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THE EVALUATION AND THE IMPLEMENTATION OF GENETIC/GENOMIC APPLICATIONS:

AN HEALTH TECHNOLOGY ASSEMENT EXERCISE?

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The PRECeDI project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 645740.

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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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PRECeDI Recomendations

Domain 2

EVALUATION

Domain 5

IMPLEMENTATION

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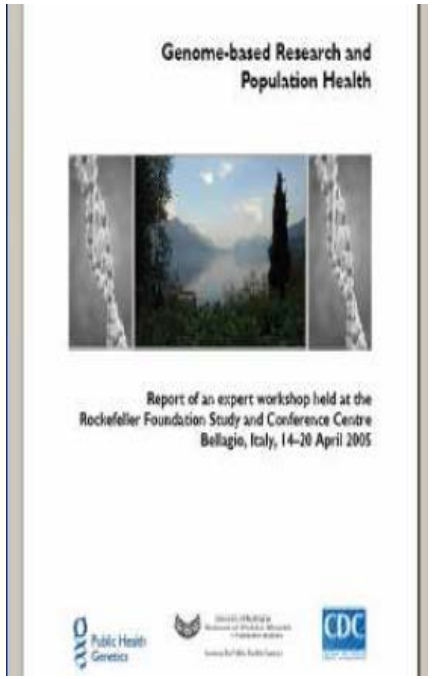
GENOMICS IN PUBLIC HEALTH

"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

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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

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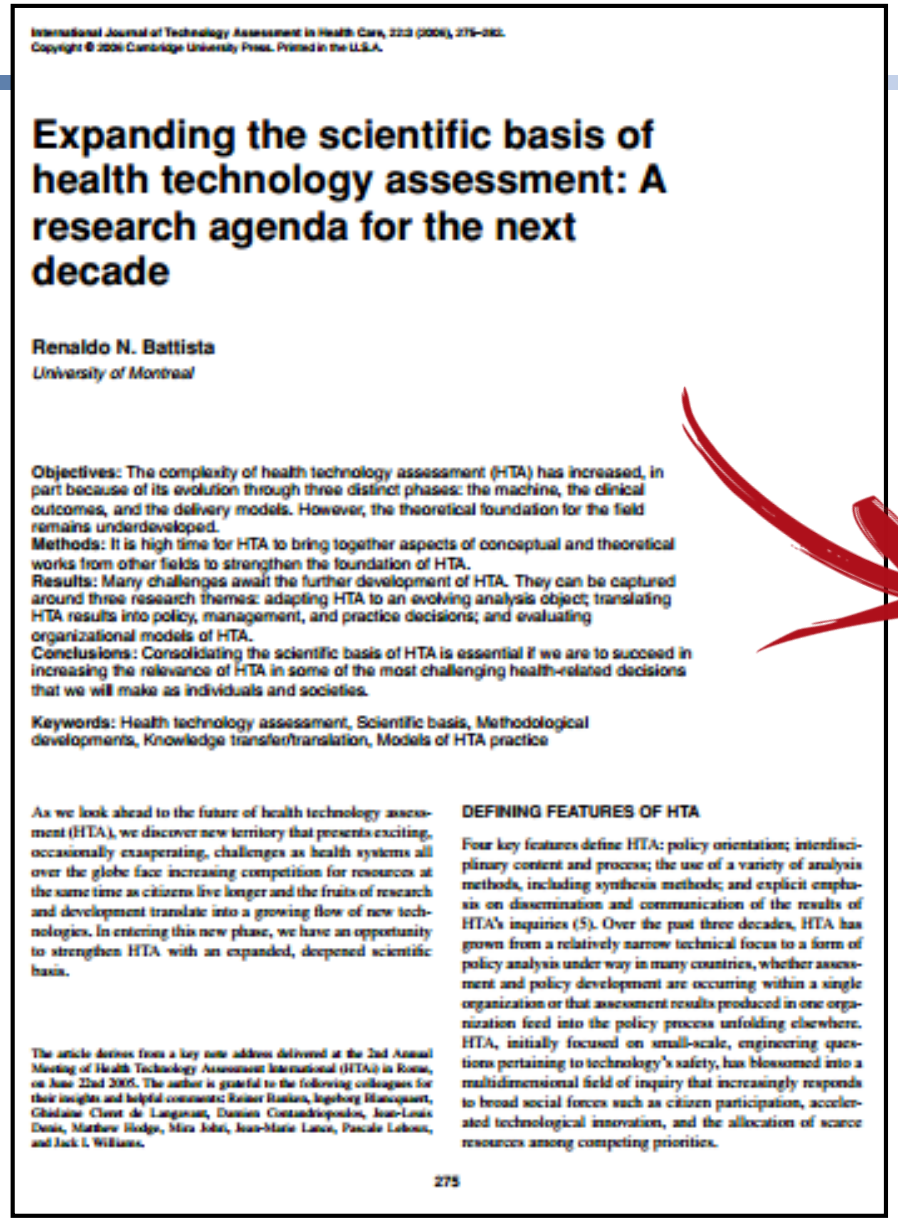
FROM THE EVALUATION TO THE EVALUATION FOR MANAGEMENT AND DELIVERY



