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Population Health Impact of Incorporating a Multi-Cancer Early Detection (MCED) Test To Existing Cancer Screening Among Immunocompromised Individuals

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INTRODUCTION

- Current standard of care (SoC) for cancer screening involves screening one cancer type at a time (e.g., breast, colorectal, cervical, and lung cancer) based on age and other risk factors.
- A previous modeling study[1] has shown that adding a multi-cancer early detection (MCED) test to SoC screening improves screening efficiency among the general population aged 50-79 years, yielding a true-positive to false-positive (TP:FP) ratio of 1:1.8 with an incremental MCED test, compared to 1:43 with SoC screening alone.
  - To detect one person with cancer with an incremental MCED test, approximately 2 people without cancer may undergo diagnostic investigations following a screen-positive result, compared to 43 people with SoC screening alone.
- The potential screening efficiency of an incremental MCED test has not yet been assessed among those aged 50-79 years with additional risk factors.

OBJECTIVES

- To estimate the potential screening efficiency of an incremental MCED test among immunocompromised individuals with a history of solid organ or hematopoietic stem cell transplant (SOT/HSCT) or diagnosed with primary or secondary immunodeficiency disorders (PID/SID).
- To assess the costs associated with diagnosing cancers following a positive test.

KEY RESULTS: THE ADDITION OF A MULTI-CANCER EARLY DETECTION (MCED) TEST TO COMPLEMENT CURRENT EXISTING SCREENING IS A POTENTIALLY EFFICIENT STRATEGY AMONG IMMUNOCOMPROMISED INDIVIDUALS

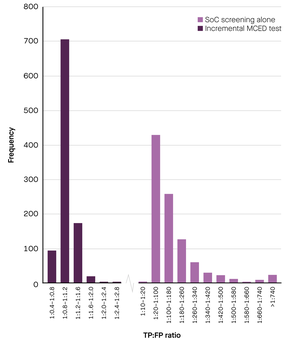
- The TP:FP ratio was higher (i.e., greater screening efficiency) with the addition of an MCED test at 1:1, compared to SoC screening alone at 1:99 (**Table 1**).
- The diagnostic yield was higher with an incremental MCED test (5.15/1000 tests), compared to SoC screening alone (1.23/1000 tests), indicating that a higher proportion of screening tests conducted yielded true positives (**Table 1**).
- Compared to the CDR of 5% for SoC screening alone, more cancers were likely to be detected with an incremental MCED test, exceeding an 8-fold increase (**Table 1**).
- Based on the distribution of values generated from the PSA, the TP:FP ratio, diagnostic yield, and CDR of an incremental MCED test remained superior to those of SoC screening (**Figures 1-3**).
- The total diagnostic workup costs for the entire patient cohort following screen-positive results for SoC screening alone and an incremental MCED test were $154,850 and $99,638, respectively. The diagnostic workup costs per cancer detected following positive screens for SoC screening alone and an incremental MCED test were $48,577 and $3,925, respectively (**Table 1**).

Table 1. Screening Outcomes of SoC Screening Alone and an Incremental MCED test

	SoC Screening Alone	Incremental MCED Test*
Total positives*	318	50
True positives*	3	25
TP:FP ratio	1:99	1:1
Diagnostic yield†	1.23 per 1000 tests	5.15 per 1000 tests
Cancer detection rate‡	5%	42%
Total diagnostic cost^	$154,850	$99,638
Diagnostic cost/cancer^	$48,577	$3,925

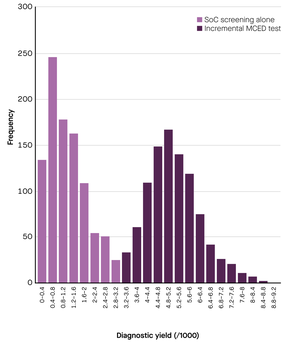
*Outcomes represent efficiency of an additional MCED test conducted after SoC cancer screening. *Rounded to closest whole number of cases.
†Diagnostic yield = Total cancers detected/Number of screening tests performed.
‡Cancer detection rate = Total cancers detected/Total expected number of cancer cases.
^All positive screening results were assumed to received diagnostic workup.
Abbreviations: SoC, standard of care; MCED, multi-cancer early detection; TP:FP, true-positive to false-positive

Figure 1. Distribution of TP:FP Ratio for SoC Screening Alone and an Incremental MCED Test



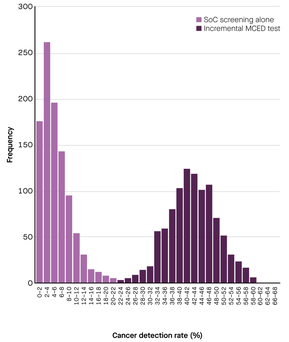
Abbreviations: SoC, standard of care; MCED, multi-cancer early detection

