

Quality by Design Principles Document for Health Services Research

INTRODUCTION

Dissemination and Implementation (D&I) science is the study of translation of research findings into practice in order to improve health outcomes in the broader community (Colditz, 2012). This toolkit adapts the principles of Quality by Design (QbD) to support proactive discussions and decision making at the time of study development about (1) what aspects of the study are critical to generating reliable data and providing appropriate protection of research participants (“critical to quality” [CTQ] factors) and (2) what strategies and actions will effectively and efficiently support quality in these critical areas. The document generally assumes that a clinical study will address a relevant scientific question for which there is a legitimate research need and is not intended as a primer on how to design a clinical study.

We have developed questions to consider for each CTQ factor to *support evaluation of the factor’s relative importance for a particular study* as well as to *inform subsequent evaluation of what events may occur that would be likely to significantly impede the conduct of the study, place trial participants at unnecessary risk, or impede usability of the resulting data* (in other words, to become “errors that matter”). These discussions can then be used to develop *formal plans to avoid these events* (e.g., through tailoring study design or implementation) or mitigate their consequences.

The document is an adaptation of a similar QbD tool, CTTI Quality by Design project - Critical To Quality Factors Principles Document.

STUDY DESIGN														
Factor	Considerations													
Design	<p>Is the design appropriate for the study goals? <i>Considerations in D&I study design:</i></p> <ol style="list-style-type: none"> Does an evidence-based intervention or practice exist? <ul style="list-style-type: none"> If Y → <i>effectiveness research</i>: examining how efficacious interventions work in real-world settings and its variations <ul style="list-style-type: none"> Role of D&I: implementation outcomes can be studied as contributing factors; implementation outcomes can be primary or secondary aims using hybrid design If Y, is the evidence-based practice applied adequately? D&I research is the primary focus If N → <i>innovation development, safety testing, efficacy testing (not D&I)</i> Can the exposure be assigned? <ul style="list-style-type: none"> If N → <i>observational</i> (cohort, cross-sectional, case-control) If Y, can the exposure be <i>randomized</i>? <ul style="list-style-type: none"> If Y → <i>experimental</i> (RCT, cluster RCT, stepped wedge, adaptive, hybrid design) If N → <i>quasi-experimental</i> (controlled before/after, interrupted time series design, regression-discontinuity design) <p>Hybrid Effectiveness-Implementation Designs:</p> <table border="1"> <thead> <tr> <th>Hybrid</th> <th>Intervention Effectiveness Focus</th> <th>Implementation Focus</th> </tr> </thead> <tbody> <tr> <td>Hybrid 1</td> <td>Primary</td> <td>Secondary</td> </tr> <tr> <td>Hybrid 2</td> <td>Equal focus</td> <td>Equal focus</td> </tr> <tr> <td>Hybrid 3</td> <td>Secondary</td> <td>Primary</td> </tr> </tbody> </table> <p> https://toolkitsc.herokuapp.com/ https://cpb-us-w2.wpmucdn.com/sites.wustl.edu/dist/6/786/files/2017/08/DIRC-intro-toolkit-2016.12.9-edits-1l2x1m8.pdf https://sites.wustl.edu/wudandi https://cpb-us-w2.wpmucdn.com/sites.wustl.edu/dist/6/786/files/2017/07/DIRC-designs-toolkit_7-27-17-2ir4zil.pdf </p>		Hybrid	Intervention Effectiveness Focus	Implementation Focus	Hybrid 1	Primary	Secondary	Hybrid 2	Equal focus	Equal focus	Hybrid 3	Secondary	Primary
Hybrid	Intervention Effectiveness Focus	Implementation Focus												
Hybrid 1	Primary	Secondary												
Hybrid 2	Equal focus	Equal focus												
Hybrid 3	Secondary	Primary												
Conceptual Model and Theoretical Justification?	<p>Is there a clear conceptual framework/theory/model that informs the design and variables being tested?</p>													

