A Proposed Framework for Designing Trials Evaluating the Effectiveness and Implementation of Digital Interventions for Substance Use

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Digital interventions
Software, websites, mobile apps used by patients to improve health outcomes
Digital interventions for substance use

Used for screening, brief intervention, or to deliver evidence-based treatment

Potential to address barriers and bottlenecks to substance use treatment

Evidence of efficacy but mixed evidence of effectiveness under real-world conditions
Effectiveness of digital interventions in real-world settings may depend on its implementation.
Implementation Challenges

Digital interventions have unique implementation considerations that may not fit traditional care pathways.

- Technology infrastructure
- Digital literacy
- Monitoring and follow-up
Studies on delivery of digital interventions in clinical care

**Clinical Workflows**
- Clinicians provide introduction, setup and follow-up
  (Glass et al., 2021, 2022)

**Staffing models**
- Clinical technology specialists
  (Ben-Zeev, 2015)
- Peer specialists
  (Fortuna et al., 2019)
- Health coaches
  (Glass et al., 2023; Park et al., 2022)

**Specialized Clinics**
- Digital clinics
  (Rodriguez-Vila et al., 2020)
Implementation strategy studies

• Map implementation strategies to digital intervention barriers (Graham et al., 2020)
Few trials testing new delivery approaches
Motivation for this framework

- Few trials test these approaches in the real world
- Lack of studies that seek to answer how to deliver digital interventions
- Trials need to be harmonized
We propose a framework for designing trials that seek to address questions about the implementation and effectiveness of digital interventions in real-world care.
METHODS

Methods

- Draws on literature from trial design, expert perspectives, lessons learned
METHODS

Methods

• Draws on literature from trial design, expert perspectives, lessons learned
• We apply this framework to a working example
DIGITS Trial: Optimizing the implementation of digital therapeutics for substance use disorders in primary care

**Interventions**
- reSET® and reSET-O®
- Practice facilitation
- Health coaching

**Comparator:** Standard Implementation

**Population:** Primary care patients with substance use disorder

**Outcomes:** Reach, fidelity, cost effectiveness

**Timeline:** 1-year active implementation and 1 year sustainment
Framework

Phase 1: Frame the research question

Phase 2: Delineate components being studied

Phase 3: Specify core features of trial design
Trial Components

At each phase, consider three trial components critical to effectiveness and implementation of digital interventions:

- **Digital Interventions**  
  (Philippe et al., 2022; Bewick et al., 2017)

- **Clinical Support Services**  
  (Hermes et al., 2019)

- **Implementation Strategies**  
  (Powell et al., 2015; Graham et al., 2021)
Phase 1: Frame the research question

- All aspects of the trial design should follow the research questions.
- Identify timely, relevant question **worthy of an experimental design**
- Frame the question in terms of the components to be tested…
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<thead>
<tr>
<th>Research question</th>
<th>Digital intervention</th>
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<tbody>
<tr>
<td>Does the digital intervention work in this population or setting?</td>
<td>Stakeholders want to know:</td>
</tr>
<tr>
<td>Which digital intervention to use?</td>
<td>• whether to invest</td>
</tr>
<tr>
<td></td>
<td>• in which product to invest</td>
</tr>
<tr>
<td>Rationale</td>
<td>Example</td>
</tr>
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<td>Stakeholders want to know:</td>
<td>Secondary in DIGITS Trial</td>
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<td>Does the digital intervention work in this population or setting?</td>
<td>What approaches for offering digital interventions are needed to support delivery in real world?</td>
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<tr>
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</tr>
<tr>
<td>Rationale</td>
<td>Stakeholders want to know:</td>
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</tr>
<tr>
<td></td>
<td>• whether to invest</td>
<td>• how to reorganize resources</td>
</tr>
<tr>
<td></td>
<td>• in which product to invest</td>
<td>• hire new staff</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• contract out to a 3rd party</td>
</tr>
<tr>
<td>Example</td>
<td>Secondary in DIGITS Trial</td>
<td>Primary in DIGITS Trial</td>
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<td>Does the digital intervention work in this population or setting? Which digital intervention to use?</td>
<td>What approaches for offering digital interventions are needed to support delivery in real world?</td>
<td>How to encourage adoption, implementation, and sustainment of digital interventions in clinics?</td>
<td></td>
</tr>
</tbody>
</table>

