












## ORIGINAL RESEARCH

## Impact of COVID-19 vaccinations on emergency department presentations

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## Abstract

**Objective:** The aim of the present study was to describe the burden of patients presenting to the ED with symptoms occurring after receiving a COVID-19 vaccination.

**Methods:** This was a retrospective cohort study performed over a 4-month period across two EDs. Participants were eligible for inclusion if it was documented in the ED triage record that their ED attendance was associated with the receipt of a COVID-19 vaccination. Data regarding the type of vaccine (Comirnaty or ChAdOx1) were subsequently extracted from their electronic medical record. Primary outcome was ED length of stay (LOS) and secondary outcomes included requests for imaging and ED disposition destination.

**Results:** During the study period of 22 February 2021 to 21 June 2021, 632 patients were identified for inclusion in the present study, of which 543 (85.9%) had received the ChAdOx1 vaccination. The highest proportion of COVID-19 vaccine-related attendances occurred in June 2021 and accounted for 21 (8%) of 262 total daily ED attendances. Patients who had an ED presentation related to ChAdOx1 had a longer median ED LOS (253 vs 180 min,  $P < 0.001$ ) compared to Comirnaty and a higher proportion had haematology tests and imaging requested in the ED. Most patients ( $n = 588$ , 88.8%) were discharged home from the ED.

**Conclusion:** There was a notable proportion of ED attendances related to recent COVID-19 vaccination administration, many of which

## Key findings

- There was a notable proportion of ED attendances related to recent COVID-19 vaccination administration, many of which were associated with lengthy ED stays and had multiple investigations.
- The vast majority of these patients did not have serious vaccine-related complications and were able to be discharged home. Nonetheless, given the large volume of patients in this cohort, they place a notable burden on the finite existing ED resources.

were associated with lengthy ED stays and had multiple investigations. In the majority of cases, the patients were able to be discharged home from the ED.

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## Introduction

COVID-19 has had a profound impact on both the healthcare system and the economy, and as such, significant emphasis has been placed on COVID-19 vaccinations as a strategy to mitigate the future toll of COVID-19 on the Australian population.<sup>1</sup> On 22 February 2021, Australia launched a staged implementation of the government's COVID-19 vaccination strategy to

strengthen our nation's protection against COVID-19. Following this COVID-19 vaccination rollout, there was a view among some ED clinicians that there were increased patient attendances with symptoms that patients perceived as being potentially because of their recent COVID-19 vaccinations.

The two COVID-19 vaccinations available in Australia for the first half of 2021 were the Comirnaty BNT162b2 mRNA vaccination (manufactured by Pfizer) and the ChAdOx1 nCoV-19 viral vector vaccination (manufactured by AstraZeneca).<sup>2</sup> Both of these COVID-19 vaccinations have been proven to be effective in preventing severe complications and death from COVID-19 in adults of all ages.<sup>3</sup> They are considered safe, with minor symptoms after vaccination being accepted as common potential side effects,<sup>4</sup> and serious COVID-19 vaccination adverse events remaining relatively rare.<sup>5</sup> There has been substantial public scrutiny and media attention around the vaccination rollout with particular focus on reported serious adverse complications. In particular, thrombosis with thrombocytopenia syndrome (TTS) associated with the ChAdOx1 vaccination, also known as vaccine-induced immune thrombotic thrombocytopenia (VITT), has been reported internationally and in Australia.<sup>6,7</sup>

An observation in some EDs was the rise in patients presenting with symptoms that they are concerned may be a consequence of a COVID-19 vaccination. Anecdotally, patients are worried that their symptoms could be attributed to their recent COVID-19 vaccination or may represent a post-COVID-19 vaccination clotting complication. There was the potential for increased demand on EDs as clinicians devote their already stretched resources to perform thorough clinical assessments for this patient cohort and to determine the cause for the symptoms.

The aim of the present study was to describe the patient demographics of those who attended the ED with COVID-19 vaccine-related presentations and to determine the subsequent burden on

the ED with regards to length of stay (LOS), investigations (blood tests and/or imaging) and patient disposition. A further aim was to compare the data regarding the demographics, ED care and ED outcomes for patients who presented following a ChAdOx1 *versus* Comirnaty COVID-19 vaccination.

