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Financing (and Organizing) the Transition to Precision Medicine

by

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Current interest rates are close to 0 %. Thus a simple key to faster G-20 economic recovery (and to a more effective monetary policy) is to organize and frame attractive options for governments, corporations, and individuals to borrow from the trillions of dollars of available funds and create additional demand. (Merely waiting for corporations to borrow for added plant and equipment – a traditional pathway – has not been working as it did in the past.) This paper outlines a (draft) option, with ideas from a new, multi-disciplinary, rapid learning system under development for economics. It recommends a creative package, building on an initiative by the Kaiser Health Plan, that requires leadership and further work, but that probably can be structured to induce $1.5 trillion (or much more) in stimulus.

Also: 1.) The plan is politically attractive. It delivers benefits to the lives of many people. 2.) The plan is economically attractive. The transition to the 21st century Precision Medicine healthcare delivery system is a worthwhile individual and international investment to get underway. 3.) Although full implementation might require solving the political impasse in Washington and other foreign capitals, the new recovery plan can get underway quickly, with creative leadership and partnerships. 4.) The plan can leverage other investments and add confidence and excitement. 5.) It recognizes a uniquely-available pathway and opportunity to achieve two urgent global public goods: a.) Building rapid economic recoveries and sustainable economic health across the world's economies; and b.) Securing an investment to activate the world's rapid transition to the new, 21st century Precision Health delivery system.

→ The plan also has the unique characteristic that: 6.) If it is implemented as I outline it, the result is likely to be a massive train wreck and waste at least $1 trillion. A bold stimulus project on this scale is an incentive for governments, healthcare providers, and especially the private sector to develop a coherent Grand Strategy. There will be even better results if stakeholders have a thoughtful roadmap to deliver the best Precision Medicine healthcare to everyone, as quickly as this can be discovered.

The Kaiser Health Example - $1,500/Adult Borrowing

The attached announcement from the Kaiser Health Plan reports its medical, civic (and business) decision to request its 10 million adult members to participate in a new investment in their 21st century, genetics-

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based, Precision Medicine healthcare. If they do, Kaiser provides privacy guarantees and it has organized financing to pay the full cost for each member. The constellations are moving into alignment to activate a transition that secures a 21st century **Precision Health Investment** for each adult, in the US and worldwide.

> [Kaiser's initiative reflects a cost of genetic profiling that has dropped a million-fold toward the $1,000 range. Kaiser already has invested in electronic health records in standard formats (extending, in some cases, for fifteen years or more) for its 10 million members. Kaiser has gained leadership experience with making medical discoveries and improving care using these new capabilities: It is*, de facto*, adding an invitation to 9 million members after developing its California-based Research Program on Genes, the Environment and Health, a pioneering R&D biobank expanding from 500,000 to 1 million members, including statistical over-sampling to take full scientific advantage of California's social and ethnic diversity.[2]]

A reasonable estimate (that will have to be refined) is that it might cost $1,500/adult for genetic testing and administration for everybody to have equivalent access to 21st century Precision Medicine. The stimulus effects can be available as soon as individuals (perhaps, typically, intermediaries acting on their behalf) can (by mechanisms to be created) access a near-zero % Best Terms borrowing system to make this one-time infrastructure loan for each adult. If we want $1.5 trillion in added lending and expenditure, we will need to structure incentives for the first 1 billion adults. And this might be done quickly, especially since the national health systems in the other G-8 + EU countries can make more centralized decisions than in the US.[3] [4] → And – an important historical reason to move quickly – if the decision is made now, the funds do not need to be appropriated! More than enough money already is available. [5]

Expected benefits are positive, but they are not yet guaranteed for each individual. There are good reasons for many people to be in a Kaiser-like Precision Health Medical system immediately. For example: NIH (attached) has announced the exciting discovery that there actually are at least three types of Type II diabetes, possibly with different genetic profiles pointing toward improvements in prevention and better treatment and already activating rapid research projects to discover new and improved drugs for each type. ***The 10 million Kaiser members are First-in-Line to receive the benefits of new discoveries because their genetic profiles already are in Kaiser's Fast Track learning system***. Nobody else with any chronic health condition, or

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[2] The URL is rpgeh.kaiser.org

[3] Roughly 1.4 billion people at the beginning of this decade: http://www.g8.utoronto.ca/evaluations/factsheet/factsheet_demography.html; the comparable estimate for the G-20 (including China and India) was about 4.7 billion people. The government of China might have a very high priority for precision medicine borrowing, as (with 1.4 billion people) it can have extraordinary savings from even small scientific discoveries.

