

Health Systems & the Future of Personalised Medicine: A Population Health Perspective

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Structure of Talk

1. The dilemmas facing health systems
2. Personalised medicine: the new paradigm
3. Genomics and the personalisation of health care
4. Personalised prevention
5. A digression on individuals, populations and stratification
6. Ethical and political implications of personalised health care

The Dilemmas Facing Health Systems

The Problem for Health Care

There is a crisis in health care due to rising demand and financial restraint

Factors responsible for the rise in demand include

- Demography of rising elderly population
- Science & technology push
- Rising patient expectations

This has forced health services to reduce costs largely through piecemeal efficiency savings, cost reduction and managing demand

Classical public health approaches directed at structural and environmental determinants of health, and generalised health promotion programmes designed to prevent disease, have been only partially successful

Proposed Solution

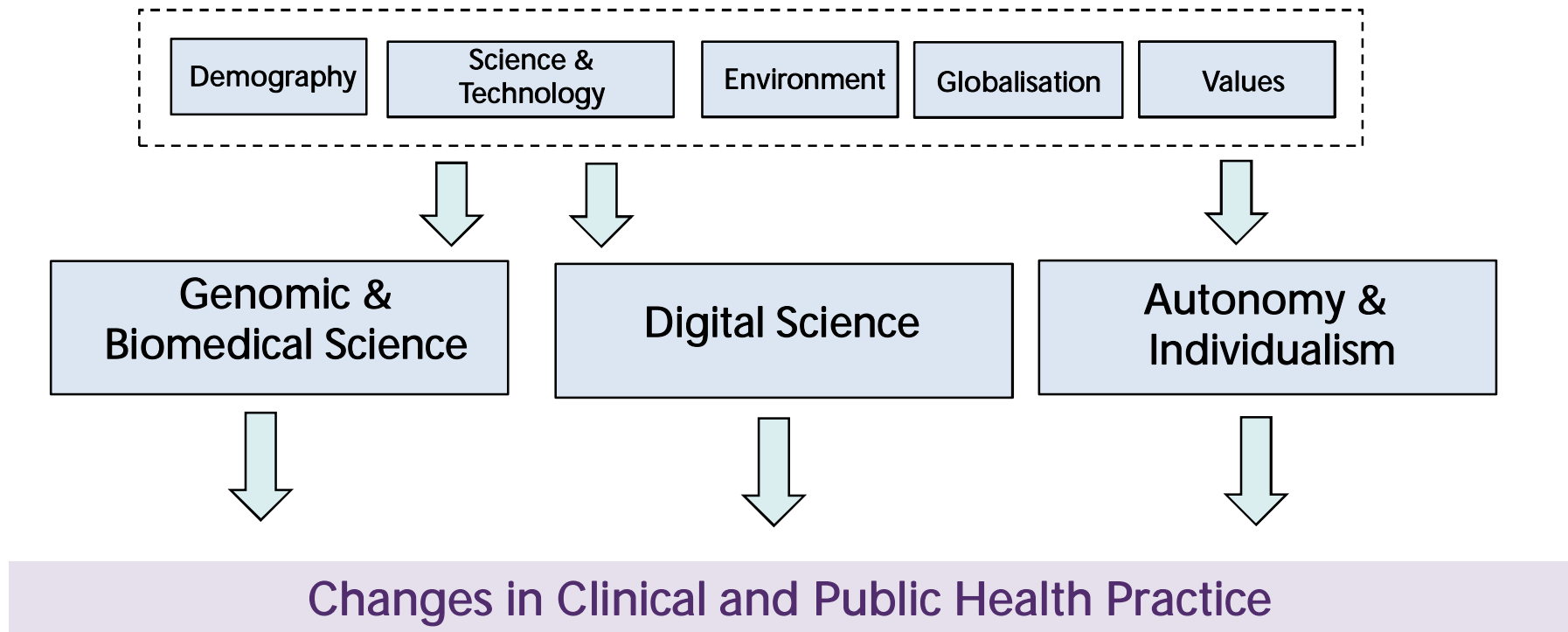
A proposed solution for a sustainable system has been to require

- a radical rethink of service organisation with movement from hospital to community
- a shift from treatment of established disease to early diagnosis and prevention
- empowerment of citizen to take greater responsibility for health

<http://www.abbvie.com/content/dam/abbviecorp/us/desktop/sustainablehealthcare/images/EU-Sustainable-Healthcare-White-paper.pdf>

New Drivers

New drivers now exist that could lead to amelioration of the problem

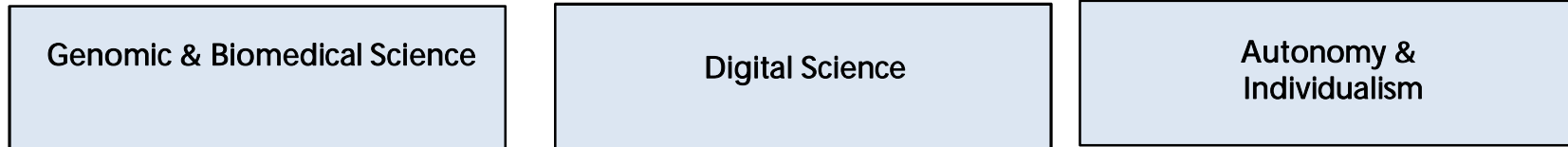


The Role of Personalised Medicine

Demography is a given and we cannot easily change it, but we can exploit to our advantage

- **biomedical and digital science & technology**
- **societal changes towards individualism**

as elements of a system of sustainable health care



New Paradigm of Personalised Medicine

Challenges

Demographic change

Greater patient expectation

Scientific and technological advances

Solutions

Placing the individual at the centre of healthcare

Increasing emphasis on prevention

Radical reorganisation of health systems by moving care from hospital to community

A New Paradigm

Personalised Medicine

and

Personalised Prevention

Personalised Medicine: The New Paradigm

Personalised Medicine

Personalised or precision medicine is complementary to existing paradigms of classical public health practice

Personalised
Stratified

Precision

We use these terms INTERCHANGEABLY to refer to an an approach which

- **treats individuals as whole persons and empowers them to take greater responsibility for their own health**
- **determines their individual biological characteristics and risk**
- **manages their care in accordance with those characteristics and with their individual values**

