Demonstrating the application of real-world evidence for health technology assessment using a federated data network

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Background

The European Health Data and Evidence Network (EHDEN.eu) is a rapidly developing large-scale federated network of real-world data from across Europe, standardised to the Observational Medical Outcomes Partnership Common Data Model (OMOP CDM). We demonstrate how EHDEN, and its associated analytical tools, can facilitate the generation of real-world evidence (RWE) to directly inform health technology assessment (HTA) in the context of cancer and COVID-19 use cases.

Natural history and real-world survival extrapolations in cancer

The problem: When assessing treatments for cancer, extrapolation techniques are used to estimate overall survival in treated and control groups beyond observed trial data[1]. This is important to inform economic evaluations used for HTA, which assess cost effectiveness over an appropriate time horizon—usually a lifetime. However, this is often a key source of decision uncertainty because it involves forecasting the future based on shorter-term observed data.

RWE can help to address this uncertainty. Country-specific, real-world survival data for patients receiving the current standard of care could be used to validate trial-based survival extrapolations typically used in HTA. Additionally, they could directly inform baseline outcomes where a treatment only has a single-arm trial.

Using data from Clinical Practice Research Datalink (CPRD) first, we are developing a user-friendly dashboard as a "proof of concept" tool allowing HTA agencies and researchers to quickly view natural history data for selected cancers and examine long-term survival projections using different parametric survival functions.

The dashboard will allow the visual fit, statistical fit and underlying hazards associated with alternative parametric functions to be compared.

Comparative effectiveness of treatments for COVID-19

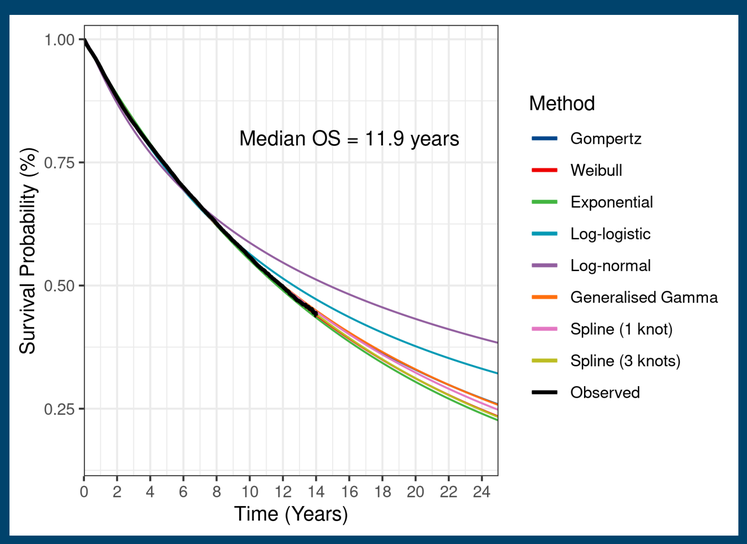
The problem: HTA relies heavily on randomised controlled trials, but often critical gaps and uncertainties remain. Randomised trials of COVID-19 treatments have been combined in several "living" network meta-analyses[2,3], however some treatments have entered clinical practice without undergoing HTA. HTA agencies will need to assess the comparative effectiveness of these treatments, and there is likely to be a wealth of RWE to facilitate this.

Using data from the EHDEN network, we aim to perform a multinational, multi-database network comparative cohort study, focusing on (1) medicines to treat COVID-19 and (2) anticoagulants used in people with COVID-19, both in the hospital setting. Specific treatments identified to compare effectiveness and safety are:

1. Tocilizumab, baricitinib & remdesivir
2. Aspirin & heparin

Study results will be summarised together with existing randomised evidence in a network meta-analysis (NMA). Sensitivity analyses will be conducted to assess the extent to which real-world outcomes from the treatments studied differs from estimates of efficacy from clinical trials.

Prostate cancer survival outputs from the EHDEN Cancer Data Dashboard

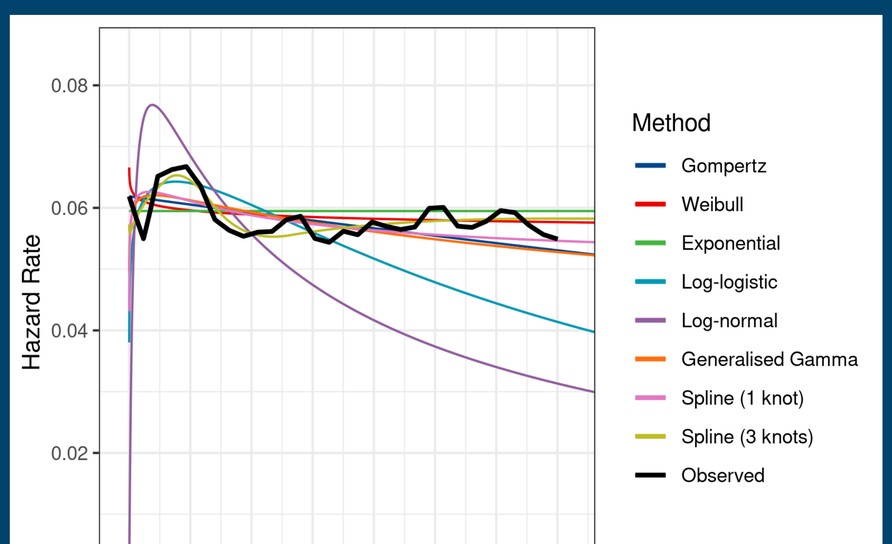


0	2	4	6	8	10	12	14
95855	65863	44771	29243	17735	9353	3835	58

Extrapolated survival curves

Method	AIC	BIC
Spline (3 knots)	196482.5	196529.9
Spline (1 knot)	196521.7	196550.1
Generalised Gamma	196526.9	196555.3
Gompertz	196536.9	196555.9
Weibull	196552.2	196571.2
Exponential	196560.8	196570.3
Log-logistic	196621.0	196639.9
Log-normal	197892.0	197910.9

Goodness of fit



Smoothed hazard plots

Conclusion

Federated data networks like EHDEN could provide evidence-based healthcare decision makers with invaluable, rapid access to relevant RWE. Our use cases demonstrate how the network can be used to quickly generate useful evidence. Additionally, our outputs will provide valuable tools to directly inform evidence gaps and reduce uncertainty in cancer and COVID-19 assessments.

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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References

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