Harnessing the power of real world data in Oncology

Luis Castelo-Branco MD, PharmD, PhD
Medical Oncologist; Doctor of Public Health

November 2026

1. Why do we need real-world evidence (RWE) research?
2. How RWE is being considered by regulators?
3. Good practices for RWE research
4. Artificial intelligence and RWE

1) Why do we need Real world evidence in oncology ?

Oncology real-world practice vs Clinical trials eligibility

Around 40% patients are ineligible/excluded from trials

Systematic Review assessing criteria for ineligibility (2004 – 2015; n = 125,316)	Patients, %
Age >75 years	25
Presence of heart disease	16
Kidney disease	5
Uncontrolled diabetes	5
Liver disease	4
Abnormal blood work	2
Prior malignancy	1
Any immunosuppression	1

…. ECOG 2-3 (?)

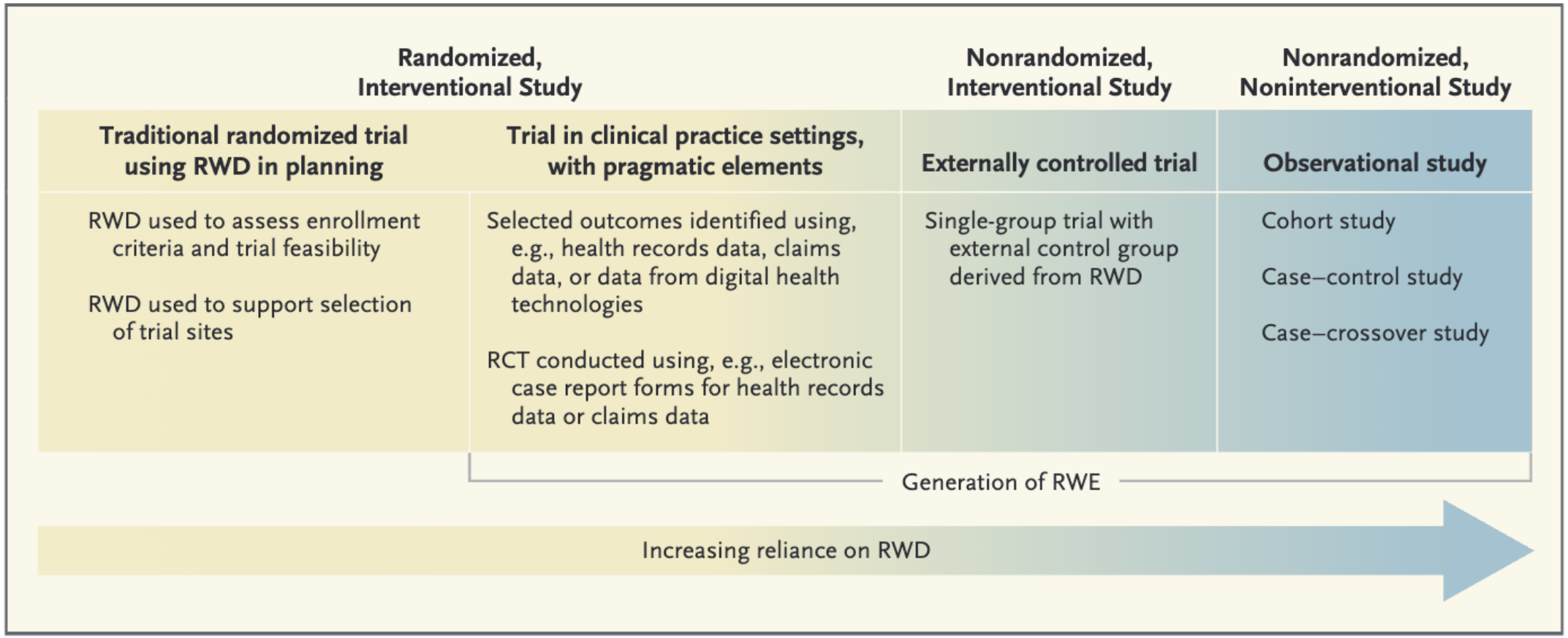
Reference(s): Karim S et al. *Clin Oncol (R Coll Radiol).* 2019;31:e160-e166. doi: 10.1016/j.clon.2019.05.003

Complementarity Clinical trials and Real world clinical evidence

Clinical trials	Real-world evidence
Highly selected population **High internal validity** Common endpoints: • Overall survival • Progression free survival • Response rate • Common adverse events • Disease Free Survival	**Broader population** **High external validity** Common endpoints: • Quality of life • Other PROMs (pain, fatigue, satisfaction…) • Real-world OS and PFS • Rarer side effects • Longer follow-up • Comparing more treatments

The utility of real-world data across clinical studies

Increased interest with hybrid, emulation and pragmatic clinical trials



Reliance on RWD in Representative Types of Study Design.

RCT denotes randomized, controlled trial; RWD real-world data; and RWE real-world evidence.

RCT, randomized controlled trial; RWD, real-world data; RWE, real-world evidence.
Concato J, Corrigan-Curay J. *N Engl J Med* 2022;386:1680–1682.

