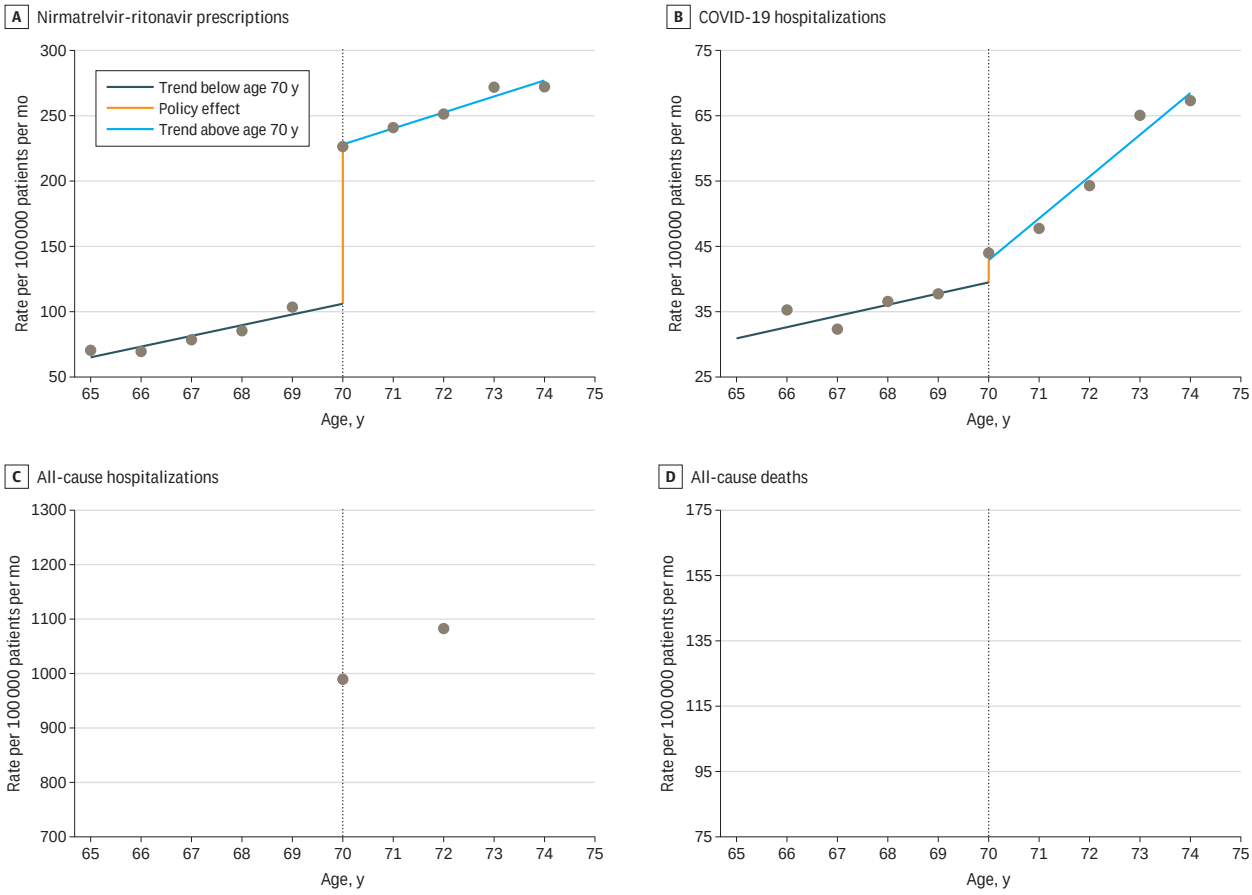
Figure. Regression Discontinuities of Nirmatrelvir-Ritonavir Prescription, COVID-19–Related Hospitalization, and All-Cause Hospitalization and Death Rates per 100 000 Older Adults, April 1–November 30, 2022, Ontario



To determine the association between nirmatrelvir-ritonavir and COVID-19–related hospitalizations (primary outcome), all-cause hospitalizations, and all-cause mortality, we used a fuzzy regression discontinuity design[5,6] to compare outcomes of patients just below vs just above age 70 years who were plausibly similar except for exposure to nirmatrelvir-ritonavir.

To validate the plausibility of this assumption, we assessed for discontinuities in 25 patient characteristics at age 70 years, including COVID-19 vaccination status and comorbidities, with significance defined as a false discovery rate–corrected $P < .10$. We also examined outcomes 1 year before nirmatrelvir-ritonavir became available (2021). Null regression discontinuity analyses in 2021 would lessen concern for imbalances in patient characteristics at 70 years old.

Multivariate linear regression models were used to estimate separate age outcome trends for 65- to 69- and 70- to 74-year-old persons. Estimated policy effects are the discontinuities (ie, gaps) between these trend lines at age 70 years, described as differences in outcome rates between those just above vs just below age 70 years. The estimated treatment effect of nirmatrelvir-ritonavir on COVID-19–related hospitalization is the COVID-19–related hospitalization discontinuity divided by the discontinuity in the prescription rate of nirmatrelvir-ritonavir. Findings were reported as model coefficients with 95% CIs, with statistical significance defined as $P < .05$ (2-sided). Analyses were conducted using R version 3.6.2. The UCLA institutional review board waived review, and ICES data do not require patient consent under Ontario law. See the eAppendix in Supplement 1 for additional details and model diagnostics.

Results | We identified 1 620 884 Ontarians aged 65 to 74 years during the study period; most (87.5%) received at least 2 COVID-19 vaccines. There were no significant discontinuities in patient characteristics at age 70 years (Table).

Nirmatrelvir-ritonavir prescriptions (n = 19 868) increased with age, rising more among patients just above vs just below age 70 years, from 106.0 to 227.9 prescriptions, or 121.9 (95% CI, 95.7 to 148.1) more prescriptions per 100 000 patients per month (policy effect: 115% increase; $P < .001$) (Figure, A). Although hospitalization and mortality outcomes also rose with age, there were no significant differences just below vs just above age 70 years (per 100 000 patients per month) in COVID-19–related hospitalizations (39.5 vs 42.9; absolute difference, 3.4; 95% CI −1.3 to 8.1; $P = .15$), all-cause hospitalizations (979.6 vs 988.4; absolute difference, 8.9; 95% CI −35.0 to 52.7; $P = .69$), or all-cause mortality (109.6 vs 115.7; absolute difference, 6.1; 95% CI, −2.7 to 14.9; $P = .17$) (Figure, B-D). Differences in outcomes were similarly null in 2021 before nirmatrelvir-ritonavir became available: absolute differences per 100 000 patients per month were 0.43 (95% CI, −4.5 to 5.4;