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Outcomes	<ol style="list-style-type: none"> 1. What is the targeted change? 2. How will you measure these changes? 3. How likely is it that your initiative will achieve key study outcomes? 4. What are some possible unintended consequences?
Implementation Outcomes	<ol style="list-style-type: none"> 1. Does your project have implementation outcomes? What are the endpoints used to measure them? Acceptability: Extent to which implementation stakeholders perceive a treatment, service, practice, or innovation to be agreeable, palatable, or satisfactory. Adoption: Intention, initial decision, or action to try or employ an innovation or evidence-based practice. Adoption may also be called “uptake.” Appropriateness: Perceived fit, relevance, or compatibility of the innovation or evidence-based practice for a given practice setting, provider, or consumer; and/or perceived fit of the innovation or evidence-based practice to address a particular issue or problem. Cost: Financial impact of an implementation effort. May include costs of treatment delivery, cost of the implementation strategy, and cost of using the service setting. Feasibility: Extent to which a new innovation or practice can be successfully used or carried out within a given agency or setting. Fidelity: Degree to which an intervention or implementation strategy was delivered as prescribed in the original protocol or as intended by program developers. May include multiple dimensions such as content, process, exposure, and dosage. Penetration: Extent to which an innovation or practice is integrated within a service setting and its subsystems. Sustainability: Extent to which a recently implemented practice is maintained and/or institutionalized within a service setting’s ongoing, stable operations.
Service Outcomes	<ol style="list-style-type: none"> 1. Does your project have service outcomes? What are the endpoints used to measure them? Efficiency Safety Effectiveness Equity Patient-centeredness Timeliness
Stakeholder engagement	<ol style="list-style-type: none"> 1. Is there a clear engagement process for key stakeholders? 2. Stakeholder Perceptions of Intervention Characteristics: Intervention source - Perception of key stakeholders about whether the intervention is externally or internally developed. Intervention strength and quality - Stakeholders’ perceptions of the quality and validity of evidence supporting the belief that the intervention will have desired outcomes. Relative advantage - Stakeholders’ perception of the advantage of implementing the intervention versus an alternative solution. Adaptability - The degree to which an intervention can be adapted, tailored, refined, or reinvented to meet local needs. Trialability - The ability to test the intervention on a small scale in the organization, and to be able to reverse course (undo implementation) if warranted. Complexity - Perceived difficulty of implementation, reflected by duration, scope, radicalness, disruptiveness, centrality, and intricacy and number of steps required to implement Design quality and packaging – perceived excellence in how intervention is presented Cost - Costs of the intervention and costs associated with implementing the intervention including investment, supply, and opportunity costs. 3. Leadership Engagement - Commitment, involvement, and accountability of leaders and managers with the implementation. 4. Characteristics of individuals

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	<p>Knowledge and beliefs about intervention Self-efficacy Individual stage of change Individual identification with organization Other personal attributes</p> <p>https://implementationscience.biomedcentral.com/articles/10.1186/s13012-022-01245-0</p>
Reach	<p>Reach: The absolute number, proportion, and representativeness of individuals who are willing to participate in a given initiative, intervention, or program, and reasons why or why not.</p> <ol style="list-style-type: none"> 1. How will this project reach the targeted population? 2. Whom do you plan to reach? 3. Define the target population 4. How and where will you reach them? 5. How will you know if those who participated are representative of your target population? <p>https://re-aim.org/applying-the-re-aim-framework/re-aim-guidance/use-when-planning-a-project/planning-tool/ https://www.re-aim.org/about/what-is-re-aim/reach/improving-reach/</p>
Maintenance	<p>Is this project sustainable within the institution/healthcare system? How will it be sustained?</p> <p>At the setting level, the extent to which a program or policy becomes institutionalized or part of the routine organizational practices and policies. Within the RE-AIM framework, maintenance also applies at the individual level. At the individual level, maintenance has been defined as the long-term effects of a program on outcomes after a program is completed. The specific time frame for assessment of maintenance or sustainment varies across projects.</p> <ol style="list-style-type: none"> 1. What will happen long-term? 2. What are likely implementation challenges that will need to be overcome? 3. What infrastructure supports will be needed to sustain the initiative? 4. Is there infrastructure or funding that will remain? 5. How will this initiative align with current and future policies, programs and priorities? 6. How will individuals be delivered the key components of the intervention over time? 7. How will you track success and provide ongoing feedback? <p>https://www.re-aim.org/about/what-is-re-aim/maintenance/</p>
STUDY CONDUCT	
Identification of Barriers and Facilitators	<p>Identify factors that affect implementation outcomes and tailor implementation strategies to overcome negative factors (barriers) and enhance positive factors (facilitators)</p> <ul style="list-style-type: none"> - Instruments for measuring barriers: Multiple-factor Assessment Instruments including combinations of innovation, provider, patient, organizational, & structural/community-level constructs; single factor assessments - Instruments for measuring facilitators <p>https://cpb-us-w2.wpmucdn.com/sites.wustl.edu/dist/6/786/files/2017/08/DIRC-BarrierFacilitators_Toolkit-1gc9m0a.pdf</p>

