Evidence-to-Recommendation Guidelines

These guidelines suggest degrees to which adoption of digital health interventions (DHIs) may be warranted by clinical evidence. Evidence is one of many critical assessment domains; others include patient experience, cost, health equity, etc. DHIs should be screened for failure to meet absolute requirements (eg, HIPAA compliance). Enrollment targets are guidelines and should have statistical justification. For conditions with few treatments or urgent need, consider increasing rating by 1-2 actionability levels, without exceeding Level 3.

Actionability Level	Criteria	Adoption level that may be appropriate	Approx. enrollment that may be appropriate
0	One or more of the following: ● Clear evidence of harm or ineffectiveness for the current DHI version ● The DHI is not clinically appropriate, per advice of clinical subject matter experts. ● The risk balance is unfavorable due to safety concerns, per subject matter experts. ● There are unaddressed concerns regarding misleading or false claims.	Adoption not recommended.	N/A
1	All of the following: ● Very low or low-quality evidence (per GRADE[41] definitions; “very low” includes no evidence) ● Low clinical risk or well-managed risk with appropriate clinical rationale ● Plausibility of clinically meaningful impact relative to usual care (or an alternate, relevant comparator) OR noninferior clinical outcomes with plausible improvement in a domain such as access, health equity, user experience, or cost. Clinically meaningful impact is defined by an effect size magnitude at or above a minimal clinically important difference, as established in credible guidelines and/or peer-reviewed literature.	Feasibility Pilot: Focus is on enrollment, engagement, user experience, safety.	$N \leq$ ~100
2	All of the following: ● Meets or exceeds all criteria for Actionability Level 1 ● Low-to-moderate quality evidence (per GRADE[41] definitions). Real-world evidence may be included. ● No or minimal uncertainty (per GRADE[41]) around value to stakeholders (often patients and their families) ● Acceptable or likely acceptable (per GRADE[41]) to stakeholders	Small Clinical Pilot: Primary outcomes are clinical.	Up to several hundred.

3	All of the following: ● Meets or exceeds all criteria for Actionability Levels 1-2 ● Moderate-to-high quality evidence (per GRADE[41]). Real-world evidence may be included.	Large Clinical Pilot: Primary outcomes are clinical.	~300 ≤ *N* ≤ ~3,000
4	All of the following: ● Meets or exceeds all criteria for Actionability Levels 1-3 ● Two or more high-quality RCTs support efficacy and safety ● Preferred: One or more RCTs have 3rd-party data monitoring and analysis ● Preferred: Real-world evidence of safety and effectiveness	May be appropriate to scale.	No limit for appropriate patients.

Abbreviations: DHI, Digital Health Intervention; RCT, Randomized Controlled Trial; HIPAA, Health Insurance Portability and Accountability Act