

THE WELLNESS REVOLUTION

The transition from disease-focused to wellness-focused medicine is within reach.

Over the last five years there has been an incredible convergence of four scientific and social thrusts to create a new medicine: *systems medicine* — which is global or comprehensive approach to disease, *big data*, the *digitalisation of self-measurements* and *consumer or social activated networks*. The convergence of these four thrusts has led to a medicine that is predictive, preventive, personalised and participatory—P4 medicine.

The first three P's are straightforward, and the essence of the fourth P is that you (each individual) will be at the centre of your own health care. P4 medicine has two major thrusts: one is to demystify disease — classically what traditional health care has focused on — and the other is to quantify wellness. About 99% of society's resources have gone to disease and because wellness has not been studied scientifically, it has a dubious reputation. We propose to make wellness scientific. To do this, we're actually going to identify blood metrics that will let us measure for each individual their degree of wellness, both psychological and physiologic.

What is important to understand is how essential wellness is going to be going forward. Consider the following calculation. If we follow the increase in average longevity over the next 10 or 15 years, one can make the calculation that in the developed world half of the children born in this calendar year will live to be 100 years of age. The question is 'what is the quality of their life physically and mentally for the last 30 or 40 years of their life.' Wellness is about bringing a productive and full life to each of us throughout our 90 to 100 years.

How do we go about bringing P4 medicine into the system? What I proposed about three years ago was that we do it by creating a longitudinal, high dimensional study of 100,000 individuals who are well — and thereby come to understand what wellness means. In fact what we did in 2014 was to identify 100 volunteers and we carried out precisely this study as a pilot project to determine how effective this wellness study would be.

So we determined the genome sequence; we took blood samples every three months to do clinical chemistries and measure proteins and metabolites; and we took stool samples to measure the microbes present in the gut that have an enormous role in determining your health. We put that together with quantised self-measurements using a fitbit that determined the amount of exercise, the quality of sleep and the pulse rate. We found we could actually integrate these data for individuals such that we could look at a catalogue we've created from the literature of close to 2000 actionable possibilities; each of which, if acted upon, had the ability to either improve your wellness or let you avoid disease.

What we did with these actionable possibilities was to use coaches to explain the actionable possibilities to the individuals and then persuade them, in the context



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of what their own health objectives were, to carry them out. To our enormous amazement, we got 70% compliance and this is testimony to the power of the coaching.

The data were incredible. In your genome sequence are the secrets to losing weight, maximising exercise and identifying your potential for various kinds of athletic injuries (and how to avoid them). In the very first clinical chemistry we analysed, 91% of the individuals had nutritional limitations, 68% had significant inflammation, 59% had cardiovascular abnormalities (e.g., lipid abnormalities) and diabetic abnormalities. In fact we found 23 pre-diabetics in this population of supposedly well individuals and we were able at the end of this time to convert seven pre-diabetics to a 'normal' status. Why the seven converted quickly and the rest didn't is a subject that we're studying.

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We were also able to demonstrate that we could use a common type of genetic marker called 'genome wide association markers' to calculate the genetic risks for each individual for about 50 different diseases. Many of them, such as Alzheimer's were non-actionable. We plan to keep track of these predispositions, and when they do become actionable we give this information to the patients to take back to their physicians for appropriate remedial action.

One of the most spectacular examples of data I've ever seen in my life was to be able to compare individual data bits in the five major categories of data types from each of these 107 individuals. We demonstrated that there were more than 35,000 statistical correlations that let us look into the dark matter of human biology providing insights into human biology and disease that we have never seen before. These were associations that told us biological systems were connected that we had no idea were interrelated; it provided associations that gave us new kinds of actionable possibilities, and even associations that gave us new approaches to therapy.

These statistical correlations will expand greatly as we increase the number of individuals analyzed a hundred-fold over the next 18 months or so. The individuals themselves:

For the most part said this was one of the most transformational personal life experiences they ever had;

For the first time they realised with information they could determine the trajectory of their own health care;

They realised that your genome is not your destiny, rather, it determines your potential but with knowledge in many cases you can circumvent the limitations of your genome; and

virtually every one of the 107 wanted to be included in the next scientific wellness study.

