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Ethical Considerations and Implications of Multi-Cancer Early Detection Screening: Reliability, Access and Cost to Test and Treat

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Abstract

This essay focuses on the ethical considerations and implications of providing a universal multi-cancer screening test as the best approach to reduce societal cancer burden in a society with limited funds, resources, and infrastructure. With 1.9 million cancer diagnoses each year in the United States, with 86% of all cancers diagnosed in individuals over the age of 50, and with screening tools approved for only four cancer types (breast, cervical, colorectal, and lung cancer), it seems that a multi-cancer screening test to detect most cancer early that is easy to administer, and is accurate and cost-effective, would be worth considering. Whole-body magnetic resonance imaging and a multi-marker blood test are the two main technologies that we will discuss as a universal screening test. However, to understand and appreciate the societal and clinical breakthrough of such a screening test, we must first consider the accessibility and efficacy of current screening methods. We conclude with a closer examination of the ethical implications of implementing the Galleri test as a multi-cancer detection screening tool as adamantly advocated by the company that developed this blood-based test.

Keywords: cancer screening; liquid biopsy; blood-based test; cancer prevention; precision prevention

Introduction

"An ounce of prevention is worth a pound of cure."[1] This immortalized quote by Benjamin Franklin in 1736 makes the perhaps not so intuitive point that allocating resources to prevent a problem is more effective than the cost of fixing the problem. For many human diseases such as cancer, diabetes, and heart disease, there are general prevention strategies to reduce risk. Cessation or limiting exposure to tobacco products and smoke, a nutritious well-balanced diet that includes fresh fruits and vegetables with limits in red meats and high sodium consumption, physically active lifestyle, and moderate alcohol use are good behaviors to reduce disease risk. Specifically for cancer, avoiding exposure to carcinogens, cancer-promoting compounds or activities (e.g., excessive ultraviolet light exposure), and receiving immunization to cancer-promoting pathogens (e.g., Human Papillomavirus [HPV] vaccination) reduces overall cancer risks. These are the most effective and low-cost strategies that can impact the general population to reduce cancer risk.

Unfortunately, even with risk reduction of these external factors, people will still develop cancer due to genetic predisposition or other circumstances (e.g., bad luck[2,3]). There are different level strategies for reducing cancer risk, depending on how likely an individual is to develop cancer, or if a patient already has cancer.[4] As we apply these different level strategies, the population or individuals who benefit becomes smaller and smaller, and the efficacy and cost per individual increases. Cancer screening is one

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such strategy that applies to a more targeted population with an elevated risk due to age, medical history (e.g., childhood cancer survivor, radiation treatment), or tobacco products usage. The premise behind cancer screening is to detect cancer early when surgery and/or other treatments can eliminate the malignant cells. Local cancer treatment has a much better outcome than treatment of cancer that has spread or metastasized to vital organs in the body. Cancer prevention is a more selected strategy for individuals at a high risk of developing cancer due to familial history or known genetic predisposition (e.g., "BReast CAncer" [BRCA] gene mutation carriers) or with a pre-malignant condition (e.g., smoldering myeloma). In these situations, the surgical removal of the primary organ in which the cancer is likely to develop (e.g., breast and/or ovaries for BRCA gene mutation carrier), or medical treatment such as chemotherapy in smoldering myeloma, is the indicated course of action to halt the development of cancer. The most targeted strategy is precision or personalized treatment of individuals that have already developed cancer. For particular mutations, these targeted treatments can provide a better outcome and sometimes cure for patients but are often much more expensive than standard chemotherapy and radiation treatment.

This essay focuses on the ethical considerations and implications of providing a universal multi-cancer screening test as the best approach[5] to reduce societal cancer burden in a society with limited funds, resources, and infrastructure. With 1.9 million cancer diagnoses each year in the United States,[6] with 86% of all cancers diagnosed in individuals over the age of 50, and with screening tools approved for only four cancer types (breast, cervical, colorectal, and lung cancer), it seems that a multi-cancer screening test to detect most cancer early that is easy to administer, and is accurate and cost-effective, would be worth considering. Whole-body magnetic resonance imaging (MRI) and a multi-marker blood test are the two main technologies that we will discuss as a universal screening test. However, to understand and appreciate the societal and clinical breakthrough of such a screening test, we must first consider the accessibility and efficacy of current screening methods.[7]

Current screening methods and their value

Breast cancer screening by mammography (X-ray imaging) in women and colorectal cancer screening by colonoscopy (brightfield imaging) in both men and women are the most widespread and successful screening programs. Cervical cancer screening in women consists of a Pap smear test and/or HPV test in collected cervical cells, and lung cancer screen for high-risk men and women (i.e., heavy smokers) consists of low-dose helical computed tomography (X-ray imaging). There are some blood marker tests that can help detect cancer early, such as CA-125 test for ovarian cancer and PSA test for prostate cancer, but they are not broadly recommended as a screening tool.