Patient Benefit Today

High Penetrance Subset

- Inherited breast & ovarian cancer
- Lynch (HNPCC)
- Long QT
- Cardiomyopathies
- Polycystic disease of the kidney

Genome based screening programmes - ffDNA

Developmental delay
Early deafness and blindness
Syndromic illness
Severely ill children

DDD project

Stem cells and regenerative medicine

Mitochondrial disease

Prevention

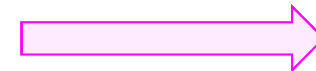
Diagnosis

Treatment

Inherited

Non-communicable

Infectious



FUTURE

Lung cancer & EGFR (gefitinib, erlotinib)
Melanoma & BRAF (vemurafinib)
Cystic Fibrosis CFTR G551D (ivacaftor)
Colorectal CA & KRAS (cetuximab)
HIV and HLA B*5701
Diabetes & MODY

Improved pathogen identification
Enhanced recognition of microbial resistance
Improved surveillance of outbreaks
Management of opportunistic infections
Implications of host susceptibility
Vaccine development

Future Science & Technologies

Genome based Sciences

- epigenetics
- proteomics
- metabolomics
- transcriptomics
- the microbiome
- DNA editing
- stem cells
- regenerative medicine

DATA
Data Sharing

Digital Sciences

- imaging
- wireless sensors
- mobile connectivity
- internet
- increased computing power
- social networking

Data sharing provides the infrastructure without which personalised and genomic medicine cannot flourish

Exponential Growth of Scientific and Medical Data

Growth of

Scientific
data

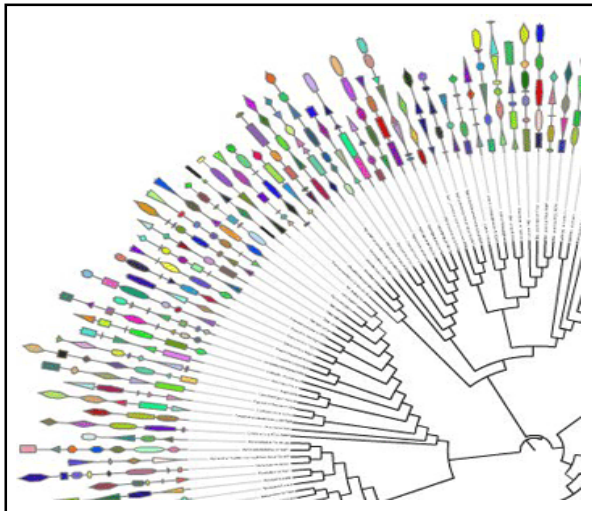
Scientific
publication

1. Analysis and synthesis of data
2. Accessibility of data
3. Transparency of information
4. Empowering individuals
5. Data sharing

