All information regarding future IHI Call topics is indicative and subject to change. Final information about future IHI Calls will be communicated after approval by the IHI Governing Board.

Topic 2: Validated, predictive approaches for clinical development of innovative personalised health technologies

Expected outcomes

Actions under this topic must contribute to both of the following outcomes:

- Validated and more predictive approaches supporting the clinical development and regulatory/health technology assessment (HTA) of innovative and personalised health technologies[1] (including medicinal products, treatment modalities, medical devices and technologies, digital tools and artificial intelligence (AI)-based solutions, diagnostics or combinatorial approaches and their combinations and integrations) contributing to personalised healthcare implementation or, where relevant, public health preparedness for the benefit of relevant stakeholders (e.g. industry, innovators, regulators, and patients).
- Acceleration of clinical development through the uptake of these approaches into clinical and industrial settings for the benefit of relevant stakeholders (e.g. industry, innovators, regulators, and patients).

Scope

Despite rapid advances in biological science, data generation, digital technologies, and analytical methods, there remains a major gap in the ability to reliably prevent diseases, predict human health outcomes and translate these predictions into actionable, evidence-based decisions to support public health preparedness, clinical development, and personalised healthcare delivery. Many potentially useful human-relevant predictive approaches lack adequate validation, defined contexts of use, interoperability, real-world demonstration, and stakeholder acceptance. This limits their uptake in clinical research and development as well as in regulatory and HTA assessment.

This topic aims to support pre-competitive research and innovation to validate approaches (e.g. tools, methods and platforms) that improve the translatability and predictability of the clinical development process and regulatory and HTA decision-making regarding health technologies, including those relevant to disease prevention. Ultimately, this should lead to an enhancement of one or more of the following: preparedness, prevention, interception, diagnosis, treatment, management of non-communicable or infectious diseases, or enabling more efficient recovery. The applicants should define the intended users, contexts of use, and decisions that are supported and the resulting actions for each predictive approach developed. Additionally, applicants should formulate a clear validation framework, considering scientific validity, analytical and clinical performance, with particular attention to data quality, representativeness, and model drift aspects.

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[1] Regulation (EU) 2021/2282 of the European Parliament and of the Council of 15 December 2021 on health technology assessment and amending Directive 2011/24/EU, recital (1): 'Health technologies encompass medicinal products, medical devices, *in vitro* diagnostic medical devices and medical procedures, as well as measures for disease prevention, diagnosis or treatment'

To achieve this aim, applicants must assemble a collaborative public-private partnership consortium reflecting the integrative and cross-sectoral nature of IHI JU and achieve one or more of the below objectives:

- Developed and validated mechanistic modelling (including, for example, disease biology and patient heterogeneity), *in-silico* trials or digital twin simulations to support prediction (e.g. in pre-symptomatic individuals) and optimisation of the clinical development of personalised health technologies (including performance simulation of medical devices, imaging systems, diagnostics, implantable devices, and AI-enabled healthcare solutions). Where relevant, these approaches should be validated across diverse clinical settings and patient populations, to demonstrate that their predictions are reliable and transferable across clinical settings.

- Developed and validated interoperable toolkits, open platforms, and implementation frameworks supporting the readiness for translation, integration and scalable adoption of new scientific and medical knowledge and of innovative/improved health technologies into clinical workflows and routine practice. This may include the following areas: scientific techniques, computational models to predict patient response and variability (e.g. due to drug-drug, drug-gene, device-patient, implant-host interaction), companion diagnostics, diagnostic-guided treatment selection, imaging biomarker-guided patient stratification, image-guided interventions, AI-supported clinical decision-making and digital health interventions and tools, as well as medical countermeasures for infectious disease outbreaks related to climate change or vector movement. Where relevant, applicants should consider reusable and interoperable mechanisms for the characterisation of implementation barriers, user needs, engagement strategies and contextual factors supporting future adoption of personalised healthcare solutions across different care settings.

- Generated evidence for approaches supporting scientific, industrial and regulatory/HTA uptake. For example, generating robust validation data and methods, consensus standards for computational models, novel endpoints relevant to personalised healthcare, stratified populations and, if relevant, risk assessment (e.g. in case of drug-drug, drug-gene, device-device, device-patient, implant-host, or software-device interactions; cybersecurity and interoperability risks; diagnostic-guided treatment selection; image-guided interventions; AI-supported clinical decision-making; digital health interventions, remote monitoring technologies; digital biomarkers; companion diagnostics; automated image analysis; and AI-enabled medical devices).

- Developed and validated predictive and data-driven methods and tools to optimise the design, conduct and analysis of observational and interventional clinical studies, enabling the evaluation of the safety, clinical benefit and real-world impact (including gender and ethnic aspects) of innovative personalised healthcare technologies as well as their combinations and integrations across the care pathway.

- Developed and validated imaging-based, biomarker-based and integrated, multi-technology tools to improve the translatability and predictability of the clinical development of innovative health technologies for disease prevention, interception, diagnosis, progression monitoring and/or treatment choice, in real-world settings.

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These approaches should be enabled, as relevant, by the following methods that leverage multimodal data pertinent to personalised healthcare (e.g. clinical/biomedical, device-generated/digital health, patient-centred/behavioural, operational/contextual/systems data):

- Federated, privacy-preserving data integration for collaborative model development and validation, enabling the integration of large-scale heterogeneous data sources. Developed components should be interoperable, quality-controlled, reusable, standardised and maintainable beyond the action. Applicants should demonstrate access to the data required for development and validation and build on existing European infrastructures, registries, standards, and federated solutions wherever appropriate.