Two important considerations for implementing a cancer screening tool are to see how well it performs and how much it costs. One way to determine how well the screen test works is the positive predictive value (PPV), that is, how likely the subject is to have cancer when the result of the test is positive. The PPV is calculated from the test sensitivity (for a particular numeric test output how many of the known individuals with cancer are correctly identified [true positive] or not [false negative]) and test specificity (for a particular numeric test output how many of the known healthy individuals are correctly identified [true negative] or not [false positive]). In a typical clinical study, a similar number of cancer patients and healthy individuals are studied to establish test performance and set a numerical threshold to call the test positive. However, in the real world, the number of healthy individuals significantly outnumbers those with cancer; cancer prevalence is about 0.5% of people over 50 and about 2% of people over 70 who are diagnosed with cancer every year in the United States. Thus, even an outstanding test with 99% sensitivity and 99% specificity when applied to a general population with only 1% cancer prevalence will have a PPV of 50%. In other words, one out of every two persons with a positive test will actually have cancer, the other person will be a false positive.

The PPV of breast cancer screening with mammography is 5%, that is, 19 false positive out of 20 individuals to detect 1 cancer patient early. Nonetheless, mammography screening may have saved more than 384,000 lives since 1990.[8] That is an impressive number when only about 50% of eligible

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women adhere to scheduled screenings. However, the process is relatively ineffective as it takes almost 3,000 women to be screened to save one life. Considering the median cost of a mammography to be about $250, it costs over $75,000 to detect one breast cancer case and over $20 billion a year to screen all eligible women.

The PPV of cervical cancer screening with pap test is about 45%. Mortality due to cervical cancer has dropped by 60% comparing data from the late 1970s to 2022. That can be attributed in part to good adherence to the screening program (Pap test cost is in the $125–$273 range), and the early age that women can be enrolled, but also to the HPV vaccination campaign launched in the mid-2000s.[9] The PPV of colorectal cancer screening with colonoscopy is an impressive 95%. Some estimates calculate that it takes about 142 persons to be screened to save one life. This is certainly a much higher number and more effective than mammography. However, part of the accuracy of colonoscopy is thanks to direct visualization of the lesions in what requires a more invasive procedure. About 1 in 100 screened individuals experience some complication, 1 in 1,000 have an intestinal perforation, and 1 in 15,000 dies during colonoscopy. Without insurance a screening colonoscopy will cost between $1,250 and $4,000.[10] It is worth noting that both for screening mammography and screening colonoscopy, additional tests are needed to make a final diagnosis of cancer that typically require more imaging procedures and a tissue biopsy.

Whole-body MRI

Annual whole-body MRI[11] has received recent interests due in part by shared experience of celebrities and movie stars.[12] MRI can typically detect a tumor mass of size larger than about 1 cm in diameter (at least 0.5 cm^3), and thus it can detect most cancers at an early stage (stage I or II). The results from recent studies showed pooled sensitivities of whole-body MRI ranging between 94% and 97%, and pooled specificities ranging between 94% and 98%,[13] what translates to a PPV of about 32% (with an estimated cancer prevalence of 1%). Some concerns with whole-body MR and similar imaging modalities are incidental findings and overdiagnosis. Some of these conditions may be indolent and not life threatening, and only revealed because the imaging study was done.[14] Several companies offer a variety of whole-body MR imaging services for early detection of cancer and other diseases.[15,16,17] The cost of these services is between $1,500 to $5,500 depending on the scanning time, organs imaged, and analysis time and depth. It is important to point out that neither of these companies is pursuing a universal cancer screening program for all individuals over 50.

