sciensano

healthy all life long

PERSPECTIVES FOR PUBLIC HEALTH GENOMICS WITHIN A HEALTH CARE SYSTEM CONTEXT

Marc Van den Bulcke

Cancer Centre

Sciensano

Geneva, 28 september 2018

.be

Disclaimer

No conflict of interest

Opinions are sole responsability of the speaker

‘Omics’ in national Health Care System of Belgium

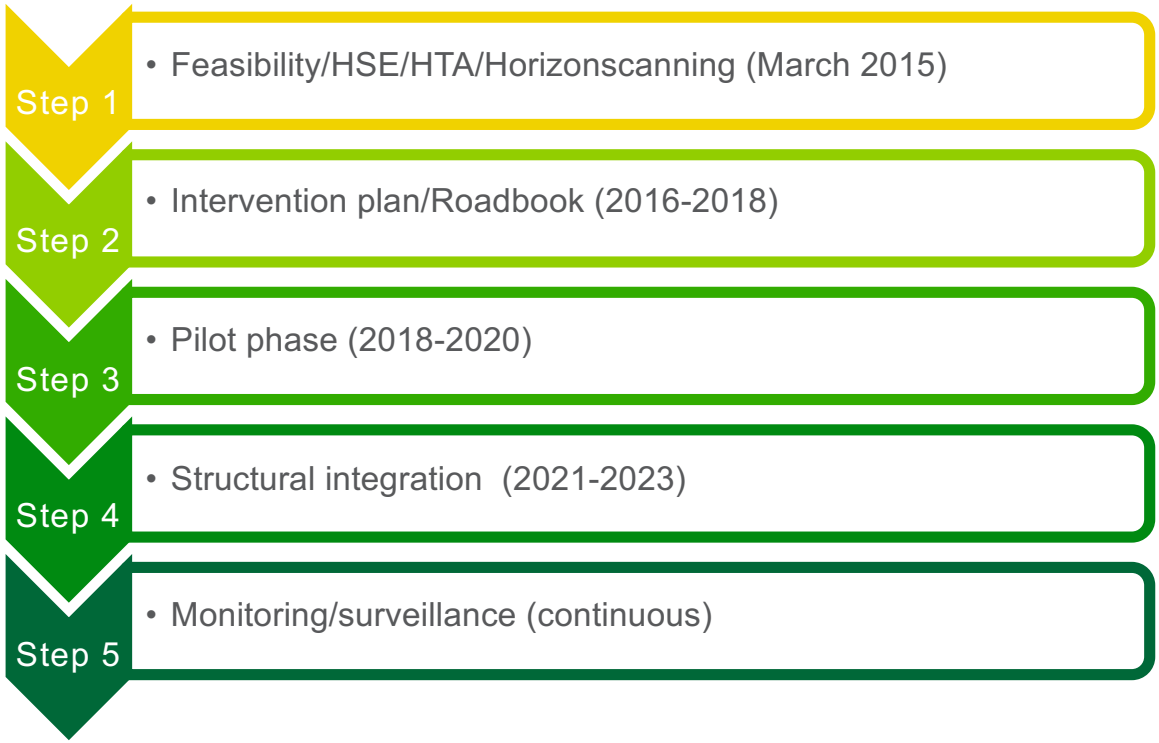
- ‘Omics’ in the clinic
- Genomic citizenship: ethics, legal and privacy
- Public Health Genomics

sciensano

.be


Omics in the clinic

‘Omics in HCS ’ : a multistep process



sciensano

.be

ROADBOOK

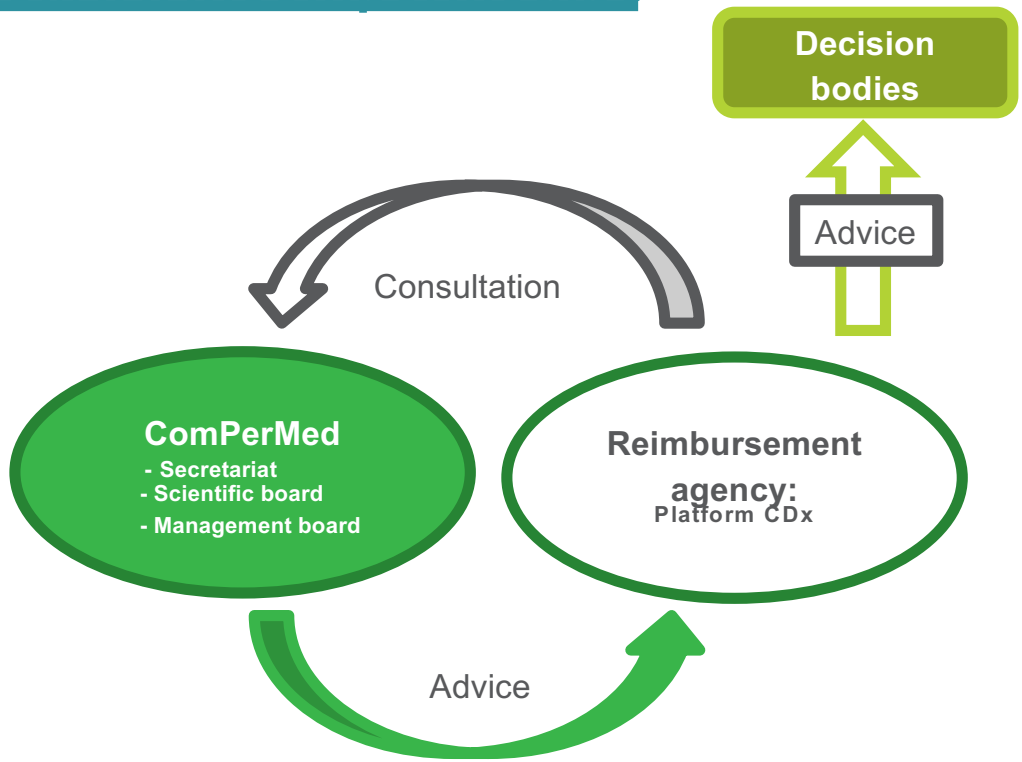
Roadbook for the implementation of next-generation sequencing in clinical practice in oncology and hemato-oncology	
ACTION 1	Establish a commission: Commission Personalized Medicine (ComPerMed)
ACTION 2	Development of guidelines for NGS use in (hemato)-oncology
ACTION 3	Development of criteria for NGS use in (hemato)-oncology
ACTION 4&5	Develop and organize a benchmarking trial and EQA for NGS use in (hemato)-oncology
ACTION 6	Implement NGS registration, storage and data management
ACTION 7	Provide NGS education and training
ACTION 8	Informed consent, legal and ethical implications of NGS use in (hemato)-oncology molecular diagnostics
ACTION 9	Pilot study 'NGS use in routine diagnostics'
ACTION 10	Build on hospital networks for NGS use in (hemato)-oncology

sciensano

.be

Action 1: Establish a commission: Commission Personalized Medicine (ComPerMed)

