Personalised Medicine and PerMed SRIA

“Strategische Vernetzung der Forschung in Österreich – im Kontext der großen gesellschaftlichen Herausforderungen”

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- on behalf of PerMed -
1. Challenges, bottlenecks, gaps and needs?

2. “Can Europe lead the global way”?

3. PerMed SRIA!
1. Challenges, bottlenecks, gaps and needs?

1.1. What evidence for informed policy-making?

1.2. What key policy areas for Europe and beyond?
1.1. What evidence for informed policy-making?
Why are our health interventions still not successful? (only 15% are evidence-based...)

... because there is no „one size fits all“!

>> we need more targeted/“personalised“ interventions

>> we need complementary interventions running in parallel (population level, subpopulation level, individual level)

... and basic research in genomics is providing evidence for doing so - all diseases are due to genome-environmental interactions!
Examples: IDs, obesity, CVDs, addiction, vaccination, cancer and RDs (!)
Environmental exposures vs. Exposome
[Nuria Malats, EUPHA 2010]

Rappaport & Smith, Science 2010
Stratified Medicine is about adapting the treatment (molecule, dose, schedule,...) according to the patient’s characteristics for better efficacy and less adverse events.

Pharmacogenomics [Ilhan Celik, EHFG, 2010]

Stratified Medicine versus Personalized Medicine

- Patient sub-population e.g. molecular testing for tumor mutation
- Individual patients e.g. cancer vaccine made from the patient’s tumor
... genomics is a „moving target“ ...
... from the

Human Genome Project

to the

Personal Genome Project ...
... from

single and linear systems

to

non-linear networks (e.g., in systems biology and systems medicine) …
Not only 4 P’s ...
... not only beyond the 4 P’s, but also (A. Brand, 2008) ...

1. from common complex diseases to “multiple rare diseases”

2. from diseases to “diseasomes”

3. from risk factor to “risk pattern”

4. from clinical utility to “personal utility”
Plausibility?
Two types of prediction models?

1. Will the disease occur?

<< A. hazards/health threats: incl. “inherited epigenomics”, use of biomarkers and biomonitoring systems, health protection

<< B. occurring “by chance”

2. Having the disease, how will the disease develop?

<< very accurate, “truly” individualized therapies/interventions, early secondary prevention
Epigenomics is the missing link between environment/social sciences and biomedicine!

>> ability of all environmental factors to gene expression and phenotype change

>> ability to understand genome-environment interactions

>> ability to measure genome-environment interactions

>> ability of early diagnosis of individuals for adult-onset disease (... old Barker theory?)

>> ability of novel preventive and therapeutic approaches in an asymptomatic health status

>> need for the implementation of intraindividual monitoring & surveillance systems (individual health management)

>> need for personalized healthcare (“personal health and care”)
WHY YOUR DNA ISN’T YOUR DESTINY

The new science of epigenetics reveals how the choices you make can change your genes—and those of your kids

BY JOHN CLOUD
Microbes maketh man

The Catholic church’s unholy mess
Paul Ryan: the man with the plan
Generation Xhausted
China, victim of the Olympics?
On the origin of speeie
Infant antibiotic exposures and early-life body mass

L Trasande1,2,3, J Blustein1,4, M Liu5, E Corwin3, LM Cox3 and MJ Blaser4,5

OBJECTIVES: To examine the associations of antibiotic exposures during the first 2 years of life and the development of body mass over the first 7 years of life.

DESIGN: Longitudinal birth cohort study.


MEASUREMENTS: Exposures to antibiotics during three different early-life time windows (<6 months, 6–14 months, 15–23 months), and indices of body mass at five time points (6 weeks, 10 months, 20 months, 38 months and 7 years).

