UNIVERSITY OF HAWAIʻI
CANCER CENTER

Mammography AI Models and Radiomic Features for Breast Cancer Risk Prediction: A Matched Case-Control Study in an Ethnically-Diverse Cohort

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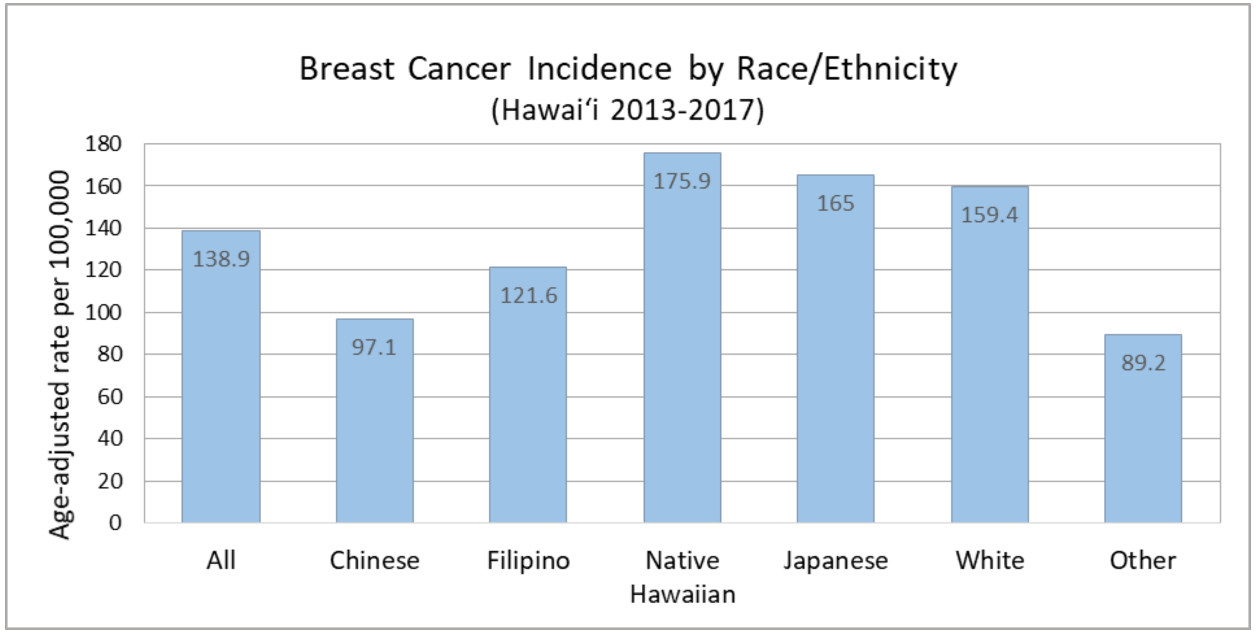
Motivation

- **Hawai‘i is the most diverse state in the USA.** 37% of Hawai‘i identifies as Asian alone and 11% as NHPI alone.
- Hawai‘i has an age-adjusted breast cancer incidence rate of 139.6 per 100,000.
    - Japanese: 167.8 per 100,000
    - Native Hawaiian: 165.9 per 100,000
    - Filipina: 119.6 per 100,000

Table 1.
10 States With the Highest Diversity Index in 2020

State	Diversity index 2010	Diversity index 2020	Percentage-point difference
Hawaii	75.1	76.0	0.9
California	67.7	69.7	2.0
Nevada	62.5	68.8	6.3
Maryland	60.7	67.3	6.6
District of Columbia	61.9	67.2	5.3
Texas	63.8	67.0	3.2
New Jersey	59.4	65.8	6.4
New York	60.2	65.8	5.5
Georgia	58.8	64.1	5.3
Florida	59.1	64.1	5.1

US Census Bureau



ANHPI – Asian, Native Hawaiian, and Pacific Islander

Motivating Questions

1. How do AI/radiomics models for breast cancer risk perform in an ethnically-diverse ANHPI population?
2. Do these AI/radiomics models retain predictive performance when models are adjusted for clinical risk factors?
3. *Exploratory:* Do conventional radiomics add to the predictive performance of the AI models?