International Journal of Technology Assessment in Health Care, 22:3 (2006), 275–282.

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

Renaldo N. Battista
University of Montreal

Objectives: The complexity of health technology assessment (HTA) has increased, in part because of its evolution through three distinct phases: the machine, the clinical outcomes, and the delivery models. However, the theoretical foundation for the field remains underdeveloped.
Methods: It is high time for HTA to bring together aspects of conceptual and theoretical works from other fields to strengthen the foundation of HTA.
Results: Many challenges await the further development of HTA. They can be captured around three research themes: adapting HTA to an evolving analysis object; translating HTA results into policy, management, and practice decisions; and evaluating organizational models of HTA.
Conclusions: Consolidating the scientific basis of HTA is essential if we are to succeed in increasing the relevance of HTA in some of the most challenging health-related decisions that we will make as individuals and societies.

Keywords: Health technology assessment, Scientific basis, Methodological developments, Knowledge transfer/translation, Models of HTA practice

As we look ahead to the future of health technology assessment (HTA), we discover new territory that presents exciting, occasionally exasperating, challenges as health systems all over the globe face increasing competition for resources at the same time as citizens live longer and the fruits of research and development translate into a growing flow of new technologies. In entering this new phase, we have an opportunity to strengthen HTA with an expanded, deepened scientific basis.

The article derives from a key note address delivered at the 2nd Annual Meeting of Health Technology Assessment International (HTAi) in Rome, on June 22nd 2005. The author is grateful to the following colleagues for their insights and helpful comments: Reiner Banken, Ingeborg Blanquaert, Ghislaine Clerc de Langavant, Damien Contandriopoulos, Jean-Louis Denis, Matthew Hodge, Mira Johri, Jean-Marie Lance, Pascale Lehoux, and Jack L. Williams.

DEFINING FEATURES OF HTA

Four key features define HTA: policy orientation; interdisciplinary content and process; the use of a variety of analysis methods, including synthesis methods; and explicit emphasis on dissemination and communication of the results of HTA's inquiries (5). Over the past three decades, HTA has grown from a relatively narrow technical focus to a form of policy analysis under way in many countries, whether assessment and policy development are occurring within a single organization or that assessment results produced in one organization feed into the policy process unfolding elsewhere. HTA, initially focused on small-scale, engineering questions pertaining to technology's safety, has blossomed into a multidimensional field of inquiry that increasingly responds to broad social forces such as citizen participation, accelerated technological innovation, and the allocation of scarce resources among competing priorities.

[…] *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

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https://doi.org/10.1038/s41431-018-0095-5

ESHG

REVIEW ARTICLE

How is genetic testing evaluated? A systematic review of the literature

Erica Pitini[1] · Corrado De Vito[1] · Carolina Marzuillo[1] · Elvira D'Andrea[1,2] · Annalisa Rosso[1] · Antonio Federici[3] · Emilio Di Maria[4] · Paolo Villari[1]

