CANCON

Cancer Control Joint Action

WP5 ’Public Health Genomics in Cancer’

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Marc Van den Bulcke| La Valetta, Malta 14 February 2017

WP5: PHG IN CANCER

Scope

- **Cancer** control as a major public health issue and being a **pathology strongly driven by genetic modification**, is closely linked to a novel field in epidemiology wherein molecular data at population scale are integrated into new strategies for from a personalized medicine as a public health perspective. This domain is generally designated as '**Public health genomics' (PHG)**.
- Here, we wish to propose guidance to three important issues where PHG can substantially advance not only our understanding of cancer control but also support policy makers, citizens and cancer patients in particular, in their common fight against cancer.
- At first, the importance of strictly regulating ***stratified screening*** by genetic testing of high-risk cancer patients, secondly key issues to be addressed within the health care system when ***implementing genomics*** as such in medical care, and thirdly how to deal with ***'Direct to Consumer' testing*** within the healthcare system

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Response to Call for experts:

18 positive replies

- Belgium: **J. Vermeesch** (KUL), **M. Peeters & C. Rolfo** (UZA), **R. Salgado** (GZA), **L. Decoster** & J. Degrève (VUB), A. Waeytens (RIZIV-INAMI**), Olga Kholmanskikh** (FAGG)
- France: **F. Nowak** & C. Berling (INCA)
- Netherlands: A. Brand (Univ Maastricht)
- Germany: C. Von Kalle (DKFZ, Heidelberg), **R. Schmützler** (Univ. Köln)
- Italy: **S. Boccia** (Univ Cath Roma), **A. De Censi** (Rome)
- EC: **J. Waligora** (DG Santé), **J. Van de Loo** (DG RTD), J. Zupan (DG JRC), **M. Huebl, A. Monsterra**t, **Isabel de Ladiges** (DG Santé)
- USA: M. Khoury (CDC, NCI)
- CanCon partners: **T. Albreht** (Slovenia), **G. Nicoletti, A. Federici** (Italy)

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Key point from first expert meeting:

The target group of this position paper is senior policy makers!

Thus: provide guidance on how to install a system that brings genomics into the health care system

- **clinical utility driven approaches**
- **who pays what**

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WP5: PHG IN CANCER

- ***Personalized risk-assessment for stratified prevention'***

  Proposal by R. Schmutzler (Germany)

- **Requirements and prerequisites for implementation of 'omics' in routine molecular diagnosis in oncology**

  Proposal by M. Van den Bulcke (Belgium)

- ***"Direct –To-Consumer" (DTC) testing***

  Proposal by S. Boccia (Italy)

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General Recommendation

- Establish a framework on the ethical, legal and social requirements related to introducing the use of 'omics' data into the health system

- Increase genetic and preventive literacy of healthcare professionals and citizens to promote responsible use of these novel options.

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PERSONALIZED RISK-ASSESSMENT FOR STRATIFIED PREVENTION'

- **Cancer screening (CS**) aims to identify cancer at a pre-symptomatic stage in order to improve patient outcomes, i.e to reduce mortality and morbidity and to improve quality of life.

  target population: mainly general population with an *average* risk to develop the disease in a specific age group.

- **Genetic screening (GS)** is defined as genetic testing for medical purposes that is systematically offered to the entire population or specific segments of the entire population as a part of **"Personalized risk-assessment for stratified prevention" (PeRaSP)**.

