

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to the Editor

Pausing cancer screening during the severe acute respiratory syndrome coronavirus 2pandemic: Should we revisit the recommendations?



Moran Amit ^{a,*}, Samantha Tam ^b, Tarif Bader ^c, Alex Sorkin ^{c,e}, Avi Benov ^{c,d}

^a Department of Head and Neck Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

^b Department of Otolaryngology, Henry Ford Health System and the Henry Ford Cancer, Detroit, MI, USA

^c Israel Defense Forces, Medical Corps, Tel Hasomer, Ramat Gan, Israel

^d The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel

^e Department of Plastic and Reconstructive Surgery, Shamir Medical Centre, Zrifin, Israel

Received 16 April 2020; accepted 17 April 2020 Available online 20 May 2020

There is already broad recognition of the challenges of cancer screening during the COVID-19 pandemic. However, if the current situation last, we anticipate that thousands of cases will be diagnosed late or in some cases will be missed. Herein, we discuss the ramifications of pausing cancer screening programs and turn a spotlight to advocate for maintaining the early detection programs running. This will hopefully prevent a 'cancer boom' that will meet an exhausted health system after the SARS-CoV-2 pandemic will subside.

Dear Editor

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which originated in Wuhan, China in late 2019, has become a major concern all over the world. By March 11, 2020, the number of cases of SARS-CoV-2 infection outside China had increased 13-fold, and the number of affected countries had tripled. With more than 118,000 people affected by

* Corresponding author.

https://doi.org/10.1016/j.ejca.2020.04.016 0959-8049/© 2020 Elsevier Ltd. All rights reserved. the virus worldwide and 4291 deaths, the World Health Organization announced that the outbreak of coronavirus disease 2019 (COVID-19) was a pandemic [1]. Shortly after the pandemic declaration, medical boards and societies released guidelines stating that medical professionals should use their clinical judgement when scheduling elective surgeries and procedures [2]. As shortages of personal protective equipment aggravated the insufficiencies of healthcare systems, many hospital and healthcare providers decided to stop all elective activity, including cancer screening [3].

The role of cancer screening in early detection and its impact on survival is well documented in breast, cervical, lung, and colorectal cancers [4]. Consequently, insurers and health officials use cancer screening participation rates as an index for the quality of care. As a result, the number of people screened for cancer and diagnosed at an early stage has been growing steadily [4]. For the first time, cancer screening has been globally interrupted. As the number of new COVID-19 cases, related deaths, and affected countries increases, interruptions of cancer screening schedules are expected to last [5]. This presents oncologists with some

E-mail address: mamit@mdanderson.org (M. Amit).

unprecedented challenges. We realize that resources will be limited until the return to a normal state and that treating established, diagnosed patients should be prioritized. However, we anticipate that the gap in cancer screening will result in delayed diagnoses, an increased proportion of patients presenting with advanced disease, delays in treatment, and, eventually, detrimental effects on survival. Here we discuss the potential ramifications of delaying cancer screening.

In the absence of data on the effects of diagnosis delays in asymptomatic individuals eventually diagnosed with cancer, our knowledge is based on the existing evidence on the effects of treatment delays. Some screenable malignancies, such as cervical and prostate cancer, are slow growing, and screening aims to detect asymptomatic precancerous lesions; in such cases, a few months' delay in diagnosis might have minimal impact on outcomes [6,7]. However, other malignancies, for instance breast and lung cancers, progress rapidly, so any delay in diagnosis or treatment risks adverse outcomes [8]. Interestingly, the literature on treatment delays in colorectal cancer is inconclusive; in accordance with some publications, delays of up to 8 months might even go unnoticed [9,10]. This further highlights the need for informed decision-making about resource sharing when the healthcare system recovers from the SARS-CoV-2 pandemic.

