RWE4Decisions REAL WORLD EVIDENCE

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Health Innovation - the European Health Data Space and Real-World Evidence

10 November 2020 14.00 - 17.30 CET

Hosted by: RWE4Decisions multi-stakeholder initiative

An event hosted under the associated programme of the Federal Ministry of Health within the German Presidency of the Council of the EU 2020.

RWE4Decisions

SESSION 1 | 14.20 - 14.50 CET

Assessing the Value of Real-World Evidence in the Innovation Process

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MERCEDES ECHAURI

Vice-President Market Access Europe and Canada, Takeda

Session 1:
Assessing the Value of Real-World Evidence in the Innovation Process

TRUST4RD

Tool for Reducing Uncertainties in the evidence generation for Specialised Treatments for Rare Diseases

Annemans and Makady *Orphanet Journal of Rare Diseases* (2020) 15:127
https://doi.org/10.1186/s13023-020-01370-3

Orphanet Journal of Rare Diseases

POSITION STATEMENT Open Access

TRUST4RD: tool for reducing uncertainties in the evidence generation for specialised treatments for rare diseases

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Dr Karen Facey, University of Edinburgh, karen.facey@ed.ac.uk
Consultant to INAMI

10 November 2020

Typology and prioritisation of evidence gaps

- Uncertainties related to the size and characteristics of the population
- Uncertainties related to the natural history of the disease and its current management
- Uncertainties related to the new treatment
- Uncertainties related to the health eco-system

Identify evidence gaps.

Agree what's key
to determining value.

Trade-off
evidence generation requirements
vs limitations of data collection

Make explicit;
set priorities

Iterative Dialogue timing – resolving uncertainties

HTA submission
Reimbursement Approval

Parallel dialogue
Market authorisation & HTA

Evidence generation

Dialogue pre-submission

Finalize value dossier

Additional evidence generation

Dialogue post-submission

Time

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REAL WORLD EVIDENCE

THE UNIVERSITY of EDINBURGH | usher institute

Real-world evidence to support Payer/HTA decisions about highly innovative technologies in the EU—actions for stakeholders

Karen M. Facey[1], Piia Rannanheimo[2], Laura Batchelor[3], Marine Borchardt[3] and Jo de Cock[4]

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Objectives. There are divergent views on the potential of real-world data (RWD) to inform decisions made by regulators, health technology assessment (HTA) bodies, payers, clinicians, and patients. This RWE4Decisions initiative explored the particularly challenging setting of highly innovative technologies, which require Payers/HTAs to make decisions on a small evidence base with major uncertainties. The aim was to go beyond strategic intent to consider actions that each stakeholder could take to improve use of RWD in this setting.

Results. Case studies of recent Payer/HTA decisions about highly innovative technologies were considered in light of recent international initiatives about RWD. This showed a lack of clarity about the Payer/HTA questions that could be answered by RWD and how the quality of real-world evidence (RWE) could be assessed. All stakeholders worked together to create a vision whereby stakeholders agree what RWD can be collected for highly innovative technologies based on principles of collaboration and transparency. For each stakeholder group, recommended actions to support the generation, analysis, and interpretation of RWD to inform decision making were developed. For HTA bodies, this includes cross border HTA/regulatory collaboration to agree RWD requirements over the technology life cycle to inform initial recommendations and reassessment, data analytics methods development for HTA, and promotion of transparency in RWE studies.

Recommendations. Stakeholders need to collaborate on demonstration projects to consider how RWE can be developed to inform healthcare decisions and contribute to a learning network that can develop systems to support a learning health system and improve patient outcomes through best use of RWD.

Regulators

Pharmaceutical Industry

Payers/HTA bodies (European & national)

RWD / analytics groups

Registry-holders

Patient groups

Clinicians

IMPACT HTA is funded by an EC H2020 grant: WP10 is Developing an Appraisal Framework for Rare Disease Treatments

The RWE4Decisions initiative is enabled by the sponsorship provided by EUCOPE, Astra Zeneca, Gilead Sciences, Novartis, Roche and Takeda

Stakeholders agree what real-world data (RWD) can be collected for highly innovative technologies
– when, by whom and how –
in order to generate real-world evidence (RWE) that informs decisions
by healthcare systems, clinicians and patients.

Transparency

Plans for RWD collection and generation of RWE should be shared publicly to ensure that data sources can be focused, coordinated and combined by:

- clarifying what questions RWD may be able to address in regulatory and Payer/HTA decisions
- publishing methods for critical assessment of RWE
- sharing information about RWD studies underway across different jurisdictions to enable data amalgamation
- use of clear processes for managing conflicts of interest among stakeholders.

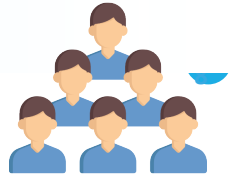
Collaboration

RWE generation is a **shared responsibility** and should be pre-specified and **planned with all stakeholders**.

Iterative dialogues should involve all stakeholders throughout the lifecycle of a technology to discuss plans for evidence generation and the potential for RWE to resolve important decision uncertainties.

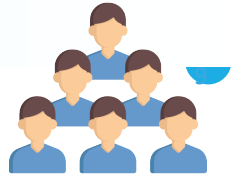
Each stakeholder needs to take responsibility for aspects they can influence and work collaboratively with other stakeholders to achieve the common goal of developing RWE that can inform Payer/HTA decisions and improve patient care.

