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Wellness Initiatives: Benefits and Limitations

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In the last decade, the public has become increasingly aware and concerned regarding their susceptibility to common conditions such as obesity and diabetes. Groups of scientists have founded initiatives that harness this desire to stay disease free and have developed public health projects using a large population base. This novel approach relies on a wide volunteer group of individuals who allow themselves to be monitored and studied over a long time period (ranging from a few months to many years). Data based on gene sequencing, sleep cycles, diets, activities, and blood sample analyses are recorded on a regular basis. By following each volunteer participant, whether they progress to disease or remain healthy, scientists hope to find lifestyle characteristics and corresponding microbiomes or genes that are key to living well. Projects such as the 100K Wellness Project, Lake Nona Life Project, and Google's Baseline Study have well-established participant groups and aim to use this information to benefit the greater public and/or to make a profit.

Because individuals vary greatly, both in biological composition and lifestyle, data collected from a ranging population may give scientists a more comprehensive data source. These data, in turn, are used to construct a personalized lifestyle plan for customers of wellness companies such as Arivale or similar company models. A customized consultant is assigned to the consumer and will potentially give advice based on monitored parameters.

Technology has built another level of data monitoring; as part of the Google Baseline Study, GoogleX has created contact lenses that constantly monitor glucose concentrations and smart trackers that can alert users of imminent heart attacks. Similar technologies such as Samsung's Simband constantly record and transmit information to a larger database, all as part of mass health studies. This recording and transmission of information, however, makes some users uncomfortable about the prospect of data leakage or other loss of privacy that may harm them.

Here, we explore this rapidly developing sector where technology and mass population testing crosses. We asked 4 experts to give their input on the development potential and perceived drawbacks of this industry.

Somebody said that the best definition of health is when you do not think about your health. Do you believe that scrutinizing your health will generate anxiety or relaxation?

Nigel Paneth: The answer to this question is to a large extent dependent on the individual. Some people, particularly when young, are relatively indifferent to factors that threaten health but do not produce symptoms. At the other extreme, some people are excessively focused on their health risks, which are often subject to exaggeration by the media covering health issues. Most people who prefer not to dwell on their health risks are unlikely to be interested in monitoring or otherwise scrutinizing their own health. The remainder—likely a small minority of the population, and concentrated in the educated classes—may find such monitoring interesting and potentially useful.

The first condition mentioned in the preface to this Q&A article discussing public awareness and concern is obesity and the second is diabetes. Is there anyone who needs special monitoring to determine that they are obese? And diabetes can be diagnosed with a simple

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blood sugar measurement. How would such conditions benefit from complex biochemical monitoring?

Henrik Vogt: When I was younger, I experienced health anxiety, and at that point such scrutiny would have generated worry, lost health, and lost youth as different findings had to be ruled out as dangerous. Now, I believe I would be less affected. As a doctor, I have become more relaxed towards most bodily symptoms and findings, trust myself as a generally self-maintaining entity, and live with the risk that comes with being alive. I definitely do not think I would be more relaxed, because I am relaxed in the first place (and should be as a healthy 39-year-old). The technology would, however, generate in me an awareness of risk, and if health equals the absence of thinking about health and risk, it would, by definition, be impossible to feel completely well anymore.

Jerry Yeo: In general, I would say scrutinizing health tends to generate some level of anxiety in most people. For example, if I subject myself to blood screening tests, I will naturally be wondering which of those tests will return as abnormal and what the consequences will be. Although I am relatively healthy, if my blood screening test shows an abnormal value, I will naturally seek to do more follow-up testing to make sure that I don't have an undiagnosed disease.

Stephen Master: I think that the answer to this question will depend entirely on the individual and their life experiences. Of course, as was pointed out during the early years of genetic susceptibility testing, everyone wants to receive a reassuring answer. However, individuals vary widely in how well they can evaluate equivocal (or possibly abnormal) results. Even some medical trainees may exhibit hypochondriasis until they have gained a sense of clinical perspective (the so-called "second-year medical student" syndrome), and a little knowledge can be dangerous. For others, however, a focus on finding better ways to monitor health may be just as normal as trying to measure their financial or career success.

