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A call for more evidence documenting human-to-dog transmission of monkeypox virus

Sophie Seang and colleagues’ description of human-to-dog transmission of monkeypox virus raised concerns about the role of pets in monkeypox virus transmission, reinforcing recommendations from public health authorities that infected people should avoid contact with animals, isolate exposed pets, and consider removing exposed pets from the homes of immunocompromised people. For example, the US Centers for Disease Control and Prevention now notes that human-to-dog transmission of monkeypox virus has occurred and that signs in dogs include development of a rash, “which to-date have been located on the abdomen and anus.”

However, the authors of this Correspondence provided insufficient evidence that the adult dog was infected with monkeypox virus: monkeypox virus was detected using PCR in scrapings from the dog’s skin lesions and from swabs from its anus and oral cavity, but whether specimens were pooled or tested separately is not stated, and cycle threshold values were not provided to quantify the DNA present. The idea that this was contaminating DNA therefore remains plausible. The lesion on the dog’s abdomen resembled a papule seen with bacterial folliculitis, and the anal lesion was barely perceptible. Biopsy proof that these lesions were pox lesions was absent, and course of the infection. Bull World Health Organ 1976; 53:13–20.

Characterising adults in Scotland who are not vaccinated against COVID-19

By Aug 10, 2022, 3497208 of the estimated 4.4 million adults living in Scotland had received three doses of a COVID-19 vaccine. However, a proportion of the adult population remains unvaccinated (defined as no record of any vaccine being administered) and susceptible to severe COVID-19 outcomes. Characterising this population can help to understand gaps in vaccine coverage and determinants of vaccine hesitancy and could support targeted public health messaging. Unlike the vaccinated population, on whom information is gathered at the point of vaccination, current estimates of the unvaccinated population are calculated using general practitioner (GP) records. However, complications arise because GP records can include people who have moved away from Scotland; estimates suggest that GP records contain a population 8% greater than National Records of Scotland population estimates.

We used data from linked national health records to estimate the number and describe the characteristics of adults living in Scotland for whom there is no record of any COVID-19 vaccination. This analysis was conducted using the Early Pandemic Evaluation and Enhanced Surveillance of COVID-19 (EAVE II) platform, a national COVID-19 surveillance platform using anonymised individual patient-level records from all 940 general practices in Scotland, deterministically linked to multiple datasets recording morbidity, mortality, virology, vaccination, and prescribing (appendix p 1). Linkage was done with a unique identifier for each resident in Scotland who is registered with a GP.

The EAVE II cohort includes all individuals registered with a GP in Scotland as of March 1, 2020, including those who have subsequently left Scotland without informing their GP. To exclude people no longer living in Scotland, we defined unvaccinated individuals as those without COVID-19 vaccination records who had at least one interaction with the National Health Service (NHS) Scotland since Jan 1, 2019. We used the EAVE II cohort at a cutoff date of Dec 8, 2020 (the start of the UK’s vaccination programme). In the appendix (p 2) we outline the process of identifying the unvaccinated population. We excluded individuals who died of any cause before the cutoff date and those recorded as having left Scotland. As individuals younger than 18 years were only invited for vaccination more recently (between August, 2021, and March, 2022, depending on age), our analysis was restricted to adults aged 18 years and older.

This identification process yielded 4712810 individuals who were recorded as eligible for COVID-19 vaccination. Linkage of vaccine eligibility data with COVID-19 vaccination records identified 842029 (17.9%) of the 4712810 eligible individuals as having no record of vaccination. Among these 842029 people, 86489 (10.3%) had documented reasons for not receiving a vaccine, including immunisation con-
Correspondence

537289 eligible individuals aged 18 years or older were identified as having no record of any COVID-19 vaccination in Scotland and at least one contact with NHS Scotland since Jan 1, 2019. We then excluded people who had died since the start of the vaccination programme, and those for whom immunisation contraindicated was recorded as the reason for non-vaccination. On Aug 10, 2022, our method identified 494288 unvaccinated individuals with no record of any COVID-19 vaccination.

This unvaccinated cohort contained similar proportions of males and females, with similar age distribution across both sexes (appendix pp 3-4). The mean age was 42.4 years. Most unvaccinated people lived in urban settings, and 143558 (29.0%) of 494288 unvaccinated individuals—compared with 719251 (18.7%) of 3847789 vaccinated individuals—resided in areas ranked by the Scottish Index of Multiple Deprivation as containing the most deprived 20% of the Scottish population.

On the basis of GP records, the majority (298866, 60.5%) of 494288 unvaccinated individuals were not known to have any comorbidities, compared with 1988751 (51.7%) of 3847789 vaccinated individuals, whereas 55122 (11.2%) of 494288 unvaccinated individuals were recorded as having three or more comorbidities, compared with 481019 (12.5%) of 3847789 vaccinated individuals. The most frequently reported comorbidities among 494288 unvaccinated individuals were chronic respiratory disease (77643, 15.7%), depression (63375, 12.8%), and hypertension (52474, 10.6%).

One in five (103505, 20.9%) of 494288 unvaccinated individuals were prescribed medications for conditions relating to the CNS, compared with 655531 (17.0%) of 3847789 vaccinated individuals, with more than a third of this unvaccinated group (40179 [38.8%] of 103505) prescribed antidepressants.

Multivariable logistic regression modelling was used to identify the factors most likely to predict COVID-19 vaccination. Male sex, high deprivation, living in large urban areas, being prescribed medication for CNS disorders, and having more than three comorbidities were most associated with unvaccinated status, although individuals with some comorbidities—such as hypertension, diabetes, and chronic respiratory disease—were more likely to be vaccinated.

