Big Databases: Outcomes Research Begins To Yield Results

By Merrill Goozner

Researchers recently unveiled the first comparative-effectiveness study in oncology that used an outcomes database.

The presentation took place at the American Society of Hematology meeting in New Orleans in December, where a research group using the National Comprehensive Cancer Network’s (NCCN) database for non-Hodgkin lymphoma reported that patients with mantle cell lymphoma, a rare but fatal form of the disease, did just as well when receiving autologous stem cell transplantation after standard chemotherapy as patients who received a highly toxic regimen of five drugs.

The five-drug regimen’s developers, mostly from the University of Texas M. D. Anderson Cancer Center in Houston, claimed that their method was superior because of a 75% progression-free survival rate at 3 years. After identifying 229 patients younger than 65 years with MCL, whose medical records had been entered into the NCCN database between August 2000 and February 2009, researchers conducted a retrospective cohort study and found that overall survival between the two treatment approaches was similar. The median progression-free survival rate at 3 years was also the same. One major difference existed, though: The median number of days in the hospital was lower in the transplant group, according to the abstract presented at the meeting.

“This [finding] validated that it is reasonable to do the auto transplant because it has the same outcome plus less toxicity,” said Ann LaCasce, M.D., of Dana–Farber Cancer Institute in Boston, who led the 10-person research team from major cancer centers that contribute data to the NCCN project. They conducted the study because MCL treatment is driven largely by physician preference and expert opinion. No randomized clinical trials or prospective observational studies have ever been done comparing the two approaches, and none are anticipated. “People [with
mantle cell lymphoma] are not all that interested in participating,” LaCasce said. “There will never be a randomized study.”

With an estimated 70% of chemotherapy drugs used off label and trials that compare competing treatments a rarity, proponents of outcomes research have been pushing oncology researchers for more than a decade to begin collecting records of patient treatments and outcomes. Their goal is to build databases that can be used to conduct retrospective comparative studies to determine what works best.

Slowly, such databases have been growing. Eighteen of the 21 large medical centers in NCCN started collecting outcomes data from breast cancer patients as early as 1997, and since then they have created similar databases for non-small-cell lung cancer, colorectal cancer, non-Hodgkin lymphoma (the one used by LaCasce and colleagues), and, most recently, ovarian cancer. The American Society of Clinical Oncology (ASCO) has also started to assemble databases. And the U.S. National Cancer Institute has invested $20 million to set up an infrastructure known as the Cancer Biomedical Informatics Grid (caBIG) to collect and use all kinds of data, including outcomes data (see accompanying news story in this issue).

Building these big outcomes databases has taken years, and even now, with the government pouring billions of dollars into electronic medical recordkeeping, questions remain about the willingness and ability of oncologists, especially those in community practice, to participate in generating the outcomes data that comparative-effectiveness researchers need. Nevertheless, signs of progress exist.

“Is the glacier moving? I think it is,” said Lynn Etheredge, Ph.D., a health policy consultant who directs the Robert Woods Johnson Foundation–funded Rapid Learning Project at George Washington University in Washington, D.C., which promotes use of electronic medical records to learn the best use of medical technologies, products, and treatments.

**Shift in Emphasis**

The databases farthest along are clearly at NCCN, which spends $6 million per year on its outcomes database program. The breast cancer database now houses records on 55,000 patients, some of them more than a decade old. About 70% of the patients are still actively followed by the institutions who inserted their initial data into the system. More than 80% of patients were diagnosed with stage II breast cancer or earlier, thus providing a rich record for tracking treatments and outcomes, according to William T. McGivney, Ph.D., CEO of NCCN. At least nine retrospective breast cancer research studies are currently under way, with the first publications based on the outcomes data expected later this year.

“We’re just doing outcomes studies now,” McGivney said.

Until recently, NCCN has used its databases to analyze practice patterns to improve the quality of care. Statisticians working with NCCN analyze treatment patterns at each institution and for the group as a whole, and then they provide individual snapshots for the participating institutions. That report enables the care providers at those institutions to compare their performance to that of the entire network and to the NCCN treatment guidelines. “We’re seeing 80%–85% [guidelines] concordance levels,” McGivney said.

One reason NCCN’s outcomes research had a slow start was the laborious nature of compiling the records, which relied on data extractors’ culling prespecified data points from deidentified paper records. The extractors submitted results quarterly to the City of Hope Cancer Center in Duarte, Calif., which maintains the data repository for NCCN. Even today, most institutions in the network are not electronically linked to the database.

