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AI-Guided Precision Medicine: A European Biotechnology Thematic Network Association Perspective on Multi-Omics, Digital Sensors, Medical Assessment, and Ethical-Regulatory Challenges

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Abstract

Artificial intelligence (AI) is increasingly integrated with genomics, multi-omics, pharmacogenomics, liquid biopsy, and digital biosensing, yet the data infrastructure, governance practices, and evidence standards remain uneven. This European Biotechnology Thematic Network Association (EBTNA) position paper includes peer-reviewed studies, regulatory reviews, and official policy surveys up to October 2026, to gauge clinical maturity and set out priorities for a responsible implementation across Europe. The review aims to identify critical gaps in governance and workforce readiness and then propose concrete lines of action. Across the World Health Organization (WHO) European Region, only 8% of Member States have a health-specific AI strategy, 24% provide in-service AI training for the health workforce, and fewer than 10% have drafted liability standards for AI in health. At the same time, the Food and Drug Administration (FDA) has authorized 903 AI-enabled medical devices as of August 2024, and 97.1% were cleared through the 510(k) pathway, for which clinical-data requirements depend on intended use and technological characteristics. Therefore, the EBTNA proposes seven lines of action whose responsible integration should link technical performance to clinical utility, equity, transparency, and continuous oversight. The European biomedical community should push for active governance to develop AI-driven precision medicine. This position paper explains the scientific rationale, provides the regulatory analysis, and lays out strategic proposals for transition.

Keywords: Artificial intelligence, precision medicine, multi-omics integration, digital sensors, health governance

Introduction

The convergence of artificial intelligence (AI) with precision medicine is expanding biomedical research and selected clinical applications, while implementation raises questions concerning evidence, infrastructure, workforce preparation, and governance. An assessment from the World Health Organization (WHO) of the European Region documented major gaps in national health AI-integrated strategies and liability frameworks.(1) Simultaneously, the US Food and Drug Administration (FDA) had authorized 903 AI-enabled medical devices, with most entering the market through the 510(k) pathway.(2,3) The European Biotechnology Thematic Network Association (EBTNA) Board provides a rationale that the European biomedical community needs to move beyond passive observation and toward active governance and co-creation of AI-guided precision medicine. The EBTNA position puts the patient, the clinical purpose and the value of the patient at the heart of responsible AI-guided precision medicine. The EBTNA advocates patient-centered AI-guided precision medicine in which technical innovation is evaluated against clinical benefit, safety, equity and accountable implementation. **Figure 1** depicts the position as a concentric, six-layer framework comprising the patient-state observation, the integration and inference through AI, the clinical assessment and action, evidence and translation, and lifecycle governance.

The outer governance ring refers to enabling factors at all stages of the process: coordination of regulation, privacy, equity evaluation, AI literacy of the workforce, independent oversight and accountability. Such factors should shape how data are collected, models are developed, validated, implemented in clinics and monitored. Participation of patients and the general public should be engaged in such processes.

Precision medicine, defined as the modification in prevention, diagnosis, and care based on each patient's own traits by integrating genetic, molecular, environmental, and lifestyle strategies, emerged as a conceptual framework in clinical settings across several disciplines. Personalized medicine is used where referring to terminology adopted by cited sources or programs, while "stratified medicine" refers to the categorization of patients according to shared attributes in relation to clinical management.(4–6) The European Union (EU) has already characterized precision medicine as a strategic priority within national programs, such as Genomic Medicine Sweden and Germany's Centers for Personalized Medicine (ZPM), which demonstrate the feasibility and clinical benefit of integrated molecular profiling.(7) The 2022 survey on personalized medicine policies across EU Member States reported that all 27 countries have taken at least some policy measures whose implementation remains inconsistent, with clear gaps in access to biomarker testing, genomic infrastructure, and reimbursement rules.(8,9) Developments in clinical AI have prompted discussion of licensing and oversight for autonomous applications.(10) Such proposals should be distinguished from comparative evidence of clinical performance. Meanwhile, clinicians did not end up beating large language models on any measured metric.(10) A network meta-analysis of 168 studies across 35,896 questions and 3,063 clinical cases found that ChatGPT-4o achieved the highest accuracy for objective medical questions (SUCRA = 0.9207), but retained superiority for top-1 diagnosis (SUCRA = 0.9001).(11) Further, a scoping review of 86 randomized controlled trials (RCTs) focused on AI in clinical practice reported that 81% of studies had positive primary endpoints, mostly tied to diagnostic yield or performance. Still, many studies were single-center and demographic details were limited, raising concerns about generalizability.(12)

The available survey evidence identifies variation in national AI strategies, workforce training, and governance arrangements across the WHO European Region.(1,13) Moreover, 24% of Member States provide in-service AI training for the health workforce, and 20% provide pre-service training. Patient associations are involved in AI governance in 42% of Member States, while the general public is engaged in 22%.(13) When

