

Precision Health: The Role of the Social and Behavioral Sciences in Advancing the Vision

Eric Hekler, PhD^{1,2,3,⊗} · Jasmin A. Tiro, PhD^{4,5} · Christine M. Hunter, PhD⁶ · Camille Nebeker, EdD, MS^{1,2,3,⊗}

Published online: 27 April 2020

© The Author(s) 2020. Published by Oxford University Press on behalf of the Society of Behavioral Medicine. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

Abstract

Background In 2015, Collins and Varmus articulated a vision for precision medicine emphasizing molecular characterization of illness to identify actionable biomarkers to support individualized treatment. Researchers have argued for a broader conceptualization, precision health. Precision health is an ambitious conceptualization of health, which includes dynamic linkages between research and practice as well as medicine, population health, and public health. The goal is a unified approach to match a full range of promotion, prevention, diagnostic, and treatment interventions to fundamental and actionable determinants of health; to not *just address* symptoms, but to *directly target* genetic, biological, environmental, *and* social and behavioral determinants of health.

Purpose The purpose of this paper is to elucidate the role of social and behavioral sciences within precision health.

Main body Recent technologies, research frameworks, and methods are enabling new approaches to measure, intervene, and conduct social and behavioral science

research. These approaches support three opportunities in precision health that the social and behavioral sciences could colead including: (a) developing interventions that continuously “tune” to each person’s evolving needs; (b) enhancing and accelerating links between research and practice; and (c) studying mechanisms of change in real-world contexts. There are three challenges for precision health: (a) methods of knowledge organization and curation; (b) ethical conduct of research; and (c) equitable implementation of precision health.

Conclusions Precision health requires active coleadership from social and behavioral scientists. Prior work and evidence firmly demonstrate why the social and behavioral sciences should colead with regard to three opportunity and three challenge areas.

Keywords: Precision medicine · Precision health · Social and behavioral sciences · Research methods · Implementation science · Research ethics

✉ Eric Hekler
ehekler@ucsd.edu

¹ Department of Family Medicine and Public Health, School of Medicine, UC San Diego, La Jolla, CA 92093-0811, USA

² Center for Wireless and Population Health Systems, Qualcomm Institute, UC San Diego, La Jolla, CA, USA

³ Design Lab, UC San Diego, La Jolla, CA, USA

⁴ Department of Population and Data Sciences, University of Texas Southwestern Medical Center, Dallas, TX, USA

⁵ Harold C. Simmons Comprehensive Cancer Center, Dallas, TX, USA

⁶ Office of Behavioral and Social Sciences Research, National Institutes of Health, Bethesda, MD, USA

Introduction

In 2015, Francis Collins, current director of the National Institutes of Health (NIH), and Harold Varmus, former director of the National Cancer Institute (NCI), articulated their vision for “*precision medicine*” as the development of “prevention and treatment strategies that take individual variability into account” [1]. Subsequently, a central thrust of precision medicine research efforts has emphasized identification of actionable genetic markers that predict response to treatment in some patients by addressing genetically driven mechanisms of cancer progression [2].

There is excitement about the potential of precision medicine to move prevention and treatment beyond approaches focused on average unit (e.g., person, community, healthcare system) responses [3], to create more specific, effective, user-friendly, and implementable interventions [4–6]. As observed by others [4–16], the full potential of precision efforts will be achieved only if precision is applied across the spectrum of health including population health and public health [17], not just medicine. In line with other definitions [10, 11, 13, 16], precision health is an ambitious conceptualization of health, which includes dynamic linkages between research and practice as well as medicine, population health, and public health. The goal is a unified approach to match a full range of promotion, prevention, diagnostic, and treatment interventions to fundamental and actionable determinants of health; to not *just address* symptoms, but *directly target* genetic, biological, environmental, *and* social and behavioral determinants of health. A comprehensive vision of precision health will only be realized through engagement and integration of the social and behavioral sciences.

The purpose of this paper is to elucidate the foundational role of the social and behavioral sciences in advancing precision health. First, we provide an overview of the history and potential future of precision health. Then, we discuss present-day changes in technologies, research frameworks, and methods within the behavioral sciences that make both precision health possible and enable the social and behavioral sciences to be actively involved. We conclude with three opportunities (i.e., new types of interventions, enhancing and accelerating linkages between research and practice, and mechanistic science in real-world contexts) and three challenges (i.e., knowledge curation, ethical conduct, and equitable implementation) to precision health that the social and behavioral sciences could take a coleadership role with others to advance precision health.

From Evidence-Based Medicine to Precision Medicine to Precision Health

Both precision medicine (called personalized medicine in the UK) and precision health are related extensions of evidence-based practice. To illustrate, it is valuable to examine varying conceptualizations of these inter-related concepts. Sackett [18] defined evidence-based medicine as:

... the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.

As illustrated in a report from the UK's National Health Service report [19] on precision/personalized medicine, new technologies afford new possibilities:

The concept of personalised medicine is not new. Clinicians have been working to personalise care, tailored to people's individual health needs, throughout the history of medicine. But never before has it been possible to predict how each of our bodies will respond to specific interventions, or identify which of us is at risk of developing an illness. New possibilities are now emerging as we bring together novel approaches, such as whole genome sequencing, data and informatics, and wearable technology. It is the interconnections between these innovations that make it possible to move to truly personalised care.

Based on this, new technologies enable increased capacity for the external evidence, foundational to evidence-based practice, to be used not only to identify “one size fits all” approaches but also interventions that are matched, with increasing specificity, to the characteristics and context of specific persons. Thus, evidence-based clinical practice would rely less on trial and error. For example, 1st, 2nd, and 3rd line cancer therapies [20] could be shifted to selection of treatment based on a combination of disease presentation characteristics. While not new, particularly when considering behavioral medicine's tailoring interventions [21], this vision is a more comprehensive and integrated approach that includes individuals and their context when selecting interventions [22].

The National Research Council report [23], which was the progenitor to the Collins and Varmus conceptualization, offers a revolutionary challenge to evidence-based practice. The National Research Council focused on understanding opportunities that could be advanced through changes in how science is conducted. Their charge was to explore “a new taxonomy of human disease based on molecular biology.” The National Research Council working group defined the vision for this new taxonomy as:

a comprehensive disease taxonomy that brings the biomedical-research, public health, and healthcare-delivery communities together [emphasis added] around the related goals of advancing our understanding of disease pathogenesis and improving health. Such a New Taxonomy would:

- Describe and define diseases based on *their intrinsic biology* [emphasis added] in addition to traditional physical “signs and symptoms.”
- Go beyond description and be directly linked to a *deeper understanding of disease mechanisms*,

pathogenesis, and treatments [emphasis added].

- Be highly dynamic, at least when used as a research tool, *continuously incorporating new emerging disease information* [emphasis added].

The National Research Council committee distinguished the vision of their taxonomy from the taxonomy of today (i.e., the International Classification of Diseases [ICD]) by highlighting that, within the ICD, there are two interrelated problems: (a) many conditions with distinct causes are classified as the same disease and, conversely, (b) multiple conditions are identified as different diseases when they share a common cause. From the perspective of the National Research Council, the creation of such a taxonomy would be foundational for a new type of science that undergirds precision medicine. Based on their definition, *precision medicine departs from evidence-based practice via a new science that would enable the selection of interventions that are directly linked with underlying causal factors, not just symptoms*. While the task of the National Research Council was focused on molecular biology, the committee alluded to the importance of bringing together the biomedical research, public health research and practice, and healthcare delivery communities toward advancing understanding of disease pathogenesis and health promotion.

Going beyond the National Research Council's focus on biology but continuing its questioning of scientific practices, an overemphasis on molecular biology as *the* fundamental determinant of health is too limiting [10, 11, 13, 16] and could be problematic [24]. The science of genetics and epigenetics is increasingly illustrating the importance of context and behavior, even if the view of determinants is limited only to “biological” determinants [25]. Current estimates indicate that genetics explain an important but incomplete portion (e.g., ~30%) of an individual's variability in health [26–28]. Health behaviors (e.g., physical inactivity, diet, tobacco use) explain an additional 40% of variance, with the remaining 30% of variance attributed to environment factors, social circumstances, and healthcare utilization and delivery [26–28]. Within sociology, some have argued that an overemphasis on biological determinants within health sciences can be damaging to individual and public health [24]. For example, when race is treated as a biological construct, it is viewed as a causal driver of suboptimal health. When race is viewed as a sociocultural construct, it is the social context that influences “race.” Thus, correlations between race and health outcomes do not equal causation; instead, third variable sociocultural mechanisms (i.e., racism) explain the association [24]. If racism is the causal issue, interventions are needed to target racism, not to do treatment matching to race, which is the likely decision one would make if viewing it as biological construct. As Roberts points out, there is clear evidence

that racism is the underlying driver and that treating race as a biological construct is not only problematic, but dangerous [24]. This example, coupled with the relatively small portion of variance explained by biological determinants, establishes a major risk of precision medicine if nonbiological determinants are not treated with equal, and possibly even greater importance.

This broad view on determinants of health establishes the need for a diverse repertoire of interventions appropriate for different determinants of health, such as behavioral, public health, community organizing, social and built environment changes, and, of course, pharmaceuticals and medical devices when appropriate [29]. Broadening the repertoire is not only essential for advancing health but it is also practical. If behaviors or social and environmental exposures are more actionable than trying to change one's biology, it is more pragmatic to target the determinants of behavior and environmental exposures over biological processes, even with the goal of influencing biological processes.

Precision Health Requires the Social and Behavioral Sciences

Figure 1 provides a visual summary of the expanded vision of precision health, using the Collins and Varmus conceptualization as an initial referent. The expansions across key areas provide clear justification for the foundational importance of the social and behavioral sciences in precision health as related to: determinants of health (i.e., from biological to a full representation of key determinants of health), targeted health domains (from disease-focused to the World Health Organization's definition of health), and intervention strategies (i.e., from interventions traditionally used in medicine to inclusion of the full repertoire of intervention strategies that span medicine, population health [17], and public health). The history and active research of the social and behavioral sciences related to tailoring interventions (illustrated in the intervention classes area of Fig. 1), data analytics, stakeholder engagement, and implementation science point to future areas of growth that could help to make precision health a reality.

What Has Changed in Technology, Methods, and Research Frameworks?

Technology

As is the case across society, digital technologies are influencing sectors including health. Many of these are not merely one-off tools but, instead, platforms [30]. Digital platforms are tools that provide an essential

