



# The IDEAL template and specific opportunities

Peter McCulloch  
Chair, IDEAL Collaboration  
Professor of Surgical Science & Practice  
Oxford University



# WHAT IS IDEAL?

An integrated evaluation pathway

REGISTRATION OF 1<sup>st</sup> in MAN (Stage 1)



PROSPECTIVE DEVELOPMENT STUDY (Stage 2a)



PROSPECTIVE EXPLORATION STUDY (Stage 2b)



RCT (Stage 3)



REGISTRY (Stage 4)



## Why was IDEAL needed?

- 1990s: Evidence Based Medicine movement began to demand rigorous evaluation of therapies
- EBM doctrine: strongly focussed on the Randomised Controlled Trial (RCT)
- Surgeons criticised for their inability to comply
- This helped to expose the real difficulties of RCTs of complex interventions





## EBM and the Pharma Paradigm

### PHARMA PARADIGM

- Theory
  - Lab demonstration
  - (animal studies)
  - First-in-man study
  - Toxicity study (Phase I)
  - Efficacy Study (Phase II)
  - RCT (Phase III)
  - Post-Marketing Surveillance (Phase IV)
- Clinical Drug development follows a relatively simple pathway because:
- Modifications of the treatment other than dose adjustment are rare
  - Most modification is done in laboratory studies before patients become involved

# ANALYSIS: 5 REAL BARRIERS TO SURGICAL RCTs

1. Need for iterative adjustment and refinement of technique in clinical practice
2. Need for definition of technique which encompasses reasonable variation
3. Variation in delivery (need to evaluate learning curves, specify quality control)
4. “ equipoise ” difficulties for the Clinician
  - a. Intimately involved with the technique – unable to be objective
  - b. (?surgical personality – naturally decisive people find equipoise uncomfortable)
5. “ equipoise ” difficulties for the Patient
  - Decision to undergo surgery usually irreversible and risks may be grave
  - Relationship of trust with surgeon – tendency to accept expert view (even if not explicit)

# IDEAL Framework

A 5 stage description of the journey of surgical innovation

- Stage 1 - **I**DEA
- Stage 2a - **D**EVELOPMENT
- Stage 2b - **E**XPLORATION
- Stage 3 - **A**SSESSMENT
- Stage 4 – **L**ONG TERM MONITORING



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		



## Key Questions at each IDEAL Stage

Each stage is defined by one key issue:

STAGE 1: What is the new treatment concept?

STAGE 2a: Have we perfected it?

STAGE 2b: Can we agree on what it is and who should get it for the purposes of an RCT?

STAGE 3: Is it better than current practice? (RCT if possible)

STAGE 4: Are there any surprises?

# Implications of the Key Questions

- Studies at each stage should be designed to answer the key question
- IDEAL Recommendations describe study formats designed to do this

# The IDEAL Recommendations

- Idea (First in Man) 1.
  - Complete technical description
  - Explanation of patient selection
  - Registration of report
- Development 2a.
  - Prospective Cohort Study (PDS)
  - Transparent Consecutive Reporting of Cases
  - Explanation of Changes in Technique, Indication
- Exploration 2b.
  - Prospective collaborative cohort study (PES)
  - Evaluation of learning curves
  - Definition of QC parameters
  - Estimation of power calculations
  - Early joint analysis leading to RCT
  - Feasibility/Pilot RCT
- Assessment 3
  - Definitive RCT
  - Removal of investigator bias from recruitment
- Long Term Study 4
  - Registry to detect late/rare events
  - Monitoring of indication and performance creep



