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Impact Of Early Detection On Cancer Curability

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Abstract

Consensus among experts regarding the potential advantages of early cancer detection is lacking across many cancer types. To address this gap, we assembled a panel of 10 practicing oncologists using a modified Delphi method based on RAND/UCLA guidelines. This panel evaluated 20 solid tumors, representing over 40 types of cancer identified by the American Joint Committee on Cancer (AJCC) and accounting for 80% of total cancer incidence, to determine which could benefit from early detection.

Before the panel meeting, experts provided estimates on the progression rates of various cancers and assessed the current curability and potential benefits (improvement in curability) of an annual multi-cancer screening blood test. Following the meeting, experts reassessed their initial estimations.

The findings revealed diverse perspectives on the potential benefits of early cancer detection, influenced by factors such as cancer stage progression and curability. Cancers deemed to progress rapidly and have high curability in early stages (e.g., stomach, eso[1]phagus, lung, urothelial tract, melanoma, ovary, sarcoma, bladder, cervix, breast, colon/rectum, kidney, uterus, anus, head and neck) were considered most likely to benefit from a screening blood test. Conversely, cancers with rapid progression but lower curability in early stages (e.g., liver/intrahepatic bile duct, gallbladder, pancreas) were seen as having moderate potential for benefit.

Cancers characterized by slower progression and high curability regardless of stage (e.g., prostate, thyroid) were viewed as having limited potential for benefit from early detection strategies. Nevertheless, the panel concluded that most solid tumors, including challenging-to-

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treat ones like pancreatic and liver/bile duct cancers, could still benefit from early-stage detection.

The consensus suggests that a comprehensive screening approach covering a wide range of cancers through blood tests holds significant potential to improve patient outcomes.

Introduction

Cancer remains a significant health concern, with an estimated 1.9 million new diagnoses projected in the United States (US) in 2022, making it the second leading cause of death with over 600,000 fatalities in 2020.

Early detection plays a crucial role in cancer prevention and reducing mortality rates. Screening aims to detect cancers or precursors early, thereby improving treatment outcomes. Current screening methods include imaging (like digital mammography), serial exams (such as colonoscopies), and tissue sampling (like Pap tests), along with individualized serum marker tests (such as the prostate-specific antigen [PSA] test). Emerging approaches include blood-based screening, including multi-cancer tests that can potentially detect multiple cancer types simultaneously. (Siegel et al., 2022)

Screening programs have demonstrated mortality reductions, such as a decrease in breast cancer mortality with mammography and a reduction in cervical cancer mortality with cytology-based screening according to a US Preventive Services Task Force (USPSTF) meta-analysis. Similarly, sigmoidoscopy screening has been associated with a decrease in colorectal cancer mortality as reported by the International Agency for Research on Cancer (IARC). Early detection, as highlighted by studies using Surveillance, Epidemiology and End Results (SEER) data, could substantially reduce cancer deaths, especially if cancers can be detected at even earlier stages. (Beer, 2020)

However, not all screening tests lead to reduced mortality. Data from SEER on thyroid, kidney, and melanoma cancers show increased diagnosis rates without corresponding increases in deaths, suggesting potential overdiagnosis and a lead time bias. (Clarke et al., 2020)

The effectiveness of early detection varies among cancer types. Screening has been successful in cancers like colon and cervical, where precursor lesions are detectable and treatable, but remains challenging for cancers like anal, where a significant portion of cases occur in individuals without perceived risk factors. (Srivastava et al., 2019)

Given these complexities, we sought expert insights from oncologists to determine which cancer types might benefit most from early detection and to understand the factors driving these differences. (Tomassi et al., 2019)

Methods

Our panel consisted of 10 experts, a size recommended by the RAND/UCLA Appropriateness Method guidelines to ensure diversity and active participation. Experts were selected based on their broad and diverse oncology experience, representing various geographic regions and practice settings . They had an average of 20 years of clinical practice, encompassing academic, community, and combined settings, and represented different regions and oncology subspecialties.

Expert panelists provided written informed consent and received honoraria for their participation.

Before the meeting, we developed a comprehensive questionnaire through individual phone interviews. This questionnaire aimed to gather expert insights on which cancers may benefit most from early detection, particularly through a hypothetical multi-cancer screening blood test. Experts assessed each cancer's curability at various stages and its progression rate. They also evaluated the risk of overdiagnosis.

