National prevalence of potential nirmatrelvir/ritonavir drug interactions in U.S. adults: implications for safe antiviral prescribing

Eurasian Clinical and Analytical Medicine Original Research

National burden of Paxlovid drug-drug interactions

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Abstract

Aim: Nirmatrelvir/ritonavir is an oral antiviral for high-risk outpatients with COVID-19, yet ritonavir-mediated drug-drug interactions can preclude use or require mitigation, delaying time-sensitive therapy. We estimated the national prevalence of significant Paxlovid drug-drug interactions in U.S. adults.

Methods: We conducted a cross-sectional analysis of National Health and Nutrition Examination Survey (NHANES) 2017-March 2020 pre-pandemic data. Prescription medications were mapped at the ingredient level to the Food and Drug Administration (FDA) Paxlovid Fact Sheet interaction table and classified as Tier 1 (contraindicated) or Tier 2 (avoid/temporary holding, dose adjustment, or monitoring). Using NHANES complex survey methods, we estimated weighted prevalence and 95% confidence intervals (CI) for exposure. A sensitivity analysis was restricted to interviewer-observed medications (prescription medication seen variable [RXQSEEN] = 1). Polypharmacy was defined as ≥5 prescription medications.

Results: Among 9,693 adults, the weighted prevalence of exposure to any Tier 1 contraindicated medication was 6.88% (95% CI, 5.63-8.13), Tier 2 exposure was 27.74% (95% CI, 26.04-29.44), and any Tier 1 or Tier 2 exposure was 31.19% (95% CI, 29.15-33.22). In the RXQSEEN-restricted sensitivity analysis, prevalence estimates were 6.08% (Tier 1), 24.86% (Tier 2), and 28.05% (any Tier 1 or Tier 2). Among adults with polypharmacy, prevalence was 22.36% (Tier 1), 79.54% (Tier 2), and 86.50% (any Tier 1 or Tier 2). Simvastatin was the most common Tier 1 ingredient (4.27%).

Conclusion: Potential clinically significant Paxlovid drug-drug interactions are common in U.S. adults and highly prevalent among those with polypharmacy, underscoring the central role of clinical pharmacy in rapid medication reconciliation, interaction mitigation, and timely access to COVID-19 therapeutics.

Keywords

COVID-19, drug interactions, ritonavir, polypharmacy, medication reconciliation

DOI: 10.4328/ECAM.25007
Received : 2026-03-26
Accepted : 2026-04-19
Published Online : 2026-04-23
Printed : 2026-05-01
Eu Clin Anal Med 2026;14(2):38-42

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How to cite this article: Taseal Ahmed. National prevalence of potential nirmatrelvir/ritonavir drug interactions in U.S. adults: implications for safe antiviral prescribing. Eu Clin Anal Med 2026;14(2):38-42. doi:10.4328/ECAM.25007

Introduction

Ritonavir-boosted nirmatrelvir (nirmatrelvir/ritonavir; Paxlovid) is a preferred oral antiviral for nonhospitalized patients at high risk for progression to severe coronavirus disease 2019 (COVID-19). Randomized trial evidence and large real-world studies demonstrate clinically meaningful reductions in hospitalization and death when treatment is initiated early in the disease course.[1-6] However, translating this efficacy into routine care depends on rapid, point-of-care therapeutic decision-making within a narrow treatment window, in which medication reconciliation and interaction screening often determine whether patients can access Paxlovid promptly or require an alternative regimen.[1-6]

A key limitation to widespread, guideline-concordant use is the drug-drug interaction (DDI) profile conferred by ritonavir, a potent inhibitor of cytochrome P450 3a (CYP3A) and P-glycoprotein. Depending on the concomitant medication, coadministration may be contraindicated or may require structured mitigation (e.g., temporary withholding, dose adjustment, enhanced monitoring) or selection of an alternate antiviral regimen.[7-9] These operational steps can delay treatment initiation and increase reliance on pharmacy support, particularly in settings with limited infrastructure for rapid interaction management.[7-10]