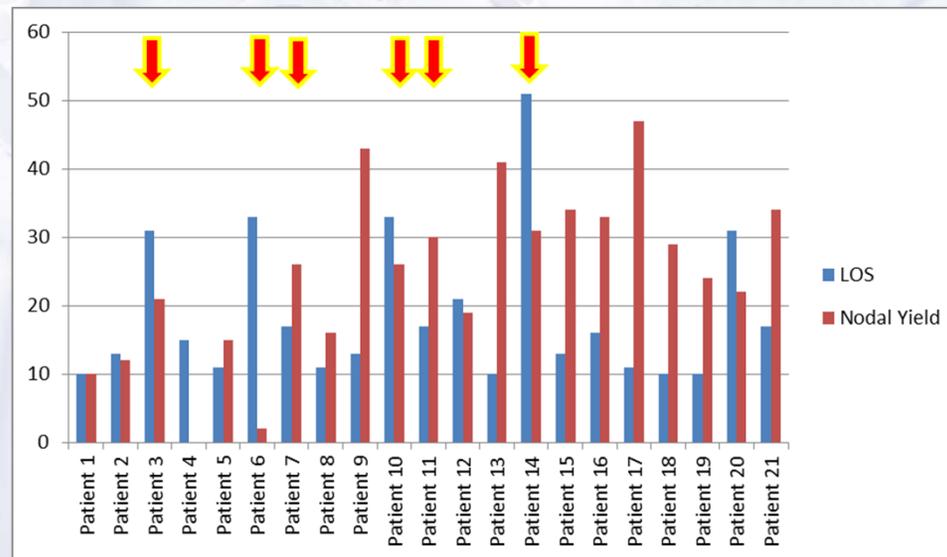
## Stage 2a: Prospective Development Studies

- **Key Specific Recommendations:**
  - 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**

# PDS Example: Development of Robotic Oesophagectomy

Arrows show 6 specific modifications to technique, described in the paper:

Modification 3 seems to improve nodal yield.



Diez del Val I, Loureiro C, McCulloch P. *Int J Surg.* 2015 Jul;19:104-11. doi: 10.1016/j.ijsu.2015.04.035.

# Why do Development studies?

- Techniques in DEVELOPMENT stage are not yet stable
- Reporting changes and their reasons allows others to learn faster and not repeat mistakes
- Therefore this approach is ethically superior to current practice
- Usually small numbers of cases, so will not slow development process or increase costs.



# Stage 2b: Prospective Exploration Study

## **Key Recommendations**

(collaborative prospective cohort study)

- To evaluate technique prospectively and co-operatively
- To agree procedure definition, quality standards & patient selection criteria
- 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

# PES example: HIFU for fibroids

Chen J, Li Y, Wang Z, McCulloch P, Hu L, Chen W, Liu G et al. Evaluation of HIFU Ablation for Uterine Fibroids: an IDEAL Prospective Exploration Study. BJOG. 2017 Apr 19. doi: 10.1111/1471-0528.14689.

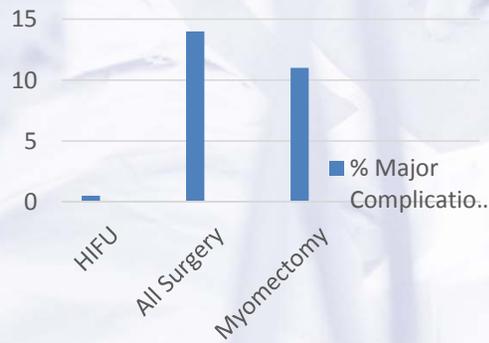
- Previous papers show progress of technology through stages 1 and 2a
- 20-centre prospective cohort offering surgery OR HIFU (patient choice)
- Tight definition of HIFU treatment
- learning curves measured
- Quality control assured
- Used results to plan RCT protocol

**Chongqing Haifu JC-200**



# HIFU Exploration study results

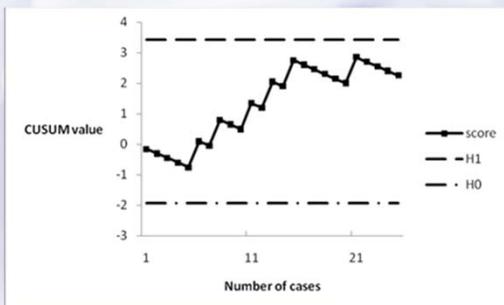
## Significant Complications



## Patients treated

- Hysterectomy 472
- Myomectomy 586
- HIFU 1353

	Hospital Stay (days)	Return to Work (days)
HIFU	3.63	4.07
Myomectomy	8.96	24.01
Hysterectomy	10.53	29.49



## Learning Curves analysed

These results don't scientifically prove the superiority of HIFU, but make it clear that an RCT using these outcomes could not be done, for lack of equipoise.