Rationale

- Stakeholders want to know:
  - whether to invest
  - in which product to invest
- Stakeholders want to know:
  - how to reorganize resources
  - hire new staff
  - contract out to a 3rd party
- Stakeholders have buy-in but want to know:
  - How to maximize uptake of digital interventions in clinics

Example

- Secondary in DIGITS Trial
- Primary in DIGITS Trial
- Primary in DIGITS Trial
FRAMEWORK PHASE 1

Digital Interventions

Clinical Support Services

Implementation Strategies
Phase 2: Delineate components under study

- Likely overlap between components
- Bring **clarity to the boundaries** of each for your study
- Critical to health system stakeholders
- Delineate based on four dimensions (Proctor et al., 2013)
# Phase 2: Delineate digital interventions under study

<table>
<thead>
<tr>
<th>Component</th>
<th>Actor</th>
<th>Activities</th>
<th>Action Target</th>
<th>Proximal Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital Intervention: reSET and reSET-O</td>
<td>Patients with substance use disorder</td>
<td>Spent time using app to engage in:</td>
<td>Substance use reductions</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1) Community reinforcement approach</td>
<td>1) Explore healthier ways to meet need</td>
<td>Treatment engagement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2) Contingency management</td>
<td>2) Incent adherence and abstinence</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3) Fluency training</td>
<td>3) Reinforce concept mastery</td>
<td></td>
</tr>
</tbody>
</table>
Phase 2: Delineate *clinical support services* under study

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<tr>
<td>Clinical Support Service:</td>
<td>“Centralized” medical</td>
<td>1) Conduct phone outreach to patients who might benefit</td>
<td>1 &amp; 2) Activate patients; reduce burden on clinicians</td>
<td>Fidelity</td>
</tr>
<tr>
<td>Health Coaching</td>
<td>assistant</td>
<td></td>
<td></td>
<td>Feasibility</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2) Monitor and encourage engagement</td>
<td></td>
<td>Health services outcomes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3) Encourage practice of skills</td>
<td>3) Support patients’ skill development</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4) Facilitate follow-up with care team</td>
<td>4) Promote collaboration between patients and providers</td>
<td></td>
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# Phase 2: Delineate implementation strategies under study

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<tr>
<td>Implementation Strategy:</td>
<td>Practice facilitator (external)</td>
<td>In the context of a supportive relationship, deliver:</td>
<td></td>
<td>Reach Adoption</td>
</tr>
<tr>
<td>Practice Facilitation</td>
<td></td>
<td>1) Education</td>
<td>1) Create clinic-wide demand</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2) Audit &amp; feedback</td>
<td>2) Clarify measurable goals to improve performance</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>3) PDSA cycles</td>
<td>3) Reinforce mastery of treatment concepts</td>
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<td>4) Engagement</td>
<td>4) Support local implementation</td>
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Phase 1: Implementation Strategies

Phase 2: Delineate implementation strategies under study

Phase 3:
Phase 3: Specify core features of the trial design

- Features of trial design should be driven by the research question
- **PICO** is a widely-known strategy for reframing research questions in a precise and testable manner
- Some applications of PICO recommend 2 additional dimensions: **PICOTS** to capture intervention complexity
Phase 3: Specify core features of the trial design using PICO

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<tr>
<th>Population of Interest</th>
<th>Intervention</th>
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| Who is the trial targeting?  
What are the important characteristics of this population? | What is the experiment or thing to be tested?  
• Digital intervention  
• Clinical support service  
• Implementation strategy | What is the control or comparator?  
How will the trial isolate the studied component |

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| What does the researcher hope to accomplish or improve?  
Is this an effectiveness, health services, or implementation outcome? | Over what period will the trial occur?  
What is the period for follow-up? | Where does the intervention occur?  
In what type of healthcare setting does this trial occur? |
## Phase 3: Specify core features of the trial design using PICO

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| Integrated mental health and primary care providers | What is the experiment or thing to be tested?  
  - Digital intervention  
  - Clinical support service  
  - Implementation strategy | What is the control or comparator?  
  How will the trial isolate the studied component |
| Patients with a drug use disorder | | |

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Phase 3: Specify core features of the trial design using PICO