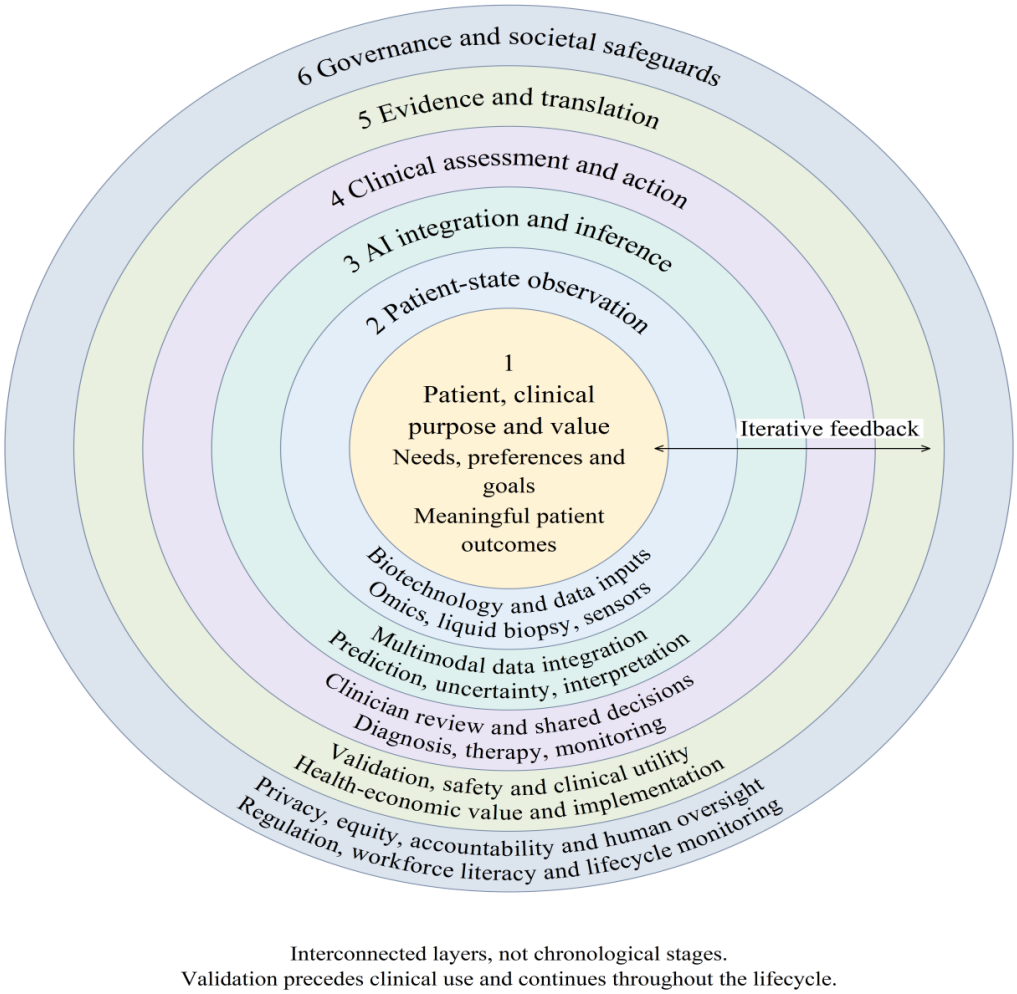


Figure 1. Concentric, patient-centered framework for responsible AI-guided precision medicine. The center identifies the patient, the clinical purpose and the intended patient value. Five rings around the center include patient-state observation and biotechnology/data inputs; AI integration and inference; clinical assessment and action; evidence and translation (validation, safety, clinical utility, and health-economic value) and governance and societal safeguarding. The bi-directional arrow symbolizes the iterative feedback across inner layers, while the outer ring of governance applies throughout the lifecycle. The ring order represents only the conceptual hierarchy, not necessarily the chronological one: appropriate validation must occur prior to the clinical application, and the evaluation occurs throughout the lifecycle. The patient value is an outcome to demonstrate – not a consequence of AI-enabled precision medicine.

asked about what blocks broader AI adoption the most, the top barriers were legal uncertainty (48%) and financial affordability (46%).(13) These findings are self-reported country-level indicators from the WHO European Region, which includes countries outside the EU. They should not be interpreted as a direct evaluation of EU legislation or evidence that governance is uniformly inadequate throughout Europe.

In this context, the EBTNA Board recommends coordinated participation by European scientific societies in the evaluation, implementation, and governance of AI-guided precision medicine. This review outlines the current dependence of clinical disciplines on AI and multi-omics technologies using quantitative data and highlights seven lines of action that require immediate attention. It also reviews the regulatory landscape by referencing specific legislative instruments and proposes clear guidance for the wider European scientific community.

Materials-Methods

Design. This position paper was developed as a structured narrative review with expert synthesis conducted by the EBTNA Board. This review was not a systematic review and did not use the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The source selection was purposive, to support an evidence-informed institutional position.

Thematic domains. The Board defined several thematic domains: (1) AI and precision medicine, (2) multi-omics integration, (3) pharmacogenomics, (4) liquid biopsy and ctDNA, (5) digital biosensing and remote monitoring, (6) federated learn-

ing, (7) regulation and governance, (8) European health-data implementation, (9) bias, equity and ethics, (10) workforce and education, (11) clinical trials and large language model evaluation, and (12) costs, health technology assessment and reimbursement.

Search strategy. A literature search was performed across multiple information sources, including PubMed, Scopus, Web of Science, and institutional repositories of European and international regulatory bodies covering publications or peer-reviewed research articles. The search strategy included an integration of several key terms related to AI, precision medicine, multi-omics, digital biosensing, liquid biopsy, data governance, regulatory frameworks, and more. Additional searches focused on WHO surveys, European Commission policy texts, FDA regulatory databases, statements from scientific societies, regulatory guidance from the European Medicines Agency and the national competent authorities were also conducted. The information was collected, arranged thematically, and critically appraised from the research articles that implement knowledge across molecular biology, clinical medicine, bioinformatics, bioethics, regulatory science, and health policy. This research was a narrative review rather than a systematic review; no formal risk of bias assessment, certainty grading, or a quantitative meta-analysis was undertaken, so the recommendations mainly reflect an evidence-informed institutional stance rather than a clinical practice guideline. We included peer-reviewed papers, systematic or scoping reviews, trials, legislation and regulation documents, if concerned the topic of AI-powered precision medicine, evidence for, governance of, or implementation of it in Europe or equivalent environments. In each theme area, we focused on the most recent, high-quality evidence, such as randomized trials, systematic reviews, official documents; and studies that reported quantitative results.

1. The Current Landscape: Evidence for AI and Omics Implementation

AI and omics technologies have expanding applications, although their clinical maturity and implementation vary by domain. As of August 2024, the FDA had authorized 903 AI-enabled medical devices, and annual authorizations increased substantially: it went from under 10 per year before 2015 to more than 220 per year by 2023.(2,3) Out of those, 76.6% were in radiology, 10.1% in cardiovascular medicine, and 3.2% in neurology. Also, 97.1% were cleared via the 510(k) pathway and only 2.4% through the de novo pathway.(3) A clinical performance study was reported for only 55.9% of these devices, while retrospective evaluations were the most frequently reported study design (38.2%), prospective studies made up just 8.1%, and randomized clinical trials were only 2.4%.(3) The FDA's first authorization for a partially AI-enabled medical device happened in 1995 (PAPNET for cervical cancer screening) and, after that, the agency has received hundreds of regulatory submissions for drugs that use AI during discovery and development, with a 10-fold jump from 2020 to 2021.(2)