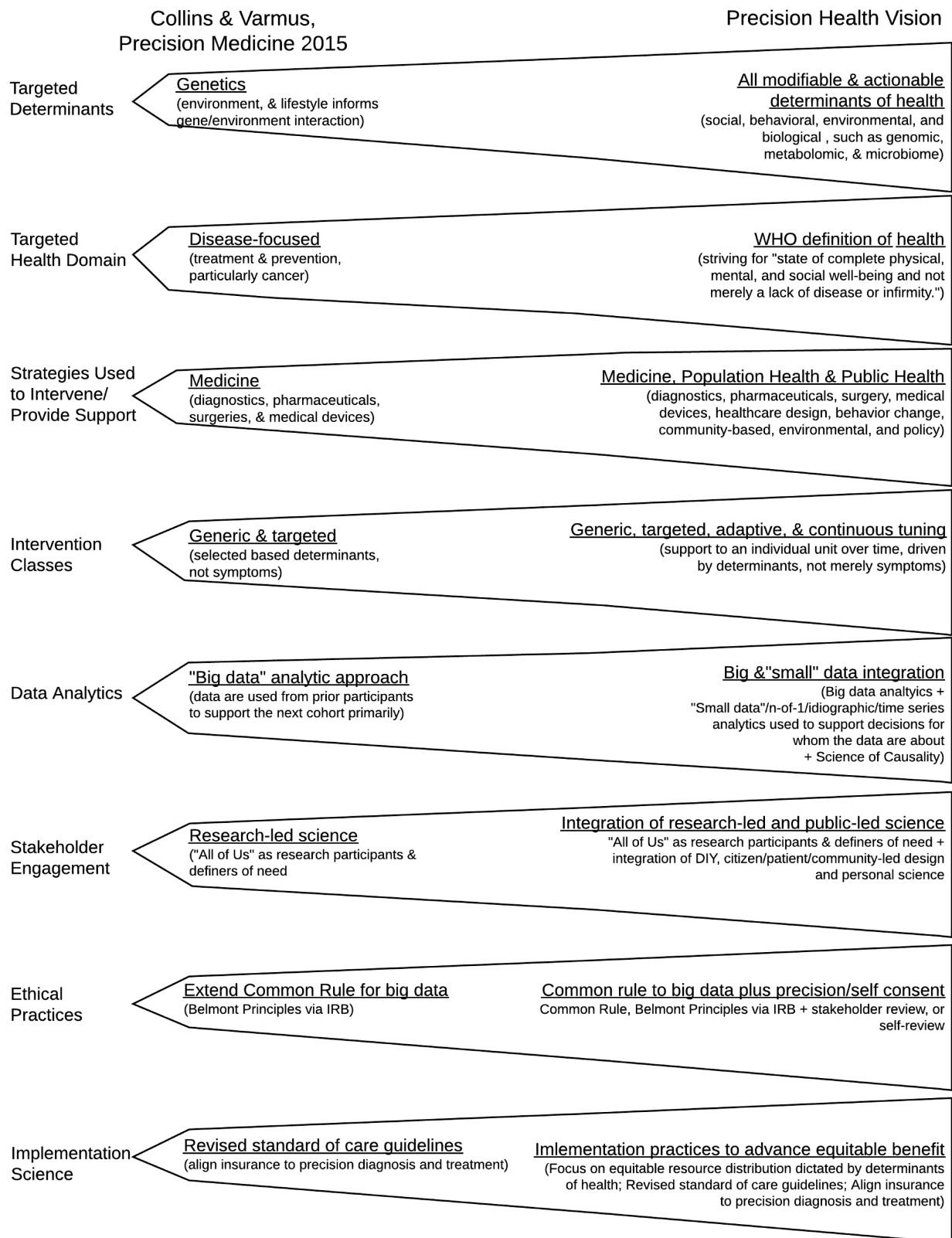


Fig. 1. A vision of precision health, with precision medicine as a referent. Collins and Varmus [1] provides an initial referent, which is then expanded to illustrate the potential future target of precision health. *IRB* Institutional Review Board; *WHO* World Health Organization.

function and act as a building block upon which other technologies can be built. One classic platform is Microsoft Windows but, of course, there are now a wide range of platforms such as the Internet/world wide web; smartphones (Android or iOS), social media platforms (e.g., Facebook, Twitter, Instagram), commerce platforms (e.g., Amazon, eBay), information platforms (e.g., Google Search), “gig economy” platforms (e.g., Airbnb, Lyft, and Uber), and, more recently, health and research platforms (e.g., Fitbit or Apple Smartwatches, ResearchKit, HealthKit). While these platforms provide a core service, these services are created modularly and are interconnected [31], which enables end-users to use these tools for a much wider range of purposes than the original creators may have envisioned.

These digital platforms have created new opportunities for measuring, intervening, and, thus, conducting research in real-world contexts related to health. Temporally appropriate time series measurement (e.g., frequent measurement for constructs that rapidly change, such as motivation, and less frequent measurement for constructs that change more slowly, such as the built environment) is required to enable precision efforts. It is possible to gather a vast amount of ecologically valid raw data and then, using algorithms, translate those data into meaningful measurement of social, behavioral, and health phenomena. These data are often obtained via smartphone sensors, tracking systems when one uses digital tools (e.g., cookies in the Internet), and contextually embedded technologies such as wearable devices [32].

These digital platforms enable an impressive array of social and behavioral data to be inferred in real-world contexts; what might be thought of as digital phenotypes [33, 34]. For example, it is now possible to do passive measurement of: a person’s health behaviors such as physical activity, eating habits [35], and smoking [36–38]; a person’s emotions, stress, mood, or depressive state [39, 40]; social interactions [41–44]; colocation of individuals [45]; driving style [46]; traffic accidents [47]; diagnostic tests such as tremors among patients with Parkinson’s [48, 49]; inferring heart rate or blood oxygen [49]; and social status and personality characteristics [50–56]. These platforms also support delivery of interventions [57], enabling delivery of support in real-world contexts, when and where it is most needed [57]. From a technical standpoint, we can measure, intervene, and conduct research within real-world environments using today’s technologies with a great deal of precision.

Research Frameworks

New research frameworks provide organizational structures on how a series of studies, when combined, produce

desired outcomes such as empirical evidence that supports intervention matching to individuals in context, better insights about mechanisms of behavior change, and more robust knowledge accumulation. Two complementary examples are the multiphase optimization strategy (MOST) and the Science of Behavior Change (SOBC).

Pioneered by Dr. Linda Collins [58], MOST is an engineering-inspired framework for optimizing behavioral and biobehavioral interventions. The MOST framework has a very practical goal; to improve interventions. MOST includes three key phases: preparation, optimization, and evaluation. The preparation phase includes steps to specify and define an empirically testable research question, such as creating a conceptual framework, selecting intervention components, conducting a feasibility study, and defining optimization criteria. Optimization criteria include measures and clinically meaningful trade-offs such as cost, time, or minimal effectiveness targets, with success (or failure) on each metric specified before running an optimization trial. For example, one optimization criteria could be that each intervention component must be significantly better, statistically, than a comparator, AND the entire intervention package must be deliverable for less than US \$500. Once these criteria have been determined, the optimization phase can proceed using an optimization trial, such as factorial trial [59–62], sequential multiple assignment randomized trial (SMART [63–66]), microrandomization trial [67, 68], or system identification experiment [69–75] (we expand on each method below). If an intervention meets the optimization criteria (e.g., an intervention package can be produced that has only effective components and costs less than \$500), then that “optimized” intervention can be evaluated in the evaluation phase via a randomized controlled trial (RCT) compared with a meaningful comparator, such as current standard of care.

Central to precision health, optimization criteria can be defined in relation to intervention matching. For example, within a factorial trial, one could include a demographic variable as a factor (e.g., equal sampling of men and women) within the factorial experiment. An optimization criterion could be that intervention components produced statistically meaningful effects among men or women as subgroups, without any requirement that the same components be used across men and women. Thus, different optimized intervention packages could be specified for different groups, with moderator analyses used to clearly test differential impact. The SMART design, which is another form of a factorial trial and, thus, supports baseline matching to different groups, can also support additional optimization of stepped-care decision-making. For example, SMART can test the decisions one might make when a person is

nonresponsive to an initial intervention or if an intensive treatment can be replaced with a less intensive intervention when a person is responsive. As these two optimization trials illustrate, the integration of optimization into intervention development enables greater precision by producing clear evidence on selection of initial treatment packages for different groups and also stepped-care decision-making. This is made possible via the MOST research framework.

While MOST focuses on the practical goal of intervention optimization, SOBC [76] has a scientific goal, "...to promote basic research on the initiation, personalization and maintenance of behavior change." SOBC applies an experimental medicine approach to understand processes or mechanisms that influence change in behavior and health outcomes [76, 77]. In the first step, a hypothesis about a putative mechanism or process driving behavior change is posited. Then, evidence for the validity of the mechanism is supported if: (a) the process can consistently and reliably be measured, and (b) those mechanistic targets can be engaged (i.e., meaningfully changed) through an intervention/experimental manipulation. Finally, the initial approach can then be expanded to test the strength and durability of findings: (a) in different subgroups of individuals based on specific measured characteristics, such as age and gender, that might be associated with a differential effect; and (b) under a variety of contexts, such as community versus healthcare settings or using different modalities of delivery such as face-to-face, technology delivered or some combination. The final step produces meaningful results on intervention matching and, thus, precision health. Further, as SOBC is ultimately focused on underlying causal mechanisms of change, it is very well matched to precision health and, specifically, the emphasis on matching interventions to underlying causal factors that drive desired outcomes and not just symptom alleviation. In summary, the SOBC experimental medicine approach systematically identifies and promulgates common mechanisms/processes of behavior change that are robust and allows for delineation of what change processes are important for whom and under what circumstances, thus making it well matched to precision health.

These are two of a wide range of research frameworks being explored to improve the efficiency, rigor, and robustness of social and behavioral scientific research. These frameworks also illustrate two different, but, ideally, complementary goals: improving interventions (e.g., MOST) and advancing understanding of underlying mechanisms of change (e.g., SOBC). A goal of precision health is to match interventions to individuals in context, with the match established, ideally, to underlying causal factors instead of symptoms. As such, MOST and SOBC provide an avenue for a robust

precision health research pipeline (a point we expand on in the opportunity section). Other frameworks potentially useful for articulating an appropriate research pipeline for precision health include, but are not limited to: the dynamic sustainability framework [78], disruptive innovations models [79], rapid relevant and responsive research model [80], the Obesity-Related Behavioral Intervention Trials model [81], the behavior change wheel [82], agile science [31, 83–85], and accelerated creation-to-sustainment model [86]. Collectively, these frameworks promote new thinking about research that are synergistic with precision health.

Research Methods

Driven by these technologies and research frameworks, there has been a similar explosion in new research methods. These include: (a) the optimization trials mentioned as part of MOST [32, 58, 87]; (b) single case experimental/"*N-of-1*"/idiographic experimental and quasiexperimental designs [70, 88–94]; and (c) methods to simultaneously investigate both intervention efficacy/effectiveness and implementation in real-world contexts, such as hybrid implementation trials [86]. While space precludes a detailed account and we have already discussed factorial trials and SMART, we expand on microrandomization trials and *N-of-1* methods for precision health.

While there is great potential with digital health tools [95–99], there is a gap between what digital health promises and intended results [36, 83, 100–104]. The concept of a just-in-time adaptive intervention (JITAI) was advanced to improve the potency of digital interventions. *JITAI*s provide support when a person is receptive to support and has the opportunity to act [105, 106]. Thus, *JITAI*s fit squarely within the precision health vision.

For *JITAI*s, a key optimization trial is the microrandomization trial [67, 84, 107]. Microrandomization trials are another variation of factorial trials and, thus, can produce the same types of insights for matching that are possible with between-person factorial trials and SMART (i.e., baseline demographics can be specified a priori to do test baseline intervention matching and insights on stepped-care decision-making can be produced). Microrandomization trials can produce additional insights to optimize the decision rules used for adapting intervention components to individuals in context [108]. A decision rule is an algorithm that defines when, where, and how an intervention component should be delivered over time and, thus, is the foundational feature of a *JITAI*. Microrandomization trials work by randomizing delivery of intervention options (e.g., sending or not an encouraging message) at decision points (e.g., each morning) on the basis of tailoring

variables (e.g., goal achievement). A proximal outcome is measured after each decision point, both when the intervention option is delivered and not, to enable causal inference of intervention component impact at decision points and test if intervention components work in certain states (e.g., only during weekdays) via time-varying moderation analyses [67, 84, 107].

To make the promise concrete, we describe *HeartSteps* [67, 84, 107]. *HeartSteps* targeted healthy sedentary adults (ages 18–60) to increase daily steps based on a combination of *pull* interventions, which participants could access on demand (previous activity suggestions, self-monitoring) and *push* interventions (contextually tailored activity and daily prompts to write implementation intentions). *HeartSteps* participants were randomized to receive or not receive an activity prompt 5 times per day (i.e., up to 210 decision points per participant). Providing a prompt (compared with random assignment to no prompt) initially increased step counts by 167 steps (66%) in the 30 min following the decision [107]. Preliminary results illustrated that context cues were particularly valuable during the first few weeks of the trial but were not as effective by week 6 and that they were more effective when delivered while a person was at home or office compared with when offered while a person was in some other location. Based on this, one could enact an evidence-based decision rule to the use of context cues during the first few weeks of an intervention and only deliver when a person was clearly at home or in their office. Implementation intentions (i.e., setting specific plans on when, where, and how to be active) were also tested within *HeartSteps* as a second intervention component. Results illustrated that writing a plan for how to be active on the next day versus not writing a plan, added 523 steps to the next day's step count, and effects stayed stable throughout the study. Preliminary results also showed that writing plans produced meaningful change on weekdays but not weekends (903 steps on weekdays). Thus, information about day of the week should be incorporated into the implementation intention decision rule. Interestingly, via the use of repeated randomization, all insights were gleaned from a properly powered [68] small sample ($N = 44$) within a short time period (6 weeks). Thus, microrandomization trials can produce valuable insights that directly align with the goals of precision health efficiently and in context.

