

Table 2. Summary of the IDEAL Framework, Recommendations and Proposals including updates.

| Stage of innovation | Updated IDEAL Framework | Updated IDEAL Recommendations for researchers | Updated IDEAL Proposals for improving the surgical research environment |
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| <p>Pre-IDEAL <i>Pre-clinical</i></p> | <p>Pre-IDEAL was not described in original IDEAL framework Purpose: Feasibility and definition of procedure Number & Types of Patients: pre-clinical Number & Types of Surgeons: Very few; innovators Output: Description addressing:</p> <ul style="list-style-type: none"> • Whether intended goal of procedure is accomplished • Level of difficulty of performing procedure or using device as compared to standard of care • Safety risks • Desirability of intervention <p>Method: Various, including simulator, cadaver, animal, modelling and cost-effectiveness studies Stage Endpoint: Any studies that could avoid predictable risks of failure or harm to the first human should have been conducted.</p> | <ul style="list-style-type: none"> • All predictable risks to patients should be investigated before human studies begin • Guidelines on best scientific practice and ethics specific to the types of study should be followed where available • A minimum dataset describing technical consistency should be made public before first-in-human testing. | <p>Journals: Editors should require publication of the Pre-IDEAL minimum dataset before or together with first-in-human reports Regulatory/legal: Regulators should develop a definition of the minimum publically available dataset required to allow First-in Human studies of new devices to proceed. Ethical aspects: general standards of research integrity apply</p> |

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| <p>Stage 1 Idea <i>First in human</i></p> | <p>Purpose: Proof of concept Number & Types of Patients: Single digit; highly selective. Number & Types of Surgeons: Very few; innovators Output: Description Intervention: Evolving; procedure inception Methods: Structured case reports Outcomes: Proof of concept; technical achievement; dramatic success; adverse events, surgeon views of the procedure Stage Endpoint: Outcomes will determine whether to proceed to stage 2a.</p> | <ul style="list-style-type: none"> • Provide full details of patient selection, technique and outcomes and patients not selected during the time frame, and why. • Use standard well-defined measures for reporting outcome and patient characteristics • Use structured reporting system eg, SCARE checklist. • Make the above information available to peers regardless of outcome | <p>Journals: Encourage or require registration of the innovation when considering for publication (E.g. IJS: Case Reports and www.researchregistry.com) Regulatory/legal: Provide public interest defence from legal discovery for registries specifically for first-in-human studies. Ensure local hospital policy on innovative procedures groups foster innovation (i.e., IRB or new procedure committee) Ethical aspects: multiple strategies required to minimise harms to patients, including formal human research ethics approval for selected planned interventions</p> |
| <p>Stage 2a Development <i>Single centre/single intervention; case series/prospective cohort</i></p> | <p>Purpose: Development of procedure Number & Types of Patients: Few; Selected Number & Types of Surgeons: Few; innovators and some early adopters Output: Technical description of procedure and its development with reasons for changes Intervention: Evolving; procedure development Methods: Prospective development studies Outcomes: Mainly safety; technical and procedural success Stage Endpoint: Procedure should be refined enough to allow replication in Stage 2b and there should be no intent to make further major modifications</p> | <ul style="list-style-type: none"> • Make protocol for study available • Use standard well-defined measures for reporting outcome and patient characteristics • Report and explain all exclusions • Report all cases sequentially with annotation and explanation of when and why changes to indication or procedure took place. • Display main outcomes graphically to illustrate the above. | <p>Journals: Support for publication of Development study formats and protocols Regulatory/legal: Ensure that patient consent includes information about known outcomes from Stage 1**, about unknown risks and – inform the patient that the surgeon has carried out few of the procedures previously Ethical aspects: formal human research ethics approval required</p> |