In the European setting, AI-assisted diagnostics are most commonly reported for AI use with deployment in 64% of WHO European Region Member States, followed by conversational platforms or chatbots at 50%.(13) In oncology, molecular profiling via next-generation sequencing (NGS) is now shaping therapy choice for the majority of advanced solid tumors. The European Society for Medical Oncology Precision Oncology Working Group also noted that AI-based algorithms are improving, including accuracy or efficiency of tumor detection classification, molecular biomarker detection, and prediction of how patients will respond to treatment. However, no prognostic or predictive AI-based biomarker has achieved level IA or IB evidence.(14) In pathology, the integration of AI with multi-omics data is governing more accurate patient stratification and those precision treatment strategies.(14) For cardiovascular medicine, AI that works off wearable sensor data has shown it can outperform older, more traditional statistical methods for forecasting cardiovascular events.(15) Evidence on AI in Europe includes the MASAI Study, which was the randomized study conducted on 80,033 women undergoing mammographic screening in Sweden. It reported 44.3% lower burden on reading the screening results when AI is used, with false-positive rate 1.5% for both groups.(86) Those are the results from particular clinical implementation of screening program. Therefore they should be perceived as the results of workflow improvement and screening outcomes, rather than evidence of reduced mortality or general benefit across all clinical AI applications.

A global survey of over 3,700 researchers projected that AI will substantially influence diagnostic medicine within the next decade, with X-ray diagnosis, heart rhythm interpretation, and skin malignancy detection identified as the most mature domains.(16) A Delphi study assumed that machine learning might help widen diagnostic access for underserved groups and uncommon diseases.(17) These results back up active preparation, but they do not establish that technical performance translates into improved outcomes across clinical settings.

2. Integrated Biotechnology Domains

2.1. *Multi-Omics Integration*

The combination of several omics layers—genomics, transcriptomics, epigenomics, proteomics, metabolomics, and microbiomics— has broadened the ability to describe disease processes and support therapeutic choices from a systems-level perspective.(18–21) In parallel, AI and machine learning tools (from older statistical methods to deep learning methods, graph/network-based models and autoencoders) have become crucial for merging high-dimensional datasets with clinical traits and measured phenotypes.(18,22) More recently, progress in mass spectrometry-based multi-omics, single-cell omics and spatial omics has increased molecular reach and granularity enabling detection of clinically meaningful patterns in cancer, cardiovascular disease, metabolic disorders, and also in rare genetic conditions.(23–25)

The critical gap is infrastructural. The European Health Data Space (EHDS) is established by Regulation (EU) 2025/327, with

phased implementation of provisions concerning primary and secondary use of electronic health data, including Health Data Access Bodies and the HealthData@EU infrastructure.(26,92) An earlier analysis of the 2022 legislative proposal raised concerns about patient control, research access, and public value; these criticisms concern the proposal and should be distinguished from the subsequently adopted regulation.(27,92) Cross-border genomic data sharing faces particular challenges: a comparative analysis of data protection rules in Germany, Greece, Latvia, and Sweden documented striking divergences in member state implementations of the General Data Protection Regulation (GDPR) that directly impede European data sharing for precision medicine research.(28) The EHDS regulation must address these divergences while ensuring that its infrastructure is ready for effective and affordable processing of large volumes of genomic and other omics data.(29)

2.2. Pharmacogenomics

Pharmacogenomics is often described as one of the most clinically mature areas of precision medicine, but in practice, implementation remains uneven across clinical settings. The Clinical Pharmacogenetics Implementation Consortium (CPIC) has put together 28 active guideline sets covering 34 genes and 164 drugs that have gained significant importance among researchers.(30) Meanwhile, the CPIC API supports over 80,000 monthly queries and is being folded into electronic health records, including the Epic foundational genomics module.(30) The FDA also lists more than 600 drug–gene interactions with potential clinical impact, indicating that over 90% of humans carry at least one impactful variant somewhere in at least one key pharmacogenomics gene.(31)

Important implementation barriers remain. CPIC member surveys suggest a shift from concerns about scientific evidence quality, toward more day-to-day, operational obstacles. Clinician training, reimbursement, and EHR integration now appear to be the main issues.(30,32) In the European picture, the Scandinavian countries have shown that pharmacogenomic-guided prescribing can work, especially for medications metabolised by cytochrome P450 enzymes, and for drugs involving Solute Carrier Organic Anion Transporter Family Member (SLCO1B1) transport. But uptake across Europe is not uniform; implementation remain uneven.(33) Evidence remains limited for some clinical indications and underrepresented populations, and thresholds for implementation vary across applications.(31,32) EBTNA considers pharmacogenomics an example of the distinction between scientific evidence and implementation readiness: clinical translation requires coordinated education, reimbursement, regulation, and informatics support.(30,32,33)

Clinical implementation evidence available in Europe is provided by the PREPARE Study including 6,944 patients from 7 European countries. Among those who had an actionable result for the index drug there were 152 (out of 725) (21.0%) with clinically relevant adverse drug reactions in those who received genotype guided treatment and 231 (833) (27.7%; odds ratio 0.70, 95% confidence interval 0.54–0.91) in the controls.(85) Therefore it serves as an evidence of implementation feasibility of pharmacogenomics in different European healthcare environments. It provides evidence on genotype-guided prescribing, but not on the usefulness of AI algorithms.

2.3. Liquid Biopsy

Liquid biopsy methods, especially circulating tumor DNA (ctDNA), have shown real clinical use across the whole cancer care pathway: selecting therapy, spotting minimal residual disease, following how a treatment is going over time, and even multi-cancer early detection (MCED).(34,35) For example, the Galleri test, which aims to screen for more than 50 cancer types by finding particular methylation signatures in ctDNA, showed a specificity of 99.5% and an overall sensitivity of 51.5% in retrospective studies. In the PATHFINDER prospective validation trial, the positive predictive value was 38%, and the negative predictive value was 98.6%.(36) The FDA authorized Guardant Health's Shield blood test for colorectal cancer screening in average-risk adults aged 45 years or older, which was a regulatory milestone for ctDNA-based screening.(37) In addition, AI-driven multi-omic and fragmentomic analyses are pushing performance upward, improving sensitivity, specificity, and even predictions about tissue origin.(38,39)

