NICE National Institute for Health and Care Excellence

EHDEN EUROPEAN HEALTH DATA & EVIDENCE NETWORK

OHDSI

RWD24

Including real-world evidence from a federated data network in a network meta-analysis of COVID-19 treatment effects

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Background

The National Institute for Health and Care Excellence (NICE) participates in international research projects, such as the European Health Data and Evidence Network (EHDEN), to collaborate on developing innovative methods and new ways of working. This supports our transformation plan to focus on what matters most, create advice that is useful and useable, and learn from data and implementation. EHDEN is a federated network of European partners, with real-world data standardised to the Observational Medical Outcomes Partnership Common Data Model (OMOP CDM). We demonstrate how EHDEN can be used to generate real-world evidence (RWE) in the context of COVID-19 and highlight how RWE may generate questions on how to interpret it when it conflicts with randomised controlled trial (RCT) data.

What we did and why

Health technology assessment (HTA) is a systematic approach to assessing the clinical and economic benefits of healthcare technologies. It has been widely adopted across Europe to inform access to healthcare that is effective and efficient. In general, HTA relies heavily on randomised controlled trials, but often critical gaps and uncertainties remain.

The COVID-19 pandemic highlighted the need for timely healthcare decisions. While randomized trials provide valuable insights, the fast-moving context demanded quicker answers. RWE can potentially fill this gap. With numerous COVID-19 treatments emerging and some entering clinical practice without HTA, RWE offers a way to assess their comparative effectiveness.

Evidence on the effectiveness of remdesivir and tocilizumab in people aged 18 years or older hospitalized with COVID-19 was collected from:

1. RCT data collected from a systematic literature review

2. RWE from a historical cohort study run using Institut Municipal Assistència Sanitària Information System (IMASIS, Spain) data.

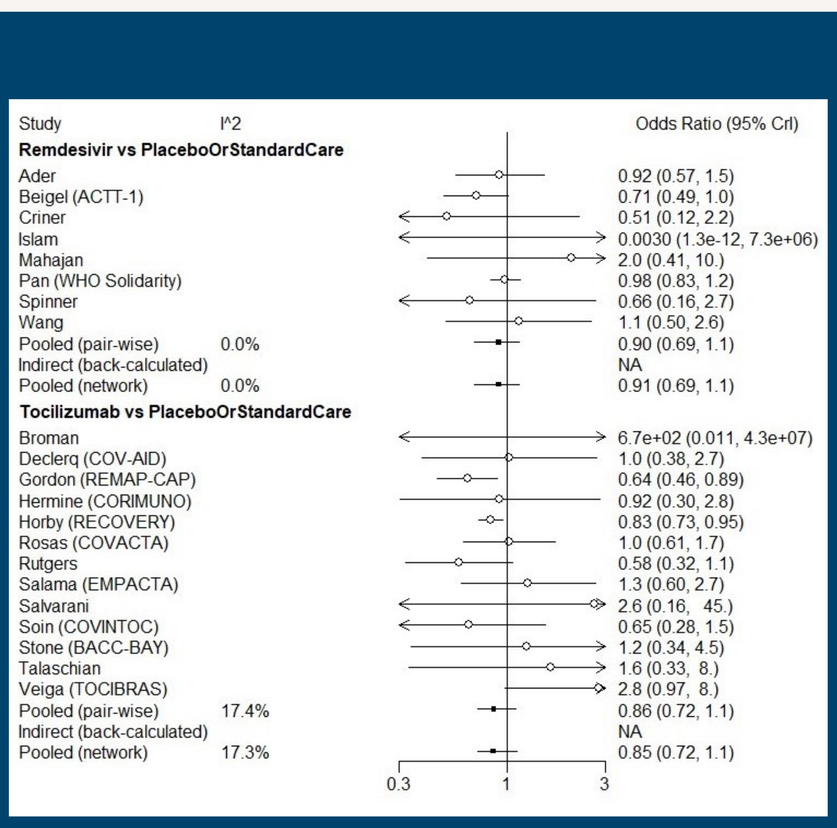
RCT data was synthesized in a Bayesian network meta-analysis (NMA). RWD were analysed using propensity score matching, logistic regression and cox proportional hazards.