Website: https://www.compermed.be



sciensano

.be

Action 2: Development of national guidelines for NGS use in oncology

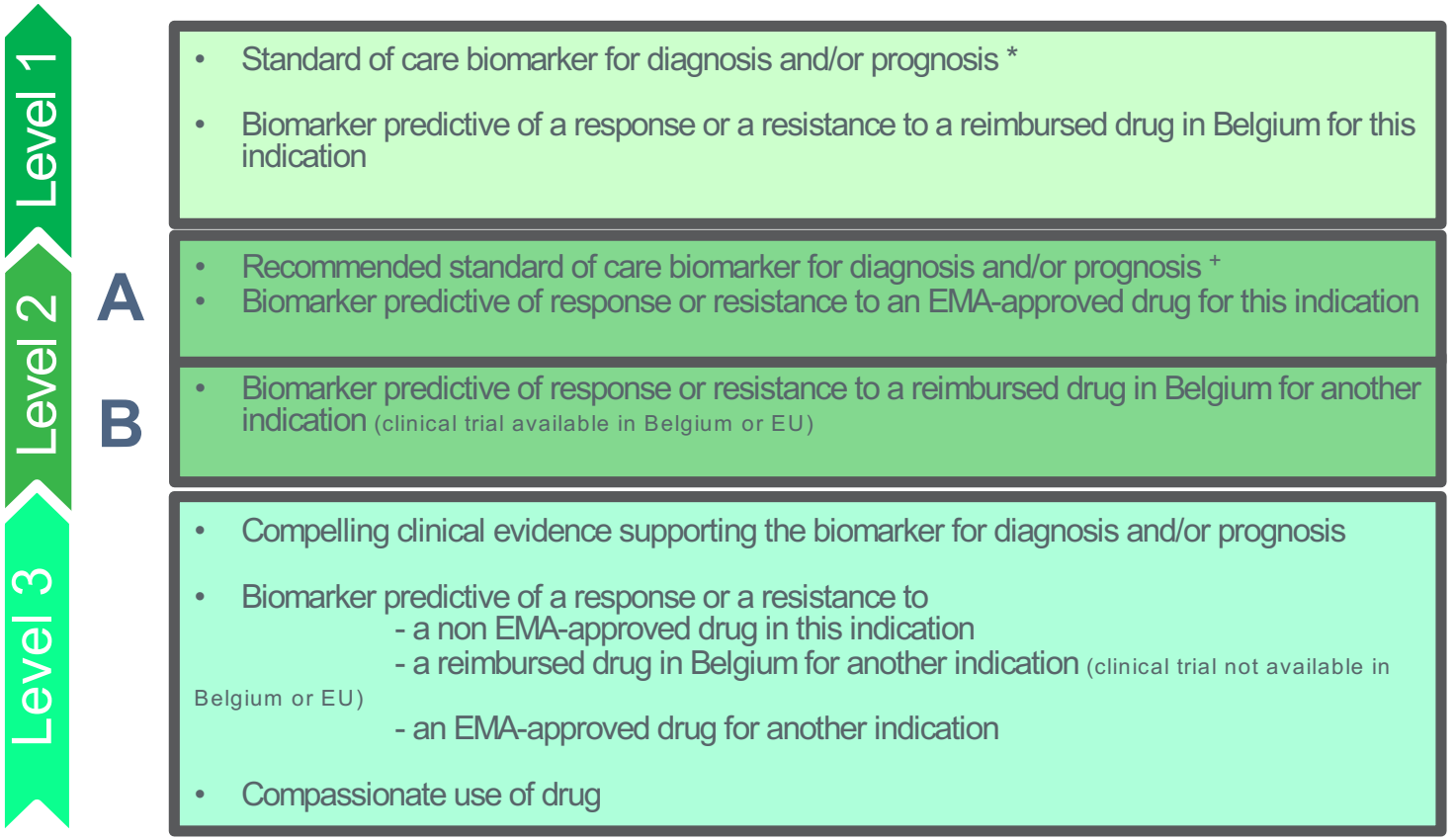
The Belgian next generation sequencing guidelines for haematology-oncology

A. Hébrant, Ir, PhD[1], G. Froyen, PhD[2], B. Maes, MD, PhD[2], R. Salgado, MD[3], M. Le Mercier, PhD[4], N. D'Haene, MD, PhD[4], S. De Keersmaecker, PhD[5], K. Claes, PhD[6], J. Van der Meulen, PhD[6], P. Aftimos, MD[7], J. Van Houdt, PhD[8], K. Cuppens, MD[9], K. Vanneste, PhD[5], E. Dequeker, PhD[8], S. Van Dooren, PhD[10], J. Van Huysse, MD[11], F. Nollet, PhD[12], S. van Laere, PhD[13], B. Denys, MD[12], V. Ghislain, PhD[14], C. Van Campenhout, PhD[14], M. Van den Bulcke, PhD[1]

sciensano

.be

TEST LEVELS



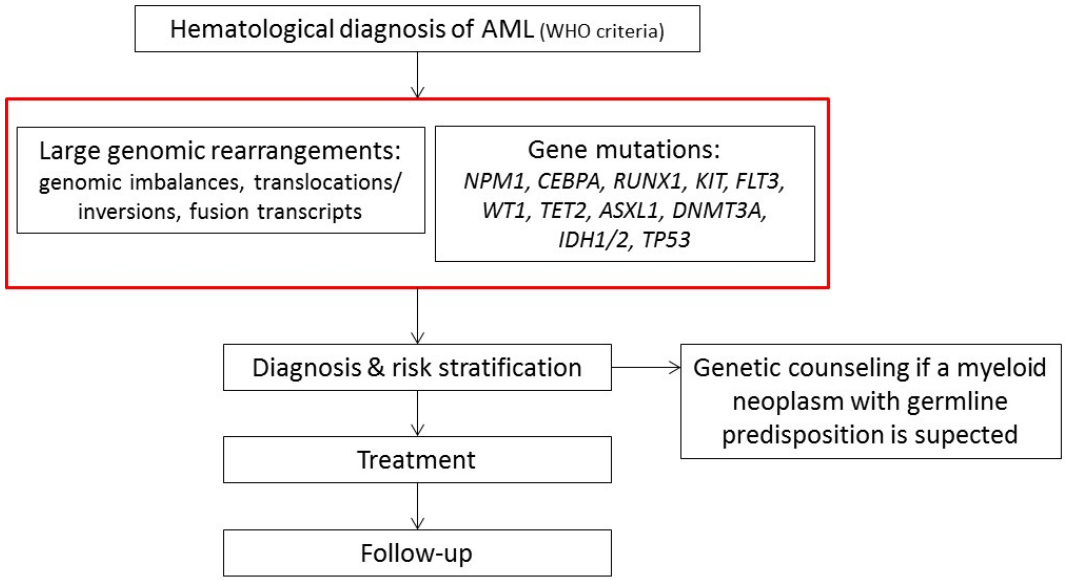
* Standard of care: Included in guidelines (WHO) AND consensus from experts ComPerMed
\+ Recommended standard of care: Clinical evidence AND consensus from experts ComPerMed

