Gaps in Health Services Research on Genetic Testing Applications

HSRProj Student Competition 2018

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Presentation Overview

- Introduction to genetic testing and relevance to health services research

- Methods

- Results

- Other evidence

- Conclusions

Introduction

- Genetic information is an increasingly important component of health service delivery.

- Uptake of genetic testing has been rapid, and the global market value in 2017 was approximately $9.4 billion with continued growth expected.[1]

- Research on genetic technology translation can be classified into four stages, T1 – T4:
    - Test development from basic science (T1)
    - Assessment of value in the clinic (T2)
    - Implementation of evidence-based guidelines (T3),
    - Population health outcome evaluation (T4).[2]

1. Modor Intelligence. *Global Genetic Testing Market - Segmented by Treatment Type, Diseases, Technology, and Geography - Growth, Trends and Forecasts (2018 - 2023)*. 2018. https://www.mordorintelligence.com/industry-reports/global-genetic-testing-market-industry
2. Khoury MJ, Gwinn M, Yoon PW, Dowling N, Moore CA, Bradley L. The continuum of translation research in genomic medicine: how can we accelerate the appropriate integration of human genome discoveries into health care and disease prevention? *Genet Med.* 2007;9:655-674.

Translational Research in Genetic Medicine

- Health services research (HSR) related to patient access, clinical uptake, implementation, process of result disclosure, cost-effectiveness, and impacts on health disparities (T2 – T4) makes up less than 3% of genetics literature.[2]

- However, research phase of research has not yet been explored using an HSR database, in which later stage evaluation is more pertinent.

Research Stage	Genetic Medicine Example
T1	Development of a genetic test from basic science research
T2	Use of the genetic test in practice and guideline development
T3	Evaluation of guidelines in clinical practice
T4	Health outcomes analysis from clinical application

2. Khoury MJ, Gwinn M, Yoon PW, Dowling N, Moore CA, Bradley L. The continuum of translation research in genomic medicine: how can we accelerate the appropriate integration of human genome discoveries into health care and disease prevention? *Genet Med.* 2007;9:655-674.

Translation Research Phases

Table 1

The continuum of translation research in human genetics: types of research and examples

Translation research phase	Notation	Types of research	Examples
TI	Discovery to candidate health application	Phases I and II clinical trials; observational studies	Is there an association between *BRCA* mutations and breast cancer?
T2	Health application to evidence-based practice guidelines	Phase III clinical trials; observational studies; evidence synthesis and guidelines development	What is the positive predictive value of *BRCA* mutations in at-risk women?
T3	Practice guidelines to health practice	Dissemination research; implementation research; diffusion research Phase IV clinical trials	What proportion of women who meet the family history criteria are tested for *BRCA* and what are the barriers to testing?
T4	Practice to population health impact	Outcomes research (includes many disciplines); population monitoring of morbidity, mortality, benefits, and risks	Does *BRCA* testing in asymptomatic women reduce breast cancer incidence or improve outcomes?

Objective

- This project aims to identify potential gaps in HSR related to genetics through comparison of HSR evaluation of genetic test and service implementation to the availability of clinical genetic tests.

Methods

- Abstracts in the HSRProj database (November 2017 full download) were searched for: "genetic", "genome", "precision medicine", and "personalized medicine".

- MeSH terms were searched for "Genetic Research".

- Each abstract was screened for relevance after duplicates were removed.

- Abstracts with an evaluation aim along the translational spectrum of a genetic test were included.

Methods – Second Database

GTR: GENETIC TESTING REGISTRY

- Clinical genetic testing landscape was assessed via the National Center for Biotechnology Information's Genetic Testing Registry (GTR), a public database of all available genetic tests.[3]

  - Goal of GTR is "to advance the public health and research into the genetic basis of health and disease."[4]

- GTR was filtered for clinical tests only. Germane abstracts were categorized by translation phase and test purpose as per GTR typology.

3. Rubinstein WS, Maglott DR, Lee JM, et al. The NIH genetic testing registry: a new, centralized database of genetic tests to enable access to comprehensive information and improve transparency. *Nucleic Acids Research.* 2013;41(D1):D925-D935.
4. https://osp.od.nih.gov/scientific-sharing/genetic-testing-registry/

Results

- A total of 181 abstracts were identified, 18 duplicates were removed, and 63 relevant abstracts were identified.

  - All 63 abstracts were archived.

- GTR contained 53,994 tests for 11,011 conditions, 5,275 genes, from 503 laboratories (as of March 18, 2018).

Figure 1 shows the number of projects initiated each year and the size of the GTR. While no projects have been initiated since 2008, the number of tests in the GTR has steadily risen since its creation in 2012.


