REAL WORLD EVIDENCE

RWE4Decisions

PUBLIC WEBINAR SERIES

Supporting HTA/Payer decision-making: Health data initiatives in Germany

Wednesday, 21 September | 15.00-16.30 CEST

@RWE4Decisions

RWE4Decisions REAL WORLD EVIDENCE

Introduction

Karen Facey, Secretariat

RWE4Decisions: A payer-inspired, multi-stakeholder learning network about use of RWE for highly innovative technologies

What?	Pragmatic and agile Learning Network about use of Real-World Evidence (RWE) to inform HTA/Payer Decisions about highly innovative technologies
Why?	Highly innovative technologies often have immature clinical evidence - could robust RWE fill gaps in clinical development, and/or post initial reimbursement? Can requirements be aligned across stakeholders and Member States?
How?	All stakeholders have their part to play Built on principles of Collaboration and Transparency

Steering Group 2022

HTA/Payers

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EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

AstraZeneca
Boehringer Ingelheim
BAYER
NOVARTIS
Roche
Takeda

Industry

FIPRA RWE4Decisions Secretariat funded by EUCOPE and member companies

RWE4Decisions: A payer-inspired, multi-stakeholder learning network about use of RWE for highly innovative technologies

What?

Pragmatic and agile Learning Network about use of Real-World Evidence (RWE) to inform HTA/Payer Decisions about highly innovative technologies

Why?

Highly innovative technologies often have immature clinical evidence - could robust RWE fill gaps in clinical development, and/or post initial reimbursement?
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How?

All stakeholders have their part to play
Built on principles of Collaboration and Transparency

Added Value?

'Learning by doing' approach

- share experience, pool resources
- sandbox approach - real problems, light-touch solutions
- build trust

Public outputs and events
Policy engagement – EUnetHTA & HTA Regulation, CADTH, CAPR, Nordic Alliance, BENELUXAI, EHDS, TEHDAS, DARWIN EU,…

Co-moderation

Dr. Karen Facey

Evidence Based Health Policy Consultant
RWE4Decisions Secretariat

Dr. Diane Kleinermans

President of the Commission of Drugs Reimbursement
Belgian National Institute of Health and Disability Insurance (INAMI-RIZIV)

Panel

Dr. Antje Behring

Keynote

Head of Pharmaceuticals Department

German Federal Joint Committee (G-BA)

Dr. Martin Danner

Managing Director

Federal Association of Self-Help Organisations for People with Disabilities and Chronic Diseases and their Relatives (BAG Selbsthilfe)

Dr. Barthold Deiters

Head of Pharmaceuticals

Society for Efficiency and Quality in Health Insurance Companies (GWQ ServicePlus AG)

Dr. Alexander Natz

Secretary General

European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)

Gemeinsamer
Bundesausschuss

Gemeinsamer
Bundesausschuss

RWE4Decisions webinar

Supporting HTA/Payer decision making
Spotlight on health data initiatives in Germany
21 September 2022

Dr. Antje Behring
Head of pharmaceuticals department
Gemeinsamer Bundesausschuss, Germany

AGENDA

- Basics: reimbursement of pharmaceuticals in Germany
- Data sources in Germany (for early benefit assessment)
- Process of routine practice data collection according to the GSAV law
  - Criteria for medicines that may go through this process
- Experiences of routine practice data collection
  - Status of medicines currently in the process
- Outlook