Previous UK data have reported on inequalities of COVID-19 vaccination coverage, with considerably lower uptake among some groups.1 Notably, although increasing age and presence of comorbidities are among the most widely recognised risk factors for COVID-19 mortality,57 people with a substantial number of comorbidities remained at increased risk of being unvaccinated.

The limitations of our approach include a lack of ethnicity data, which are important because variations in vaccine uptake among different ethnic groups are known.8 Additionally, although our approach minimises false inflation of the number of unvaccinated people, some of these individuals will have had no recent interaction with the health-care system and so will remain undetected. Unvaccinated people might also be less likely to have health-seeking behaviour, reducing the chance of them being detected through this method.9 Some individuals might have been vaccinated outside of Scotland, which was not captured in our analysis. Identifying people vaccinated in other countries will improve future estimates of unvaccinated populations.

In summary, this national analysis revealed that, even after accounting for possible overinflation of population size, a considerable proportion of the adult population of Scotland remains unvaccinated against COVID-19. We also identified predictors of unvaccinated status, which can help with formulating a revised national vaccination strategy.

AS and CR are members of the Scottish Government Chief Medical Officer’s COVID-19 Advisory Group. AS is a member of the NERVTAG Risk Stratification Subgroup and an unfunded member of AstraZeneca’s COVID-19 strategic consultancy group, the Thrombocytopenia Taskforce. CR is a member of the Scientific Pandemic Influenza Group on Modelling and the Medicines and Healthcare Products Regulatory Agency COVID-19 Vaccine Beneﬁt and Risk Working Group. JLM is a member of the COVID Scottish National Incident Management Team. CM reports research funding from the Medical Research Council, Health Data Research UK, National Institute for Health Research, and the Scottish Chief Science Office. All other authors declare no competing interests. EAVE II is funded by the Medical Research Council with the support of the Thrombocytopenia Taskforce and by the Scottish Government Chief Medical Officer’s COVID-19 Advisory Group. The limitations of our approach include a lack of ethnicity data, which are important because variations in vaccine uptake among different ethnic groups are known. Additionally, although our approach minimises false inflation of the number of unvaccinated people, some of these individuals will have had no recent interaction with the health-care system and so will remain undetected. Unvaccinated people might also be less likely to have health-seeking behaviour, reducing the chance of them being detected through this method. Some individuals might have been vaccinated outside of Scotland, which was not captured in our analysis. Identifying people vaccinated in other countries will improve future estimates of unvaccinated populations.

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led by Health Data Research UK in partnership with the Office for National Statistics and funded by UK Research and Innovation. UA and CM acknowledge funding from Health Data Research UK (Measuring and Understanding Multimorbidity using Routine Data in the UK—HDR-9006, CFC0150). The funding source had no involvement in data collection, study design, data analysis, interpretation of findings, or the decision to publish this Correspondence. We thank Dave Kelly (Albasoft, Inverness, UK) for support with making primary care data available, Iain Mclaughlin (Public Health Scotland, Glasgow, UK) for help with the identification of the unvaccinated cohort, and James Pickett (Health Data Research UK, London, UK), Wendy Inglis-Humphrey, Vicky Hammonsley, Maria Georgiou, Laura Gonzalez Rienda (Usher Institute, University of Edinburgh, Edinburgh, UK), Morna Coote, Amanda Burridge, Amie Wilson, and Megan Gorman (Public Health Scotland, Glasgow, UK) for project management and administration support. We acknowledge the support of the EAVE II Patient Advisory Group for their help with interpretation of findings and suggestions for dissemination and engagement. SSH and EH contributed equally: AS and CR contributed equally.

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**Maintenance antipsychotic trials and the effect of withdrawal**

Johannes Schneider-Thoma and colleagues1 report the results of a systematic review and network meta-analysis of antipsychotics for the maintenance treatment of adults with schizophrenia, but did not consider the effect of withdrawal-related effects when interpreting their results. They included 49 trials with a placebo group, of which we were able to access information on participants and design for 47 trials (appendix). Of those 47 trials, all used a discontinuation design, most involving people who had been taking antipsychotics for many years, and 43 trials described or implied abrupt cessation of antipsychotic treatment upon assignment to placebo, although the trial with the longest taper period stopped antipsychotics over 4–6 weeks. These rapid stopping schedules, including of depot formulations, are likely to induce somatic and psychiatric withdrawal effects (eg, anxiety), which are now established symptoms, as recently shown in an individual participant data meta-analysis.2 Withdrawal effects could be conflated with worsening of the illness and therefore interpreted as relapse,3 inflating the apparent relapse rate in the placebo group. Withdrawal might also have a destabilising effect on the illness leading to relapse, and abrupt cessation of antipsychotics could outright induce psychotic symptoms.4 Therefore, the placebo-controlled discontinuation trials included by Schneider-Thoma and colleagues5 do not inform about potential benefits of starting maintenance treatment with antipsychotics to begin with, and provide misleading information on the benefits and harms of continuing versus stopping ongoing antipsychotic treatment, by ignoring the consequences of withdrawal effects.4

JM is chief investigator of a National Institute for Health and Care Research-funded trial of gradual antipsychotic reduction. KM and MAH declare no competing interests.

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Authors’ reply

We thank Klaus Munkholm and colleagues for their valuable correspondence. First, we would like to mention that this Correspondence does...