

## Introduction

- Young lung cancer (≤50 years) is rare and biologically distinct, predominantly affecting never-smokers with targetable mutations (EGFR, ALK, ROS1)
- Following peak tobacco incidence in the mid-1980's, lung cancer incidence declined among men but not women, with rates in women continuing to rise
- This gender disparity suggests that an alternative carcinogenic pathway may be driving disease
- Agricultural worker lung cancer risk (HR 2.38)<sup>1</sup> combined with elevated oral contraceptive (OCP) use (75-100%) and consumption of pesticide-prone foods suggests food contaminants and hormonal exposures as possible drivers of female predominance in never-smoking lung cancer populations
- We characterized environmental and lifestyle exposures to understand drivers of this epidemiologic shift
- Hypothesis:** Mutation-specific environmental exposure patterns, including potential dietary contaminant consumption and hormonal factors, contribute to lung cancer risk in young patients

1. Alavanja MCR et al. *Am J Epidemiol.* 2004;160(9):876-885

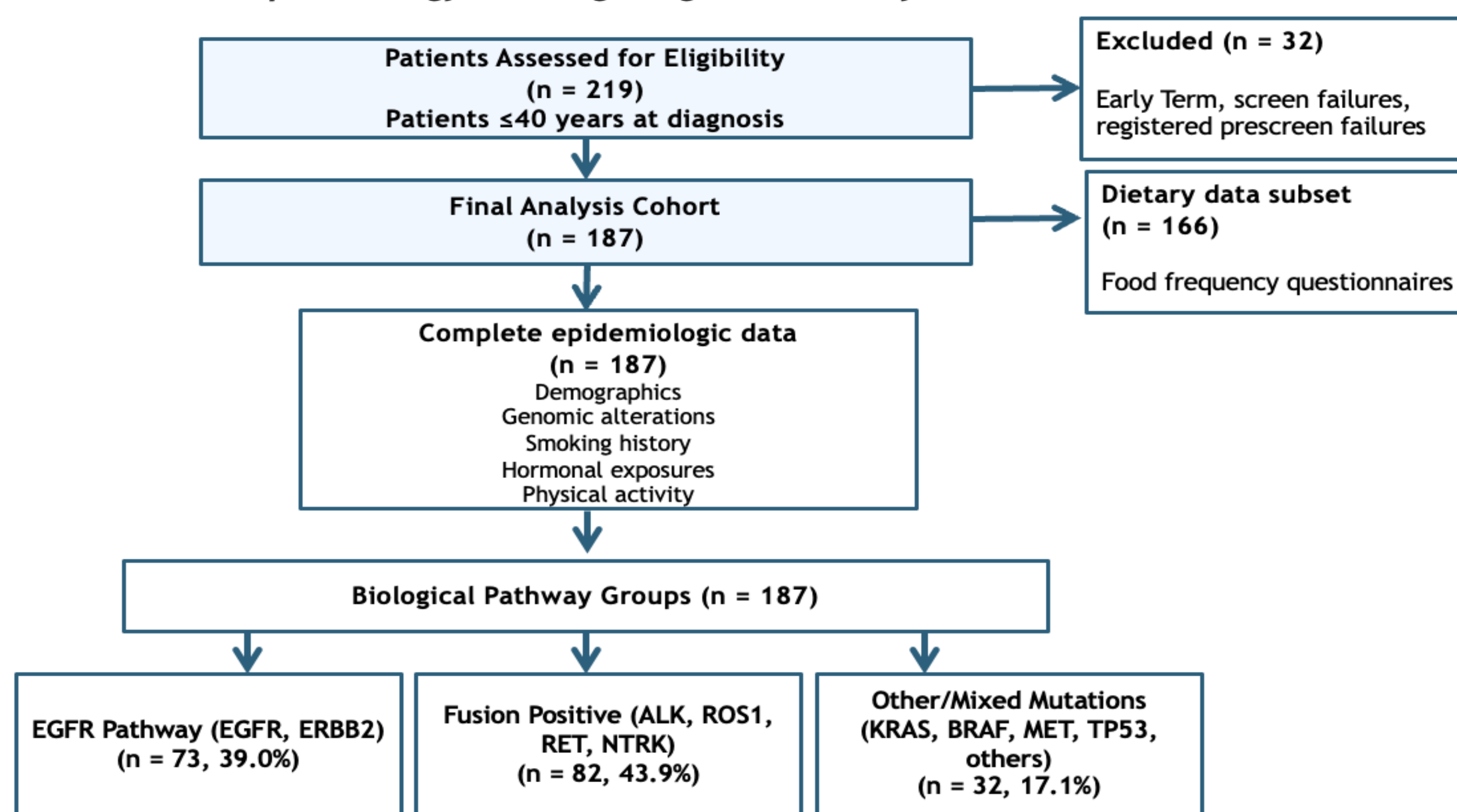
## Methods

- Study Design:** The Epidemiology of Young Lung Cancer (NCT04640259) is a multi-institutional, virtual, observational case study that explored environmental, lifestyle, and genetic factors associated with driver mutations in young lung cancer patients nationwide.
- Data Collection:** Comprehensive epidemiological surveys captured smoking history, oral contraceptive use, demographics, diet, physical activity and genomic alterations for the year prior to their lung cancer diagnosis
- Mutation Classification:** Biological pathway grouping: EGFR Pathway (EGFR+ERBB2, n=73), Fusion Positive (ALK+ROS1+RET+NTRK, n=82), Other/Mixed Mutations (KRAS, BRAF, MET, TP53, PIK3CA, additional alterations, n=32)
- Dietary Assessment:** Validated food frequency questionnaires. Dietary quality assessed using Healthy Eating Index-2020 (HEI-2020) compared to NHANES U.S. reference values. High-residue food categories identified using published literature
- Statistical Analysis:** One-sample t-tests against reference means, chi-square tests for categorical variables

Figure 1. Patient Flow Diagram

### Patient Flow Diagram

Epidemiology of Young Lung Cancer Study



## Results

### Cohort Characteristics

- Cohort was predominantly female (146/187, 78.1%) across all pathway groups
- Race/ethnicity was predominantly Non-Hispanic White (75-78%) with representation of Asian and Hispanic/Other populations
- Highly educated cohort, with the majority having college or post-graduate degrees across all pathway groups

