Public Health in the Era of Personalized Health

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Personalized Health – the Promise

Improved understanding of causal disease risks and mechanisms to prevent disease from occurring...

Screening for disease before symptoms occur, allowing timely interventions...

Diagnosing the disease more precisely, leading to more effective treatment...

Selecting the specific medication that will best treat the disease...

the focus is on the individual
Public Health – the Mission

Kass NE Am J Public Health 2001

the community rather than the **individual** is the patient

governmental and other institutional bodies rather than treating physicians are the providers

> the focus is **community** well-being
The Ethical Dilemma in Public Health

Lee LM Am J Public Health 2012

Principles of clinical ethics:

- health care provider’s responsibility to protect patient
- 4 essential principles used by hospital ethics committees: **autonomy; beneficence; non-maleficence; justice**

Principles of public health ethics:

- Public Health authority’s responsibility to use the information to maintain or improve population health
- the community is the patient

SEE ETHICAL DILEMMAS RELATED TO COVID-19
Citizen Cohorts - for Personalized & Public Health

130 of 215 Mio. USD invested into the U.S. Precision Medicine Initiative are allocated to build the 1 Mio citizen “All of Us” cohort with an associated biobank [https://allofus.nih.gov](https://allofus.nih.gov)

Cohort benefit for personalized and public health:

- Primary prevention - improve understanding of causal disease risks and of preventive behaviour
- Risk and disease screening – identify and test utility of biomarkers
- Diagnosis and treatment – evaluate health care and health systems
Cohort & Biomarker Data

Primary prevention
- improve understanding of causal disease risks
  and
  of preventive behaviour
Non-Communicable Diseases

Noncommunicable diseases account for 67% of deaths in low- and middle-income countries but only 1% of health funding addresses them.

- Tuberculosis, Malaria, and HIV: 5%
- Maternal, Neonatal, and Child Health: 7%
- Other Communicable Diseases and Injuries: 32%
- Noncommunicable Diseases: 67%
- Noncommunicable Diseases and Injuries: 28%
- 1% of total health funding in 2015 including government, philanthropy, and international organizations.

Source: Institute for Health Metrics and Evaluation.

The relevance of preventing NCDs

treatment of NCDs is costly - increasingly so due to personalized and high-technology interventions

treatment of NCDs is often lifelong and disabilities remain - years lived with disability are increasing

treatment of NCDs contributes to poverty and social stratification

treatment of NCDs overwhelms health systems in low and middle income countries and increasingly in high income countries
The complexity of NCDs which risks are causal—where to intervene

Dahlgren and Whitehead Model
Understanding causal disease risks

Challenges:

• correlation of hazards
• mixtures and diversity of hazards – with additive, competing, synergistic effects – measured or unmeasured
• measurement error in exposure and susceptibility
  • technical
  • considerable spatial, temporal, intraindividual variation
  • long latency period
• measurement error in phenotype
• small effects
• confounding
• unknown modes of action & causalities
Exposome Research

- **Questionnaires**
  - Residential, occupational, smoking history, etc.

- **GIS-based environmental model**
  - Air pollution
  - Green space
  - Noise, etc.

- **Pictures**
  - Cosmetic use
  - Food
  - Cleaning products, etc.

- **Mobile devices**
  - Smartphone
  - Accelerometer
  - Environmental sensor, etc.

- **Biomarkers in different tissues**
  - Urine
  - Blood
  - Exhaled breath condensate, etc.

- **Integrated tools and technologies for exposome assessment**
  - High-throughput ‘omics technologies
    - Epigenomics
    - Transcriptomics
    - Proteomics
    - Metabolomics, etc.
The Opportunities of Biomarkers

Wild et al. Environ Mol Mutagen 2013

improvement of exposure assessment - biomarkers of exposure
identification of susceptibilities - biomarkers of susceptibility
improvement of phenotype classification – biomarkers of disease
interrogation of biological mechanisms – mediating biomarkers
provision of short-term outcomes in intervention studies – biomarkers of early disease
Precision prevention research
Patel C Pac Sym Biocomput 2015; Sun YV Advances in Genetics 2016
Public Health relevant causal pathways

- Urban exposome
  - Physical activity
  - Obesity
  - Noise
  - Air pollution chemicals
  - Psycho-social stressors

- Mechanisms
  - Systemic inflammation
  - Insulin resistance
  - Hypothalamus-pituitary-adrenal axis

- Urban phenome
  - Changes in infection and microbiome profile
    - Respiratory diseases
    - Cardiovascular diseases
    - Diabetes
    - Cognitive function

- Urban exposome
  - Systemic inflammation
  - Insulin resistance
  - Hypothalamus-pituitary-adrenal axis
  - Changes in infection and microbiome profile

SSPH+ ETH Zürich
Proposed mediating pathophysiological mechanisms of cardiometabolic disease induced by environmental air pollution and noise

