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At the crossroads of oral health inequities and precision public health

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Abstract

Objectives: This paper reviews the precision public health literature pertaining to oral health, identifies possible threats that could inadvertently increase health inequities, and proposes potential opportunities that precision public health could utilize to reduce oral health inequities.

Methods: The health sciences literature was reviewed and supplemented with new data to identify important issues relating to precision medicine, precision oral health, precision public health, and health equity.

Results: Examples from general health and oral health were provided to illustrate salient concepts.

Conclusions: Future precision public health should utilize multifactorial, multilevel conceptual frameworks and conceptual causal models with upstream social determinants and downstream health effects, as well as a proportionate universalism perspective; and proper analytic methods, including sufficient sample sizes, appropriate statistical competitors, health disparity indices, causal modeling, and internal and external validation.

Keywords

precision medicine/ethics; precision medicine/methods; dental research; health disparities; health equity; population health

Introduction: from precision medicine to precision health to precision public health

This article reviews the precision public health literature pertaining to oral health, identifies possible threats that could inadvertently increase health inequities, and proposes potential opportunities that precision public health could utilize to reduce oral health inequities. Precision public health is a recently evolving field that proposes synergistically integrating

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Declaration of Conflicts of Interest

Dr Gansky's brother is a 3M employee, in a different division than the one that provided in-kind product. This paper includes discussion of "off-label" use of the following: The US FDA only has approved fluoride varnish as a device to be used for tooth sensitivity in a cavity lining preparation; caries prevention is an off-label use.

public health data with other health information sources to improve health status and reduce costs. Precision public health expands precision medicine's recent call for a new taxonomy of disease and a knowledge network of integrated biomedical research (1), from an emphasis on diagnosis and curative medical treatment to also include prevention and health promotion. Precision medicine advocates have called for developing a vast knowledge network with data at many levels, including the exposome, signs and symptoms, genome, epigenome, microbiome, and "other types of patient data," which can be linked to patient outcomes (Figures 1 and 2) (1). Oral health research policy makers have identified the need for similar integrated networks of multilevel data to advance personalized oral health care (2). These levels of data are then linked to permit mapping to knit the network together.

However, when transitioning from precision medicine to precision public health, the term exposome is overly general, additional terms for environmental and social factors have recently been proposed including hydrome (water), nutriome (consumed food and beverages), legome (education status), econome (financial circumstances), and ethnome (culture, race, and ethnicity) (3); importantly, among all the proposed "-omes", the new nomenclature includes one rarely explicitly included: the "H"-ome or home for the living environment including neighborhood factors. Home is a great nexus of impact and perhaps the single most important health determinant (4), so the home and family-level measures should not be neglected in such multilevel models.

To address the potential for an integrated multilevel information network to study health, President Obama in 2015 launched the Precision Medicine Initiative, now rebranded as "All of Us." The goal is to enroll a cohort of at least one million people, to examine interconnections among environment, lifestyle, and biology, to accelerate research and discover ways to improve prevention and healthcare through precision health. Many universities, private entities, and community organizations serve as partners and recruitment sites, including, for example, the San Ysidro Health Center (SYHC) in San Ysidro, CA, which is a federally-qualified health center at the US-Mexico border.

Although precision health offers the possibility of important breakthroughs, at the Precision Public Health Summit—The First 1,000 Days at UCSF, Bill and Melinda Gates Foundation Chief Executive Officer Dr. Susan Desmond-Hellmann discussed possible threats resulting from precision health (5), which have been echoed by others (6), including the real possibility of actually exacerbating health disparities. Some groups (e.g. those with higher SES status, higher health literacy, more leisure time to participate) may benefit more than others, and those gaining from precision health may be the same people who already have advantages from their insurance coverage, access to technologies, or their societal stratum. Additional serious concerns include lack of cohort diversity and representativeness, which may result from insufficient participant and community engagement. Privacy and security issues about the data, as well as post-collection data usage policies remain unanswered (6). Additional questions have been previously raised about whether genomic medicine specifically increases disparities (7). Stratifying on race/ethnicity for genomic medicine has the potential to widen disparities due to patients' unequal access to both screening and treatment. Reversing this process is possible, but will take considerable effort from the global health community.