Figure 2. Race/Ethnicity

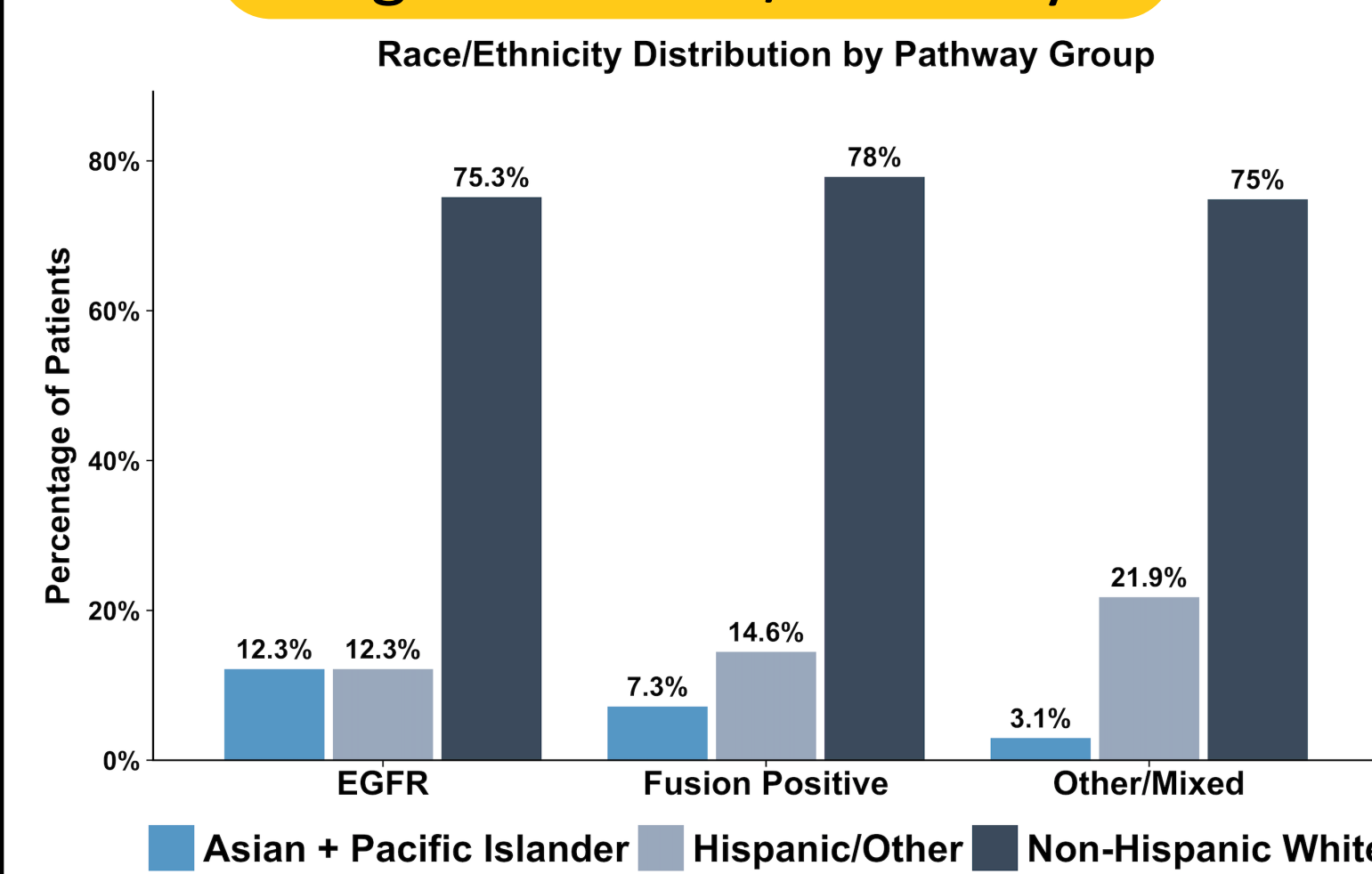


Fig 2. Race/Ethnicity distribution shows predominantly non-Hispanic White patients across all pathway groups.