In your opinion, will patients actually follow instructions from coaches and make lifestyle changes?

Nigel Paneth: Practitioners know that it is very hard to convince people to undertake lifestyle changes. As a cardiologist friend of mine once said, "The most I can achieve with my patients is to get them to quit smoking and take their medicines." On the other hand, there is evidence that focused and detailed advice, such as from dieticians, can be adopted, but this is in relation to clear health risks such as obesity and diabetes. If established clinical disease engenders lifestyle changes only with difficulty, then how likely is it that asymptomatic biochemical abnormalities will? The few people who are willing to undertake intensive monitoring are probably those most likely to be coached into lifestyle changes. But for the majority of the population, this is unlikely to be an effective strategy.

Henrik Vogt: Some no doubt will, but neither previous evidence on general health checks and lifestyle counselling, nor new evidence on the impact on communicating genetic risks on risk-reducing behavior, suggest that the general population will change behavior substantially. This makes the promise that great health benefits and cost-reductions are just around the corner quite dubious. Advocates of this "surveillance medicine" suggest that even more monitoring and constant feedback will change this picture, but a recent randomized controlled trial performed by researchers at Scripps suggested no differences in healthcare utilization or costs from an intervention employing different monitoring devices in people with common, chronic disease. However, advocates of so-called P4 medicine (predictive, preventive, personalized, and participatory) seem to continue with their bold promises as if this evidence is not there, suggesting that they are partly based on faith.

Jerry Yeo: I believe that, in general, patients who have paid for an assessment of their health are more likely to listen to their coaches and to alter their lifestyles towards better health. However, there may be some variability in responses that is dependent on the level of difficulties in lifestyle alterations to achieve the intended outcomes. More motivated individuals are more likely to follow through while less motivated ones may find the prescribed changes too difficult to achieve. Thus it is a multifactorial consideration, including the patient's per-

ceived risk of not following the recommendations based on the screening results.

Stephen Master: Making lifestyle changes can be hard, and even direct advice from a physician is no guarantee that individuals will follow basic, well-established diet and exercise guidelines (I do not exempt myself from this difficulty). On the other hand, there are clearly patients who have had, for example, clinically significant cardiac events and have made radical behavioral changes as a result. Since detailed monitoring leads to personalized rather than general advice, I think that it is worthwhile to try and identify those patients who may benefit from the motivation that is provided by wellness data.

Is there the potential that findings from such programs could be harmful to the individuals and in what ways?

Nigel Paneth: A subset of patients willing to be monitored will have their health concerns exacerbated and may make untoward demands on the healthcare system. There is also the very real risk of excessive intervention, either for diagnosis or therapy, with the possibility of side effects. Every practitioner has seen examples of this, which multiply in proportion to the extent of testing of asymptomatic patients. To quote another internist friend of mine, "no one is really healthy—they just haven't been tested enough."

Henrik Vogt: Yes. Firstly, there are false-positive test results indicating that something is wrong when it in fact it is not. Secondly, there is overdiagnosis, meaning findings that represent a real abnormality, but that will actually never pose an actual health problem. Such findings can cause unnecessary worry and initiate a spiral of further testing and treatments with potential side effects and costs. It is hard to know who is overdiagnosed at the point of diagnosis, meaning who with an abnormality will actually suffer and who will not. Theoretically, these people can only lose from diagnosis and treatment. While concerns about anxiety as a result of predictive testing may not be sufficiently supported in isolated case control trials, screening may still instill a more general awareness of risk or suboptimal health in the population that is supposed to be alleviated by this testing.

Jerry Yeo: Practitioners of laboratory medicine are well versed with the concept that the more you test (as in health assessment screening) a healthy population, the higher the risk of getting false-positive results. False-positive results can provoke anxiety and depression, leading individuals to seek medical help, which undoubtedly results in more diagnostic tests that are costly and may be unnecessary. Others may choose to believe the screening results and immediately seek treatment to ameliorate a perceived pathological condition. Additional testing and treatments may have associated risks and side effects that could lead to physical and psychological harm to the individual.

