-20 minutes of continuous dance and brisk walks four times weekly." These specific recommendations are generated by our web platform and are reviewed by our team of health practitioners and health scientists before being released to users. Although not shown, users will be able to build a grocery shopping list from their shortlist of foods from their diet recommendations. And users will be able to use the web platform to construct, either by themselves or with the help of a health coach, weekly meal and exercise plans using their specific diet and exercise recommendations and can adjust the servings and frequency as needed.

Normalization of health risks and biomarker levels following 100-day action plan period

We analyzed and compared the health risks and biomarker levels of our study population reported by our platform before and after participants completed their action plans (Figure 4). We had previously developed a proprietary method of computing risk based on two factors: (1) the number of metabolite biomarkers that are associated with a

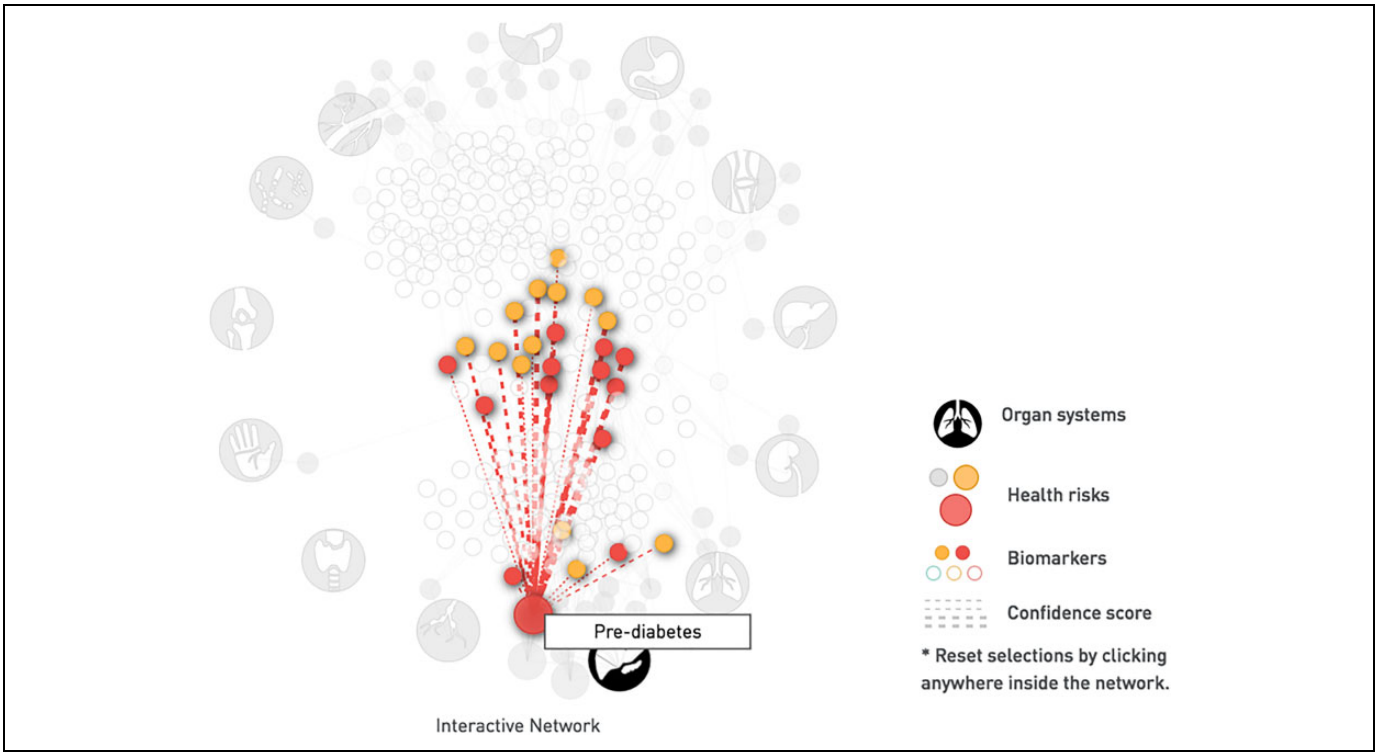

Figure 2. Our health intelligence platform allows users to visualize their biomarkers with abnormal physiological levels and explore how these biomarkers are connected to their body's network of health risks and organ systems. In this representative example, the user is able to explore the various abnormal biomarkers associated with their elevated risk of pre-diabetes. So far, the biomarkers all cluster together to contribute to this elevated risk; however, we can also see some biomarkers also clustering closer to other organ systems, such as brain and kidney health. Users can select brain or kidney health to see the connecting biomarkers that were also part of the pre-diabetes risk. The strength of evidence for each of these links between biomarkers and health risks and organ system is represented by increasing thickness of the dotted lines. The thicker the dotted line, the more scientific evidence is present that positively correlates abnormal levels of that biomarker with that specific health risk or organ system dysfunction.