Health technologies can increase health disparities

Thus, it may be instructive to review some cautionary tales of situations where health technologies have actually increased health disparities, in various phases, in both medical and dental health (Table 1). In diagnosis, for example, colonoscopy and Papanicolaou tests have had differential uptake, while in dentistry oral cancer diagnosis has been differential, resulting in some groups having been diagnosed at later stages. In terms of prevention, hypertension medications in medicine and sealants in dentistry have not been provided uniformly. Carey and colleagues (8) saw curious findings in hypertension-reducing drugs. Even though new hypertension drugs had better efficacy than older, generic drugs, wide variations in public clinic patients existed. Patients taking generics had better hypertension control than those on brand new drugs that were supposed to work better. This was an example of Simpson's paradox (9), since they found in real-life patients were not adhering properly to medications but were stopping when they finished their free samples, skipping doses, or splitting pills, because they could not afford the new drugs, but they could afford the generic. Thus sometimes unintended consequences with large health ramifications occur. In dentistry, efficacious technologies have not been provided universally to all or even targeted to those who need it the most. One important example of that phenomenon is dental sealants. There are numerous examples in both medicine and dentistry of new efficacious technologies not being provided equitably to specific population subsets. In terms of treatment, in medicine an example is coronary artery bypass graft, while in dentistry an example is tooth implants or root canals versus extractions; groups of people make different treatment choices based on their insurance coverage and out of pocket costs. This potential problem of differential dissemination of new health technologies exists in many historical examples.

While there is much excitement about the new technology of precision health, because of its potential to advance health, there are also some important concerns. Some have called precision health and personalized medicine a Faustian Bargain (10). (Or, perhaps more appropriately for this colloquium, a Johnsonian bargain, in the context of having convened at the historic Gunter Hotel in San Antonio where in Room 414 in 1936 the blues musician Robert Johnson recorded the song "Cross Road Blues" which refers to the place where he allegedly sold his soul to the devil in exchange for technical prowess.) Pauwels and Dratwa (10) warn that research not only has used genetic material of donors without sharing revenues with them, but many of those donors would not be able to afford the newly developed genomic treatments or personalized medicines. Postman summarized that "… technological change is always a Faustian bargain: Technology giveth and technology taketh away, and not always in equal measure. A new technology sometimes creates more than it destroys. Sometimes, it destroys more than it creates. But it is never one-sided" (11). Not only do the net societal benefits need to be calculated, but also appropriate weighting needs to be placed on any increased gaps in health outcomes between advantaged and disadvantaged groups.

So standing now at the crossroads of precision health, public health researchers and leaders have the opportunity to choose the directions and craft the path of the precision public health field. As Desmond-Hellmann said at the Precision Population Health Summit, potential threats might unintentionally increase health disparities, but those threats can be transformed into opportunities, including reducing health disparities using these technologies.

All of Us is trying to address the concerns of representativeness and generalizability by going to diverse communities around the country in mobile units. They are going where the people are, trying to engage them to recruit them, as members of diverse communities, to be part of this effort and not be left out. For example, in November and December 2017, they visited throughout the South-west, while in January 2018, they were in California. Some of these centers serve very specific groups, to attempt to represent people who need prevention the most.

Omics methods may increase disparities

Even with proper cohort representativeness, there are other ways that precision health might increase disparities. Another important potential source of precision health increasing disparities involves the precision health research methodologies used. Alyass and colleagues (12) discussed concerns that the United States already has a 2-tiered health-care system; they warn that adding -omics will not only create a 2-tiered P4 (predictive, preventive, personalized, and participatory) health-care system in the United States, but also will greatly exacerbate global health inequities among higher and lower income countries.

Some important methodological issues in precision public health

From a methodological perspective, Alyass *et al.* (12) also summarize the bias-variance tradeoff in developing personalized medicine models. Precision public health modeling needs to be performed correctly. The bias-variance tradeoff leads to the so-called curse of dimensionality. Precision health and precision public health involve integrating many big data sources. The bias-variance tradeoff notes that as the dimensionality (the number of variables) increases, there are both pros and cons to emphasizing either low bias or low variance trade-offs. On one hand, models would have high reproducibility, producing robust models, but have fewer novel findings; for example, integrating multilevel data sources may result in only using poverty to identify people at-risk. Alternatively, too many variables in final models might result in decreased estimate precision, unstable models, and poor calibration, so when adding more information, models perform poorly. The bias-variance tradeoff must be balanced just right. There are sources of variability from both noise and true biological heterogeneity. Noise would come from sources like sampling variation and measurement error. While true heterogeneity would result from biological variability in people's genes and other sources.

