

Worldwide Exome and Genome Sequencing: Who Has Access, Who Pays, and What are Solutions for Implementation Challenges?

Most published studies on exome/genome sequencing (ES/GS) are focused on the US and other high-income countries such as the UK. However, although interest in using ES/GS in routine clinical care has grown around the world, there have been few analyses examining where testing is available, how it is funded, and how different health systems are addressing implementation challenges.

Countries have different availability of testing and approaches to payer coverage and public funding for ES/GS. This variation can lead to differences in an individual's chance of disease diagnosis and potential treatments according to which country they live in and where in that country they reside. Understanding the differences in availability and funding and the evolution of these differences may help inform future challenges and potential solutions for implementation of genomic technologies into practice.

We examined the availability and funding of exome and genome sequencing for suspected genetic diseases worldwide (ES/GS). Given that there are few peer-reviewed data sources describing testing in countries other than the U.S., we compiled data from the gray literature (e.g., white papers, market analyses, industry websites) and interviews with global experts. We also used exploratory case studies across three diverse health care systems:

- (1) publicly funded/national (UK)
- (2) publicly funded/provincial (Canada)
- (3) mixed private/public system (US).

These case studies were used to illustrate funding challenges and approaches used to address those challenges that might be adopted by other countries.

We found that ES/GS tests are now available in a range of countries in every region of the world (Table 1), and that public and private funders are covering these tests in some clinical scenarios. Tests have become available not only in high-income countries with robust genomic programs such as the US and the UK but also countries with middle-income economies. There are many initiatives, such as those in Asian countries, to implement ES/GS into clinical care.

Table 1: Availability of Exome and/or Genome Sequencing Across World Regions and Countries

North America	Central/ South America	Europe	Middle East	Asia/Oceania	Other Countries
United States Canada Mexico	Brazil Argentina Colombia Argentina Peru	United Kingdom, Germany Belgium, Denmark, Netherlands, Sweden, Italy, Spain, Ireland, Estonia, Finland, France	Saudi Arabia Qatar Turkey Israel	Australia China Japan South Korea Taiwan	South Africa

Our case studies identified the current funding situation, key factors influencing funding, and illustrative solutions that are being implemented to address challenges (Table 2). We found key leverage points that can be adopted by other countries to facilitate implementation, including developing coordinated, standardized, systematic testing infrastructures as well as using stakeholder engagement to develop consistent, efficient, and equitable practices and policies.

Table 2: Comparison of ES/GS Funding Approaches and Solutions to Implementation Challenges Across Three Diverse Health Care Systems

Themes	UK	Canada	US
Current funding	- Funding provided at national level for WES and WGS w/in National Health Service	- WES funding varies by province and generally requires pre-approval - WGS generally not covered	- Funding varies by payer and test type/clinical scenario - Greater funding of WES vs. WGS and for rapid WES in neonatal intensive care (NICU)

Key factors influencing funding	<ul style="list-style-type: none"> - 100,000 Genomes Project provided evidence of increased diagnostic yield and reduced costs - Political support to invest in genomic testing and infrastructure 	<ul style="list-style-type: none"> - WES emerged from funding of multi-gene panels for other conditions - WGS funding has been viewed as infeasible due to higher cost 	<ul style="list-style-type: none"> - Evidence of clinical utility, particularly for rapid testing in the NICU - Acceptance by payers of broader measures of clinical utility
Solutions for challenges	<ul style="list-style-type: none"> - Mainstreaming and coordinating testing through centralized labs, test directory, and clinical services - Developing consistent policies for patients with the same conditions 	<ul style="list-style-type: none"> - Mainstreaming and centralizing testing through development of infrastructures and clinical workflows to enable in-province test processing - Developing infrastructure for timely testing to enhance equitable access 	<ul style="list-style-type: none"> - Use of inclusionary, consensus-building approach with stakeholders - Focus on developing narrowly defined coverage policies that are not only medically appropriate but also feasible to implement

In conclusion, we found that there are wide gaps in available data on ES/GS implementation. We conclude that these tests are now available in every major region of the world, and thus we need to better track and understand where and how testing is used.