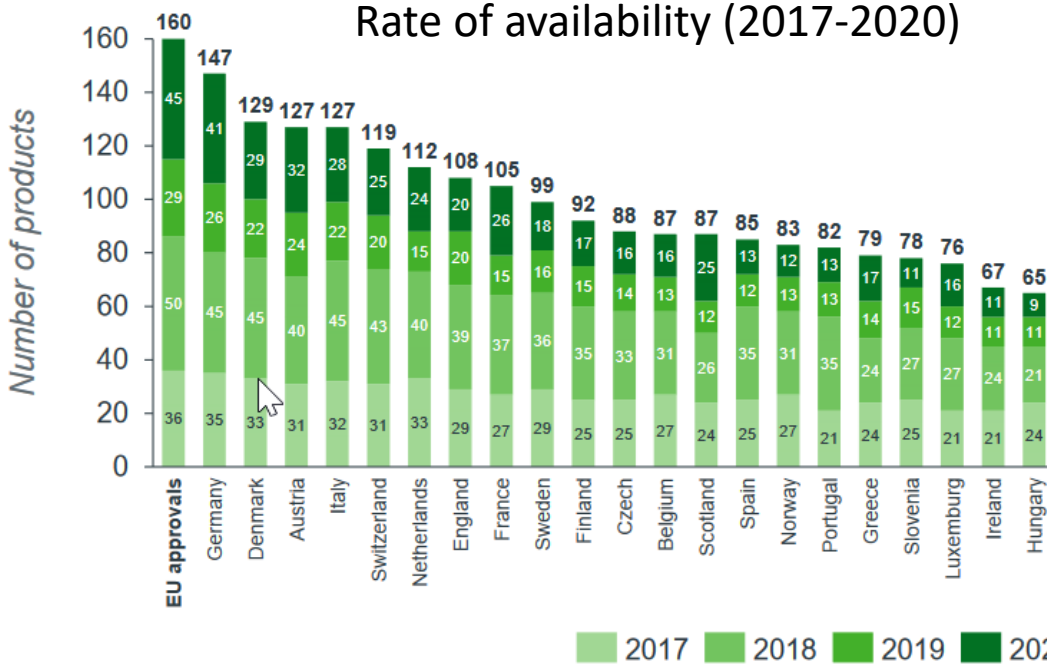
Reimbursement of medicinal products
reimbursable according to §31 SGB V

- All (prescription) medicines that come onto the market are reimbursed (§31 SGB V),
- Date of reimbursement: immediately from market entry (listing in "sales list" = so called "Lauer – Taxe").
  - Exceptions apply e.g. for OTC, lifestyle medicines or by decision of the G-BA (only applies to a few medicines e.g. sleeping pills).
- New medicinal products since 2011: a drug is assessed by G-BA at launch and for each of its following extensions of indications. (§35 a SGB V, AMNOG)
- One year: free pricing
- Price negotiations between manufacturer and National Association of Statutory Health Insurance Funds (SHI) on the basis of the G-BA resolutions (ratings)
- The reimbursed price applies for all indications of the drug.

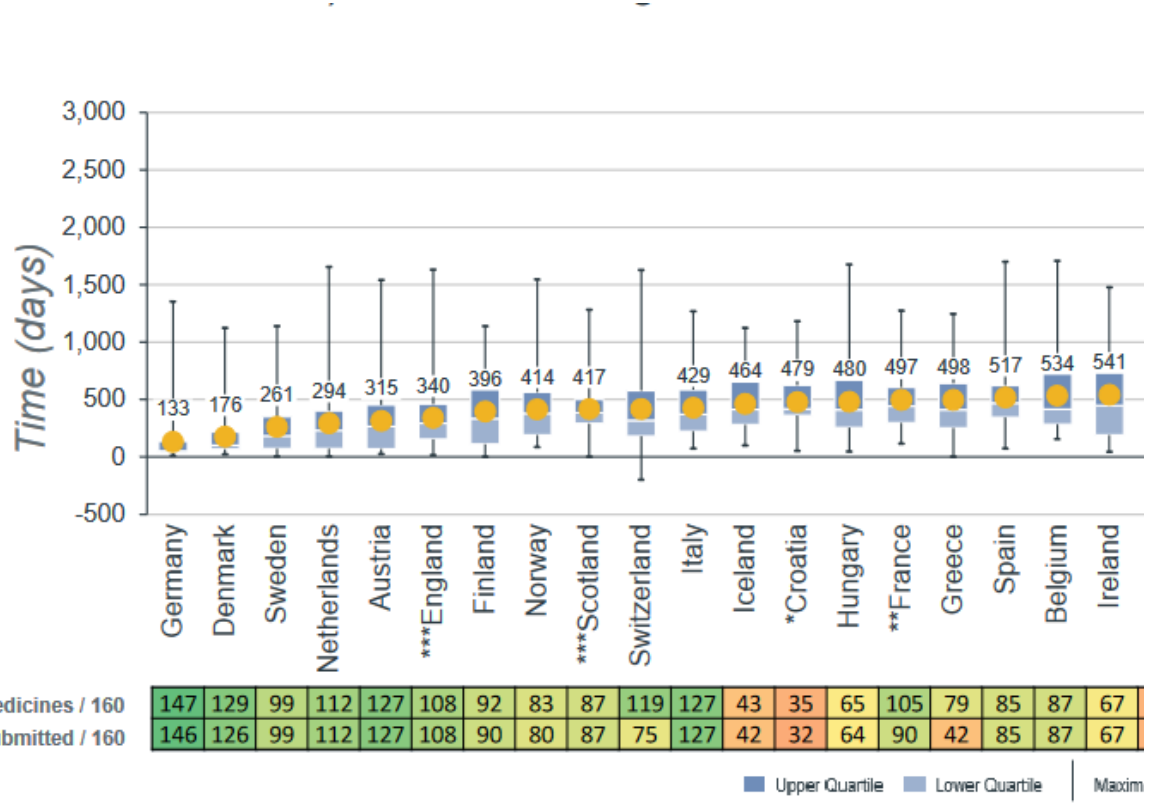
AMNOG reform bill "Financial stabilisation of Germany's SHI system" planned for this year: pricing reform

