Value & Outcomes Spotlight had the opportunity to sit down with Don Husereau, BScPharm, MSc adjunct professor at the University of Ottawa, and Shelby Reed, RPh, PhD, professor at Duke Clinical Research Institute, to discuss the implications of emerging curative therapies for health economics outcomes research (HEOR) and the health system. Don is a past ISPOR board member, health policy consultant, and chair of the ISPOR Task Force, CHEERS (Consolidated Economic Evaluation Reporting Standards), who has previously presented and written on the Value of Cures.1 Shelby, an ISPOR past president, is currently working on studies to evaluate patients’ views on the value of potentially-curative therapies and their inclusion in value frameworks. Both played integral parts as invited associate editors, overseeing the June 2019 Curative Therapies themed section of Value in Health, which features 8 peer-reviewed research papers from distinguished international authors. This themed section and papers address the potential future impact of curative therapies, how global HTA bodies and payers may respond to challenges of evaluating and paying for cures, what additional factors technology assessors may need to consider, potential spillover effects from cures, and optimal models for payment.

Value & Outcomes Spotlight: We seem to be increasingly hearing about cures, whether they are from chronic hepatitis C therapies, chimeric antigen receptor (CAR) T-cell therapies, or even curing human immunodeficiency virus (HIV) or sickle-cell disease through transplant. Is the era of cures upon us?

Husereau: Well interestingly, that depends on how you define “cure.” A number of researchers in our special issue call attention to the fact there is no standard definition for “cure.” Hepatitis C has been called “cureable” by the US FDA, although they are really referring to clearing virus rather than any promises of avoiding illness. The word “cure” certainly doesn’t appear on the label. I think a lot of payers are skeptical of calling remedies for hepatitis C or HIV cures when there is a chance of re-infection.

Reed: One research paper in our themed section cited a 2018 study by the National Association of Managed Care Physicians and Alliance for Regenerative Medicine that made distinctions between “transformative” therapies and “curative” ones. Both terms are on a continuum with curative therapies thought to have a much longer duration of disease stabilization and no other treatment. Yet another paper that involved interviewing US payers highlighted that curative therapies imply no downstream costs. So, clinicians may have one opinion about what a cure is, but payers may have other thoughts about when to call something a “cure.”

Husereau: I think many would be surprised at the pipeline for curative therapies. Another research paper in our themed section, from researchers based at the Massachusetts Institute of Technology Center for Biomedical Innovation, identified 628 gene and cellular therapies that are currently under development. Assuming similar failure rates to historical small molecules, the research team predicted that by 2030 up to 50,000 patients annually might be treated in the United States alone.

Some might argue there is nothing special about evaluating and paying for cures—that they are simply a variation of the current model of chronically treating patients; except with cures, it is one upfront treatment. Do you think that is a fair point?

Reed: It certainly may be a fair point. One could imagine a cure equivalent to the total lifetime costs and benefits of other treatments. However, cures also seem to imply a large magnitude of benefit or return to a “perfect” health state. They may also mean treatments for rare and more serious outlier conditions. Again, without a standard definition of “cure” it’s hard to generalize. It’s possible we may have to distinguish between
cures for specific types of diseases, like genetic diseases, or specific types of therapies, like gene therapies, that may halt disease symptoms or progression rather than using the term “cure” more broadly.

**Husereau:** I certainly don’t get the sense that there is consensus on this point among health economists and outcomes researchers. When CAR-T emerged, there were various arguments made both for and against special value frameworks or considerations. If a cure really means an upfront treatment for rare or severe conditions, some have argued that providing robust clinical evidence is difficult (due to population sizes). But this is not often accepted by payers, who have raised concerns about single-arm trials and trials of short duration and questioned what is actually feasible in a global clinical development program. Uncertainty about durability of effect is an issue that emerges across many of the invited papers. Others have suggested there may be novel aspects of value to cures (such as spillover effects or societal preferences) that need to be addressed by HTA bodies. But it begs the question as to whether these same things might apply to other therapies. Certainly a few papers in our themed section highlight an issue that is more unique to the US—churn—paying for cures under one insurance plan, which then goes on to benefit another insurance plan when patients move, and what to do about that. Affordability is also something that all payers seem to be consistently concerned about. Apparently no one expects cures to be cheap!

