CORE-MD

Coordinating Research and Evidence for Medical Devices

The CORE-MD study of introducing novel methodology for clinical evidence development

Aims of CORE-MD Workstream 2.1

- To understand factors facilitating and inhibiting the uptake of novel methodology for regulatory clinical evidence development

- To evaluate the uptake and use of IDEAL format studies as clinical evidence for CE marking under MDR

Open access Analysis

BMJ Surgery, Interventions, & Health Technologies

IDEAL as a guide to designing clinical device studies consistent with the new European Medical Device Regulation

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To cite: Fleetcroft C, McCulloch P, Campbell B. IDEAL as a guide to designing clinical device studies consistent with the new European Medical Device Regulation. *BMJ Surg Interv Health Technologies* 2021;**3**:e000066. doi:10.1136/bmjsit-2020-000066

Received 22 September 2020
Revised 06 January 2021
Accepted 01 February 2021

INTRODUCTION

The evidence demanded by European medical device regulators is getting tougher, especially for high-risk devices. The new European (EU) Medical Device Regulation[1] (MDR) has changed the evidence requirements for CE certification. The regulation states, in general terms, what kind of evidence is required for market approval and for subsequent surveillance, but it does not specify the types of studies which may be most appropriate in providing the evidence. This can pose a major challenge for innovators and developers of devices, many of whom are relatively inexperienced in planning clinical studies and limited in their capacity to fund studies. A framework specifying methodology for producing evidence throughout the lifecycle of new products would therefore be both useful and timely.

Key messages

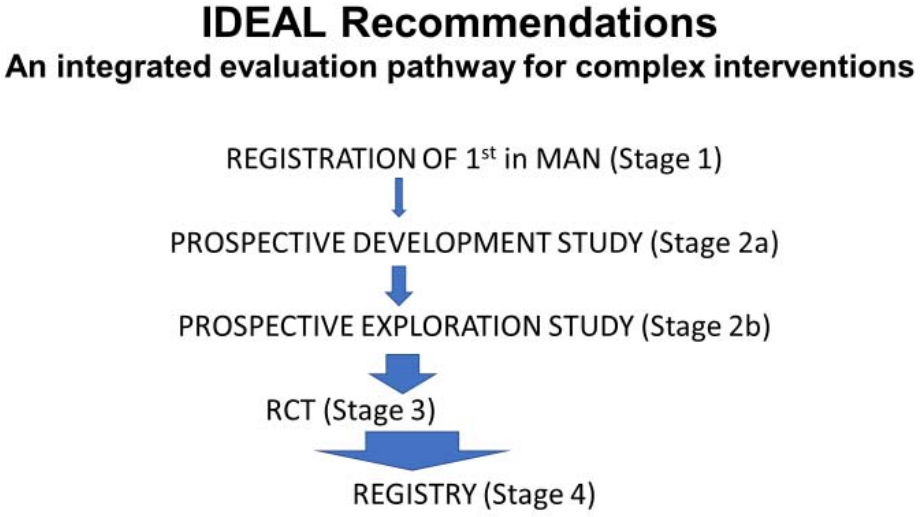
- Regulation for therapeutic devices is getting more stringent but regulators worldwide avoid providing specific advice on study design and reporting, for market access and surveillance.
- IDEAL provides guidance on appropriate methodology at each stage in the life cycle of therapeutic procedures and devices.
- IDEAL is well aligned with the principles of the new EU Medical Device Regulation, so suggesting IDEAL as a template could facilitate production of appropriate evidence compliant with the new regulation, for specific devices.
- Since IDEAL provides an integrated evaluation pathway, it could also prove useful in developing evidence for health technology assessment, commissioning and other purposes.

THE MEDICAL DEVICE REGULATION

The MDR was developed in the context of

What is IDEAL?