DDI burden is expected to be highest in older adults and those with polypharmacy, groups that also carry disproportionate risk for severe COVID-19 and are therefore most likely to meet indications for outpatient antiviral treatment.[9-12] Nationally representative estimates of potential DDIs can inform the scale of medication-reconciliation and pharmacist resources required for safe outpatient implementation, and can guide targeted decision support for the most common contraindicated agents.[11,12] Prior National Health and Nutrition Examination Survey (NHANES) based work has quantified the prevalence of potential DDIs with ritonavir-containing COVID-19 therapy in the U.S. population, underscoring DDIs as a common and clinically relevant barrier to outpatient antiviral prescribing at scale.[11] In parallel, expert guidance has emphasized that Paxlovid prescribing requires systematic recognition and management of interactions driven by potent CYP3A and transporter inhibition, with a practical distinction between agents that are contraindicated versus those that may be used with temporary holding, dose adjustment, or close monitoring.[9,10]

While this prior NHANES-based work represented an important first national estimate, that analysis was restricted to the cytochrome p450 3a4 (CYP3A4) metabolic pathway alone and applied a generic ritonavir interaction framework rather than Paxlovid-specific regulatory guidance.[11] Critically, it did not distinguish between agents that are contraindicated with nirmatrelvir/ritonavir, requiring a switch to an alternative antiviral, versus those that require only structured management strategies such as temporary medication holding, dose adjustment, or enhanced monitoring.[8,9] This distinction is central to the clinical decision at the point of prescribing. Our study addresses these gaps by anchoring the DDI classification directly to the Food and Drug Administration (FDA) Paxlovid Fact Sheet interaction table, incorporating interactions mediated by CYP3A4, cytochrome p450 2d6 (CYP2D6), and P-glycoprotein inhibition by ritonavir, and applying a two-tier classification scheme that maps directly to the distinct management pathways faced by prescribers and pharmacists.[8,9]

Building on this literature, our study provides Paxlovid-specific, nationally representative estimates anchored directly to the FDA Fact Sheet interaction table, applying transparent Tier 1 (contraindicated) and Tier 2 (avoidance/hold/dose adjustment/monitoring) classifications via ingredient-level exact matching to NHANES prescription inventory, and evaluates robustness in a sensitivity analysis restricted to interviewer-observed medications.[8] Using NHANES 2017-March 2020 pre-pandemic public-use data, we quantified the U.S. population prevalence of potential clinically significant DDIs with nirmatrelvir/ritonavir using a transparent DDI dictionary derived from the FDA Fact Sheet interaction table.[8] We report weighted national prevalence estimates overall and by age, sex, and polypharmacy, and identify the most common contraindicated medication ingredients.

Materials and Methods

Study Design and Data Source

We conducted a cross-sectional secondary analysis of the NHANES 2017-March 2020 pre-pandemic cycle. This cycle combines the 2017-2018 cycle with the partial 2019-March 2020 cycle using adjusted weights to support nationally representative inference.[13-15] NHANES is a complex, multistage probability sample of the noninstitutionalized U.S. civilian population.[15]

Study Population

Adults aged ≥18 years with valid interview weights and prescription medication questionnaire data were included. Medication exposure reflected self-reported prescription use in the prior 30 days, with container verification when available.