Bioinformatic
Support

' Data intensive'
science

From Sewerage to Bioinformatics

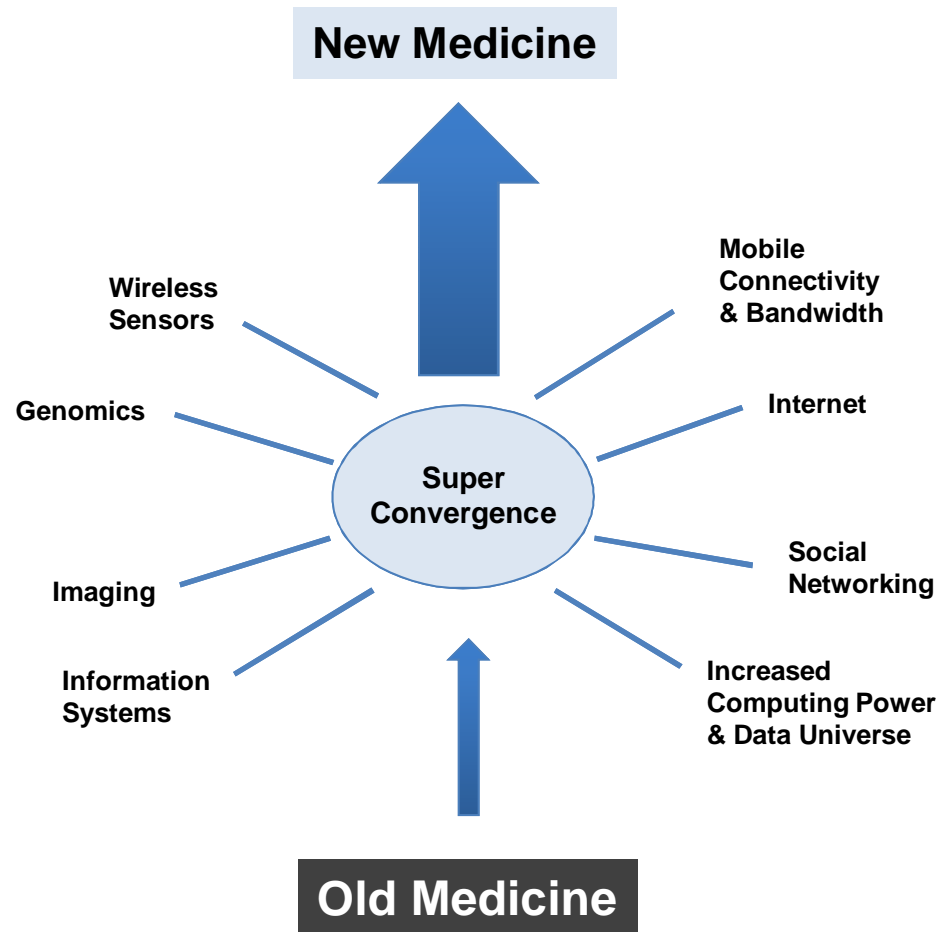


19 C Sanitary Engineer

20 C Social Engineer

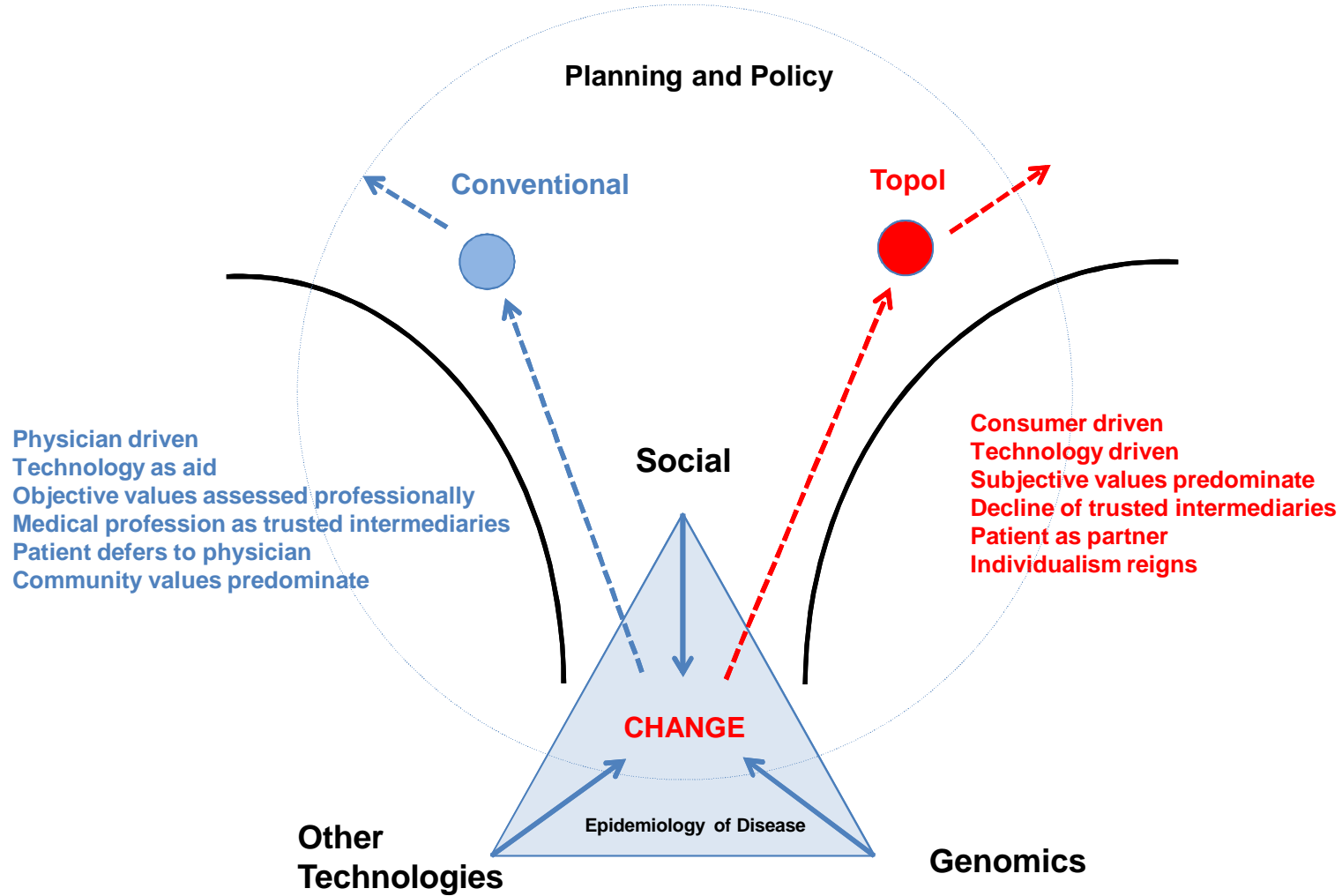
21 C Information Engineer

The Creative Destruction of Medicine



Adapted from Fig 1: The transformation of medicine today to new individualised medicine enabled by digitising humans. Eric Topol (2012)

Change, Scenarios and the Trumpet of Uncertainty



Genomics and the Personalisation of Health Care

Public Health Genomics

The responsible and effective translation of
genome-based knowledge and technologies for
the benefit of population health

Genetics and Genomics

1. Genetics as inheritance ('genetics')

single gene disorders inherited in a Mendelian fashion
genetic services
familial association

Clinical Genetics

The branch of biology dealing with heredity and variation of individual members of a species.

The branch of medicine that studies inherited disorders

2. Genetics as cell and molecular biology ('genomics')

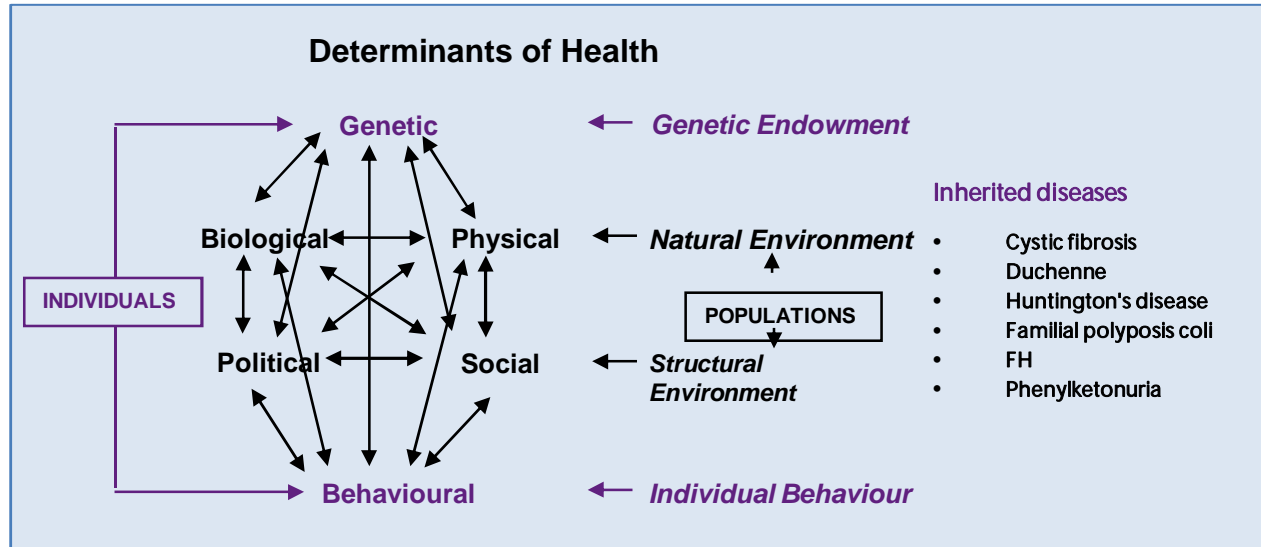
the genetic component of all human traits and diseases
the basis of development
modern biology

