Opportunities and Challenges of Developing Information Technologies on Behavioral and Social Science Clinical Research

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Introduction

> Digital Health is the blending of mobile health (mHealth) and health information technology (smartphones, wearable sensors, Internet resources, and electronic health records) with genetic, biological, social, and behavioral science to help consumers, clinicians, and researchers measure, manage, and improve health and productivity. Digital Health also has an important role in enhancing efficiencies in health care delivery by increasing patient access to health information, extending the reach of health care experts into communities with noted access barriers (e.g., rural and low income populations), and potentially reducing the overall cost of health care through the automation of services.
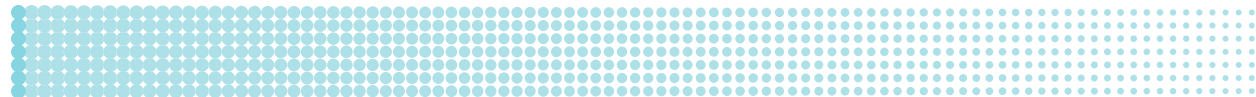
Digital Health is no longer limited to the technologically savvy. Around the world, 2.19 billion people own a smartphone[1,2] including approximately 60% of minority and low income populations who use these devices[3-5] for Internet-based activities[6]. In addition, wearable sensors with wireless connections (e.g., autographs (smartwatch devices that verify the wearer's handwritten signatures), pedometers, devices with GPS, continuous heart rate monitors) are growing in availability and adoption for health and fitness purposes[7].

In the realm of mental health, Digital Health tools such as assessment and tracking application software (apps), online communities, and asynchronous coaching have increased dramatically in the last few years, with 29% of health-related apps focused specifically on mental health[8]. Sensors, such as health bands, have also been used to measure behavioral correlates of mental health (e.g., sleep, physical activity). Large health care systems offer their members online tools for managing mental health problems and co-occurring conditions such as PSTD, sleep disturbance, depression, and even psychosis management.

Because of their ubiquitous nature, Digital Health tools have the potential to truly improve our understanding of mental illness, to track the course of illnesses, and to provide as-needed mental health

care. For the purposes of science, these tools can help amass large quantities of physiological, social, emotional, and behavioral data in real time with limited burden on the consumer.

Over the past five years, there has been a notable increase in the use of Internet-based and mobile device-based data collection for studies ranging from simple survey studies to intervention studies[9-29]. Industry has also contributed tools for mobile research, with innovative efforts like open source research kits, that help with the recruitment of very large samples into medical research. Indeed, the rapid recruitment of large samples has been demonstrated several times. For example, one recent remote clinical trial not only rapidly recruited 1,200 adults into a randomized controlled trial, but recruited a sample that was identical to the demographics of the United States, without any special efforts to recruit these populations[9]. The promise of these technologies is such that the NIH Office of the Director has invested significant resources into the All of Us Research Program (formerly the Precision Medicine Initiative Cohort Program) that will rely heavily on mobile technology to recruit, retain, and collect behavioral information, and will also leverage information available in electronic health records, with an eye toward better understanding the causes and consequences of disease.

At several open sessions of the National Advisory Mental Health Council questions were raised about future directions for behavioral and clinical research in the context of new and developing digital tools. Council members suggested a workgroup be convened to review the state of behavioral research and offer guidance to researchers on how behavioral science should move forward. In response to this discussion, Dr. Insel, then Director of NIMH, elected to form a Workgroup of Council to address the topic.

THE NATIONAL ADVISORY MENTAL HEALTH COUNCIL

Workgroup on Behavioral and Social Science Research was tasked with exploring the opportunities and challenges of using new information technologies to study human behaviors relevant to the NIMH mission. The Workgroup began by reviewing the existing NIMH clinical portfolio in behavioral and social sciences to identify areas in which NIMH is already using 21st century tools and to identify potential new opportunities. Next, the workgroup looked to what may be possible in the context of the NIMH Strategic Plan for Research and Strategic Research Priorities. Finally, the workgroup approached the question of how to develop and use technology-driven information science at several levels of analysis, including the individual (cognition and behavior), social, and cultural contexts.

FRAMING THE WORKGROUP AGENDA

Workgroup members met by teleconference to set the agenda and identify participants who could discuss opportunities to leverage technology, including:
- Technologies to advance assessment (including the assessment related to the risk, etiology, diagnosis, and course of psychopathology);
- Technologies to advance research on and delivery of preventive and therapeutic interventions; and
- Technologies to study and improve service delivery (i.e., to improve the reach, efficiency, and quality of mental health services).

Workgroup members also identified maany cross-cutting issues, including those related to research, infrastructure, privacy, safety, and ethics. These topics were organized into six key questions:

1. What technologies currently exist and/or could be developed to understand the life course and etiology of mental disorders in terms of their developmental trajectory, course, and epidemiology?
2. How can these new technologies be used to predict and prevent mental illness?
3. How can these new technologies be used to achieve more efficient and effective diagnoses and treatments of mental illnesses?
4. How can these new technologies be used to improve quality in mental health practice?
5. How can these new technologies address new questions as well as enable more rapid and nimble research?
6. How can technology-enhanced research be conducted ethically and in a manner that protects participant data?

OVERVIEW OF THE REPORT

The remaining sections of this report provide an overview of the discussion and recommendations from the workgroup's deliberations. The next seven chapters summarize the discussion and corresponding recommendations related to each of the six key questions as well as a set of cross-cutting recommendations, respectively. The report includes a discussion on how Digital Health technology can facilitate mental health research (Chapters 1 and 2), potential avenues for research into the use of digital technology to improve treatment access and outcomes (Chapters 3 and 4) and the challenges of a Digital Health approach to research, including ethical and human subject protection concerns (Chapters 5 and 6). Additional cross-cutting considerations (Chapter 7) and recommendations are addressed, followed by an overall conclusion.

Developing Technologies for Understanding the Life Course and Etiology of Mental Disorders

ACCORDING TO THE **NIMH STRATEGIC RESEARCH PRIORITIES – PRIORITIES FOR STRATEGY 2.1**, NIMH SEEKS TO:

"...support research that fundamentally breaks new ground in understanding the development of mental illness from early life through illness course to guide the development of preventive or preemptive interventions. NIMH encourages studies that seek to characterize developmental processes across biological and behavioral domains of analysis that give rise to mental illnesses throughout the lifespan; to identify sensitive periods for typical and atypical mental health trajectories; and, to determine modifiers of maturational and illness trajectories, emphasizing periods of sensitivity to perturbation and/or potential for intervention."

Important to this Strategic Research Priority is the ability to capture cognitive, social, emotional, and functional behavior accurately and continuously, with as little burden to the consumer as possible. Historically, these data have been captured using self-report and clinical and lab-based assessment tools (e.g., sleep laboratory tools). These traditional methods of assessment have proven to be invaluable in the study of developmental psychopathology but are limited in important ways. First, self-report measures are subject to inaccuracies due to retrospective memory, and to survey bias (the tendency to respond to questions in a prosocial way). Second, the clinical and lab-based assessments measure behavior outside the typical environment in which it occurs, thus introducing potential artifacts in the data. Finally, both methods collect information at specific time intervals, rather than continuously, potentially missing critical information about how mental illness develops and progresses. Even with the use of ecological momentary assessment (EMA), where research participants report on symptoms at random intervals during the day or after pre-determined times during the day, assessment may be burdensome and demands a level of engagement that may present a challenge to many people[30,31].

