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Genomics-based Personalised prevention:

FEAM Spring Conference, 20 May 2016

Dr Hilary Burton, PHG Foundation Director

Outline of talk

- New genomic technologies may help 'solve the problems' of healthcare
- Primary and secondary prevention
- Genomic approaches to prevention
  - Understanding and acting on risk
  - Spotting early disease
- Challenges
- Highlighting work of PHG Foundation

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About us

The PHG Foundation is a pioneering independent think-tank with a special focus on **genomics** and other **emerging health technologies** that can provide more accurate and effective personalised medicine.

- Active since 1997
- Member of Cambridge University Health Partners and Cambridge Institute of Public Health
- Funded by philanthropy, grants, and fees for commissioned work
- Undertakes analysis, knowledge brokering, advocacy for policy makers

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We are located within the heart of the Cambridge biomedical hub

Cambridge Institute of Public Health

CAMBRIDGE UNIVERSITY Health Partners

Knowledge-based healthcare

Three challenges to healthcare

- Demographic changes
- Greater patient expectation
- Scientific and technological advances

Three solutions

- Increasing emphasis on prevention
- Placing the individual at the centre (empowerment)
- Radical re-organisation with care moved from hospital to community

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Disease prevention

- Primary and secondary prevention
  - Reducing risk
  - Finding and treating early disease

Genomic contribution to understanding of disease risk

And new biomarkers for detecting disease early

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Primary prevention

Traditional epidemiology and public health studies determinants of disease…

Environmental exposures

- Housing
- Water
- Infectious disease
- Nutrition
- Chemical and physical agents

Social and behavioural factors

- Poverty
- Lifestyle

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Tackling risk factors: Geoffrey Rose

Strategies aimed at populations

- Many people must take precautions in order to prevent disease in a few – some may actually be harmed
- A prevention measure that brings large benefits to the community offers little to each participating individual
- How can individuals be motivated to change

High risk strategy

Segregation of a minority with special problems from the rest who need no attention

- Requires an active approach to identifying those at high risk
- Risks medicalising (and stigmatising) the high risk minority

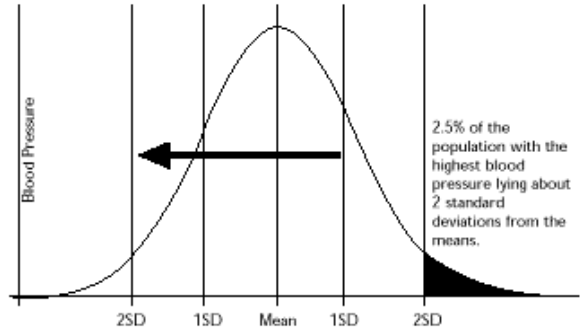

FIGURE 2. THE NORMAL DISTRIBUTION OF BLOOD PRESSURE IN A HUMAN POPULATION

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Personalised primary prevention

- Recognises different types and levels of disease risk
- Tailors prevention according to risk
  - More effective
  - More cost effective
  - Avoids over-diagnosis
- Requires
  - Effective tests
  - Effective interventions

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Genes and disease

Genes, environment and their interaction

- Single gene disorders
- Multifactorial disease
- Genes and environmental exposures (*e.g.* smoking, environmental hazards, foods, medicines, infectious agents)

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Personalised preventive interventions

- Newborn screening
- Single gene disorders in adult life
  - Breast cancer or cardiac arrhythmias
  - Familial hypercholesterolaemia

Relevant to individual and family members

In the UK 120,000 individuals with FH go undetected

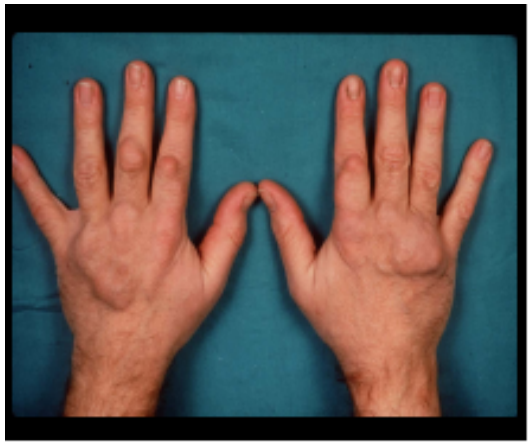

Baby screening: Life-saving scheme expanded

By James Gallagher
Health editor, BBC News website

5 January 2015 | Health

Newborn babies across England will be screened for more debilitating genetic diseases from Monday.

Cystic fibrosis and sickle cell disease are already picked up in the heel-prick blood test. Four rarer conditions will now also be tested for.



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New opportunities arising from WGS

Whole genome sequencing revealed Mr Hedley's kidney failure was caused by a particular genetic variant. His family is also being tested and their blood pressure can now be effectively controlled by drugs available on the NHS.

He said:

> "I was keen to take part in the project as I felt it was important to try and find out as much as possible about my condition for my daughter and granddaughter. Now that my daughter, Terri, has been given a diagnosis it means that her condition can be monitored every year to see if there are any changes.