Figure 3. Education Level

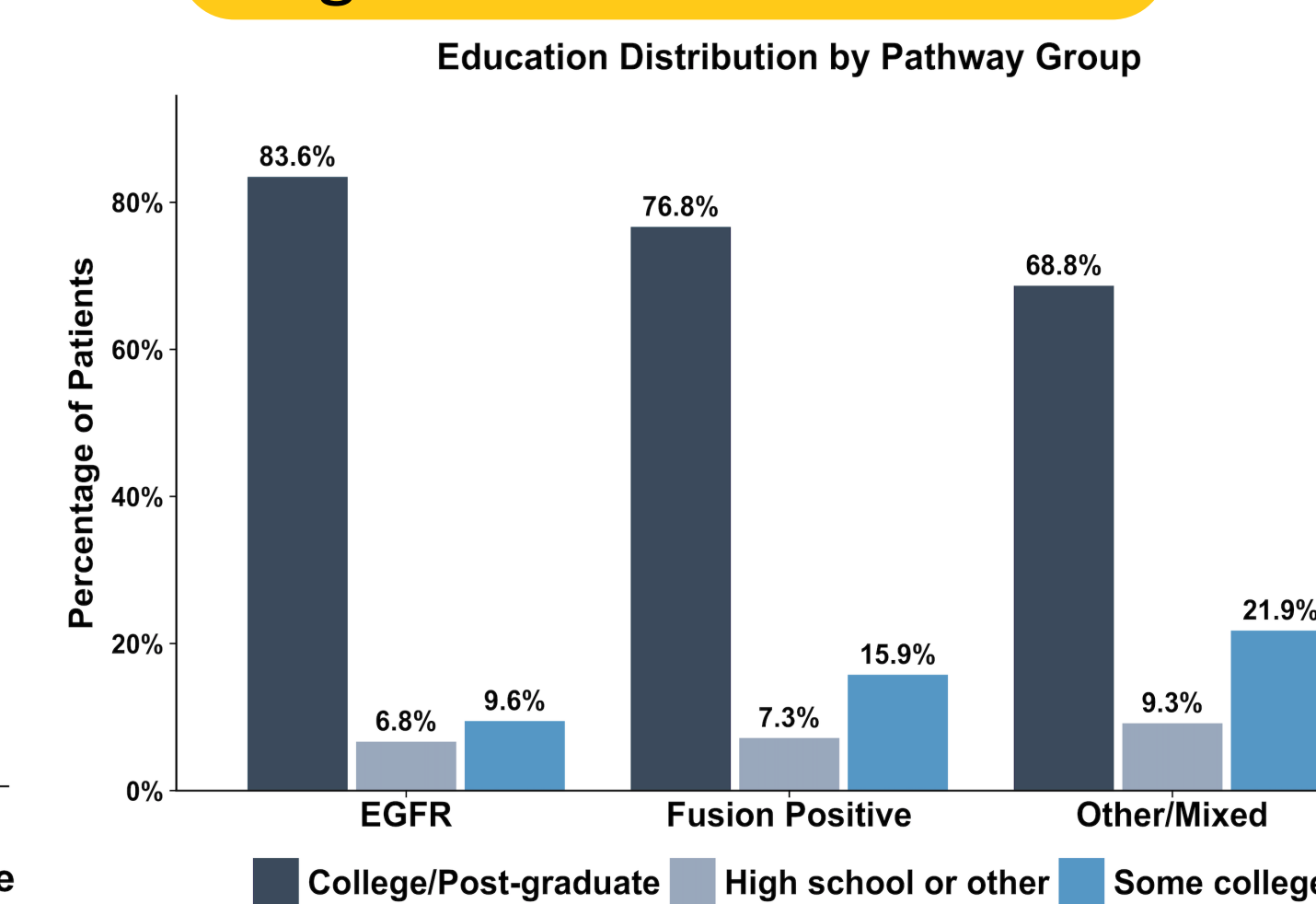


Fig 3. Educational attainment demonstrates highly educated cohort with majority having college or post-graduate degrees.

### Smoking and Hormonal Exposures

- Tobacco patterns diverged from expected associations (p=0.014). EGFR Pathway showed unexpected tobacco exposure (32.9%) despite being classically associated with never-smokers, while Fusion Positive showed expected never-smoking patterns (79.3%)
- Oral contraceptive use consistently elevated (75-100%) across all pathway groups (p>0.05)