Stephen Master: For low-prevalence disease, a test needs extraordinary performance to provide any predictive value. Given the reported deficiencies within our own medical community when it comes to understanding positive predictive value, I am concerned that including more rare diseases within a "wellness profile" would be actively misleading. While it is possible that this problem could be reduced through an intensive focus on reporting tools that help patients understand such data, I think that the near-term risks of misinterpretation need to be carefully considered.

Should participants worry about breach of privacy from constant monitoring through smartphones?

Nigel Paneth: In today's world, one must be worried about breaches of privacy every time one makes a connection with any electronic device.

Henrik Vogt: Yes, information is volatile and there is no way one can be completely sure that it does not end up in the wrong hands, especially in countries with poor respect for individual freedom and human rights. To speculate about the future: Our society is concerned about 2 major fears or risks, terror attacks and the failure of our own bodies. A confluence of these 2 fears and the technologies we have developed for prediction and control of them may lead to the ultimate societal surveillance. In the future, what may be hacked from our smart-phones will not be a few data, but a computational avatar based on big data about most aspects of your being ("avatar" is actually a metaphor used by the European Digital Patient project to describe a future virtual mirror image of all of us). A state or company that wishes to monitor people, for example with reference to risk of terror, could access such an avatar containing our physiology, sociometrics, psychometrics, and environmental exposures.

Jerry Yeo: Absolutely! Anyone who uses smartphones or wireless devices should be concerned about the risk of being hacked. Constant monitoring of health data via the Internet or wireless devices can be intercepted by unscrupulous parties, who can then use the information for various nefarious purposes, ranging from blackmail/ransom to theft of personal identity. Determined hackers will attempt to steal these data (especially from celebrities or government officials) and either leak embarrassing information or use them inappropriately for commercial purposes.

Stephen Master: There are substantial privacy implications in at least 2 areas. First, the inherent volume of data may reveal fundamental aspects of the individual's health that would not be gleaned from a simple sample at one time point. Second, location, activity, and health data may reveal non–health-related aspects of a person's life (for example, when they typically leave their house to go running). Societal views on the acceptable level of privacy risk may change; after all, many of us willingly use Gmail despite the fact that we know that Google "reads" our mail to provide targeted advertising. Nonetheless, the privacy risks inherent in any continuous electronic monitoring should be clearly laid out by manufacturers and providers.

Will there be important traits of participants' lifestyles that are unquantifiable? Could you cite examples?

Nigel Paneth: One of the greatest limitations of the monitoring described is the contemporary time period that is monitored. Many important health risks are set down in very early life. In fact, for most chronic diseases of adults in the western world, etiologic agents are operating decades before any clinical manifestations. The assumption that we can detect these etiologies years after they operate is mistaken. We are more likely to be able to detect the earliest manifestations of clinical disease, as when we detect mild hypertension or prediabetes. These easily recognized conditions are often noted many years before the onset of clinical disease. How much earlier in pathophysiology are we likely to detect lifestyle risk factors of importance of which we are now unaware by using intensive monitoring? We will not detect early exposures that we know for certain are major causes of disease (intrauterine life and the perinatal period, childhood trauma and poverty, familial environment)? These factors may not be recognized by participants in the monitoring, or may not be remembered. The ability to detect imminent heart attacks not producing symptoms that would bring the patient to a doctor might be valuable, but we would need to know the screening parameters of such detection systems (clinical sensitivity, specificity, predictive value) and whether such earlier detection improves survival.

Henrik Vogt: One could no doubt measure substantial aspects of the "exposome," which by definition includes every exposure an individual is subjected to from conception to death, including social, economic, and psychological influences. However, the scientific idea that one can measure every aspect of human life, which is extremely context-dependent and defined by an immense social complexity, remains what biologist René Dubos already in 1959 described as "the mirage of health." It is tempting to go into an argument about why it is impossible to measure everything. However, instead it should really be the other way around. Those who propose that one may measure every relevant facet of human existence are making a very bold claim, which also reduces human beings to something quantifiable, and have a lot of explaining to do.

