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Updates on the best practices for conducting and publishing Real-World Evidence studies

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Co-Chair of EMWA MedComm SIG and member of RWE subgroup

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Disclaimer

The views expressed in this presentation are those of the presenters and do not necessarily reflect those of Lumanity.

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RCTs vs RWE studies

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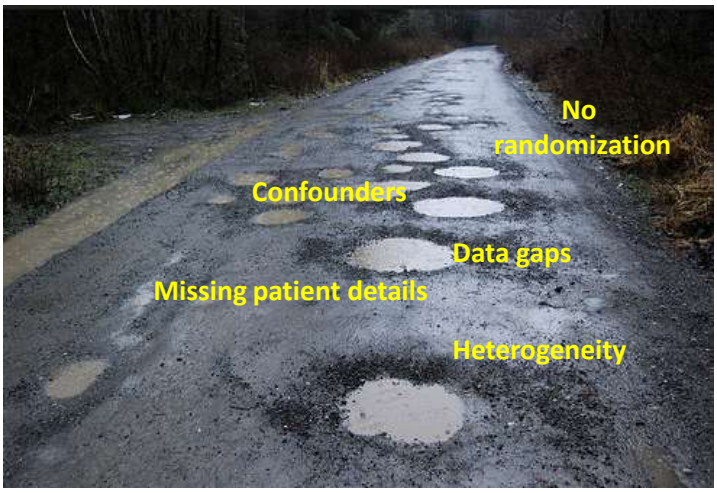
RCTs vs RWE studies



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Reporting Guidelines

Increasing transparency and reproducibility in RWE

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RWE Reporting Guidelines in peer-reviewed journals

- Consistency in reporting RWE data is important
  - Comparison of data from different studies
  - Planning future studies and interventions
  - Transparency/Reproducibility

STROBE Statement
Strengthening the reporting of observational studies in epidemiology
strobe-statement.org/

RECORD
REporting of studies Conducted using Observational Routinely-collected Data
record-statement.org/

CONSORT TRANSPARENT REPORTING of TRIALS
consort-statement.org/extensions/overview/pragmatic-trials

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RWE Reporting Guidelines in peer-reviewed journals

- Pragmatic Trials – CONSORT Guidelines [1]
- STROBE-ME: Observational studies - Molecular epidemiology [2]
- STROME-ID: Molecular epidemiology for infectious diseases [2]
- STROBE-RDS: Observational studies in epidemiology for respondent-driven sampling studies [2]
- STROBE-AMS: epidemiological studies on antimicrobial resistance [2]
- STREGA: Genetic association studies [3]
- RECORD: Observational Routinely-collected health Data (http://www.record-statement.org/pubs.php) [4]
- RECORD – PE : non-interventional pharmacoepidemiological studies using routinely collected health data [5-6]
- REporting recommendations for tumour MARKer prognostic studies (REMARK) [7]

1. Zwarenstein M, et. al. for the CONSORT and Pragmatic Trials in Healthcare (Practihc) group. Improving the reporting of pragmatic trials: an extension of the CONSORT statement. BMJ 2008; 337;a2390. http://www.consort-statement.org/extensions/overview/pragmatic-trials. 2. STROBE Statement. Available at: http://www.equator-network.org/reporting-guidelines/strobe/ 3. Little, et al. (2009), STrengthening the REporting of Genetic Association studies (STREGA) – an extension of the STROBE statement. European Journal of Clinical Investigation, 39: 247-266. https://doi.org/10.1111/j.1365-2362.2009.02125.x 4. Benchimol EI, et al.(2015) The Reporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. PLoSMed12(10):e1001885. 5. Langan SM et al. BMJ 2018;363:k3532 http://dx.doi.org/10.1136/bmj.k3532 . 6. RECORD - PE: record-statement.org/checklist-pe.php. 7. McShane, et al. REporting recommendations for tumour MARKer prognostic studies (REMARK). Br J Cancer 93, 387–391 (2005). https://doi.org/10.1038/sj.bjc.6602678.