A recent advancement of *N-of-1* methods is the use of system identification [69–75], which evolved from the field of control systems engineering, for understanding human health. System identification is an experimental and analytic suite of methods to generate/validate dynamical models for future predictions on a per unit (e.g., person, system, community) basis [93, 109–111]. System identification “excites” variance within a unit/person via plausible intervention options to test what happens

in different states and contexts of the unit/person over time. For example, a system identification study was conducted to improve steps per day among adults [74] using adaptive step goals and points received when meeting goals as intervention components. Points translated into financial rewards, which were systematically varied over time and across different states, such as different days of the week or when stressed or not [73]. Results illustrated: (a) system identification can be used to generate individualized dynamical models that are predictive of each person's steps/day over time; (b) different variables (e.g., weekend/weekday, stress, busyness) appeared to be predictive for different individuals; and (c) compared with an aggregate-based model (i.e., traditional mixed model analyses), the individual-based models identified unique tailoring variables to use for each person, suggesting a potential mismatched tailoring variable for 75% of the sample if a nonindividualized tailoring variable were used [74]. This trial and other *N-of-1* trials [112–114] show increased capacity and rigor with which the social and behavioral sciences are able to systematically account for individual differences and use those insights for advancing precision behavioral interventions. Collectively, these methods, particularly when also including implementation science methods, showcase a much wider range and deeper sophistication of research questions that social and behavioral scientists can now address to advance the goals of precision health.

Opportunities for the Social and Behavioral Sciences Within the Realm of Precision Health

Clearly, new technologies, research frameworks, and methods afford opportunities for social and behavioral sciences to drive facets of the precision health agenda. The next section highlights how the social and behavioral sciences, particularly the behavioral medicine community, provide the basic building blocks to advance three opportunities: (a) building “continuous-tuning interventions” that match the complexity of some health phenomena; (b) integrating research within practice to enable equitable, robust, rapid, iterative learning; and (c) enabling mechanistic science in real-world contexts.

Building Interventions That Match Complex Behavioral and Health Phenomena

The first key opportunity is to expand our capacities in matching interventions to people and contexts. Many health issues, such as obesity, diabetes, cardiovascular disease, and cancer, are highly complex [94]. Complexity can be unpacked in terms of the degree to which a problem is dynamic, multicausal, and manifests

idiosyncratically. For example, obesity is dynamic, in that a person's weight fluctuates; it is multicausal as a variety of factors influence a person's weight in any given moment [115]. Further, while universal mechanisms, such as energy balance, exist, how these mechanisms manifest is idiosyncratic (e.g., each person "eats less" differently based on issues like food preference, culture, and availability). These three factors (dynamic, multicausal, and idiosyncratic) are orthogonal; the more each is true, the more likely there will be a need for complex interventions and, by extension precision health. And, as an aside, the less complex a phenomenon is, the less likely precision health is needed. As discussed above, only now are the technologies, frameworks, and methods being developed to match the complexity of some of our most intractable health issues.

Prior work on tailoring [22] provides a solid foundation both conceptually and methodologically. Tailoring is defined as:

Any combination of information or change strategies *intended to reach one specific person*, based on characteristics that are unique to that person, related to the outcome of interest, and have been *derived from an individual assessment*. [Note, italics were in the original].

Prior work offers distinctions in types of interventions from generic [22] and targeted [22] to adaptive [116] interventions (see Table 1), which exist on a continuum. The distinctions are illustrative and particularly valuable from the perspective of precision health. Briefly, targeted interventions support matching based on relatively static traits, such as demographics or personality characteristics. Empirical work about moderation from factorial trials or RCTs is needed to generate evidence-based targeting interventions. Adaptive interventions support dynamic decision-making of match over time with the adaptation algorithms generated based on insights from prior individuals from previous studies. Developing evidence-based adaptive interventions can use moderation, rigorous empirical testing of decision rules, as in SMART, or time-varying moderation related to when/where an intervention component may produce desired effects versus not, which can be gleaned from microrandomization trials, as illustrated with the *HeartSteps* study. Arguably, most precision medicine efforts focus on targeted interventions only and do not leverage methods, such as SMART and microrandomization trials, for optimizing intervention packages and stepped-care decision-making. Because behavioral scientists have addressed these complexities, they can play a leadership role in creating targeted and adaptive interventions.

Work on JITAIs [105, 106] and individualized and perpetually adapting behavioral interventions driven by control systems engineering methods [70] provide a conceptual and methodological foundation for a new class of interventions, continuous-tuning interventions (see Table 1). While the definition of tailoring emphasizes providing the right strategies of change for an individual, methodologically, adaptive interventions select options based on responses from prior individuals in previous studies, not the individual themselves. Continuous-tuning interventions can technically achieve the logical extreme of evidence-based tailoring to a specific individual, which was postulated by Kreuter [22]. By continuous tuning, we mean interventions that adjust and "tune" the intervention to the changing needs of individuals, based on their own data, not merely prior participants' responses to interventions.

The key distinction between adaptive and continuous-tuning interventions is how data are used to define adaptation over time. Adaptive interventions are driven by prespecified adaptation algorithms generated and evaluated based on the response of prior individuals. For example, the Extending Treatment Effectiveness of Naltrexon (ExtEND) study, which used a SMART design to test a decision rule, produced an if/then algorithm to guide adaptation for when individuals are nonresponders to first-line treatment (i.e., if a person does not respond to first-line support of Naltrexon + medical management within 8 weeks, then provide more-intensive behavioral treatment, as second step response [108]). Adaptive interventions are valuable for providing a "warm start" initial decision when no data about a specific individual's response is available. However, once data from an individual are available, it becomes possible to go beyond warm start decisions and deploy continuous-tuning techniques and deliver interventions based on the individual's own data. Specifically, continuous-tuning interventions include *real-time optimization algorithms*, which can further adjust intervention support to a specific individual, using methods such as reinforcement learning [117] control systems engineering [70, 75], and *N-of-1* study methods [94]. An example is MyBehavior [117], which used reinforcement learning to identify and deliver message types a person actively responded to instead of messages the person tended to ignore.

Continuous-tuning interventions match the dynamic, multicausal, idiosyncratic complexities of behavior change and health far more effectively than prior work. For example, the previously discussed study to improve steps per day among adults [74] illustrated the potential for tailoring variable mismatch for 75% of the sample if using aggregate-based statistics (i.e., those used for generic, targeted, and adaptive interventions) compared with individual-derived tailoring variable (i.e., used for continuous tuning). A recent paper examining six studies

Table 1. Summary of four types of interventions to support tailoring

Intervention classes			
	Generic	Targeted	Adaptive
Frequency of intervention selection	Single selection, based on inclusion/exclusion criteria or clinical expertise	Single selection, based on status of moderator variable	Repeated selection
Relevant experimental designs	RCTs and FTs	RCTs and FTs with moderation hypotheses specified a priori	MRT + RL, COT
How are data from prior participants from prior studies used?	Intervention chosen based on main effect estimates of prior clinical trials; selection based on inclusion/exclusion criteria	Intervention chosen based on results from moderation tests from prior clinical trials	Insights from prior studies used as a “warm start” for identifying plausibly meaningful intervention component type, frequency, dosing, or adaptation algorithms
Targeted insights from studies conducted with prior individuals, to inform the intervention class	If the intervention produces a statistical and clinically meaningful effect compared with a meaningful control	If the intervention, for a subgroup as specified via a baseline variable as a moderator, produced a statistical and clinically meaningful effect among the subgroup	For MRT + RL, if an intervention option produces a meaningful effect within a particular state of the person, as defined by time-varying moderation variables; for System ID/COT, if a dynamical model can be produced that is sufficiently stable and predictive of an individual’s future states, to inform plausible future dynamical models of individuals that can be selected at baseline as a “warm start” model
How data from the current participant is used to select the intervention?	Data related to inclusion/exclusion criteria are used to select the intervention	Baseline data previously shown as a reliable moderator are used to select, at one time point, one intervention over another	Via MRT + RL, same points as MRT described for adaptive plus current data on a person’s ongoing responsibility to an intervention is used to adjust the probability with which a person receives an intervention type, frequency, or dose; intervention type, frequency, or dose that a person responds more favorably to are selected more often; Via a COT, same as system ID, described in adaptation + intervention option selection is based on simulated predictions of future responses of a person based on a dynamical model generated for each person, coupled with a controller “closing the loop” to drive adaptive decision-making

COT control optimization trial; FT factorial trial; MRT micro-randomized trial; RCT randomized controlled trial; RL reinforcement learning; SMART sequential multiple assignment randomized trial.

that used a repeated measures design (what we have been calling time series data) suggested that insights gleaned by aggregating across groups versus individuals was very different [118], establishing that it is not necessarily appropriate to generalize insights gleaned from a group to an individual.

Social and behavioral scientists are uniquely suited to drive application of continuous-tuning interventions within precision health. We can advance continuous tuning by:

- 1) Increasing the collection of time series data (i.e., same variables measured repeatedly, ideally multiple variables across the determinants of health).
- 2) Using small data/*N*-of-1 study designs and idiographic data analytic methods to glean insights from time series data to move beyond warm start decisions, particularly microrandomization trials + reinforcement learning, control engineering methods, and *N*-of-1 study designs (see [94, 119, 120] for similar calls to action).
- 3) Cultivating partnerships with researchers with expertise in these analytic methods, particularly control systems engineers, computer scientists, and statisticians working on idiographic data analyses [119, 120].

Integrating Research into Practice

Precision health challenges the basic assumption that research and practice should remain separate. The National Research Council report actively called for the integration of research and practice [23] such as through

learning healthcare systems [8]. Scientifically, the advantage of integrating research into practice is to speed the pace of learning, such that health sciences can more quickly contribute to improving care. Practically, precision health will only be valuable if it can be advanced equitably. One could easily imagine top-tier research institutions making rapid advancements in precision health that, because of the individuals who have access, contexts they exist within (e.g., wealthier neighborhoods), and resources available to the institution, are difficult, if not impossible to implement elsewhere. To be of value, precision health must be prioritized among underresourced settings for underserved, marginalized, and rural populations. Doing this will very likely require respectfully and ethically integrating research within practice, particularly with the communities being served playing coleadership roles if we wish to advance precision health (a point we return to in the challenges section).

Two tasks to advance integration will involve aligning goals and realigning cultures. For the former, the social and behavioral sciences have a robust science to build on. For the latter, the social and behavioral sciences can facilitate the transition by using methods such as community-based participatory research [121, 122] and capacity building as well as insights from sociology to equitably cultivate productive shifts in belief systems, cultural norms, and embedded worldviews engrained in disciplines and communities of practice.

Starting with goals, research classically seeks generalizable knowledge first, with the hope that this will eventually translate into helping future people. Practice, in contrast, is focused on the people who need support right now, including people helping themselves. As such,

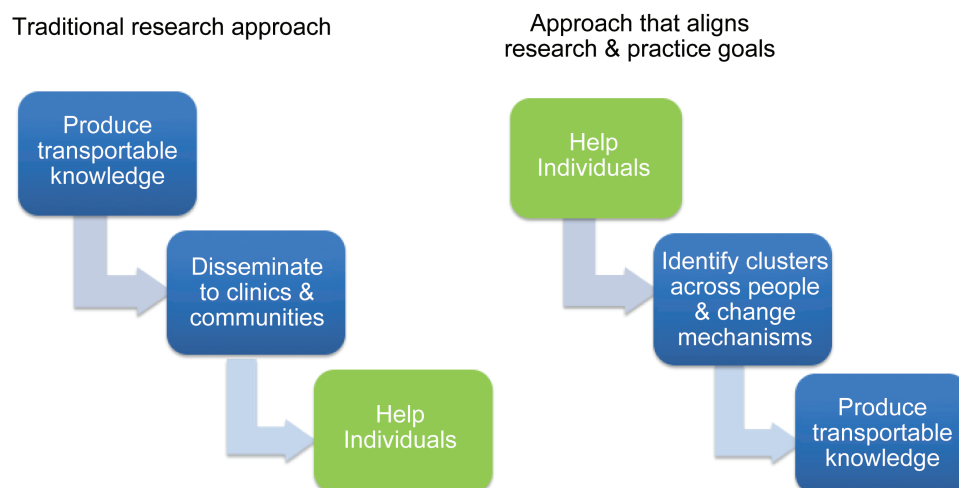


Fig. 2. Two pathways to generalizable/transortable knowledge. The above visualizes two pathways to generalizable (labeled “transportable”) knowledge. The left pathway is the traditional research approach, which starts with generalizable knowledge as the target. The right pathway is an alternative strategy, which would enable better alignment of initial goals between research and practice. Image from Hekler et al. [94].

research and practice share the same broad goals, but research supports that goal in a delayed fashion.

