THE EVALUATION AND THE IMPLEMENTATION OF GENETIC/GENOMIC APPLICATIONS: AN HEALTH TECHNOLOGY ASSEMENT EXERCISE?

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PRECeDI Recomendations

Domain 2
Economic evaluation of predictive genomic applications

Domain 5
Identification of organizational models for the provision of predictive genomic applications

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“A multidisciplinary field concerned with the effective and responsible translation of genome-based knowledge and technologies to improve population health” (Bellagio Statement, 2006)

As genome-based research generates new ideas for healthcare innovation, there is a critical need for an evaluation process, based in ongoing integration of knowledge within and across multiple disciplines (including ELSI) to determine the outcomes, both health-related and social, of new genome based applications. In the absence of a robust evaluation strategy, a trial-and-error process of innovation occurs. Resulting commercial incentives tend to promote the value of genetic tests based on the intuitive appeal of risk knowledge in the absence of proven benefit. This approach is already evident in direct-to-consumer and -physician marketing of genetic tests, and represents a potential drain on healthcare resources.

There is also a risk that effective innovations will not be implemented, or implemented haphazardly

Burke, 2006
INAPPROPRIATE USE vs CITIZENS’ RIGHTS

GENETIC/GENOMIC APPLICATIONS SHOULD BE EVALUATED RIGOROUSLY BEFORE ENTERING INTO CLINICAL AND PUBLIC HEALTH PRACTICE

GENETIC/GENOMIC APPLICATIONS WITH PROVED EFFICACY AND COST-EFFECTIVENESS SHOULD BECOME CITIZENS’ RIGHTS
FROM THE EVALUATION TO THE EVALUATION FOR MANAGEMENT AND DELIVERY

Expanding the scientific basis of health technology assessment: A research agenda for the next decade

Renaldo N. Battista
University of Montreal

HTA has evolved through three distinct phases: the machine, the clinical outcomes, and the delivery models, with the third of these still under way. As the focus has shifted from a single machine to choosing among interventions for specific disease conditions to service delivery approaches, HTA has drawn on research and modes of discourse from a growing variety of disciplines.

Battista, 2006
29 tools published between 2000 and 2017 (USA n.12, Canada n.4, Europe n.9, Australia n.2, International n.2).

They are mostly based on the ACCE model (n.13 tools) and on the HTA model (n.6 tools) or both (n.2 tools).

17 tools address all types of genetic test, while the others take into account a specific type of genetic test (newborn screening, predictive genetic tests, genetic susceptibility tests).
RESULTS - Evaluation components and methodological aspects

<table>
<thead>
<tr>
<th>Evaluation components</th>
<th>N (29)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overview diseases/last under study</td>
<td>25</td>
<td>86</td>
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<tr>
<td>Analytic validity</td>
<td>27</td>
<td>93</td>
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<tr>
<td>Clinical validity</td>
<td>28</td>
<td>96</td>
</tr>
<tr>
<td>Clinical utility</td>
<td>29</td>
<td>100</td>
</tr>
<tr>
<td>Ethical, legal and social implications</td>
<td>22</td>
<td>76</td>
</tr>
<tr>
<td>Delivery models</td>
<td>8</td>
<td>27</td>
</tr>
<tr>
<td>Organizational aspects</td>
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<td>52</td>
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<tr>
<td>Economic evaluation</td>
<td>29</td>
<td>100</td>
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<tr>
<td>Patient/citizen’s point of view</td>
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<table>
<thead>
<tr>
<th>Methodological aspects</th>
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<td>Format</td>
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<tr>
<td>Key questions</td>
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<td>41</td>
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<tr>
<td>Card</td>
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<td>17</td>
</tr>
<tr>
<td>Checklist</td>
<td>2</td>
<td>7</td>
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<tr>
<td>Set of principle/methodological guidance</td>
<td>10</td>
<td>34</td>
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<tr>
<td>Evidence collection and evaluation</td>
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<tr>
<td>Source of evidence</td>
<td>13</td>
<td>45</td>
</tr>
<tr>
<td>Quality of the evidence</td>
<td>12</td>
<td>41</td>
</tr>
<tr>
<td>Evidence gaps/research priorities</td>
<td>12</td>
<td>41</td>
</tr>
<tr>
<td>Recommendations</td>
<td>5</td>
<td>17</td>
</tr>
</tbody>
</table>

Most used evaluation criteria are analytic and clinical validity, clinical utility and ethical, legal and social implications.

