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making science work for health

Genes, Privacy and Discrimination
Challenges raised by novel genomic technologies

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PHG Foundation, Cambridge, UK

- PHG Foundation is an international independent not-for-profit policy research organisation
- Links to Cambridge University, Institute of Public Health and hospital trust
- Multi-disciplinary
- Active since 1997

The PHG Foundation's aim is to make science work for health by supporting the effective and responsible use of biomedicine and genomics.

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www.phgfoundation.org

PHG = Population Health Genomics

1. **Population / public health**

" the science and art of preventing disease, prolonging life and promoting health through the organised efforts and informed choices of society, organisations, public and private, communities and individuals"

2. Genomics / genetics

- Genetics = biological basis of inheritance and variation
- Genomics = wider study of genes and how they work

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Whole genome sequencing
Managing Incidental findings

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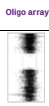
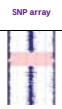
Whole genome technologies

	Light microscope	G-banded karyotype	Oligo array	SNP array	Exome sequencing	Full sequencing
Appearance					CGGATGATTACCCGTG ....GCTCTAGCTA GCTATAGA	CGGATGATTACCCGTG ATATAGCTCTCGCTCG CTCTAGCTAGCTATAG GCTATGGG

- 3 billion loci (6 billion diploid)
- 3-4 million bases which differ from the reference genome
- 30 megabases of information
- Multiple uses
  - targeted clinical (diagnostic)
  - public health use (asymptomatic at high risk)

➢ WGS likely to yield unprecedented amounts of data including incidental findings

➢ More systematic creation, retention and sharing of genomic data and samples

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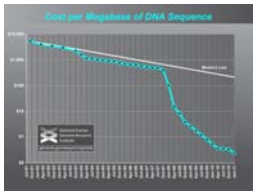
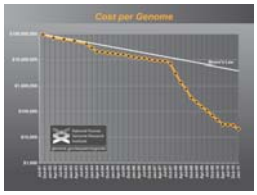
Cost of sequencing





Wetterstrand KA. DNA Sequencing Costs: Data from the NHGRI Large-Scale Genome Sequencing Program Jan 2011

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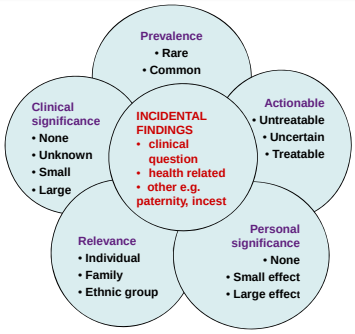
Different dimensions of incidental findings



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WGS: Managing incidental findings

Wolf et al (2008) Managing Incidental Findings in Human Subject Research

Net Benefit	Strong	Possible	Unlikely
DISCLOSE?	Disclose	May disclose	Do not disclose

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Personalised medicine, stratification and targeted approaches to screening: *Understanding risk*

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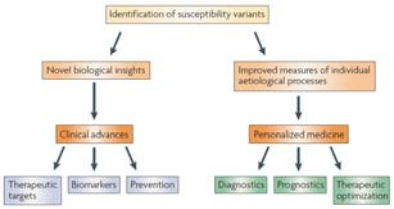
Personalised medicine

Using information about an individual's genetic profile to discriminate between those who should receive a treatment or intervention and those who should not



McCarthy et al. *Nat Rev Gen* (2008) 9:356-369

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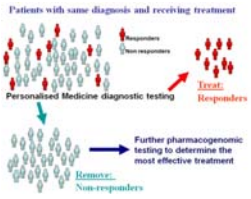
Stratified medicines

Treating groups of patients differently based on the genetic nature of their disease.



CANCER RESEARCH UK

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COGS and targeting screening

- Current NHS breast cancer screening programme:
  - Offered to women aged 50 and above
  - A fifty year old woman has a 1.9% chance of getting breast cancer before age 60
  - Used as a threshold at which screening becomes "worthwhile"
  - How could using genetic information change this?

Relative GENETIC risk	Risk (%) by 70	10 yr risk (%) at 50	Age at which R_{10}>1.9
0.67	4.1	1.3	**75**
0.80	4.9	1.6	**58**
1.25	7.6	2.4	**44**
1.50	9.0	2.9	**40**

Collaborative Oncological Gene-environment Study

Pharoah *et al*. New England Journal of Medicine 2008

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Reclassification and consent

Table 3 Reclassification of population of 100 00 women 35–79 years eligible for screening and in whom breast cancer could be detectable, under age-based or personalised screening strategies.

Personalised screening Polygenic risk threshold	Age-based screening <47 years	≥47 years	Total
Population			
<2.5%	30 276	19 926	50 202
≥2.5%	4429	45 368	49 798
Total	34 705	65 295	100 000
Cases			
<2.5%	26	38	64
≥2.5%	9	162	172
Total	35	200	236

Eligibility based on age 47 or polygenic risk equivalent to 10-year absolute risk for age 47 (2.5% 10-year absolute risk): England 2002–2006.

Collaborative Oncological Gene-environment Study

Pasharan N et al British Journal of Cancer (2011) doi:10.1038/bjc2011.118

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Personalised medicine: some implications

- Calculating risk
  - Integrating genetic and environmental risks
  - Integrating multiple small genetic risks
- Implications of long term data storage, interrogation and data security
- Managing those at high and low risk
  - Avoiding discrimination in insurance and employment
  - Ensuring equity
- Avoiding genetic exceptionalism or fatalism in individuals
- Medicalisation of childhood and parenthood

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Direct-to-consumer and genetic predisposition

- Direct-to-consumer genetic testing
- Purpose of test
- Expected health benefit
- What will be done with results

- Electronic consent?
- Ensuring identity
- Children and vulnerable groups

@ Nature 20 Jan 2011

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@ BMJ 29.1.11

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