The implied pathway whereby research translates eventually into helping individuals involves three broad steps (Fig. 2, left side pathway [94]). First, research is conducted to produce generalizable knowledge relevant to clinical practice (e.g., intervention A, on average, influences outcome B for population C, in context D). These results enable the creation of “evidence-based” interventions and, ideally, insights about how they “work” in general. With this evidence base, the second step of translation can occur, whereby the intervention is disseminated and implemented in similar contexts compared with where the intervention was studied. Assuming successful implementation, these evidence-based practices can produce meaningful real-world results (step 3). This pathway hinges on the assumption that differences between people and contexts are only minimally important for the translation of evidence-based interventions into practice. When that is true, the process works well (e.g., matching blood transfusions to different blood types). However, for complex behaviors and health phenomena, differences between people and contexts can very likely influence if an intervention will produce desired effects or not. Therefore, the three steps for translating research to practice may not be appropriate for some types of interventions, particularly those targeting complex phenomena, as argued by implementation science. Indeed, the entire field of dissemination and implementation science is a response to this problem as it investigates intervention adaptations to context to explain why real-world results vary [78].

One alternative pathway is to embed research into practice, by aligning research and practice goals initially and then enabling researchers to build on top of that foundation (Fig. 2, right side pathway [94]). In brief, both research and practice could start with the goal of helping individuals, groups, and communities first. This is similar to “positive deviant” research [123–125] whereby those individuals or groups who are achieving meaningful success are carefully monitored and documented, with those insights used to guide future work for others. This approach also aligns very well with continuous-tuning interventions as, ultimately, continuous-tuning interventions are adjusting to each individual’s need, just like in practice [94]. As clinically meaningful results are produced, the second step can occur whereby researchers use methods from machine learning and statistics to cluster intervention and intervention components that produce favorable effects in relation to differences in people, place, and time. With sufficient clusters of successful interventions identified across different people and contexts, causal hypotheses about matching different interventions to different people or contexts can then occur. Using the emerging science of causality [126, 127],

systematic tests of the transportability of findings from one group or context to the next can take place, thus producing generalizable knowledge. While only a concept, the alternative pathway illustrates a viable, complementary approach to generalizable knowledge that would align early efforts of researchers, patients/people, and practitioners as everyone would be seeking to achieve meaningful, real-world outcomes for the people being supported right now.

Beyond advancing methods that enable goal alignment, the social and behavioral sciences can play a role in shifting the cultures of practice and research toward a more equitable and inclusive and also open and transparent process that honors the value and insights from all stakeholders in medicine, population health, and public health. Patient-centered outcomes research [128], community-based participatory research [121, 122], youth participatory action research [129], lead user innovation [130], participatory design, and citizen science [131], all establish the foundational importance of those people being served by science being given voice and coleadership roles within research endeavors.

This also points to the opportunity to broaden conceptualizations on who can act as a scientist and how their voices can be meaningfully integrated into scientific discourse. The work of Eric Von Hippel [130] on “lead user innovation” illustrates a long history of those with lived experience coupled with technical expertise solving their own problems. The movement of self-innovation is being applied in the health domain across biological to behavioral to social and environmental determinants of health [132–135]. It is quite plausible that finding ways to meaningfully include those with lived experience into scientific discourse will strengthen the trustworthiness of any consensus that emerges on the topic [94] and the degree to which scientific priorities align with the priorities of the people being served.

The social and behavioral sciences, with its long history in single case experimental designs (for aligning goals and supporting the alternative pathway), community-based research (for building inclusive cultures), and capacity to work and think at multiple levels of the social ecological model, can play a critical role in helping to explore new approaches to science that better align efforts of research and practice and facilitate more inclusive cultures of diverse stakeholders. While there are many plausible next steps, three concrete ones could be:

- 1) Embed research within real-world contexts of practice. This would involve first, aligning the goals and success criteria of researchers and practitioners. Second, the use of time series data (as discussed with continuous-tuning interventions) as one key referent to evaluate progress toward desired success criteria. Third, the use of more advance methods,

research frameworks, and methods that support this type of work. In light of the high risk of propagating inequities if poorly implemented, it is essential that precision health research be conducted with historically marginalized communities first, instead of high resource settings. If that does not occur, it is quite likely that precision health will exacerbate inequities.

- 2) Expanding patient/participant-centric efforts to include patient-led research and innovation, with the goal of developing understanding on how nontraditional scientists with lived experience of a phenomena could meaningfully add to scientific discourse and reallocating research resources to support these types of contributors.
- 3) Advancing “deimplementation” efforts to enable more stakeholders (e.g., clinicians, people formerly known as patients) the time and energy to reflect, cultivate community-academic partnerships that support patients, care for all stakeholders, and provide insights needed to integrate more of a research mindset into practice.

Mechanistic Science in Real-World Contexts

As implied by the classic separation between research and practice, the health sciences, broadly, balance two separate but complementary goals; to improve: (a) understanding of fundamental determinants of health; and (b) individual and population health. These two goals have been separated in the past with “basic” science occurring, often in labs and controlled settings, and “applied” science seeking to translate insights into real-world impact. It is quite likely that differences in people, place, and time matter causally, for a wide range of complex health phenomena, such as obesity. The more likely that a phenomenon is causally complex, the less likely anything meaningful can be learned about mechanisms and determinants of health within lab-based “basic science” studies, which would lack variance on differences in people, place, and time. Based on this and the need to match interventions with underlying determinants of health, there is a need for a third type of research within precision health; what we call mechanistic science in real-world contexts.

Mechanistic science in real-world contexts primarily involves a change in study goals to those that explicitly seek to advance both practical goals and mechanistic science goals simultaneously. Interventions, particularly intervention component(s), play a dual role; they can be used to support individuals to improve health outcomes and, simultaneously, these interventions could be thought of as experimental manipulations meant to activate hypothesized mechanisms of change for

influencing fundamental determinants of health. If the dual purpose of interventions is recognized, then single research studies can be designed that explicitly advance these dual purposes and, thus, enact mechanistic science in real-world contexts. Arguably, the dual role is implicitly present when evaluating pharmaceuticals within double blind RCTs because the RCTs provide a clear and robust isolation of the mechanistic impact of the pharmaceutical agent upon targeted health outcomes. Pharmaceuticals have had a distinct advantage, scientifically, based on the power of the placebo as a control condition to enable studies to inform the basic understanding of a phenomenon while also informing clinical decision-making and practice. As such, for pharmaceuticals only, one could think of classic RCTs as mechanistic science in real-world contexts. Within the social and behavioral sciences, the placebo is often not an appropriate control condition [136]. With new technologies and methods, the social and behavioral science can begin to localize effects in contexts to support both clinical decision-making and mechanistic science (see earlier discussion of HeartSteps microrandomization trial in the methods section, which illustrates this possibility).

Next steps include:

- 1) Increased focus on advancing digital phenotypes of social and behavioral constructs [33, 34, 137, 138] to enable measurement of mechanisms and determine if interventions are activating mechanisms in context, per the SOBC approach.
- 2) Increased use of appropriate research methods, particularly factorial trials, SMART, microrandomization trials, system identification, and control optimization trials [70] should occur as they enable far more localized conclusions about intervention components and dosing in context [84].
- 3) As the causal complexity of a phenomenon increases, the behavioral science community will likely need to adopt techniques from the emerging science of causality [126, 127]. The science of causality enables far more complex causal models to be specified in an empirically testable fashion compared with traditional health sciences, which, within clinical evaluation studies, implicitly biases toward simple causal linkages (e.g., intervention X → outcome Y).
- 4) It would be valuable to advance research frameworks that honor and advance these dual roles, such as a research framework that melds MOST and SOBC.

Summary of Opportunities and Next Steps

The vision of precision health, as outlined in Fig. 1, is broad and will require robust collaboration and

synergistic activities across diverse stakeholders. The social and behavioral sciences are well suited to:

- 1) drive advancement of an emerging new class of intervention, continuous-tuning interventions, in partnership with control systems engineers, computer scientists, and statisticians advancing idiographic methods.
- 2) facilitate shifts in methods and cultural norms that better align research and practice to enable more equitable, rapid, iterative, and efficient learning across stakeholders and to increase the likelihood that precision health can be used to reduce disparities, not increase them.
- 3) conduct mechanistic science in real-world context, with increased use of more advanced study designs that enable localized effect estimates of intervention components and, likely, in partnership with those advancing the science of causality, the study of causally complex health phenomena.

Challenges to Precision Health and Ways the Social and Behavioral Sciences Can Help

The vision of precision health introduces three challenges (see bottom of Fig. 1) briefly summarized as: (a) knowledge organization and curation, (b) ethical implications, and (c) inequitable implementation.

Knowledge Organization and Curation Challenges

Accumulation of precision health research will fundamentally change how we organize and find relevant information. Presently, scientific knowledge is largely organized and digested via scientific articles. Searching the literature successfully may have occurred when a person paid attention to a few key journals on focused topics [139]. Precision health synergizes efforts across a wide range of stakeholders, which makes the classic strategy of staying informed untenable. For example, the same scientific study would be described very differently depending on the publication venue it is presented within, be it medicine, psychology, computer science, control engineering, and so forth. Interdisciplinary teams increasingly publish across these diverse publication venues. Depending on the discipline and venue, the insights offered will be accessible to one audience (e.g., computer science) but not others and, by extension, may not be immediately found by other audiences (e.g., behavioral science). If the goal of precision health is to integrate medicine, population health, and public health, and research and practice, then new forms of information

sharing are needed that supports translation between groups.

While, of course, scientific articles will always have value for sharing information within scientific communities, other forms of knowledge organization and curation are necessary for communicating information and tools that will be necessary for precision health. One concept is development of codifiable knowledge representation tools that can effectively search, organize, and curate large amounts of information to facilitate translation of evidence and insights gleaned from one discipline or stakeholder to another discipline or stakeholder [139]. Without innovative tools to support cross-sector and disciplinary access and curation, the vision of precision health may become a proverbial Tower of Babel that is largely inaccessible and, therefore, of questionable value. Organizing and curating knowledge as complex as that associated with precision health is no small task with no simple answers. Space precludes a full discussion, but interested readers looking for steps forward could review the Human Behaviour Change Project out of University College London [140] and results from a recent National Science Foundation workshop in the USA focused on advancing knowledge curation in the social and behavioral sciences [139].

Ethical Challenges

The new technologies, frameworks, and methods supporting precision health research require careful consideration of the ethical, regulatory/legal, and social implications (ELSI) throughout the process. The accepted ethical principles of respect for persons, beneficence and justice, first published in 1979 [141], have provided a useful framework to assess whether the research will generate knowledge and, subsequently benefit society—but, whether they remain comprehensive and relevant is in question. For example, the emerging and widespread change in the research enterprise introduced by information and communication technologies prompted leaders in the Department of Homeland Security to propose an additional principle of respect for law and public interest [142]. As precision health advances, it is critical that social and behavioral scientists are supported to carry out research to qualify and quantify related risks and risk management strategies, including barriers to informed consent and accessibility. In Table 2, we suggest research questions against the backdrop of current ethical principles described in the Belmont Report.

