Implementing precision medicine in a regionally organized healthcare system in Sweden

To the Editor—An increasing number of precision medicine initiatives have been launched worldwide, with Genomics England as the pioneering flagship project[1]. Although some governments have created national strategies for precision medicine and utilized centralized infrastructures, the process has proven more challenging for countries like Sweden with a regionally organized healthcare system[2,3]. In Sweden, the key to a successful implementation of precision medicine has instead been a bottom-up approach in which academia and healthcare joined forces to build a nationally distributed infrastructure[3]. In this way, an innovative framework was established to continuously develop and implement precision diagnostics, thereby facilitating equal access to precision medicine at the national level (Fig. 1).

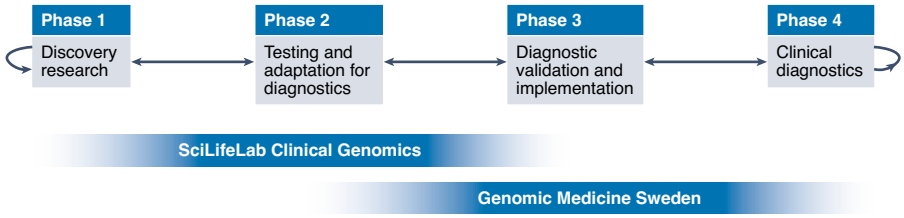

Fig. 1 | Key phases of the research-implementation framework developed in Sweden for precision diagnostics and medicine. The technology-driven SciLifeLab Clinical Genomics platform develops, adapts and optimizes new technologies for diagnostics and has nodes at all seven universities with a medical faculty, while Genomic Medicine Sweden validates and implements precision diagnostics/medicine in Swedish healthcare and has established Genomic Medicine Centers at all seven university hospitals. For a continuous development of new methods and treatment strategies, data generated in healthcare will be fed back to research through the National Genomics Platform.

An important step toward leveraging new technologies, including genomics, in diagnostics was the launch of a national infrastructure for molecular biosciences, the Science for Life Laboratory (SciLifeLab), in 2010. SciLifeLab provides expertise and services through a range of technology platforms, and established the Clinical Genomics platform in 2014 to further advance the translation of genomic sequencing into clinical utility. The platform, with nodes at all medical faculties in Sweden, supports translational and clinical research projects and adapts and optimizes new technologies for diagnostics (Table 1). Illustrating its cutting-edge activities, Sweden became one of the first healthcare systems to implement whole-genome sequencing in rare disease diagnostics[4,5].

To further leverage genomics into clinical practice, the Clinical Genomics platform in 2017 initiated Genomic Medicine Sweden (GMS). To achieve nationwide access to precision medicine, all university healthcare regions and medical faculties agreed to collaborate. GMS received governmental funding from the Swedish innovation agency, Vinnova, and public co-funding from collaborating parties. A national steering board was formed with representation from academia, healthcare, industry and patient organizations. Genomic Medicine Centres (GMCs) were established at the university hospitals to facilitate nationally harmonized implementation, while taking into consideration regional requirements and strengths.

GMS focuses on patients with rare diseases, cancer and infectious diseases. Through the joint efforts of Clinical Genomics and GMS, three GMCs have implemented whole-genome sequencing as a first-line diagnostic test in rare diseases, also serving other GMCs. In a report on the first 3,200 patients who underwent whole-genome sequencing, 40% of previously undiagnosed patients received a molecular diagnosis, underscoring the dramatic impact of introducing this approach in routine diagnostics[6]. In 2021, more than 5,000 such analyses were performed within Swedish healthcare, which also contributed to the discovery of novel disease genes[6–8].

In cancer, capture-based gene panels were designed at the national level, including pharmacogenomically relevant genes that are essential for treatment dosing. For hematological malignancies, a panel of 199 genes was launched in 2020, and last year more than 3,800 analyses were performed, with a major impact on patient stratification and therapy selection.

For solid tumors, molecular profiling by amplicon-based targeted sequencing has had a nation-wide coverage since 2017, with more than 10,000 samples analyzed yearly within healthcare. A national collaboration is implementing a comprehensive DNA/RNA panel, which is ongoing at all GMCs. This panel includes 560 genes and covers all types of predictive and diagnostic aberration, including microsatellite instability, tumor mutation burden and homologous recombination deficiency. Government grants support pilot implementation in patients with breast, ovarian and lung cancers. This panel will also be used in clinical trials such as the Swedish MEGALiT study, which includes patients with metastatic disease in treatment baskets defined by detected genomic aberrations.

