Value in cancer drug spending: assessing the clinical risks and benefits from a decade's worth of innovation

by Sebastian Salas-Vega and Elias Mossialos

There are growing questions about the value from spending on what seem like ever-more expensive cancer medicines. Rising expenditures may make it difficult for patients to access or remain compliant with life-extending therapies. Yet, some have argued that high prices may be justified if new and innovative treatments offer significant clinical benefits. Even as studies point to gains in overall survival from innovative cancer medicines, efforts to examine the value from related expenditures remain stymied by a dearth of systematic evidence on their clinical risks and benefits. This lack of evidence makes it difficult to demand more from innovation, and, where costs factor into the decision-making process, for clinicians and patients to balance preferences for the expected impact from treatment against rising drug costs.

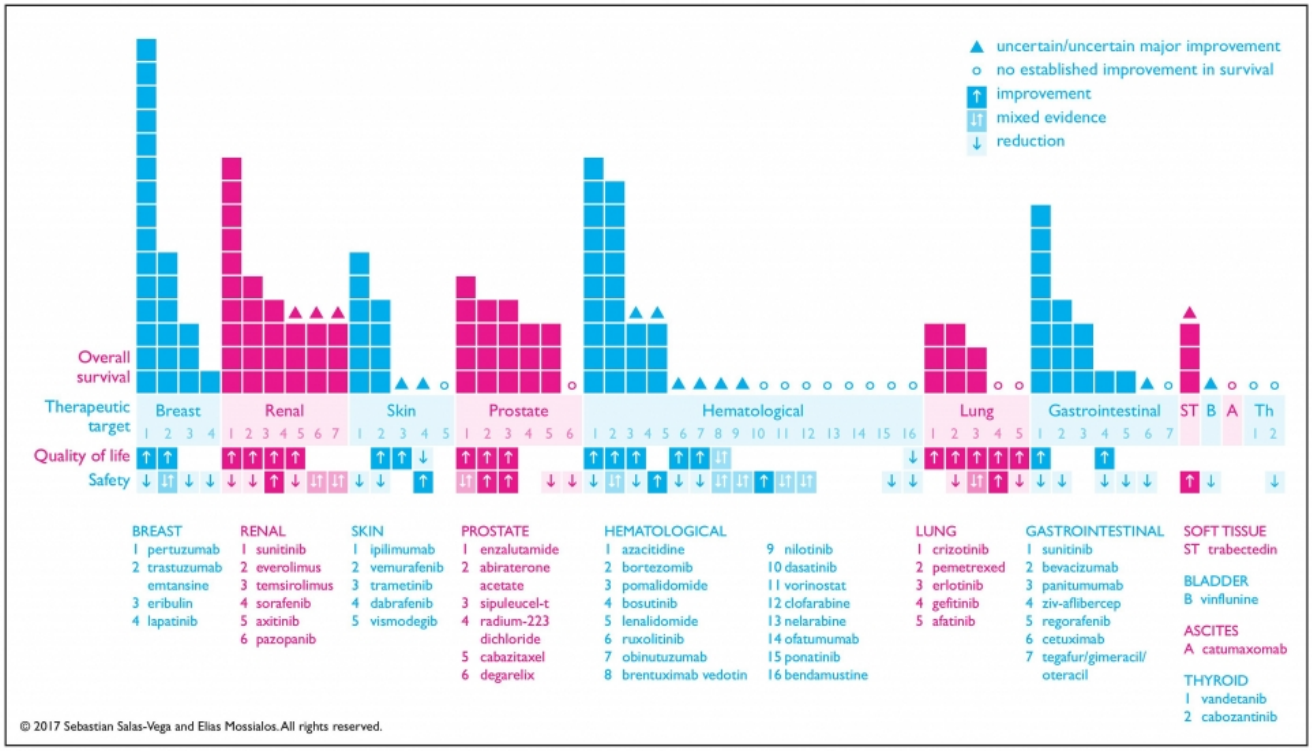
To shed light on the clinical risks and benefits from new cancer medicines, we took a narrative synthesis approach to review regulatory assessments of the impact on overall survival, quality of life, and safety from all cancer medicines newly licensed in the US and EU between 2003-2013. For this, two researchers evaluated appraisals from English (National Institute of Health and Care Excellence, NICE), French (*Haute Autorité de Santé*, HAS) and Australian (Pharmaceutical Benefits Advisory Committee, PBAC) health technology assessment (HTA) agencies that were published through May 2015.