specific disease or biological function with a measured concentration that is outside of normal physiological ranges and (2) the strength of scientific evidence that supports each biomarker's association with the specific disease or biological function.[2] This allows us to calculate a risk score (referred to "risk grade") for each specific disease and biological function which we used to identify changes to the study participants' health status. Before their action plan recommendations, several of the healthy participants had various health risks and biomarkers associated with aberrant biological systems were identified, including high and moderate risk scores in cardiovascular diseases, insulin resistance, type 2 diabetes, metabolic syndrome, and perturbations with biomarker levels associated with inflammation, immune health, and dietary health. The computed risk grade is relatively high, especially for insulin resistance, type 2 diabetes, metabolic syndrome, and cardiovascular disease (Figure 4; left). After the completion of their action plan, all study participants had decreased their health risks for these reported conditions. Furthermore, many biomarker levels associated with functional biological systems, such as inflammation, immune function, and dietary health, also showed reduced risks in the participants' second assessment (Figure 4; right).

Discussion and recommendations

If physicians and health practitioners were to solely rely on the traditional clinical tests of using fasting blood glucose levels as the only method to identify the risk of future type 2 diabetes, there is a potential for mis-categorizing patients who may be at significant risk of developing the disease. In our study, we identified a group of individuals who present with normal fasting blood glucose levels that were identified to have several early indicators of risks to their health, including type 2 diabetes, insulin resistance, and diabetes-associated co-morbidities, such as cardiovascular diseases (Figure 1). Furthermore, these study participants did not self-report any diseases or clinical symptoms during the initial intake for blood sample collection. However, looking at the different health risks and biomarker levels, it is easy to come to the conclusion that although these individuals were not experiencing any clinical symptoms related to type 2 diabetes, disease development may have been initiated and the progress of declining health was unknown to the individual. Their risk of type 2 diabetes and deteriorating health may only become apparent when symptoms may appear in the future or fasting glucose levels suddenly

