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ISPOR Report

The PICOTS-ComTeC Framework for Defining Digital Health Interventions: An ISPOR Special Interest Group Report

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ABSTRACT

Objectives: Digital health definitions are abundant, but often lack clarity and precision. We aimed to develop a minimum information framework to define patient-facing digital health interventions (DHIs) for outcomes research.

Methods: Definitions of digital-health-related terms (DHTs) were systematically reviewed, followed by a content analysis using frameworks, including PICOTS (population, intervention, comparator, outcome, timing, and setting), Shannon-Weaver Model of Communication, Agency for Healthcare Research and Quality Measures, and the World Health Organization's Classification of Digital Health Interventions. Subsequently, we conducted an online Delphi study to establish a minimum information framework, which was pilot tested by 5 experts using hypothetical examples.

Results: After screening 2610 records and 545 full-text articles, we identified 101 unique definitions of 67 secondary DHTs in 76 articles, resulting in 95 different patterns of concepts among the definitions. World Health Organization system (84.5%), message (75.7%), intervention (58.3%), and technology (52.4%) were the most frequently covered concepts. For the Delphi survey, we invited 47 members of the ISPOR Digital Health Special Interest Group, 18 of whom became the Delphi panel. The first, second, and third survey rounds were completed by 18, 11, and 10 respondents, respectively. After consolidating results, the PICOTS-ComTeC acronym emerged, involving 9 domains (population, intervention, comparator, outcome, timing, setting, communication, technology, and context) and 32 optional subcategories.

Conclusions: Patient-facing DHIs can be specified using PICOTS-ComTeC that facilitates identification of appropriate interventions and comparators for a given decision. PICOTS-ComTeC is a flexible and versatile tool, intended to assist authors in designing and reporting primary studies and evidence syntheses, yielding actionable results for clinicians and other decision makers.

Keywords: definition, health economics and outcomes research, patient-facing digital health intervention, PICOTS-ComTeC, systematic review.

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Highlights

- Abundant, yet vaguely defined definitions in digital health represent a challenge for clinicians, decision makers, developers, and researchers. Despite having several guidelines/checklists for the standardization of evidence generation and assessment for digital health interventions (DHIs), the identification of comparable DHIs remains difficult because of their personalized nature, complex technologies, and linkages to larger systems. This may restrict the validity of evidence syntheses.
- We introduce the PICOTS-ComTeC (population, intervention, comparator, outcome, timing, setting, communication, technology, and context) framework, a newly developed, flexible, and versatile tool to help the formulation of sufficiently specific and detailed definitions for patient-facing digital health interventions and related research questions.
- To overcome the limitations of terminology in digital health, the PICOTS-ComTeC framework of patient-facing DHIs should be specified in sufficient detail, to allow the identification of comparable interventions and allow for the selection of appropriate comparators that deliver similar effects to patients; therefore, the fit of DHIs in clinical, financing or development decision contexts, and specific research questions can be assessed.

Introduction

Digital health involves technologies including artificial intelligence (AI), virtual reality, digital therapeutics, wearables, remote monitoring, and software.[1] Acknowledging the bewildering array of terms in use,[1-6] we denote these technologies as digital health interventions (DHIs). Technological advances, movement toward patient-centered care, and the COVID-19 pandemic have driven the adoption of DHIs.[7-15] Although DHIs can potentially enhance decision making, equity, and access,[16,17] concerns persist regarding the reporting quality and ambiguous terminology of DHI studies.[4,18-20]

Several guidelines aim to standardize the methodological and reporting quality of DHI studies. CONSORT-EHEALTH focuses on randomized controlled trials of DHIs.[21] The mHealth Evidence Reporting and Assessment (mERA) checklist proposes a minimum information set to define the content, context, and technology of mHealth interventions to support their replication.[18] The Guidelines and Checklist for the Reporting on Digital Health Implementations (iCHECK-DH) guides the reporting of real-world implementation studies.[22] A checklist is available for DHI usability studies.[23] The Digital Health Checklist for Researchers addresses ethics, data security, and privacy when selecting DHIs for research.[24,25] The eHealth Resource Checklist guides the search and assessment of eHealth resources for a personalized health promotion program.[26] The Evaluating Connected Sensor Technologies (EVIDENCE) framework focuses on performance evaluation studies of digital measurement products.[27] Over 20 guidelines were developed for medical AI studies in various contexts.[28]

Further guidelines address the systematic evidence appraisal of DHI studies. The Evidence in Digital Health for EFfectiveness of INterventions with Evaluative Depth checklist provides guidance on the assessment of evidence quality for DHIs.[19] The Target User, Evaluation Focus, Connectedness, Health Domain framework guides the systematic app review process.[29] Kolasa et al[30] have systematically reviewed 11 DHI value frameworks. Over 40 frameworks exist for the health technology assessment of DHIs.[30-32] As of September 2022, payers have adapted 6 evidence frameworks to inform DHI financing decisions.[33]

Despite the abundance of checklists, standardizing evidence generation and assessment for DHIs remains difficult because of their personalized nature, complex technologies, and linkages to larger systems. Although results from individual DHI studies are hardly generalizable, identifying comparable interventions for systematic evidence syntheses presents a further challenge. Systematic reviews of digital health technologies often cover diverse, difficult to compare technologies.[34] Digital-health-related terms (DHTs) are abundant, and definitions are frequently vague or overlapping.[4,20] The absence of comprehensive terminology in existing taxonomies and classification systems for DHIs may restrict the validity of evidence syntheses.[3,35,36] A systematic scoping review conducted by the ISPOR Digital Health Special Interest Group (DH-SIG) concluded that, when focusing on evidence summaries for health economics and outcomes research (HEOR) or health technology assessment purposes, umbrella DHTs (eg, digital health, eHealth, mHealth, telehealth/telemedicine) should be accompanied by Medical Subject Headings terms reflecting population, intervention, comparator, outcome, timing, and setting (PICOTS).

