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Feasibility of cohort event monitoring and assessment of reactogenicity and adverse events among a cohort of AstraZeneca and Moderna COVID-19 vaccine recipients in Nigeria, 2021

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Authors' contribution

All authors attest they meet the ICMJE criteria for authorship.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dale Nordenberg reports financial support was provided by The Task Force for Global Health. Comfort Ogar reports financial support was provided by The Task Force for Global Health. Robert Chen reports a relationship with Coalition for Epidemic Preparedness Innovations that includes: funding grants. Dale Nordenberg reports a relationship with Coalition for Epidemic Preparedness Innovations that includes: funding grants. Robert Chen reports a relationship with Task Force for Global Health, Brighton Collaboration that includes: board membership and serves as Associate Editor, Elsevier Vaccine. The other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Disclaimer

The findings and conclusions are those of the authors and do not necessarily represent the official position, policies or views of the US Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry.

Ethics approval and consent to participate

Informed consent was obtained from all participants. The protocol was approved by the National Health Research Ethics Committee, Nigeria (approval number NHREC/01/01/2007). The U.S. Centers for Disease Control and Prevention (CDC) determined the protocol to be non-research.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2025.126907>.

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Abstract

Background: To generate COVID-19 vaccine safety data in Nigeria, passive reporting was supplemented with cohort event monitoring (CEM), an active surveillance system. We described reactogenicity within 7 days and adverse events up to 3 months after each AstraZeneca or Moderna COVID-19 vaccine dose while assessing the feasibility of implementing CEM in a low- to middle-income country (LMIC) during a mass vaccination campaign.

Methods: Participants were aged ≥18 years with access to mobile phones who received the first dose of an authorized COVID-19 vaccine from participating health facilities in 6 states of Nigeria during September and October 2021. Data collectors interviewed participants via phone on days 0, 3, 7, and thereafter every 7 days for 3 months. The same schedule was restarted if a participant received a second vaccine dose. Proportions of participant-reported adverse events following COVID-19 vaccine receipt were calculated. Investigation and causality assessment were conducted on deaths using the World Health Organization causality guidelines.

Results: We enrolled 12,317 participants (AstraZeneca 6990; Moderna 5327); 6167/6990 (88.2 %) AstraZeneca and 4879/5327 (91.6 %) Moderna recipients completed a follow-up interview days 0–7 after the first dose; among them, 2685/6167 (43.5 %) AstraZeneca and 3533/4879 (72.4 %) Moderna recipients reported local reactions and 2456/6167 (39.8 %) AstraZeneca and 2087/4879 (42.8 %) Moderna recipients reported systemic reactions. Overall, 3891/6990 (55.7 %) AstraZeneca and 3978/5327 (72.8 %) Moderna recipients received a second dose of COVID-19 vaccine, among whom 897/3891 (23 %) AstraZeneca and 1979/3978 (49.7 %) Moderna recipients reported local reactions and 727/3891 (18.7 %) AstraZeneca and 1680/3978 (42.2 %) Moderna recipients reported systemic reactions. Among all enrolled, 11 died; there was no evidence to suggest any deaths were vaccine-related.

Conclusions: No unexpected patterns of adverse events were detected, providing additional data on the safety of these COVID-19 vaccines in Nigerian adults. We demonstrated that implementing CEM was feasible and may be valuable for safety monitoring of vaccines introduced in LMICs.

Keywords

Adverse events following immunization; Nigeria; Reactogenicity; Cohort event monitoring; Serious adverse events; AstraZeneca COVID-19 vaccine; Moderna COVID-19 vaccine; Vaccine safety; Post-introduction surveillance; Feasibility

1. Background

The urgent development, regulatory fast-tracking, and widespread use of vaccines against the SARS-CoV-2 virus was an essential strategy for mitigating the COVID-19 pandemic [1]. Previous experiences and technological advancements in vaccine development (e.g., for the Ebola vaccine) facilitated the rapid development and emergency use of COVID-19 vaccines [2]. Vaccines approved for use in National Immunization Programmes— including COVID-19 vaccines— have met safety and efficacy criteria as specified for regulatory approval [3]. However, post-introduction monitoring is important to detect serious, unexpected, or rare adverse events following immunizations (AEFI) that might not be identified during clinical trials [4,5]. High-income countries like the United States have well-established systems and protocols for post-introduction vaccine safety monitoring [6,7], which are under development in many low- and middle-income countries (LMICs) [8].

In Nigeria, vaccination against COVID-19 disease first began in March 2021 with the AstraZeneca vaccine (Covishield), an adenovirus vector vaccine manufactured by the Serum Institute of India [9]. An mRNA vaccine produced by Moderna was introduced in July 2021, both under the World Health Organization (WHO) Emergency Use Listing. Since clinical trials for COVID-19 vaccines were conducted outside of Nigeria, immunization safety stakeholders in the country planned to supplement the existing spontaneous (passive) reporting system in the country with active, post-introduction safety surveillance using cohort event monitoring (CEM), a prospective observational cohort design to generate safety data quickly. The CEM methodology monitors the safety of a new drug or vaccine in the post-marketing phase during which a selected group of recipients is followed at defined intervals to obtain information on reported adverse events, regardless of severity or suspected relatedness to the drug/vaccine of interest [10,11]. CEM methodology is beneficial to generate reactogenicity data and evaluate health impact events over time. This active surveillance methodology has supplemented traditional passive surveillance systems for new drug and vaccine introductions in LMICs, including for anti-malarials and H1N1 and COVID-19 vaccines, and has provided valuable safety information in mass immunization campaigns [12–14].

A pilot CEM evaluating the safety of the first available COVID-19 vaccine (AstraZeneca) in Nigeria among 1284 recipients has been published [15]. Our CEM expands the safety assessment to ten-fold more eligible Nigerian adults to estimate reactogenicity within 7 days as well as the percentage of participants reporting AEFI after each COVID-19 vaccine dose, including recipients of the Moderna vaccine. Moreover, we aimed to demonstrate the

feasibility of implementing CEM in this setting during a mass immunization campaign to inform health messaging, including expected events following immunization, and to provide an example for future safety monitoring efforts in LMICs.