To European or multi-country HTA or payer collaboratives (1/2)



- Collaborate with academia to better understand the potential of new statistical, econometric and modelling approaches to develop robust RWE for use in Payer/HTA decisions.
- **Encourage industry to engage in multi-stakeholder dialogues to discuss evidence generation plans including RWD collection.**
- **Use joint processes (multi-HTA and with regulators) to document evidence gaps and key uncertainties in the clinical (and economic) evidence and identify which areas might be addressed by patient-relevant RWE.**
- Document the regulatory post-licensing evidence generation (PLEG) obligations and the additional Payer/HTA PLEG needs. Establish what PLEG is needed on national, regional, and European level.

To European or multi-country HTA or payer collaboratives (2/2)



- **For individual HTAs, agree the core dataset that is required for HTA reappraisal, within a reasonable timeframe, so that common data collection protocols can be agreed across countries and joint analyses performed.**
- Engage with the clinical community (particularly ERNs) to avoid conflicting or duplicative data collection.
- Develop methods guides to show how RWE will be critically assessed and how the validity and applicability of RWD/RWE from another country/health setting will be determined.
- Encourage the development of a public portal registering RWE studies that may be used in decision-making and when fully established only accept studies previously registered and reported on the portal.

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SESSION 2 | 14:50 - 15:50 CET

Stakeholder actions and collaboration to improve learnings on real-world evidence. Proposal for a EU Learning Network on RWE

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DR. MARC VAN DE CASTEELE

Coordinator - expertise phamaceuticals,
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Director General of Strategic Affairs
and Chief Medical Officer,
Finnish Ministry of Health

DR. PETER ARLETT

Head of the Data Analytics Methods Task Force,
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Secretary General, European Confederation
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Session 2: Stakeholder actions & collaboration to improve learnings on RWE

Diane Kleinermans, President of the Commission of Drugs Reimbursement, in collaboration with
Marc Van de Casteele, Coordinator – expertise pharmaceuticals,
Belgian National Institute for Health and Disability Insurance (INAMI/RIZIV)

INAMI-RIZIV

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RWD in the life-cycle of the pharmaceutical

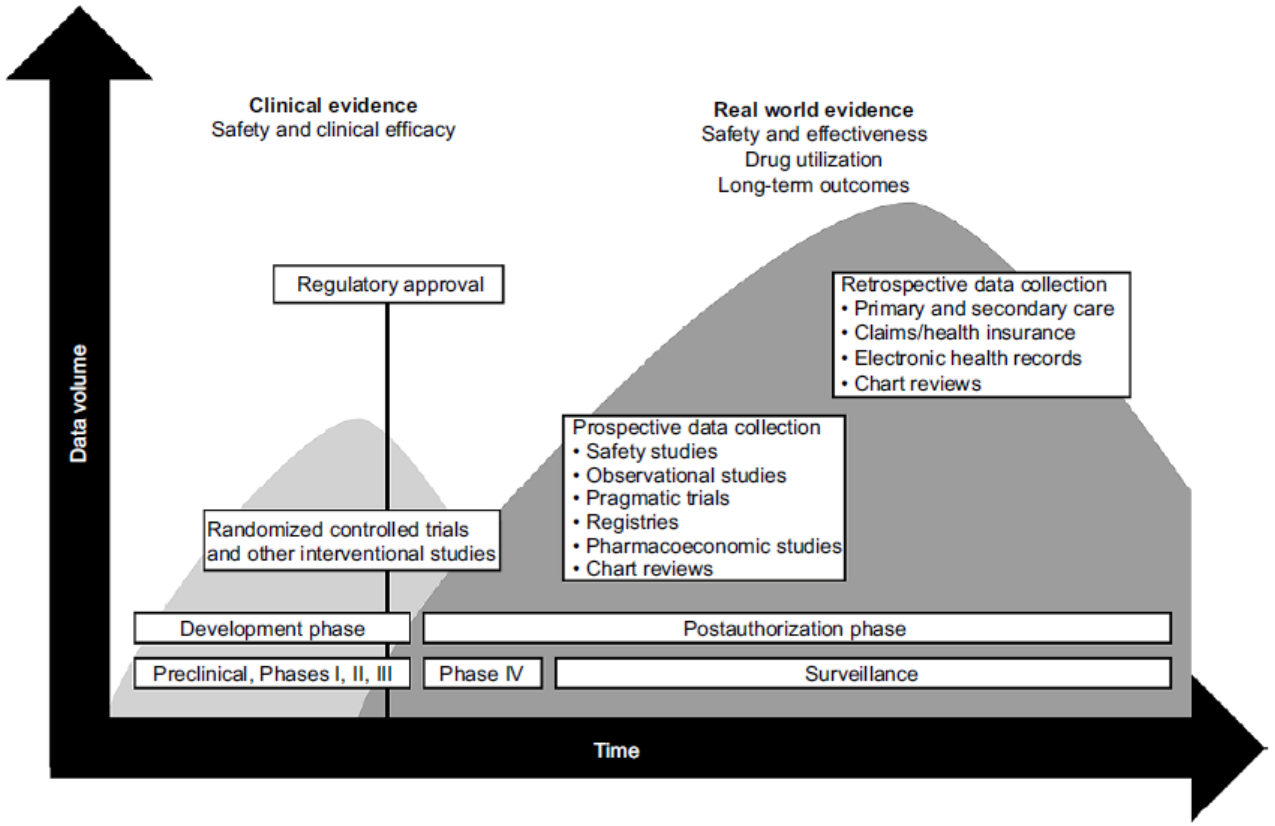


Figure 2 Schematic illustration of the utilization of randomized controlled trial data and real world data through the lifecycle of a medical intervention.

