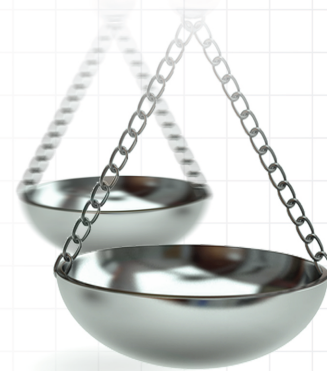




RWE ready for reimbursement? A round up of developments in real-world evidence relating to HTA: part 3

Journal of **Comparative Effectiveness Research**

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In this round up, we discuss a number of recent publications that have utilized real-world evidence to explore the value that innovative treatments have brought to patients.

First draft submitted: 23 July 2021; Accepted for publication: 11 August 2021; Published online: 20 August 2021

Keywords: health technology assessment • HTA • innovation • oncology • patient access • real-world evidence • reimbursement • RWE

The value of innovation: seeing the wood from the trees

The past decade has been characterized by the increasing availability of innovative treatments, particularly in oncology. The desire to avoid delays in providing patients with access to these treatments given the significant unmet need has led to their marketing approval and reimbursement with perhaps more limited data regarding their benefits than would traditionally have been required. As such, these products have entered use with outstanding questions regarding their benefits to patients and health systems. In order to address this, these treatments have sometimes been re-evaluated after a period of time, with real-world evidence occasionally playing a role in such reassessments. Reassessments which fail to confirm the initial perceived value of a specific treatment often stimulate debate around the appropriateness of allowing patient access to these treatments. However, in considering the benefit of expediting patient access, it is important not to solely focus on specific cases and to maintain some focus on the extent to which access to a host of innovative treatments have provided benefits to patient populations and health systems as a whole. In this regard, a number of recent papers have utilized real-world data (RWD) to provide interesting insights into the population level benefits and value of treatment innovation in oncology.

First, in an analysis published last year, lung cancer survival was explored using data from Surveillance, Epidemiology and End Results – the USA's National Cancer Institute cancer surveillance program [1]. This demonstrated that mortality in non-small-cell lung cancer (NSCLC) had decreased more rapidly than the incidence of the condition and that improvements in survival had occurred shortly following the introduction of innovative treatments for this indication. Interestingly, this study also reported relatively stable survival over time in small-cell lung cancer, a condition in which little treatment innovation had been observed over the period in question. Given that certain other time-based confounders would be common to both analyses, the small-cell lung cancer data provides somewhat of a negative control, supporting the indirect link the authors draw between treatment innovation and survival improvements.

Additionally, Snee *et al.* [2] reported data from a UK perspective on the impact of innovative treatments in NSCLC. Their data, from a large NHS university teaching hospital, demonstrated improvement in median and 1 year survival among NSCLC patients treated with systemic anticancer therapies in the 2013–2017 period compared with 2007–2012. Notably the use of checkpoint inhibitors and later generation tyrosine kinase inhibitors in both first-line and second-line settings had been observed to increase in the later period.

Finally, a study published very recently by Grinda *et al.* [3] utilized data from Epidemio-Strategy-Medico-Economical, a French nationwide observational cohort, to provide a similar perspective in metastatic breast cancer (MBC). They demonstrated that survival in MBC patients had improved over a 12-year period beginning in 2008, primarily driven by improvements in the HER2+ subgroup of patients and that the use of anti-HER2 therapies had

increased substantially over the same period. Notably, the MBC subgroups in which survival was not observed to increase (triple-negative MBC, HR+/HER2- MBC) again provided a negative control of sorts, as use of innovative treatments in these groups did not increase greatly over time.

While these studies focused on the population level clinical benefit of innovation, a recent Belgian study [4] utilized RWD to provide both a clinical and economic perspective. This extensive study, carried out by Belgian Healthcare Knowledge Centre, at the request of the National Institute for Health and Disability Insurance, linked RWD from the Belgian Cancer Registry with survival data, drug utilization and costing data from two other Belgian RWD sources. Researchers investigated the relationship between improvements in survival in 12 oncology indications between 2004 and 2017, and increases in the costs of treating patients with these indications over the same period. The study found that in NSCLC improvements in survival were observed to occur at the same time as significant increases in spending on innovative drugs; however, in many other indications, including breast cancer, major improvements in survival had not been observed despite substantial increases in spending on innovative drugs over the same period. While this analysis raises questions regarding the overall value of innovative treatments in oncology, the authors acknowledge that the broad perspective of the analysis is not well aligned with the targeted nature of some innovative treatments and may, therefore, have underestimated the clinical benefits innovative treatments have brought in certain indications. Furthermore, this study also did not consider the humanistic value that innovation can bring to families as a whole. Such innovations, which can result in extra months or years of increased life for many hundreds of thousands of patients can have tremendous importance for families as they are gifted extra treasured time with their loved ones. In an age where economies have been shut down at the expense of saving lives – this population level humanistic value should not be ignored. It is also pertinent to stress the importance of having high quality, complete data with good population coverage when making these sorts of assessments. Lack of major improvements in survival despite the introduction of innovative treatments could be explained by the lack of granularity in the data to undertake a detailed assessment. In this regard, we can see from the results of Grinda *et al.* that innovations in breast cancer treatment and improvements in survival were isolated to HER2+ breast cancer [3], the Belgian team's focus on stage IV breast cancer as a whole may, therefore, have masked important subgroup effects.

The findings of the studies above must of course be considered in the context of their observational nature and as such alternative explanations for the improvements in survival over time may exist. However, the studies do suggest that real world data can support Health Technology Assessment policy makers in discerning the proverbial wood from the trees when considering the value of innovative treatments, and as such can aid them in considering whether the clinical and economic risks associated with expediting patient access to treatments are worthwhile. In light of this, we expect to see further, more nuanced real-world analyses of this nature emerge in the future.

Financial & competing interests disclosure

SV Ramagopalan has received an honorarium from Future Science Group for the contribution of this work. A Simpson and SV Ramagopalan are employees of F Hoffmann-La Roche. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

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