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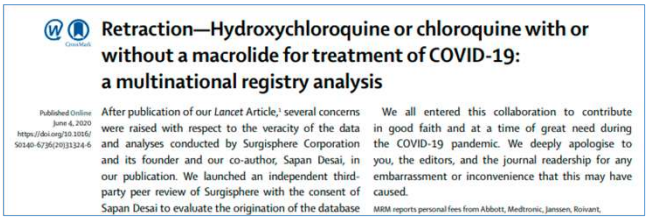
Reporting Guidelines - Failures



Retraction—Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis

Published Online June 4, 2020 https://doi.org/10.1016/S0140-6736(20)31324-6

After publication of our *Lancet* Article,[1] several concerns were raised with respect to the veracity of the data and analyses conducted by Surgisphere Corporation and its founder and our co-author, Sapan Desai, in our publication. We launched an independent third-party peer review of Surgisphere with the consent of Sapan Desai to evaluate the origination of the database

We all entered this collaboration to contribute in good faith and at a time of great need during the COVID-19 pandemic. We deeply apologise to you, the editors, and the journal readership for any embarrassment or inconvenience that this may have caused.

MRM reports personal fees from Abbott, Medtronic, Janssen, Roivant.

- RECORD and RECORD-PE items were not adequately reported (methods, confounders, outcomes, programming codes, etc..)
- When confronted, three of the authors claimed they were unable to access the raw data due to legal circumstances
  - RECORD 22.1:"provide information on how to access any supplemental information such as the study protocol, raw data, or programming code"

- Full story: https://retractionwatch.com/2020/07/10/a-month-after-surgisphere-paper-retraction-lancet-retracts-replaces-hydroxychloroquine-editorial/

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Regulatory and HTA agencies guidance on reporting RWE studies

- European Medicines Agency. Real-world evidence framework to support EU regulatory decision-making (2023) [1]
- European Network for Health Technology Assessment. REQueST Tool (2023) [2]
- European Organisation for Research and Treatment of Cancer (2023)[3]
- National Institute for Health and Care Excellence. NICE real-world evidence framework. (2023) [4]
- Canada's Drug and Health Technology Agency. Guidance for Reporting Real-World Evidence. (2023) [5]
- ISPE/ISPOR task force. (2022) [6]
- US Food and Drug Administration. Framework for FDA's real-world evidence program. (2023) [7]

1. European Medicines Agency. Real-world evidence framework to support EU regulatory decision-making. Available at https://www.ema.europa.eu/en/documents/report/real-world-evidence-framework-support-eu-regulatory-decision-making-report-experience-gained-regulator-led-studies-september-2021-february-2023_en.pdf . Published 2023. Accessed Oct 2024. **2.** European Network for Health Technology Assessment. REQueST Tool and its vision paper. Available at https://www.eunethta.eu/requesttool-and-its-vision-paper/ . Published 2023. Accessed Oct 2024 **3.** Robbe Saesen, et al. Defining the role of real-world data in cancer clinical research: The position of the European Organisation for Research and Treatment of Cancer, European Journal of Cancer, Volume 186, 2023, Pages 52-61, ISSN 0959-8049, https://doi.org/10.1016/j.ejca.2023.03.013. **4.** National Institute for Health and Care Excellence. NICE real-world evidence framework. Available at https://www.nice.org.uk/corporate/ecd9/resources/nice-realworld-evidence-framework-pdf-1124020816837 Accessed Oct 2024. **5.** Canada's Drug and Health Technology Agency. Guidance for Reporting Real-World Evidence. Guidance for Reporting Real-World Evidence | CDA-AMC. Published 2023. Accessed Oct 2024. **6.** Shirley V. et al. HARmonized Protocol Template to Enhance Reproducibility of Hypothesis Evaluating Real-World Evidence Studies on Treatment Effects: A Good Practices Report of a Joint ISPE/ISPOR Task Force, Value in Health, Volume 25, Issue 10, 2022, Pages 1663-1672, ISSN 1098-3015, https://doi.org/10.1016/j.jval.2022.09.001. **7.** US Food and Drug Administration. Framework for FDA's real-world evidence program. Available at https://www.fda.gov/media/120060/download . Published 2018. Accessed Oct 2024

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

The first expert-based guidance specifically for reporting oncology RWE studies

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ESMO-GROW Recommendations

- **Why:** The use of multiple complementary guidelines can be demanding and burdensome for both authors and journals and, most importantly, may not capture all the relevant oncology research-specific considerations.
- **How:** Multidisciplinary experts of the ESMO Real-World Data and Digital Health Working Group have developed the first specific guidance for reporting oncology RWE studies in peer-reviewed journals: the ESMO Guidance for Reporting Oncology real-World evidence (ESMO-GROW).
- **Results:**
  - A guidance for reporting descriptive (e.g. epidemiological) or analytical (e.g. explanatory, predictive) oncology RWE studies and for pragmatic studies, such as 'target trial emulation' designs
  - Thirty-five reporting recommendations developed for each of the following sections:
    - Title
    - Introduction
    - Methods
    - Results
    - Discussion and conclusions
    - Final considerations

