Precision Medicine and Black-White Health Disparities

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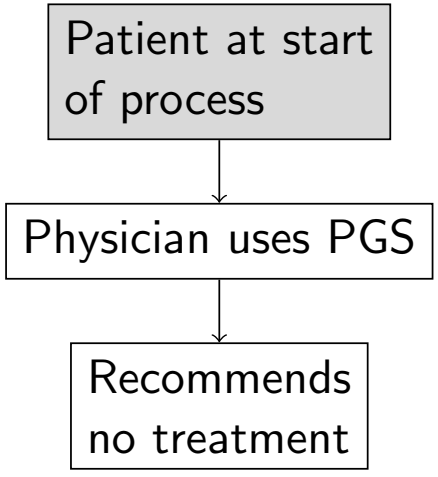
1. Princeton University; 2. Stanford University

IGSS 2019

Motivation: past research focuses on how clinical use of polygenic scores (PGS) may widen Black-White disparities through mechanism of unequal accuracy



Duncan et al. (2019); Martin et al. (2019) Mills and Rahal (2019); Mostafavi et al. (2019)

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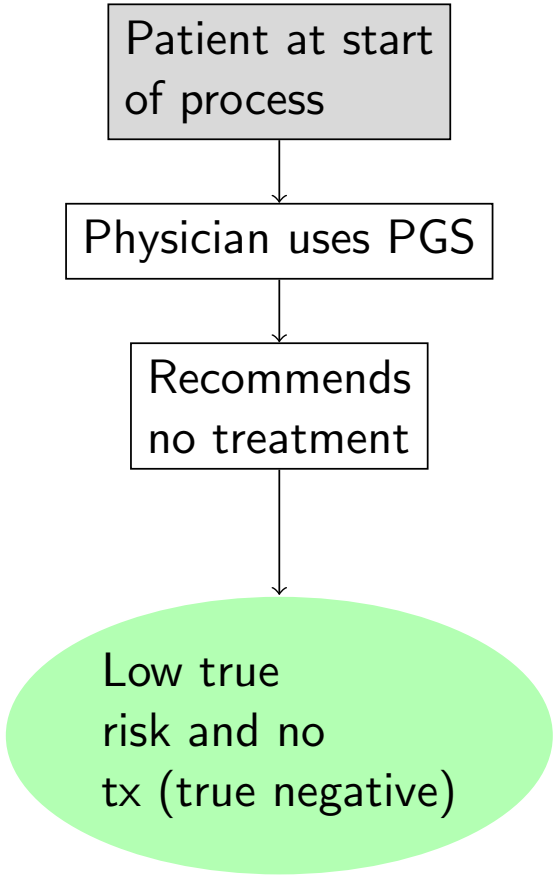

