

# Public health genomics

João Lavinha

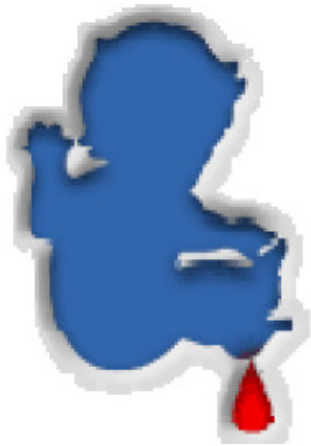
Departamento de Genética Humana

Instituto Nacional de Saúde Ricardo Jorge, Lisboa

[joao.lavinha@insa.min-saude.pt](mailto:joao.lavinha@insa.min-saude.pt)

# Outline

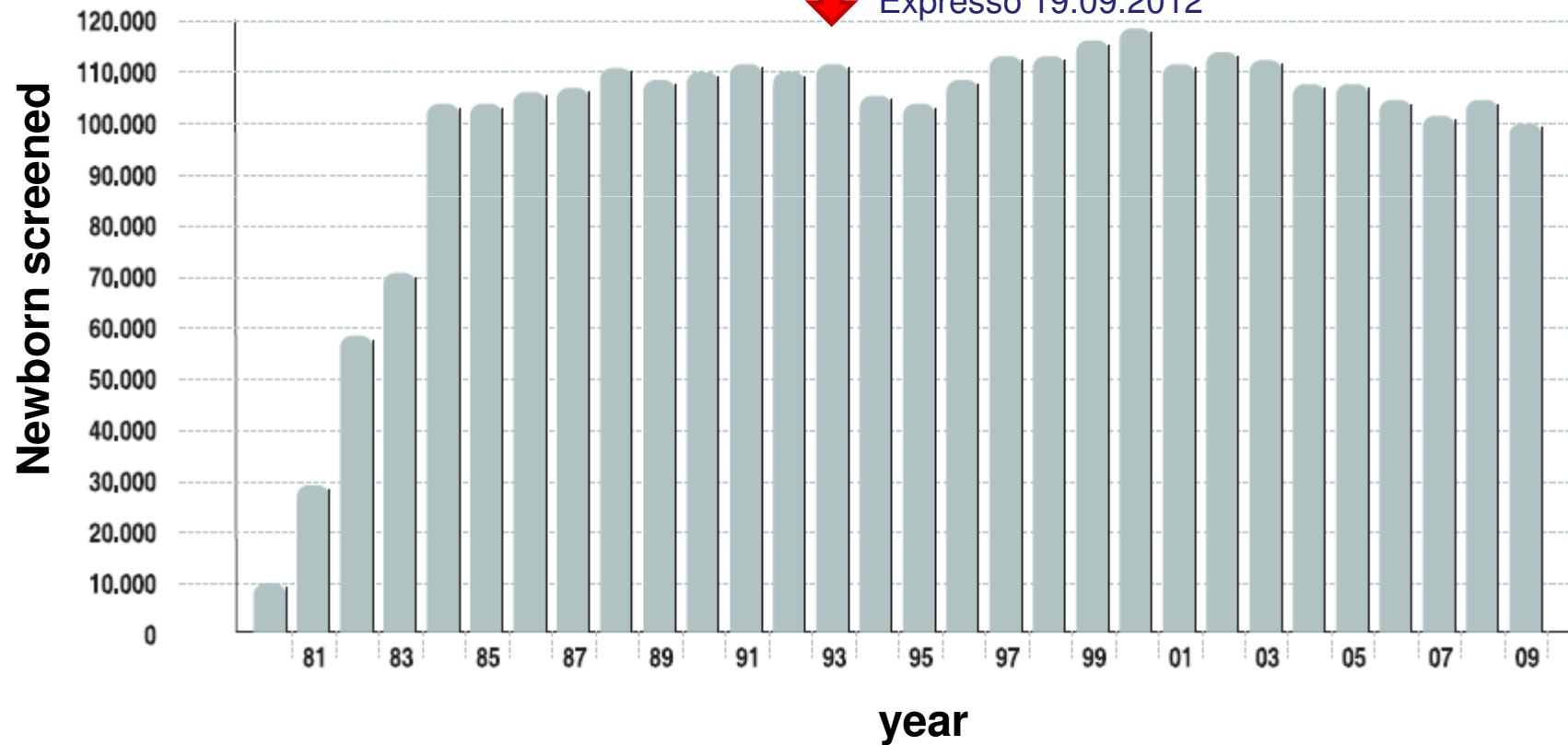
- Professional *genomic and molecular medicine and consumer genetics*
- The *health field* concept and the *public health wheel*
- The enterprise of Public Health Genomics (PHGEN)
- Genetic exceptionalism
- Ethical benchmarks
- Introduction and use of genome-based knowledge in the health services
- Stakeholder involvement



# Newborn screening towards an earlier diagnosis and treatment

Nascimentos continuam a descer:  
menos 5235 em Agosto do que em  
mês homólogo de 2011

Expresso 19.09.2012



# The dawn of professional genomic and molecular medicine

Inherited thrombotic risk factors (Factor V, Factor II, PAI-1, MTHFR).

Demand (DGH):

2006 – 310 samples

2007 – 389 samples

**How to turn the knowledge of the genetic profile into action to prevent/control disease?**

# Genes on the Web — Direct-to-Consumer Marketing of Genetic Testing or *Genetic horoscopes*?

A J Wolfberg. *NEJM* 2006;355:543-5.



