

# INPLASY

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## Protocol deviations in NIHR-funded multicentre randomised controlled trials of surgical and medical device interventions: a scoping review informed by aviation safety principles

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## ADMINISTRATIVE INFORMATION

Support - NIHR Bursary.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202680016

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 3 August 2026 and was last updated on 3 August 2026.

## INTRODUCTION

**Review question / Objective** What insights from operational aviation principles can inform how protocol deviations are described, attributed, and managed in NIHR-funded multicentre RCTs of surgical and medical device interventions?

**Background** The RCT is the methodological gold standard for healthcare interventions, but its credibility depends on whether it was conducted as its protocol intended. ICH E3 (1996) defines a protocol deviation broadly as any departure from the study design, giving limited guidance on which deviations warrant reporting.

Terminology, deviation, violation, breach, non-compliance, non-adherence, varies between organisations and is often used interchangeably, limiting judgement of what occurred. Standardisation efforts include the ICH E3(R1) Q&A (2012), recommending "deviation" over "violation", and the TransCelerate Protocol Deviations Initiative, which proposed revised terminology

before concluding in January 2023 with unclear uptake outside industry trials.

This review adopts the ICH E6(R3) (2025) definition of Important Protocol Deviations: deviations that may significantly affect data completeness, accuracy or reliability, or a participant's rights, safety or wellbeing, with oversight directed at the deviations most likely to affect these areas.

Surgical and device trials carry features likely to raise deviation rates relative to pharmacological trials: operator dependence, learning curves, blinding difficulty, and design iteration. The NIHR, England's largest public research funder (around £1.7 billion annually), offers established governance and a best-case setting, and its Journal Library provides more methodological detail than journal publications, aided by the Health Research Classification System (HRCS) for consistent identification.

Aviation offers a comparator: both fields are proceduralised, multi-site operations under formal protocols, where deviations are rarely attributable

to one individual. Aviation has built mechanisms, confidential non-punitive reporting, standardised terminology, systems-based classification, to treat deviations as data for aggregation and learning; equivalent cross-trial mechanisms are largely absent in clinical research.

**Rationale** Protocol deviations, departures from the approved trial protocol, are the condition under study. The focus is deviations arising in NIHR-funded multicentre randomised controlled trials of surgical procedures and medical device interventions, a population structurally prone to such deviations because intervention delivery is operator-dependent, blinding is often not feasible, and devices introduce technical and implementation variability rarely seen in pharmacological trials. How these deviations are described, classified, attributed and reported across this trial population remains poorly characterised.

## METHODS

**Strategy of data synthesis** Descriptive quantitative and qualitative thematic analysis will be integrated into a narrative synthesis with the aviation literature. Categorical variables will be summarised as frequencies and proportions, continuous variables as medians and interquartile ranges. Outputs include the proportion of trials reporting deviations, applying formal classification, deviation types against TransCelerate's categories, and corrective actions.

Thematic analysis, following Braun and Clarke (2006), will examine how deviations are conceptualised, combining deductive coding (terminology, classification, attribution, response) with inductive coding of emergent themes in Microsoft Word, refined iteratively. Analysis will focus on how responsibility is framed (individual, procedural, systemic), whether corrective-action language is reactive or proactive, and alignment with ICH GCP and CONSORT. Quantitative summaries will use Microsoft Excel.

**Eligibility criteria** Criteria follow the JBI Population, Concept, Context framework, preferred over PICO as the review specifies no intervention, comparator or outcome.

Population: NIHR-funded multicentre RCTs of surgical or device interventions in the NIHR Journal Library; trials, not patients, are the unit of analysis. Concept: how deviations are described, attributed and managed, potentially reframed through aviation principles, with attention to IPDs as

defined in ICH E6(R3), including terminology, classification, frequency, attribution, corrective actions, and links to ICH E6(R3) and CONSORT. Context: UK NIHR-funded trials published between January 2016 and June 2026, spanning ICH E6(R2) and the finalisation of E6(R3).

## Source of evidence screening and selection

The primary search combines four HRCS codes with OR: 5.3/6.3 (devices) and 5.4/6.4 (surgery), covering development and evaluation, filtered to January 2016–June 2026, with a supplementary title-field keyword search to prevent HRCS miscoding.

A separate aviation and human factors search (PubMed, Scopus, Google Scholar) will use terms including "aviation safety", "ASRS" and "human factors", unconstrained by date, with manual reference searching.

As all studies are full text within the Journal Library, no separate abstract screening stage is required; records are assessed directly against criteria, piloted, with a 10% sample independently checked by the supervisor, and selection reported via a PRISMA-ScR flow diagram.

**Data management** A standardised Excel charting form, piloted on five reports, will be used. Reports will be searched using anchor terms (deviation, violation, breach, non-adherence, non-compliance, adverse event) before relevant sections are read in full, charting six domains: study characteristics, deviation reporting, frequency and type, attribution, responses, and reporting standards. Extraction will be by a single reviewer, with piloting and supervisor-checked samples as quality controls.

**Language restriction** English language publications only.

**Country(ies) involved** United Kingdom (England) – the review addresses NIHR-funded trials published in the NIHR Journal Library, and draws on aviation safety literature without geographic restriction.

**Keywords** Protocol deviations; scoping review; surgical trials; medical devices; NIHR; aviation safety; human factors; ICH E6(R3); clinical trial conduct.

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