1.ESMO Guidance for Reporting Oncology real-World evidence (GROW) Castelo-Branco, L. et al. Annals of Oncology, Volume 34, Issue 12, 1097 - 1112

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ESMO-GROW Recommendations

Table 1. Summary of recommendations on reporting RWE studies

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 real-world evidence studies
2.2	Identify the gaps in evidence and explain why and how they can be suitably addressed by real-world evidence 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)
3.3	Provide relevant information to describe and classify the study design used to address the research question
3.4	Give a clear definition of the eligibility criteria used to select the patients or objects under study, particularly regarding cancer-related aspects
3.5	Report the specific type and purpose of real-world data source(s) used, providing a detailed description and the reason(s) why the source was considered appropriate for the study objectives
3.6	When multiple real-world data sources are used, provide details on interoperability, including identification of duplicated cases or data linkage from separate databases
3.7	Provide details and timings of source and study data management. Consider specifying methods of raw data collection, updates and completeness, data extraction, cleaning and/or quality controls and validation
3.8	Provide core details on database and/or study registration, governance, ownership, metadata and full data accessibility in the main text or supplementary material
3.9	Identify the data source of each core variable, its definition, if the variable was derived or coded, and describe how the derivation or coding was conducted and validated
3.10	Specify the time points of core variables in relation to the cancer disease trajectory
3.11	Provide a complete list of core variables included in the study. Variables can be grouped as baseline characteristics, exposure, and outcomes or endpoints
3.12	For biomarker-related studies, provide details on biomarker description, timing, and methods of assessment and analytical validation
	Statistical analysis and artificial intelligence methods
3.13	Summarise the main aspects of the statistical analysis
3.14	When applicable, provide details on the pre-planned sample size requirements and power of the study
3.15	Specify the pre-planned strategies to identify and mitigate the main sources of bias
3.16	Clearly distinguish prespecified from *post hoc* analyses, especially for subgroup analyses
3.17	Provide information on internal and external validity, as well as any sensitivity analyses
3.18	For analytical studies, the full version of the statistical analysis plan should be provided in the supplementary material, including a brief explanation of any amendments
3.19	When applicable, specify which machine learning, deep learning or alternative artificial intelligence method has been used
3.20	When reporting real-world data analysis with artificial intelligence (e.g. machine learning and deep learning) algorithms, include comprehensive aspects on data pre-processing techniques, feature engineering strategies and model development
3.21	Address the artificial intelligence model explainability and interpretability, and present the plan for integration into clinical practice, if applicable
3.22	When applicable, briefly describe the multidisciplinary team required for the study and explain how these needs were met

1.ESMO Guidance for Reporting Oncology real-World evidence (GROW) Castelo-Branco, L. et al. Annals of Oncology, Volume 34, Issue 12, 1097 - 1112

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ESMO-GROW Recommendations

4. **Results**
4.1 Provide the number of cases excluded or nonparticipating and reasons at each stage of sample selection, as well as numbers lost to follow-up. Compare the cases excluded with those included in the analyses. Illustrate this with a flowchart
4.2 Describe the baseline characteristics of the cases included (e.g. clinico-demographic and tumour characteristics). The baseline characteristics of different groups under analysis should be compared, if applicable
4.3 Report the results of the primary analysis of study outcomes. Briefly describe the results of exploratory analyses if relevant (prespecified and/or *post hoc*). Provide details of how readers can access the full results
5. **Discussion and conclusions**
Discussion
5.1 Summarise the core results that address the primary research question(s) and objectively discuss the data in relation to the best available evidence on the topic. Avoid a convenient selection of literature to support a point
5.2 Discuss the strengths and limitations of the current study, including the main biases, how the strategies applied contributed to bias avoidance or mitigation and, if applicable, in which direction the authors estimate that residual bias may influence the core results of the study
5.3 Discuss the generalisability of the study results and their potential implications for clinical practice, health policies or public health and for the generation of hypotheses for future research
Conclusions
5.4 Provide a balanced summary of core results relating to the primary research question and the main implications for clinical practice, health policies and/or public health. Suggest further research considering the remaining unmet needs and limitations from the reported study
6. **Final considerations**
6.1 Specify all relevant study sponsorship(s) as well as direct and/or indirect or in-kind funding
6.2 Specify all relevant acknowledgements, author disclosures, individual contributions and other final considerations as per journal regulations

