essary contact with health professionals of all types, only listen to the news for a short time each day, do not wash your hands repeatedly if you have had no possible contact with another person, and keep yourself occupied as much as possible.

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Smartphone relapse prediction in serious mental illness: a pathway towards personalized preventive care

Imagine a smartphone app that knows when a patient is at risk of relapsing on alcohol use based on geolocation data indicating proximity to a liquor store and real-time surveys suggesting elevated craving. The smartphone detects this imminent risk, alerts a clinician, and the patient receives a personal check-in within minutes. Such a system does not sound futuristic in 2020, neither was it a decade ago, when the Alcohol - Comprehensive Health Enhancement Support System (A-CHESS) study, described above, was conducted[1]. Ten years later, smartphone relapse prediction systems are catalyzing a paradigm shift in mental health care that is now further accelerated by the COVID-19 pandemic. As these approaches continue to enable dynamic and longitudinal modeling of risk, personalized preventive care is within reach.

The evidence for smartphone relapse prediction across major mental disorders is impressive. Today it is possible to build dynamic digital proxies for symptoms, functioning, cognition and physiology using smartphones and wearables – often referred to as digital phenotyping[2]. For example: passive smartphone data from sensors like global positioning system (GPS) can inform about location; accelerometer about sleep; active data from surveys (often referred to as ecological momentary assessment) can capture real time symptoms; metadata from phone interactions can characterize cognition; and data from wearables can inform on physiological measures.

Capturing these diverse data streams is highly feasible. Open-source and free platforms such as mindLAMP have permitted teams across the world to engage in this work[2]. Using varying combinations of these digital data streams, studies have shown clinically actionable assessment of relapse risk in schizophrenia[3], depression[4], bipolar disorder[5] and substance abuse[1]. Furthermore, data around spoken and written language as well as social media use (often accessed via smartphones) is also augmenting relapse prediction. Since at least 2018, an effort has been made to predict suicide attempts in the US through real time natural language processing[6].

The success in accurate assessment of relapse risk is encouraging and highlights the need for the field to advance towards studies of predictive validity and reproducibility. In the suicide prevention field, a recent review highlighted that even the good global classification accuracy of current suicide risk models still yields a predictive validity of less than 1%[7]. The predictive validity of smartphone relapse models remains untested, but targets for ensuring reproducibility have already emerged, including data accessibility, standards and methods.

Data accessibility from smartphones is constantly in flux, as Apple and Google (which control over 99% of the world's smartphone operating systems) change accessible data sources each year in response to both technical and privacy considerations. For example, in June 2020, both Apple and Google announced that access to Bluetooth data (which can be used to infer social context – a key element in many relapse models) would become limited given growing privacy concerns. Balancing ethical data uses and surveillance risks from this work requires renewed attention. For available data streams, differences in sensors and phone models and brands often yield divergent metrics for the same behaviors, generating a need to control for device characteristics in a standardized way.

Furthermore, assuming a case where all smartphone sensors are sampling at 10Hz, theoretically up to 65GB of data can be generated for one patient in one month. Appropriate use of statistical methods is critical, as spurious findings should be considered the norm with this amount of digital data. Sharing data – a challenge in this work given the personal and identifiable nature of digital phenotyping data – will be critical to success, and new efforts in the spirit of the openfMRI project (see https://openfmri.org) are necessary. Ensuring that these new dynamic models of relapse are not biased, as is being realized today for some medical treatment algorithms that misuse race[8], will require diverse and representative research.

Careful assessment of the prospective validity, reproducibility and clinical applicability of these new smartphone relapse prediction models is a clear next step. Many current models are not utilized in routine care because they are based on static risk factors (e.g., age and gender) and explain a low percentage of relapse variance. While there are some sophisticated models that allow for time varying factors, they often assume that mental health processes are ergodic, i.e. that group level data are generalizable to an individual[9]. In the past, when data collection was limited at the individual level, this assumption has been necessary, but now it is recognized to be incorrect[9].

