CHIEF SCIENTIST OFFICE

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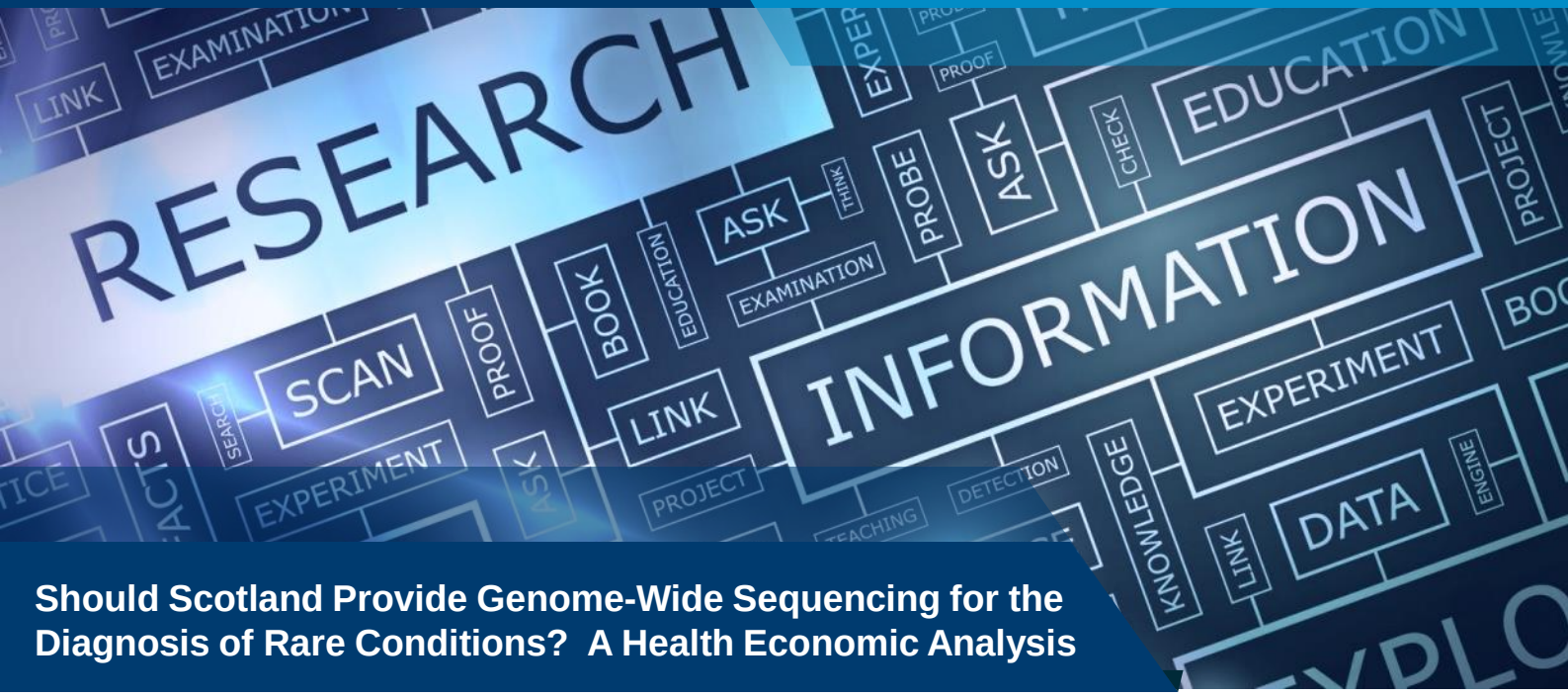
RESEARCH PROJECT BRIEFING



Should Scotland Provide Genome-Wide Sequencing for the Diagnosis of Rare Conditions? A Health Economic Analysis

AIMS

Genetic testing looks for changes in a person's DNA that might cause a medical condition. Standard genetic testing focus on one gene (single gene testing), a group of related genes (gene panel testing), or missing or extra sections of DNA using chromosomal microarray testing. New genomic tests, such as whole genome sequencing (WGS) analyse a person's entire DNA at the same time, whereas whole exome sequencing (WES) focuses on the part of DNA that makes proteins. WGS and WES can diagnose rare genetic conditions more quickly and effectively than standard genetic testing. This project investigated whether these genomic tests provide value for money in the Scottish healthcare system, focussing on the diagnosis of rare complex developmental delay conditions.

