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Cell-free DNA Indicates Potential Preclinical Detectability of Cancer Signals up to 30 Months Prior to Diagnosis

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DECLARATION OF INTERESTS

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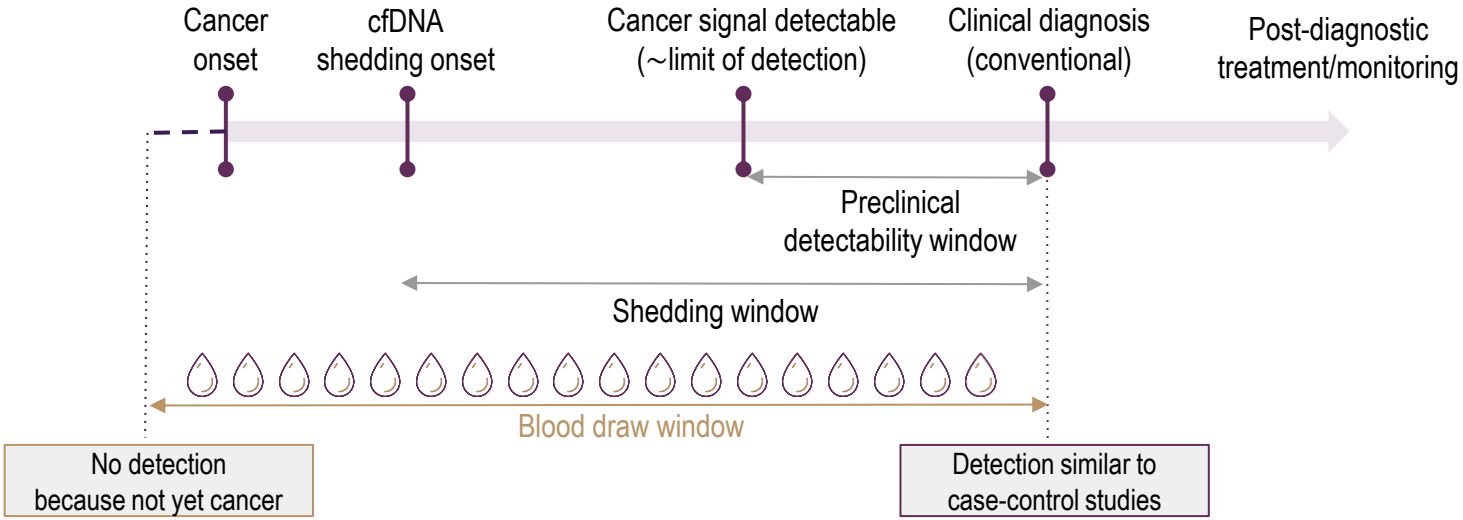
Methylation-Based Cancer Signals Can Be Detected and Quantified from Blood Samples

Early detection of cancer can occur in the preclinical phase



American Cancer Society Cancer Prevention Study-3[1]

323 days

average time between blood draw and diagnosis among those detected

How early can we detect preclinical cancer signals?

[1]Patel AV, et al. Presented at ASCO Annual Meeting. June 2-6, 2023. ASCO 2023.
cfDNA, cell-free DNA.

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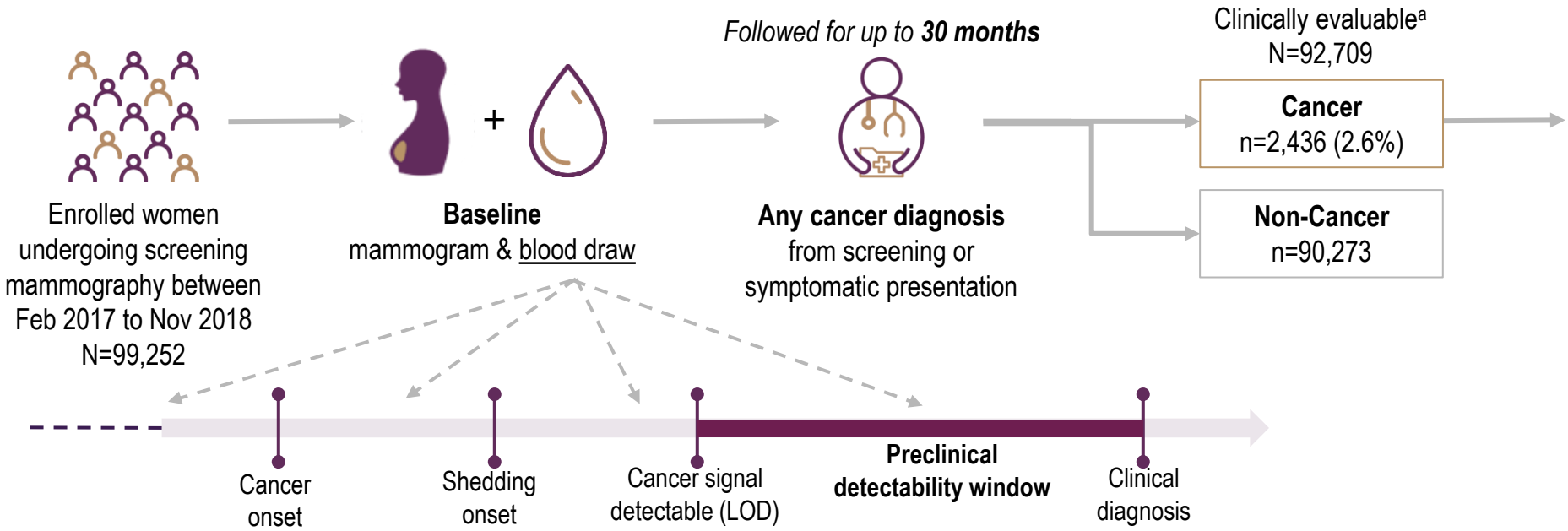
STRIVE (NCT03085888): A Multicenter, Prospective, Observational Cohort Study



