

# EUROPEAN INITIATIVES FOR HEALTH RESEARCH AND DEVELOPMENT

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This report summarises the “European initiatives for health research and development” workshop that was held at the World Health Summit in Berlin on Sunday 29<sup>th</sup> October 2019. The workshop was hosted by the **BioMed Alliance**, **Charité – Universitätsmedizin Berlin** and the **M8 Alliance**.

Europe leads in many areas of health research and has developed powerful models of cross-border, cross-sectoral research cooperation. These have helped to increase the EU’s attractiveness as a place for research and innovation, produced high-quality patents and created jobs and growth. The Scientific Panel for Health, one of the expert groups tasked by the Commission, included in its recommendations a proposal for a European Council for Health Research as a multi-stakeholders’ platform to provide a comprehensive policy for health research in Europe, and facilitate cross-border collaboration.

Global partnerships in health research create opportunities for enhanced learning, innovation and better health. Different models for participation, for data sharing and leadership co-exist. Through examples and stakeholders’ debate, **the session aims to explore needs and opportunities for future design of European health research and global partnerships.**

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## CHAIRS

### **Axel Pries**

BioMed Alliance | President | Belgium

Berlin Institute of Health (BIH) | Chairman of the Executive Board | Germany

### **Karin R. Sipido**

KU Leuven | Professor of Medicine and Head of Experimental Cardiology | Belgium

## SPEAKERS

### **Gilles Bloch**

INSERM | Chairman and CEO | France

### **Alberto De Negri**

KPMG Italy | Head of Healthcare | Italy

### **John P. A. Ioannidis**

Stanford Prevention Research Centre | Professor and Director, Meta-Research Innovation Centre at Stanford | United States of America

Einstein fellow, Berlin Institute of Health | Germany

### **Britta Siegmund**

German Research Foundation (DFG) | Vice-President | Germany

### **Päivi Sillanaukee**

Ministry of Social Affairs and Health | Permanent Secretary | Finland

*Acknowledgment: this report was prepared by Sally Jackson and Karin Sipido. It was reviewed by all speakers.*

## FOREWORD BY THE CHAIRS

### **Axel Pries**

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In its consensus document proposing a European Council for Health Research, the Horizon 2020 Scientific Panel for Health (SPH) emphasized the need for a new approach for health research to have more impact, to enable better health. Creating more synergies for health research across sectors and borders necessitates an EU-wide vision and strategy: More cohesive and better-aligned funding, programs and initiatives will benefit health research. Continuity in a long-term vision will increase efficiency and facilitate sustainable results. Research into mechanisms that delay implementation and uptake into health care can identify measures for more equality between European countries. This call for leadership in health at EU level and for strong multi-stakeholders' collaboration, comes from different groups, such as the EU Health Coalition, including among others the BioMed Alliance, EFPIA and the patient-led PACT coalition.

The presentations and panel discussion in this workshop explore different aspects of such a future scenario. Partnerships for multi-sectoral and cross-border collaborations enhance research value. How can we develop a common agenda with stakeholder participation? With research as a path to better health and as a means to improve health care outcomes and costs, what funding mechanisms are in place, and how will we ensure that the research data that guides policies is of high quality? Well-being and prevention research and implementation should be embedded in a comprehensive health research policy. How can this concept be developed into practice?

**INSERM** is a large public research organization in France that represents 13,000 people (8,000 of whom are on INSERM's payroll), across 14 clinical research centres connected to university hospitals. With much of INSERM's primary external funding stemming from the EU, INSERM has a major commitment to EU research initiatives. Its motto "**from science to health**" is reflected in INSERM's new strategic plan, which comprises 10 goals and priorities to strengthen public health research in France. These include prevention and health services research; open data policy to address a need to work collectively on shared data; and strengthening the connection between science and society. Dr. Bloch described three initiatives that INSERM is strongly involved in which demonstrate where a more global approach can make a difference:

**Conect4children** is a collaborative network for European clinical trials for children that is facilitating research on a large scale. **Children of all ages and their families are engaged at the centre** of vital medical progress for new paediatric therapies in Europe. A large initiative within the Innovative Medicines Initiative 2 (IMI2) joint undertaking and supported by Horizon 2020 and EFPIA, the project will mobilise 140 million Euros and includes many hospitals and clinical centres: 43 academic and industrial partners and 500 affiliated partners from 19 European countries. Four studies have currently been launched and will provide insight in the operation and added value of the network.

