payment for cancer care will change radically over the next decade as the nation struggles to hold down health care costs, experts told an early October Institute of Medicine forum, Delivering Affordable Cancer Care in the 21st Century.

Traditional fee-for-service medicine, in which oncology reimbursement relies disproportionately on profits from expensive chemotherapy drugs, will give way to a variety of alternative payment mechanisms that Medicare and insurance companies are now testing. These systems include bundled payments for episodes of care, value-based insurance design, and shared savings models linked with pay-for-performance programs that reward physicians who adhere to standardized treatment protocols.

“If you think it's been a tough reimbursement environment up to now, just wait. It's going to be much, much tougher in a year or two,” said Mark McClellan, M.D., Ph.D., former administrator of the Centers for Medicare and Medicaid Services and now director of the Engelberg Center for Health Care Reform at the Brookings Institution. Given societal demands to hold down health care spending, “the unavoidable conclusion is that we can’t keep doing things the way we've been doing things.”

Many institutions and community oncology practices are already experimenting with treatment alternatives that lower costs while preserving quality. Sometimes the alternatives are part of Centers for Medicare and Medicaid Services pilot programs. Sometimes the practices are moving forward on their own. Those efforts are likely to become more widespread in the next few years, the experts said.

Most of the experiments shift financial risk from payers—either the government or insurers—to providers, such as hospitals or community oncology practices. Different approaches shift the risk in different ways. Under bundled or episode-of-care payments, for instance, the provider must allocate resources, who then is at financial risk if the total cost of the episode exceeds the payment. “This is very different from fee-for-service, where the only risk is if someone doesn't pay you,” said Peter B. Bach, M.D., director of the Center for Health Policy and Outcomes at Memorial Sloan-Kettering Cancer Center in New York.

It can work only where alternative approaches to treating a condition are available, he warned. It could work well in treating metastatic non–small-cell lung cancer, for instance, because the medical literature on that illness includes eight different approved and equally effective chemotherapy protocols. With monthly costs ranging from $1,322 for paclitaxel–cisplatin to $7,092 for pemetrexed–cisplatin, payers that switch to bundled payments could set their reimbursements at about the average, about $3,500 per month. “Once oncologists see that, they will be shyer about prescribing a regimen that costs them over $3,500,” Bach said.

Sometimes they may refuse to use certain regimens. Memorial Sloan–Kettering recently announced that it would not pay for the newly approved colorectal cancer drug ziv–aflibercept (Zaltrap) because it costs more than $11,000 per month. “The drug has proved to be no better than a similar medicine that we already have for advanced colorectal cancer,” three oncologists from the institution, including Bach, wrote in the New York Times.

United Healthcare, the nation’s largest insurer, is taking a different approach. It has launched an experimental bundled payment program with five community oncology practices (see J. Natl. Cancer Inst. 2011;103:8–10) that takes drugs out of the equation. It required the five practices to choose a common protocol for 19 different cancer conditions and then pays a bundled payment for adhering to those protocols. Whatever the chosen protocol, the insurer pays the full cost of any drugs, which removed any incentive for the practices to choose pricier drugs if they didn’t work any better.

The program is already showing positive results by lowering costs while improving outcomes. Lee Newcomer, M.D., director of oncology at United Healthcare, told the forum. Although full release of the pilot program’s results were available, the program has lowered costs by substantially reducing variation between practices. For instance, per-patient diagnostic radiology costs for metastatic breast cancer at the five practices before the program ranged from less than $2,000 to more than $5,700. “The variation we deal with is huge,” he said. “When we cut that variation in half, we cut our expenses in half.”