We find that while most new cancer drugs approved between 2003 and 2013 extended overall survival or improved the quality of life of cancer patients, their clinical benefits vary widely. Improvements in overall survival and quality of life also often come at the cost of safety, and there are reasons to question whether claims of clinical benefits have been matched by those observed in real-world settings.

Overall survival, quality of life, and safety benefits

Of 53 new cancer drugs analysed, researchers found no known improvement in overall survival from new medicines for thyroid cancers and malignant ascites from 2003 to 2013, but an average improvement of 8.48 months for breast cancers over this period. The average improvement in overall survival for people with lung, haematological, gastrointestinal, prostate, skin, and renal cancers equalled 2.09, 2.61, 2.90, 3.17, 4.65, and 6.27 months, respectively. Within indications as well, there was often a wide range in the overall survival benefits associated with new medicines. On average, all newly licensed cancer drugs extended overall survival by 3.43 months over the past decade (Figure 1).

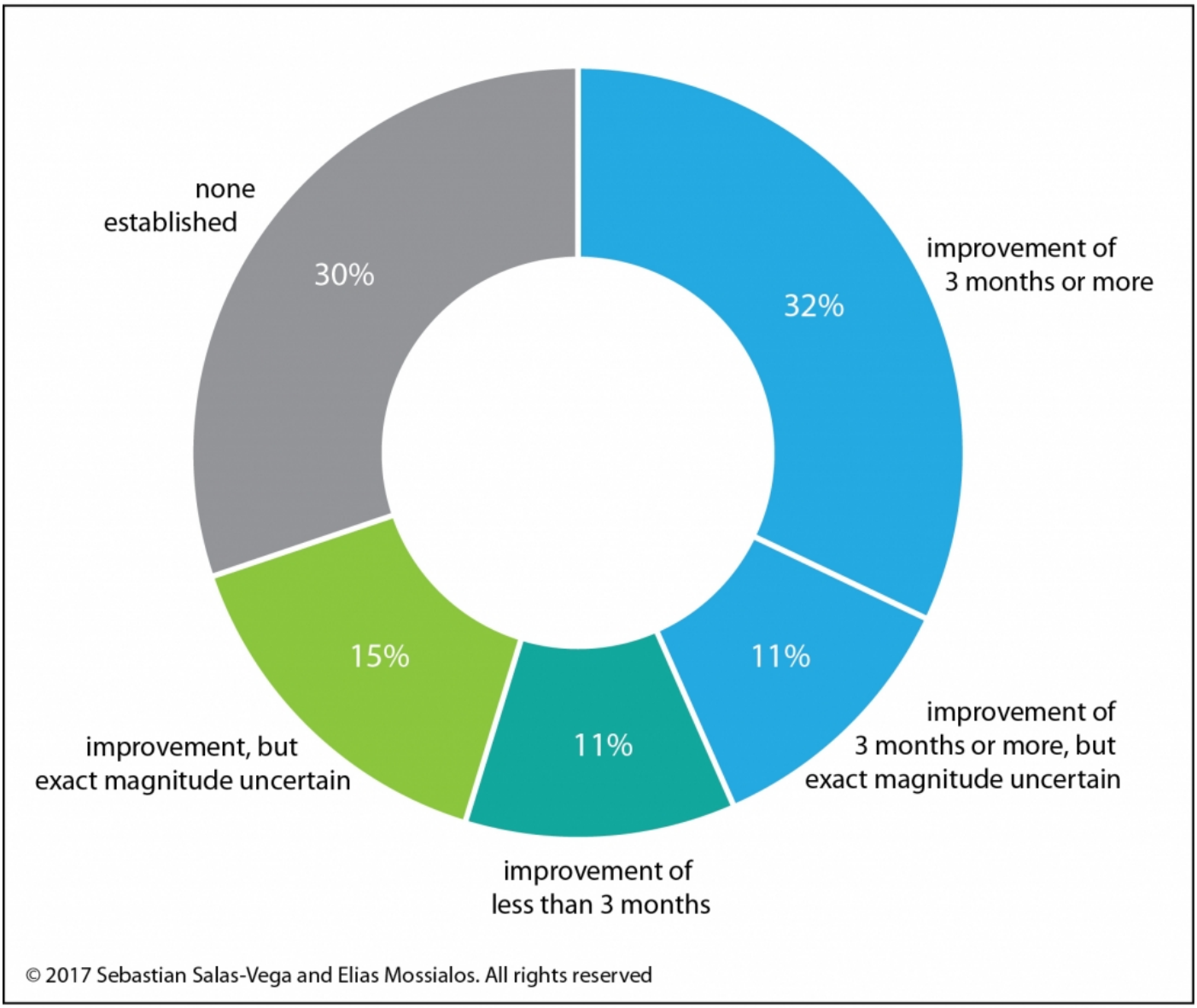
Figure 1. New cancer medicines grouped by therapeutic target and effect on overall survival, quality of life and safety