“With a more global approach, we can make a difference”

The **European Joint Program on Rare Diseases (EJP RD)** was launched in January 2019 and INSERM is a coordinating institution. An ambitious EU-funded program, EJP RD brings over 130 institutions from 35 countries together to address the challenges in rare diseases in Europe. The aim is to **better integrate the very rich and complex research ecosystem** on rare diseases, and create a comprehensive, sustainable ecosystem that allows a virtuous cycle between research, care and medical innovation.

The **European and Developing Countries Clinical Trials Partnership (EDCTP)** started 15 years ago and is now a vibrant success. It aims at accelerated development of new and approved drugs, vaccines, microbicides, and diagnostics for poverty related infectious diseases. Hundreds of projects have been funded, hundreds of millions of euros have been spent, hundreds of institutions have been involved, and hundreds of junior and senior African scientists have been trained. This European Program is now a key player in the global health arena, and a really **good example of what can be done together**. EDCTP has helped build knowledge, research capacity, research systems, and new institutions like the African Vaccine Regulatory Forum (AVAREF).

**KPMG** covers 46 countries with over 4,500 professionals specialised in health care across the globe. The focus of KPMG services to clients in the sector is quite broad and spans from care system redesign to operational excellence, through value-based care, supporting universal coverage, and health information technology. At the core of all of these activities is one common theme - the sustainability of health care systems. That is because it is challenging to provide good quality of care with financial constraints, and **all health care systems across the globe are under financial pressure.**

A number of health research mega-trends are affecting health care systems, including precision medicine, advanced therapy, and medicinal products. All are becoming increasingly patient-specific and therefore targeted at increasingly selective groups of patients. This increases the cost of conducting research; and for those innovations that are found to be effective and are brought to the market, the number of patients impacted also tends to be relatively low. **The more personalised the intervention, the higher the unit cost. We therefore need to balance the healthcare benefits of the targeted few with the costs that an innovation has on the whole healthcare system.** The choices that need to be made are well illustrated by the range of interventions that we have available for hepatitis C. The per unit cost per patient for some innovations is in the magnitude of thousands, whereas others are in the range of tens to hundreds of thousands; and the work conducted on individual patients is presumably in the range of millions of Euros.

“We need to find a way to really study the clinical, organisational and financial dimensions together, and earlier in the research process”

Considerations about the sustainability of innovations that get to the market should be a key point in discussions within the early days of health research. Instead of thinking in a one-dimensional clinical space, it makes sense to consider a three-dimensional space that includes clinical, organizational and payment dimensions. Does the innovation enable re-organisation opportunities that improve the efficiency of the system and save costs, and do those savings cover and sustain the cost of the innovation? Consider Hepatitis C. If innovations help us eliminate this as a pathology, how will that affect the hospital departments that were treating it? While impact of these innovations within current systems is quite low, if we redesign care pathways to facilitate a high impact will that in turn contribute to the innovations’ sustainability? **When we consider innovation, we should be considering an organizational process – not just an isolated product,** like a pill.

Currently, organisational and payment dimensions are approached on a country by country basis, but that is insufficient. Non-clinical dimensions are also only considered late in the process, when an innovation is already on market and is being paid for or about to be paid for, at the earliest. At this late stage, it is difficult for health systems to get all the efficiency improvement potential out of innovations and just finding additional financing for new products is more and more difficult. **We need to find a way to really study the clinical, organisational and financial dimensions together, and earlier in the research process.** By considering new payment models and by improving our ability to evaluate the organisational benefits through linking innovations with measurable outcomes, we will be better able to make innovations self-sustainable. Support from the European Commission in developing such an agenda is key.

## JOHN P. A. IOANNIDIS

Stanford Prevention Research Centre | Professor and Director, Meta-Research Innovation Centre at Stanford | United States of America  
Einstein fellow, Berlin Institute of Health | Germany

The **Meta-research Innovation Centre at Stanford (METRICS)** was launched in 2014. It is a university-wide research centre within the Stanford University that aims to try to be a connector hub, facilitating research around the world with the goal to improve the quality, reliability, credibility, and efficiency of health-related research. In 2019, the European sister of METRICS was founded in Berlin – **METRIC-Berlin**.