Münzel T et al. European Heart Journal 2017;38, 557–564
Meet-in-the-Middle Concept
Vineis P et al. Environmental Molecular Mutagenesis 2013

Prospective Study

risk-predictive biomarkers associated with exposure
risk-predictive biomarkers associated with disease

exposure
intermediate biomarkers of effect
disease
SAPALDIA – Swiss-wide chronic disease biobank
complex data towards understanding of complex diseases
9651 participants, 8 communities, 30 years of follow-up and address history, 5 surveys

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Vineis P et al. Environmental Molecular Molecular Mutagenesis 2013

Epigenome-Wide Association with Transportation Noise

Enrichment for published DNA-methylation signals associated with insulin resistance?
Arner et al. Diabetologica 2016;59

Noise-related DNA-methylation signals predicting the incidence of diabetes?
The Urban Exposome: H2020 Expanse
PI: Vermeulen R; Vermeulen R et al. Science 2020;367:392

**Ecosystems**
- Food outlets, alcohol outlets
- Built environment and urban land uses
- Population density
- Walkability
- Green/blue space

**Lifestyle**
- Physical activity
- Sleep behavior
- Diet
- Drug use
- Smoking
- Alcohol use

**Social**
- Household income
- Inequality
- Social capital
- Social networks
- Cultural norms
- Cultural capital
- Psychological and mental stress

**Physical–Chemical**
- Temperature/humidity
- Electromagnetic fields
- Ambient light
- Odor and noise
- Point, line sources, e.g., factories, ports
- Outdoor and indoor air pollution
- Agricultural activities, livestock
- Pollen/mold/fungus
- Pesticides
- Fragrance products
- Flame retardants (PBDEs)
- Persistent organic pollutants
- Plastic and plasticizers
- Food contaminants
- Soil contaminants
- Drinking water contamination
- Groundwater contamination
- Surface water contamination
- Occupational exposures
Expanse Project
PI: Vermeulen R; Vermeulen R et al. Science 2020;367:392

Exposome Map:
Assign exposome scores to geographical locations
Identify hotspots of elevated health risk

Internal Exposome
Identify molecular pathways
Wearables—evaluate long-term utility

Wearables promise to promote healthy lifestyles

Test this hypothesis in the context of cohorts:

What are characteristics of cohort participants who do or do not use wearables?

Does wearing a fitness tracker lead to sustained increases in physical activity?
Cohort & Biomarker Data

Risk and disease screening

identify and test utility of biomarkers
Population-attributable fraction for genetics in various disease groups

Genetic Factors Are Not the Major Causes of Chronic Diseases except for monogenetic/familial disorders

Precision – Prevention: Genetic Risk Prediction?
Rappaport SM. PloS One 2016; 016; 11(4): e0154387
Utility of polygenic genetic risk test – non-small cell lung cancer


The Impact of Communicating Genetic Risks of Disease on Risk-Reducing Health Behaviour: Systematic Review With Meta-Analysis

Hollands et al. BMJ 2016

Expectations that communicating DNA based risk estimates changes behaviour is not supported by existing evidence.

Increase in motivation to not smoke/stop smoking

unless everybody sequenced at birth

absolute risks remain relatively low does not justify screening in all

Red: Chinese; Blue: Europeans; ORs 1.0 – 1.5 absolute risks remain relatively low does not justify screening in all
Risk/Disease screening: time variant biomarkers

Pase M et al. JAMA Neurol 2019;76:598; Mirzaei et al. Rev Neurosci 2019;27:857

Plasma total Tau level measured in prospectively sampled blood predicting dementia

Relevance of the «Healthy Reference»
Cohort & Biomarker Data

Diagnosis and treatment – evaluate health care and health systems
Personalized Lung Cancer Treatment

• lung cancer comprises a multitude of genetically distinct diseases.
• EGFR tyrosine kinase inhibitors are used as first and second-line treatments in lung cancer
• EGFR testing is required before treatment decision

Improvements in cancer treatments (survival; quality of life) have come at a very substantial cost, and in the past decade, the average price of new anticancer agents has more than doubled, from $4500 to >$10 000 per month

Temporal change in average monthly lung cancer-attributable costs in the U.S.
Global Access to EGFR Tests & Treatments

Carbonnaux et al. ERJ 2016;47:1331
The need for large sample size: sufficient endpoints
UK cohort 500 000 men & women 40–69 years

Example: Lung cancer:

- Social equity in access to
  - Lung cancer screening
  - Timely diagnosis
  - Personalized treatments
A Swiss Cohort Platform

Schweizer Gesundheitsstudie
Für mich – Für uns
pilot study with 1000 citizens

- Swiss-wide
- 100’000+ citizens 20-69
- interview-examination-sensoring-biosampling-imageing
- interdisciplinary collaboration
- duration > 10 years
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