

DIYgenomics Crowdsourced Health Research Studies: Personal Wellness and Preventive Medicine through Collective Intelligence

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Abstract

The current era of internet-facilitated bigger data, better tools, and collective intelligence community computing is accelerating advances in many areas ranging from artificial intelligence to knowledge generation to public health. In the health sector, data volumes are growing with genomic, phenotypic, microbiomic, metabolomic, self-tracking, and other data streams. Simultaneously, tools are proliferating to allow individuals and groups to make sense of these data in a participatory manner through personal health tracking devices, mobile health applications, and personal electronic medical records. Health community computing models are emerging to support individual activity and mass collaboration through health social networks and crowdsourced health research studies. Participatory health efforts portend important benefits based on both size and speed. Studies can be carried out in cohorts of thousands instead of hundreds, and it could be possible to apply findings from newly-published studies with near-immediate speed. One operator of interventional crowdsourced health research studies, DIYgenomics, has several crowdsourced health research studies in open enrollment as of January 2012 in the areas of vitamin deficiency, aging, mental performance, and epistemology. The farther future of intelligent health community computing could include personal health dashboards, continuous personal health information climates, personal virtual coaches (e.g.; Siri 2.0), and an efficient health frontier of dynamic personalized health recommendations and action-taking.

Introduction

Bigger Data, Better Tools, and Collective Intelligence Computing Communities

The internet has facilitated the advent of new models of collective intelligence that are shaping and advancing

humanity in ways that may have been unthinkable previously. Millions of people creating and using content on the internet has generated large data sets and tools for interpreting and manipulating these data that are themselves recursive enablers of subsequent advance. Artificial intelligence is one area that has realized substantial benefits from the new era of bigger data and better tools, particularly regarding machine learning, anomaly detection (e.g.; fraud and spam), and natural language processing (e.g.; question answering systems like IBM's Watson). A quintessential example is Google's success in spelling correction and language translation: progress in natural language machine learning allowed statistical methods to be applied to the large datasets that have arisen on the web (Halevy 2009). Simple data analysis techniques were successful after decades of specially-designed algorithms showed little progress; a key point was finally having a very large corpus of data.

One effect of bigger data and better tools is that humans themselves start to serve as a computing community, both as individual nodes and through mass collaboration. Individuals take in data, process it, and turn it back into the network in new forms with added value. One public good that has arisen through community computing and collective intelligence is the wikipedia (Fallis 2008). The annotation of street map data, creating crowdsourced wikipedias of the Earth, is another example (Kamel Boulos 2011). Community computing models are arising in the health sector as well. All of these examples display the predicted progression of engagement in online communities, escalating in three stages from information-sharing to cooperating to participating in collaborative action (Shirky 2008). Another benefit of internet-based models is that a wide range of diverse participants can be engaged. Crowdsourcing can be used to obtain needed participants, services, ideas, or content at low cost by

soliciting contributions from a large group of people via the internet. Better quality outcomes may be obtained through wisdom-of-the-crowds benefits that accrue as people with diverse backgrounds analyze data and propose novel interpretations. On average, the wisdom of crowds arrives at a better answer than any individual can provide, including outperforming small groups of experts in making decisions and predictions (Surowiecki 2004).

Participatory Health: Bigger Data, Better Tools, and Collective Intelligence Models

Health may be generating big data faster than any other sector: the number of people participating is growing, the amount of data per person is growing, and the demand for easy accessibility and robust searchability of these data is growing. In 2009, it was estimated that all human-created content to date comprised one zettabyte of information, but that within five years, it would be routine to be generating one zettabyte of information in much shorter time frames, particularly in the field of medicine, due to imaging and personalized profiling (Enriquez 2010) where billions of data points per individual could become the norm (Hood 2011). Better tools are also proliferating in participatory medicine and health 2.0, for example with self-tracking devices, mobile health applications, personal electronic medical records, health social networks, and crowdsourced research studies. A next generation of tools will be required to integrate burgeoning health data streams (genomic, phenotypic, microbiomic, metabolomic, self-tracking data, etc.) into personally meaningful recommendations.

