The Health Outcomes, Utility and Costs of Returning Incidental Results from Genomic Sequencing: A Mixed-Methods Randomized Clinical Trial

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Introduction

Genomic sequencing (GS) has rapidly transitioned into clinical practice, yet large-scale implementation of GS faces challenges with regard to the return of incidental results (IR), which refer to genetic variants uncovered during testing that are unrelated to the primary disease under investigation, but of potential clinical significance.

Aims

To evaluate the health outcomes and costs of receiving incidental results for patients undergoing genomic sequencing.

Methods

A Mixed-methods randomized controlled trial comparing the health outcomes and costs of receiving, versus not receiving, incidental results.

Table 1: Study Description

Participants	Adult patients with cancer or polyposis (N=260 patients) who had genetic testing for cancer and received negative or uninformative results.
Intervention	Participants in the intervention arm will receive cancer-related GS results and the option to learn IR from up to 5 categories of results.
Comparison	Participants in the control arm will only learn cancer-related GS results, if found.
Outcomes	Psychological distress; clinical utility; personal utility; health behavioural consequences; healthcare system costs; personal costs

Table 2: Categories of Incidental Results and Examples

Category #	Category Type	Examples
Category 1	Medically Actionable	Lynch Syndrome
Category 2	Common Disease Risks	Type 2 Diabetes
Category 3	Rare Mendelian Disorders	Muscular Dystrophy
Category 4	Early-onset Neurological Conditions	Early Onset Alzheimer's disease
Category 5	Carrier Status	Cystic fibrosis

Figure 1: Study Design

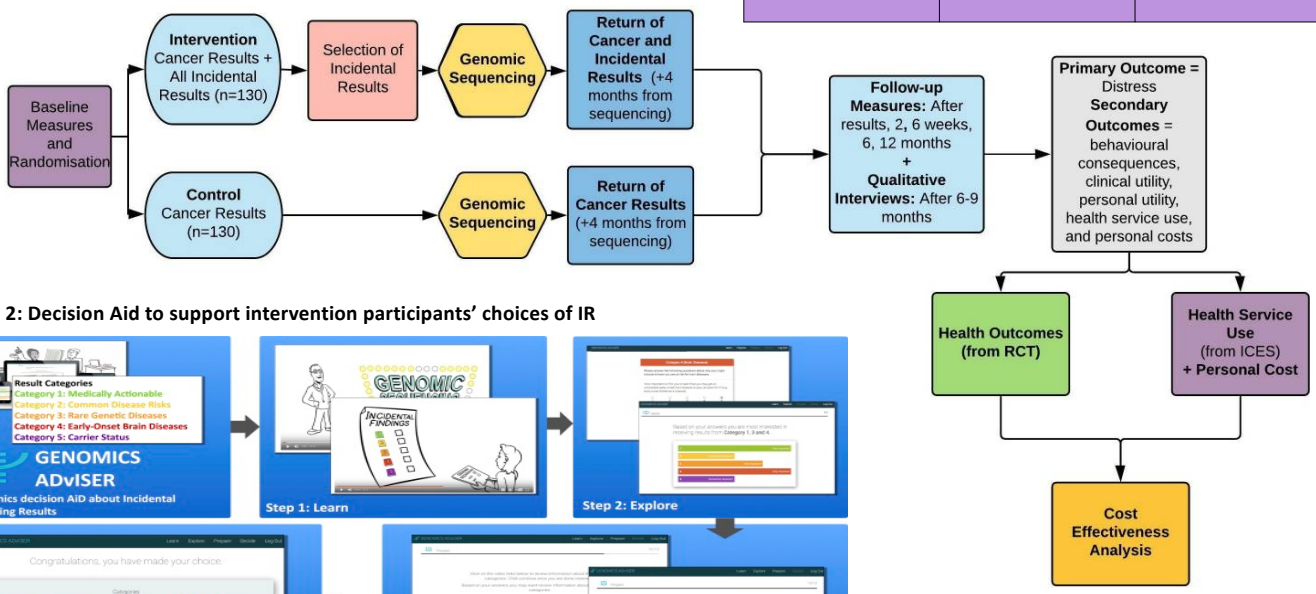

Figure 2: Decision Aid to support intervention participants' choices of IR

Conclusion

This clinical trial is the first to provide high-quality evidence evaluating health outcomes and costs of receiving all clinically significant incidental genomic results. This evidence is critical for informing the clinical implementation of genomic sequencing and to understand the unintended consequences of the adoption of genomic sequencing in practice.

Further information

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Trial Registration: clinicaltrials.gov Identifier: NCT03597165

Reference: Shickh et al. *BMJ Open.* 2019 7;9(10).