

## **Supplementary file B: complementary methods to embed within implementation research for global health**

### **Economic evaluation**

An economic evaluation is particularly important in implementation research as it provides insight as to whether implementation efforts are likely to make effective and efficient use of the limited availability of resources. (64) Economic evaluation for implementation research uses comparative analysis of the cost consequences and the benefits arising from improved implementation success (including improved health outcomes) to determine whether implementation strategies have been effective.

Implementation costs are essential to test for in the pre-implementation phase of research, to avoid the possibility of providing a service that has the potential to improve health, especially where provision of health services are particularly poor, only to remove it due to excessive costs.(65) Economic modelling in the pre-implementation phase can provide insight as to whether the interventions are feasible for scale-up after an intervention is completed. If results suggest the intervention is unsustainable, it may be possible to modify aspects of the intervention, that will help to ensure longer-term sustainability.(66) However, a recent review of the types of health economic modelling in implementation programmes found that this was a neglected aspect of the pre-implementation phase of research.(28)

### **Literature reviews**

In the pre-implementation phase of research, a review of the literature is important to not only establish the most effective evidence-informed practice to address the identified gap in the local setting, but also contextual and behavioural barriers that influence the delivery of this care and potential mechanisms behind which this occurs.

Ideally such reviews are guided by methods such as implementation science theories and frameworks; in particular determinant frameworks. Findings from such a review can help to guide future implementation research programmes including an understanding of barriers/enablers in the local context that will influence the effectiveness of implementation efforts for a set of selected implementation strategies on implementation outcomes. Not to be overlooked, is the importance of literature reviews guided by middle-range theories (i.e. a realist review) that can be used to help develop a programme theory relevant to the local setting to theorise how contextual determinants influence the mechanisms introduced by the implementation strategies on implementation outcomes. The initial programme theory, can then be tested and modified throughout the implementation and evaluation phase.(67)

#### **Implementation-effectiveness hybrid trial designs**

There have been significant methodological developments that improve our ability to effectively implement evidence-informed practice that are inherently different to methods such as a randomised controlled trial used to test the effectiveness of a novel treatment (i.e. drug, therapy, device). Effectiveness-implementation hybrid trials are one such advancement that blend the design components of randomised controlled trials/quasi-experimental trials with those of implementation trials.(68) These trials focus on evaluating the effectiveness of the implementation strategies in delivering evidence-informed practice on both clinical and implementation outcomes. Hybrid trials also incorporate methodology to help understand how contextual and behavioural barriers influence the effectiveness of implementation strategies in delivering evidence-informed practice. In turn, this can help to ensure the longer-term sustainability of implementation efforts in a novel context.

Broadly, there are three types of Hybrid Trials (i.e. Type 1, Type 2, and Type 3) where the type of trial selected depends on the availability of evidence for both the clinical components of the intervention as

well as the interventions selected to deliver the evidence-based clinical intervention for a given context.<sup>(32)</sup> One can anticipate that a Hybrid Type 1 trial using a randomised controlled trial design may be appropriate when the literature review and findings from the pre-implementation phase of research indicates that several additional implementation strategies are required to deliver the evidence based practices. However, if only a few adaptations are required, it is likely that a Hybrid Type 3 trial is required that involves the ongoing monitoring of the influence of context on the effectiveness of implementation strategies on implementation outcomes. Table 1 describes the key differences between the types of Hybrid trials.

**Table 1 Different hybrid trial designs, associated aims, recommendations for use and suggested level of care offered to the control arm**

Hybrid trial design	Research aims	Required evidence base for use	Recommended level of care to the control arm
Type 1	Primary aim: determine clinical effectiveness of clinical intervention. Secondary aim: understand context of implementation.	Existing evidence for effectiveness of the clinical intervention in a different context, that is applicable to the relevant local setting.	Treatment as usual, enhanced usual care.
Type 2	Copriamary aim: effectiveness of clinical intervention. Copriamary aim: effectiveness of implementation intervention/strategy.	Existing evidence for the effectiveness of both the clinical intervention and the interventions that deliver the evidence-informed practice in a different context, that would support applicability to the new setting.	Enhanced usual care, or quasi-experimental designs without a control arm.
Type 3	Primary aim: effectiveness of interventions (strategies) to deliver evidence-informed practice. Secondary aim: evaluate clinical outcomes associated with implementation trial.	Strong evidence base for the clinical effectiveness, but ambiguity exists as to what are the most effective interventions (strategies) to deliver the evidence-informed practice within the new setting.	Quasi-experimental designs without a control arm.