1.ESMO Guidance for Reporting Oncology real-World evidence (GROW) Castelo-Branco, L. et al. Annals of Oncology, Volume 34, Issue 12, 1097 - 1112

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ESMO-GROW Recommendations – Online tool

ESMO

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

ESMO-GROW checklist and informative score

The ESMO Guidance for Reporting Oncology real-World evidence (GROW) online and interactive checklist integrates all recommendations from the ESMO-GROW manuscript and can be used by authors, journals or readers when assessing the report of an oncology real-world evidence (RWE) study.

The output generated is an assessment report sheet, and an informative score, which can be considered for improvements or final appraisal on the study's general adherence to reporting standards. Please note that the height of the score does not necessarily reflect the quality of the manuscript, since the weight/relevance of individual items might differ, depending on the study design and setting.

There is also an option to add notes (if useful) for each recommendation. You will then be able to include or not include these notes in the final report.

Start →

https://grow.esmo.org/

1.ESMO Guidance for Reporting Oncology real-World evidence (GROW) Castelo-Branco, L. et al. Annals of Oncology, Volume 34, Issue 12, 1097 - 1112

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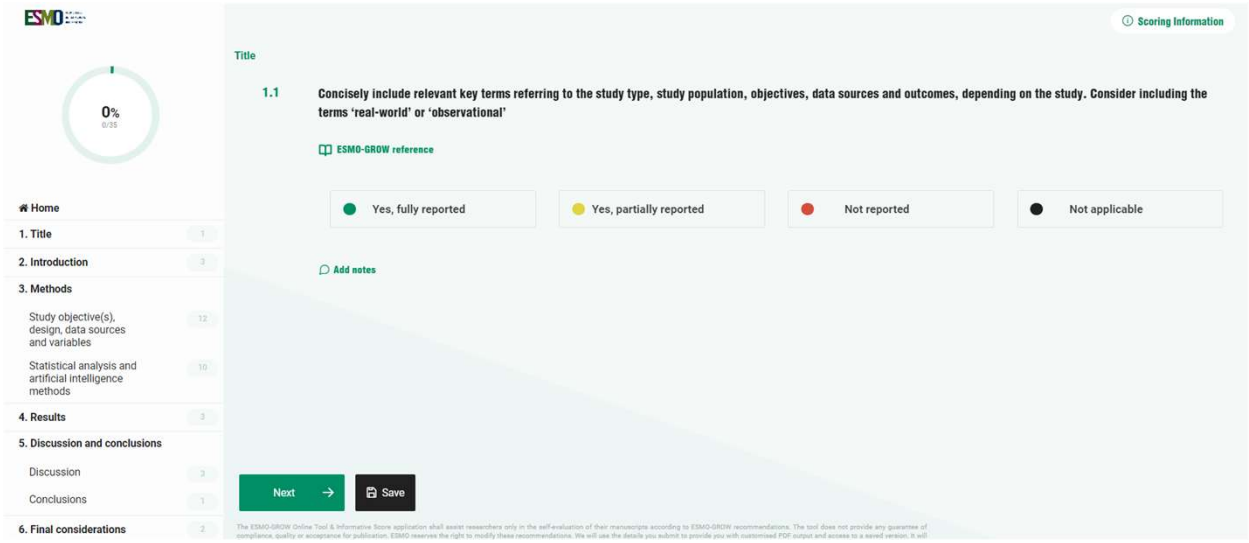
ESMO-GROW Recommendations – Online tool



1.ESMO Guidance for Reporting Oncology real-World evidence (GROW) Castelo-Branco, L. et al. Annals of Oncology, Volume 34, Issue 12, 1097 - 1112

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Acknowledge the use of ESM-GROW tool in your manuscript

Cancers (Basel). 2024 Apr 22;16(8):1609. doi: 10.3390/cancers16081609.