Source: Katkade et al, Journal of Multidisciplinary Healthcare 2018;11:295-304

RWD in the life-cycle of the pharmaceutical

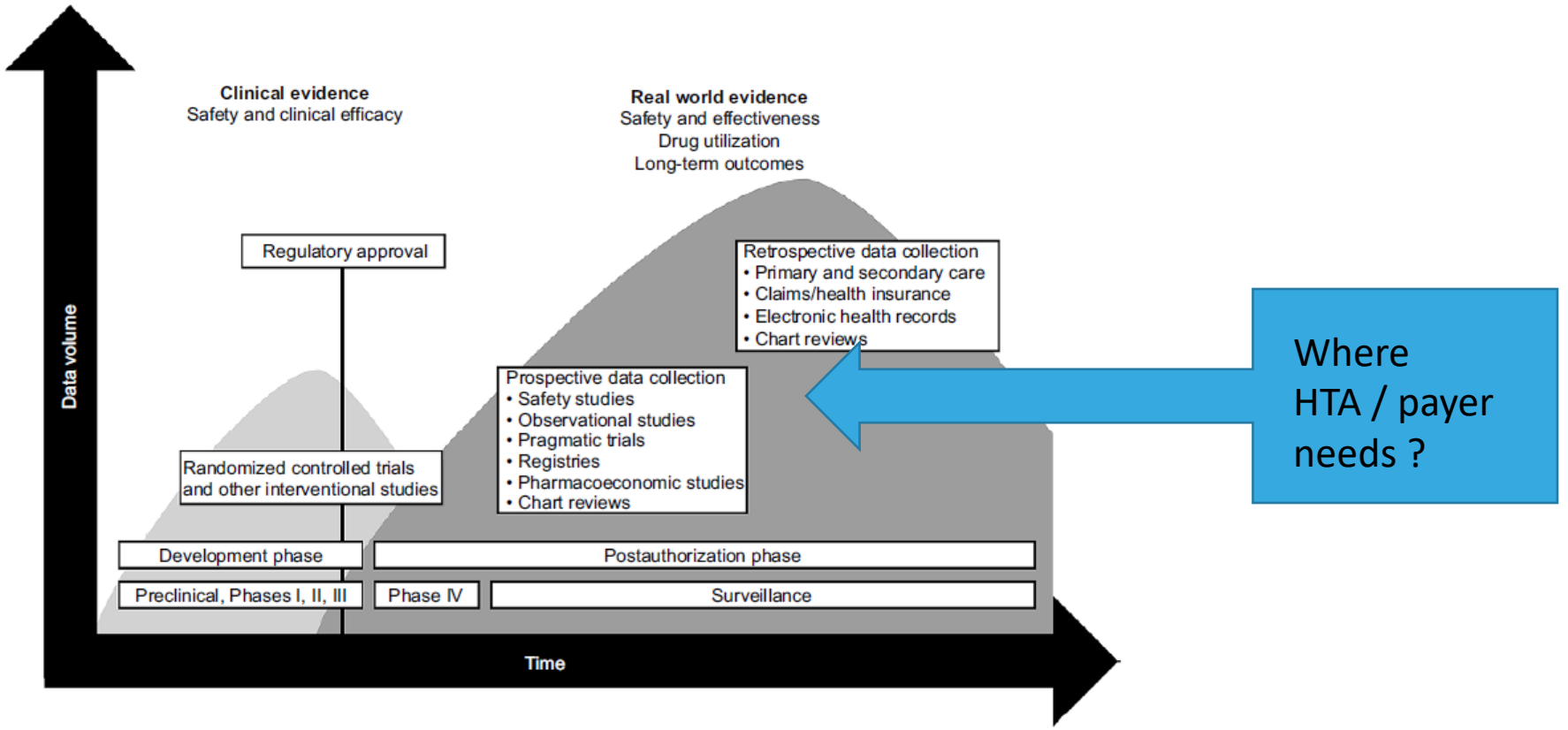


Figure 2 Schematic illustration of the utilization of randomized controlled trial data and real world data through the lifecycle of a medical intervention.

