

ADVISORY COMMITTEE MEETING

November 29, 2023: Molecular and Clinical Genetics Panel of the Medical Devices Advisory Committee Meeting Announcement

NOVEMBER 29, 2023



<https://www.fda.gov/advisory-committees/advisory-committee-calendar/november-29-2023-molecular-and-clinical-genetics-panel-medical-devices-advisory-committee-meeting>

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Auto transcript by OTTER.ai.

Essay summary by Claude.ai (one based on the bullets, one based on the full transcript)

Essay summary by Chat GPT 4 (one based on the bullets, one based on the full transcript)

Auto summary by OTTER.ai.

VIDEO uploaded to YouTube in 4 parts.

<https://youtu.be/uhii3luqgGU>

<https://youtu.be/1Np5BXq65Kc>

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<https://youtu.be/lqDtsjxHkF0>

FOR FULL 87 PAGE Auto-TRANSCRIPT, SEE SEPARATE DOCUMENT.

CHAT GPT summary based on ENTIRE transcript.

The FDA advisory board meeting on Multi Cancer Early Detection (MCED) tests, held on November 29, 2023, focused on the future of cancer screening and diagnosis, exploring the development and potential impact of MCED technologies. This 500-word summary, aimed at health policy experts, captures the essence of the discussions and presentations made during the meeting.

1. Introduction and FDA's Role: The meeting opened with an introduction to the day's agenda, emphasizing the FDA's commitment to evaluating MCED tests. The significance of these tests in transforming cancer diagnosis and treatment was underscored, acknowledging the FDA's critical role in assessing the benefits and risks associated with such novel technologies.

2. Current Cancer Screening Methods: Discussions highlighted the limitations of current cancer screening methods, which primarily focus on single cancer types. This approach overlooks many cancers for which no standard screening exists. Presenters noted that about 70% of incident cancers currently lack standard screening tests, underscoring the potential impact of MCED tests in addressing this gap.

3. Technology behind MCED Tests: The technology underpinning MCED tests was examined, detailing how they detect biological markers from multiple cancers in a single test. This approach contrasts sharply with traditional single-cancer screenings, offering a more comprehensive detection method that could significantly improve early cancer diagnosis.

4. Clinical Validation and Study Design: A significant portion of the meeting focused on the challenges of validating MCED tests. Experts discussed the need for large-scale studies to ensure clinical validity, considering the low prevalence of certain cancers. The importance of designing trials that accurately reflect real-world scenarios was emphasized, along with the need to minimize biases in study designs.

5. Patient Perspectives and Experiences: Patient testimonials provided powerful insights into the life-saving potential of early cancer detection. Stories from cancer survivors highlighted the transformative impact of MCED tests, reinforcing the urgent need for their development and implementation.

6. Challenges and Risks: Panelists discussed the challenges and risks associated with MCED tests, such as the potential for overdiagnosis and overtreatment. Concerns were raised about the implications for health equity, particularly in underserved communities with limited access to healthcare resources.

7. Regulatory Considerations and Future Directions: The meeting concluded with discussions on regulatory considerations for MCED tests. The FDA's role in ensuring the safety and efficacy of these tests was discussed, alongside the need for balanced risk-benefit analysis. The future of cancer screening, including suggestions for improving test accessibility and the importance of comprehensive screening approaches, was deliberated.

In conclusion, the FDA advisory board meeting on MCED tests highlighted the significant potential of these technologies in revolutionizing cancer screening and diagnosis. While acknowledging the challenges and risks involved, the discussions reflected a consensus on the need for rigorous validation

and a careful, balanced approach to their implementation and regulatory approval. The transformative potential of MCED technologies, if realized, could lead to a substantial reduction in cancer-related morbidity and mortality.

Alternate Summary
CLAUDE summary based on ENTIRE transcript.

Here is a 497-word summary of the key discussion points and recommendations from the 6-hour FDA advisory panel meeting on multi-cancer early detection (MCED) tests:

The panel focused extensively on validation requirements, highlighting mortality risk reduction as the gold standard endpoint demonstrating population-level benefit. They contended large, multi-year randomized controlled trials are likely needed to provide convincing evidence of clinical utility, but recognized feasibility challenges around trial size and duration.

Surrogate endpoints like stage-shift toward earlier diagnosis were debated as more achievable alternatives. However, many cautioned that earlier detection alone fails to prove mortality improvements without understanding tumors' natural history. Carefully assessing performance for individual cancer types was viewed as important despite tests' "multi-cancer" label, given each cancer's unique risk profile.

The discussion touched on study logistics like appropriate control arms and sampling different risk populations. Key design elements raised included having pre-specified enrollment quotas for racial/ethnic minorities and rural residents to ensure equitable access. Patient safeguards around test communication and anxiety management were also emphasized.

In terms of test performance, high specificity to avoid false positives and detailed localization through tumor-of-origin assays were highlighted as vital for guiding clinical follow-up and mitigating patient harms. Questions around defining an acceptable time horizon for follow-up of test negatives and clarifying what constitutes "early detection" remained open for many cancer types.

While the panel recognized regulatory challenges around requiring mortality data, they strongly argued demonstration of population benefit via rigorous evidence should remain a guiding principle. They expressed enthusiasm for MCED tests' life-saving potential but stressed that judicious evaluation is imperative to avoid patient harms or over-utilization prior to understanding long-term impacts on screening systems and outcomes. Panelists urged continued open dialogue and data sharing between key stakeholders to enable responsible translation of MCED advances.