# “The science from the lab to your living room”



## *MyCellf Program:*

A combined analysis of **nineteen genes** that may play an important role in how your body manages **bone health, heart health, antioxidant and detoxification function, insulin sensitivity and inflammation**. Perfect for those who want a complete snapshot of their overall health profile and recommendations for achieving **optimal health** without a specific disease focus.

Price: **\$269.00**

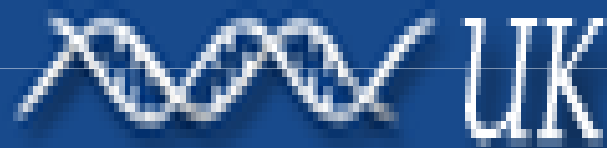


**23andMe** genetics just got personal.

A **web-based service** that helps you read and understand your DNA. After providing a saliva sample using an **at-home** kit, you can use our interactive tools to shed new light on your distant ancestors, your close family and most of all, yourself.

Discover how your genes may affect **your chances** of developing various **diseases** and **conditions**, as well as **traits** as athletic ability.

*Gene Watch*



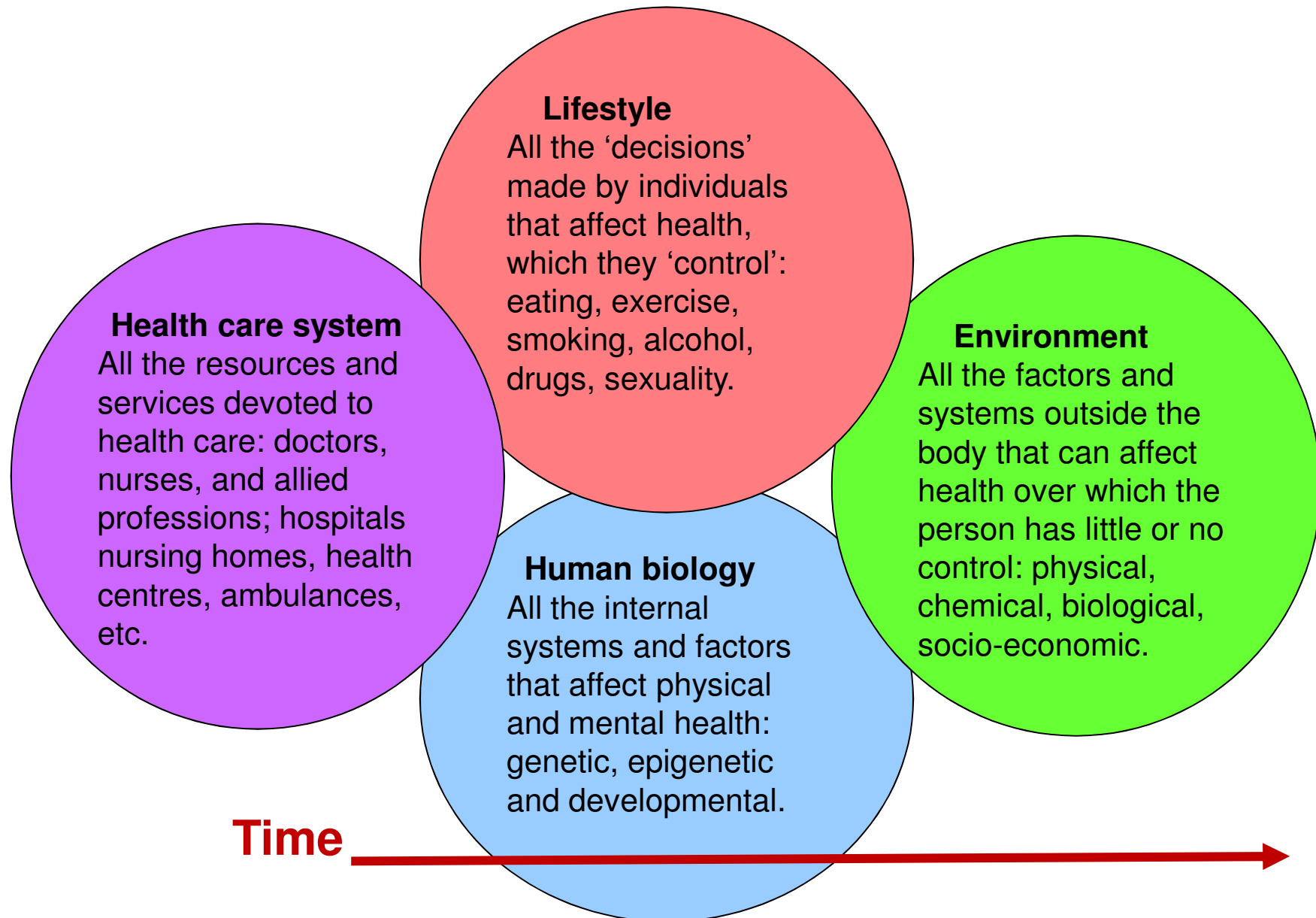
NicoTest:

**“Sales pitch not science”**

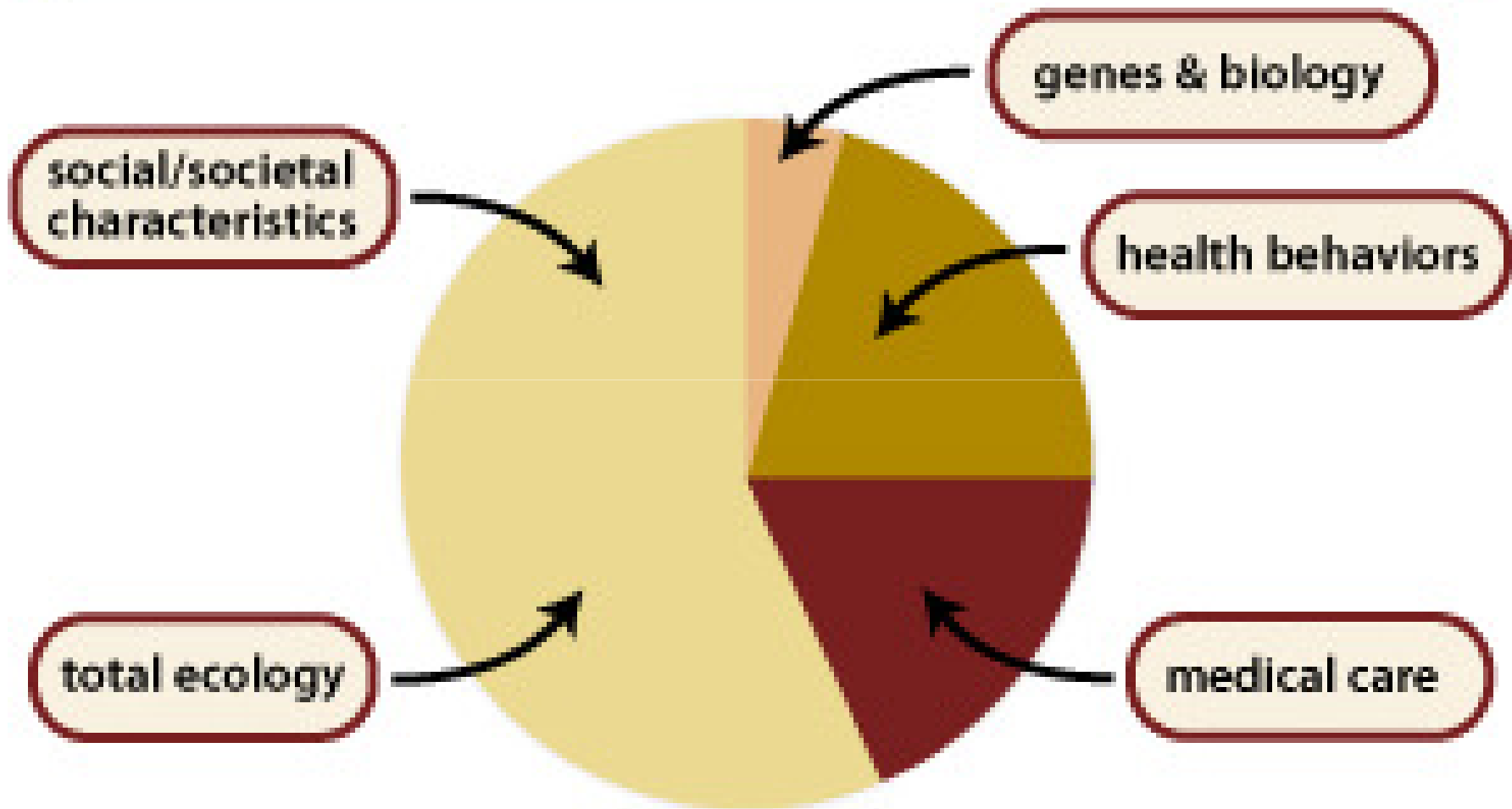
[www.genewatch.org](http://www.genewatch.org)