sciensano

.be

Test Algorithms

- 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



sciensano

.be

Action 4: QA/QC in NGS oncology

Benchmarking trials

- SOLID tumours
- Haematological tumours
- BRCA trial

- Reports

sciensano

.be

Reimbursement of NGS

Nomenclature: art. 33*ter*

Drug: Chaper VIII

scope: ‘Marker’ and ‘Medicine’ linked by a molecular test

Also prognostic & diagnostic markers

sciensano

healthy all life long

PITTER-NGS VIA HEALTHDATA

Central data registration with a link to the national cancer register

support.healthdata@sciensano.be

.be

Action 6: Implement NGS registration, storage and data management

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

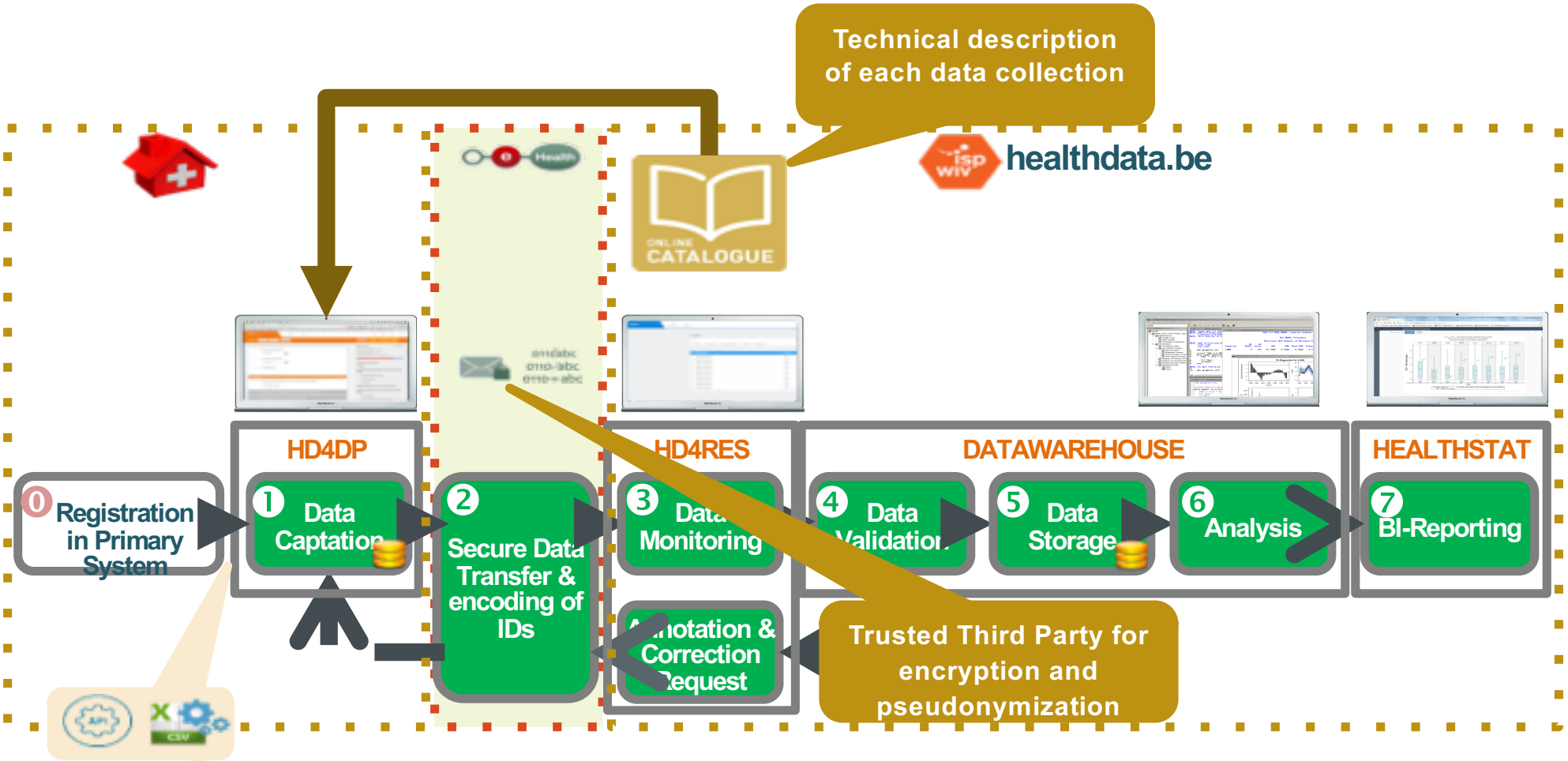
→ improving access to data for clinical research

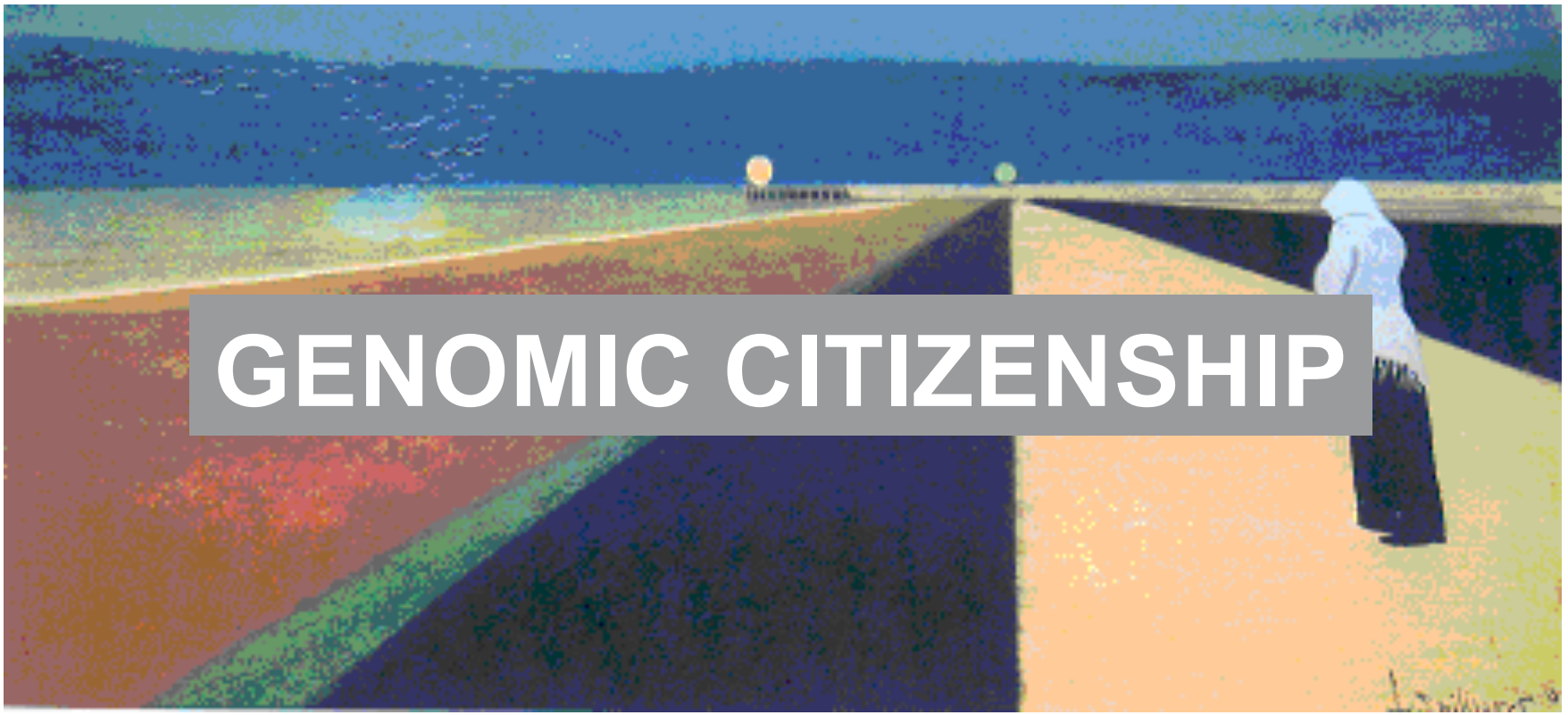
→ facilitating evaluation and decision making for policy makers