Figure 1. Number of Tests and Project Initial Year
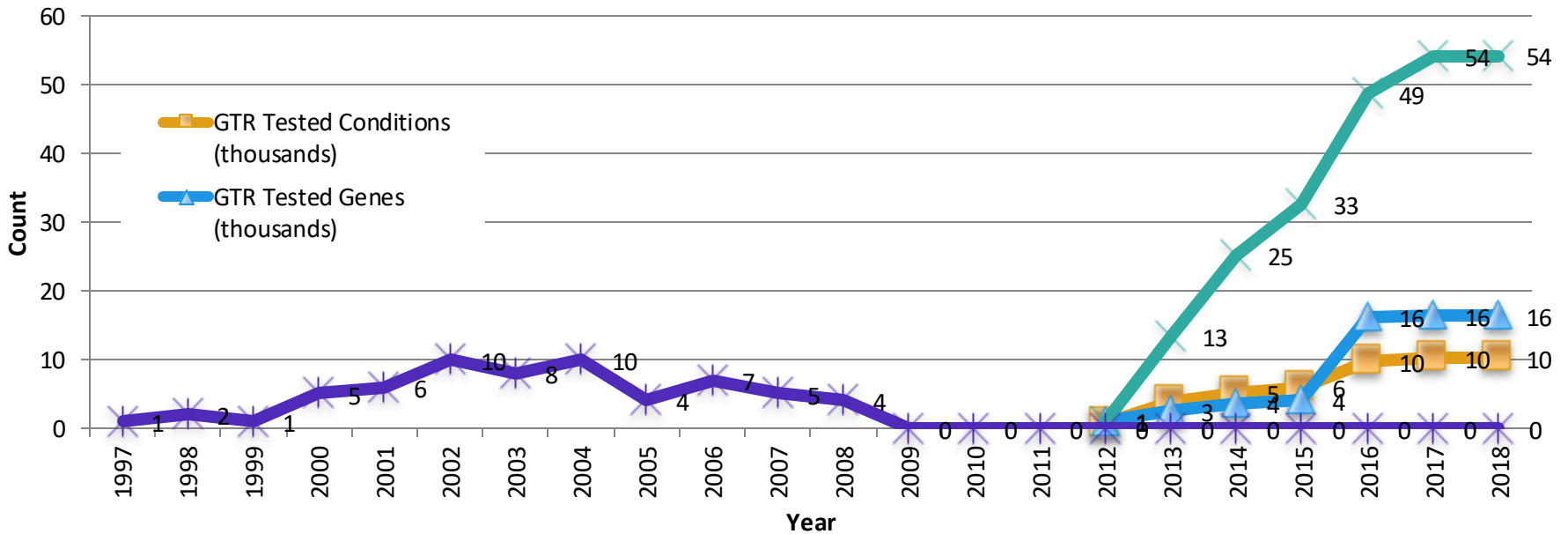
Proposed research in each abstract was classified as T1 (n=18), T2 (n=31), T3 (n=14), while no T4 studies were identified (Figure 2).

Most evaluations were of diagnostic tests (n=25) and predictive tests (n=18), followed by therapeutic management (n=9), mutation confirmation (n=7), pre-implantation genetic diagnosis (n=2), and pre-symptomatic detection (n=2).