Inclusion and representativeness beyond eligibility

CHALLENGES AND OPPORTUNITIES WITH EQUITABLE ACCESS TO **CANCER CLINICAL TRIALS** IN THE EUROPEAN UNION

By: Luis Castelo-Branco, Florian Tille, Eva Jolly, Iwona Ługowska, Dario Trapani, Jose Luis Perez-Gracia and Dheepa Rajan

European Observatory on Health Systems and Policies 25 years

World Health Organization Europe



- More inclusiveness
- Expanding access to **more countries**
- Expanding access **inside countries**
- Reducing Bias of selection in the **same centre**

More pragmatism in clinical research – closer to real life conditions, across regions

*Eurohealth 2025, Castelo-Branco et all.

Real World data useful everywhere in Cancer research

Epidemiology/ Public Health

Heath Systems Performance

Health-economics



Clinical Evidence

Trials Validation

Comparative effectiveness

Subgroups and biomarkers-driven research

Larger Toxicity and PROMs data

Longer data analysis

Source: Original

2) How regulators are looking into RWE in Oncology?

U.S. FOOD & DRUG ADMINISTRATION

Real-World Evidence

Selected Guidance

- Framework for FDA's Real-World Evidence Program
- Use of Electronic Health Records in Clinical Investigations
- Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision-Making for Drug and Biological Products
- Data Standards for Drug and Biological Production Submissions Containing Real-World Data
- Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products
- Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products
- Submitting Documents Utilizing Real-World Data and Real-World Evidence to FDA for Drugs and Biologics
- Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products
- Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices
- Use of Real-World Data and Real-World Evidence to Support Effectiveness of New Animal Drugs

GUIDANCE DOCUMENT

Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products

Guidance for Industry

JULY 2024

Source: Real-World Evidence | FDA; Access: 1.june.2024

Use of real-world evidence in regulatory decision making – EMA publishes review of its studies

23 June 2023

News Human Data on medicines

- Big data: Use of real-world evidence
- EMA-HMA Big Data Steering Group
- Monitoring of COVID-19 pandemic: Observational reserach
- Measuring the impact of pharmacovigilance activities
- Data Analysis and Real World Interrogation Network (DARWIN EU)
- Regulatory science strategy to 2025
- European medicines network strategy to 2025
- Multi-stakeholder workshop on Real World Data (RWD) quality and Real World Evidence (RWE) use (26-27/06/2023)

HMA
Heads of Medicines Agencies

EMA
EUROPEAN MEDICINES AGENCY

Real-world evidence framework to support EU regulatory decision-making

Report on the experience gained with regulator-led studies from September 2021 to February 2023



Data Analysis and Real World Interrogation Network (DARWIN EU)

Collecting data

Healthcare professionals collect patient health information in various formats.

Accessing data

DARWIN EU collaborates with hospitals, registries, insurance claims, biobanks, and other sources to access the data collected from patients.

Standardising data

DARWIN EU's data partners standardise all data into a single format, the Observational Medical Outcomes Partnership (OMOP) common data model, so it can be analysed faster.

Analysing data

Experts at DARWIN EU use analytical methods to analyse the data and create study reports summarising the findings.

Interpreting results

EMA committees and EU regulators use the generated reports to complement other evidence when making regulatory decisions on medicines.

Supporting regulatory decisions

Regulators use the reports to support regulatory decisions that help make medicines safer and more effective for patients.

- EMA and European Medicines Regulatory Network collaboration
- Aim for Timely evidence on the use of medicines
- From real world healthcare databases across the European Union

Sourcce: Data Analysis and Real World Interrogation Network (DARWIN EU) | European Medicines Agency (europa.eu). Access 1.June.2024



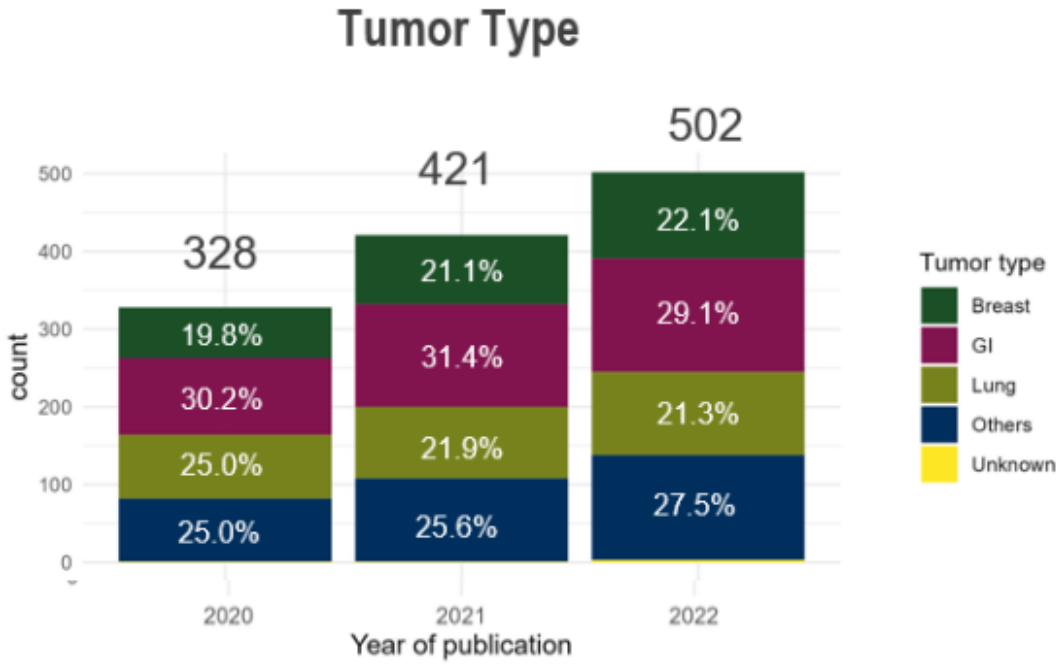
- Description of RWE use in authorisation of targeted therapies for solid malignancies by EMA
- **RWE** use was **reported in 21% of indications** between 2018 and 2022, **increasing over time**
- RWE ‘supportive’ in 75% of EPARs reporting RWE of clinical efficacy.