Patients with Advanced or Metastasised Non-Small-Cell Lung Cancer with *Viscum album* L. Therapy in Addition to PD-1/PD-L1 Blockade: A Real-World Data Study

Friedemann Schad [1,2], Anja Thronicke [1], Ralf-Dieter Hofheinz [3], Harald Matthes [4,5], Christian Grah [6]

Affiliations + expand

"The reporting of data was performed in accordance with the ESMO-GROW criteria for the optimal reporting of oncological real-world evidence (RWE) studies".

Immunotherapy with PD-1/PD-L1 inhibitors has significantly improved the survival rates of patients with metastatic non-small-cell lung cancer (NSCLC). Results of a real-world data study investigating add-on VA (*Viscum album* L.) to chemotherapy have shown an association with the improved overall survival of patients with NSCLC. We sought to investigate whether the addition of VA to PD-1/PD-L1 inhibitors in patients with advanced or metastasised NSCLC would have an additional survival benefit. In the present real-world data study, we enrolled patients from the accredited national registry, Network Oncology, with advanced or metastasised NSCLC. The reporting of data was performed in accordance with the ESMO-GROW criteria for the optimal reporting of oncological real-world evidence (RWE) studies. Overall survival was compared between patients receiving PD-1/PD-L1 inhibitor therapy (control, CTRL group) versus the combination of anti-PD-1/PD-L1 therapy and VA (combination, COMB group). An adjusted multivariate Cox proportional hazard analysis was performed to investigate variables associated with survival. From 31 July 2015 to 9 May 2023, 415

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What to include in your manuscript

The Experts' view and suggestions

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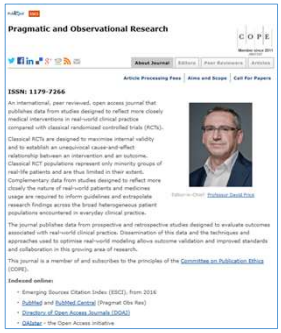
Reporting RWE studies – The voice of experts



REG Respiratory Effectiveness Group

rkkp regionernes kliniske kvalitetsudviklingsprogram

RECIF Réseau d'Epidémiologie Clinique International Francophone

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Manuscript preparation

- Clarify in detail the rationale of the study[1]
- All studies (regardless of size!), well conducted, novel and address an important clinical question are worth publishing
  - RWE studies often cover a population that is difficult to study by 'traditional' study designs. (e.g.: elderly, children, pregnant women)
- Provide details of pre-registration of the study in a public repository, with the commitment to publish the results
- Address all the strengths, limitations and potential confounders in a *Strengths and Limitations* paragraph within the Discussion

Roche, Reddel, Martin,et al.: Quality Standards for Real-World Research – 2014 - https://doi.org/10.1513/AnnalsATS.201309-300RM Accessed Feb 2020

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Manuscript preparation

- Statistical Analyses and Data extraction:
  - Qualified statisticians with expertise in data extraction should be among the authors and their contribution clearly stated in the Authors' Contribution section
- A detailed protocol of data extraction, including:[1]
  - Key variables and combinations for defining study subjects
  - List and codes of key variables, such as measurements of exposures, outcomes, possible confounders, or subjects general characteristics
  - State which author or company performed the data extraction

Roche, Reddel, Martin,et al.: Quality Standards for Real-World Research – 2014 - https://doi.org/10.1513/AnnalsATS.201309-300RM Accessed Feb 2020

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Manuscript preparation

- If dealing with missing data in your study, work closely with a statistician for:
  - Adequately reporting the bias in the manuscript
  - Fully describe all the analyses taken for minimising bias[1]
- Be careful when using significance testing (p-value, or confidence limits) as measure of effect.[2–8] Correlation does not prove causation!

1. Petersen I et al. Clinical Epidemiology 2019:11 157–167 **2.** Significance Testing is the Reason that Scientific Results have Poor Reproducibility. Video at https://epiresearch.org/serlibrary/sertalks/sertalks-archives/significance-testing/: Society for Epidemiologic Research; 2017 **3.** Rothman KJ, Greenland S, Lash TL. Modern epidemiology. 3rd ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2008. **4.** Goodman S. A dirty dozen: twelve p-value misconceptions. Semin Hematol. 2008;45(3):135-140. **5.** Rothman KJ. Six persistent research misconceptions. J Gen Intern Med. 2014;29(7):1060-1064. **6.** Farland LV, et. Al.. P-values and reproductive health: what can clinical researchers learn from the American Statistical Association? Hum Reprod. 2016;31(11):2406-2410. **7.** Harvey LA. Statistical power calculations reflect our love affair with P-values and hypothesis testing: time for a fundamental change. Spinal Cord. 2014;52(1):2-2. **8.** Wasserstein RL, Lazar NA. The ASA's Statement on p-Values: Context, Process, and Purpose. American Statistician. 2016;70(2):129-131.