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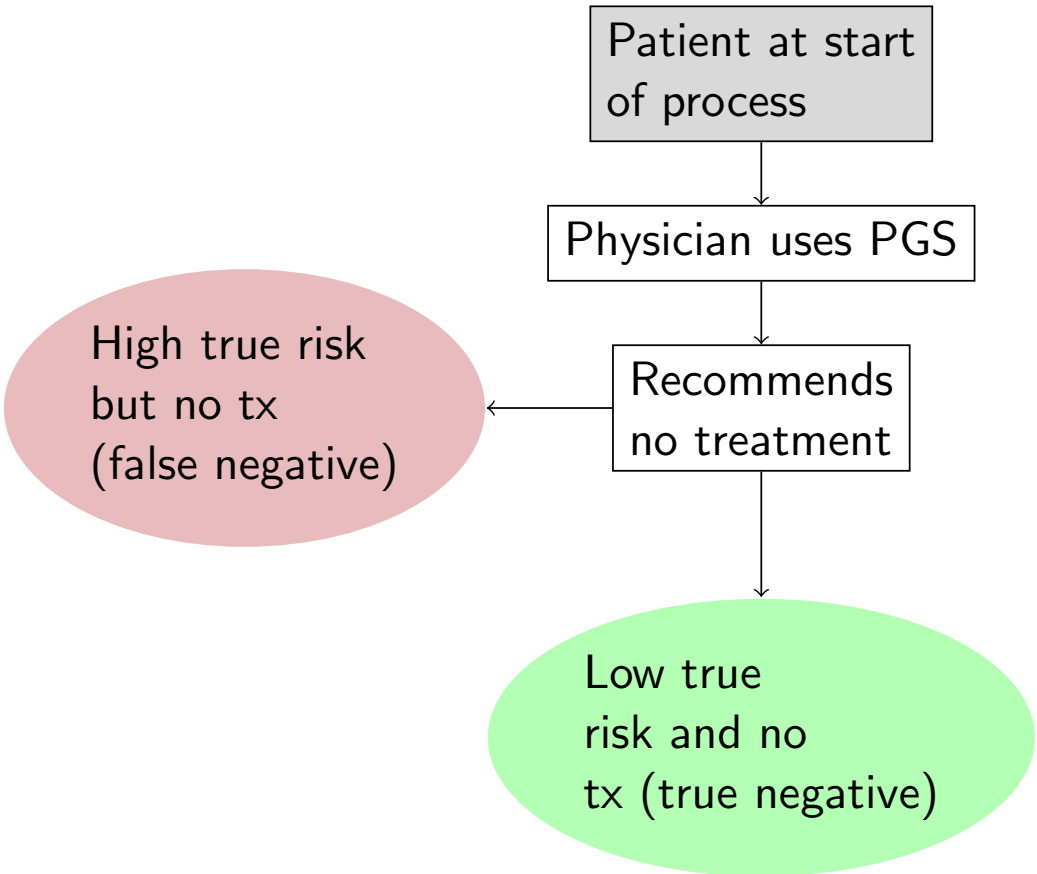

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Gaps and present study

1. **Unequal accuracy:**
high true risk
but not given high-risk
label (false negative)

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high true risk
but no scoring by PGS
(false negative)