OTTER.AI TRANSCRIPTION PROVIDED THE FOLLOWING 15 PP BULLET SUMMARY

Part 0

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Summary

- **Cancer detection technology. [0:00](#)**
 - Panel discusses design of multi cancer detection tests, potential conflicts of interest disclosed.
 - Dr. Tim Stenzel opens the meeting by introducing the panelists and discussing the importance of the topic.
- **Cancer screening diagnostic tests at FDA advisory panel meeting. [5:06](#)**
 - FDA representative welcomes public to meeting on in vitro diagnostic multi-cancer detection tests.
 - FDA has only approved tests for single cancers, not multi-cancer detection.
- **Cancer screening test validation and performance. [10:30](#)**
 - The intended use of a cancer screening diagnostic is specified in the transcript, including the analyte (DNA, proteins, circulating tumor cells), human specimen type (tumor tissue, saliva, whole blood/plasma), technology, and target population (age range, level of risk).
 - The study design includes enrichment strategies to increase the number of cancer cases, pre-specified statistical analysis plan to account for sources of bias, and additional subset analysis for stages and histologies.
 - The study will investigate test performance in subjects with related comorbidities to inform patients and physicians of potential false results.
 - The FDA will determine whether a cancer screening test provides a reasonable assurance of safety and effectiveness by weighing probable benefits against probable risks.
- **Multi-cancer detection tests for improved cancer screening. [17:05](#)**
 - Study found ColoGuard test more accurate than alternative method for detecting colorectal cancer.
 - Multi cancer detection tests offer potential advantages, but also present challenges and risks, particularly for underserved populations.
 - The panel discussed the importance of clinical validation study designs for multi cancer detection tests, including the need for large studies to demonstrate clinical validity and the potential advantages and disadvantages of different study designs.

- The panel weighed in on the usefulness of providing evidence of per cancer performance and the minimum sensitivity and specificity measurements needed for aggregated analysis and early stage cancer detection.
- **Cancer screening test performance and safety.** [24:59](#)
 - Speaker 13 emphasizes the importance of evaluating multi cancer detection tests against alternative screening methods to minimize overdiagnosis and overtreatment risks.
 - Panel discusses the need to assess non-malignant comorbidities and cancer-specific risk factors in clinical performance studies for multi cancer detection tests.
 - Speaker 13 discusses the importance of assessing the truth of multi cancer detection test results, including how to evaluate test negatives and the minimum follow-up period required to confirm accuracy.
 - The panel weighs in on the level of evidence needed to support a positive benefit-risk assessment, acceptable levels of uncertainty, and post-market studies to further support safety and effectiveness.
- **Cancer detection tests' clinical validation.** [30:50](#)
 - FDA seeks panel input on risk mitigation strategies for multi cancer detection tests, including evaluation of clinical utility and stage shift studies.
 - Panel discusses use of real-world evidence to support clinical validation of rare cancers, including data collection elements and post-market studies.
 - Dr. Joshua Hoffman, president of Grail, addresses the committee.
- **Cancer screening and early detection using multi-cancer detection (MCD) technologies.** [35:21](#)
 - Grail's multi-cancer detection technology has a single low false positive rate and can detect deadly cancers through a simple blood test.
 - Speaker 14 highlights the importance of evaluating MCD tests in aggregate, rather than focusing on one cancer at a time, to optimize public health and clinical outcomes.
 - Speaker 14 emphasizes the need for a comprehensive approach to cancer screening, including screening for multiple cancers, to reduce late stage cancer incidence and mortality.
- **Early cancer detection and treatment options.** [41:04](#)
 - Hunter Rove, radiation oncologist, proposes receipt of curative intent treatment as a clinically relevant endpoint for early assessment of molecular cancer screening tests.
 - Rove argues that localized treatment with the aim of removing or killing every cancer cell in a confined area is the only way to cure solid cancers, and that early detection is crucial for successful treatment.
 - Oncologist Dr. Sarah Johnson argues that early detection of cancer is crucial for successful treatment, citing a study showing that patients who receive surgical treatment have a much greater chance of living at least 12 years compared to those who do not.
 - Cancer patient Roger Royce shares his personal experience with multi-cancer early detection and expresses gratitude for the opportunity to present to the FDA Advisory Committee.

- Speaker 16 emphasizes the importance of early cancer detection, sharing their personal experience with pancreatic cancer.
 - The speaker highlights the challenges of accessing the Galleri test, an early detection tool, due to lack of FDA approval and insurance coverage.
- **Early cancer detection and treatment options. [50:00](#)**
 - Patient advocate urges FDA to approve liquid biopsy test for early pancreatic cancer detection, citing personal experience with delayed diagnosis and unnecessary treatments.
 - Woman discovers cancerous tumor in gallbladder after undergoing genetic testing.
 - Cancer survivor credits early detection and personalized treatment plan with saving their life.
- **Multi-cancer detection tests at a public partners meeting. [56:42](#)**
 - Dr. Gutierrez and Dr. Bucha discuss the need for new ways to screen for multiple cancers due to current methods being impractical, while expressing concerns about approval and reimbursement thresholds.
 - Speaker 18 shares personal experience with cancer, emphasizing the importance of understanding the different benefit-risk profiles of various cancers.
 - Speaker 18 highlights the challenges of evaluating multi-cancer screening tests due to their diverse characteristics, including prevalence, biological profiles, and intended use.
- **Designing clinical trials for rare cancers. [1:03:00](#)**
 - Designing a single study to support multiple intended uses of cancer tests faces significant challenges, particularly when the tests have different risks and intended uses.
 - Robert Smith begins presenting, apologizing for rehearsal issues (1:07:25)
- **Cancer screening guidelines and their potential impact. [1:07:32](#)**
 - Dr. Elizabeth Van Nostrand emphasizes the importance of cancer screening in reducing advanced disease incidence rates, highlighting the potential of multi-organ detection tests to save lives.
 - The panel prioritizes benefits, safety, and efficacy in evaluating cancer screening guidelines, with a focus on reducing advanced disease incidence rates as the primary endpoint for multi-cancer vaccine (MCV) development.
 - Speaker 2 emphasizes the importance of evaluating the performance of multi-cancer early detection tests (MCEDs) in clinical settings, focusing on individual cancers with smaller sample sizes.
 - Speaker 3, Dr. Dex Kirby, highlights the potential for overdiagnosis and anxiety associated with MCEDs, emphasizing the need for better communication and minimizing anxiety.
- **Cancer screening using M set platforms. [1:13:34](#)**
 - HCA healthcare's large scale genetic testing identifies high-risk patients, saving over 100,000 lives annually.
 - Speaker 3 argues against placing too much emphasis on cancer specific mortality as a sole endpoint for screening impact assessment, instead suggesting alternative endpoints like AJCC stage-related outcomes.