This work is important because health investment should be a priority for all of us. While health research has led to great progress, empirical evaluation conducted by METRICS indicates that evidence quality is dismal, including at the supposedly highest levels of evidence, such as meta-analyses and guidelines. Scientists agree we have a problem in research and that we need to fix it. Provided we can align the interests and priorities of different stakeholders, we have an opportunity. We need to change the paradigm by encouraging:

- **Patient centeredness** – patients are beneficiaries and payors, know the needs and should determine priorities. Research should connect with real-life.
- **Transparency** so that methods, data, and analysis are verifiable, unbiased, and transparent. Better dissemination of clinical trial protocols, amendments, and analysis plans so that we can better assess the evidence is fundamental.
- **Large scale collaboration and sharing** to resolve our currently fragmented efforts and have translational impact. As an example of data sharing, BMJ and PLOS medicine have adopted data sharing for all clinical trials as a norm.
- **Research on research** to help us focus on solving the right problems. We need to be able to reliably appraise the information gained from different studies, and systematically appraise research findings to reduce biases and better determine next steps.
- **Workforce capacity building** so that we are well equipped to handle new challenges and make the most of new opportunities, for example big data.
- **Re-engineering of the rewards system**. We need to be able to better assess what research is value for money, and reward it. Instead of incentivising volume of publications, we need to incentivise other indicators such as research quality, reproducibility, sharing, and translational impact. We also need to decide as a society who should be the authors of sensitive information. For example, research on the cost effectiveness of interventions should not be controlled by companies with conflicts of interest.
- **Progress monitoring** by tracking indicators of transparency (funding and conflict of interest declarations), reproducibility (including computational methods), sharing and credibility.
- **Better visibility** so that when ambitious projects are abandoned, our learnings don't disappear.

“Scientists agree we have a problem in research and that we need to fix it. Provided we can align the interests and priorities of different stakeholders, we have an opportunity”

The German Research Foundation, DFG, has implemented several initiatives for collaborative research that address health-related questions and promote excellence and impact. The DFG's function is to provide the pre-requisites for innovation to respond to science-driven research needs.

DFG's platform **facilitates collaboration** through national scientific infrastructure. Strong and efficient **stakeholder participation** in health research policy and design is facilitated at the national and European levels. **Cooperation and competition irrespective of national borders** is promoted including the free exchange of ideas, international cooperation in funding programs, and institutions implemented jointly with international partners. A recent position paper of the DFG has identified the need for translational hubs – the infrastructure to perform translation at a reasonable time point.

“For a vibrant research ecosystem, DFG considers all research disciplines (not just health) and balances applied vs. curiosity-driven research.”

For a vibrant research ecosystem, DFG **considers all research disciplines (not just health) and balances applied vs curiosity-driven research**. Innovations in other fields can result in unexpected innovations that can benefit health.

Assessment of impact needs to be considered carefully. Innovation does not happen only because of economic need - it is driven by research that need to be done in unconfined environment. Curiosity-driven, exploratory research is essential as it leads to disruptive innovations. As objectives and missions in health change over time, if we confine research only to the known problems at the time of research, impact is short-term and predictable. If we have already filled in some of the 'unknowns' through curiosity-driven research, we are better able to respond when new priorities emerge. Necessitating that initiatives deliver immediate impact could widen the gap between applied and exploratory research; and while delivering impact could strengthen societal trust in research, making undeliverable promises would undermine it.

We need to address our strong limitations in the process of translation. We lack clinician scientists, and under the economic pressure of medical universities it is difficult to maintain the translation mindset. The community of clinical scientists has addressed the need for educating young clinician scientists, and has attracted funding from different organisations including the German Research Foundation.

Investment is also required in areas where there is no economic interest for industry, for example novel strategies and structural efforts for rare diseases.

The principle of subsidiarity regulates the functional differentiation of funding measures at the national and European levels. DFG safeguards the scope and resources for European research in the future European framework programs, enables interaction between national and European funders, and funds cooperation between national systems and organisations.

