

Assessing the Consistency of Carrier Screening Guidelines Across Seven Populations and 265,000 Individuals

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INTRODUCTION

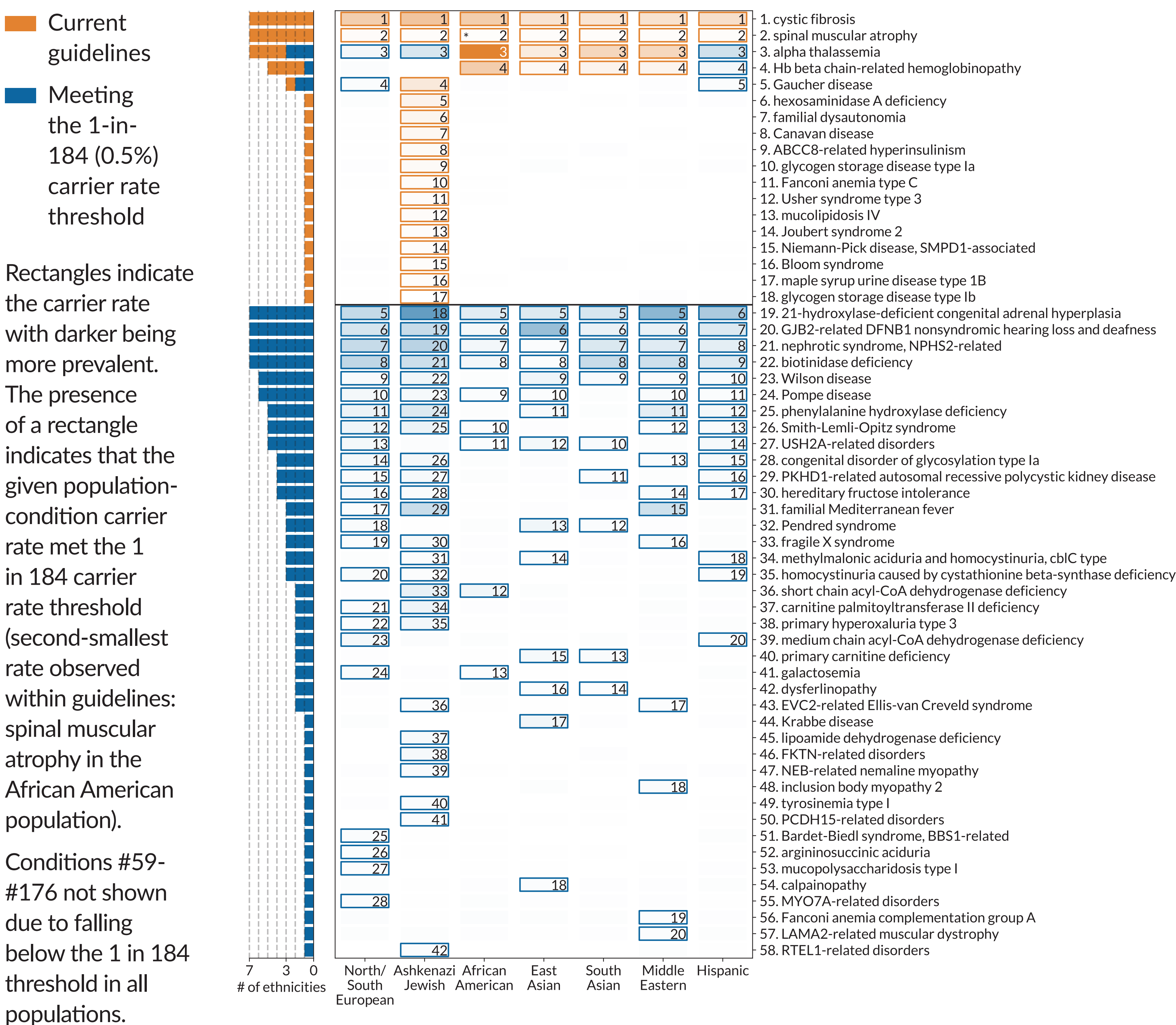
- Current ACMG and ACOG carrier screening guidelines for Mendelian conditions recommend pan-ethnic screening for cystic fibrosis and spinal muscular atrophy, motivated by the pan-ethnic incidence of the conditions. Population-specific guidelines exist for additional diseases due to elevated incidence.
- We posited that disorders that are more common than those included in current guidelines should also be considered for carrier screening.

