

R in HEOR modelling for HTA submissions: An assessment

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>>> Executive Summary

This paper, published in September 2024, discusses the growing importance of R programming language in Health Economics and Outcomes Research (HEOR) modelling, particularly for Health Technology Assessment (HTA) submissions. The authors, representing Parexel, a global CRO that offers HEOR modelling expertise as part of its Access Consulting services, highlight the advantages of using R over traditional tools like MS Excel or TreeAge. They emphasise R's ability to enhance transparency, simplify bug tracking, and enable more complex model structures.

The paper outlines how R can be integrated throughout the entire model development process, from initial decision-making to final reporting. It mentions various R packages specifically designed for HEOR, such as heemod and darthpack, as well as general-purpose packages that support documentation, testing, and reporting. The authors also note using version control systems and AI tools to optimise the modelling process further.

The adoption of R by HTA agencies is discussed, focusing on NICE (UK) and ZIN (Netherlands). While these agencies are beginning to accept R-based models, the authors acknowledge that widespread adoption is still limited. They highlight NICE's pilot program using R for a reusable reference model in advanced renal cell carcinoma, demonstrating the potential for R to improve consistency and efficiency in HTA decision-making.

The paper concludes by emphasising R's readiness to become the primary tool for health economics modelling. It notes that R's versatility and large community support make it well-positioned to adapt to future changes in the HTA landscape, such as increased use of AI and potential shifts towards generalised cost-effectiveness modelling. The authors call for stakeholder collaboration to integrate R into the HEOR field fully. They also offer you Parexel's expertise in developing R-based health economic models across various therapeutic areas.

HEOR (Health Economics and Outcomes Research) modelling consulting involves creating health economic models for HTA (Health Technology Assessment) submissions on behalf of pharmaceutical and medical device companies. Our goal at Parexel, a global CRO that offers HEOR modelling expertise as part of its Access Consulting services, is, therefore, to bridge the best of these different worlds, ensuring excellent client outcomes:

1. To learn from state-of-the-art academic modelling techniques and expand and scale them, giving them practical meaning and applications.
2. To get the most out of the client's data (including RWD) and fully exploit this data's value for patients (we are also helping our clients generate the right data at the right time; more on this in a following piece on early modelling), we create models that more readily adapt to newly available data and different HTA bodies/countries.
3. To navigate the ever-changing and evolving HTA landscape, making the most of current guidelines and their applications (with our multiple applications in various HTA agencies and various TAs (Technology Appraisals)) but also anticipating changes ahead (including JCA and IRA regulation, increased use of AI (Artificial Intelligence), potential move towards Generalized Cost-Effectiveness Modelling)

R is a powerful and versatile programming language that brings [many benefits](#) compared to the *de facto* submission standard, MS Excel (or previous proprietary software like TreeAge or Decision Programming Language). In R, analyses are easy to follow: the scripting nature of R makes it easy to understand the successive modelling steps (no jumps between several dozen sheets to understand one formula, for instance). This enhances transparency, especially when modellers use comments liberally. In R, bugs are easy to spot, track and correct. R has a much greater computational facility than MS Excel, allowing more complex model structures (and consequently closer to reality) to be implemented more efficiently—for example, microsimulations and more advanced probabilistic sensitivity analysis. R-based models can be launched through web applications, such as R-Shiny, which can be easier to use and update than an Excel-based model. R also benefits from many packages (“extensions”) that simplify or amplify its capabilities in code analysis, health economics, data and statistical analyses, graphical representation, reporting, quality assurance, etc.

The table below summarises the advantages and disadvantages of using R for HEOR Modelling (based on literature and our experience).

Use of R for HEOR Modelling	
Advantages	Disadvantages
Transparency (code and data, no complex maze of formulae)	Unfamiliarity (coding)
User-accessibility can be improved with packages like Shiny, offering a user-friendly web interface to more complex models	Accessibility (not yet considered default software by IT infrastructure)
Built-in statistical analysis capabilities to appropriately quantify decision uncertainty in expected treatment benefit estimates with limited data	
Robust ecosystem of extensions (“packages”) to solve HEOR modelling needs	
Integration in data analytics upstream (clinical trial, survival analyses e.g.) and downstream (RWD analyses, managed-entry agreement modelling, etc.)	
Speed of analysis (and possibility to fully utilise multi-threaded and/or cluster environments)	
	Currently small (but growing) acceptance by HTA bodies for reimbursement submissions
Creation of reproducible, reusable and adaptable models	

This paper will first show to what extent R now accompanies our health economics model development from start to finish. It will then give an update about adopting R in HTA agencies. This paper’s main conclusion is that since R is now more than ready to tackle health economics modelling projects, its widespread adoption will necessitate collaboration from all stakeholders. This collective effort is crucial for successfully integrating R into the HEOR landscape.