**Population of Interest**
- Integrated mental health and primary care providers
- Patients with a drug use disorder

**Intervention**
1) Clinical support service: Health coaching
2) Implementation strategy: Practice facilitation

**Comparator**
- “Standard implementation”

**Outcome**
- Fidelity
- Reach

**Timing**
- Over what period will the trial occur?
- What is the period for follow-up?

**Setting**
- Where does the intervention occur?
- In what type of healthcare setting does this trial occur?
**Phase 3: Specify core features of the trial design using PICO**

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<td>12-week intervention (fidelity)</td>
<td></td>
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<td></td>
<td>1-year active implementation period (reach)</td>
<td></td>
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**Outcome**
- Fidelity
- Reach

**Timing**
- Where does the intervention occur?
- In what type of healthcare setting does this trial occur?
**Phase 3**: Specify core features of the trial design using PICO

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| Fidelity  
Reach | 12-week intervention (fidelity)  
1-year active implementation period (reach) | Integrated healthcare setting |
Phase 3: Specify core features of the trial design

1) HEALTH COACHING (clinical support service)
In the context of an integrated healthcare setting (S), do primary care clinics randomized to health coaching (I) compared to standard implementation (C) have a higher mean number of weeks in which patients with documented drug use disorder (P) use reSET and reSET-O as recommended [fidelity] (O) over the 12-week intervention (T)?
Phase 3: Specify core features of the trial design

1) HEALTH COACHING (clinical support service)
In the context of an integrated healthcare setting (S), do primary care clinics randomized to health coaching (I) compared to standard implementation (C) have a higher mean number of weeks in which patients with documented drug use disorder (P) use reSET and reSET-O as recommended [fidelity] (O) over the 12-week intervention (T)?

2) PRACTICE FACILITATION (intervention strategy)
In the context of an integrated healthcare setting (S), do primary care clinicians who care for patients with a drug use disorder (P) in clinics randomized to practice facilitation (I) compared to standard implementation (C) prescribe reSET and reSET-O to a higher proportion of eligible patients with documented drug use disorder [reach] (O) during a 1-year active implementation period (T)?
Phase 3: Specify hybrid trial design

- Hybrid trials allow the researcher to address questions related to implementation while gathering data on effectiveness
Phase 3: Specify hybrid trial design

- Hybrid trials allow the researcher to address questions related to implementation while gathering data on effectiveness.
Phase 3: Specify hybrid trial design

- Hybrid trials allow the researcher to address questions related to **implementation** while gathering data on **effectiveness**
- Well-suited when effectiveness is lacking/limited but there is **political will to implement**

**Effectiveness**
- patient health outcomes (typically)
- real-world settings with researchers delivering interventions

**Implementation**
- clinic/provider outcomes (typically)
- real-world setting with clinicians delivering intervention

---

Hybrid Trials
Phase 3: Specify hybrid trial design

**Hybrid Type I** studies have a primary research question about effectiveness and a secondary focus on implementation.

**Hybrid Type II** studies have an equal focus on effectiveness and implementation.

**Hybrid Type III** studies have a primary research question about implementation and a secondary focus on effectiveness.
Phase 3: Specify hybrid trial design

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- Well-suited when effectiveness is lacking/limited but there is **political will to implement**

Effectiveness
patient health outcomes (typically)
real-world settings with researchers delivering interventions

Implementation
clinic/provider outcomes (typically)
real-world setting with clinicians delivering intervention

Hybrid Trials
Type I  Type II  Type III

DIGITS Trial (Glass et al.)
Phase 3: Specify hybrid trial design

Where do Clinical Support Services fit?

- Could be considered Type I, II, or III
- Consider research question and primary outcome(s)
- Important to clarify and report rationale
CONCLUSION

Implications

Helps researchers **design**, **review**, and **execute** trials of digital interventions; helps **communicate** to decision-makers

Considers the impact **clinical support services** have on effectiveness and implementation of digital interventions

Advocates for the use of **hybrid trials** to advance evidence-to-practice and applicability in real-world settings

Trials need to be harmonized

Lack of studies that seek to answer how to deliver digital interventions

Few trials test these approaches in the real world
This is a working framework.
We welcome your questions, comments, and feedback!
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✉️ Tessa.e.matson@kp.org or Joseph.e.glass@kp.org
References


Park LS, Chih MY, Stephenson C, et al. Testing an mHealth System for Individuals With Mild to Moderate Alcohol Use Disorders: Protocol for a Type 1 Hybrid Effectiveness-Implementation Trial. JMIR Res Protoc. 2022;11(2):e31109. doi:10.2196/31109