Genomic Medicine

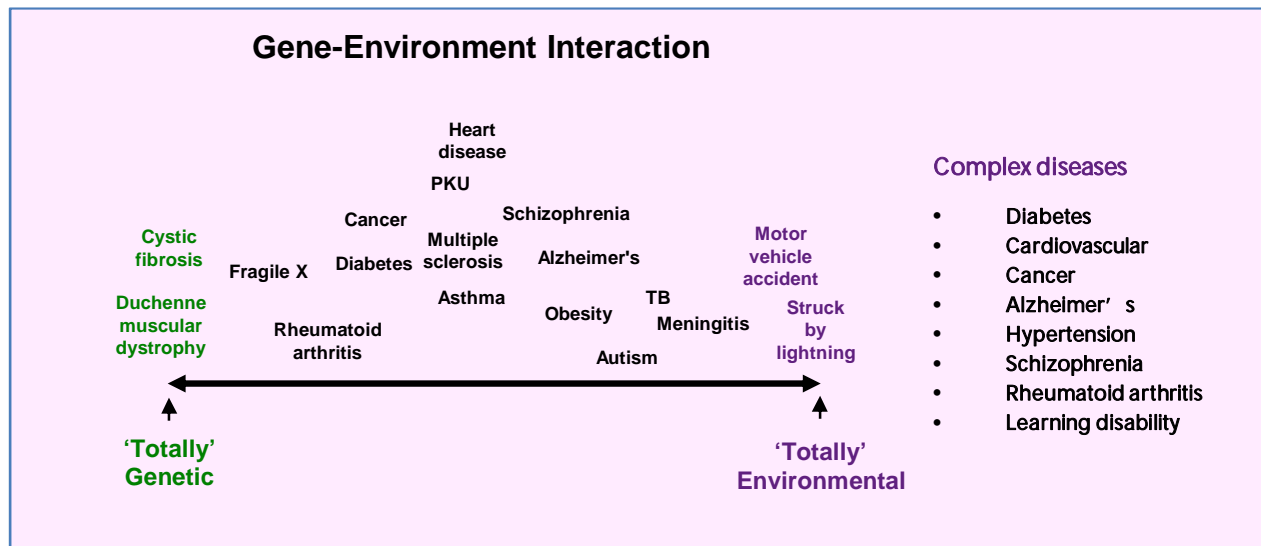
The study of genes and their function

The use of genomic information and technologies to determine disease risk and predisposition, diagnosis and prognosis, and the selection and prioritisation of therapeutic options