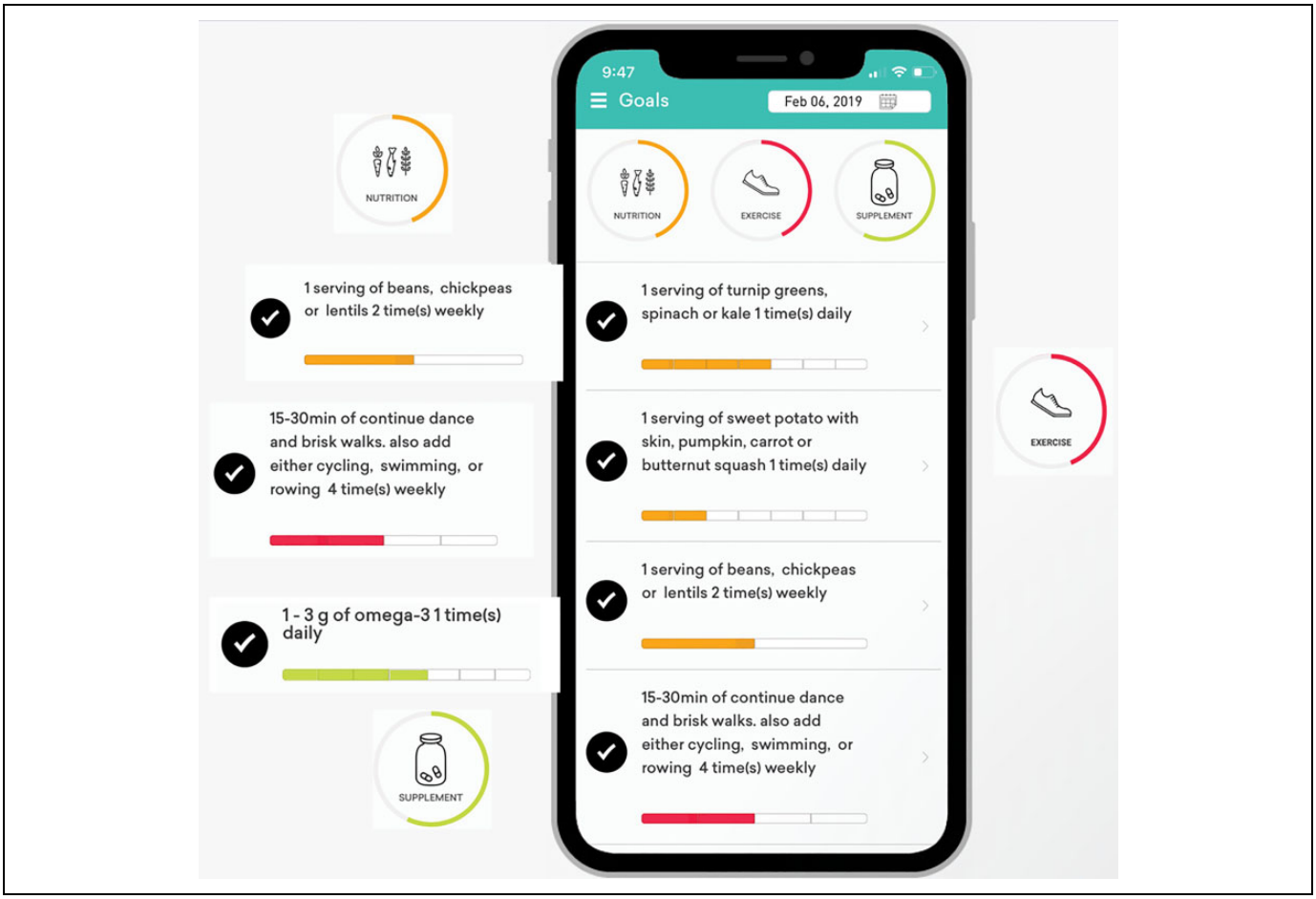

Figure 3. Representation of a diet and exercise action plan recommendation for an individual with high risk for type 2 diabetes in our health intelligence platform. Our platform can recommend nutrition, exercise, and supplement actions from our comprehensive database for individuals to follow to potentially mitigate their risks of disease. Users can also explore each of the different actions on our mobile app to see how they are linked to disease risks or biomarkers, such as metabolites, that are being targeted by their personalized lifestyle recommendations.

become too high. However, at the stage where clinical symptoms appear, it may be far more difficult to reverse the damage that has already occurred and many individuals may be forced to manage the disease through medication.

As mentioned, type 2 diabetes is also associated with a number of co-morbidities, including cardiovascular, liver, and kidney diseases.[36] In our analysis, we readily found moderate and high risks for a number of associated conditions, including Alzheimer disease, atherosclerosis, heart attack, metabolic syndrome, rheumatoid arthritis, liver cirrhosis, and chronic kidney disease. Even without the loss of glycemic control and no clinical symptoms, our study participants had perturbations in metabolites associated with these specific diseases. Therefore, it becomes more prudent to investigate early perturbations of metabolites to not only prevent type 2 diabetes but also to prevent many of these associated co-morbidities.

We developed a web-based reporting platform that identifies these various health risks and health insights for each participant. Our reporting platform also allows users to explore their metabolite levels and how these metabolites interconnect with their health risks and organ systems (Figure 2). Participants can also explore how the different metabolite biomarkers are interconnected by their relative network links, all of which may be contributing to their elevated risk of disease. Our platform can also group these metabolite biomarkers based on their functional roles which provide insights into each participants' health status, particularly when it comes to inflammation, immune health, and nutritional status, for example. Our hope is that patients, physicians, and other health practitioners will be able to use the web-based platform to explore the interconnectedness of metabolite biomarkers and how they may be impacting health status and disease risks.

As the participants in our study have normal fasting blood glucose levels and present with no clinical symptoms, it does not make sense to recommend medications for their type 2 diabetes or other health risks. Instead, our platform also leverages a comprehensive curated database of lifestyle recommendations, specifically diet, exercise, and nutritional