Source: Katkade et al, Journal of Multidisciplinary Healthcare 2018;11:295-304

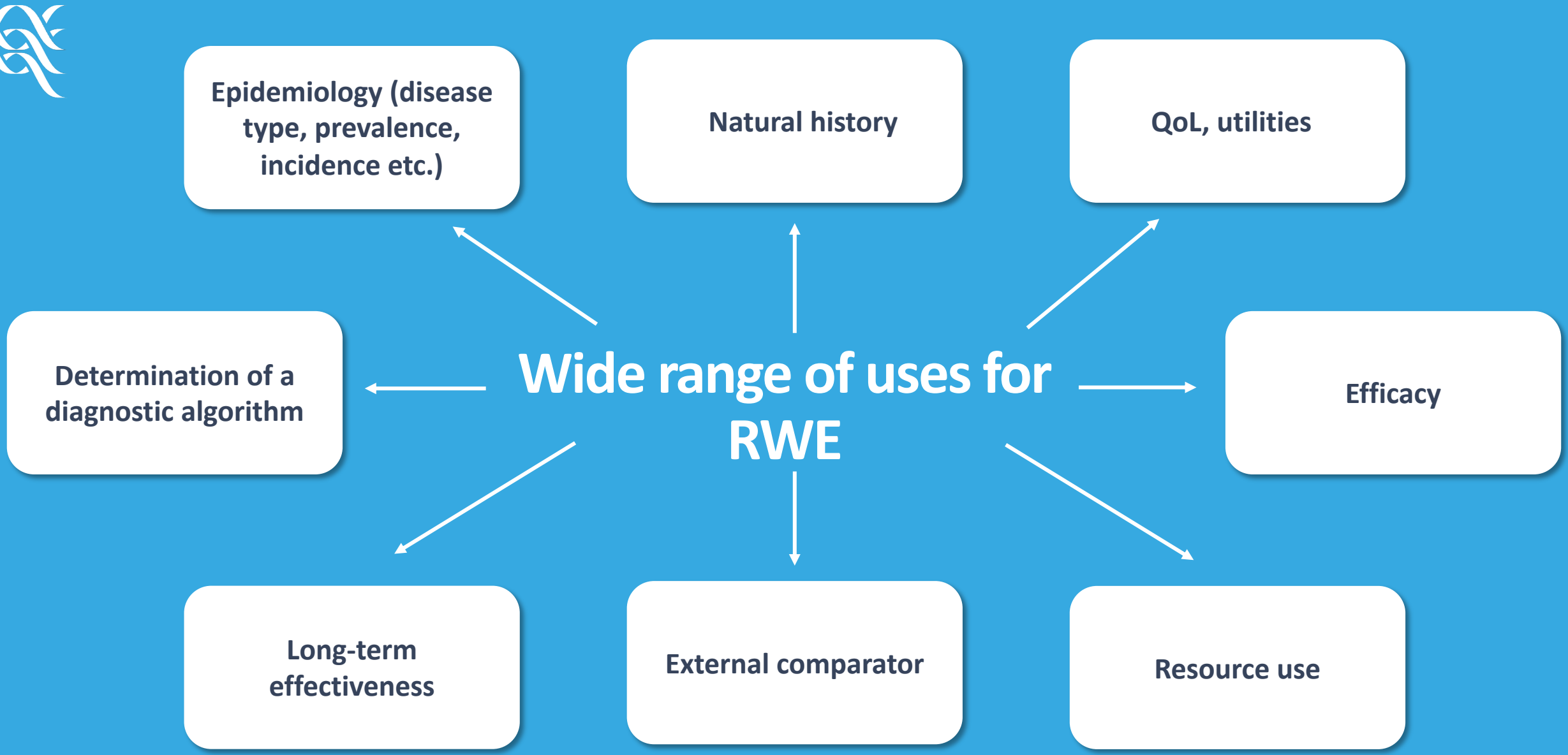
RWE4Decisions Case Study Workshops – Key Learnings

10 September 2020

RWE4Decisions Case Study Workshop (Sept 2020)

Demonstration project of a light-touch multi-stakeholder dialogue meeting about highly innovative technologies in development. Can we address any of the RWE4Decisions stakeholder actions?

INAMI-RIZIV


Epidemiology (disease type, prevalence, incidence etc.)
Natural history
QoL, utilities
Determination of a diagnostic algorithm
Wide range of uses for RWE
Efficacy
Long-term effectiveness
External comparator
Resource use

Workshop outcomes

Open and confidential discussion of RWE generation plans

Consideration of

1. Challenges
2. Pros and cons of different RWE designs/data sources
3. Propositions for long-term evidence generation post-launch
4. Practicalities of data collection (responsibility & approaches to reduce duplication/maximize use)
5. Be clear that RWE may not resolve important uncertainties

Plan iterative dialogues

RWE4Decisions proposes iterative dialogues to discuss RWE requirements

HTA/Payers need to agree which questions should be discussed when (create a timeline) - Link to life cycle of RWD availability

Use of RWE studies

RWE studies to create matched external controls should have clear protocols and analytical plans with robust data capture (e.g. via eCRF) and quality control mechanisms, including analyses to show sensitivity of the cohort to different data rules.

Applicability of RWE studies to different jurisdictions should be considered.

A plan for the use of RWE studies should be developed that does not cherry pick elements.

Recommendations

International disease based registries

Recommended – but practicalities of use for an individual product is complex and needs further discussion (content, funding, management, ownership).

Collaboration across EU

Engage with ERNs and EJPRD to ensure HTA/Payer needs are understood when disease registries are developed and to ensure Payers can have access to relevant data.

