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Violations of independence: ethnicity and COVID-19 in Brazil

Pedro Baqui and colleagues (August 2020)¹ did a cross-sectional observational study of hospital mortality from COVID-19 in Brazil to assess variations in mortality according to ethnicity and region, adjusting for many clinical features. The study revealed the presence of societal inequities in the effects of COVID-19: mortality was significantly higher in *Pardo* (mixed ethnicity) and Black Brazilians than in White Brazilians (hazard ratio [HR] 1.45, 95% CI 1.33–1.58 for *Pardo* Brazilians; 1.32, 1.15–1.52 for Black Brazilians).

The authors used a mixed-effects Cox regression survival analysis to estimate the effects of ethnicity while allowing the baseline hazard function to vary by state. Beyond exploring variation across entities of interest (here, the Brazilian states), an important advantage of mixed-effects models compared with standard methods is their capacity to adjust for violations of the assumption of independent observations.² In the context of health care, assuming that clinical outcomes for patients receiving care within the same hospital are independent is not appropriate. Ignoring this issue could lead to unreliable estimations and, in conventional terms, increases the risk of incorrectly rejecting a null hypothesis.³

Instead of allowing the baseline hazard function to vary only across states, Baqui and colleagues' model should also have incorporated hospitals within those states as sources of variation and dependence between patients, which would have reflected the hierarchical nature of the data more accurately.

Indeed, using public data and code provided by the authors, I re-ran the model to incorporate hospitals within states, which altered the findings. The HR for *Pardo*

Brazilians decreased from 1.45 to 1.28 (95% CI 1.17–1.41) and the HR for Black Brazilians decreased from 1.32 to 1.12 (0.96–1.30), making the HR no longer statistically significant. These two HRs were outside the 95% CIs of the original estimates. The differences were substantial in size and uncertainty (appendix), regardless of the excessive focus on statistical significance in quantitative research.⁴

Although incorporating hospitals into the mixed-effects model yielded smaller HRs for Black and *Pardo* Brazilians, these HRs remained higher than those for White Brazilians. Furthermore, differences in the quality of care across hospitals are also related to the ethnicity of patients, which calls for additional work. An accompanying Comment by Helena Ribeiro and colleagues⁵ highlighted the racial, socioeconomic, and environmental determinants of Brazilians' health, and charted a way forward for further research.

I declare no competing interests.

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- 1 Baqui P, Ebara S, Bica I, Marra V, Ercol A, van der Schaar M. Ethnic and regional variations in hospital mortality from COVID-19 in Brazil: a cross-sectional observational study. *Lancet Glob Health* 2020; **8**: e1018–26.
- 2 Austin PC. A tutorial on multilevel survival analysis: methods, models and applications. *Int Stat Rev* 2017; **85**: 185–203.
- 3 Aarts E, Verhage M, Veenvliet JV, Dolan CV, van der Sluis S. A solution to dependency: using multilevel analysis to accommodate nested data. *Nat Neurosci* 2014; **17**: 491–96.
- 4 McShane BB, Gal D, Gelman A, Robert C, Tackett JL. Abandon statistical significance. *Am Stat* 2019; **73**: 235–45.
- 5 Ribeiro H, Mendes Lima V, Alves Valdman E. In the COVID-19 pandemic in Brazil, do brown lives matter? *Lancet Glob Health* 2020; **8**: e976–77.



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