With new access to unprecedented amounts of data over intervals that can range up to years per individual, the methods used to analyze data need to evolve alongside the technology that has enabled this new potential data resource. Digital phenotyping creates the potential for a new generation of relapse prediction models that do not fall victim to the ergodic fallacy, and can make personal and more preventive psychiatry a reality.

This reality is approaching faster now, as the COVID-19 pandemic has accelerated the field's use of telehealth and acceptance of smartphone data to supplement care. As patients can no longer fill out paper-and-pencil surveys and hand them to clinicians, use of patient-reported outcomes captured via computers and smartphones has become necessary for everyday care. As barriers to using smartphone data continue to fall, and the evidence for benefit continues to expand, the real question is not when but how relapse prediction data will be used.

While it is easy to imagine ideal uses for smartphone relapse prediction, as outlined in the A-CHESS study, the broader realities must also be considered. In Fall 2019, the concept of using smartphone prediction not towards relapse, but rather violence prediction among people with serious mental illness, was floated. This idea was met with concerns around ethics, feasibility and stigma, but highlights how easily a seeming boon to the field can turn into a potential liability.

Another pressing challenge is how health systems can respond to smartphone relapse prediction data. Relapse may happen at 2am on Sunday morning, and the clinical team can be alerted at the same time. The real solution is designing new clinical services that are able to respond to digital data. Designing these new services along with new technologies in an inclusive, collaborative, iterative manner across disciplines will result in solutions that will bridge the research to practice (or code to clinic) gap and help prevent relapse.

The digital clinic of tomorrow may not look like the traditional clinic of today. Our teams in Boston, New York and Philadelphia are piloting digital clinic models where we have learned first-hand the rewards and challenges of this approach. In relapse prediction, the new technology can offer a first line of response with just-in-time adaptive interventions in a stepped care manner – in some cases removing the need for an immediate personal response from the clinical team. But there is always the need for a personal connection with every patient. For example, a patient recently appeared at risk for a manic relapse given elevated levels of phone activity but, upon reaching out, he informed us that he had started letting his roommate use his smartphone when working the night shift. This explained the lack of sleep and increased activity captured by the smartphone, which had been interpreted incorrectly as elevated risk. Fully automated interventions could be problematic with respect to false positives and should instead be seen as complementary to the human element of care.

The potential of personalized preventive mental health care is within reach with smartphone-based relapse prediction. As the next generation of studies explore prospective validity, the clinical need for these models will drive further innovation. The convergence of these approaches is not a decade away, but will likely be as swift as it is transformative.

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Brain networks and cognitive impairment in psychiatric disorders

Cognitive impairments are a prominent feature of all psychiatric disorders. The goal of mapping each disorder to individual brain areas has now been largely abandoned, and supplanted by systems neuroscience approaches which focus on distributed circuits and large-scale brain organization[1].

Although the nature of cognitive impairments varies across disorders, a common underlying feature is the inability to adaptively regulate or control behavior in relation to changing goals and saliency of external stimuli and internal mental events. Dysregulation of the brain's cognitive control systems thus lies at the crux of most behavioral impairments. Cognitive control is a dynamic process, which relies on flexible goal-relevant modulation of brain networks, and investigations of dynamic network interactions are advancing fundamental knowledge of the neurobiological basis of psychiatric disorders[2].

The human brain is intrinsically organized into networks, each consisting of a distinct set of cortical and subcortical areas linked by temporally synchronous neural activity[1]. The intrinsic connectivity of brain networks displays close correspondence with task-related co-activation of brain regions, and this correspondence has allowed intrinsic and task-related connectivity to be demarcated and studied under a common systems neuroscience framework[3].

Brain networks not only provide a unifying framework for characterizing functional organization of the neurotypical brain, but also for probing the neurobiological basis of psychiatric disor-