Recognizing the terminology limitations in digital health,[4] our goal was to develop a patient-facing DHI definition framework for HEOR purposes, which allows the identification of comparable DHIs with similar intended effects. DHIs are plentiful and most have unique features or intended use. Therefore, we aimed to achieve consensus on a minimum information framework that is sufficiently specific and detailed; therefore, the appropriateness of DHIs in clinical, delivery system, financing or development decision contexts, or specific research questions can be formulated or assessed. Specifically, we aimed to extend the PICOTS framework to capture relevant aspects of patient-facing DHIs.

Methods

This study was conducted by volunteers from the DH-SIG, who interacted online. ISPOR provided administrative support. We broadly followed the Enhancing the QUAlity and Transparency Of health Research guidance for development of health research reporting guidelines.[37] Decisions were made by a core team, the authors of this article. The DH-SIG leadership, all DH-SIG members, and the ISPOR Health Science Policy Council's Science/Research Committee were invited to review and comment on the draft manuscript. Ethical approval was not required for this study. Delphi expert panelists provided written consent. ISPOR provided anonymous survey responses to the core team.

Systematic Literature Review and Content Analysis

We conducted a systematic scoping review of DHTs' definitions occurring in systematic reviews of digital health.[4] Reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews[4,38] (Appendix 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2024.01.009). After reviewing umbrella DHTs,[4,39] in this study we analyzed the content of secondary DHT definitions. Eight researchers worked in pairs using predefined concepts from research frameworks covering evidence-based medicine, information and communication technologies, health systems research, and digital health. Detailed descriptions were extracted to show how the concepts appeared in the definitions, and researchers agreed whether they were explicitly present, implicitly present (could be implied from the context) or absent. The 24 concepts were from the PICOTS framework, reflecting the structure of clinical evidence summaries[39]; the Shannon-Weaver Model of Communication (sender, message, encoder, channel/medium, decoder, receiver, and information exchange/transmission pattern), reflecting that digital health or eHealth are applications of information communication technology in healthcare[40,41]; the Institute of Medicine's quality measures adopted by the Agency for Healthcare Research and Quality (safe, effective, patient-centered, timely, efficient, and equitable), representing a broad set of benefits DHIs may aspire to deliver[42,43]; further concepts concerned the geographic scope (Geography), technological features (Technology) of the DHTs, and the domains of the WHO's Classification of Digital Health Interventions (functionality of DHI, health system challenge, and system category of DHI).[3] Terms were mapped to umbrella DHTs and bibliographic details were recorded. Occurrence of concepts per definition were summarized via descriptive methods.

Delphi Consensus Survey Study

The varying, limited information content of secondary DHT definitions (see results) called for a Delphi study. Following the Conducting and Reporting Delphi Studies guideline,[44] we aimed to develop consensus on the minimum information set needed to define patient-facing DHIs for HEOR purposes. We developed a predefined protocol. The study methods and first-round questionnaire are provided in Appendix 2 and 3, respectively, in Supplemental Materials found at https://doi.org/10.1016/j.jval.2024.01.009. We recruited a geographically and professionally diverse expert panel from the DH-SIG (goal $\geq$ 10 third-round respondents), proposed an initial PICOTS-ICT (information, communication, and technology) framework derived from the content analysis, provided the rationale and supporting evidence for the initial items, conducted a Delphi survey, incorporated feedback from the expert panel, and consolidated the results. For consensus, 70% of panelists had to vote "important" or "very important" in the final third-round survey. The core team reviewed and consolidated survey findings and then reorganized consensus items under the proposed PICOTS-ComTeC acronym, in which "Com" stands for Communication, "Te" for Technology, and "C" for Context.

Pilot Testing of the PICOTS-ComTeC Framework

Based on the example of breast cancer, 5 core team members developed DHI descriptions and parallel decision situations. We explored how PICOTS-ComTeC can help specifying the details of the DHIs that are important for a particular decision.

Results

Systematic Literature Review

After deduplication, the search retrieved 2610 records. 545 full-text articles were assessed for eligibility, 214 articles were selected for data extraction, out of which 76 contained 101 unique definitions of 67 secondary DHTs. The list of included studies, secondary DHTs, and their definitions are provided in Appendix 4 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2024.01.009. We found the most unique definitions for telerehabilitation (n = 10), electronic health record (EHR) (n = 6), and DHI, electronic consultation, and telemonitoring (n = 5) followed by clinical decision support, mHealth intervention, mobile health app, and personal health record (n = 3). We found a single definition for the remaining 58 terms. We mapped secondary DHTs to our conceptual framework for umbrella terms,[4] 24 to eHealth/digital health, 12 to telehealth, 24 to telemedicine, 3 to mHealth, and 5 to the intersection of telemedicine and mHealth (Appendix 5 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2024.01.009).

Content Analysis

Explicit and implicit occurrences of concepts in secondary DHT definitions were merged. We found 95 different patterns among the 101 unique definitions. Any concepts from PICOTS, Shannon-Weaver, Agency for Healthcare Research and Quality, technology, geography, and WHO were mentioned in 79.6%, 92.2%, 31.1%, 52.4%, 0.0%, and 88.4% of definitions, respectively. The most prevalent concepts were system from WHO (84.5%), message from Shannon-Weaver (75.7%), intervention from PICOTS (58.3%), and technology (52.4%). Details are provided in Figure 1.

