

Digital mental health: challenges and next steps

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APPENDIX

This appendix contains tables which highlight particular details about, or examples of, concepts relevant to the paper 'Digital mental health: challenges and next steps'. The explanations and examples are not exhaustive; instead they are presented to illustrate and to provide some examples of the concepts explained in the main paper.

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Table 1. EMA and digital phenotyping, definitions and examples.

EMA (ecological momentary assessment) in mental health describes, in its broadest sense, repeatedly collecting data in participants' daily lives using real-time measures [1,2]. **Digital phenotyping** can be defined as the 'moment-by-moment quantification of the individual-level human phenotype in situ using data from personal digital devices' [3]. Personal data gathered from mobile devices and sensors is analysed to provide health information (and can be used as a basis for providing advice). This provides the opportunity to access continuous assessments of symptomatology in patients' daily lives, and therefore the potential to overcome some of the challenges in mental health [4].

There is some variability in the exact use of these individual terms. A detailed exploration is beyond the scope of this paper, but in some settings, EMA is used to refer to actively acquired data, and digital phenotyping to passive data (see for example [5]), whereas in others, digital phenotyping is used to cover both passively and actively acquired data as a whole [for example, [6]]. These differences may demonstrate the use of multiple terms to represent similar methodologies, which all have the common goal of using research to assess daily life [7].

Some examples to illustrate the potential uses of this type of data come from mood disorder research. Actively acquired data as described above involves active input from users: for example, in bipolar disorder patients can evaluate their level of symptoms, which map well onto clinical evaluations [8,9,10]. This active data has great potential for long-term monitoring or as outcome measures of the early effect of interventions. By contrast, passive data can be collected without active data entry from participants: for example, voice features collected during telephone calls may represent both a supplementary objective marker discriminating bipolar disorder from unipolar disorder and healthy individuals, and also serve as a state marker within bipolar disorder

[11,12]. Additionally, mobility patterns (from mobile location data) can contribute as a digital diagnostic marker in discriminating between patients with bipolar disorder and unipolar disorder, and serve as a state marker within bipolar disorder [13,14].

Table 2. An example of a transdiagnostic digital approach: adolescent mental health

In adolescence, prevalence of mental disorders is about one in four [15] but may be even higher for subthreshold conditions, which may then evolve into different psychiatric diagnoses [16]. As young people develop, their symptom presentation may change or evolve, either within a diagnostic category, or moving through several separate psychiatric diagnoses according to traditional classifications [17]. In addition, comorbidity is the norm rather than the exception in children and adolescents with mental health conditions [15]. Some underlying constructs, such as affect regulation, inhibitory executive control, or stress sensitivity, are also related to the onset and persistence of different psychiatric conditions in children and adolescents [18].

These factors taken together all suggest that the use of digital mental health in a transdiagnostic approach may help by integrating categorical and dimensional assessments. Tracking dynamic behavioural, physiological, cognitive, and symptom patterns (rather than solely episodes of categorised illness) may produce more meaningful data for the clinician and patient, such as prediction of episode onset or remission. This also has implications for treatment and is consistent with a wider consensus (led by the Neuroscience-based Nomenclature (NbN) task force, <https://www.ecnp.eu/research-innovation/nomenclature>) to move from traditional disease-based psychopharmacology classifications to those which categorise using factors such as the relevant neuroscientific evidence or mechanism of action. Perhaps the novel naturalistic and longitudinal data afforded by digital phenotyping could help in the development of such transdiagnostic approaches.

Table 3. Machine learning methods in mental health: possible applications.

In parallel with the rapid development of digital phenotyping technology, machine learning methods have emerged as powerful tools to explore high-dimensional, time-series data (such as electroencephalography, resting-state functional magnetic resonance imaging, or natural language) [19]. Therefore, possible applications of machine learning in mental healthcare range from diagnostic and prognostic markers [20,21,22], to the potential use of generative deep learning models as conversational chatbots for broadly psychotherapeutic treatment delivery [23].

However, as highlighted by a recent review [24], these methods have so far rarely been used to extract predictive markers from digital data streams, and their application has mainly focused on the prediction of affective states in mood disorders [13,25,26]. Thus, it remains unclear if these mood-predictive models could be employed transdiagnostically to forecast abnormal affective and psychomotor states across other conditions such as schizophrenia, borderline personality disorder, or substance abuse disorders. In addition, the potential power of multimodal predictive information extracted across multiple parallel data streams, such as voice, geolocation, and EMA data, using machine learning methods, is only just beginning [27].