Exposure definition: We created a DDI dictionary based on the FDA Paxlovid Fact Sheet for Healthcare Providers table of clinically significant drug interactions.[8] Tier 1 (contraindicated) agents were defined as medications primarily metabolized by CYP3A for which elevated plasma concentrations are associated with serious or life-threatening toxicity, or strong CYP3A inducers for which co-administration would significantly reduce nirmatrelvir or ritonavir plasma concentrations and risk loss of virologic response and possible resistance.[8] Tier 2 agents were defined as medications for which co-administration requires avoidance, temporary withholding, dose adjustment, or therapeutic drug monitoring due to clinically meaningful pharmacokinetic interactions mediated by CYP3A4 inhibition and, to a lesser extent, CYP2D6 and P-glycoprotein inhibition by ritonavir.[8,9] These mechanistic tier distinctions map directly to the binary clinical decision at the point of prescribing: Tier 1 interactions require switching to an alternative antiviral regimen, whereas Tier 2 interactions may permit Paxlovid use with structured mitigation strategies. Operationally, an ingredient was assigned to Tier 1 if it appeared under the FDA Fact Sheet's contraindicated or "not recommended for co-administration" categories due to risk of serious toxicity or virologic failure; all remaining listed interactions requiring avoidance, dose adjustment, or monitoring were assigned to Tier 2. Generic ingredients were normalized and mapped to NHANES generic medication names. The final dictionary contained 149 unique ingredients (39 Tier 1 and 111 Tier 2), represented by 150 rows including headings, synonyms, and mapping variants.

Outcomes

Primary outcomes were the weighted prevalence of (1) any Tier 1 contraindicated medication, (2) any Tier 2 medication requiring avoidance/management, and (3) any clinically significant interaction (Tier 1 or Tier 2). Secondary outcomes included prevalence stratified by age group (18-49, 50-64, ≥65 years), sex, and polypharmacy (defined as ≥5 concurrent valid prescription medications), and identification of the most common Tier 1 contraindicated ingredients in the U.S. population.

Ethical Approval

This study used publicly available, de-identified NHANES data and did not constitute human subjects research under U.S. regulations.

Statistical Analysis

We followed National Center for Health Statistics (NCHS) analytic

guidance for NHANES 2017-March 2020 pre-pandemic analyses, incorporating interview weights (WTINTPRP), strata (SDMVSTRA), and primary sampling units (SDMVPSU) to produce nationally representative estimates and valid variance estimates.[13-15] Weighted prevalences and 95% confidence intervals (CIs) were estimated using Taylor series linearization. Sensitivity analyses restricted medication reporting to prescriptions observed by the interviewer (prescription medication seen variable [RXQSEEN] = 1).

Reporting Guidelines

This study was reported in accordance with the STROBE guideline.

Results

The analytic sample included 9,693 adults, representing approximately 247.9 million U.S. adults. In weighted estimates (Supplementary Table 1), 53.9% (95% CI 51.4-56.3) were aged 18-49 years, 25.7% (95% CI 24.2-27.2) were aged 50-64 years, and 20.4% (95% CI 18.2-22.6) were aged ≥65 years. Females comprised 51.8% (95% CI 50.2-53.3) and males 48.2% (95% CI 46.7-49.8). Race/ethnicity distribution was 62.2% (95% CI 57.4-66.9) non-Hispanic White, 11.5% (95% CI 8.7-14.3) non-Hispanic Black, 8.6% (95% CI 6.4-10.8) Mexican American, 7.7% (95% CI 6.3-9.2) other Hispanic, and 10.0% (95% CI 8.1-12.0) other race (including multi-racial) (Supplementary Table 1). National prevalence of potential clinically significant DDIs with nirmatrelvir/ritonavir was substantial (Table 1). Overall, 6.9% (95% CI 5.6-8.1) of adults had at least one Tier 1 contraindicated medication, 27.7% (95% CI 26.0-29.4) had at least one Tier 2 medication requiring avoidance/management, and 31.2% (95% CI 29.1-33.2) had any Tier 1 or Tier 2 medication. These correspond to approximately 17.1 million adults with Tier 1 contraindications and 77.3 million adults with any clinically significant DDI.