Delphi Consensus Survey

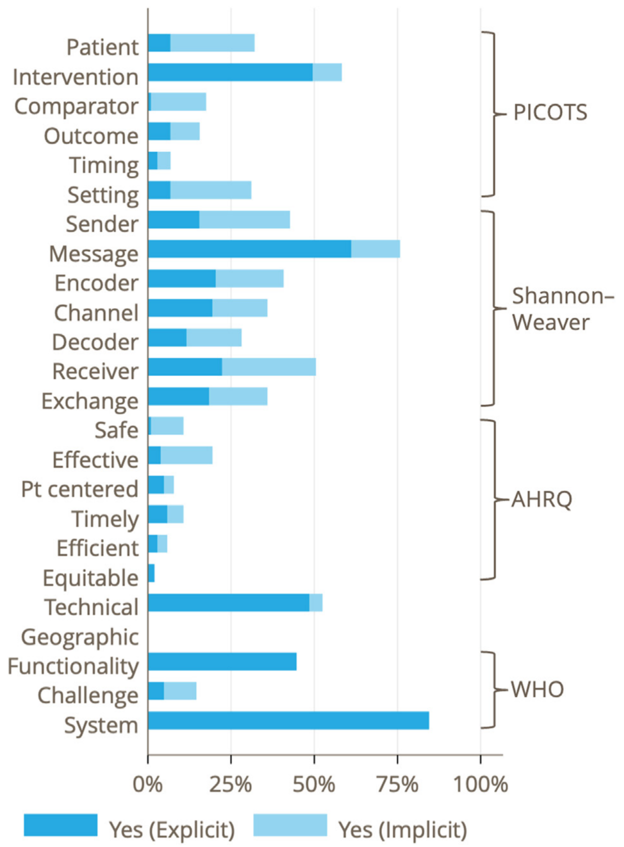
Panel characteristics

An online screening questionnaire was distributed to all members of the DH-SIG (n = 249) and completed by 47 members. SIG members who indicated at least moderate familiarity with digital health (n = 31) were selected for the first survey round. Respondents to round 1 (n = 18) became the Delphi expert panel and were invited to consecutive rounds. Demographic characteristics of the panel (recorded in round 1) were diverse in terms of geography, work experience, and professional background (Table 1). Rounds 2 and 3 were completed by 11 and 10 experts, respectively. The predefined consensus thresholds were applied on the completed responses, ignoring missing items.

Results of the consensus survey

In round 1, 37 items were included (9 PICOTS-ICT domains and 28 subcategories). Six domains and 18 subcategories reached the final round consensus threshold. No items met the exclusion criterion. One additional domain (context) and 4 subcategories were proposed by the panel. Forty-two items were advanced to rounds 2 and 3 in an abbreviated questionnaire. In round 2, no items were excluded, and the early stopping criteria were not met; therefore, a final, third round was required. The summary of results is reported in Table 2. The proportion of "important" and "very important" ratings is denoted as P_{45}. No items were rated as "not important" (P_1), except for a single vote for 3 subcategories in round 1: (1) non-health-related risks, (2) efficacy, convenience, and economic benefits, and (3) channel/medium. According to predefined consensus rules, all items were retained in the final framework, except for the information domain (P_{45} = 0.60). From the information domain 2 qualifying subcategories were moved to other domains: message to communication, and data management to technology.

Figure 1. Concepts in the definitions of secondary digital-health-related terms.



The PICOTS-ComTeC Framework

After reviewing the survey results and comments, we proposed the PICOTS-ComTeC framework (Table 3 and Appendix 6 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2024.01.009). The following is a brief elaboration of the framework domains.

Population

DHIs may act differently within seemingly homogenous patient groups, eg, in a systematic literature review of the diagnostic accuracy of teledermatology in skin cancer, the diversity of malignancy definitions and positive findings hindered the pooling of results.[34] When specifying 1 or more target populations/diagnoses in a decision-making situation, authors should consider that, within a therapeutic area, some conditions may be more-or-less suitable for DHIs.[45] Furthermore, demographic characteristics, such as age, gender, or socioeconomic status,[46,47] or special user characteristics, such as culture, beliefs, attitudes, health behaviors, or health literacy,[48,49] may impact suitability of DHIs. Some DHIs are designed with consideration to these issues.[48,50,51]

Intervention

DHIs may be complex with multiple components and objectives. Research questions should specify how DHIs intend to deliver their desired impact, including key components and how

Table 1. Demographic characteristics of the Delphi expert panel.