>>> R for Health Economics Model development

R's potential as the next modelling standard is evident. Some first publications date back nearly a decade ago; [the first HEOR-focused packages were published in 2017](#), and several health economics academic groups and consultancy firms remain heavily involved in developing and using R for modelling. This trend is not new and not isolated in the pharmaceutical world, where R is also gaining traction in clinical trial analysis and submission with a robust open-source movement.

When mapping a typical model development activities timeline (Figure 1), R can be brought in when decisions about the model type are considered. This is dictating the future development “from scratch” or using HEOR-oriented packages like heemod, darthpack, BCEA, hesim, etc. Each package was developed with a precise goal or a specific modelling technique in mind. Their development rhythm may vary, but they can be considered mature. They can also be extended beyond their initial modelling coverage. Alternatively, models can be developed “from scratch” in R using data frames for Markov traces or solving differential equations for dynamic models. In addition, regardless of the use of packages, Parexel continues to develop its own model templates and good modelling practices to increase efficiency, reproducibility, transparency, and quality. From that perspective, more recently, the [package assertHE](#) started helps us review models' structure and our QC/QA process.

R accompanies model development from start to finish

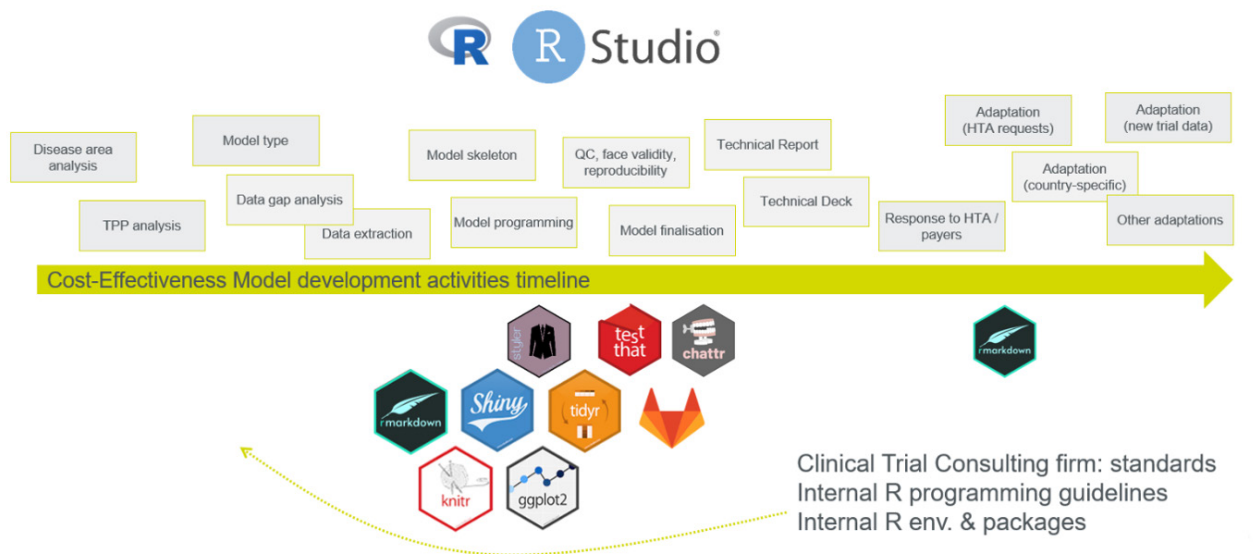


Figure 1. Cost-Effectiveness Model development activities and R impact

A group of non-HEOR packages also supports our model development. For instance, roxygen2, testthat, and styler help document the code, unit test and maintain a cohesive style, respectively. R Markdown and the more recent development with Quarto help us efficiently automate reporting to a wide range of documents (protocol, technical report, slides, ...) with the possibility to adopt our clients' report templates easily.