## Methods

This retrospective cohort study was conducted at Alfred Health in Melbourne, Australia. It included all patients attending the EDs of both The Alfred Hospital which is an adult major metropolitan tertiary public hospital and Sandringham Hospital which is an urban district metropolitan public hospital. Alfred and Sandringham Hospitals, together, manage approximately 110 000 ED attendances per annum.

All patients attending Alfred Health EDs during the 4-month study period from 22 February 2021 to 21 June 2021 were included in the present study. Keywords used to search the ED triage nursing notes included: Astra, AZ, Zeneca, Pfizer, vac, vaccine, vax and immunisation. Additional variables collected included patient age, sex, mode of arrival, ED LOS, triage nursing documentation, blood test results (platelet count and D-dimer result), imaging requested (CT and/or ultrasound [US]), ED discharge diagnosis and ED disposition destination. Further chart review was performed for all patients to exclude those patients where the ED attendance was because of a non-COVID-19 vaccination (e.g. an influenza vaccination) and to determine which type of COVID-19 vaccination (Pfizer or AstraZeneca) was administered and how long after COVID-19 vaccination administration the patients attended the ED. Patients were excluded if the type of COVID-19 vaccination administered was not recorded in any of their ED medical or nursing documentation. Manual chart review was also performed for all patients who underwent CT and/or US imaging to determine whether an abnormality was

identified on imaging. For those with an abnormality that was a thrombus, analysis was performed of haematology discharge summaries to determine whether this was a case of TTS. Data regarding COVID-19 vaccination rates within Victoria were obtained from data published by the Australian Government.<sup>8</sup>

The primary outcome variable was ED LOS, defined as the time, in minutes, between registration of the patient's ED presentation and their discharge from either the ED or emergency short-stay unit (ESSU). Secondary outcomes included ED disposition destination, imaging requests and pathology results (D-dimer and platelet results).

For the unadjusted analysis, ED LOS was determined to be asymmetrical (right-skewed). Therefore, the measure of association used to determine the unadjusted association between ED LOS and vaccine-type was the difference in medians. Statistical significance was tested using the Wilcoxon rank-sum test. To determine the independent association between ED LOS and vaccine-type in the adjusted analysis, the dependent outcome variable (ED LOS) was log-transformed. This was necessary because it did not fulfil the assumptions necessary for linear regression (i.e. normal distribution). A limited selection of potential confounders was included in a multivariable linear regression analysis according to whether or not they had a statistically significant association with both the primary exposure variable (vaccine-type) and the primary outcome variable (log ED LOS). The measure of association used to summarise the effect sizes in the univariable and multivariable models was the coefficient for the vaccine-type variable.

Symmetrical numerical data were summarised using mean (SD), whereas skewed numerical data and ordinal data were summarised using median (interquartile range [IQR]). Nominal data were summarised using frequency (percentage). Between-group differences in means and medians were tested for statistical significance, using Student's *t*-test and the Wilcoxon rank-sum test,

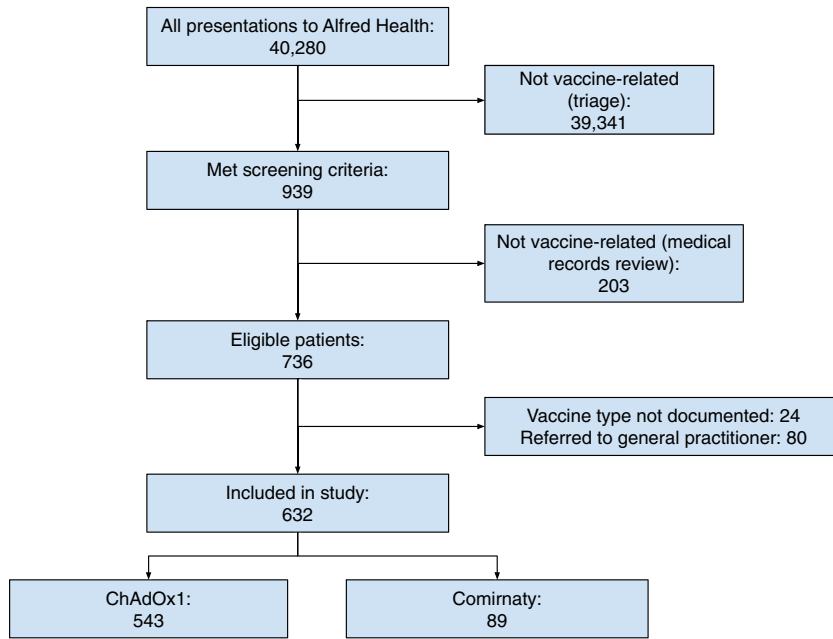


Figure 1. Eligible patient population for inclusion in the present study.