The economic dimension is always considered even if in little detail.

Attention for delivery models, organizational aspects and consumer’s point of view is often lacking.

Only few models highlight research priorities or criteria to recommend the use of the test.
Overall structure

**Section I – The genetic test**
- Overview of the test and the clinical condition
- Analytic validity
- Clinical validity
- Clinical utility
- Personal utility

**Section II – Delivery of the genetic test**
- Overview of the delivery programs
- Organizational aspects
- Economic evaluation
- Ethical, legal and social implications
- Patient’s/individual’s point of view

**Section III – Research priorities**

**Section IV – Criteria to establish recommendations on the use of the genetic test**
- Net benefit of the delivery program
- Cost-effectiveness of the delivery program
- Organizational and feasibility aspects
GENETIC TEST vs GENETIC TEST PROGRAM

Genetic test program = Health care program including the genetic test

1. Target population
2. Genetic counseling
3. Genetic test
4. Diagnosis of carrier status
5. Health care pathway based on carrier status
Which BRCA genetic testing programs are ready for implementation in health care? A systematic review of economic evaluations

Elvira D’Andrea, MD,1, Carolina Marzuillo, BS,1 Corrado De Vito, MD,1 Marco Di Marco, MD,1 Erica Pitini, MD,1 Maria Rosaria Vacchio, BS,1 and Paolo Villari, MD, MPH1

Purposse: There is considerable evidence regarding the efficacy and effectiveness of BRCA genetic testing programs, but whether they represent good use of financial resources is not clear. Therefore, we aimed to identify the main health-care programs for BRCA testing and to evaluate their cost-effectiveness.

Methods: We performed a systematic review of all published economic evaluations of health care programs involving BRCA testing.

Results: Nine economic evaluations were identified. Two categories of BRCA testing programs were noted: population-based genetic screening of individuals at high risk for BRCA mutation; and (b) carrier-based genetic screening, i.e., testing individuals with a family history of BRCA-related cancer.

Conclusions: Currently, there are few population-based screening programs with known familial BRCA mutation, and (b) carrier-based genetic screening, i.e., testing individuals with an FB suggestive of BRCA mutation, is still not recommended.

The Cost-effectiveness of Genetic Screening for Familial Hypercholesterolemia: a Systematic Review

A. Rosso1, E. Pitini2, E. D’Andrea1, A. Massimi1, C. De Vito1, C. Marzuillo1, P. Villari1

Key words: Familial Hypercholesterolemia, cost-effectiveness, cost-utility, economic evaluation, genetic screening.

Purpose: Familial Hypercholesterolemia (FH) is a genetic disorder that leads to elevated plasma cholesterol concentrations, which increases the risk of cardiovascular disease (CVD). This study aimed to evaluate the cost-effectiveness of genetic screening programs for familial hypercholesterolemia: a systematic review of full economic evaluations that assessed the cost-effectiveness of genetic screening programs for FH.

Methods: We performed a systematic review of full economic evaluations of genetic screening for FH in different target populations. We included studies that were published in peer-reviewed journals and that reported on the cost-effectiveness of genetic screening programs for FH.

Results: Overall, 20 studies were included in the systematic review. Based on the study populations, we identified six categories of FH screening programs: universal screening, age-targeted screening, and combination screening. In five studies, universal programs were effective, and in combination with the BRCRAF test, were cost-effective compared to no screening, while in two studies age-targeted programs plus universal programs were cost-effective.

Conclusion: Universal or age-targeted FH screening programs are cost-effective and should be implemented in the “real world.”