Variables	Category	Delphi panel (n = 18)		ISPOR DH-SIG membership (n = 249)	
		n	%	n	%
Age group (y)	20-29	3	16.7	NA	
	30-39	4	22.2		
	40-49	8	44.4		
	50-59	3	16.7		
Gender	Female	6	33.3	142	57.0
	Male	12	66.7	105	42.2
	Prefer not to respond			2	0.8
Area of residence	Asia Pacific	3	16.7	36	14.6
	Central & Eastern Europe	3	16.7	4	1.6
	Latin America	1	5.6	8	3.2
	Middle East	2	11.1	8	3.2
	North America	4	22.2	139	56.3
	Western Europe	5	27.8	48	19.4
	Africa	0	0.0	4	1.6
Professional expertise	Clinical/clinical research	4	22.2	NA	
	DHI development/technical	1	5.6		
	Health economics/outcomes research	12	66.7		
	Health technology assessment	1	5.6		
Professional experience	Junior level	1	5.6	NA	
	Mid-level	7	38.9		
	Senior level	10	55.6		
Work environment (multiple answers permitted)	Academia	5	27.8	34	13.8
	Clinical/hospital	2	11.1	7	2.8
	Communications/advertising	0	0.0	1	0.4
	Consulting firm	3	16.7	26	10.5
	Contract research organization	0	0.0	12	4.9
	Digital health	1	5.6	0	0.0
	Government	1	5.6	6	2.4
	Information technology	1	5.6	3	1.2
	Managed care/insurance	0	0.0	5	2.0
	Medical technology (devices/diagnostics)	3	16.7	26	10.5
	Non-profit, NGO	2	11.1	5	2.0
	Other	0	0.0	5	2.0
	Patient organization	0	0.0	1	0.4
	Pharmaceutical/biotech	5	27.8	68	27.5
	Self-employed	1	5.6	7	2.8
	Student	1	5.6	41	16.6
ISPOR SIG Membership (multiple answers permitted)	Digital health	18	100	NA	
	Biosimilars	3	16.7		
	Clinical outcome assessment	4	22.2		
	Health equity research	2	11.1		
	Health preference research	2	11.1		
	Medical Devices and Diagnostics	7	38.9		
	Medication adherence and persistence	3	16.7		
	Nutrition economics	2	11.1		
	Oncology	3	16.7		
	Open-source models	2	11.1		
	Patient-centered	3	16.7		
	Precision medicine and advanced therapies	4	22.2		
	Rare disease	2	11.1		
	Real-world evidence	8	44.4		
	Statistical methods in HEOR	4	22.2		

DHI indicates digital health intervention; DH-SIG, Digital Health Special Interest Group; HEOR, health economics and outcomes research; NA, not applicable; NGO, non-governmental organization.

Table 2. Summary of the consensus survey results in each round.

Item	Round 1		Round 2		Round 3	
	n	P_{45}	n	P_{45}	n	P_{45}
Population domain	18	0.94	11	1.00	10	1.00
• Target population/diagnosis	16	0.94	11	1.00	10	1.00
• Demographic characteristics	16	0.88	11	0.91	10	1.00
• Special user characteristics	16	0.69	11	0.73	10	0.90
Intervention domain	16	0.94	11	1.00	10	1.00
• Key function/intended use	16	0.81	11	0.91	10	0.90
• Modality	16	0.88	11	0.82	10	0.80
• Limits of intervention	-	-	11	0.82	10	0.80
Comparator domain	16	0.88	11	1.00	10	0.90
• Model of care	16	0.88	11	0.91	10	1.00
• Alternative digital health interventions	16	0.56	11	0.82	10	0.80
• Usual care alternatives	16	0.81	11	0.73	10	0.90
Outcomes domain	16	1.00	11	1.00	10	1.00
• Health benefits	15	0.93	11	1.00	10	1.00
• Improved care structure or process	15	0.80	11	0.91	10	1.00
• Social/societal benefits	15	0.67	11	0.91	10	1.00
• Safety	15	0.87	11	0.82	10	1.00
• Non-health-related risks	15	0.53	11	0.64	10	0.70
• Efficiency, convenience, and economic benefits	15	0.87	11	0.91	10	1.00
Timing domain	15	0.40	11	0.82	10	0.90
• Timeliness	14	0.71	11	0.82	10	0.90
• Frequency and duration of intervention	14	0.79	11	0.82	10	0.90
Setting domain	14	0,71	11	1.00	10	1.00
• Care setting	14	0.71	11	1.00	10	1.00
• Patient location	14	0.57	11	1.00	10	0.90
• Geographic scope	14	0.71	11	0.91	10	0.90
Information domain	14	0.64	11	0.64	10	0.60
• Message*	14	0.43	11	0.73	10	0.80
• Data management†	14	0.43	11	0.73	10	0.70
Communication domain	14	0.64	11	0.82	10	0.80
• User	14	0.79	11	0.73	10	0.80
• Interaction pattern	14	0.29	11	0.82	10	0.70
• User experience	14	0.64	11	0.91	10	0.90
Technology domain	14	0.71	11	1.00	10	1.00
• Channel/medium	14	0.71	11	1.00	10	0.90
• Device	14	0.64	11	1.00	10	0.90
• Software	14	0.71	11	0.82	10	0.80
• System	14	0.79	11	1.00	10	1.00

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Table 2. Continued

Item	Round 1		Round 2		Round 3	
	n	P_{45}	n	P_{45}	n	P_{45}
Context domain	-	-	11	0.64	10	0.70
• Regulatory status	-	-	11	0.73	10	0.80
• Medical/legal liability	-	-	11	0.64	10	0.80
• Financing	-	-	11	0.64	10	0.90

P45 indicates the proportion of "important" and "very important" ratings.
*Moved to the Communication domain in the final framework.
†Moved to the Technology domain in the final framework.

they interact.[52] Within the same population, the key function or purpose of DHIs may be fundamentally different (ie, intended use). For example, mobile health apps for breast cancer disease management had a variety of functions, such as symptom tracking, survivorship education, information sharing, scheduling follow-up visits, personal reminders, and social networking.[53] Similar functional diversity was reported for opioid management apps.[54] DHIs may differ in modality, how they deliver their intended core function, (ie, underlying communication or behavioral theories and human, technological, or design components). For example, modalities of DHIs for weight-management included self-monitoring, self-motivation, goal setting, personalized feedback, participant engagement, psychological empowerment, persuasion, digital literacy, and efficacy to credibility.[55] Just-in-time, adaptive interventions adjust to the changing status of patients to better support their individual needs.[56] The limits of intervention are worth stating, such as the threshold beyond which a DHI needs to be replaced by face-to-face care (eg, non-response within a certain period).