Curability and progression were rated on scales, with experts referring to SEER data for guidance. Additionally, experts estimated the potential benefit of an annual screening blood test for patients aged 50 years and older, assuming 100% sensitivity and specificity and not replacing existing screening tests. They considered both typical and best available care standards.

Experts evaluated curability and progression across stages I to IV for 20 solid organ cancers, covering a wide range of cancer types. Subtypes were not considered. Ratings were completed before and after a panel meeting, where disagreements were discussed and consensus statements were developed.

The group consensus statements from the second-round ratings were reviewed and approved by all experts.

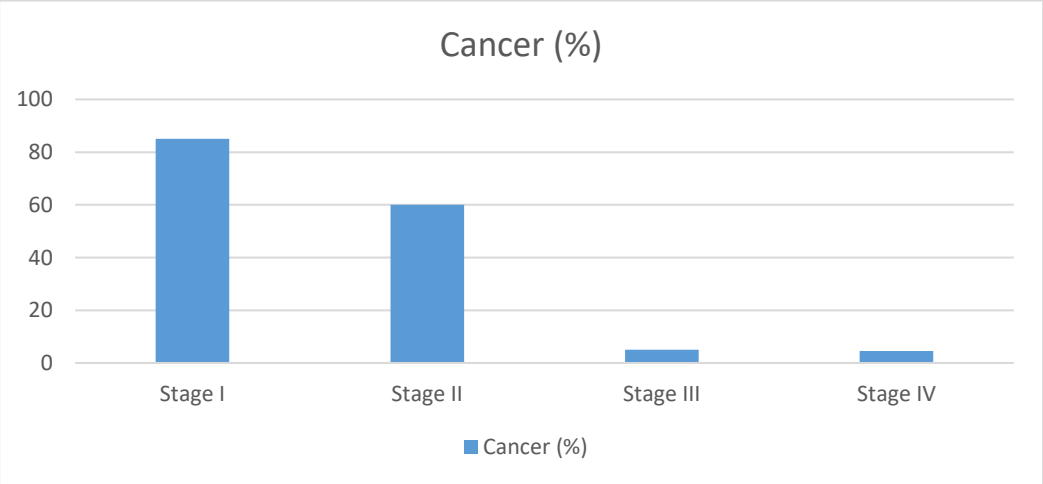
Results

Following a group discussion, panelists reached consensus on 99% of the 540 ratings, compared to 13% disagreement after the initial ratings.

Cancer Curability and Progression

Experts rated the curability of cancers across stages as follows:

- 85% (n = 17) of cancers were rated as somewhat likely to extremely likely to be cured in stage I.
- 60% (n = 12) in stage II were rated similarly.
- Only 5% (n = 1) in stage III were considered curable.
- None were rated as curable in stage IV.



Experts estimated the preclinical progression of cancer as provided in Table 2. Prostate and thyroid cancers were perceived as the slowest growing, taking about 7 and 5 years, respectively, to progress through stage I, 5 years for stage II, and 3 and 4 years, respectively, for stage III. On the other hand, esophageal, lung, liver/intrahepatic bile duct, gallbladder, and pancreatic cancers were seen as progressing rapidly through stages I to III (1 to 2 years per stage).

Benefit from Early Detection

Experts identified three groups of cancers regarding the potential benefit from early detection. Cancers that progress quickly and are currently considered curable were seen as benefiting the most from early detection, encompassing 75.0% of all rated cancers. These included stomach, esophagus, lung, urothelial tract, melanoma, ovary, sarcoma, bladder, cervix, breast, colon/rectum, kidney, uterus, anus, and head and neck. Cancers that progress but are less curable (liver/intrahepatic bile duct, gallbladder, pancreas) were rated as potentially showing some benefit. However, cancers that progress slowly and are curable (prostate, thyroid) were not expected to benefit significantly from early detection.

Typical Treatment versus Best Available Care

Panelists generally perceived a higher benefit from early detection when best-available care was provided compared to typical care, particularly evident in stages II and III

Table 1 Median (range) rating scores of the likelihood of cancer curability today.