Payers

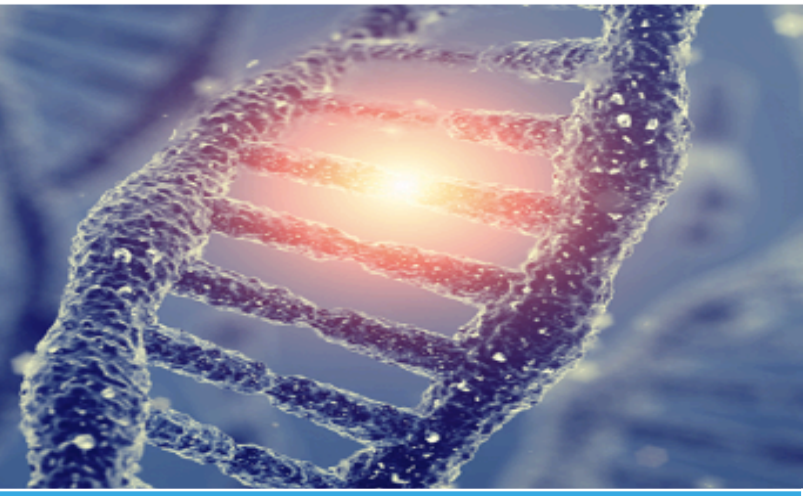
Be clear about what data is required post-HTA/reimbursement and collaborate to define a layered core dataset outlining data that is

- essential
- important
- nice to have

Other initiatives

Avoid duplication with other initiatives (Early Dialogues, etc). Identify purpose of a light-touch process focussed on RWE and where it can contribute given insufficient capacity in other systems.

Call to Action



RWE4Decisions calls for a Multi-Stakeholder EU Learning Network on Real-World Evidence within the European Health Data Space

RWE4Decisions calls for the creation of a **multi-stakeholder EU Learning Network on Real-World Evidence**, which is based on a transparent governance mechanism. This Learning Network, designed for Member States to implement evidence-based decision-making, should be supported by EU funding, and:

1. clarify **when, by whom and how** real-world data should be collected in order to generate real-world evidence that **meets the needs of patients and healthcare systems;**
2. be based on a **voluntary mechanism**;
3. be underpinned by **robust methodologies** in alignment with other initiatives.

Can we create a multi-stakeholder Learning Network on RWE?

The Learning Network needs to:

be premised on open governance, reciprocity and legitimacy through comprehensive membership

enable knowledge sharing and dialogue, and operate on the basis of shared responsibilities and clear roles

be able to develop actions, to reach goals efficiently and be able to question goals and practices to develop new learning methods

enable the attainment of common goals, develop network members' own work, skill and capabilities

In order to deliver on the goals, the Learning Network must be:

- owned by a public institution
- enabling the multi-stakeholder interaction
- sustainable through long-term funding

Thank you for attention

Acknowledgements:
Francis Arickx
Laura Batchelor
Marine Borchardt
Jo De Cock
Karen Facey

RWE4Decisions REAL WORLD EVIDENCE

SESSION 3 | 16.00 - 16.40 CET

Cancer as a Case Study for the Use of Real-World Evidence

eu2020.de

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Vice-Chair of Horizon Europe Mission Board for Cancer

DR. ANJA TEBINKA-OLBRICH

Head of Unit AMNOG EBV, GKV-Spitzenverband

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Head of the Centre for Health Care, National Institute of Public Health of Slovenia

DR. TOMÁŠ SKACÉL

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ROBERT GREENE

Patient Advocate, Founder of HungerNdThirst Foundation, Advisory Board Member for EPF's Data Saves Lives initiative & Board Member of the European Cancer Patient Coalition (ECPC)

DR. DENNIS LACOMBE

Executive Director, European Organisation for the Research and Treatment of Cancer(EORTC)

Horizon Europe
Mission on Cancer

Professor Christine Chomienne
Vice-Chair Mission Cancer Board

European Commission

European Commission

Horizon Europe Missions

#HorizonEU #EUmissions

This presentation is based on the Commission Proposal for Horizon Europe, the common understanding between the co-legislators and the Partial General Approach. It does not represent an engagement on behalf of the European Commission. Please refer to official documents

Research and Innovation

The Mission-oriented Research and innovation approach

« Missions provide a solution, an opportunity, and an approach to address the numerous challenges that people face in their daily lives ».