sciensano

.be

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

sciensano

.be

Dealing with difficult problems

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

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

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

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

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

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

$$\begin{pmatrix}-i\hbar\frac{\partial}{\partial x_0} & -i\hbar\vec{\sigma}\cdot\vec{\nabla}\\ i\hbar\vec{\sigma}\cdot\vec{\nabla} & i\hbar\frac{\partial}{\partial x_0}\end{pmatrix}\begin{pmatrix}\psi_A\\ \psi_B\end{pmatrix}+mc\begin{pmatrix}\psi_A\\ \psi_B\end{pmatrix}=0$$

sciensano

.be

The use of genomic information in healthcare as a wicked problem

sciensano

.be

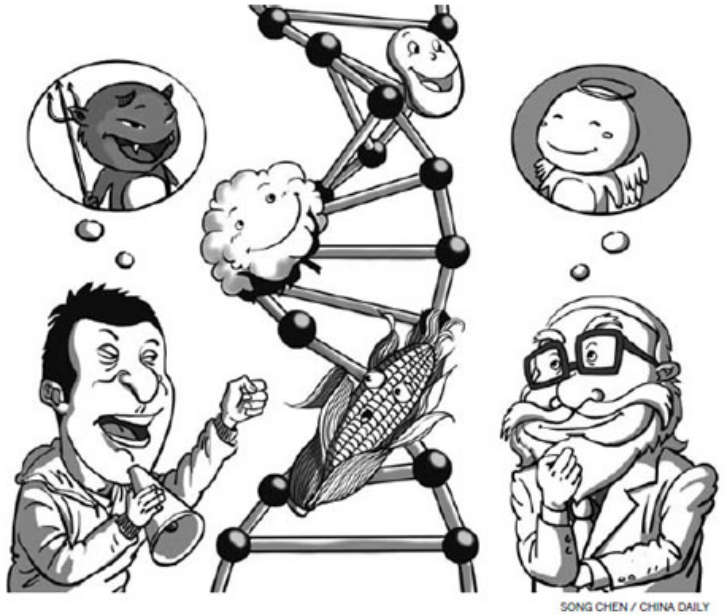
Wicked problems and societal debate

Dealing with wicked problems:

Authoritative

Competitive

Collaborative



sciensano

.be

“Genomic citizenship” in Belgian

Focus group study

- Involving **patients** in implementation of genomics in the clinic

Citizens forum

- Gaining insight in **citizens’ perspectives** on ELSI regarding genomics

sciensano

.be

Focus groups: goal

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

sciensano

.be

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

sciensano

.be

CITIZENS FORUM

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)

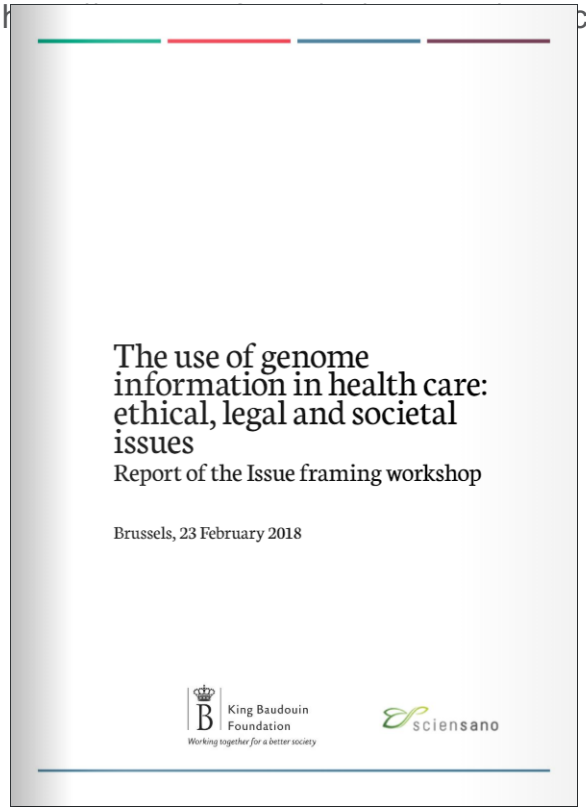
SECOND REPORT -> **SYMPOSIUM** (End of 2019)