[4] For governments to create credit at near-zero% interest, without requiring co-payment, is close to simply encouraging governments to print money – which, historically, has been risky. However, these Precision Health Investment loans probably can be structured with little risk of default

[5] I.e., the money is available as credit. The Obama Administration, and each national government, will need to work with central banks and the financial system to structure access to near-zero % interest and repayment packages (perhaps beginning in several years?) and assure credit-worthy individuals or intermediaries. If desired, the Precision Health Investments could be structured primarily as a voluntary individual option and a personal obligation, with a repayment schedule of $100/year added to income tax bills, beginning in three years, until the loan is amortized.

at risk, can benefit quickly from equivalent discoveries until their DNA profile is linked to a Fast Track, rapid learning system. Everybody else in the world, who does not make such a Precision Health Investment under this plan (or have someone arrange for financing on their behalf), must wait – possibly for too many years – while established institutions, with slow economic recoveries, go through the delayed pushing-and-hauling process, and often the political process, of informing themselves, debating ideology, setting agendas, and adjudicating competing claims in an appropriations process. It is wiser to solve the problem now.

Additional Comments

- The new Precision Health Investment System needs to be structured carefully. Participation *must* be financed through new borrowing. (If the money redirects current expenditures, it does not have a new stimulus effect.) It should not be tax deductible. If insurance companies or other healthcare providers offer incentives or co-payments, these should be financed by new borrowing.

- To design the stimulus package, these behavioral economics/reframing ideas improve monetary policy by working around the need to improve economic confidence or restore trust in governments and the financial sector. The project requires only confidence in the progress of biomedical science and clear and vivid examples of how individuals can expect personal, future health benefits for themselves and others who they care about.

- To encourage enrollment, the stimulus investment package might be time-limited and available only while interest rates are near zero percent.

- It would be useful to develop a marketing strategy with the private sector that facilitates rapid signups and borrowing. Many healthcare providers will see competitive advantages to join Kaiser in offering the best quality medical care and First-in-Line notifications of relevant new discoveries for existing chronic or at-risk conditions. Universities and other progressive employers might step forward to create these options quickly for members of their own health plans.

- There should be early consultation with the private sector to assure that the FDA-certified Lab and other investments will be available as national and global DNA testing scales upward. Secure storage, DNA testing, interpretation, and notification systems will require planning on a global scale, as will the training of health professionals to implement the new capabilities for the best interest of their patients.

- Priority signups might be organized for all patients diagnosed with breast and other cancer, or other serious diseases for which precision medicine discoveries, linked to a genetic profile, are available or can be expected.[6] All enrollees might receive initial Kaiser-level confidential reports, by means that they specify, of relevant discoveries that already have been made.

[6] When DNA testing becomes established as essential to the diagnosis or treatment of specific diseases, it typically will be covered by existing health plans. There are strategic calculations that can be made, by

- The private sector might facilitate access to near zero % financing and participation by national health systems in other countries and individual foreigners. Currently, for example, US companies are among the leaders: There will be networks of FDA-approved labs and Big Data providers (e.g., Amazon Web Services, IBM and a network of international partners) who can get a share of global demand and markets from these investments. Also, citizens of other countries – including foreign employees of US-based multinationals – should have participation rights even if their own national health systems and governments are not yet ready to write direct contracts.

- The strategy for full global coverage – all UDCs and G-20 populations – deserves attention. A rollout might begin with loans and repayment guarantees by multinational corporations who can provide upgraded clinics and services to their employees and families in UDCs. [7]

- For individuals, this is a one-time, lifetime investment in better health.[8] It is the kind of infrastructure (and individual) investment that really does justify borrowing, especially at near zero % interest and with easy repayment terms.