A vital key to balancing bias and variance in precision public health models is validation, both internal and external, with all the groups of people to whom the model would be applied in real life (12,13). A very simple example demonstrates the danger of overfitting in only two dimensions; that is, one covariate of interest ($k = 1$) and one outcome measure (Figure 3). A simple linear regression model (dotted line) and the highest possible degree polynomial (N-1 = 6) model (dashed line) have been fitted to illustrate the two extremes of low bias—high variance and high bias—low variance, respectively. Any new data added to the 6-degree polynomial will very probably differ greatly from the fitted dashed line, showing poor calibration (low reproducibility and validation). In practice with high-dimensional data (a large number of covariates), the bias-variance tradeoff issue increases exponentially.

The discipline of knowledge discovery and data mining (KDD) at the interface of artificial intelligence, machine learning, computer science, engineering, and statistics has been defined as a "semi-automatic discovery of patterns, associations, anomalies, and statistically significant structures in data." (14) In 2001, *MIT Tech Review* called KDD one of the top ten breakthrough technologies (15) because these new algorithms can help guide finding patterns in the oncoming and growing tidal wave of information. KDD was in the first wave of tools for the Big Data to Knowledge (BD2K) initiatives leading up to precision medicine and precision public health. KDD tools (e.g. see the Glossary in Gansky, 2003 (13)) include traditional statistical methods and modern statistical and computational techniques, such as technologies like random forests, support vector machines, and newer algorithms like machine learning and deep learning. They can be supervised learning where the outcome measures are included in the modeling or unsupervised learning, which clusters risks or potential risk factors akin to factor analytic methods (but without the outcome measures). KDD is a multistep iterative approach: collect and store data; sample, merge, and warehouse data; preprocess data, which is an important step involving cleaning, imputation, and standardization (transformation and registration); analyze using visualization (supervised or unsupervised); validate both internally and externally; and act to intervene and set policy (see Figure 1 in Gansky 2003 (13)). However, KDD steps are not a strictly linear process, as learning might require repeating iterations to further clean data, standardize different measures, and so forth. For example, different clinics may measure or record information differently so harmonizing variables may be needed or standardization may be required based on which laboratory performed assays. There are both internal (single database) and external (multiple database) validation methods. There are many different internal validation methods: splitting samples, cross-validating, bootstrapping, and jackknifing. External validation uses new data bases representing the wide spectrum of the target populations, but not used to develop the model or perform any initial analyses, to see how well they replicate (calibrate). The goal is to create data-driven interventions for individual patients and health policies that improve health.

To evaluate precision health and precision public health research, cross-referencing lessons learned from KDD and BD2K can be quite helpful, such as referring to a list of common mistakes with artificial neural net models; issues include too many parameters for the sample size, no validation, no model complexity penalty (e.g. Akaike Information Criterion (AIC), Bayes Information Criterion (BIC), Mallow's C_p), incorrect misclassification estimation, implausible function, incorrectly described network complexity, inadequate statistical competitors, insufficient comparison to competing models (16).

An underutilized precision public health research area involves analyzing text data through text mining tools such as natural language processing (NLP). A vast amount of health data is free form text including chart subjective, objective, assessment, and plan (SOAP) notes and other electronic health record (EHR) open-ended response fields, as well as health portal communications. A few recent papers have used text from EHRs and processed the information to discover interesting patterns in health using tools. For example, early adverse childhood experiences (ACEs) like abuse and homelessness, lack of safe environment, and food insecurity were found in EHR text; researchers then found ACEs were correlated with subsequent poor health outcomes (17). Another example is care coordination, which helps overcome psychosocial distress. Investigators discovered patients with care coordination documented in EHR notes overcame psychosocial distress more frequently than those who did not have care coordination (18).