Different timepoints of cancer development can be captured in sampling population

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[a]Excludes participants who withdrew (n=6394), had active cancer (n=42), or had uncertain cancer outcomes (n=107).
LOD, limit of detection.

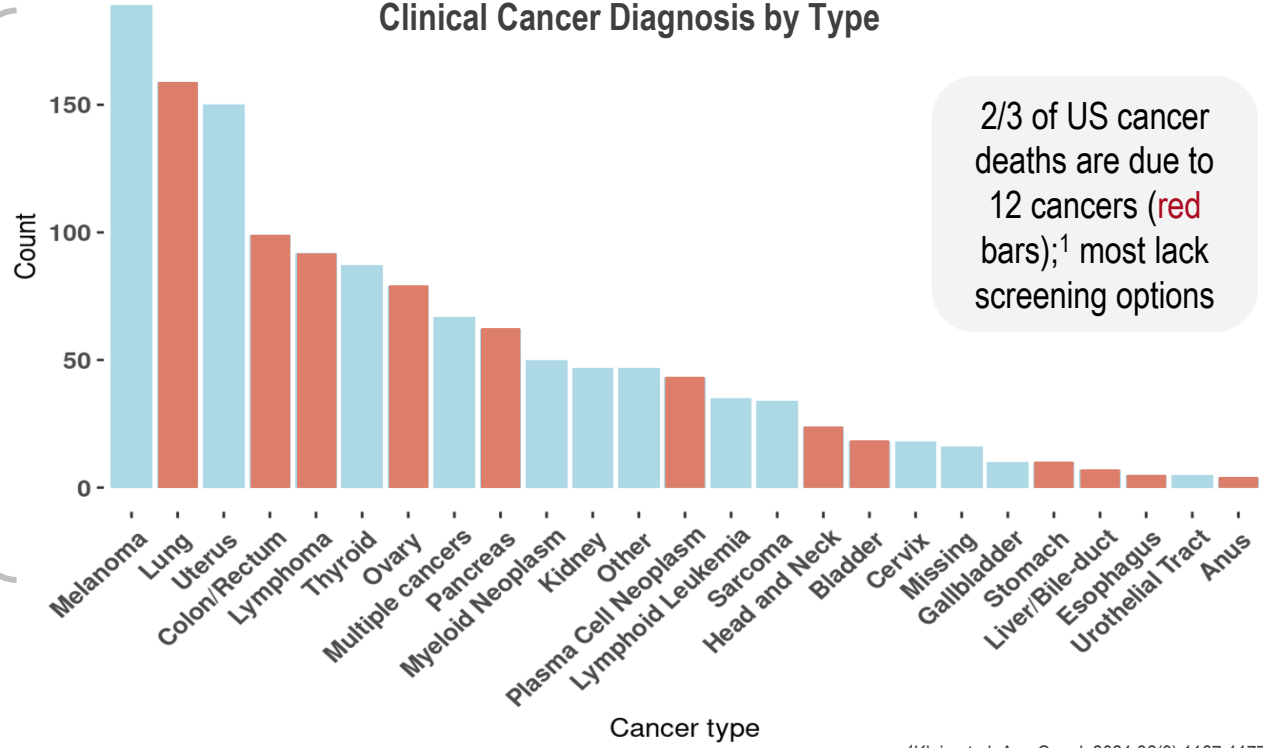
STRIVE (NCT03085888): A Multicenter, Prospective, Observational Cohort Study

Cancer
n=2,436
(2.6%)

Non-Breast Cancer
n=1,358
(55.7%)

+

Breast Cancer
n=1,078
(44.3%)



2/3 of US cancer deaths are due to 12 cancers (red bars);[1] most lack screening options

[1]Klein et al. Ann Oncol. 2021;32(9):1167-1177.