R-agnostic modelling practices, such as using version control (Git), are also widely beneficial. AI, represented by our own internal Large Language Model, ParexelGPT (currently based on Claude 3.5 Sonnet, ensuring client and patient data is not comingled with other data in less secure servers), is now part of R development to support new modellers in R or to further optimise our code, for instance.

Finally, R Studio, an integrated development environment, is the hub that centralises all of this. It allows for simpler code organisation and supports the integration of all packages and tools.

This abundance of packages and tools and the necessity of learning each one can be daunting for new modellers, especially when their modelling curriculum is focused on using MS Excel during their Master's.

»»» Updates on the HTA adoptions of R

In developing and implementing patient access and HTA strategies, the sponsor is widely expected to seek to launch and gain favourable access/ payment in many countries. Therefore, our modelling work must anticipate both adaptations and the different levels of technical proficiency of HTA agencies worldwide. If NICE (National Institute for Health and Care Excellence for England & Wales), ZIN (Zorginstituut Nederland), and others start to openly accept R-based models in their guidelines, most agencies around the world remain uncertain about their acceptance or just do not accept them.

For a few years, [NICE process and methods guidance](#) for health technology evaluations “accepts fully executable economic models using standard software.” But not *any* software: NICE immediately specifies it will accept “Excel, DATA/Treeage, R or WinBUGs.” Although capturing the proportion of these four software packages used in models submitted to NICE is difficult, it is safe to assume that only a small proportion of submissions use R at the current time.

This may change as, in parallel, NICE is developing [a new proportionate approach](#) to technology appraisals. This should allow NICE to speed up technology appraisals and increase capacity to accommodate a larger volume of applications and more complex treatments. As part of a pilot with PenTAG at the University of Exeter, NICE built a reusable reference model for advanced renal cell carcinoma in R. This pilot model will assess ways to reduce repetition and improve consistency in NICE decision-making. R was chosen for its ability to handle extensive computation requirements and the possibility of version control (via Github). [In a paper](#), Lee, Burns and Wilson explained some of their hurdles and successes with R. These pilot programs show the commitment of HTA agencies to explore innovative solutions where R takes centre stage.

On its side, ZIN has been consulting with other organisations since 2021 to pilot model submission in R (but technically would accept other programming languages). [ZIN guidelines](#) are prescriptive, describing everything from general principles to folder structure, coding conventions, allowed packages (and versions), etc. Fortunately, those guidelines mostly follow broader R programming conventions (like the Tidyverse style guide or the DARTH coding framework), minimising rework specifically for submissions to ZIN – or setting the standard for other HTA submissions with less stringent guidelines.

As we submit to and discuss with HTA agencies worldwide, we discover more and more agencies open to considering R models. Still, broader official adoption of R models by HTA agencies is necessary to make departing from Excel an attractive proposition for pharmaceutical companies.

»»» Conclusion

For HEOR Modelling, as for various statistical and analytical tasks for years now, R has become an essential tool to create health economic models at Parexel. By leveraging an array of packages and good programming practices and tools, R and its HEOR ecosystem have shown that it is ready to take centre stage in health economics modelling. Major HTA agencies have taken considerable steps to build highly complex pilots and test new modelling guidelines. As a versatile programming language supported by a large community, R is also ready to anticipate changes ahead (JCA and IRA regulation, increased use of AI, potential move towards Generalized Cost-Effectiveness Modelling, etc.). We look forward to a steady increase in models and submissions and an overall increased programming literacy to successfully integrate R into the HEOR landscape.

With Heart™

>>> We're always available for a conversation

[Connect with us](#) for more information or to discuss your next modelling project.

With a team of experienced modellers in R (also MS-Excel) and several therapeutic areas (oncology, neurology, infectious diseases, etc.), Parexel's HEOR modelling team is ready to accompany you to develop your next health economic models successfully, be it a cost-effectiveness or a budget impact model (or other, less common types of simulations). The modelling team is surrounded by competent teams specialising in literature review, value communication, dossier creation and other advanced analytics topics.

This paper was elaborated on from a talk by Jep and discussions at R-HTA. *The authors are indebted to the R-HTA community for the vibrant discussions.*

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