Received: 22 May 2017 / Revised: 7 November 2017 / Accepted: 19 December 2017

Abstract

Given the rapid development of genetic tests, an assessment of their benefits, risks, and limitations is crucial for public health practice. We performed a systematic review aimed at identifying and comparing the existing evaluation frameworks for genetic tests. We searched PUBMED, SCOPUS, ISI Web of Knowledge, Google Scholar, Google, and gray literature sources for any documents describing such frameworks. We identified 29 evaluation frameworks published between 2000 and 2017, mostly based on the ACCE Framework ($n = 13$ models), or on the HTA process ($n = 6$), or both ($n = 2$). Others refer to the Wilson and Jungner screening criteria ($n = 3$) or to a mixture of different criteria ($n = 5$). Due to the widespread use of the ACCE Framework, the most frequently used evaluation criteria are analytic and clinical validity, clinical utility and ethical, legal and social implications. Less attention is given to the context of implementation. An economic dimension is always considered, but not in great detail. Consideration of delivery models, organizational aspects, and consumer viewpoint is often lacking. A deeper analysis of such context-related evaluation dimensions may strengthen a comprehensive evaluation of genetic tests and support the decision-making process.

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).

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RESULTS - Evaluation components and methodological aspects

	N (29)	%
Evaluation components		
Overview disease/test under study	25	86
Analytic validity	27	93
Clinical validity	28	96
Clinical utility	29	100
Ethical, legal and social implications	22	76
Delivery models	8	27
Organizational aspects	15	52
Economic evaluation	29	100
Patient/citizen's point of view	2	7
Methodological aspects		
Format		
Key questions	12	41
Card	5	17
Checklist	2	7
Set of principle/methodological guidance	10	34
Evidence collection and evaluation		
Source of evidence	13	45
Quality of the evidence	12	41
Evidence gaps/research priorities	12	41
Recommendations	5	17

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.

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GENETIC TESTS EVALUATION FRAMEWORK

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

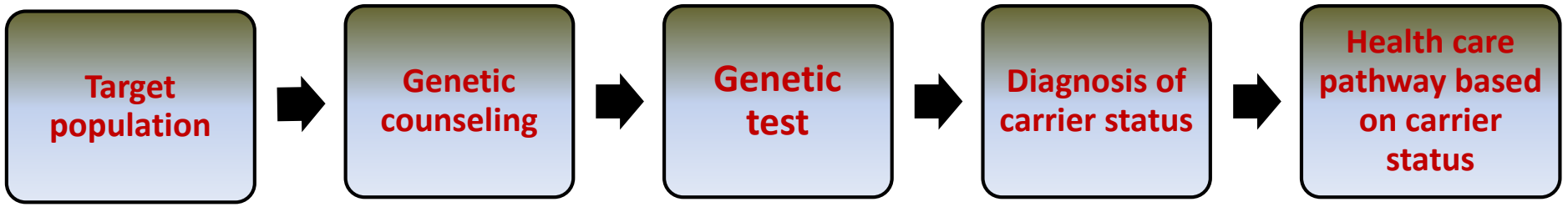
Net benefit of the delivery program

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



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GENETIC TESTING PROGRAMS

Official journal of the American College of Medical Genetics and Genomics

SYSTEMATIC REVIEW | Genetics inMedicine

Open

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, MPH[1]

Purpose: 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 re
uations of health-care programs involving

Results: Nine economic evaluations wer
categories of *BRCA* testing programs wer
based genetic screening of individuals w
prehensive or targeted based on ancestry
based genetic screening, i.e., testing indi
with FH suggestive of *BRCA* mutation; (i
based genetic screening, i.e., testing indi

with known familial *BRCA* mutation; and (iv) cancer-based genetic screening, i.e., testing individuals with *BRCA*-related cancers.

Conclusions: Currently *BRCA1/2* population-based screening rep-
resents good value for the money among Ashkenazi Jews only. FH-

Ann Ig 2017; 29: 464-480 doi:10.7416/ai.2017.2178

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

A. Rosso[1], E. Pitini[1], E. D'Andrea[1], A. Massimi[1], C. De Vito[1], C. Marzuillo[1], P. Villari[1]

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

Parole chiave: Ipercolesterolemia familiare, costo-efficacia, costo-utilità, valutazione economica, screening, test genetico.

