https://doi.org/10.1038/s41591-026-04232-w

Embedding equity in clinical research governance

Johanna M. C. Blom, Ciara Staunton, Sophie Tascedda, Neil Slabbert, Luca Pani & Melodie Labuschaigne

Inclusion by Design is a governance blueprint for auditable representation across trials and data infrastructures

Underrepresentation in clinical trials is not only an ethical concern, it is also a reproducibility and safety concern that propagates bias into evidence-based care and downstream clinical artificial intelligence (AI). We propose 'Inclusion by Design': a policy and governance approach that makes representation measurable, auditable and correctable within existing trial and data infrastructures. The EQUITRIAL framework we have developed operationalizes this approach with a ten-domain model of exclusion, across individual, contextual and cultural dimensions. EQUITRIAL adopts two lightweight indicators (representation ratio and intersectionality score) to embed inclusion as a measurable parameter, not an ethical aspiration. It also includes a practical inclusion plan template to translate EQUITRIAL into policy actions aligned with global regulations. This is key as regulators enter a unique policy window for action.

Global importance

Persistent underrepresentation across sex, age, pregnancy, disability, migration status and socioeconomic disadvantage continues to undermine external validity and weakens trust in biomedical innovation[1,2]. There is now an opportunity for change as several regulations are under review: the European Medicines Agency (EMA) is improving diversity expectations for trials, the European Health Data Space (EHDS) is setting the infrastructure for secondary data use and cross-border learning, and the European Union AI Act is codifying dataset representativeness and bias mitigation for high-risk systems used in healthcare[3–5].

Yet a familiar implementation gap remains: policy documents state that diversity is important, but trial teams still lack a shared, auditable way to plan, monitor and report inclusion. Inclusion by Design addresses this gap by treating representation as a design specification and a governance deliverable — comparable to quality management, safety monitoring and data integrity — rather than a retrospective narrative.

From ethical aspiration to operational equity

Research ethics has historically emphasized protection from harm. In a data-intensive era, exclusion creates a second structural harm: groups missing from trials become missing from evidence and are more likely to receive care based on extrapolation[6,7]. Operational equity reframes inclusion as a scientific parameter that can be assessed, audited and improved. Operational equity does not require that every study perfectly mirrors population demographics. Instead, it requires that deviations are visible, justified and actively managed. This shifts inclusion from 'best efforts' to accountable practice. In this framing, inclusion functions not as a moral aspiration but as a scientific quality parameter, comparable to reproducibility, risk management, and data integrity.

Table 1 | The EQUITRIAL ten-domain model of structural exclusion

Cultural level	Contextual level	Individual level
Race, ethnicity and indigeneity	Socioeconomic position	Demography and life stage
Migration and displacement	Legal and admin status	Disability and function
Language, culture and literacy	Geography and infrastructure	Gender and sexuality
		Disease and risk profile

The ten-domain model groups determinants of underrepresentation across individual, contextual and cultural levels. Each domain reflects a modifiable dimension. The domains are used to identify likely points of exclusion during trial design and delivery, and to structure a response through protocol choices, site strategy, participant support, and monitoring.

EQUITRIAL at a glance

EQUITRIAL is presented here as a governance and policy framework. It provides a structured way to anticipate where exclusion arises, to translate that assessment into protocol-level actions, and to enable routine oversight (Table 1). The framework is intentionally lightweight so it can be piloted within existing infrastructures and refined by therapeutic area[8].

Lightweight indicators to support planning and oversight

Two indicators within EQUITRIAL can support auditing of trial designs. The representation ratio compares planned (or achieved) enrollment proportions for key subgroups to an external benchmark such as disease burden or service utilization. The intersectionality score summarizes cumulative exclusion risk across domains to prompt tailored mitigation (for example, language support, transport, accessibility or documentation assistance).

Importantly, the representation ratio and intersectionality score are intended as governance indicators to support piloting and continuous improvement. Thresholds should be treated as illustrative starting points and refined through EMA-led learning cycles by therapeutic area.

The inclusion plan template

A practical inclusion plan translates intersectionality into protocol-level actions aligned with global regulatory expectations via stepwise operation. First, trial sponsors and investigators identify underrepresented groups for the target condition, including intersectional combinations likely to face access barriers. Then, they specify benchmarks for the representation ratio (for example, based on disease burden, registry data or service utilization) and document assumptions. Using the ten domains, teams anticipate barriers and assign mitigation actions across eligibility criteria, sites, support services and communications.