Digital Health technology deployed over smartphones and wearable sensors can mitigate many of the problems of traditional assessment. These technologies allow scientists to capture participants' symptoms and functioning in real time, with far less burden than traditional methods. New technologies can improve engagement of patients, including their participation in therapeutic practice skills that may enhance the effectiveness of the therapy[32,33]. These methods also allow scientists to measure how behavior varies over time, and between different social contexts (work versus home)[34,35]. Digital Health measures can take the form of brief surveys delivered over text messaging or an assessment app. Such measures can also capture information on physical and spatial activity from the GPS and accelerometers in smartphones or wearable devices, as well as collect physiological data such as heart rate, blood pressure, and respiration, which are good measures of disability associated with many mental illnesses[36,37]. Digital Health tools in the form of electronic health records, can also provide valuable information about illness, injuries, and toxin exposures early in the life span, or prior to the onset of mental illness. Table 1 provides a list of Digital Health tools and the information they collect.

As is noted in Table 1 (pg. 20), there is a considerable amount of data available that has the potential to measure social, environmental, and behavioral markers of psychopathology. However, there is still work to be done to determine the construct validity and reliability of these measures, and to determine their predictive value in isolating deviations from normal function. Studies, such as the Sleep, Networks, Affect, Performance, Stress, and Health using Objective Techniques study, SNAPSHOT study, are needed to test the validity and reliability of these measures. (SNAPSHOT is an NIH-funded collaborative research project between the Affective Computing group and Macro Connections group at the MIT Media Lab and Brigham & Womens' Hospital.) As data become available, it will be important to warehouse and open-source the data, such as through the NIMH Data Archive, so that investigators can begin developing algorithms that indicate normal developmental processes, algorithms that signal aberrant development, and algorithms that identify toxic exposures, such as sedentary lifestyle and negative social interaction. Approaches might include recording multiple signals at single points in time as well as passively collecting data over months/years to evaluate long term outcomes and trajectories. To make sense of these data, the development of new analytic tools for compiling, analyzing, and combining data with other sources (e.g., genetic databanks, health registries, NIMH Data Archive) is necessary. The use of digital analytics for precision health is now possible given advances in machine learning models that can extract complex patterns from multiple sources of high-dimensional data over time. For example, recent work has shown that building mathematical models not only of groups, but also of individuals, longitudinally, can lead to stronger models that can be used to forecast changes tomorrow, based on behavior today[38].

CHAPTER 1 RECOMMENDATIONS

» Encourage the development and use of strategies for managing and combining large streams of data from multiple measures/sources, including Electronic Medical Records, biobanks, and registries.

» Pursue more powerful analytic strategies for combing information from various measures (information collected via various channels) for improved predictive power.

» Encourage the development of analytic strategies to advance prediction and identification of potential problems before they happen.

» Promote the collection of passive, real-time data from people who are well, yet at risk for mental illness, across locations and age groups, to identify the diversity of data corresponding to aberrant and normal developmental processes.

» Develop predictive models capable of identifying individual patterns both within individuals (over time) and across individuals (finding similar clusters of predictors across a group).

» Develop strategies to engage people in providing data over the long term.

Note: All the recommendations above are also applicable to Chapter 2

Using Technology To Predict And Prevent Mental Illness

THE GOALS OF STRATEGY 2.2 OF THE **NIMH STRATEGIC RESEARCH PRIORITIES** ARE TO:

"...identify, early in the development of major mental illnesses, biomarkers and behavioral indicators with high predictive value to guide the use of preventive interventions. ...to develop biomarkers and assessment tools to predict illness onset, course, and intervention response across diverse populations...for stratification purposes, (to) examine novel potential risk factors and the complex relationships between risk and mental illness, focus on defining directed intervention targets or health outcomes, and examine factors that can predict disease development or progression."

As discussed in Chapter 1 and outlined in Table 1, Digital Health technologies can be very useful for measuring behaviors associated with mental health states and for identifying strategies for preventing impending mental health problems. Digital Health technology could be used to identify early behavioral warning signs, such as disturbed sleep, pressured speech on video chats, failure to respond to texts, and changes in activity, as they occur in real time. This could, in turn, offer opportunities to intervene before warning signs turn into mental health problems.

Although promising, there is still a considerable amount of research to be done to determine if Digital Health data of this nature can accurately predict when someone may be in the early phases of a new mental illness or relapsing from the recovery of a mental illness. Most research to date has focused on proof of principle, feasibility, and acceptability of these tools for prediction purposes. These studies find that many technology-based approaches (e.g., texting one's clinical status, using web or mobile self-management software, behavioral sensing) are feasible and acceptable assessment approaches in clinical populations, particularly when designed with the characteristics of the target population in mind. Therefore, while the use of highly novel technology or innovative combinations of technology are exciting new directions that warrant continued development, scientific efforts in the Digital Health space can progress towards larger evaluations of efficacy and effectiveness in predicting and preventing mental illness, as well as developing and evaluating technology implementation models in the context of real-world care.

To support this research, many of the resources and methods discussed in Chapter 1 apply here. First, although digital data collection is acceptable by clinical populations participating in research, their construct validity and reliability still must be determined. Second, large repositories of Digital Health data are needed to create predictive algorithms, both at the group level (how do people at risk for depression behave differently than the general population?) and at the individual level (what is an individual's digital signature like, and how well does deviation from that signature predict an event?). The data analytic methods discussed in Chapter 1 (e.g., machine learning approaches) could be applied to these needs as well. Therefore, multi-modal data collection is encouraged to fully capitalize on what contemporary personal devices offer (e.g., accelerometry, GPS, device use logs, in-home sensors, social media data).

Specific to prevention research is identifying strategies that could mitigate the occurrence or reoccurrence of a mental health event. As an example, just-in-time-interventions for people who are coping with active symptoms, need to be further studied in order to identify:

- The most efficacious interventions,
- The optimal timing between early indication of an event and the actual event, and
- The best way to alert patients, family or clinicians that an event is imminent.

Just In Time Adaptive Intervention (JITAI) methods[39] are ideal for developing decision rules that link a patient's information to intervention options, specifying if, when, and what type/dose of an intervention should be offered. Developing these decision rules requires large-scale clinical trials. Likewise, the basket (treating to a phenotype) and umbrella (treating to a specific disease) trial designs can save valuable resources by matching the right intervention to the right subgroup of patients through Digital Health markers. While basket and umbrella trial designs are used almost exclusively in oncology trials, these trial designs can be used effectively in large scale mental health trials. Participant-based research methods will also be critical to determining whether the way warnings about impending illness states and information about preventative interventions are delivered will impact patients' reactions to warnings, and their subsequent use of recommended strategies.