Key words: genetic screening, cost-effectiveness, FH screening programs, systematic review.
DELIVERY MODELS

Definition

THE BROAD CONTEXT WITHIN THE PHG FRAMEWORK IN WHICH GENETIC SERVICES ARE OFFERED TO INDIVIDUALS AND FAMILIES WITH OR AT RISK OF GENETIC DISORDERS

In other words, a genetic delivery model is a combination of personal healthcare services provided by healthcare professionals to individuals and families (i.e., diagnosis, treatment/management, and information) and PH services and functions (i.e., population screening, financing, policy development, workforce education, information/citizen empowerment, service evaluation, and research).
DELIVERY MODELS FOR GENETIC TESTS (I)

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Original Paper
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Genetics in Health Care: An Overview of Current and Emerging Models

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Abstract
Background: With advances in genetic and genomic medicine, the optimal integration of genetic services into the health care system remains of major concern in many countries. Objectives: To review the current organisation of genetic services, mostly in Europe, North America and Australia, explore emerging service delivery models, and probe challenges inherent in the transition process. Methods: We conducted a literature review of genetics in clinical practice: testing, diagnosis, counselling, and treatment. We examined the basic structures of genetic services, examples of integrated networks, and existing professional resources. We investigated services belonging traditionally in medical genetics as well as those developed for more common diseases. Results: Multidisciplinary specialist clinics and coordinated services appeared to be key to delivering proper care in rare genetic disorders. For oncogenetics, neurogenetics and cardiogenetics, interprofessional collaboration between geneticists and other specialists seemed to be favoured. On the other hand, there was also a tendency toward the integration of genetic services directly into primary care. Among the most pressing challenges was the merging of paediatric care into adult care. Conclusion: The coordination of activities between professionals in first-, second- and third-line medical care is a primary objective calling for the reconfiguration of professional roles and responsibilities. This entails the forging of new relationships as well as an enhanced sharing of expertise and genetic information, including information regarding services. Barriers to overcome include the redistribution of roles, sharing of data and databases, and the lack of preparedness of non-genetics professionals and of the health care system in general.

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Identification of Delivery Models for the Provision of Predictive Genetic Testing in Europe: Protocol for a Multicentre Qualitative Study and a Systematic Review of the Literature

Brigid Unimir, Tyra Lagerberg, Erica Pittini, Corrado De Vito, Maria Rosaria Vacchlo, Giovanna Adamo, Annalisa Rosso, Elvira D'Andrea, Carolina Marzullo and Paolo Villari

1 Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy; 2 Better Value HealthCare, Ltd., Oxford, United Kingdom

Introduction: The appropriate application of genomic technologies in healthcare is surrounded by many concerns. In particular, there is a lack of evidence on what constitutes an optimal genetic service delivery model, which depends on the type of genetic test and healthcare context considered. The present project aims to identify, classify, and evaluate delivery models for the provision of predictive genetic testing in Europe and in selected Anglophone extra-European countries (the USA, Canada, Australia, and New Zealand). It also sets out to survey the European public health community's readiness to incorporate public health genomics into their practice.
OUR CLASSIFICATION

- **GENETICISTS MODEL**
  - Patient - GP/medical specialist - Counsellor - Lab
  - Patient - Counsellor - Lab

- **PRIMARY CARE MODEL**
  - Patient - GP - Counsellor - Lab
  - Patient - GP - Lab

- **MEDICAL SPECIALIST MODEL**
  - Patient - Medical specialist - Lab
  - Patient - Medical specialist - Counsellor - Lab

- **POPULATION SCREENING PROGRAMMES MODEL**
  - Patient - GP/Medical specialist - Counsellor - Lab
  - Patient - GP/Medical specialist - Lab
  - Patient - Counsellor - Lab

- **DIRECT TO CONSUMER (DTC) MODEL**
  - Patient - Lab
  - Virtual clinic
DELIVERY MODELS IDENTIFIED IN THE LITERATURE

**BRCA1/2**
- Model I: Genetic services led by geneticists
- Model II: Primary care model
- Model III: Medical specialists model
- Model IV: Genetic services integrated into population screening programs
- Model V: Direct-to-consumer (DTC) model

**Lynch syndrome**
- Model I: Genetic services led by geneticists
- Model II: Primary care model
- Model III: Medical specialists model
- Model IV: Genetic services integrated into population screening programs
- Model V: Direct-to-consumer (DTC) model

**Familial hypercholesterolemia**
- Model I: Genetic services led by geneticists
- Model II: Primary care model
- Model III: Medical specialists model
- Model IV: Genetic services integrated into population screening programs
- Model V: Direct-to-consumer (DTC) model
IMPLEMENTATION ISSUES
PHARMACOGENETICS VS PREDICTIVE GENETIC TESTS

PREDICTIVE GENETIC TESTS

• PHYSICIANS AND OTHER PHG PROFESSIONALS
• TRAINING
• GUIDELINES
• LABS
• HEALTH CARE INTERVENTIONS

Health promotion
Preventive measures
Public health services

Treatments

PHARMACOGENETICS

PRECeDI
Prevention of Chronic Diseases of Diabetic Patients
Why this survey?