2. Methods

2.1. Design and setting

The CEM program was prospective, active surveillance designed to monitor the reactogenicity and AEFI with AstraZeneca and Moderna COVID-19 vaccines in Nigeria in alignment with the WHO protocol template for CEM for safety signal detection after vaccination with COVID-19 vaccines [11]. The CEM took place in one state in each of the 6 geo-political zones in Nigeria. The states—Bauchi, Edo, Enugu, Federal Capital Territory, Kaduna, and Lagos— were selected based upon security, stability, and the existence of infrastructure to conduct vaccine safety surveillance. In each state, one tertiary health facility and five primary health facilities were purposively selected for inclusion in the surveillance program. These sites all contained COVID-19 vaccination clinics offering both AstraZeneca and Moderna COVID-19 vaccines and were high-volume health facilities with adequate staffing, administration spaces, functional information technology infrastructure, and with an average of 25 persons vaccinated daily with a COVID-19 vaccine.

2.2. Surveillance population

Consenting individuals aged ≥ 18 years who received the first dose of any COVID-19 vaccine from the selected health facilities were enrolled. Individuals who were already vaccinated against COVID-19 before the day of enrollment and those unable to comply with surveillance program procedures were excluded. To facilitate timely data collection during the pandemic, participation was limited to persons with access to mobile phones (applies to $>90\%$ of Nigerian adults), defined as ownership of or access to a family member's mobile phone.

2.3. Sample size estimation

A total sample size of 10,000 participants was estimated to rule out events with a frequency of 1 per 3333 at an alpha level of 0.05 if no event was detected [16]; this allows for the detection of uncommon events ($\geq 1/1000$ and $< 1/100$) and potentially the detection of rare events ($\geq 1/10,000$ and $< 1/1000$), as defined by the Council for International Organizations of Medical Sciences [17,18]. With a 10 % buffer for loss to follow-up, the target for enrollment was 12,000 (approximately 2000 participants per state).

2.4. Data collection

Enrollment occurred at the selected health facilities from 1 September to 30 October 2021. The enrollment target was equally allocated across the 36 selected facilities: 334 participants per facility. Participants were enrolled sequentially at each facility until the day the facility enrollment quota was met. Some facilities exceeded their quota due to the high volume of vaccine recipients on the last enrollment day. Eligible, consenting participants were enrolled at the time of vaccination using a tablet-based questionnaire adapted from the WHO adverse drug reaction reporting tool [19], using CSPro (Census and Survey Processing

System) software. Questionnaires were administered face-to-face by data entry clerks at the enrollment facilities and information was entered directly into tablets. The questionnaire collected information on demographic characteristics, vaccine exposure, participant-reported pre-existing medical conditions (defined below), solicited systemic symptoms experienced within three days prior to vaccination, and contact information of the participant and next-of-kin for follow-up data collection.

Data collectors conducted follow-up interviews over a three-month period via phone calls. Consenting participants were called on days 0 (within 24 h of vaccination), 3, 7, and every 7 days thereafter for three months, asking about events experienced since the last follow-up call. The same follow-up schedule was restarted if a participant received a second dose of any of the approved COVID-19 vaccines, per the country vaccination guidance. Information collected at enrollment was hosted on a custom CEM Activity Management Information System database. The follow-up information, obtained during phone call interviews, was captured via a web form interface of the CEM Activity Management Information System on a tablet or laptop. Response data were linked to the enrollment data using the participant's unique identifier. Information on reactogenicity was collected on days 0, 3, and 7 after the first and second-dose vaccination; participant-reported medically attended events, hospitalization, and COVID-19 testing were solicited at every follow-up call. At the time of surveillance, mixed vaccine series were not permitted in Nigeria; therefore, there were no heterologous first and second-dose vaccine schedules. When surveillance personnel were unable to reach the participant directly after 5 attempts, they called the listed next-of-kin for follow-up. The follow-up of participants was concluded in March 2022.

The main outcome variables were local and systemic reactogenicity, medically attended events (MAEs), and serious adverse events (SAEs). Local reactogenicity was defined as inflammatory changes around the injection site, including pain, swelling, hardening (induration), warmth, redness (erythema), bruise, or itching occurring within 0–7 days of the first or second vaccine dose. Systemic reactogenicity was defined as fever, chills, headache, malaise, tiredness, joint pain, muscle ache, dizziness, cough, or nausea occurring 0–7 days post-vaccination. In addition to these specific symptoms solicited, any other participant-reported symptoms were captured during the 0–7-day period and at subsequent follow-up calls. Pre-vaccination systemic symptoms were defined as fever, nausea, malaise, chills, headache, joint pain, muscle ache, or fatigue within 3 days prior to the first dose COVID-19 vaccination. History of medical conditions was defined as one or more of the following participant-reported conditions: chronic respiratory, heart, or liver conditions, renal diseases, diabetes, immunocompromised/immunosuppressed conditions, obesity, and allergies [11].

Reported events that led participants to seek medical care from a health practitioner or pharmacist during any period of follow-up were classified as MAEs. SAEs, according to the WHO definition, included “events that result in death, are life-threatening, require in-patient hospitalization or prolongation of existing hospitalization, result in persistent or significant disability/incapacity, or are congenital anomalies or birth defects” [20]. Events that resulted in inpatient hospitalizations or death were identified and reported by the participant or next-of-kin. All SAEs were documented but participants with more than one SAE were only counted once (e.g., if a person was hospitalized and subsequently died).

2.5. Causality assessment

All deaths reported during the CEM surveillance program were investigated by the Disease Surveillance and Notification Officers (DSNOs) at the local government area where the event occurred. Per routine surveillance, the local DSNOs sent an investigation report and laboratory findings to the State DSNO, who sent the dossier to the National Primary Health Care Development Agency (NPHCDA), where it was then collated and presented at the National Expert Committee (NEC), an independent group to assess potential causal association of conditions with the two COVID-19 vaccines. The NEC conducted causality assessments using the WHO standards, including the WHO AEFI reporting form and the AEFI causality assessment user manual for classification (2019 update) [1,21].

Hospitalizations that did not result in death were not assessed by the NEC. The surveillance team conducted an internal classification exercise to document reported reasons for hospitalization, but no causality assessments were made.