- There are elements of risk, because scientists cannot prove that there will be $1,500 of lifetime benefits to each individual. For now, the Precision Health Investment system should be viewed as transitional and voluntary – although eventually it might become standard.[9]

- Kaiser has introduced a degree of political pressure on the federal government. Its 10 million members include many federal employees in the Washington, DC area. These federal employees – but not federal employees elsewhere, or the Armed Forces or Veterans – now have privileged access to 21st

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each individual, about when to participate and whether to delay (although there may not be enough information to decide with confidence). Participating now for a one-time $1,500 investment also is a form of buying insurance, inviting a calculation about the rate of medical discoveries and the useful discoveries that will be available to Fast Track participants before this later point of routine DNA analysis in the daily practice of medicine. For intermediaries (like Kaiser) this also is a form of civic, professional, and business decision by organizations who believe that they can better serve all of their patients or members, or gain market share, or develop better treatments, save costs or increase profitability, or acquire new knowledge or make new discoveries that have marketable value. For governments, borrowing to assure the full coverage of Veterans and their families might be a civic decision.

[7] Hopefully, the full DNA analyses in the early research phase will yield specific sub-analysis requirements for any specific diagnosis – e.g., DNA sub-analysis to distinguish among only seven causal pathways producing asthma and seven Best Treatment options. These treatment sub-analyses might eventually be provided at the cost of a simple blood test. For UDCs, a key ethical question is whether the DNA analysis is the highest current public health priority.

[8] There may be further data investments, including biome analysis and neuroscience-informed analysis of brains, but the R&D costs to pioneer these methods still should be the current responsibility of NIH.

[9] There might be creative, but unusual, ways to structure assured repayment. For example, a one-time $1,500 Precision Health Investment individual loan could be repaid by a (healthier, longer-lived) individual who agrees, now, to slide his/her future social security eligibility by three weeks.

century Precision Medicine although others pay the same premium. The same *de facto* favoritism and two-tier health system also is created between federal employees in the Washington, DC area and all other Americans. This violates a fundamental American norm and many patient advocacy and other groups might be political allies to structure borrowing packages.

- Politically, in America, it may be possible to activate a Precision Health Investment national option (N=320 million) within existing legal authority, although full implementation or specific, targeted, lending mechanisms also might require Congressional approval. It can be a voluntary option for people covered by the Affordable Care Act, or Medicare or Medicaid, for all public employees, for all members of the Armed Services and for Veterans.[10] It can even be structured as a nearly-automatic Precision Health Investment loan to all standard health plans (with an opt-out that requires individual initiative) with borrowing and repayment options handled behind the scenes. (Everything, including the borrowing, can be almost routine: participation actually requires only a standard blood sample.) [11]

- It might not be necessary to enroll 1 billion adults before there is a major economic stimulus effect. A bold Precision Health Investment option sends messages, creates excitement, and can leverage the early investment. The new era of genetics-based Precision Medicine offers a cornucopia of new business opportunities, including new Big Data resources for all countries who want their companies to compete in global pharmaceutical development.

- This full global Grand Strategy can be phased-in, with part of the infrastructure investment in Precision Health held in reserve as a fast-trigger option if there is a threat of recession.

Enclosures:

- Kaiser Permanent Research Bank, "Enrollment Request to 10 Million Members" (http://research-bank.kaiserpermanente.org/). Downloaded 4/15/2016
- Francis Collins, "Big Study Reveals Possible Subtypes of Type II Diabetes," blog posted on 11/10/2015.
- Foundation for NIH, "The FNIH Announces $4 M Grant Award to Support Building of First International Arm of AMP Type 2 Diabetes Knowledge Portal" (http://www.fnih.org/news/announcements/fnih-announces-4-million-grant-award), 12/9/2015.