Cancer Type	Stage I	Stage II	Stage III	Stage IV
Thyroid	9 (8–9)	8 (7–9)	7 (6–9)	5 (1–7)
Colon/Rectum	9 (8–9)	8 (7–8)	5 (3–6)	1.5 (1–3)
Kidney	9 (7–9)	8 (6–8)	5 (4–6)	2 (1–2)
Uterus	9 (8–9)	8 (7–8)	5 (5–7)	1 (1–3)
Anus	9 (8–9)	8 (6–8)	5 (5–7)	1 (1–3)
Head and Neck	9 (7–9)	7.5 (6–8)	5 (3–6)	3 (1–5)
Breast	9 (7–9)	7.5 (6–8)	5.5 (4–6)	1 (1–2)
Cervix	9 (8–9)	7 (6–8)	5 (4–6)	1 (1–3)
Melanoma	9 (8–9)	7 (6–8)	4 (3–6)	1.5 (1–8)
Prostate	8.5 (7–9)	8 (7–9)	5.5 (4–8)	1 (1–5)
Sarcoma	8 (6–8)	7 (4–7)	4 (2–5)	1 (1–2)
Ovary	8 (7–9)	7 (5–8)	3 (2–5)	1 (1–3)
Bladder	8.5 (7–9)	6.5 (6–8)	4 (3–5)	1 (1–2)
Urothelial Tract	8 (6–9)	5.5 (5–7)	4 (3–5)	1.5 (1–3)
Lung	7 (6–9)	5 (3–8)	3 (1–5)	1 (1–2)
Stomach	7 (6–8)	4.5 (2–7)	2 (1–5)	1 (1–1)
Esophagus	7 (5–8)	4 (3–7)	2 (1–5)	1 (1–1)
Gallbladder	5 (4–6)	3 (2–5)	2 (1–3)	1 (1–1)
Liver/Intrahepatic Bile Duct	4 (2–7)	3 (2–7)	1.5 (1–5)	1 (1–1)
Pancreas	4 (3–7)	2.5 (1–5)	1 (1–3)	1 (1–1)

Table 2 Estimated median (range) number of years for each cancer type to progress from one stage to the next.

Cancer Type	Stage I	Stage II	Stage III

Prostate	7 (5–8)	5 (4–6)	3 (2–5)
Thyroid	5.5 (4–8)	5 (3–7)	4 (2–5)
Kidney	5 (<1–7)	3 (<1–5)	2 (<1–2)
Uterus	4 (3–5)	3 (<1–5)	1.5 (<1–3)
Cervix	4 (<1–5)	2.5 (<1–4)	<1 (<1–2)
Colon/Rectum	3.5 (2–5)	3 (2–5)	<1 (<1–2)
Sarcoma	3.5 (<1–6)	2 (<1–4)	<1 (<1–2)
Breast	3 (2–4)	2 (<1–3)	1.5 (<1–2)
Melanoma	3 (<1–5)	2 (<1–4)	<1 (<1–2)
Head and Neck	3 (2–6)	2 (<1–4)	<1 (<1–2)
Bladder	3 (2–5)	2 (<1–5)	<1 (<1–2)
Ovary	3 (<1–3)	2 (<1–2)	<1 (<1-<1)
Stomach	3 (2–5)	2 (<1–2)	<1 (<1–2)
Urothelial Tract	3 (2–7)	2 (2–5)	<1 (<1–4)
Anus	3 (2–7)	2 (2–5)	<1 (<1–3)
Esophagus	2.5 (2–5)	<1 (<1–2)	<1 (<1–2)
Lung	2 (2–3)	<1 (<1–2)	<1 (<1-<1)
Liver/Intrahepatic Bile Duct	2 (<1–3)	<1 (<1–2)	<1 (<1-<1)
Gallbladder	2 (<1–3)	<1 (<1-<1)	<1 (<1-<1)
Pancreas	<1 (<1–2)	<1 (<1–2)	<1 (<1-<1)

Discussion

The panel consensus emphasized the potential benefits of early cancer detection across most solid tumors, with exceptions noted for prostate and thyroid cancers, which are generally associated with good long-term survival rates even when diagnosed early. This aligns with existing medical practice and screening recommendations, highlighting the importance of tailored screening strategies based on cancer type and individual risk factors. (Rocque et al., 2018)

Cancers that were identified as most likely to benefit from early detection were those with rapid progression and a high likelihood of curability in earlier stages. These included a range of cancers such as anus, bladder, breast, cervix, colon/rectum, esophagus, head and neck, kidney, lung, melanoma, ovary, sarcoma, stomach, urothelial tract, and uterus. Notably, many of these cancers lack established screening tests, and their curability varies significantly by the stage of diagnosis. For instance, ovarian cancer exhibited a high likelihood of curability in stage I but a substantially lower likelihood in stage III. This pattern was consistent across several cancers without established screening protocols. (Richardson et al., 2018)