Availability of medicinal products

Rate of availability (2017-2020)



Time from central approval to availability (2017-2020)



Source: EFPIA Patients W.A.I.T. Indicator 2021 Survey

Data sources, Types of evidence for early benefit assessment

- Adequate RCTs and adjusted indirect comparisons in general acceptable
  - Assumption of exchangeability → assumptions of sufficient similarity and homogeneity (and consistency)
- Non – randomized controlled studies (depends on context)
- Single arm trials: in general not accepted,
  - Exceptions apply for orphan drugs: approval studies must be taken into account.
- Registry data have not been able to demonstrate sufficient quality to be used for the benefit assessment
  - Confounder: e.g. despite confirmed relevance of confounder, the lack of data was not discussed adequately
  - Incompleteness (e.g. safety data, only selected endpoints reported, missing patient characteristics)
  - Insufficient methodology (e.g. naïve comparisons)
  - Accepted for epidemiological data
- Electronic health records not sufficiently elaborated in Germany
  - Incomplete,
  - No lifelong ID, incomplete with regard to therapeutic interventions and outcomes

Data sources: examples of central data collection laid down by law

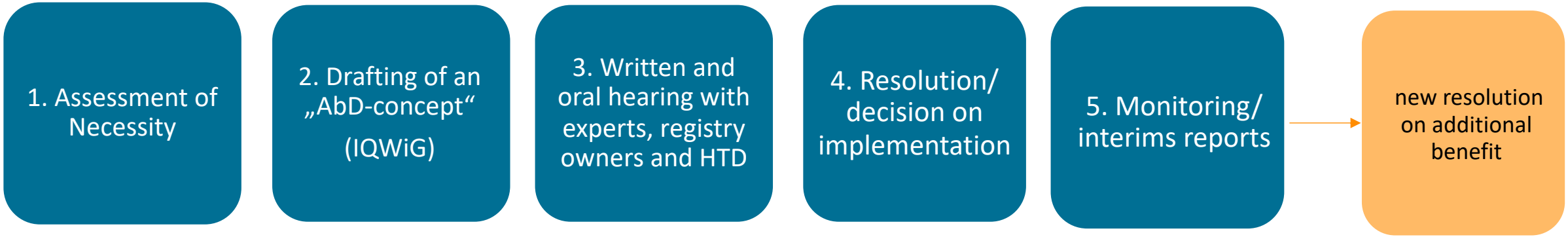
- The Research Data Centre (FDZ)
  - Makes it possible to access the medical billing data of all people with statutory health insurance in Germany. The FDZ is currently in the process of development.
  - Section 303a Social code book V: Performance of data transparency tasksNo PID exists in Germany,
  - Patients difficult to follow (e.g. change of health insurance company ect.)
- Federal Cancer Registry
  - The Federal Cancer Registry Data Act (BKRG/ KFRG) came into force in April 2013. Purpose: early cancer detection and quality assurance through clinical cancer registries.
  - The federal states are responsible for the organization.
  - The Centre for Cancer Registry Data compiles this data and checks it for completeness and plausibility, so that nationwide figures are available for all new cancer cases.
  - Completeness of the cancer registries: remaining deficits are to be eliminated in the next few years….

Routine practice data collection (AbD) according §35a Abs. 3b SGB V

- G-BA requests submission of routine practice data collection and evaluation thereof for the purpose of benefit assessment by the company within a reasonable period of time.
    - In the case of conditional marketing authorisations
    - Approval under exceptional circumstances
    - Orphan drugs.
- ATMPs are not explicitly mentioned, but are mostly orphan drugs
- Specifications in terms of the research question (e.g. patient population, endpoints, comparative therapy), type and duration of data collection must be defined by the G-BA
- In case of non-quantifiable additional benefit: Price must be lower than original price

Routine practice data collection (AbD) according §35a Abs. 3b SGB V

- Permission for Prescription can be limited to those clinicians who participate in the required data collection
- Disease specific collection preferred, no product specific data collection
- Consider ongoing and future studies, especially regulatory requirements
- Discussions should involve national regulatory bodies
- G-BA to review whether and how data collection is carried out every 18 months