2.6. Data analyses

Participant characteristics and vaccine information at enrollment were summarized using descriptive statistics. All data were included until the time of participant completion in the surveillance program or until lost to follow-up; participants with at least one follow-up were included in the MAE and SAE analyses. Missing values were not replaced. All reported events and diagnoses were coded using MedDRA Preferred Terms for analysis. Frequencies of participants reporting reactogenicity, MAEs, and SAEs were stratified by vaccine brand and reported as percentages grouped by age, sex, history of medical condition, pre-vaccination systemic symptoms, and previous COVID-19 diagnosis. Proportions of participants with reported events were calculated from the post-vaccination observational period. Data were analysed using STATA version 16.

2.7. Ethical considerations

The protocol was approved by the National Health Research Ethics Committee, Nigeria (approval number NHREC/01/01/2007) and the University of Maryland, Baltimore institutional review board. The U.S. Centers for Disease Control and Prevention (CDC) determined the protocol to be non-research.

Participation was voluntary. Written informed consent was obtained from all participants, who were able to withdraw from the CEM program at any time.

3. Results

3.1. Participation

Overall, 12,317 participants were enrolled across the 6 states (Fig. 1), with a range of 2024–2078 participants per state. Among those enrolled, 6990 (56.7 %) received AstraZeneca vaccine, and had a median age of 39 years (interquartile range (IQR) 29–51 years), and over half (4062, 58.1 %) were male. Among the 43.3 % (5327) of participants who received Moderna vaccine, the median age was 37 years (IQR 29–49 years), and 2973 (55.8 %) were male (Table 1).

Of the 12,317 enrolled participants, 11,911 (96.7 %) (AstraZeneca 6662 (95.3 %), Moderna 5249 (98.5 %)) participants' phone numbers were reachable (Fig. 1). Loss to follow-up over time point ranged from 0.4 to 5.6 %, with 10,618 (85.8 %) participants completing all surveillance timepoints.

3.2. Reactogenicity

Among those reached, 11,046/11,911 (92.7 %) (AstraZeneca 6167 (56 %), Moderna 4879 (44 %)) completed at least one follow-up interview on day 0, 3, or 7 following the first dose vaccination and were included in the reactogenicity analyses. Of 6167 AstraZeneca vaccine recipients included in the reactogenicity analyses, 2685 (43.5 %) reported local reactions and 2456/6167 (39.8 %) reported systemic reactions within 7 days of receiving the first vaccine dose. Among those reporting local reactions within 7 days following vaccination, 47.7 % (1281/2685) were female, 23.5 % (629/2685) reported history of a medical condition, and 37.0 % (994/2685) reported experiencing systemic symptoms within 3 days pre-vaccination. Among people reporting systemic reactions within 7 days of vaccine receipt, 45.6 % (1119/2456) were female, 23 % (564/2456) reported history of a medical condition, and 37.7 % (926/2456) reported systemic symptoms within 3 days pre-vaccination (Table 2A). Among AstraZeneca vaccine recipients who experienced local reactions within the first 7 days, the majority reported pain at injection site after both vaccine doses, while bruising around the injection site was the least reported reaction. Fever was the most reported systemic reaction after receiving both doses of AstraZeneca vaccine, while cold and cough and shortness of breath were least reported (Fig. 2B).

Of the 6167 AstraZeneca recipients, 3891 (63.1 %) received a second vaccine dose. Among them, local and systemic reactions were reported by 23.1 % (897) and 18.7 % (727), respectively. Among people reporting local reactions following the second dose of AstraZeneca vaccine, 48.6 % (436/897) were female, 26.5 % (237/897) reported history of a medical condition, and 39.6 % (355/897) experienced pre-vaccination systemic reactions before the second dose. Among those reporting systemic reactions, 46.9 % (341/727) were female, 25.6 % (186/727) reported history of a medical condition, and 38.2 % (278/727) reported pre-vaccination systemic reactions (Table 2A).

Among the 4879 participants who received a first dose of Moderna vaccine, local and systemic reactions within 7 days of vaccination were reported by 72.4 % (3533/4879) and 42.8 % (2087/4879), respectively. Among people reporting local reactions within 7 days of a first dose of Moderna vaccine, 46.7 % (1612/3533) were female, 24.9 % (880/3533) reported history of a medical condition, and 25.7 % (1389/3533) experienced pre-vaccination systemic symptoms. Among those reporting systemic reactions, 46.7 % (975/2087) were female, 24.9 % (535/2087) reported history of a medical condition, and 39.3 % (891/2087) reported systemic symptoms 3 days pre-vaccination (Table 2B).

Overall, 3978/4879 (81.5 %) Moderna vaccine recipients received a second dose vaccine; 49.7 % (1979) and 42.2 % (1680) reported local and systemic reactions within the first 7 days, respectively. Among those reporting local reactions, 47.5 % (941/1979) were female, 26.5 % (523/1979) reported history of a medical condition, and 39.3 % (778/1979) reportedly experienced pre-vaccination systemic reaction. Among those reporting systemic

reactions post second Moderna dose, 45.7 % (768/1680) were female, 26.7 % (449/1680) reported history of a medical condition, and 40.1 % (673/1680) experienced pre-vaccination systemic reaction (Table 2B). Injection site pain was the most commonly reported local reaction after receiving the first and second doses of Moderna vaccine (Fig. 2A). Fever was the most reported systemic reaction (Fig. 2B).

3.3. Reported MAEs and SAEs

Overall, 5.3 % (355/6662) of AstraZeneca and 8.2 % (431/5249) of Moderna vaccine recipients reported a MAE during the surveillance period (Table 3). The most common reasons for seeking any type of care were fever (AstraZeneca 10.1 %, Moderna 11.8 %), body pain (AstraZeneca 7.6 %, Moderna 7.7 %), and respiratory symptoms (AstraZeneca 6.5 %, Moderna 6.5 %) (Fig. 3).

Overall, 84/11,911 (0.7 %) participants reported a SAE; (0.7 % (48/6662) AstraZeneca recipients and 0.7 % (36/5249) Moderna recipients) (Table 4); 75/11,911 (0.6 %) of those participants were hospitalized during the surveillance, with fever and tiredness among the most reported events that led to hospitalization (Fig. 4). Two hospitalized patients died. Nine other participants died, per their next-of-kin. Causality assessment was conducted for all 11 reported deaths. Autopsy was not conducted and there was insufficient evidence to classify these cases without a valid diagnosis (cause of death). However, per the NEC, there was no evidence to suggest that the deaths were vaccine-related (Supplementary Table 1).