Outcomes and next steps

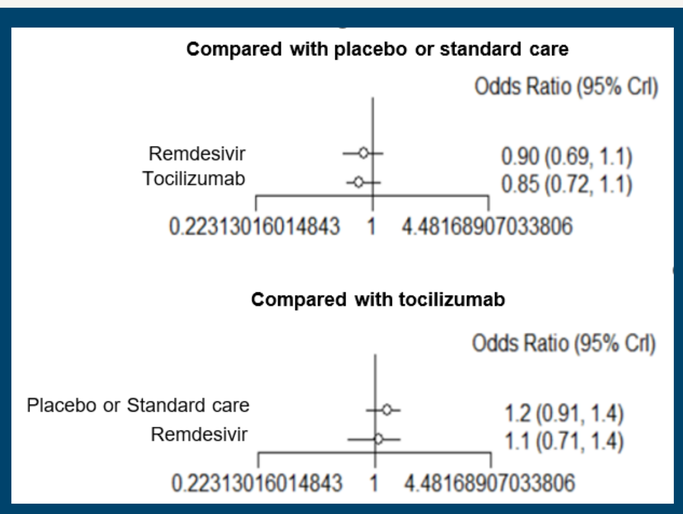
The RCT data (n = 15,246) did not show an effect on all-cause mortality for remdesivir vs tocilizumab (odds ratio: 1.10, 95% confidence interval 0.71-1.40). RWE evidence (n = 475) showed lower odds of mortality for people treated with remdesivir compared with those treated with tocilizumab (adjusted odds ratio: 0.39, 95% confidence interval 0.20-0.67 , P value 0.002).

Federated data networks like EHDEN can be used to generate RWE. However, with the data analysed thus far, the RWE results are not consistent with RCT data. This difference may be attributable to remdesivir and tocilizumab being given at different stages of the disease course in people hospitalized with severe COVID-19. Caution should also be taken when interpreting the results from the non-randomised study due to the relatively small sample size. How HTA and regulatory bodies make decisions when presented with conflicting RCT and RWE evidence warrants special consideration.

Future work will focus on the recruitment of more hospitals to produce a larger sample of non-randomised evidence. We are currently working with EHDEN data partners from Hospital Universitario 12 de Octubre, Spain; Ben-Gurion University of the Negev, Israel; and Unidade Local de Saúde de Matosinhos, Portugal. We then aim to combine these results in an NMA with the RCT evidence using an ISPE endorsed framework. This study demonstrates the feasibility of collecting RWE using the EHDEN network and synthesizing this observational evidence with randomised evidence.



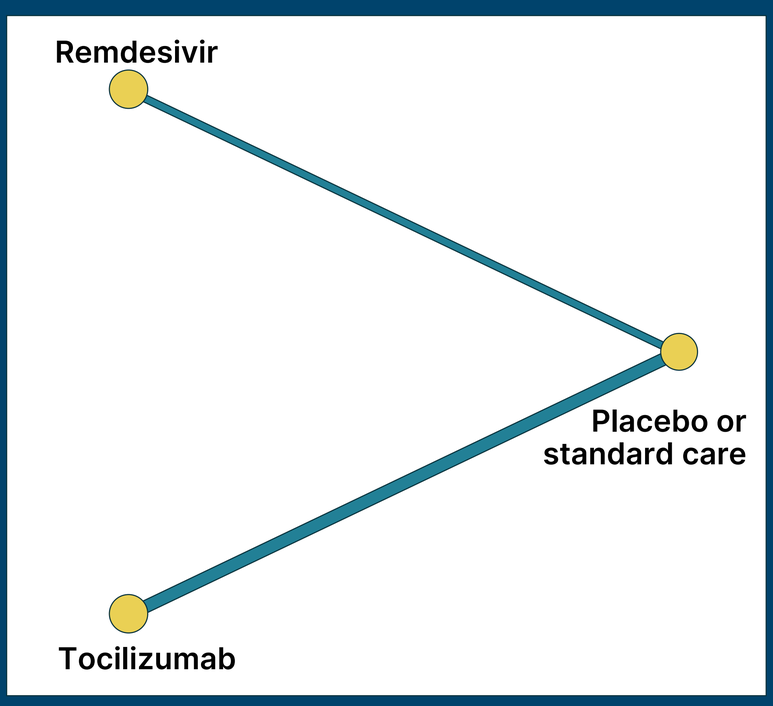
Meta-analysis of RCTs



NMA results of RCTs

Remdesivir vs Tocilizumab	Odds ratio (95% Confidence interval)	P-value
30-day all-cause mortality (unadjusted)	0.38 (0.20 to 0.69)	0.002
30-day all-cause mortality (adjusted)	0.39 (0.20 to 0.67)	0.002

Non-randomised results



Network plot

Reference

[1]Sarri G, *et al.* "Framework for the synthesis of non-randomised studies and randomised controlled trials: a guidance on conducting a systematic review and meta-analysis for healthcare decision making." BMJ Evidence-Based Medicine 27.2 (2022): 109-119.

EHDEN Academy

To learn more about EHDEN and the basics of HTA, consider signing up to the EHDEN academy. A free learning resource for anyone interested in RWE.

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imi innovative medicines initiative efpia

The European Health Data & Evidence Network has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 806968. The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.