Derksen, Martins-Branco et al 2024, https://doi.org/10.1016/j.esmorw.2024.100039

RWE publications in Oncology growing, mainly published in low impact factor journals

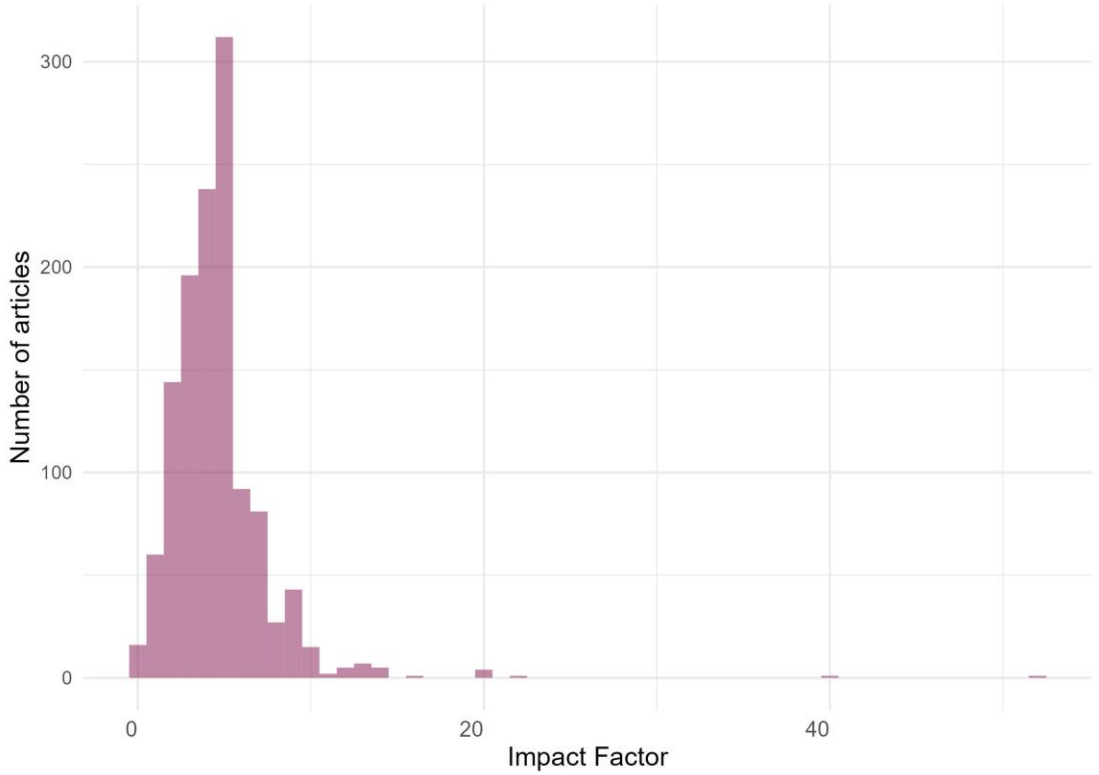


RWE publications with targeted therapies (2020-2022)



Mainly published in low impact factor journals

(Median IF 4,4 (3-5,3))



Source: kind permission and adapted from Dr. Anna Pellat. Originally presentation at ESMO congress 2023, Madrid.

3) Good practices for cancer real-world evidence research

Learning lessons from the COVID-19 pandemic for real-world evidence research in oncology—shared perspectives from international consortia

ESMO OPEN | SCIENCE FOR OPTIMAL CANCER CARE

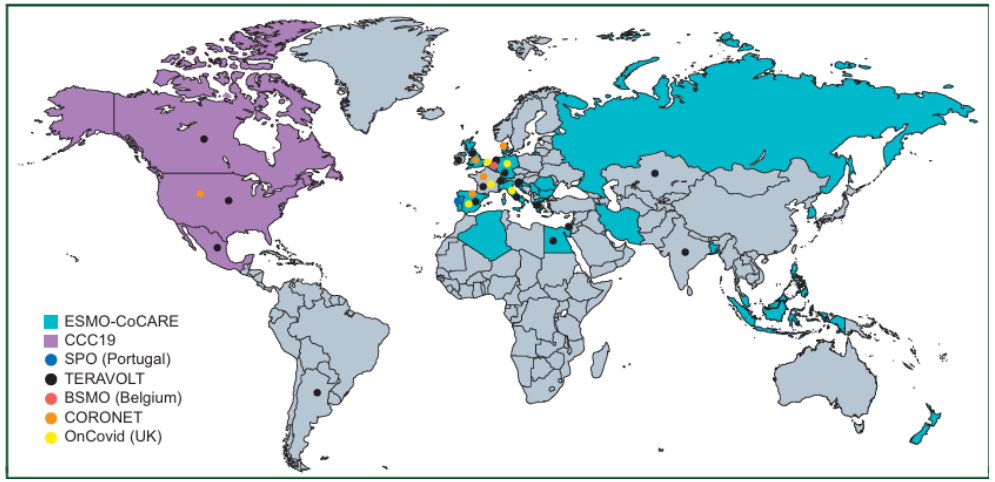
L. Castelo-Branco ✉ • R. Lee • M. Brandão • A. Cortellini • A. Freitas • M. Garassino • T. Geukens • P. Grivas • S. Halabi • J. Oliveira • D.J. Pinato • J. Ribeiro • S. Peters • G. Pentheroudakis • J.L. Warner • E. Romano •