More than 70% of women between ages 50 and 74 in the U.S. reported a recent mammogram, and similar rates were noted in other Western countries [11,12]. There are nearly 50 million women in this age range in the U.S., which means that 1,412,000 women have mammograms each month. Based on a recent crossnational comparison of screening mammography accuracy measures, the positive predictive value (i.e., the number of screening-detected breast cancers divided by the number of recalls due to positive mammographic findings) in the U.S. is 4.9% (range: 4.8–16.7%) [13]; and the number of women who need to be recalled to undergo an invasive procedure to detect 1 breast cancer in the U.S. is 20.3 (range: 6 to 20.7) [14]. Thus, for each month that breast cancer screening programs are shut down due to the SARS-CoV-2 pandemic, 69,629 patients with breast cancer will go undiagnosed, increasing their risk for delayed treatment and poor prognosis [15].

Lung cancer is a time-sensitive malignancy; it is estimated that early-stage lung cancer diagnosis could save more than 70,000 lives a year [16]. The average 5year survival rate for lung cancer (17%) is among the lowest of all types of cancer but is higher (52%) when the disease is diagnosed at an early, asymptomatic stage. However, only 15% of lung cancer cases are diagnosed at such a stage [17]. In accordance with the U.S. Census data, 13.2% of adults aged 55–80 years nationwide are eligible for low-dose computed tomography lung cancer screening. Given national participation rates, each month approximately 25,000 adults are screened, and more than 1200 patients with positive screening results are diagnosed with lung cancer [18].

The large numbers of patients eligible for screening will make it difficult for screening programs to recuperate once they resume their normal schedules, especially as the duration of the pandemic increases. Moreover, with the large expected financial ramifications of the pandemic, funds directed towards screening efforts are at risk of being diverted to other causes even after the pandemic is over. At first glance, the cost of screening programs appears higher than delaying treatment until there is clinical evidence of disease, owing to the number needed to screen for each of the screening tests. However, previous studies have demonstrated that cost of a screening program increases the cost of care in exchange for decreased patient morbidity and mortality [19–23]. In breast, for example, cost of care with a screening program is estimated to be \$63 billion (2000 USD) more than cost of care without a screening program over 10 years [23]. However, this results in a gain of 1.7 million quality-adjusted life-years (QALYs), with an estimated incremental cost-effectiveness ratio (ICER) of \$37,000 USD per QALY. Generally, an ICER of less than \$50 000 USD per QALY is accepted as a price worth paying for a decrease in patient morbidity and mortality. Lung cancer screening programs have also been demonstrated to be cost-effective, with an estimated ICER of \$49,200 USD per QALY [22]. Thus, although cancer screening efforts result in increased upfront expenses, the longer term benefits to patient quality of life and longevity need to be considered.

As the duration of the SARS-CoV-2 pandemic increases, the backlog of patients awaiting their routine screening will also increase. In the intervening time period, patients may develop clinical disease, and we may face an increasing proportion of patients presenting with advanced-stage breast and lung cancer that will require multimodal treatment and will cause increased morbidity and mortality. Although the absolute costs of screening efforts exceed those of no screening, consideration of the quality life-years gained is essential to the long-term wellness of the population. The SARS-CoV-2 pandemic has created a new reality that many of us have not experienced before. Given the amount of uncertainty, the aggressive response of most health authorities was needed. Today, a few weeks into the crisis, as data accumulates, we still do not know how long the pandemic will last, and this 'knee-jerk' response should be revisited. Considering the lower mortality rate of COVID-19 than of breast or lung cancer in similarly aged populations, the postponement of timesensitive screening tests should be avoided or at list minimized. As resources are diverted to treat the acute needs of patients with COVID-19, a thoughtful approach is needed to determine how to allocate any remaining resources to usual healthcare functions. Especially in the aftermath of the pandemic, we can expect a large surge in healthcare activity as systems attempt to play 'catch-up' for the months