The main theme for the Finnish Ministry of Social Affairs and Health during the EU presidency has been the Economy of Wellbeing, which is central when we consider the broader picture of health research impact. **The 'Economy of Wellbeing' relates to the interdependent and mutually reinforcing relationship between economic growth and well-being:** a healthy population is vital for a stable sustainable and inclusive society and improvements in health play a key role in reduce poverty, fostering social progress, and prosperity in increasing economic growth.

We know that peoples' physical and mental health can be influenced by their individual situation, as well as the broader societal context that they are living in. **Wellbeing is all about interlinkages** such as income, education level, and societal and gender aspects; all of which impact upon health and disease risk. The Economy of Wellbeing (EoW) therefore underlines the **importance of collaboration between different sectors to strengthen knowledge-based policy making and identify synergies that maximise the long-term impact of policy decisions.**

An EoW approach aims to enhance the wellbeing of both people and the environment and contributes to the implementation of the UN agenda 2030, which highlights the balance between economic, social and environmental policies. **Promoting wellbeing is central objective of the EU.** EoW is a continuation of the European pillar of social rights, supporting its efficient implementation. Council conclusions on EoW were adopted by the Employment, Social Policy, Health and Consumer Affairs Council on Thursday 24<sup>th</sup> October and include four calls for actions for the EC which aim at more **people centred policy making at the European level:** 1) To propose a New long term post-Europe 2020 strategy aimed at ensuring that the union becomes the world's most competitive and socially inclusive economy, 2) To issue a Communication addressing the EoW, 3) To promote cross-sectoral collaboration and continue strengthening the role of employment, health, and social education policies within the European Semester process, and 4) To strengthen the assessment of the impact of legislative and major policy decisions for wellbeing, including in the field of economic policy.

We are facing novel, newly emerging and persisting challenges. During the Finnish presidency, the approach of turning ageing into an opportunity rather than seeing it as a burden was supported. People living and staying healthier for longer is the success story of modern society. This major success brings along several challenges which require new policy models. **Our response needs to be multigenerational and multisectoral,** as was highlighted at the high-level forum on the "Silver economy" held in Helsinki in July.

“We need to collaborate between countries and with diverse stakeholders to learn and provide better health together”.

**Research and Innovation as well as public-private and civil society partnerships are the key components for the wellbeing of people and sustainability of solutions,** and investing in them is critical. We need a broader perspective to look at how investments today generate wellbeing impact in the longer run. R&I provides us with evidence-based and concrete tools to convert ageing into an opportunity and strength, and science-policy dialogue is important. Governments play an important role by establishing an open innovation environment and procedures, legislation and regulation for public-private cooperation that fully respects rights for ethics and privacy. In Finland, the health research and innovation policy ecosystem has been a success: a joint public-private venture, its highlights and strengths are well educated citizens who are positive about innovations and participate in research, and a global network of enterprises including start-ups. Finland aims to be in the frontline of a new technology, open, real-world data approach for better evidence evidence-based policy and decision making. In November 2019 the FinData public operator will begin to operate, offering a one-stop shop for public sector organisations, academia and private-sector

companies to access anonymous and aggregated health and socioeconomic data in public registers as well as licencing for trials.

## BREAK-OUT DISCUSSION

**A participant noted that although the EU has highly invested in research there is an innovation gap, and lack of translation and product development.**

**The panel responded on three dimensions – incentives, impact on budgets, and data availability.**

On incentives, Gilles Bloch noted that translating good research into innovation is a systemic question. One needs to have the best science to do innovation. Dr. Bloch described how in some countries in Europe we are doing fair science and good science - but not excellent science. He gave some examples of how we may improve our systems to do it, notably France's strong policy to have research hubs and clusters; cultural change for young people who want to become entrepreneurs; and the need to have the tools to fund start-ups to remove the major bottlenecks that prevents ideas from being translated into products for patients.

On impact on budgets, Alberto De Negri described the silos and tools for financing in Italy, noting that funds for innovation alone are insufficient. He stressed that in healthcare, innovation and reorganisation comes last; and that to promote innovation we need to re-organise so that it is self-funded by the process itself.

