

Q&A: Ned Sharpless on COVID-19 and Cancer Prevention



The pandemic has raised concerns about cancer screening, while also presenting research opportunities.



Norman E. "Ned" Sharpless, M.D.
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Over the past year, the COVID-19 pandemic has affected every facet of oncology care, including cancer prevention efforts. NCI (Bethesda, MD) director Norman E. "Ned" Sharpless recently shared his thoughts on COVID-19 and cancer screening and diagnosis, and outlined key research questions that have emerged during the pandemic.

His conversation with *Cancer Prevention Research* Editor-in-Chief Michael Pollak, director of the Division of Cancer Prevention in the Department of Oncology at McGill University in Montreal, Canada, also touched on other aspects of cancer prevention, including lung cancer screening and modifiable risk factors.

What are your concerns about COVID-19 and cancer screening?

This is an area of tremendous concern. Very disparate sets of data from academic medical centers, electronic health records, CMS claims, and NCI networks, are coming together and giving a common answer, which is that the pandemic has affected cancer screening in a dramatic way. During the height of the pandemic last spring and summer, cancer screenings—mammography, PAP smears, low-dose CT screening for lung cancer, colonoscopy, and other colorectal cancer screening tests—were down on the order of 95% across the country. How long that stayed down and how quickly that's recovering is still an area of scientific interest, but this has created a massive screening deficit over the last 12 months—millions of screening events have been missed, and it's unlikely we have the infrastructure to fully catch up. I think this is going to lead to cancers being diagnosed at later stages. The other bad piece of news is that diagnoses of cancer were down on the order of 50% for several months during the pandemic. There's no reason to believe that the incidence of cancer is down that much; we just think those cancers are going to become apparent at a later stage.

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You're saying patients with symptoms are not seeking care?

Right. This is an important point. I think screening has gotten a lot of the focus because it's familiar to patients, but most cancers get diagnosed when a symptomatic patient seeks evaluation, and those diagnoses are down, too. We've seen decreased rates of diagnosis for pancreatic cancer and other malignancies that are not typically screen detected. So, we believe that decreased diagnosis is, in part, from screening, but it's also from patients not going to the doctor for symptomatic evaluation.

An optimistic spin on this would be that a lot of screen-detected cancers are indolent, and if you diagnose them 6 months or a year later, that's not going to be a big deal. But I think you would really have to be a Pollyanna to think that the 50% decline in cancer diagnoses is all just screen-detected, insignificant cancers. I think most of us, including me, believe that this is the substrate for diagnosis at a later stage. One piece of evidence I've already seen is from a single institution showing that there was a big drop in low-dose CT screening during the pandemic, and now that they're starting to screen again, they're finding bigger lung nodules than they used to.

How will the NCI use this unfortunate "experiment of nature" to study cancer screening?

We've worked hard to get the word out regarding our concerns about missed screening and diagnosis. The good news is that I think most caregivers are now aware of this problem and talking about solutions. Groups like the American Society of Clinical Oncology, the American Society for Radiation Oncology, the American Association of Cancer Institutes, the National Comprehensive Cancer Network, the American College of Surgeons, and others have started to put out recommendations about how we can do screening and cancer care during the pandemic. The American Cancer Society has a big return-to-screening initiative, and academic institutions and cancer centers have reopened and are trying to catch up. The NCI is a research organization, so our main objective now is to ask the critical research questions that this pandemic has raised, including those related to screening and prevention. One question is: What is the value of at-home screening? This includes self-collection for cervical sampling and for colon cancer detection kits. We have already seen some data that, although colonoscopy was dramatically affected by the pandemic, self-collection was not really affected in some places. I think that's a promising thing to learn. If we can enhance screening through at-home sampling, particularly for difficult-to-reach and underrepresented populations, we might do a better job of screening.

Another question is: Can we use this dramatic pause in screening to study overdiagnosis and overtreatment? Such

trials are very hard to do because they are massive and require many years of observation. I think it would be a missed opportunity if the NCI did not take the dramatic change in screening behavior caused by an act of nature to try to understand the role of cancer screening in discerning indolent from aggressive malignancy.

Do you expect the resumption of screening to be homogeneous across all populations?