- An analysis of the life-cycle of complex therapeutic interventions including operations & devices
- An analysis of the evaluation needs at each stage in the life cycle
- An integrated evaluation pathway using study methods suited to the needs of each stage in the life cycle



Hirst, A., Philippou, Y., Blazeby, J., et al (2019). No Surgical Innovation Without Evaluation: Evolution and Further Development of the IDEAL Framework and Recommendations. *Annals of surgery*, *269*(2), 211–220. doi.org/10.1097/SLA.0000000000002794

The IDEAL Framework

IDEA (Stage 1)	DEVELOPMENT (2A)	EXPLORATION (2B)	ASSESSMENT (3)	LONG TERM STUDY (4)
Initial report	"Tinkering" (rapid iterative modification)	Technique now more stable	Gaining wide acceptance	Monitoring late and rare problems, changes in use & quality of surgical performance
Innovation may be planned, accidental or forced	Small experience from one centre	Replication by others	Considered as possible replacement for current treatment	
Focus on explanation and description	Focus on technical details and feasibility	Focus on adverse effects and potential benefits	Comparison against current best practice (RCT if possible)	
		Learning curves important		
		Definition and quality parameters developed		

SPECIFIC DIFFICULTIES IN EVALUATING COMPLEX INASIVE THERAPIES

1. Need for iterative **modification**
2. Need for **definition** of the treatment including variants
3. Variation in **delivery** quality
4. "**equipoise**" difficulties for the Clinician
5. "**equipoise**" difficulties for the Patient

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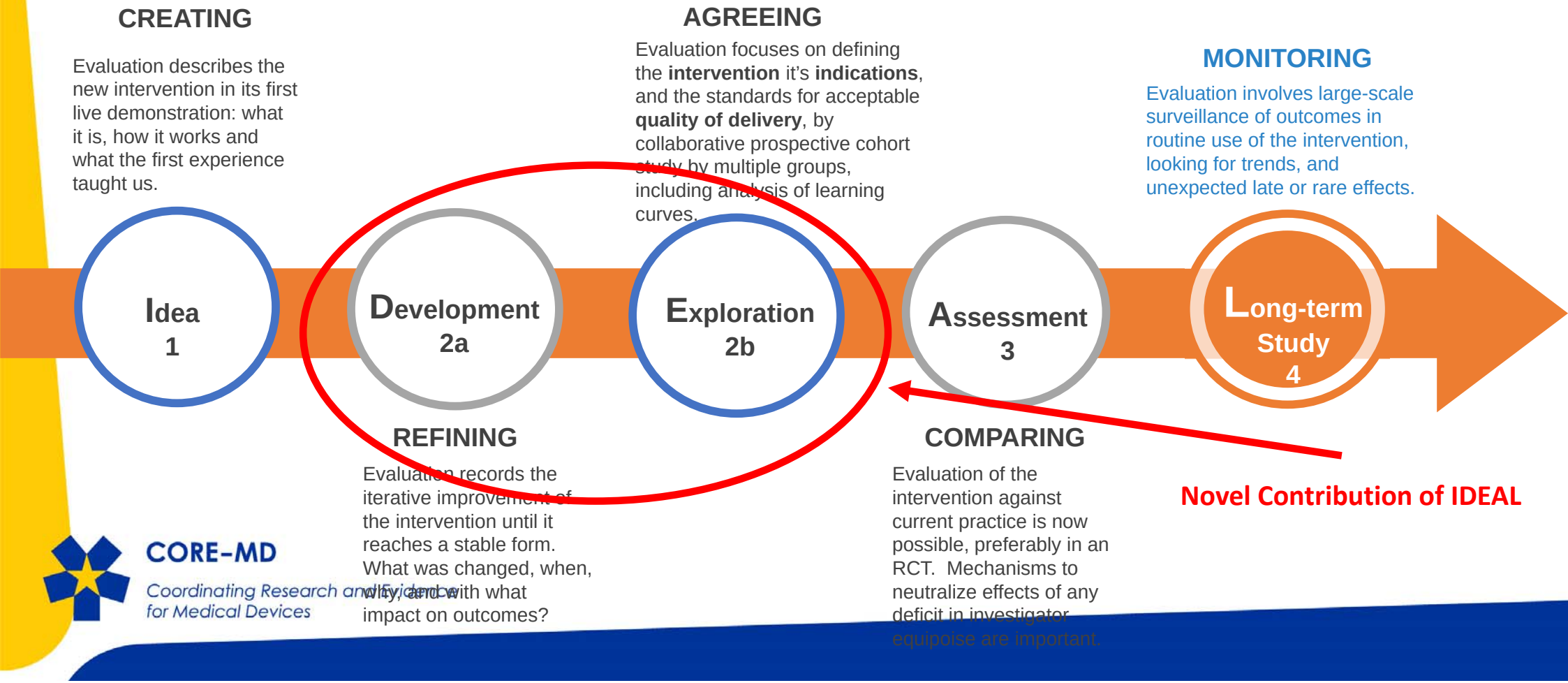
The IDEAL evaluation pathway