Figure 2. Distribution of Diagnostic Yield for SoC Screening Alone and an Incremental MCED Test



Abbreviations: SoC, standard of care; MCED, multi-cancer early detection

Figure 3. Distribution of Cancer Detection Rate for SoC Screening Alone and an Incremental MCED Test



Abbreviations: SoC, standard of care; MCED, multi-cancer early detection

CONCLUSIONS

- Adding an MCED test to SoC screening is estimated to further improve the screening efficiency among immunocompromised individuals.
- The higher diagnostic yield and CDR with an incremental MCED test were driven by a higher number of true positives, given the wider range of cancers detected.
- The high specificity of the MCED test also resulted in an improved TP:FP ratio and fewer false positives, resulting in a lower diagnostic cost per cancer detected among screen-positive cases.
- Limitations of the study included having a small sample of size of immunocompromised individuals from a single institution, from which the cancer incidence was extrapolated. As a result, the incidence of some cancers, such as cervical cancer, may not be representative of the wider population of immunocompromised patients. Also, this model did not simulate the potential for missing a cancer due to cancer development in these individuals.

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Disclosures

This project received funding from GRAIL, LLC, a subsidiary of Illumina, Inc.*
*GRAIL, LLC is currently held separate from Illumina, Inc.under the terms of the Interim Measures Order of the European Commission dated 29 October 2021.

METHODS AND SUPPORTING DATA

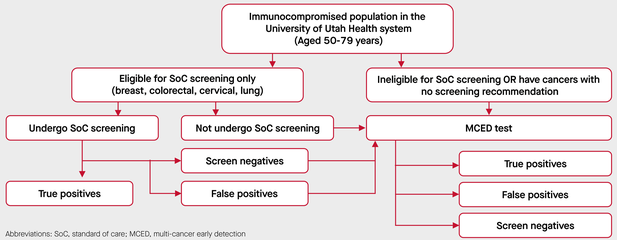
- The impact of incorporating an MCED test to SoC screening over 1 year was modeled in a real-world cohort of patients aged 50-79 years who either (i) underwent a SOT/HSCT or (ii) were diagnosed with a PID/SID (e.g., HIV) between 1/1/2000 and 2/28/2018 in the University of Utah Health system.[2] The predictive model is illustrated in **Figure 4**, and the model parameters are described in **Table 2**.
- Screening efficiency was evaluated based on the following outcomes: (i) total number of individuals with a positive test; (ii) total number of individuals diagnosed with cancer following a positive test (true positives); (iii) TP:FP ratio; (iv) the number of cancers detected as a proportion of the total number screened (diagnostic yield); (v) the number of cancers detected divided by the total number of cancers expected in the population (cancer detection rate, CDR). The costs of diagnosing a cancer case following a positive screening test result to differentiate true cancer cases from false positives were also estimated.
- A probabilistic sensitivity analysis (PSA) was performed to test the robustness of our model to parameter uncertainty. A Monte-Carlo simulation was conducted with 1,000 iterations and varied model inputs including cancer incidence rates, adherence to SoC screening, and test performance.

Table 2. Model Parameters and Data Sources

Model Parameter	Data Source
Cancer incidence rates (**Figure 5**)	Linkage of patient cohort identified from the University of Utah data warehouse to tumor registry[2]
Screening eligibility	SoC screening: based on demographic characteristics of real-world cohort [2] and guideline recommendations[3-6]
Adherence to screening	SoC screening: Utah-specific self-reported adherence rates from the Behavioral Risk Factor Surveillance System survey[7]; National lung cancer screening registry[8] MCED test: Assumed to be 100%
Screening performance	SoC screening and MCED test: published literature [9-13]
Diagnostic workup cost	Estimated using a micro-costing approach based on published procedure charges assuming each recommended diagnostic procedure was performed once following a positive screen[14]

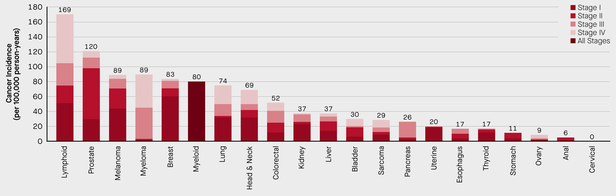
SoC, standard of care; MCED, multi-cancer early detection

Figure 4. Schematic Diagram of Predictive Model



Abbreviations: SoC, standard of care; MCED, multi-cancer early detection

Figure 5. Site-Specific Cancer Incidence in Real-World Patient Cohort



- Among immunocompromised patients aged 50-79 years in the University of Utah Health system (n=4,932), the cancer incidence was approximately 1,225/100,000 person-years, which equates to a total of 60 cancer cases in one year. The most common cancer type in our patient cohort was lymphoma, followed by prostate cancer (**Figure 5**).