Prof. Patrick Chinnery (centre) with Leslie Hedley and his daughter Terri Parker. *Photo courtesy of Newcastle University and photographer Mike Urwin*

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Multifactorial conditions: example of diabetes

Lifestyle and genes in the development of diabetes

- Multifactorial
  - Obesity
  - Lack of exercise
- Genetic susceptibility
  - Type 1 (factors affecting autoimmunity to pancreatic beta cells)
  - Type 2 (over 60 loci over many genes)
- Monogenic forms
  - Neonatal diabetes (known defects in several genes)
  - MODY mutations in various genes

Obesity: www.phgfoundation.org/briefing_notes/184
Diabetes: www.phgfoundation.org/reports/13538/

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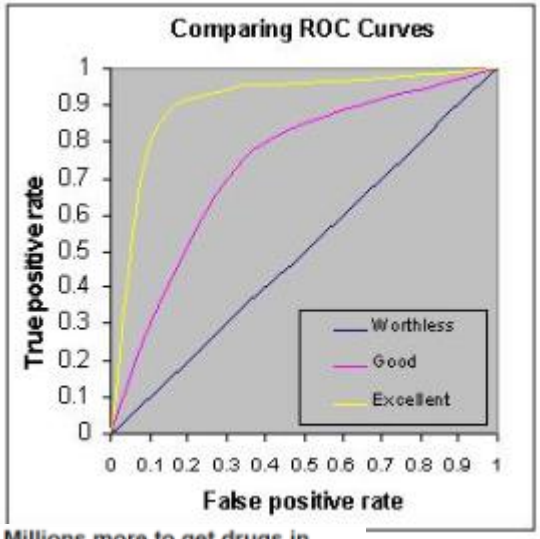
Prevention in multifactorial conditions (*e.g.* CHD)

- Fine tuning risk estimates
- Does it change the 'intervention' or advice?
- Does it help people to change lifestyle?
- How can we improve this?



Statins: Millions more to get drugs in controversial plans

Effects of communicating DNA-based disease risk estimates on risk-reducing behaviours (Review)

Marteau TM, French DP, Griffin SJ, Prevost AT, Sutton S, Watkinson C, Attwood S, Hollands GJ

THE COCHRANE COLLABORATION®

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Gene environment interaction

- Food (*e.g.* PKU, coeliac disease, coronary artery disease)

- Environmental pollutants
- Medicine (*e.g. CYP2D6* slow metabolisers)
- Infectious agents
- Vaccines

e.g. mutations in *MHC* genes confer susceptibility to Dengue shock syndrome

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Challenges in personalised prevention

- Developing the evidence base
- Integrating with other technologies
- Patient empowerment
- Ethics, legal and regulatory considerations
- Competence of health professionals
- Finding complementarity with public health programmes

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The evidence base

- Limits of conventional epidemiological studies and randomised trials as data that gives us information about individual risk and effect
- Complexity of modelling and long timescales
- Constantly evolving technologies

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Genomics and other relevant technologies contribute to personalised prevention

Data generation: omics, imaging, sensors, mobile phone apps

Data integration: big data, cloud computing, mobile connectivity and social networking

Data analysis: algorithms, machine learning, learning support systems

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Empowering individuals for personalised prevention

Empowerment means:

- Self-determining own health and healthcare
- Shared decision-making

Empowerment requires capacity building:

- *e.g.* education, counselling, coaching
- Potential for self-education facilitated by internet, patient organisations or community activism

Comments

- Understanding risk and genetics is complex
- Changing lifestyle is hard
- Health professionals are not well prepared
- Danger of worsening health inequalities

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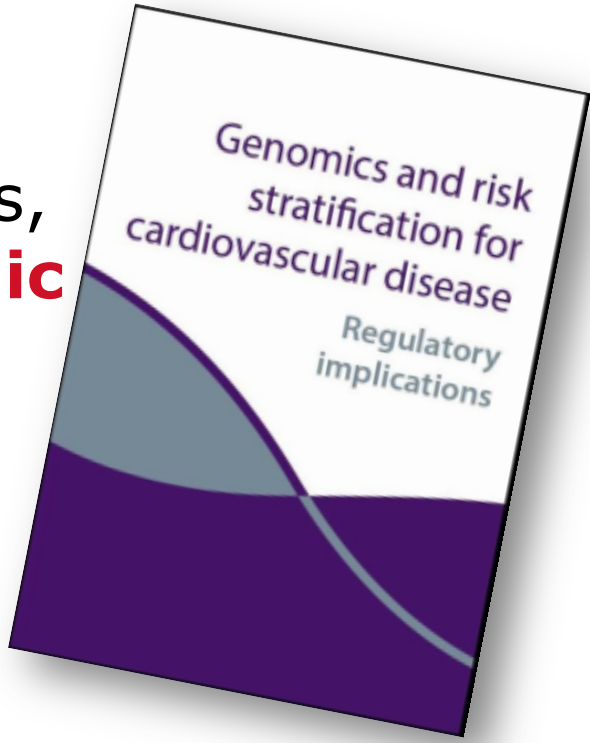
ELSI example: genomics, risk stratification and the law: cardiovascular disease

- Risk estimates based on family history, physiological measurements, biomarkers, lifestyle ….**and genomic susceptibility variants**



Regulatory complexities

- International movement of data
- Who can offer genetic tests
- Are the tools IVDs?