defines the types of evaluation which are appropriate at successive stages in the life cycle of complex interventions



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IDEAL Recommendations for Stages 2a and 2b

Stage 2a

- **Detailed technical description of procedure**
- **Detailed description of patient selection criteria**
- **Description of ALL modifications, when made in the series, and why**
- **Prospective account of ALL cases consecutively, showing results**

Stage 2b

- **To agree procedure *definition*, *quality* standards & *patient selection criteria***
- **To examine differential outcomes in pre-specified sub-groups**
- **To accumulate *data* for *power calculations***
- **To evaluate *learning curves***
- **To evaluate *preferences* and *values* amongst patients and clinicians**
- **To achieve consensus on future *trial question and comparator***
- **To develop a multi-centre randomised trial**

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Research Plan for Task 2.1 CORE-MD

- Engage with partners in CORE-MD (especially EFORT and European Cardiology Soc members)
- Seek additional partners though the IDEAL Advisory service (see www.IDEAL-net)
- Identify innovators conducting or preparing early clinical studies for regulatory approval
- Co-design IDEAL 2a and/or 2b format studies
- Evaluate value and barriers to implementation

STUDY DETAILS

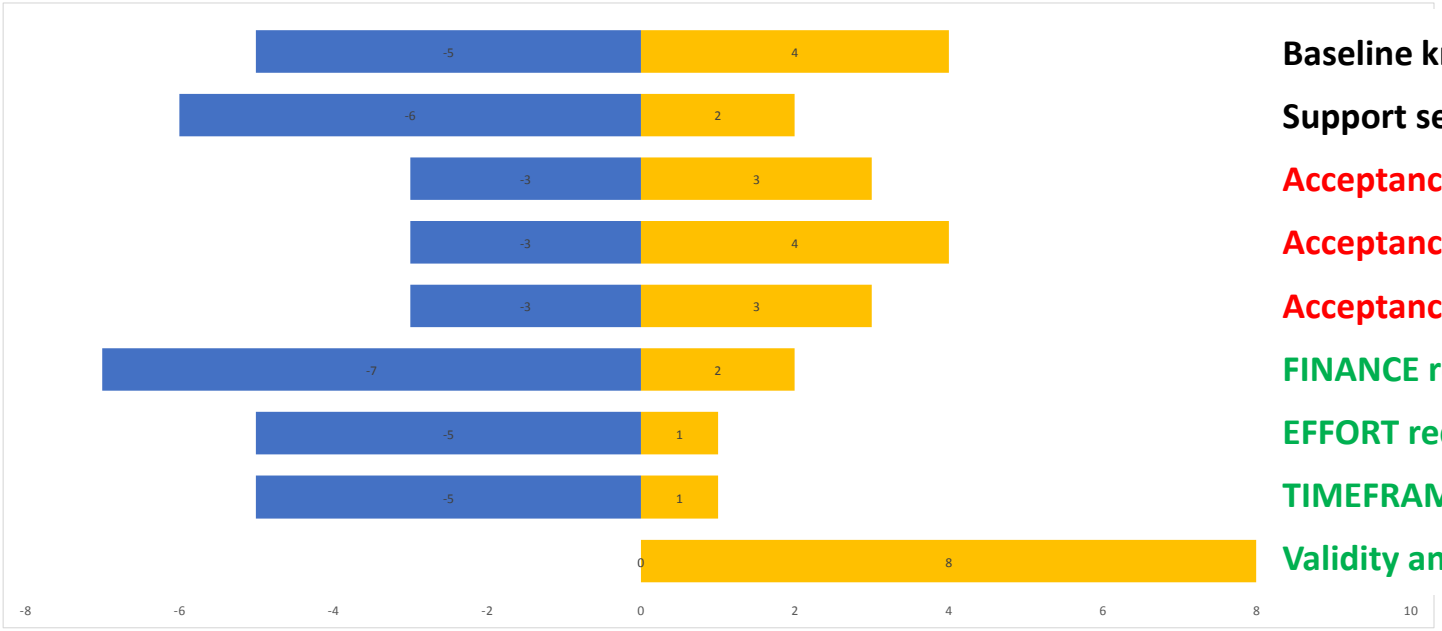
- Recruited 11 groups from CORE-MD and 9 from other sources
- All developing Class 2/3 devices for CE marking
- Interest in IDEAL format studies and approval of theory high
- Supported all groups in designing IDEAL format proposals for clinical evidence development
- Followed process of evidence development & outcome
- Explored user views and motivation in qualitative studies