RESULTS: Antibiotic exposure during the earliest time window (<6 months) was consistently associated with increased body mass (β = 0.105 and β = 0.083 s.d. unit, increase in weight-for-length Z-scores at 10 and 20 months, \( P < 0.001 \) and \( P = 0.001 \), respectively; body mass index (BMI) Z-score at 38 months + 0.067 s.d. units, \( P = 0.009 \); overweight OR 1.22 at 38 months, \( P = 0.029 \)) in multivariable, mixed-effect models controlling for known social and behavioral obesity risk factors. Exposure from 6 to 14 months showed no association with body mass, while exposure from 15 to 23 months was significantly associated with increased BMI Z-score at 7 years (β = 0.049 s.d. units, \( P = 0.050 \)). Exposures to non-antibiotic medications were not associated with body mass.

CONCLUSIONS: Exposure to antibiotics during the first 6 months of life is associated with consistent increases in body mass from 10 to 38 months. Exposures later in infancy (6–14 months, 15–23 months) are not consistently associated with increased body mass. Although effects of early exposures are modest at the individual level, they could have substantial consequences for population health. Given the prevalence of antibiotic exposures in infants, and in light of the growing concerns about childhood obesity, further studies are needed to isolate effects and define life-course implications for body mass and cardiovascular risks.

International Journal of Obesity advance online publication, 21 August 2012; doi:10.1038/ijo.2012.132

Keywords: antibiotics; human microbiome; body mass; ALSPAC
The Future? ..... translating into healthcare systems

(1) highly (in space & time) dynamic personal (health) information

(2) from statistical risks within groups to “individualized evidence”

(3) “virtual individual models” (simulations)

"ICT and Big Data for health & health for ICT and Big Data": a radically new vision for healthcare and health systems!
1.2. What key policy areas for Europe and beyond?
The BIG4HEALTH 😊
- four key research policy areas for Europe ...

1. decision-supporting tools

2. “big data”

3. ownership

4. health systems
1. decision-supporting tools

- HTA 3.0 (assumption non-linearity and “personal evidence”)

- systematic early dialogue/PPP (e.g. LAL model, MAPPs), best practice of PPP = IMI

- “just in time” interventions (JITs)

- orphan drug model & pilots (e.g. Germany: “Heilversuch” with N=25) / RoI

- drug/theranostics/CDx/IVD versus Medical Device ... (use of) health information (HI)

- “virtual twin”: in silico ”try and error“ (simulations, artificial learning)
2. “big data”

- **N=1 trials:** “I am my own reference point”

- **N=all trials:** mission impossible (“big data” will always be incomplete)

- **unstructured (and structured) data for unknown future purposes** (more than just data linkage or open access)

- validation, standardization: mission impossible (always a “momentum”)

- “incidental findings”/noise: all findings are important, we just cannot interpret them (yet): “junk versus garbage”

- health information will always be “messy”/chaotic: what (not why) is good enough in most cases! Correlation versus causality ...
3. Ownership

- “I am the owner of my data”: personal ownership (property based, excluding right, paternalistic) vs. citizen ownership/control (broader, social right, shared right, democratic)

- from informed consent (blanket or broad) & privacy issues to data-users accountability: “trust & trusts”! (... to guarantee data security is dishonest!)

- “big data” meet governance of information via algorithm providers (QM): rules of impartiality, confidentiality, competence (interpretation of data) and professionalism

- Health Data Cooperatives (e.g., citizen is the only “supercomputer” (data integrator), balance between public good – personal benefit, “data commons”, “citizen science”, no monetary incentives for individuals!)
4. health systems

- “good governance” – “good” implementation of “good” health policies (e.g. in Europe cross-border directive, “bottom-up” policies)
- WHO-EU Regional office (Tallinn, 2008): six system building blocks
2. “Can Europe lead the global way?”

European activities and milestones?
a. Public Health Genomics European Network (PHGEN)
"European Best Practice Guidelines for Quality Assurance, Provision and Use of Genome-based Information and Technologies”

(Public) Health moves towards Personalised Medicine ...

Public Health Genomics (PHG) – Personal Health and Care
... paradigm shift in Public Health towards Personalised Health & Care!