Researchers will need to plan for new types of data storage and data management challenges (e.g., raw data, feature extraction, data security measures, data transmission) and prepare to use and develop new data modeling and analytics as discussed above. New digital sources of

CHAPTER 2 RECOMMENDATIONS

» **Develop data modeling and inference techniques to detect clinical signals based on changes within an individual over time.**

» **In addition to the collection of passive data, promote the use of "real time" data collection of self-reported measures as predictors.**

» **Couple data from varying technologies (e.g., data from Ecological Momentary Assessment (EMA) and social media) to improve assessment/prediction.**

Note: See recommendations from Chapter 1.

information will provide more nuanced and granular information about illness and expression of illness within the individual. For example, in the NIMH-funded CrossCheck study, individuals with schizophrenia were given a multi-modal smartphone system that collected comprehensive behavioral sensing, device use, and self-report data to identify behavioral indicators of relapse and hospitalization[40]. The results showed that digital warning signs of hospitalization were idiosyncratic, with data combinations and patterns that were meaningful indicators for one individual, but not for all. Researchers will need to look beyond group differences and develop new data modeling and inference techniques that will enable more tailored clinical signal detection—examining changes within each individual, over time.

Using Technologies For Diagnosing and Treating Mental Illnesses

UNDER STRATEGY 3 OF THE **NIMH STRATEGIC RESEARCH PRIORITIES**:

"NIMH encourages applications that identify new targets for intervention, and that develop new treatments based on these targets." (Strategy 3.1). "NIMH encourages efficient research designs that can be used to examine prescriptive approaches for matching individuals to optimal care." (Strategy 3.2). "Given the resources necessary to launch large-scale trials and conduct intervention research in community/practice settings, studies must be justified in terms of potential impact, use innovative platforms and designs, and advance treatment personalization." (Strategy 3.3).

To this end, Digital Health technology, particularly online interventions, mobile health applications (apps), and electronic patient portals have tremendous potential to increase the reach of existing evidence-based treatments, to deliver interventions targeted to the unique symptom profile of the individual, and to do so in a manner that allows for as-needed and timely delivery. Technology can extend care to those who cannot access it by overcoming access barriers related to time constraints, transportation problems, and cost. Many people who are hesitant or unwilling to talk with mental health professionals due to problems such as social anxiety or mistrust of therapists may be willing to use technology based tools[41,42]. Technologies may be able to improve the efficiency of existing treatments, by reducing the amount of therapist time required in psychotherapy[43]. They may also be able to improve processes and quality of pharmacotherapy for depression in primary care[44]. By embedding data collection in the context of people's lives, technology may aid in the diagnosis, as well as the identification of actionable treatment strategies.

Web-based technologies have been investigated for more than 15 years[45-48]. Evidence shows that coach-facilitated, Internet-based treatment is as effective as face-to-face treatment, but far better than stand-alone Internet interventions, where no coaching or interaction with a clinician is offered[49], and that this form of treatment is largely acceptable. The evidence for smartphone app interventions is emerging. While some of the early interventions used the phone primarily for in-the-moment mood assessment[50] or text messaging[51] in the context of other forms of web-based or standard treatments, more recently apps have been developed that provide interventions in ways that are quite different from web-based treatments. These apps are designed to be used in short but frequent interactions targeting specific behavioral strategies. Rather than using psychoeducation, these apps can successfully reduce symptoms and improve well-being by prompting beneficial behaviors[52,53]. An emerging area of investigation is the use of Digital Health with more traditional face-to-face therapy. Both web-based interventions and mobile-based intervention apps have been shown to decrease the amount of therapist time required[43,54], although some studies have also suggested that the introduction of technology into standard face-to-face therapies may increase the amount of time in treatment[55].

In spite of the overwhelming evidence that technology-based treatments can be effective,

particularly when coupled with some human support, there are almost no instances of successful and sustainable implementation in real world clinical settings[56]. There are many potential reasons for this.

One reason is that much of the design and development of technology-based interventions has been top down, with clinicians designing tools that try to get patients to do things that treatment models suggest would reduce symptoms. Other design methods, such as user-centered or participatory design, engage patients from the very earliest phases of development and keep them involved throughout the design process. Indeed, user-centered design could also help to develop targeted behavioral treatments by combining Digital Health assessment and digital phenotypic responses to treatments, in conjunction with patients' reports on the helpfulness of the interventions. User-centered design should involve all key stakeholders in the design of those services, including patients, providers, administrators, and IT experts.

Another issue is that while there may be some people who can fully benefit from standalone digital interventions, the vast majority require human support or coaching to obtain more consistent engagement and outcomes, as was noted earlier in this chapter. Historically, web-based tools for computers did not work because people did not consistently use them[57], and therefore the addition of human support to get individuals to use the tools was developed[58]. Thus, rather than thinking of these tools as digital interventions (or intervention technologies), they should be thought of as technology-enabled services[56]. The use of this term has several implications. Most importantly, it focuses on the service to be provided and what technology or technologies are needed to support that service (rather than developing the service to match and be supported by the technology).

Moving forward, there are a number of opportunities and caveats in pursuing the conduct of mental health assessments and interventions through electronic technologies. As the real time, low burden detection of behaviors and states related to mental health and mental health treatment becomes possible, there is an opportunity to develop treatments that harness this information to support JITAI, as discussed in Chapter 2[41,56]. Advances in assessment could also lead to stepped approaches to care, maximizing the workforce capacity by offering online tools to consumers who both like and can benefit from this form of treatment, reserving the scarce workforce for those who require more intensive, face-to-face care. Natural language processing is improving rapidly, to the point where chatbots can interact with people on specific tasks. It is unlikely in the near term that chatbots will be able to provide therapy, as artificial intelligence cannot yet manage the required complexities of human speech and experience[60,61]. However, chatbots may be able to perform more limited functions such as assessment or training of the individuals with whom they interact.

There are opportunities in other technologies as well. Virtual reality technology has become increasingly accessible in recent years. A growing number of smaller studies have demonstrated its use in supporting the treatment of anxiety disorders, PTSD[62], and persecutory delusions in schizophrenia[63]. Serious gaming, that is, the use of games designed for purposes other than pure entertainment, such as the use of interactive games to teach treatment principles and promote behavior change, has shown, for example, good potential in the treatment of depression among youth[64].