# The *health field* concept (Lalonde 1974)

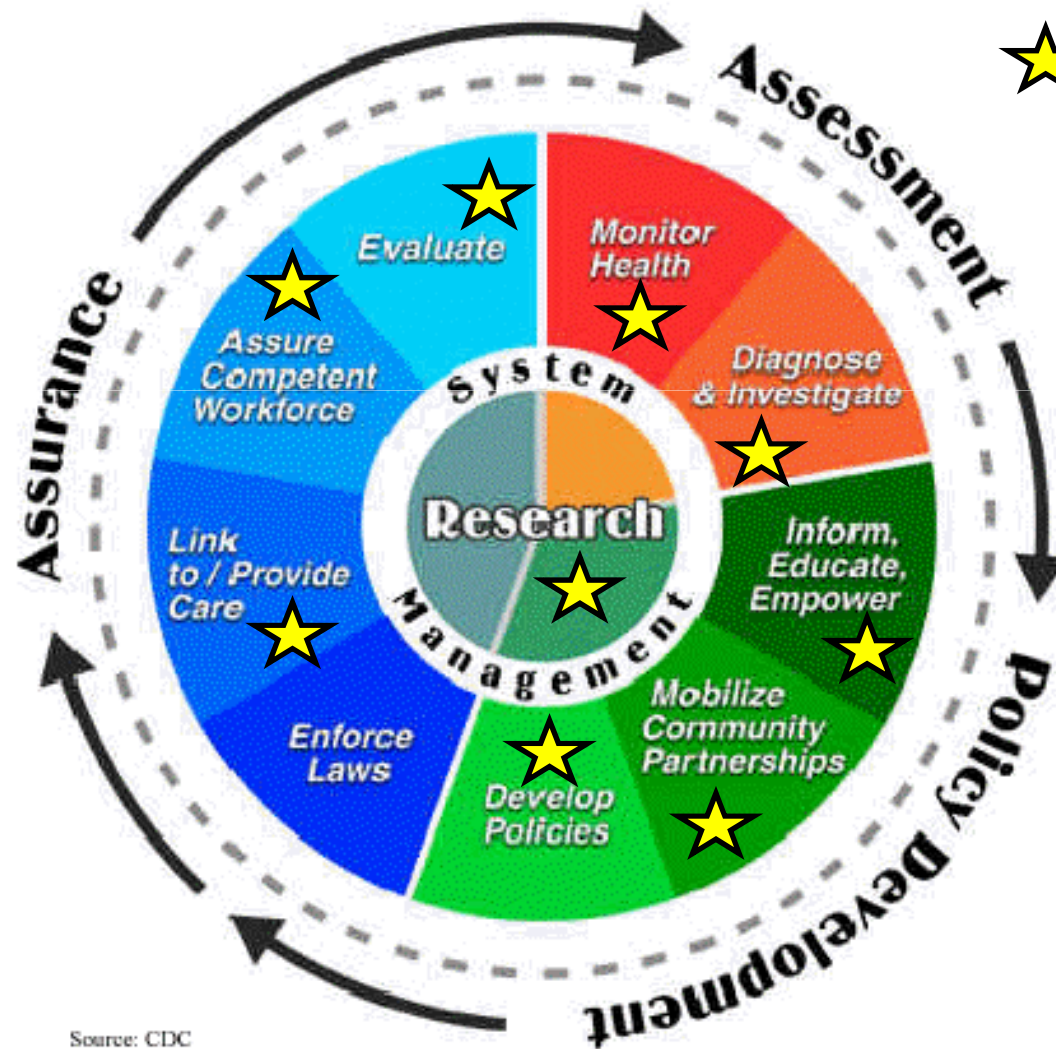


# DETERMINANTS OF POPULATION HEALTH



# ***Public Health Wheel:*** **core functions, specific responsibilities and essential public health services**

★ DGH, INSA



Source: CDC

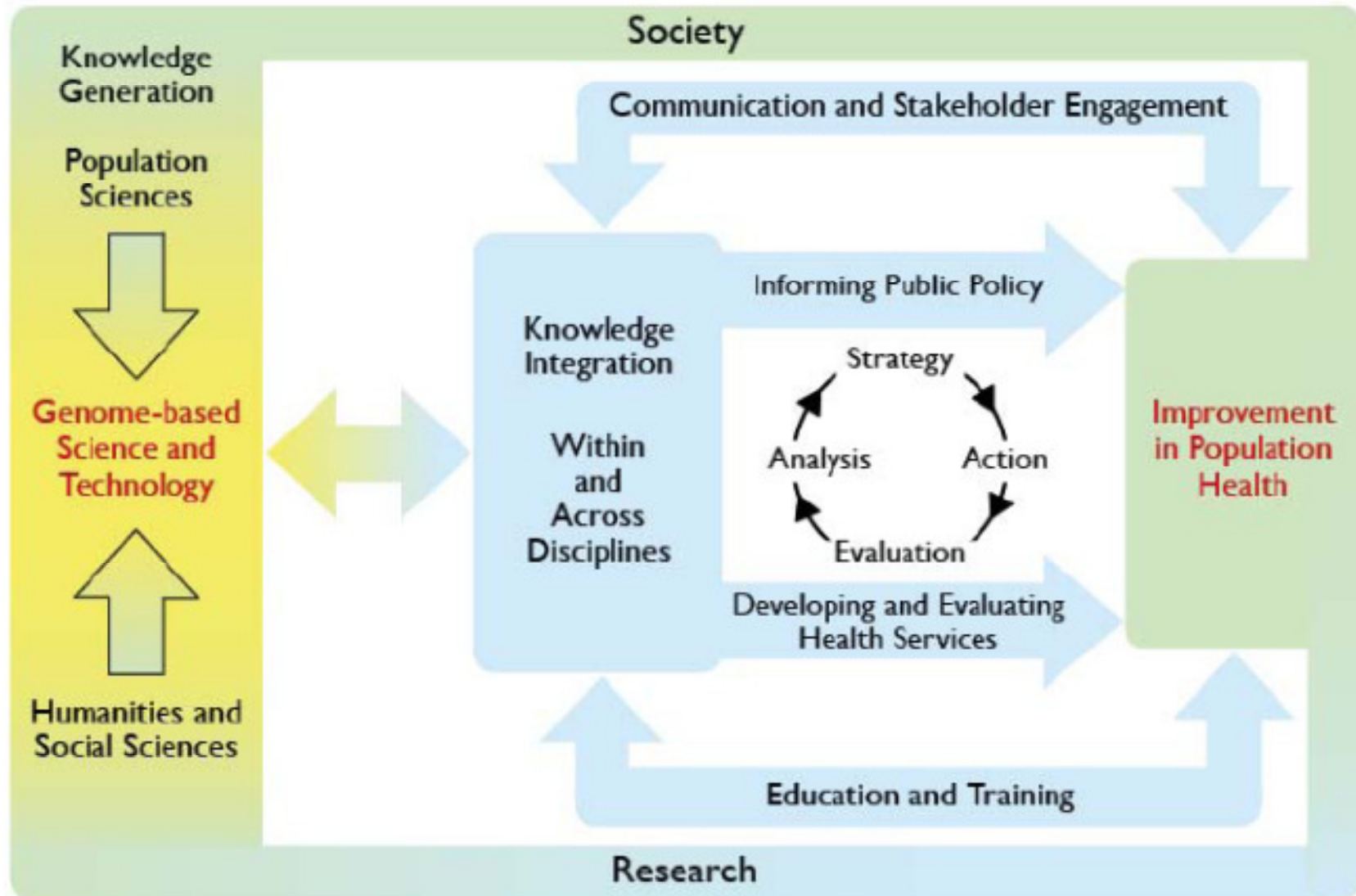
## **Public health genomics:**

**The responsible and effective translation of genome-based knowledge and technology for the benefit of population health.**