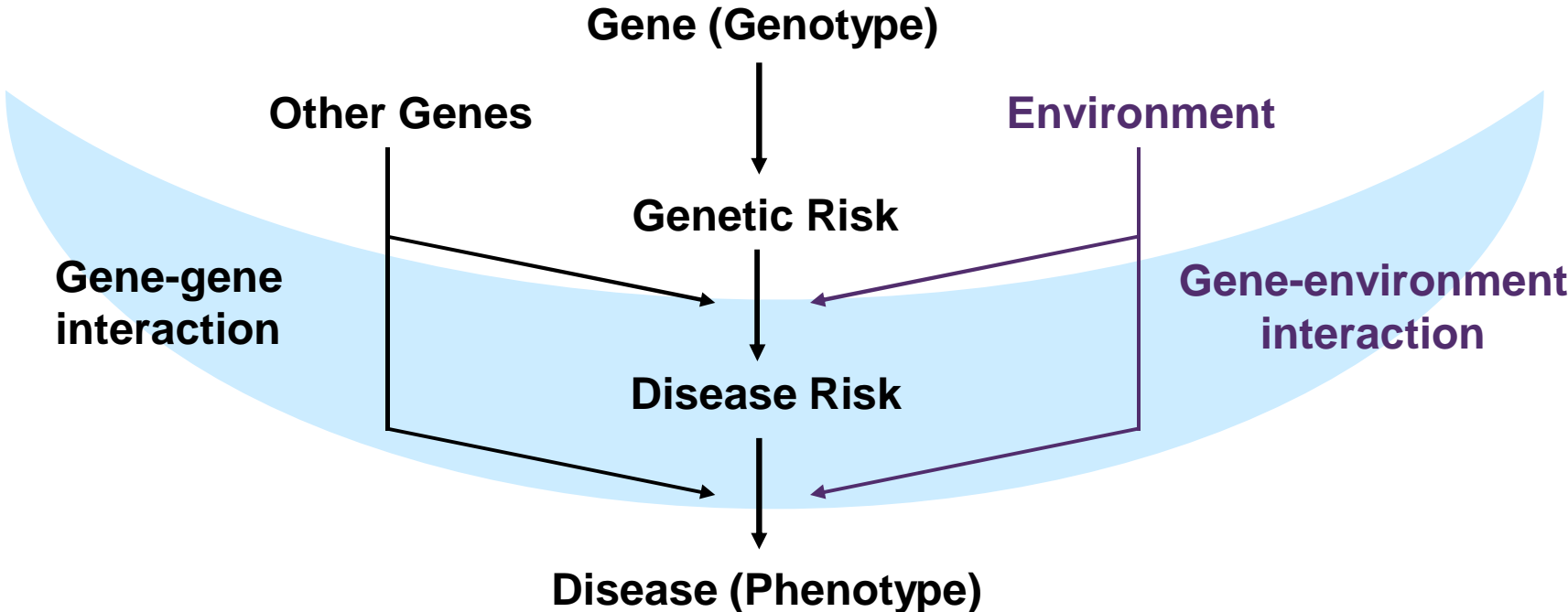
Basic Tenets of Public Health Genomics



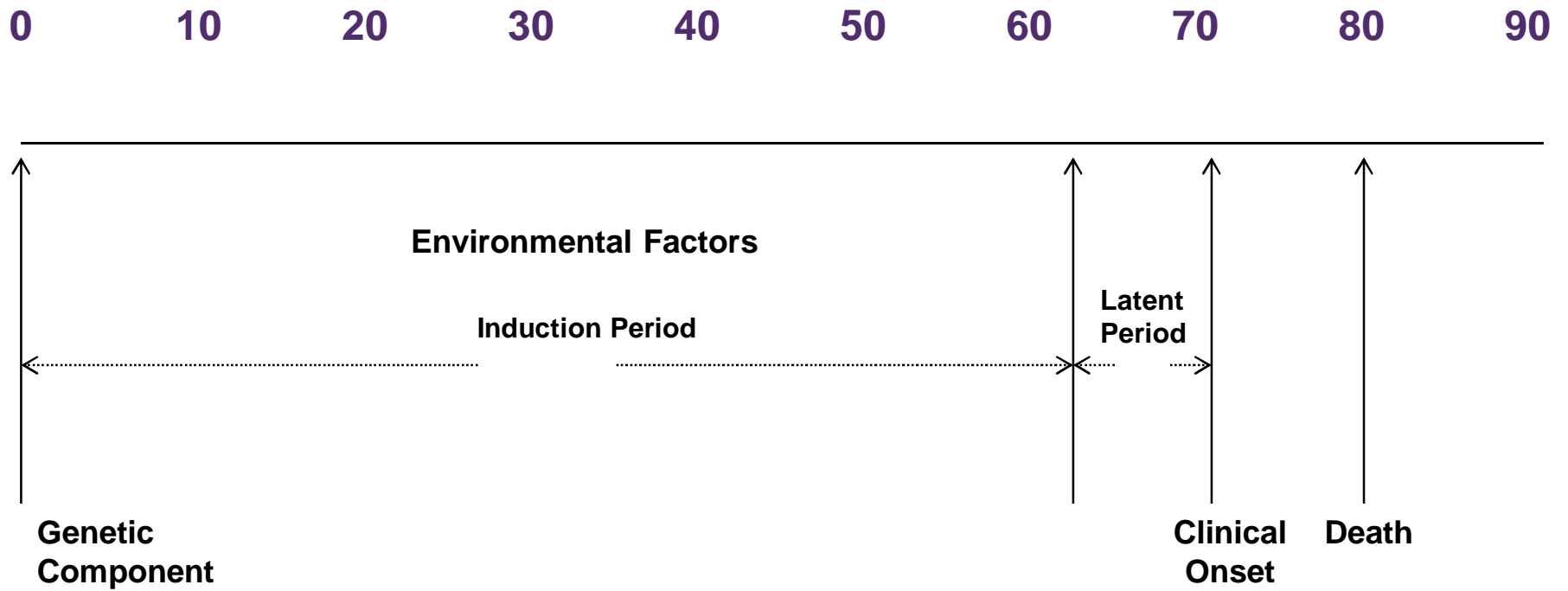
- ### Sub-domains of G-E Interaction
- Nutrigenomics**
Food
 - Pharmacogenetics**
Medicines
 - Ecogenetics**
Environmental pollutants
 - Vaccinogenomics**
Vaccines
 - Susceptibility to Infection**
Protozoa, Bacteria, Viruses



Penetrance



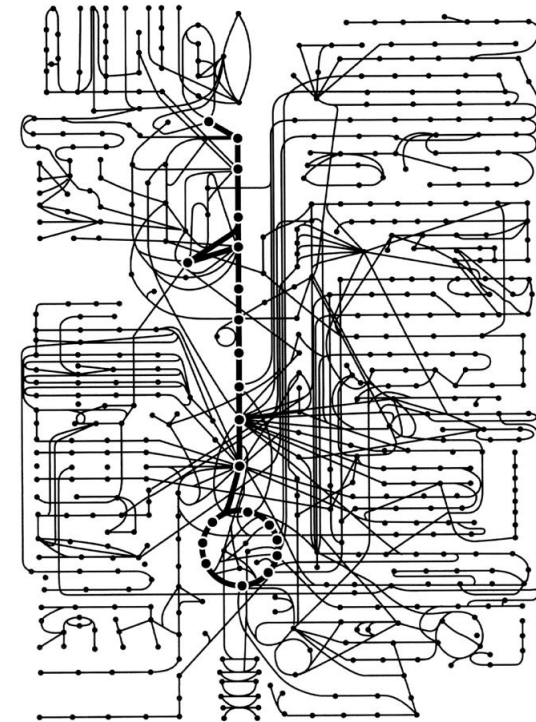
Development of Disease



Idea from Khoury and Cohen (1988) J Clin Epid 41, 1181

Complexity in Genetic Science

1. CpG Methylation
2. Histone modification
3. Gene-gene interaction
4. Alternative splicing
5. Post translational modification
6. Temporal effects



