PERSPECTIVE

Share your values

Paying for cancer immunotherapy will require new ways of cooperation between drug companies, insurers and policymakers, says **Scott Ramsey**.

Immunotherapy has moved to the forefront of cancer research and is being adopted rapidly into oncology practice. It is good news for people with cancer, but the success comes at a cost.

The price of cancer immunotherapy drugs ranges from US$9,000 to $18,000 a month — around 10 times more expensive than conventional chemotherapy. The treatments can take months or, unlike chemotherapy, even years to complete. Moreover, many combination treatments involving immunotherapy drugs are being tested and some, including nivolumab with ipilimumab for advanced melanoma, are already being used in the clinic, pushing costs even higher.

The wholesale replacement of conventional chemotherapy by immunotherapy in the near future is unlikely, but the extraordinary incremental costs of replacing older treatments with such agents, together with the rising number of cases of cancer as the population ages, is creating great concern. By 2030, 2.1 million people in the United States will be diagnosed each year[1]. As the treatments replace older and cheaper ones, immunotherapies will add billions of dollars to the nation's health-care spend.

It is important to consider two issues that are pertinent to costly new medical treatments: budgetary impact and value.

Budgetary impact refers to the added financial burden of a treatment or group of treatments on the total health-care spend of the system. Spending matters because, in the short term, insurers have fixed pools of funds that are tied to premiums. Large, unexpected increases in spending can strain the budget and create pressure to cut costs elsewhere. Although one immunotherapy drug is unlikely to be a budget buster, in aggregate, they raise that risk.

Beyond budgetary impact, the most controversial issue that concerns immunotherapy is its value. Value compares the cost of a treatment with its benefits such as quality of life and survival time, and drug payment schemes need to set value thresholds (a willingness to pay for selected benefits). But estimates of cost-effectiveness for most immunotherapeutic agents often fail to meet the value thresholds widely cited in health care.

Consider the quality-adjusted life year (QALY), a measure of disease burden used by gatekeepers of treatment such as the UK National Institute for Health and Care Excellence. Estimates of the cost-effectiveness of checkpoint-inhibitor immunotherapy drugs as a second-line treatment for non-small-cell lung cancer, for instance, range from $219,000 for atezolizumab to $416,000 for nivolumab per QALY. Those figures, which come from the US Institute for Clinical and Economic Review in Boston, Massachusetts, are much higher than the widely used threshold of $100,000 to $150,000 per QALY[2].

Reducing expenditure while maintaining access for patients to immunotherapy will require new thinking on the part of pharmaceutical companies, health insurers, providers of cancer care and policymakers.

Many economists support the practice of setting prices on the basis of agreed-on benchmarks of cost-effectiveness. Such value-based pricing arrangements are, in fact, common outside the United States.

The main problem with estimating value for most immunotherapy drugs today is that it is too early to know whether the tumour responses seen in trials (ranging from 10% to more than 80% of participants) will translate into long-term improvements in overall survival.

In the meantime, patients and policymakers must understand that most immunotherapy drugs provide only incremental benefits such as reduced toxicity and modest gains in survival.

Solutions may come from other drug payment schemes grouped under the term performance-based risk-sharing agreements (PBRSAs). These are contracts between organizations that pay for drugs and drug manufacturers in which reimbursement is tied to product performance in the clinic[3].

PBRSAs have the advantage of allowing patients to access treatments for which the evidence of benefit is not yet conclusively established or agreed on. PBRSAs might apply, for example, when a drug is approved on the basis of an intermediate endpoint such as progression-free survival.

Alternatively, payment for long-term survival might be required, in which case the payer (a government health-care agency or private insurer) and the manufacturer must agree on a time point after which that outcome is achieved.

Barriers to value-based pricing or PBRSAs may be falling — for example, this year the US Centers for Medicare and Medicaid Services announced a PBRSA programme for tisagenlecleucel, a one-time treatment for a subtype of acute lymphoblastic leukaemia that costs $475,000. The agency will pay the manufacturer only if a patient shows evidence of a clinical response after one month. (However, in clinical studies, some people initially respond to the treatment, but relapse within a year.)

In oncology, the movement towards PBRSAs faces the 'death by 1,000 cuts' problem: implementing a single PBRSA is costly and affects only a small number of patients, even though in aggregate the cost of immunotherapy will be an extraordinary burden for payers. To reduce the cost of PBRSAs and the uncertainty about their effects, independently funded experiments on these agreements would do much to answer questions about their benefits and limitations. ■

IMMUNOTHERAPIES WILL ADD **BILLIONS** OF DOLLARS TO THE UNITED STATES' **HEALTH-CARE SPEND.**

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Scott Ramsey *is a physician, health economist and director of the Hutchinson Institute for Cancer Outcomes Research in Seattle, Washington.*
e-mail: sramsey@fredhutch.org

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