According to internal classification by the surveillance team (not causality assessment) among the 73 hospitalized patients who experienced 151 symptoms at admission, 37/73 (50.7 %) patients were hospitalized for a known infectious etiology or pre-existing medical condition (Supplementary Table 2).

4. Discussion

This CEM active surveillance program, implemented six months after COVID-19 vaccines were introduced in Nigeria, provided further information from all six geopolitical zones in the country on reactogenicity, MAEs, and SAEs after the administration of AstraZeneca or Moderna COVID-19 vaccines. These locally generated safety data complement the data generated from clinical trials and post-marketing surveillance from high-income countries, providing additional information on the safety of AstraZeneca and Moderna COVID-19 vaccines in Nigerian adults.

The findings from this surveillance program, citing mostly local reactions, fever, and general malaise, are consistent with those from other COVID-19 vaccine safety studies for both mRNA vaccines, including the Moderna vaccine, and adenovirus vaccines, including AstraZeneca [22,23]. We found that the Moderna vaccine was more reactogenic than the adenovirus vector vaccine, AstraZeneca. Based on our surveillance, reactogenicity was highest among participants aged 25–34 years and lowest among those older than 55 years, similar to the findings from v-safe, a U.S. self-reporting vaccine safety system [24]. Similarly, phase 2 clinical trials of AstraZeneca vaccine in United Kingdom showed higher reactogenicity among persons younger than 55 years [25].

As observed in several high and upper middle-income countries, the Nigeria CEM detected a low number of MAEs and SAEs [26–29], with a higher number of MAEs among participants who received Moderna when compared to AstraZeneca [23]. Hospitalization and death were uncommon in our cohort and occurred four times more often in participants over 55 years old and in those aged 25–34 years, as older adults are generally more likely to have preexisting conditions. People with reported chronic illness reported more MAEs and SAEs when compared with the general population, as was found elsewhere [30]. Similarly, over half of deaths identified from our surveillance had participant-reported chronic illnesses. However, with available evidence, no causal association was identified between the reported deaths following vaccination, highlighting the expected occurrence of certain serious health events in the general population [31].

Safety is a critical element of vaccine confidence and acceptance. Studies have found that the perceived lack of safety is a barrier to COVID-19 vaccination and is associated with vaccine hesitancy [32]. Given the rapid development and authorization of COVID-19 vaccines, many countries felt compelled to gather better post-introduction safety surveillance data rather than relying solely on traditional passive surveillance, with its known limitations (e.g., underreporting) [33]. Given its simplicity, CEM was recommended by WHO to help meet this need [11], and was a popular method adopted by many countries during the pandemic, especially LMICs [34]. In Nigeria, these CEM COVID-19 vaccine safety surveillance data were important to promote public confidence in the immunization program; the results were incorporated into vaccine communications and strategies to address vaccine hesitancy to reassure the public. While the number of participants enrolled in Nigeria was lower than those included in pre-clinical trial data and post-licensure surveillance broadly conducted in the United States and other high-income countries, this CEM program provided Nigeria-specific safety data affordably and timely enough to utilize reactogenicity data to inform healthcare providers and vaccine recipients of what to expect following vaccination.

There are challenges to implementing CEM in a LMIC, including securing the human, financial, and technological resources required. Classifying SAEs requires robust clinical data. There exist challenges with obtaining complete medical information, including lack of diagnostic capacity, including autopsy, or lack of available clinical documentation, to enable complete classification. Despite these challenges, we demonstrate the feasibility of establishing this active surveillance during a mass vaccination campaign in a LMIC. Across Nigeria, we found that participation throughout the surveillance program was high. Many LMICs do not have robust electronic medical records that can be queried for specific health events following vaccination. These self-reported data from the CEM program are beneficial in settings without electronic records and for health events that did not require medical care, including reactogenicity symptoms. Using phone calls to obtain self-reported data may allow interviewers to probe further into responses to obtain more relevant information while also encouraging more inclusive participation as compared to methods requiring literacy (e.g., text messaging) [35]. Other LMICs regionally and globally could implement CEM studies in future large-scale vaccination campaigns to generate substantive real-world vaccine safety data while strengthening overall vaccine safety surveillance to detect and respond to AEFI [36].

4.1. Limitations

There were limitations to this surveillance program. Because events were solicited from vaccine recipients, there was the potential for overreporting. All events were participant-reported and were not validated by clinical personnel or by medical chart review. However, all deaths detected were reported to the Nigerian regulatory authority for investigation and causality assessment. No autopsies were performed, limiting available information for assessment. There was potential variability of the qualifications and professional experience of the personnel administering the vaccines, which could influence the incidence of certain adverse events. Further, there was the potential for recall bias on concurrent medications or other medical interventions that could confound the relationship between the vaccination and reported AEFI. Reported SAEs that did not result in death were not investigated by the NEC, thus some events resulting in hospitalization may or may not have been vaccine-related (e.g., high fevers). Participation in this surveillance program was only offered to individuals with access to mobile phones; however, current data on mobile phone subscriptions indicate that over 90 % of Nigerian households have access to a mobile phone [37]. While we do not expect differences in AEFI between vaccine recipients with and without access to mobile phones, the healthcare-seeking behaviours, hence the incidence of reported MAEs and SAEs may vary, as there is evidence of an association between mobile phone ownership and healthcare-seeking behaviour and access to health services [38–40]. Because two vaccines were in use at the time of implementation, our sample size was not reflected per vaccine product. Similarly, our sample size was insufficient to detect rare but potentially life-threatening conditions, such as thrombosis with thrombocytopenia syndrome, a rare AEFI recognized to be causally associated with adenoviral vector COVID-19 vaccines [41]. Data on symptom onset from the time of vaccination were not available. Future studies should include information on symptom onset to allow for identification of clustering of AEFI. We did not collect the number of all vaccine recipients screened and therefore do not know the proportion of vaccinated individuals that refused or were ineligible to participate. Last, we did not assess AEFI in persons younger than 18 years old. Since completing this surveillance program, COVID-19 vaccines have been permitted for use in younger age groups (<18 years old) and other special populations, such as pregnant women. To address this gap in locally generated data, immunization and regulatory authorities in Nigeria are implementing an expanded CEM among a larger cohort and with a longer duration of follow-up.