Professor Mariana Mazzucato

European Commission

Goals of Missions

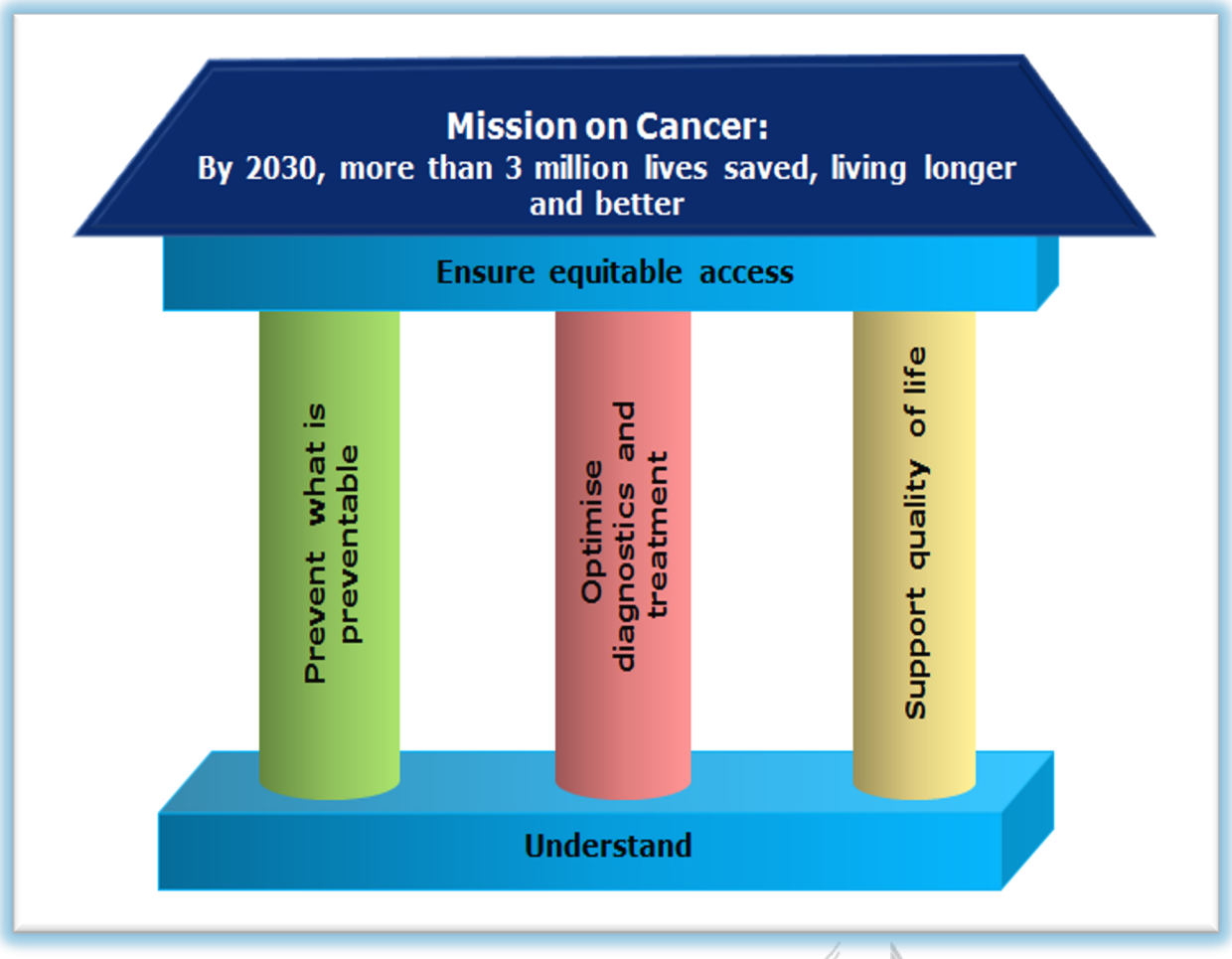
- to give direction to European research and innovation in solving society's pressing challenges and produce tangible results

- to involve citizens and stakeholders more closely in setting research priorities, but not only, which will lead to equal access for everyone in Europe to the best of European innovation & research resources, and global know-how