KEY FINDINGS

- **Replacing standard gene panel testing with trio WES** (testing a child and both parents) diagnoses 14% more conditions and saves £1,029 per family tested. This results in better outcomes for patients, and budget savings for NHS Scotland.
- **Trio WGS provides 4% more diagnoses than trio WES.** However, WGS costs between £3,750 - £5,576 per trio. Focusing on cost per diagnosis, WGS would need to cost less than £1,753 per trio to be cost effective.
- **Genomic testing significantly shortens the time to diagnosis,** reducing the 'diagnostic odyssey' from 3-4 years with standard testing, to under 12 months with WGS or WES.
- **Patients and families with rare conditions highly value *early* genomic testing** compared to later testing or standard genetic testing. When the value of benefits to patients and families is included, WGS becomes cost effective if it costs less than £3,750 per trio.

WHAT DID THE STUDY INVOLVE?

Cost-Effectiveness Analysis (CEA)

Using data from the Scottish Genomes Partnership's (SGP) involvement in the UK 100,000 Genomes Project and the Deciphering Developmental Disorders (DDD) study, we:

- Estimated the cost and diagnostic yield (% of patients diagnosed) of standard genetic testing, trio WES and trio WGS for the diagnosis of rare conditions
- Compared the cost per diagnosis of five genomic testing strategies versus standard genetic testing. This included WGS and WES at different points in the testing process

Budget Impact Analysis (BIA)

For genetic and genomic testing to help diagnose rare conditions, it must be affordable for NHS Scotland. We:

- Calculated the five-year budget impact of each genetic and genomic testing strategy evaluated in the CEA
- Assessed how changes in the cost of WGS and WES could affect the Scottish NHS budget

Cost-Benefit Analysis (CBA)

Patients and families with rare conditions value the benefits of genomic testing, such as providing information, or reducing waiting times and clinic visits. We:

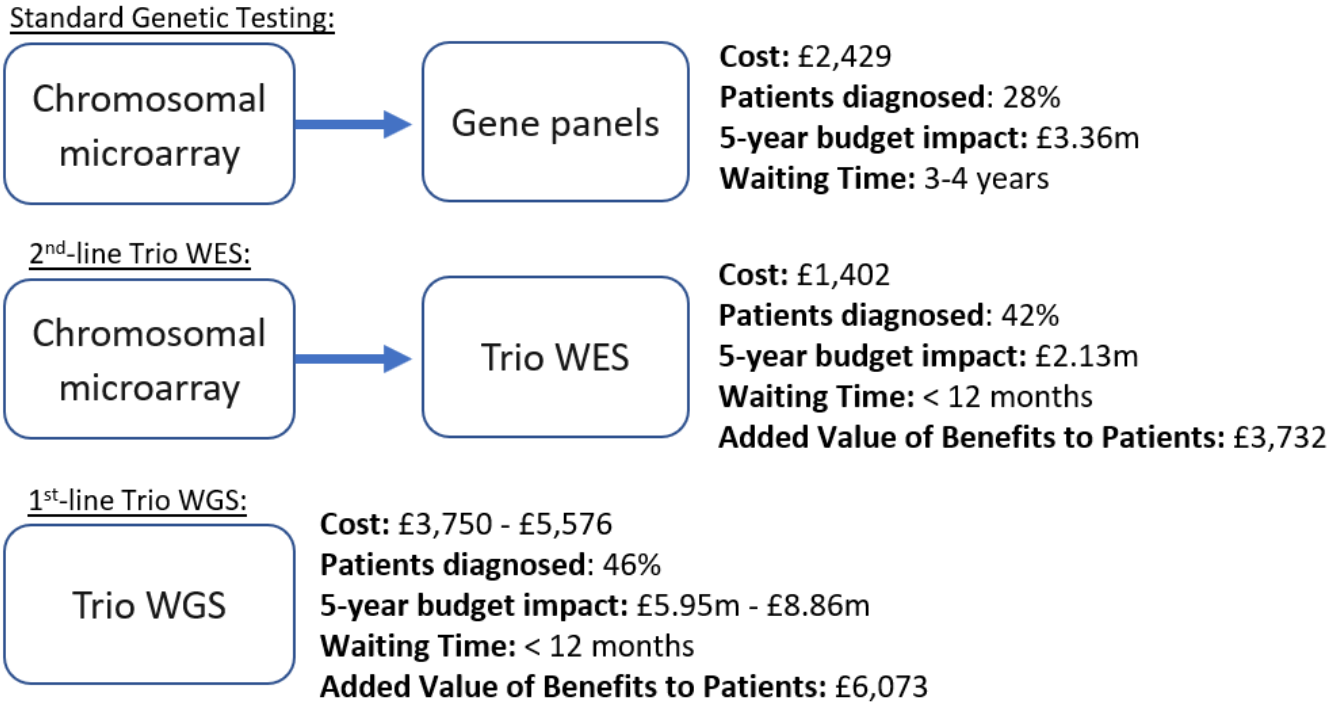
- Surveyed patients and families from the SGP and DDD studies who had experience with WGS or WES to understand their preferences
- Measured how much patients and families value these tests by estimating their "willingness to pay" (WTP) – a way to measure the overall importance of a test to users in monetary terms
- Used these WTP values to calculate the net benefits (value of the benefits minus the costs) of each testing strategy in a user-centred cost-benefit analysis