Prevalence increased with age. Any clinically significant DDI prevalence was 16.9% (95% CI 15.5-18.4) in adults 18-49 years, 36.3% (95% CI 33.0-39.7) in adults 50-64 years, and 62.3% (95% CI 59.1-65.4) in adults ≥65 years. Tier 1 contraindications increased from 1.6% (95% CI 1.2-2.0) (18-49 years) to 8.4% (95% CI 6.1-10.7) (50-64 years) and 18.9% (95% CI 16.0-21.8) (≥65 years); Tier 2 interactions increased from 15.8% (95% CI 14.4-17.2) to 32.4% (95% CI 29.3-35.5) and 53.3% (95% CI 49.9-56.8). By sex, any clinically significant DDI prevalence was 29.5% (95% CI 26.6-32.3) in males and 32.8% (95% CI 30.7-34.9) in females.

Table 1. Weighted prevalence of potential nirmatrelvir/ritonavir (Paxlovid) drug-drug interaction exposure

Variable	n	Weighted % (95% CI)
Any Tier 1 contraindicated medication	748	6.88 (5.63-8.13)
Any Tier 2 medication requiring avoidance /hold/dose adjustment/monitoring	2957	27.74 (26.04-29.44)
Any Tier 1 or Tier 2 medication	3304	31.18 (29.15-33.22)

Definitions: Tier 1 = contraindicated with nirmatrelvir/ritonavir; Tier 2 = requires avoidance/temporary holding, dose adjustment, or close monitoring. Tiers derived from FDA Paxlovid Fact Sheet and applied via ingredient-level exact matching.
Abbreviations: CI = Confidence Interval; FDA = Food and Drug Administration.

Polypharmacy was common: 17.1% (95% CI 15.7-18.6) of U.S. adults used ≥5 concurrent prescription medications. Among adults with polypharmacy, 86.5% (95% CI 83.6-89.4) had any clinically significant DDI, and 22.4% (95% CI 19.0-25.8) had a Tier 1 contraindication. Among adults without polypharmacy, 19.8% (95% CI 18.1-21.4) had any clinically significant DDI, and 3.7% (95% CI 2.8-4.6) had a Tier 1 contraindication (Supplementary Table 2). The most common Tier 1 contraindicated medication ingredients included simvastatin (4.27% [95% CI 3.35-5.19]); lovastatin (0.84% [95% CI 0.49-1.19]); colchicine (0.27% [95% CI 0.09-0.45]); carbamazepine (0.21% [95% CI 0.02-0.41]); lurasidone (0.21% [95% CI 0.05-0.37]) (Supplementary Table 3). In sensitivity analyses restricted to prescriptions observed by the interviewer (RXQSEEN = 1), prevalence estimates were modestly lower but remained high: Tier 1 6.1% (95% CI 4.8-7.3), Tier 2 24.9% (95% CI 23.3-26.4), and any DDI 28.0% (95% CI 26.1-30.0) (Supplementary Table 4).

Discussion

In this nationally representative analysis, nearly one-third of U.S. adults used at least one medication with potential clinically significant interaction with nirmatrelvir/ritonavir as listed in FDA labeling, and approximately 7% used contraindicated (Tier 1) medications that may preclude use without switching therapies.[8] The interaction burden was strongly age-graded and concentrated among adults with polypharmacy, highlighting that patients at the highest baseline risk for severe COVID-19 also face the greatest DDI-related prescribing complexity. These findings are concordant with prior U.S. population-level estimates of ritonavir-related interaction risk and with studies focused on older adults showing high prevalence of interacting medications.[10,11] Although many interactions can be managed safely (e.g., time-limited holding of selected lipid-lowering agents, dose adjustment, or monitoring), feasibility depends on rapid medication reconciliation, clear protocols, and timely access to clinical pharmacy support.[7,9,12]