dedicated to fighting the pandemic. It is easy to imagine that cancer screening may become a low priority and be further deferred. However, considering the prognostic effect, costutility ramifications, and the large populations affected, cancer screening needs to be continually brought to the table when considering how to allocate rare resources. Risk stratification strategies may need to be refined and used to triage patients within disease systems to identify those who might benefit most from screening efforts. Most importantly, cross-disciplinary discussions need to be open and collaborative to allow for an organized and thoughtful plan to optimally distribute resources for the benefit of the population. Cancer screening programs may need to merge their efforts to jointly prioritize screening resources to minimize long-term morbidity and mortality for the largest group of patients at the lowest cost.

Funding

Nothing declared.funding.

Conflict of interest statement

The authors declare no conflict of interest

Acknowledgement

The authors thank Amy Ninetto of the Department of Scientific Publications at The University of Texas MD Anderson Cancer Center for editing the manuscript.

References

- WHO Director-General's opening remarks at the media briefing on COVID-19 [Internet][cited 2020 Apr 2] Available from: https://www. who.int/dg/speeches/detail/who-director-general-s-opening-remarksat-the-media-briefing-on-covid-19—11-march-2020; 11 March 2020.
- [2] Radiology preparedness for COVID-19: radiology scientific expert review panel - YouTube [Internet][cited 2020 Apr 2] Available from: https://www.youtube.com/watch?v=1T98zMYxrKU.
- [3] News article | ASBrS [Internet][cited 2020 Apr 2] Available from: https://www.breastsurgeons.org/news/?id=45.
- [4] Smith RA, Andrews KS, Brooks D, Fedewa SA, Manassaram-Baptiste D, Saslow D, et al. Cancer screening in the United States, 2019: a review of current American Cancer Society guidelines and current issues in cancer screening [Internet] CA Cancer J Clin 2019;69:184–210 [cited 2020 Apr 2] Available from: http://www. ncbi.nlm.nih.gov/pubmed/30875085.
- [5] COVID-19 map Johns Hopkins coronavirus resource center [Internet][cited 2020 Apr 2] Available from: https://coronavirus. jhu.edu/map.html.
- [6] Perri T, Issakov G, Ben-Baruch G, Flder S, Beiner ME, Helpman L, et al. Effect of treatment delay on survival in patients with cervical cancer: a historical cohort study [Internet] Int J Gynecol Cancer 2014;24:1326–32 [cited 2020 Apr 2] Available from: http://www.ncbi.nlm.nih.gov/pubmed/25054445.
- [7] Castellsagué X. Natural history and epidemiology of HPV infection and cervical cancer [Internet] Gynecol Oncol 2008;110:

S4-7 [cited 2020 Apr 2] Available from: http://www.ncbi.nlm.nih. gov/pubmed/18760711.

