A little-noticed risk model may help identify good candidates for lung cancer screening, adding to the arsenal of tools to help physicians target their ministrations at those most likely to benefit.

Unlike risk-based treatment and prevention strategies, risk-based screening is still in its infancy, but “it’s becoming more important,” said David Levy, Ph.D., a professor at Georgetown University and an expert on modeling. Risk stratification “tells us who can be most effectively screened—which candidates are most likely to have true positives,” he said. “But at the same time you want to take into account the probability of false positives, because those impose heavy psychic as well as medical costs.”

A misconception lingers that testing asymptomatic patients for cancer is an unmixed blessing because of the potential to detect disease earlier, when it’s often more treatable. But that is rarely the case for any given screening test. According to the U.S. Preventive Services Task Force, colonoscopy for adults aged 50–75, Pap tests for women aged 21–65, and mammograms for women aged 50–74 are the only cancer screening tests for the general population whose benefit (cancer deaths prevented) exceeds their harms (unnecessary treatment of those who don’t have cancer). Mammography for women in their 40s and prostate-specific antigen tests for men have been controversial, as have chest X-rays and computed tomography (CT) scans for those considered at high risk of developing lung cancer.

In 2011, the National Lung Screening Trial showed a 20% decrease in lung cancer deaths and a 6% decrease in all-cause mortality when current or former smokers aged 55–74 with a history of at least 30 pack-years were screened with low-dose CT annually for 3 years. However, not all lung cancer screening trials have found a benefit. And in all the trials, CT scanning found suspicious nodules in an average of 20% of participants, more than 90% of whom did not have lung cancer. Expert panels, including the International Association for the Study of Lung Cancer, have called for better ways to flag individuals at high risk for the disease to maximize screening’s benefit–harm ratio.

Liverpool Lung Project
Researchers have developed several risk models to predict individual risk for lung cancer within a specified period. One of those models, the Liverpool Lung Project, has now been validated in three independent populations who underwent CT screening. John Field, Ph.D., of the University of Liverpool, and colleagues reported their results in the Aug. 20, 2012, issue of Annals of Internal Medicine.

The Liverpool model was developed to identify smokers’ and nonsmokers’ absolute 5-year risk for lung cancer. In addition to smoking duration, it used information on history of pneumonia, history of cancer, family history of cancer, and asbestos exposure. Researchers evaluated the model for accuracy by using data from the European Early Lung Cancer and Harvard case-control studies and the Liverpool Lung Project prospective cohort study. The model was simple, could distinguish between persons who will and will not develop lung cancer, and performed better than smoking duration alone as a tool to decide who should be screened.

Although agreeing with the authors that the Liverpool model requires more prospective evaluation, Barnett S. Kramer, M.D., M.P.H., director of the Division of Cancer Prevention at the National Cancer Institute, called it a step in the right direction.

The model does not take into account actual health outcomes, Kramer said, and “the average clinician is not going to incorporate it into practice at this point, so it’s still a research tool. [But] it leads into new directions that come closer to precision medicine.”

Kramer was hard-pressed to think of many other examples of risk-based cancer screening. The most notable is breast cancer, where “we have a number of pretty good models for predicting risk of getting breast cancer, and some people have tried to personalize the approach to breast cancer screening for women in their 40s.” He was referring to the recent work of researchers from the Cancer Intervention and Surveillance Modeling Network (CISNET) and the Breast Cancer Surveillance Consortium, published last May in the Annals of Internal Medicine. The researchers found that women aged 40–49 with very dense breasts or a first-degree relative with breast cancer had the same risk as an average woman in her 50s and, therefore, could expect to benefit from mammography screening. Another possible example, Kramer said, is cervical cancer, “where they’re refining screening decisions based on [human papillomavirus] status.”
By Charlie Schmidt

Conflicting Clinical Guidelines

When the U.S. Preventive Services Task Force (USPSTF) issued guidelines against prostate-specific antigen (PSA) screening last May, the American Urological Association responded with a scathing rebuttal: The move was outrageous, claimed the association, whose own guidelines take a far more favorable view of the PSA screen. Covered widely in the media, the volatile debate over PSA tests pitted one set of clinical practice guidelines against another. But that's hardly unusual. Recent decades have seen a surge of guidelines, now numbering up to 3,700, according to the Institute of Medicine (IOM)—and many give inconsistent or opposing recommendations on the same clinical topics. “It’s a jungle out there,” said David Ransohoff, M.D., a professor at the University of North Carolina School of Medicine in Chapel Hill. “This is a huge topic that goes to the heart of our profession. Anyone can make guidelines, and our evidence-based medical system is coming under attack by special-interest groups.”

Conflicts of Interest on the Chopping Block

Experts in medicine and health policy are trying to identify and root out conflicts of interest that might skew guideline recommendations. Those efforts are aided by a 2011 IOM report, Clinical Practice Guidelines We Can Trust, which created a standardized framework to ensure transparency and scientific credibility in guideline development. The American Cancer Society (ACS), for instance, which IOM singled out as a model for how not to create guidelines, has revised its own process to make them more transparent, with input from clinicians with no stake in the outcome. ACS now takes public comments into account before issuing final guidelines, said Otis Brawley, M.D., chief medical officer and executive vice president. Brawley said this newer approach, a response to the IOM report and involving an extensive literature review guided chiefly by generalists, departs from the back-room discussions ACS previously relied on. “We’ve got to get away from this black-box methodology,” he said. “Trustworthy guidelines need to be developed out in the open.”

Brawley cites two conflict-of-interest categories as a concern: those based on financial interest, which are relatively easy to identify, and those with an “emotional” component, which tend to be more troubling. John Santa, M.D., director of the Heath Ratings Center at Consumer Reports, agreed. “Specialists and academic researchers can be wedded to their idea or hypothesis about how something works, and it’s very hard for them to accept that there could be an [alternative] explanation,” he said.

Meanwhile, professional societies take pride in their guidelines and see them as a