Important validation gaps remain. Sensitivity in stage I disease is quite low—24% in the GRAIL symptomatic population report—and ctDNA detection in early-stage cancers is still tough because the analytes are rare, plus molecular heterogeneity complicates things.(36,40) There's also clonal hematopoiesis, which can act like a confounder and trigger false positives. If a 0.5% false-positive rate is carried into screening at the population scale, that could result in hundreds of thousands of people without cancer getting sent into prolonged, extensive evaluation.(41) So basically, that systematic review on blood-based ctDNA assays, for colorectal cancer screening in people without symptoms, sort of concluded that none of the reviewed assays showed enough sensitivity, for both advanced adenomas and early-stage CRC, to be something you can call a future screening tool. And it also says ctDNA screening hasn't really proven yet that it's better than fecal immunochemical testing.(42) There are prospective randomized trials underway that would demonstrate a mortality reduction, but they're not finished, and they are ongoing for any MCED test.(43) The EBTNA also points out that the potentially transformative power of liquid biopsy has to be paired with careful, prospective, population-based validation before it can be rolled out widely in regular clinical practice.

2.4. Digital Biosensing

Wearable and implantable digital biosensing technologies are generating continuous streams of physiological data that, when integrated with AI architectures, enable patient profiling, risk prediction, and closed-loop therapeutic systems.(44,45) The systematic review and meta-analysis of digital sensor alerting systems showed a mean reduction in length of stay in hospital

of 1.043 days, about 25 hours.(46) Findings regarding hospitalization and mortality differed based on the analytical method and cannot be generalized to all monitoring systems and patient populations. A large-scale implementation study of an FDA-cleared wireless monitoring device (BioButton) across 11,977 patient encounters demonstrated that 73% of clinical deteriorations had at least one notification within 24 hours prior, and hospital length of stay exhibited a decreasing trend from 3.07 to 2.75 days over 12 months.(47) The implementation study presented here describes notification performance and trend in length of stay, it does not establish that the device caused the reduction.

Yet the evidence base remains thin relative to the scale of deployment. A systematic review of FDA-approved digital medical devices for just-in-time interventions found that only 13.2% of product summaries included results of clinical studies assessing effectiveness, and only 26.3% allowed a full understanding of how the device operated.(48) The regulatory classification of these technologies under both the EU Medical Devices Regulation and the AI Act creates overlapping requirements that manufacturers and healthcare systems struggle to navigate.(49,50) Reimbursement remains a critical barrier: although CPT codes for remote patient monitoring exist, health insurance companies often require evidence of cost reduction before reimbursement, and drivers of inequitable access — heterogeneous coverage, provider bias, limited English proficiency — considerably restrict availability.(51) These coding and insurance examples concern the US healthcare system. European coverage and reimbursement depend on national arrangements and require country-specific assessment of clinical benefit, affordability, and equitable access. The EBTNA calls for the development of clinical validation pathways and reimbursement models that match the pace of technological innovation while ensuring equitable access.

3. Cross-Cutting Implementation Challenges

3.1. *The European Regulatory Interface*

Applicability of AI and medical device laws of Europe is based on the purpose and characteristics of the system. As per the AI Act Article 6(1), an AI system related to a regulated product will be regarded as a high-risk system if the criteria for the relevant product and safety component and the conformity assessment by a third party are satisfied. Not all AI systems which are used for healthcare purposes will be considered high risk. The analysis should follow the current consolidated AI Act and its phased application, including the 2026 amendments. (54,87,98) The Act defines an AI system as "a machine-based system designed to operate with varying levels of autonomy, that may exhibit adaptiveness after deployment and that, for explicit or implicit objectives, infers, from the input it receives, how to generate outputs such as predictions, content, recommendations, or decisions that can influence physical or virtual environments."(53)

The interaction between the AI Act and the Medical Devices Regulation/In Vitro Diagnostic Regulation creates specific regulatory challenges. Even medical devices in lower MDR/IVDR risk categories may be classified as high-risk under the AI Act, because the classification criteria and implications differ between the frameworks despite similar terminology.(49) An analysis of the use of AI software in radiology for prostate cancer provides an example of how the needs for documentation, performance assessment, oversight, and monitoring overlap with practical uncertainties regarding updates and the duties of health-care providers.(50) These differences should not be interpreted as a complete absence of oversight or safety obligations under medical-device legislation. AI Act Article 43(4) distinguishes predetermined changes in learning that are documented and assessed during the initial conformity assessment from changes that are considered substantial and require new assessment. Consequently, adaptive operation requires a change management approach.(87) EBTNA recommends version control, local performance monitoring, predefined escalation criteria, update testing, and roll-back procedure, combined with medical device surveillance.

The GDPR adds a further layer of complexity. A comparative analysis of data protection rules across four EU Member States documented striking divergences in the implementation of GDPR provisions relevant to health data sharing, with the destructive effect of these divergences depending on the legal qualification of the EU provisions they rely on.(28) In multi-country, multi-partner projects developing and validating medical AI systems, the regulatory landscape is characterized by complexity, evolution, and conflicting principles, particularly regarding data anonymization, cross-border data flows, and intellectual property.(55)

The article level mapping highlights complementary obligations. The AI Act Articles that are pertinent are those on risk management (Article 9), data governance (10), documentation and logging (11–12), transparency (13), human oversight (14), accuracy, robustness and cybersecurity (15), quality management (17), provider and deployer obligations (25–26) and post-market monitoring and incident reporting (72–73). (87) The MDR Articles 51–52 pertain to classification and conformity assessment, Article 61 to clinical evaluation and Articles 83–88 to surveillance and vigilance, with Annex VIII Rule 11 being particularly relevant for medical software. (88) With respect to the IVDR, Articles 47–48 deal with classification and conformity assessment, Article 56 and Annex XIII with performance evaluation and Articles 78–83 with surveillance and vigilance. (89)

For personal health data, the GDPR Articles 6 and 9 provide for a lawful basis and condition for processing of special category data. The pertinent Articles include those on information and access (13–15), data protection by design and controller–processor relationships (25–28), security (32) and data protection impact assessment (35) where required. Article 89 provides for specific measures in the context of research processing. (90) These requirements should be mapped separately from clinical consent and device conformity assessment.