Data Source

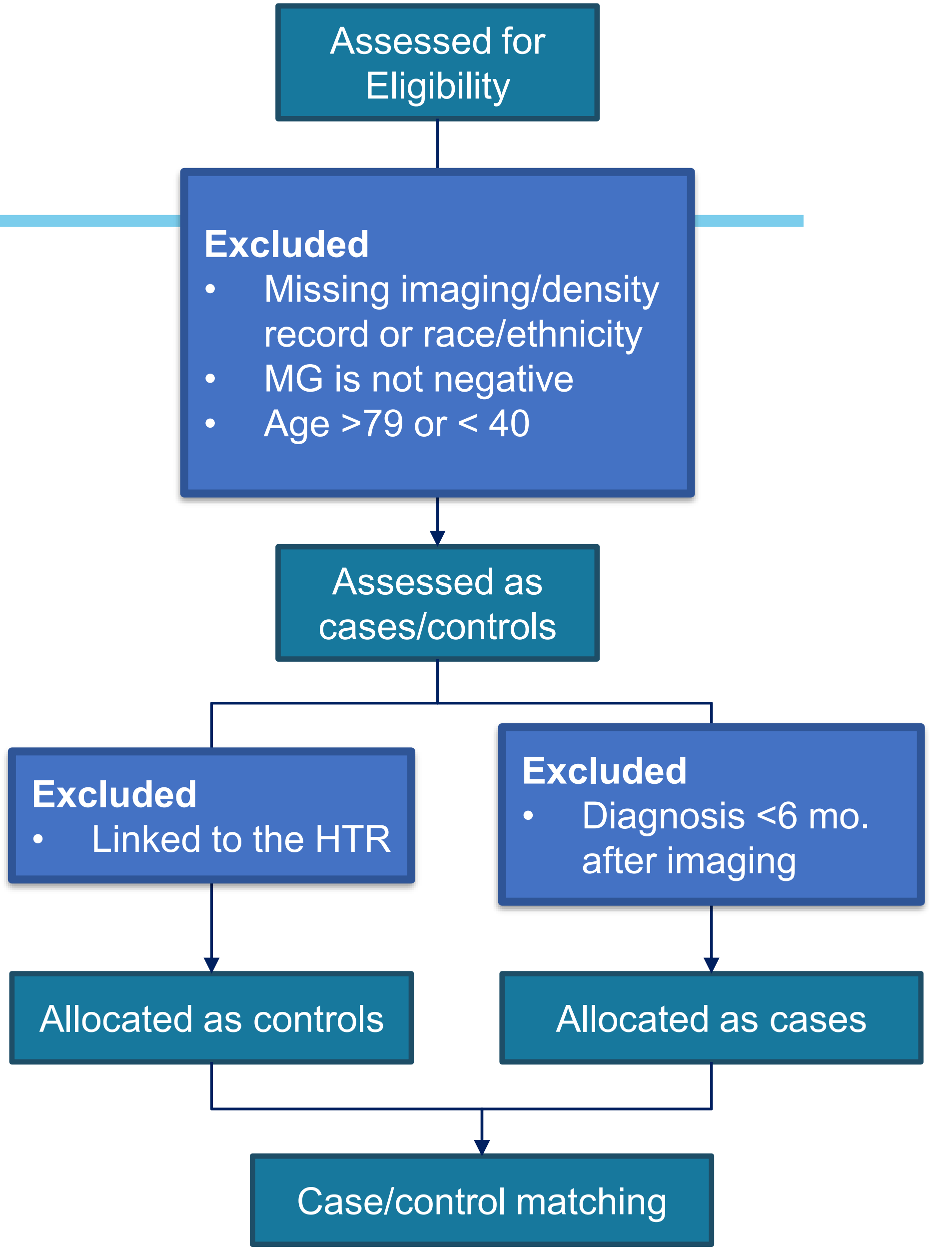
- The data used in this study are sourced from the Hawai‘i and Pacific Islands Mammography Registry (HIPIMR)
  - Prospective cohort of women
  - Collects breast imaging and breast health information (2009-*present*)
  - Linked to the Hawai‘i Tumor Registry to identify cases

- HIPIMR data consist of imaging, metadata, clinical variables, patient characteristics, and biopsy-confirmed cancer status

https://hipimr.shepherdresearchlab.org/

Selection Criteria

- Population is all patients with a record of MG imaging in the HIPIMR
- Exclusion Criteria
  - MG is not negative (BI-RADS 1 or 2)
  - Imaging <6 months before diagnosis date
  - Missing R/L CC/MLO views
  - Age <40 or >79
  - Missing race/ethnicity or density
- 1:3 case-control matching on age, race/ethnicity, first visit date, and MG machine type