Opportunities abound for public health researchers to discover novel information from text records, including copious troves of documents relating to possible industry influences (such as big tobacco, big pharma, big chemical, and big sugar) on health policies. UCSF houses a vast and growing repository of tobacco industry papers as well as papers on the pharmaceutical and chemical industries (currently numbering over 12 million documents); sugar industry papers have recently been made public online. These can all be accessed and searched for free at https://Industrydocuments.ucsf.edu.

Social determinants of health in precision public health

In precision public health, another set of important measures are known collectively as social determinants of health (SDOH), which operate at individual, family, and community levels. Poverty, education, health literacy, and home conditions are some examples. Focusing on housing conditions, there have been some ground-breaking precision public health efforts, which have used individual patient level information to positively intervene in ways that affect larger groups of people exposed to deleterious conditions, essentially “taking the handle off the pump” for neighborhoods or clusters of people. One seminal example has been happening at Cincinnati Children’s Hospital (19,20), where clinicians asked about the rental home conditions in pediatric visits with a 7-item social risk screening checklist. When pest infestation and other signs of substandard housing were reported in 16 cases, they connected parents via a medical legal partnership to someone who could provide family legal services including ordinance enforcement. Substandard housing was abated in 10 (71%) of 14 multi-unit buildings improving living conditions for at least 45 children in those buildings in Cincinnati communities. Thus, they have taken that potential problem of exacerbating health disparities with technology and reversed it into a solution to positively impact community health.

With SDOH, as with all precision public health factors, it is important to properly evaluate classification models. (All primary research reported in this paper was performed with institutional review board approvals.) For example, using an older 2004–2005 version of the American Association of Pediatric Dentistry’s Caries-risk Assessment Test (CAT) (21), questionnaire data from the 1993–1994 California Oral Health Needs Assessment of Children (COHNAC) (22) were used to classify children as low or moderate/high caries risk. In 2648 children where 48% actually had caries, CAT estimated 5% at low risk and 95% at moderate/high risk with corresponding sensitivity of 98% and specificity of 8% because only about half of those classified as moderate/high risk actually had caries (high percent of false positives). Among the 52% of children with no caries, the 2004–2005 CAT classified

93% of those as moderate or high risk. One item in CAT is a parent/caregiver with low socioeconomic status, which may over identify children as moderate/high risk.

Multifactorial, multilevel conceptual frameworks

The UCSF Center to Address Disparities in Children's Oral Health has used a multidimensional framework—the Fisher-Owens framework (23)—to conceptualize the child, family, and community influences on children's oral health outcomes. For precision public health, expanding this framework to an Integrative Social Molecular Pathologic Epidemiology (ISMPE) perspective can be useful. ISMPE combines social epidemiology with molecular pathological epidemiology. Social epidemiology provides insights on social, economic, cultural, and behavioral factors; to address disparities the Fisher-Owens framework can be expanded to include global-level factors. The molecular-pathological perspectives can potentially yield mechanistic and pathogenic insights, refine effect size estimates for specific subtypes, and foster causal inference (24). Another relevant conceptual framework connects upstream impacts such as social and environmental contextual factors to downstream disease interventions via a causal model (25).

These conceptual frameworks along with recently developed analytic methods can help provide more information on interventions and policies. For example, mediation model methodology has recently been adapted for non-Normal discrete count outcome data often seen in oral health studies using caries indices. The original caries management by risk assessment trial showed a strong association between the intervention and caries risk but only a modest and not statistically significant relationship to the caries increment outcome (26). This mechanism of action was posited to change caries risk, which would then change caries increment. Cheng *et al*. (27) have been developing mediation models for non-Normally distributed discrete count data. The mediation effect was statistically significant, showing that the intervention (anti-bacterial and fluoride treatments) changed the mediators (risk levels), which then changed the outcomes (less new DMFS) two years later in adults. About 36% of the intervention effect on 24-month DMFS increment was through the intervention's indirect effect on the 12-month overall risk ($P = 0.03$) (27).