Patient & Public Involvement

- Feedback from our Project Advisory Group, including patient representatives, helped shape the user preference survey, CEA and CBA models and the final report
- The user preference survey was designed based on interviews with SGP and DDD study participants, who had experience of genomic testing for the diagnosis of a rare condition
- Throughout the project, findings were shared and discussed at patient engagement events, organised and hosted by Genetic Alliance UK

WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

Figure 1: Economic Evaluation of Genetic and Early Genome-Wide Sequencing Strategies



- Early implementation of WGS or WES (*Figure 1)* was always cost effective compared to using WES or WGS later in the diagnostic process
- Standard genetic testing often involves multiple gene panel tests over several years. WGS and WES reduce the need for repeated testing and provide faster diagnoses for rare conditions
- **Cost-Effectiveness Analysis:** When we only focus on *cost per diagnosis,* WGS would need to cost less than £1,753 per trio, or diagnose more than 89% of patients to be cost effective
- **Cost-Benefit Analysis:** When we include the value of genomic testing to patients and families with rare conditions – such as reducing uncertainty and waiting times – WGS would be cost-beneficial if it costs less than £3,750 per trio or diagnoses more than 46% of patients
- Over 70% of the cost of WGS comes from sequencing the DNA, analysing the data (bioinformatics), and storing the results. Reducing these costs would have the greatest impact on the cost effectiveness of WGS

WHAT IMPACT COULD THE FINDINGS HAVE?

- Providing a trio WES service in NHS Scotland would diagnose more patients, more quickly, and at a lower cost than standard genetic testing
- Replacing standard genetic testing with WGS would reflect users' preferences, and offer value for money if the cost of WGS decreases
- Accounting for the preferences and values of patients and families with rare conditions aligns with the Scottish Government's goal of delivering person-centred genomic testing services

HOW WILL THE OUTCOMES BE DISSEMINATED?

- Cost-effectiveness results have been presented to the Scottish Strategic Network for Genomic Medicine (SSNGM) Oversight Board. Going forward, we will work with SSNGM to ensure our project findings inform the development of a Scottish genomic testing strategy.
- Our findings have been discussed at patient and public engagement events hosted by Genetic Alliance UK. We will continue to collaborate with Genetic Alliance UK to disseminate our results.
- To reach health professionals, such as health economists and clinical geneticists, we will disseminate our findings through academic publications and conferences.

CONCLUSION

- Early genomic testing offers value for money to the Scottish healthcare system and benefits patients and families with undiagnosed rare conditions.
- Providing WES diagnoses more patients, more quickly, at a lower cost than standard genetic testing.
- Including the value of genomic testing to users – such as reducing uncertainty, providing answers sooner, and avoiding unnecessary tests – WGS does not need to be as cheap or effective to offer value for money to NHS Scotland.

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