What have we done from a clinical point of view? We have a catalogue of close to 2000 actionable possibilities, we've been able to use those on the 107 pioneers to optimise wellness and minimise or avoid disease. We've actually begun to set up the blood metrics that will allow us to quantify wellness. We've been able to see transitions from wellness to disease; and this is really important because in the future we'll look at the earliest disease transitions and use systems approaches to be able to understand their biology. This will provide insights into early diagnostic biomarkers and eventually the therapeutics that will be necessary to take individuals at the very earliest stage of their disease and bring them back to wellness immediately. This will save the health care system enormous amounts of resources.

Matt Trau and his colleagues are thinking about new types of assays that could be miniaturised, and hence could be made far less expensive for the future. We'd like to have a watch you could take home and take virtually all measurements we need for scientific wellness at home. We have a long way to get there but that is the direction we'd like to go.

We have a database now with all these wellness-to-disease transitions, which is going to create the possibility for a whole array of new companies—that are going to populate this new industrial sector of scientific wellness. And this pilot project is the very essence of P4 medicine because it will increase the quality of health care; it will decrease the cost

of health care and it will open up the possibility for innovation.

What I will argue is wellness has created a whole new thrust in health care, a whole new industrial thrust — denoted scientific wellness. I'll argue that in a 10 to 15-year period the market capital for scientific wellness will far exceed that of the disease industry or the old-fashioned health care industry.

So for society what can we do? A variety of things — we can see the digitisation of medicine is going to make wellness assays far less expensive—and this is by far the largest expense of scientific wellness. We can also see that it is going to create new wealth as we populate this new sector with companies.

Scientific wellness will trigger innovation. If you think about the Industrial Revolution, the steam engine that triggered this revolution was a macro invention that threw out many micro inventions that expanded the reach of the Industrial Revolution. Similarly, P4 medicine will be a macro invention that will throw out many micro inventions in the future. For the first time, we're going to be able to deal with the challenge that every nation state has: how to reduce the cost of health care which takes ever increasing fractions of their national budgets. Furthermore, we're in a wonderful position to optimise human potential through wellness to let everybody be all that they can.

In the future we at the Institute for Systems Biology will be taking two approaches to scientific wellness. The first is that we have created a company called Arivale that is going to provide scientific wellness with a focus on consumers — and already we're far oversubscribed for a company that just barely got started. In this company context we plan to accumulate 10,000 additional individuals undertaking scientific wellness in the next 18 months. This will produce a transformational amount of data that I'll argue will alter how pharmaceutical companies, how biotechnology companies, how nutrition companies and how diagnostic companies operate in the future.

At the Institute for Systems Biology we will continue to carry out academic projects. For example, one attractive possibility is to bring scientific

wellness to the Indigenous (Aboriginal) Australians to see if we can change their early average age of death and bring to them scientific wellness. We will also bring scientific wellness to individuals who've gone through the horrors of breast cancer treatment and make them well.

My dream for the future is that P4 medicine would become the central tenet of health care. It's proactive, it focuses on the individual, it's all about pushing wellness, creating these dense data clouds and of course using the social networks of individuals and patients for education, crowdsourcing and for advocacy to change the health care system that itself is intrinsically conservative. We'll be able to see strikingly the wellness-to-disease transitions for all major diseases and we'll push the revolution that will lead to the early conversion from disease back to wellness.

We'll take women who want to get pregnant, we'll follow them through pregnancy and indeed follow the individual all the way through the rest of their life.

We'll be able to participate in this exploding scientific wellness industry and create companies that will be the Googles of this new industry.

We'll be able to, through digitization of medicine cut the costs of health care to the point that we can bring it to the developing world — and that will lead to a democratization of health care that was utterly inconceivable even just a few years ago.

Finally, what I hope to be able to do in the context of aging is answer the question I often get asked: 'how are you going to avoid the last three or four years of death (when you spend half your health care dollars and so forth), even if you've lived beautifully up until then?' I do have an answer now because we, over the past five years, have studied centenarians (100–115 years of age) and what we've discovered is that when they die, they die rapidly with complete systems failures. So, all I have to do for you is keep you alive with the scientific wellness program until you reach 100 — and then you're on your own.