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P054

Agenda of the novel Special Interest Group for Medical Devices: Finding similarity within the diversity of Medical Devices

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eSIG Medical Devices

Introduction

There are **fundamental differences** in the scientific, clinical, and regulatory pathways for the development of medical devices compared to drugs and biologics.

Hence, the **Special Interest Group for Medical Devices (SIG MedDev)** was formed as part of the PSI and EFSPI organizations in December 2025 to study the implications of these differences for the application of statistical methods.

Join us to contribute to the identified **high-impact topics** with special relevance for medical devices !
https://www.psiweb.org/sigs-special-interest-groups/medical-devices-sig

Holistic health model of the patient

Medical device as a multi-domain intervention …

Anatomical	Physiological	Biochemical
Implants, prosthetics, bone fixation devices	Insulin pump, ventilator, pacemaker	Inhaler, dialysis filter, glucose monitor
Psychological	**Functioning**	**Social**
Neurofeedback, brain stimulation, biofeedback	Limb prosthetics, exoskeletons, mobility aids	Hearing aids, telehealth devices, communication aids

… With specific challenges

Device
Materials, mechanics, software

Procedure (clinician)
Technique and protocol

Mechanisms of action
Broad and multimodal, not chemical

User (patient)
Patient ability, operator skill

Performance
Depends on device, procedure and user

Medical device development
A multi-domain intervention

Clinical perspective
Intended use and context of use

Shapes the statistical design
The effect must disentangle device, procedure and operator interactions — not isolate a single molecule

Statistics

Clinical topics

Estimand Framework (ICH E9 R1, 2020)

Originally an addendum for drugs and biologics, but increasingly applied to medical devices.

Adoption for medical devices since ISO14155 (Mars 2026)

For devices, specifying the estimand is harder: intercurrent events, the comparator, and the operator all shape what the effect means

Applied well, it gives device trials a common language for aligning design, analysis, and interpretation

Intercurrent events (IE), comparator & standard of care (SoC)

Identification & definition especially challenging for medical devices

Example of IE
Mobile app: discharged battery
Assessed by likelihood & impact

Comparator arm
Drugs, devices or non-interventional
Wide range of competitors vs. drugs

Sham comparator
A group receiving a procedure/device appearing identical to the active one but containing no active processes or components

Study designs

RWE
Observational data from routine clinical practice & registries

RCT
Randomised controlled trial; may include sham comparator arm, predicates or SoC

No clinical study
Based on SOTA evidence (state-of-the-art bibliography) when sufficient prior evidence

Post-Market Clinical Follow-up
Registries, single-arm trials, trials with historical controls

Statistical modeling of endpoints

Heterogeneity of endpoints	anatomical, physiological, social, ...
Endpoint nature	mechanical, electronic, or functional performance vs. biological response
Distributional assumptions	non-normal, time-to-event, or measurement-error structures are common in device trials
Causal estimand	the treatment effect must account for the device, the procedure and the operator

Hybrid treatments

Combining medical devices with drugs or biologics

Examples
Drug-eluting stents, insulin pump + CGM

Challenge
Disentangling device vs. drug contribution

Statistical methods & emerging topics

Blinding
Often infeasible - implants, procedures, worn devices reveal allocation. Mitigated by sham comparators and blinded outcome assessors (single-blind).

Bayesian methods
Informative priors of particular interest for medical device studies

AI methods (e.g. LLMs)
Evaluated against emerging legislation (EU AI Act) - developments ongoing

Other challenges

Safety
e.g. late adverse device reactions due to material wear, sometimes only occurring after 10+ years

Device interactions
Imminent interactions between multiple medical devices per participant