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Analysis Objective: Assess the time between preclinical cancer signals at baseline and future cancer diagnosis in a mammography screening cohort

Sampling Scheme

Cancer: Down-sampling in Breast, Melanoma, and Thyroid

Non-Cancer: Stratified by network and age (+/-50)

Analysis Set

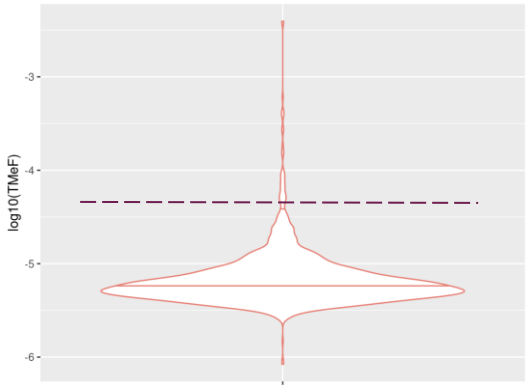
Samples analyzed for **tumor methylated fraction (TMeF)**, an estimate of the amount of tumor-derived cfDNA in blood

Cancer: n=1,519
Breast (n=492)
Non-breast (n=1,027)

Non-Cancer: n=1,616

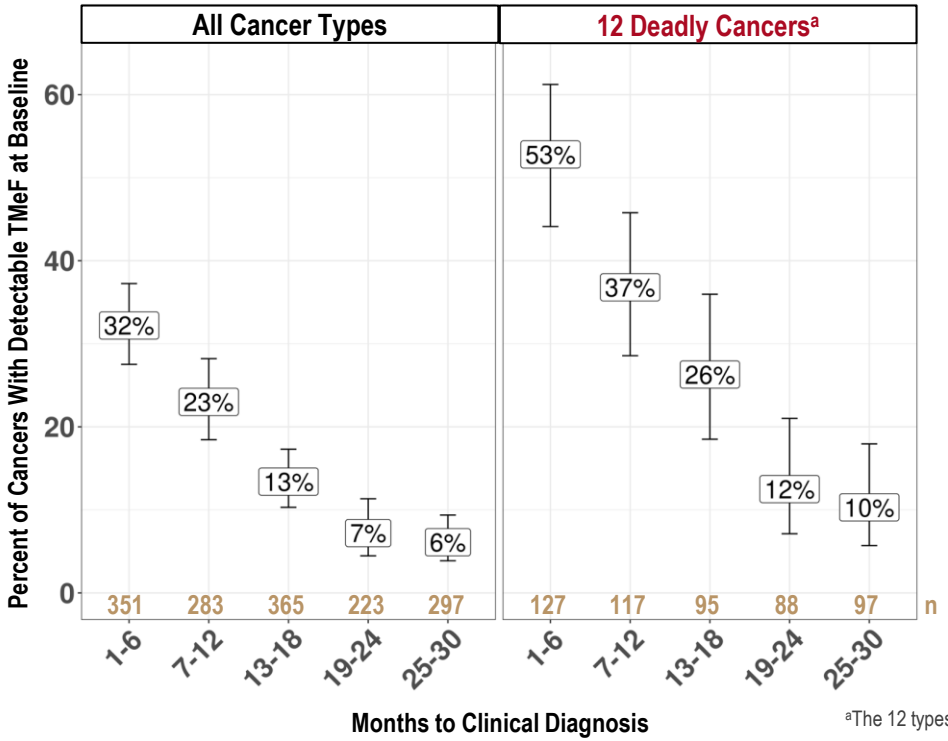
Analysis Methods

"Detectable TMeF" a proxy for MCED test detectability[1]
>98th percentile of TMeFs in non-cancer samples



[1]Melton et al. Cancers. 2024;16(1):82.
cfDNA, cell-free DNA; MCED, multi-cancer early detection.

Cancers Diagnosed Closer to Blood Draw Were More Likely to Have Detectable TMeF at Baseline