The novelty of emerging technology, methods and tools associated with precision health naturally draws diverse stakeholders who are learning to work together. Over the past decade, we have seen a rise in patient-initiated research [143], citizen science [144],

Table 2. Recommendations for research on research ethics

Principle	Application	Considerations for precision health research
Autonomy, respect for persons	The process of obtaining study information to facilitate decision-making Used to document voluntary participation Protect persons who have diminished capacity to make decisions	Are digital strategies for conveying study information appropriate? Do participants understand the granularity and volume of data collected? Is the consent content and process appropriate for people with limited technology and data literacy? What consent process is useful for an <i>N</i> -of-1 study
Beneficence	Evaluation of the probability and magnitude of potential harms to participants Assessment of risks and mitigation strategies against potential benefits to the individual, persons represented by participants and society	What data management strategies (wireless transmission, encryption, etc.) are appropriate to ensure confidentiality of potentially sensitive digital data? What system-wide strategies are effective in capacity building? When data are obtained using commercial products, what terms of service and privacy protections are appropriate? Does the technology have sufficient evidence to support the use of the device/app?
Justice	Persons who participate should reflect those most likely to benefit from the study outcomes Considerations for vulnerable populations	What potential barriers to study access exist in digitally deployed studies? What methods increase participant representation and involvement as partners? Do preferences for privacy vary across lifespan or groups identified as underrepresented in research?

and Do-it-Yourself [DIY] [145] types of research. Major technology companies have launched large-scale, longitudinal bio/behavioral research initiatives (e.g., Apple ResearchKit, Alphabet's, Verily, and Microsoft Research). All conceivably fall within the continuum of precision health, but project staff may vary considerably in terms of their formal research training and ethics socialization, requiring that experts be identified to fill the governance gaps [146].

New tools combined with variable ethics acculturation may place strain on the traditional institutional review board (IRB) model [147]. The IRB model, while an essential perspective in human research protections, has been criticized in recent years [148–150] for being inefficient and focused more on institutional protections over that of participants. With precision health research, IRBs must be able to evaluate several risk-to-benefit profiles as well as a diverse set of tools, methods, and stakeholders. Clearly, resources are needed to support risk-to-benefit assessments and mitigation strategies, which will assist those planning safe and ethical research as well as those responsible for its review.

Related to the diversity of tools and methods used in precision health, we have acknowledged the ability to collect and combine granular multidimensional data from genetic, behavioral and environmental sources. How people consent to participate as well as how these data are collected, transferred, secured, and shared are, in some cases governed by regulations (i.e., Office of Human Research Protections [OHRP] [151], Health Insurance Portability and Accountability Act [HIPAA] [152]) yet, there are regulatory gaps. For example, a

behavioral intervention carried out in a free-living environment using real-time using pervasive sensors (e.g., Fitbit) and/or social media platforms (Facebook [153]) lack clear guidelines for deploying these interventions. Regardless of the health focus of the research (e.g., HIV, healthy pregnancy, sedentary behavior) the data collected may not be part of the participant's health records and, as such, neither HIPAA nor Health Information Technology for Economic and Clinical Health Act (HITECH) regulations [154] may be relevant. Researchers and IRBs have little guidance on how to manage consent, expectations for privacy nor strategies to reduce risks of a data breach. When using commercial products, potential risks are introduced when the quality of the device or app is unknown, the participant does not use the technology correctly or the data are owned by commercial entities. These complexities may not be well understood by IRB members and, lacking relevant expertise, can lead IRBs to a determination that a proposal is acceptable, not based on a careful understanding of risk. Alternatively, IRBs may reject a new and potentially fruitful line of research by applying standards from noncomparable research or fear of the “unknown unknowns” and, thus squelching innovation.

In addition to the fact that no one IRB member has all the requisite knowledge, ever-changing technologies may create potential harms that were not present or known when a project first starts, out of no fault, conscious action, or even awareness of the researcher. Clearly, we are at a critical juncture whereby social and behavioral scientists must continue to play an important role in development of responsive ethical guidelines. This will

involve conducting empirical research to inform how best to obtain informed consent, calculate study benefits and harms and promote inclusivity such that the research is translational to practice (see [Table 2](#)). Likewise, new models that authentically engage and promote community input are necessary, as we can no longer afford to “outsource” ethics and hope for the best. All precision health stakeholders must be actively involved in shaping responsible practices.

Initiatives that can support a broader precision health “ethical intelligence” are beginning to emerge. For example, the Connected and Open Research Ethics (CORE) initiative is a digital health ethics “learning” commons where conversations about the ethical issues noted above take place [[155](#)]. The CORE platform, developed with support of the Robert Wood Johnson Foundation (RWJF), was designed with input from scientists, technologists, regulators, and ethicists [[156](#)]. Features include a forum where community members can post questions and offer expertise, a Resource Library that includes IRB-approved protocols and consent language and evidence-based Tools to support decision-making [[157](#)]. There are other efforts underway to provide ethical guidelines for areas such as unregulated research by citizen scientists or data scientists in industry [[158–160](#)]. Further, professional societies are launching efforts to elevate awareness of the ELSI of precision health research to support members [[161](#), [162](#)].

Given the potential personal and societal value of precision health, empirical research can inform responsive standards of practice to ensure meaningful outcomes. Social and behavioral scientists are already conducting studies to better understand aspects of research that impact scientific integrity and, subsequently research ethics. For example, researchers are evaluating wearable sensors to ensure they are measuring what they claim to measure [[163](#)]. Likewise, studies are using wearable sensor technologies to gather “in the wild” behavioral data as an alternative to self-report and lab-centered studies [[164](#)] and researchers are also looking at adoption barriers [[165](#)], which can influence data fidelity and inclusion of diverse populations.

Inequitable Implementation Challenges

Implementation science can help assure that precision health efforts are adopted into routine healthcare across diverse settings and do not propagate health disparities. The latter is of particular risk in the USA because of our fragmented network for financing and delivering healthcare that constrain individuals’ ability to access healthcare resources. For precision health, disparities may occur if particular geographic areas are able to deliver precision health initiatives better than others (e.g.,

urban vs. rural); similarly, disparities by socioeconomic status and race/ethnicity may result if healthcare systems and communities serving the poor and uninsured (i.e., safety-net providers) struggle to implement precision health efforts [[166](#)].

In past decades, patients, providers, health systems, community organizations, and policymakers, have often been unprepared when interventions were deployed in real-world settings because factors necessary to systematically deploy these interventions had not been tested. Recognizing the implementation gap, social and behavioral scientists have developed new tools, including theories and frameworks [[167](#)], measures, strategies to balance implementation fidelity with the need for adaptability, and new study designs like hybrid effectiveness–implementation designs [[168](#)]. To avoid propagating disparities, we illustrate below how implementation science research needs to address: (a) valid measurement of individual-reported risk factors; (b) patient-centered and public health communication; (c) building capacity of healthcare provider teams, low-resource healthcare settings, and policymakers; and (d) reach of these new precision health approaches across diverse settings.

Putting precision health interventions into practice will require that individuals/patients and healthcare teams measure and document individual-risk factors to deliver the right treatment, at the right time, to the right individuals or local communities. Measuring risk factors often relies on patient self-report, which can present challenges in obtaining valid and reliable measures [[169](#), [170](#)]. Further, accuracy of self-report measures may vary across subgroups; some have shown lower sensitivity and specificity estimates for racial and ethnic minorities [[171](#)]. Many have recognized that individuals’ education, literacy, culture, and past experiences influence how they respond to risk factor measures [[172–174](#)]. Strategies like cognitive interviewing [[175](#)] and other psychometric methods will be needed to ensure that these measures are conceptually equivalent (e.g., interpreted similarly) by different subgroups. Incorporating validated measures into existing electronic patient portals and population-based health surveillance systems (e.g., Behavioral Risk Factor Surveillance System) can improve reporting of risk factors at the health system and community-level (see extended discussion in *Capturing Social and Behavioral Domains in Electronic Health Records, Phase 2* [[176](#)]). In addition, recent efforts to advance digital phenotyping may enhance and complement self-reported measures [[33](#), [138](#)]. Identification of particular geographies with large numbers of individuals at risk can inform the planning of policies supporting precision health interventions. Integrating validated measures into clinical information and population surveillance systems will be critical.

After obtaining reliable risk information, patient-centered communication and shared decision-making will be essential for delivering precision health interventions. Treatment recommendations are likely to become more complex and challenging for individuals with low health literacy to understand and enact, which may increase health disparities. We will need innovative strategies to instruct and assess providers' communication skills particularly with respect to precision health [177]. Similarly, we will need to develop health communication strategies to explain to policymakers and the public about genetic, behavioral and environmental risk factors and the evidence supporting precision health interventions. Clear communication can help policymakers design policies ensuring interventions reach all who could benefit, and the public recognize the value of interventions; thus, be willing to use the interventions (see [178] for implementation challenges in lung cancer screening). Future precision health initiatives should involve implementation scientists early in the intervention development process to ensure fit with the environmental context and improve the quality of care.

We must also build capacity to support delivery of precision health interventions particularly in low-resource healthcare settings. Delivery cannot solely rest on the shoulders of physicians, given the large number of topics that must be covered during a primary care visit [179]. Multidisciplinary teams have been shown to improve the efficiency and effectiveness of cancer care delivery [180–183]. Important considerations include the roles and responsibilities of team members, coordination among team members, and necessary resources and support. Fortunately, midlevel providers, such as physician assistants, nurse practitioners and navigators, genetics counselors, and case managers, may be just as well equipped to help deliver these services as physicians. Tools embedded within electronic health records can assess individual-risk factors to: (a) facilitate identifying eligible patients; (b) provide clinical decision support concordant with guidelines; (c) document provider recommendations and patient decisions; and (d) track management of results and health outcomes. Ensuring electronic health records systems have these capabilities will be imperative to prevent disparities when deploying precision health interventions [184–186].

Application of models like the Consolidated Framework for Implementation Research [187] highlight that the range of stakeholders should be expanded beyond healthcare providers and include government agencies, nonprofit community organizations, faith-based organizations, and other groups involved in case management. Attention to the social determinants of health by these stakeholders can illuminate the larger societal context that hinders effectiveness of interventions. To

call attention to this issue, the RWJF created a research initiative on how organizations, institutions, and leaders outside of healthcare systems can collaborate and build a national culture of health. To avoid exacerbating disparities, precision health research needs to use models that describe how upstream determinants may support or undermine precision health interventions and how various sectors of society could collaborate to deploy strategies addressing these upstream determinants.

As one final note on implementation, it is important that anyone interested in precision health think through the intended and unintended consequences of this work. For example, shifting toward precision health could be highly disruptive to a wide range of people and health sectors. Based on this, it is important to think carefully on when and where it is most appropriate to advance precision health versus not. One key consideration is the inherent complexity of the phenomenon being targeted. Precision health will only really be needed and appropriate for complex health issues, such as obesity. Beyond complexity, inequities should also be considered. We contend that the benefits would be greatest and, thus, likely be worth the disruption, if historically marginalized communities were prioritized over more well-resourced areas as a mechanism to reduce inequities. That said, that type of work should only be done when historically marginalized groups agree and play coleadership roles in advancing the vision. Precision health will fully and equitably realize its potential only if the right intervention is effectively delivered to all population members who would benefit. Engagement of social and behavioral scientists with expertise in implementation science research can ensure broad, equitable reach.

Summary and Next Steps

Precision health is an ambitious conceptualization of health, which includes dynamic linkages between research and practice as well as medicine, population health, and public health. The goal is a unified approach to match a full range of health promotion, prevention, diagnostics and treatments to fundamental and actionable determinants of health that cut across genetic, biological, environmental, *and* social and behavioral determinants (see Fig. 1). The research necessary to advance precision health requires the social and behavioral sciences to take part alongside others.