Abstract

olemia (FH) is a genetic disorder that leads to elevated plasma coronary heart disease (CHD). An understanding of the mutations s of statins in lowering the risk of CHD in FH patients has increased to improve FH diagnosis. In this study, we aimed to evaluate the

view of full economic evaluations that assessed the cost-effectiveness used relevant search terms to investigate Medline, Scopus, Web of Reviews of Effects, the Health Technology Assessment Database, and Evaluation Database. Data extraction and assessment of the quality dently by two reviewers. The key features of the included studies are

evaluations that assessed the cost-effectiveness of genetic screening tween 2002 and 2015. Most studies had a no-screening strategy as a ex cases with genetic or clinical diagnosis of FH (cascade screening), pted a health care payer viewpoint. Cascade screening, based on case with confirmed clinical or genetic diagnosis of FH, was shown

cost-effectiveness of cascade genetic screening for the diagnosis of to assess the cost-effectiveness of cascade screening following the erapeutic regimes and next-generation sequencing.

Official journal of the American College of Medical Genetics and Genomics

SYSTEMATIC REVIEW | Genetics inMedicine

Open

Which Lynch syndrome screening programs could be implemented in the "real world"? A systematic review of economic evaluations

Marco Di Marco, MD[1], Elvira D'Andrea, MD, MPH[1,2], Nikola Panic, MD, PhD[3,4], Valentina Baccolini, MD[1], Giuseppe Migliara, MD[1], Carolina Marzuillo, BS[1], Corrado De Vito, MD, PhD[1], Roberta Pastorino, MSc, PhD[4], Stefania Boccia, MSc, PhD[5] and Paolo Villari, MD, MPH[1]

Purpose: Lynch syndrome (LS) screening can significantly reduce cancer morbidity and mortality in mutation carriers. Our aim was to identify cost-effective LS screening programs that can be implemented in the "real world."

Methods: We performed a systematic review of full economic evaluations of genetic screening for LS in different target populations; health outcomes were estimated in life-years gained or quality-adjusted life-years.

Results: Overall, 20 studies were included in the systematic review. Based on the study populations, we identified six categories of LS screening program: colorectal cancer (CRC)–based, endometrial cancer–based, general population–based, LS family registry–based, cascade testing–based, and genetics clinic–based screening programs. We performed an in-depth analysis of CRC-based LS programs, classifying them into three additional subcategories: universal, age-targeted, and selective. In five studies, universal programs based on immunohistochemistry, either alone or in combination with the *BRAF* test, were cost-effective compared with no screening, while in two studies age-targeted programs with a cutoff of 70 years were cost-effective when compared with age-targeted programs with lower age thresholds.

Conclusion: Universal or <70 years–age-targeted CRC-based LS screening programs are cost-effective and should be implemented in the "real world."

Genet Med advance online publication 4 January 2018

Key Words: colorectal cancer; cost-effectiveness; Lynch syndrome; screening program; systematic review

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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).

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DELIVERY MODELS FOR GENETIC TESTS (I)

Original Paper

Public Health Genomics

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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 morphing 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.

frontiers in Public Health

PROTOCOLS
published: 22 August 2017
doi: 10.3389/fpubh.2017.00223

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 Unim[1], Tyra Lagerberg[2], Erica Pitini[1], Corrado De Vito[1], Maria Rosaria Vacchio[1], Giovanna Adamo[1], Annalisa Rosso[1], Elvira D'Andrea[1], Carolina Marzuillo[1] and Paolo Villari[1]*

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OPEN ACCESS

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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.

