Baseline Participant Characteristics From PATHFINDER 2, a Prospective Interventional Study of a Multi-Cancer Early Detection Test in a Population Setting

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INTRODUCTION

- Multi-cancer early detection (MCED) tests are being established as a novel approach to simultaneously screen for multiple cancer types with 1 test
- A blood-based MCED test that uses targeted methylation patterns in cell-free DNA to detect a shared cancer signal and predict the cancer signal origin has demonstrated feasibility as a screening tool in large-scale clinical trials (CCGA [NCT02889978]; PATHFINDER [NCT04241796])[1,2]
- This MCED test (Galleri®) is commercially available and >350,000 tests have been administered in clinical settings[3]
- The MCED test has shown consistent performance across racial and ethnic groups,[4] though generalizability of these results may be limited by sample size and participant demographics that do not fully reflect the diversity of a broad screening population (eg, 91.7% of PATHFINDER participants were White[2])
- It is increasingly recognized that certain demographic groups shoulder disproportionate cancer burdens while being historically underrepresented in cancer screening trials[5,6]
- The PATHFINDER 2 study (NCT05155605) will further evaluate safety and performance of the MCED test in a large and diverse intended-use population (individuals aged ≥50 years and without clinical suspicion of cancer)[7]

OBJECTIVE

- To understand the generalizability of PATHFINDER 2 study results by assessing participant baseline characteristics relative to the general US population based on data from the National Health and Nutrition Examination Survey (NHANES)

METHODS

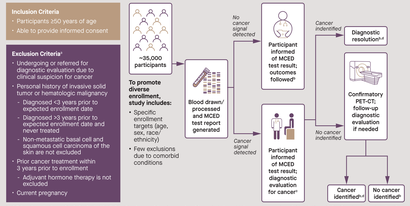
PATHFINDER 2

- PATHFINDER 2 is a prospective, multicenter, interventional study that enrolled participants aged ≥50 years from diverse clinical settings in North America[7] (**Figure S1**)
  - Key exclusion criteria included clinical suspicion of cancer or cancer diagnosis/treatment within 3 years prior to enrollment
- Enrollment targets for sex and race/ethnicity were established from the 2019 American Community Survey (US Census Bureau)
- Enrollment targets for age were enriched for the 60-69 years and 70-79 years age categories relative to the US population (based on 2020 Census data)
- Recruitment strategies were implemented to maximize enrollment for groups historically underrepresented in clinical studies (**Figure S2**)
- Data on baseline demographics (age, sex, race/ethnicity) and key characteristics associated with cancer risk (education, marital status, smoking status, BMI, and alcohol use) were collected at enrollment

NHANES Comparison Data

- The PATHFINDER 2 study population was compared with a nationally representative sample of US adults aged ≥50 years from the 2017-2020 NHANES[8]
- NHANES assesses overall health and nutrition of adults and children in the US and is conducted by the National Center for Health Statistics[9]
  - NHANES uses a complex, multistage probability sampling design that allows for the generation of a nationally representative sample[8]
  - NHANES participants are selected from the noninstitutionalized US civilian population
  - The 2017 to March 2020 (pre–COVID-19 pandemic) NHANES data were used to ensure a sample that would be an appropriate comparison for the PATHFINDER 2 population
- Analytic weights provided by NHANES were applied in all analyses to ensure estimates were representative of the US population, which was assessed by comparison to demographic data from the US Census Bureau's 2018 5-year American Community Survey

Figure S1. PATHFINDER 2 Study Design Overview.



[a]Additional exclusion criteria included individuals who could not comply with protocol procedures, were not registered at participating centers, previously participated in a GRAIL-sponsored study, or were current employees/contractors of GRAIL. [b]All participants will be actively followed by enrolled institutions for 3 years to assess cancer status and utilization of guideline-recommended cancer screening. [c]Diagnostic evaluations based on CSO are recommended in the protocol. [d]Clinical information including, but not limited to, cancer type, histology, and staging information will be captured.
CSO, cancer signal origin; MCED, multi-cancer early detection; PET-CT, positron-emission tomography-computerized tomography.

Figure S2. Strategies to Promote Diverse Recruitment.

- Multiple translations available for study documents, including consent form, participant-reported outcomes, educational, and outreach materials
- Participant- and provider-centric educational and outreach materials in digital and printed formats
- Resourcing for site-led community outreach and enrollment events
- Network collaboration at sites that include multiple subspecialties and/or practice locations

KEY RESULTS: THE PATHFINDER 2 STUDY POPULATION LARGELY REFLECTS THE MCED TEST INTENDED-USE POPULATION IN THE US

Overall Enrollment

- Of 35,878 participants enrolled in PATHFINDER 2, this analysis included 35,307 **(98.4%)** who were clinically eligible and evaluable
- Strategies to promote diverse recruitment (**Figure S2**) were utilized to enroll participants from 32 clinical sites across 19 US states, the District of Columbia, and 1 Canadian province[7]