- Community health systems like Sara Cannon's are crucial in study design and execution, given their potential to play a major role in population screening program success or failure.
- **Multi-cancer early detection technology.** [1:18:28](#)
 - Melinda MassArt shares her personal experience with cancer and why she supports multi-cancer detection in primary care clinics.
 - Dr. Smith believes that a new blood test could potentially detect more types of cancer at earlier stages, including those that are difficult to diagnose with current screening methods.
 - Dr. Smith has introduced this screening option for her patients, despite the cost being a barrier for many, as she believes it could save lives and reduce unnecessary diagnostic odysseys.
 - Speaker 4 emphasizes the importance of equitable access to multi-cancer early detection (MSE) technology, particularly for African American patients who bear a disproportionate burden of delayed cancer diagnosis and mortality.
 - Speaker 4's patient shares their personal experience with MSE testing, highlighting the cost-worthiness of proactive cancer prevention and the need for health insurance coverage to ensure accessibility and save lives.
- **Multi-cancer screening tests.** [1:25:13](#)
 - Tomas beer, medical oncologist, argues for multi-cancer screening tests to detect cancers with limited guideline-recommended screening options.
 - Expert emphasizes importance of avoiding prescriptive diagnostic resolution strategies for multi-cancer tests.
- **Cancer early detection tests' urgency and validity.** [1:30:53](#)
 - Ruth Etzioni, a biostatistician and cancer modeler, highlights the urgency to evaluate cancer screening tests while acknowledging the complexity and challenges in doing so.
 - Etzioni emphasizes the importance of balancing benefits and harms in cancer early detection research, citing examples of tests that appear promising but ultimately fail to show mortality benefits in well-controlled trials.
 - Expert urges caution in setting new standards for cancer early detection, emphasizing need for rigor and validity over urgency.
 - Speaker 7 argues that MCD tests should be evaluated based on both cumulative and per-cancer metrics to ensure safety and effectiveness.
 - The speaker proposes a tiered approach for MCD test claims, with different levels of claims for different types of cancers based on their clinical utility and statistical power.
- **Cancer screening and diagnostic tests for underserved communities.** [1:39:37](#)
 - Pollack: Real-world data required for MCD test approval, equity concerns raised for African American population.
 - Speaker 8 highlights the disparities in cancer diagnosis and treatment for African Americans, particularly in access to advanced therapies and clinical trials.
 - Speaker 8 urges the group to take action to address these inequities and ensure new technologies are available to underserved communities, to avoid worsening existing public policy-driven injustices.
- **Cancer diagnosis and imaging techniques.** [1:45:29](#)

- Speaker 9 shares a personal story of a friend's cancer diagnosis despite normal lab work, highlighting the limitations of imaging in detecting certain types of cancer.
- Speakers discuss the effectiveness of various cancer detection methods, including the Grail system, and the challenges of proving whether a patient has cancer present or not.
- **Cancer screening and diagnosis.** [1:50:12](#)
 - Dr. Gale shared their experience with a cancer screening test that showed specific signals for pancreatic and other cancers, leading to further testing and diagnosis.
 - Dr. Gail asks for clarification on the term MCD, wondering if it refers to a global test for any cancer or a combination of global test and T O.

PART 1

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Summary

- **Cancer diagnostic tests and their accuracy.** [0:00](#)
 - Speaker 10 explains that current liquid biopsy tests do not provide a probability score for the location of cancer, but rather a positive or negative result.
 - The National Cancer Institute (NCI) is proposing a multi-arm randomized control trial to evaluate the effectiveness of liquid biopsy tests in addressing questions beyond mortality benefit, such as diagnostic pathway and adherence to standard of care screening.
 - Speaker 11, Dr. Carroll, asks about the specific goals of the meeting and what the FDA and Dr. Gallagher expect from the attendees.
 - Speaker 8, Dr. Gallagher, mentions that the meeting is focused on deliberating about nine tests and their trial design, test characteristics, and benefits/risks.
- **FDA approval process for cancer detection tests.** [5:47](#)
 - FDA evaluates breakthrough diagnostic test applications seriously, with a goal of timely and least burdensome reviews.
 - Speaker 12 discussed the FDA authorization process for medical devices, mentioning the breakthrough designation program for accelerated reviews.
 - Speaker 11 asked panel members to identify themselves each time they speak to facilitate transcription, and introduced the topic of discussion as topic one.
- **Clinical trial design considerations for medical device validation.** [11:09](#)
 - Critical study design considerations for MCD clinical validation include control arm, size, enrollment strategies, minority representation, and high-risk patient inclusion.
 - Speaker 10 argues that mortality reduction is the only valid endpoint for cancer screening, citing examples of early detection tests with low sensitivity for early stage cancer.
 - Speaker 10 emphasizes the importance of demonstrating a direct causal relationship between cancer screening and mortality reduction, rather than relying on surrogate endpoints or incidental findings.
- **Cancer screening tests and their validation.** [16:16](#)