Health community computing models may offer some help, for example health social networks and crowdsourced health research studies are emerging to support both individual activity and mass collaboration. Health social networks are online communities for individuals to discuss and inform themselves about conditions, symptoms and treatments, provide and receive support, track disease progression, and potentially engage in health studies. At present, there are dozens of health social networks, for example, general communities like PatientsLikeMe which has over 125,000 patients in 1,000+ conditions as of January 2012, and condition-specific communities like SugarStats for diabetes.

Crowdsourced health research studies are investigative projects conducted by individuals or groups for the purpose of understanding and/or improving a health-related issue. Studies may be researcher-organized or participant-organized. So far, researcher-organized studies have been non-interventional studies organized by professional researchers using crowdsourced cohorts or crowdsourced data as the input or research focus, for example studies organized by PatientsLikeMe and 23andMe. Participant-

organized studies have been interventional studies designed and operated by citizen scientists, for example those conducted by PatientsLikeMe patients, DIYgenomics citizen scientists, and Quantified Self individual experimenters (Swan forthcoming 2012). The studies organized by DIYgenomics serve as a particular example of the emerging collective intelligence health model that is becoming a complement to traditional clinical trials and defining a new ecosystem of preventive medicine (Swan *Personalized Medicine* 2012).

DIYgenomics Health Research Studies

DIYgenomics is a non-profit research organization established in 2010 for the purpose of organizing group collaboration health research studies with the goal of realizing preventive medicine. Inspired by the democratization of health experimentation, studies seek to apply the wisdom of crowds to personal health management. The generalized hypothesis for studies is that one or more genetic polymorphisms (e.g.; mutations) may lead to out-of-bounds phenotypic measures (for example, deficient vitamin B levels) that may be ameliorated with personalized intervention. Part of realizing preventive medicine is establishing individualized baseline markers of wellness, for example a normal level of total cholesterol for one person might be 130 mg/dL whereas for another 180 mg/dL would be normal. It is important for individuals to have a sense of their own normal levels, and effective measurement tools for learning if there is deviation from these norms. At present, the focus of DIYgenomics studies is linking genetic mutation with phenotypic evidence and personalized intervention. Additional health data streams such as microbiome profiling and whole human genome sequencing will be integrated as they become feasibly available to consumers. Seven studies have been launched in the areas of vitamin deficiency, aging, mental performance, and epistemology, and are available for ongoing open enrollment. These studies are operated on the Genomera personal health collaboration and genome sharing platform, and links to the studies are available from the DIYgenomics.org homepage.

Vitamin Deficiency Studies

DIYgenomics has two vitamin deficiency studies underway, investigating the possibility that one or more genetic polymorphisms (e.g.; mutations) may lead to current blood marker levels that are already out-of-bounds per recommended levels, and that simple vitamin supplementation may be able to restore blood markers to recommended ranges. The flagship study “Vitamin B-9 and MTHFR variants” examines the potential role of MTHFR genetic polymorphisms in vitamin B deficiency

and homocysteine levels, and attempts to determine which supplement solutions are best from an individual perspective.

In the MTHFR gene (methylenetetrahydrofolate reductase), two small variations in DNA (SNPs rs1801133/C677T and rs1801131/A1298C) may prevent vitamin B9 (or folic acid) from being metabolized into its active form (folate). Without this form of vitamin B, homocysteine can accumulate which may lead to nutritional deficiencies and symptoms associated with cardiovascular disease, diabetes, vascular damage, nerve damage, and blood clots and pregnancy loss. Over 50% of the population may have some form of MTHFR mutation.

The Vitamin B study protocol is to find individuals with MTHFR polymorphisms by collecting genotype data from volunteers who have used genetic testing services like 23andMe, try simple interventions like vitamin B supplements available over-the-counter, and see if they work by asking participants to share results from blood tests performed at commercial labs. Drug companies will not do this type of study as there is little money to be made in over-the-counter treatments, but citizen science cohorts can, and the results could be extremely useful to individuals. The tools to do this kind of experiment, looking at genomic information, measuring treatment results, and analyzing the data, are now cheap or free.

The participant tasks are to review a list of Frequently Asked Questions (FAQs), submit data regarding MTHFR genetic variants, and participate in at least 3 different 2 week trials involving taking over-the-counter vitamins and measuring homocysteine levels with a blood draw each time (blood tests are about \$70 each). Participant exclusions (self-selected) are those with known vitamin B deficiencies, those that might not be able to follow the outlined vitamin protocol, or those who might have health problems related to high homocysteine levels. Two MTHFR gene variants are reviewed, rs1801131 and rs1801133. Blood test and genomic profile data results are available to study organizers and all participants.