5. Conclusion

Data from this cohort of Nigerian adults receiving AstraZeneca and Moderna COVID-19 vaccines contribute to the growing body of reactogenicity data and are consistent with those of other surveillance programs. No unusual or unexpected patterns of MAEs or SAEs were detected among our cohort, information that was beneficial to Nigerian health communications efforts around these COVID-19 vaccines. Continuous vaccine safety monitoring through an effective AEFI surveillance system, such as CEM, is critical to maintain public trust in the immunization program and for potential signal detection. CEM surveillance programs are beneficial to supplement the existing surveillance to generate longer-term, post-introduction safety data for large-scale vaccination programs.

We demonstrate this type of surveillance can be successfully implemented in a LMIC and can be tailored to monitor adverse events of special interest, the safety of vaccines in persons under 18 years old and other special sub-populations, and for new, underutilized, or booster vaccines.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

The datasets used and/or analysed during the current surveillance are available from the corresponding author, with permission from the Government of Nigeria's National Agency for Food and Drug Administration and Control (NAFDAC), on reasonable request.

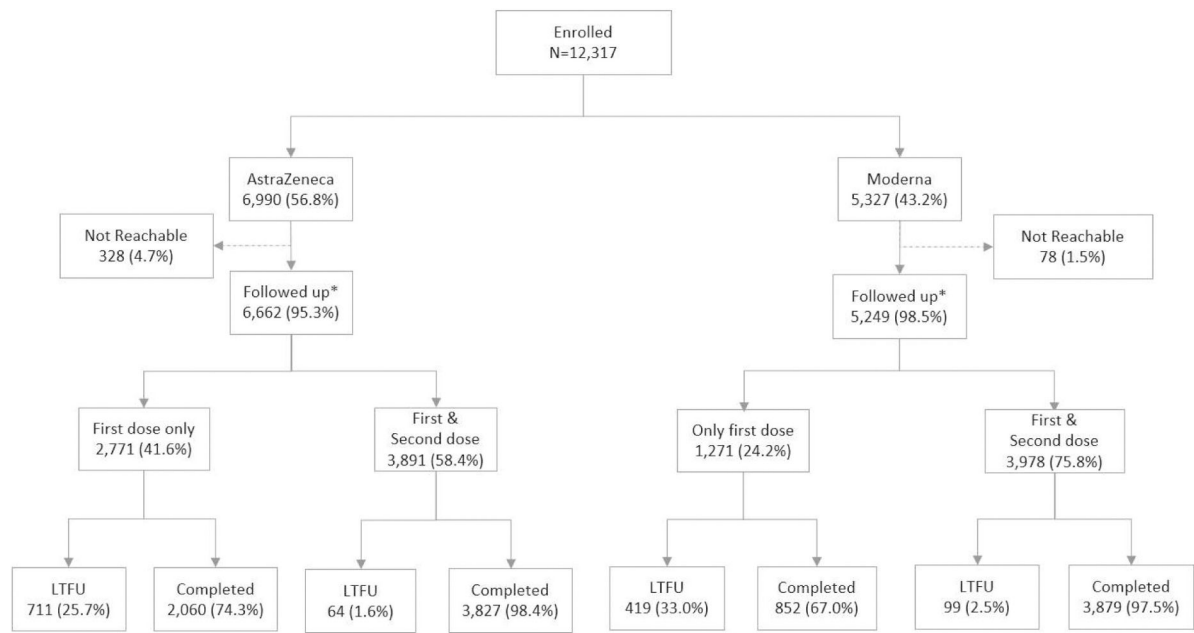
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**Fig. 1.**

Flow diagram for the enrolled participants, by COVID-19 vaccine, cohort event monitoring surveillance, Nigeria, 2021. *Followed up at any time during the surveillance program; 865 (7.3 %) participants did not complete the reactogenicity questions but did participate in subsequent interview points as they were not officially lost to follow-up. LTFU = lost to follow-up, any time during the surveillance program.