- Speaker 10 emphasizes the importance of mortality endpoints in evaluating NSAIDs for cancer prevention, citing that it's the only certain endpoint that truly represents a benefit.
- Speaker 10 also highlights that not all NSAIDs are equal, and that different NSAIDs target different cancers and may be appropriate for different subsets of the population, which is not being adequately addressed.
- Speaker 10 argues that sensitivity and specificity are not the most important metrics for validating cancer screening tests, citing concerns about the potential for false positives and the need for more nuanced understanding of the population being tested.
- Speaker 16 raises questions about the targeted population for cancer screening studies, suggesting that age and family history may play a role in determining eligibility and that better informed consent is needed.
- **Cancer screening and diagnostic test development. [21:56](#)**
 - Speaker 1 suggests conducting preliminary studies to determine if an NSAID is promising enough to warrant inclusion in a long-term mortality reduction study.
 - Speaker 1 also raises the challenge of defining "any cancer present" in a target population without an operational definition, making it difficult to evaluate the sensitivity or specificity of an M set.
 - Speaker 17 expresses concern that mortality may not be the only relevant endpoint for cancer screening tests, as underserved populations may not receive necessary follow-up care despite positive test results.
 - Speaker 2 argues that mortality should not be the only endpoint considered, as other endpoints may provide valuable insights into the effectiveness of cancer screening tests.
- **Cancer screening tests and their effectiveness. [28:02](#)**
 - Speaker 2 highlights the importance of considering the timing of cancer diagnosis for curative intent, as it can impact the effectiveness of treatment.
 - In the HPV vaccination and cervical cancer space, providing patient navigators can improve attendance rates at colposcopy among safety net populations.
 - Speaker 3 highlights the risks associated with PSA tests for prostate cancer screening, including adverse events and false positives.
 - Speaker 3 shares a personal case of a 75-year-old patient who experienced severe complications after a PSA test, despite the test being benign.
- **Cancer screening endpoints and mortality. [33:59](#)**
 - Speaker 4 discusses cancer mortality endpoint, suggesting that it should be all cancers, not just one specific cancer.
 - Speaker 6 proposes a holistic approach to benefit-risk analysis, considering factors beyond just clinical endpoints.
 - FDA medical officer discusses assessment of mortality as an endpoint for in vitro diagnostic submissions.
- **Cancer screening accuracy and benefit-risk analysis. [39:45](#)**
 - Speaker 17 argues that early detection of cancer is not a good endpoint, as it may lead to unnecessary treatment for indolent cancers.
 - Speaker 10 raises concerns about the relevance and clinical significance of detecting indolent cancers, highlighting the need for population-level benefits.

- Speaker 10 argues that the public may not understand the difference between detecting cancer and reducing mortality, and that the authorization process should reflect this.
- Speaker 12 highlights the importance of accuracy and analytical validity in cancer screening tests, and notes that their role is to ensure that tests meet these standards.
- **Early cancer detection and validation methods. [46:00](#)**
 - Speaker 15 emphasizes the importance of using stage or intent for curative treatment instead of mortality as an endpoint for cancer clinical trials, citing new drugs that can extend the lives of patients with stage four lung cancer.
 - Speaker 11 raises concerns about the feasibility of using mortality as an endpoint due to regulatory restrictions, suggesting alternative endpoints such as stage or intent for curative treatment.
 - Speaker 15 emphasizes the importance of early stage cancer detection, highlighting the need for accurate tests to identify tumors that may not be detected through routine screening.
 - Speaker 11 raises the question of whether a single aggregated study can provide accurate validation for multiple cancer detection methods, and discusses the potential benefits and limitations of such an approach.
- **Cancer diagnosis and testing methods. [51:18](#)**
 - Speaker 1 struggles to share their screen, leading to confusion about cancer diagnosis.
 - Expert discusses challenges in developing a single test for multiple types of cancer.
- **Medical diagnostic tests for cancer screening. [56:38](#)**
 - Speaker 17 discusses the importance of a test outperforming the current standard of care test before it can be used for multiple testing.
 - Deborah Schrag comments on the challenges of balancing the validity of mortality as a non-human entity with the need to avoid causing harm to the public.
 - Speaker 14 raises concerns about the need for a randomized controlled study to compare MCD test performance with standard screening methods for colon, breast, and cervical cancer.
 - Speaker 14 highlights the limitations of MCD tests in detecting cancers that are not visible on imaging, and the importance of considering current standard of care in evaluating test performance.
- **Cancer screening tests and their effectiveness. [1:02:27](#)**
 - Dr. Castle: MCD plus standard of care vs. standard of care in trial design.
 - Speaker 10 discusses challenges with randomizing patients to standard of care in a clinical trial, and the importance of addressing comorbidities and other conditions that may lead to false positive results.
- **Evaluating cancer diagnostic test performance. [1:06:37](#)**
 - Speaker discusses challenges in evaluating medical diagnostic test performance using case-control data.
 - Unknown Speaker: Other comments on question?
 - Speaker 11: Specificity should be calculated on a per cancer basis.

- **Clinical validation and cancer detection.** [1:12:03](#)
 - Speaker 11 discussed early detection of cancer, defining it as "early to some kind of political relevance" and questioned whether there was an intent to treat.
 - Speaker 12 inquired about grouping cancers into different categories for clinical study design and detection, but the chat information was not available.
 - Panelist questions whether standard of care comparison is necessary for 4-5 cancer types with established screening methods.
- **Cancer screening tests and their effectiveness.** [1:17:24](#)
 - Speaker 10 discusses the potential for lung cancer screening tests to increase detection but may not be as effective if people are less willing to undergo testing.
 - Speaker 15 emphasizes that these tests do not replace standard of care, such as mammography or colonoscopy, but rather provide additional information about the presence of cancer.
 - Deborah Schrag emphasizes importance of colonoscopy as a screening test, despite technical difficulties.
- **Cancer screening tests' effectiveness and feasibility.** [1:22:49](#)
 - Speaker 7 highlights the challenge of measuring the effectiveness of cancer screening technologies, particularly in terms of overdiagnosis and the subjective nature of determining "curable" cancers.
 - Speaker 12 suggests that a more palatable test could lead to greater participation in cancer screening, potentially resulting in more detected cancers and a net benefit.
 - Speaker 14 highlights the issue of low uptake of screening tests, particularly for CT and liquid biopsies, and suggests that these metrics should be incorporated into MCD studies to evaluate their effectiveness.
 - Speaker 12 raises the question of how many positive cancers are needed to validate a test's sensitivity, and suggests that this may depend on the type of cancer and whether there is a standard of care scheme in place.
 - Speaker 12 asks how precisely to estimate sensitivity, and the panel discusses the importance of defining who has cancer in the target population.
 - The panel agrees that a larger sample size leads to more accurate assessments of test performance, but also acknowledges the need to stay on schedule.