An example of a liability issue could be the case of a prostate

imaging test where the test's accuracy drops after an update in a hospital population. Pertinent issues are whether the manufacturer tested the update properly, whether the hospital added an unauthorized update or did not react to monitoring indications, and whether the clinicians ignored any limitations. Responsibility will depend on the circumstances, causation, and product liability and national medical negligence laws, and will not be automatically assigned to the treating physician. Significant changes can also affect the obligations of the provider under Article 25 of the AI Act. The updated EU Product Liability Directive explicitly includes software, but its applicability is different from that of national clinical negligence laws.(87,91)

Member state differences are still important even under a unified GDPR framework. Comparison of the four member states shows differences concerning genetic and health data research. (28) In the case of an illustrative cross-border genomic study, all involved institutions should check all research grounds, national conditions, permissions, and controllership arrangements before access.(28,55,90)

The US regulatory approach offers a contrasting model. The FDA regulates AI-enabled medical devices through a risk-based total product life cycle approach, with three clearance pathways (De Novo, 510(k) clearance, and Premarket Approval pathways), and has articulated four areas of focus: fostering collaboration, promoting harmonized standards, advancing regulatory approaches supporting innovation, and supporting research on AI performance evaluation and monitoring.(2) The FDA co-leads an AI working group of the International Medical Device Regulators Forum to promote global harmonization.(2) The US evidence also identifies limitations in publicly accessible reporting of clinical performance and benefit–risk information for AI-enabled medical devices.(3,56)

Different sources of evidence need to be considered in respect to their remit. Reflection Paper on AI in the medicinal product lifecycle published by EMA should be distinguished from the general authority to authorize medical device software because EMA has no such authority.(93) EUDAMED provides with tools to identify devices and transparency of medical device regulation in Europe. Four out of its six modules will become obligatory as of 28th of May 2026 and entries in this register can neither be treated as evidence on clinical benefits nor as a comprehensive list of AI products used in Europe.(94) At the national level, the DiGA register provides with detailed information on assessed digital health applications, but it reflects only the category of applications, which receive reimbursement, but not all of the AI devices used in Europe.(95) Evidence on HTA can be further supplemented with the evidence standards framework provided by NICE, taking into account the UK setting and separation of market access and reimbursement.(96)

As a consequence the pathways for marketing authorization of AI in the EU and in the USA are different. In the EU devices fall under the scope of MDR or IVDR with the involvement of notified body and additional obligations of the AI Act, where required. Different pathways in the USA include 510(k), De Novo Classification, and premarket approval. (2,88,89) As far as planned updates of AI algorithms are concerned, FDA guidance describes predetermined change control plans, while Article 43(4) of the AI Act describes predetermined changes to be assessed during initial conformity assessment procedure. (87,97) Neither pathway can prove superiority of the product compared to other interventions nor its reimbursement, so it would be inaccurate to transfer authorization counts and publicly available proportions of randomized studies to the denominator from the European setting.

A comparative governance analysis across five jurisdictions (including the EU and US) found increasing convergence around core principles such as transparency, accountability, and human-centric AI, but significant divergence in regulatory maturity, enforcement mechanisms, reimbursement pathways, and implementation capabilities.(57) EBTNA recommends regulatory harmonization in Europe and alignment with international standards in order to minimize unnecessary duplication while retaining necessary requirements for patient safety and clinical validation. This regulatory burden falls disproportionately on small and medium-sized enterprises and start-ups, which typically lack the dedicated regulatory-affairs capacity that larger manufacturers can deploy to navigate overlapping AI Act, MDR, and IVDR requirements.(58)

Recommendations from EBTNA include harmonized guidance produced in collaboration between AI, medical devices and data protection authorities with clinical, legal, and patient input. Priorities are intended-purpose categorization, acceptable updating practices, common incident reporting, and allocation of responsibilities for both developers and healthcare providers. AI Act articles 57 to 59 provide for regulatory sandboxes, while articles 60-61 address real-world testing.(87) EBTNA calls for development of healthcare sandboxes that should be elaborated to include eligibility criteria, clinical oversight, rules on consent and protection of health data, independent monitoring, stopping criteria, and paths to report harm. Participation in sandboxes should not be treated as an exemption from medical devices, data protection, and liability requirements.

3.1.1. Western Balkan Implementation Priorities

Western Balkans offer an appropriate case to implement the EBTNA position. While recognizing the achievements in terms of personal-data-protection legislation, the EU Commission's assessment for Albania in 2025 identified needs for stronger implementation capacity and alignment with the EU AI Act. (59) Regional cooperation in this area is emerging: the Regional Cooperation Council and UNDP hosted the first meeting of the Western Balkans Six AI Working Group in May 2026 aimed at policy coordination and development of the regional AI roadmap.(60)

In the case of precision medicine, the EBTNA suggests the need to translate this development into specific procurement requirements in the field of healthcare, proper delineation of responsibilities, proper data governance, local validation and ongoing safety monitoring. Existing models should be evaluated

in their intended populations and settings, including analysis of calibration, subgroup performance and disparities in access. Regional collaboration should involve patients, clinicians, regulators and researchers, distinguishing the suggested measures from those required by the national legislation.

3.2. Algorithmic Bias, Health Equity, and Generalizability

The deployment of AI in healthcare introduces risks of amplifying existing health disparities through algorithmic bias — the tendency of AI models to reproduce or amplify pre-existing inequalities in training data.(61–63) The Agency for Healthcare Research and Quality and the National Institute for Minority Health and Health Disparities have articulated five guiding principles for mitigating algorithmic bias: (1) health equity as a fundamental objective, (2) transparency and explainability, (3) authentic community engagement, (4) explicit identification of fairness trade-offs, and (5) accountability for equitable outcomes.(62)

The evidence base for these concerns is substantial. A JAMA Network Open analysis of 903 FDA-authorized AI-enabled medical devices found that publicly reported clinical performance studies were found for 505 of 903 devices (55.9%). Of these 505 devices, 193 (38.2%) had retrospective studies, 41 (8.1%) prospective studies, and 12 (2.4%) randomized studies. So, publicly reported randomized evidence concerned 12 of all 903 devices (1.3%), not 2.4% of the whole population of devices.(3) Lack of public report of study does not mean lack of all clinical data submitted to regulator. The New England Journal of Medicine (NEJM) perspective argued that biased data should be considered informative artifacts rather than simply noise to be eliminated, and that understanding the social and structural processes that generate biased data is essential for developing AI systems that do not perpetuate inequities.(63) Europe faces particular challenges: the diversity of populations, languages, healthcare systems, and data collection practices creates unique risks that AI models trained in one context may systematically disadvantage populations in another. The EBTNA insists that algorithmic fairness must be a design principle embedded from the earliest stages of AI system development, validated across diverse European populations, and subject to independent, ongoing audit.