The methodology and pilot study results were published in December 2010 (Swan *JOPM* 2010). The study continues in ongoing open enrollment and has 25 participants as of January 2012.

A second vitamin deficiency study, the “Vitamin D Study,” examines vitamin D serum levels and tests how different supplementation doses and vitamin D receptor gene polymorphisms may interrelate in attaining optimal vitamin D levels. Low levels of Vitamin D have been linked to cancer risk (Laino 2011), and since some individuals are unable to raise their blood levels despite supplementation, genetic factors may be involved which could be worthwhile to study (Jacobs 2010).

The participant tasks are to take a vitamin D3 supplement, obtain a 25-hydroxyvitamin D test, record

results, and review their genetic data for the main vitamin D receptor gene polymorphism, rs10735810. Participants self-experiment regarding optimal supplement dosage, using Vitamin D Council guidelines recommending 1,000 IU per 25 pounds of body weight as a starting dosage (Cannell 2011). A person who weighs 150 pounds, for instance, would start taking 6,000 IU per day. A blood test would test results after at least eight weeks, and then supplement dosage can be modified. Each 1,000 IU increase in vitamin D is estimated to produce an approximate 10 ng/ml increase in vitamin D blood level. Participant exclusions are those that have underlying kidney disease or a history or genetic risk of vitamin D problems. The study has 15 participants as of January 2012.

Aging Studies

Aging is an important systems biology and preventive medicine challenge where crowdsourced cohorts can make a contribution with detailed self-tracking, data reporting, and longitudinal analysis. DIYgenomics has three aging-related studies. The first is “Aging: telomere length and telomerase activation therapy” which investigates telomere length (shorter telomeres are thought to cause earlier-onset disease and aging (Willeit 2011)) the efficacy of a natural product based remedy, TA-65, and potential linkage with telomerase-related TERT and TERC gene polymorphisms.

With aging, telomeres shrink by about 100 base pairs per year. Research from 2009 Nobel Prize winner Elizabeth Blackburn and former Geron Chief Science Officer Cal Harley has been used to develop a potential remedy in the form of the TA-65 telomerase activation therapy (Harley 2011). More than one thousand individuals are currently taking TA-65. This study seeks to establish quantitative and qualitative measures of the efficacy of TA-65 or astragalus supplements, and whether personal genome profiles make a difference, specifically whether individuals with TERT and TERC polymorphisms have shorter telomeres to start with and therefore may be more likely to benefit from telomerase activation therapies.

The participant tasks are to have telomere length measured (from commercial vendors such as SpectraCell or RepeatDiagnostics), take an over-the-counter astragalus supplement or TA-65 (available from TA Sciences or Recharge Biomedical), journal product reactions and take a photo on a weekly basis, and re-measure telomere length at 6 months or 1 year. TERT and TERC polymorphisms are reviewed: rs10511887, rs12696304, rs16847897, rs2293607, and rs610160. The study has 20 participants as of January 2012 and a 250-member randomized cancer study is currently in design (breast and prostate cancer chemotherapy patients in

remission will be sought) to examine the potential benefits of TA-65 in rebuilding the immune system.

A second aging study, "Aging: risk reduction for common aging conditions through monitoring and intervention," is a longitudinal study of aging to establish personal baseline norms for 50 blood markers, their potential correspondence to 1,000 gene variants associated with aging, and to experiment with personalized intervention. The study provides an opportunity to apply the dozens of genome-wide association studies (GWAS) which relate to general and specific conditions of aging in a comprehensive preventive medicine approach. Genomic data is linked with corresponding measures of phenotypic biomarkers and interventions. The top twenty biological mechanisms of aging in GWAS include: neurodegenerative disease, osteoporosis, IGF-1/insulin signaling, lipoprotein metabolism, inflammation, immune system function, DNA damage repair, telomere length, transcription (ex: RNA editing), catabolism, mitochondrial health, cell cycle/stem cell health, protein function, and blood operations. The top twenty phenotypic biomarkers of aging include: blood pressure and hypertension, cholesterol (HDL, LDL, and triglycerides; LDL particle size), BMI, Framingham Risk Score, VO2 max, erythrocyte glycosylation, telomere length, lymphocyte growth capability, and granulocyte strength. The participant tasks are to complete an annual blood test (a comprehensive panel of approximately 50 markers available through DirectLabs (\$79) or another source), and if willing, share the data with the cohort, and self-experiment with relevant interventions. 1,000 genetic variants are reviewed that have been linked to a variety of conditions of aging (Swan 2011). The study has 15 participants as of January 2012.