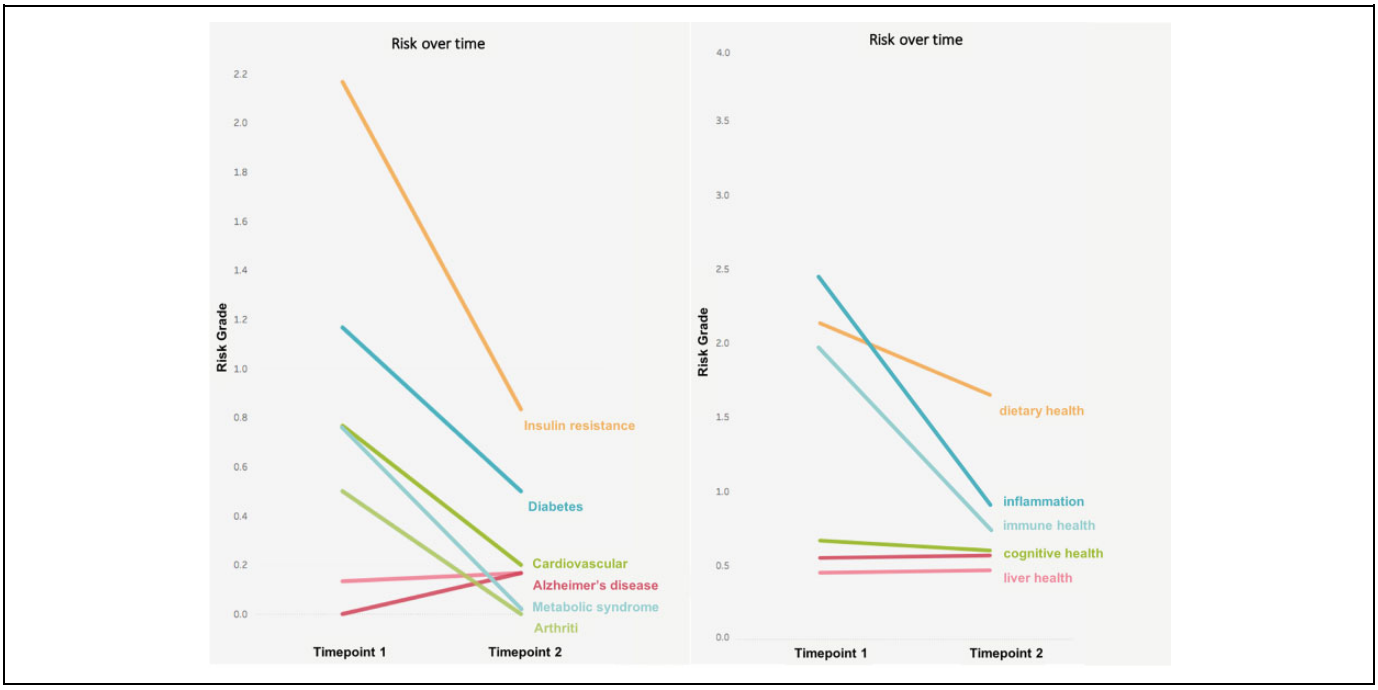

Figure 4. Aggregate data analysis of health risks and biomarker functional groups of study participants shows that many risks decreased in the second assessment (left). We computed risk scores for a number of health risks for our study participants, including insulin resistance, type 2 diabetes, cardiovascular disease, Alzheimer disease, metabolic syndrome, and arthritis. These health risk scores for various diseases were reduced in the second time point, particularly insulin resistance, type 2 diabetes, cardiovascular disease, and metabolic syndrome (right). We also computed risk scores for biological functions for our study participants, such as inflammation, dietary health, immune health, cognitive health, and liver health. Perturbations to many of these biological systems were also reduced in the second time point, particularly inflammation, dietary health, and immune health.

supplement that have been shown to influence specific metabolite levels according to scientific research, to develop a personalized action plan for each participant. Each action plan is reviewed by our team of health professional and health scientists before being released to the participants so as to verify the accuracy and validity of the information. An example of an action plan that may be reported to one of the participants is outlined in Figure 3. Each action and lifestyle recommendation is linked to the specific health risk or metabolite that it is supposed to impact and is clearly shown to the participant, through user-friendly and easy-to-navigate web and mobile app platforms (Figure 3).

Our health intelligence platform can aggregate metabolites together that are involved in specific disease risks and compute risk scores on a proprietary algorithm based on the number of metabolites that are outside of their normal biological ranges and on the strength of the research evidence. We performed an aggregate analysis of all our study participants at time point 1 (baseline) to show the average computed risk scores for each health risk levels identified on our platform through metabolomics analysis. We noticed that proportion of our study participants had moderate and high risks for insulin resistance, type 2 diabetes, and cardiovascular diseases, including heart attack and atherosclerosis (Figure 4). However, a similar aggregate analysis of our study participants at time point 2, where the participants were able to follow a personalized lifestyle action plan for 100 days, reveals that most of the health risks have decreased scores and none indicates low risk (Figure 4). Our platform also enables us to explore specific metabolite biomarkers that were previously outside of normal range, and we were able to confirm that these outlying metabolites in time point 1 had indeed returned to normal ranges after the action plan period and hence reduced potential health risks in time point 2 (data not shown).

