

Appendix III: Factors of the Precision Medicine ecosystem.

Factors	Description / related ideas	Numbers (from Appendix I) of the articles
Treatment	Health, wellness, prevention, vaccination, diagnostic, diseases, treatment decision, informed choice, shared decision-making, decision-making process, prediction, predictive power, predict treatment outcomes, prognostic, treatment strategies, patient care, treatment as a continuum, early detection and intervention, responsiveness, uncertainty, surgery, genomic medicine, overtreatment, clinical practice, medical mediation, point-of-care devices, risk-benefit, psychological risk, quality of life, physical activities, effects of physical activity on health.	1-35, 37-45
Data	Clinical data, family history data, phenotype, genotype, biological data, omics data, DNA, metabolome, microbiome, genetic alterations, rare variants, epigenetic modifications, environment, imaging, omics data, big data, data source, public databases, EHRs data, mHealth data, data collect, data management, sequencing, interpretation, integration, integrating heterogeneous sources, data governance, data access, data sharing, biobanking.	1, 3-21, 23-36, 38-45
Testing	Genetic test, utility and validity, uncertainty and complexity, biomarker, communication, delivery information, incidental results, re-identification, companion diagnostics, interpretation, continuous genetic education, translation of genomics language into lay language.	1, 3-8, 10-17, 19-21, 23-33, 35, 37-45
Research	Understand how genes affect health and disease, clinical research, genomic research, pharmacogenetic studies, cohorts of patients, dissemination of general study results, longitudinal studies, system approaches, multidisciplinary, education program, research infrastructure.	1, 3-8, 14, 16-21, 23-31, 33, 35-43
Technologies	Computing, algorithms, big-data analytics, bioinformatics, cloud computing, machine-learning, network analysis, computational biomedicine, apps, mathematical and computer simulation models, signal processing, technological advances, inflated expectations, novel screening technologies, advanced materials, synthetic biology, network and collaboration, applications that allow measuring, sharing and assessing data, open-source algorithms, warning systems, global partnership platforms and standards, standardizing genotyping platforms, trusted and transparent interaction platform, ambient sensors, remote sensing, wireless sensor network, behavioral change, mobile health technology, geolocation, personal smart devices ubiquity, wearable sensors, implanted technology.	3, 5, 7, 12, 14-26, 28, 30-35, 38, 40-42, 44, 45
Drugs	Pharmacogenetics, pharmacogenomic markers, pharmamicrobiomics, molecular pharmacology, product information, drug development, orphan drug status, drug discovery, drug response variability, understanding of drug effects, drug repositioning, tailor-made drug supply, drug dosage, printing medicines, drug usage, drug side-effects, toxicity.	1, 2, 4-8, 10, 14, 16-20, 22-27, 30-32, 34, 39, 41, 44, 45
Individuality	Patient's perspective, patient and citizen empowering, patient seeking for information, need for genetic counseling, fear of stigmatization, discrimination, life planning, human enhancement, self-medicalize, consent, information ownership, susceptibility, genetic predisposition, germline, customization, custom-made medications.	1, 5, 6, 9, 10, 14-17, 21-23, 26-28, 30-32, 34, 35, 37, 40-45
Heterogeneity	Disease classification, catalog of genetic variations, stratification, risk stratification for public health programs, subpopulations, genetic stratification, geographic information, ethnicity, ethnic minority groups, gender, age, motivating high-risk groups, understanding the human genome across populations, diverse socio-economic patient population, identify cluster and correlations, heterogeneity, differences between individuals, multiplicity of molecular characteristics, tailored solutions.	5-8, 11, 14-16, 21, 23, 25-28, 30, 31, 35, 35, 37-45
Funding and Costs	Funding strategies, continuous support from public funders and institutions, economics of biobanks, long-term financial sustainability, health care costs, cost-effectiveness, price of NGS technologies, low-cost sequencing, high-cost tests, premium priced drugs, transparency of testing costs, economic evaluation of pharmacogenomics, paying, insurance coverage, reimbursement, lack of reimbursement for genetic testing, sequencing for lowering costs, costs tending to fall, 1000-dollar-genome, 1-dollar-genome.	1, 3, 5, 6, 8, 12, 14, 16-20, 23-26, 29, 30, 32, 35, 38, 40-43, 45
Ethical-Social	Ethics, data-sharing ethics, social, cultural differences, inequity or unequal access to new technologies, social justice, ageing society, marketing, market demand, DTC advertising, e-commerce, market for selling health data, market value of personal data.	1, 5, 6, 14, 16, 25, 26, 28-30, 32, 35, 37, 39-43, 45

Regulation	Legal consequences. regulatory policies. legal challenges. legislative gaps. Health Insurance Portability and Accountability Act (HIPAA). ambiguity and inconsistency in policies. diversity across jurisdictions.	1. 3. 6. 12-14. 16. 17. 20. 21. 25. 26. 29. 31. 32. 35. 40. 43. 44
Privacy and Security	Privacy risks. patient confidentiality. DNA data cannot truly be anonymized. local privacy requirements. security. patient information protection. secure-computing environment. data security. data protection legislation.	1. 3. 5. 6. 10. 14. 24. 26. 30. 31. 34. 35. 40. 42. 43