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<p>Organizational Constructs/Inner Setting</p>	<ol style="list-style-type: none"> 1. Is the organization ready to implement change? 2. Does the organization’s members believe in their collective capability to change? 3. What is the organizational culture surrounding change? 4. How do the employees perceive the impact of their work? 5. To what extent do employees collectively perceived that the adoption, implementation, and use of the program is expected, rewarded, or supported by the organization? To what extent do they perceive it is important to implement? <p>Organizational Readiness for Change: Organizational members' shared commitment to implement a change and belief in their collective capability to do so.</p> <p>Organizational Culture: The set of expectations and norms that influence behavior within an organization; it includes the historical values and collective experiences of the organization and is often viewed as “the way things are done around here.”</p> <p>Organizational Climate: Employees’ collective perceptions of the psychological impact of their work environment on their own functioning and well-being. This involves the perceived meaning of organizational practices and procedures, as well as perceptions of the kinds of behaviors that are rewarded or expected, aggregated at the organization level.</p> <p>Implementation Climate: The extent to which employees collectively perceive that the adoption, implementation, and use of an innovation such as an evidence-based program or practice is expected, rewarded, and supported by the organization. This refers to employees’ shared perceptions of the importance of implementing a particular innovation within the organization.</p> <p>Tension for change: The degree to which stakeholders perceive the current situation as intolerable or needing change.</p> <p>Compatibility: The degree of tangible fit between meaning and values attached to the intervention by involved individuals, how those align with individuals’ own norms, values, and perceived risks and needs, and how the intervention fits with existing workflows and systems.</p> <p>Relative priority: Individuals’ shared perception of the importance of the implementation within the organization.</p> <p>Organizational incentives and rewards: Extrinsic incentives such as goal-sharing awards, performance reviews, promotions, and raises in salary, and less tangible incentives such as increased stature or respect.</p> <p>Goals and Feedback: The degree to which goals are clearly communicated, acted upon, and fed back to staff, and alignment of that feedback with goals.</p> <p>Learning climate: A climate in which: a) leaders express their own fallibility and need for team members’ assistance and input; b) team members feel that they are essential, valued, and knowledgeable partners in the change process; c) individuals feel psychologically safe to try new methods; and d) there is sufficient time and space for reflective thinking and evaluation.</p> <p>Readiness for implementation: Tangible and immediate indicators of organizational commitment to its decision to implement an intervention.</p> <p>https://cpb-us-w2.wpmucdn.com/sites.wustl.edu/dist/6/786/files/2017/08/DIRC-implementation-organizational-measures-tool_12.9.16-edits-2253kxf.pdf</p> <p>https://implementationscience.biomedcentral.com/articles/10.1186/s13012-022-01245-0</p>
<p>Implementation Strategies</p>	<ol style="list-style-type: none"> 1. Have you developed an implementation strategy (see below)? How will the initiative be delivered, adapted, adjusted? <ul style="list-style-type: none"> - What are the key elements that must be delivered to be successful? 2. To what extent will the key aspects of the program be delivered as intended? <ul style="list-style-type: none"> - How will you assess program delivery? 3. What adaptations or modifications do you think will be necessary to help implement the initiative to different settings? <ul style="list-style-type: none"> - Possible implementation challenges to overcome? 4. How will you know what adaptations or modifications were made during the program? <ul style="list-style-type: none"> - Who can help you keep track of modifications/adjustments?