There are a few caveats to consider when exploring technology for diagnosis and treatment. To succeed, investigators need to carefully consider their approaches to research and development. While it is likely that the use of technology will continue to have a transformative effect on mental health, it is essential that technology-enabled services focus on the use of evidence-based treatment models. While technology can accomplish some things clinicians

cannot do (e.g., provide immediate information about function in real time readouts), the burden that a real-time intervention has on a consumer is relatively unknown. While some in-the-moment interventions may be highly effective, some may also be highly disruptive and unacceptable to some participants. The heterogeneity of needs, preferences, and types of responses make it difficult to fully anticipate what the future of Digital Health holds. To some degree this will depend on research interventionists, and their ability to embrace looking forward rather than being reactive to new technological developments. Closer collaborations with experts outside of the mental health field (e.g., engineers, computer scientists, anthropologists, ethicists, business entrepreneurs, marketers) will not only provide their expertise, but will likely stimulate mental health researchers to consider new strategies and manage assumptions. For example, clinicians/ researchers will need to adapt as new technologies develop and make current ones obsolete or ineffective. One possible consideration along these lines is whether apps will continue to be the dominant tools on the smartphone, or will there be another shift to a new form of interaction. Whatever the case, the researchers will also need to nimbly adapt to such changes.

CHAPTER 3 RECOMMENDATIONS

» Encourage new paradigms for developing intervention content/formats, including deployment-focused development and/or testing

» Promote the design and evaluation of interventions in real-world environments with input from end-users (consumers, clinicians, administrators).

» Consider new paradigms for developing, refining, and testing Just-In-Time Adaptive Interventions (JITAIs), via nimbler platforms, including:

  » Web-based platforms for launching and conducting clinical trials, rapidly enrolling participants and refining and testing interventions;

  » Iterative, nimble evaluations that allow for optimization of Behavioral Intervention Technologies (BITs) while the study is ongoing; and

» Analyzing data from commercial applications and other sources that could yield valuable information about patterns of use and outcomes.

» Promote the development of analytic strategies for informing decision rules and developing/testing algorithms for personalized approaches, including:

  » Decision rules for stepped interventions (when and how to advance individuals to treatments of differing intensity across illness phases); and

  » Strategies for intensively adaptive interventions and just-in-time interventions.

Note: See recommendations from Chapter 1.

Using Technology To Improve Quality In Mental Health Practice

> STRATEGY 4 OF THE **NIMH STRATEGIC RESEARCH PRIORITIES** CALLS FOR RESEARCH TO:
>
> "...develop and test innovative care models of care that eliminate traditional shortcomings of mental health care provided in various sectors and utilize advanced tools to better reach populations in need and deliver appropriate and progressively improving care." (Strategy 4.3) and "...develop and validate tools and platforms to conduct robust, rigorous, and efficient practice-based research and foster better integration of research methods and measures within multiple service systems and community settings, to promote ongoing care improvement." (Strategy 4.4).

Since health organizations first began to adopt telehealth in the early 1990s, improvements in technology have contributed to a rapid growth and usefulness of these modes of treatment, with an even more rapid expansion anticipated in the coming years[65]. Telehealth services delivered via telephone, videoconferencing, and mHealth appear to be well-accepted and many are as effective as face-to-face visits for delivering mental health care[66-69], as noted in prior chapters. Asynchronous modalities such as remote consultation between providers and secured emails between providers and patients are also being used to supplement clinical visits[70]. Medicare, Medicaid, and private insurers increasingly support billing for these services[71].

Once patients are in treatment, tools such as electronic health records (EHRs) and personal health records can be used to improve quality and outcomes of mental health care. Electronic health records coupled with a registry function can be used to track and monitor symptoms for patients who are not improving[72,73]. Provider dashboards can provide clinicians with: real-time data about the course of patient's illnesses and responses to treatment; passive data about patient activity; and reminders and prompts about indicated clinical interventions. Personal health records can integrate information across multiple systems of care, including medical

and mental health records, supporting coordination of care and patient engagement[74]. Insurance claims data can be used to identify high users of service and guide quality improvement efforts[75].

NIMH is supporting several large-scale efforts to pool data from health care systems to advance knowledge. The Mental Health Research Network, a consortium of 13 health system research centers, is currently being used as a platform to conduct research on mental health: epidemiology; health services; economics; disparities; outcomes and quality assessment; and pragmatic clinical trials[76].

In the public sector, NIMH has sponsored collaborative research projects to pool data from all-payer warehouses across states to advance policy research[77]. NIMH is currently leading efforts to better understand the epidemiology and best clinical practices for individuals with clinical high-risk (CHR) and first episode psychosis (FEP) patients through the Early Psychosis Intervention Network (EPINET) program, which will collect and aggregate clinical, biological, and administrative data from academic and community-based early psychosis treatment programs around the country[78].

Several factors have limited the adoption and clinical utility of health information technologies

in routine clinical practice. First, due to lack of funding and fragmentation, the use of health information technology in mental health care delivery has lagged behind the general medical sector, particularly in the public mental health sector[79]. Second, most commercial mental health EHRs are primarily used as a means of storing medical information, and lack capabilities such as registry functions that can be used to drive better care[72]. Third, many of these systems lack the interoperability and privacy safeguards needed to exchange information with medical EHRs[80,81].

Finally, many health information technologies have not paid adequate attention to the preferences, needs, and time constraints of end users. Google discontinued its personal health record, Google Health, in 2012, due to low perceived usefulness and high burden involved in data entry[82]. Many practices continue to struggle to achieve meaningful use of their EHRs which are often viewed by providers as time consuming to complete, and a barrier to interacting with patients[80].

Population-based health information technology is likely to continue to migrate from provider-generated electronic health records to cloud-based, patient-owned records that combine health care records with passively collected health data from wearable devices, as well as data that are manually entered by patients on symptoms, functioning, and health goals. These platforms will create new opportunities for both coordinating care, and for recruiting and tracking patients enrolled in research studies[83]. They will also create new challenges for patient consent and privacy, as lines blur between research and care delivery.

Using health technologies to improve population health requires that they be both effective and widely utilized. Research is needed to test the best strategies, including training and payment structures, for encouraging meaningful use of health technologies by the full range of end users including patients, providers, and managers.

CHAPTER 4 RECOMMENDATIONS

» Promote the development of strategies for coupling patient data from personal devices with Electronic Health Records (EHRs).

» Identify predictive analytics that can be used with EHR data to identify individuals at risk for illness or relapse.

» Encourage the use of health information exchanges and all-payer databases to facilitate population-level approaches.

» Explore deployment-focused approaches that anticipate the needs of providers who are on the receiving end of devices.

» Conduct research to demonstrate the return value of new technologies.

Using Technology For More Rapid and Nimble Research

STRATEGY 4 OF THE **NIMH STRATEGIC PLAN FOR RESEARCH** CALLS FOR:

"New research designs, measures, and statistical approaches will be needed to support rapid testing of system improvement efforts and to facilitate analysis of complex data arising from the growing digital enterprise. To achieve high-impact public health research, new training models will be required that embrace new opportunities, including advanced information and communication technologies, and assessment and analytic strategies for complex data. Finally, we need to harness new opportunities afforded by citizen-centered science and crowdsourcing." (Strategy 4.4).

Over the past several years, there have been a number of developments in research that are leveraging digital and passive sensing strategies through personal mobile technologies such as smartphones and wearables. Apple's ResearchKit studies have shown that it is possible to recruit tens of thousands of people into research in as little as a day. The NIMH-funded BRIGHTEN study, a feasibility randomized controlled trial comparing three mobile apps for depression, recruited and randomized 1,200 adults representative of the United States population and completed data collection in under one year[9]. Studies like these also find that smartphones and wearable sensors can capture a more accurate picture of participants' symptoms in real time, with far less burden than is typical in a clinical or behavioral study. Clinical and behavioral research may be conducted more quickly, efficiently, and to greater scale than ever imagined.