To take the next step in precision cancer diagnostics, whole-genome sequencing is offered to all pediatric cancer patients in Sweden, comprising 350 cases a year. On the basis of the first 100 patients, diagnosis and risk-assessment was refined for most patients, while also enabling the detection of genetic predisposition and drug targets. In an ongoing study in acute leukemias, combined whole-genome and whole-transcriptome sequencing is performed in parallel to standard-of-care diagnostics in patients diagnosed since May 2021 (150 cases so far) to assess whether an all-in-one test can replace current testing[9].

In infectious diseases, implementation of whole-genome sequencing significantly reduces the risk of microbial and viral spread through accurate species determination, molecular typing and determination of antibiotic resistance. SciLifeLab, Clinical Genomics and GMS have jointly established SARS-CoV-2 sequencing across Sweden and are actively engaged in the national pandemic preparedness program.

A challenge has been the lack of a coordinated information technology (IT) infrastructure for patients' genomic data.

Table 1 | Key services provided by the SciLifeLab Clinical Genomics platform and Genomic Medicine Sweden

Entity	Service
Clinical Genomics platform[a]	Translational and clinical research support
	Method development for clinical diagnostics
	Clinical trial support
	Technological support for Genomic Medicine Sweden
Genomic Medicine Sweden[b]	Implement precision diagnostics and treatment for rare diseases, solid tumors, hematology, pediatric cancer, infectious diseases, pharmacogenomics and complex diseases
	Supportive working groups on informatics, ethics and legal implications, industry collaboration, health economy and education

[a]The Clinical Genomics platform provides expertise and services to the research and industrial communities, as well as to Genomic Medicine Sweden. [b]Genomic Medicine Sweden encompasses six national diagnosis-specific working groups and five working groups that support the GMS infrastructure. The GMS strategy plan 2021–2030 outlines the plans for the next 10 years and is closely linked to the government's life science strategy.

To overcome this, GMS established the National Genomics Platform, enabling unified analysis, interpretation and sharing of genomic data. The pandemic accelerated this infrastructural investment, whereby common bioinformatic workflows were established on the platform for SARS-CoV-2 analysis. The opportunity to combine genomic data with Sweden's renowned national registers will provide an invaluable resource for future research. However, for full benefits from the technical solutions established at the National Genomics Platform to be achieved, the Swedish legislation relating to secondary use of data requires changes;[10] a governmental inquiry was recently commissioned to address this issue.

In the coming years, the Clinical Genomics platform will continue developing and adapting new techniques of relevance for precision diagnostics, whereas GMS will continue implementing precision diagnostics/medicine in Swedish healthcare. Within SciLifeLab, other technology platforms are currently providing services such as proteomics and spatial and single-cell biology to the research community, and as clinical demand for such services increases, a similar research-implementation model will be applied.

GMS recently initiated pilot projects in complex diseases, such as autoimmune and psychiatric diseases[11]. Taking advantage of other omics technologies and integration with health data, GMS will move towards precision health, including early detection and disease prevention. Other emerging opportunities will be explored in immune oncology and liquid-biopsy-based diagnostics.

The National Genomics Platform enables critically important data-sharing within healthcare and provides an opportunity for collaboration with the research community and life science sector. An important national initiative on Data-Driven Life Science was recently launched by SciLifeLab and the Knut and Alice Wallenberg Foundation, with one focus area being precision medicine and diagnostics. To promote international collaboration, strategic alliances have also been formed with similar initiatives in France, Germany and Denmark, and GMS is actively involved in the European 1+ Million Genome Initiative.

Remaining challenges to unlocking the full potential of precision medicine include dealing with legal and regulatory issues, such as how to facilitate data sharing and comply with upcoming regulations; provision of competence and know-how, with an increasing demand for IT and bioinformatics expertise as well as cross-disciplinary education among all stakeholders; and financial matters, including sustainable, long-term funding models and health-economic assessments to study cost effectiveness. Many of these challenges are currently being addressed by the Swedish and international precision medicine ecosystems, and lessons learned from different national initiatives should be shared so that precision medicine can be widely delivered for the benefit of patients and society at large. ❐

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Author contributions

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Competing interests

T.F. is a co-founder, board member and scientific advisor of Qlucore AB and Cantargia AB. V.W. has received honoraria from Illumina and Roche. B.J. has performed NIPT (fetal diagnostics) clinical diagnostic trials with Ariosa, Vanadis and Natera, with expenditures reimbursed per patient. A.E. has received honoraria from Amgen, AstraZeneca, Bayer, Diaceutics and Roche. H.E. has received honoraria from AstraZeneca. M.L. is the founder, a board member and chief scientific officer of MetaCurUm Biotech AB aiming for precision medicine for cancer patients. A.L. has received honoraria from Illumina. C.E.W. has received honoraria from Abitec and GossamerBio. R.R. has received honoraria from AbbVie, AstraZeneca, Illumina, Janssen and Roche.