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To conclude

- Before submission check the following:
- Pre-registration details have been included
- Limitations, missing data and confounders have been clearly described in full
- A statistician should ideally be among the authors and their contribution clearly stated in the manuscript
- Conclusions must be in line with the data presented

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Pre-registration of RWE studies

Increasing transparency and reproducibility in RWE

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Pre-Registering Studies – What Is It, How Do You Do It, and Why?

- Pre-registration is the practice of deciding your research and analysis plan prior to starting your study and sharing it publicly, like submitting it to a registry.
- There are many reasons to pre-register studies
  - May prevent researchers from overfitting to their data (i.e. making analysis decisions that are too specific to a particular sample or study)
  - May prevent the use of questionable research practices, like p-hacking, cherry picking, or hypothesizing after results are known (sometimes called “HARKing”).
  - Increase the transparency and rigor of research and evaluation, which, in turn, may help to bolster public confidence

Pre-Registering Studies – What Is It, How Do You Do It, and Why?: https://www.acf.hhs.gov/opre/blog/2022/08/pre-registering-studies-what-it-how-do-you-do-it-and-why

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What about the regulators: EMA

- EMA has recently issued its final guideline on registry-based studies, which includes the following recommendations:
- For non-interventional PASS: Imposed studies initiated, managed or financed by an MAH shall be registered by the MAH in the EU PAS Register. Non-imposed studies required in the RMP or conducted voluntarily in the EU should also be registered in the EU PAS Register. Registration should include the study protocol and the study report
- For non-interventional PAES: Studies initiated, managed or financed by an MAH should be registered in the EU PAS Register, independently from whether they are imposed or not
- All non-interventional PASS/PAES initiated, managed or financed by other parties than an MAH should also be registered in the EU PAS Register together with their protocols and studies results when available.
- *"Making this information available will help increase transparency, reduce publication bias and support collaborations between centres and any other parties"*.

PASS: Post- Authorisation Safety Study; PAES: Post-Authorisation Efficacy Study; MAH; Marketing authorisation holder; RMP: Risk Management Plan

- https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-registry-based-studies_en-0.pdf

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What about the regulators: FDA

- FDA suggests to follow the published task force recommendations from the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and the International Society for Pharmacoepidemiology (ISPE) as good procedural practices for RWE treatment effectiveness studies, including transparency and reproducibility[1,2]
- To ensure transparency regarding their study design, sponsors should post their study protocols on a publicly available website, such as ClinicalTrials.gov or the web page for the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) for post-authorization studies[3]
- Updated guidance in August 2023 is more explicit – Sponsors should:
  - Describe in the study protocol, or as an appendix to the protocol, the data sources evaluated when designing the study, including results from feasibility evaluations or exploratory analyses of those data sources.
  - Provide a justification for selecting or excluding relevant data sources from the study.
  - Describe how the choice of the final data sources, study design elements, and analytic approaches aligns with the research question of interest and that the data sources, study design elements, and analytic approaches were not selected to favor particular study findings[3]
- The crux of this guidance is to maintain the reliability of RWD and data integrity from the point of origin through curation, transformation, and reporting of results.

1. Berger, M.J, Sox, H., Willke, R.J., Brixner, D.L., Hans-Georg, E., Goettsch, W., Madigan, D., Makady, A., Schneeweiss, S., Tarricone, R., Wang, S.V., Watkins, J., and Mullins, C.D. (2017). Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making, Pharmacoepidemiology and Drug Safety, 26(9):1033- 1039. doi:10.1002/pds.4297 **2.** Wang, S.V., Schneeweiss, S., Berger, M.L., Brown, J., de Vries, F., Douglas, I., Gagne, J.J., Gini, R., Klungel, O., Mullins, C.D., Nguyen, M.D., Rassen, J.A., Smeeth, L., and Sturkenboom, M. (2017). Reporting to Improve Reproducibility and Facilitate Validity Assessment in Healthcare Database Studies V1.0, Pharmacoepidemiology and Drug Safety, 26(9):1018-1032. doi:10.1002/pds.4295. **3.** Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products (fda.gov) : https://www.fda.gov/media/171667/download