A third aging study, "Retin-A: wonder cream for acne and wrinkles?" examines a potential connection between skin-related genetic variants and the widely-experienced negative side effects of using Retin-A skin care products. Retinoids (vitamin A compounds), particularly a tretinoin product Retin-A, are often used to treat acne and wrinkles. Remedies are available by prescription or over-the-counter. Retin-A peels or thins the outer layer of the epidermis, and thickens the layers below by stimulating collagen production. When first using a Retin-A product, some individuals experience a period of irritation with red, flaky, peeling skin. This study investigates whether underlying genetic profiles might make a difference and predict product response ahead of time. The participant task is to complete a 10 minute online survey of regarding experience with Retin-A products. Gene variants related to skin allergy and irritation are reviewed: rs1800629, rs3793784, rs6661961, rs6700998, rs7538876, rs7927894, and rs8011 (Wadyka 2006). The study has 8 participants as of January 2012.

Mental Performance Study

There are many health studies which can be performed without the cost and other drawbacks of blood tests, linking genomics with phenotype per online tests. DIYgenomics has such a study, "Processing Reality: Impact of Dopamine Modulation on Memory Filtering," examining how genetic variants may be related to dopamine processing in the brain and how this may impact the processing of memories.

The brain is able to adapt to the unexpected using an inbuilt network that makes predictions about the world and monitors the results of those predictions. An area at the front of the brain, called the orbitofrontal cortex, plays a central role and studies have shown that patients with damage to this area confuse memories with reality and continue to anticipate events that are no longer likely to happen (Elsevier 2011, Nahum 2011). This study seeks to determine if genetic variants in the dopamine processing pathway impact this process in normal, healthy volunteers.

The study is being conducted in collaboration with the Center of Cognitive Neurorehabilitation at the Geneva University Hospital in Switzerland. The participant tasks are to complete a background demographic survey (10 minutes), and a memory filtering task (30 minutes), which shows a series of images and asks the viewer whether the image has been shown previously. Genetic variants in dopamine-processing genes are reviewed: COMT (VAL158MET rs4680), DRD2 (rs1076560, rs2283265, rs7131056), and SLC6A3 (rs40184, rs27048, rs27072). Participant exclusions include those with psychological or neurologic disorders (e.g.; bipolar disorder, schizophrenia, epilepsy, Parkinson's disease, prior stroke, traumatic brain injury, or dementia). The study has 27 participants as of January 2012.

Epistemology Study

Self-experimentation studies conducted individually and in groups are emerging as an important complement to traditional clinical trials and other established mechanisms of health knowledge generation. To validate crowdsourced health research studies, it is important not only to conduct and report on these efforts in a scientifically-acceptable manner, but also to provide a philosophical context for understanding their role and impact. The epistemology project seeks to investigate, characterize, and provide a structure and context for knowledge derived through individual and group-based self-experimentation. Participants are asked to complete an online questionnaire (15-20 min) regarding self-experimentation activities in any area including health, time-management, stress-reduction, or nutrition, exercise, sleep optimization, etc.

