Scottish Medicines Consortium (SMC) Position Statement on the Use of Real-World Evidence (RWE)

July 2025

Introduction

The Scottish Medicines Consortium (SMC) recognises the value and growing importance of Real-World Evidence (RWE) as part of the supporting evidence for the assessment of medicines. RWE, which is derived from Real-World Data (RWD), provides valuable insights into the effectiveness, safety and use of medicines in routine clinical practice.[1-4]

Randomised Controlled Trials (RCTs) remain the gold standard design to evaluate the efficacy of medicines. However, they are not always feasible due to ethical and time constraints, particularly in rare diseases, small populations or rapidly evolving therapeutic areas. In these circumstances, evidence may be based on open-label, single arm or non-randomised early phase I or II studies. RWE can complement and strengthen these data by providing additional, relevant evidence that helps to bridge evidence gaps and inform decision-making.[5] In addition, where robust RCT evidence is available, study populations may not fully represent local populations, in such cases RWE can add value by demonstrating generalisability of study results to NHSScotland.

This position statement outlines SMC's approach to the use of RWE in health technology assessment (HTA), emphasising the need for robust methodological standards, transparency and relevance. RWE provides further evidence and insights where evidence gaps exist or where clinical study data are limited or not feasible, thereby supporting the SMC Committees to carry out informed decision-making.

Definitions

RWD

RWD is data collected from everyday healthcare, outside of the highly controlled environment of clinical studies. This data can come from a variety of sources, such as patient medical records, electronic health records, patient registries, healthcare billing data and information reported by patients themselves. RWD is useful in understanding how treatments work in real-life settings and can provide insights into people's health and the care they receive.[1, 3, 6]

RWE

RWE is clinical evidence regarding the use, benefits and risks of medical interventions derived from the analysis of RWD. RWE provides additional insights into the performance of treatments in

broader, more diverse patient populations and real-world settings, particularly in circumstances where clinical study data are limited, unavailable or not feasible.[1, 3, 6, 7]

SMC's Position on the Use of RWE

SMC recognises the value of RWE as supplementary evidence to address evidence gaps in clinical study data, including RCTs, early phase or non-randomised, open-label studies or where real-world outcomes provide further understanding about a medicine's efficacy on the local NHSScotland population. SMC acknowledges the value of RWE to support the assessment of medicines in the following contexts:

When RCTs Are Not Feasible or Ethical

RWE is particularly valuable in situations where conducting RCTs is ethically challenging (for example, withholding potentially life-saving treatments) or logistically impractical, such as small patient populations.[2, 3, 5]

Rare Diseases

RWE can provide evidence to address evidence gaps for rare conditions, where it is often not possible to conduct large-scale RCTs because of limited patient populations. In these cases, RWE offers vital insights into the effectiveness and safety of treatments that may not be captured by conventional study designs.[2, 4, 5]

Long-Term Outcomes

RWE offers insights into the long-term safety and effectiveness of treatments, which may not be fully captured by clinical studies due to their limited duration. This is especially relevant for chronic conditions or treatments requiring ongoing management.[2, 4 5]

Integration with Other Evidence

RWE should not be viewed as a standalone solution; where robust RCT data is available, RWE can be integrated to provide a more comprehensive understanding of a treatment's impact. Where RCT data are limited, unfeasible or unavailable, RWE can offer important insights that inform decision-making.[2, 5, 8]

SMC's Methodological Requirements for the Use and Assessment of RWE

Data Source: The source of the data must be transparent. Information on the data's origin (for example, electronic health records, registries, claims databases) should be provided, including details about how the data was collected, how it was curated or processed, and by whom. The timelines during which the data was collected must also be provided, ensuring the data is up to date and reflects current medical practice. Governance and privacy compliance should be demonstrated.[1, 5, 6, 9]

Data Management: Details regarding the management of data must also be transparent, with clear documentation about who was responsible for collecting, curating and processing the data.