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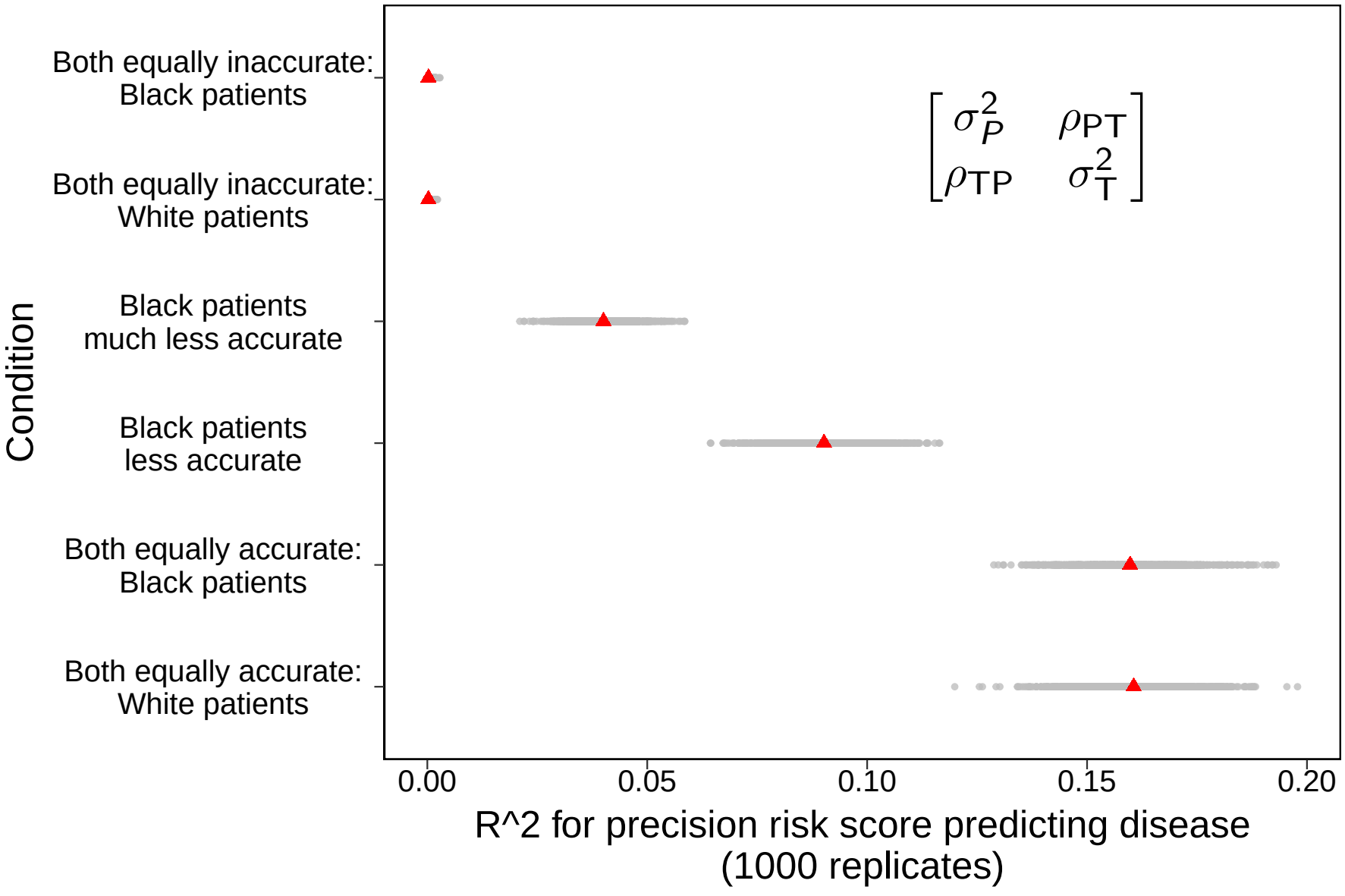
Present study:
use agent-based modeling (ABM),
informed by HRS data;
start with false negatives due
to unequal accuracy as baseline;
investigate *relative magnitude*
of unequal accuracy as mechanism for disparities
vs. other mechanisms that persist
after equalizing accuracy