The use of these analytical methods requires large-scale and harmonised data collection efforts. This is not a trivial undertaking, as the technological basis of digital phenotyping, such as smartphone operating systems and the hardware itself, is rapidly evolving. Also, for the ultimate clinical translation of digital phenotyping-based prediction models into clinical care, evidence of out-of-sample generalisability, transdiagnostic generalisation, and therapeutic specificity must be submitted to regulatory bodies [19]. It is well-established that AI models themselves can be highly biased depending on the input data they have been trained upon, and so it is key that they use representative and diverse models in training. These requirements can only be met through

internationally agreed standards that harmonise the data acquisition, training, and validation steps of models operating on digital phenotypes [19]. However, encouraging efforts towards these are now underway in large international projects involving digital phenotyping [28, <https://www.nimh.nih.gov/research/research-funded-by-nimh/research-initiatives/accelerating-medicines-partnership-program-schizophrenia-ampr-scz>]

Table 4. Choice of placebos in digital intervention studies

Placebos are needed to control for the considerable noise arising in clinical trials, including natural history, regression to the mean, response biases, Hawthorne effects (the potential for participants to change their behaviour when monitored), and placebo/nocebo effects (genuinely positive/adverse health changes arising as a result of psychobiological expectancy responses that a treatment will be effective/harmful) [29]. Without adequate placebo controls, researchers risk overestimating effect sizes of active interventions [30] leading to inaccurate inferences about the treatment's effectiveness.

Placebos should therefore be matched to the active intervention on as many variables as possible (ideally all) except the hypothesised therapeutic component(s); the 'essence' of the intervention [29,31]. However, in digital intervention studies this is often not known, or not clearly described. This problem is not unique to digital interventions. For example, in drug studies, fewer than 10% report on placebo characteristics [30], and in psychotherapy studies there are additional challenges, as clinicians cannot be blinded to allocation [32,33].

An example of an approach addressing these complex issues would be the use of so-called 'dismantling' or 'additive' studies. For example, in studying a hybrid clinic that offers synchronous telehealth visits with a clinician, asynchronous support from a digital navigator, and real-time services from an app, it is important to assess the impact of each intervention, as well as their combinations, in order to understand the mechanisms behind efficacy and drive further improvement. To date, few if any studies report on the actual drivers of efficacy in hybrid care models [34] (for example therapeutic alliance with the clinician, coach or app, increased self-efficacy, increased emotional self-awareness) which has precluded both the development of new theories on engagement and the development of more effective services.

Table 5. Addressing the physical health needs of those with mental illness

The delivery of preventative/behavioural health interventions in the general population is increasingly relying on digital technologies, and there is currently a variety of research, innovation and investment towards using apps, wearables and remote support to create a physically fitter and healthier society [35]. Although people with severe mental illness (SMI) die approximately 15-20 years younger than the general population, primarily due to cardiovascular and metabolic diseases [36], the extent to which digital innovations for physical health can reach mental health populations has not been widely considered [37,38]. People with SMI may therefore be 'left behind', increasing pre-existing disparities.

Psychiatric research has started to examine how digital technologies may be able to increase the accessibility and scalability of behavioral health interventions for people with mental illness, for instance through app-based approaches for smoking cessation [39], wearable or virtual reality-supported physical activity programs [40,41,42], and gamified mHealth platforms for healthy living [43]. Such innovations could improve not only physical health, but also mental health outcomes, as lifestyle interventions have been shown to have beneficial effects on cognitive and functional outcomes in people with mental illness [44].

Table 6. Examples of integrating intervention with real time assessment

Real-time analyses of mobile sensor technology can be used to increase adherence to interventions. For example, in the PROUD study (Prevention of comorbid depression and obesity in attention-deficit/ hyperactivity disorder), patients were treated preventively via light and exercise therapy [45]. Endurance training and strengthening exercises were implemented on a smartphone with short video clips. Real-time analyses of the completed training were performed, logging training videos and using accelerometers. Performance parameters were calculated in real time, for example steps per day, and sent to the participants as motivational cues to keep up the training or to motivate them for a certain physical activity of the day that had not yet been performed.

Another example of integrating real-time analyses of mobile sensor technology into interventions is the Bipolife study [46], where digital phenotypes of patients with bipolar disorders are tracked and analysed in real time. A fully automated algorithm sends alarms to treating psychologists and psychiatrists, if a set of predefined parameters surpasses individualised, adapting thresholds.