Table 2 | Policy alignment and operational leverage

Policy instrument	What it already requires/encourages	How Inclusion by Design can operationalize it
EU clinical trials regulation (EU no. 536/2014)	Protects participants and data integrity; requires justification of eligibility choices.	Add a structured inclusion plan annex and consistent documentation of deviations and mitigations.
EMA regulatory-science priorities or diversity guidance	Calls for inclusion of underrepresented groups and improved generalizability.	Provide an operational template (representation ratio or intersectionality score and plan) that can be recommended, piloted and scaled via guidance.
US FDA Diversity Action Plans	Requires prospective plans with enrollment goals and strategies.	Offer harmonizable indicators and monitoring fields suitable for multi-regional trials.
EHDS	Enables secondary use and cross-border learning through interoperable data governance.	Support equity metadata and dashboards that link trial inclusion to real-world denominators and learning cycles.
EU AI Act	Requires representativeness and bias mitigation for high-risk AI systems.	Improve upstream evidence and datasets; enable auditable equity monitoring in AI-enabled trial tools.
WHO resolution WHA 75.8	Promotes equitable participation and stronger trial capacity.	Provide a practical governance mechanism and common language to plan inclusion across contexts.

Finally, they set recruitment targets, phases for monitoring uptake, and predefined triggers for correcting shortfalls.

For the inclusion plan to deliver, governance must be clearly defined: this includes specifying who within the study team is accountable for monitoring inclusion metrics, the pathway for escalating concerns to ethics committees, sponsors or regulators, and commitments to transparency in reporting both successes and shortfalls.

Implementation levers: what can change now

Inclusion by Design is designed to work with existing regulatory and operational expectations. Key points of alignment and operational leverage across existing policy instruments are summarized in Table 2.

For clinical trial protocols, regulatory agencies such as the EMA and US Food and Drug Administration (FDA) should encourage sponsors to add an Inclusion Plan annex to trial protocol templates and submissions, to be reviewed alongside feasibility and risk management[9]. Trial sponsors would then use the representation ratio/intersectionality score fields as structured prompts for justification and mitigation, with ethics committees and regulators monitoring compliance during periodic reviews.

The Innovative Health Initiative (IHI), established by the European Commission to support collaborative research and innovation across the healthcare spectrum, brings together researchers, industry, healthcare users and regulatory agencies to co-design solutions addressing unmet health needs. IHI and Horizon Europe programs should adopt inclusion planning as a performance indicator with staged milestones and shared learning across funded consortia[3,10]. Program managers can use pilots to refine benchmarks and thresholds and to identify where additional support (budget, sites, community partners) is needed.

To enhance transparency, the EMA and national regulatory authorities should publish aggregate inclusion performance (representation ratio or intersectionality score summaries) by therapeutic area and geography through public, privacy-preserving dashboards, analogous to pharmacovigilance transparency initiatives. Data governance teams would ensure benchmarking across sponsors and regions while protecting individuals and small-group identifiability.

Digital infrastructures: equity as metadata

Digital transformation can either amplify inequity or help to correct it[11]. If the representation ratio or intersectionality score (or comparable structured fields) are treated as equity metadata within data registries and secondary-use datasets, inclusion oversight can move from retrospective reporting to near real-time monitoring. A pragmatic first step is to add standardized fields for planned and achieved representation (relative to a declared benchmark) and to require a short narrative of mitigation actions when gaps persist. When such gaps remain invisible at the trial stage, they are carried forward into secondary data use and increasingly into clinical AI systems, where they can be amplified rather than corrected.

The EHDS provides a natural testing ground for this approach: real-world denominators (disease burden or service utilization) can inform realistic benchmarks, and federated analytics can enable privacy-preserving dashboards[4]. In parallel, the AI Act creates a strong incentive to ensure that clinical datasets used to develop or validate high-risk AI tools are demonstrably representative and mitigate against bias[5].

Models that return participant data to them, including the European FACILITATE initiative, reinforce this infrastructure by strengthening reciprocity and transparency. When participants receive meaningful data back, and can see how their participation contributes to representation, they become stakeholders in a learning system — not merely data sources[12].

Trust and culture: inclusion fails without relationships

Operational tools are necessary but insufficient for inclusion. Trust in this context is not an individual disposition but an emergent property of systems in which governance, communication and participant experience are aligned over time. For communities that have experienced exclusion or harm, participation depends on perceived relevance, reciprocity and trust[13]. Inclusion by Design therefore includes a cultural dimension: responsibilities, roles and practices that make equity a lived part of trial delivery.