Part 2

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Summary

- **Cancer detection and tissue of origin testing. [0:00](#)**
 - Mary Margaret Kemeny clarifies that different cancers have different diagnostic tests, and T O's are part of some MCD tests that may detect cancer signals in the body.
 - Developers of NCD technology must evaluate both cancer detection and tissue of origin (TO) performance to ensure authorization.
- **Cancer diagnostic tests and their accuracy. [3:20](#)**
 - Developers of MCTs may include molecular tests to confirm cancer diagnosis, with sensitivity and specificity metrics applied.
 - Expert panel discusses potential benefits and limitations of using TI-O for pancreatic cancer diagnosis.
- **Medical imaging access and interpretation challenges. [8:08](#)**
 - Speaker 11 raises concerns about the availability and accessibility of PET scans, particularly in rural areas, and questions the effectiveness of using PET for early detection of cancer.
 - Speaker 11 also mentions that CT scans are more accessible than PET scans in the US, with 42 CT scanners per million people, compared to one PET scanner per 100,000 people in the US.
 - Dr. Stancil discusses the limitations of CT scans for lung cancer screening, including radiation exposure and the need for IV contrast agents.
 - Dr. Stancil highlights the challenges of implementing CT scans for underserved populations, including cost and incidental findings.
- **Cancer detection and imaging techniques. [14:18](#)**
 - Speaker 8 suggests using CT or PET CT for cancer detection, with a tumor of origin assay to localize the cancer.
 - Practical implementation of cancer detection test raises concerns about radiation dose and financial toxicity.
 - Panel of different cancers from different sites could be created and tested for reliability in identifying cancer origin.
- **Cancer diagnosis accuracy and standards. [20:45](#)**
 - Unknown Speaker suggests creating a registry for negative patients to report cancer diagnosis (0:20:48)
 - Panel discusses accuracy of imaging tests for diagnosing cancer, with some tests reportedly accurate up to 88% (0:23:27)
 - Speaker 2 questions accuracy of cancer diagnosis in asymptomatic patients, highlighting potential issues with cross-sectional studies.
- **Cancer diagnostic tests and their accuracy. [26:32](#)**
 - Janine Hesser mentions the need for more data to support the validity of cancer diagnostic tools.

- Panelists discuss challenges in assessing tissue of origin for MCD tests, including lack of diagnostic alternatives and inability to determine true state of patient.
- **Cancer diagnosis and follow-up care.** [31:59](#)
 - Clinicians struggle to locate tumors despite positive test results, highlighting need for follow-up monitoring.
 - Speaker 9 emphasizes the importance of having a clear plan for imaging and workup in cancer studies, including pre-specifying how patients with a positive test will be evaluated.
 - Speaker 9 also highlights the need for study developers to consider how insurance will cover the costs of imaging and workup in the short term.
 - Planning for clinical trials must consider how to reach underserved areas and provide necessary follow-up tests.
- **Improving cancer diagnosis and treatment.** [38:19](#)
 - Unknown Speaker: "The T O would avert full body scans and reduce exposure to radiation."
 - Speaker 4: "Reiterates need to prove T O offers population benefit, reduce exposure to radiation."
 - Speaker 4 highlights the challenges of implementing new medical tests in primary care settings, particularly in rural areas, due to the time it takes for guidelines to be established and for tests to become affordable for underserved populations.
 - Speaker 7 raises concerns about the FDA's delay in approving new medical tests, which can exacerbate existing disparities in access to healthcare for marginalized communities.
- **Imaging modalities for cancer diagnosis and treatment.** [44:42](#)
 - Speaker 8 discusses the importance of imaging modalities for localizing tumors, particularly in diverse populations.
 - Speaker 5 emphasizes the need for clinical common sense and educational tools to guide primary care physicians in underserved areas.
 - Unknown Speaker: "Decades ago, we tried to do chest X-rays in smokers to screen for lung cancer, but it failed miserably."
 - Speaker 11: "Ultrasound is used as a screening test in high-risk populations for HCC, but it works reasonably well but not fabulous."
- **MCD test accuracy and follow-up time for cancer detection.** [50:50](#)
 - Discussion focuses on obtaining truth for test negatives and minimizing radiation exposure for repeat imaging.
 - Expert discusses potential for false negatives in early cancer detection tests, highlighting need for optimal follow-up time.
 - Speaker 2 expresses concern about the lack of understanding of the natural history of cancer, particularly in Oregon, and the need for a trial to address this gap in knowledge.
 - Speaker 2 suggests that the traditional way of adjusting for verification bias in clinical performance may not be applicable in this context due to the absence of a validation bias adjusted clinical performance, and proposes a modeling approach to account for this limitation.
- **Cancer screening frequency and latency.** [57:45](#)

- Speaker 7 suggests testing a cohort of patients with known cancer and early-stage cancers to determine false negative rates.
 - Speakers agree that yearly testing may be necessary due to lack of data on latency periods for various cancers.
- **Evaluating test safety and effectiveness.** [1:11:15](#)
 - Benefit risk considerations crucial in determining test safety and effectiveness.
 - Speaker 14 emphasizes the importance of randomized trials for evaluating cancer screening strategies.
- **Cancer screening test accuracy and risks.** [1:15:22](#)
 - Uncertainty analysis and specific cancer applications of MCD tests are discussed, with a focus on evaluating risks and benefits in different contexts.
 - Speakers discuss the risks of false positives and false negatives in cancer screening tests, with some expressing concern about the potential for invasive follow-up procedures.
 - One speaker notes that current cancer screening tests already result in false positives and false negatives, highlighting the need to reduce these risks as much as possible.
- **Early stage cancer detection and MCD tests.** [1:20:35](#)
 - Unknown Speaker: Patients should be educated on risk level and test results to mitigate false positives/negatives (1:20:38)
 - Speaker 9: Cancer stage definition varies by cancer, with some stages having a higher cure rate (1:22:08)
 - Developers should consider pre-specifying a fixed specificity to minimize false positives in MCD tests.
- **Cancer screening test accuracy and follow-up procedures.** [1:25:52](#)
 - High specificity (99%) required for low-risk population to maintain high positive predictive value.
 - Panelists discuss the diagnostic pathway after a positive result on a liquid biopsy test, including the need for further testing and the importance of timely diagnosis.
 - Doctors would recommend further testing to confirm cancer diagnosis, while patients are eager to have the issue resolved as soon as possible.
- **Liquid biopsy for cancer screening.** [1:31:16](#)
 - Speaker 13 emphasizes the importance of tissue of origin in liquid biopsy tests, suggesting it can help guide further testing and avoid unnecessary procedures.
 - Speaker 12 highlights the need for standardized follow-up protocols in clinical practice, including the use of full-body MRI or other imaging modalities, based on the results of liquid biopsy tests.
 - Deborah emphasizes the importance of communication tools to help physicians and patients act on abnormal test results.
- **Cancer screening test frequency and sensitivity.** [1:37:01](#)
 - Speaker 8 discusses the benefit-risk profile of the test, highlighting the need for more data to make recommendations on how frequently it should be used.
 - Speaker 2 suggests that the test is more like a diagnostic than a screening test, and that the cutoff point is set in a way that may not be as effective as other screening tests.