As with the history of precision medicine, new technologies, frameworks, and methods are enabling new ways to measure and intervene in real-world contexts. With these technologies, frameworks, and methods, the next generation of social and behavioral sciences offers

three opportunities to help lead in precision health: (a) a new intervention type, continuous-tuning interventions, that match the inherent complexity of some behavioral and health phenomena; (b) strategies to integrate research into practice that enable more efficient, iterative learning across stakeholders interested in health; and (c) conducting mechanistic science in real-world contexts that supports improved understanding of underlying determinants of health. While there is great excitement, there are also challenges to precision health that the social and behavioral sciences could mitigate: (a) knowledge organization and curation; (b) ethical conduct of research; and (c) equitable implementation of the vision. For those places where the benefits overcome the disruptions, social and behavioral scientists working in the health sector can help to ethically and responsibly advance precision health with others.

Acknowledgments The content is solely the responsibility of the authors and does not necessarily represent the official views of the Office of Behavioral and Social Science Research, the National Institutes of Health, or the U.S. Department of Health and Human Services. This manuscript grew out of a debate that occurred at the Society of Behavioral Medicine’s annual conference in 2017. The authors thank the Theories and Techniques in Behavior Change Interventions SIG for organizing the event and for Dr. Alex Rothman for providing support on organizing the paper. The authors also thank Dr. Jerry Suls for meaningful review and contribution to earlier drafts of this manuscript as well as Drs. Kevin Patrick and Susan Michie for informing this manuscript. Thank you, also, to Drs. Coleen McBride and Matthew Kreuter, for reviewing a draft of this manuscript and providing feedback.

Funding: Tiro supported by the National Cancer Institute (2P30CA142543-08). E.H., C.N., and C.M.H., have no financial support to disclose.

Compliance with Ethical Standards

Authors’ Statement of Conflict of Interest and Adherence to Ethical Standards Authors Eric Hekler, Jasmin A. Tiro, Christine M. Hunter, and Camille Nebeker declare that they have no conflict of interest.

Authors’ Contributions E.H., J.T., C.H., and C.N. made substantial contributions to conception of the paper, participated in drafting the article, critically revised the intellectual content, and approved the final version.

Ethical Approval This work did not require a review/approval from an ethics board.

Informed Consent No human participants were involved in this study.

References

- Collins FS, Varmus H. A new initiative on precision medicine. *N Engl J Med*. 2015;372:793–795.
- Lee J, Hamideh D, Nebeker C. Qualifying and quantifying the precision medicine rhetoric. *BMC Genomics*. 2019;20:868.
- Fradkin JE, Hanlon MC, Rodgers GP. NIH Precision Medicine Initiative: implications for Diabetes Research. *Diabetes Care*. 2016;39:1080–1084.
- Vaithinathan AG, Asokan V. Public health and precision medicine share a goal. *J Evid Based Med*. 2017;10:76–80.
- Arnett DK, Claas SA. Precision medicine, genomics, and public health. *Diabetes Care*. 2016;39:1870–1873.
- Yanovski SZ, Yanovski JA. Toward precision approaches for the prevention and treatment of obesity. *JAMA*. 2018;319:223–224.
- Akdis CA, Ballas ZK. Precision medicine and precision health: building blocks to foster a revolutionary health care model. *J Allergy Clin Immunol*. 2016;137:1359–1361.
- Chambers DA, Feero WG, Khoury MJ. Convergence of implementation science, precision medicine, and the learning health care system: a new model for biomedical research. *JAMA*. 2016;315:1941–1942.
- Dolley S. Big Data’s role in precision public health. *Front Public Health*. 2018;6:68.
- Dorsey SG, Resnick BM, Renn CL. Precision health: use of omics to optimize self-management of chronic pain in aging. *Res Gerontol Nurs*. 2018;11:7–13.
- Gambhir SS, Ge TJ, Vermesh O, Spittle R. Toward achieving precision health. *Sci Trans Med*. 2018;10(430): e3612.
- Gillman MW, Hammond RA. Precision treatment and precision prevention: integrating “below and above the skin”. *JAMA Pediatr*. 2016;170:9–10.
- Kellogg RA, Dunn J, Snyder MP. Personal omics for precision health. *Circ Res*. 2018;122:1169–1171.
- Khoury MJ, Galea S. Will precision medicine improve population health? *JAMA*. 2016;316:1357–1358.
- Khoury MJ, Iademarco MF, Riley WT. Precision public health for the era of precision medicine. *Am J Prev Med*. 2016;50:398–401.
- Riveroll A, Thompson K, Robertson K, Salijevec A, Montelpare W. Precision health: a personalized approach to active health management. *CMBES Proc*. 2018;41:1–5.
- Kindig D, Stoddart G. What is population health? *Am J Public Health*. 2003;93:380–383.
- Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn’t. *BMJ*. 1996;312:71–72.
- England NHS. Improving outcomes through personalised medicine. 2016. Available at <https://www.england.nhs.uk/wp-content/uploads/2016/09/improving-outcomes-personalised-medicine.pdf>. Accessibility verified January 5, 2020.
- Leighl NB. Treatment paradigms for patients with metastatic non-small-cell lung cancer: first-, second-, and third-line. *Curr Oncol*. 2012;19:S52–S58.
- Noar SM, Benac CN, Harris MS. Does tailoring matter? Meta-analytic review of tailored print health behavior change interventions. *Psychol Bull*. 2007;133:673–693.
- Kreuter MW, Skinner CS. Tailoring: what’s in a name? *Health Educ Res*. 2000;15:1–4.
- National Research Council. *Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease*. Washington, DC: National Academies Press; 2011.

24. Roberts D. *Fatal Invention: How Science, Politics, and Big Business Re-create Race in the Twenty-First Century*. New York City, NY: New Press/ORIM; 2011.
25. McBride CM, Graves KD, Kaphingst KA, et al. Behavioral and social scientists' reflections on genomics: a systematic evaluation within the Society of Behavioral Medicine. *Transl Behav Med*. 2019;9:1012–1019.
26. Gakidou E, Afshin A, Abajobir AA, et al. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390:1345–1422.
27. McGinnis JM, Williams-Russo P, Knickman JR. The case for more active policy attention to health promotion. *Health Aff (Millwood)*. 2002;21:78–93.
28. Herbert A, Gerry NP, McQueen MB, et al. A common genetic variant is associated with adult and childhood obesity. *Science*. 2006;312:279–283.
29. Sabatello M, Appelbaum PS. The Precision Medicine Nation. *Hastings Cent Rep*. 2017;47:19–29.
30. Gawer A. *Platforms, Markets and Innovation: An Introduction*. Northampton, MA: Edward Elder Publishing; 2009.
31. Hekler EB, Klasnja P, Riley WT, et al. Agile science: creating useful products for behavior change in the real world. *Transl Behav Med*. 2016;6:317–328.
32. Consolvo S, Bentley FR, Hekler EB, Phatak SS. Mobile user research: a practical guide. *Synth Lect Mob Pervasive Comput*. 2017;9(1):1–215.
33. Jain SH, Powers BW, Hawkins JB, Brownstein JS. The digital phenotype. *Nat Biotechnol*. 2015;33:462–463.
34. National Institutes of Health. Ancillary studies to identify behavioral and/or psychological phenotypes contributing to obesity (R01). Available at <https://grants.nih.gov/grants/guide/pa-files/PAR-18-105.html>. Accessibility verified May 16, 2018.
35. Thomaz E, Zhang C, Essa I, Abowd GD. Inferring meal eating activities in real world settings from ambient sounds: a feasibility study. *IUI*. 2015;2015:427–431.
36. Kumar S, Nilsen WJ, Abernethy A, et al. Mobile health technology evaluation: the mHealth evidence workshop. *Am J Prev Med*. 2013;45:228–236.
37. Kumar S, Nilsen W, Pavel M, Srivastava M. Mobile health: revolutionizing healthcare through trans-disciplinary research. *Computer*. 2013;46:28–35.
38. McGarraugh G. The chemistry of commercial continuous glucose monitors. *Diab Technol Ther*. 2009, 11: S-17–S-24.
39. Canzian L, Musolesi M. Trajectories of depression: unobtrusive monitoring of depressive states by means of smartphone mobility traces analysis. Proc ACM Intern Joint Conf Perv Ubiq Comp (UbiComp), Osaka, Japan; 2015:1293–1304.
40. Saeb S, Zhang M, Karr CJ, et al. Mobile phone sensor correlates of depressive symptom severity in daily-life behavior: an exploratory study. *J Med Internet Res*. 2015;17:e175.
41. Wyatt D, Choudhury T, Bilmes JA. Conversation detection and speaker segmentation in privacy-sensitive situated speech data. In: Wyatt D, Choudhury T, Bilmes JA, eds. *Conversation Detection and Speaker Segmentation in Privacy-Sensitive Situated Speech Data*. Conf Internat Speech Comm Assoc, Antwerp, Belgium; 2007.
42. Choudhury T. Using smartphones to sense, assess, and improve well-being. Proc Workshop on Physical Analytics, Bretton Woods, NH; 2014:1–15.
43. Lu H, Frauendorfer D, Rabbi M, et al. StressSense: detecting stress in unconstrained acoustic environments using smartphones. Proc ACM Conf Perv Ubiq Comp (UbiComp), Pittsburgh, PA; 2012:351–360.
44. Choudhury T, Consolvo S, Harrison B, et al. The mobile sensing platform: an embedded activity recognition system. *IEEE Perv Comp*. 2008;7:32–41.
45. Cattuto C, Van den Broeck W, Barrat A, Colizza V, Pinton JF, Vespignani A. Dynamics of person-to-person interactions from distributed RFID sensor networks. *Plos One*. 2010;5:e11596.
46. Johnson DA, Trivedi MM. Driving style recognition using a smartphone as a sensor platform. 2011 14th International IEEE Conf Intell Transport Syst (ITSC), Washington, DC; 2011:1609–1615.
47. White J, Thompson C, Turner H, Dougherty B, Schmidt DC. WreckWatch: automatic traffic accident detection and notification with smartphones. *Mob Netw Appl*. 2011;16:285–303.
48. Bot BM, Suver C, Neto EC, et al. The mPower study, Parkinson disease mobile data collected using ResearchKit. *Sci Data*. 2016;3:160011.
49. Trister AD, Dorsey ER, Friend SH. Smartphones as new tools in the management and understanding of Parkinson's disease. *NPJ Parkinsons Dis*. 2016;2:16006.
50. Zuckerman I, Cheng K-L, Nau DS. Modeling agent's preferences by its designer's social value orientation. *J Exp Theor Artif Intell*. 2018;30(2):257–277.
51. Estrin D. Small data, where n = me. *Comm ACM*. 2014;57:32–34.
52. Golbeck J, Robles C, Turner K. Predicting personality with social media. Proc SigCHI, Vancouver, Canada; 2011:253–262.
53. Hekler EB, Klasnja P, Traver V, Hendriks M. Realizing effective behavioral management of health: the metamorphosis of behavioral science methods. *IEEE Pulse*. 2013;4:29–34.
54. Pentland A. *Social Physics: How Good Ideas Spread—The Lessons from a New Science*. New York, NY: Penguin; 2014.
55. Zhou MX, Nichols J, Dignan T, et al. Opportunities and risks of discovering personality traits from social media. Proc SIGCHI, Toronto, Canada; 2014:1081–1086.
56. Tausczik YR, Pennebaker JW. The psychological meaning of words: LIWC and computerized text analysis methods. *J Lang Soc Psychol*. 2010;29:24–54.
57. Arigo D, Jake-Schoffman DE, Wolin K, Beckjord E, Hekler EB, Pagoto SL. The history and future of digital health in the field of behavioral medicine. *J Behav Med*. 2019;42:67–83.
58. Collins LM. *Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: The Multiphase Optimization Strategy (MOST)*. New York, NY: Springer; 2018.
59. Chakraborty B, Collins LM, Strecher VJ, Murphy SA. Developing multicomponent interventions using fractional factorial designs. *Stat Med*. 2009;28:2687–2708.
60. Collins LM, Dziak JJ, Kugler KC, Trail JB. Factorial experiments: efficient tools for evaluation of intervention components. *Am J Prev Med*. 2014;47:498–504.
61. Collins LM, Dziak JJ, Li R. Design of experiments with multiple independent variables: a resource management perspective on complete and reduced factorial designs. *Psychol Methods*. 2009;14:202–224.
62. Dziak JJ, Nahum-Shani I, Collins LM. Multilevel factorial experiments for developing behavioral interventions: power, sample size, and resource considerations. *Psychol Methods*. 2012;17:153–175.
63. Almirall D, Nahum-Shani I, Sherwood NE, Murphy SA. Introduction to SMART designs for the development of adaptive interventions: with application to weight loss research. *Transl Behav Med*. 2014;4:260–274.
64. Almirall D, Nahum-Shani I, Wang L, Kasari C. Experimental designs for research on adaptive interventions: singly and