Methods for collecting biometric, behavioral, and survey data discussed in previous sections are all potentially useful tools for collecting clinical and behavioral research data. However, the process of recruiting, consenting, and compiling these data necessitates accessible platforms. Online research platforms typically include a web-based or app-based landing page explaining the purpose of the

study and an initial eligibility screening process. Study information to aid in the consent process is provided here, either using a text modality (e.g., PDF) or a brief video. Assessment and treatment tools are downloaded by the participant from this page. An example of this is the Center for Behavioral Intervention Technologies (CBITS) Participant Registration Intervention Management (PRIM) system at Northwestern University. PRIM offers a standardized toolkit for research websites that include the capacity to screen and consent participants for eHealth and mHealth behavioral intervention research trials. Also, the University of California, San Francisco was recently awarded funds from the NIH to develop a robust recruitment platform for conducting research into common health problems using digital and mobile technologies. These platforms are customizable for specific projects, allowing research teams to develop their own online research portals without having to rebuild the necessary infrastructure and databases from scratch. Commercial and open-sourced research platforms are also available through companies such as Apple's ResearchKit and Arivale. Arivale currently collects a combination of biological, physical activity, and Ecological Momentary Assessment (EMA)-driven survey data to better understand the development and physical health of

the population. ResearchKit has specific research projects (e.g. on cancer, heart disease, Parkinson's Disease) that collect passive and EMA data, which are available via open-access protocols to any investigator interested in using the data. ResearchKit also provides guidelines to researchers to develop their own tools and research platform using CareKit. These commercial- and academic-led projects have the potential to facilitate the development of novel methods for conducting mental health research, either by providing a wealth of existing data to be analyzed, or by offering easily accessed methods for large scale, mobile data collection.

CHAPTER 5 RECOMMENDATIONS

» Partner with existing research networks and social networking platforms, e.g., for understanding risk patterns; for delivery of JIT interventions.

» Identify mechanisms to rapidly test ideas and conduct exploratory research, including the possibility of partnering with small businesses.

Facilitating Ethical Conduct Of Technology-Enhanced Research And The Protection Of Participants

THE **NIMH STRATEGIC PLAN** FOR RESEARCH INCLUDES AN INTRODUCTORY SECTION ON "ADAPTING TO A CHANGING ECOSYSTEM" IN WHICH A SECTION ON "TECHNOLOGY" IS ADDRESSED

"The rapidly evolving health technology sector has the potential to radically transform the way all people (i.e., patients, providers, researchers, payers) interact within the mental health care system. Mobile technologies are changing the world of mental health care in ways that could scarcely have been imagined before the social media revolution. .... The promise is enticing, but there are still many unanswered questions about effectiveness, concerns about privacy, and challenges for regulation of these nascent technologies."

RECRUITMENT/RETENTION & EVOLUTION

Researchers embarking on research leveraging mobile and digital data must be aware of three key issues:

- Challenges with participant recruitment and retention, and measurement coherence
- Protection of participant data (privacy, security) and safety, and
- The rapid evolution of the field.

Addressing this range of challenges in recruitment, retention, measurement coherence, privacy, security and the ever rapid changes to the field, is critical to the success of research leveraging mobile technology.

RECRUITMENT: Although there has been success in using technology platforms to recruit participants from the general population to participate in research, the evaluation processes for including/ excluding participants with specific characteristics (e.g., age, diagnostic history, chronicity, etc.) and retaining participants throughout the study lifecycle remains problematic. While researchers have been successful in rapidly recruiting participants in large numbers, the success of remote recruitment strategies changes drastically and unpredictably

over time. Early mobile research easily relied on search engines as a method for Internet-based recruitment[84]. However, within a year, that method was no longer successful, and it is currently deemed by many in the field as a low yield recruitment source[9]. Furthermore, the ability to remotely assess and screen individuals to confirm eligibility criteria remains a significant challenge.

RETENTION: Some mobile studies suffer from poor long-term retention, with dropout rates as high as 90% over the course of only a few weeks[85]. A recent study of mental health app use found that even with push reminders, retention dropped from a low of 63% at one month to 46% by three months' use[86]. Conversely, some studies demonstrate relatively high levels of user engagement in mobile interventions over longer timeframes. For example, Ben-Zeev and colleagues (2016)[87] reported on a technology-assisted relapse prevention program for 342 people with schizophrenia that involved the use of an mHealth intervention called FOCUS. In the study, engagement was encouraged and supported by regular check-in calls and meetings with clinical research staff and approximately three quarters of study participants used the intervention regularly, for 3 to 6 months. However, even the most motivated participants exhibit variable use patterns, such as

switching apps or devices as their goals or lives change[88].

It is clear there are many opportunities for behavioral scientists, working with experts in human centered design, to study how to best involve, motivate, and continuously engage participants in research that is conducted remotely. Exploring better research designs, including evaluating incentives and allowing participants to choose which data to share with researchers would be invaluable in improving the retention rates in these studies.

Another important challenge in conducting research of this nature is the pace at which technology changes. The technology specified in an initial research application may be out-of-date by the time the study is funded and ready to launch. This means that researchers and funders will need to be flexible about allowing for changes in technologies for data collection, during the conduct of the study. It also means that studies will need to move quickly for the outcomes to be meaningful. There currently exist several barriers to modifying an intervention during the course of the research study including limitations in study designs, data analytic challenges, and navigating lengthy Institutional Review Board (IRB) approval processes each time the intervention undergoes a new iteration.

PROTECTION OF PARTICIPANT DATA AND SAFETY: Electronic technology studies are subject to problems such as cyber-attacks, physical disasters, submission of corrupted or fraudulent data, loss and corruption of collected data, insider data theft, unauthorized data sharing, Private Health Information (PHI) leaks, and participant re-identification. There are additional challenges with the volume and granularity of data collected via passive sensing technologies (e.g., wearable or phone app) and the lack of standards to securely store and share these data.

Participant protection is a key issue. The data collected from research participants may not be part of their medical record and, as such, privacy protections offered through HIPAA do not apply. The personal health data collected by researchers using both research grade and commercial wearable sensors or mobile-based apps introduce new concerns for data management. For devices controlled by the researcher, data management is an internal process that can be dictated by institutional policy and IRB mandates, however, for many institutions, policies detailing how to manage the volume of data produced by these technologies do not yet exist. When using a commercial product as a research tool (e.g., Fitbit, MapMyFitness, etc.), research participants may be asked to set up an account with the vendor, which likely involves the review of Terms and Conditions and Privacy Agreements. Even if the participant opted to review these in detail, they are not written at the 4-6th grade reading level that IRBs strive for in documents related to informed consent and may lead to difficulty in fully understanding the risks. Additionally, the legal context of Terms and Condition agreements is likely to conflict with regulations to protect research participants' rights to litigate, if harmed as a direct result of study participation. These are a few safety and security concerns that should be carefully considered to ensure appropriate protections of research participants.