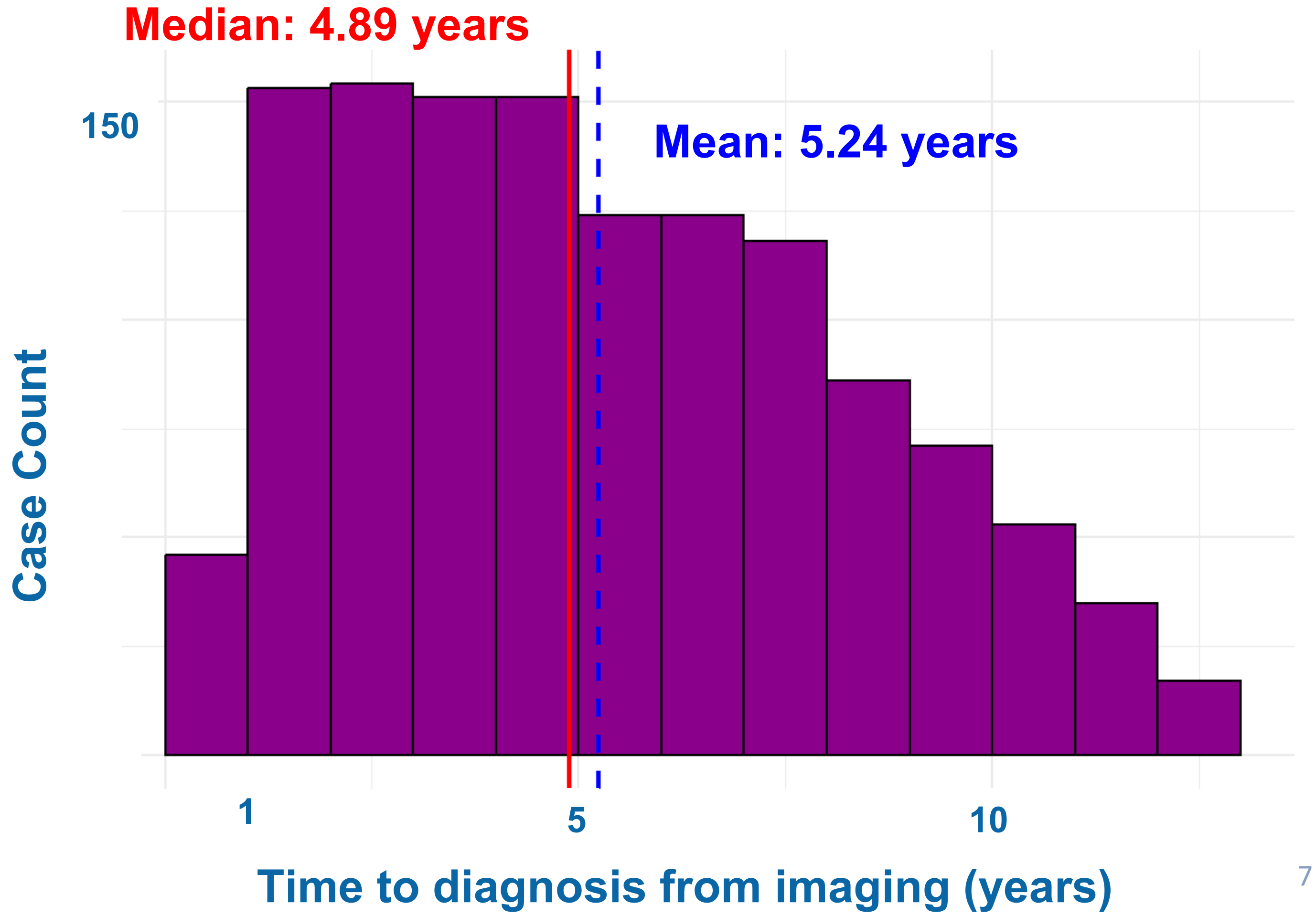


Data Selection Results – All Women

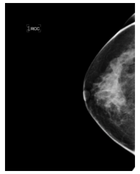
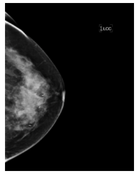
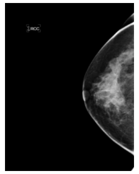
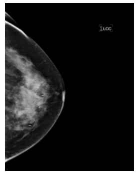
		Controls	Cases
	Women, N	**3,159**	**1,283**
Race/Ethnicity	NHPI	773	272
	White	508	182
	Chinese	138	99
	Filipina	178	161
	Japanese	476	444
	Hispanic	174	62
	Other/NOS Asian	869	47
	Other	43	16
Breast Density	Fatty (A)	189	34
	Scattered (B)	1,438	610
	Heterogeneous (C)	1,272	515
	Extremely dense (D)	260	124
Menopause	Menopausal	2,314	904
	Pre-menopausal	845	379

Case Selection

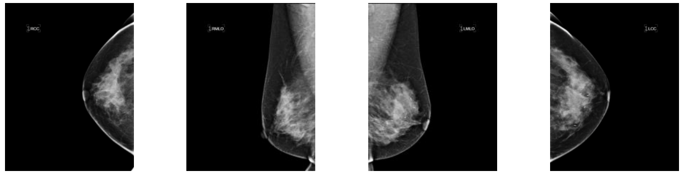
- **Time to diagnosis from imaging:**
  - 8.2% of cases diagnosed after 10 years
  - 3.6% of cases diagnosed before 1 year