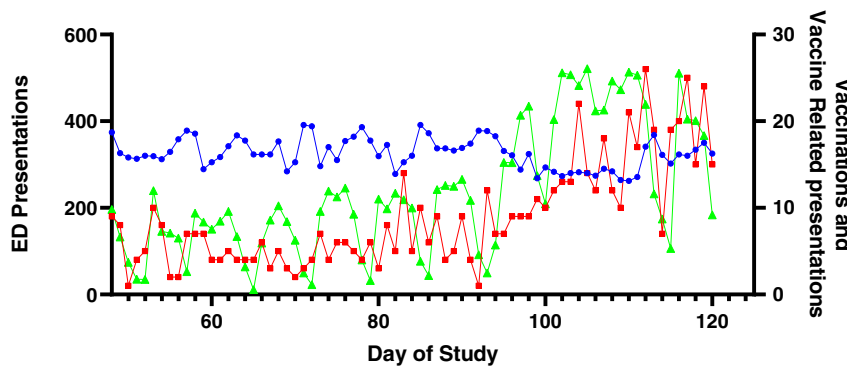


Figure 2. Graph indicating the rate of Alfred Health COVID-19 vaccination-related presentations as compared to the total ED presentations and the state-based vaccination rate for the present study. (—+), ED presentations, (—+), vaccine-related presentations and (—+), vaccinations/100.

respectively. For categorical data, the measure of association and statistical test used were the odds ratio (95% confidence interval [CI]) and the  $X^2$  test, respectively. For all analyses, a  $P$  value of less than 0.05 was considered to be statistically significant. All analyses were conducted using STATA version 15.0 (College Station, TX, USA).

Ethics approval for the present study, as a nested study of the REC Project, was obtained from the Alfred Human Research Ethics Committee (project no. 282/20), in June 2021.

### Results

A total of 40 280 patients attended an Alfred Health ED during the 4-month study period. Of these, 939 patients had an ED triage comment that included the predefined search terms. Of these, there were 736 (1.8%) ED attendances in which the ED triage nurse documentation indicated that the ED attendance was felt to be related to a recent COVID-19 vaccination. Of these patients, 24 (3.2%) were excluded as the type of COVID-19 vaccination that had been administered was not documented in the medical or nursing notes. A further 80 (10.9%) patients who attended Sandringham Hospital ED were immediately redirected from triage to receive care at an on-site GP clinic and were therefore excluded from the study. Of the remaining 632 (85.9%) eligible patients, 543 (85.9%) had received the

TABLE 1. Baseline characteristics, comparing those who had ChAdOx1 versus Comirnaty vaccine

Variable	Both (n = 632)	ChAdOx1 (n = 543)	Comirnaty (n = 89)	Difference† or odds ratio (95% CI)	P-value for difference
Age (years), mean (SD)	56 (16)	59 (14)	41 (16)	18 (15–21)	<0.001
Female, n (%)	431 (68.2)	363 (66.9)	68 (76.4)	1.6 (1.0–2.7)	0.13
Arrived by ambulance, ‡ n (%)	83 (13.1)	68 (12.5)	15 (16.9)	0.7 (0.4–1.3)	0.26
Days since vaccine, median (IQR)	7 (2–14)	7 (4–14)	1 (0–5)	6 (4.2–7.8)	<0.001

†Difference in mean, median or %. ‡Ambulance defined as private ambulance, police service or road ambulance service in comparison to private transport (other or public transport). CI, confidence interval; IQR, interquartile range.

ChAdOx1 COVID-19 vaccination and 89 (14.1%) had received the Comirnaty COVID-19 vaccination (Fig. 1).