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Transparency in RWE studies

- Real-World Evidence Transparency Initiative[1,2]
- Pre-registration of hypothesis-testing RWE studies in an open repository is becoming an important requirement
- EU-PAS, ClinicalTrials.gov and the new Real-World Evidence Registry (ISPOR, ISPE, NPC, and Duke Margolis)[3]

ISPOR Improving healthcare decisions

Duke MARGOLIS CENTER for Health Policy

National Pharmaceutical Council

ispe International Society for Pharmacoepidemiology

- 1. https://www.ispor.org/strategic-initiatives/real-world-evidence/real-world-evidence-transparency-initiative
- 2. Orsini, Lucinda S. et al. Improving Transparency to Build Trust in Real-World Secondary Data Studies for Hypothesis Testing—Why, What, and How: Recommendations and a Road Map from the Real-World Evidence Transparency Initiative Value in Health, Volume 23, Issue 9, 1128 – 1136
- 3. Real-World Evidence Registry - https://osf.io/registries/rwe/discover

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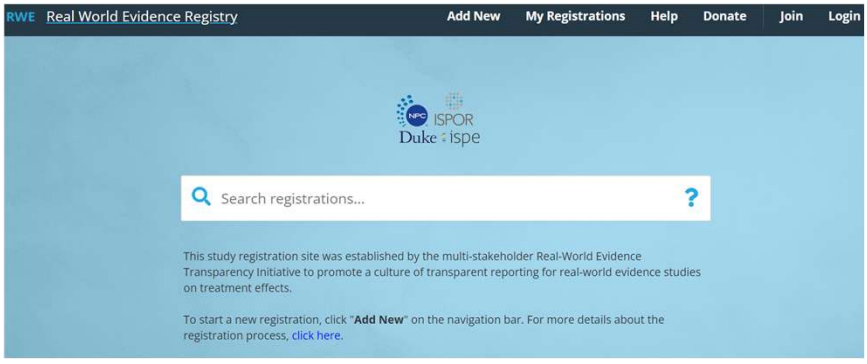
Real World Evidence Registry



Real-World Evidence Registry - https://osf.io/registries/rwe/discover

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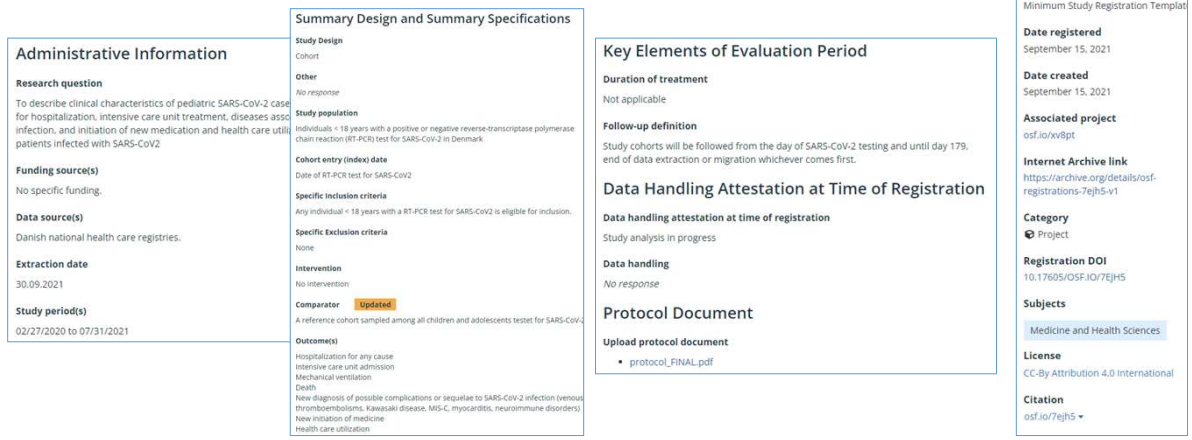
Real World Evidence Registry

- Comprehensive assessment of pediatric SARS-CoV-2 infection



Administrative Information

Research question
To describe clinical characteristics of pediatric SARS-CoV-2 case
for hospitalization, intensive care unit treatment, diseases assc
infection, and initiation of new medication and health care utili
patients infected with SARS-CoV2

Funding source(s)
No specific funding.

