PERSPECTIVES FOR PUBLIC HEALTH GENOMICS
WITHIN A HEALTH CARE SYSTEM CONTEXT

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No conflict of interest

Opinions are sole responsibility of the speaker
‘Omics’ in national Health Care System of Belgium

- ‘Omics’ in the clinic
- Genomic citizenship: ethics, legal and privacy
- Public Health Genomics
Omics in the clinic
‘Omics in HCS’ : a multistep process

- **Step 1**: Feasibility/HSE/HTA/Horizonscanning (March 2015)
- **Step 2**: Intervention plan/Roadbook (2016-2018)
- **Step 3**: Pilot phase (2018-2020)
- **Step 4**: Structural integration (2021-2023)
- **Step 5**: Monitoring/surveillance (continuous)
<table>
<thead>
<tr>
<th>ACTION 1</th>
<th>Establish a commission: Commission Personalized Medicine (ComPerMed)</th>
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<tbody>
<tr>
<td>ACTION 2</td>
<td>Development of guidelines for NGS use in (hemato)-oncology</td>
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<td>ACTION 3</td>
<td>Development of criteria for NGS use in (hemato)-oncology</td>
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<td>ACTION 4&amp;5</td>
<td>Develop and organize a benchmarking trial and EQA for NGS use in (hemato)-oncology</td>
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<td>ACTION 6</td>
<td>Implement NGS registration, storage and data management</td>
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<td>ACTION 7</td>
<td>Provide NGS education and training</td>
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<td>ACTION 8</td>
<td>Informed consent, legal and ethical implications of NGS use in (hemato)-oncology molecular diagnostics</td>
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<td>ACTION 9</td>
<td>Pilot study ‘NGS use in routine diagnostics’</td>
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<td>ACTION 10</td>
<td>Build on hospital networks for NGS use in (hemato)-oncology</td>
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Action 1: Establish a commission: Commission Personalized Medicine (ComPerMed)

Website: https://www.compermed.be
Action 2: Development of national guidelines for NGS use in oncology

The Belgian next generation sequencing guidelines for haematology-oncology

A. Hébrant, Ir, PhD, G. Froyen, PhD, B. Maes, MD, PhD, R. Salgado, MD, M. Le Mercier, PhD, N. D’Haene, MD, PhD, S. De Keersmaecker, PhD, K. Claes, PhD, J. Van der Meulen, PhD, P. Aftimos, MD, J. Van Houwt, PhD, K. Cuppens, MD, K. Vanneste, PhD, E. Dequeker, PhD, S. Van Dooren, PhD, J. Van Huysse, MD, F. Nollet, PhD, S. van Laere, PhD, B. Denys, MD, V. Ghislain, PhD, C. Van Campenhout, PhD, M. Van den Bulcke, PhD
**TEST LEVELS**

**Level 1**
- Standard of care biomarker for diagnosis and/or prognosis *
- Biomarker predictive of a response or a resistance to a reimbursed drug in Belgium for this indication

**Level 2**
- Recommended standard of care biomarker for diagnosis and/or prognosis +
- Biomarker predictive of response or resistance to an EMA-approved drug for this indication
- Biomarker predictive of response or resistance to a reimbursed drug in Belgium for another indication (clinical trial available in Belgium or EU)

**Level 3**
- Compelling clinical evidence supporting the biomarker for diagnosis and/or prognosis
- Biomarker predictive of a response or a resistance to
  - a non EMA-approved drug in this indication
  - a reimbursed drug in Belgium for another indication (clinical trial not available in Belgium or EU)
  - an EMA-approved drug for another indication
- Compassionate use of drug

* Standard of care: Included in guidelines (WHO) AND consensus from experts ComPerMed
+ Recommended standard of care: Clinical evidence AND consensus from experts ComPerMed
Test Algorithms represent a sequential of molecular tests to be performed for a particular cancer, documented in addition with the clinical utility (diagnosis, prognosis or therapy), test level and a brief description of the molecular test.

To define the specific conditions for NGS testing
Action 4: QA/QC in NGS oncology

Benchmarking trials

- SOLID tumours
- Haematological tumours
- BRCA trial
- Reports
Reimbursement of NGS

**Nomenclature:** art. 33ter

**Drug:** Chaper VIII

**Scope:** ‘Marker’ and ‘Medicine’ linked by a molecular test

Also prognostic & diagnostic markers
PITTER-NGS VIA HEALTHDATA

Central data registration with a link to the national cancer register

support.healthdata@sciensano.be
NGS comes with the generation of large amounts of data and the management of such information can represent an important added value for quality, outcome analysis and reimbursement reallocation as well as for clinical and public health research.

→ develop a technical platform for central collection and storage of NGS data

→ Healthdata platform with linkage to the national Cancer Registry

Ultimate goal: a central molecular registry with the results of all molecular tests

→ improving access to data for clinical research

→ facilitating evaluation and decision making for policy makers
HEALTHDATA AT A GLANCE

Registration in Primary System

HD4DP
1. Data Captation
2. Secure Data Transfer & encoding of IDs

HD4RES
3. Data Monitoring
4. Data Annotation & Correction Request

DATAWAREHOUSE
5. Data Storage
6. Analysis

HEALTHSTAT
7. BI-Reporting

Technical description of each data collection

Trusted Third Party for encryption and pseudonymization

HEALTHDATA AT A GLANCE
GENOMIC CITIZENSHIP
Genomic Citizenship: why a societal debate?