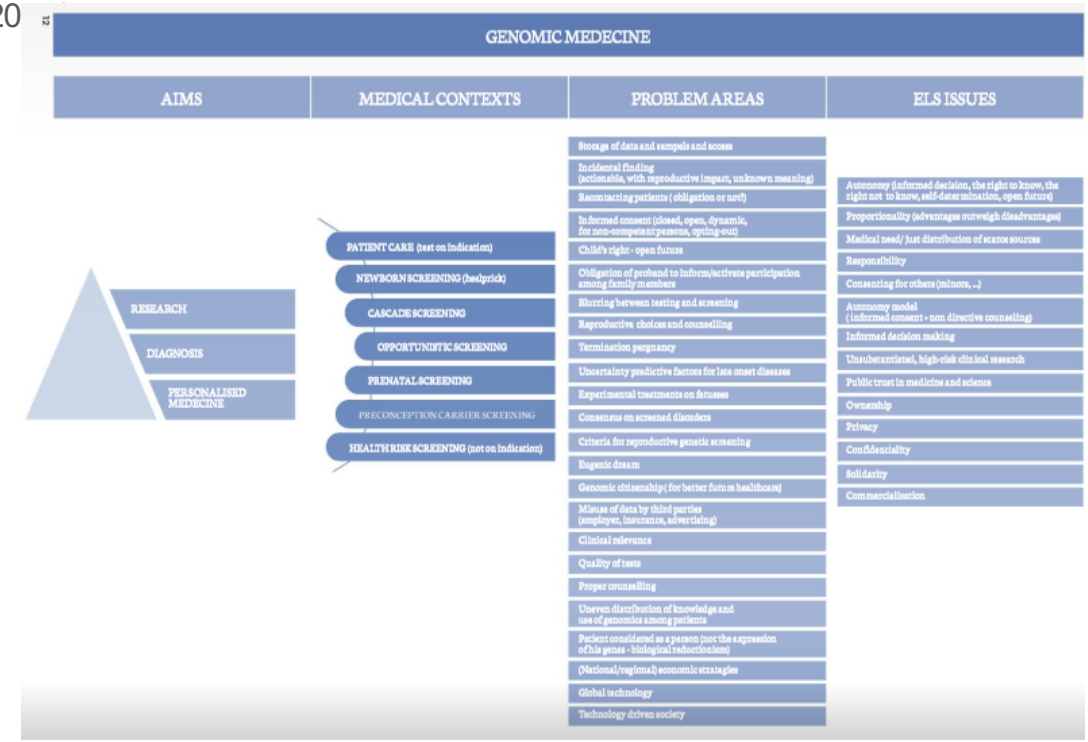
sciensano

.be

ISSUE FRAMING workshop

h…cations/20…

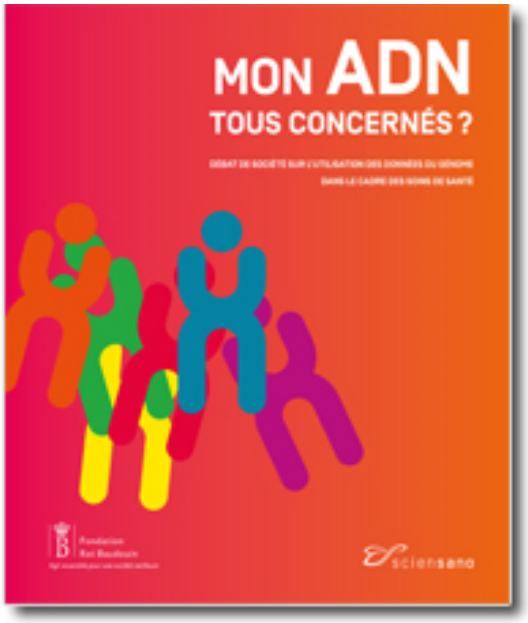




sciensano

.be

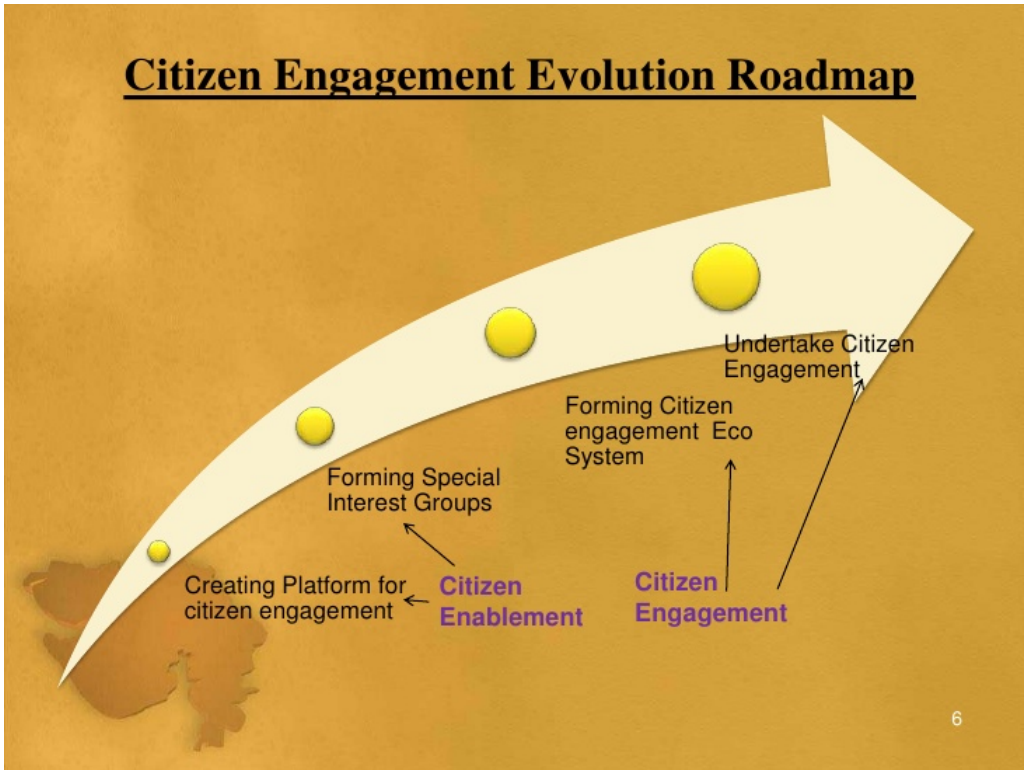
Information brochure



https://www.kbs-frb.be/fr/Activities/Publications/2018/20180704PP

sciensano

.be



EC Perspective:

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

Joint Action **IPAAC** Work packgae on Genomics

AIM: ROADMAP on sustainable implementation of recommendations made on cancer control and care

Co-funded by the Health Programme of the European Union


PUBLIC HEALTH GENOMICS

PUBLIC HEALTH GENOMICS

"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)."

sciensano

.be

Health Interview Survey

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

sciensano

.be

GENETIC VARIABILITY

Van den Eynden et al. Human Genomics (2016) 10:6
DOI 10.1186/s40246-016-0130-8

Human Genomics

PRIMARY RESEARCH Open Access

The genetic structure of the Belgian population

Jimmy Van den Eynden[1,2*], Tine Descamps[1], Els Delporte[1], Nancy H. C. Roosens[1], Sigrid C. J. De Keersmaecker[1], Vanessa De Wit[1], Joris Robert Vermeesch[3], Els Goetghebeur[4], Jean Tafforeau[1], Stefaan Demarest[1], Marc Van den Bulcke[1] and Herman Van Oyen[1,2*]

Abstract

Background: National and international efforts like the 1000 Genomes Project are leading to increasing insights in the genetic structure of populations worldwide. Variation between different populations necessitates access to population-based genetic reference datasets. These data, which are important not only in clinical settings but also to potentiate future transitions towards a more personalized public health approach, are currently not available for the Belgian population.

Results: To obtain a representative genetic dataset of the Belgian population, participants in the 2013 National Health Interview Survey (NHIS) were invited to donate saliva samples for DNA analysis. DNA was isolated and single nucleotide polymorphisms (SNPs) were determined using a genome-wide SNP array of around 300,000 sites, resulting in a high-quality dataset of 189 samples that was used for further analysis. A principal component analysis demonstrated the typical European genetic constitution of the Belgian population, as compared to other continents. Within Europe, the Belgian population could be clearly distinguished from other European populations. Furthermore, obvious signs from recent migration were found, mainly from Southern Europe and Africa, corresponding with migration trends from the past decades. Within Belgium, a small north-west to south-east gradient in genetic variability was noted, with differences between Flanders and Wallonia.