Comparison with prior NHANES-based work: Our estimates extend and differ from the prior NHANES-based DDI analysis by Igho-Osagie et al. in three important ways.[11] First, our DDI dictionary was anchored to the FDA Paxlovid Fact Sheet, reflecting the specific interaction profile of nirmatrelvir/ritonavir, including interactions mediated by CYP2D6 and P-glycoprotein inhibition in addition to CYP3A4, rather than a broader CYP3A4-only framework applied to ritonavir-containing COVID-19 therapy generically.[11] Second, our two-tier classification operationalizes the clinically critical distinction between contraindicated agents (which preclude Paxlovid use without therapy switching) and manageable agents (which may permit Paxlovid use with time-limited mitigation), a distinction that is central to real-world prescribing decisions but absent from prior NHANES-based estimates. Third, by providing Tier-stratified national prevalence estimates, our study enables direct quantification of the proportion of U.S. adults who face absolute prescribing barriers versus those for whom DDI-informed management protocols could expand access. This is a policy-relevant distinction not previously derivable from population-level data. In brief, this study estimates the national prevalence of absolute versus manageable Paxlovid prescribing barriers, not merely overall ritonavir-related DDI burden.

Clinical implications: Our results support embedding DDI screening as a default, workflow-based step in outpatient antiviral prescribing and suggest the need for such integration. Despite Paxlovid's proven real-world effectiveness, with large-scale target trial emulation estimating reductions in hospitalization risk of approximately 39% and in mortality of approximately 61%, antiviral prescribing remains markedly suboptimal in the highest-risk populations.[16] A 2026 MMWR analysis found that fewer than one-quarter of eligible adults aged ≥65 years received a COVID-19 antiviral during several recent seasonal periods, with concerns about drug interactions cited as a primary barrier.[17] A parallel study similarly documented that lack of prescriber familiarity with Paxlovid's interaction profile contributes to underutilization, specifically among older adults, the very population for whom antiviral benefit is greatest.[18] The convergence of our population-level prevalence data with real-world pharmacovigilance findings is particularly notable: simvastatin was the most prevalent Tier 1 agent in our analysis (4.27%), consistent with pharmacovigilance data identifying simvastatin as the most frequently reported drug associated with potential DDI adverse events in nirmatrelvir/ritonavir-exposed patients

globally (Supplementary Table 3).[19] This alignment between population-level risk estimates and observed real-world harm events supports the clinical relevance, and not merely descriptive value of our prevalence findings. Furthermore, among adults with polypharmacy, where our estimates show 86.5% carry any DDI and 22.4% a Tier 1 contraindication, proactive deprescribing strategies may represent an underutilized tool for expanding treatment eligibility (Supplementary Table 2). The COVID-SAFER analysis found that 68% of hospitalized older adults with polypharmacy had a nirmatrelvir-ritonavir DDI and that 21% were taking at least one potentially inappropriate medication, many of which required complex deprescribing strategies rather than simple holding.[20] Our nationally representative estimates suggest this burden extends across the broader outpatient population, supporting the need for anticipatory medication optimization integrated into routine chronic disease management. Standardized medication reconciliation and patient counseling may benefit from integration with decision support and pharmacist escalation pathways for common interaction classes. Systems should also maintain readiness to deploy alternate therapies when contraindications or management complexity would delay treatment beyond the effective window.[7-9,12]

Implications for guidelines and health practice: Current clinical guidance prioritizes nirmatrelvir/ritonavir for many high-risk outpatients while acknowledging that DDIs may necessitate alternate antivirals.[11] By quantifying the national scale of potential clinically significant DDIs, our findings support guideline-concordant investment in medication management infrastructure and targeted decision support, particularly for older adults and those with polypharmacy.

Strengths include the use of nationally representative NHANES data, complex-sampling variance estimation, and a transparent, FDA-label-anchored DDI operationalization. Limitations include reliance on pre-pandemic medication patterns; incomplete capture of nonprescription agents; and inability to incorporate dose, renal function-based adjustments, timing, or clinician-supervised holding strategies. Consequently, these estimates should be interpreted as potential interaction prevalence requiring clinical adjudication at the point of care.