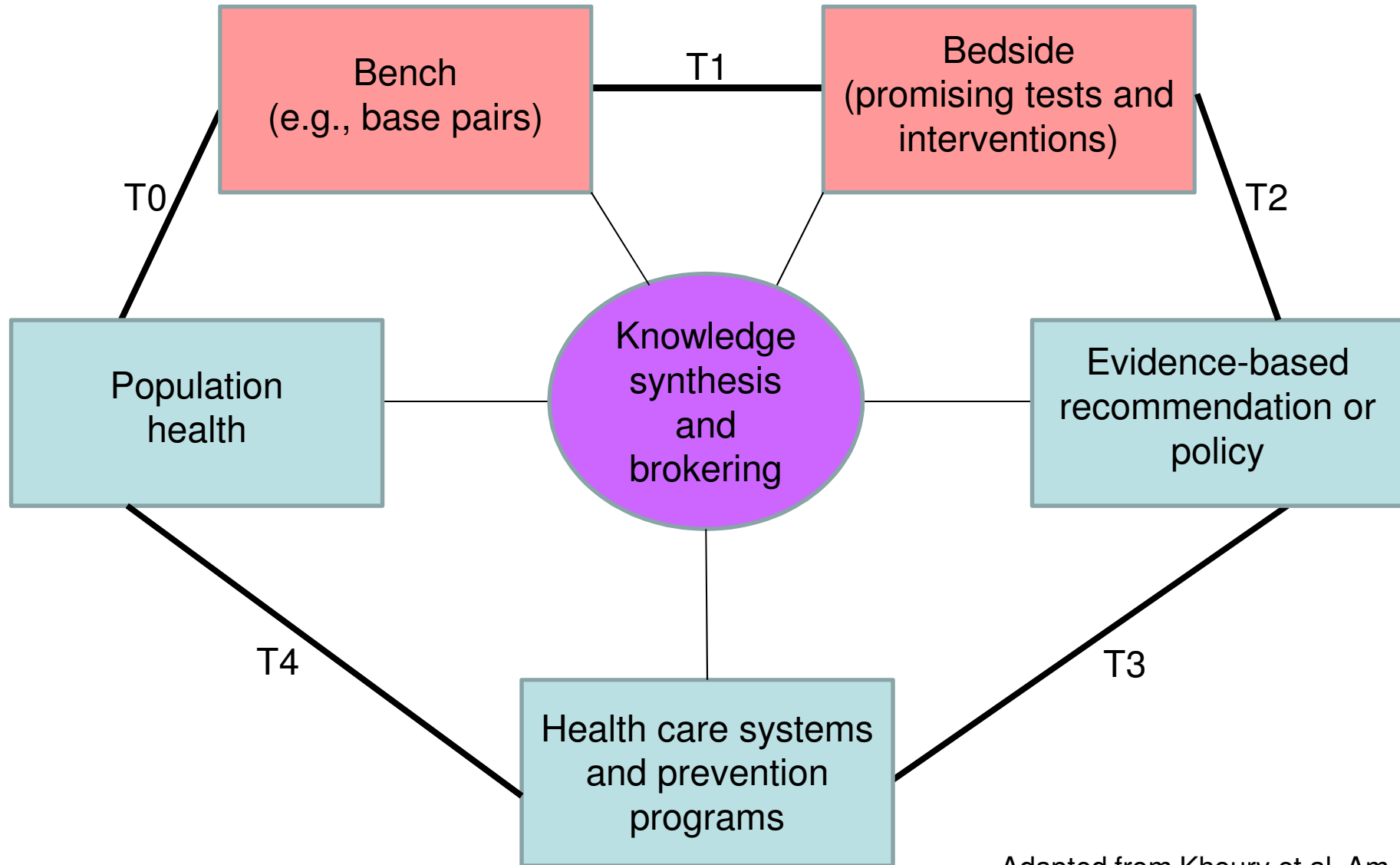


**Genome-based Research and Population Health, Bellagio 2005.**

# PHGEN at the crossroads of science, health technology and society



# Beyond the bench-to-bedside model of translational research



Adapted from Khoury et al. Am J Public Health. 2012;102:34-7.

# Genetic exceptionalism

Genetic information fundamentally differs from other kind of health information and – compared to non-genetic health information – should *per se* be protected in a special way.

## Is this true?

Ref: Hedgecoe A (1998) *Medicine, Health Care and Philosophy* 1: 235-43.

# Genetic *versus* non-genetic information - I

- *Concern for kin:* genes can be passed on to children and as such can affect the family
- *Concern for stigmatisation and discrimination:* knowledge derived from analysing DNA provides potential for stigmatising and discriminating persons or risk groups
- *Concerns for easy accessibility of information and identification:* DNA is a unique material to identify persons and is ubiquitous
- Tuberculosis or sexually transmitted diseases
- Leprosy and HIV
- IR thermal cameras at airports screen the body temperature of passengers; identical twins have different irises.