Simulating unequal accuracy (T: true disease risk; P: measured PGS)



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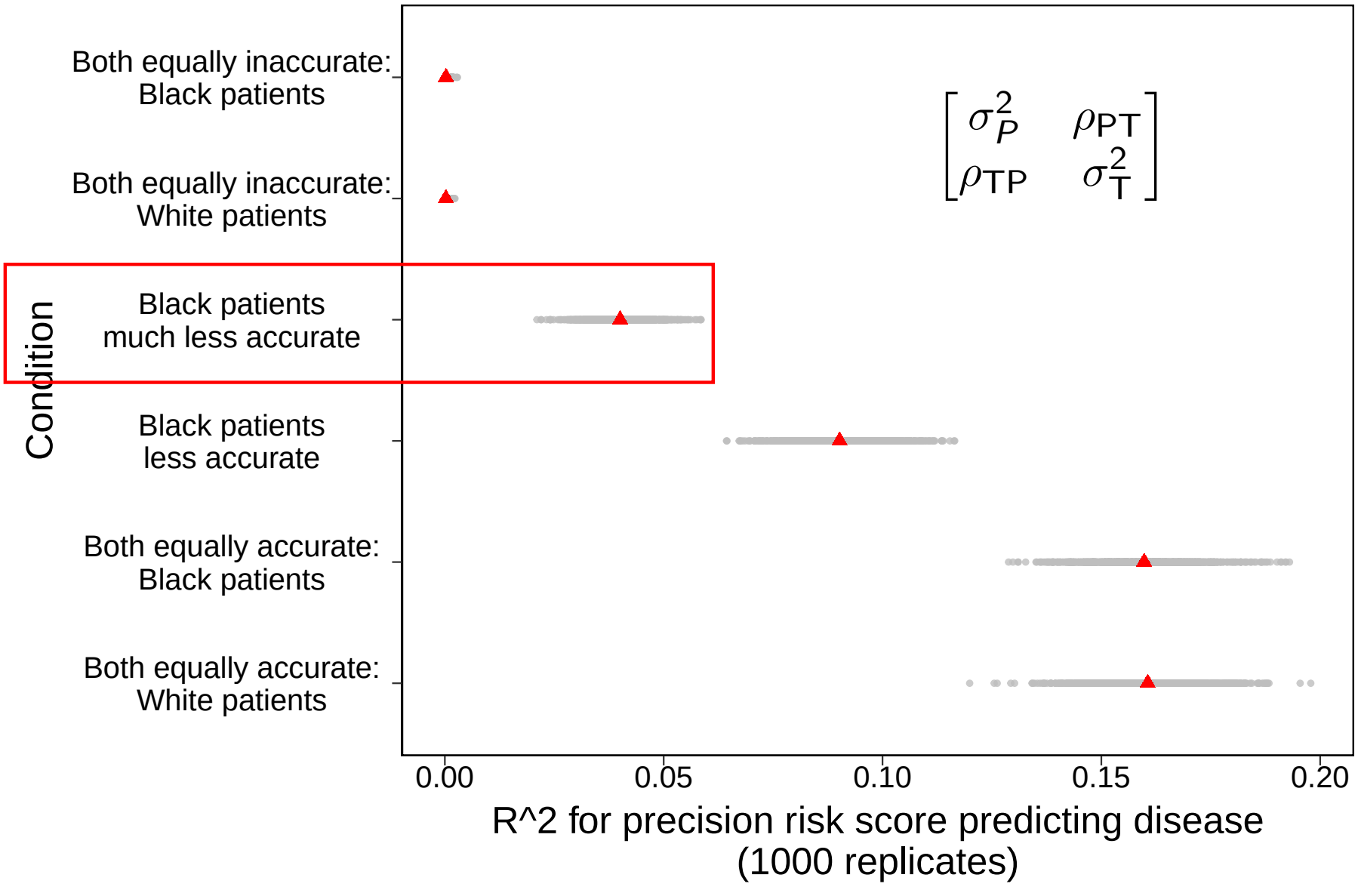
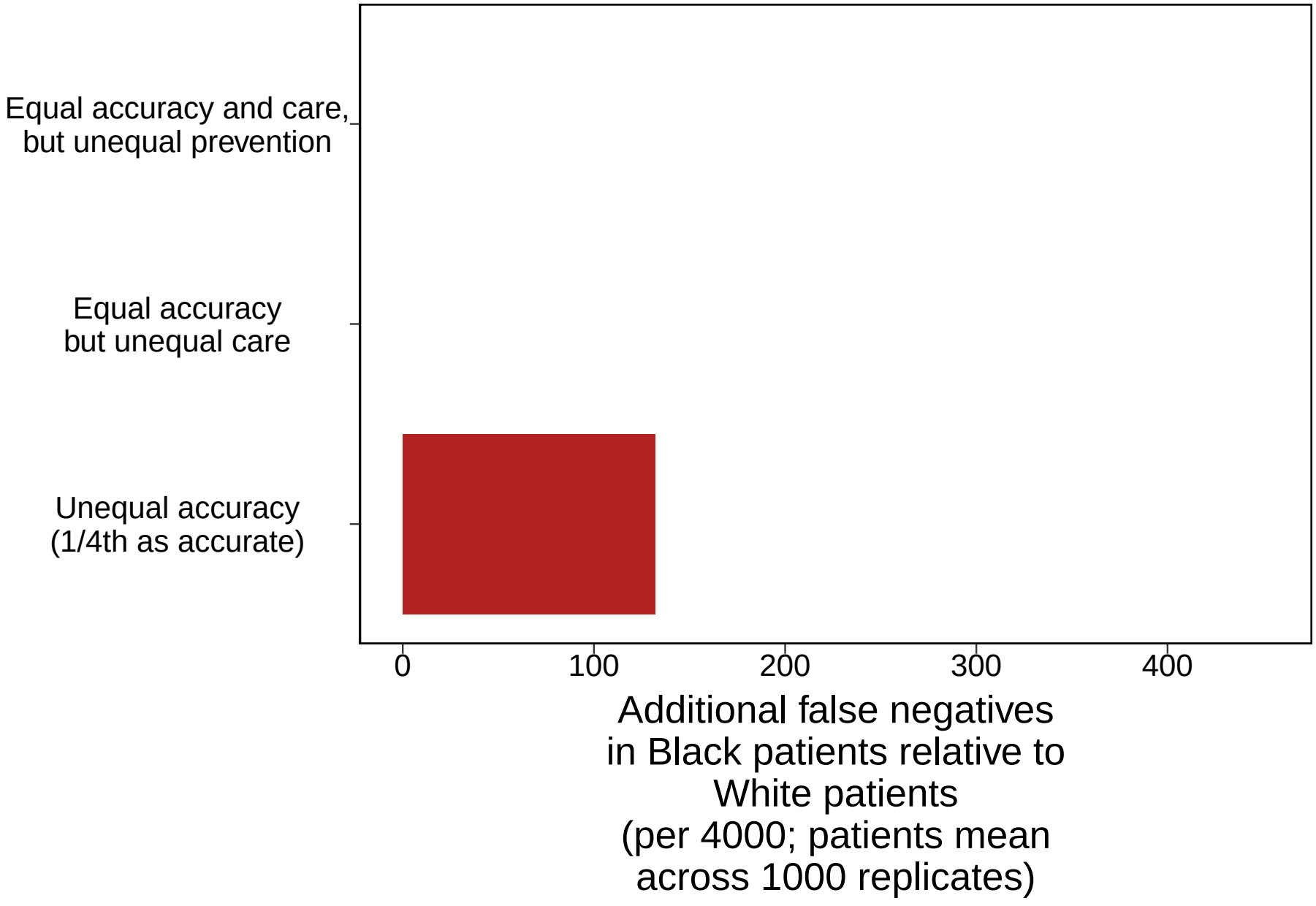