Figure 4. Smoking History and OCP Use

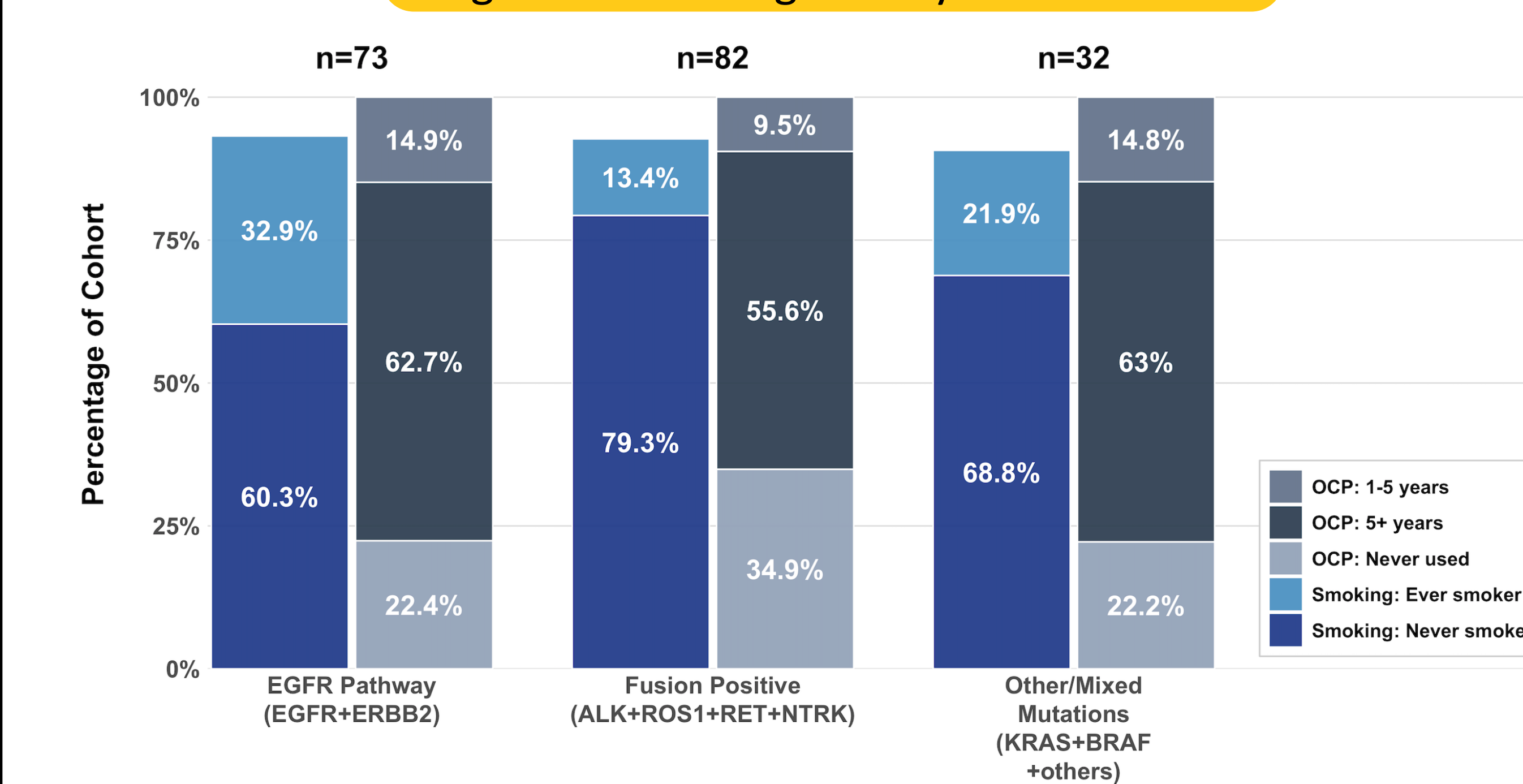


Fig 4. Smoking history and oral contraceptive use by biological pathway group. Stacked bars show percentage of patients by smoking status (never-smoker vs ever-smoker) and OC use duration (never used, 1-5 years, 5+ years) for EGFR (n=73), Fusion Positive (n=82), and Other/Mixed (n=32) groups. Smoking status significantly differed across groups (p=0.014); OCP use patterns were similar (p>0.05).

### Dietary Quality

- EGFR Pathway and Fusion Positive patients demonstrated higher HEI-2020 scores: EGFR 64.94 ± 10.65, Fusion Positive 65.26 ± 9.89 vs. US reference 57
- These patients consumed significantly higher fruits, vegetables, and whole grains, which may have been pesticide-prone (HEI-2020 component scores out of 5): Total vegetables 4.12 vs. 3.4, Fruits 3.3 vs. 2.4, Whole grains 4.12 vs. 2.3 (US reference)