**So what advice then, if any, do you have for HEOR researchers who are being asked to evaluate curative therapy?**

**Husereau:** I would say for starters, ask yourself what is meant by “curative” and whether this will be acceptable or of any relevance whatsoever to payers. Rather than focusing on the word cure, focus on what is known about the costs and benefits of treatment. Focus on what the true unmet need is. This is what payers will do.

**Reed:** Designs of trials, and particularly length of trials and plans for ongoing data collection will be important. How benefits are extrapolated will need to be addressed. We have already seen this to be the case with therapies like Glybera (alipogene tiparvovec), Yescarta (axicabtagene ciloleucel) and Kymriah (tisagenlecleucel). Payers will understandably be concerned about how uncertainty about the duration of effect impacts cost-effectiveness estimates. And although, as one research paper in our themed section shows, this uncertainty might optimally be addressed through outcomes-based risk-sharing arrangements, we also know that these agreements are not currently widespread. In fact, 2 other research papers describing interviews with US payers suggest these types of arrangements may not be the most desirable solution for payers due to difficulties in administration and expense.

**Husereau:** I think challenges with clinical evidence will remain front and center for payers. Certainly, despite analysts treating a QALY as a QALY regardless of who receives it, we know payers are likely to put some premium on treatments with a convincingly large magnitude and duration of benefit in patients with severe and debilitating conditions and for which there are no available treatments. Innovators are starting to understand that more robust evidence can have payoffs, and that starting with a thin evidence base, often to satisfy regulatory requirements and global rare-disease frameworks, can create downstream challenges for themselves along with payers.

**So do we expect HTA bodies and payers to change approaches in the future era of cures?**

**Reed:** I think it’s hard to say, and a lot will also depend on whether innovators change their approaches to generating evidence beyond regulatory requirements. We know it is difficult to implement such change quickly, whether we are talking about large, global pharmaceutical companies or large private and public insurers. Until these stakeholders come together to tackle barriers to generating real-world data on relevant patient outcomes, it will be difficult to implement risk-sharing agreements. Given the stakes involved and the understanding that all stakeholders could benefit from coverage with evidence development, curative therapies might provide the tipping point.

**Husereau:** I think many of the lessons from funding prevention also apply to cures. I know in the Canadian province I live in, like many other jurisdictions worldwide, we have had citizens’ councils saying they would put a premium on preventive therapies; however, just how much of a premium (what they would be willing to give up in treatments to receive prevention) has never been elucidated. And preventive things are often considered lower priority in reality. Another interesting aspect of cures with long-term effects is how discount rates will affect the value proposition. Cures may draw much more attention to this important aspect of research that needs to reflect societal preferences. My personal feeling is that neither HTA bodies nor innovators will make significant changes in how they approach things in the near future, despite the increasing emergence of cures. Clinical evidence will be king, as always, and therapies that fall below a threshold of credibility will simply not be funded. Similarly, companies will simply react to an austere payer environment and choose not to commercialize promising innovation, because of commercial viability. Anyway, I like saying things about the future, because I can’t be wrong (at least, for now). As the old saying goes, “Prediction is difficult, especially about the future”.

**REFERENCE**


**ADDITIONAL INFORMATION**

The Curative Therapies themed section will be available in the June 2019 issue of Value in Health (www.ispor.org/valueinhealth). For more information on curative therapies, visit our Personalized / Precision Medicine Special Interest Group page at www.ispor.org/specialinterestgroups. The SIG is expanding to include curative and regenerative therapies and they will have forum at ISPOR 2019 in New Orleans on Tuesday, May 21, 2019, from 12:30 to 1:45PM titled, “Leveraging Real World Evidence To Address Uncertainty For Transformative And Curative Therapies.”