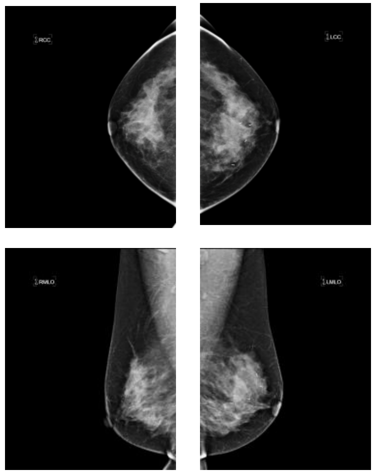
Radiomic Features

Algorithm	Input	Output
OpenBreast Pertuz+ 2019	    Any view(s)	32 texture features (GLC, GRA, GLH, SFA, GLR)
CaPTk Zheng+ 2019		328 features (LBP, FD, GLC, GLH, GLR)
Malkov Malkov+ 2016	 	17 fractal (FD) features

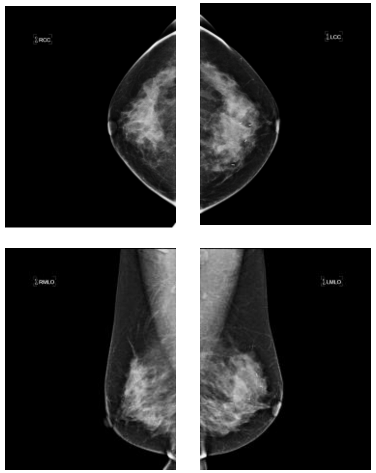
Density Models

<table>
<tr><th>Algorithm</th><th>Input</th><th>Output</th></tr>
<tr><td>LIBRA
Keller+ 2012</td><td>Any view(s)</td><td>Percent density</td></tr>
<tr><td>Wu et al.
Wu+ 2018</td><td rowspan="2">
R/L CC/MLO views</td><td>Probability of BI-RADS density
[P(A), P(B), P(C), P(D)]</td></tr>
<tr><td>Transpara</td><td>Volumetric density</td></tr>
</table>

AI Models (Academic)

<table>
<tr><th>Algorithm</th><th>Input</th><th>Output</th></tr>
<tr><td>GMIC
Shen+ 2019</td><td rowspan="3">
R/L CC/MLO views</td><td>[P(benign finding), P(malignant finding)]</td></tr>
<tr><td>Mirai
Yala+ 2021</td><td>1-, 2-, 3-, 4-, and 5-year risk</td></tr>
<tr><td>Zhu et al.
Zhu+ 2021</td><td>[P(normal), P(screen-detected), P(interval)]</td></tr>
</table>

AI Models (Commercial)

<table>
<tr><th>Algorithm</th><th>Input</th><th>Output</th></tr>
<tr><td>ProFound Detection</td><td rowspan="2">
R/L CC/MLO views</td><td>Case score (1-100)</td></tr>
<tr><td>Transpara</td><td>Exam score (1-10)</td></tr>
</table>

Statistical Methods

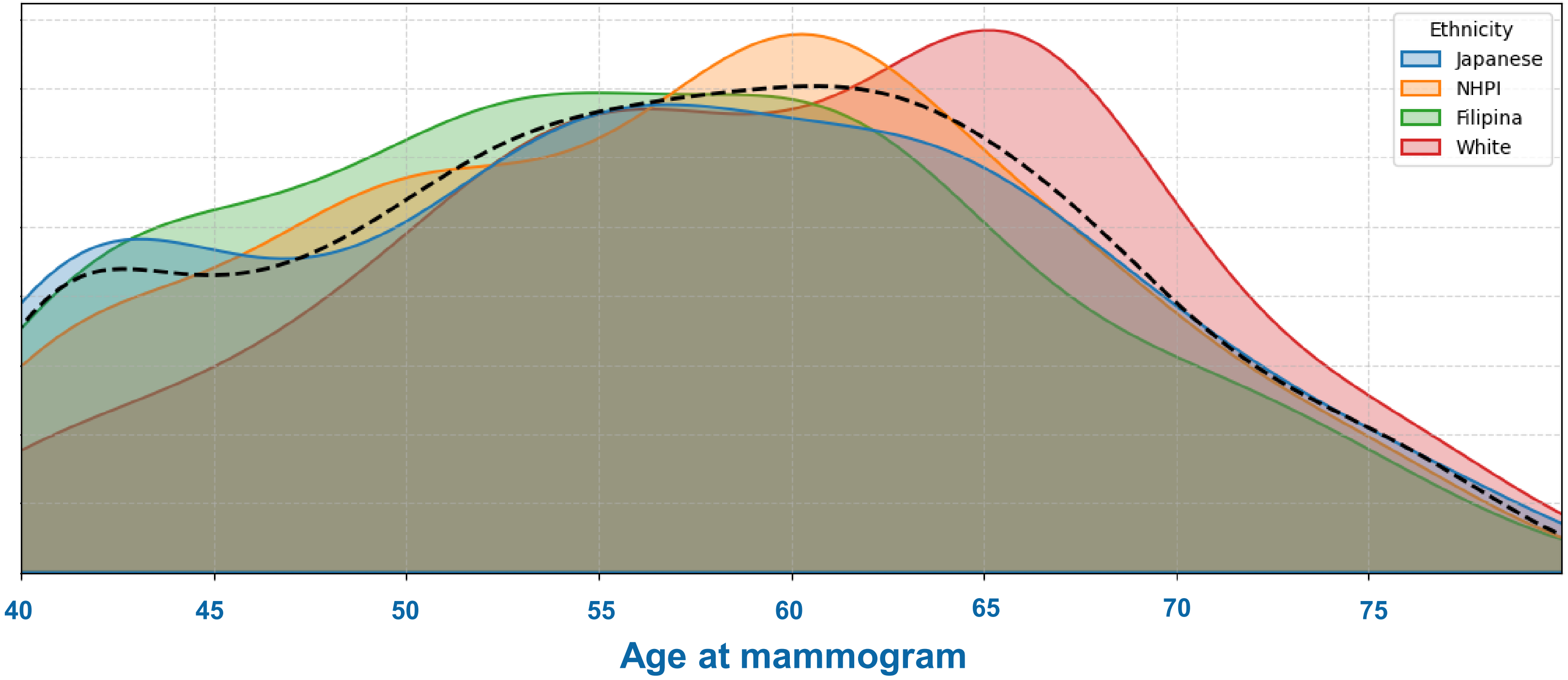
- Features were dropped out when they had Pearson's r > |0.7| with another feature *in their same family.*
- This reduced the number of features from 401 to 58 features
    - CaPTk → reduced from 328 to 32 features
    - Malkov → reduced from 11 to 4 features
    - Mirai → reduced from 5 to 1 feature
    - OpenBreast → reduced from 32 to 9 features