Figure 2. Evaluation Research by Translation Stage
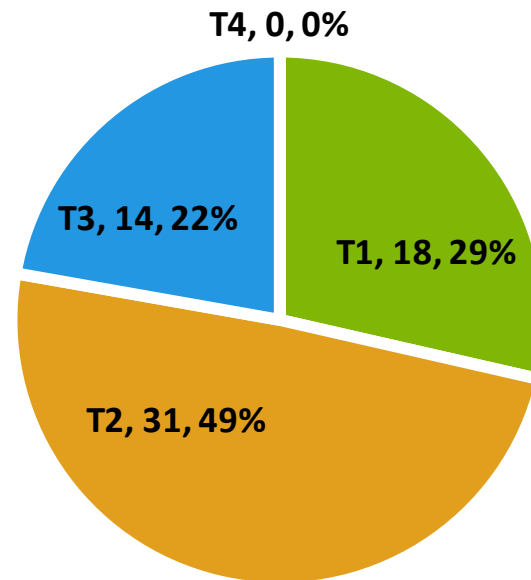
Figure 3. Tests and Evaluations According to Test Purpose
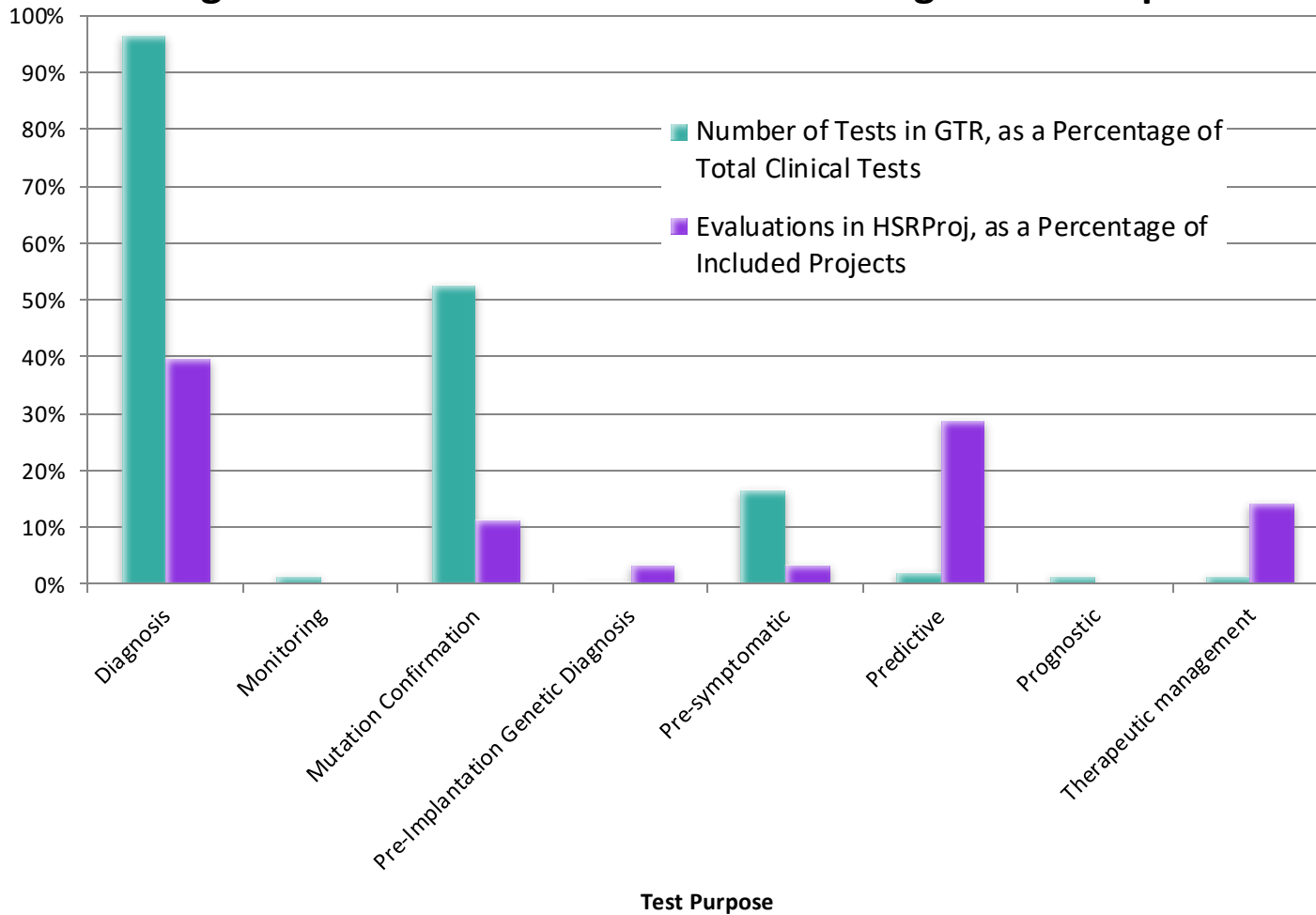
Number of evaluations relevant to each test type is compared to the number of tests of each type currently in the GTR in Figure 3. The proportion of evaluations for therapeutic management and predictive tests is relatively higher than the proportion of tests available.

Corroborating Findings – Systematic Literature Reviews

■ Overall, systematic reviews conclude lack of consistent measurement of outcomes, clinical utility, and economic evaluation; need for increased HSR research of genetic tests

Payne K, Gavan SP, Wright SJ, Thompson AJ. Cost-effectiveness analyses of genetic and genomic diagnostic tests. *Nature Reviews Genetics*. 2018;19:235.
"It is now time to direct funding to support the empirical research needed to develop the use of decision analytic model-based CEAs of genomic tests while being cognizant of the known methodological, technical, practical and organizational challenges to maximize the potential benefits to patient populations."

Phillips KA, Deverka PA, Sox HC, et al. Making genomic medicine evidence-based and patient-centered: a structured review and landscape analysis of comparative effectiveness research. *Genetics In Medicine*. 2017;19:1081.
"In summary, we found a very limited body of evidence about the effect of using genomic tests on health outcomes and many evidence gaps for CER to address."

Schwarze K, Buchanan J, Taylor JC, Wordsworth S. Are whole-exome and whole-genome sequencing approaches cost-effective? A systematic review of the literature. *Genetics In Medicine*. 2018.
"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. "

Smith HS, Swint, JM, Lalani, SR, Yamal, J-M. de Oliveira Otto MC, Castellanos S, Taylor A, Lee BH, Russell HV. Clinical Application of Whole Genome and Whole Exome Sequencing as a Diagnostic Tool: A Scoping Review of the Literature. Forthcoming *Genet Med*.
Lack of consistent outcome measurement, clinical utility assessment, robust economic evaluation

Conclusion

- Genetic tests are increasingly available; however, HSR lags behind.

- HSR on stages T2-T4 is needed to inform the evidence-based use of genetic tests and study the population health impact of these costly yet promising tools.

- Evaluation of genetic services is critical in the development of clinical policy and payer policy, which, in turn, influence clinical uptake.

- Given the identified gap in HSR research, evaluations of genetic services should be prioritized to keep pace with availability and use.