Experts also recognized the potential benefits of early detection for pancreatic, gallbladder, and liver/intrahepatic bile duct cancers, albeit to a lesser extent compared to the aforementioned cancers. These cancers face challenges in survival outcomes, particularly when diagnosed at later stages. Early detection could offer opportunities for improved treatment efficacy, especially considering the advancements in treatment options for early-stage cancers over time. (Spees et al., 2019)

Prostate and thyroid cancers were deemed less suitable for early detection screening programs. These cancers have shown good long-term survival rates, especially in stages I and II, and screening may lead to overdiagnosis and unnecessary interventions. Current screening

guidelines and recommendations reflect these considerations, advocating for a balanced approach to screening that considers individual risk factors and preferences. (Singhi et al., 2019)

The discussion also touched on the importance of providing best-available care alongside early detection efforts. Panelists noted that optimal treatment strategies, particularly in stages II and III, could significantly enhance the benefits of early detection. However, they acknowledged that guideline-concordant care is not always consistently delivered across all cancer types and stages, highlighting the need for improvements in healthcare delivery and access to specialized care. (Lamartina et al., 2020)

While discussing the potential benefits of multi-cancer screening blood tests, experts weighed the benefits against potential harms such as false positives and increased costs. They recognized the value of convenience and accessibility offered by such tests but emphasized the importance of maintaining screening specificity to minimize unnecessary interventions and associated harms. (Hugosson et al., 2019)

This study's limitations include its reliance on expert opinion rather than objective data on mortality rates from screening tests. The expert panel's composition, primarily from the US, may also limit the generalizability of the findings to other regions with different cancer burdens and healthcare systems. Further research with a broader expert representation and inclusion of granular cancer subtypes could provide additional insights into the complexities of early cancer detection strategies. (Shoag et al., 2020)

Conclusion

In summary, the panel emphasized the potential for enhancing cancer treatment outcomes by detecting cancers earlier. This notion is supported by both clinical trials and real-world evidence, which consistently show improved survival rates with early detection. Even for challenging cancers like pancreas, liver/intrahepatic bile duct, and gallbladder cancers, early-stage detection was seen as beneficial. The consensus among the panel members suggests that expanding the coverage of cancer types in screening tests would offer substantial advantages to patients.

References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72:7–33. doi: 10.3322/caac.21708
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020;70:7–30. doi: 10.3322/caac.21590
3. Beer TM. Novel blood-based early cancer detection: diagnostics in development. Am J Manag Care. 2020;26(14 Suppl):S292–9. doi: 10.37765/ajmc.2020.88533
4. Gøtzsche PC, Nielsen M. Screening for breast cancer with mammography. Cochrane Database Syst Rev. 2011. Jan 19;(1):CD001877. doi: 10.1002/14651858.CD001877.pub4
5. Pace LE, Keating NL. A systematic assessment of benefits and risks to guide breast cancer screening decisions. JAMA. 2014;311:1327–35. doi: 10.1001/jama.2014.1398
6. US Preventive Services Task Force, Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, et al. Screening for cervical cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2018;320:674–86. doi: 10.1001/jama.2018.10897
7. Lauby-Secretan B, Vilahur N, Bianchini F, Guha N, Straif K, International Agency for Research on Cancer Handbook Working Group. The IARC Perspective on Colorectal Cancer Screening. N Engl J Med. 2018;378:1734–40.
8. Clarke CA, Hubbell E, Kurian AW, Colditz GA, Hartman A-R, Gomez SL. Projected reductions in absolute cancer–related deaths from diagnosing cancers before metastasis, 2006–2015. Cancer Epidemiol Prev Biomark. 2020; 29:895–902. doi: 10.1158/1055-9965.EPI-19-1366