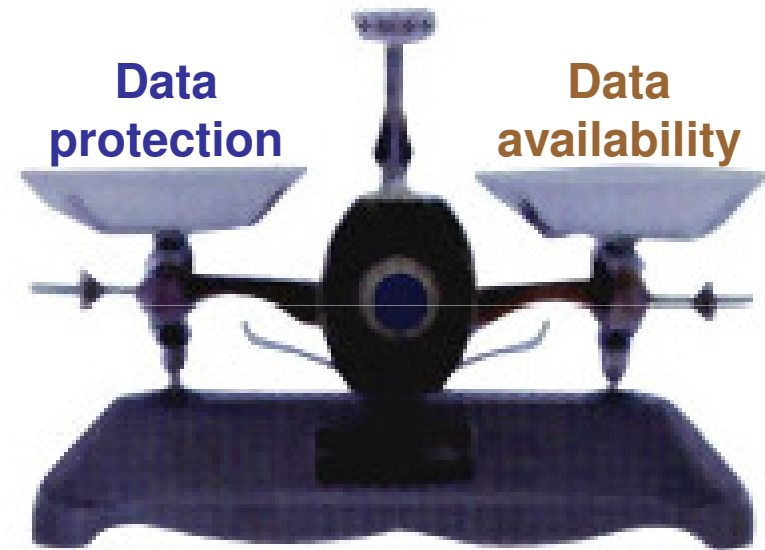


# Genetic *versus* non-genetic information - II

- *Long-term storage and use for other purposes than originally consented for*
- *Concern for prophecy: knowing genes has a potential to tell with some probabilities something about a person's future health*
- *The origination of health information: Health information in some cases stem from the analysis of a person's genome*
- In the Dutch Bloodbank 14 years after samples had been taken they were searched for antibodies for other purposes than originally intended
- HIV, Hepatitis B or high cholesterol can also foretell the risks and probabilities of a person's future health
- It can also come from analyses at the phenotype level

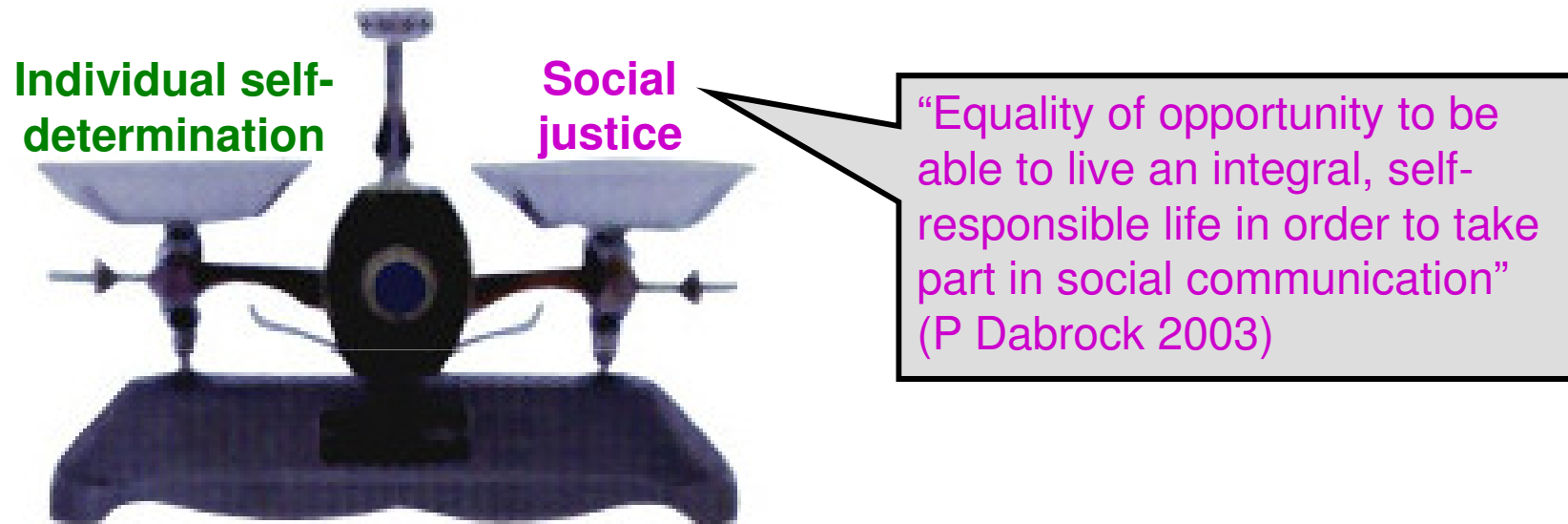
# Ethical benchmarks of PHGEN - I

Respecting autonomy / self-determination



# Ethical benchmarks of PHGEN - II

## Social justice



Empowerment of people to act as co-producers of their own health

Health and genetic literacy promotion as an ethical duty

R Veatch (2000) Doctor doesn't know best: Why in the new century physicians must stop trying to benefit patients. J Med Phil 25:701-21

# Introduction and use of genome-based knowledge in health services - I

- To what extent, when and in what order and manner genomic knowledge and technologies will give rise to effective and affordable clinical and public health interventions?

**Prepare the ground**

**Anticipate all eventualities**

# Introduction and use of genome-based knowledge in health services - II

- Genomic R&D findings are clinically valid and useful for human health
- Equity of access to clinical genetic services
- Adequate capacity and funding to respond to scientific developments

