Smoking Cessation and Low-Dose Computed Tomography Screening: A Necessary Pair

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The primary health benefits of cancer screening are realized by improved cancer-specific or overall mortality. Low-dose computed tomography (LDCT) screening is a relatively recent addition to the repertoire of methods that the health care system uses to improve mortality from lung cancer.[1] However, a recent analysis of the benefits of health care on premature mortality shows that the effects of behavioral factors far outweigh deficiencies in health care access or delivery.[2] The clinical utility of LDCT is driven by smoking, which has a long well-established history of causing a spectrum of adverse health conditions resulting in a 10-year shortened life expectancy.[3] Whereas smoking has decreased in developed countries such as the United States over the past 50 years, smoking worldwide has unfortunately increased.[1,4,5] Proven methods to curb smoking include research, educational campaigns, taxation, and regulatory initiatives to enact broad-based smoking restrictions.[4] Throughout, one emphasis has remained constant: strategies that help tobacco users quit are critical to reducing cancer and mortality from cancer and other causes.[6] It is not currently clear what smoking cessation approaches are best in combination with LDCT.[7] Given the health benefits of quitting, behavioral research on ways to maximize quit rates are needed.

In the accompanying article, Tremblay et al.[8] report that telephone-based smoking cessation counselling did not improve quit rates in active smokers undergoing LDCT screening. The study is an important contribution for the oncology field and helps advance the research agenda on smoking cessation in patients at high risk of cancer. The authors randomized 345 active smokers undergoing LDCT screening to receive a telephone intervention (an "opt-out" approach where all patients are contacted with an offer for smoking cessation services) versus a mailed pamphlet containing contact information (an "opt-in" approach where patients must independently seek services themselves). The primary endpoint was self-reported 30-day abstinence at 12 months. Ultimately, 74% of patients randomized to the telephone intervention completed at least one counseling session (versus 7% of those randomized to mailed pamphlets), with 42% completing at least two. At 6 months, there was a trend toward increased current (25.1% versus 17.2%, $p = 0.072$) and 7-day abstinence (23.3% versus 15.5%, $p = 0.065$). However, the primary endpoint of 30-day abstinence at 12 months was not significantly different (14.0% versus 12.6%, $p = 0.704$). Although a "negative" study, results are thought-provoking, and the authors are commended for their efforts in conducting a rigorous randomized trial with more than 300 participants.

The question remains as to why the primary objective failed in a carefully conceived trial. The study certainly has many strengths. The study's parallel trial design emulated a more real-world setting where patients already enrolled in a screening study were randomized regardless of quit motivation. Such an approach minimizes the selection bias inherent in studies that enroll patients willing to participate specifically in a smoking cessation study. Study procedures appeared rigorous with very few patients lost to follow-up (0.6%) for the primary objective at 12 months. Results were also similar to observed quit rates from other large LDCT trials referenced by the authors. Even so, in addition to the negative primary endpoint, there were no differences in use of nicotine replacement therapy (NRT), pharmacologic aids, or even "intent to quit in the next 30 days" between the intervention and control groups at 6, 12, or 24 months.

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Several possibilities may help explain these findings. Although LDCT screening is a convenient opportunity to contact patients, it may be particularly difficult to change behavior in this particular cohort. As the authors themselves acknowledge, "such participants are likely already thinking about their health, their cancer risk, and their tobacco habits, many (39%) had already tried to quit in the past year [and they have been] unable to quit despite widespread societal cues to quit, have failed previous attempts or were not necessarily seeking quitting assistance." Strikingly, those with a history of cancer appeared less likely to quit smoking, possibly reflecting an established recalcitrance to quitting. More intensive interventions, including in-person counseling, possibly family therapy, and increased use of pharmacotherapy, may be needed in the face of the obstacles facing this particular patient population.

There were no differences in proximal endpoints such as use of NRT, pharmacologic aids, or "intent to quit" that could signal subsequent abstinence, raising concerns about the effectiveness of telephone intervention. Patients randomized to intervention received their initial telephone call at a median of 16 days (range, 11–21 days) after being informed of their LDCT screening results, and 26% did not receive any phone intervention as randomized. It is possible that intervention at, or closer to, the time of screening may have been more effective. Given that 86% of patients had a negative screening result, patients could feel relieved at being cleared of cancer and have even lower motivation to quit smoking when contacted several weeks later. This is in direct contrast to the cancer population, where bad news has just been delivered and potentially galvanizes action. It is encouraging, however, that patients who actually had one or more contacts with cessation counselors as randomized trended toward a higher 12-month abstinence rate (16.7% versus 6.7%, respectively, $p = 0.13$). Differences in access to smoking aids such as NRT may also play an important role, with the relatively low use of NRT contributing to lower quit rates. Finally, the authors acknowledge the study was powered to detect a 13% absolute improvement in quit rates, and it was underpowered to detect smaller but still clinically significant differences.

A notable strength of the study by Tremblay et al.[8] was the opt-out strategy used in the intervention arm. This opt-out approach was innovative and showed the powerful ability to increase contact rates by providing smoking cessation counseling as the "default." Opt-out approaches such as these have been proposed to be the standard of care when dealing with efforts targeting addiction and other high-risk behaviors.[9] When applied to patients with cancer diagnoses, opt-out approaches show consistently high participation rates, with subsequent reductions in mortality for lung cancer patients who quit smoking.[10-12] That the opt-out telephone intervention was unsuccessful in this case may reflect differences between screening and cancer populations. Patients with cancer may have increased motivation for behavioral change and more frequent contacts for treatment, with more opportunities for counseling. Screening patients, on the other hand, may have infrequent medical visits and less impetus to motivate change. More research on the opt-out concept is clearly needed to test innovative approaches for smoking cessation in these settings. To this end, the National Cancer Institute has formed the Smoking Cessation at Lung Examination (SCALE) Collaboration.[13] Funded across eight projects, the SCALE Collaboration will evaluate methods to provide smoking cessation using quitlines, LDCT medical providers, and trained cessation specialists across a variety of institutional and community settings. Researchers will investigate intervention type, intensity, timing, duration, and scale, in addition to the use of telehealth, incentivization, and other behavioral exercises.

Although Tremblay et al.[8] did not find increased abstinence with targeted phone interventions in the context of LDCT screening, it is critical to retain perspective on the magnitude of clinical benefit provided by smoking cessation. The financial and societal effects of continued smoking are profound with annual estimates of $1 trillion in economic damages internationally and nearly $300 billion in health care costs in the United States alone.[14] Long-term follow-up of nearly 1 million people shows that current smoking substantially increases mortality, but lung cancer caused a relatively small percentage of deaths (7%), comparable to stroke (7%) but less than 23% for ischemic heart disease and 8% for other heart diseases.[6] LDCT in the absence of effective methods for smoking cessation would appear to limit access to a proven method to improve premature mortality. As LDCT advances, efforts to reduce the burden of lung cancer should be coupled with continued efforts to reduce overall risks for premature mortality. Plenty of room exists for improvement and progress, not only in the setting of LDCT screening, but in general medicine clinics, cancer hospitals, and society at large. Results from Tremblay et al.[8] assist in refining efforts to improve smoking cessation in combination with LDCT and support the need for continued investigation on effective methods to improve overall health.

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