Conclusions: This is the first study on the genetic structure of the Belgian population and its regional variation. The Belgian genetic structure mirrors its geographic location in Europe with regional differences and clear signs of recent migration.

Keywords: Genetic variability, Population genomics, Public health genomics

Background

After the completion of the Human Genome Project in 2003, international efforts were initiated to map human genetic variation between populations. This variation has been described for 26 populations worldwide via the 1000 Genomes Project [1, 2]. While this is a valuable resource for studying global genetic variation, both the number of samples per population and the total number of populations studied are relatively low. To gain sufficient statistical power and avoid false positives/negatives due to unmatched control populations in genotype-phenotype association studies, population-based genetic reference data are required from more specific and extended populations [3]. To address this, population-based whole genome sequencing initiatives have been performed at the national level throughout Europe [4–7]. From these genetic population studies, it has become clear that there is a strong correlation between the geographical location and the genetic structure of different populations [8, 9], also at the more regional level (e.g., along a north-south axis in the Netherlands) [6, 7, 9, 10]. Currently, this genetic information is not available for the Belgian population.

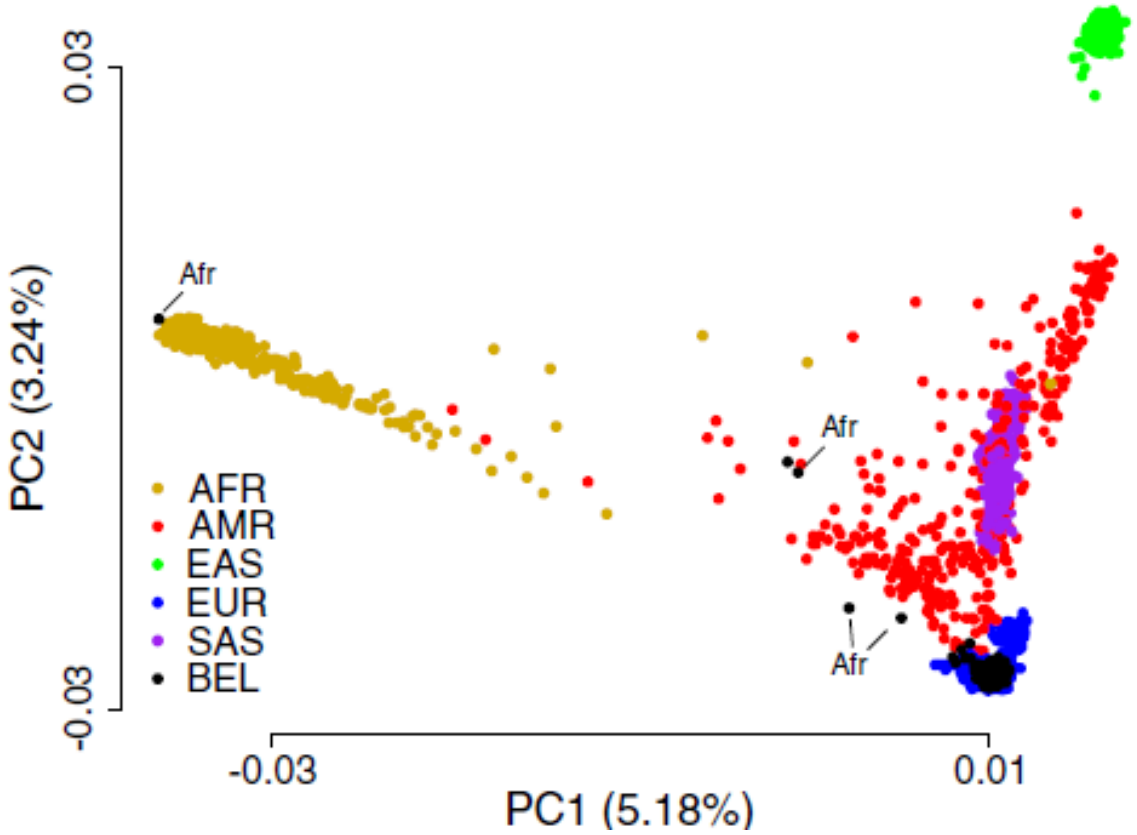
Therefore, a population-based cross-sectional study, called BelPHG-21 (Belgian Public Health Genomics in the twenty-first century), was organized that aims at describing the genetic variability in the Belgian population and relating

*Correspondence:
jimmy.van.den.eynden@gmail.com; herman.vanoyen@wiv-isp.be
[1]Scientific Institute of Public Health, Brussels, Belgium
Full list of author information is available at the end of the article