Data source(s)
Danish national health care registries.

Extraction date
30.09.2021

Study period(s)
02/27/2020 to 07/31/2021

Summary Design and Summary Specifications

Study Design
Cohort

Other
No response

Study population
Individuals < 18 years with a positive or negative reverse-transcriptase polymerase chain reaction (RT-PCR) test for SARS-CoV-2 in Denmark

Cohort entry (index) date
Date of RT-PCR test for SARS-CoV2

Specific Inclusion criteria
Any individual < 18 years with a RT-PCR test for SARS-CoV2 is eligible for inclusion.

Specific Exclusion criteria
None

Intervention
No intervention

Comparator Updated
A reference cohort sampled among all children and adolescents testet for SARS-CoV-

Outcome(s)
Hospitalization for any cause
Intensive care unit admission
Mechanical ventilation
Death
New diagnosis of possible complications or sequelae to SARS-CoV-2 infection (venous thromboembolisms, Kawasaki disease, MIS-C, myocarditis, neuroimmune disorders)
New initiation of medicine
Health care utilization

Key Elements of Evaluation Period

Duration of treatment
Not applicable

Follow-up definition
Study cohorts will be followed from the day of SARS-CoV-2 testing and until day 179, end of data extraction or migration whichever comes first.

Data Handling Attestation at Time of Registration

Data handling attestation at time of registration
Study analysis in progress

Data handling
No response

Protocol Document

Upload protocol document
- protocol_FINAL.pdf

Registration type
Real World Evidence Recommended Minimum Study Registration Templat

Date registered
September 15, 2021

Date created
September 15, 2021

Associated project
osf.io/xv8pt

Internet Archive link
https://archive.org/details/osf-registrations-7ejh5-v1

Category
Project

Registration DOI
10.17605/OSF.IO/7EJH5

Subjects
Medicine and Health Sciences

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Citation
osf.io/7ejh5

- Real-World Evidence Registry - https://doi.org/10.17605/OSF.IO/7EJH5

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EMA and HMA Launch Real-Word Data Catalogues

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EMA and HMA Launch Real-Word Data Catalogues

https://catalogues.ema.europa.eu/

Catalogue of RWD sources replaces the ENCePP Resources Database

Catalogue of RWD studies enhances the EU PAS Register®

- Freely available access via the catalogues webpage, hosted on EMA public website
- User-friendly platform for researchers, regulators, pharmaceutical companies, data source holders and general public
- Facilitation of search of data sources and studies related to medicines, ultimately supporting evidence-based decision-making

1. EMA-HMA Catalogues: https://www.ema.europa.eu/en/documents/presentation/presentation-multi-stakeholder-webinar-hma-ema-catalogues-real-world-data-sources-studies_en.pdf

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EMA and HMA Launch Real-Word Data Catalogues: Examples of use

A researcher would like to identify suitable data sources for a planned study	The catalogues provide information (metadata) on the data source content. It allows benchmarking of different data sources referring to similar population when planning a study.
A study protocol submitted uses a data source. The assessor needs to understand the suitability of the data source proposed	The study in question or other similar studies can be retrieved using the studies catalogue; the protocol is available. A comparison of data sources used in similar research is also possible.
An assessor reads a study report for which they need to evaluate the data source(s) used in the study	Other studies conducted using this particular data source can be consulted using the catalogues and provide orientation on the suitability of the data.

1. EMA-HMA Catalogues: https://www.ema.europa.eu/en/documents/presentation/presentation-multi-stakeholder-webinar-hma-ema-catalogues-real-world-data-sources-studies_en.pdf

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EMA and HMA Launch Real-Word Data Catalogues: Good Practice Guide

- The EMA and HMA have published the draft Good Practice Guide to guide the use of catalogues and description of data elements:

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

HMA
Heads of Medicines Agencies

1 September 2022
EMA/787647/2022
European Medicines Agency

To be updated soon!

Good Practice Guide for the use of the Metadata Catalogue of Real-World Data Sources
V 1.0

- 1. Good Practice Guidance: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/good-practice-guide-use-metadata-catalogue-real-world-data-sources_en.pdf

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Thank you!

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