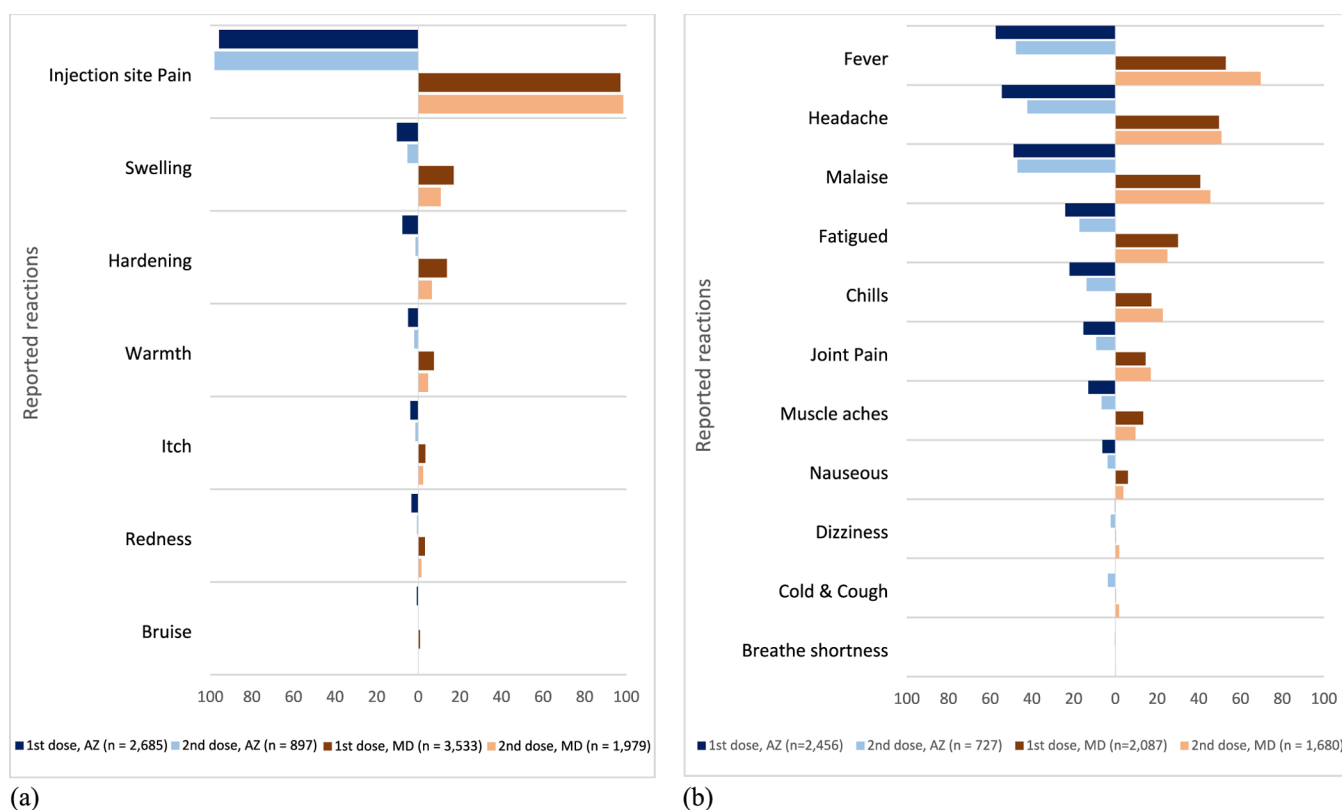


Fig. 2.
 (A) Distribution of reported local reactions by dose, cohort event monitoring surveillance, Nigeria, 2021. AZ – AstraZeneca, MD – Moderna. (B) Distribution of reported systemic reactions by dose, cohort event monitoring surveillance, Nigeria, 2021.

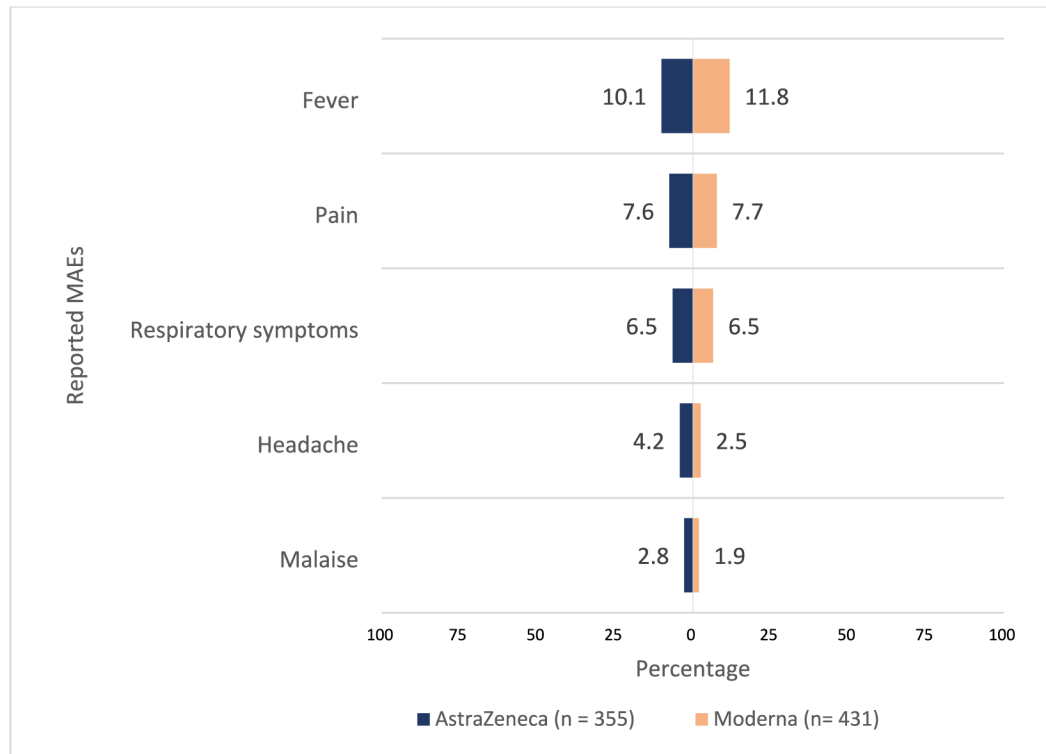


Fig. 3.

Most reported medically attended events during surveillance period, cohort event monitoring surveillance, Nigeria, 2021. Reported events during any time of the surveillance period.

*Others: routine check-ups and follow-up (6.2 %), medical consultations (1.9 %), surgery (0.5 %), malaria (6.0 %), typhoid (2.1 %), car and motorbike accident (0.4 %), ulcer (0.8 %), abnormal blood sugar (0.2 %), and antibiotics (1.6 %).

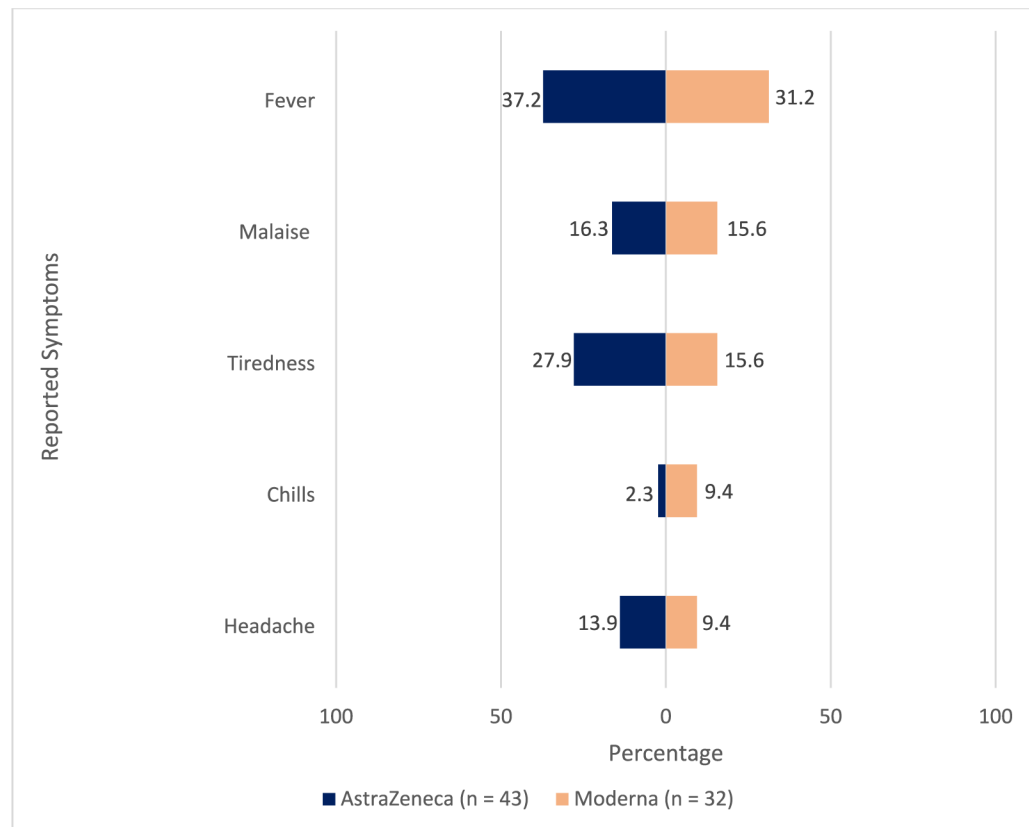


Fig. 4.