Criteria considered in the selection of medicines that may go through this process

General	• Conditional, ATMP • Conditions imposed by the regulatory authorities • Available registries, ongoing registry studies
Population	Are all relevant patient populations [according to the (planned) marketing authorization] covered by the available / planned studies?
	Not investigated or insufficently investigated patient population ? (e.g. specific mutation, children, therapeutic sequence, more severely or mildly affected patients, comorbidities]
Intervention	?
Comparator	• No comparative evidence available or • therapeutic alternatives in practice available, that were not the subject of clinical trials
Outcome	• Patient centered outcomes missing, only surrogate endpoints available
	• Study duration too short (e.g. long-term effects uncertain, specific safety concerns)

Assessment of necessity

assessment of the existing evidence	Assessment of the appropriateness and feasibility of data collection
Clinical development programme appropriate?	Recruitment → sufficient number of patients?
Study duration appropriate?	Existing registries?
Patient population complete?	Further requirements imposed by the regulatory authorities
Mode of action new with high degree of uncertainty about future effects?	Studies in other therapeutic lines?
No patient relevant endpoints.	Availability of other therapeutic options?

Status of current „AbD“

Selected products	Indication	Status
Onasemnogen-Abeparvovec	spinal muscular atrophy	First check of status-report (09/22)
Risdiplam	spinal muscular atrophy	decision on implementation (07/22)
Brexucabtagen Autoleucel	Mantle cell lymphoma	decision on implementation (07/22)
Fedratinib	Myelofibrosis	Oral hearing (08/22)
Valoctocogen roxaparvovec	severe haemophilia A	IQWiG concept pending (10/22)
Etranacogene Dezaparvovec	Haemophilia B	IQWiG concept pending (01/23)

Overarching documents:

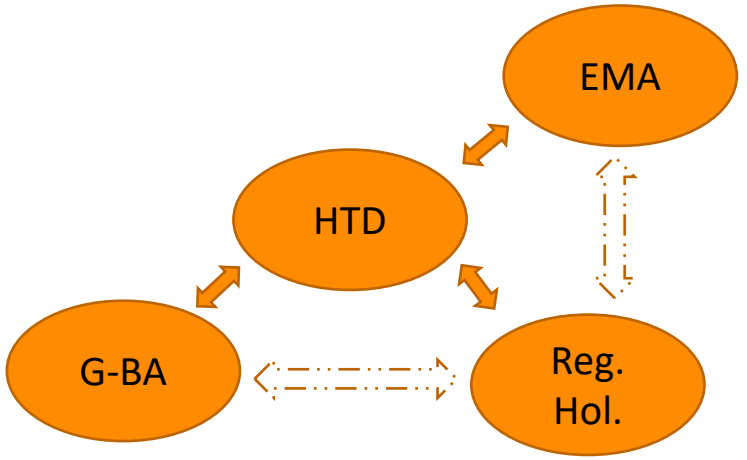
- IQWiG Rapid Report of 01.10.2020: Concepts for routine practice data collection and their evaluation for the purpose of the benefit assessment of drugs according to § 35a SGB V
- IQWiG Rapid Report of 27.04.2022: Concepts for routine practice data collection and their evaluation for the purpose of the benefit assessment of drugs according to § 35a SGB V in the situation of market access of several drugs of the same class (publication on 27.05.2022)

Status of routine data collection for Onasemnogen-Abeparvovec (Zolgensma®)

Population	Patients with 5q-associated SMA with a biallelic mutation in the SMN1 gene (3 groups)
	Patients older than 6 months or 6 weeks at the time of gene therapy.
Intervention	Onasemnogen-Abeparvovec
Comparator	Nusinersen
Outcome	e.g. motor functions, respiratory functions (need for continuous ventilation), ability to swallow and speak, need for non-oral nutritional support
	e.g. deaths, serious specific adverse events (hepatotoxicity, thrombocytopenia, cardiac events, spinal ganglion cell inflammation, renal toxicity, hydrocephalus).
Other:	• Registry: SMArtCARE as primary registry, • Duration: 60 months • Recruiting: ca 500 patients • Inclusion of other sources (e.g. RESTORE Registry) recommended • Combination of „historical data“ and prospective data recommended