Detailed information should be provided about who owns and manages the data, ensuring that privacy and governance standards are adhered to it.[1, 6, 10]

Data Quality and Relevance: The data used should be high-quality and relevant to the research question. RWE should be representative of the target population and accurately reflect the real-world settings in which the intervention is being used. The data must be as complete, accurate, and consistent as possible, and any limitations in these areas should be disclosed.[1, 6, 10, 11]

Sample Size and Follow-Up: In RWE studies, sampling should be planned carefully to avoid selection bias. Use probability-based sampling methods where possible. Clear sampling criteria should be provided, addressing how the sample represents the target population, especially when using non-probability sampling. The dataset must include a sufficiently large sample size and an appropriate follow-up period to allow for robust assessment of the outcomes of interest. There should be a description of how the sample size and duration of follow-up relate to real-world treatment practices and patient characteristics. Any missing data must be addressed accordingly and sample size calculations should be included within the documentation.[9, 12]

Study Design and Conduct: RWE studies should employ appropriate designs (for example, cohort, case-control or cross-sectional). RWE studies should be conducted in line with best methodological practices for observational studies, with clear descriptions of inclusion and exclusion criteria and a transparent study protocol.[7, 9, 12, 13]

Outcome Relevance: Outcomes measured in RWE studies must be relevant to the research question and may include outcomes that are not typically assessed in conventional clinical studies . They should reflect real-world clinical effectiveness, long-term safety and patient-centred outcomes. All outcomes used in RWE studies, supporting HTA should be validated in both clinical and patient-reported settings. If surrogate outcomes are used, clearly explain how they relate to meaningful clinical outcomes.[4, 9, 10, 13]

Bias Minimisation: Efforts to minimise selection bias, confounding and information bias must be clearly documented. It is expected that statistical adjustments will be implemented for confounding factors and ensure standardisation in data collection. Techniques such as propensity score matching, inverse probability weighting and multivariate adjustments should be employed as appropriate to ensure the robustness of the findings.[3, 11, 12]

Analytical Methods: Statistical methods must be justified, and the choice of models should reflect the data structure and research question. Methods such as regression models, sensitivity analyses and appropriate confounding adjustments should be used to ensure the validity of the results.[3, 11, 14]

Reporting and Transparency: Comprehensive and transparent reporting of the study design, data sources and methodologies is essential.[4, 11, 14] Established reporting guidelines should be followed (for example, STROBE or RECORD).

Internal Validity Assessment: RWE studies should employ rigorous methods to ensure internal validity, minimising biases and confounding factors. Interventions and outcomes must be clearly

defined. In addition, when needed, there should be provision of detailed sensitivity analyses to demonstrate the robustness of any findings.[4, 14]

External Validity Assessment and Generalisability: The findings from RWE must be generalisable to the broader population and applicable to real-world clinical practice.[4, 15 16] There should be an explanation of how the study population compares to the target population in the healthcare system (that is, Scotland) and whether the results are generalisable. This includes a thorough examination of how the treatment practices, healthcare delivery systems and patient demographics in the study setting compare with those in Scotland. Any clinical and contextual differences that could influence the generalisability and applicability of the results to the NHSScotland patient population should be explicitly addressed.

Economic Evaluations and RWE: SMC acknowledges that RWE can also inform economic evaluations, including resource use, costs, and longer-term outcomes. Where RWE is included in submissions, companies should provide appropriate scenario and sensitivity analyses to explore uncertainties associated with RWD. These analyses should demonstrate how different assumptions might affect cost-effectiveness estimates and overall decision-making.

SMC Appraisal of RWE

SMC will appraise RWE and point out any limitations, considering the specific disease context, quality of the evidence and its potential to address unmet clinical and patients' needs. The inclusion of RWE in a submission will be assessed based on its ability to add insights to existing clinical evidence, bridge any evidence gaps and provide meaningful information on the use of the medicine in practice.

Conclusion

SMC is committed to ensuring that its assessment processes are informed by robust, transparent and relevant evidence. RWE, when used appropriately and in conjunction with other evidence, can enhance the understanding of a medicine's real-world effectiveness and safety. SMC encourages adherence to the methodological standards outlined in this position statement to ensure that assessments including RWE are of the highest quality and contribute to informed decision-making in the best interests of patients in NHSScotland.

References

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