Potential Future Studies

DIYgenomics has several other potential future studies, and has been designing studies at two levels, one for ongoing on-demand citizen science participation, and one for professional studies that have at least 100 participants in a randomized, controlled, double blind format (Swan Personalized Medicine 2012). One such study is being designed to investigate cholesterol, in possible collaboration with the California Walnut Commission, examining genetic polymorphisms and remedies including statins, niacin, green tea, and walnuts in lowering LDL and raising HDL, and in increasing LDL particle size. Another study is in design to investigate calcinosis, which is an aging disease of the arteries like atherosclerosis, in this case where calcium builds up unhealthily. In collaboration with a Silicon Valley-based biotechnology firm, novel biomarkers for calcinosis will be sought, their potential link to vitamin K metabolism polymorphisms investigated, and vitamin K2 tested as a supplement intervention. A sleep study is contemplated in potential collaboration with Zeo to investigate genetic polymorphisms and sleep performance. An extension of the Blueberry Study (www.BlueberryStudy.com) is under discussion to examine genetic linkage as a follow-on to the demonstration of blueberry consumption leading to enhanced mental performance. Another potential study is testing the efficacy of an anti-aging supplement (Juvenon, based on acetyl-L-carnitine and alpha lipoic acid) in a genetically-stratified cohort. Finally, there is a possible collaboration to investigate loving style preference and genomics in collaboration with the University of Pavia, Italy to extend a 'genetic loading on human loving styles' study (Emanuele 2007) in a citizen science cohort.

Conclusion

Summary

The current era of internet-facilitated bigger data, better tools, and collective intelligence community computing is accelerating advances in many areas ranging from artificial intelligence to knowledge generation to public health. In the health sector, data volumes are growing with genomic, phenotypic, microbiomic, metabolomic, self-tracking, and other data streams. Simultaneously, tools are proliferating to allow individuals and groups to make sense of these data in a participatory manner through personal health tracking devices, mobile health applications, and personal electronic medical records. Health community computing models are emerging to support individual activity and mass collaboration through health social networks and crowdsourced health research studies. Large groups, both patient registries and communities of healthy individuals,

are searchable publicly in real-time based on deep attributes. One operator of interventional crowdsourced health research studies, DIYgenomics, has several crowdsourced health research studies in open enrollment as of January 2012 in the areas of vitamin deficiency, aging, mental performance, and epistemology.

Limitations of Participatory Health

There are important challenges to the conduct of participatory health efforts. Perhaps less than 10% of individuals are interested in health, perceiving it as a deterministic area where the only incoming information will be negative, and that health is a physician's responsibility, not one's own. It could take a while for widespread responsibility-taking for health to arise as few individuals may have the time, interest, or incentive to self-manage their health. Crowdsourced cohorts may be too slow to help with the more fundamental public health system problems of budget shortfalls, rising health care costs, expected physician shortages, and the exorbitant cost of bringing new drugs to market (currently estimated at \$1.3 billion (Gavura 2011)). Health social network participation is growing but slowly. Only some few 100,000 individuals have subscribed to personal genome services since they launched in 2007, even though costs have dropped to \$99 with 23andMe. Consumers are still wondering about the meaning and use of the non-deterministic genetic information, and questions about the validity and utility of services persist as risk interpretations vary across services (e.g., the risk of heart attack is high according to 23andMe, but low according to deCODEme) (Swan *Gen Med* 2010). Even if the cost of genotyping has fallen, blood-testing and other monitoring and experimental measures remain prohibitively expensive.

Future Implications

However, in the end, the bigger data, better tools, and intelligent community computing models of participatory health might be the right solution at the right time. Participatory health efforts portend important benefits in both size and speed. Studies can be carried out in cohorts of thousands instead of hundreds (Do 2011, Dufau 2011), and it could be possible to apply findings from newly-published studies immediately in crowdsourced cohorts.

Participatory health efforts and health social networks are providing direct value to participants, and have also become useful in a broader social context for clinical trial recruitment. Pharmaceutical companies and researchers can recruit crowdsourced cohorts much more quickly and expeditiously than traditional cohorts, and at lower cost and with lower study drop-out rates. Self-organized studies by health social networks and personal health collaboration communities could help to surface interesting new

findings, particularly related to preventive medicine. Not everyone needs to be engaged, with the 'Wikipedia effect,' 1% of individuals actively participating could create a public asset for all. A million social health collaborators could benefit hundreds of millions of others.

In the not too far future, it may be possible to see the next levels of intelligent health community computing: personal health dashboards integrating multiple health data streams, a continuous personal health information climate and body area network that makes unobtrusive behavioral suggestions, personal virtual coaches in the vein of Siri 2.0, and an efficient health frontier of dynamic personalized health recommendations and action-taking.

Conflicts of Interest

The author is the founder of DIYgenomics.

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