Figure 2 displays the daily incidence of COVID-19 vaccination presentations relative to the total number of ED attendances. This graph also indicates the total COVID-19 vaccinations administered during the study period, commencing from day 49 (9 April 2021) of the study period, which is the date when state-wide daily vaccination rates were first published by the government.<sup>8</sup> The highest proportion of total ED attendances during the study period, related to COVID-19 vaccination, occurred on day 110 of the study (10 June 2021), in which 21 (8.0%) of the 262 ED attendances that day were related to COVID-19 vaccination-related presentations. The highest individual number of attendances of COVID-19 vaccination-related presentations on a single day occurred on day

112 of the study period (12 June 2021), in which 26 (7.6%) of the 341 ED attendances were COVID-19 vaccination related. There was a statistically significant daily increase in vaccine-related presentations (relative to total ED presentations) during the study period ( $P < 0.001$ ), which was expected in accordance with rising state-wide vaccination rates. However, there was no statistically significant increase in vaccine-related presentations, relative to daily state-wide vaccination rates during the study period ( $P = 0.89$ ). There was also an observed decrease in total ED attendances of all patients in early June 2021, which coincided with the timing of a 2-week COVID-19 lockdown in Melbourne.

Key demographic features of patients attending the ED with presentations related to a recent COVID-19 vaccination are outlined in Table 1. Patients with an ED attendance related to Comirnaty vaccination were typically younger than

the ChAdOx1 cohort (mean age 41 *vs* 59 years, difference 18 years; 95% CI 15–21,  $P < 0.0001$ ) and presented earlier (median time between vaccine administration and presentation 1 (IQR 0–5) *vs* 7 (IQR 4–14) days, difference 6 days [95% CI 4.2–7.8,  $P < 0.001$ ]). This age-related difference in ED attendances between the two vaccination groups was not unexpected, as at the time of the study, government policy encouraged ChAdOx1 COVID-19 vaccination usage among older patients.

Table 2 summarises the ED LOS, disposition and investigations required for patients attending with concerns related to recent COVID-19 vaccinations. The median ED LOS for ChAdOx1 recipients was 253 min (IQR 171–389), whereas the median ED LOS for Comirnaty recipients was 180 min (IQR 100–291), a difference in median ED LOS of 73 min between the two cohorts ( $P < 0.001$ ). A higher proportion of

TABLE 2. ED LOS and disposition

Variable	Both ( $n = 632$ )	ChAdOx1 ( $n = 543$ )	Comirnaty ( $n = 89$ )	Difference† or OR (95% CI)	$P$ -value for difference
ED LOS‡ (min), median (IQR)	239 (163, 384)	253 (171, 389)	180 (100, 291)	73 (26.9–119.5)	<0.001
ED disposition, $n$ (%)					
Home	561 (88.8)	480 (88.4)	81 (91.0)	–	Reference
Ward	38 (6.0)	36 (6.6)	2 (2.3)	3.0 (0.7–12.9)	0.13
ICU	3 (0.5)	3 (0.6)	0 (0)	–	–
Left after advice	3 (0.5)	3 (0.6)	0 (0)	–	–
Left at own risk	24 (3.8)	18 (3.3)	6 (6.7)	0.5 (0.2–1.3)	0.16
Transfer to another hospital	3 (0.6)	3 (0.6)	0 (0)	–	–
Admit,§ $n$ (%)	44 (7.0)	42 (7.7)	2 (2.3)	3.6 (0.9–15.3)	0.08
CT or US, $n$ (%)	121 (19.2)	114 (21.0)	7 (7.9)	3.1 (1.4–6.9)	0.004
Platelets, $n$ (%)	476 (75.3)	429 (79.0)	47 (52.8)	3.4 (2.1–5.4)	<0.001
D-dimer, $n$ (%)	235 (37.2)	225 (41.4)	10 (11.2)	5.6 (2.8–11.0)	<0.001

†Difference in median. ‡ED LOS includes the total length of stay in both the ED and the ESSU. §Admission to ward or ICU as well as those who left at own risk or were transported to another hospital. CI, confidence interval; ESSU, emergency short-stay unit; IQR, interquartile range; LOS, length of stay; OR, odds ratio.

TABLE 3. Linear regression

Variable	Regression coefficient (univariable) (95% CI, <i>P</i> -value)	% Change in ED LOS (univariable) (95% CI)	Regression coefficient (adjusted) (95% CI, <i>P</i> -value)	% Change in ED LOS (adjusted) (95% CI)
Vaccine type	0.36 (0.20–0.52, <0.001)	+43 (+22 to +68)	0.05 (–0.11 to 0.21, 0.54)	+5 (–10 to +23)
Age	0.01 (0.01–0.01, <0.001)	+0.9 (+0.5 to +1.2)	0.00 (0.00–0.01, 0.02)	+0.4 (+0.01 to +0.70)
Imaging	0.65 (0.51–0.79, <0.001)	+91 (+66 to +120)	0.49 (0.36–0.62, <0.001)	+63 (+42 to +85)
Platelets	0.72 (0.60–0.84, <0.001)	+105 (+82 to +132)	0.57 (0.44–0.70, <0.001)	+77 (+55 to +101)
D-dimer	0.31 (0.19–0.42, <0.001)	+36 (+21 to +52)	0.07 (–0.05 to 0.18, 0.25)	+7 (–5 to +20)