European Commission

Conquering cancer: mission possible

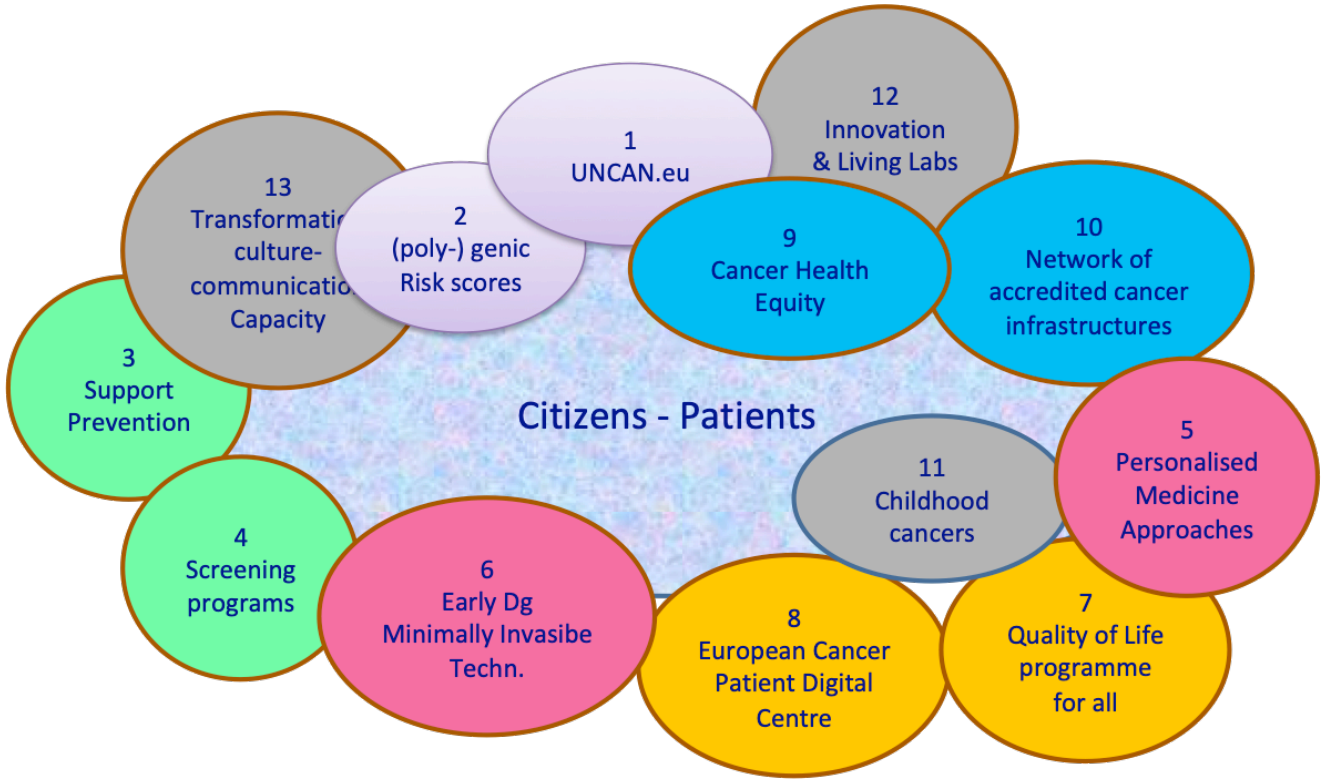
Mission Outline September 2020



https://op.europa.eu/en/web/eu-law-and-publications/publication-detail/-/publication/d0235612-b68a-11ea-bb7a-01aa75ed71a1

European Commission

13 Citizen- and patient–centred recommendations for actions of the Mission on Cancer



Existing EU/national/ Regional structures

European Commission

Work of the Mission Board
Advise on Mission Actions:
Cross Sectors-Cross Borders

- ✓ Citizens, patients, carers
- ✓ Member states authorities
- ✓ EU and National Stakeholders
- ✓ European Commission –DGs
- ✓ Members of the European Parliament

European Commission

Citizen engagement and Board member ambassador activities

Since May 2020 : more than 80 meetings

Citizen engagement

- citizen engagement events in nat'l language
- stakeholder events in nat'l language or English
- 2 EU-wide Focus Groups in English

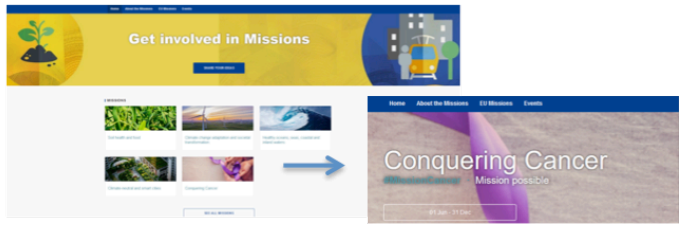
*Austria**
*Belgium**
*Bulgaria**
*Croatia**
*Cyprus**
*Czech Republic**
*Denmark**
*Estonia**
*Finland**
*France**
Germany
*Greece**
*Hungary**
*Ireland**
*Italy**
Latvia
*Lithuania**
*Luxembourg**
*Malta**
*Netherlands**
*Poland**
*Portugal**
*Romania**
*Slovakia**
*Slovenia**
*Spain**
*Sweden**

Board as 'Ambassadors

- Meeting with Ministry of Research, Health, Economics or Education
- Citizen engagement (citzens, patients and caregivers) on outline and/or several recommendations
- Meeting nat'l and EU stakeholders all sectors
- Support from Assembly members if deemed useful
- Take into account written/published input from range of stakeholders all sectors

EU-Missions

survey



missions-get-involved.ec.europa.eu

☞**Recommendation 8: Create a European Cancer Patient Digital Centre where cancer patients and survivors can deposit and share their data for personalised care**

This recommendation involves the cr
Patient Digital Centre (ECPDC), i.e.
controlled (national) health data infrastru
and survivors can deposit their health
care providers (e.g. imaging, genetic
lifestyle data) in a standardised, ethical
repository would include a summary of t
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For
e on cancer, cancer prevention and
atment and supportive care. For
CPDC will also be a global point of
ort on returning to work, addressing
financial issues and asserting survivors' rights.
Data within the ECPDC will serve as a valuable resource for research to improve understanding of cancer and its impact on patients' and
surviv
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First goal for people living with and after cancer and their carers

- ✓ Provide a health passport (health data provided by their medical care providers (e.g. imaging, genetics, blood markers, clinical and lifestyle data) in a standardised, ethical and interoperable manner
- ✓ Provide a personalized center of knowledge including information on treatments and follow-up recommendations, and foster a (long-term) personalised care plan

Second goal for research & innovation

Data within the ECPDC will serve as a valuable resource for research to improve understanding of cancer and its impact on patients' and survivors' lives, thus contributing to the development of improved diagnostics, treatment, care and quality of life support

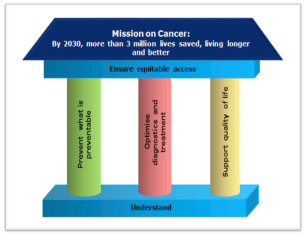
(recommendations 1 and 2, 4 to 7, 9, 13)

Overall aim:

give a voice to patients and survivors, enable them to enforce their rights, and increase their confidence in sharing their data for cancer research, innovation and policy development.