However, he warned that the degree to which the new payment systems can hold down costs will be limited if the prices of the latest cancer drugs continue to skyrocket. Drugs now account for 12% of all payments for cancer patients at United Healthcare, up from 10% just 5 years ago. He gave the example of pertuzumab (Perjeta), a new treatment for metastatic breast cancer that extends average progression-free survival by 6–18 months at a cost of $188,000. “When a new compound comes out, it’s generally unique . . . I don’t have a way to say to a company, ‘We have a competitor; let’s have a bidding [war].’ And in most states, I’m required by law to pay for it,” he said.
Cancer Vaccines: Always a Bridesmaid, Never a Bride?

Anna Azvolinsky

The saying “Always a bridesmaid, never a bride” is apt for therapeutic cancer vaccines, which manage to garner excitement in early trials but despite many attempts do not achieve clinical efficacy. “This is an area that has been studied for a very long time, but there are, to my knowledge, no effective therapeutic vaccines for cancer,” said Steven A. Rosenberg, M.D., Ph.D., chief of surgery and head of the tumor immunology section at the National Cancer Institute, who has been studying immunotherapy for more than 30 years.

Perhaps this time things will change. In the wake of many disappointments, new vaccine approaches have reached late-stage development, having conceivably learned from the pitfalls of predecessors.

In an August 2012 Nature Medicine study, researchers demonstrated early promise of IMA901, a 10-peptide therapeutic vaccine for renal cell cancer (RCC). Harpreet Singh-Jasuja, Ph.D., chief scientific officer of Immatics Biotechnologies, based in Germany, and colleagues developed the vaccine by isolating antigens directly from RCC patients’ primary tumors.

Phase II results showed a 64% rate of immune response among 64 patients, 26% of whom responded to multiple antigens. Patients who responded to multiple antigens in the vaccine had extended survival. At 30 months, overall survival was approximately 25% for patients who responded to a single antigen, compared with more than 50% for those who responded to two or more antigens.

According to Carsten Reinhardt, M.D., Ph.D., and chief medical officer of Immatics, this result confirms that a broad immune system attack on multiple targets is a promising approach.

“The clinical utility of cancer therapeutic vaccines probably depends on many factors, including the potency of the vaccine, the inherent immunogenicity of the patient’s tumor, and the ability to eradicate the tumor before it develops suppressive features that shut down the immune response,” said Howard L. Kaufman, M.D., director of the Rush University Cancer Center in Chicago. Identifying the patients most likely to respond, whose cancer is inherently immunogenic, may be key.

A phase III trial is now testing whether adding IMA901 to sunitinib treatment will improve the survival of treatment-naïve RCC patients. The trial uniquely evaluates whether either of two serum biomarkers can predict patients who are more likely to achieve a survival benefit.

More May Be Better

Reinhardt believes the failure of previous vaccines stemmed from not having enough quality antigens. Having more antigens may reduce the chance that a tumor can down-regulate the antigens and escape immune system detection. “Only one antigen is not enough,” said Hans-Georg Ramnensee, Ph.D., head of the department of immunology at the University of Tuebingen, in Germany, who serves on the scientific advisory board of Immatics. “The tumor is proliferating and is mutating, so it is easy for the tumor to get rid of one antigen.”

Ramnensee is taking the multipeptide approach further. Using antigen data from prostate, colorectal, and ovarian cancer patients, he and colleagues are creating cocktails of 25–30 peptides for vaccines against those cancers. Personalized vaccines, based on selection of antigens mutated in a patient’s tumor but not in healthy tissue, are also in the works.

Other vaccine developers are also taking the personalized approach. Argos Therapeutics, in Durham, N.C., is developing AGS-003, a vaccine made from a patient’s own dendritic cells and modified with a CD40 ligand and the patient’s own tumor mRNA. Researchers are testing AGS-003 on RCC patients in combination with sunitinib in a phase III clinical trial.

MAGE-A3 is another vaccine being tested as an adjuvant melanoma therapy in a phase III trial. A different version of the vaccine is being tested as adjuvant therapy for non–small-cell lung cancer patients. The MAGE-A3 protein is a tumor-specific antigen expressed on various tumors, including...