Table 2. Key recommendations to start and conduct collaborative RWE studies in oncology

Before starting—preparedness
- Pre-define agreed aims and research questions of the project(s);
- Carry out a literature review to ensure there is no research duplication. In addition, consider discussing with other groups opportunities to collaborate;
- Build a multi- and inter-disciplinary team with relevant skills for the research proposed;
- Be inclusive with different research centers and early career-motivated members; include diversity of thought, experience and professional backgrounds;
- Involve patient advocates in the research design, whenever appropriate;
- Follow best guidelines for that research field;
- Establish a central (and/or regional) coordinating team and define tasks for each member. Carry out training and quality control to deliver objectives properly and accurately;
- Ensure sufficient funds are in place, including for infrastructure maintenance and administrative support;
- Anticipate and mitigate barriers for data sharing;
- Embrace compliance and ethics principles but remove unnecessary barriers to research.

The research protocol
- Develop a protocol to be approved in all geographies and participating centers, flexible to accommodate emerging research questions;
- Define the statistical plan considering guidelines for RWE studies;
- Engage different centers on protocol development;
- Define the essential data fields required to address the research goals, distinguishing mandatory from optional variables if relevant;
- Specify methods for data sharing, interoperability and metadata details. If needed, have a dedicated and qualified team working on interoperability;
- Consider the use of novel methods for data collection and analysis, use of open software for data collection, artificial intelligence and machine learning. Such methods may require validation before or during the study.

During the study and reporting findings
- Regularly assess all processes and eventual obstacles with team members; pursue quality control checks;
- Agree and prioritize goals and deadlines, estimating the time allocated for different tasks (e.g. full data collection per patient);
- Promote the project amongst the communities for broader collaboration;
- Reward centers and collaborative members accordingly to their contributions, such as with adequate authorship positions, early access to data, public recognition, congress participation and/or financial support;
- Be open to new research ideas led by different team members;
- Ensure that good governance (e.g. steering committee) is achieved and documented;
- Be ready to adjust priorities upon new important unmet needs;
- Follow available guidance on reporting RWE studies when submitting for publication;
- Follow scientific rigor and principles. Report ethical misconduct in a timely manner.



JCO® Global Oncology
An American Society of Clinical Oncology Journal

Leveraging Real-World Evidence to Drive Advances in Oncology Care in the Asia-Pacific Region: Recommendations From the Asia-Pacific Oncology Drug Development Consortium Working Group

Authors: Herbert H. Loong, MBBS (HK), PDipMDPath (HK), MRCP (UK), FRCP Edin, FHKCP, FHKAM (Medicine), FASCO, Pankaj Kumar Panda, BDS, MSc, Ben Tran, MBBS, FRACP, Toshio Shimizu, MD, PhD, Pei Jye Voon, MD (UNIMAS), MRCP (UK), MMED (NUS), Frederic Ivan Leong Ting, MD, MAN, MCM (MO), FPCP, FPSMO, FSASS, FPSO, Takafumi Koyama, MD, PhD, Daphne Day, MBBS (Hons), FRACP, K. Arnold Chan, MD, ScD, FISPE, Grace L. Wong, MBChB (CUHK), MD (CUHK), FRCP (Lond, Edin), FHKCP, FHKAM (Medicine), and Daniel S.W. Tan, BSc (Hons), MBBS (London), MRCP (UK), PhD | AUTHORS INFO & AFFILIATIONS

JCO Glob Oncol **12**, e2600217(2026) • Volume 12, Number 10 • DOI: 10.1200/GO-26-00217

ESMO > About ESMO > Organisational Structure > Educational Committee

ESMO Real World Data and Digital Health Working Group

Activities and responsibilities

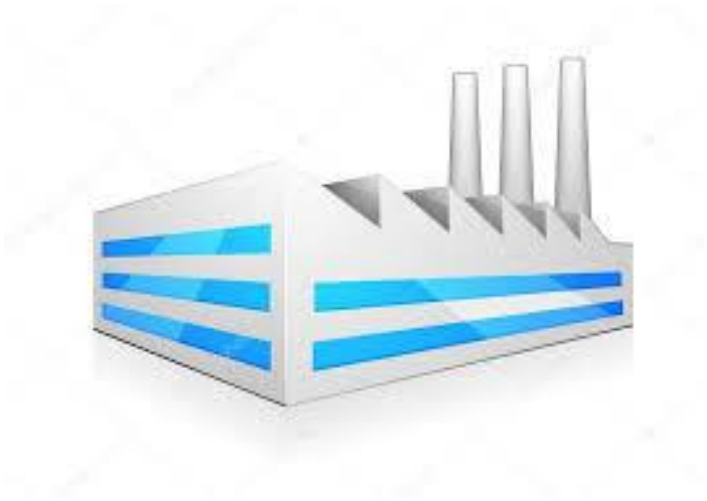
- Identify a pilot network of non-commercial, clinicopathologic RWD groups and facilitate joint scientific snapshot analyses on focused queries
- Develop a framework for Governance and Methodology for the scientific collaborations
- Develop Digital Health in Oncology/RWE education programmes for ESMO members
- Develop position papers on RWE, Digital Health
- Optimise interactions with stakeholders