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[10] The Veterans Administration already has underway a One Million Veterans, genetics-based, initiative. The program is not financed through new borrowing, which should be the VA package for the new one-time system upgrade for all Veterans. See: http://www.research.va.gov/mvp/

[11] The Kaiser project involves added research questionnaires to study social relationships and behaviors and the physical environment (e.g., access to safe parks and recreation, pollution levels and workplace exposures to various chemicals). Structuring a near-zero % loan option for individuals might be organized with an equivalent package to participate in research that might provide useful information.

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DNA Could Help the KP Research Bank Discover New Ways to Prevent Disease

What causes diseases like cancer, asthma, and Alzheimer's? What are the impacts of lifestyle and history on a person's risk of disease? Scientists working with the Kaiser Permanente (KP) Research Bank are using DNA and other information to find new ways to help people live healthier lives.

What Could this Research Mean?

It could lead to breakthroughs in ways to prevent or treat diseases. In the future, patients may receive health care based on their individual DNA, environmental, and lifestyle information.

DNA information could be used to:

- Test earlier for diseases;
- Prescribe the most effective medicines;
- Better understand the warning signs of disease;
- Predict the risk of getting a disease;
- Understand new ways to prevent disease.

The KP Research Bank has gathered DNA and information from thousands of people and used it in research about many diseases. Researchers need to collect DNA from people of all

ages, genders, ethnicities, and backgrounds so discoveries can benefit even more people.

The KP Research Bank invites all adult KP members to participate.

The KP Research Bank is asking all adult members of Kaiser Permanente to participate. Participation is voluntary and there's no cost to you. New participants can click join, and returning participants can log in below.

JOIN LOG IN

Follow These 3 Steps to Begin

1. **Review and sign a consent form.**

   This form explains your rights as a participant. Click here to review it. If you agree, sign the consent form to give samples, and past and future health information to the KP Research Bank.
2. **Fill out a health survey.**

   Provide information about your health, lifestyle, and history. When you complete the consent form, this survey will automatically pop up. You can take the survey at any time.
3. **Provide a blood sample.**

   Give a small sample of blood, about 2 tablespoons, at any Kaiser Permanente clinic or lab. This is collected at no cost to you. You can provide your sample before or after you take the survey.

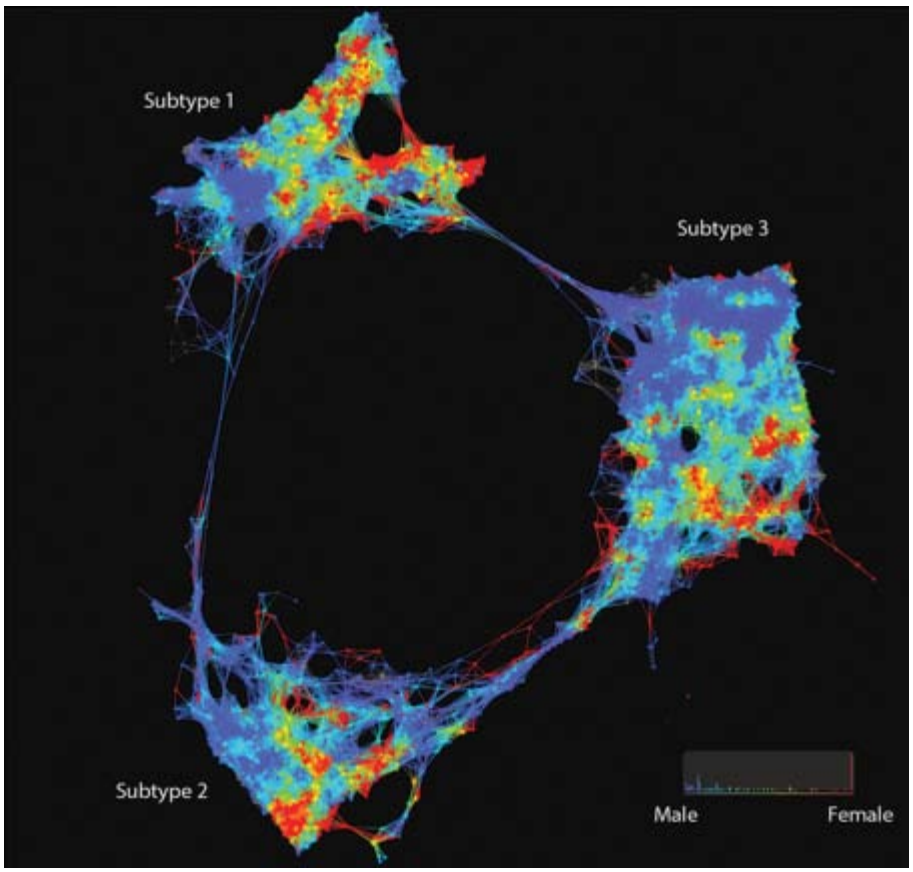
Questions? Please call the KP Research Bank at 844-268-2947, Monday through Friday 8am-6pm