Jerry Yeo: I am not a social scientist, but I would state that, in general, lifestyle traits such as work life, sex life, spiritual life, relationship life, mental and emotional life, creative life, and a healthy life (balanced nutrition, sleep, avoidance of addictions and stress, and sufficient exercise) can be quantifiable, but in a more subjective way. The relevant question is how translatable are these subjective data of lifestyle traits since the data obtained are highly dependent on the construct used by the researchers? For example, a construct used in our Western culture may not have the same meaning in another culture and so it might elicit a very different response. However, there is no doubt that these (lifestyle) environmental factors have large modulating effects in addition to various "omics" factors in determining the final health disposition of an individual.

Stephen Master: As previously mentioned above, the effects of a patient's past medical history may be difficult to capture using current metrics. In fact, a substantial amount of what is and is not quantifiable depends on the sensors that are available at any given time. At present, there is no consumer-style sensor that I am aware of to directly measure, say, coronary artery blood flow. However, this is something that could be achievable in principle. Other aspects of an individual's health, such as psychiatric and behavioral factors, are more difficult to quantify in a "wellness testing" setting. However, to the extent that the intangible aspects of human behavior directly affect physiological parameters, it may be possible to indirectly infer personal traits that have an actionable influence on health.

Should public health systems or private insurers cover this type of preventive medicine? If not, would the rich have an unfair health advantage compared to those who cannot afford it?

Nigel Paneth: It should only be covered by third parties if it is demonstrated to be effective. First, show whether it is effective, then consider issues of coverage. If effective, it should be covered by third parties. If not effective, it should not be covered.

Henrik Vogt: If it worked, and was deemed to be responsible and sustainable for society, it should be covered. It would be unfair that some individuals could buy better health than others. Coming from Scandinavia, I would worry that a medicine that could provide the affluent with substantial advantages over the poor in terms of

longevity and quality of life would create an inequality that damages the social fabric.

Jerry Yeo: If there is good evidence linking certain preventive medicine measures to better health outcomes, then it is a cost-effective practice that should be funded by a combination of public health system for those who cannot afford it and private insurers for those who are employed. Otherwise it will cause a huge health disparity where the less well-off population sector will have higher risk of poorer health outcomes, causing a drain on public health resources that eventually will be borne by society as a whole.

Stephen Master: If there are data to support its efficacy, it should be covered; prevention is almost certainly less expensive than treatment. In the case of private insurers (and even large employers), there seems to be an increasing trend toward recognizing this fact and incentivizing healthy behavior. Thus, the self-interest of third-party payers should lead them to support this technology if it is shown to positively influence population health.

Is there scientific evidence that such initiatives produce more good than harm?

Nigel Paneth: There are no well-evaluated programs of intensive monitoring, such as are described in the preface to this Q&A article, upon which we can determine benefit or harm. Moreover, it does not seem that programs such as the 100K Wellness Project and others have been set up so as to produce evaluable data. Are controls to be selected? If not, to whom should the participants be compared in light of the near-certainty that they will be selected for high education, income, and health awareness? These are people who will have better health outcomes even without the monitoring. I worry that claims will be made based on the better health of the monitored that are in fact not attributable to the monitoring itself.

Henrik Vogt: On the whole, no. What is staged is essentially the most massive medicalization of human life in history. As shown, for example, by the "Too Much Medicine" campaign initiated by the *British Medical Journal*, screening and preventive medicine are already at a tipping point where it is questionable whether benefits really outweigh the damages and costs. The promise of P4 medicine is that substantially more medical testing, data, and intervention will produce less waste and harm in already well people. It will take years to assess if and how that is possible. Disconcertingly, very little has so far been published from the Hundred Person Wellness Project, making it what John Ioannidis recently called "stealth research," i.e., biomedical innovation that is happening outside the peer-reviewed literature.

Jerry Yeo: I think currently there isn't a lot of evidence that mass screening of a healthy population leads to more good than harm. In fact, there is evidence of the opposite effect (as alluded to above). However, with rapid advancements in technology, biomedical discoveries, and the ability to gather and process big data, it is possible that in the near future complex data sets encompassing many factors could be used to generate predictive algorithms for individuals that will lead to better health outcomes while minimizing harmful effects.