  target population: individuals *at elevated risk* for certain tumour diseases

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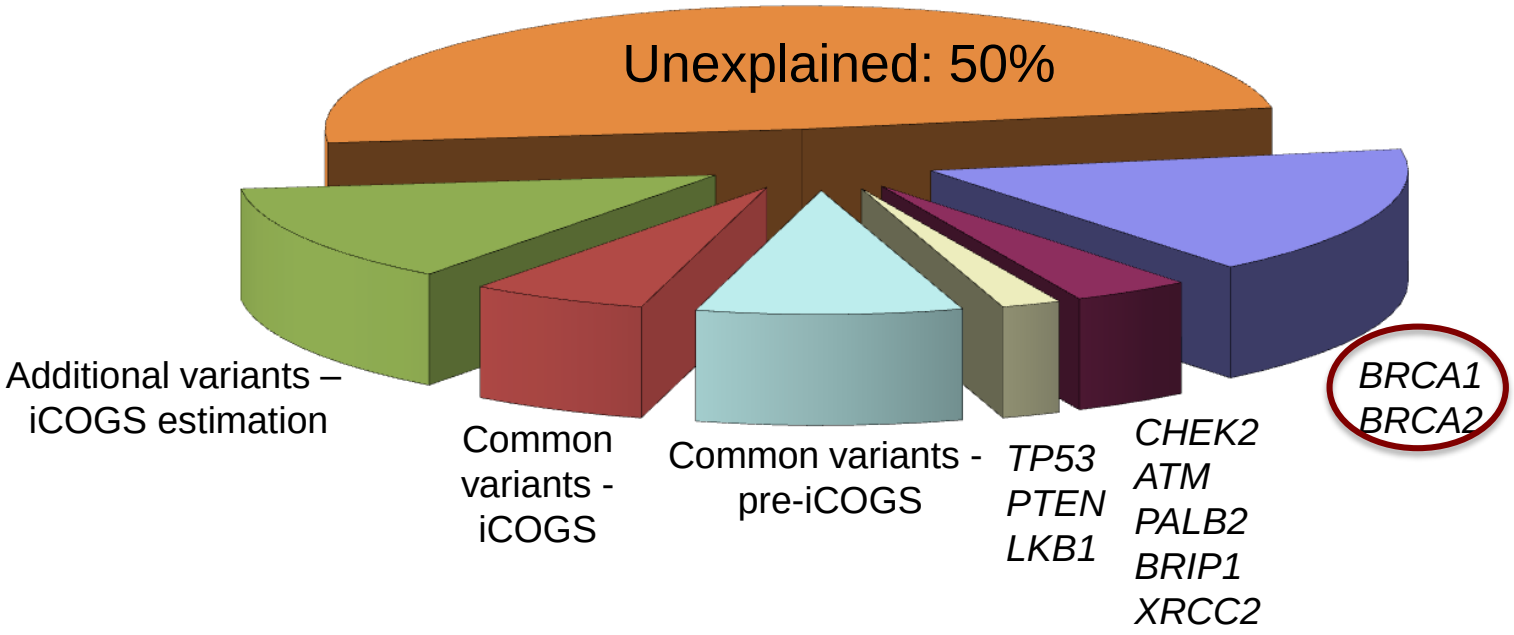
DEUTSCHES KONSORTIUM
für familiären Brust- und Eierstockkrebs
unterstützt durch die Deutsche Krebshilfe e.V.

CONTRIBUTION OF KNOWN GENETIC FACTORS TO FAMILIAL AGGREGATION OF **BREAST CANCER**



PERSONALIZED RISK-ASSESSMENT FOR STRATIFIED PREVENTION'

Recommendation 1: Develop harmonized common entrance criteria for PeRaSP throughout Europe

Recommendation 2: Establish and promote specific multi-disciplinary professional structures for the indication, evaluation and provision of PeRaSP

Recommendation 3: Increase genetic and preventive literacy of health care professionals (i.e. literacy on risk assessment, risk communication, clinical interpretation of genetic test results, indication of preventive measures)

Recommendation 4: Increase genetic and preventive literacy of citizens to allow a responsible handling of cancer preventive options and resources of the health care system

Recommendation 5: Establish new genotype-/phenotype data bases to enable prospective cohort studies and QA as a prerequisite for the evaluation of the effectiveness of PeRaSP (preferentially to be linked to existing cancer registries)

Recommendation 6: Establish a harmonized framework on the ethical, legal and social requirements of PeRaSP in cancer

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EU Roadmap

Implementation of ‘omics’ in routine molecular diagnosis in oncology

Definition ‘Personalized Medicine’

… no commonly agreed definition of the term “personalised medicine”. However, it is widely understood that