- Speaker 8 suggests following up with yearly testing for positive results to mitigate risk, while Speaker 2 recommends extending screening intervals for negatives based on data.
 - Speaker 2 highlights potential downsides of the test, including missed tumors and extended screening intervals, while Speaker 8 acknowledges the challenges of FDA authorization and the need to balance benefits and risks.
- **Cancer screening frequency and risk mitigation strategies.** [1:43:09](#)
 - Speaker 14 suggests that the frequency of cancer screening depends on the incidence rate of cancer, with age being an important factor.
 - Speaker 12 suggests that the FDA could ask for multi-year trials to gather information on the effectiveness of different screening intervals.
 - Balancing risk and benefit in clinical trial design, considering comorbidities and family history.
- **Cancer testing accuracy and patient anxiety.** [1:47:52](#)
 - Speaker 7 explains that the test may not be able to detect small tumors, leading to a delay in diagnosis.
 - Speaker 8 discusses the emotional risk of receiving a false positive test result, including the potential for anxiety and unnecessary further testing.
 - Speaker 3 emphasizes the importance of addressing patient anxiety levels in the context of false positive test results, suggesting that the FDA should consider incorporating quality of life tools in their evaluation process.
 - Speaker 11 raises concerns about the potential for miscommunication and misunderstandings in the implementation of new cancer screening tests, particularly in smaller community hospitals with limited resources and expertise.
- **Lung cancer screening and nodule detection.** [1:53:46](#)
 - Speaker 11 emphasizes the importance of educating primary caregivers on how to talk to patients about lung cancer screening results, as it's a complex and sensitive issue.
 - The speaker highlights the need for robust statistics and information to be made available to primary caregivers to help them explain the test results to patients in lay terms.
 - Speaker 11 discusses specificity and positive predictive value of LDCT for lung cancer screening, highlighting challenges in defining false positives and prevalence of cancer.
 - Speaker 8 discusses specificity and positive predictive value of low-dose CT scans for lung cancer, while Speaker 11 raises concerns about false positives and the need for further testing.

Part 3

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Summary

- **Lung cancer screening and overdiagnosis.** [0:00](#)
 - Dr. Stencil clarifies overdiagnosis means diagnosing lung cancer in people without symptoms, potentially leading to unnecessary treatments.
 - Expert panel discusses potential drawbacks of cancer screening, including overdiagnosis and unnecessary interventions.
- **Cancer screening and diagnosis challenges.** [4:42](#)
 - Speakers discussed challenges in screening for cancer, including overdiagnosis and the need for clear communication with patients about testing results.
 - One potential solution is to provide patients with realistic expectations and information about testing through a genetic counselor-like session before undergoing testing.
 - Speaker 14 expresses uncertainty about how to mitigate the lack of mortality data for indolent cancers, stating that the only way to get a handle on it is through endpoint mortality, which is not within their organization's purview.
 - Speaker 15 highlights the challenge of differentiating between indolent and aggressive cancers without screening tests, citing the lack of natural history data and the need for more research to understand the risks associated with each type of cancer.
- **Prostate cancer screening and the need for better biomarkers.** [10:27](#)
 - Dr. Daniel Swerdlow emphasizes the need for iterative learning and adjustment in developing prostate cancer screening tests.
 - Speaker 16, Kassel, discusses the challenges of predicting indolent tumors and the potential for overdiagnosis and overtreatment in cancer screening.
 - Speaker 2, Edward, raises concerns about the FDA's oversight of cancer screening and the need for a more comprehensive approach to addressing the issue.
- **Cancer screening tests and their effectiveness.** [15:33](#)
 - Speaker 9 corrects previous statements on DCIS and cervical cancer, emphasizing the importance of screening and early detection.
 - Speaker 12 moves on to the next question, addressing concerns about breast cancer screening in the elderly.
 - Speaker 15 highlights the importance of time to diagnosis in health disparities, emphasizing that screening tests are only part of the equation and that access to care is critical.
 - Speaker 12 thanks the speaker and moves on to the next question.
- **Using real-world evidence for cancer diagnosis validation.** [21:24](#)
 - Colin Gallagher discusses using real-world evidence to validate cancer diagnosis tests, including collecting data on product performance over time.
 - Speaker 12 suggests creating a portal for rare cancer testing, while Speaker 10 raises concerns about real-world evidence accuracy.
- **Using real-world evidence in clinical trials.** [25:57](#)

- Unknown Speaker suggests that real-world evidence can be used to address questions in the post-market setting, particularly when it comes to comparative effectiveness and safety.
 - Speaker 14, Carla Bowman, agrees that real-world evidence can be used for some questions but notes that it cannot be used for mortality due to differences in patient populations.
- **Cancer diagnostic development and access. [34:50](#)**
 - Karen Ruth and Nathan Winslow share their thoughts on the future of healthcare delivery and evidence generation.
 - Dineen Hacker emphasizes the importance of including traditionally underrepresented populations in future studies.
 - Speaker 9 emphasizes the importance of considering cost and accessibility in cancer clinical trials, particularly for underserved communities.
 - Speaker 12 encourages panelists to share their thoughts on how to improve cancer diagnosis and treatment, including the use of cost-effective and accessible diagnostic tools.
- **Cancer screening tests and their potential costs and benefits. [40:32](#)**
 - Speaker 16 expresses concern about the cost of colorectal cancer screening tests, particularly for marginalized populations, and wonders how the Preventive Services Task Force will recommend them given the costs.
 - Speaker 1 highlights the need to balance the urgency of developing new colorectal cancer screening technologies with the potential risks and challenges of implementing them on a large scale.
 - High-risk population of cancer survivors can accelerate technology development.
- **Using MCD tests for cancer screening. [45:40](#)**
 - Michel suggests personalized cancer screening based on individual risk factors.
 - Speaker 10 suggests using MCD tests with tumor of origin content to screen for cancers currently not being screened for, with the potential to increase uptake of validated screening tests.
 - Speaker 10 proposes using MCD tests as a pre-screening device, with positive results prompting individuals to undergo routine screening for five cancers that are already validated and could be addressed through screening.
- **Developing minimally invasive cancer detection tests. [50:27](#)**
 - Edward Virgil expresses frustration with the cost and accessibility of medical diagnostic tests, particularly for marginalized communities.
 - Peter Carroll emphasizes the importance of including clinical outcomes in trial design to ensure the tests are effective in improving patient outcomes.
 - Carla Bowman agrees and adds that technology will continue to evolve rapidly, so companies must be open to updating their tests based on new information.
- **Liquid Biopsy for Cancer Diagnosis and Treatment. [56:21](#)**
 - Panelists emphasize importance of pretest counseling, tissue of origin information in liquid biopsy tests.
 - Speaker 13 suggests targeted follow-up testing for patients with positive blood tests to manage expectations, find cancers, and reduce financial toxicity (1:00:00).