But a shift in emphasis to effectiveness is clearly under way. About one-third of NCCN’s participating institutions have begun supplying data for the other four databases. It now has comprehensive records for more than 3,000 lung cancer patients, 5,500 colorectal cancer patients, 4,500 NHL patients, and 700 ovarian cancer patients. Many of the records are now old enough with enough consistent follow-up to allow meaningful retrospective studies. At least eight are under way, using those four cancer databases in addition to the nine breast cancer studies.

“We ultimately see these databases as a tremendous resource for conducting comparative-effectiveness research,” McGivney said. “We can slice and dice it and look at specific subpopulations.”

**ASCO**

The American Society of Clinical Oncology (ASCO) has also been compiling data on treatment patterns since 2002 in its Quality Outcomes Performance Initiative (QOPI). As its name implies, the effort is focused on encouraging community oncologists to bring their practice patterns in line with standards contained in guidelines. QOPI, which is advised by Outcome Sciences of Cambridge, Mass., collects data twice a year from 300 practices with 600 treatment sites. They review an estimated 15,000–20,000 charts, extract dozens of quality measures, and provide practitioners with reports on their performance vis-à-vis their peers and guidelines.

“Right now, it’s a performance-based quality improvement program,” said Allen Lichter, M.D., CEO of ASCO. But that’s starting to change because of pressure from advocates for turning cancer care into a learning system that can generate better outcomes.

Last year, ASCO set up a pilot project to collect outcomes data from 20 of the practices signed up with QOPI. “We’re taking the first baby steps in breast cancer to create a registry,” Lichter said. “Will practices participate? Will it be too onerous? We’re still some years away from having that one nailed down, but we understand where the path is heading and we’re determined to help lead practitioners down that path.”

Skeptics abound, of course. Critics point to gaps in the data, such as the lack of input from community cancer centers. “QOPI only covers a sliver of community practices,” said Sharon Murphy, M.D., who once led another NCI clinical trial group, the Pediatric Oncology Group, and now directs the Institute of Medicine’s National Cancer Policy Forum.

Another issue is the strength of evidence generated by retrospective studies of outcomes, which will never reach the level of randomized clinical trials. “These sorts of registries don’t constitute level 1 evidence,” said Richard Schilsky, M.D., a professor at the University of Chicago Medical School.
and outgoing chief of the NCI-funded clinical trial group known as Cancer and Leukemia Group B (CALGB).

Yet CALGB has launched its own breast cancer registry, which 7 years ago began enrolling about 1,000 women older than 65 years with early-stage breast cancer. Researchers have recorded detailed information about their demographics, cancer, treatments, outcomes, quality of life, and satisfaction with treatment. “If we observe compelling trends, these results could influence guidelines,” Schilsky said. “In this era of comparative-effectiveness research, we’re going to see more and more of this kind of stuff. Randomized clinical trials are just too long and too expensive. We need to come up with alternatives.”

He’s also optimistic about using retrospective research to advance personalized medicine. “You can go back and figure out who responded [to a treatment],” he said. “We may be able to better match available drugs to specific patients. This could change standards of care without randomized, controlled clinical trials.”

Government will play a major role in advancing the field. CaBIG has thus far concentrated on creating software programs and facilitating access to basic research tools such as biospecimen and cancer genome databases. And although it has handed out $60 million in grants to use those databases, it still lacks electronic interoperability to collect outcomes data from the 49 NCI-designated cancer centers and its 100 affiliated hospitals and independent care providers. “This is a new part for us,” said Kenneth Buetow, Ph.D., director of caBIG. “We’re in discussions how to capture the data in their electronic systems.”

ASCO and caBIG, working together, are developing a set of core requirements for extended oncology health records, and they hope to persuade the 30 electronic medical record vendors operating in the field to adopt a common standard. Buetow is also working to persuade community cancer centers to participate in collecting and reporting outcomes data by using caBIG. “We’re hoping by the end of this year to have five of 10 community cancer centers online,” he said.

Like ASCO, caBIG cannot predict how community cancer centers will respond to such efforts. And that, in the end, may be the major stumbling block to turning the outcomes of cancer care in community settings—where 85% of cancer care takes place—into a fully searchable record for improving oncology outcomes.

“Where’s the incentive to put in the data?” asked Murphy of the Institute of Medicine. “Until you have these databases become part of pay for performance or require reporting data from electronic medical records, it’s just not there. Who’s going to use it?”

Eutheredge at the Rapid Learning Project thinks he has the answer. “Medicare can create a data system where you don’t get paid until you provide the required data,” he said. “It would be a travesty for Medicare to pay for creating electronic health records and not require the reporting of data that could be used to improve the quality of care.”

© Oxford University Press 2010. DOI: 10.1093/jnci/djq034