Source: ESMO Real World Data and Digital Health Working Group. Assessed on 02.June.2024

Real-world evidence ecosystem

Database infrastructure



Good Quality

Poor Quality

Quality Standards for RW Database

Data



Good Quality

Poor Quality

Quality Standards for RW Data

Report



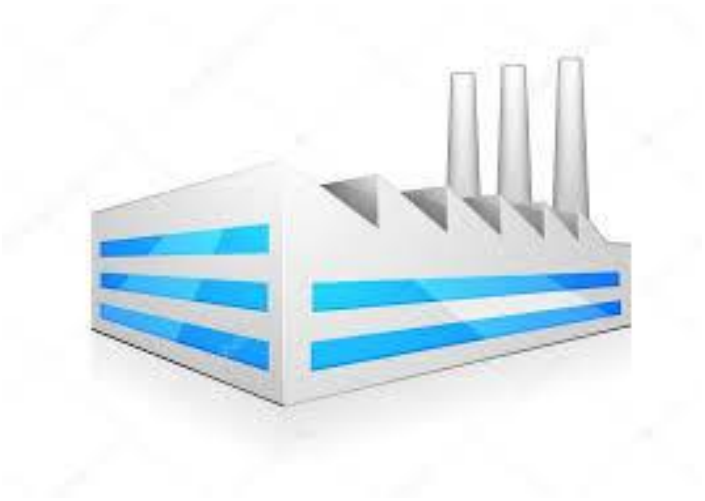
Good Quality

Poor Quality

Quality Standards for RWD Reporting

Real-world evidence ecosystem

Database infrastructure



Data



Report



Guidelines useful for observational and real-world data publications (2022)

Unmet need for reporting modern RWE in Oncology

Guideline	Topics considered	Limitations and comments
STROBE, 2007	**Three main study designs: cohort, case–control, and cross-sectional studies considered** **A checklist of 22 items: title, abstract, introduction, methods, results, and discussion**	**Not a tool for designing or conducting studies** **Not an instrument to evaluate the quality of observational research.** **Focused on good reporting, not if research was of good quality**
RECORD, 2015	Checklist of 13 items related to the title, abstract, introduction, methods, results, and discussion	Not designed to recommend the methods used to conduct research, but rather to improve its reporting
MOOSE, 2000	Specifications on: Background; Search strategy; Methods; Results; Discussion; Conclusion.	For meta-analysis (not primary observational studies); General but not very specific guidance
CONSORT, 2010 (update)	A checklist of 25 items on: Title and abstract; Introduction; Methods; Results; Discussion; Other information.	Designed for Clinical trials, not for Observational studies; Not recommendations for designing, conducting, and analyzing studies
REMARK, 2005	Topics: Introduction; Materials and methods (patients; specimen characteristics; assay methods; study design; statistical analysis); Results (data; analysis and presentation); Discussion.	Not intended to dictate specific designs or analysis strategies. To predict particular therapies, such as molecular targeted therapies, need additional considerations
OSQE, 2021	Cohort- studies; Case-control	Only four authors, from one country; No multi-disciplinary extensive discussion A complex tool with many items and steps; unclear the applicability
NOS, 2011	A 'star system' in which a study is judged on three broad perspectives. Selection; Comparability; Exposure/Outcome;	Designed for metanalysis (and/or systematic reviews?) not primary observational studies Not published in a peer review journal; Not specific for Oncology
ISPOR, 2012	Study Design and Analytical Strategies; Design Tools; Study Execution; Reporting Study Findings; Interpretation;	General report
ROBINS-I, 2016 (Cochrane)	Pre-intervention; At-intervention; Post-intervention.	Primarily for use in the context of a systematic review; Focused on “study bias”

Source: original

ESMO Guidance for Reporting Oncology real-World Evidence (ESMO-GROW)

ESMO GROW
GUIDANCE FOR REPORTING ONCOLOGY REAL-WORLD EVIDENCE



ESMO-GROW Publications

Online available on
- Annals of Oncology
- ESMO Real World Data and Digital

Online Tool & Informative Score
Interactive tool generating a final assessment report of a RWE study in Oncology
Access →

Checklist in PDF
To assess the reporting standards of a RWE study
Download

Flowchart
For reporting case selection for analysis in a RWE study
Download

SPECIAL ARTICLE

ESMO Guidance for Reporting Oncology real-World evidence (GROW)

L. Castelo-Branco[1*], A. Pellat[2,3†], D. Martins-Branco[1,4†], A. Valachis[5†], J. W. G. Derksen[6†], K. P. M. Suijkerbuijk[7], U. Dafni[8,9], T. Dellaporta[9], A. Vogel[10,11,12], A. Prelaj[13,14], R. H. H. Groenwold[15], H. Martins[16], R. Stahel[17], J. Bliss[18], J. Kather[19,20], N. Ribelles[21], F. Perrone[22], P. S. Hall[23], R. Dienstmann[24,25], C. M. Booth[26,27], G. Pentheroudakis[1†], S. Delaloge[28†] & M. Koopman[7†]

