Bridging Trials and Practice: Real-World Evidence in Diabetes from the REDDIE Project

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Summary

- RCTs offer high internal validity but limited real-world generalisability, while real-world data (RWD) from registries and digital health sources can complement evidence in diabetes care.
- REDDIE develops methods and standards—including fit-for-purpose data assessment, target trial emulation, and synthetic data—to strengthen the use of RWD for regulatory and HTA decision-making.
- By integrating RCTs, RWD, and patient perspectives, the REDDIE (Real-World Evidence for Decisions in Diabetes) project aims to improve the generation and application of real-world evidence to support better diabetes treatment decisions.

Introduction

Randomised controlled trials (RCTs) remain the cornerstone of evidence-based medicine. However, trial populations are typically highly selected and may not reflect the diversity, multimorbidity, and treatment patterns seen in routine clinical practice.

In diabetes, this gap is particularly relevant. Management is long-term, multifactorial, and increasingly supported by digital technologies and there is growing recognition RCT-derived evidence alone may not fully capture how therapies perform in real-world settings.

The increasing digitalisation of healthcare, through electronic health records, registries, and devices has enabled large volumes of real-world data (RWD). RWD offer an opportunity to complement RCTs by providing insights into effectiveness, safety, and use of therapies across broader populations.

The European Health Data Space is creating a regulatory and technical framework to enable secure, cross-border use of health data for both care and research. As access to large-scale, routinely collected data increases, the key challenge is no longer data availability but ensuring translation into reliable and actionable evidence.

Background and aims

REDDIE, brings together researchers, clinicians, regulators, and patient representatives (1). Its central aim is to develop methods, standards, and tools that enable RWD to complement RCTs in the evaluation of diabetes interventions.

The project focuses on supporting regulatory and health technology assessment (HTA) decision-making by improving how RWD are assessed, analysed, and interpreted. A key feature of REDDIE is the use of large-scale national registries from Sweden, Denmark, Germany, and England (2). By leveraging these complementary data sources, REDDIE aims to generate evidence that better reflects routine clinical practice.

Assessing Data Quality: Fit-for-Purpose Approaches

A fundamental challenge in using RWD is determining whether a dataset is suitable to answer a specific question. To address this, REDDIE has systematically identified and characterised over 600 diabetes-related databases across 58 countries (3), and developed a "fit-for-purpose" framework. A dataset may be adequate for one purpose (e.g. describing treatment patterns) but insufficient for another (e.g. estimating causal treatment effects). For clinicians and decision-makers, such tools are essential to build confidence in RWE.

From Real-World Data to Synthetic Cohorts and Simulated Trials

REDDIE is advancing methods to generate artificial datasets i.e. synthetic data that preserve the statistical properties of real-world populations without exposing individual-level information. REDDIE has demonstrated that synthetic datasets can reproduce key characteristics of clinical trial populations (4). In addition, simulation frameworks for in silico trials—computer-based experiments that mimic clinical studies, are being developed. These approaches do not replace empirical evidence but offer valuable tools to explore scenarios that are difficult to study, such as long-term outcomes or rare events.

Emulation of target trials using real-world data

A central objective of REDDIE is to compare findings from RCTs with those derived from RWD using target trial emulation. This approach replicates the design of a hypothetical randomised trial using observational data. Studies evaluating sodium–glucose cotransporter-2 inhibitors (SGLT2i) in people with type 2 diabetes and cardiovascular disease have shown reductions in cardiovascular events consistent with RCT findings (5). Interestingly, the absolute risk reductions observed in routine clinical practice appeared larger than those reported in trials, likely due to higher baseline risk in real-world populations. Similarly, glucagon-like peptide-1 receptor agonists (GLP-1RA) compared with dipeptidyl peptidase-4 inhibitors demonstrated benefits in cardiovascular outcomes, all-cause mortality and glycaemic control (5,6). This highlight both the

potential and the challenges of RWE; results can reinforce trial evidence, differences in effect size and population characteristics underscore the importance of careful interpretation.

Patient Involvement and Trust in Data Use

The increasing use of health data raises important questions about trust, governance, and patient involvement. REDDIE addresses this through an active Patient Advisory Committee (PAC), which brings together individuals living with type 1 and type 2 diabetes from across Europe.

The PAC contributes to discussions on how data is collected, accessed, and used, ensuring embedded patient perspectives throughout the project. Such involvement is essential. Without patient trust and engagement, the full potential of RWD cannot be realized.

From Data to Impact

REDDIE illustrates both the promise and the complexity of using RWD in diabetes. While large datasets and advanced analytical methods offer new opportunities, they also raise important questions about data quality, bias, and interpretability. Importantly, RWE should be viewed as a complementary source of evidence, not a replacement for RCTs. Together, these approaches can provide a more complete understanding of treatment effects combining the internal validity of trials with the external relevance of real-world practice.

For clinicians, this means that future evidence may better reflect the patients they see in daily practice. For regulators and payers, it offers the potential for more adaptive and context-sensitive decision-making.

As diabetes care becomes increasingly data-driven, the ability to generate and interpret real-world evidence will be critical. REDDIE represents a crucial step towards building the methodological and conceptual foundations needed to achieve this.

By combining large-scale registry data, advanced analytics, and meaningful patient involvement, the project aims to bridge the gap between clinical trials and real-world practice. In doing so, it contributes to a broader shift in evidence generation and use, with the goal of improving outcomes for people living with diabetes.

References

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