While the focus has been on phone apps and mobile/wearable technologies, it would be remiss not to acknowledge data that can be leveraged for research that is collected on social network platforms like Instagram, Facebook and Twitter. For example, Tweets are publically available and can be used for research purposes; however, most are geo-tagged and, with somewhat sophisticated analytics, researchers can identify public health threats and make inferences about individuals who may be at risk.

At this time, the ideal approach is to inform research participants about the precautions employed to protect data and to clearly state that the researchers are not able to guarantee the confidentiality of data and that techniques to anonymize data are limited in terms of protecting participants' private information. Researchers may want to consider the use of software that can remove information that identifies a participant even if the person chooses to self-identify during their electronic participation.

PROTECTION OF PARTICIPANTS AND INSTITUTIONAL REVIEW BOARDS: Researchers also must present their research plan to an IRB responsible for applying regulations and ethical principles designed to protect human research participants. The IRB is charged with evaluating the probability and magnitude of risks and benefits associated with the research. New technologies and methods may introduce new challenges for IRBs. Given there are upwards of 6,000 IRBs in the United States, it may be unreasonable to expect IRB members to be sufficiently well versed with all technologies, which may contribute to either overlooking potential risks of harm to participants or making overly conservative decisions[89]. There is considerable variability in how IRBs view the ethical dimensions because of the novelty of passive sensing and mobile research methods and the lack of guidelines. Furthermore, an underlying problem for IRBs is that the federal regulations used to guide research participant protections (45 CFR 46) have not been updated since 1991. An exploration of the gap between 21st century research methods and static regulations should include individuals with expertise in research, privacy, bioethics, research ethics, technology, computer science, and research regulations convened to imagine a responsive and dynamic ethics review process[90].

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CHAPTER 6 RECOMMENDATIONS

» Promote the testing of strategies for using technology to enhance the consent process (e.g., alternative formats for low-literacy populations and "quizzes" to test/ensure comprehension).

» Explore the use of consenting strategies that allow participants to select which information they chose to share.

» Disseminate best practices for safety monitoring and management, considering the use of software that removes identifying information even if the participant voluntarily self-identifies during their participation.

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Additional Cross-Cutting Considerations and Recommendations

STRATEGIES 2-4 OF THE **NIMH STRATEGIC PLAN** FOR RESEARCH AS WELL AS THE SECTION ON "ADAPTING TO A CHANGING ECOSYSTEM" HAVE PROVIDED THE FRAMEWORK FOR THE PRIOR RECOMMENDATIONS DESCRIBED IN THIS REPORT. THESE SAME STRATEGIES PROVIDE THE FRAMEWORK FOR ADDITIONAL CROSS-CUTTING RECOMMENDATIONS AND CONSIDERATIONS.

In the discussions captured in the preceding chapters, several other recommendations regarding Digital Health research were identified. These can be divided into the following topics: infrastructure, training/collaboration, study design/methodology, dissemination/implementation, and technology design.

INFRASTRUCTURE RECOMMENDATIONS:

- *Facilitate access to existing mHealth data sources.* Access to mHealth data sources may be promoted through data sharing, which would include incentivizing researchers to share their data e.g., through the use of the NIMH Data Archives and/ or repositories.
- *Support conferences and workshops.* Leverage existing conferences on mHealth, wireless health technology, allied health fields, and consumer technology. The researchers and stakeholders at these meetings could come together to discuss mental health applications in the context of those meetings.

TRAINING/COLLABORATION RECOMMENDATIONS:

- *Develop new training models that integrate a wide range of experts.* Encourage new training models for researchers, physicians, and psychologists (particularly those facing the challenges of mid-career) in the areas of data use and intervention development, from a wide perspective. Encourage the collaborations of multi-disciplinary experts.
- *Develop and test generalizable strategies for task shifting.* Test approaches for training and supporting the implementation of technology-assisted approaches by para-professionals, including those who can translate and interpret data and know how to respond when technology is deployed on a large scale.

STUDY DESIGN/METHODOLOGY RECOMMENDATIONS:

- *Utilize study designs that allow technology to evolve during the research lifecycle.* The phases of traditional research contrast with studies on technology-enhanced assessment and intervention. Technologies adapt to how people use them and to users' demands, therefore it is critical that ability for making modifications are built into the study designs, allowing for quick adaptation.[91]
- *Consider the balance between pilot studies and later stage research.* There should be a well-considered balance of pilot studies versus full-scale, late-stage research, as well as a consideration of the nature and amount of pilot data that are optimal before larger-scale testing is proposed.
- *Test principles rather than technology.* Support research that tests principles (e.g. behavioral science principles) rather than products or applications.

DISSEMINATION/IMPLEMENTATION RECOMMENDATIONS:

- *Evaluate existing mental health apps.* Numerous mental health applications are available online, but there is a need for rigorous evaluation, and development of an evaluation structure of these apps.
- *Promote new models for implementation.* The large-scale use of technology in this area will not happen on its own. There is a need for well-articulated models for implementation of these technologies in the real world.
- *Promote Dissemination.* Since dissemination is an important driver of uptake, various avenues for dissemination should be stimulated, including those of an open-source environment.
- *Consider factors that impact the ultimate adoption of technology.* Within the context of the research, larger provider organizations are well equipped to promote support of technology, for example, providing smartphone technology as part of insurance plans, especially for people with serious mental illness. Such support will likely help to scale up adoption of this technology.

TECHNOLOGY DESIGN RECOMMENDATIONS:

- *Weave interventions into existing technology.* Emphasize user-centered design. The field should ask patients about their needs and develop technological solutions that are built into the fabric of their lives (i.e., are invisible) to support behavioral change.
- *Consider user factors.* Technology users need to have options. Factors such as literacy levels and dexterity must be considered during hardware and software development.
- *Simple is sometimes better.* Capitalize on simple, user-friendly technologies—for both patient and clinician-facing tools.

CONCLUSIONS

Digital Health technology has rapidly evolved to play many important roles: in research studying the etiology and course of mental illnesses; in uncovering opportunities for early identification and intervention in those illnesses; in supporting the delivery of evidence-based treatments; and in improving the delivery of mental health care. These tools are also useful in conducting large scale research to answer questions more efficiently and rapidly. The contribution of such cutting edge technology has also been discussed at a National Academies Workshop on Neuroscience Trials of the future.