TABLE 4. Investigation results

Variable	<i>n</i> * (ChAdOx1)	ChAdOx1	<i>n</i> (Comirnaty)	Comirnaty	Difference or odds ratio (95% CI)	<i>P</i> -value for difference
Platelet result, † mean (SD) (x10 <sup>9</sup> /L)	420	248 (64)	47	249 (63)	0.44 (–19.07 to 19.94)	0.97
D-dimer result, ‡ mean (SD) (mg/L)	222	1.03 (5.33)	10	0.37 (0.28)	–0.66 (–3.99 to 2.66)	0.69
Imaging abnormal, § <i>n</i> (%)	106	29 (27.4)	5	1 (20.0)	1.5 (0.2–14.0)	0.72

†Platelet counts were requested but results were missing for nine patients. ‡D-dimer levels were requested but results were missing for three patients. §Imaging reports were ambiguous for 10 patients.

patients in the ChAdOx1 COVID-19 vaccination recipient group had CT/US imaging (21.0% *vs* 7.9%,  $P = 0.004$ ). Similarly, certain pathology investigations, such as D-dimer testing, were requested more frequently for ChAdOx1 COVID-19 vaccination recipients than Comirnaty COVID-19 vaccination recipients (41.4% *vs* 11.2%,  $P < 0.001$ ). There were 561 (88.8%) of the patients involved in the study who were discharged directly home from the ED.

Table 3 displays the results of the univariable and multivariable analysis for ED LOS following log transformation. There was a crude association between the log of the ED LOS and vaccine type (0.36; 95% CI 0.20–0.52,  $P < 0.001$ ). The antilog equivalent, expressed as the

percentage increase in ED LOS for ChAdOx1 patients, was 43 (22–68). Following adjustment for age, alone, there remained an independent association between the log of the ED LOS and both vaccine type (0.23; 95% CI 0.06–0.41,  $P = 0.01$ ) and age (0.01; 95% CI 0.00–0.01,  $P < 0.001$ ). Following further adjustment in the multivariable linear regression model for the requesting of ED tests (platelet count, D-dimer and imaging), there was no independent association between ED LOS and vaccine type (0.05; 95% CI –0.11 to 0.21,  $P = 0.54$ ).

The results of specific ED investigations for patients presenting following ChAdOx1 vaccination *versus* Comirnaty COVID-19 vaccination are displayed in Table 4. Investigation outcomes were largely similar

between the ChAdOx1 and Comirnaty recipients attending the ED, as can be seen in Table 4. There was no statistically significant difference in mean platelet counts or D-dimer results between the ChAdOx1 and Comirnaty COVID-19 vaccination recipients respectively. The majority ( $n = 81$ , 73.0%) of patients who underwent CT and/or US imaging with known results had a normal result with no statistically significant difference in the proportion of abnormal imaging results between the two groups ( $P = 0.72$ ). There were only two patients diagnosed with TTS following a ChAdOx1 COVID-19 vaccination during the present period. Both of these patients were initially admitted under the haematology service and were ultimately able to be discharged home. The other abnormal

imaging results were largely incidental findings and not diagnosed as TTS.

## Discussion

These data indicate that there are a significant proportion of ED attendances in which patients cite a recent COVID-19 vaccination as a component related to their presentation. The majority of these patients (543/632, 85.9%) had received the ChAdOx1 vaccination and were ultimately discharged from the ED.

This is the first study reported in Australia exploring the burden of COVID-19 vaccine-related presentations to the ED. During the study period, the number of COVID-19 vaccination-related presentations to ED was highest in early June 2021, which correlated with a period of increased COVID-19 vaccinations being administered to the Victorian population, as well as a timeframe during which the media was reporting widely on TTS cases secondary to ChAdOx1 vaccinations.<sup>8</sup> Additionally, at a similar time, the Australian Technical Advisory Group on Immunisation guidance was evolving with regard to which age groups are recommended to receive the Comirnaty vaccination preferentially over the ChAdOx1 vaccination.<sup>9</sup> All of these factors may have contributed to concern in the general public that their symptoms may represent a serious COVID-19 vaccination complication and prompt them to attend the ED for review.