Examples of precision public health analyses

Newer analytic tools and approaches can help better understand health phenomena. Another precision public health analytic method assesses heterogeneity of treatment effects (HTE) to identify subgroups of the population that benefit more from a particular intervention. To assess whether fluoride varnish better prevents caries in some preschoolers HTE methods called the Johnson-Neyman (J-N) approach. For 376 preschool children in a fluoride varnish trial (28), any fluoride varnish versus no fluoride varnish reduced the odds of 2-year caries incidence (odds ratio (OR) = 0.33). J-N showed that children with more baseline MS (those with at least $\log_{10}$ 0.649 CFU/ml) had significantly greater preventive benefit from FV and the greater the baseline MS level, the greater the benefit from FV; for example, for children with $\log_{10}$ MS of 5.0, OR = 0.18) (29).

In the 2004−2005 COHNAC statewide stratified complex survey of 186 schools with the Association of State and Territorial Dental Directors Basic Screening Survey, screenings were performed on 21,399 kindergarteners or third graders measuring rampant caries (defined as the number of decayed or filled primary (dft) or permanent teeth (DFT) ≥7) and, among third graders, whether they had dental sealants on first permanent molars. Various factors potentially related to caries were assessed: demographics (race/ethnicity, gender, age, and grade), socioeconomic status (free/reduced cost lunch (FRL) program participation, both for the individual child, and the percent of children at school), and acculturation (non-English language at home, both for the individual child and the percent of children at school).

Absolute differences from reference groups and 95% confidence intervals (CIs) were estimated using survey logistic regression (accounting for strata, clusters, and weights) for rampant caries prevalence by race/ethnicity and socioeconomic position (Figure 4). All racial/ethnic groups had significantly higher prevalences than non-Hispanic Whites with Hispanic children having the highest prevalence—about 15% more than non-Hispanic Whites. Being a FRL program participant related to significantly higher prevalence (more than 10%) than not being a participant for individual children. But the school-level FRL effect was even greater. A child in a school with 75% or more of children in the FRL program, regardless of whether he or she was in it him- or herself, had significantly higher prevalence (about 20%) than a child in a school with <25% FRL participation; that group difference was greater than the difference for Hispanics and the difference for individual FRL participation. Thus, community impacts can matter even more than individual ones.

Community impacts beyond economic ones can be quite important. Using the 2004–2005 COHNAC survey, Mejia and colleagues examined FRL (individual and school-level) and English language (individual and school-level) by the lack of dental sealants. Using health disparities indices of slope index of inequality, relative index of inequality (mean), and absolute concentration index with 95% CIs, no statistically significant effect was seen for individual-level or school-level FRL program participation, but there were statistically significant effects for all three health disparity indices for percent English language learners (school level) with lacking sealants; moreover, a language other than English being spoken at home (individual level) was statistically significant (30). So this is an example of SDOH, other than the typical income or poverty disparities, being important—here as linguistic disparities.

Targeted, universal, and proportionate universalism approaches

Precision public health typically considers an “either-or” choice with two alternative intervention approaches: whole population or targeted high risk. The targeted risk approach (31) posits that preventing disease in higher risk individuals is an efficient use of resources to change population health. However, there are reasons why the targeted approach has not resulted in improving public health. In some cases, the targeted approach blames the victim. Moreover, the targeted approach continues *ad infinitum* with those at high risk. Finally, it is frequently difficult to deliver care to high risk individuals, because it is often challenging to reach the highest risk individuals.

The whole population approach (32) eliminates the need for the step of targeting and identifying those at highest risk and instead aims to increase overall public health. The main drawback is that the whole population approach frequently results in increasing health disparities. Cerdá and colleagues compared population health effects of targeted and whole population (universal) approaches *in silico* (via computer simulation), finding that although the universal approach can better impact population health with an efficacious intervention, disparities can still increase (33). Additionally, intervening on the whole population typically yields differential uptake, reaching fewer of the individuals needing the intervention the most.

However, a third way exists: the targeted vulnerable population approach, which seeks to reduce health inequities, while also improving overall public health (34). The targeted vulnerable population approach seeks to foster proportionate universalism not only to acknowledge the typically socioeconomic gradient in health outcomes, but to specifically focus actions proportional to the subgroups' need. Interventions would be focused through communities, rather than individuals (35).

In precision proportionate universalism, public health investigators need to answer the following questions:

Who are the vulnerable groups?

What is the public health prevention/intervention?

Where are the populations?

How is precision public health delivered?