Our platform can also group metabolites together that are involved in specific biological functional roles, such as inflammation, dietary health, and immune function, and similarly compute risk scores based on the number of metabolites that are outside of their normal biological ranges and on the strength of the research evidence. When we looked at an aggregate analysis of all our study participants at time point 1, we are able to see that metabolites associated with several functional pathways, such as inflammation, immune health, and dietary health, are reported to be perturbed by our platform, as indicated by a high computed risk score, for study participants at time point 1. A similar aggregate analysis of all our participants at time point 2, where the participants were able to follow a personalized lifestyle action plan for 100 days, reveals that metabolites in the majority of their functional pathways, including inflammation, immune health, and dietary health, have returned to their normal physiological

levels (data not shown) and thereby contribute to a reduced risk score for these functional pathways (Figure 4). Interestingly, risk scores for Alzheimer disease show a slight increase in the participants' second assessment. We attribute this slight increase to noise in the risk computations and did not deem as significant. We also determined this increase is not material since we did not see a substantial increase in risk scores for cognitive health.

Although for this study we were not able to track the participants to verify their adherence to their action plans, the results show there is still quite a substantial shift and improvement in health assessments from what the analysis revealed from their first test. It is important to also mention that although many of the health risks and biomarkers returned to no risk and normal levels (data not shown) and computed risk scores decreased (Figure 4), respectively, not all biomarkers were influenced by the action plan. Several nutrition-associated biomarkers are still outside of the normal ranges in the second test. It could be that some biomarkers are not as readily influenced by diet and exercise changes or it may also be likely that certain biomarkers require more than the 100 days to normalize, and a longer term strategy of healthy lifestyle support system is needed. With that being said, we believe our metabolite-based assay health risk and lifestyle recommendation platform is a novel and significant tool for health professionals and health leaders to use to identify individuals who are on early trends toward disease and adopt a more proactive and preventative approach in their clinical practice. As traditional medicine routinely employs a one size fits all approach, we believe our platform and comprehensive panel of biomarkers will help usher in a more personalized side of healthcare that can be tailored specifically to each unique individual.

Furthermore, with an aging demographic that is growing larger and larger every year with a life expectancy that continues to rise as well, the incidence of chronic disease is projected to increase, thereby increasing the financial demands on our already burdened healthcare system.[18] A central challenge to our healthcare system in the near future will be the implementation of new approaches in healthcare delivery to address the changing and complex health needs of this aging population. We believe the healthcare system must seriously consider a multidisciplinary evidence-based and personalized approach to ensure patients are receiving better case management and attention to their unique aspects of care. The benefits of a value-based healthcare system that is also focused on the preventative rather than reactive will be of value to patients, healthcare practitioners, payers, and suppliers. Value-based healthcare models focus on helping patients recover from illnesses more quickly and aim to avoid chronic disease in the first place. As a result, patients face fewer clinic or hospital visits, medical tests, and procedures and spend less money on prescriptions. Although healthcare practitioners may need to spend more time on new, prevention-based services, such as our biomarker-based risk assessment and lifestyle platform, they will spend less time on chronic disease and long-term disability management. In addition, the metrics around quality and patient engagement will improve when the focus is on delivering value instead of volume. Insurance companies know that risk can be reduced by diversification, or in other words, spreading the risk across a larger patient population. A healthcare system that strives to identify and reduce chronic disease incidence will translate to a healthier population and less risk on payers' investments. Suppliers will benefit from aligning their products and services with positive patient outcomes and reducing their costs. Many healthcare industry stakeholders are calling on manufacturers to tie drug prices to their actual value to patients, a process that is likely to become easier with the shift toward personalized medicine.

Moving away from the traditional medical norms of fee-for-service model and fixed prescriptive protocols for patients to a more proactive, preventative, and personalized focus on improving patient health outcomes via a value-based model may take time and a concerted effort from multiple stakeholders and players in the healthcare industry. As the healthcare landscape continues to evolve and providers increase their adoption of value-based healthcare models, it would not be surprising to see short-term financial losses before we see longer term costs decline. However, industry transition toward delivering value to patients is the best method for lowering healthcare costs while increasing quality care and helping people lead healthier lives.

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