- sequentially randomized trials. In Collins LM, Kugler KC, eds. *Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: Advanced Topics*. New York, NY: Springer; 2018.
65. Collins LM, Nahum-Shani I, Almirall D. Optimization of behavioral dynamic treatment regimens based on the sequential, multiple assignment, randomized trial (SMART). *Clin Trials*. 2014;11:426–434.
 66. Sherwood NE, Butryn ML, Forman EM, et al. The BestFIT trial: a SMART approach to developing individualized weight loss treatments. *Contemp Clin Trials*. 2016;47:209–216.
 67. Klasnja P, Hekler EB, Shiffman S, et al. Microrandomized trials: an experimental design for developing just-in-time adaptive interventions. *Health Psychol*. 2015;34S:1220–1228.
 68. Liao P, Klasnja P, Tewari A, Murphy SA. Sample size calculations for micro-randomized trials in mHealth. *Stat Med*. 2016;35:1944–1971.
 69. Freigoun MT, Martín CA, Magann AB, et al. System identification of Just Walk: a behavioral mHealth intervention for promoting physical activity. 2017 Am Control Con (ACC), Seattle, WA; 2017:116–121.
 70. Hekler EB, Rivera DE, Martin CA, et al. Tutorial for using control systems engineering to optimize adaptive mobile health interventions. *J Med Internet Res*. 2018;20:e214.
 71. Martin CA, Deshpande S, Hekler EB, Rivera DE. A system identification approach for improving behavioral interventions based on Social Cognitive Theory. Am Control Conf (ACC), Chicago, IL; 2015:5878–5883.
 72. Martin CA, Rivera DE, Hekler EB. An identification test monitoring procedure for MIMO systems based on statistical uncertainty estimation. IEEE Conf Dec Control (CDC); Osaka, Japan; 2015:2719–2724.
 73. Martin CA, Rivera DE, Hekler EB. A control engineering approach for optimizing physical activity behavioral interventions. 2016 IEEE Ecuador Technic Chapter Meet (ETCM), Guayaquil, Ecuador; 2016.
 74. Phatak SS, Freigoun MT, Martín CA, et al. Modeling individual differences: a case study of the application of system identification for personalizing a physical activity intervention. *J Biomed Inform*. 2018;79:82–97.
 75. Rivera DE, Martín CA, Timms KP, et al. Control systems engineering for optimizing behavioral mHealth interventions. In: Rehg JM, Murphy SA, Kumar S., eds. *Mobile Health: Sensors, Analytic Methods, and Applications*. Cham: Springer International Publishing; 2017:455–493.
 76. Nielsen L, Riddle M, King JW, et al.; NIH Science of Behavior Change Implementation Team. The NIH Science of Behavior Change Program: transforming the science through a focus on mechanisms of change. *Behav Res Ther*. 2018;101:3–11.
 77. Riddle M; Science of Behavior Change Working Group. News from the NIH: using an experimental medicine approach to facilitate translational research. *Transl Behav Med*. 2015;5:486–488.
 78. Chambers DA, Glasgow RE, Stange KC. The dynamic sustainability framework: addressing the paradox of sustainment amid ongoing change. *Implement Sci*. 2013;8:117.
 79. Rotheram-Borus MJ, Swendeman D, Chorpita BF. Disruptive innovations for designing and diffusing evidence-based interventions. *Am Psychol*. 2012;67:463–476.
 80. Riley WT, Glasgow RE, Etheredge L, Abernethy AP. Rapid, responsive, relevant (R3) research: a call for a rapid learning health research enterprise. *Clin Transl Med*. 2013;2:10.
 81. Czajkowski SM, Powell LH, Adler N, et al. From ideas to efficacy: the ORBIT model for developing behavioral treatments for chronic diseases. *Health Psychol*. 2015;34:971–982.
 82. Michie S, Atkins L, West R. The behaviour change wheel: a guide to designing interventions. *Implement Sci*. 2011;6:42.
 83. Klasnja P, Hekler EB. Wearable technology and long-term weight loss. *JAMA*. 2017;317:317–318.
 84. Klasnja P, Hekler EB, Korinek EV, Harlow J, Mishra SR. Toward usable evidence: optimizing knowledge accumulation in HCI research on health behavior change. Proc SIGCHI Conf Hum Factor Comput Syst, Denver, CO; 2017;2017:3071–3082.
 85. Patrick K, Hekler EB, Estrin D, et al. The pace of technologic change: implications for digital health behavior intervention research. *Am J Prev Med*. 2016;51:816–824.
 86. Mohr DC, Lyon AR, Lattie EG, Reddy M, Schueller SM. Accelerating digital mental health research from early design and creation to successful implementation and sustainment. *J Med Internet Res*. 2017;19:e153.
 87. Collins LM, Kugler KC. In: Collins LM, Kugler KC, eds. *Optimization of Behavioral, Biobehavioral, and Biomedical Interventions, Advanced Topics*. New York: Springer; 2018.
 88. Kravitz R, Duan N, Eslick I, et al. In: A. Publication, ed. *Design and Implementation of N-of-1 Trials: A User's Guide*. Vol. 13. Rockville, MD: Agency for Healthcare Research and Quality; 2014, EHC122-EF.
 89. Schork NJ. Personalized medicine: time for one-person trials. *Nature*. 2015;520:609–611.
 90. Lillie EO, Patay B, Diamant J, Issell B, Topol EJ, Schork NJ. The n-of-1 clinical trial: the ultimate strategy for individualizing medicine? *Per Med*. 2011;8:161–173.
 91. Dallery J, Raiff BR. Optimizing behavioral health interventions with single-case designs: from development to dissemination. *Transl Behav Med*. 2014;4:290–303.
 92. Dallery J, Cassidy RN, Raiff BR. Single-case experimental designs to evaluate novel technology-based health interventions. *J Med Internet Res*. 2013;15:e22.
 93. Ljung L. *System Identification: Theory for the User*. 2nd ed. Upper Saddle River, NJ: Prentice Hall; 1999.
 94. Hekler EB, Klasnja P, Chevance G, Golaszewski NM, Lewis D, Sim I. Why we need a small data paradigm. *BMC Med*. 2019;17:133.
 95. Cui M, Wu X, Mao J, Wang X, Nie M. T2DM self-management via smartphone applications: a systematic review and meta-analysis. *Plos One*. 2016;11:e0166718.
 96. Marcolino MS, Oliveira JAQ, D'Agostino M, Ribeiro AL, Alkmim MBM, Novillo-Ortiz D. The impact of mHealth interventions: systematic review of systematic reviews. *JMIR Mhealth Uhealth*. 2018;6:e23.
 97. Pfaeffli Dale L, Dobson R, Whittaker R, Maddison R. The effectiveness of mobile-health behaviour change interventions for cardiovascular disease self-management: a systematic review. *Eur J Prev Cardiol*. 2016;23:801–817.
 98. Rathbone AL, Prescott J. The use of mobile apps and SMS messaging as physical and mental health interventions: systematic review. *J Med Internet Res*. 2017;19:e295.
 99. Payne HE, Lister C, West JH, Bernhardt JM. Behavioral functionality of mobile apps in health interventions: a systematic review of the literature. *JMIR mHealth uHealth*. 2015;3:e20.
 100. Jakicic JM, Davis KK, Rogers RJ, et al. Effect of wearable technology combined with a lifestyle intervention on long-term weight loss: the IDEA randomized clinical trial. *JAMA*. 2016;316:1161–1171.
 101. Klasnja P, Hekler EB. Rethinking evaluations of mHealth systems for behavior change. *Getmobile*. 2018;22:11–14.

102. Fanning J, Mullen SP, McAuley E. Increasing physical activity with mobile devices: a meta-analysis. *J Med Internet Res*. 2012;14:e161.
103. Dobkin BH, Dorsch A. The promise of mHealth: daily activity monitoring and outcome assessments by wearable sensors. *Neurorehabil Neural Repair*. 2011;25:788–798.
104. Whittaker R. Issues in mHealth: findings from key informant interviews. *J Med Internet Res*. 2012;14:e14.
105. Nahum-Shani I, Hekler EB, Spruijt-Metz D. Building health behavior models to guide the development of just-in-time adaptive interventions: a pragmatic framework. *Health Psychol*. 2015;34S:1209–1219.
106. Nahum-Shani I, Smith SN, Spring BJ, et al. Just-in-time adaptive interventions (JITAI) in mobile health: key components and design principles for ongoing health behavior support. *Ann Behav Med*. 2018; 52(6):446–462.
107. Klasnja P, Smith S, Seewald NJ, et al. Efficacy of contextually tailored suggestions for physical activity: a micro-randomized optimization trial of HeartSteps. *Ann Behav Med*. 2019;53:573–582.
108. Lei H, Nahum-Shani I, Lynch K, Oslin D, Murphy SA. A “SMART” design for building individualized treatment sequences. *Annu Rev Clin Psychol*. 2012;8:21–48.
109. Ljung L. *System Identification Toolbox for Use with MATLAB: User’s Guide*. The MathWorks, Natick, MA; 2011.
110. Ljung L. Experiments with identification of continuous time models. 15th IFAC Symposium on System Identification. Saint-Malo (France); 2009.
111. Ljung L, Glad T. *Modeling of Dynamic Systems*. New Jersey: Prentice-Hall, 1994.
112. Shaffer JA, Kronish IM, Falzon L, Cheung YK, Davidson KW. N-of-1 randomized intervention trials in health psychology: a systematic review and methodology critique. *Ann Behav Med*. 2018;52:731–742.
113. Shechter A, Julian J, Davidson KW, Cheung K, Lee J, Kronish IM. A within-subject comparison of the effect of two putative sham light therapies on mood and fatigue in cancer survivors: results from a series of N-of-1 trials. *Psychiatry Res*. 2019;279:385–386.
114. Conroy DE, Hojjatinia S, Lagoa CM, Yang CH, Lanza ST, Smyth JM. Personalized models of physical activity responses to text message micro-interventions: a proof-of-concept application of control systems engineering methods. *Psychol Sport Exerc*. 2019;41:172–180.
115. Vandebroek P, Goossens J, Clemens M. *Foresight: Tackling Obesities: Future Choices. Obesity System Atlas*. Government Office for Science, London, UK; 2010.
116. Collins LM, Murphy SA, Bierman KL. A conceptual framework for adaptive preventive interventions. *Prev Sci*. 2004;5:185–196.
117. Rabbi M, Aung MH, Zhang M, Choudhury T. MyBehavior: automatic personalized health feedback from user behavior and preference using smartphones. Proc Intern Join Conf Perv Ubiq Comp (Ubicomp), Heidelberg, Germany; 2016:707–718.
118. Fisher AJ, Medaglia JD, Jeronimus BF. Lack of group-to-individual generalizability is a threat to human subjects research. *Proc Natl Acad Sci USA*. 2018;115:E6106–E6115.
119. Molenaar P, Campbell C. The new person-specific paradigm in psychology. *Curr Direct Psychol Sci*. 2009;18:112–117.
120. Molenaar PC. A manifesto on psychology as idiographic science: bringing the person back into scientific psychology, this time forever. *Measurement*. 2004;2:201–218.
121. Israel BA, Schulz AJ, Parker EA, et al. Critical issues in developing and following community-based participatory research principles. In: Minkler M, Wallerstein, N, eds. *Community-Based Participatory Research for Health*. San Francisco, CA: Jossey-Bass; 2003.
122. Minkler M, Wallerstein N. *Community-Based Participatory Research for Health: From Process to Outcomes*. San Francisco, CA: Jossey-Bass; 2010.
123. Bradley EH, Curry LA, Ramanadhan S, Rowe L, Nembhard IM, Krumholz HM. Research in action: using positive deviance to improve quality of health care. *Implement Sci*. 2009;4:25.
124. Marsh DR, Schroeder DG, Dearden KA, Sternin J, Sternin M. The power of positive deviance. *BMJ*. 2004;329:1177–1179.
125. Spreitzer GM, Sonenshein S. Toward the construct definition of positive deviance. *Am Behav Sci*. 2004;47:828–847.
126. Pearl J, Glymour M, Jewell NP. *Causal Inference in Statistics: A Primer*. New York City, NY: John Wiley & Sons; 2016.
127. Pearl J, Mackenzie D. *The Book of Why: The New Science of Cause and Effect*. New York, NY: Basic Books; 2018.
128. Selby JV, Beal AC, Frank L. The Patient-Centered Outcomes Research Institute (PCORI) national priorities for research and initial research agenda. *JAMA*. 2012;307:1583–1584.
129. Anyon Y, Bender K, Kennedy H, Dechants J. A systematic review of Youth Participatory Action Research (YPAR) in the United States: methodologies, youth outcomes, and future directions. *Health Educ Behav*. 2018;45:865–878.
130. Von Hippel E. Lead users: a source of novel product concepts. *Manage Sci*. 1986;32:791–805.
131. Petersen C, Austin RR, Backonja U, et al. Citizen science to further precision medicine: from vision to implementation. *JAMIA Open*. 2019:ooz060.
132. Pauwels E. The New Bio-citizen: How the Democratization of Genomics Will Transform Our Lives from Epidemics Management to the Internet of Living Things. Washington, DC: Wilson Briefs, Wilson Center; 2017.
133. MakerNurse. MakerNurse. Available at <http://makernurse.com/>. Accessibility verified April 14, 2020.
134. Mehta RH. Atlas of Caregiving. Available at www.atlasofcaregiving.org. Accessibility verified April 17, 2020.
135. OpenAPS. OpenAPS. Available at www.openaps.org. Accessibility verified April 17, 2020.
136. Freedland KE, King AC, Ambrosius WT, et al.; National Institutes of Health Office of Behavioral and Social Sciences Research Expert Panel on Comparator Selection in Behavioral and Social Science Clinical Trials. The selection of comparators for randomized controlled trials of health-related behavioral interventions: recommendations of an NIH expert panel. *J Clin Epidemiol*. 2019;110:74–81.
137. Williams DM, Dunsiger S, Jennings EG, Marcus BH. Does affective valence during and immediately following a 10-min walk predict concurrent and future physical activity? *Ann Behav Med*. 2012;44:43–51.
138. Onnela JP, Rauch SL. Harnessing smartphone-based digital phenotyping to enhance behavioral and mental health. *Neuropsychopharmacology*. 2016;41:1691–1696.
139. Larsen K, Hekler EB, Paul M, Gibson B. Improving usability of social and behavioral sciences’ evidence: a call to action for a National Infrastructure Project for mining our knowledge. *Comm Assoc Information Sys*; 2020:46.
140. Michie S, Johnston M, West R, et al. Human Behaviour Change Project. Available at <https://www.humanbehaviourchange.org/>. Accessibility verified June 20, 2019.