- AI and machine learning methods:
  1. to de-risk development of medical countermeasures;
  2. to predict disease prevalence, clinical outcomes, safety profiles, device performance, operational performance or disease progression;
  3. for patient stratification;
  4. for personalised intervention planning;
  5. for clinical decision support; and/or
  6. for workflow orchestration.

Where relevant, these methods should incorporate explainability, uncertainty quantifications, privacy-preserving approaches, quality control, standardisation, auditability, and appropriate human oversight to support trustworthy uptake in personalised healthcare settings.

Additionally, where relevant, applicants are expected to consider the potential regulatory and health economics impact of the results and develop a corresponding strategy and interaction plan for engagement with regulators and HTA bodies (e.g. EU national competent authorities and notified bodies for medical devices and *in-vitro* diagnostics, the European Medicines Agency (EMA), and HTA agencies) in a timely manner through existing opportunities for regulatory support services, such as the Innovation Task Force and qualification advice.

Where applicable (e.g. the approaches are intended for clinical or patient facing use), the applicants should consider their clinical utility, usability, explainability, and workflow fit, as well as any effects on professional and patient decision-making, including how insights from clinical, patient-generated or remotely collected data are translated into actionable monitoring, treatment or personalised support. Accordingly, patients, patient organisations and healthcare professionals should be actively involved in co-design and prospective validation.

Applicants are expected also to explore and/or implement synergies and complementarities with relevant initiatives/projects, at national, European and international level, thus avoiding unnecessary overlap, and duplication of efforts and funding.

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Expected impacts

Actions under this topic are expected to achieve the following impacts:

- improved validated predictive approaches for assessing the efficacy, performance, and safety of health technologies, supporting faster development and the adoption of personalised healthcare strategies for improved diagnosis, intervention selection and/or monitoring;
- reduced late-stage attrition in health technology R&D through improved prediction of clinical outcomes, safety, performance and patient response;
- strengthened regulatory confidence in innovative evidence sources (e.g. AI models, *in-silico* trials, biomarkers and real-world evidence), including their use in personalised healthcare contexts, leading to more efficient regulatory evaluations and the alignment of evidence generation with EU HTA needs;
- the consolidation of Europe's leadership in translational and regulatory science, contributing to the faster introduction of innovative, personalised healthcare solutions and improving global competitiveness of the EU healthcare sector;
- strengthening of the competitiveness of the EU's healthcare industry, via increased economic activity in the development of health technologies and solutions.

Actions funded under this topic are expected to consider and contribute to EU programmes, initiatives and policies on personalised medicine and prevention including the Safe Hearts Plan, Europe's Beating Cancer Plan, the European Health Data Space (EHDS) — Regulation (EU) 2025/327, the HTA Regulation (EU) 2021/2282, the 1+ Million Genomes initiative and linked projects (such as: Genomic Data Infrastructure, Genome of Europe) and different objectives listed under the European Commission's Strategy for European Life Sciences.

Why the expected outcomes can only be achieved by an IHI JU action

Science and technologies are changing rapidly, and their successful implementation requires increased cross-sectoral integration of technologies, know-how, products, services, and workflows for delivering people-centred, personalised healthcare. Laying the groundwork for the development of innovative tangible health solutions that are suitable for end-users requires expertise, resources, and knowledge from all stakeholders in the innovation value chain.
IHI JU provides a unique framework to stimulate a co-creation/co-ideation approach, bringing together the private (pharmaceutical and medical technology industry sectors) and public partners (academia, healthcare professionals and providers, patients and carers, regulators, health technology assessment bodies, payers) as well as small and medium-sized enterprises (SMEs), and charitable foundations / philanthropic organisations, with a view to ensuring that the solutions developed are comprehensive, evidence-based, and aligned with public health needs whilst offering new market opportunities to companies and improving their translational potential.

Indicative budget

Applicant consortia will be competing for the maximum financial contribution from IHI JU of up to EUR 37 831 000.

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IHI JU estimates that an IHI JU financial contribution in the range of EUR 12 000 000 to EUR 15 000 000 would allow a proposal to address these outcomes appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.

Applicant consortia must ensure that at least 45 % of the action's eligible costs and costs for the action-related additional activities are provided by in-kind contributions to operational activities ('IKOP'), financial contributions ('FC'), or in-kind contributions to additional activities ('IKAA'). While 45 % is the threshold for eligibility, applicant consortia are strongly advised to aim for 50 % to provide a margin e.g. for unforeseen changes during the project lifetime.
IKOP and FCs may be contributed by the constituent and affiliated entities of both the private members and the contributing partners. IKAA may be contributed by constituent and affiliated entities of the private members only. Contributing partners and their affiliated entities cannot contribute IKAA. See the call conditions in the annual Work Programme for further information (also in the document 'call text' published on the IHI website).

Indicative duration of the action

Applicants should propose a project duration that matches the project's activities and expected outcomes and impacts.

Dissemination and exploitation obligations

The specific obligations described in the conditions of the calls and call management rules under 'Specific conditions on availability, accessibility and affordability' do not apply.

Glossary

Acronym	Meaning
AI	Artificial Intelligence
EC	European Commission
EU	European Union
EMA	European Medicines Agency
EHDS	European Health Data Space
FC	Financial contribution
HTA	Health Technology Assessment
IHI JU	Innovative Health Initiative Joint Undertaking
IKAA	in-kind contributions to additional activities
IKOP	in-kind contributions to operational activities

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SMEs	Small & Medium-sized Entreprises
R&D	Research & Development

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