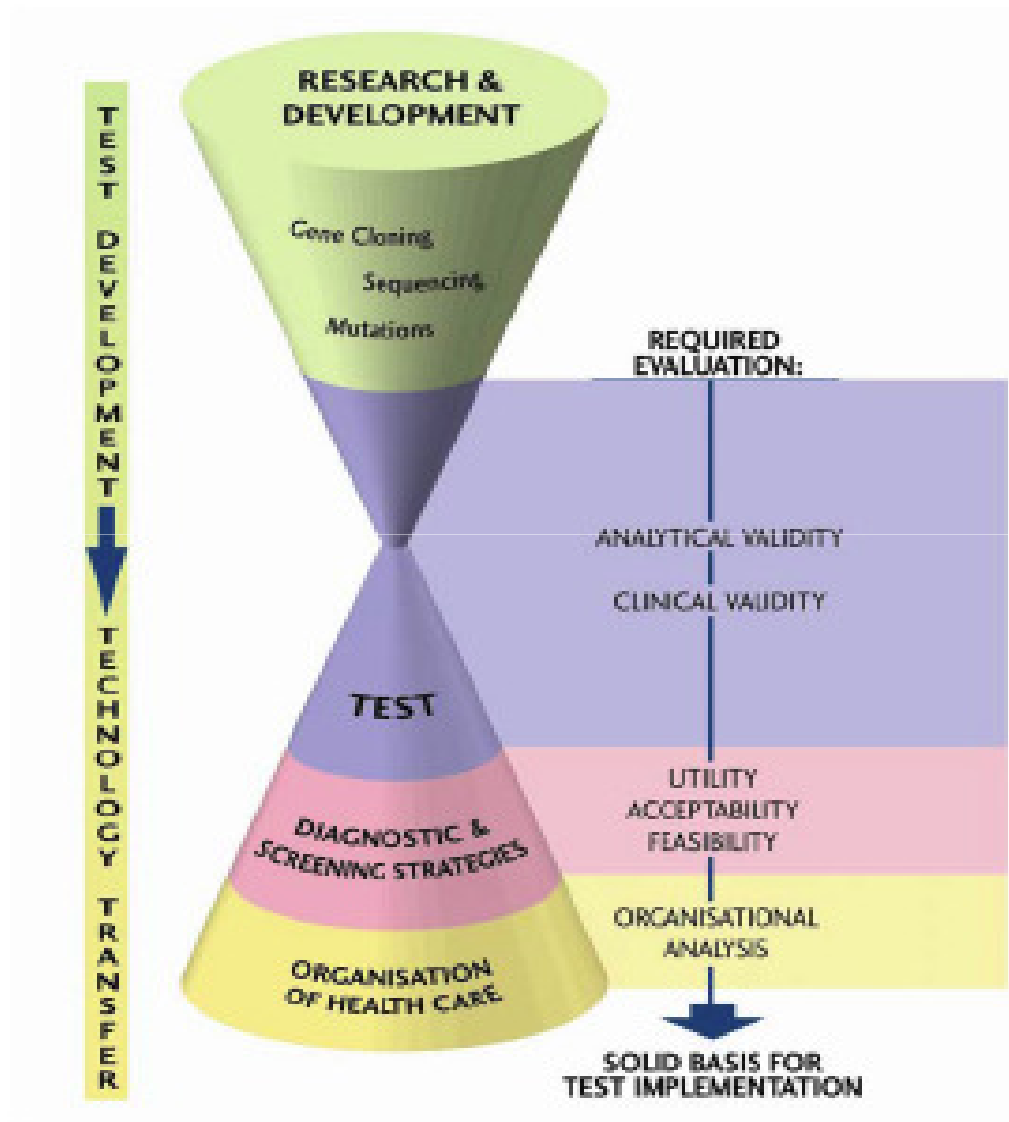
**Assessment tools are needed to systematically evaluate genome-based knowledge for public health purposes**

# Introduction and use of genome-based knowledge in health services – III

## Assessment tools

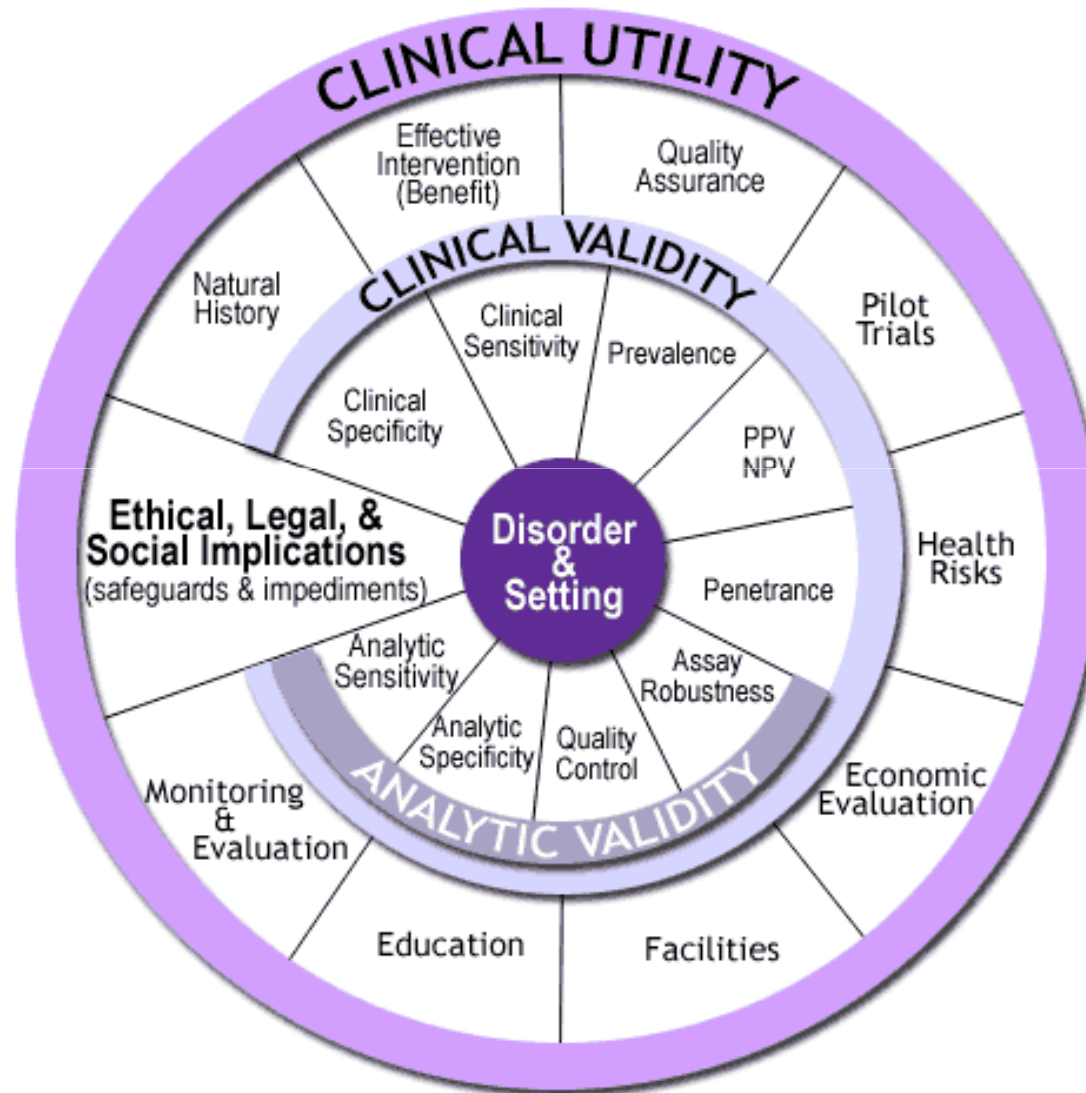
- Public health approach:
  - **H**ealth **N**eeds **A**ssessment (unmet needs; priorities; resource allocation)
  - **H**ealth **T**echnology **A**ssessment (safety; efficacy; effectiveness; comparative effectiveness research; social and ethical implications)
  - **H**ealth **I**mpact **A**ssessment (*Health in all policies*)
- Clinical genetics approach:
  - **ACCE** model