Multi-marker blood test or liquid biopsy

Blood tests are the workhorse of human medicine. Many diseases can be diagnosed by changes of single marker (higher or lower than normal range) in the blood. Blood samples are easy to collect in a noninvasive and fast fashion that fits well with any routine office visit or annual checkup examination. Given the readily available blood samples and development of new technologies to detect many markers at the same time in a single sample, there has been a research explosion of tests that can detect cancer early based on a signature or combinatorial changes of selected markers. Tumors as they grow and become bigger secrete and shed more and more of their cell content (DNA, RNA, and protein) in blood. These tests aim at identifying and measuring those markers that uniquely come from the cancer cells.[18] One of the cancer cell markers that is more amenable to high-level interrogation is DNA, so called cell-free DNA (cfDNA). High-throughput sequencing techniques allow us to detect changes in the DNA, either mutations in the base composition (A, T, C, and G changes) or changes in marks that decorate and regulate the DNA (such a methylation marks involved in epigenetic regulation). Two salient multi-cancer detection (MCD) tests are CancerSeek by Exact Sciences and the Galleri test by Grail.[19] The CancerSeek test measures in blood DNA mutations from cfDNA of 16 genes known to be frequently altered in cancer as well as 8 proteins known to come from specific cancer types or organ sites.[20] The Galleri test measures in blood DNA methylation patterns from cfDNA of 100,000 gene fragments. This is

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an unprecedented large number of data points that help to determine whether cancer cell DNA is present and the most likely organ site due to specific changes in DNA methylation patterns (mostly regulatory CpG islands).[21]

These two tests follow a similar strategy to set specificity at 99% to minimize the number of false positives, that is, a positive test result in a healthy individual. This strategy is problematic for sensitivity or how many cancers are missed. Both studies with about an overall sensitivity of 60% will miss 40% of cancer cases, that is, false negatives, a negative test result in cancer patient. The best feature of both tests is that they can detect a high percentage (>70%) of aggressive cancers, such as esophageal, head and neck, ovarian, liver, stomach, and pancreatic for which there are no approved screening methods. A limitation of both tests is that they miss detection of many tumors at stage I (<40% sensitivity). Note that the lower the stage of the tumor, the better the impact on treatment and outcome. This is a challenging limitation of these blood-based tests because the tumor has to reach a relatively large size, at least 3 cm in diameter, to reliably be able to detect its shed, that is, secreted content in blood.[22,23] The Galleri test is better at predicting the organ site where the tumor is, which is important for follow-up diagnostic procedure and eventual treatment. The PPV of the Galleri test was reported to be 51% in the original study and at 44% in a large retrospective validation study with more than 4,000 participants (2,823 of which were known to have cancer).[24] As we mentioned above, in the real world, cancer prevalence, which is relatively low and age-dependent (<3%), affects the PPV. In an effort to have a more direct measurement of PPV, a clinical trial named Pathfinder[25] (https://clinicaltrials.gov/study/NCT04241796) was designed to enroll prospectively more than 6,000 participants over 50 years of age. About 50% of participants were known to have an elevated risk of developing cancer.[26] In this Pathfinder study, enrolled individuals were followed up for 1-year after they took the Galleri test to see how well a positive result indicated a cancer diagnosis or not. The Galleri test identified 35 of 121 cancers that develop in patients and the PPV was 43.1%.[27] This PPV still is reasonably good. For every 10 positive tests, 4 persons would have cancer and 6 would be healthy individuals; a screening mammography has a much lower PPV of 5% (4 cancer cases and 76 false positives). Like mammography and colonoscopy screening, a positive result from Galleri, CancerSEEK, or similar MCD test would require additional procedures to diagnose if a tumor is present and where it is.

Regulatory considerations of MCD tests

These MCD tests or similar blood tests can be provided to consumers as FDA-reviewed in vitro diagnostics or Clinical Laboratory Improvement Amendments (CLIA)-compliant laboratory-developed tests (LDTs). An FDA-reviewed test needs to meet a series of parameters and provide specific documentation about the test that LDTs may not need to provide.[28] FDA review or clearance of a test is required for insurance reimbursement consideration, whereas LDTs are just paid out of pocket. In either case, the FDA reviewed tests or the LDTs do not need to show clinical utility such as an effect on reducing mortality to be offered to health providers and patients/individual persons.[29] In the case of the Galleri test, it can be provided as an LDT as direct-to-consumer sales, or an employer can choose to provide this test to their employees as a perk or enhancement to the health benefits package. For the Galleri test to be reimbursed by insurance companies or covered by Medicare, it would need to be reviewed and/or cleared by the FDA first. The FDA has cleared other cancer detection kits either blood-based or stool-based with a much lower PPV than the Galleri test. For example, ColoGuard® is an FDA-cleared stool-based test and is Shield™ FDA-approved blood test as less invasive alternatives to detect colorectal cancer. The PPV of either of these tests is about 5%.[30,31] What is unprecedented is how extensively Grail, the company that makes the Galleri test, has interacted with health systems in the United States and United Kingdom to bring the Galleri test to so many individuals so quickly. At present, it is adamantly lobbying in the United States for Medicare to cover the Galleri test before the test is reviewed or cleared by the FDA or other regulatory agencies. The fact that large health systems in the United States and the United Kingdom have partnered with Grail suggests the perceived value of such an MCD test by the clinicians and health providers that lead these prestigious organizations.[32,33,34] An

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argument for an early roll out to a large number of individuals is that this real-world scenario could help further improve the algorithm and enhance sensitivity parameters (specificity is set at 99%).