Limitations

This study has several limitations. First, medication exposure was based on NHANES self-reported prescription use in the prior 30 days, which may incompletely capture true medication use despite interviewer verification when available. Second, NHANES does not fully capture over-the-counter, herbal, recreational, inpatient, or procedure-administered medications, and we could not account for dose, treatment duration, renal function, timing of coadministration, or clinician-directed temporary holding strategies; therefore, these findings represent potential rather than adjudicated contraindications. Third, because the analysis used 2017-March 2020 pre-pandemic data, prescribing patterns may not fully reflect the therapeutic landscape during later phases of COVID-19 antiviral use. These limitations likely result in conservative estimates and support the interpretation of our findings as population-level prescribing complexity rather than definitive patient-level ineligibility.

Conclusion

Approximately 31.2% (95% CI 29.1-33.2) of U.S. adults, about 77.3 million people, use medications with potential clinically significant interactions with nirmatrelvir/ritonavir, and 6.9% (95% CI 5.6-8.1) have contraindicated medications. These results underscore the need for rapid, standardized DDI assessment and management to maximize equitable access to guideline-recommended outpatient antiviral therapy while minimizing preventable adverse drug events.

Declarations

Ethics Declarations

Ethics approval and consent to participate: This study used de-identified, publicly available data from the National Health and Nutrition Examination Survey (NHANES) 2017-March 2020 pre-pandemic public-use datasets provided by the National Center for Health Statistics, Centers for Disease Control and Prevention. As no human participants were directly involved and all data were fully de-identified and publicly accessible, ethics committee approval and informed consent were not required.

Animal and Human Rights Statement

This study did not involve any human participants or animal subjects.

Informed Consent

Not applicable.

Data Availability

The datasets used and/or analyzed during the current study are not publicly available due to patient privacy reasons but are available from the corresponding author on reasonable request.

Conflict of Interest

The authors declare that there is no conflict of interest.

Funding

None.

Author Contributions (CRediT Taxonomy)

Conceptualization: T.A.
Methodology: T.A.
Software: T.A.
Validation: T.A.
Formal Analysis: T.A.
Investigation: T.A.
Resources: T.A.
Data Curation: T.A.
Writing – Original Draft Preparation: T.A.
Writing – Review & Editing: T.A.
Visualization: T.A.
Supervision: T.A.
Project Administration: T.A.
Funding Acquisition: T.A.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content, including study design, data collection, analysis and interpretation, writing, and some of the main line, or all of the preparation and scientific review of the contents, and approval of the final version of the article.

Abbreviations

CI: confidence interval
COVID-19: Coronavirus disease 2019
CYP3A: Cytochrome p450 3a
CYP3A4: Cytochrome p450 3a4
CYP2D6: Cytochrome p450 2d6
DDI: Drug-drug interaction
FDA: Food and drug administration
NHANES: National health and nutrition examination survey
NCHS: National center for health statistics
RXQSEEN: Prescription medication seen variable
SDMVPSU: Masked variance pseudo-primary sampling unit
SDMVSTRA: Masked variance pseudo-stratum
STROBE: Strengthening the reporting of observational studies in epidemiology
WTINTPRP: Interview sample weight variable

References

1. Hammond J, Leister-Tebbe H, Gardner A, et al. Oral nirmatrelvir for high-risk, nonhospitalized adults with COVID-19. N Engl J Med. 2022;386(15):1397-1408. doi:10.1056/nejmoa2118542
2. Arbel R, Sagy YW, Hoshen M, et al. Nirmatrelvir use and severe COVID-19 outcomes during the Omicron surge. N Engl J Med. 2022;387(9):790-798. doi:10.1056/nejmoa2204919
3. Lewnard JA, McLaughlin JM, Malden D, et al. Effectiveness of nirmatrelvir-ritonavir in preventing hospital admissions and deaths in people with COVID-19: a cohort study in a large US health care system. Lancet Infect Dis. 2023;23(7):806-815. doi:10.1016/s1473-3099(23)00118-4

