treatment by detailed personal and clinical characteristics. Our finding that only 20% of potentially eligible patients received treatment could be of concern, although this proportion might only reflect the limitations discussed above. Although sotrovimab was the first line treatment available during the majority of the study period, almost 50% of patients received molnupiravir or paxlovid; this finding might be explained by sotrovimab requiring an infusion in a clinic setting, presenting greater logistical challenges. Focusing on the three groups (Down's syndrome, rare neurological conditions, and immune deficiencies) where sotrovimab was not first choice might be a pragmatic first step for investigations on the reasons for these choices.

Paxlovid was implemented as a first line treatment next to sotrovimab on 10 February 2022, reflected by a slowing in the uptake of molnupiravir from that date.[11] Both the antiviral drugs molnupiravir and paxlovid are used orally.[13] The low uptake of remdesivir might be explained by logistical challenges, because remdesivir is given intravenously in a three day course.[11] In addition, concerns were raised about the low efficacy of sotrovimab against the omicron BA.2 sublineage,[27] the dominant circulating variant from mid-February.[28] Our findings of discrepancies in treatment between different groups is notable and consistent with our analysis of sociodemographic and ethnic group variation in the receipt of covid-19 vaccinations.[14] Additionally, the finding of lower coverage among those patients aged ≥80 years requires investigation, particularly because age is associated with covid-19 death and admission to hospital.[29]

Further research and investigation is required to understand and deal with the causes of any inequity, such as the identification of barriers to the uptake of covid-19 vaccines.[30] Additionally, understanding variation in the choice of individual treatment option beyond clinical indications and cautions will be of utmost importance as more information on the relative efficacy emerges from ongoing trials.

Finally, all our analytical code is openly available for reuse and can be used to underpin observational work on clinical effectiveness and safety of treatments. To our knowledge, no head-to-head comparative interventional research has been reported to date for these treatments. The effectiveness of these covid-19 treatments is supported by the original randomised controlled trials.[31–33] Observational studies are starting to emerge on the effectiveness of these treatments in the clinical setting.[34–39] The timeliness, granularity, and scale of the data available via OpenSAFELY offers unprecedented opportunity to carry out rapid observational work to inform the roll-out of new treatments.

The reasons underpinning variation in treatments delivered by CMDUs are not yet understood, and information presented here should not be misinterpreted as a criticism of the rapidly established CMDUs in the context of high levels of infection,[40] but rather as an example of the value of rapid turnaround data monitoring to help optimise the successful delivery of an ambitious national treatment programme. We will produce routine data updates at https://reports.opensafely.org/ to assist with ongoing monitoring and targeted initiatives to resolve gaps in coverage as well as informing development of study designs on the efficacy and safety of these new treatments.

## Conclusions

The NHS in England has rapidly deployed facilities to offer novel therapeutics for the rapid treatment of covid-19 in the community. Targeted activity might be needed to resolve lower treatment rates observed among certain geographical areas and key groups including ethnic minority groups, people aged ≥80 years, people living in areas of higher deprivation, and care home residents. Near real time data monitoring can help support individuals on the front line making complex operational decisions around treatment delivery.


## AUTHOR AFFILIATIONS

[1]Bennett Institute for Applied Data Science, Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK
[2]London School of Hygiene and Tropical Medicine, London, UK
[3]Oxford Health NHS Foundation Trust, Oxford, UK
[4]TPP, Leeds, UK

Twitter Viyaasan Mahalingasivam @viyaasanm, Christopher T Rentsch @DarthCTR, Colm D Andrews @ColmResearcher and Brian MacKenna @brianmackenna



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Data availability statement Data may be obtained from a third party and are not publicly available. Access to the underlying identifiable and potentially re-identifiable pseudonymised electronic health record data is tightly governed by various legislative and regulatory frameworks, and restricted by best practice. The data in OpenSAFELY are drawn from general practice data across England where TPP is the data processor. TPP developers (CB, JC, and SH) initiate an automated process to create pseudonymised records in the core OpenSAFELY database, which are copies of key structured data tables in the identifiable records. These are linked onto key external data resources that have also been pseudonymised via SHA-512 one-way hashing of NHS numbers using a shared salt. Bennett Institute for Applied Data Science developers and principal investigators (BG, CEM, SCJB, AJW, WJH, HJC, DE, PI, SD, GH, RMS, ID, TW, JM, MW, RYP, KB and CTR) holding contracts with NHS England have access to the OpenSAFELY pseudonymised data tables as needed to develop the OpenSAFELY tools. These tools in turn enable researchers with OpenSAFELY Data Access Agreements to write and execute code for data management and data analysis without direct access to the underlying raw pseudonymised patient data, and to review the outputs of this code. All code for the full data management pipeline—from raw data to completed results for this analysis—and for the OpenSAFELY platform as a whole is available for review at github.com/OpenSAFELY.