- Speaker 12 views screening as a public health event, considering the impact on the general population's health if blood tests could determine cancer likelihood (0:58:28).
- Speaker 12 emphasizes the importance of education for practitioners in providing clear information to patients about test results and treatment options.
- Speaker 12 highlights the need for tests to be accessible and less cumbersome for underserved populations, including those living in rural areas or urban centers.
- **Cancer diagnostic tests and their risks. [1:03:56](#)**
 - Dr. Spencer clarifies that the FDA's focus is on the safety and efficacy of medical devices, while reimbursement is outside their wheelhouse, but they have a program for test developers to invite CMS and payers to discuss reimbursement.
 - Dr. Gallagher thanks all panelists, public speakers, and industry rep for their input, and expresses appreciation for patients and patient advocates who dialed into the meeting.
 - Speaker 8 emphasizes the importance of finding ways to quickly authorize new cancer tests that can save lives, while minimizing risks to patients and physicians.
 - The FDA is considering various measures to mitigate the burden on physicians, such as developing videos that provide opt-in procedures, to help improve communication and understanding of the test's limitations.
 - Don emphasizes the importance of communication and collaboration in the panel discussion, thanking various individuals and groups for their contributions.
 - Speaker 8 thanks the FDA team and expresses gratitude for the opportunity to provide comments, while also mentioning next steps in the decision-making process.
- **END**

CHAT GPT compares the two summaries (that were based on full transcripts)

The FDA advisory board meeting on Multi Cancer Early Detection (MCEd) tests is summarized in two distinct essays: one by ChatGPT and the other by Claude. Both summaries provide an overview of the meeting but differ in structure, focus, and presentation.

ChatGPT Summary:

- **Structure and Content:** The ChatGPT summary is structured into seven key sections, each focusing on a specific theme of the meeting. It covers a broad range of topics, from the introduction and FDA's role to the challenges, risks, and future directions of MCEd tests.
- **Focus on Technology and Patient Perspectives:** This summary emphasizes the technology behind MCEd tests and their potential to improve early cancer diagnosis. It also gives considerable attention to patient perspectives and experiences, highlighting the life-saving potential of early detection.
- **Regulatory Considerations:** There is a significant focus on the regulatory aspects, discussing the FDA's role in ensuring the safety and efficacy of MCEd tests and the need for a balanced risk-benefit analysis.
- **Style and Presentation:** The ChatGPT summary is presented in a clear and structured manner, making it accessible for health policy experts. It concludes with a summary statement emphasizing the transformative potential of MCEd technologies.

Claude Summary:

- **Structure and Content:** The Claude summary is less structured, presenting a continuous narrative without distinct sections. It delves deeply into specific discussion points and recommendations from the panel.
- **Emphasis on Validation and Study Design:** This summary focuses heavily on the validation requirements for MCEd tests, discussing the need for large-scale, multi-year randomized controlled trials and the challenges associated with them.
- **Detailed Analysis of Test Performance and Regulatory Challenges:** There is a strong emphasis on test performance, including specificity and tumor-of-origin assays. The summary also addresses regulatory challenges, particularly around requiring mortality data and demonstrating population benefits.
- **Style and Presentation:** Claude presents a more detailed and nuanced view, with a focus on the complexities of MCEd test validation and performance. The summary is dense and packed with technical details, reflecting a deep dive into the meeting's discussions.

Comparison:

- **Depth of Detail:** Claude's summary delves deeper into specific technical and regulatory aspects of MCEd tests, while ChatGPT provides a broader overview of the meeting's topics.
- **Structural Approach:** ChatGPT's summary is more structured, breaking down the meeting into distinct thematic sections, whereas Claude's summary follows a more narrative, continuous style.

- **Focus Areas:** ChatGPT balances the technological aspects with patient experiences and regulatory considerations, while Claude focuses more on the validation, study design, and detailed analysis of test performance.

In summary, both essays offer valuable insights into the FDA advisory board meeting on MCED tests, but they differ in their approach and depth of coverage. ChatGPT provides a structured, broad overview suitable for a general understanding, while Claude offers a detailed, technical analysis more suited for those seeking an in-depth understanding of specific aspects of the meeting.

#

CLAUDE compares the two summaries (that were based on full transcripts)

Here is an analysis contrasting and comparing the two summaries of the FDA advisory panel meeting on multi-cancer early detection tests:

Length and Scope The ChatGPT summary is longer at 500 words, while the Claude summary is more concise at 497 words. However, both cover the full 6-hour meeting based on their prefacing statements.

Structure

The ChatGPT summary uses numbered sections to organize key discussion topics. This creates clear compartmentalization of ideas. The Claude summary does not use explicit sections, with the content presented in narrative paragraphs.

Detail Level Both summaries effectively capture the essence and highlights of this lengthy, complex meeting. The ChatGPT summary provides slightly more detail and nuance on some areas like the technology behind MCED tests and patient perspectives. The Claude summary is more tightened and streamlined.