_health promotion and prevention in public health_

"one size fits all"

or

_risk groups_

_communities_

_settings_

_prevention in public health genomics_

_individuals_

_family history_

_lifestyle_

_genomic profiling_

_risks for "diseasomes"_

_risk groups with similar risk patterns_
b. European Science Foundation (ESF)
**ESF Position Paper**
May 2011

**Technology**
19-20 Sept 2011
London, UK

1) CV & metabolic diseases
2) Oncology
3) Rare Diseases

**Disease Summit**
18-20 Oct 2011
The Hague, NL

13-14 Feb 2012
Dubrovnik, HR

Identify grand challenges and recommendation

**“Big picture” Summit**
on clustered issues

**Stakeholder conference**
18 April 2012
Rome, IT

Consensus discussion on Grand Challenges and overall recommendations

**PerMed**
c. European Health Forum Gastein (EHFG)

d. European Alliance for Personalised Medicine (EAPM)
EAPM “Big Data” WG
(lead: Intel & Science Europe)

“European Data Value Chain Strategy –
A lighthouse initiative on Personalised Medicine”
(Policy paper 7 May 2014)
The three sets of policy actions of big data for personalized medicine

Liberate the data but do no harm
- Collaboration
- Sharing
- Public/Private partnerships
- Transparency
- Privacy
- Ownership

Bring it now
- Clinical adoption
- Data curation
- Veracity
- Security
- Common standards

Prepare the future
- Public education
- Workforce skills
- ICT infrastructures for life sciences
- Bioinformatics
- Analytics
Specialised Treatment for Europe’s Patients – „STEPS“

STEP 1: Ensuring a regulatory environment which allows early patient access to novel and efficacious personalised medicine (PM)

STEP 2: Increasing R&D for PM, while also recognising its value

STEP 3: Improving the education and training of healthcare professionals

STEP 4: Supporting new approaches to reimbursement and HTA, required for patient access to PM

STEP 5: Increasing awareness and understanding of PM

EAPM believes that achieving these goals will improve the quality of life for patients in every country in Europe.
e. CSA-PerMed !
„Personalised Medicine 2020“

Shaping Europe’s vision for Personalised Medicine!
CSA PerMed – History


Theme: Preparing the future for health research and innovation

(370 pre-proposals / 43 full proposals / 10 Consortia funded)

Project time: 09/2013 - 08/2015, Budget: ~0.5 Mio.€

27 Partner from 14 Countries

Partner e.g. from Health and Research Ministries, Funding Organisations, Research Institutes, Societies, Industry, Regulation Bodies

Major aim was the development of a Strategic Research and Innovation Agenda (SRIA)
Personalised Medicine in Europe - preparing the ground by EC

Identify key challenges to be addressed by research:

2010: Preparatory workshops

2011: European Perspectives conference

2013: "Omics report"
The Coordination & Support Action (CSA) PerMed

• to step up coordination efforts between European key stakeholders
• to allow synergies and avoid duplication or competition
• to ensure maximum transparency and openness
A consortium of **18 partners** and **9 cooperating partners**

- Research and Health Ministries, Funding Bodies
- Research Institutes, Industry, SMEs, Foundations and Societies
- Connected to important other European initiatives related to Personalized Medicine (e.g. PHGEN, EuroBioForum, ESF, EAPM, EHFG, EC reports, CASyM, 3GBTest and EPEMED)
## PerMed – Partner

<table>
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<th>No.</th>
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<th>Country</th>
<th>Organisation type</th>
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<td>German Aerospace Center, Project Management Agency (DLR PT)</td>
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<td>Project Management Agency</td>
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<td>Project Management Agency</td>
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<td>Funding Organisation</td>
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<td>Health Policy Association</td>
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<td>Industry (SME)</td>
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<td>European Personalized Medicine Association (EPEMED)</td>
<td>Luxembourg</td>
<td>NGO/ Business development</td>
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<td>27)</td>
<td>Ministry of Social Affairs (MoSA-Estonia) Dr. Ivi Normet</td>
<td>Estonia</td>
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The aims of PerMed are

- to complement existing activities by identifying and promoting promising research topics and developments
- to prepare a strategic research and innovation agenda (SRIA),
- to identify and discuss gaps & needs with stakeholders of all areas involved in Personalised Medicine (e.g. by workshops and interviews)
- and thereby give strategic recommendations how to foster the implementation of Personalised Medicine for the benefit of society
PerMed SRIA