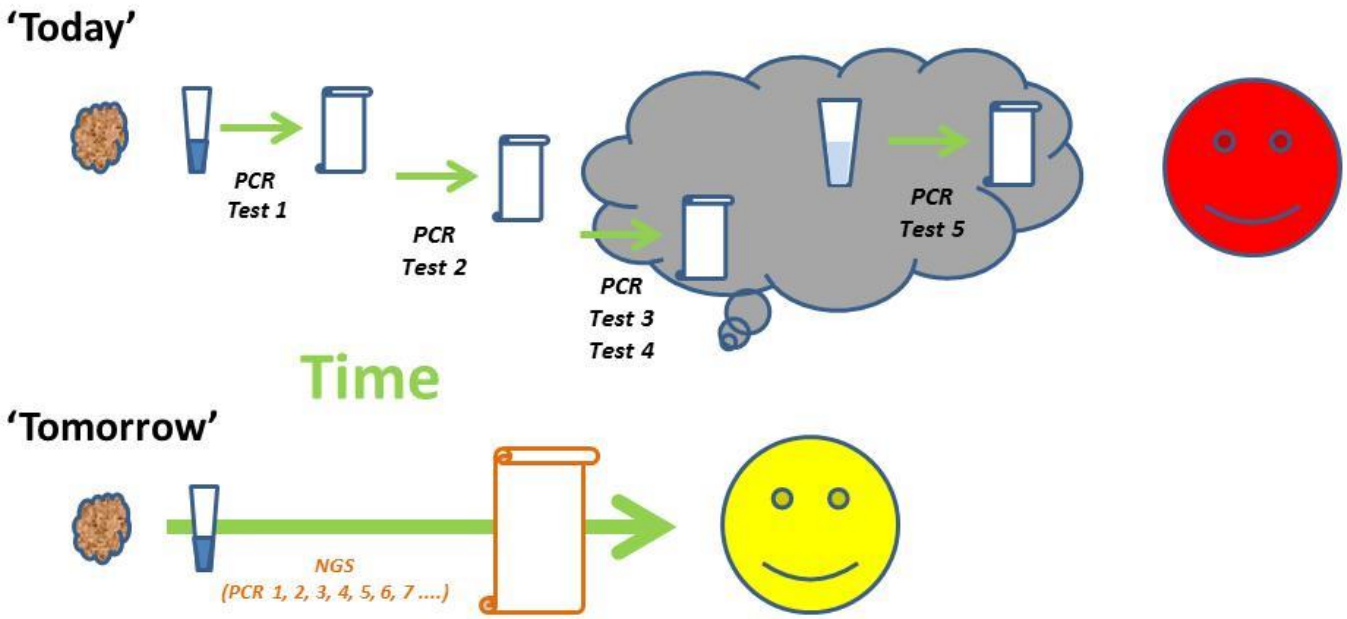
Personalised Medicine refers to

“a medical model using characterisation of individuals' phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention.”

Personalized medicine relates to the broader concept of patient-centred care, which takes into account that, in general, healthcare systems need to better respond to patient needs”

Council conclusions on Personalised medicine for patients (2015)