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| <p>Stage 2b Exploration <i>Bridge from observational to comparative evaluation. Purpose is to gain data to decide if and how to test in a robust RCT or other appropriate pivotal design.</i></p> | <p>Purpose: Achieving consensus between surgeons and centres Number & Types of Patients: Many; broadening indication to include all potential beneficiaries Number & Types of Surgeons: Many; innovators, early adopters, early majority Output: Effect estimate based on large sample; Analysis of learning curves; estimate of influence of pre-specified technical variants and patient subgroups on outcome. Intervention: Stable; acceptable variants defined Method: Prospective multi-centre exploration cohort study (disease or treatment based); pilot/feasibility multicentre RCTs. Outcomes: Safety; clinical outcomes (specific/graded); short-term outcomes; patient centred/reported outcomes; feasibility outcomes Stage Endpoints: fall in to two main groups; Demonstrate that technique can be more widely adopted; and, Demonstrate that progression to RCT is desirable and feasible</p> | <ul style="list-style-type: none"> • Make protocol for study available • Use standard well-defined measures for reporting outcome and patient characteristics • Participate in collaborative multi-centre co-operative data collection, incorporating feasibility issues such as: <ul style="list-style-type: none"> ○ estimating effect size, ○ defining intervention quality standards, ○ evaluating learning curves, ○ exploring subgroup differences, ○ eliciting key stakeholder values and preferences, ○ analysis of adverse events: • Pre-planned consensus meeting prior to progressing to an RCT to identify feasibility and ability to recruit, intervention and comparator definitions, appropriate patient selection criteria, primary endpoint. | <p>Funders: Support Stage 2b Exploratory cohort studies as preliminary “pilot/feasibility” phases for RCT proposals. Journals: Support publication of IDEAL Exploration studies and protocols Ethical aspects: formal human research ethics approval required. Ensure that potential harms from the learning curve are minimised by training and mentoring prior to progressing to Stage 3</p> |
| <p>Stage 3 Assessment <i>Definitive comparative evaluation of main efficacy and safety aspects of new technique against current best treatment.</i></p> | <p>Purpose: Comparative effectiveness testing Number & Types of Patients: Many; expanded indications (well-defined) Number & Types of Surgeons: Many; early majority Output: Comparison with current standard therapy Intervention: Stable</p> | <ul style="list-style-type: none"> • Register on an appropriate international register (e.g., clinicaltrials.gov) • Use standard well-defined measures for reporting outcome and patient characteristics • Incorporate information about patient and clinician values and preferences in consent information and outcome measure design • Reporting guidelines: | <p>Funders: Support trial proposals incorporating preparatory Stage 2b work Journals: Encourage authors to refer to work on innovation in prior IDEAL stages preceding RCT. Support use of appropriate reporting guidelines. Mandate registration of RCT in trials register prior to publication. Ethical aspects: formal human research ethics approval required</p> |

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| | <p>Method: RCT with or without additions/modifications; alternative designs (cluster, preference RCTs, stepped wedge, adaptive designs)</p> <p>Outcomes: Clinical outcomes (specific and graded); potentially Patient Reported outcomes , Health Economic outcomes</p> <p>Stage Endpoints: two main endpoints; Clear valid evidence on relative effectiveness of innovation; and, Identification of issues requiring long term monitoring.</p> | <p>CONSORT update of 2010 with extension for non-pharmacological treatments COMET TIDieR SPIRIT (for RCT protocol design)</p> | |
| <p>Stage 4 Long term monitoring</p> | <p>Purpose: Surveillance</p> <p>Number & Types of Patients: All eligible</p> <p>Number & Types of Surgeons: All eligible</p> <p>Output: Description; audit; regional variation; quality assurance; risk adjustment</p> <p>Intervention: Stable</p> <p>Method: Registry; routine database; rare-case reports</p> <p>Outcomes: Rare events; long-term outcomes; quality assurance</p> <p>Additions: Registries for devices – IDEAL-D Registries at earlier stages of IDEAL</p> | <ul style="list-style-type: none"> • Registries may begin from the earliest stages of human use • Registry datasets should be defined by the clinical community with patient input • Datasets should be simple, cheap and easy to collect • Curation of registries by clinical community is desirable • Funding of registries should be agreed between government and commercial interests but kept separate from curation • Consent for use of registry data in research should be broad and where possible automatic | <p>Funders: Link funding for purchasing treatment to delivery of adequate long term follow up</p> <p>Ethical aspects: resolve issues of consent for data use and especially for nested RCTs</p> |

*Registries should be organised according to the IDEAL recommendations and should be available for enrolment at *any Stage*

**Patient consent should always include outcomes from previous IDEAL Stage

Actions for Professional societies:

- Ensure guidelines explicitly support IDEAL model of technical development and evaluation
- Require members to use appropriate registers for the various stages of innovation as a condition of specialist recognition