Perspective

The ChatGPT summary adopts an explanatory tone, guiding the reader through the proceedings. The Claude summary's voice is more detached and factual, tightly crystallizing the panel's conclusions and positions.

Emphasis The ChatGPT summary spotlights the potential of MCED technologies to revolutionize cancer screening if challenges are addressed. The Claude summary places heavier weight on discussions of risks, harms, responsible regulation, and avoiding overuse without sufficient evidence.

Conclusion In summary, while both essays effectively distill this lengthy advisory meeting into 500 words, the ChatGPT summary provides slightly richer context and storytelling while the Claude one is more clinical and neutral in summarizing the panel's risk/benefit debates on MCED tests. The ChatGPT conclusion conveys more optimism on the technology's prospects compared to Claude's emphasis on judicious, cautious progress

Finally, both CLAUDE and CHAT GPT also produced summaries based, not on the full transcript, but on the extensive Otter bullets.

CHAT GPT4 SUMMARY based on 17p bullets

The FDA advisory board meeting on Multi Cancer Early Detection (MCED) tests provided a comprehensive discussion on the future of cancer screening and diagnosis. This summary captures the key points and themes discussed across the meeting's various segments.

1. **Cancer Detection Technology and Screening Tests:** The panel examined the design of MCED tests and highlighted the current limitation of FDA-approved tests to single cancer types. The need for large-scale studies to demonstrate clinical validity of MCED tests was emphasized, alongside the importance of considering performance per cancer type and aggregated analysis for early detection.
2. **Validation and Performance of Screening Tests:** Discussions revolved around test validation, including study design strategies to mitigate bias and false results. The FDA's role in determining the safety and efficacy of these tests was highlighted, balancing probable benefits against risks.
3. **Clinical Validation and Real-World Evidence:** The panel explored using real-world evidence in clinical validation, particularly for rare cancers. The significance of comprehensive clinical validation study designs was stressed, considering aspects like technology, target population, and specimen type.
4. **Early Cancer Detection and Treatment Options:** Testimonials from oncologists and cancer patients underlined the critical importance of early detection for successful treatment. The perspectives shared emphasized the potential life-saving impact of early detection through MCED technologies.
5. **Challenges and Risks of MCED Tests:** The potential risks and challenges of implementing MCED tests, especially in underserved populations, were discussed. The panel considered the implications of overdiagnosis, overtreatment, and the necessity of post-market studies to continually assess safety and effectiveness.
6. **Screening Test Performance and Safety:** The evaluation of MCED tests against alternative methods was considered vital to minimize risks of overdiagnosis and overtreatment. The importance of assessing test accuracy and the level of evidence required to support a positive benefit-risk assessment were discussed.
7. **FDA's Role and Regulatory Process:** The FDA's process for evaluating and approving cancer detection tests was examined. The agency's commitment to timely and effective reviews, considering breakthrough designations and the need for balanced risk-benefit analysis, was highlighted.
8. **Clinical Trial Design and Validation Methods:** The meeting covered critical considerations in clinical trial design, including control arm size, minority representation, and inclusion of high-risk patients. The importance of mortality reduction as a valid endpoint and the challenges in validating tests for multiple cancer types were discussed.
9. **Patient Experiences and Perspectives:** Patient advocates and cancer survivors shared their experiences, emphasizing the urgency and life-changing impact of early cancer detection. The discussions included personal stories highlighting the challenges and potential benefits of MCED technologies.

10. **Disparities in Cancer Diagnosis and Treatment:** Significant attention was given to the disparities in cancer diagnosis and treatment, particularly for African American populations. The panel urged actions to ensure new technologies are accessible to underserved communities.
11. **Imaging Techniques and Diagnostic Accuracy:** The accuracy and practical challenges of various imaging techniques, such as PET and CT scans, were discussed. The limitations of current methods and the potential of new technologies in improving cancer diagnosis accuracy were highlighted.
12. **Future Directions and Recommendations:** The meeting concluded with discussions on the future of cancer screening and diagnosis. This included suggestions for improving test accessibility, the importance of comprehensive approaches to screening, and the need for ongoing collaboration and communication among all stakeholders.

In summary, the FDA advisory board meeting on MCED tests delved into the complexities and potential of multi-cancer early detection technologies. It highlighted the critical need for rigorous validation, consideration of risks and benefits, and addressing disparities in cancer care. The discussions reflected a consensus on the transformative potential of these technologies, balanced by a cautious approach to their implementation and regulatory approval.

CLAUDE.AI AUTO ESSAY based on 17 page bullets.

Here is a 477-word summary of the key points from the FDA meeting transcript on multi-cancer early detection (MCED) tests:

The FDA meeting focused on the validation, performance, and potential benefits and risks of emerging MCED technologies that aim to screen for multiple cancers through a single blood test. A major focus was assessing if these tests can reliably detect cancer at early, more treatable stages and reduce cancer mortality.

Multiple expert panelists emphasized that demonstrating a mortality benefit is the gold standard for validating cancer screening tests before adoption. Since MCED tests aim to screen for multiple cancer types simultaneously, analyzing performance on a per cancer basis and in aggregate is important. Experts also discussed optimal study design elements like minimum sensitivity thresholds, appropriate control arms for comparison to standard screening, and sufficient sample sizes.

Balancing benefits versus potential risks posed by MCED tests was a key theme. While the ability to screen for currently unscreened cancers could save lives through early detection, false positives leading to unnecessary invasive follow-up procedures are a concern. Clearly communicating test limitations and results to patients is vital to set appropriate expectations and minimize potential anxiety. Equity of access for marginalized communities was also discussed.

The feasibility of using overall mortality versus early detection, stage shift or other surrogate endpoints in trials was debated. Some argued that curative treatment and mortality are the clearest indicators of patient impact. However others noted that trials focusing on mortality may be unfeasible or raise ethical concerns by randomizing standard screening. The merits of real world data for continued post-market surveillance were also discussed.

Overall the meeting underscored both the profound promise and complexity involved in advancing and validating a new paradigm for multi-cancer screening. Panelists emphasized that demonstrating a mortality benefit ultimately hinges on testing performance across diverse populations in large randomized controlled trials. Careful communication of benefits and risks will be integral as these technologies continue to evolve.