OXFORD POPULATION HEALTH

UNIVERSITY OF OXFORD

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Breakout session 8

Addressing Equity Challenges in Genome Sequencing: What Can Health Economics Contribute?

Moderator

James Buchanan (University of Oxford)

Panelists

Deborah Marshall (University of Calgary)

Maarten IJzerman (Erasmus School of Health Policy and Management)

Jeroen Jansen (University of California – San Francisco)

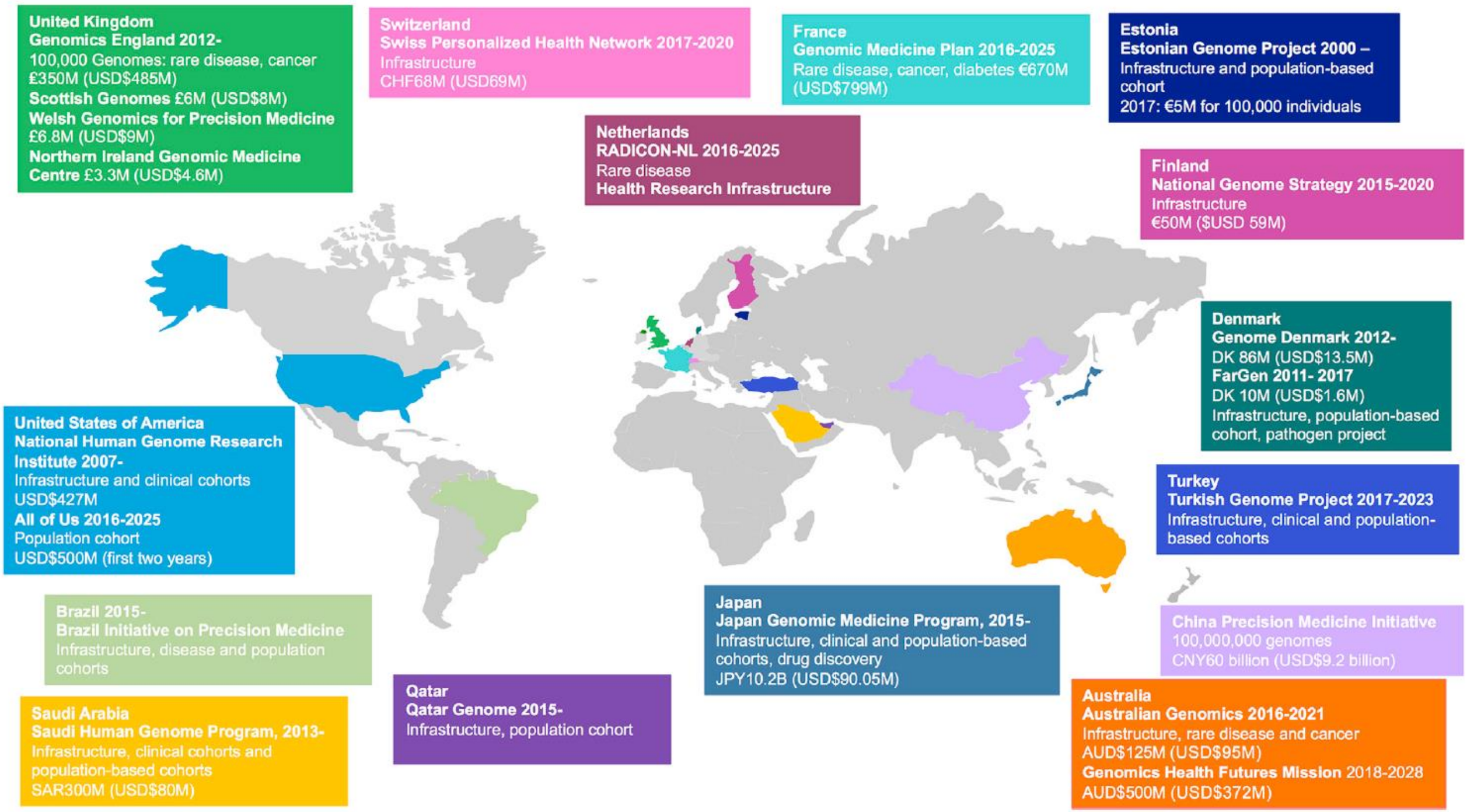
Session outline

- Introduction (5 mins)
- Panelist presentations (20 mins)
- Panel discussion (20 mins)
- Audience questions and discussion (15 mins)

Genome sequencing: a primer

- **Genome ➔ the complete DNA sequence of an individual**
- Virtually identical in every human
- Small differences (mutations) make us unique, and can also be associated with disorders and disease
  - In particular, rare diseases and cancer
- Identifying these differences can inform treatment and clinical management
- **Genome Sequencing ➔ the process of determining an individual's entire DNA sequence**
- (Exome Sequencing ➔ focuses more narrowly on the protein-coding regions of the genome)
- Genome/exome sequencing increasingly embedded in research practice over past 15 years, but testing still relatively expensive

Genome sequencing at scale



Stark et al. (2019) doi: 10.1016/j.ajhg.2018.11.014

Health economics evidence for sequencing?