NGS: Added value to current molecular diagnostics

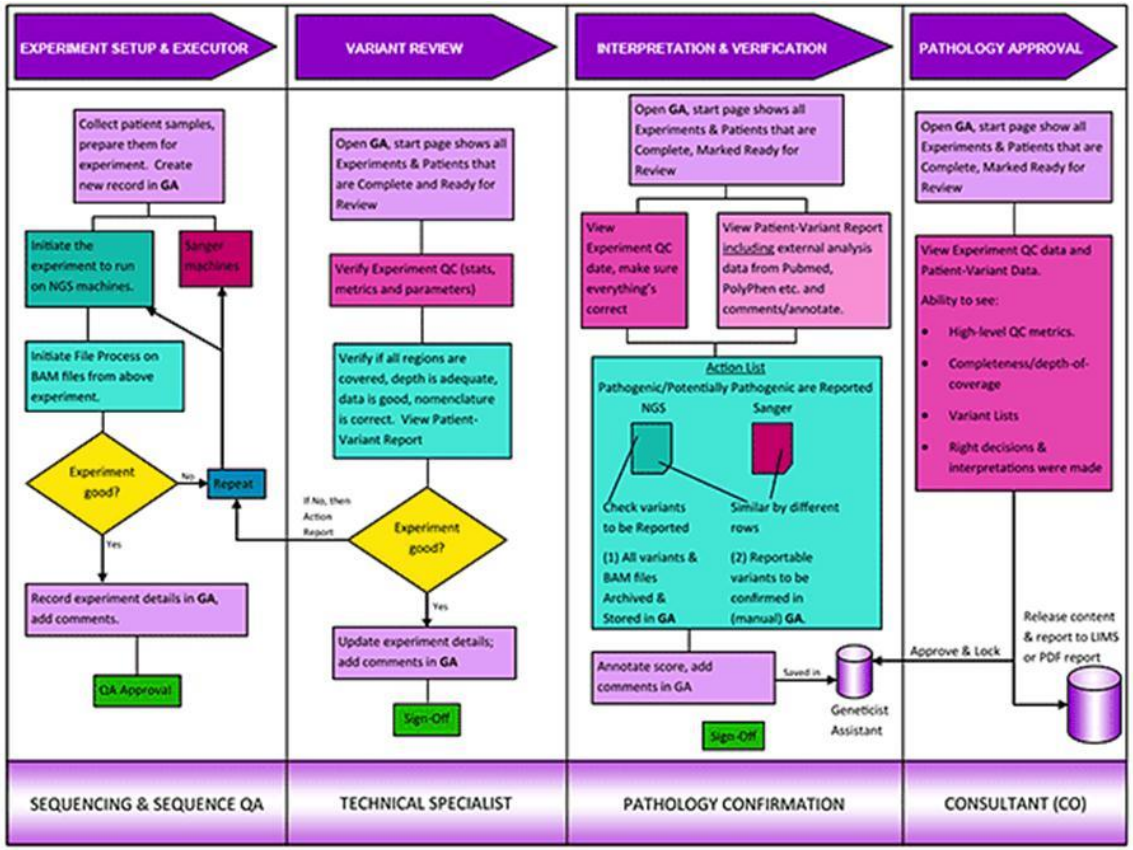


Advantages:

- ***Less*** material for ***more*** info
- Info at the DNA sequence level (***precision*** higher)
- Parallel analysis, ***faster*** conclusive results

Disadvantages:

- ***New*** paradigm (privacy, legal, ethical aspects)
- Major primary ***investment***
- ***Complex*** interpretation
- Does ***not substitute*** for all molecular testing (e.g. translocations)


EXPERIMENT SETUP & EXECUTOR
VARIANT REVIEW
INTERPRETATION & VERIFICATION
PATHOLOGY APPROVAL
Collect patient samples, prepare them for experiment. Create new record in GA
Initiate the experiment to run on NGS machines.
Sanger machines
Initiate File Process on BAM files from above experiment.
Experiment good?
No
Repeat
Yes
Record experiment details in GA, add comments.
QA Approval
Open GA, start page shows all Experiments & Patients that are Complete and Ready for Review
Verify Experiment QC (stats, metrics and parameters)
Verify if all regions are covered, depth is adequate, data is good, nomenclature is correct. View Patient-Variant Report
If No, then Action Report
Experiment good?
Yes
Update experiment details; add comments in GA
Sign-Off
Open GA, start page shows all Experiments & Patients that are Complete, Marked Ready for Review
View Experiment QC date, make sure everything's correct
View Patient-Variant Report including external analysis data from Pubmed, PolyPhen etc. and comments/annotate.
Action List
Pathogenic/Potentially Pathogenic are Reported
NGS
Sanger
Check variants to be Reported
Similar by different rows
(1) All variants & BAM files Archived & Stored in GA
(2) Reportable variants to be confirmed in (manual) GA
Annotate score, add comments in GA
Saved in
Geneticist Assistant
Sign-Off
Open GA, start page show all Experiments & Patients that are Complete, Marked Ready for Review
View Experiment QC data and Patient-Variant Data.
Ability to see:
High-level QC metrics.
Completeness/depth-of-coverage
Variant Lists
Right decisions & interpretations were made
Approve & Lock
Release content & report to LIMS or PDF report
SEQUENCING & SEQUENCE QA
TECHNICAL SPECIALIST
PATHOLOGY CONFIRMATION
CONSULTANT (CO)