Source: Authors' analyses.
Notes: Clinical benefits of new medicines approved between 2003 and 2013 by US and EU authorities with a primary anti-cancer indication, as evaluated by health technology appraisals. Overall survival benefits are rounded to the nearest integer and represented as blocks, where each block corresponds to an improvement of one month relative to existing regimens or treatments. 'Uncertain major improvement' refers to increases in overall survival of at least three months, where the exact magnitude is unknown. Uncertain improvements are those where no further information is provided

Across the entire sample, 32% increased overall survival by three months or more; 11% by an unknown magnitude of greater than three months; 11% by less than three months; and 15% by some unknown amount. A further 30% did not improve overall survival relative to alternative treatments (Figure 2).

Figure 2. Improvements in overall survival: clinical benefits from cancer medicines licensed between 2003 and 2013



Note: Percentages may not sum to 100 because of rounding errrors.

Just under half of new cancer drugs increased cancer patients' quality of life, yet the largest share (45%) reduced patient safety. Taken as a whole, approximately 1 in 3 newly approved cancer medicines were not associated with any overall survival benefit, while 1 in 5 neither extended life nor improved quality of life or safety.

Regulatory decision-making

There were however a number of reasons to question whether claims of clinical benefits perfectly reflected those observed in real-world settings. Regulatory evidence, for instance, may be based on modelled, rather than real-world, data; health technology assessment agencies do not always agree on the clinical benefits associated with new cancer medicines, particularly those that claim to bring the largest health benefits; and outside factors may shape the interpretation of scientific evidence. For example, English authorities were most likely to attribute overall survival, quality of life, and safety improvements to new cancer medicines; Australian authorities, in contrast, were more conservative in doing so.

Clinical impact from a decade's worth of cancer drug innovation

All new cancer medicines licensed between 2003 and 2013 by the FDA and EMA extended OS by an average of 3.43 months relative to the treatments that were available in 2003. While perhaps modest, this extension in overall survival represents an important step forward for patients and society, as even minor improvements in survival can have a significant effect on reducing mortality at the population level. It is, at the same time, encouraging to find that most new cancer drugs were associated with some known (55%) or at least unknown (70%) overall survival benefit, with the largest share (43%) extending life by greater than or equal to 3 months, an amount that English and Australian regulators consider to be clinically meaningful.