sciensano

.be

GENETIC VARIABILITY:
Belgian vs. Continental

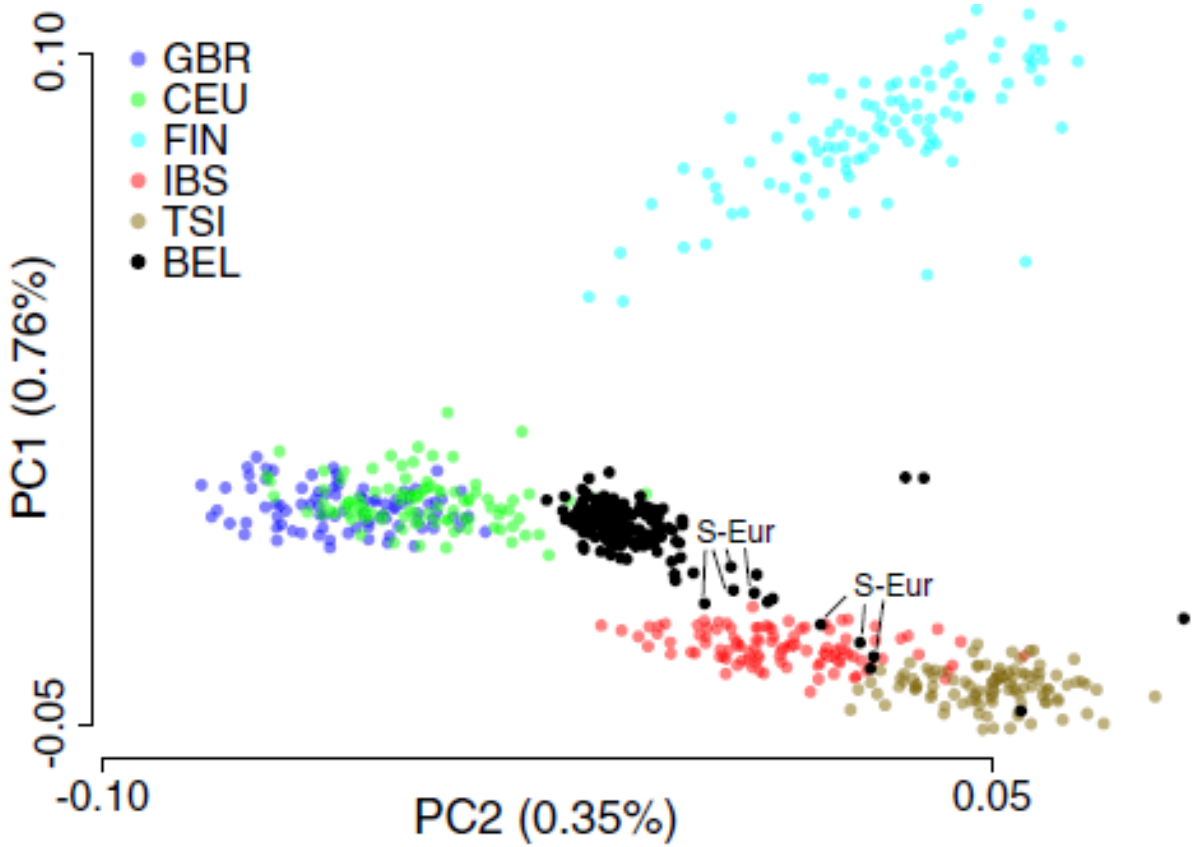


sciensano

Van den Eynden *et al* (2018) Human Genomics

.be

GENETIC VARIABILITY: Belgian vs. European

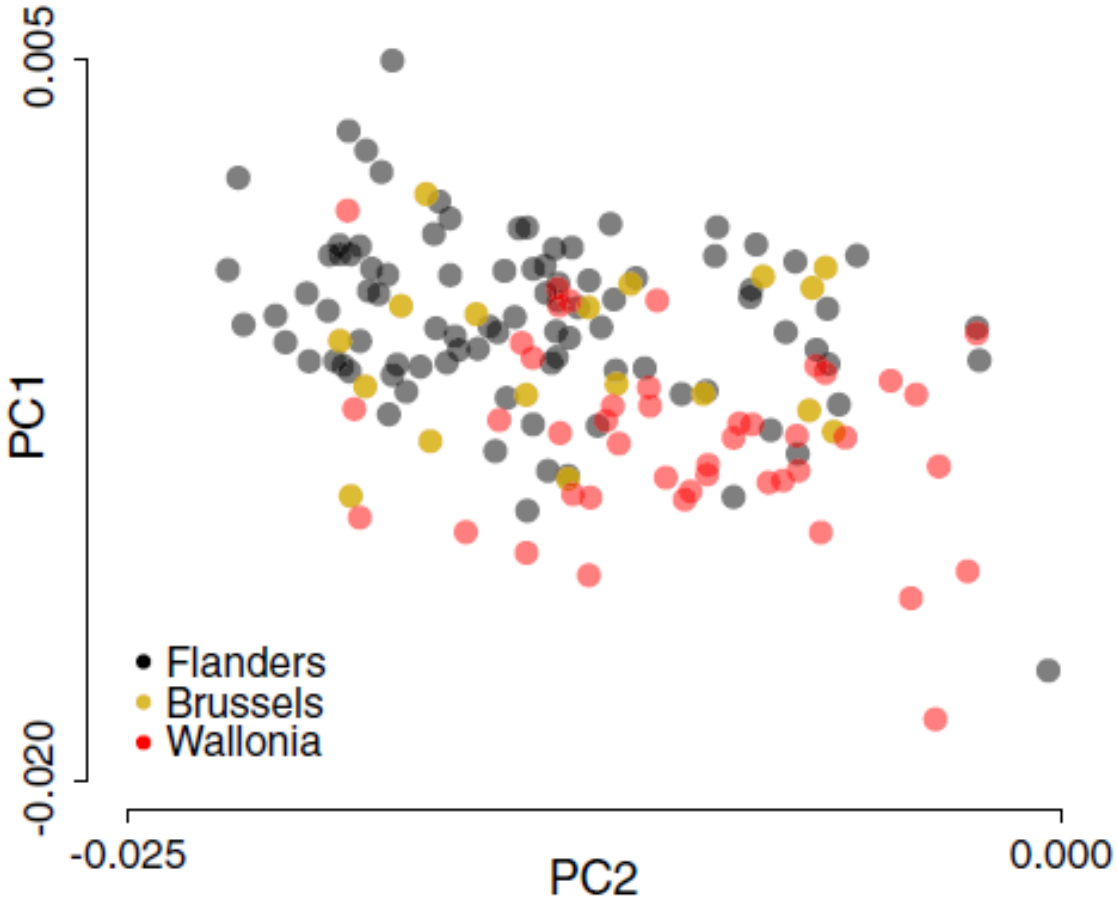


sciensano

Van den Eynden *et al* (2018) Human Genomics

.be

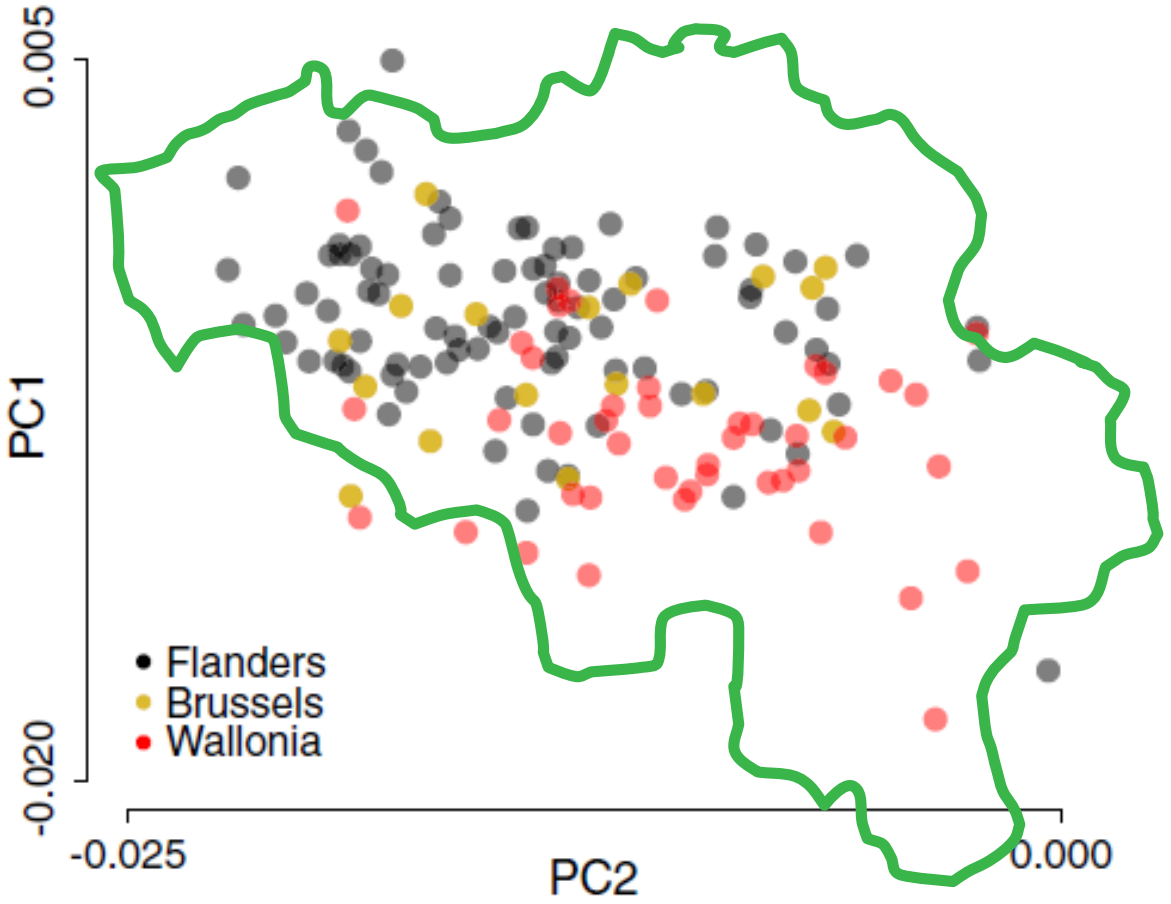
GENETIC VARIABILITY: Within Belgium



sciensano

.be

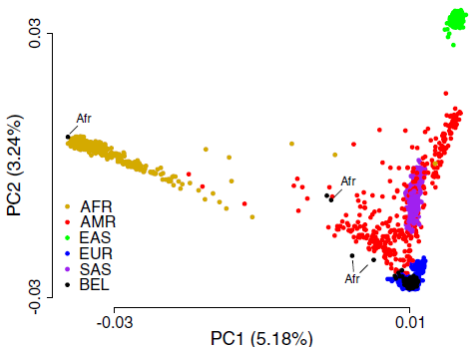
GENETIC VARIABILITY: Within Belgium

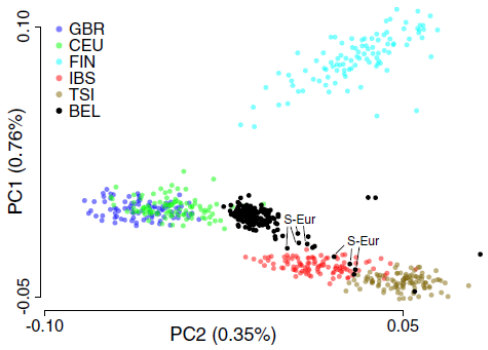


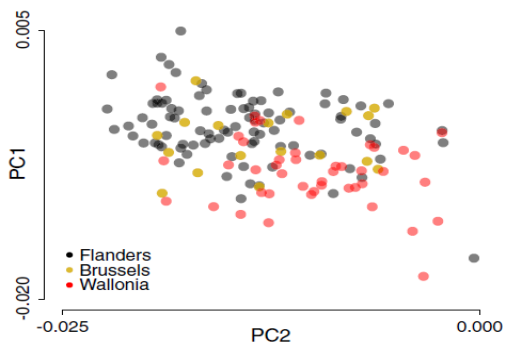
sciensano

.be

GENETIC VARIABILITY: Conclusions