Distribution of the most commonly reported symptoms resulting in hospitalization during surveillance period, cohort event monitoring surveillance, Nigeria, 2021. *Others: surgery, cataract, malaria, stooling, cancer, food poisoning,

Table 1

Self-reported participant characteristics at enrollment into the cohort event monitoring surveillance program, Nigeria, September – October 2021.

	<u>AstraZeneca; n (%)</u> <i>n</i> = 6990	<u>Moderna; n (%)</u> <i>n</i> = 5327	<u>Overall; n (%)</u> <i>N</i> = 12,317
State			
Bauchi	1592 (22.8)	432 (8.1)	2024 (16.4)
Edo	1791 (25.6)	272 (5.1)	2063 (16.7)
Enugu	761 (10.9)	1282 (24.1)	2043 (16.6)
Federal Capital Territory	498 (7.1)	1580 (29.7)	2078 (16.9)
Kaduna	1336 (19.1)	698 (13.1)	2034 (16.5)
Lagos	1012 (14.5)	1063 (20.0)	2075 (16.8)
Age group			
18–24 years	1014 (14.5)	695 (13.0)	1709 (13.9)
25–34 years	1688 (24.1)	1459 (27.4)	3147 (25.6)
35–44 years	1744 (24.9)	1421 (26.7)	3165 (25.7)
45–54 years	1270 (18.2)	861 (16.2)	2131 (17.3)
55+ years	1274 (18.2)	891 (16.7)	2165 (17.6)
Sex			
Female	2928 (41.9)	2354 (44.2)	5282 (42.9)
Male	4062 (58.1)	2973 (55.8)	7035 (57.1)
History of medical condition			
None	5391 (77.3)	4035 (75.8)	9426 (76.7)
Yes	1581 (22.7)	1285 (24.2)	2866 (23.3)
Pre-vaccination (3 days prior) symptoms			
No	4524 (64.7)	3323 (62.4)	7847 (63.7)
Yes	2466 (35.3)	2004 (37.6)	4470 (36.3)
Previous COVID-19 diagnosis			
No	6650 (95.1)	5074 (95.3)	11,724 (95.2)
Yes, not laboratory-confirmed	270 (3.9)	118 (2.2)	388 (3.2)
Yes, laboratory-confirmed	70 (1.0)	135 (2.5)	205 (1.7)

Table 2A

Local and systemic reactogenicity within the first seven days of COVID-19 vaccination by participant characteristics among those who received AstraZeneca vaccine, cohort event monitoring surveillance program, Nigeria, 2021.

	First dose		Second dose		
	Overall, n(%)	Local, n(%)	Systemic, n(%)	Overall, n(%)	Systemic, n(%)
	N* = 6167	n = 2685 (43.5)	n = 2456 (39.8)	N* = 3891	n = 727(18.7)
Age group					
18–24 years	894 (14.5)	466 (17.4)	416 (16.9)	493 (12.7)	89 (12.2)
25–34 years	1491 (24.2)	737 (27.4)	685 (27.9)	899 (23.1)	185 (25.4)
35–44 years	1541 (25.0)	677 (25.2)	668 (27.2)	950 (24.4)	206 (28.3)
45–54 years	1108 (18.0)	435 (16.2)	384 (15.6)	725 (18.6)	132 (18.2)
55+ years	1133 (18.4)	370 (13.8)	303 (12.3)	824 (21.2)	115 (15.8)
Sex					
Female	2515 (40.8)	1281 (47.7)	1119 (45.6)	1618 (41.6)	341 (46.9)
Male	3652 (59.2)	1404 (52.3)	1337 (54.4)	2273 (58.4)	386 (53.1)
History of medical condition					
None	4759 (77.4)	2050 (76.5)	1885 (77.0)	2900 (74.6)	541 (74.4)
Yes	1391 (22.6)	629 (23.5)	564 (23.0)	987 (25.4)	186 (25.6)
Pre-vaccination (3 days prior) symptoms					
No	4027 (65.3)	1691 (63.0)	1530 (62.3)	2520 (64.8)	449 (61.8)
Yes	2140 (34.7)	994 (37.0)	926 (37.7)	1371 (35.2)	278 (38.2)
Previous COVID-19 diagnosis					
No	5854 (94.9)	2554 (95.1)	2324 (94.6)	3718 (95.6)	690 (94.9)
Yes, not laboratory-confirmed	250 (4.1)	90 (3.4)	97 (3.9)	128 (3.3)	26 (3.6)
Yes, laboratory-confirmed	63 (1.0)	41 (1.5)	35 (1.4)	45 (1.2)	11 (1.5)

* Cohort size of participants reached between day 0–7. Participants could have reported both local and systemic reactogenicity.
Local reactogenicity is defined as the presence of pain, redness, warmth, swelling, hardening/induration, haematoma, or itching at, or near, the injection site.
Systemic reactogenicity is defined as the presence of fever, chills, headache, nausea, muscle ache, joint pain, or malaise.

Local and systemic reactogenicity within the first seven days of COVID-19 vaccination, by participant characteristics among those who received Moderna vaccine, cohort event monitoring surveillance program, Nigeria, 2021.