141. Health UDo, Services H. *The Belmont Report*. Rockville, MD: Office for Human Research Protections; 1979.
142. Dittrich D, Kenneally E. *The Menlo Report: Ethical Principles Guiding Information and Communication Technology Research*. Washington, DC: US Department of Homeland Security; 2012.
143. Pauwels E, Denton SW. *The Rise of the Bio-citizen*. Wilson Center, Raleigh, NC: NC State University; 2018.
144. Irwin A. *Citizen Science: A Study of People, Expertise and Sustainable Development*. Abingdon, Oxfordshire, UK: Routledge; 2002.
145. Lewis D. DIYPS. Available at <https://diyyps.org/>. Accessibility verified May 25, 2018.
146. Grant AD, Wolf GI, Nebeker C. Approaches to governance of participant-led research: a qualitative case study. *BMJ Open*. 2019;9:e025633.
147. Nebeker C, Harlow J, Espinoza Giacinto R, Orozco-Linares R, Bloss CS, Weibel N. Ethical and regulatory challenges of research using pervasive sensing and other emerging technologies: IRB perspectives. *AJOB Empir Bioeth*. 2017;8:266–276.
148. Schneider C. *The Censor's Hand: The Misregulation of Human-Subject Research*. Boston, MA: MIT Press; 2015.
149. Klitzman R. The ethics police? IRBs' views concerning their power. *Plos One*. 2011;6:e28773.
150. Bloss C, Nebeker C, Bietz M, et al. Reimagining human research protections for 21st century science. *J Med Internet Res*. 2016;18:e329.
151. Health UDo, Services H. *Office for Human Research Protections (OHRP). Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects Subpart C, Code of Federal Regulations Title*. 2006; Office for Human Research Protections, Rockville, MD USA.45.
152. Control CfD, Prevention. HIPAA privacy rule and public health. Guidance from CDC and the US Department of Health and Human Services. *MMWR*. 2003;52:1–19.
153. Thomas JG, Bond DS. Behavioral response to a just-in-time adaptive intervention (JITAI) to reduce sedentary behavior in obese adults: implications for JITAI optimization. *Health Psychol*. 2015;34S:1261–1267.
154. Health UDo, Services H. Health information technology: initial set of standards, implementation specifications, and certification criteria for electronic health record technology. *Fed Regist*. 2010;75:44590–44654.
155. Torous J, Nebeker C. Navigating ethics in the digital age: introducing Connected and Open Research Ethics (CORE), a tool for researchers and institutional review boards. *J Med Internet Res*. 2017;19:e19.
156. Harlow J, Weibel N, Al Kotob R, et al. Using participatory design to inform the Connected and Open Research Ethics (CORE) commons. *Sci Eng Ethics*. 2020;26:183–203.
157. Nebeker C, Bartlett Ellis RJ, Torous J. Development of a decision-making checklist tool to support technology selection in digital health research. *Translat Behav Med*. 2019, online first ibz074.
158. Bietz M, Fiesler C, Metcalf J, et al. PERVADE: Pervasive Computing Ethics for Computational Research. Available at <https://pervade.umd.edu/about/general/>. Accessibility verified April 17, 2020.
159. Simonite T. Should data scientists adhere to a Hippocratic Oath? *Wired*. 2018. Available at <https://www.wired.com/story/should-data-scientists-adhere-to-a-hippocratic-oath/>. Accessibility verified April 17, 2020.
160. Nebeker C, Torous J, Bartlett Ellis RJ. Building the case for actionable ethics in digital health research supported by artificial intelligence. *BMC Med*. 2019;17:137.
161. IEEE Standards Association. The IEEE Global Initiative on Ethics of Autonomous and Intelligent Systems. Available at https://standards.ieee.org/develop/indconn/ec/autonomous_systems.html. Accessibility verified July 11, 2018.
162. AMIA Ethical L, Social Issues Working Group. Ethical, Legal, and Social Issues Working Group. Available at <https://www.amia.org/programs/working-groups/ethical-legal-and-social-issues>. Accessibility verified July 12, 2018.
163. Düring P, Fuss FK, Holmberg H-C, Sperlich B. Recommendations for assessment of the reliability, sensitivity, and validity of data provided by wearable sensors designed for monitoring physical activity. *JMIR mHealth uHealth*. 2018;6:e102.
164. Nebeker C, Lagare T, Takemoto M, et al. Engaging research participants to inform the ethical conduct of mobile imaging, pervasive sensing, and location tracking research. *Transl Behav Med*. 2016;6:577–586.
165. Nebeker C, Murray K, Holub C, Haughton J, Arredondo EM. Acceptance of mobile health in communities underrepresented in biomedical research: barriers and ethical considerations for scientists. *JMIR Mhealth Uhealth*. 2017;5:e87.
166. National Academies of Sciences E, Medicine, Health, et al. In: Baciu A, Negussie Y, Geller A, Weinstein JN, eds. *Communities in Action: Pathways to Health Equity*. Washington, DC: National Academies Press; 2017.
167. Tabak RG, Khoong EC, Chambers DA, Brownson RC. Bridging research and practice: models for dissemination and implementation research. *Am J Prev Med*. 2012;43:337–350.
168. National Cancer Institute Division of Cancer Control & Population Sciences. *Research Resources and Tools*. Bethesda, MD: National Cancer Institute; 2018 <https://cancercontrol.cancer.gov/brp/research/index.html>
169. Vernon SW, Meissner H, Klabunde C, et al. Measures for ascertaining use of colorectal cancer screening in behavioral, health services, and epidemiologic research. *Cancer Epidemiol Biomarkers Prev*. 2004;13:898–905.
170. Newell SA, Girgis A, Sanson-Fisher RW, Savolainen NJ. The accuracy of self-reported health behaviors and risk factors relating to cancer and cardiovascular disease in the general population: a critical review. *Am J Prev Med*. 1999;17:211–229.
171. Rauscher GH, Johnson TP, Cho YI, Walk JA. Accuracy of self-reported cancer-screening histories: a meta-analysis. *Cancer Epidemiol Biomarkers Prev*. 2008;17:748–757.
172. Stewart AL, Nápoles-Springer AM. Advancing health disparities research: can we afford to ignore measurement issues? *Med Care*. 2003;41:1207–1220.
173. Nápoles-Springer AM, Santoyo J, Houston K, Pérez-Stable EJ, Stewart AL. Patients' perceptions of cultural factors affecting the quality of their medical encounters. *Health Expect*. 2005;8:4–17.
174. Karliner LS, Napoles-Springer A, Kerlikowske K, Haas JS, Gregorich SE, Kaplan CP. Missed opportunities: family history and behavioral risk factors in breast cancer risk assessment among a multiethnic group of women. *J Gen Intern Med*. 2007;22:308–314.
175. Willis G. *Cognitive Interviewing: A Tool for Improving Questionnaire Design*. New York, NY: Sage Publications; 2005.
176. Institute of Medicine. *Capturing Social and Behavioral Domains and Measures in Electronic Health Records: Phase 2*. Washington, DC: The National Academies Press; 2014.
177. King A, Hoppe RB. "Best practice" for patient-centered communication: a narrative review. *J Grad Med Educ*. 2013;5:385–393.

178. National Academies of Sciences Engineering and Medicine; Health and Medicine Division; Board on Health Care Services; National Cancer Policy Forum. Implementation of Lung Cancer Screening: Proceedings of a Workshop; Washington, DC; 2016.
179. Yarnall KS, Pollak KI, Østbye T, Krause KM, Michener JL. Primary care: is there enough time for prevention? *Am J Public Health*. 2003;93:635–641.
180. Taylor C, Munro AJ, Glynne-Jones R, et al. Multidisciplinary team working in cancer: what is the evidence? *BMJ*. 2010;340:c951.
181. Fennell ML, Das IP, Clauser S, Petrelli N, Salner A. The organization of multidisciplinary care teams: modeling internal and external influences on cancer care quality. *J Natl Cancer Inst Monogr*. 2010;2010:72–80.
182. Chin MH, Clarke AR, Nocon RS, et al. A roadmap and best practices for organizations to reduce racial and ethnic disparities in health care. *J Gen Intern Med*. 2012;27:992–1000.
183. Chan IS, Ginsburg GS. Personalized medicine: progress and promise. *Annu Rev Genomics Hum Genet*. 2011;12:217–244.
184. Mitchell J, Probst J, Brock-Martin A, Bennett K, Glover S, Hardin J. Association between clinical decision support system use and rural quality disparities in the treatment of pneumonia. *J Rural Health*. 2014;30:186–195.
185. Kruse CS, Kristof C, Jones B, Mitchell E, Martinez A. Barriers to electronic health record adoption: a systematic literature review. *J Med Syst*. 2016;40:252.
186. Adler-Milstein J, Holmgren AJ, Kralovec P, Worzala C, Searcy T, Patel V. Electronic health record adoption in US hospitals: the emergence of a digital “advanced use” divide. *J Am Med Inform Assoc*. 2017;24:1142–1148.
187. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci*. 2009;4:50.