Lessons learned

- Education and higher transparency of the process to allow the health technology developer (HTD) better implementation of the requirements of the G-BA, process more efficient. → adjustment of rules of procedure
- The registry landscape in Germany or Europe is not suitable for the “AbD”: registries need adjustments to the primary data source to be adequate for Early benefit assessment
    - →In fact, setting up RCT would be lower workload for the company.
- G-BA cannot make any demands on the registry holder and G-BA
- Requirements of regulatory authority usually not suitable and the protocol is usually not available to the regulatory authorities.
- Prolongation of the time until AbD begins due to various adjustment loops.
- Desirable: Start of AbD with market entry.
- Company is unfamiliar with registry studies:
    - Lack of concept for the study planning
    - Registry study: planning almost similar to the study planning of RCTs (assumptions must be made)
    - Early engagement with G-BA, regulatory authorities



Lessons learned

- first drafts for the SAP and SP discussion too late
  - SAP and SP should already be started after receipt of the IQWiG concept
  - Ensure comprehensibility of the drafts of the SAP and SP,
  - mark changes in the interims reports or amendments
  - Make it transparent: SAP, SP required from regulatory bodies , and also the requirement of the G-BA
  - G-BA aimes for highest possible transparency
- Specific questions should be ready at the time of the expert exchange
  - (currently focus on overarching methodological aspects and discussion of specific approaches is missing)
  - Interaction with registry holder before,
  - Draw attention to the challenges of implementation
- The lack of a request for an AbD is not synonymous with "acceptance of weak evidence"
  - Request of an AbD is independent of the outcome of the re-assessment. Allows the G-BA to determine the value of the medicinal product in routine practice,
- Currently prioritization needed: limitations with regard to capacity of the G-BA/IQWiG: learning system

Conclusion

- AbD is "ultima ratio": if no higher-quality evidence can be expected later (for the purpose of the benefit assessment)
- Verification of the sustainability of the results from clinical trials in routine practice
- AbD methodological standards of evidence-based medicine:
  - Predefined research question according to PICO scheme, study design incl. statistical analysis plans, etc.
  - Quality requirements of data sources/ registries
  - Supplementary evidence for benefit assessment
- Coordination between regulatory authorities and HTA necessary.
- AbD must be a useful knowledge enhancement (for patients and physicians) and must be therefore publicly available

National Health Data Spaces


Austria


Belgium


Denmark


England


Finland


Norway


Scotland


Spain

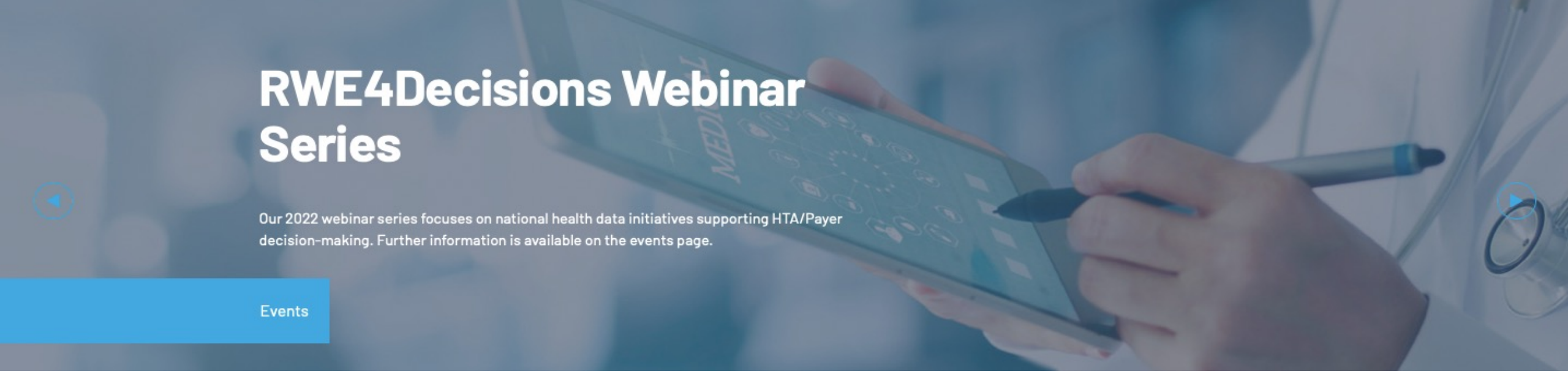

Sweden

Coming soon:


Germany


Portugal

https://rwe4decisions.com/documents/country-responses/



Thank you for your attention!

The recording, slides & webinar report will be available on http://www.rwe4decisions.com/events

For any questions or suggestions, please email secretariat@rwe4decisions.com

RWE Symposium on 24 November 2022 (09:00-13:00)
Registration now open for online attendance!

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