4. Bajema KL, Berry K, Streja E, et al. Effectiveness of COVID-19 treatment with nirmatrelvir-ritonavir or molnupiravir among US veterans: target trial emulation studies with one-month and six-month outcomes. Ann Intern Med. 2023;176(6):807-816. doi:10.7326/m22-3565
5. Xie Y, Choi T, Al-Aly Z. Nirmatrelvir and the risk of post-acute sequelae of COVID-19. Nat Med. 2023;29(7):1806-1813.
6. Gottlieb RL, Vaca CE, Paredes R, et al. Early remdesivir to prevent progression to severe COVID-19 in outpatients. N Engl J Med. 2022;386(4):305-315. doi:10.1056/nejmoa2116846
7. National Institutes of Health. Coronavirus disease 2019 (COVID-19) treatment guidelines: therapeutic management of nonhospitalized adults with COVID-19; drug-drug interactions between ritonavir-boosted nirmatrelvir (Paxlovid) and concomitant medications. Accessed February 12, 2026.
8. US Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization for Paxlovid—clinically significant drug interactions. Accessed February 12, 2026.
9. Marzolini C, Kuritzkes DR, Marra F, et al. Prescribing nirmatrelvir-ritonavir: how to recognize and manage drug-drug interactions. Ann Intern Med. 2022;175(5):744-746. doi:10.7326/m22-0281
10. Ross SB, Bortolussi-Courval É, Hanula R, et al. Drug interactions with nirmatrelvir-ritonavir in older adults using multiple medications. JAMA Netw Open. 2022;5(7):e2220184. doi:10.1001/jamanetworkopen.2022.20184
11. Igho-Osagie E, Brzozowski K, Jin H, et al. Prevalence of potential drug-drug interactions with ritonavir-containing COVID-19 therapy in the United States: an analysis of the National Health and Nutrition Examination Survey. Clin Ther. 2023;45(3):390-399.e4. doi:10.1016/j.clinthera.2023.03.012
12. Abraham S, Bukhari S, McKinnon JE, et al. Cardiovascular drug interactions with nirmatrelvir/ritonavir in patients with COVID-19. J Am Coll Cardiol. 2022;80(20):1912-1924. doi:10.1016/j.jacc.2022.08.800
13. Akinbami LJ, Chen TC, Clark J, et al. National Health and Nutrition Examination Survey, 2017-March 2020 prepandemic file: sample design, estimation, and analytic guidelines. Vital Health Stat 12. 2022;(190):1-36.
14. Centers for Disease Control and Prevention; National Center for Health Statistics. NHANES 2017-March 2020 prepandemic: brief overview and analytic guidance. Accessed February 12, 2026.
15. Centers for Disease Control and Prevention; National Center for Health Statistics. NHANES survey methods and analytic guidelines. Accessed February 12, 2026.
16. Bhatia A, Preiss AJ, Xiao X, et al. Effect of nirmatrelvir/ritonavir (Paxlovid) on hospitalization among adults with COVID-19: an electronic health record-based target trial emulation from N3C. PLoS Med. 2025;22(1):e1004493. doi:10.1371/journal.pmed.1004493
17. Raykin J, Rochin I, Wiegand R, et al. COVID-19 antiviral prescription receipt among outpatients aged ≥65 years—United States, June 1, 2023–September 30, 2025. MMWR Morb Mortal Wkly Rep. 2026;75(6):69-76. doi:10.15585/mmwr.mm7506a1
18. de Arpe CF, Homen R, Valls-Carbó A, et al. Underutilization of nirmatrelvir/ritonavir in eligible COVID-19 patients. Eur J Clin Microbiol Infect Dis. 2025;44(9):2283-2286. doi:10.1007/s10096-025-05150-4
19. Quercia R, Di Perri G, Pein C, et al. Pharmacovigilance of drug-drug interactions with nirmatrelvir/ritonavir. Infect Dis Ther. 2024;13(1):2545-2561.
20. Ross SB, McDonald EG, Lee TC, et al. COVID-SAFER: deprescribing guidance for nirmatrelvir-ritonavir drug interactions in older adults. medRxiv. Published online March 4, 2022. doi:10.1101/2022.03.01.22271254