Increasing the standards and harmonizing the report of RWE in Oncology

- **First Guidance for Reporting Oncology RWE** studies (all types: descriptive and analytical)
- Addresses **trends in treatments, molecular-based epidemiology, and patient-reported outcomes**
- Considers **digital health, artificial intelligence, and machine learning in RWE research**
- Different products**: Article, RWE flowchart, Checklist and Interactive tool**
- Recommendations for **authors, editors, and readers**

https://www.esmo.org/scales-and-tools/esmo-guidance-for-reporting-oncology-real-world-evidence-esmo-grow

ESMO-GROW article

35 recommendations:

(i) Title

(ii) Introduction

(iii) Methods,

(iv) Results,

(v) Discussion and conclusions

(vi) Final considerations

Suplementary material

. Definitions for modern cancer RWE

. RWD sources

. Main variables and their specificities

. Commmon sources of Bias with RWE studies

SPECIAL ARTICLE

ESMO Guidance for Reporting Oncology real-World evidence (GROW)

L. Castelo-Branco[1*], A. Pellat[2,3†], D. Martins-Branco[1,4†], A. Valachis[5†], J. W. G. Derksen[6†], K. P. M. Suijkerbuijk[7], U. Dafni[8,9], T. Dellaporta[9], A. Vogel[10,11,12], A. Prelaj[13,14], R. H. H. Groenwold[15], H. Martins[16], R. Stahel[17], J. Bliss[18], J. Kather[19,20], N. Ribelles[21], F. Perrone[22], P. S. Hall[23], R. Dienstmann[24,25], C. M. Booth[26,27], G. Pentheroudakis[1‡], S. Delaloge[28‡] & M. Koopman[7‡]

Multidisciplinarity for design, conduction and report of RWE in Oncology

3.22: When applicable, briefly describe the multidisciplinary team required for the study and explain how these needs were met.

The growing complexity of RWE research in oncology often demands multidisciplinarity (inclusion of different and complementary scientific backgrounds and knowledge), which can be important for the design, conduct and reporting of studies.

Depending on the type of research, RWE studies may include clinical oncologists, other health professionals, public health experts, epidemiologists, statisticians, methodologists, data scientists, AI experts and patient representatives, among others. For example, a study applying an AI algorithm to assess the association between risk factors and incidence or mortality from colon cancer in a specific region will require input from, at a minimum, experts in several oncology specialities, epidemiology, data science and AI.

This information could be concisely reported in the methods section or in the supplementary material; for example, as reported for this guidance (see Supplementary Material Section 1, Table S2, available at https://doi.org/10.1016/j.annonc.2023.10.001).

ESMO-GROW checklist and informative score

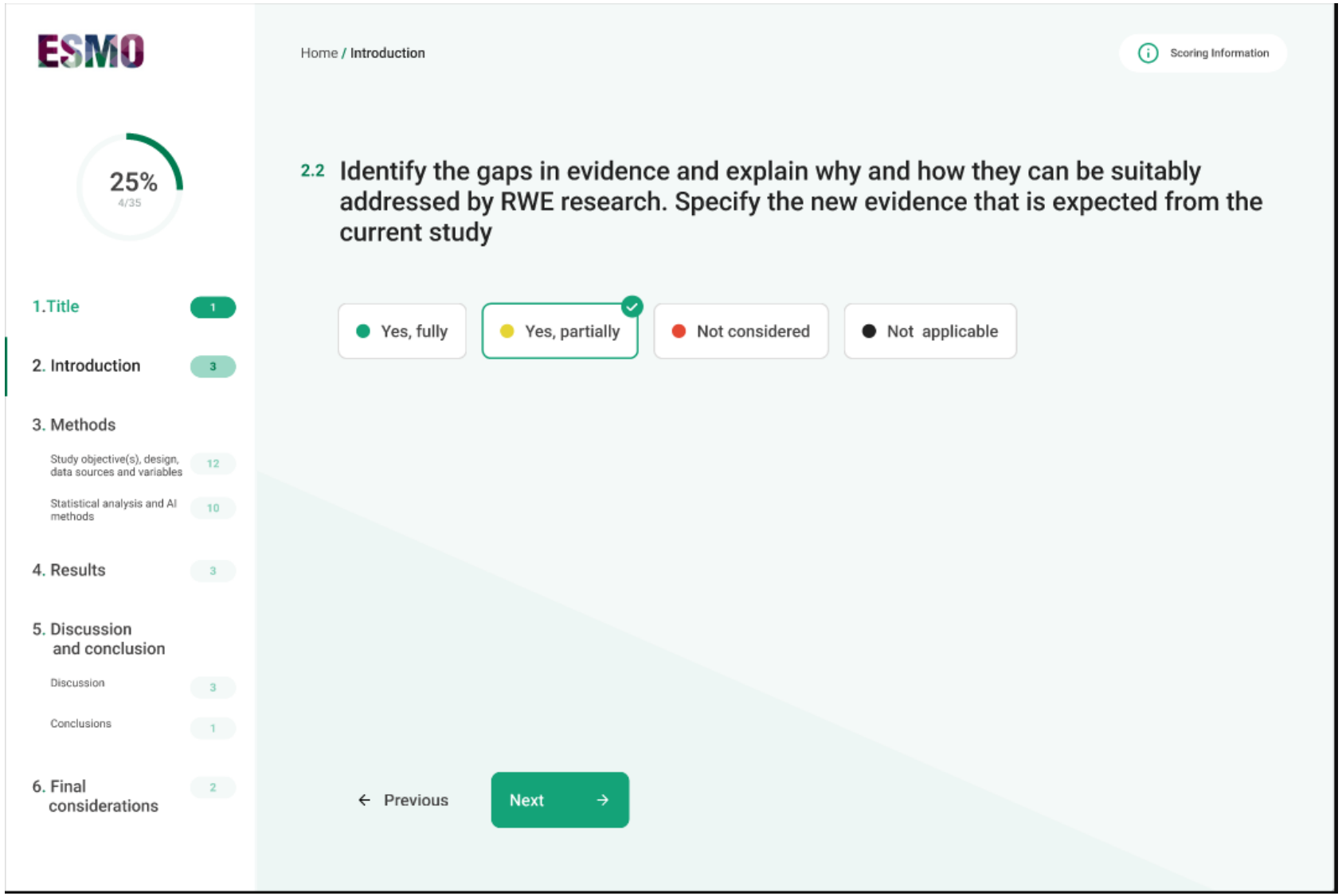
ESMO Guidance for Reporting Real World Evidence Studies checklist for authors and journals.