Comparator

When demonstrating value, comparators of DHIs can be established software or medical devices,[57] alternative DHIs, sham apps,[19] or even non-digital interventions. The intended use of the DHI (standalone, companion, or in a combination) can drive the comparator choice.[2] For DHIs with transformative effect, an alternative model of care may be the right comparator, eg, for a service redesign project for community palliative care.[58] The choice of suitable comparators among alternative DHIs may require care even if the functional category is narrowly defined, eg, COVID-19 tracing apps have been shown to differ markedly in data privacy and public health profiles, rendering some as potentially inappropriate comparators.[59] Given the ubiquity of digital technologies in current healthcare systems, the delineation of what constitutes a usual care alternative may be challenging. Although some studies compared DHIs with non-digital alternatives,[60,61] especially post-COVID-19, the widespread adoption of digital technologies in health systems could be considered as a new standard for usual care.[62]

Outcomes

Although value-based healthcare defines value in terms of improvement in patients' health outcomes, separating those from quality of care or patient satisfaction,[63] some regulatory and payer frameworks acknowledge that DHIs deliver a wide range of effects relevant to patients, organizations, or the society.[2,6,33] Depending on the evaluation perspective, relevant outcomes may include health benefits measured as improvements in symptoms, quality of life,[30] disease duration or survival.[31] DHIs may benefit patients indirectly through improved care structure or processes affecting their role, information, decision making, health behaviors, everyday life, or individual needs.[2] Examples include better coordination of care,[64] adherence,[65] access to care,[66] health literacy,[67] autonomy,[14] self-management,[68] or caregiver burden.[69] Social or societal benefits of DHIs related to humanistic or holistic values beyond the biomedical model may be measured such as well-being or happiness,[70] equity,[71] or social support.[68,72] Safety may be the core outcome for DHIs when they are designed to reduce adverse effects of other interventions,[73] replace in-person care in high-risk populations,[74] or when their dysfunction has potentially serious consequences.[75] Beyond safety, non-health-related risks of DHIs involve their potential for algorithmic bias,[76] contributing to inequity,[77] deterioration of the patient-HCP relationship,[17] or data security and privacy risks.[59] Efficiency, convenience and economic benefits may be relevant determinants of the value delivered by DHIs.[78,79]

Timing

Timeliness is a critical aspect of some DHIs, eg, although telestroke systems aim to shorten time to thrombolysis in acute care, timeliness is less important when telemedicine is used for long-term rehabilitation and education of stroke patients.[80,81] Furthermore, the emerging field of dose-response research suggests that optimal frequency and duration of intervention should be determined for DHIs to maximize their value.[82] For example, in cardiac rehabilitation patients the association between DHI usage and effect varied by outcomes such as weight, diet, or exercise.[83]

Setting

For the same condition, DHIs may target a different care setting, such as primary care, emergency room, or inpatient setting. Examples include apps for COVID-19[84-86] or stroke.[87] Also, DHIs may be delivered at specific patient locations, such as digital health kiosks,[88] patients' homes,[89] or intensive care units.[90] The geographic scope of DHIs should be considered when evaluating their value, eg, despite similar challenges in reaching rural populations, telemedicine systems aiming to improve access to primary care differ considerably in Brazil and Canada.[91] Some DHIs may target a specific geographic location, such as rural Alaska.[92]

Communication

DHIs may differ in who their users are, what their roles are, how the communication process takes place, or what is the user experience, eg, users of a Fitbit-based lifestyle intervention may include patients only, or also physicians, other health professionals, and even peer patients interacting with them.[93] Message refers to the unit of information collected or communicated by the DHI, eg, dietary assessment apps use a range of input data from photos to text messages.[94] The interaction pattern between users (ie, how the

Table 3. The PICOTS-ComTeC framework.

Item	Explanation
Population domain	Characterization of patients/population(s)
Target population/diagnosis	• Diagnosis/condition/population (may be more than 1)
Demographic characteristics	• Sociodemographics of population (eg, age, gender, education)
Special user characteristics	• DHI relevant user characteristics (eg, digital literacy, PC access)
Intervention domain	Description of DHI Intervention including key components and interactions
Key function/intended use	• Intended function (eg, online screening to identify high-risk patients)
Modality	• Design elements to achieve key function (eg, behavioral, communication)
Limits of intervention	• To specify those situations or thresholds where the DHI can be used, and beyond which the DHI should be replaced by face-to-face care
Comparator domain	Non-DHI(s) or alternative DHI(s) with same function
Model of care	• Current model of care or clinical pathway, may be redesigned by DHI
Alternative digital health interventions	• DHI(s) with the same purpose (eg, smart phone vs PC retinal screening)
Usual care alternatives	• Usual treatment or care (eg, compare with paper-based surveillance)
Outcomes domain	Outcomes relevant to patients and other stakeholders
Health benefits	• Clinical and patient-reported outcomes
Improved Care Structure or Process	• Health care system improvements (eg, access to care, adherence to guidelines, patient health literacy, self-management)
Social/societal benefits	• Humanistic, social, or societal effects (eg, DHI could improve social support, or reduce stigma of a condition)
Safety	• May reduce health-related risks or improve patient safety
Non-health-related risks	• Non-health-related risks including data privacy (eg, unauthorized access and use of personal data)
Efficiency, Convenience, and Economic Benefits	• DHIs could deliver the same outcome with greater efficiency, or less effort
Timing domain	Timing and duration of treatment and follow-up
Timeliness	• Timely delivery of services could improve outcomes (eg, telestroke DHI to shorten time to thrombolysis could improve survival)
Frequency and duration of intervention	• Increased DHI use may improve outcomes (eg, increased use in cardiac rehabilitation associated with greater weight-loss)
Setting domain	DHIs may increase access to or improve quality of health care. Potential benefits may vary by setting
Care setting	• Settings where DHI may be useful include pre- and post-hospitalization, emergency care, primary and community care
Patient location	• DHIs can bring care to the patient's location (eg, in-home hospital care during COVID-19, public kiosks providing access to nurses)
Geographic scope	• DHIs can improve access to health care (eg, rural Alaska). Culture may limit use (eg, telehealth differences in Brazil vs Canada)
Communication domain	DHIs may have different users with different roles. Function impacts frequency of interaction (eg, post-surgical vs routine monitoring)
User	• DHI users may vary (eg, activity monitoring for patient lifestyle modification involving healthcare providers, or support groups)
Message	• Unit of information collected and communicated by DHI (eg, text, diagnostic image, or machine-readable data) impacts function
Interaction pattern	• Differences in interactions (eg, synchronous (real-time) or asynchronous) could affect outcomes in critical situations
User experience	• Improving user experience may improve outcomes (eg, when human factors were considered in digital interface design)
Technology domain	Use of different technologies (ie, communication channel, device, software, or system) may affect DHI performance
Channel/medium	• Channel selection may affect patient access and DHI effectiveness (eg, DHIs that exclude patients without telephone access)
Device	• DHIs involve devices or user interfaces that may vary in cost and accessibility (eg, patient access to mobile phone vs PC)
Software	• Algorithms (eg, for machine learning) and software components (eg, for security) used by DHIs may affect performance
System	• Compatibility with data standards (eg, FHIR) and interoperability with larger healthcare systems may affect DHI potential
Data management	• Considerations include data quality, timeliness, interoperability (eg, with EHR), security, patient privacy, and legal requirements
Context domain	Capture additional information that may influence the usability, access, or overall value of DHIs