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	<p>5. What are some of the possible obstacles to consistent implementation? - Are there competing projects or programs to consider?</p> <p>6. What cost and resources (including time, burden) need to be considered?</p> <p>Intervention Strategies</p> <p>Evaluative and iterative strategies: Assess for readiness and identify barriers and facilitators, Audit and provide feedback</p> <p>Provide interactive assistance: Provide facilitation, Provide clinical supervision, Provide local technical assistance</p> <p>Adapt and tailor to context: Promote adaptability, Tailor strategies, Use data experts</p> <p>Develop stakeholder relationships: Build a coalition, Identify and prepare champions, Conduct local consensus discussions</p> <p>Train and education stakeholders: Conduct educational meetings, Develop and distribute educational materials</p> <p>Support clinicians: Facilitate relay of clinical data to providers, Remind clinicians</p> <p>Engage consumers: Intervene with patients/consumers to enhance uptake and adherence, Use mass media</p> <p>Utilize financial strategies: Access new funding, Alter patient/consumer fees, Allow incentives/allowance structures</p> <p>Change infrastructure: Change physical structure or equipment, Change record systems</p> <p>https://re-aim.org/applying-the-re-aim-framework/re-aim-guidance/use-when-planning-a-project/planning-tool/ https://sites.wustl.edu/wudandi/ https://cpb-us-w2.wpmucdn.com/sites.wustl.edu/dist/6/786/files/2017/11/DIRC-implementation-strategies-tool-1v33amk.pdf</p>
<p>Feasibility of Proposed Research Methods & Contingency Plans</p>	<p>Do you have contingencies in place, should methods not work as planned?</p>
<p>Participant accrual and retention</p>	<p>1. Describe the enrollment process.</p> <p>2. How will participants be identified? How will they be reached? Are there stakeholders who can help with identification of eligible participants?</p> <p>3. How will you retain participants?</p>
<p>Participant Safety</p>	<p>1. Informed consent: What are the key elements of the informed consent for this project? Have various stakeholders been involved in development of the informed consent? Does it use plain language principles (eg focus on symptoms rather than disease states)? How does the consent process fit in with study processes? Is there potential for vulnerable trial participants, those with impaired cognition or capacity?</p> <p>2. Withdrawal Criteria: Describe situations in which participants should or may be withdrawn. What are the steps required prior to deeming participant lost to follow up? Are there advocacy groups who should be involved?</p>
<p>Training</p>	<p>1. Is there a training protocol in place for all stakeholders?</p> <p>2. Will stakeholders need booster sessions?</p> <p>3. How will you ensure consistent conduct?</p> <p>4. Do staff need training for data collection?</p>
<p>Data Recording and Reporting</p>	<p>1. Where will data be collected?</p> <p>2. Can IT systems be leveraged for data collection?</p> <p>3. Will data be captured in parallel with routine clinical assessments?</p>

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	<ol style="list-style-type: none"> 4. Will multiple data systems be utilized, requiring transfer and integration? 5. Where will data be stored? 6. Where and how will the data be used?
Data Monitoring and Management	<ol style="list-style-type: none"> 1. Identify departures from study conduct that may generate “errors that matter.” 2. Which data are not critical to study analysis? 3. By what methods will data be monitored while the study is ongoing? At what frequency? 4. Approaches be used in combination with onsite monitoring activities? 5. What functional lines will be involved in ongoing data monitoring? 6. Identify which function/individual is ultimately responsible for the decision to lock and unlock the database. 7. What types of issues is the monitoring plan designed to detect? Is it sufficiently comprehensive? 8. Define critical data elements for data management during protocol development
DISSEMINATION	
Dissemination Plan	<ol style="list-style-type: none"> 1. Does team agree on the dissemination plan? 2. Who are the targets of dissemination? 3. How will information be used? 4. Plan for dissemination to the community? 5. How will information be communicated to study participants? 6. Who has rights to publish? 7. Agreement on authorship? 8. How will you get the word out about the initiative and lessons learned? 9. What are likely modifications or adaptations that need to be made?