## ORCID iDs

George Hickman http://orcid.org/0000-0002-6691-4046
Alex J Walker http://orcid.org/0000-0003-4932-6135
Ben Goldacre http://orcid.org/0000-0002-5127-4728
Brian MacKenna http://orcid.org/0000-0002-3786-9063

## REFERENCES

1 Agarwal A, Rochwerg B, Lamontagne F, *et al*. A living WHO guideline on drugs for covid-19. *BMJ* 2020;370:m3379. doi:10.1136/bmj.m3379
2 COVID-19 Treatment Guidelines. Hospitalized adults: therapeutic management. Available: https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults-therapeutic-management/ [Accessed 23 Feb 2022].
3 NICE. Recommendations: COVID-19 rapid guideline: managing COVID-19: guidance. Available: https://www.nice.org.uk/guidance/ng191/chapter/Recommendations [Accessed 23 Feb 2022].
4 Department of Health and Social Care. Government launches COVID-19 antivirals Taskforce to roll out innovative home treatments this autumn, 2021. Available: https://www.gov.uk/government/news/government-launches-covid-19-antivirals-taskforce-to-roll-out-innovative-home-treatments-this-autumn [Accessed 23 Feb 2022].
5 Department of Health and Social Care. UK's most vulnerable people to receive life-saving COVID-19 treatments in the community, 2021. Available: https://www.gov.uk/government/news/uks-most-vulnerable-people-to-receive-life-saving-covid-19-treatments-in-the-community [Accessed 23 Feb 2022].
6 Department of Health, Social Care. UK secures millions more antivirals to help fight omicron, 2021. Available: https://www.gov.uk/government/news/uk-secures-millions-more-antivirals-to-help-fight-omicron [Accessed 19 Sep 2022].
7 Kanja C, Bunn S, UK Parliament. Drug therapies for COVID-19, 2022. Available: https://post.parliament.uk/drug-therapies-for-covid-19/ [Accessed 20 Sep 2022].
8 NHS Digital. Population health: COVID-19 treatment methodology. Available: https://digital.nhs.uk/coronavirus/treatments/methodology [Accessed 22 Jan 2022].
9 UK Government Health Departments, Central Alerting System. Interim clinical commissioning policy: neutralising monoclonal antibodies or antivirals for non-hospitalised patients with COVID-19 (2021-12-08), 2021. Available: https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103184 [Accessed 26 Sep 2022].
10 UK Government Health Departments, Central Alerting System. Interim clinical commissioning policy: neutralising monoclonal antibodies or antivirals for non-hospitalised patients with COVID-19 (2021-12-24), 2021. Available: https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103186 [Accessed 26 Sep 2022].
11 UK Government Health Departments. Interim clinical commissioning policy: antivirals or neutralising monoclonal antibodies for non-hospitalised patients with COVID-19 (2022-01-27); 2022.
12 UK Government Health Departments, Central Alerting System. Interim clinical commissioning policy: antivirals or neutralising monoclonal antibodies for non-hospitalised patients with COVID-19 (version 5) (2022-02-24), 2022. Available: https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103191 [Accessed 26 Sep 2022].
13 UK Government Health Departments, Central Alerting System. Interim clinical commissioning policy: antivirals or neutralising monoclonal antibodies for non-hospitalised patients with COVID-19 (version 6) (2022-05-30), 2022. Available: https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103208 [Accessed 26 Sep 2022].
14 Curtis HJ, Inglesby P, Morton CE, *et al*. Trends and clinical characteristics of COVID-19 vaccine recipients: a federated analysis of 57.9 million patients' primary care records in situ using OpenSAFELY. *Br J Gen Pract* 2022;72:e51–62. doi:10.3399/BJGP.2021.0376
15 Williamson EJ, Walker AJ, Bhaskaran K, *et al*. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 2020;584:430–6. doi:10.1038/s41586-020-2521-4
16 OpenSAFELY. Antivirals and nMABs for non-hospitalised COVID-19 patients: coverage report. Available: https://reports.opensafely.org/reports/antivirals-and-nmabs-for-non-hospitalised-covid-19-patients-coverage-report/ [Accessed 10 May 2022].
17 LSHTM. National chronic kidney disease audit (NCKDA). Available: https://www.lshtm.ac.uk/research/centres-projects-groups/ckdaudit [Accessed 25 Feb 2022].
18 NHS England. Interim clinical commissioning policy: neutralising monoclonal antibodies or antivirals for non-hospitalised patients with COVID-19, 2022. Available: https://www.england.nhs.uk/coronavirus/documents/c1603-interim-clinical-commissioning-policy-antivirals-or-neutralising-monoclonal-antibodies-for-non-hospitalised-patients-with-covid-19-version-5/ [Accessed 1 May 2022].
19 NHS data model and dictionary. Lower layer super output area, 2022. Available: https://www.datadictionary.nhs.uk/nhs_business_definitions/lower_layer_super_output_area.html
20 Department for Environment, Food & Rural Affairs. 2011 rural urban classification, 2013. Available: https://www.gov.uk/government/statistics/2011-rural-urban-classification [Accessed 1 Jun 2022].