Summary and conclusions

Thus, at the crossroads of precision public health, what directions will we choose? What bargains will we strike in order to get there? Now is the time for the dental public health community to strategically plan to integrate precision methodology into the discipline to increase the chances of meeting its goals to improve the health of the public.

In the future, precision public health should be sure to utilize:

- multifactorial, multilevel conceptual frameworks and conceptual causal models with upstream social determinants and downstream health effects, as well as a proportionate universalism perspective; and
- proper analytic methods, including sufficient sample sizes, appropriate statistical competitors, health disparity indices, causal modeling, and internal and external validation.

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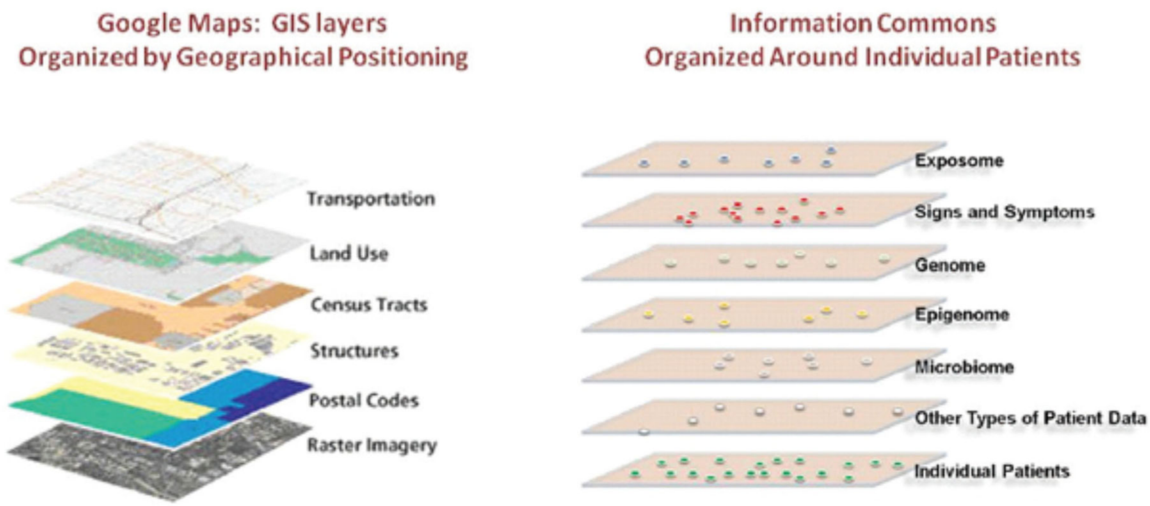

Figure 1.

An information commons might use a GIS-type structure (1). The proposed, individual-centric information commons (right panel) is somewhat analogous to a layered GIS (left panel). In both cases, the bottom layer defines the organization of all the overlays. However, in a GIS, any vertical line through the layers connects related snippets of information since all the layers are organized by geographical position. In contrast, data in each of the higher layers of the information commons will overlay on the patient layer in complex ways (e.g., patients with similar microbiomes and symptoms may have very different genome sequences). SOURCE: FPA 2011 (left panel), NRC 2011 (right panel). (Reprinted with permission from *Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease*, 2011, the National Academy of Sciences, Courtesy of the National Academies Press, Washington, DC.)