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Table 3. Continued

Item	Explanation
Regulatory status	• The relevant regulatory category and authorization status for the DHI to identify appropriate comparators. (eg, FDA approved or investigational)
Medical/legal liability	• Specify if certain legal provisions influence the availability or effect of the DHI (eg, can a medical expert give advice or only tests results can be communicated)
Financing	• Specify if certain reimbursement or financing rules or pricing schemes influence the availability of functionality of the DHI (in-app purchases, free from health service provider, subscription fee, etc)

DHI indicates digital health intervention; EHR, electronic health record; FDA, Food and Drug Administration; FHIR, Fast Healthcare Interoperability Resources; PC, personal computer; PICOTS-ComTeC, population, intervention, comparator, outcome, timing, and setting, communication, technology, and context.

information flows or users are connected) can influence outcomes. For example, interactive web-based patient education programs are the most effective forms,[95] or synchronous tele-exercise programs are more successful than asynchronous forms.[96] An emerging field of research, user experience (eg, usability) may be a critical barrier or key success factor for DHIs.[9,27,97,98]

Technology

For the same purpose, DHIs may use different technologies, such as the communication channel, device, software algorithm, or system, which may affect their performance or feasibility, eg, the channel/medium for postoperative pain management ranges from short message services to synchronous videoconferencing.[99,100] In some settings, patient access to DHIs may be limited by the available infrastructure.[101,102] The accessibility or usability of DHIs may depend on the applied device or interface, eg, pain management interventions involve a range of devices, such as online controlled pumps for nerve blockade,[103] videoconferencing,[100] or virtual reality devices.[104] A plethora of devices may be used for improving physical activity[105] or rehabilitation. User interface was a main component in a classification framework of mental health DHIs.[106] The underlying software technology (including AI) may affect the efficacy, safety, or security profile of DHIs, eg, glucose monitoring algorithms differ in their input parameters, prediction window, and accuracy.[107] Videoconferencing software for telemedicine are diverse in terms of their technical, or security profiles and compliance with EU/US regulations.[108] The compatibility or dependence of DHIs on larger systems may affect their feasibility. Apps may be compatible with different quality[109] and interoperability standards[110] and EHR systems,[111] whereas a platform benefits patients by enhancing the connectivity and interoperability of a plethora of devices and apps developed for type 1 diabetes.[112] Data management considerations include data quality, security, privacy or findability, accessibility, interoperability, and reusability for open research (FAIR principles[113]) or legal requirements, eg, centralized or decentralized COVID-19 tracing apps differ in their efficacy and data privacy profiles.[59]

Context

This domain captures additional information that may influence the use, access, or overall value of DHIs. In 2020, approximately 250 apps were introduced every day globally, most were wellness products, and only a fraction obtained an authorized regulatory status allowing them to treat, prevent, or manage certain conditions.[7] Furthermore, it is worth considering the medical/legal liability aspects of DHIs, a frequently neglected area with diverse regulations across jurisdictions.[114] Involvement of healthcare professionals in DHIs may range from simple observation through distant intervention[115] to complex networks involving interaction of humans with AI.[116] Financing or reimbursement rules may influence availability or functionality of DHIs. Cost is a key factor affecting the choice of apps by patients and physicians.[117,118] To offer full functionality, some apps require in-app purchases.[119] DHIs included in public financing are expected to undergo rigorous evaluation processes,[33] and the experience is accumulating with the first publicly financed DHIs.[120] Even if not reimbursed, customers have greater willingness to pay for apps endorsed by authorities.[121] Some apps may offer financial incentives for the adoption of favorable behaviors from a public health perspective.[122]