Demographic Distribution

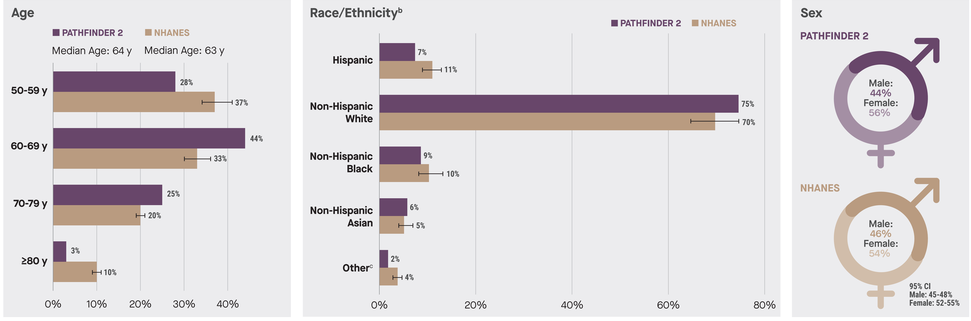
- PATHFINDER 2 participant demographics were generally reflective of the weighted NHANES population sample aged ≥50 years (**Figure 1**)
  - The median age was 64 years in the PATHFINDER 2 dataset and 63 years in the NHANES dataset
  - The age distribution was generally comparable between the PATHFINDER 2 and NHANES datasets
    - The percentage of people aged ≥65 years was 49% in the PATHFINDER 2 dataset and 44% (95% CI 41-48%) in the NHANES dataset
  - **Sex and racial/ethnic distributions were similar** between PATHFINDER 2 participants and the NHANES dataset

Lifestyle Characteristics

- PATHFINDER 2 participants had a generally similar distribution of lifestyle characteristic data as the NHANES dataset, but were more likely to report characteristics associated with better health (**Figure 2**)
- Compared with the weighted NHANES dataset:
  - A higher percentage of PATHFINDER 2 participants were highly educated (bachelor's degree or higher)
  - A lower percentage of PATHFINDER 2 participants were former or current smokers
  - A higher percentage of PATHFINDER 2 participants were married/living with a partner
  - A lower percentage of PATHFINDER 2 participants were overweight or obese (body mass index [BMI] ≥25 kg/m²)
  - A higher percentage of PATHFINDER 2 participants reported moderate or heavy alcohol use

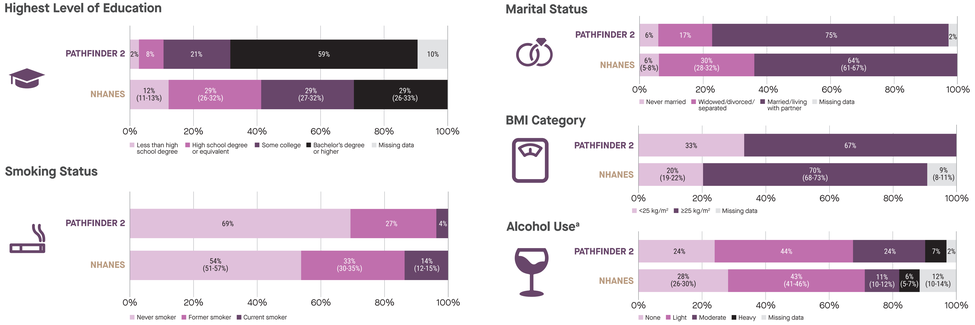
Figure 1. PATHFINDER 2 Participant Demographic Distribution Aligned With Weighted NHANES Data.

PATHFINDER 2 (N=35,307[a]) **NHANES (N=114,420,685)**



Weighted NHANES data presented with 95% CI. [a]Clinically eligible and evaluable population. [b]Missing race/ethnicity data: 1.8%. [c]Other includes non-Hispanic Native American, non-Hispanic multiracial, and non-Hispanic Native Hawaiian or other Pacific Islander.
CI, confidence interval; NHANES, National Health and Nutrition Examination Survey; y, years.

Figure 2. Lifestyle Characteristics Were Generally Similar Between PATHFINDER 2 and NHANES, With PATHFINDER 2 Participants More Often Reporting Characteristics Associated With Better Health.



Weighted NHANES data presented with 95% CI. Totals may not add up to 100% due to rounding.
[a]None is defined as 0 drinks per week; Light is ≤3 drinks per week; Moderate is >3 and ≤7 drinks per week for women and >3 and ≤14 drinks per week for men; Heavy is ≥7 drinks per week for women and ≥14 drinks per week for men.
BMI, body mass index; NHANES, National Health and Nutrition Examination Survey.

CONCLUSIONS

- PATHFINDER 2 enrolled a diverse participant population that matches the demographics of the US population aged ≥50 years
  - 25% of PATHFINDER 2 participants were from demographic groups historically underrepresented in cancer screening trials[a]
- As has been observed in prior cancer screening trials,[10] a higher percentage of PATHFINDER 2 participants reported characteristics associated with better health compared with the NHANES participants
- Safety and performance results from PATHFINDER 2 are expected to reflect real-world clinical experience given that the study population largely reflects the intended-use population for the MCED test

[a]Historically underrepresented demographic groups include Hispanic, Non-Hispanic Black, Non-Hispanic Asian, and Other.

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Disclosures

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