3.2.1. Patient Autonomy and Ethical Accountability

Ethical implementation requires protection of patient autonomy, human supervision and accountability besides technical performance. As part of its recommendations, the EBTNA emphasizes that clear communication regarding the role and limitations of AI, informed consent and lawful use of data, and mechanisms for questioning of AI-informed decisions and subsequent clinical consultation should be ensured. Responsibilities for supervision, incident reporting and remedial actions must be specified among developers, health institutions and clinicians. Active engagement of patients and the public is needed in determining acceptable applications, prioritizing outcomes and assessing the equitable benefits.(52, 64)

It is worth mentioning that clinical consent and legal basis for processing health data are two different requirements. GDPR article 22 refers to decisions made solely based on automated processing and producing legal or similarly significant effects. The latter is not applied automatically to all the clinical decisions made with assistance of AI. Recommendations from EBTNA imply explanation of the system used and its limitations, identification of the clinician who makes the decision, documentation of clinical overrides, and a possibility for a person to have his/her case re-evaluated by human.(90)

3.3. Federated Learning as a European Strategic Asset

Federated learning (FL) allows collaborative model training without disclosing the underlying data set; effective privacy protection, however, presupposes the correct governance and appropriate measures for security and confidentiality.(65–67) The clinical evidence supporting FL is still growing, and becoming more solid. For example, the EMR CXR AI Model (EXAM) model, trained across 20 institutions worldwide with FL, reportedly reached an Area under the curve (AUC) higher than 0.92 for forecasting oxygen needs in COVID-19 patients at 24 and 72 hours. It also showed an approximately 16% increase in average AUC, and a 38% gain in generalizability compared to single-site models.(68) A multicenter study in 21 hospitals in Brazil demonstrated improvement relative to locally trained model in some institutions with data limitation. In the smallest hospital (n = 86) the federated random forest training showed the difference in AUC of +0.3682 compared with local training (95% confidence interval 0.0908-0.6307), not an absolute AUC of 0.3682.(69) The benefit was different for each hospital. This result shows the potential for improvement in predictive performance when there is local data limitation, but does not show the improvement in patient outcomes or health equity. And in neurosurgery, a collaboration across five departments in the US found that FL reached an AUC of 0.9487 for intracranial hemorrhage detection, hitting 99% of the centralized model's quality. Even more, it kept landing in the top three performance consistently, no matter which site's data you used for validation.(70,71)

Recent advances include the integration of differential privacy, homomorphic encryption, and blockchain-based verification. The Health-FedNet framework achieved 92% accuracy and AUC-ROC of 0.94 for chronic disease prediction on MIMIC-III data, with a 20% to 5% reduction in membership inference risk and a 41.6% decrease in communication overhead compared to baseline federated approaches.(72) The FLAME platform, developed within the German PrivateAIM project, has demonstrated the feasibility of conducting federated analyses on clinical and genomic data across university hospitals with fine-grained access control and minimal computational overhead.(73) However, a scoping review of FL applications on structured medical data found that existing applications lack sufficient evaluations of clinically meaningful benefits compared to single-site analyses, and only 14 of 34 included studies discussed comparisons between local and federated models.

(74) The EBTNA views FL as a foundational infrastructure for European precision medicine research and calls for its prioritization in EU funding programs, with rigorous evaluation of clinical benefit. The scaling of FL infrastructure exhibits environmental costs, given that distributed model training and large-scale AI processing required substantial power. Infrastructure considerations must then take into consideration the issues not only of finances but also of energy consumption and its environmental consequences along with privacy concerns and medical importance of the expected results.(75)

3.4. Workforce Preparation: Evidence and Implementation Needs

The WHO survey identifies gaps and variation in workforce preparation across responding countries in the WHO European Region. Only 12 of 50 European Member States (24%) offer in-service AI training for the health workforce, and only 10 (20%) offer pre-service training.(13) A Flanders-based study found that only 13.8% of clinicians felt their training adequately prepared them for AI integration, while 85% expressed interest in introductory AI courses tailored to healthcare; nurses and physiotherapists showed the lowest AI familiarity, despite their pivotal role in AI-enabled workflows.(76) A mapping review of digital public health training across five European countries identified 367 training initiatives, but conference sessions (54.5%) and webinars (22.3%) predominated, while structured courses (18.3%) and degree programs (3.3%) were rare; scientific associations delivered 69.5% of initiatives, with academic institutions accounting for less than one-third.(77)

Scientific societies have begun to respond, but unevenly. The American Medical Informatics Association published AI principles emphasizing transparency, accountability, and equity(78), while the Society of General Internal Medicine issued recommendations for clinicians, technologists, and healthcare organizations on generative AI use.(79) The American Academy of Otolaryngology published an AI report addressing clinical applications and governance.(80) In Europe, the landscape remains fragmented. The EBTNA Board recommends coordinated investment in workforce preparation so that clinicians can critically evaluate AI tools, supervise their use, and contribute to assessment of safety and clinical utility. **Table 1** consolidates the quantitative signals supporting the EBTNA priorities.

3.5. Financial Requirements and Implementation Costs

Initial costs include computing infrastructure, secure data storage, interoperability and harmonization of the data, integration with clinical information systems, local validation, cybersecurity measures, regulatory documentation and training of the workforce. Recurrent expenses include software licenses, maintenance of the model and updates, security auditing and incident management, technical support and training of the workforce. Additional expenses could appear from the necessity to conduct confirmatory studies, false-positives and increase in workload.

Evidence does not support the existence of Europe wide estimates of the implementation costs of AI and therefore bottom-up costing is recommended for particular intended purpose application. It should include the measurements of the locally available resource needs and cost calculation. Pilot and scale up scenarios should report initial expenditures, annual operational costs and costs per patient or per one clinical episode of care. Sensitivity analysis should consider patient flow, staffing, infrastructure and frequency of the model updates.

Economic analysis should differentiate between cost-effectiveness and affordability/budget impact and should consider AI-supported full care pathway compared to usual care.