Using PICOTS-ComTeC

Given the diversity, flexibility, and highly individualized nature of DHIs, PICOTS-ComTeC aims to help with the formulation of sufficiently specific and detailed definitions to allow identification of comparable DHIs delivering essentially the same effect and comparators that deliver similar effect but differ in relevant determinants of value (ie, improvement of patient outcomes for their cost).[63] Although focusing on DHI's value to patients, PICOTS-ComTeC can be used in many situations, such as writing study reports, framing clinical, financing, or development decision questions, formulating research questions for evidence syntheses, or applying for approval or reimbursement.[2,6] PICOTS-ComTeC can augment descriptions of DHIs when used in parallel with general reporting guidelines, such as the Consolidated Health Economic Evaluation Reporting Standards[123] or evaluation frameworks, such as the National Institute for Health and Care Excellence Evidence Evidence standards framework for digital health technologies.[124] We suggest that the main domains (population, intervention, comparator, outcome, timing, setting, communication, technology, and context) should be considered and specified if appropriate, whereas the 32 subcategories can be used flexibly to add optional detail. As a minimum information framework, PICOTS-ComTeC was not intended to serve as a comprehensive DHI taxonomy. We suggest that if feasible, authors should refer to established classifications when specifying details for the items (eg, the WHO classification of DHI uses[125]) or provide additional information if pertinent.

Pilot Testing of the PICOTS-ComTeC Framework

Four hypothetical breast cancer DHI examples illustrate differences between various DHIs and the information needs for specific decisions (Table 4[126]). The mobile breast cancer management DHI_1 and DHI_2 have similarities, eg, both involve physician monitoring of breast cancer patients and provide for 2-way

Table 4. Examples using the PICOTS-ComTeC framework to characterize breast cancer digital health interventions and decisions related to those interventions.

	DHI_1	DHI_2	DHI_3	DHI_4
Digital Health Intervention	US multifunction, EHR integrated mobile app for breast cancer management	European, hospital based mobile e-wound monitoring app integrate into a hospital pathway for breast cancer surgery; objectives of improving quality of care and resource utilization	Oncomasto Cirurgia App, Brazilian mobile app for patient-initiated breast cancer education on surgical treatment[126]	US mobile app for patient-initiated breast cancer education
Decision context	IHS clinic-based oncologist to recommend best mobile app with EHR integration for women in US with breast cancer; objectives of improving patient outcomes and satisfaction.	Developer decision on best mobile e-wound monitoring app design for an ex-European hospital, drawing from existing apps and collaborating with local hospital experts.	Decision on national implementation of this mobile app in the Brazilian health care system.	US HCP (eg, physician, nurse, pharmacist) to recommend a mobile app for patient-initiated breast cancer education.
Population	Women in the US with breast cancer in an IHS with an EHR	Ex-European breast cancer patients undergoing surgery in a hospital	Brazilian breast cancer patients including foreign and indigenous populations	US male and female breast cancer patients
Intervention	Required functions: symptom, diagnostic and treatment tracking; patient satisfaction assessment; personalized messages and education modules to bridge period of time between clinic visits and HCP interaction or getting test results. Optional functions: routine clinic scheduling and reminders	Mobile app for post-surgical wound monitoring and support for breast cancer patients	Standalone educational patient-facing mobile app about procedures, treatments, and self-care related to breast cancer surgery	Patient-facing US mobile app with breast cancer education modules, including diagnosis, treatment, and other patient resources in English. Optional functions: access in other languages (eg, Spanish), and for those with disabilities (eg, audio interface)
Comparator	Usual care with patient access to EHR portal	Conventional follow-up in breast cancer surgery (predefined post-surgery hospital stay, regular in-person visits, no patient-surgeon encounters after discharge)	Other non-digital sources of breast cancer information (eg, educational pamphlets, clinic visits, telephone conversation)	Other similar mobile apps, or online patient sites containing breast cancer information from credible US sources (eg, American Cancer Society)
Outcomes	Must have outcomes for episode of care; short-term patient adherence to treatment, improved self-management. Preferred but not required: satisfaction with care	Primary outcomes: reduced frequency of complications, unscheduled visits, and hospital readmission Secondary outcomes: improved patient satisfaction and adherence, reduced psychological distress and anxiety	Breast cancer surgery-related knowledge including pre- and postoperative care, and types of surgery. Optional: patient satisfaction with care	Required; improved breast cancer-related knowledge. Optional; patient satisfaction with various aspects of mobile app use and content

continued on next page

Table 4. Continued

	DHI_1	DHI_2	DHI_3	DHI_4
Timing	Accessible at any time, reminders as set by provider	After discharge, patients submit non-urgent data and messages at any time. Clinicians/ nurses evaluate responses as part of routine EHR updates	Accessibility at any time for target users	Information should be available at any time for patients
Setting	Patient at home in the community. Treatment is provided in outpatient and inpatient settings	Patient at home; clinicians, nurses, and surgeons in the hospital	Patients at home, remote access to educational information	Patients in the community
Communication	Interface should be "user friendly." Patient accesses functions within the app. Asynchronous communication between patient and physician. Optional: app accesses patient EHR for scheduling and sends automatic reminders.	Mobile app with user friendly patient interface that does not require special training. Able to send image, respond to predefined questions, have virtual contact with clinicians/nurses. Online portal for HCP access. Asynchronous communication between patient and HCP.	Mobile app with user friendly interface and relevant language (eg, Portuguese, German, English). User accesses information.	Mobile app interface should be "user friendly." Patient accesses information within app. No patient-HCP communication. Education content is tailored to an appropriate health literacy level. Optional: app supports other languages (eg, Spanish)
Technology	Mobile app must be accessible by US smartphones (iOS or Android) and compatible with the IHS EHR	Existing apps in Europe are accessible by European smartphones (iOS or Android) and are interoperable with the HIS based on a specific standard (eg, Health Level 7) The mobile app should be widely accessible by local smartphones and can be integrated with the local networks in the ex-European country	Access to a mobile device (mobile phone or computer) required. Ideally, non-digital access should also be available for those lacking mobile phone or computer (eg, printed brochures)	Mobile app must be accessible by US smartphones (iOS or Android). Optimal: the app supports other interfaces (eg, audio)
Context	App free to the user and in-app financial incentives not required. FDA approval is not required.	Free to patients during the prescribed time. Costs to be covered by hospital or national budget. Regulatory approval is required.	Information from literature review and content validation with physicians, usability validation with patients. Regulatory approval not required. App should be free to user.	Information from a credible US source (eg, American Cancer Society). Mobile apps that are free to the user are preferred. FDA approval is not required.