Moreover, roughly four out of every five new cancer medicines licensed in the US and EU between 2003-2013, and evaluated by English, French, and Australian HTA agencies, demonstrated at least some evidence of an OS, QoL, or safety benefit over alternative treatments. Therefore, for the most part, innovation in the oncology drug market appears to be bringing real value to patients and society.

Seen from another perspective, however, this means that approximately 30% of new cancer medicines introduced over the past decade may not provide overall survival benefits to patients, while 20% may not improve their overall survival, quality of life, or safety. While perhaps reflective of non-active comparisons, the approval of new medicines for orphan indications with no alternative treatment, or the growing use of surrogate efficacy endpoints during regulatory evaluations, this finding suggests that expenditures for up to 1 out of every 5 new cancer drugs may be spent without any overall survival, quality of life, or safety benefit to the patient.

In the absence of real-world observational data, our study reviewed technological appraisals from HTA agencies in England, France, and Australia. To better reveal the real-world benefits from new cancer medicines, future studies should periodically repeat this analysis using post-marketing, observational or pragmatic clinical trial evidence. The National Cancer Institute's upcoming National Cancer Knowledge System—a component of the US Precision Medicine Initiative® that will integrate genomic information with clinical response data and outcomes information—may provide crucial insights in this regard and help to inform value-based decision-making.

Patient access to medicines should be a goal that all health systems strive for—how patients respond to treatments can be very diverse, and it is possible for at least some patients to benefit from most new medicines. Clinical decision-making in the case of cancer is an incredibly personal matter, and should be tailored to the unique circumstances of each patient. As our paper demonstrates, we have seen a significant amount of innovation over the past decade in cancer medicines. New medicines frequently enter into the clinic, providing patients with additional choice that can help them personalize their treatment. Given the diversity in clinical response that is possible, we see this as a positive development.

Yet, it is important for patients to understand the circumstances under which any treatment would be expected to produce the greatest clinical benefits and the lowest risks, given costs. This study adds to the evidence that can be used to inform clinical decision-making. At the same time, our results point to the notion that new cancer treatments may not always provide patients with greater clinical benefits, or lower risks, over existing treatments. This is especially important to consider if costs are of significant concern, e.g. if costs make it difficult for patients to complete the prescribed course of treatment. In this way, this study reminds us of the importance of the patient-physician relationship—patients should work with their physicians to consider all available evidence that exists in support of individual treatments. For their part, physicians owe it to their patients to provide them with as thorough of an overview of the scientific evidence as possible, and to work with patients to identify individualized goals of care. This can help patients make fully informed decisions on personalized treatment plans that best meet their own medical and personal circumstances.

In conclusion, our findings suggest that spending on new cancer drugs may not always be proportional to their clinical benefits, which raises a number of important questions about value-based decision-making in oncology. This study also gives greater transparency to the clinical

impact from new cancer medicines, and the basis for regulatory decision-making. And, it provides an additional resource to patients and clinicians who, in personalizing treatment, may have to consider the economic implications of drug prescriptions alongside individual preferences for treatment-related risks and benefits.

Further information

Salas-Vega S, Iliopoulos O, Mossialos EA (2016) Assessment of overall survival, quality of life, and safety benefits associated with new cancer medicines, *JAMA Oncology*. Published online 29 December.

About the Authors

Sebastian Salas-Vega is Scholar and Research Officer in Pharmaceutical Policy and Economics within LSE Health. His academic interests focus on value-based policy, pharmaceutical innovation, healthcare delivery, and patient outcomes.

Elias Mossialos is Professor of Health Policy at the LSE, Director of LSE Health, and Professor of Health Policy and Management at Imperial College London.

Othon Iliopoulos is Associate Professor of Medicine at Harvard Medical School and Attending Oncologist at Massachusetts General Hospital.

January 5th, 2017 | Health Care | 0 Comments