On data availability, John P. A. Ioannidis noted that while Electric Health Records (EHR) and databases can be wonderful resources in themselves that we need to look more at how they can be better used to fill in the gaps in evidence that trials cannot answer. Database research is not applicable to all problems and is not easy to do well (e.g. handling missing data; good interpretation of results), and observational data cannot replace RCTs for certain problems. Observational research is an opportunity - it is complementary to RCTs. The issue is in selecting the right research methods to best address the problem.

**A participant followed on from the first question by asking a question related to how assessment of the quality of scientific evidence is conducted in grant proposals.**

John P. A. Ioannidis responded by expressing that there is no perfect funding system, and explaining how the appropriateness of assessment methods varies by setting: in some 'informed' settings it is better to conduct grant assessment of proposals than do nothing, whereas in some settings, using a random scheme could be appropriate and save a lot of resources. He emphasized that some of the best models have evaluated the scientists as opposed to the proposals, which could work well for discovery and early stage research whereas for later stages (e.g. 3 or 4) the proposal is much more important.

**A participant noted that the Finnish and German Presidency has opened initiatives on the framework of global health. They asked if this initiative would result in a redesign of the existing Commission's policy.**

Päivi Sillanaukee expressed that when talking about the EUs role in global health we also need to talk about other partnerships and countries that are needed to have more impact on global health discussions. She stated that while there are no council conclusions as yet, discussions have taken place, and that several countries need to work together to define the EUs role in global health.

**A participant expressed that we have very good data on how much things cost, but few data on treatment outcomes. The question was raised if this will be covered in the future by an expansion of a clinical program?**

The question provoked many comments. The panel noted that:

- Research in treatment cost is much less structured than in other areas.
- To support decision-making, regular health records are not sufficient. We need to conceptualise new ways of collecting data so that in the future we are better able to tackle different diseases. A diabetes study of the EPICOM group was provided as an example: Epidemiological data is collected from patients with diabetes all over Europe, including determinants, costs, treatment and outcomes.
- There is a distinction between research conducted inside the healthcare system, and that conducted outside of it. We normally think of research as something that is happening outside of the system - funded by the Ministry of Science etc; but we need research within the system.
- It is difficult to measure many of the indicators that we need to using existing data collection methods. We need to agree upfront about what data we specifically need, and what is sufficient to measure. Data about cost is available, although we tend to measure possible benefits in terms of costs and variable costs. These don't always reflect the reality - costs vary case by case. For example, if we increase the number of occupied bed days it doesn't necessarily convert into saved costs.
- Health and the healthcare system is one aspect, but we need to look at the bigger picture: the health impact of the environment. Organising this at the country level is very difficult, and addressing this at the European level (i.e. European biomonitoring for EU) in terms of biocoohorts would really make a difference.
- Health promotion and prevention sits at the other side of spectrum and is a long-term investment
- In the context of Horizon Europe, the framework program is an important budget, but we need to look at both the EU and the country levels. That means prioritising which partnerships are imperative, and addressing funding silos. We have to look at the entire budgetary and financial decision system, and this comprises many sectors. This is particularly challenging within countries and when looking at bringing this to European level. For example, some countries provide funding for medicines, and others do not. A bigger system may be required to establish equality.
- We need to find a way to bridge existing disparities, and to do this we need to provide the EU with the capacity to bring countries into EU policy.

## CLOSING WORDS BY THE CHAIRS

### **Axel Pries**

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### **Karin R. Sipido**

KU Leuven | Professor of Medicine and Head of Experimental Cardiology | Belgium

Europe is excellent in science but weaker in translating excellence into value, and we need to address this link. Current scientific efforts are not unified but fragmented both across administrative borders and over time, with turnover in leadership at the EU level hindering a long-term view. A fragmented scientific landscape where some entities dominate over others threatens scientific progress.

We need to find a way to work together effectively so that we can leverage Europe's diverse landscape as a strength. Building on the ideas from our diverse communities and balancing curiosity-driven vs. application-driven research would help us create a unified scientific ecosystem that builds on our subsidiarity, as opposed to being compromised by it.

An overarching body involving diverse stakeholders including clinicians, scientists, and society, could reduce fragmentation and unpredictability. By bringing a longer-term perspective to Europe's health challenges, a multi-stakeholders' platform, e.g. a European Council for Health Research, would help to translate excellence into value and strengthen Europe's position and contribution to global health.