Personalised Prevention

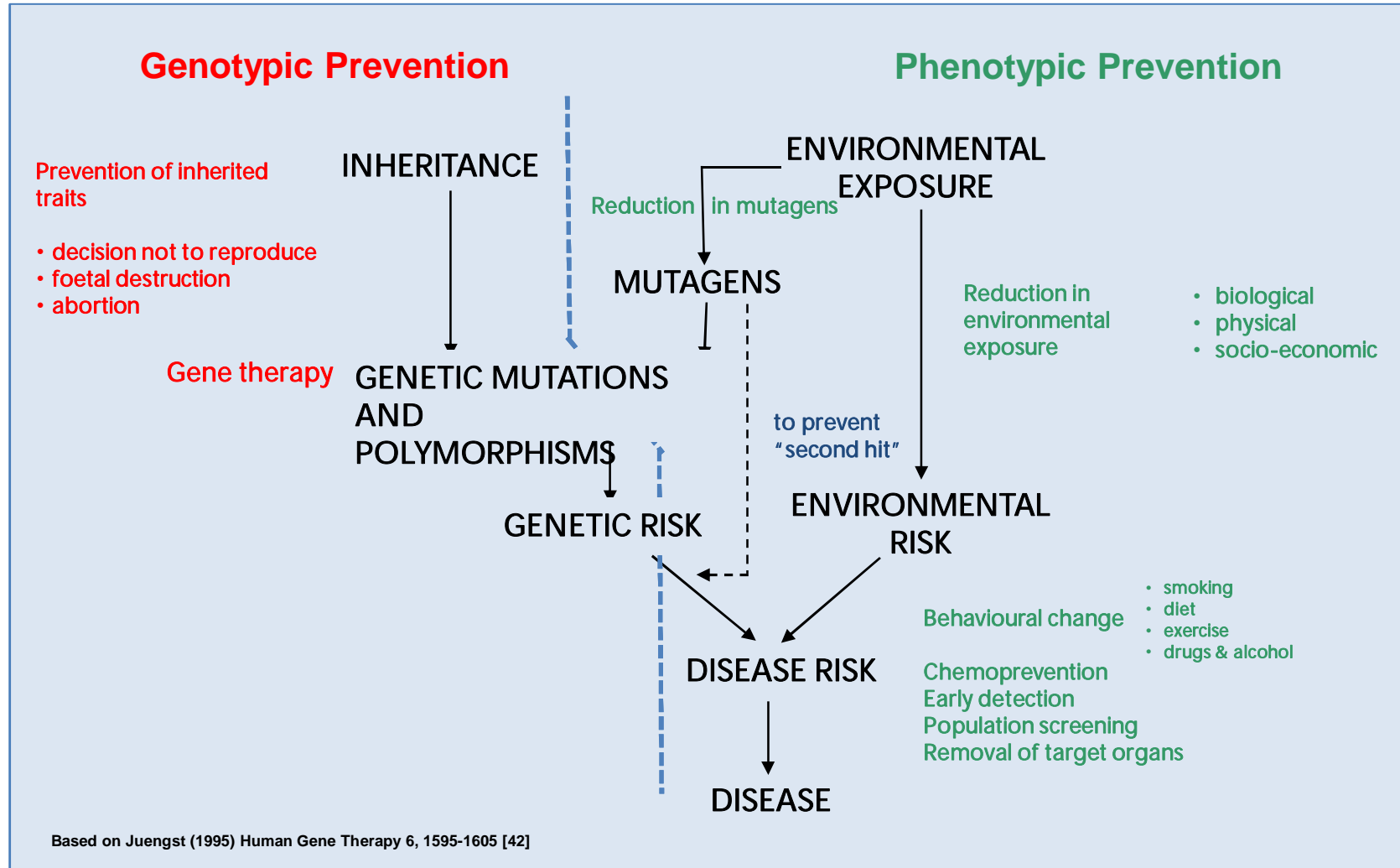
Personalised Prevention (versus Classical)

Personalised prevention is the use of genome based science and technologies to assess individual risk and the risk in sub-populations followed by specific interventions to prevent disease

Elimination of disease	Classical	Genotypic	Primary
Reduction in probability of developing disease	Personalised	Phenotypic	Secondary
Reduction in development of disease complications			Tertiary

Disease Prevention	Classical Directed at more distal structural and environmental factors Population based	External
	Personalised Directed at more proximal genetic and biological factors Risk based	Human Agency

Genotypic versus Phenotypic Prevention



Diagnostic and Predictive Markers

(Primary Secondary Distinction)

PRIMARY PREVENTION

RISK MARKERS

Genes



Bio-marker_{Pre}

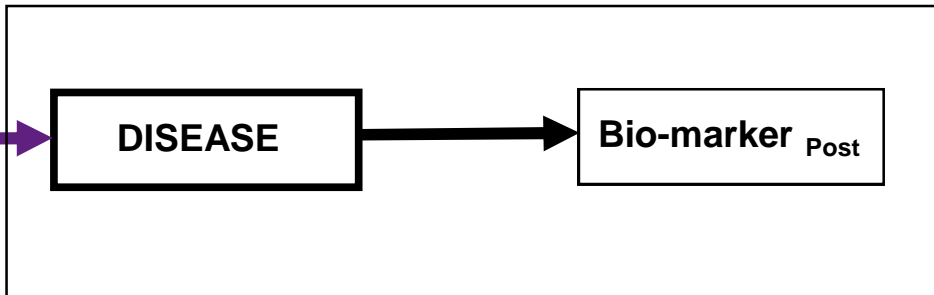
Environment



Predict future risk of disease
Monitor risk
Intervene to prevent disease

SECONDARY PREVENTION

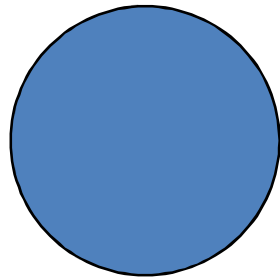
DISEASE MARKERS



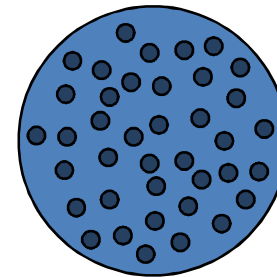
Early diagnosis of disease
Follow course of disease
Monitor treatment