13 Recommendation

UNCAN.eu would encompass relevant stakeholders and enable integration of innovative models and technologies with longitudinal patient



WGS EU data base for the implementation of genomic and informatic infrastructures for data collection and dissemination

1	Launch UNCAN.eu – a Europ
2	Develop an EU-wide research programme to identify (poly-
3	
4	
5	Advance and implement personalised medicine approaches fo
6	De
7	Develop an EU-wide research programme and policy support family members and carers, and all persons with an increase
8	Create a European Cancer Patient Digital Centre where
9	
10	Set up a network of Comprehensive
11	g adults: cure more and cure better
12	Accelerate innovation and imple
13	Transform cancer culture, communication and capacity building

Collect evidence of policy interventions

Big-data analysis and machine learning integrated in screening and early detec programmes to generate new insights

large-scale inter-sector, EU-collaboration and advanced data analyses in personalised medicine.

Collect data on health related and social and legal needs; short & long term toxicities

successful research in the development of effective early diagnostic tools, integrated and driven by AI, as well as in minimally invasive treatment strategies and -technologies may lead to more cure and a better quality of life

Ava patient

CCI tumor boards to integra
Data quality assurance and

Cross linkage of data bases for understanding, prevention of toxicities, efficacy of innovative therapies; health ip passeports

er States to increase quality of

Traditional and non traditional innovators for digital science.

ogy-focused Living Labs to conquer cancer

Lay language and national language dissemination of cancer data

European Commission

Citizen/patients inputs

- *Support for a **European Cancer Patients Data Centre***
- ***Support for a Health passport** that not only contains relevant information on patients clinical history and received treatments, but may also serve as an educational tool.*
- *For senior patients such a passport might be difficult to use and also concerns were raised about the security of such a database.*
- *A health passport with all relevant patient information is appreciated, but not sufficient to improve shared decision making.*
- *Patients should also have easy access to their own health data to strengthen the position of patient in shared decision making .*
- *There was support for more **personalised prevention**, based on assessment of individual risk **based on big data***

Summary

To fulfill our goal of conquering cancer

- *Use all data available from every stakeholder including patients/citizens*
- *All stakeholders should define the level of evidence they need to make decisions*
- *Patients/citizens should participate with their data in decison making to answer their needs*
- *Equity requires cross border-cross MS collaborations*

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CONCLUDING SESSION | 16.40 - 17.30 CET

Evidentiary Challenges for Higly Innovative Technologies
The Way Forward to Improve Shared Learnings on Real-World Evidence for Decision-Makers

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DR. WIM GOETTSCH

Special Advisor HTA, Zorginstituut Nederland (ZIN)

Concluding session:
The way forward to improve shared learnings on RWE for decision-makers

Jo De Cock, CEO, Belgian National Institute for Health and Disability Insurance (INAMI-RIZIV)

INAMI-RIZIV

10 November 2020

RWE4Decisions REAL WORLD EVIDENCE

The Way Forward

In light of the proposal for an EU Health Data Space, a revised EU Pharmaceutical Strategy and a Regulation for EU collaboration on HTA, there is a need for an **EU Real-World Evidence Action Plan** to stimulate alignment and collaboration amongst ongoing initiatives and responding to key challenges by:

- ❑ Ensuring the development of a framework for cross country collaboration on analyses;
- ❑ Supporting an infrastructure for sharing of evidence generation plans and post-licensing evidence generation;
- ❑ Ensuring data quality and accessibility as well as data security and privacy;
- ❑ Developing evidence standards and agreeing on common data sets;
- ❑ Promoting comprehensive and aligned guidance across bodies;
- ❑ Ensuring systematic patient involvement in order to capture real world experience;
- ❑ Promoting the use of digital data in health care.

Call for a Multi-Stakeholder Learning Network on RWE

WHAT?

A Network including HTA bodies/payers, the EMA, patient representatives, researchers, clinicians, industry and academics…

To improve evidence-informed decisions for market access and reimbursement of highly innovative technologies

WHY DISTINCTIVE?

Multi-stakeholder in approach, HTA/payer led

Sustainable collaboration (beyond pilots)

WHY?

To harness the use of data in the evaluation of the truly added-value of pharmaceuticals

To address the operational, technical and methodological gaps

ADDED VALUE?

To develop practical learnings on the potential use of RWE through a 'learning by doing' approach

Share experience - pool resources - build trust

Where next? Opportunities in 2021 and beyond

Continue Demonstration Projects

- INAMI-RIZIV to drive forward demonstration projects
- Welcomes interest from stakeholders, including all HTA authorities and payers willing to contribute to case study workshops in 2021
- Identification of case studies in collaboration with International Horizon Scanning Initiative (IHSI)

INAMI–RIZIV

EU RWE Action Plan & EU Funding for RWE Learning Network

- Dialogue with DG CONNECT & DG SANTE on the need for a EU Real-World Evidence Action Plan
- Explore sustainable funding for EU multi-stakeholder Learning Network on RWE
- Collaboration with ERNs

Opportunities to share Learnings with policy- and decision-makers

- RWE4Decisions appreciated the support of the German EU Presidency and looks forward to working with the Portuguese and Slovenian Presidencies to progress policy thinking on the value of RWE
- Share learnings on RWE for decisions - e.g. meetings of the Pricing and Reimbursement Authorities (CAPR)
- Share learnings within context of OECD

OECD

Thank you for participating in our virtual conference!

For further information about RWE4Decisions, visit the website www.rwe4decisions.com

For any feedback or questions, contact secretariat@rwe4decisions.com