IMPLEMENTATION OF 'OMICS' IN ROUTINE MOLECULAR DIAGNOSIS IN ONCOLOGY

Recommendation 1: For each country, establish a system and infrastructure that oversees the rapid evolution within oncological clinical use and utility of molecular variants

Recommendation 2: Develop an integrated outcome evaluation framework allowing linkage between different healthcare information registries/repositories invoking standardized data formats and data transmission protocols to gain evidence by clinical trials setups tailored to framework of personalized genome context

Recommendation 3: Launch the public debate on the use and limits of use of genomic information for public health and healthcare support improvement with citizens, cancer patients, professionals, scientists, industry and government responsibles

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GENDIA (GENETIC DIAGNOSTIC NETWORK)

Wat is een Kanker Risico test?

- De Kanker Risico test bepaalt uw risico op erfelijke kanker door de analyse van 30 genen die betrokken zijn bij een erfelijke aanleg voor kanker.

- De Kanker Risico test spoort dus geen bestaande kanker op, maar een verhoogd risico om kanker te ontwikkelen, voornamelijk kanker van de borst, eierstokken (ovaria), baarmoeder (uterus), darm, maag, alvleesklier (pancreas), huid (melanoom) en prostaat. Wanneer met de Kanker Risico test een genvariant wordt gevonden die een verhoogd risico op kanker geeft, kan een kanker screening en preventieplan voor u worden opgesteld.

- De **Kanker Risico test** analyseert **30 genen** die betrokken zijn bij de ontwikkeling van erfelijke tumoren zoals kanker van de borst, eierstokken, baarmoeder, darm, maag, alvleesklier (pancreas), huid (melanoom) en prostaat. De 30 genen die met de Kanker Risico test worden geanalyseerd zijn: ***BRCA1, BRCA2, APC, ATM, BAP1, BARD1, BMPR1A, BRIP1, CDH1, CDKN2A CDK4, CHEK2, EpCAM, GREM1, MLH1, MSH2, MSH6, MITF, MUTYH, NBN, PALB2, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, SMAD4, STK11 en TP53.***

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"DIRECT – TO - CONSUMER" TESTING

The 'Direct-To-Consumer' genetic testing industry has sparked significant controversy not only among the scientific community, but also among professional societies and government agencies. Although our understanding of the human genome holds much promise in the realm of cancer prevention and treatment, DTC genomic profiling for cancer risk prediction is unlikely in its current form to have any significant impact on the health of the public.

CAUTION

Legal framework

Counseling needs

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DIRECT –TO - CONSUMER" TESTING

Recommendation 1: DTC GT for cancer risk prediction is unlikely in its current form to have any positive impact on the health of citizens. Citizens' and health care professionals' awareness and education in this framework is urgently needed

Recommendation 2: Policy makers should regulate the offering of DTC being aware that legislation should balance consumer protection with the 'freedom of opinion'

Recommendation 3: Each citizen should have access to organized certified genetic counseling in his country provided by a national health care system

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PHG IN CANCER: FUTURE COLLABORATIVE PERSPECTIVES

EC DG Santé

- **New Joint action on Cancer: 'Innovative Partnership on Action against Cancer**

Making use of recent scientific advances, this Joint Action is expected to reinforce prevention of cancer via population based programmes on cancer screening, further developing the principles of the 2003 Recommendation on Cancer Screening, paying particular attention to genetic screening and personalised medicine.

- **Ongoing Joint actions on Chronic diseases, Rare Cancers**

EC DG RTD

- **Horizon 2020**
- **EC PERMED initaitive**

EC initiatives on 'Big data'

- **DG Connect**

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THANKS

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