Figure 5. Diet Quality vs US ref  
HEI-2015 Scores: Produce and Whole Grains

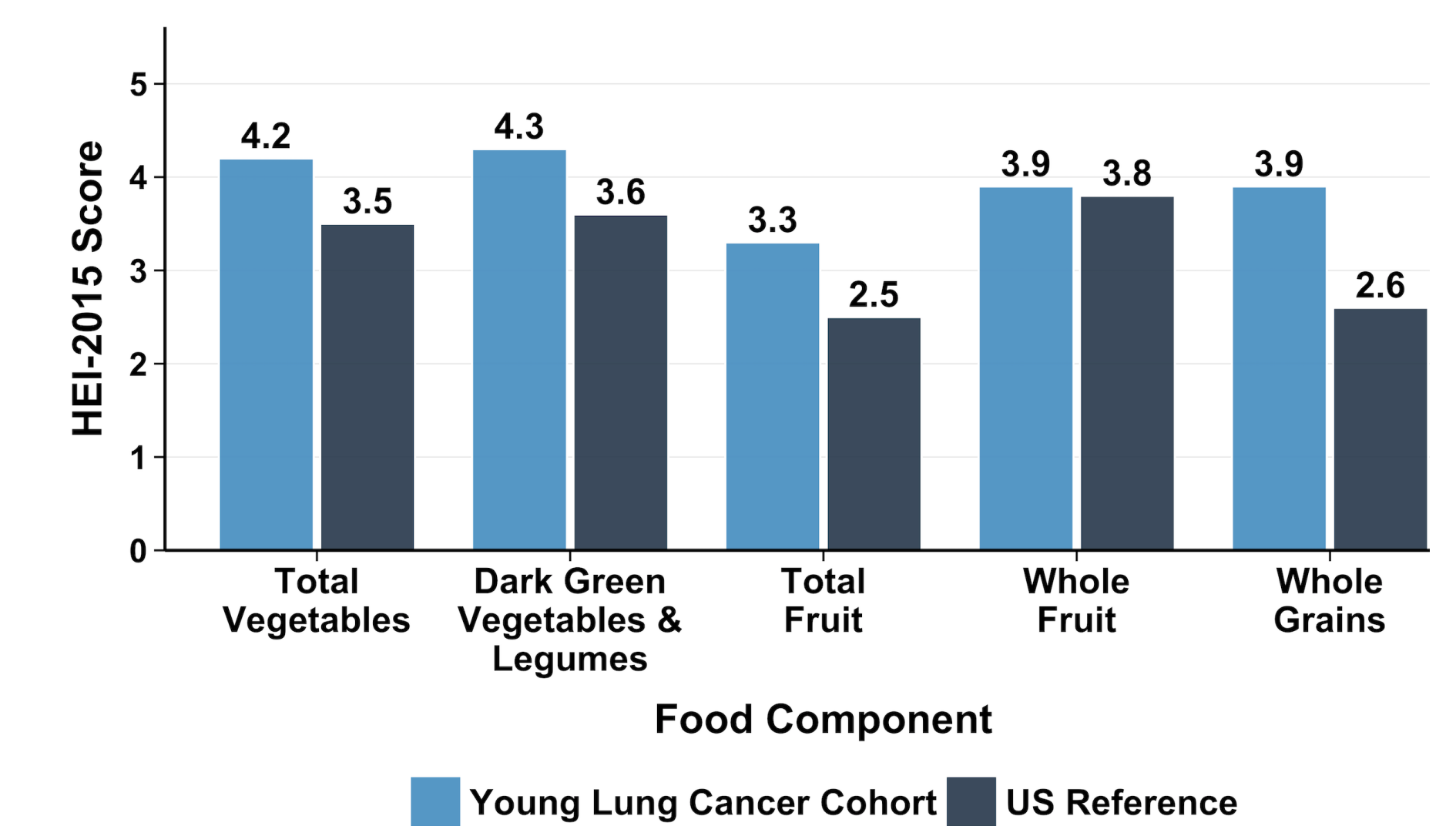


Fig 5. HEI-2020 component scores for pesticide-prone food categories in young lung cancer cohort versus U.S. reference population (NHANES).