Most cost-effective and accessible universal cancer screening program

If we consider the cost of screening with current methods and some of the recommended single marker blood tests for everyone over 50 annually, such as mammography for breast cancer (only women), the pap test for cervical cancer (only women), the PSA test for prostate cancer (only men), low-dose CT scan for lung cancer, and colonoscopy for colorectal cancer, it would cost over $250 billion just to detect five cancer types. Considering the cost of screening with high-end full-body MRI everyone over 50 annually would cost over $400 billion to potentially detect any cancer type and any other human disease. To do an MRI scan for everyone over 50, assuming 10 people are scanned per day every day of the year would require us to have over 27,000 MRI units in the United States. Currently, there are fewer than 13,000 MRI units.[35] Assuming that current units are only used at 50% capacity at least 20,000 MRI units would need to be procured with a cost more than $10B just in capital equipment purchases and much more in infrastructure and unit operation. In comparison, the cost of screening with the Galleri test everyone over 50 annually would be about $100 billion to potentially detect more than 50 cancer types. Because the Galleri test is a blood test and uses DNA sequencing technology, it would be relatively easy to pool and/or process many samples in parallel, automate, and high throughput the sample processing and analysis—what should bring down the cost per individual test to the $200–$500 range. Thus, the cost of the Galleri test would not be prohibitively expensive and would be more cost-effective than other strategies that we considered above. In addition, because a blood draw is a very common procedure than can be done in any doctor's visit, the Galleri test would be readily accessible, and individuals could have a high compliance and adherence to the screening program.

Most sensitive universal cancer screening program

The main challenges for the Galleri test, and similar blood-based MCD tests, are that they are not very sensitive to detect smaller tumors and that they are not particularly good at detecting breast and colorectal cancer.[36,37] MCD tests will miss up to 85% of stage I tumors depending on the cancer types. Arguably, the most clinical impactful benefit of a universal screening program would be to detect all cancers at stage I or II. The benefit of "downstaging" of most cancers detected at stage III rather than stage IV seems much more limited. With known performance and PPV parameters of the Galleri test, it would need to be implemented alongside mammography and colonoscopy since it cannot compete with these screening methods for breast and colorectal cancer—but would offer benefit to detect pancreatic cancer, gastric cancer, and ovarian cancer. In contrast, whole-body MRI should be able to detect most cancer types at stage I or II, including breast and colorectal cancer. Whole-body MRI would have the added benefit of detecting other human diseases and ailments not just cancer (though, as noted earlier, misleading incidental findings of suspected cancerous and non-cancerous lesions would be a significant problem).

Consequences of implementing a universal cancer screening program

Since the start of the U.S. Preventive Services Task Force recommendations for screening for breast, colorectal, cervical, and lung cancer, a mathematical model estimates aggregated life-years gained of more than 12 million and a monetary benefit value of more than $6 trillion.[38] These estimates are based on actual adherence to these recommended screening methods of less than 75%. Assuming the same level of adherence to and cancer stage at early detection of a universal cancer screening program for all individuals over 50 years of age, the aggregated life-years gained and monetary benefit value could likely

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double or triple, given that a universal cancer screening program would encompass almost all cancer patients whereas current screening methods only apply to 25% of all cancer patients.