It's an interesting question. Clearly, coronavirus incidence and mortality has disproportionately been felt by certain underserved populations in the United States, particularly African American and Hispanic patients. One also wonders whether the disruption in cancer screening, diagnosis, and treatment has been uniformly felt across all populations, or whether there are people experiencing a double whammy of coronavirus and decreased access to cancer care. I'd say that's still an open research question. I've seen some Centers for Disease Control and Prevention (CDC; Atlanta, GA) data that suggest screening was pretty much wiped out for everybody. There may be a hint now in some of the data that screening for African American and white patients has resumed at a greater rate than for, say, American Indian patients. So, there appear to be some disparity issues emerging with the return to screening, although that bears watching—the data are early and the sample sizes are still small. I have been saying a lot lately that if you're an implementation scientist, your moment has arrived. That's because the pandemic has provided an opportunity to address some important research questions: Why does this happen? How do you address a problem like that?

Changing gears, is there a concern that SARS-CoV-2 could increase cancer risk?

That's an interesting topic given that about a third of human cancers worldwide are associated with a viral infection. Often, it's a virus that integrates in the host genome or exists episomally, but not in all cases. For example, with some types of viral hepatitis, it appears that the virus itself is not driving the cancer as much as the inflammation and fibrosis promoted by the virus. So, the effects of viruses on cancer can be somewhat indirect. I think this is an important research question. I would not expect coronaviruses to cause cancer, but I don't think expectations should drive what we do—we really have to pay attention to this issue.

There are a number of ways that we can study this. The NCI and other parts of the NIH (Bethesda, MD) have prospectively identified longitudinal cohorts that we'll be able to follow to see whether there are unexplained or adverse long-term effects related to coronavirus. Most of the focus right now is on so-called long COVID (i.e., post-acute sequelae of COVID or PASC), but I think those same cohorts will be valuable for looking at secondary diseases like malignancy. We have some registry studies that may be valuable as well. Often with epidemiologic studies, the problem is that there are not enough cases, but that is not the issue with coronavirus.

Moving beyond COVID-19, what are your thoughts on the expansion of the U.S. Preventive Services Task Force (USPSTF) lung cancer screening guidelines?

When Cancer Intervention and Surveillance Modeling Network (CISNET) researchers showed me their modeling efforts, I asked them, "What is going to happen to lung cancer in the next 50 years?" I was thinking about tobacco control and new therapies, but what I hadn't understood is that the opportunity presented by lung cancer screening is significant. We can make a big difference in lung cancer mortality if we get broad adoption, and the data for this are not subtle: Large randomized trials in the United States and Europe have shown that lung cancer screening is something we ought to do, and CISNET has done its modeling about who exactly should be the relevant population, which is what led to the recent change to the U.S. Preventive Services Task Force (USPSTF) recommendations. That change will increase the number of people eligible for screening on the order of a factor of 2, including many more women and underrepresented minority patients—African American patients, in particular. So, I think this is all headed in the right direction. The technology is clearly ready, and we have a proven modality to reduce mortality, so we just have to get people to do it. Hopefully the new USPSTF announcement, which got a lot of favorable attention, will get some patients asking their doctors whether they should be screened.

Of course, we're also worried about overdiagnosis or overtreatment, and then there is this moral hazard of, "I can keep smoking if I get screened." I think data will be emerging in the not-too-distant future that shows any kind of lung cancer screening program is much better if it's paired with cessation efforts. Even if cessation therapies are moderately effective when paired with screening, the impact on lung cancer diagnosis and other nonmalignant diseases is huge. I think we as caregivers have to try to incentivize broad adoption of paired screening and cessation.

How else can we help people understand and minimize their cancer risk?

Education is a very important part of this messaging. The CDC and the FDA have funds that are appropriated to them for educational initiatives, as do local public health authorities, and I'm a big believer in those efforts. The NCI's role is in measuring the impacts of these efforts. But is there more we could do? Or are there different things we could do?

I believe that obesity probably is not getting enough attention in the United States. The ability of obesity to induce cancer is often the fifth thing people think about with obesity, but it is becoming a very important modifiable risk factor for cancer in the United States, and it may soon be the leading modifiable risk factor. The cancers that are increasing in incidence are, for the most part, those associated with obesity. This is a topic where I think more education is needed, but frankly more science is needed. We need more effective approaches to help patients deal with obesity, and we need to better understand why it happens in the first place.

Is there anything else you'd like to mention about cancer prevention?

Maybe the last thing to say is, we have a new administration that is very focused on cancer, and has made a lot of very strong statements about cancer, including President

Joe Biden saying that we would like to end cancer as we know it. I think any success in that regard will involve prevention and screening—that kind of goal will only happen by dramatically reducing the incidence of cancer through prevention measures.

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