There is considerable promise to the new approaches brought about by the technology, in assessment, treatment, service delivery, and research methods. Nonetheless, investigators must be careful to consider the limitations and challenges to this form of data collection, the role that technology plays in treatment and service delivery, and the potential burdens of Digital Health technology for end-users. Investigators should employ user-centered designs in developing tools, use novel data analytic techniques that are better suited for Big Data analysis, and pursue an interdisciplinary team science approach to research, that will involve collaborations with engineers, data scientists, health system experts, and technology designers. This research should specifically be conducted in collaboration with health systems and communities, so that the data collected, and the interventions developed have the greatest chance of being generalized and adopted.
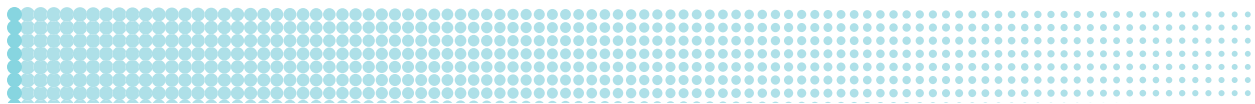
With this report's recommendations and cautions in mind, collecting behavioral data objectively in real-time on potentially thousands of consumers and participants, will result in far-reaching mental health treatment and service innovations in the future.

Table 1: Digital Health Tools for Collecting Data

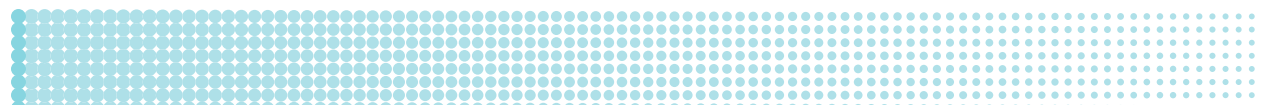| DATA TOOL/TYPE	USEFUL FOR MEASURING	STATUS FOR USE IN RESEARCH
GPS/Wi-Fi • Time spent at different locations • Distance covered during a day • Variability in geospatial activity	Social and occupational functioning (time spent at school, friends, work), time engaged in activities outside of home and work, change in routine.	Pros: technology exists Cons: requires participant to have phone and sensors with them and GPS activated
Physiological sensors • Heart rate • Heart rate variability • Galvanic Skin Response • Blood pressure	Autonomic activity, cardiac and muscular function, arousal	Pros: devices and apps widely available Cons: Devices and apps vary widely in accuracy
Accelerometers/ Actigraphy • Movement	Activity (active vs. sedentary, walking, running, cycling) and sleep inference	Pros: data are available Cons: correlation with activity and sleep still in development. Does not currently measure quality of sleep or activity
Light sensor	Ambient brightness	Pros: data are available Cons: what activities (e.g., sleep) can be accurately inferred from these data are still TBD
Ingestible sensor • Ingestion detection	Oral medication use	Pros: Objective indicator of medication use/adherence Cons: technology exists but is proprietary. Acceptability by different clinical populations TBD
Social media • Sites • Frequency of activity • Group membership • Photos posted	Degree of on-line social engagement, changes in activity	Pros: technology exists to have participants download data for up to 2 years Cons: security

DATA TOOL/TYPE	USEFUL FOR MEASURING	STATUS FOR USE IN RESEARCH
Calendar • # events • event type	Work and activity demands	Pros: technology exists Cons: requires participant to enter data
Device use • when and how often device is open • time on device	Nighttime activity as proxy for sleep quality	Pros: technology exists Cons: may need to capture data from various devices
SMS/MMS/Phone/Email • # of contacts • messages sent • messages received • time spent in response • when contacting and for how long	Social network, social behavior	Pros: data can be accessed Cons: but on only Android devices
Keyboard • Typing errors • Typing speed	Cognitive load	Pros: data can be captured Cons: unclear utility, requires a baseline
Microphone • Human speech • Heart rate • Ambient sound	Conversation turn taking, speech rate and fluency, time in social environment (proximal to human speech) affect, cognition, sleep inferences	Pros: much could be learned about social, emotional and cognitive performance from vocal behavior Cons: still in proof of concept phase; ethical issues related to collecting data from people interacting with participant
Search Engine data • Websites visited • Website types • On-line shopping	Interests, concerns	Pros: Participant can download search data from 18 months to two years Cons: Cannot distinguish if different person uses same computer, or if participant uses different computers for work or personal use

DATA TOOL/TYPE	USEFUL FOR MEASURING	STATUS FOR USE IN RESEARCH
Video data • Facial expression • Eye movement • Vocal data	Cognitive load, social behavior, emotional state	Pros: data is available Cons: not ready for routine use, association with cognition, emotion and social behavior still being researched
Health history • Illness exposure • Injuries • Frequency of common illnesses (colds, flu, infections) • Family illness history • Prescription	Health status	Pros: Many big health plans have this data electronically Cons: for many, past history is still retrospective (existed before electronic health records), data hard to combine
Service Use • Frequency of visits • Types of services used • Time between appointments • Interventions prescribed • Provider type • Clinical notes	Quality of care; effects of treatment	Pros: Data currently being collected Cons: Missed information when participant moves or switches between hospitals and clinics, as well as insurance plans

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National Advisory Mental Health Council Workgroup

Co-Chairs

PATRICIA A. AREÁN, PH.D.

Professor
Director of Targeted Treatment Development
Department of Psychiatry and Behavioral Sciences
University of Washington
Seattle, WA

ALAN LESHNER, PH.D.

American Association for the
Advancement of Science
Washington, DC

Members

DEANNA M. BARCH, PH.D.

Gregory B. Couch Professor of Psychiatry
Department of Psychology, Psychiatry and
Radiology
Washington University
St. Louis, MO

DROR BEN-ZEEV, PH.D.

Associate Professor of Psychiatry
Director, mHealth for Mental Health Program
Dartmouth Psychiatric Research Center
Department of Psychiatry
Geisel School of Medicine at Dartmouth College
Lebanon, NH

DAVID A. BRENT, M.D.

Academic Chief
Child & Adolescent Psychiatry
Endowed Chair in Suicide Studies
Professor of Psychiatry, Pediatrics and
Epidemiology
Director, Services for Teens at Risk
University of Pittsburgh School of Medicine
Pittsburgh, PA

RANDALL L. CARPENTER, M.D.

Chief Scientific Officer
Rett Syndrome Research Trust
Trumbull, CT

BJ CASEY, PH.D.

Sackler Professor
Department of Psychiatry and Neuroscience
Sackler Institute for Developmental Psychobiology
Weill Medical College of Cornell University
New York, NY

JOHN W. DAVISON, M.B.A., PH.D.

Chief, Conditioned-Based Specialty Care Section
Clinical Support Division
Defense Health Agency
Department of Defense
Office of the Chief Medical Officer (OCMO)
TRICARE Management Activity, OASD (HA)
Falls Church, VA

BENJAMIN G. DRUSS, M.D., M.P.H.

Rosalynn Carter Chair in Mental Health and Professor
Department of Health Policy and Management
Rollins School of Public Health
Emory University
Atlanta, GA

MICHAEL F. HOGAN, PH.D.

Consultant and Advisor
Hogan Health Solutions LLC
Delmar, NY

MARSHA M. LINEHAN, PH.D.

Professor and Director
Behavioral Research and Therapy Clinics
Department of Psychology
University of Washington
Seattle, WA

DAVID C. MOHR, PH.D.