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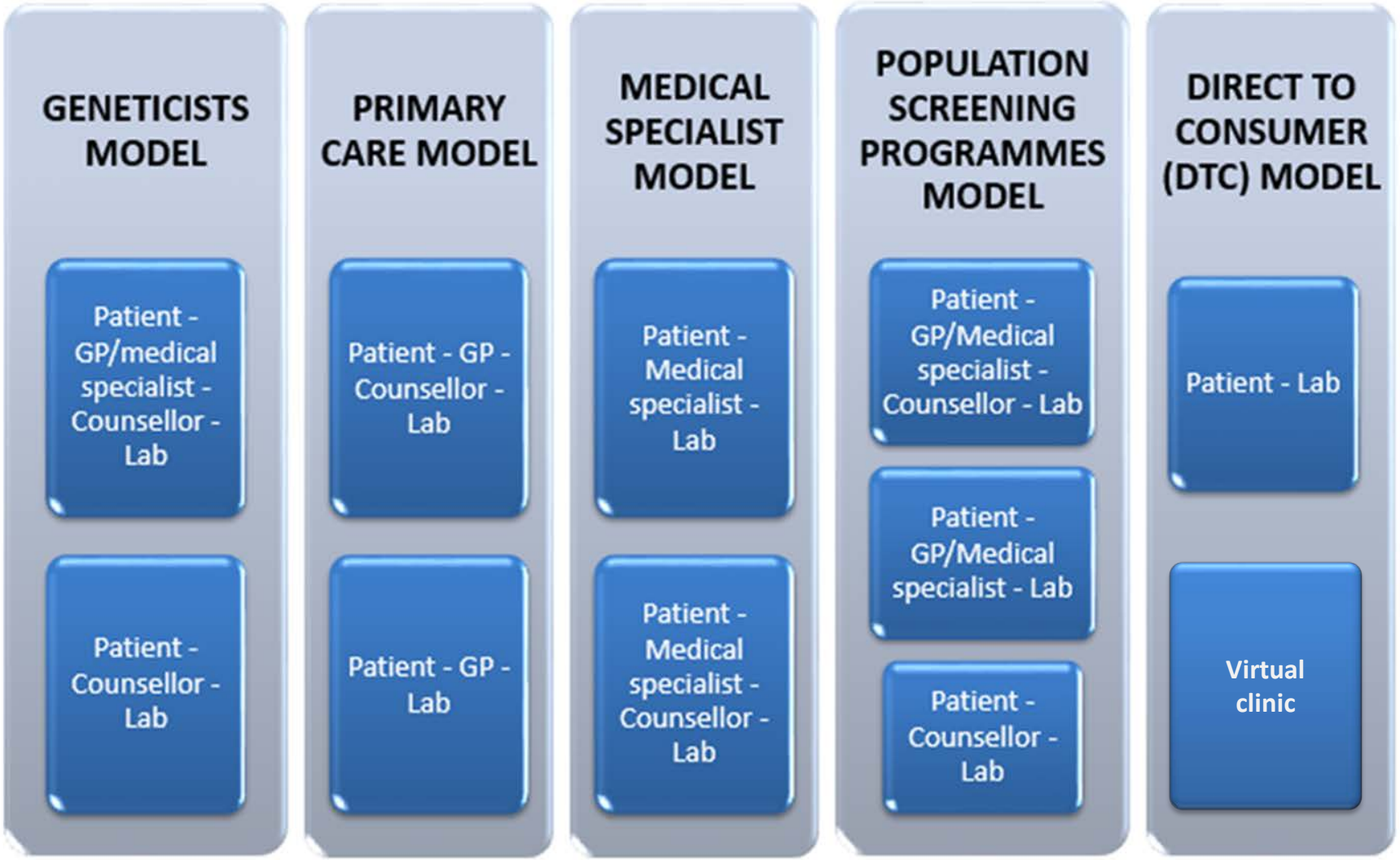
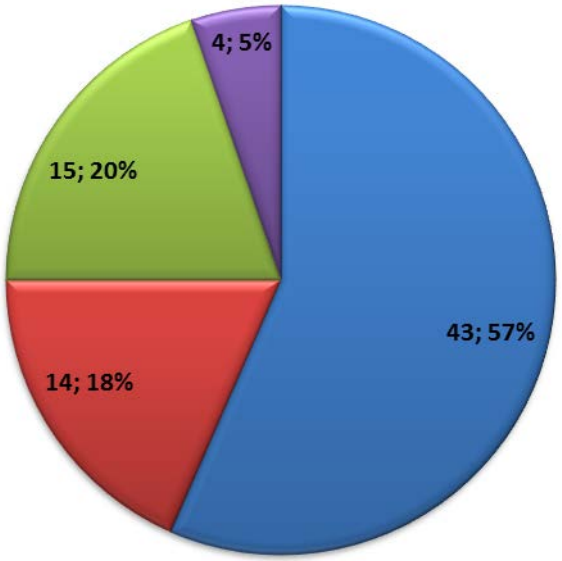
OUR CLASSIFICATION