Just-in-time adaptive interventions (JITAs) are interventions that adapt over time to an individual's changing status and circumstances, to address the individual's need for support, whenever this need arises [47]. They show great potential, but there is a lack of current real-world clinical examples in mental health [48,49].

Table 7. Clinical decision making using digital data: some concepts and examples

Using digital data in clinical decision-making not only allows for the addition of extra information, but as this extra information is generated in real time by the patient, it may also help to identify or confront the bias in information-gathering encountered via other routes [50]. This benefit in reduction of bias might occur at several levels:

1. At the 'micro-systemic' level (the clinical interaction with patients) this could reduce errors of judgment (in the patient or clinician) related to incomplete clinical information processing (for example memory bias, choice of salient information, influence of theoretical a priori knowledge). In addition, the patient/physician relationship could also be positively impacted by the increased emphasis on the patients' information, and act as a powerful empowerment tool.
2. At the 'meso-systemic' level (the organisation of care), the digital phenotype data may reduce heterogeneity in clinical practice and management, and therefore increase efficiency and reduce disparities in care.
3. At the 'macro-analytical' level (systems of care), these efficiencies and increased consistency could allow better acceptability by organisations in terms of financial support and implementation.

An example of clinical decision making using digital data is in the so-called 'digital clinic' model of integration of asynchronous telehealth with apps into synchronous telehealth models of care through video (or in person) visits [51,52]. There are several potential advantages in this approach including both improved access and quality of care, as the use of digital tools can enhance evidence-based care and shared decision-making. Digital clinics can use a variety of asynchronous technologies (for example apps, and sensors) to collect comprehensive data and inform care decisions. These can supplement in-person or synchronous telehealth visits, and because of their asynchronicity, also allow for the potential to increase efficiency.

However, there are challenges in implementing digital tools in the clinical setting which go beyond any immediate technological difficulties [53]. In real world implementation, aspects such as the type of digital innovation (for example the complexity and utility of the app), the users (patients, carers, clinicians, and their familiarity and wish to use the digital tools), and the overall context (the healthcare system, reimbursement, and regulation policies) are also key areas to consider [51,52,54]. There are strategies which can facilitate implementation including: co-production of the technology with users (see Table 8), training for staff and patients, creation of new team members with complementary skills (such as 'digital navigators'), and re-design of the structure and flow through the clinic [55].

Table 8. Case studies highlighting co-design

Although initial engagement with digital interventions can be high, this is often not sustained. For example, the majority of users abandon apps within a few days [56,57]. Engagement can be improved by human support alongside app use [58], but this human interaction is often a limiting factor. To realise the full potential for interventions such as apps to expand access to care and enable scalability, there is increasing interest in co-design and co-production with users and stakeholders, to ensure that digital tools reflect their self-identified specific needs and preferences [59].

An example is in children and young people, where rates of mental illness and mental health difficulties are high, but rates of availability of intervention and support are much lower [60]. This may be an ideal population for digital intervention as a potential route to improve the reach and access to therapies. With 97% of teens reporting that they use the internet daily, and 46% saying they use the internet almost constantly [61], a digital approach could have a significant impact in this population. However, although there is some initial evidence to support this [62,63], engagement, uptake and adherence outside the research setting is a significant challenge and perhaps an “Achilles’ heel” for the paradigm [62,64,65].

Co-design involves a process throughout the life and research cycle of the programme, involving all relevant stakeholders. For adolescents, these might include families, carers and friends, and also experts in youth services (for example in education, health, social care), experts in the content of the intervention (for example clinicians, researchers) and experts in digital technologies (for example designers, information technology specialists, animators) [64]. Parents’ opinions and concerns about the use of technology, and the logistics of its use within families will highly impact the acceptability and utility of innovations and so it is key to include patients and families. It is

especially important to encompass diverse populations and include those young people living in communities facing health and social disparities. Teens with socially complex needs may be more in need of mental health resources, but also experience the greatest systemic barriers to accessing care, and have previously been overlooked or excluded from collaborative research designs for mHealth [66].

Table 9. Ethical issues in digital interventions

There are a variety of potential ethical concerns in the use of digital mental health interventions [67]. Firstly, epistemology is deeply entwined with ethics. The quality of evidence on which digital interventions are based carries ethical consequences for clinical practice, both in terms of what diagnostic or treatment tools are employed, and what is conveyed to patients about these tools. In addition, due consideration must be given to informed consent when it comes to the inclusion of patient data in generating insights in the domain of digital mental health. There may be great scope for digital markers to improve the precision and timeliness of care; but establishing the benefits and balancing these against the potential harms of digital health interventions will be essential.