# HTA framework for genetic tests



Blancquaert et al., 2001

# ACCE model for evaluating genetic tests



Source: CDC, Public Health Genomics



# Critical ACCE questions

In what clinical context is the genetic test going to be conducted? Confirmation of diagnosis, screening, predictive?

Has an internal quality control programme been defined and has it been monitored externally?

What is known about other genetic or environmental factors that can modify the effect of the genotype under study?

Is there any effective and acceptable intervention or other kind of benefit derived from performing the genetic test?

What human, material and economic resources are required for the provision of the necessary services?

What information is available on the impact of the test in terms of stigmatisation, discrimination and inequality in health? Orphan genotypes.

## Sensitivity (r), specificity (s), predictive values (PPV, NPV), relative risk (RR) and efficiency (Eff) of a discrete test for the presence of a disease

$$r = a/(a+c)$$

$$s = d/(b+d)$$

$$PPV = a/(a+b)$$

$$NPV = d/(c+d)$$

$$RR = [a/(a+b)]/[c/(c+d)]$$

$$Eff = (a+d)/(a+b+c+d)$$

		Status		Total
		Diseased	Non-diseased	
Diagnostic test	+ve	a (true +ve)	b (false +ve) <i>Type I error</i>	a+b
	-ve	c (false -ve) <i>Type II error</i>	d (true -ve)	c+d
Total		a+c	b+d	a+b+c+d



# ESHG Clinical utility cards - I

- DISEASE CHARACTERISTICS:
  - gene(s) involved, mutational spectrum;
  - analytical method validation;
  - incidence at birth ('birth prevalence') or population prevalence;
  - diagnostic setting (differential diagnosis, predictive testing, risk assessment in relatives, prenatal).
- TEST CHARACTERISTICS:
  - analytical and clinical sensitivity and specificity;
  - clinical PPV and NPV.



# ESHG Clinical utility cards - II

- CLINICAL UTILITY:
  - (Differential) diagnosis:
    - Can a diagnosis be made other than through a genetic test?
    - Describe the burden of alternative diagnostic methods to the patient.
    - How is the cost effectiveness of alternative diagnostic methods to be judged?
    - Will disease management be influenced by the result of a genetic test?
  - Predictive setting:
    - Will the result of a genetic test influence lifestyle and prevention?
    - Which options in view of lifestyle and prevention does a person at risk have if no genetic test has been done?
  - Genetic risk assessment in family members of a diseased person:
    - Does the result of a genetic test resolve the genetic situation in that family?
    - Can a genetic test in the index patient save genetic or other tests in family members?
    - Does a positive genetic test result in the index patient enable a predictive test in a family member?
  - Prenatal diagnosis:
    - Does a positive genetic test result in the index patient enable a prenatal diagnosis?



# ESHG Clinical utility cards - III

## CLINICAL UTILITY GENE CARD

### Clinical utility gene card for: Centronuclear and myotubular myopathies

Valérie Biancalana<sup>\*,1,2</sup>, Alan H Beggs<sup>3</sup>, Soma Das<sup>4</sup>, Heinz Jungbluth<sup>5,6</sup>, Wolfram Kress<sup>7</sup>, Ichizo Nishino<sup>8</sup>, Kathryn North<sup>9</sup>, Norma B Romero<sup>10</sup> and Jocelyn Laporte<sup>2</sup>

*European Journal of Human Genetics* (2012) **20**, doi:10.1038/ejhg.2012.91; published online 23 May 2012

A molecular confirmation of the diagnosis will limit unnecessary further diagnostic investigations, which can be invasive (and expensive).

Patients and family may find encouragement and support by becoming members of associations that welcome affected families.

A molecular diagnosis enables carriers to make informed reproductive decisions.

# **Stakeholder involvement:**

## **Areas of public policy of concern to PHGEN**

- Reproductive decision making (PND, PGD, population screening, ART, ...)
- Consent to testing and biobanking
- Privacy and confidentiality
- Discrimination in employment and insurance
- Test provision and laboratory performance
- Pharmacogenetics/genomics (personalised medicine)
- Gene and (stem) cell therapies
- Clinical R&D, including clinical trials
- IPR and patents
- R&D capacity
- Training of health professionals
- Genetic literacy of lay people



“Public health genomics:  
A population perspective  
on how genomics can  
improve health.”

**Muin J. Khoury, MD, PhD**  
Founding director of CDC's  
National Office of Public Health  
Genomics