ASCENT
Advancing the Science of Palliative Care Across the Lifespan

Stage Ib Feasibility/Pilot Study Guidance Document

A key formative step in the development of an intervention is feasibility and pilot testing. This is performed at Stage Ib of the NIH Stage Model prior to full-scale efficacy testing. **This document is provided to support investigators in developing rigorous Stage I testing.** Poor design choices in Stage Ib can limit the potential of a future Stage II / III clinical trial, and thus a rigorous Stage Ib study is imperative for moving serious illness intervention research forward.

Purpose of a Stage Ib Feasibility/Pilot Study

The purpose of a Stage Ib feasibility/pilot study is to examine the feasibility and acceptability of *both* the intervention and its implementation. It should test the elements of the trial to inform a future stage II or III efficacy trial in the way it would be performed at full-scale. Stage Ib testing should occur after Stage Ia intervention generation, adaptation, or tailoring. Stage Ia testing is not within the scope of this guidance.

Feasibility and Acceptability Metrics

1. Feasibility/Pilot studies have primary and secondary outcomes that are measures of feasibility and / or acceptability. These studies must demonstrate the feasibility of collecting the proposed primary outcome for a fully powered trial but are usually not powered to evaluate efficacy.
2. Each study should have *a priori* feasibility and acceptability goals. These should cover at a minimum: recruitment, screening:enrollment ratio, retention, participant engagement and adherence, ability to collect outcome measures including completeness/missingness, fidelity of intervention implementation, and measures of acceptability and/or usability of the intervention.
3. Measurable and achievable metrics should be specified for each goal. For example, 85% participant retention at 3 months. Alternatively, the stop/amend/go approach may be used. If the minimum statistic or “go” definition is not achieved, amendments or refinements may need to be performed prior to advancing to a stage II/III trial.

Number of Study Arms

1. Randomization/multi-armed trials should be considered where there are unanswered questions around recruitment, retention, comparator condition (e.g. usual care vs. attention control), equipoise, or other methodological elements that cannot be predetermined. The decision to conduct a multi-arm trial will depend on costs, as a larger sample size will be required.

2. For funding mechanisms that do not permit NIH-defined clinical trials, investigators should ensure that the study objectives and planned analyses are limited to feasibility objectives (e.g., recruitment, retention, acceptability, implementation, and the feasibility of collecting clinical outcome measures) and should confirm that the proposed design is consistent with the NIH clinical trial definition and the specific funding opportunity. See NIH's definition of a clinical trial and decision support tool for further guidance.

Sample Size Justification

1. Sample size should be chosen so that, if the expected feasibility outcome is observed (e.g., 80% retention), the lower bound of the 95% confidence interval exceeds a prespecified acceptable value. Trials do not necessarily need to be powered for all feasibility outcomes but must be powered to ascertain key feasibility outcomes (e.g. primary, secondary) that are necessary for showing ability to move to a full-scale trial.

Other Design Considerations

1. An intervention should have a clear hypothesized mechanism(s) of action, which is often visualized in a conceptual model. An intervention should include one or more components that are intended to change specific processes (mechanisms) that are believed to improve outcomes. These mechanisms should be on the causal pathway between the intervention and the primary and secondary outcomes. Both the mechanisms and the outcomes should be measurable using self-report questionnaires, behavioral assessments, or objective measures such as performance-based measures or instrumented measures.

2. During Stage Ib studies, researchers should examine whether the intervention changes the proposed mechanism(s) (mechanistic target engagement) and whether change in those mechanisms are associated with favorable changes in the outcomes (mechanistic target validation). Target engagement should be operationalized descriptively by examining pre-post change in the proposed mechanistic target using effect sizes with confidence intervals. This is analogous to the NIMH Fast-Fail approach, where the primary question is simply whether the intervention engages the target, not whether target engagement causally mediates the outcome. Target validation should be assessed by reporting the direction and magnitude of the association between change in the mechanism and change in the outcome (e.g., correlation coefficients with confidence intervals), explicitly framed as preliminary and hypothesis-generating rather than confirmatory causal inference. The NIH Science of Behavior Change CLIMBR Tool is a helpful resource for performing this work. Because Stage Ib studies are typically small, these analyses should focus on estimation rather than formal hypothesis testing, and any attempt at formal mediation or moderation analysis would be underpowered and risk exaggerated conclusions. These preliminary

findings serve as go/no-go decision points that inform the design of a fully powered Stage II/III efficacy trial, where mediation can be properly tested.

3. The proposed design should address all pilot and feasibility CONSORT extension elements.
4. Consider key elements and potential scalability of your intervention early in the design phase. If uncertainty still exists after the pilot regarding which intervention elements or dosage of elements should be utilized, other methods such as an optimization study may be appropriate to perform prior to a full stage II/III efficacy trial.
5. Qualitative or mixed methods approaches can increase the robustness of feasibility/pilot testing and support refinement to a future stage II/III study protocol.

What Stage I Feasibility/Pilot Studies Should Not be Used For

1. Unlike definitive trials, feasibility/pilot studies are not powered for efficacy, and not designed for *a priori* hypothesis testing around clinical efficacy. **They therefore should not be used to determine "preliminary efficacy" which is a problematic scientific concept.** They can however be used to examine variability and floor/ceiling effects of measures.
2. Data from a feasibility/pilot study should not be used as the sole data for generating power estimates, as they may generate biased outcome estimates and tend to underestimate variability. However, they can be used as one point of data to inform power calculations by developing a range of variance estimates based off the pilot study findings to use in addition to published full-scale trials in determining power and sample size for a future full-scale trial.

Note: These recommendations, as of publication date, are considered best practices for obtaining rigor and meeting the goals of a feasibility/pilot study. While these items provide some key guidance on decision points, it is by no means an exhaustive list and both the citations below, and discussion with design experts should be performed as you go about designing your study, either through your institution, the ASCENT Lab, or otherwise.

To Cite this Document

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Key Citations

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