- **Model definition:** Conditional logistic regression with woman-level clustered standard errors. Radiomic features/AI model outputs were all standardized.
    - Benjamini-Hochberg adjustment was used to correct for multiple testing.

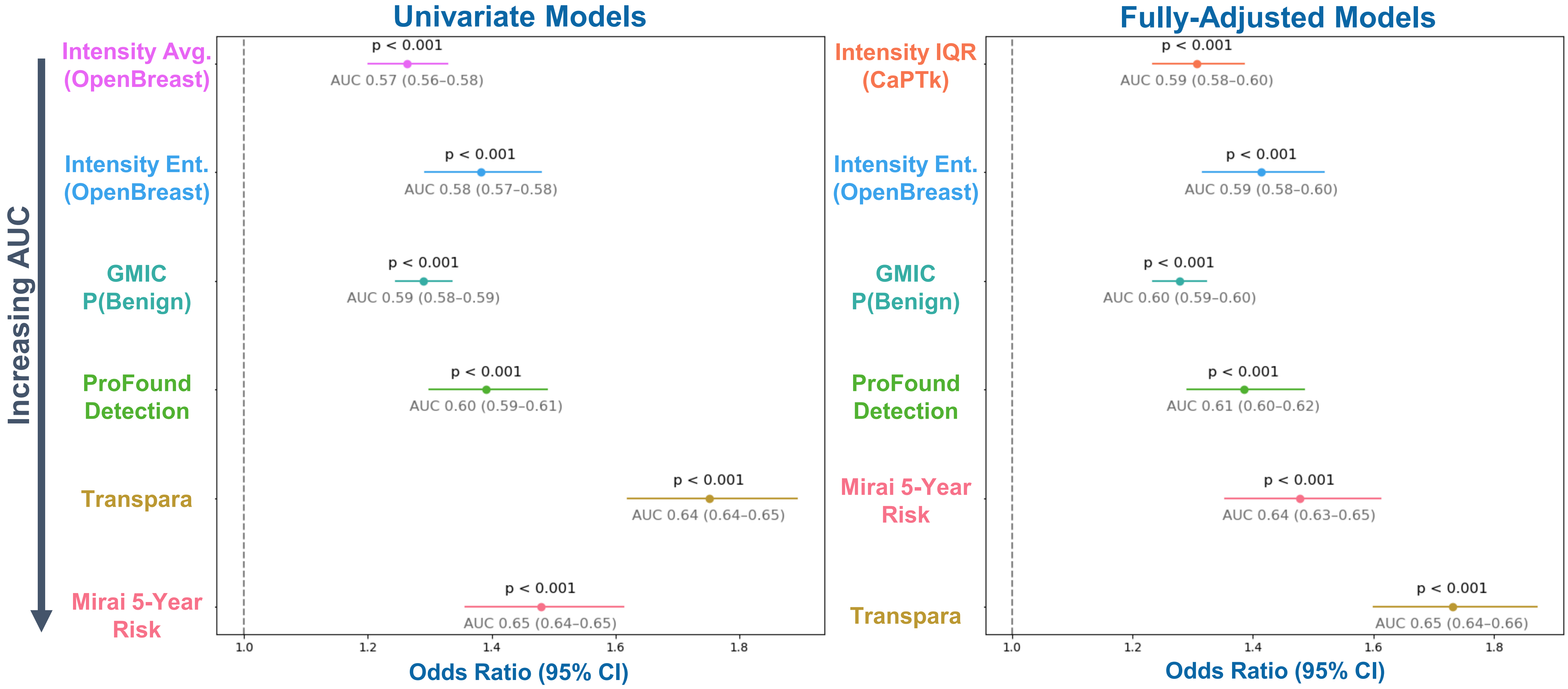
Baseline Models

Baseline models were constructed with *only* clinical risk factors to assess added benefit of radiomics.