- [8] Yousaf-Khan U, Van Der Aalst C, De Jong PA, Heuvelmans M, Scholten E, Lammers JW, et al. Final screening round of the NELSON lung cancer screening trial: the effect of a 2.5-year screening interval [Internet] Thorax 2017;72:48–56 [cited 2020 Apr 2] Available from: http://www.ncbi.nlm.nih.gov/pubmed/ 27364640.
- [9] Pruitt SL, Harzke AJ, Davidson NO, Schootman M. Do diagnostic and treatment delays for colorectal cancer increase risk of death? Cancer Causes Control 2013;24:961–77.
- [10] Pita-Fernández S, González-Sáez L, López-Calviño B, Seoane-Pillado T, Rodríguez-Camacho E, Pazos-Sierra A, et al. Effect of diagnostic delay on survival in patients with colorectal cancer: a retrospective cohort study [Internet] BMC Cancer 2016;16:664 [cited 2020 Apr 2] Available from: http://www.ncbi.nlm.nih.gov/ pubmed/27549406.
- Breast cancer screening | cancer trends progress report [Internet] [cited 2020 Apr 2] Available from: https://progressreport.cancer. gov/detection/breast_cancer.
- [12] Hall IJ, Tangka FKL, Sabatino SA, Thompson TD, Graubard BI, Breen N. Patterns and trends in cancer screening in the United States [Internet] Prev Chronic Dis 2018;15:170465 [cited 2020 Apr 2] Available from: http://www.cdc.gov/pcd/issues/ 2018/17_0465.htm.
- [13] Lehman CD, Arao RF, Sprague BL, Lee JM, Buist DS, Kerlikowske K, et al. National performance benchmarks for modern screening digital mammography: update from the Breast Cancer Surveillance Consortium [Internet] Radiology 2017;283: 49–58 [cited 2020 Apr 2] Available from: http://www.ncbi.nlm. nih.gov/pubmed/27918707.
- [14] Domingo L, Hofvind S, Hubbard RA, Román M, Bankeser D, Sala M, et al. Cross-national comparison of screening mammography accuracy measures in U.S., Norway, and Spain [Internet] Eur Radiol 2016;26:2520–8 [cited 2020 Apr 2] Available from: http://www.ncbi.nlm.nih.gov/pubmed/26560729.
- [15] Li Y, Zhou Y, Mao F, Guan J, Lin Y, Wang X, et al. The influence on survival of delay in the treatment initiation of screening detected non-symptomatic breast cancer [Internet] Sci Rep 2019;9: 10158 [cited 2020 Apr 2] Available from: http://www.ncbi.nlm.nih. gov/pubmed/31308467.
- [16] Goldberg SW, Mulshine JL, Hagstrom D, Pyenson BS. An actuarial approach to comparing early stage and late stage lung cancer mortality and survival. Popul Health Manag 2010;13: 33-46.
- [17] Screening for lung cancer: systematic review to update the U.S. Preventive services task force recommendation. PubMed - NCBI [Internet][cited 2020 Apr 2] Available from: https://www.ncbi.nlm. nih.gov/pubmed/24027793.
- [18] Lung cancer screening | cancer trends progress report [Internet] [cited 2020 Apr 2] Available from: https://progressreport.cancer. gov/detection/lung_cancer.
- [19] Rim SH, Allaire BT, Ekwueme DU, Miller JW, Subramanian S, Hall IJ, et al. Cost-effectiveness of breast cancer screening in the national breast and cervical cancer early detection program [Internet] Cancer Causes Control 2019;30:819–26 [cited 2020 Apr 4] Available from: http://www.ncbi.nlm.nih.gov/pubmed/ 31098856.
- [20] Ralaidovy AH, Gopalappa C, Ilbawi A, Pretorius C, Lauer JA. Cost-effective interventions for breast cancer, cervical cancer, and colorectal cancer: new results from WHO-CHOICE 11 medical and health sciences 1117 public health and health services 11 medical and health sciences 1112 oncology and carcinogenesis [Internet] Cost Eff Resour Alloc 2018;16:38 [cited 2020 Apr 4] Available from: http://www.ncbi.nlm.nih.gov/pubmed/30450014.
- [21] Arnold M. Simulation modeling for stratified breast cancer screening - a systematic review of cost and quality of life assumptions [Internet] BMC Health Serv Res 2017;17:802 [cited

2020 Apr 4] Available from: http://www.ncbi.nlm.nih.gov/pubmed/29197417.

- [22] Criss SD, Cao P, Bastani M, Ten Haaf K, Chen Y, Sheehan DF, et al. Cost-effectiveness analysis of lung cancer screening in the United States. Ann Intern Med 2019;171:796–804.
- [23] Stout NK, Rosenberg MA, Trentham-Dietz A, Smith MA, Robinson SM, Fryback DG. Retrospective cost-effectiveness analysis of screening mammography [Internet] J Natl Cancer Inst 2006;98 [cited 2020 Apr 4] Available from: http://www.cdc.gov/ nchs/nhis.htm.