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Case Study

Victor Grann Uses Decision Analysis to Weigh Treatment Options for Patients at High Risk of Developing Cancer

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Victor Grann
Clinical Professor of Medicine and Public Health
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Profile

As Clinical Professor of Medicine and Public Health at Columbia University's School of Public Health, Victor Grann wears a number of hats – working with students, conducting research and practicing medicine. But he is perhaps best known for directing a number of studies on cancer risks and prevention strategies, including research on the progression of breast cancer, ovarian cancer, lung cancer and colon cancer.

Challenge

Grann developed an interest in studying the benefits of genetic testing when he was a student in the Masters in Health Policy program at Columbia. It was the mid-1990s, and the first cancer genes had just been identified. That breakthrough made it possible to test individuals for the presence of genes believed to increase the risk of developing cancer. But Grann knew the value of genetic testing would depend on what those who tested positive could do to reduce their risks. He wondered how at-risk individuals would do if they chose to pursue one or more prophylactic measures, and what would happen to those who tested positive but decided against preventive treatments. How would these

decisions affect their survival and quality of life?

It would take many years to answer such questions with the help of clinical trials. Meanwhile, at-risk individuals and their doctors were faced with making critical decisions without the benefit of knowledgeable guidance. And policy makers and insurance providers charged with making reimbursement decisions would need to act in the absence of data demonstrating the cost-effectiveness of available treatments.

Solution

Grann needed a way to model the progression of various cancer and treatment scenarios.
At first he tried using Excel spreadsheets. But soon a colleague suggested TreeAge Software's DATA, the decision analysis software now superseded by TreeAge Pro. Grann has been building and analyzing models with the software ever since.

"With decision analysis modeling, you can find out really quickly if a treatment will be better or not," Grann said. In contrast, "with a randomized [clinical] trial, it would take 10 years to find out how effective preventive treatment would be," he said. And although computer modeling doesn't substitute for randomized trials, there are many times when such trials aren't practical, as when researchers are studying women who have tested positive for breast cancer. "You can't randomize them into 'You'll get a mastectomy, you won't,'" Grann said.

In one of Grann's first studies, he built a model that demonstrated that the life expectancy of a hypothetical 30 year old woman who had tested positive for a breast cancer gene could be increased by several years if she chose to undergo both a preventive mastectomy and an oophorectomy (surgery to remove both ovaries). In a subsequent study, he looked at how those decisions would affect a woman's quality of life.

Since then, Grann has expanded his early models for use in a number of additional cancer studies, refining the data using updated information from the medical literature as well as the results of his own research. He now has what he describes as a huge database of information and an invaluable set of models that can be modified and used for additional investigations. "When there's a new medicine or a diagnostic procedure – especially for breast cancer – I can look at it and see if it pays to use it in terms of living longer, and if it makes sense for society to pay to have the procedure done," he said.

When randomized controlled trials suggested that taking tamoxifen or raloxifene might prevent invasive breast cancer, Grann undertook a decision analysis study comparing the outcomes of chemoprevention with tamoxifen, raloxifene or oral contraceptives with the outcomes of prophylactic surgery. The study suggested that although surgery might yield more substantial survival and cost benefits, quality of life issues may make chemoprevention a more attractive option for young women at high genetic risk.

In 2002, Grann published a study updating his earlier findings regarding the effects of prophylactic surgery, chemoprevention and surveillance (involving the use of screening tests such as mammograms) on the survival and quality-adjusted survival of women who test positive for BRCA 1/2 mutations. The study looked at eight cancer prevention strategies and used Markov modeling to "observe" a hypothetical at-risk woman for 70 years (Markov cycles) starting at age 30. The use of Markov modeling allowed researchers to calculate the age-dependent probabilities of each of several possible outcomes, ranging from remaining healthy to death.

Like many of Grann's studies, the decision analysis also relied on TreeAge Pro's sensitivity analysis features to help isolate the impact of particular variables. Grann looked at how outcomes change when you vary assumptions about factors including time, treatment efficacy, cancer risk and cancer mortality, and explored the possible outcomes of preventive strategies when they are used in combination.

The study found that women who test positive for BRCA 1/2 mutations may derive greater survival and quality adjusted benefits than previously reported from chemoprevention, prophylactic surgery or a combination. For example, by combining tamoxifen and oophorectomy, a 30 year-old woman at risk of developing ovarian cancer could prolong her survival beyond that associated with surveillance alone by 6.3 years.

Today Grann is following up on the study using TreeAge Pro's cost-effectiveness capabilities. The results will help society determine if it pays to have a particular procedure done, he said. "Based on my modeling, I can say to insurance companies, 'Why not pay for a prophylactic mastectomy if a woman wants it? It will save you money in the long run," Grann said.

Grann couldn't have accomplished his studies without the help of user-friendly decision analysis software, he said. And over the years, he has found that the TreeAge software has become even more powerful, flexible and easy to use. "Now my models are very complex, but I can run thousands of simulations without any problem," he said. "And making changes to the software is so much easier to do. It also runs much faster. And it's much easier to see errors. Debugging and improving models is easier now," he said.

Whenever Grann has turned to the TreeAge team for help and advice, he has been very happy with the results. "They are truly so user-friendly. And they're always so responsive to me when I call, even at night. I can't tell you how helpful it's been," he said.

To date Grann's decision analysis studies have helped hundreds of patients, clinicians and health management organizations weigh the risks, costs and benefits of healthcare options. And the possibilities are practically unlimited. "Now that I have the data and the models, I can do a lot of other things with the software. I have a grant now to look at other mutations and other genes for breast cancer and also for other cancers," Grann said.