Correlation does not imply causation: it is imperative to ensure that data collected are predictively valid and support safe and accurate diagnoses and prognoses [68]. Harms may arise if digital data lead to overdiagnoses or inaccurate predictions of mental health. Ensuring reliability and validity may require data to be collected from a diverse variety of populations [69]. For example, both individual and cultural differences may lead to differences in linguistic markers in digital phenotyping; analyses of content that use irony or sarcasm might incorrectly identify users as depressed or suicidal among some patients but be predictive among others. Without due caution and oversight, digital phenotyping could perpetuate or exacerbate health disparities via biases if trained on limited populations of patients [70]. Limitations with datasets combined with the opacity of some algorithms on which insights are based, might exacerbate healthcare inequalities, by restricting the usefulness of these tools among some patient populations or directly leading to harms via inaccuracies.

Other ethical problems arise if the processes of collecting digital data incur adverse influences on patient behaviour [71]. For example, preoccupation with checking health tracking data via downloadable apps and wearable devices might increase anxiety or unwanted nocebo effects [72],

or lead to increased time spent online. Although the relationship between screen time and adverse mental health has not been fully resolved, there is a risk that under certain conditions, some social media platforms might be detrimental to mental health [73,74], displace more healthful behaviours, or be sources of misinformation.

Perhaps the most prominent ethical concerns with respect to digital mental health are patient privacy, confidentiality, and trust in healthcare. Data collection may involve tracking patients beyond traditional health information to include a variety of data embedded in (for example) social media posts, fitness trackers, telephone and text traffic, and geolocation. The secure storage and usage of this information including patient consent [75] and adequate data governance pose real and persistent challenges for healthcare, providers [76], and civic privacy laws. This is particularly relevant with the passive nature of data collection in digital phenotyping; ensuring patients are fully aware and consent to how data is collected, managed, and used, will be critical to preserving trust in clinicians.

Examples of ethical issues

Ethical challenges frequently appear, such as that around the Crisis Textline in the United States. In mid-2022 it was revealed the company had been sending all text messages (often about suicidal thoughts) to a partner company which used the messages for building AI-informed customer service software (<https://www.bbc.co.uk/news/technology-60218894>). Only when the public was made aware of this and amidst the subsequent outcry did the company stop this practice and agree that the prior terms of conditions of use were not ethical (agreeing to share data by texting for help).

Often, ethical challenges are difficult to track, as in the case of Facebook which, again in the United States, may send the police to a user's door if they write messages around self-harm that are

detected by natural language processing run by Facebook [77]. While there is no sharing of results to show if Facebook's approach prevents suicide and saves lives, or results in harm by sending police to people's homes, there is currently no means to opt in or out of this program.

Table 10: specific populations

Child and adolescent mental health is a public health priority worldwide [78]. Smartphone use among this population is high, suggesting that this could be an ideal mode of delivery for mental health interventions [79]. The desire for digital media is aligned with the biology of the adolescent brain, as it offers social connection, novelty and the potential for making choices with low failure cost during a developmental period in which there are extensive brain and neurotransmitter system changes [80]. However, the evidence of the effectiveness of digital mental health interventions for youth is still limited to short-term treatments for conditions such as anxiety or depression, with very few data on long-term outcomes, younger age groups, youth with developmental disorders, minimum dose required, and on the generalisability of findings to adolescents and young people with different socioeconomic, cultural, racial or other backgrounds [81,82].

This is not the only group which might be relevant for digital interventions. For example, the elderly are also an important population to target, but have so far been left out of many digital data studies even though innovations like digital phenotyping may be especially practical [83]. A recent systematic review identified factors such as ease of use, opportunities for social interactions, human support and having tailored interventions as related to the success of digital mental health interventions [84]. People with intellectual disability experience high rates of mental illness, but have also been excluded from the development and implementation of new interventions. Barriers to using digital technology could be overcome in many cases by appropriate support and adaptations, and there is some early evidence of the value of incorporating digital technologies for promoting health, educational, vocational and leisure opportunities in this population [85,86,87]. Those with chronic physical conditions also experience higher rates of mental illness, and digital health interventions might help to overcome barriers to accessing mental health support for these

individuals. However, there is still work to be done in assessing the design and implementation of digital health interventions in this population [88,89].

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