Figure 1: Overview of Medical Device Categories

Regulatory

Regulatory framework: Pharma vs. Medical Device

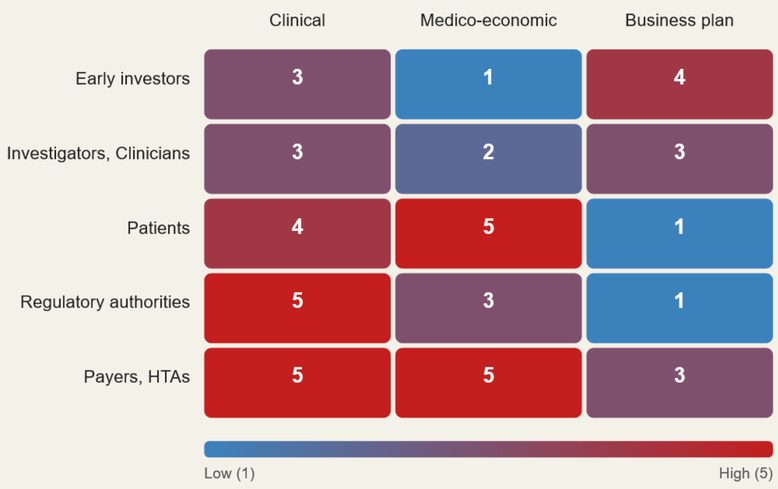
Topic	Drugs / Biologics	Medical devices
Regulatory framework*	• ICH guidelines (E6, E8, E9…) • GCP / GMP — CTD dossier • Uniform global framework EU, US, Japan, China, Asia-Pacific EU Clinical Trials Information System (CTIS)	• ISO13485 & 14155:2026 + CE MDR/IVDR (EU) • 510(k) / PMA / De Novo (US) • Fragmented across regions with some international framework such as MDSAP EU European Databank on Medical Devices (Eudamed)
Competent authorities	• EMA (EU), FDA CBER CDER (US), PMDA (JP) • National drug agencies • Centralised review FR ANSM	• Notified Bodies (EU) + country-authorities • FDA CDRH, CBER, CDER (US) • EMA when device & drug combination FR Notified Bodies + ANSM
Development stages*	• Long timelines (10–15 years) • Preclin. → Phase I → II → III → IV • Linear, frozen product	• Faster to market (2–10 years) • Feasibility → Prototype → Non-clinical Tests → Clinical Evaluation(s) → Certification • Potential biocompatibility • Potential versioning & software updates
Clinical evidence*	• RCT mandatory (Phase III) • Placebo-controlled standard • Large sample sizes required • Post-marketing studies (Phase IV)	• RCT, RWE or SOTA biblio. • Sham comparator or gold standard • Predicates comparator (US) • PMCF (EU, >Class I) • Vigilance & surveillance
Reimb. Agency assessment & HTA*	• Agency approval → HTA → pricing • Benefit/risk ratio central • EUNETHTA Joint Clinical Assessment FR Commission Transparence (HAS) SMR / ASMR evaluation	• Country-dependent, HTA → pricing • EUNETHTA for high-risk devices FR CNEDiMTS: ASSD/SSED Added clinical benefit evaluation
Reimburse-ment strategy*	• Standard reimbursement pathway • Pharmacoeconomic dossier required FR Early access: ATU/AAP Negotiated pricing (CEPS) Liste en Sus / MEA-RSA Remboursement Séc. Sociale	• Direct reimb. with SOTA biblio. (country-dependent) FR PECAN (Class I): anticipated reimb. LPPR / LPP: liste des produits Telesurveillance: dedicated pathway DMDIV: CNEDiMTS + CEPS Post-market FU replaces prior RCT
Market strategies*	• Marketing authorisation required • Phase IV post-approval studies • Regulators, payers, HCPs, patients	• Depend on country, business model, product & industrialization • Post-market FU • Regulators, payers, investors, patients
Challenges	• Long & costly approval process • Rigid protocol amendments • Harmonisation across regions • AI/ML & Bayesian adoption • EUNETHTA Joint Clinical Assessment	• Applying regs to AI, ML, evolving tech • High regulatory costs & admin. burden for small companies • Device class & potential versioning • Classification mismatch across regions • Post-market surveillance burden • EU AI Act compliance for SaMD

Key difference: regulatory pathway & market strategy

- Pharma: mandatory RCT → marketing authorisation → HTA → reimbursement. One fixed molecule. Harmonized across molecules.
- Med Dev: RCT not mandatory (SOTA/predicate) → direct reimbursement (PECAN, telesurveillance).
- There are too many differences between Med. devices to be fully harmonized (e.g. non-harmonized reimbursement in EU).
- Med Dev: marketing authorization could be approved by Notified Bodies (private) or auto-certified.
- When Med Dev = treatment: agency assessment → HTA pathway as for drugs applies (with same ICH & GCP requirements).

* : Med Dev class-dependent

Figure 2: Map of Evidence Requirement Levels



Case-study

AN AI RETINAL SCREENING TOOL CLEARED BY FDA — WITHOUT A SINGLE RANDOMISED CONTROLLED TRIAL

WHAT IS IDX-DR?

- AI software analysing retinal fundus photographs in primary care
- Binary output: diabetic retinopathy detected / negative
- Operable by non-specialist staff
- Designed to scale screening where eye specialists are scarce
- First autonomous AI diagnostic device authorised in the US (2018)

DRUGS / BIOLOGICS

Efficacy proven by a **pre-specified RCT**: fixed protocol, fixed population, fixed comparator. Evidence generated before approval, then product is frozen.

MEDICAL DEVICE / AI

Performance validated on a **real-world dataset** of 900 patients across 10 US primary care sites. Algorithm locked at submission; deployment performance monitored post-market.

- ✓ IDx-DR was authorised via De Novo pathway — not a traditional PMA.
- ✓ FDA reviewed analytical & clinical validation studies showing 87.2% sensitivity / 90.7% specificity against a grader reference standard.
- ✓ No drug-style Phase III trial was required or expected.

Iterative by design: Software updates require re-validation, not a new clinical trial — a notion absent in pharma

RWE replaces RCT as primary evidence: Site diversity, patient mix, and camera models all shape algorithmic performance — not just the molecule

Algorithm lock vs. drug batch release: In pharma, the molecule is stable; in AI devices, the "product" is the model weights — frozen at a commit hash

Key takeaway: Medical device regulation evaluates *performance in context* — how a tool behaves across sites, operators, and patient populations — not just whether an active ingredient works. AI amplifies this difference dramatically.

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