# Why do Exploration (2b) studies?

- Organising surgical RCTs is difficult: it requires TRUST and UNDERSTANDING between surgeons
- 2b studies improve trust and understanding by improving joint ownership and belief in data
- 2b studies allow questions which hold up agreement on RCTs to be answered, e.g.
  - Which variations of the procedure are acceptable?
  - Are some colleagues still learning?
  - Which patients are suitable?
  - How many patients will we need?
  - What questions are important to patients – and surgeons?
- In this way 2b studies should improve the FEASIBILITY of RCTs
- Sometimes 2b studies may alternatively show that an RCT is not feasible

## Is IDEAL just for surgeons?

- Development studies are appropriate wherever complex interventions require refinement in live settings
- AND
- Exploration studies are appropriate wherever both the intervention and the threshold for acceptable quality of delivery require definition to allow meaningful comparisons

# Where could IDEAL be useful?

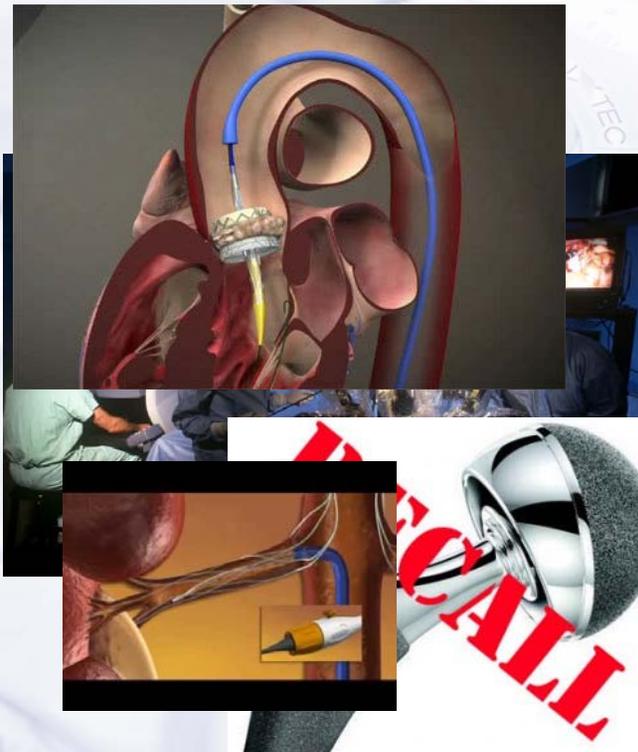
## QUASI-SURGICAL THERAPIES

- Endoscopic manoeuvres
- Radiologically guided manoeuvres
- Invasive therapeutic devices

## WIDER USES

- Physiotherapy
- Radiotherapy
- Psychological therapies
- Quality Improvement projects
- Complex public health interventions

# IDEAL for Devices: IDEAL (D)



## **DELPHI consensus process conclusions**

- Need a Stage 0 with minimum declared dataset
- Need a flexible approach to mixes of Development (2a) and Exploration (2b) stages
- Need Registries from an early stage, developing and changing with needs

**IDEAL-D: a rational framework for evaluating and regulating the use of medical devices**  
*BMJ* 2016; 353 doi: <http://dx.doi.org/10.1136/bmj.i2372> (Published 09 June 2016)

## How can IDEAL be useful?

- Research: Development (2a) and Exploration (2b) studies could prepare the way for RCTs of complex interventions better than current (heterogeneous) approaches
- Regulation: Clinical evidence requirements for regulatory approvals could be simplified by requiring Development or Exploratory study results (depending on risk)
- Purchasing & Commissioning: Evidence based purchasing decisions could be strengthened by agreeing to fund treatments with a limited evidence base only in the context of appropriate IDEAL studies which would increase this