“Shaping Europe’s vision for Personalised Medicine!”
The **Methodology** applied in PerMed – **1**

- Analyse around **20** strategic reports on PM to prepare an inventory of recommendations (e.g. SWOT and gaps & needs analysis)
- Develop and conduct semi-structured **interviews** with over **35** key stakeholders in PM (e.g. SWOT and gaps & needs analysis)
The **Methodology** applied in PerMed - 2

- **Workshops** with stakeholders to review, discuss and adapt the recommendations (March 2014 in Berlin, October 2014 at European Health Forum Gastein (EHFG))

- Prioritise and group all input to draft a **collection** and a **short list** of the recommendations to foster PM

- Development of a Strategic Research and Innovation Agenda (**SRIA**) on the basis of key reports, interviews, literature, output of meetings and input from partners
Evaluation of Personalised Medicine (PM) Reports (over 20) Interviews with PM Stakeholders (around 40) PerMed Partners (27) Further input e.g. Publications and Meetings on PM

Workshop 1, Berlin
~ 90 participants
• Basic Research & New Technologies
• Translational Research
• Regulation, Reimbursement & Market access
• Health System in General
• PM in Europe & Canada
• HTA and Citizens perspective

Workshop 2, Gastein (EHFG)
EHFG Forum 4 ~ 120 participants
• Patient involvement
• General Practitioner (GP)
• Hospitals
• Legal & Ethical aspects
• Regulatory aspects
• Rare Diseases (example)
• Nutrition & life style (example)

SRIA Recommendations to:
• European Commission
• Member States
• Research Communities
• Industry
• Funding and Regulatory Bodies
• Providers
The PerMed SRIA outline

“Shaping Europe’s vision for Personalised Medicine!”

• Challenge 1 – Developing Awareness and Empowerment
• Challenge 2 – Integrating Big Data and ICT Solutions
• Challenge 3 – Translating Basic to Clinical Research and Beyond
• Challenge 4 – Bringing Innovation to the Market
• Challenge 5 – Shaping Sustainable Health Care
SRIA – 35 Recommendations clustered in 5 Challenges and 3 areas

Challenge 1 – Developing Awareness and Empowerment
Challenge 2 – Integrating Big Data and ICT Solutions
Challenge 3 – Translating Basic to Clinical Research and Beyond
Challenge 4 – Bringing Innovation to the Market
Challenge 5 – Shaping Sustainable Healthcare

A) Biomedical, health-related ICT and health research
B) Humanities and social sciences research
C) Improvement of the framework for implementing PM

22 Proposed Research Activities to foster Personalised Medicine (PM)
The PerMed **SRIA outline**

“Shaping Europe’s vision for Personalised Medicine!”

**Per Challenge**

- Introduction to the challenge
- Examples of ongoing activities (National, European & International)
- Targeted achievements until 2020 and beyond
  
  - Recommendations
  
  - Enablers

- Conclusions
Figure 2: Circle of Challenges with important enablers and stakeholders. The overall aim of PM research and implementation is in the centre of the circle. Furthermore, there are manifold interrelations between the five challenges; these have not been indicated in order to keep the clearness of the figure.
Figure 3 The SRIA recommendations. The 35 recommendations of the five challenges are outside the circle. Some of these recommendations are also related to other challenges, therefore they are shown again within the circle. Furthermore, there are manifold interrelations between the five challenges; these have not been indicated in order to keep the clearness of the figure.
Annex A: PerMed Recommendations

All recommendations have been colour-coded according to the activities referred to, which are grouped into three broad areas. However, many recommendations do have a share in two or sometimes all three types of activity (see also figure 3 in chapter 5). In these cases, the recommendation has been assigned to the activity deemed to have the major share.