3.6. Role of Universities and Higher Education Institutions

An interdisciplinary curriculum combining knowledge of clinical medicine, genomics, statistics, computer sciences, ethics, law and health economics in universities and other institutions of higher education can provide with means for successful implementation of AI in clinical practice. Undergraduate and postgraduate programs should address issues like quality of data, model evaluation, uncertainty, algorithmic bias and distinction between performance metrics of models and clinical benefit from the use of AI. Continuing professional development should provide role-specific training for clinicians, laboratory professionals, nurses, and health-system managers, with competence assessed through practical clinical tasks rather than attendance alone.(30,76,77)

Clinical-academic partnerships can provide settings for independent external validation, prospective evaluation, and assessment of clinical utility and cost-effectiveness. Universities can also contribute expertise in data governance, cybersecurity, research ethics, and regulatory interpretation. EBTNA recommends collaboration among universities, healthcare providers, patient organizations, industry, and policymakers, supported by protected teaching time, shared research infrastructure, and transparent management of conflicts of interest. These contributions should connect workforce development with the evidence and governance required for sustainable implementation.

4. EBTNA Position and Lines of Direction

As illustrated in **Figure 1**, the evidence considered above lends weight to the EBTNA position and gives rise to seven strategic directions. This agenda links patient needs and intended clinical benefits with biotechnological inputs, inferences enabled by artificial intelligence, clinical action, evidential and governance translation across the lifecycle.

The seven strategic directions outlined above represent goals for institutions. Their implementation will be based on assessment of capacity, need, feasibility, availability of resources, and consensus among stakeholders. Suggested actors and indicators are provided in **Table 2**; they are not funded commitments. Expansion goals numerically should not be set until the European baselines and needs have been assessed.

EBTNA's institutional position is that European scientific so-

Table 1. Quantitative evidence underpinning the EBTNA position with their associated priorities.

Domain	Quantitative evidence from the reviewed literature	Interpretation and EBTNA priority
AI-enabled medical devices	903 FDA-authorized devices by August 2024; 97.1% used 510(k). Public clinical performance studies were reported for 505/903 devices (55.9%). Among those 505 devices, 41 (8.1%) had prospective studies and 12 (2.4%) randomized studies; the latter represent 1.3% of all 903 devices.(2,3)	Public clinical reporting was limited; prioritize application-appropriate prospective comparative evaluation and ongoing monitoring
European governance	Among 50 responding countries in the WHO European Region, 4 (8%) reported a health-specific AI strategy, 24% in-service training, and 20% pre-service training; 48% reported legal uncertainty as a barrier.(1,13)	Coordinate strategy, liability guidance and workforce preparation across Member States
Multi-omics integration	All 27 EU countries exhibit some activity of personalized medicine policy, but access to biomarkers and genomic infrastructure remains uneven.(8,9)	Harmonize data standards, access mechanisms and cross-border governance through the EHDS
Pharmacogenomics	28 CPIC guidelines cover 34 genes and 164 drugs.(30)	Embed decision support in electronic records and align education, reimbursement and evidence thresholds
Liquid biopsy	Performance varies by assay, disease stage, intended use, and study population. Retrospective and prospective estimates should be interpreted separately. (35,36,40,42)	Do not equate analytical performance with population benefit; prioritize prospective trials and mortality outcomes.
Digital biosensing	Meta-analysis: mean reduction in length of stay of 1.043 days. BioButton observational study: 11,977 encounters; 73% of deteriorations had a notification within the preceding 24 hours.(46,47)	Standardize validation, transparency, reimbursement evidence and equitable access.
Federated learning	EXAM involved 20 institutions and reported AUC > 0.92 for specified oxygen-requirement predictions. The Brazilian study reported ΔAUC +0.3682 relative to local random forest training at the smallest hospital, rather than an absolute AUC of 0.3682.(68,69)	Scale privacy-preserving infrastructure to enable comparison with local and centralized models.
Workforce readiness	In the Flanders survey, 13.8% considered their training adequate for AI integration and 85% expressed interest in introductory training. Degree programs represented 3.3% of 367 mapped initiatives across five countries. (76,77)	Develop accredited, role-specific and continuously updated AI-literacy. Develop accredited, role-specific and continuously updated AI-literacy programs.

AI: Artificial intelligence; AUC: Area under the curve; CPIC: Clinical Pharmacogenetics Implementation Consortium; EHDS: European Health Data Space; PPV: Positive predictive value; ΔAUC: difference in area under the curve between federated and local models.

cieties should be involved actively in the process of evaluation and governance of AI-guided precision medicine. Evidence from the literature suggests that the readiness for certain applications can be ensured, yet the pace and scope of application depend on clinical utility, safety, costs, public acceptance, and regulation compliance. The recommendations below express an institutional interpretation of these implementation needs rather than evidence of an inevitable or universal transition.

4.1. European multi-omics harmonization

The EBTNA recommends a European Multi-Omics Data Harmonization Initiative, building on the EHDS framework, to support consensus standards for multi-omics data collection, curation, and sharing. The idea is that these standards should be compatible with the GDPR, the AI Act, and the MDR/IVDR, prioritize interoperability across Member States, and include principles of safeguarding public value when publicly funded data contributes to commercially patentable AI assets.(26–29)

4.2. Regulatory-interface guidance

The EBTNA calls for the urgent development of harmonized regulatory guidance, meant to clarify the interplay between the AI Act (Regulation (EU) 2024/1689), the MDR (Regulation (EU) 2017/745), the IVDR (Regulation (EU) 2017/746), and the GDPR (Regulation (EU) 2016/679). Particular attention should go to how self-learning AI systems are classified, what post-market surveillance requires, and how regulatory sandboxes for controlled innovation will be established.(49,50,81) The EBTNA further calls for explicit guidance on the allocation of legal liability across the physician, software developer, and data-harmonizing institution within the human-in-the-loop decision chain – an area where fewer than 10% of Member States currently have drafted standards – to prevent responsibility gaps as systems adapt post-deployment.(1,13)

4.3. Pan-European AI literacy

The EBTNA proposes developing pan-European continuing professional development programs focused on AI literacy for healthcare professionals, working together with other European scientific societies. These programs should foster development of AI literacy according to the article 4 of the amended AI Act, while it should provide with necessary skills to use this technology safely. The educational program proposed by EBTNA should not be considered a legal requirement that will ensure the same level of skills for all users.(13,76,77,98)

4.4. Lifecycle equity assurance

The EBTNA endorses lifecycle-based frameworks for algorithmic fairness and calls for mandatory bias auditing, equity impact assessments, and diverse stakeholder engagement, including patient and citizen representation, in the development and deployment of all healthcare AI systems across Europe, consistent with the AHRQ/NIMHD guiding principles.(62) Current omics datasets and clinical AI models are concentrated in Western/Northern European and high-resource academic centers; fairness auditing and infrastructure scaling should explicitly target Eastern, Southern European, and low-resource institutions.(82) Such collaboration should involve Western Balkan partners by way of collaborative validation, training of the workforce and engagement of patients, with evaluation of performance and access across the participating health systems.