21 NHS England. Safeguarding adults. Available: https://www.england.nhs.uk/wp-content/uploads/2017/02/adult-pocket-guide.pdf [Accessed 26 Sep 2022].
22 NHS Digital. COVID medicine delivery unit directory. Available: https://digital.nhs.uk/coronavirus/covid-medicine-delivery-unit-directory?key=h58vqkRUup40027K04xOrtfh7ZXqwRQoOLhXTkGWlbOrVSkwzfTeetw39uGFlc28 [Accessed 18 May 2022].
23 Github. antibody-and-antiviral-deployment github rEpo. Available: https://github.com/opensafely/antibody-and-antiviral-deployment [Accessed 21 Feb 2022].
24 Andrews C, Schultze A, Curtis H, *et al.* OpenSAFELY: representativeness of electronic health record platform OpenSAFELY-TPP data compared to the population of England. *Wellcome Open Res* 2022;7:191. doi:10.12688/wellcomeopenres.18010.1
25 Brown M, Saund J, Qureshi A, *et al.* Demographics and outcomes of COVID-19 medicines delivery units across 4 UK centres during the initial B1.1.529 omicron epidemic: a service evaluation. *SSRN Journal* 2022. doi:10.2139/ssrn.4123333
26 Bhaskaran K, Rentsch CT, MacKenna B, *et al.* HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform. *Lancet HIV* 2021;8:e24–32. doi:10.1016/S2352-3018(20)30305-2
27 Mahase E. Covid-19: has the spread of omicron BA.2 made antibody treatments redundant? *BMJ* 2022;377:01009. doi:10.1136/bmj.01009
28 UK Health Security Agency. SARS-CoV-2 variants of concern and variants under investigation in England, 2022. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1060337/Technical-Briefing-38-11March2022.pdf
29 Romero Starke K, Reissig D, Petereit-Haack G, *et al.* The isolated effect of age on the risk of COVID-19 severe outcomes: a systematic review with meta-analysis. *BMJ Glob Health* 2021;6:e006434. doi:10.1136/bmjgh-2021-006434
30 GOV.UK. Factors influencing COVID-19 vaccine uptake among minority ethnic groups, 17 December 2020, 2021. Available: https://www.gov.uk/government/publications/factors-influencing-covid-19-vaccine-uptake-among-minority-ethnic-groups-17-december-2020 [Accessed 20 Sep 2022].
31 Jayk Bernal A, Gomes da Silva MM, Musungaie DB, *et al.* Molnupiravir for oral treatment of Covid-19 in nonhospitalized patients. *N Engl J Med* 2022;386:509–20. doi:10.1056/NEJMoa2116044
32 Hammond J, Leister-Tebbe H, Gardner A, *et al.* Oral Nirmatrelvir for high-risk, nonhospitalized adults with Covid-19. *N Engl J Med* 2022;386:1397–408. doi:10.1056/NEJMoa2118542
33 Gupta A, Gonzalez-Rojas Y, Juarez E, *et al.* Early treatment for Covid-19 with SARS-CoV-2 neutralizing antibody Sotrovimab. *N Engl J Med* 2021;385:1941–50. doi:10.1056/NEJMoa2107934
34 Huang DT, McCreary EK, Ryan Bariola J. Effectiveness of casirivimab and imdevimab, and sotrovimab during delta variant surge: a prospective cohort study and comparative effectiveness randomized trial. *medRxiv* 2021.
35 Solera JT, Árbol BG, Alshahrani A, *et al.* Impact of vaccination and early monoclonal antibody therapy on COVID-19 outcomes in organ transplant recipients during the omicron wave. *Clin Infect Dis* 2022. doi:10.1093/cid/ciac324. [Epub ahead of print: 21 Apr 2022].
36 Aggarwal NR, Beaty LE, Bennett TD, *et al.* Real world evidence of the neutralizing monoclonal antibody Sotrovimab for preventing hospitalization and mortality in COVID-19 outpatients. *J Infect Dis* 2022. doi:10.1093/infdis/jiac206. [Epub ahead of print: 16 May 2022].
37 Chavarot N, Melenotte C, Amrouche L, *et al.* Early treatment with sotrovimab monoclonal antibody in kidney transplant recipients with omicron infection. *Kidney Int* 2022;101:1290–3. doi:10.1016/j.kint.2022.04.003
38 Ganatra S, Dani SS, Ahmad J, *et al.* Oral Nirmatrelvir and ritonavir in non-hospitalized vaccinated patients with Covid-19. *Clin Infect Dis* 2022. doi:10.1093/cid/ciac673. [Epub ahead of print: 20 Aug 2022].
39 Zheng B, Green ACA, Tazare J, *et al.* Comparative effectiveness of sotrovimab and molnupiravir for prevention of severe covid-19 outcomes in patients in the community: observational cohort study with the OpenSAFELY platform. *BMJ* 2022;379:e071932. doi:10.1136/bmj-2022-071932
40 UK Government. UK summary of COVID-19 in the UK. Available: https://coronavirus.data.gov.uk/ [Accessed 24 Feb 2022].


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