Clinical risk factors: Breast density, age, menopausal status



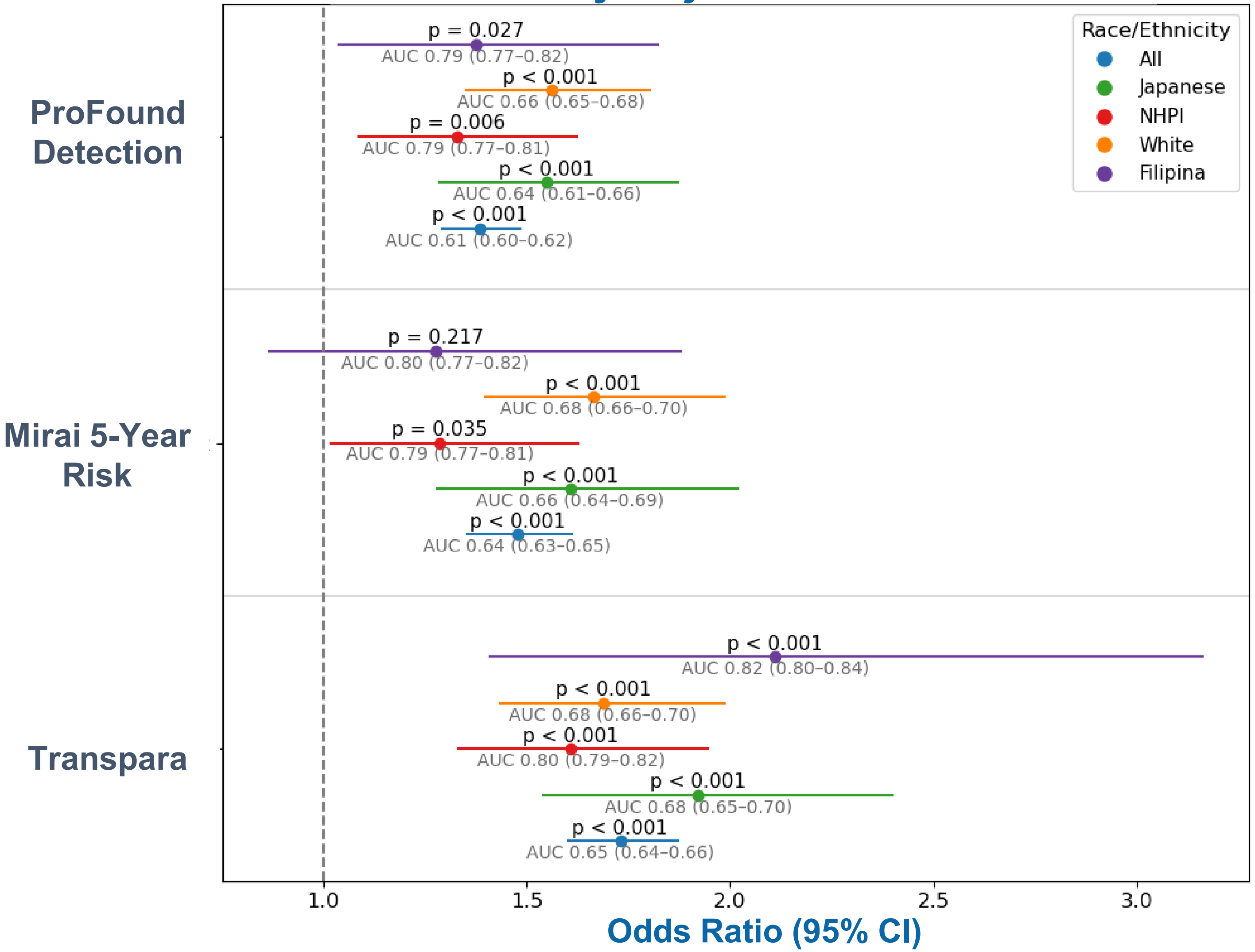
Results – All Women



Race/Ethnicity Subgroups