Support

• No genomics without data sharing

Value laden

• Genetics, medical research, privacy, … - ELSI

Good governance

• Taking the perspective of citizens into account

➢ Many questions, no easy solution
Dealing with difficult problems

\[-i\hbar \sigma \cdot \vec{\nabla} (\phi^R - \phi^L) - i\hbar \frac{\partial}{\partial x_0} (\phi^R + \phi^L) + mc(\phi^R + \phi^L) = 0\]

\[i\hbar \sigma \cdot \vec{\nabla} (\phi^R + \phi^L) + i\hbar \frac{\partial}{\partial x_0} (\phi^R - \phi^L) + mc(\phi^R - \phi^L) = 0\]

\[-i\hbar \frac{\partial}{\partial x_0} (\phi^R + \phi^L) - i\hbar \sigma \cdot \vec{\nabla} (\phi^R - \phi^L) + mc(\phi^R + \phi^L) = 0\]

\[i\hbar \sigma \cdot \vec{\nabla} (\phi^R + \phi^L) + i\hbar \frac{\partial}{\partial x_0} (\phi^R - \phi^L) + mc(\phi^R - \phi^L) = 0\]

\[-i\hbar \frac{\partial}{\partial x_0} \psi_A - i\hbar \sigma \cdot \vec{\nabla} \psi_B + mc\psi_A = 0\]

\[i\hbar \sigma \cdot \vec{\nabla} \psi_A + i\hbar \frac{\partial}{\partial x_0} \psi_B + mc\psi_B = 0\]

\[\begin{pmatrix}
-i\hbar \frac{\partial}{\partial x_0} & -i\hbar \sigma \cdot \vec{\nabla} \\
i\hbar \sigma \cdot \vec{\nabla} & i\hbar \frac{\partial}{\partial x_0}
\end{pmatrix}
\begin{pmatrix}
\psi_A \\
\psi_B
\end{pmatrix}
+ mc
\begin{pmatrix}
\psi_A \\
\psi_B
\end{pmatrix}
= 0\]
The use of genomic information in healthcare as a wicked problem
Dealing with wicked problems:

Authoritative

Competitive

Collaborative
Focus group study
• Involving patients in implementation of genomics in the clinic

Citizens forum
• Gaining insight in citizens’ perspectives on ELSI regarding genomics
The goal of the focus groups is to draft ‘informed’ informed consent guidelines, based on the experiences and opinions of patients.

**Balancing** data from
- focus groups,
- international guidelines
- legal and normative arguments

**Stakeholder working group**
CITIZENS FORUM

With King Baudoin Foundation
Internationally validated method: wicked societal problems

32 informed citizens share their views

- Dialogue, no need for consensus
- Help from a support team
- Information provided by experts
- Working towards balanced policy recommendations
ISSUE FRAMING WORKSHOP (23/02/2018): EXPERTS
The use of genome information in health care: identifying and discussing the ethical, legal and societal issues

INFORMATION BROCHURE (28/06/2018): CITIZENS

THREE WEEKENDS (September – December 2018): CITIZENS

FIRST REPORT -> STAKEHOLDER WORKSHOP (February 2019)

SECOND REPORT -> SYMPOSIUM (End of 2019)
The use of genome information in health care: ethical, legal and societal issues
Report of the Issue framing workshop
Brussels, 23 February 2018
Information brochure

**EC Perspective:**

Joint Action CanCon Policy paper on ‘Public Health Genomics in cancer »

Joint Action IPAAC Work package on Genomics

AIM: ROADMAP on sustainable implementation of recommendations made on cancer control and care
“Through better understanding and integrating information on the role of the genome in fighting diseases and in adaptation to environmental factors, novel approaches in the control or cure of diseases are envisaged. The latter is generally designated as ‘personalized’ or ‘precision’ medicine, the former when studied at the population level as ‘Public Health Genomics’ (PHG).”
Pilot study: link between the national Health Interview Survey (HIS) and genome information

Goals:

- Map the **genetic variability** in the Belgian population (n = 200)
- Link this variability to **health** and **environment**: Smoking
GENETIC VARIABILITY
GENETIC VARIABILITY: Belgian vs. European

GENETIC VARIABILITY: Within Belgium
GENETIC VARIABILITY: Within Belgium
- Typical European population (recent migration from the African continent)
- Belgium has unique properties mirroring geographical orientation (recent migration from Southern Europe)
- Regional differences within Belgium
Smoking behaviour: cessation

- Non-genetic factors: NHIS-2013
- Genetic factors: GWAS

Predictive model: Non-genetic & genetic factors ➔ better prediction?

PUBLIC HEALTH & GENOME: The smoking model
THE SMOKING MODEL: Genetic variables

! Multiple testing correction

A Manhattan plot GWAS smoking cessation

B Distribution rs728341 and rs4937755

C Relative risk smoking cessation

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<tr>
<th></th>
<th>mean [95% CI]</th>
<th>P-value</th>
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<tbody>
<tr>
<td>AB/AA</td>
<td>2.87 [1.44, 4.30]</td>
<td>0.011</td>
</tr>
<tr>
<td>BB/AA</td>
<td>1.40 [1.07, 1.72]</td>
<td>0.016</td>
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THANK YOU