This checklist integrates all recommendations from ESMO-GROW guidance and could be used by authors and journals when assessing the reporting standards of a RWE study in Oncology. *The output generated will be an "informative score" (and not a quantitative assessment on the quality of the report).*

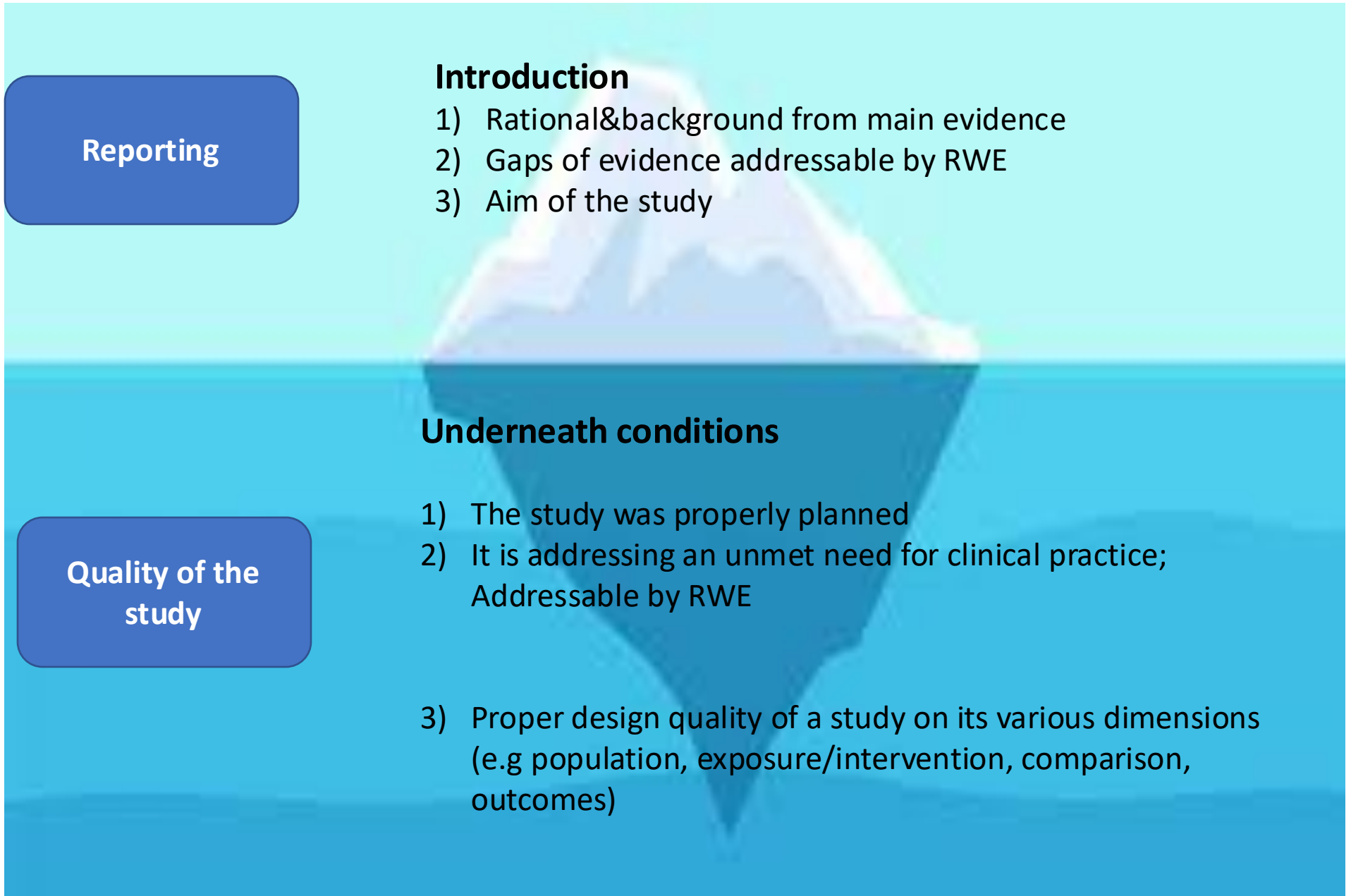
The following rules apply for scoring:
Yes, fully – recommendation fully incorporated in the manuscript. (1 point); green colour.
Yes, partially - recommendation incorporated in the manuscript but some aspects not considered. (0,5 point); yellow colour.
Not considered – recommendation not considered, while it should be applicable (o points) Red colour
Not applicable – recommendation not applicable for this manuscript (recommendation does not count for final score); Black colour.