Table 2B

	First dose			Second dose		
	Overall, n(%)	Local, n(%)	Systemic, n(%)	Overall, n(%)	Local, n(%)	Systemic, n(%)
	N* = 4879	n = 3533 (72.4)	n = 2087 (42.8)	N* = 3978	n = 1979 49.7	n = 1680 (42.2)
Age group						
18–24 years	632 (13.0)	457 (12.9)	257 (12.3)	455 (11.4)	212 (10.7)	176 (10.5)
25–34 years	1342 (27.5)	1051 (29.7)	655 (31.4)	1059 (26.6)	552 (27.9)	478 (28.5)
35–44 years	1294 (26.5)	939 (26.6)	565 (27.1)	1077 (27.1)	554 (28.0)	469 (27.9)
45–54 years	778 (15.9)	560 (15.9)	311 (14.9)	667 (16.8)	322 (16.3)	293 (17.4)
55+ years	833 (17.1)	526 (14.9)	299 (14.3)	720 (18.1)	339 (17.1)	264 (15.7)
Sex						
Female	2143 (43.9)	1612 (45.6)	975 (46.7)	1748 (43.9)	941 (47.5)	768 (45.7)
Male	2736 (56.1)	1921 (54.4)	1112 (53.3)	2230 (56.1)	1038 (52.5)	912 (54.3)
History of medical condition						
None	3681 (75.6)	2648 (75.1)	1548 (74.3)	2959 (74.5)	1453 (73.5)	1230 (73.3)
Yes	1191 (24.4)	880 (24.9)	535 (25.7)	1013 (25.5)	523 (26.5)	449 (26.7)
Pre-vaccination (3 days prior) symptoms						
No	3038 (62.3)	2144 (60.7)	1196 (57.3)	2479 (62.3)	1201 (60.7)	1007 (59.9)
Yes	1841 (37.7)	1389 (39.3)	891 (42.7)	1499 (37.7)	778 (39.3)	673 (40.1)
Previous COVID-19 diagnosis						
No	4644 (95.2)	3347 (94.7)	1960 (93.9)	3780 (95.0)	1865 (94.2)	1572 (93.6)
Yes, not laboratory-confirmed	115 (2.4)	86 (2.4)	57 (2.7)	93 (2.3)	49 (2.5)	48 (2.9)
Yes, laboratory-confirmed	120 (2.5)	100 (2.8)	70 (3.4)	105 (2.6)	65 (3.3)	60 (3.6)

* Cohort size of participants reached between day 0–7. Participants could have reported both local and systemic reactogenicity. Local reactogenicity is defined as the presence of pain, redness, warmth, swelling, hardening/induration, haematoma, or itching at, or near, the injection site. Systemic reactogenicity is defined as the presence of fever, chills, headache, nausea, muscle ache, joint pain, or malaise.

Characteristics of participants reporting medically attended events throughout surveillance program, cohort event monitoring surveillance, Nigeria, 2021.

Table 3

	AstraZeneca		Moderna		Overall	
	N	n (%)	N	n (%)	N	n (%)
	N = 6662	n = 355	N = 5249	n = 431	N = 11,911	n = 786
Age group						
18–24 years	961	42 (4.4)	683	48 (7.0)	1644	90 (5.5)
25–34 years	1605	102 (6.4)	1439	127 (8.8)	3044	229 (7.5)
35–44 years	1666	87 (5.2)	1399	121 (8.6)	3065	208 (6.8)
45–54 years	1207	55 (4.6)	852	60 (7.0)	2059	115 (5.6)
55+ years	1223	69 (5.6)	876	75 (8.6)	2099	144 (6.9)
Sex						
Female	2761	143 (5.2)	2319	187 (8.1)	5080	330 (6.5)
Male	3901	212 (5.4)	2930	244 (8.3)	6831	456 (6.7)
History of medical condition						
None	5133	260 (5.1)	3972	310 (7.8)	9105	570 (6.3)
Yes	1511	95 (6.3)	1270	119 (9.4)	2781	214 (7.7)
Pre-vaccination (3 days prior) symptoms						
No	4321	223 (5.2)	3276	236 (7.2)	7597	459 (6.)
Yes	2341	132 (5.6)	1973	195 (9.9)	4314	327 (7.6)
Previous COVID-19 diagnosis						
No	6331	333 (5.3)	4997	400 (8.0)	11,328	733 (6.5)
Yes, not laboratory-confirmed	264	16 (6.1)	118	12 (10.2)	382	28 (7.3)
Yes, laboratory-confirmed	67	6 (9.0)	134	19 (14.2)	201	25 (12.4)

Reported throughout the entire surveillance program.

Medically attended events are those that led the participant to seek medical care from a health practitioner or pharmacist at any time during the surveillance period.

Table 4

Characteristics of participants reporting serious adverse events throughout surveillance program, cohort event monitoring surveillance, Nigeria, 2021.

	<u>AstraZeneca</u>		<u>Moderna</u>		<u>Overall</u>	
	<u>N</u>	<u>n (%)</u>	<u>N</u>	<u>n (%)</u>	<u>N</u>	<u>n (%)</u>
	N = 6662	n = 48	N = 5249	N = 36	N = 11,911	n = 84
Age group						
18–24 years	961	3 (0.3)	683	1 (0.1)	1644	4 (0.2)
25–34 years	1605	18 (1.1)	1439	14 (1.0)	3044	32 (1.1)
35–44 years	1666	8 (0.5)	1399	6 (0.4)	3065	14 (0.5)
45–54 years	1207	5 (0.4)	852	4 (0.5)	2059	9 (0.4)
55+ years	1223	14 (1.1)	876	11 (1.3)	2099	25 (1.2)
Sex						
Female	2761	18 (0.7)	2319	16 (0.7)	5080	34 (0.7)
Male	3901	30 (0.8)	2930	20 (0.7)	6831	50 (0.7)
History of medical condition						
None	5133	34 (0.7)	3972	20 (0.5)	9105	54 (0.6)
Yes	1511	14 (0.9)	1270	16 (1.3)	2781	30 (1.1)
Pre-vaccination (3 days prior) symptoms						
No	4321	32 (0.7)	3276	19 (0.6)	7597	51 (0.7)
Yes	2341	16 (0.7)	1973	17 (0.9)	4314	33 (0.8)
Previous COVID-19 diagnosis						
No	6331	43 (0.7)	4997	34 (0.7)	11,328	77 (0.7)
Yes, not laboratory-confirmed	264	3 (1.1)	118	0 (0)	382	3 (0.8)
Yes, laboratory-confirmed	67	2 (3.0)	134	2 (1.5)	201	4 (2.0)

Reported throughout the entire surveillance program.

Serious adverse events included those that resulted in death, were life-threatening, required in-patient hospitalization or prolongation of existing hospitalization, or resulted in persistent or significant disability/incapacity.