A Digression on Individuals, Populations and Stratification

Populations and Individuals

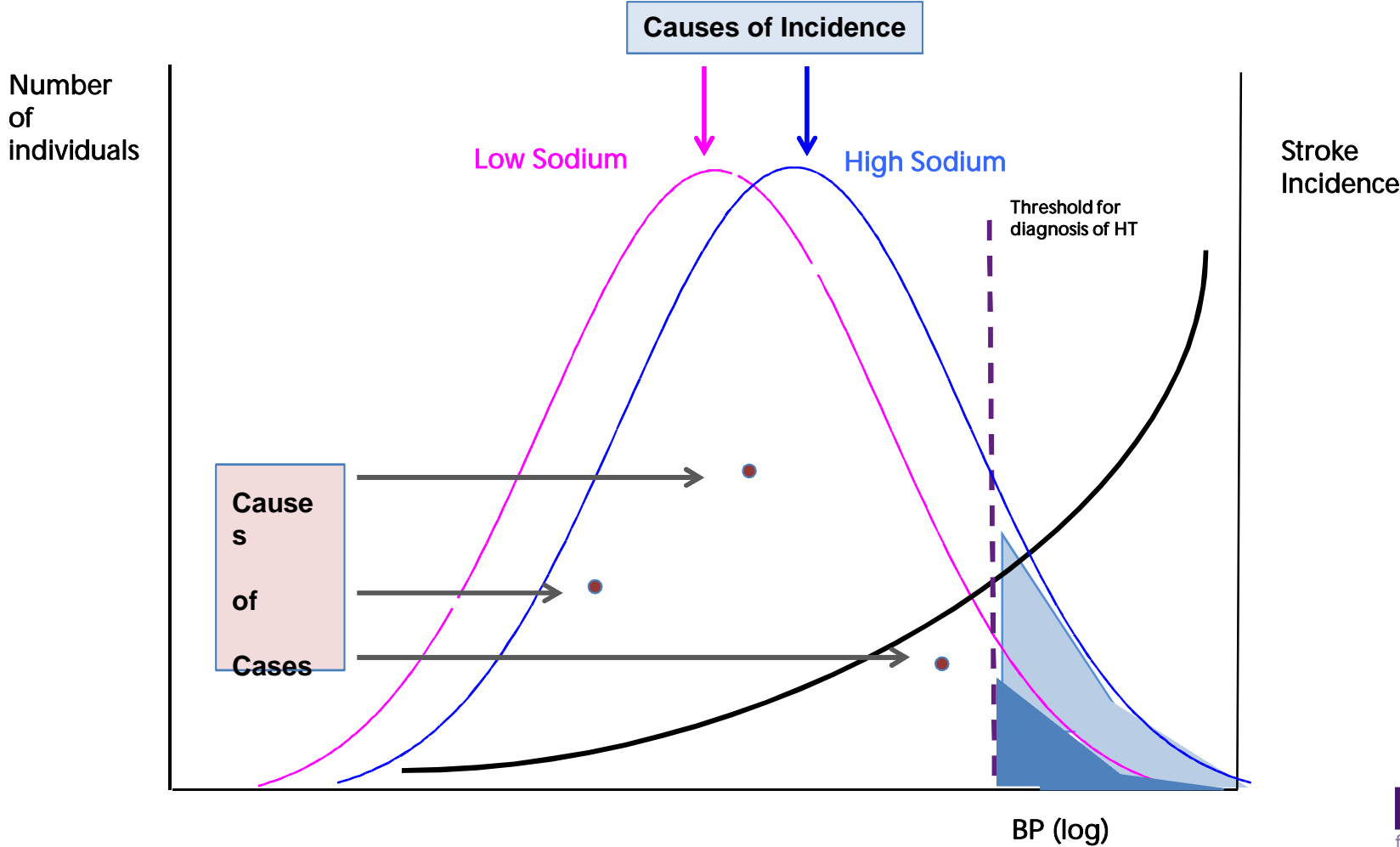


Homogenous population
Single ontological entity

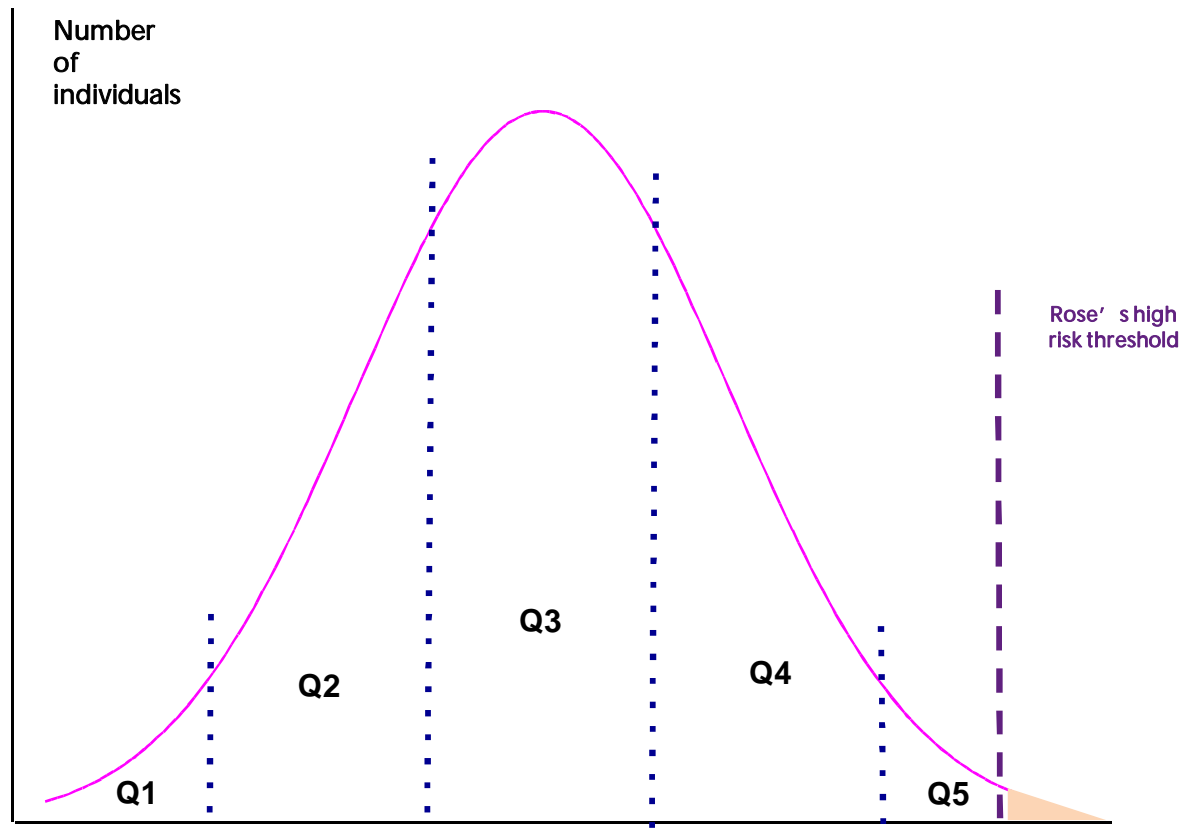


Heterogeneous population
A set of individuals

Geoffrey Rose: Population vs. High Risk and Incidence vs. Cases



The Use of Stratification



1. Relies on risk measurement

2. Multiple segments

1. Differential interventions

2. Individual directed

Ethical and Political Implications of Personalised Health Care

Health Service Organisation and Development

Seamless service from hospital to community to social care and move from hospital to community care