Figure 6. Diet Quality by Pathway

HEI-2015 Scores: Produce and Whole Grains

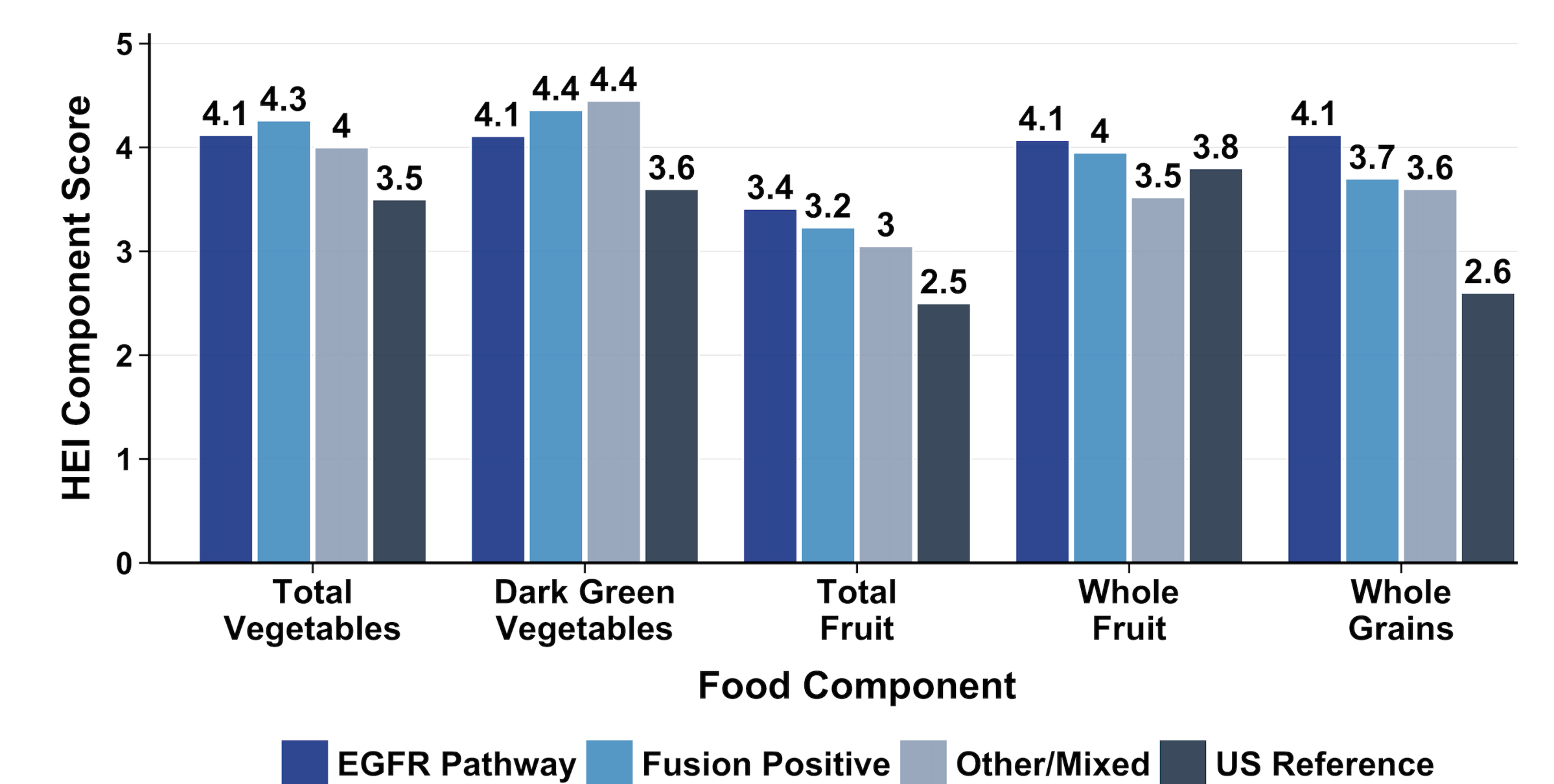


Fig 6. HEI-2020 component scores by pathway group. EGFR Pathway and Fusion Positive groups show highest consumption of pesticide-prone food categories compared to U.S. reference.

## Conclusions

- Young Lung Cancer patients have relatively low tobacco exposure, elevated OCP use, and higher quality diets than the general US population
- Higher diet quality is driven by higher fruit, vegetable and whole grain consumption, which may have subjected these individuals to higher pesticide consumption, and may link dietary factors in young lung cancer patients to increased lung cancer rates observed in agricultural sprayers
- Future research should validate dietary-contaminant-mutation pathways through prospective urinary or blood-based pesticide metabolite biomarker studies

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