The Intensive Care Platform Trial (INCEPT)

Core protocol synopsis

Protocol version and date
Version 1.3, 2025-02-13

Website
www.incept.dk

Applicable protocol registration numbers
European Union Clinical Trials Information System (CTIS) EUCT number: 2024-516208-41-00.
ClinicalTrials.gov identifier: NCT06667999.
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Protocol synopsis

Background

Randomised clinical trials (RCTs) are the gold standard for evaluating intervention effects, however, conventional RCTs are bureaucratic, costly, inflexible, and often inconclusive. Adaptive platform trials are increasingly used as they can reduce barriers and are more flexible, and thus come with a higher probability of obtaining conclusive results faster at lower costs.

Objectives

This core protocol describes the methodological framework for the *Intensive Care Platform Trial (INCEPT)*, which will be used to assess the effects of interventions used in adults acutely admitted to the intensive care unit (ICU).

Design

INCEPT is an investigator-initiated, pragmatic, randomised, embedded, multifactorial, domain-based, international, adaptive platform trial. *INCEPT* uses adaptive stopping and arm-dropping rules, as well as fixed and response-adaptive randomisation.

Domains and interventions

Comparable groups of interventions will be nested in domains, which have conceptual similarities with stand-alone randomised trials. Specific domains may be either open label or blinded. Domains will continuously be added to *INCEPT* and conducted following domain-specific appendices to the core protocol. Domains will be *closed*, i.e., arms will not be added to domains once started.

Inclusion and exclusion criteria

Adults acutely admitted to the ICU will be screened if they are eligible for at least one active domain. The only platform-level exclusion criteria are 1) informed consent after inclusion expected to be unobtainable and 2) patients admitted under coercive measures. Additional inclusion and exclusion criteria will be domain-specific.

Stakeholder involvement

Stakeholder involvement is central in *INCEPT* and ensured through a central advisory board comprising various key stakeholder and national and international research panels consisting of ICU survivors, family members, clinicians, and researchers. Stakeholders have been involved in the development of the overall platform trial and continued involvement is planned with pre-specified minimum requirements for involvement in *INCEPT* and all domains.

Outcomes

The following core outcomes will be evaluated in all *INCEPT* domains:

- All-cause mortality at 30, 90, and 180 days
- Days alive without life support at 30 and 90 days
- Days alive and out of hospital at 30 and 90 days
- Days free of delirium at 30 days
- Health-related quality of life at 180 days evaluated using EQ-5D-5L index values and EQ VAS
- Cognitive function at 180 days evaluated using the Mini MoCA test
- One or more domain-specific safety outcomes

Each domain will use one of the core outcomes as the primary outcome and the *guiding* outcome driving all adaptations.

Statistical methods

Primary analyses will generally be conducted in the intention-to-treat population of each domain. *INCEPT* primarily uses Bayesian statistical methods with neutral priors conveying either minimal information or some scepticism, although specific domains may use conventional, frequentist statistical methods. Outcomes will generally be analysed using logistic and linear regression models adjusted for pre-specified anticipated prognostic baseline characteristics, followed by calculation of sample-average estimates and intervention effects using G-computation. Results will be presented for each intervention and comparisons presented on both the absolute (risk differences and mean differences) and relative (risk ratios and ratios of means) scales with 95% credible intervals and probabilities of superiority. *INCEPT* will generally use constant, symmetric stopping rules for superiority/inferiority based on the guiding outcome; domains may use stopping rules for practical equivalence or futility based on the posterior distribution of the guiding outcome on the absolute scale. All stopping rules will be binding. Response-adaptive randomisation, either with or without restrictions, may be used based on the posterior distribution for the guiding outcome. Missing data will be multiply imputed. Additional secondary analyses (e.g., per-protocol analyses), sensitivity analyses, and analyses of heterogeneity in intervention effects according to pre-defined baseline characteristics may be specified for each domain and undertaken once a domain has stopped. Domains will be designed and evaluated using statistical simulation.

Estimated timeline

We expect that *INCEPT* will launch and include the first participant in the first quarter of 2025. *INCEPT* has been designed to run perpetually with domains continuously added and stopped and without a planned stopping date for the overall platform.

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