METHODS

- We estimated the “population-condition carrier rates” of 176 Mendelian conditions in a cohort of over 265,000 individuals undergoing routine expanded carrier screening.
- Self-reported ethnicity was used.

RESULTS

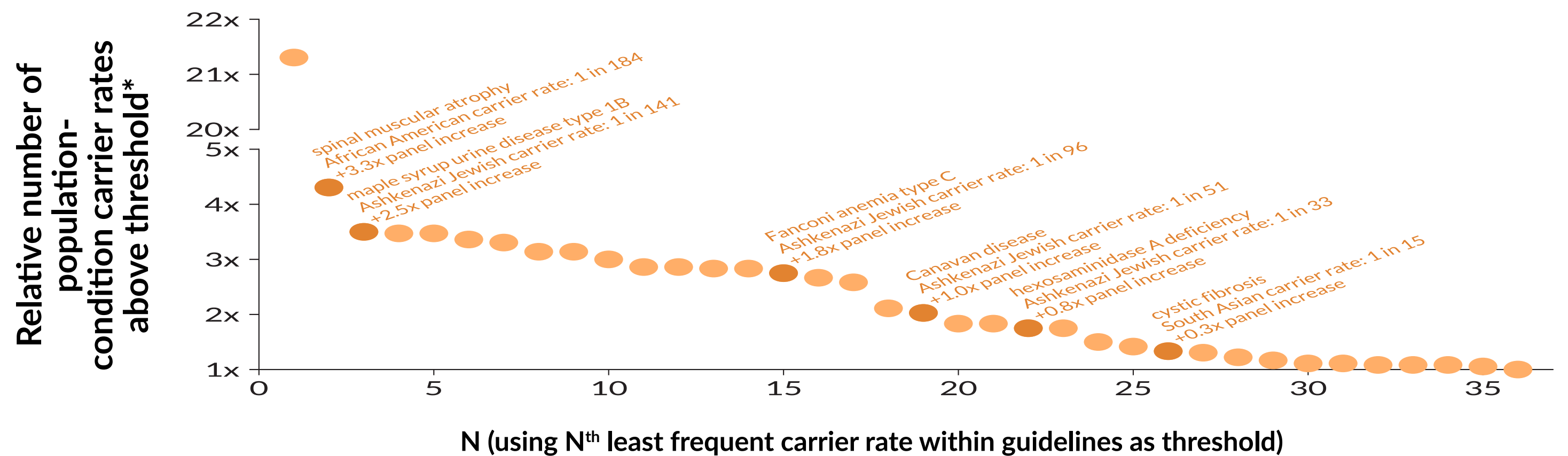
Figure 1. Population-condition carrier rates



- The second-to-least frequent condition out of the studied 36 population-condition combinations in current ACMG/ACOG guidelines was spinal muscular atrophy (SMA) in the African American population, with an estimated population-condition carrier rate 1 in 184 (0.5%).
- Our analysis revealed 119 (>3x) additional population-condition carrier rates in excess of 1 in 184, suggesting that current guidelines are not consistently capturing reproductive risk across populations or conditions (Figure 1).
- Even if a more common guideline-condition is used as the threshold, many additional conditions meet the carrier rate criterion (Figure 2).

Figure 2. Changing the minimum carrier rate threshold

*Current guidelines always included



CONCLUSIONS

- Many conditions have population-specific incidence comparable to SMA in the African American population—the second rarest population-condition pair currently recommended for carrier screening by both ACMG and ACOG.
- Expanding guidelines to include additional conditions with comparable or higher incidence in select populations would improve equitability of medical care across populations. The added complexity of three times more population-specific recommendations could be mitigated by adopting pan-ethnic expanded carrier screening as the recommended approach to carrier screening.