Website

EU funded EPIC-CVD project

www.phgfoundation.org/reports

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Getting genomic medicine right: The need for a competent workforce

In the UK

- 73,000 physicians in specialist practice
- 60,000 in general practice

'Few of these specialists will escape the impact of genomics in the next few years'

'Most specialties are unprepared'

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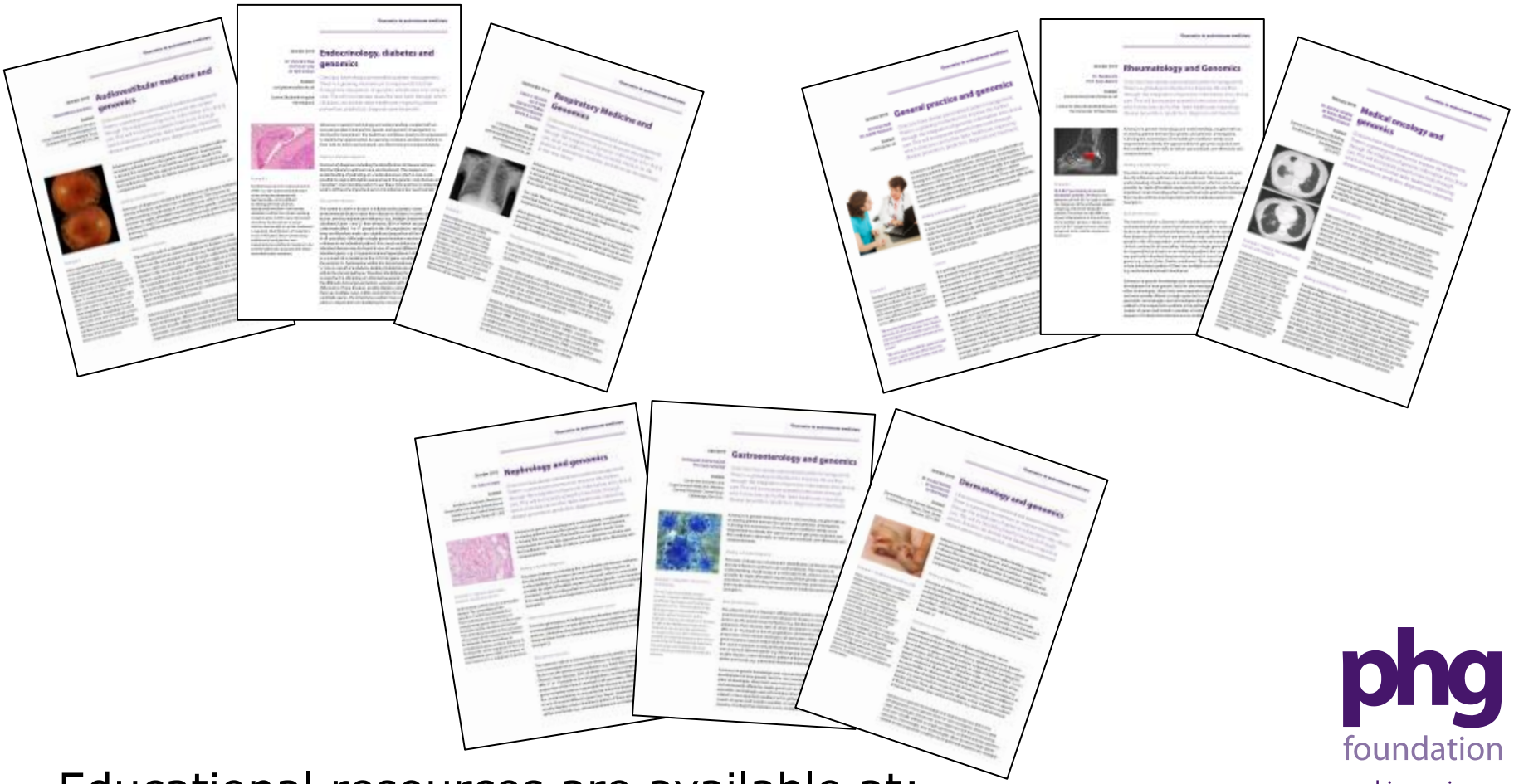
Competent workforce

The RCP group on genomics medicine



Educational resources are available at:
www.phgfoundation.org/education

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Personalisation and the public health perspective

- Finding complementarity between major public health programmes aimed at population determinants of health and personalised prevention
- Cultural and educational shift for public health practitioners

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Conclusions

- Prevention – an important aspect of the genomics personalisation agenda not widely discussed
- Relevant in inherited and multifactorial disease
- Issues in implementation include:
  - Evidence, integration with other technologies, empowerment, regulatory issues around data, healthcare development, integration with public health programmes, developing the evidence base

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