DHI indicates digital health intervention; EHR, electronic health record; FDA, Food and Drug Administration; HCP, healthcare professional; HIS, hospital information system; IHS, integrated healthcare system; PICOTS-ComTeC, population, intervention, comparator, outcome, timing, and setting, communication, technology, and context.

patient-doctor communication. However, differences exist because DHI_1 tracks all breast cancer treatments and interacts with the EHR, whereas DHI_2 is specifically for post-surgery wound follow-up and is integrated with the hospital treatment pathway. The decisions are different. In DHI_1, an oncologist is tasked with recommending the best mobile app for use in an integrated healthcare system, whereas in DHI_2, a developer is looking for an app design that could be adapted for a different geographic location. What is important to the decision-maker varies, eg, the comparator for DHI_1 is usual care with patient access to an EHR portal, whereas the comparator for DHI_2 is conventional breast cancer surgery follow-up. DHI_1 requires multiple functions, episode of care outcomes, and EHR integration, whereas DHI_2 requires an accredited information exchange protocol and potential for regulatory approval. DHI_3 and DHI_4 are standalone patient-facing mobile education apps; however, differences in healthcare systems and access to technology between Brazil and the United States and the decisions being made (reimbursement in DHI_3 and patient referral in DHI_4) are reflected in the decision-maker requirements.

Discussion and Conclusions

Lack of clear terminology in digital health hinders evidence synthesis and may impede the adoption of DHIs. To overcome this barrier, we propose the PICOTS-ComTeC framework to define patient-facing DHIs for HEOR purposes. Following PICOTS-ComTeC, patient-facing DHIs can be specified in sufficient detail that allows the selection of appropriate interventions and comparators for a given decision. PICOTS-ComTeC is a flexible and versatile tool, aiming to help authors in designing and reporting evidence syntheses or research questions with actionable results for clinicians and other decision makers. PICOTS-ComTeC may also help developers and researchers conducting studies on individual DHIs to report sufficient detail about the intervention to allow the use of results in evidence syntheses.

Several reporting checklists proposed items to comprehensively define DHIs. Relevant parts of CONSORT-EHEALTH,[21] mERA,[18] and iCHECH-DH[22] overlap with PICOTS-ComTeC. However, CONSORT-EHEALTH puts greater emphasis on how the DHI was implemented in the trial and asks fewer details about how the DHI works (technology) or about its real-world implementation (context). Although focusing more on technology and context, details of the target population and outcomes are omitted from mERA. iCHECK-DH does not explicitly address timing and setting domains. WHO classifies DHIs by the main user, with further details covered by the intervention and communication domains of PICOTS-ComTeC. In addition, health system challenges (related to outcomes) and information system categories (related to technology) can be specified.[3] The Target User, Evaluation Focus, Connectedness, Health Domain framework for app reviews defines the research question in terms of target population and health domain (ie, population), evaluation focus (ie, outcomes), and connectedness (ie, technology), whereas several proposed data extraction items cover the PICOTS-ComTeC intervention and communication domains, allowing for the integration of established app evaluation frameworks.[29]

The strength of our research is that PICOTS-ComTeC integrates relevant pieces of digital technology information with the widely recognized PICOTS framework. PICOTS-ComTeC relies on the consensus of experts with diverse geographic and professional backgrounds. Although overlapping with established DHI reporting checklists, PICOTS-ComTeC aims to define DHIs in sufficient detail for multiple purposes from a HEOR perspective. PICOTS-ComTeC has been developed by a volunteer group of HEOR professionals and academics without funding. A possible limitation of our research is that the voluntary Delphi panel was not representative of the DH-SIG membership. Despite the sample diversity, Africa and some professional areas (patient groups, contract research organizations, and managed care/health insurance organizations) were not represented. However, our panel was anonymous and willing to participate in an iterative consensus building process. Although in the lower end, the panel size was within the usual range used in healthcare research[127] and within the optimal panel size of 7 to 15 recommended by the Conducting and Reporting Delphi Studies guidelines.[44] Volunteers with low self-reported familiarity with DHIs were excluded. Despite some attrition of respondents, the consensus remained stable over the survey rounds. Furthermore, PICOTS-ComTeC has not been externally validated and tested with a broader group of stakeholders beyond HEOR (eg, professional societies, regulatory agencies, and patient groups), which presents an avenue for future research. We anticipate that PICOTS-ComTeC could serve as a robust foundation for the development of a comprehensive international terminology and classification system for DHIs.

In conclusion, to overcome terminology limitations in digital health, we propose that the population, intervention, comparator, outcome, timing, setting, communication, technology, and context (PICOTS-ComTeC) of patient-facing DHIs be specified in sufficient detail, to allow for the identification of comparable interventions and the selection of appropriate comparators that deliver similar effects to patients.

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Links to the disclosure forms provided by the authors are available here.

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