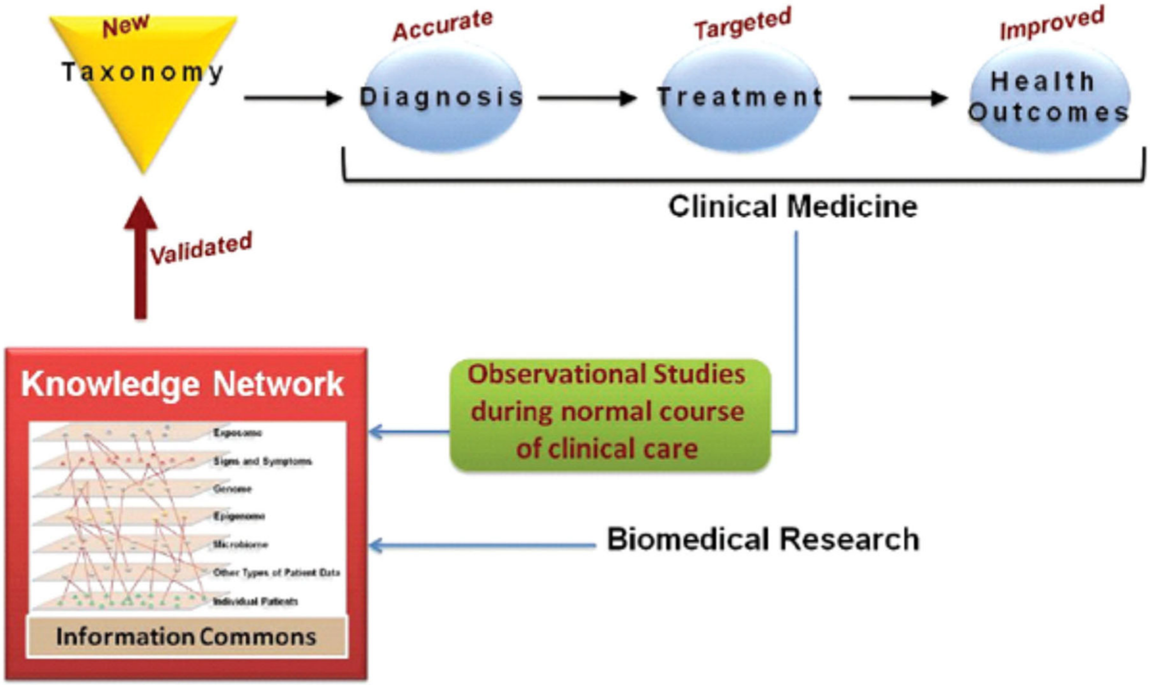

Figure 2.

A knowledge network of disease would enable a new taxonomy (1). An individual-centric information commons, in combination with all extant biological knowledge, will inform a Knowledge Network of Disease, which will capture the exceedingly complex causal influences and pathogenic mechanisms that determine an individual's health. The Knowledge Network of Disease would allow researchers to hypothesize new intralayer cluster and interlayer connections. Validated findings that emerge from the Knowledge Network, such as those which define new diseases or subtypes of diseases that are clinically relevant (e.g., which have implications for patient prognosis or therapy) would be incorporated into the New Taxonomy to improve diagnosis and treatment. SOURCE: Committee on A Framework for Developing a New Taxonomy of Disease. (Reprinted with permission from *Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease*, 2011, the National Academy of Sciences, Courtesy of the National Academies Press, Washington, DC.)