We propose strengthening trust-building capacity within multicenter studies through a dedicated trust liaison officer function. This could be implemented by expanding the mandate of existing patient liaison officers or community engagement coordinators rather than creating entirely new positions, thereby minimizing additional bureaucratic burden. The trust liaison officer would: (i) track inclusion commitments; (ii) document barriers encountered by specific groups; (iii) support two-way communication with communities; and (iv) ensure course corrections are implemented and reported. The aim is to embed accountability in people and processes, not only in documents.

Training and shared resources are also needed so that investigators and ethics committees can interpret inclusion plans consistently

and avoid stigmatizing or reductive use of demographic categories. The goal is procedural fairness: making the pathway into trials accessible, meaningful, and transparent.

Outlook: a practical agenda for the next 24 months

A feasible near-term agenda for EQUITRIAL is to issue joint regulator–funder recommendations that define what 'good' inclusion planning looks like and how deviations should be justified, and to pilot an inclusion plan template and a minimal set of equity metadata fields in selected EU-regulated trials through IHI and aligned sponsors. Regulatory agencies should publish aggregate inclusion dashboards through existing pharmacovigilance transparency portals, with clear governance to avoid small-group re-identification and to support constructive benchmarking. In addition, shared benchmark datasets for representation ratio by therapeutic area should be developed using EHDS-compatible real-world denominators, and trust-building functions (including expanded patient liaison roles) and participant-centric data return should be evaluated, especially for underserved communities.

We recognize concerns about bureaucratic burden in clinical trials, particularly in Europe. Our proposal aims to work within existing structures rather than adding parallel systems: the inclusion plan integrates into existing protocol annexes, the indicators leverage data already collected, and the trust liaison officer function can expand existing liaison roles. Some additional effort is unavoidable when embedding any new quality parameter, but the goal is to make inclusion measurable, improvable, and auditable within systems that already demand quality, transparency, and accountability. If Europe couples its regulatory ecosystem with its emerging health-data infrastructure, it can help harmonize global expectations and improve the trustworthiness of evidence for everyone[3,4,14,15].

Johanna M. C. Blom[1,2] ✉, Ciara Staunton[1,3], Sophie Tascedda[4,5], Neil Slabbert[6], Luca Pani[1,2,7] & Melodie Labuschaigne[8]

[1]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia (UNIMORE), Modena, Italy. [2]Center for Neuroscience and Neurotechnology, University of Modena and Reggio Emilia (UNIMORE), Modena, Italy. [3]School of Law, University of KwaZulu-Natal, Durban, South Africa. [4]Department of Biomedical Engineering, Faculty of Medicine, University Hospital Basel and University of Basel, Basel, Switzerland. [5]Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), University Hospital Basel and University of Basel, Basel, Switzerland. [6]Pepkor NexTech Group IT – Machine Learning Engineering, Stellenbosch, Western Cape, South Africa. [7]Department of Psychiatry and Behavioral Sciences, University of Miami, Miami, FL, USA. [8]Department of Jurisprudence, School of Law, University of South Africa, Pretoria, South Africa.
✉e-mail: joan.blom@unimore.it

Published online: 13 February 2026

References

1. Cherubini, A. et al. *Eur. Heart J.* **44**, 3201–3210 (2023).
2. Krumholz, H. M. et al. *BMJ* **380**, e0725 (2023).
3. EMA. *EMA Regulatory Science to 2025. Strategic Reflection* (2020).
4. EC. *Proposal for a Regulation on the European Health Data Space* (COM(2022) 197 final) (2022).
5. EU. *Artificial Intelligence Act* (Regulation (EU) 2024/1689) (2024).
6. CIOMS. *International Ethical Guidelines for Health-related Research Involving Humans* (2016).
7. Retzer, A. et al. *Nat. Med.* **29**, 3259–3267 (2023).
8. Bowleg, L. *Am. J. Public Health* **102**, 1267–1273 (2012).
9. EU. *Regulation (EU) no 536/2014 on Clinical Trials on Medicinal Products for Human Use* (2014).
10. MRCT Center. *Diversity, Equity, and Inclusion in Clinical Research Toolkit* v1.1. (2021).
11. Obermeyer, Z., Powers, B., Vogeli, C. & Mullainathan, S. *Science* **366**, 447–453 (2019).
12. FACILITATE Consortium. *White Paper on the Return of Individual Participant Data by Design* (2024).
13. Blom, J. M. C. et al. *Front. Pharmacol.* **16**, 1570899 (2025).
14. WHO. *WHA 75.8: Strengthening Clinical Trials to Provide High-quality Evidence on Health Interventions* (2022).
15. US FDA. *Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies* (2024).

Competing interests

The authors declare no competing interests.