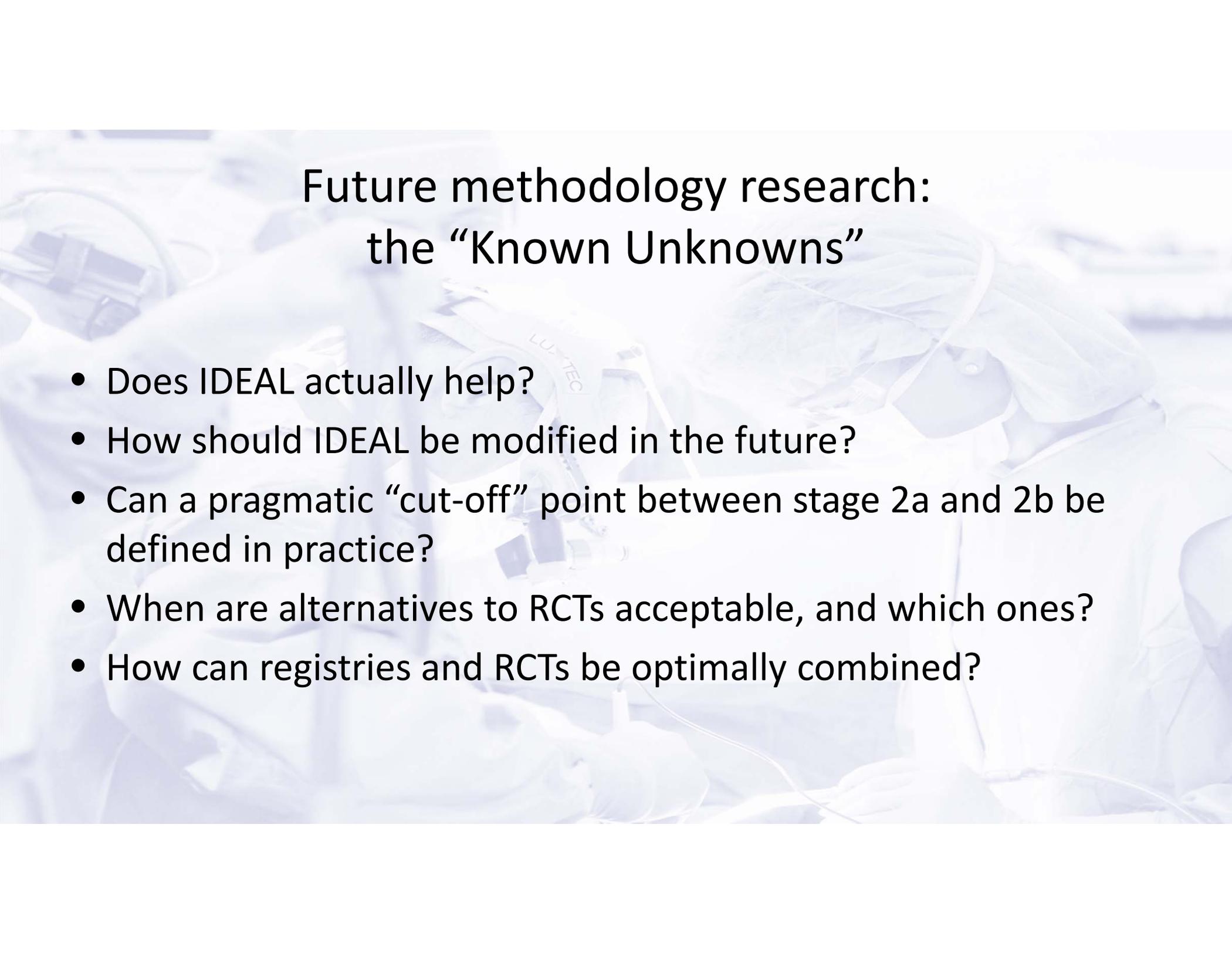


## Some current IDEAL Adoption in Rx evaluation

- EpiCOR programme in Canada (Martin J et al) using IDEAL to make purchasing decisions
- Radboud University Medical Centre, Nijmegen, Netherlands (Rovers et al) – using IDEAL to advise on Health Technology Assessment reports.
- EXCITE International – an new international body offering end-end expert 3<sup>rd</sup> party evaluation for therapeutic devices
- HTA Programme (NIHR) has issued calls for IDEAL 2b (Exploration) studies for:
  - Fenestrated aneurysm stenting
  - Pilonidal sinus
  - Surgery for Crohns' disease

# How to “weaponise” IDEAL

- **In treatment purchasing decisions:** The integrated nature of the IDEAL pathway allows graduated approval for use and for purchase – small Development study, then larger Exploration study then definitive RCT
- Payment only within confines of a study limits costs without slowing innovation, whilst providing evidence
- Established techniques already in practice could be challenged to produce convincing evidence or face disinvestment.
- **In research:** Development and Exploration studies are cheaper, MUCH faster and in many ways more appropriate than RCTs for early phase evaluations
- Bolting IDEAL 2a and 2b studies on appropriately at the “front end” of research programmes should increase their success in developing high quality RCTs of complex interventions, thereby reducing research waste.



## Future methodology research: the “Known Unknowns”

- Does IDEAL actually help?
- How should IDEAL be modified in the future?
- Can a pragmatic “cut-off” point between stage 2a and 2b be defined in practice?
- When are alternatives to RCTs acceptable, and which ones?
- How can registries and RCTs be optimally combined?