9. Welch HG, Black WC. Overdiagnosis in cancer. J Natl Cancer Inst. 2010;102:605–13. doi: 10.1093/jnci/djq099
10. Carter SM, Barratt A. What is overdiagnosis and why should we take it seriously in cancer screening? Public Health Res Pract. 2017. Jul 26;27(3):2731722. doi: 10.17061/phrp2731722
11. Srivastava S, Koay EJ, Borowsky AD, De Marzo AM, Ghosh S, Wagner PD, et al. Cancer overdiagnosis: a biological challenge and clinical dilemma. Nat Rev Cancer. 2019;19:349–58. doi: 10.1038/s41568-019-0142-8
12. Pinsky PF. An early- and late-stage convolution model for disease natural history. Biometrics. 2004;60:191–8. doi: 10.1111/j.0006-341X.2004.00023.x
13. Landy R, Pesola F, Castañón A, Sasieni P. Impact of cervical screening on cervical cancer mortality: estimation using stage-specific results from a nested case-control study. Br J Cancer. 2016;115:1140–6. doi: 10.1038/bjc.2016.290
14. Tomassi MJ, Abbas MA, Klaristenfeld DD. Expectant management surveillance for patients at risk for invasive squamous cell carcinoma of the anus: a large US healthcare system experience. Int J Colorectal Dis. 2019;34:47–54. doi: 10.1007/s00384-018-3167-7
15. Fink A, Kosecoff J, Chassin M, Brook RH. Consensus methods: characteristics and guidelines for use. Am J Public Health. 1984;74:979–83. doi: 10.2105/ajph.74.9.979
16. Campbell SM. Research methods used in developing and applying quality indicators in primary care. Qual Saf Health Care. 2002;11:358–64. doi: 10.1136/qhc.11.4.358
17. Fitch K, editor. The Rand/UCLA appropriateness method user's manual. Santa Monica (CA): Rand; 2001.
18. Rocque GB, Williams CP, Kenzik KM, Jackson BE, Azuero A, Halilova KI, et al. Concordance with NCCN treatment guidelines: relations with health care utilization, cost, and mortality in breast cancer patients with secondary metastasis: effect of treatment nonconcordance. Cancer. 2018;124:4231–40.
19. Richardson PG, San Miguel JF, Moreau P, Hajek R, Dimopoulos MA, Laubach JP, et al. Interpreting clinical trial data in multiple myeloma: translating findings to the real-world setting. Blood Cancer J. 2018;8:109. doi: 10.1038/s41408-018-0141-0
20. Spees LP, Wheeler SB, Varia M, Weinberger M, Baggett CD, Zhou X, et al. Evaluating the urban-rural paradox: The complicated relationship between distance and the receipt of guideline-concordant care among cervical cancer patients. Gynecol Oncol. 2019;152:112–8. doi: 10.1016/j.ygyno.2018.11.010
21. Hundal R, Shaffer EA. Gallbladder cancer: epidemiology and outcome. Clin Epidemiol. 2014;6:99–109. doi: 10.2147/CLEP.S37357
22. Bruix J, Reig M, Sherman M. Evidence-based diagnosis, staging, and treatment of patients with hepatocellular carcinoma. Gastroenterology. 2016;150:835–53. doi: 10.1053/j.gastro.2015.12.041
23. Singhi AD, Koay EJ, Chari ST, Maitra A. Early detection of pancreatic cancer: opportunities and challenges. Gastroenterology. 2019;156:2024–40. doi: 10.1053/j.gastro.2019.01.259
24. Lamartina L, Grani G, Durante C, Filetti S, Cooper DS. Screening for differentiated thyroid cancer in selected populations. Lancet Diabetes Endocrinol. 2020;8:81–8. doi: 10.1016/S2213-8587(19)30324-9
25. Davies L, Welch HG. Current thyroid cancer trends in the United States. JAMA Otolaryngol Neck Surg. 2014;140:317–22. doi: 10.1001/jamaoto.2014.1
26. US Preventive Services Task Force, Grossman DC, Curry SJ, Owens DK, Bibbins-Domingo K, Caughey AB, et al. Screening for prostate cancer: US Preventive Services Task Force recommendation statement. JAMA. 2018;319:1901–13. doi: 10.1001/jama.2018.3710
27. Nyame YA, Gulati R, Tsodikov A, Gore JL, Etzioni R. Prostate-specific antigen screening and recent increases in advanced prostate cancer. JNCI Cancer Spectr. 2020;5(1):pkaa098. doi: 10.1093/jncics/pkaa098
28. Hugosson J, Roobol MJ, Månsson M, Tammela TLJ, Zappa M, Nelen V, et al. A 16-yr follow-up of the European Randomized study of Screening for Prostate Cancer. Eur Urol. 2019;76(1):43–51. doi: 10.1016/j.eururo.2019.02.009
29. Shoag JE, Nyame YA, Gulati R, Etzioni R, Hu JC. Reconsidering the trade-offs of prostate cancer screening. N Engl J Med. 2020;382(25):2465–8. doi: 10.1056/NEJMsb2000250