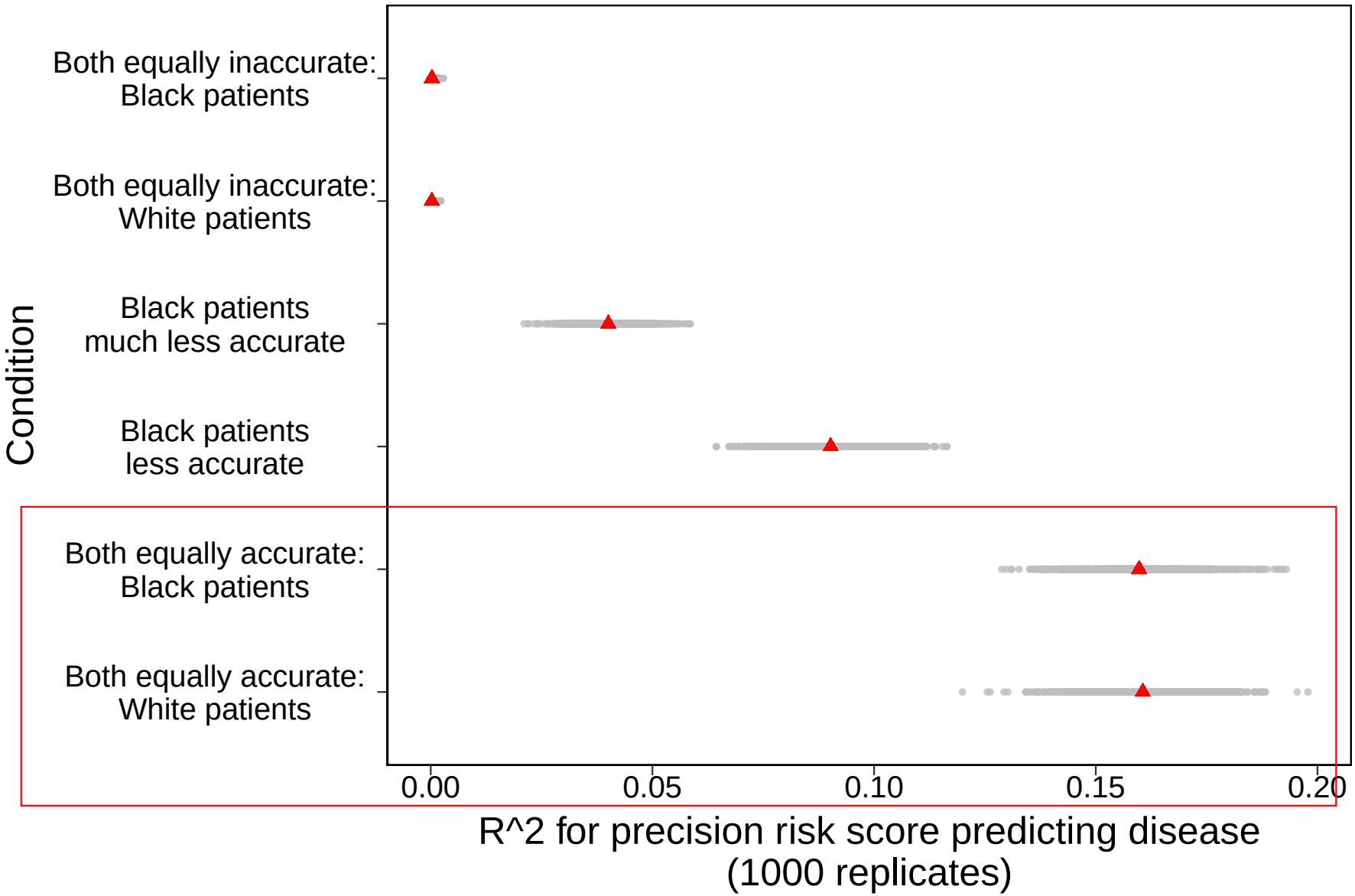
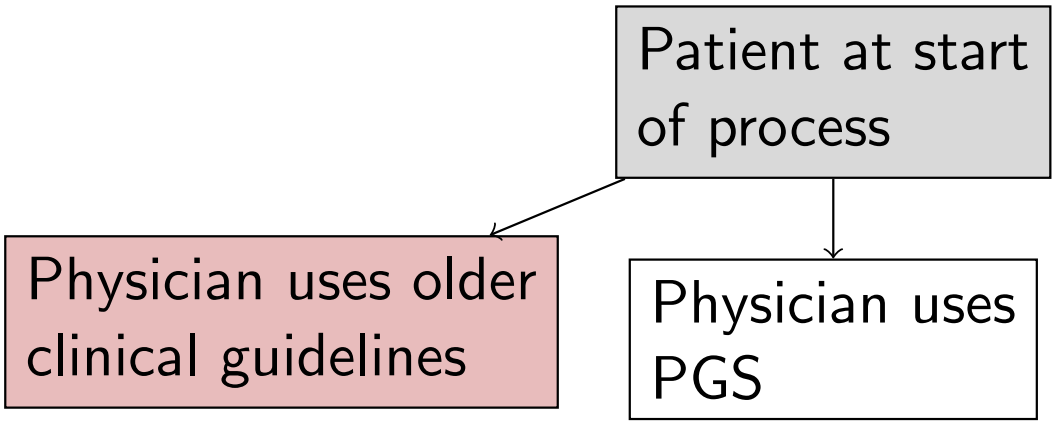