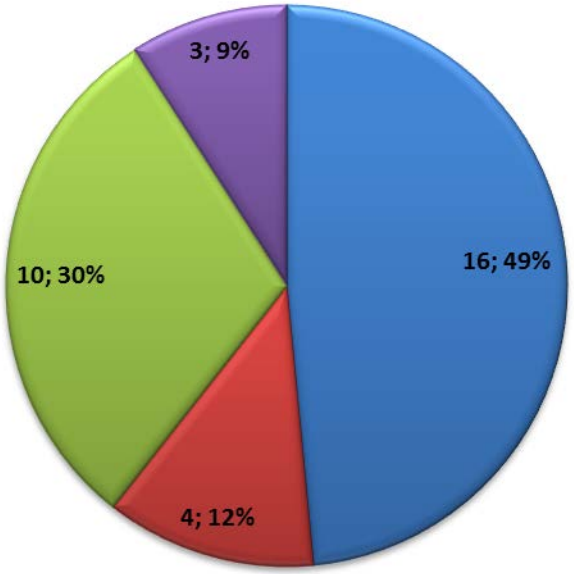


DELIVERY MODELS IDENTIFIED IN THE LITERATURE

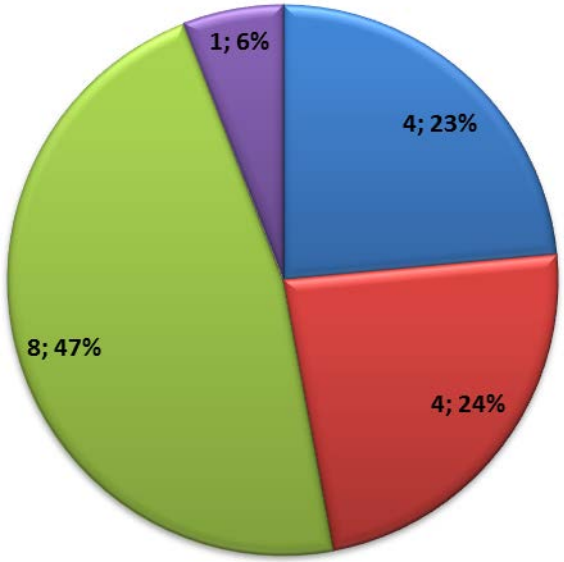
BRCA1/2



Lynch syndrome



Familial hypercholesterolemia



Model I Model II Model III Model IV

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

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IMPLEMENTATION ISSUES
PHARMACOGENETICS *vs* PREDICTIVE GENETIC TESTS

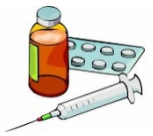
PREDICTIVE GENETIC TESTS

Health promotion
Preventive measures
Public health services

Treatments

PHARMACOGENETICS

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



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BARRIERS TO IMPLEMENTATION: THE EUPHA SURVEY

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.

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RESPONDENTS

493 Respondents
382 Completed the survey

+44 non EU

CHARACTERISTICS	N (%)
Gender	
Female	245 (56.2)
Male	191 (43.8)
Age	
25-40	120(29.7)
41-55	179 (41.1)
56-75	127 (29.2)
Type of health professional	
PH professional not involved in PHG	153 (75.0)
PH professional involved in PHG	26 (12.7)
Not PH professional not involved in PHG	22 (10.8)
Not PH professional involved in PHG	3 (1.5)
Area of degree	
Medicine	212 (50.5)
Health professions (e.g nursing)	35 (8.3)
Biology	27 (6.4)
Public health	56 (13.3)
Other (e.g. statistics, political sciences)	90 (21.4)
Sector of work	
Academic	322(65.3)
Hospital	22 (4.4)
Government (national or local)	74(15.0)
Public health service	33 (6.7)
Other (e.g. NGO, technical agency)	42 (8.5)
Information on genetic screening in undergraduate training	
Yes	182 (43.4)
No	237 (56.6)
Information on genetic screening in postgraduate training	
Yes	184 (47.1)
No	198 (43.8)
Not applicable	38 (9.1)

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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**

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