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Supplementary Material

Article Title: Defining the Clinical Role of Digital Therapeutics in Major Depressive Disorder Treatment: A Consensus Panel Perspective

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Supplementary Material

Appendix 1

Future Research Priorities

The panel identified four priorities for research that would improve the scientific understanding of digital therapeutics for MDD. These priorities emerged from the evidence gaps identified by the panel throughout the manuscript. The research priorities, including study-design examples and clinical-practice impact are summarized in **Supplementary Table 1**.

The first priority the panel addressed was the need for real-world evidence studies to examine effectiveness across MDD severity levels and demographic subgroups to improve our understanding of which patients are most likely to benefit from digital therapeutics. Second, research examining specific intervention features and mechanisms of action is needed to help identify which components of a digital therapeutic drive patient engagement and symptom improvement, allowing interventions to be better matched to patient needs. Third, the panel identified the need for active comparator effectiveness studies to guide decision making when multiple evidence-based digital therapeutics are available and to clarify how digital therapeutics compare with other treatment approaches. Finally, research evaluating the durability of treatment effects beyond the acute treatment phase is needed to determine whether digital therapeutics function primarily as a short-term intervention or can also be used as durable companion treatments. Together, these

research priorities address many of the evidence gaps identified by the panel and provide a roadmap for future research.

Across the priorities, the panel emphasized several methodological considerations. Future studies should prioritize real-world effectiveness studies, focus on active-comparator and comparative-effectiveness designs that move beyond wait-list controls, which can worsen depressive or functional symptoms, and include longitudinal follow-up of patients.

Supplementary Table 1. Four Research Priorities with Example Study Designs and Impact on Clinical Practice

Research priority	Issue addressed	Example study designs	Impact on clinical practice
Real-world evidence across patient subgroups	Limited evidence in severe and treatment resistant MDD; underrepresentation of diverse populations.	• Phase IV effectiveness studies conducted in routine practice • Studies stratified by depression severity, age, sex, race/ethnicity, education, and socioeconomic status • Large pragmatic implementation studies in diverse healthcare settings	Improves understanding of which patients are most likely to benefit from digital therapeutics and supports more equitable, personalized treatment recommendations.
Research on design features	Limited understanding of which intervention components drive engagement, adherence, and symptom improvement.	• Component-analysis evaluating individual intervention elements (eg, reminders, check-ins, content modules) • Studies matching intervention features to patient subtypes	Identifies which components are driving symptom improvement, enabling more effective intervention design and more precise treatment matching.
Comparative effectiveness	Lack of evidence to guide selection when multiple digital therapeutics are available; uncertainty regarding how digital	• Pragmatic comparative-effectiveness trials comparing digital therapeutics to one another	Helps clinicians determine which digital therapeutic is most appropriate for specific patients when multiple

	therapeutics compare with pharmacologic or psychotherapeutic augmentation.	• Randomized trials comparing digital therapeutics with pharmacologic or psychotherapeutic augmentation • Indirect comparison network meta-analysis	evidence-based options are available.
Durability of benefit	Unresolved question regarding whether digital therapeutics function primarily as acute interventions or durable companion treatments.	• Prospective longitudinal cohort studies • Maintenance and relapse-prevention studies evaluating continued versus discontinued use	Clarifies the role of digital therapeutics in long-term treatment planning, patient communication, and can aid reimbursement decisions.

Abbreviation: MDD=major depressive disorder.