For patients who received either the ChAdOx1 or Comirnaty COVID-19 vaccinations, there was a notable burden placed on the ED because of both the large number of ED attendances as well as the multi-hour LOS within the ED and the co-located ESSU. The median LOS was longer for patients who had received the ChAdOx1 vaccination. This difference in ED LOS between ChAdOx1 and Comirnaty COVID-19 vaccine recipients remained when data were adjusted for age, but disappeared when the data were adjusted for whether or not investigations had been performed. This comparative analysis suggests that

the increased investigations performed in the ChAdOx1 COVID-19 vaccination recipient cohort translated to a longer ED LOS because of the requirement to wait for the results of these investigations.

Various algorithms have been suggested to help support emergency clinicians to identify and diagnose TTS among patients who have received the ChAdOx1 COVID-19 vaccination.<sup>9</sup> These typically involve a clinical assessment of patient symptomatology, timeframe from ChAdOx1 COVID-19 vaccination administration as well as pathology tests to detect thrombocytopenia and either a significantly elevated D-dimer count or significantly reduced fibrinogen count. This could translate to patients who are being assessed for possible TTS to be more likely than their Comirnaty recipient counterparts to have certain investigations, such as D-dimer testing, and therefore this ChAdOx1 vaccination recipient cohort may need to remain longer within the ED while awaiting their results. Given the majority of patients were not found to have a serious condition after their COVID-19 vaccination, there would also likely have been significant time spent by the ED clinicians explaining to patients their assessment findings and providing appropriate reassurance.

There are multiple limitations to the study. This includes recall bias among those patients who developed symptoms after COVID-19 vaccination prompting them to indicate to the ED triage nurse that they have had a recent COVID-19 vaccination. Triage nurse documentation is not always a verbatim account of the patient's presenting complaint, and therefore there may have been some cases in which the patient reported a recent COVID-19 vaccination, and this was not captured in the ED triage documentation. As this was a retrospective study and COVID-19 vaccination status was not routinely recorded as part of the ED's medical or nursing assessment, the study may have underestimated the true size of the population attending with symptoms after COVID-19 vaccination. Additionally, it must be acknowledged

that the scope of the present study was to assess the burden of suspected COVID-19 vaccination-related presentations on ED attendances and not whether the patient's symptoms were definitively caused by the vaccination. Within the ED consult, the treating clinician often is not able to determine causality between the patient's symptoms and the recent COVID-19 vaccination administration. Adverse events following immunisations are typically investigated in greater detail by other organisations such as the Therapeutic Goods Administration to assess whether or not there was potentially causality between a new vaccination administration and a patient's medical condition.

These data indicate the need for future prospective studies to monitor the ongoing impact of COVID-19 vaccination-related ED attendances to support public health leaders and health services to refine their response to this COVID-19 vaccination challenge. It also indicates the need for potential greater community education about common early minor COVID-19 vaccination side effects, particularly in the immediate few days after vaccination administration. Similarly, there may be scope to help support community GPs in arranging urgent blood tests and imaging in patients who meet the clinical risk profile of TTS, to empower GPs to play a greater role in managing COVID-19 vaccination-related presentations and reduce the current burden this cohort is placing on overcrowded EDs. Considering the importance of ensuring a successful vaccination programme, the study also highlights the need for community-based supports to ensure further follow up of these patients. This could include counselling, education, advice and reassurance to mitigate vaccination hesitancy, particularly, for those patients presenting following their first COVID-19 vaccine dose.

## Conclusions

A large number of patients attending the ED with perceived concerns relating to their recent COVID-19

vaccinations may be because of a combination of strong community COVID-19 vaccination uptake, as well as public awareness as to the possible rare complications that can occur after certain COVID-19 vaccinations. The vast majority of these patients did not have serious vaccine-related complications and were able to be discharged home. Nonetheless, given the large volume of patients in this cohort, they place a notable burden on the finite existing ED resources and often require multiple investigations prior to discharge home.

### *Competing interests*

MLG is a member of the Australian Technical Advisory Group on Immunisation. LB, PAC, BM and GMOR are section editors for *Emergency Medicine Australasia*.

### *Data availability statement*

Research data are not shared.

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