- 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

sciensano

.be

PUBLIC HEALTH & GENOME:
The smoking model

Smoking behaviour:
cessation

Non-genetic factors:
NHIS-2013

Genetic factors:
GWAS

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

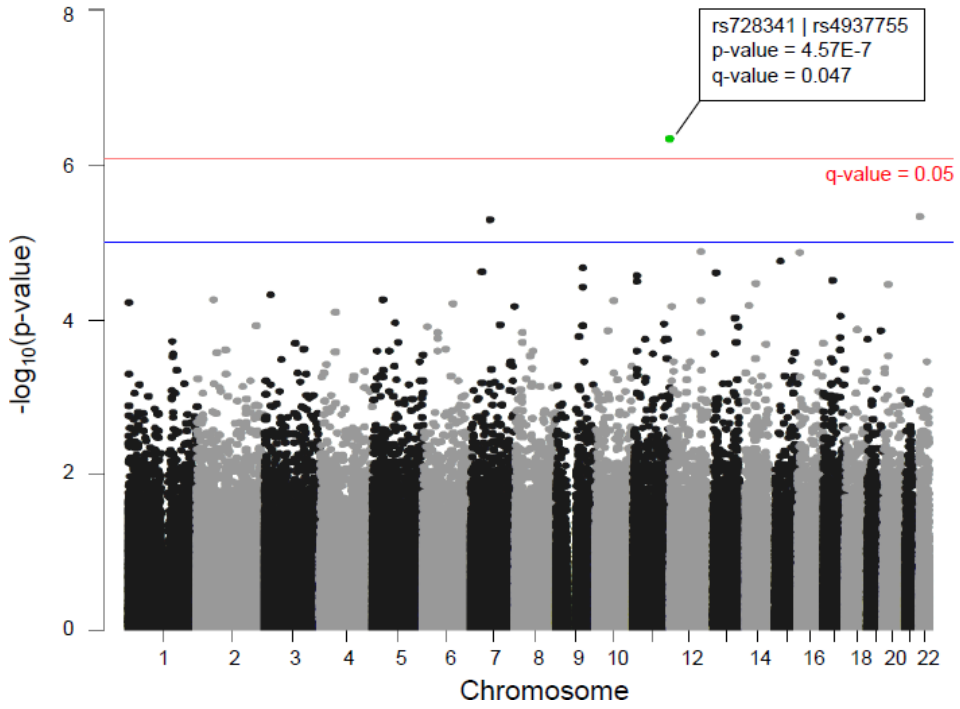
sciensano

.be

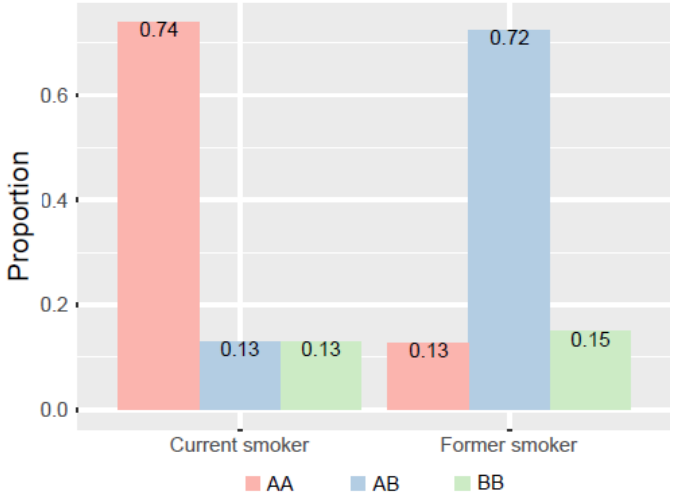
THE SMOKING MODEL:
Genetic variables

! Multiple testing correction

A Manhattan plot GWAS smoking cessation



B Distribution rs728341 and rs4937755



C Relative risk smoking cessation

	mean [95% CI]	P-value
AB/AA	2.87 [1.44, 4.30]	0.011
BB/AA	1.40 [1.07, 1.72]	0.016

sciensano

.be

THANK YOU

sciensano

.be