A universal cancer screening program most certainly would empower individuals to have more information about cancer risks and early intervention options, make more informed decisions about lifestyle choices, proactively seek actions to reduce cancer risk and address early cancer detection, and follow additional diagnostic tests recommendation by healthcare providers. The quality of life and life-years gained by early detection outweighs any potential savings of only treating patients with clinical symptoms. Any downstaging of tumor afforded by universal screening would improve the clinical outcome of a patient and provide for a less aggressive treatment plan. Even the most expensive targeted treatments have limited benefit for advanced cancer cases. With the average cost of cancer treatment per patient at $200,000/year,[39] allocation of those funds for a universal cancer screening could provide tests for 100–200 individuals per year. Assuming a PPV of 50% of the MCD test regardless of the specific technology implemented, this would result in cancer diagnosis and a false positive for every two positive tests. This would mean that about 500,000 healthy individuals will need to undergo additional diagnostic procedures associated with some worries about cancer and additional costs, but it would also mean that 500,000 cancer cases could be caught earlier each year (about 25% of all expected cancer diagnoses at 2 million/year). Yes, these would mean that more individuals would receive cancer treatment, but likely the treatment cost per individual would be less. Moreover, if we consider the number of false positives if screening mammography with a PPV of 5% was provided to all women over 50 (about 50 million), it would mean that more than 4.5 million women would have a false positive[40] result and undergo additional diagnostic procedure just to rule out one cancer type. If 50 independent tests, each for a particular cancer type and all with a PPV of 50% were applied to the same 110 million population for universal cancer screening, there would be more than 10 million individuals with false positive results. Thus, while not perfect, an MCD test for universal cancer screening would be more affordable, accessible, and efficient as a strategy to reduce overall cancer burden and treatment cost.

Ethical assessment of the Galleri test

Since Grail company is the only one aggressively pursuing and adamantly advocating for implementation of their Galleri test for universal and equitable screen program for everyone over 50, we are exclusively in the last section of this essay on the ethical assessment of the Galleri MCD test. We have already noted that 610,000 Americans die of cancer each year. This is a tremendous loss of life. If it were the case that we had no ability to treat or cure cancer, this would be a sad and tragic fact. However, more than half of the cancers diagnosed today will be treatable and will result in a cure. This is due to both the availability of powerful cancer therapies and the fact that many of these cancers are diagnosed in an early stage before metastasis has occurred. Still, cancers that are identified as a result of clear presentation of symptoms associated with cancer will frequently have a poor prognosis. It is obviously preferable to identify cancers at the earliest possible stages, which is why annual screening is seen as a desirable strategy for saving more lives at a lower cost. However, as noted above, only four screening strategies are currently available. Those screening strategies can be costly and some are invasive, which has the unfortunate side effects of discouraging individuals from using these strategies. In addition, they cover only about 25% of the cancers that will be diagnosed in a year.

The Galleri test developed by Grail promises to overcome many of those obstacles. It is a simple blood test. It is noninvasive. It is capable of identifying more than 50 cancers with 99% specificity. In addition, it is capable of identifying correctly (>80% accuracy) the tissue of origin associated with a cancer it has identified. Clinicians who are familiar with the test are strong advocates for broad dissemination of the test. Grail is advocating that this test be publicly funded for everyone over age 50 in the United States. That would be about 110 million Americans. The cost of the test is $950. That would be a cost of about $100 billion annually for the broad dissemination of the test. No one would doubt that is a very substantial sum. However, researchers at Grail contend that if this test were this widely disseminated, the result would be reducing cancer deaths in the United States by up to 160,000 lives.[41] This would

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clearly be a clinically and ethically significant accomplishment. Some of those individuals might only be 52 years old; others might be 75 years old. In some cases, the test might save 10 life-years for an older individual but 30 life-years for a somewhat younger individual. If the average number of life-years saved were about 20 life-years, that would amount to saving 3.2 million life-years each year for that $100 billion investment. That means that the cost per life-year saved would be about $30,000. That number is well within the $100,000 figure generally used as a test of cost-effectiveness for some new therapeutic intervention. In addition, substantial savings would be achieved as a result of not having to pay for advanced cancer treatment for those 160,000 individuals. If the average cost of such advanced cancer treatment with targeted therapies or immunotherapies were about $200,000, the result would be a savings of $32 billion. Those savings would in turn reduce the cost per life-year saved to about $20,000, which is well within the range of what is ethically and economically reasonable.

If we are assessing from an ethical perspective Grail's proposal for public funding that would cover everyone for annual access to this test, then it is surely equitable that *everyone* over the age of 50 would be covered. Insurance status would be irrelevant, along with employment status, financial status, age, gender, race, or ethnicity. Such access to the test would emphasize the value of every human life. Everyone would be equally protected from cancer, at least from a preventive perspective. That is, individuals would be protected from a preventable premature death from cancer. No financial barriers would get in the way of access to that preventive option.