Pacific Time (11am – 9pm Eastern, 9am – 7pm Mountain, 5am – 3pm Hawaii), or email ResearchBank@kp.org.

EMAIL THE KP RESEARCH BANK

Big Data Study Reveals Possible Subtypes of Type 2 Diabetes

Posted on November 10, 2015 by Dr. Francis Collins



Caption: *Computational model showing study participants with type 2 diabetes grouped into three subtypes, based on similarities in data contained in their electronic health records. Such information included age, gender (red/orange/yellow indicates females; blue/green, males), health history, and a range of routine laboratory and medical tests.*
Credit: *Dudley Lab, Icahn School of Medicine at Mount Sinai, New York*

In recent years, there's been a lot of talk about how "Big Data" stands to revolutionize biomedical research. Indeed, we've already gained many new insights into health and disease thanks to the power of new technologies to generate astonishing amounts of molecular data—DNA sequences, epigenetic marks, and metabolic signatures, to name a few. But what's often overlooked is the value of combining all that with a more mundane type of Big Data: the vast trove of clinical information contained in electronic health records (EHRs).

In a recent study in *Science Translational Medicine* [1], NIH-funded researchers demonstrated the tremendous potential of using EHRs, combined with genome-wide analysis, to learn more about a common, chronic disease—type 2 diabetes. Sifting through the EHR and genomic data of more than 11,000 volunteers, the researchers uncovered what appear to be three distinct subtypes of type 2 diabetes. Not only does this work have implications for efforts to reduce this leading cause of death and disability, it provides a sneak peek at the kind of discoveries that will be made possible by the new Precision Medicine Initiative's national research cohort, which will enroll 1 million or more volunteers who agree to share their EHRs and genomic information.

In the latest study, a research team, led by Li Li and Joel Dudley of the Icahn School of Medicine at Mount Sinai, New York, started with EHR data from a racially and socioeconomically diverse cohort of 11,210 hospital outpatients. Of these volunteers, 2,551 had been diagnosed with type 2 diabetes, which is the most common form of diabetes.

Without focusing on any particular disease or condition, the researchers first sought to identify similarities among all participants, based on their lab results, blood pressure readings, height, weight, and other routine clinical information in their EHRs. The approach was similar to building a social network with connections forged, not on friendships, but medical information. When the resulting network was color-coded to reveal participants with type 2 diabetes, an interesting pattern emerged. Instead of being located in one, large clump on this "map," the points indicating people with type 2 diabetes were actually grouped into several smaller, distinct clusters, suggesting the disease may have subtypes.

To take a closer look, the researchers rebuilt the network to include only participants with type 2 diabetes. They then reanalyzed the EHRs based on 73 clinical characteristics, including gender, glucose levels, and white blood cell counts. That work confirmed that there were three distinct subtypes of type 2 diabetes among study participants.

Type 2 diabetes is associated with potentially serious complications, including nerve damage, vision problems, kidney disease, and an increased risk for cardiovascular disease. The study found differences in the distribution of such complications among the three subtypes of type 2 diabetes. People with subtype 1 were more likely to be diagnosed with microvascular complications, including blindness/vision defects. This group of participants was also the youngest and most likely to be obese. People with subtype 2 showed the greatest risk for tuberculosis and cancer. As for subtype 3, such people were more likely than others to be HIV positive, have high blood pressure, and develop arterial blood clots. Both subtypes 2 and 3 displayed a greater risk for heart disease than subtype 1.