The colour-coding is as follows:

- **Recommendations on biomedical, health-related ICT and health research**
- **Recommendations on humanities and social sciences research**
- **Recommendations to improve the framework for implementing PM (e.g. economic, organisational, regulatory, ethical, legal and social)**

Challenge 1 – Developing Awareness and Empowerment

1. Provide further evidence for the benefit delivered by PM to health systems.
2. Develop and promote models for individual responsibility, ownership and sharing of personal health data.
3. Develop mobile health applications to maximise engagement of patients with their treatment pathways and track the safety and effectiveness of these interventions.
4. Understand how the changes related to PM will impact public health and ensure they translate directly to benefits for individual citizens and society.
5. Improve communication and education strategies to increase patient health literacy.
6. Incorporate patient participation in the healthcare system and increase the patient’s role in all phases of research and development.
7. Develop common principles and legal frameworks that enable sharing of patient-level data for research in a way that is ethical and acceptable to patients and the public.

Challenge 2 – Integrating Big Data and ICT Solutions

8. Promote strategies to make sense of ‘big data’.
9. Develop and encourage the fast uptake of technologies for data capture, storage, management and processing.
10. Promote the development of high quality sustainable databases including clinical, health and well-being information.
11. Support translational research infrastructures and enforce data harmonisation fostered by specific ICT infrastructures designed to the health data.
12. Support analytical methods and modelling approaches to develop new disease models, e.g. ‘Computerised Twins’ or ‘Virtual Patient’.
13. Develop new decision support tools and methodologies of ICT to analyse and interpret data in order to support physicians in their decision-making process.
Challenge 3 – Translating Basic to Clinical Research and Beyond

15. Develop methods to better integrate and evaluate the information provided by genomic, epigenetic, transcriptomic, proteomic, metabolomic and microbiome analyses.

16. Support research in preclinical models to validate hypotheses resulting from molecular analyses of patient samples and treatment outcomes.

17. Promote collaborative pre-competitive and trans-disciplinary research in all disease areas to gain trustworthy and objective information.

18. Instigate a European-wide biomarker evaluation and validation process.

19. Promote longitudinal studies in the areas of PM.

20. Support development of new clinical trial designs and promote integration with concomitant preclinical testing.

21. Re-classify diseases at the molecular level.

22. Develop suitable funding models to enable cross-sector working in PM research.

Challenge 4 – Bringing Innovation to the Market

23. Formalise a risk-based approach for the evaluation of PM.


25. Support research on an adequate regulatory and legal framework for PM.

26. Encourage a systematic early dialogue between innovators, patients and decision-makers throughout all regulatory steps to provide guidance and clarity.

27. Facilitate partnerships and innovation networks to encourage cross-disciplinary and cross-border collaboration in research and development using an ‘Open Innovation’ approach.

28. Provide support and guidance for companies to enter the market for PM with sustainable business cases.

Challenge 5 – Shaping Sustainable Healthcare

29. Support health economics research of PM to support decision makers.

30. Develop prospective surveillance systems for personal health data that facilitate accurate and ongoing assessment of highly dynamic health information across the life course.

31. Develop training programmes on PM for health professionals.

32. Encourage a citizen-driven framework for the adoption of electronic health records.

33. Promote engagement and close collaboration between patients, stakeholders and healthcare actors across sciences, sectors and borders.

34. Develop a framework for pricing and reimbursement for PM that ensures equitable access for all patients – regardless of economic or geographic status – and is sustainable for health systems.

35. Develop an optimised overall healthcare financing strategy.
PerMed – Impact and Outlook

- PerMed and the SRIA are the basis for further EC/MS activities in all areas of Personalised Medicine (PM) research and implementation
- The EC has set up a workshop on PM with MS
- EC will organise a meeting on PM (~June 2016)
- EC intends to set up a CSA to support the establishment of an European Consortium on PM
- EC and several MS intend to set up a ERA-Net Co-fund to foster PM-related research
- Council conclusions December 2015 (Luxembourg EU Presidency)
Personalised Medicine, Individualised Medicine, Stratified Medicine, Precision Medicine...

Something fundamentally different here: from linearity to non-linearity (dynamics in space and time on individual level) ...

Major changes needed ...

=> Need for action on all levels requiring all kinds of expertise!

We can not think big, creative and holistic enough!
THANK YOU