The ABCs of Real Option Value of Medical Technologies

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Estimating real option value requires estimating and incorporating future survival and quality of life improvements from adopting new medical technologies, better use of existing technologies, and other changes that can affect survival or quality of life.

In 2018, the International Society for Pharmacoeconomics and Outcomes Research published a series of Special Task Force reports on US value assessment frameworks, with the goal of informing the shift towards a more value-based healthcare system in the United States. In the reports, several potential novel elements of value—beyond conventional quality-adjusted life-years (QALY) gained and net costs—were identified and defined: insurance value, reduction in uncertainty, fear of contagion, insurance value, severity of disease, value of hope, real option value, equity, and scientific spillovers.[1-2] So far, many of these novel elements of value have been omitted in the theoretical and applied health technology assessment (HTA) literature, and the reports called for more research on developing sound methodologies to estimate them.

This article will address 5 key questions related to one of the novel elements of value—real option value (ROV):

1. What is ROV?
2. What is the origin of real option theory?
3. How large is ROV in healthcare?
4. Does ROV really exist?
5. How does ROV affect value assessment of medical technologies?

1. What is ROV?

Real option value is generated when a medical technology that extends the life of patients creates opportunities to benefit from future medical advances. Suppose cancer drug A can extend survival for 1 year, and while patients are on drug A, a new drug B is approved and becomes available to patients that can extend survival for another 1 year after the patients fail drug A. The conventionally calculated survival benefit and QALYs gained of A generally do not account for the possible arrival of B. However, longer survival from drug A is not only valuable in itself, but it also opens up opportunities for patients to benefit from the new drug B in the future. The ROV of drug A is therefore primarily the additional survival (and QALY gain) from the new drug B conditional upon patients surviving to its arrival. Besides ROV from disease-specific technology advancement, there is also ROV from general background improvements in mortality (ie, for reductions in other causes of death).

2. What is the origin of real option theory?

Originating from corporate finance, real options theory recognizes that managers have managerial operating flexibilities—rights, with no obligations to take certain course of action in the future—when operating in a market full of changes, uncertainty, and interrelated decisions.[3] These rights, which are called real options, include deferring, expanding, contracting, abandoning, or altering a project in other ways after it is initiated, as more information about market conditions becomes available. In some cases, especially in infrastructure-based or strategic industries, initial investments (eg, a lease on undeveloped oil reserves) may create subsequent investment opportunities (production and commercializing of oil).[4] These managerial operating flexibilities, or real options, can affect a project's value because management can revise the initial operating plans based on new market development and move its cash flow distribution toward a higher rate of return. By analogy, with real options, payment is made now for the option to make further investments in the future; investing in the current life-extending medical technology can be interpreted as buying an option to benefit from medical advances that are coming through the pipeline.

3. How large is ROV in healthcare?

In the current HTA literature, ROV has been measured prospectively in several studies as an increase in expected survival or QALY gain for several drugs in oncology—tyrosine kinase inhibitors, nivolumab, and ipilimumab—in several cancers including chronic myelogenous leukemia, renal cell carcinoma (RCC), squamous non-small cell lung cancer, nonsquamous non-small cell lung cancer, and metastatic melanoma.[5-7] The estimated ROV, measured as additional survival or QALY gain, ranged from 5% of the conventional value for nivolumab for squamous non-small cell lung cancer to 18% for renal cell carcinoma. The size of ROV depends primarily on 2 factors: (1) the survival benefit of the current

life-extending therapy, and (2) the speed of medical technology advancement in the disease area. The greater the survival benefit of the current treatment, the greater the ROV. The faster the technological progress, the greater the ROV. Additionally, many cancer drugs have multiple indications and the ROVs from different indications are potentially additive.

4. Does ROV really exist?

Real option theory implies that a forward-looking patient (optimally informed by a physician agent) would consider both existing treatments and those that are in the pipeline in their current treatment decision making: the future treatment opportunities are the real options here. As a result, their current treatment decisions may change as their expectations about future treatment opportunities change. For example, if a phase II clinical trial demonstrates that an investigational new drug can significantly prolong survival for patients with lung cancer, a rational, well-advised, forward-looking patient may undergo more active treatments so that he/she can live long enough to benefit from the new lung cancer drug. A recent analysis of real-world treatment decisions by melanoma patients with regional or distant metastasis showed that the public disclosure of ipilimumab's phase II result was associated with a nearly twofold immediate increase in the probability of receiving surgical resection of metastasis relative to no treatment.[8] Surgical resection was shown to improve overall survival for metastatic melanoma patients, and this prolonged survival combined with technology advancement (the arrival of ipilimumab) creates ROV. By contrast, the utilization of systemic therapy, which was shown to have no impact on overall survival, did not change significantly in this patient population.

> Real option value is generated when a medical technology that extends the life of patient creates opportunities to benefit from future medical advances.

5. How does ROV affect value assessment of medical technologies?

In HTA relying on conventional cost-effectiveness analysis (CEA), current practice is to evaluate the effect of a treatment in a world where medical technology is fixed and patients passively commit to the treatment assigned, thus neglecting the effect of today's treatment on future treatment opportunities. With the rapid advancement of medical technology and the adoption of a lifetime horizon by many CEAs, these assumptions can be clearly unrealistic in some disease areas. Accounting for ROV in HTA will likely increase the projected QALYs gained of life-extending therapies, as technology is improving and mortality from nearly all causes has been declining in recent decades. Current estimates indicate that the percentage increase ranged from 5% to 18% for a single indication for recent targeted cancer therapies. As a result, a life-extending therapy would be seen as more valuable by a rational, well-informed plan member than a therapy that provides the same (conventionally calculated) QALYs gained but primarily improves the quality of life. (Improved quality of life may, in theory, generate some ROV as well, as frailty may limit what treatment a patient can use and its effectiveness.) A life-extending intervention in a disease area with a stronger pipeline and, therefore, with a brighter future would also be seen as more valuable by such a plan member. In addition to the implications for health gains, accounting for ROV in HTA may also be cost-increasing, as future technologies tend to be more expensive than the current ones, due in part to the system-wide rising cost of producing new molecular entities.[9] In the case of ipilimumab for metastatic melanoma, consideration of ROV resulted in approximately a 3% to7% increase in the incremental cost of ipilimumab.[5] The change in the cost-effectiveness of the therapy, as measured by the incremental cost-effectiveness ratio (ICER), depends on the relative increase in QALYs gained versus the change in cost. In the case of ipilimumab for the treatment of metastatic melanoma, accounting for ROV decreased the ICER by less than 1%.[5]

Estimating ROV requires estimating and incorporating future survival and quality-of-life improvements from adopting new medical technologies, better use of existing technologies, and other changes that can affect survival or quality of life. Existing studies have used pipeline data projection and mortality data projection for several cancers and have generated relatively consistent findings. As the ISPOR Special Task Force recommended, next steps are to expand the evidence base to other disease areas and to incorporate any trends in quality-of-life improvement over time. Furthermore, work is needed to better understand any interactions among related novel elements of value—especially ROV with insurance value, the value of hope, severity of disease, and scientific spillovers.

References

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Additional information

The preceding article was based on an issue panel presented at ISPOR 2019. Presentations from this meeting can be found at www.ispor.org/conferences.