Next, the researchers performed a genomic analysis, identifying hundreds of genetic variants that were enriched non-randomly in each of the three groups. Interestingly, some of the genetic variants linked to each subgroup were associated with genetic pathways that appeared relevant to the distinguishing clinical features of those subgroups.

These findings suggest that some of the clinical differences observed between the different type 2 diabetes subtypes are rooted in lifestyle or environment, and others may be influenced by inherited factors. Still, more research needs to be done to replicate and expand upon these findings. The hope is that by gaining a more nuanced understanding of type 2 diabetes, we may be able to identify more precise ways of helping to detect, manage, and, ultimately, prevent this serious, chronic disease that currently affects about 1 out of every 11 Americans [2].

References:

[1] Identification of type 2 diabetes subgroups through topological analysis of patient similarity. Li L, Cheng WY, Glicksberg BS, Gottesman O, Tamler R, Chen R, Bottinger EP, Dudley JT. Sci Transl Med. 2015 Oct 28;7(311):311ra174.

[2] Diabetes Latest Fact Sheet. 2014 June 17. (Centers for Disease Control and Prevention)

[http://fnih.org/news/announcements/fnih-announces-4-million-grant-award#.VmhdmottRfY]

The FNIH Announces $4M Grant Award to Support Building of First International Arm of AMP Type 2 Diabetes Knowledge Portal

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The Foundation for the National Institutes of Health (FNIH) has awarded a 4-year grant award in the amount of $4 million to the European Molecular Biology Laboratory — European Bioinformatics Institute (EMBL-EBI), the University of Oxford, and the Broad Institute of the Massachusetts Institute of Technology and Harvard University to support the buildout of a European arm of the Type 2 Diabetes (T2D) Knowledge Portal. The award is part of the Accelerating Medicines Partnership Type 2 Diabetes (AMP T2D) initiative. This is the first in what the project hopes to be a buildout of a broader network of interconnected, international portal sites.

The AMP T2D Knowledge Portal is a sophisticated research tool that allows the public to search and analyze genetic and clinical information on individuals with type 2 diabetes and serious complications of the disease, while maintaining strict confidentiality of individual level data. The Knowledge Portal is intended to generate new understanding of the disease by revealing relationships between human genome-wide sequence variation in potential targets and either risk for or protection from diabetes and its complications. The portal is planned to contain data integrated from existing genetic studies from close to 100,000 individuals by early 2016.

In June 2015, the FNIH issued a Request for Proposals (RFP), which solicited applications to build and maintain secure, distributed database hubs for the project's Knowledge Portal outside of the United States. Establishing one or more new hubs outside of the United States allows researchers to store their data at any of the portal's hubs and enables analyses across global datasets while maintaining compliance with regional data privacy regulations. This FNIH award funds the buildout of a European hub, based in the United Kingdom, over the 4 year period. AMP T2D hopes to expand this pilot hub to various other international federated sites that could allow participation from groups on any continent.

The portal's U.S. hub resides at the Broad Institute in Cambridge, MA, and is funded by a grants from both the National Institute on Digestive and Kidney Disease (NIDDK)/National Institutes of Health (NIH) and the FNIH.

Funding Partners:

American Diabetes Association, Janssen Research and Development LLC, JDRF International, Eli Lilly and Company, Merck Sharp & Dohme Corp., NIDDK/NIH, Pfizer Inc., and Sanofi US Services. Read more about the AMP T2D initiative

About the Accelerating Medicines Partnership:

A public private partnership that brings together NIH, biopharmaceutical companies, and not-for-profit organizations, AMP's mission is to transform the current model for developing new diagnostics and treatments by jointly identifying and validating promising biological targets of disease. AMP's goal is to generate diverse, high quality, pre-competitive, disease-specific clinical data to be made publicly available for the purpose of accelerating drug development. The FNIH raises and distributes private sector funds for AMP, provides central project management to AMP initiatives, and convenes the governing committees that oversee the partnership on behalf of all the stakeholders.