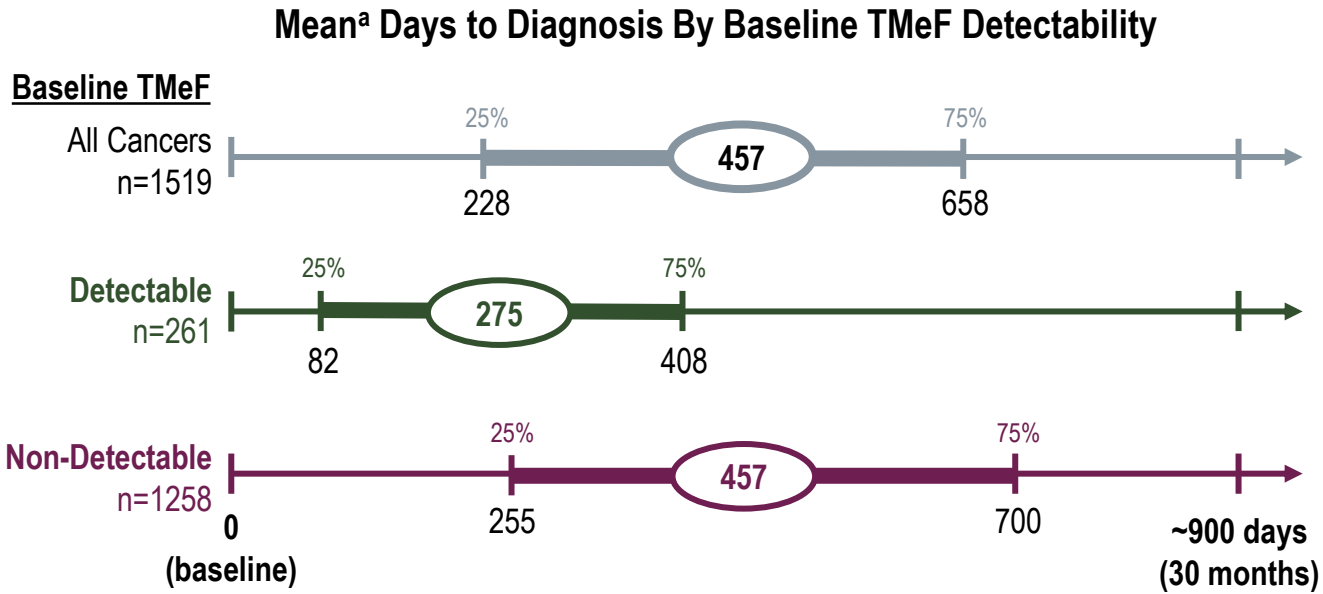


cfDNA Shedding Dynamics

- cfDNA shedding tends to increase as cancers move closer to diagnosis
- For certain cancers, preclinical signals can be detected many months prior to diagnosis
- 17% (261/1519) of all cancers in the analysis set had detectable baseline TMeF
- Aggressive and lethal cancers tend to shed more cfDNA,[1] making them more likely to have detectable baseline TMeF
  - 30% (156/524) of these 12 deadly cancers had detectable baseline TMeF
  - For these 12 cancers, the percent with detectable baseline TMeF was significantly higher than for all *other* cancers ($p < 0.001$)

[a]The 12 types of cancer that account for ⅔ of US cancer deaths (Klein et al. Ann Oncol. 2021;32(9):1167-1177).
[1]Chen et al. Clin Cancer Res. 2021;27(15):4221-4229.
cfDNA, cell-free DNA; PC, plasma cell; TMeF, tumor methylated fraction.

Detectable Signal Preceded Clinical Diagnosis by 275 Days on Average



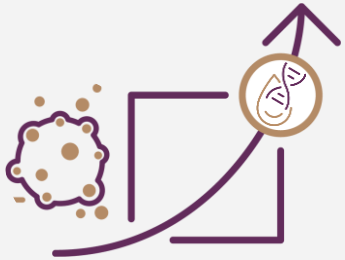
Results in Context:
The average time to diagnosis of 275 days for those with preclinical detectability in this mammography screening cohort[b] is less than that observed in the ACS study (323 days) of low-risk volunteers; factors of **age** and **cancer composition** may explain this difference

Timelines include mean days to diagnosis and interquartile range.
[a]Mean is the natural parameter for summarizing exponential distributions such as sojourn time.
[b]As this study followed a screening mammography cohort, diagnosed cancers were likely enriched for day 0 (baseline) breast cancer diagnoses, which may have shortened the average time to diagnosis.
ACS, American Cancer Society; TMeF, tumor methylated fraction.

Cancer Signals in Blood Can Be Detected Prior To Diagnosis

The average preclinical detectability window is consistent with an annual screening interval

In this cohort, TMeF detectability suggests that MCED screening can potentially identify cancers **up to 30 months** before clinical presentation (eg, a stage II pancreatic cancer diagnosed at day 896)



TMeF was consistently and significantly **more detectable in 12 deadly cancers** compared with other cancers

The mean time of 275 days between detectable baseline TMeF and cancer diagnosis suggests that the average preclinical detectability window by MCED test is **within 1 year** for this screening adherent population

MCED, multi-cancer early detection; TMeF, tumor methylated fraction.

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We acknowledge the contributions to this effort of the patients, staff, and healthcare providers who provided clinical data

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For more on cancer signal dynamics, see poster 1184P “Early Real-World Experience With Positive Multi-Cancer Early Detection (MCED) Test Cases And Negative Initial Diagnostic Work-Up”

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