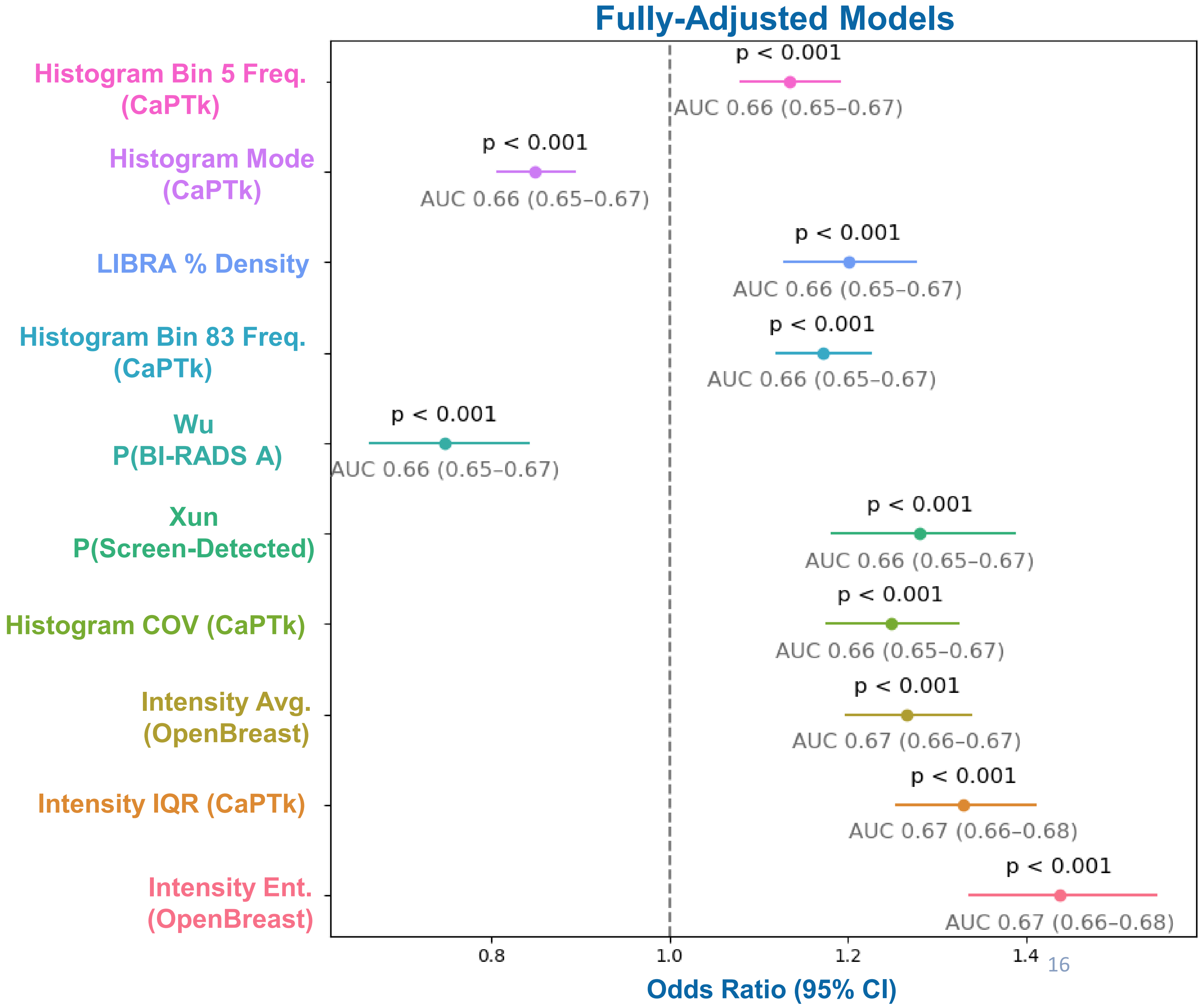
Subgroup	Baseline Performance (AUC)
Japanese	0.78 (0.77-0.80)
NHPI	0.61 (0.59-0.63)
White	0.57 (0.54-0.59)
Filipina	0.79 (0.77-0.82)