Equal accuracy and care, but unequal prevention
Equal accuracy but unequal care
Unequal accuracy (1/4th as accurate)
0
100
200
300
400
Additional false negatives in Black patients relative to White patients (per 4000; patients mean across 1000 replicates)

Now suppose we equalize accuracy...



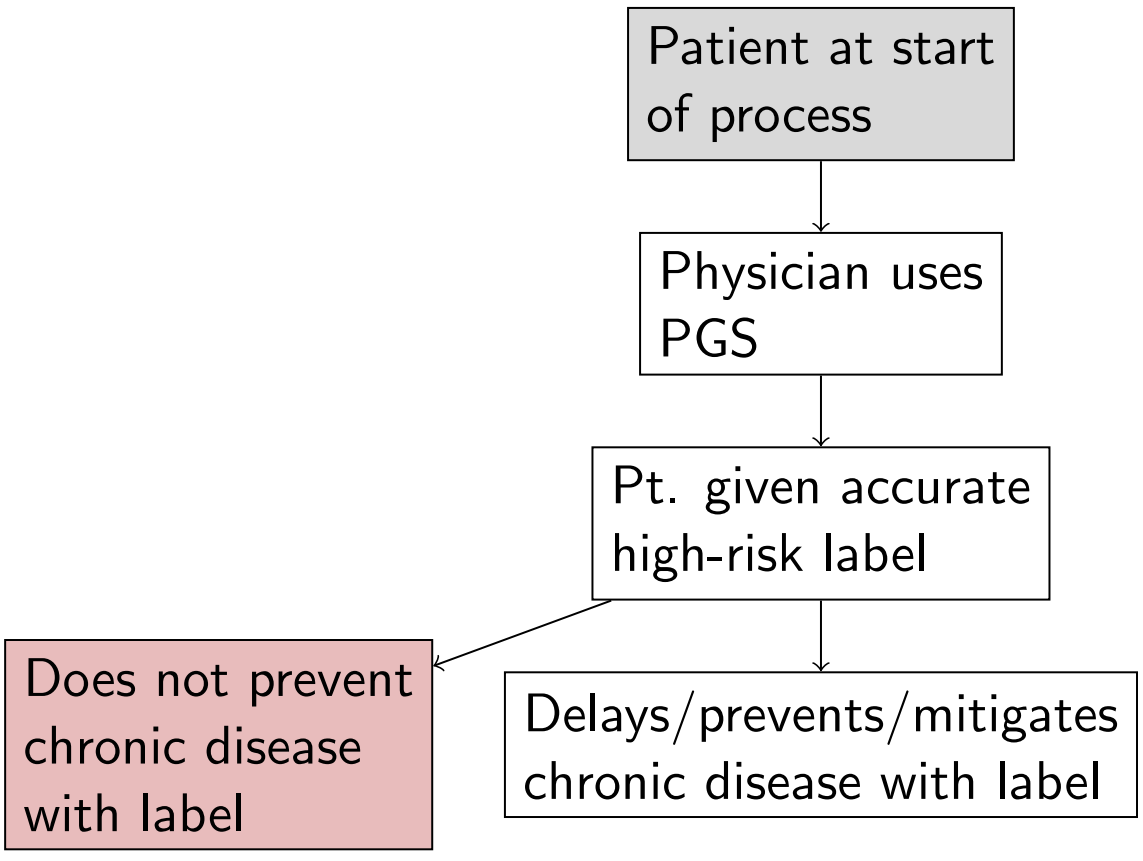
Two additional mechanisms



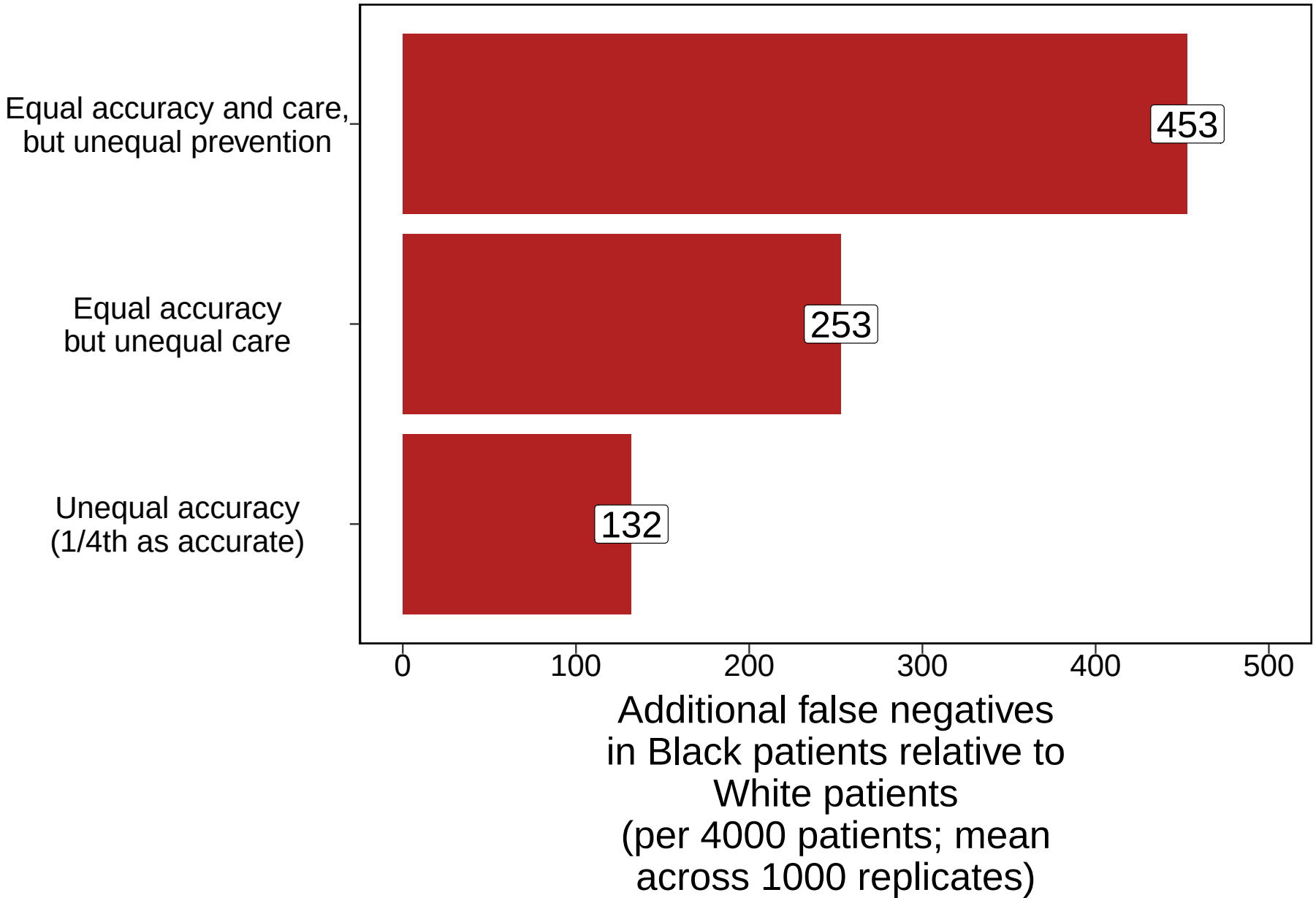
Parameters:
1. Redundancy between PGS and existing risk assess. methods (less redundant; more it matters)
2. How race affects Doctors using new tech./evidence-based care

Torkamani et al. 2018; Khera et al. 2018

Two additional mechanisms



Parameters:
1. Correlation between race and SES
2. Disparities in chronic disease management among those at high risk


Equal accuracy and care, but unequal prevention
Equal accuracy but unequal care
Unequal accuracy (1/4th as accurate)
453
253
132
0
100
200
300
400
500
Additional false negatives in Black patients relative to White patients (per 4000 patients; mean across 1000 replicates)

Future directions: improve simulation + supplement work on improving accuracy disparities with work investigating other mechanisms

Mechanism	**Example research**
Whose care features newer risk assessment methods?	Pr(Dr. offers); Pr(Pt. accepts|Dr. offers) (how much does the selection into genotyping in pop. cohort studies–White, healthier, higher-SES–generalize to clinical contexts?)
How does disclosure of polygenic risk affect health behaviors?	RCTs of candidate gene disclosure (e.g., Green et al. ApoE4 REVEAL study)...similar RCTs for PGS? How does interpretability of risk info. influence its impact?

Thanks!

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https://github.com/rebeccajohnson88/precisionmed_disparities