Recommendation	Yes, Fully	Yes, Partially,	Not Considered	Not Applicable
1. Title				
1.1: Concisely include relevant key terms referring to the study type, study population, objectives, data sources and outcomes, depending on the study. Consider including the terms 'real-world' or 'observational'				
2. Introduction				
2.1: Explain the scientific rationale for the research question(s), providing concise background information on previous core evidence from systematic reviews, meta-analyses, clinical trials and/or RWE studies				
2.2: Identify the gaps in evidence and explain why and how they can be suitably addressed by RWE research. Specify the new evidence that is expected from the current study				
2.3: Briefly introduce the aim(s) of the study				
3. Methods				
Study objective(s), design, data sources and variables				
3.1: Provide the study research question(s) including a description of the patients or the object under study and the target outcome(s)				
3.2: Provide the study objective(s) and consider classifying the type of research as descriptive and/or analytical (explanatory or predictive)				

ESMO-GROW digital tool generating an informative score on the report of a RWE study in Oncology



GROW: From reporting to quality standards



Reporting

Introduction

1) Rational&background from main evidence
2) Gaps of evidence addressable by RWE
3) Aim of the study

Quality of the study

Underneath conditions

1) The study was properly planned
2) It is addressing an unmet need for clinical practice; Addressable by RWE

3) Proper design quality of a study on its various dimensions (e.g population, exposure/intervention, comparison, outcomes)

GROWing from GROW

- Series of publications vs One big article
- Promotion and engagement with community and stakeholders
  - Testing GROW on real-life publications (ongoing)
  - Abstract – a parallel and new project (probably soon by ESMO)

4) **Artificial Intelligence for** cancer RWE research

Super-Intelligence?

Super Artificial Intelligence?

Digital Intelligence?

Artificial intelligence everywhere (also in Oncology)

Data collection

Data Analysis

Manuscript drafting



Literature revision

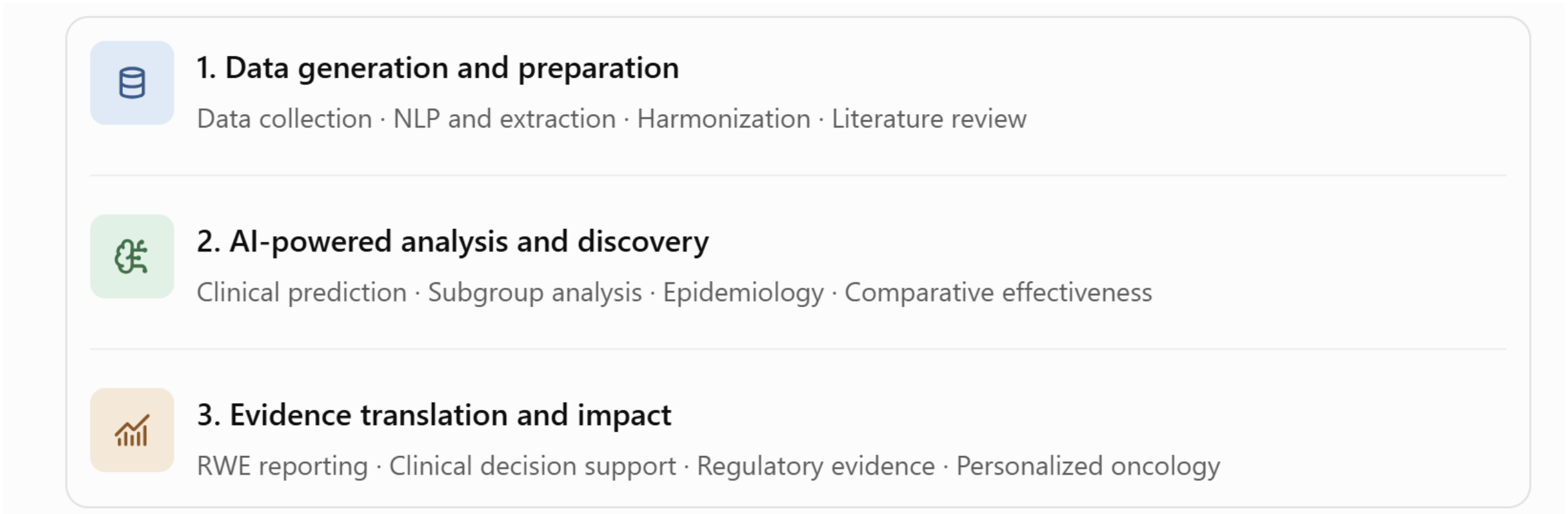
Guidelines summary

Personalized decisions

Source: Original

hoje às 10:52

I am preparing a slide on role of AI in clinical Oncology and real world evidence research. Tell me concisely the main topics I sould consider.



Source: Prepared with the assistance of ChatGPT (OpenAI).

Real-World Evidence in Oncology

Real-world practice different from trials and guidelines

- Several relevant subgroups of patients excluded
- Guidelines are not sufficient for each individual decisions
- **Needed Complementary, high-quality, real-world evidence**

Are regulators considering more RWE in Oncology?

Yes, if good quality addressing unmet needs

Good standards for RWE research in Oncology?

Following guidance such as ESMO-GROW

What is the role of Artificial Intelligence for RWE research?

Supportive, under proper regulation and ethical use