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*Resolving the enigma of Iquitos and Manaus: A modelling analysis of multiple COVID-19 epidemic waves in two Amazonian cities*

The nearby cities of Iquitos (Peru) and Manaus (Brazil) experienced the world's highest infection and mortality rates during the first COVID-19 wave in 2020. Key studies suggested that  $>70\%$  of the city populations were infected in this wave and thus close to herd immunity and protected. It remains an enigma as to why a deadly second wave followed in Manaus worse than the first. To resolve this, we present a data-driven model of epidemic dynamics in Iquitos which we use to help explain and model events in Manaus. The partially observed Markov process model simultaneously fits a flexible "variable  $R_0$ ", estimates long-term immunity waning and impulsive immune evasion, and thus provides a comprehensive framework for characterizing and modeling new variants of concern.