• 2003 Human Genome Project debate on the utility of genomic science for public health purposes

• Public health genomics (PHG): diverting resources or providing useful prevention opportunities?

Aim of the survey
To assess the attitudes of European Public Health (PH) professionals belonging to EUPHA network regarding their role in the implementation of PHG, and their knowledge and attitudes regarding genetic testing and the delivery of genetic services.
# RESPONDENTS

493 Respondents
382 Completed the survey

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
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</tr>
<tr>
<td>Female</td>
<td>245 (56.2)</td>
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<tr>
<td>Male</td>
<td>191 (43.8)</td>
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<tr>
<td><strong>Age</strong></td>
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</tr>
<tr>
<td>25-40</td>
<td>120 (29.7)</td>
</tr>
<tr>
<td>41-55</td>
<td>179 (41.1)</td>
</tr>
<tr>
<td>56-75</td>
<td>127 (29.2)</td>
</tr>
<tr>
<td><strong>Type of health professional</strong></td>
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<tr>
<td>PH professional not involved in PHG</td>
<td>153 (75.0)</td>
</tr>
<tr>
<td>PH professional involved in PHG</td>
<td>26 (12.7)</td>
</tr>
<tr>
<td>Not PH professional not involved in PHG</td>
<td>22 (10.8)</td>
</tr>
<tr>
<td>Not PH professional involved in PHG</td>
<td>3 (1.5)</td>
</tr>
<tr>
<td><strong>Area of degree</strong></td>
<td></td>
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<tr>
<td>Medicine</td>
<td>212 (50.5)</td>
</tr>
<tr>
<td>Health professions (e.g nursing)</td>
<td>35 (8.3)</td>
</tr>
<tr>
<td>Biology</td>
<td>27 (6.4)</td>
</tr>
<tr>
<td>Public health</td>
<td>56 (12.3)</td>
</tr>
<tr>
<td>Other (e.g. statistics, political sciences)</td>
<td>90 (21.4)</td>
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<tr>
<td><strong>Sector of work</strong></td>
<td></td>
</tr>
<tr>
<td>Academic</td>
<td>322 (65.3)</td>
</tr>
<tr>
<td>Hospital</td>
<td>22 (4.4)</td>
</tr>
<tr>
<td>Government (national or local)</td>
<td>74 (15.0)</td>
</tr>
<tr>
<td>Public health service</td>
<td>33 (6.7)</td>
</tr>
<tr>
<td>Other (e.g. NGO, technical agency)</td>
<td>42 (8.5)</td>
</tr>
<tr>
<td><strong>Information on genetic screening in undergraduate training</strong></td>
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<tr>
<td>Yes</td>
<td>182 (43.4)</td>
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<tr>
<td>No</td>
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<tr>
<td><strong>Information on genetic screening in postgraduate training</strong></td>
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<td>184 (47.1)</td>
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<td>No</td>
<td>198 (43.8)</td>
</tr>
<tr>
<td>Not applicable</td>
<td>38 (9.3)</td>
</tr>
</tbody>
</table>

+44 non EU
RESULTS

• The analysis shows a low level of knowledge on PHG among EUPHA members, while attitudes on the use of genetic testing and genetic services and on the possible roles of PH professionals in PHG are generally positive.

• Positive attitudes are associated with higher level of knowledge and younger age.

• *Initiatives to increase culture on PHG among EUPHA members may contribute to fostering the incorporation of genomic applications in PH activities.*
CONCLUSIONS

- Genetic/genomic applications: inappropriate use vs citizens’ rights
- Need of an Health Technology Assessment approach
- Systematic reviews of economic evaluations are important
- Culture and training are strategic