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Themed Section: Curative Therapies

A Beginner's Guide to Understanding Curative Therapies

Don Husereau, BSc Pharm, MSc*, *School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON, Canada*
Shelby D. Reed, RPh, PhD, *Duke University School of Medicine, Duke University, Durham, NC, USA*

Headlines from late-breaking sessions at scientific conferences herald exciting advances in medicine. Yet, what is often whispered between physicians, and more obvious to market access specialists and health technology assessors, are the relatively small health gains associated with most new medical treatments. This is not a fault of innovation—advances in nutrition, sanitation, and improved socioeconomic conditions have already created a high bar for life expectancy in developed countries.[1] Similarly, we have already benefitted from advances in medicine introduced decades ago—vaccines and antibiotics—curing and eradicating prematurely fatal conditions that have long plagued humanity. The past 50 years also has marked significant declines in cardiovascular mortality and improvements in cancer outcomes.

Not surprisingly then, scientific discovery has shifted its attention toward the outliers—rare occurrences of disease that lead to significant early loss of life or prolonged suffering. The 21st century has already witnessed the introduction of therapies for chronic hepatitis C viral infection, leukemia, lymphoma, cystic fibrosis, lysosomal storage disorders, and rare retinal conditions. These treatments have restored health or have prevented prematurely fatal conditions. And with them, the word "cure" seems to have made a return to medicine.[2] To paraphrase Pearson,[3] cures have created a "heartening dilemma" for healthcare administrators, insurers, patients, and innovators who must reconcile how to determine a fair price and how we can afford to pay for them. Putting a price on life has once again reached center stage.

At the advent of this new era, we are all beginners. It is for this reason we have worked to provide this themed section of *Value in Health*. It is our hope that these articles provide ISPOR members and others with an up-to-date understanding of what we are about to face: what the potential impact of curative therapies might be, whether HTA bodies and payers are ready for them, what aspects of evaluation may need to be modified or expanded, and how we might pay for them. We have invited authors for this issue who have previously presented on these topics at ISPOR meetings or in ISPOR journals.

To begin the themed section, Quinn and colleagues use a modeling approach to help us appreciate what the future holds for cures.[4] Starting with an impressive 628 gene and cellular therapies that are currently under development, and assuming similar failure rates to current small molecules, they predict by 2030 up to 50 000 patients might be treated annually in the United States alone. They also identify what types of patients are most likely to be affected. The results and insights from this analysis may be surprising to some; but it should be seen as a best guess for the future of curative therapy.

It also begs the question as to whether HTA bodies and payers are ready for cures. Faulkner and colleagues conduct a sizeable piece of market access scholarship, examining the output of 100 HTA recommendations from Australia, Canada, France, the United Kingdom, and the United States of currently disruptive technologies.[5] Using examples from regenerative and advanced therapies, precision medicine, molecular diagnostics, and rare diseases, they identify what will likely be future issues for HTA globally. The article addresses concerns about uncertainty of the magnitude and duration of effect owing to "study design issues," and reflects on how cures are best defined. These insights should be helpful for those trying to understand how payers will respond to cures in the future.

Two studies by Jane Barlow and Kai Yeung and colleagues attempt to illuminate concerns among payers in the United States.[6,7] Through structured interviews, both groups revealed payers' perception of the desirability of outcomes-based, risk-sharing agreements, a strategy to managing uncertainty often proffered by academics and innovators (with benefits shown by Towse and Fenwick[8] later). These studies indicate that most payers see current payment methods as sufficient, citing technical and administrative barriers to risk-sharing and outcome-based payment models. This research also reveals that most payers are aware of the challenges from cures that await them and provide some unique insights into how cures may also need to be defined in economic, rather than just clinical, terms. Not surprisingly, all payers viewed affordability of curative treatments as a major challenge.

Whether we can afford curative therapies or not, Pearson reminds us that there is still a question "… of how to determine what a fair, reasonable, value-based price should be for a potential cure."[3] To aid evaluators and address challenges with clinical evidence and social values that may need to be considered, Drummond and colleagues provide a checklist that groups these additional considerations into curative therapy-specific domains.[9] One such factor is spillover effects from cures. Research conducted by Julia Snider and colleagues[10] further describes one such spillover effect—the potential to reduce wait times for liver transplants from current use of antiviral medications and its associated social value. They remind us that these are not often considered in traditional economic evaluations.

* Address correspondence to: Don Husereau, BSc Pharm, MSc, 879 Winnington Avenue, Ottawa, ON, Canada K2B5C4. Email: donh@donhusereau.com

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In his article, Steve Pearson also provides some helpful suggestions for evaluators and those translating evaluations of cures into pricing and reimbursement decisions by HTA bodies and payers.[3] He considers approaches to adjusting prices or using incremental cost-effectiveness ratios to inform prices based on considerations of social and economic value. A unique insight from this article is that unlike patented medicines today, curative therapies do not allow for a future sharing of social value between consumers and producers once patents have expired. He suggests that we may need to adjust prices to ensure "shared savings" between consumers and producers.

Lastly, and assuming that HTA bodies can determine a fair and reasonable price, Towse and Fenwick then address the issue of how to pay, specifically how payment schemes could be structured to avoid biasing health systems for or against a one-time curative treatment (ie, upfront payment) versus a chronically administered treatment (ie, ongoing payments) that offers the same level of health benefit. Their illustrative example (a cure at a bargain price of $296 741 that reduces the monthly chance of mortality from 5 to 0 in 1000) highlights the consequences of decisional uncertainty for curative therapies. It also highlights the economic advantages of evidence collection or outcomes-based agreements, something that we now know payers have largely been reluctant to pursue. But, with increasing numbers of pricy curative therapies on the way, the tipping point for a new era of value-based contracting may finally be on the horizon.

Taken together, it is our hope that this Beginner's Guide gives *Value in Health* readers insights into the current state of curative and transformative therapies. After a read of each article, cross-cutting themes that will need to be addressed by those in HTA and outcomes research should become more apparent. In particular, payers' concerns about duration of effect, perceptions of unaffordability, social values, and the desirability and feasibility of performance-based risk-sharing agreements will all need to be addressed in our soon-to-be future.

At last, the era of cures is upon us.

Be careful what you wish for.

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