4.5. Federated learning infrastructure

The EBTNA recommends the scaling of federated learning infrastructures across European research networks, supported by standardized governance frameworks and sustained public funding, building on demonstrated successes such as the EXAM model (AUC > 0.92 across 20 institutions) and the FLAME platform.(68,73) Expansion should occur after an inventory and feasibility assessment of the current European network including participating institutions, governance, infrastructure, validation locally, and recurrent funding. Timing and scope of expansion should be determined by that assessment.

4.6. Prospective clinical and economic evaluation

The EBTNA recommends prospective and multicenter clinical studies evaluating the clinical utility, safety, and cost-effectiveness of artificial intelligence tools across diverse European populations according to the study design that is appropriate to the intended clinical application of the AI tool.(3,12) This evidence generation should be paired with early engagement of Health Technology Assessment (HTA) authorities, so that clinical-utility data are structured to support reimbursement decisions rather than accumulating without a pathway to adoption. Progress should be measured according to a European population of devices and indicators such as comparative evidence, patient outcomes, safety, and economic impact. Baseline numbers from the United States for device reporting should not be used for Europe. Randomized trials should be prioritized where appropriate to the clinical question.

4.7. Standing working group on AI and precision medicine

The EBTNA proposes establishing a standing Working Group on AI and precision medicine that will be responsible for continuous monitoring of the scientific, regulatory, and ethical landscape, delivering periodic updates to this position paper, and representing the association in European and international policy arenas, including the International Medical Device Regulators Forum (IMDRF), Artificial Intelligence/Machine Learning-Enabled Working Group and European Commission consultations supporting implementation of AI Act.(83, 84)

Limitations

This position paper has several limitations. It is a structured narrative review rather than a systematic review, so source selection and interpretation involve expert judgment. The field is changing rapidly, and device counts, regulatory timelines and performance estimates may become outdated. Much of the quantitative device evidence comes from the United States and may not directly represent European approval pathways or clinical practice. Evidence across AI, digital sensors and federated learning remains heterogeneous, often retrospective or single-center, and technical metrics do not necessarily establish patient benefit.(3,12,73) Finally, the proposed actions require consultation with patients, clinicians, regulators, industry, educators and Member-State institutions before implementation. The evidence that supports this position paper is concentrat-

Table 2. Implementation framework proposed for seven EBTNA strategic directions. Baseline values require measurement before implementation; responsible actors are proposed and subject to agreement.

Strategic Direction	Baseline to Establish	Indicators of Progress	Proposed Responsible Actors	Principal Resource Requirements
Multi-omics harmonization	Participating datasets, standards, and interoperability	Data quality, interoperability, and population coverage	Hospitals, universities, data custodians, and patient representatives	Data stewardship, harmonization expertise, and secure infrastructure
Regulatory-interface guidance	Existing guidance and unresolved implementation questions	Guidance produced and consistency of classification, update, and reporting procedures	EU and national authorities, legal experts, and professional societies	Regulatory expertise, coordination, and consultation
AI literacy	Available courses and assessed workforce competence	Participation and demonstrated practical competence	Universities, employers, and professional societies	Educators, protected training time, and learning platforms
Lifecycle equity assurance	Existing subgroup validation and access assessments	Subgroup performance, monitoring coverage, and access disparities	Developers, healthcare providers, and patient organizations	Representative data, statistical expertise, and audit capacity
Federated learning	Functioning networks, participating sites, and governance arrangements	Participation, local validation, reliability, and demonstrated clinical value	Research networks, hospitals, data custodians, and funders	Computing, privacy safeguards, coordination, and maintenance
Clinical and economic evaluation	European applications and their available comparative evidence	Patient outcomes, safety, cost-effectiveness, and budget impact	Clinical research networks, HTA bodies, regulators, and funders	Recruitment, follow-up, statistics, and health-economic expertise
Standing working group	Existing association capacity and governance arrangements	Published updates, consultations, and completed review cycles	EBTNA, clinical and technical experts, legal specialists, and patient representatives	Protected staff time, administrative support, and specialist input

ed in oncology, radiology, and rare-disease settings, where AI and omics-driven precision medicine are the most mature; extrapolation to high-volume, time-constrained settings like emergency medicine or primary care requires another level of translational validation. The regulatory discussion synthesizes published analyses, primary legislation, and official guidance. Application of the discussed regulation to a certain AI product, institution, or a member state requires legal and regulatory expertise, especially regarding liability, national research provisions, and updates to adaptive systems.

Conclusions

The convergence of AI with multi-omics, digital biosensing, pharmacogenomics, liquid biopsy, and advanced clinical decision support is increasingly influencing biomedical research and selected clinical applications. The evidence shows a technical and clinical promise, but at the same time there is a mismatch between market adoption and prospective validation, fragmented European governance, and insufficient workforce development. Responsible implementation should try to link innovation with interoperable data, clinical utility, equity, transparency, human oversight, and continuous monitoring. Through the seven lines of action, EBTNA drives European biotechnology societies toward coordinated participation in education, research, standard setting, and governance.

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Conflict of Interest

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Ethical Review and Approval

Ethical review and approval were not required because this position paper is based exclusively on previously published literature and publicly available regulatory and policy documents, and it did not involve human participants, identifiable personal data, or animal experiments.

Data Availability

No new data sets were generated or analyzed for this article. All quantitative information that appears in the manuscript was gathered from the cited publications and from publicly available regulatory and policy sources.

Disclaimer

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