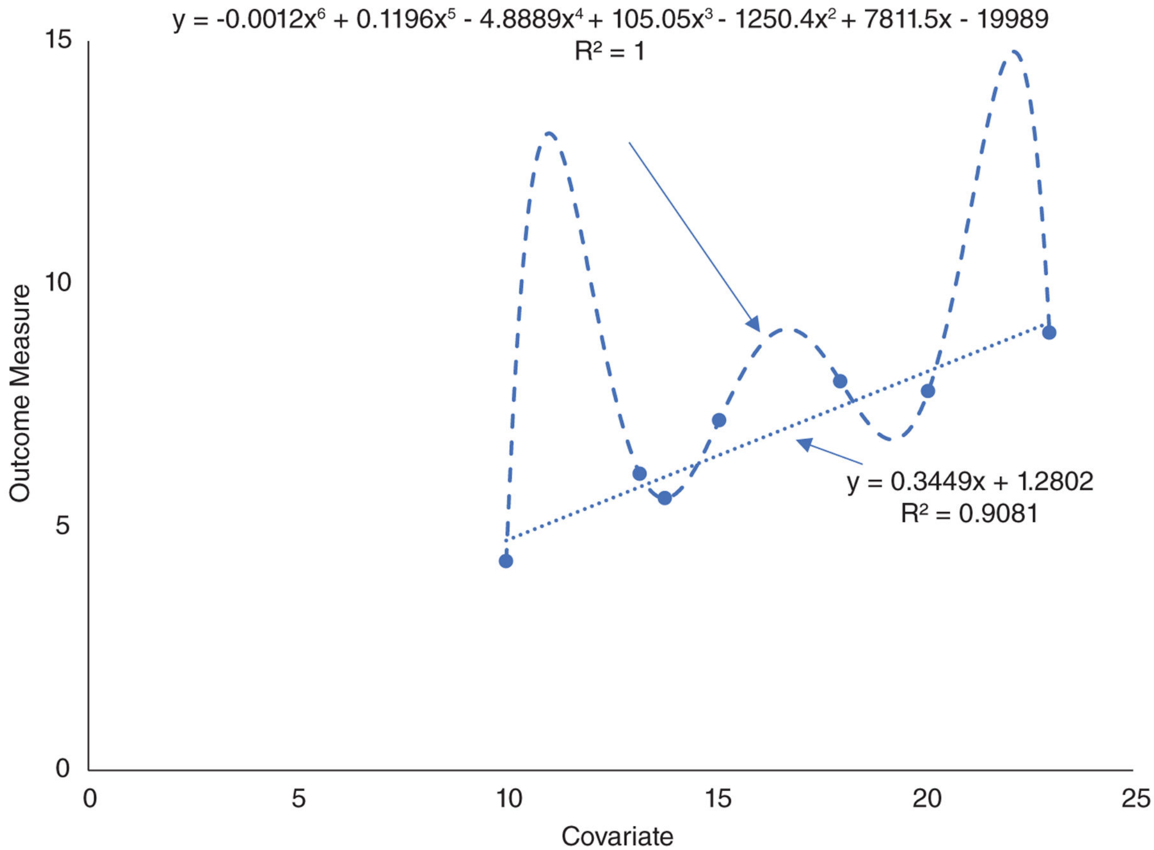

Figure 3.
Simple example of overfitting in only 2-dimensions ($N = 7$).

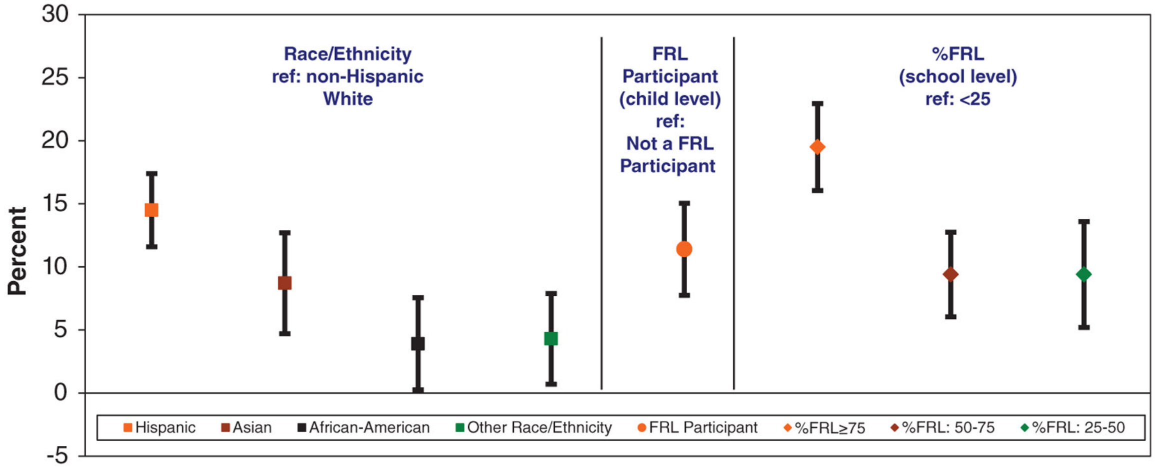

Figure 4.

Absolute difference (95% CI) in rampant caries (dft or DFT ≥7) prevalence by race/ethnicity and socioeconomic position, California Oral health needs assessment of children, 2004–5 (*N* = 21,399). CI = confidence interval. dft = number of decayed or filled primary teeth. DFT = number of decayed or filled permanent teeth. FRL = free/reduced cost lunch program. ref = reference group.

Table 1

Examples of Health Technologies Which Exacerbated Health Disparities

Health area	Medicine	Dentistry
Diagnosis	Colonoscopy	Oral cancer staging
	Papanicolaou (Pap) test	
Prevention	Hypertension medication (8)	Dental sealant
Treatment	Coronary artery bypass graft	Tooth implant Root canal therapy