Fully-Adjusted Models



Adding to Transpara – All Women

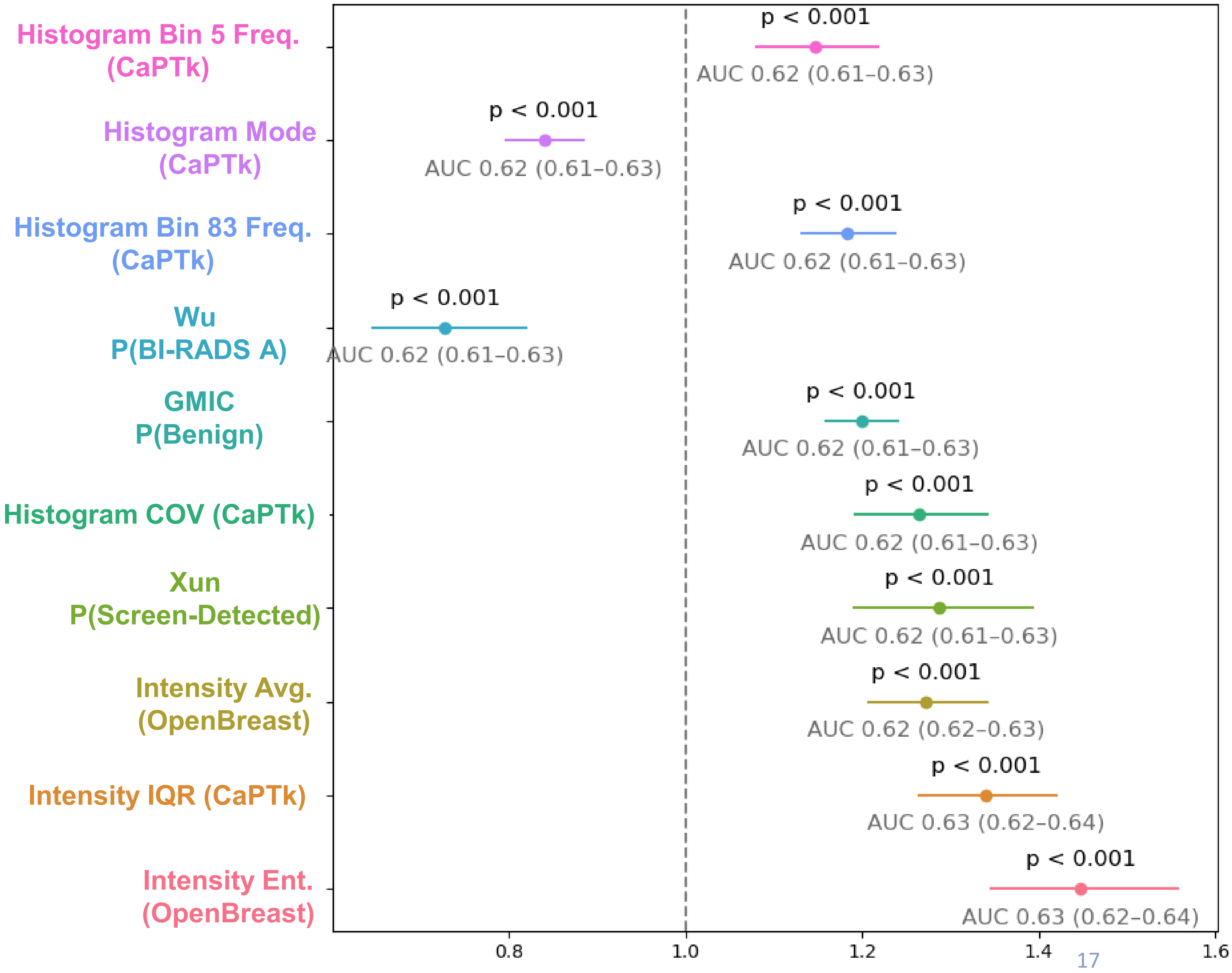
Baseline = 0.65 AUC



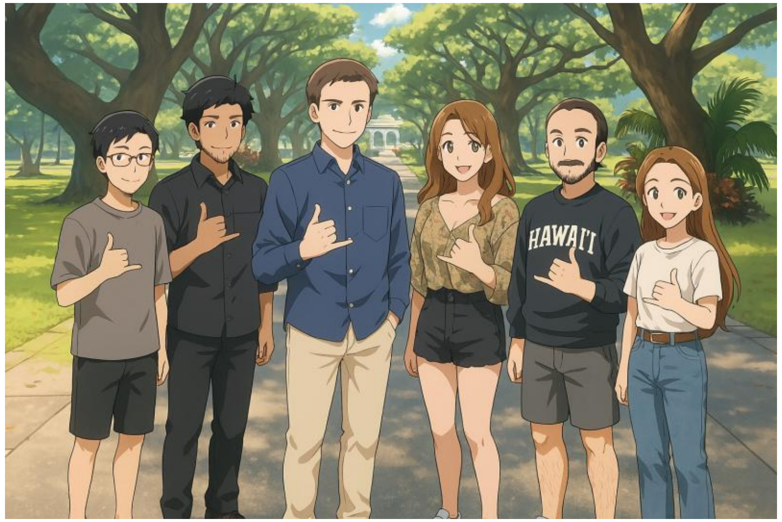
Adding to Profound Detection – All Women

Baseline = 0.60 AUC

Fully-Adjusted Models



Mahalo nui loa!



Sadowski Group

SHEPHERD RESEARCH LAB

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Future Work

20% of Hawaiʻi identifies as mixed-race, how can we account for this in our models?

Exploring multivariate, cross-family modeling with risk factors. Which radiomics add information?

Can we condense down risk information from multiple radiomics into a single “super radiomic”?