Stephen Master: I'm not aware of data that support this hypothesis. However, given the potential for genuinely new kinds of data (focused, for example, on intraindividual longitudinal changes rather than on the relationship to a population mean) and their proposed effects on human health, it is reasonable to propose that well-designed studies to determine the effects of these initiatives would be worthy candidates for federal funding.

Should anonymized data derived from these initiatives be available for public usage?

Nigel Paneth: The lack of a structure to the data—no systematic comparisons set up in advance, no randomization of the intervention, absence of data on time periods of maximum exposure risk—make me wonder about the value of anonymized data for any useful purpose.

Henrik Vogt: It should be up to the individual participant. However, I find it notable that advocates of P4 medicine find it necessary to stress that patients must understand that it is their societal responsibility to make their data available to scientists, invoking for example images of future relatives that will be at a loss if they do not. This looks more like coercion; it should also be viewed in light of the abovementioned privacy concerns and the fact that the promised revolution of healthcare is not an inevitable, but a largely unsubstantiated promise.

Jerry Yeo: Yes, public access will spur further research and advancement of knowledge that can benefit society as a whole. However, data in the public domain could be used by nonexperts or unscrupulous individuals to make outrageous claims to sell products to the general public, who may not be sophisticated enough to understand the interpretations and limitations of the data. Especially with the proliferation of non–peer-reviewed publications/blogs on the Internet and the rapid accessibility via search engines like Google, the lay public could be deceived by "shady publications" being used to scam the public into buying worthless products.

Stephen Master: Yes, with caveats. Although the utility of the data set would be maximized by including every-

one, individual consent is necessary. With enough detailed medical data, it becomes increasingly questionable whether it is still truly possible to "anonymize" a data set. I'm not as concerned about bad conclusions being drawn from the data; after all, many publically accessible, data-rich repositories already exist, and we rely on peer review to weed out spurious conclusions drawn from them. I'm more concerned about messy data with respect to unknown, confounding factors. Some valuable inferences may be achievable, but selection bias is still likely to exist.

If cost were not an issue, would you subscribe to such programs and could you comment on your decision?

Nigel Paneth: I would not subscribe to such a program, for free or for payment, until it had been demonstrated to be effective at preventing disease. We are a long way from that now, and, unfortunately, not clearly headed towards a means of assessing the value of this kind of monitoring.

Henrik Vogt: All in all, no. I would want to spend my limited time, focus, and resources on other things given the evidence. But of course, it would be interesting to observe my own dynamic physiology, and to learn more about how I function from a quantitative viewpoint. I think many people monitoring their bodies are motivated more by a sense of identity and self-knowledge than the prospect of better health. The quantified self-movement has even adopted the old Greek maxim to "know thyself" as a slogan. Much can be learned from scrutinizing one's own computational "avatar"—which can be seen as a kind of advanced medical "selfie." Still, there is a difference between knowing thyself and knowing thyselfie.

Jerry Yeo: I would consider subscribing to such a program if sufficient evidence exists to substantiate the benefits (and risks) of joining the program affecting my health outcome. If the screening program identifies areas of risk to my current health status that could be ameliorated by changes in lifestyle habits (e.g., healthier nutrition, exercise, rest, etc.) or being put on a certain medication regimen, I would definitely subscribe to it. In contrast, if the screening program identifies a genetic condition that I will eventually develop with no known cure, I would avoid such program since all it does is to cause great psychological duress without any possibility of relief. So before signing on to any screening program I would want to know the scope of assessment as well as the limitations of the testing program.

Stephen Master: So long as there were reasonable privacy safeguards and I was able to directly access the raw data, yes. To put this in context, I would also volunteer to get my full genome sequenced, my metabolome profiled, or any number of other biological tests performed. I fully acknowledge that this may not change a single thing in my healthcare, wellness, or life expectancy. Further, acting on any of this information without a healthy dose of clinical context and experience could be actively detrimental to my health. At the end of the day, though, I am just curious.

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