SYSTEMATIC REVIEW | Genetics inMedicine

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Are whole-exome and whole-genome sequencing approaches cost-effective? A systematic review of the literature

Katharina Schwarze, BSc, MA[1], James Buchanan, MA, DPhil[1], Jenny C. Taylor, MA, DPhil[2,3] and Sarah Wordsworth, MSc, PhD[1,2]

Purpose: We conducted a systematic literature review to summarize the current health economic evidence for whole-exome sequencing (WES) and whole-genome sequencing (WGS).

Methods: Relevant studies were identified in the EMBASE, MEDLINE, Cochrane Library, EconLit and University of York Centre for Reviews and Dissemination databases from January 2005 to July 2016. Publications were included in the review if they were economic evaluations, cost studies, or outcome studies.

Results: Thirty-six studies met our inclusion criteria. These publications investigated the use of WES and WGS in a variety of genetic conditions in clinical practice, the most common being neurological or neurodevelopmental disorders. Study sample size varied from a single child to 2,000 patients. Cost estimates for a single test ranged from $555 to $5,169 for WES and from $1,906 to $24,810 for WGS. Few cost analyses presented data transparently and many publications did not state which components were included in cost estimates.

Conclusion: The current health economic evidence base to support the more widespread use of WES and WGS in clinical practice is very limited. Studies that carefully evaluate the costs, effectiveness, and cost-effectiveness of these tests are urgently needed to support their translation into clinical practice.

Genet Med advance online publication 15 February 2018

Key Words: cost; economic evaluation; outcome; whole-exome sequencing; whole-genome sequencing

Economic evaluation challenges in genomics

- Key challenges well-documented:
  - **Selecting an appropriate analytical approach and comparator**
    - Positioning of tests in clinical pathways
    - Selecting an appropriate current practice comparator for tests spanning multiple disorders
    - Selecting an appropriate comparator if a test fulfils multiple clinical applications
  - **Complexity of modelling approach**
    - How to incorporate all potential results and clinical trajectories
    - Accommodating interactions between results
  - **Test outcomes**
    - Health and non-health (personal utility)
    - Patient / current family / future generations

Issues surrounding equity are a growing concern

- Initial analyses in population sequencing studies have highlighted issues surrounding test access and outcomes
- These inequalities could be inequities, and could lead to bias in cost-effectiveness analyses
- Also concerns about the transferability of findings between countries/biomarkers/ethnicities
  ➔ impacts on the generalisability of economic evaluation results

nature medicine

SERIES | PERSPECTIVE

https://doi.org/10.1038/s41591-021-01672-4

A roadmap to increase diversity in genomic studies

Segun Fatumo[1,2] ✉, Tinashe Chikowore[3,4], Ananyo Choudhury[3], Muhammad Ayub[5], Alicia R. Martin[6,7] and Karoline Kuchenbaecker[5,8]

Two decades ago, the sequence of the first human genome was published. Since then, advances in genome technologies have resulted in whole-genome sequencing and microarray-based genotyping of millions of human genomes. However, genetic and genomic studies are predominantly based on populations of European ancestry. As a result, the potential benefits of genomic research—including better understanding of disease etiology, early detection and diagnosis, rational drug design and improved clinical care—may elude the many underrepresented populations. Here, we describe factors that have contributed to the imbalance in representation of different populations and, leveraging our experiences in setting up genomic studies in diverse global populations, we propose a roadmap to enhancing inclusion and ensuring equal health benefits of genomics advances. Our Perspective highlights the importance of sincere, concerted global efforts toward genomic equity to ensure the benefits of genomic medicine are accessible to all.

Evidence from the 100,000 Genomes Project

- For probands with rare diseases undergoing sequencing:
  - Probands of lower socioeconomic status had **lower odds**, while probands of European ancestry had **higher odds**, of having **two or more relatives enrolled in the study**
  - Probands of **lower socioeconomic status** had **more** emergency care episodes and **higher** emergency care costs
  - Probands of **European ancestry** had **fewer** inpatient care episodes but **higher** inpatient care costs
  - Episodes and costs were **concentrated** among more deprived individuals

Addressing data diversity challenges in genomics: a health economics perspective

Pauline Herscu, James Buchanan, Laurence Roope, Patrick Fahr, Sarah Wordsworth

Just as we, in our daily lives, face the challenge of allocating a finite monthly income across priorities such as food, housing or education, health economics is the discipline evaluating the allocation of scarce resources in healthcare. Attempting to answer the question 'Is this money well spent?', health economic evaluations (for example cost-effectiveness analyses) reconcile any changes in costs from introducing a new healthcare intervention with associated changes in health

Over to the panelists…

- **Professor Deborah Marshall:** “Data Diversity Challenges in Genomics”
- **Professor Maarten IJzerman:** “HTA of Cancer Genomics: Perspectives, Transferability and Access”
- **Dr Jeroen Jansen:** “Distributional cost-effectiveness analysis: a promising tool?”