This last point suggests another ethically relevant consideration, that is, respect for patient autonomy. For 80% of Americans, an annual cost of $950 for the Galleri test would be an insurmountable financial barrier if they had to pay that from their own pockets. Public funding gives everyone the freedom to pursue that option. What are the consequences of failing to provide public funding for the Galleri test? That would mean 130,000 lives would be lost prematurely to cancer that could have been saved if their cancer had been detected when it was still curable and equally important treatment more affordable. That is the ultimate loss of autonomy. It will still be the case that 450,000 individuals will die of cancer annually, even with public funding for the Galleri test. That is tragic and regrettable. The fact of the matter is that no curative therapies are available for many cancers, even if detected early. However, the loss of those other 130,000 lives is ethically problematic because those lives clearly could have been saved if we made the right sort of social investment.

Many will express concerns about the size of that social investment: $100 billion. The relevant question to ask is whether there is some other preventive or curative modality for cancer that would represent a better use of that $100 billion, which could save more lives and more life-years. The short answer to that question will be negative, as we argued above. Cancers have proven to be extraordinarily complex and virtually impossible to cure once a cancer has become metastatic. For the present and foreseeable future, there will be no single therapeutic strategy, the proverbial magic bullet, that will yield a cure for the 200 or so cancers that have been identified. That suggests that for now we are better off funding access to the Galleri test as a preventive screening strategy. There are some other MCD screening strategies being developed. However, none of them promise as much as the Galleri test, as discussed above. Still, we recognize that there are challenges the Galleri test must meet in order to justify that $100 billion investment.

Critics will say the test is too expensive to be provided to 110 million Americans annually. Researchers at Grail believe that in the future the cost of the test could be reduced by 50%. That would be a major accomplishment. Some may harbor the hope that the cost of the test could be reduced to $100. That seems entirely unrealistic, given the necessary technological complexity.

Critics also point out that the sensitivity of the test is disappointing, especially with regard to stage I and II cancers, the stages at which the opportunity for cure would be most realistic. The sensitivity of the Galleri test for a stage I cancer is only 16%, which means 84% of such cancers are missed. And for stage II, the sensitivity is only 42%. Again, researchers at Grail believe that with time they will be able to improve those numbers.

Critics also point to the problem of false positives as an ethics issue. The fact of the matter is that the false positive rate is very low, around 0.8%. However, if we are screening 110 million Americans annually, that translates into 800,000 individuals. Further, it takes a lot of effort and cost to resolve those false

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positives. To be precise, the median time to resolve a false positive will be 162 days and the cost will be $5,000.[42] In addition, it is easy to imagine considerable patient anxiety during that period of time. No one can doubt that these are harms that have ethical relevance. Further, we should not be cavalier regarding how we think about these harms. However, these are not deadly harms, whereas the 160,000 lives that would be lost without Galleri screening clearly represent a much more serious harm. All things considered, the trade-off in this case, regrettable as it is, should be regarded as being ethically acceptable.

Finally, critics will point out that the most important claims made on behalf of the Galleri test rest upon a very slim empirical basis and surrogate end points from which Grail researchers have extrapolated those very large numbers of lives that could be saved. In other words, in the real world, the Galleri test *may have saved* a few thousand lives, but not 160,000 lives in a year. Critics would put "may have saved" in italics because it might take as long as 10 years to know that the result of detecting a cancer with Galleri actually resulted in the saving of a life. What can be said is that the cancer that was discovered was treated with the best therapy available, that no evidence of residual cancer cells could be found, and that often resulted in a cure, but there was no guarantee of such an outcome. Recurrence was still possible, and in some cases that recurrence would be deadly.

Given the potential for recurrence in a 10-year window, critics want the Galleri test subjected to the same rigorous evidential standards that any other cancer intervention might be subjected to. However, the CEO of Grail, Joshua Ofman, contends that such strict requirements would be ethically and economically objectionable. Strict standards would require trials that would extend for 10 or 15 years. Ofman has contended that by the time those trials ended, the technology they evaluated would be obsolete. Of course, if that were likely to be the case, investors would abandon the technology as too economically risky. There would be an ethical cost to that as well. Imagine that the trials had to last only 10 years in order to gain FDA approval. That would still imply that 1.6 million lives would have been lost over those 10 years that could have been saved if the FDA gave tentative approval with the expectation of careful follow-up for data collection. Further, if you were to query the broad public, as well as practicing physicians, you would find that they would vigorously object to such strict scientific validation if the cost of that would be those 1.6 million lives lost.

In conclusion, clinical, economic, and ethical considerations would all support the wide dissemination of the Galleri MCD screening test through a public funding mechanism for all those over the age of 50 annually.

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Notes

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