Reconfiguration of laboratory and clinical services with use of point of care diagnostics

Capacity building and training of workforce to understand the impact of personalisation and stratification and to interpret and use risk information: bioinformatics, epidemiology, health economics

Policy makers, physicians and third party payers (NHS commissioners and private insurers) to better understand effectiveness or otherwise of new technologies, both biological and digital, to better prevent and manage disease

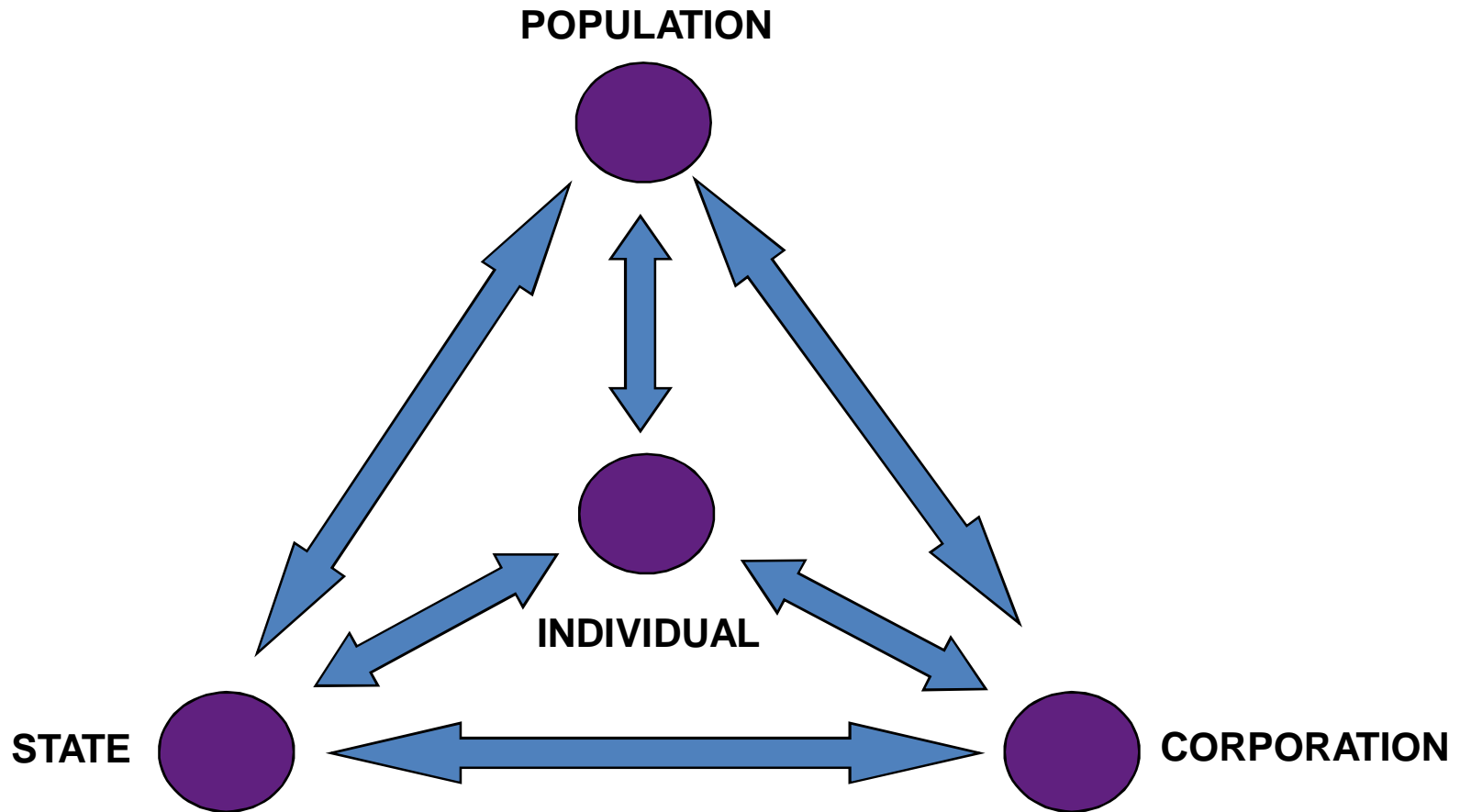
Empower citizens to take control of their own health

Providing citizens with access to information through the internet and establishment of EHRs and biobanks

Encourage data sharing with appropriate governance

Catalyse public policy to better governance of data and bio-banks, new diagnostics and other technologies and direct to consumer services

Pluralism in Population Health



Questions for Public Policy

To what extent should governments

- **aim to explicitly empower citizens through programmes of public engagement to take greater responsibility for their health?**
- **encourage the promotion of personalised health care and the determination of personal risk profiles?**
- **explicitly use legislation, funding mechanisms, public policy interventions to ensure the appropriate balance between individuals and populations ?**
- **be explicit that the subjective views of its citizens (subjective utility) be respected?**
- **draw the balance between individual privacy and the benefits that can come from data sharing?**
- **regulate the commercial sector, device and diagnostics, and direct to consumer products and services**

General Conclusions

Health policy in the twenty first century can no longer ignore the knowledge derived from genomics, cell and molecular biology

Biological and social models of disease must be regarded as complementary paradigms by policy makers in their efforts to improve population health

Health leadership and practice must:

- 1. take into consideration the scientific and technological advances that will prevail in the coming years**
- 2. understand and acknowledge the role of the pharmaceutical and biotechnology industries, of information, IT and telecommunications, and the importance of innovation**
- 3. acknowledge existing social trends and move from a collectivist towards a more individual patient focused framework**

The personalisation of health care cannot and should not be considered a thing in itself and of its own right. It must be grounded in the transformation of health care in its entirety, fitting within plans to produce a sustainable health system, ethically, practically and financially

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