Device
specialist robot for spine surgery
Neurosurgery image guided tumour resection system
Neurosurgery DB for sleep disorder
Dermatology laser for vulval LS
Liver trauma haemorrhage compression device
Colonoscopic device for polyp detection and resection
General purpose surgical robot
Distraction orthosis for thumb base OA
Intraoperative Neurosurgical AR Guidance Product
Versius robot for intraoral cancer surgery
Various knee surgery trials
Knee replacement prosthesis
Stem cell treatment for patello -femoral OA
Robotic knee surgery device
Range of AI related devices
Range of RWD studies of cardiac devices
Paediatric cardiology devices for valve and septal defects
Mitral valve and atrial appendage devices
Minimally invasive cardiac valve devices
Range of cardiac devices

Entities, Devices and Outcomes

	DEVICE TYPES	OUTCOME	
CORE – MD RECRUITMENT	11	1 0 11	Progressed
Cardiac	5	0 0 5	In process/partial
Orthopaedic	5	1 0 4	Not taken up
Other	1	0 0 1	
IDEAL Advisory RECRUITMENT	9	4 4 1	
Neurosurgery	4	2 2 0	
Robotic	2	0 2 0	
Other	3	2 0 1	

Factors affecting use of IDEAL: Questionnaire data



Baseline knowledge of IDEAL

Support services available

Acceptance by REGULATORS

Acceptance by JOURNAL EDITORS

Acceptance by FUNDERS

FINANCE required to complete study

EFFORT required to complete study

TIMEFRAME required to complete study

Validity and credibility of IDEAL

*Neutral responses removed

Emerging themes from interview studies

- High confidence in the validity and usability of IDEAL
- Little concern about difficulties in use but support and advice very helpful
- No concerns about effects on cost or delays due to use of IDEAL
- **Significant concerns expressed about uncertainty how IDEAL would be received by Notified Bodies and Regulators in the absence of any guidance**
- "Safety First" risk management strategy led to avoidance of novel methodology despite obvious potential benefits, because of lack of transparency about evidence expectations
- **Methodological innovation will not occur in the current system unless this barrier is removed**

Conclusion

- Current EU systems prevent any communication between innovator and NB about the design of clinical studies
- This is a strong inhibitor on innovation and improvement in clinical evidence development
- Ways of neutralising this barrier to predictability in assessment are urgently required

CORE-MD, Coordinating Research and Evidence for Medical Devices, aims to translate expert scientific and clinical evidence on study designs for evaluating high-risk medical devices into advice for EU regulators.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945260

For more information, visit: www.core-md.eu

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