Director
Northwestern University Center for
Behavioral Intervention Technologies
Chicago, IL

CAMILLE NEBEKER, ED.D., M.S.

Assistant Professor,
Behavioral Medicine and Global Health
Department of Family Medicine and Public Health
University of California, San Diego School of Medicine
La Jolla, CA

ROSALIND PICARD, SC.D.

Director of Affective Computing Research
Co-director of Advancing Wellbeing Initiative
Professor of Media Arts and Sciences
Massachusetts Institute of Technology
Cambridge, MA

RUSSELL POLDRACK, PH.D.

Professor of Psychology
Department of Psychology
Stanford University
Stanford, CA

GENE E. ROBINSON, PH.D.

Director,
Carl R. Woese Institute for Genomic Biology
Swanlund Chair Center for Advanced Study
Professor in Entomology And Neuroscience
University of Illinois at Urbana-Champaign
Urbana, IL

RHONDA J. ROBINSON BEALE, M.D.

Senior Vice President and Chief Medical Officer
Senior Vice President and Chief Medical Officer
Blue Cross of Idaho
Meridian, ID

MARY JANE ROTHERAM, PH.D.

Bat-Yaacov Professor of Child Psychiatry
  And Behavioral Sciences
Director, Global Center for Children and Families
Director, Center for HIV Identification Prevention
  And Treatment Services (CHIPTS)
Semel Institute and the Department of Psychiatry,
University of California, Los Angeles
Los Angeles, CA

KARAN SINGH, M.B.A.

Co-founder
Ginger.io
San Francisco, CA

National Institutes of Health Staff

YANCY BODENSTEIN, M.S., M.P.H.

Office of Science Policy, Planning
and Communications
National Institute of Mental Health
NSC Building
Rockville, MD

MINDY CHAI, PH.D.

Office of Science Policy, Planning
and Communications
National Institute of Mental Health
NSC Building
Rockville, MD

DAVID CHAMBERS, D.PHIL.

Deputy Director for Implementation Science
Division of Cancer Control & Population Sciences
National Cancer Institute
Rockville, MD

KAREN GAVIN-EVANS, PH.D.

Division of Extramural Activities
National Institute of Mental Health
NSC Building
Rockville, MD

ADAM HAIM, PH.D.

Office of Clinical Research
National Institute of Mental Health
NSC Building
Rockville, MD

JEAN NORONHA, PH.D.

Director
Division of Extramural Activities
National Institute of Mental Health
NSC Building
Rockville, MD

JANE PEARSON, PH.D.

Chief, Suicide Preventive Interventions Programs
National Institute of Mental Health
NSC Building
Rockville, MD

BILL RILEY, PH.D.

Director
Office of Behavioral and Social Sciences Research
National Institutes of Health
Rockville, MD
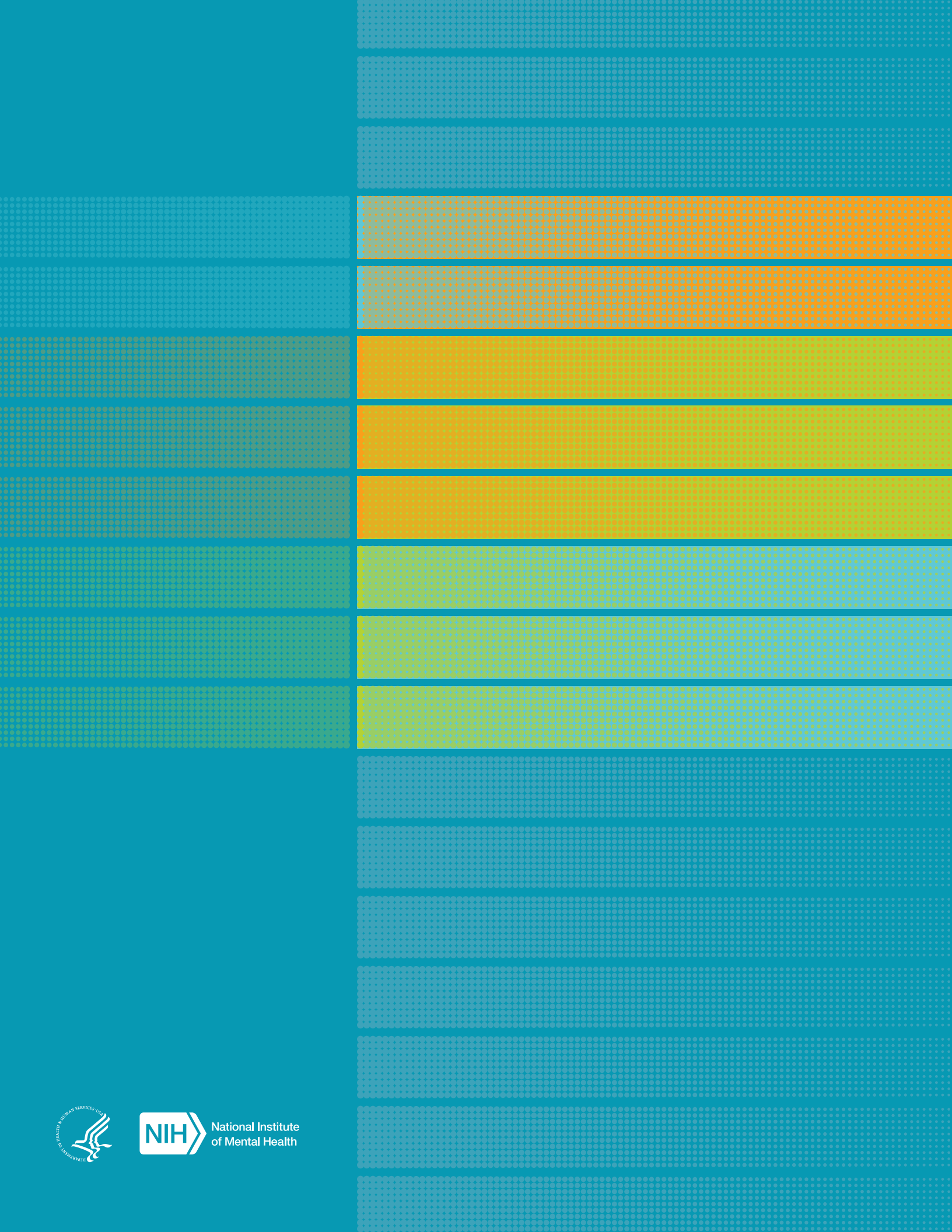
JOEL SHERRILL, PH.D.

Acting Deputy Director
Adult Treatment Intervention Research Branch
Division of Services and Intervention Research
National Institute of Mental Health
NSC Building
Rockville, MD

JANINE SIMMONS, M.D., PH.D.

Division of Behavioral Science and Integrative
Neuroscience Research Branch
National Institute of Mental Health
NSC Building
Rockville, MD

TRACY WALDECK, PH.D.

Acting Deputy Director
Division of Extramural Activities
National Institute of Mental Health
NSC Building
Rockville, MD
(now, Deputy Director,
Association for Psychological Science)