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Risk stratification through allergy history: single-centre experience of specialized COVID-19 vaccine clinic

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Abstract

Anaphylaxis is a rare side-effect of COVID-19 vaccines. To (a) provide direct advice and reassurance to certain persons with a history of anaphylaxis/complex allergy, in addition to that available in national guidelines, and (b) to provide a medically supervised vaccination, a specialist regional vaccine allergy clinic was established. The main objective was to determine if risk stratification through history can lead to safe COVID-19 vaccination for maximum population coverage. A focused history was taken to establish contraindications to giving COVID-19 vaccines. People who reported a high-risk allergy history were given a vaccine not containing the excipient thought to have directly caused previous anaphylaxis. All vaccines were monitored for 30 min after administration. A total of 206 people were vaccinated between 6 July 2021 and 31 August 2021; Comirnaty (Pfizer-BioNTech) ($n = 34$), and Janssen ($n = 172$). In total, 78% were women. Ninety-two people (45%) reported a high-risk allergy history. There were no cases of anaphylaxis. Three people developed urticaria and one of these also developed transient tachycardia. One vaccinee developed a pseudoseizure. Two of 208 people (<1%) referred during this time declined vaccination based on personal preference, despite the assessment of low clinical risk. In our experience, all vaccines with high-risk allergy histories were administered Pfizer BioNTech or Janssen Covid-19 vaccines uneventfully following screening based on allergy-focussed history. Our data support that drug allergy is not associated with a higher risk of vaccine-related anaphylaxis but may act to guide the administration of alternate vaccines to people with polyethylene glycol/polysorbate 80/trometamol allergies or anaphylaxis after the first dose.

Keywords: allergy, public health, vaccination, COVID-19

Abbreviations: HSE: health service executive; NIAC: National Immunisation Advisory Committee; PEG: polyethylene glycol; PS80: Polysorbate 80; ROI: Republic of Ireland; WHO: World Health Organisation

Introduction

Achieving population immunity by mass vaccination against COVID-19 has been one of the greatest challenges for health services in recent times [1]. The Republic of Ireland (ROI) has achieved one of the highest adult vaccination rates in the world with 85.69% of eligible persons in ROI (over five years old) fully vaccinated as of 29 May 2022 [2]. Anaphylaxis is a very rare side effect of COVID-19 vaccines, estimated to occur in 10.67 cases per million COVID-19 vaccines [3]. It is also important to consider that the criteria used to define anaphylaxis cases may be prone to overestimation [4]. The WHO recommends avoiding the administration of a vaccine to persons with anaphylaxis to the first dose or with an identified allergy to a vaccine component [5].

At the initiation of the vaccine programme, it was anticipated that there would be concerns in relation to certain individual's suitability for vaccination because of their personal history of suspected drug/vaccine allergy. In order to address these concerns, which might cause personal vaccine hesitancy or vaccinator reluctance to vaccinate, the National Immunisation Advisory Committee/Irish Association of Allergy and Immunology and the Royal College of Physicians of Ireland developed and released a guidance document in early 2021 to try to clarify cautions and contraindications to COVID 19 immunization aimed at community doctors and vaccination centres to ensure the maximum vaccination rates amongst this cohort. This was further developed and revised in April 2022 [6]. Despite this reassurance, a significant number of individuals were not vaccinated because of personal concerns, or even being refused vaccination when they attended for it, leading to numerous referrals for vaccination advice being received

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by local clinical immunology departments. Such referrals could increase vaccine hesitancy and reduce overall vaccine coverage.

The worldwide COVID pandemic has necessitated the review of health service delivery and the introduction of novel models of care, including the formation of clinics off-site from acute hospital bases [7].

We describe a specialized COVID-19 vaccine allergy clinic set up to address the COVID-19 vaccination needs of persons who are 16 years and older receiving primary vaccination who had been considered at increased risk of vaccine allergy or who had been refused vaccination in the community, despite the advice documents provided.

Methods

The clinic consisted of two rostered clinical immunologists, one consultant anaesthesiologist, and a full nursing team. The team was responsible for both vaccination and patient monitoring post-vaccination. A specific email address was established and information about the clinic, including referral criteria (Table 1), was circulated to vaccination centres and coordinators in the Dublin metropolitan area (1.5 million population). The clinic was set up in an existing and active mass vaccination centre in the community with full resuscitation capabilities and access to a standby paramedic team. All people who attended the specialist clinic between 6 July 2021 and 31 August 2021 were included.

Full hospital medical records were not available, merely the information was provided in the referral source. A focused allergy history was taken from each person. In part, this consisted of whether a prior COVID-19 vaccine had been administered if a reaction occurred to the same or whether they had been referred based on a prior history of suspected drug/other allergies. This clinic therefore worked on the basis of a risk reduction strategy rather than a definitive assessment for excipient or other allergies. Anonymized data were collected for each attendee including the referral source, clinical history, vaccine administered, vital signs post-vaccine, details of an adverse event, if any, and management of any post-vaccination event that occurred.

Each person who attended the clinic was offered either the Comirnaty (Pfizer-BioNTech) or Janssen vaccines depending on the reported history. These were the only two vaccines available at this vaccination clinic. People reporting a history of severe immediate hypersensitivity reaction to a previous COVID-19 vaccine were given the vaccine which did not contain the excipient profile unique to the first vaccine. An extended monitoring period of 30 min post vaccine was observed. Abnormal findings prompted further medical review. If no adverse event was noted the patient was discharged.

Table 1: referral criteria to specialist vaccine allergy clinic

Referral criteria
Anaphylaxis to a COVID-19 vaccine
Anaphylaxis to a constituent of a COVID-19 vaccine
Anaphylaxis to multiple drugs of different classes
Unexplained anaphylaxis

Results

A total of 206 people were vaccinated between 6 July 2021 and 31 August 2021. One hundred and sixty-six people (80.5%) were referred from a mass vaccination centre. Thirty-four people (16.5%) were general practitioner referrals and the remaining six (3%) were referred from a hospital clinical immunology service. Seventy-eight (78%) were female (Table 2).

Ninety-two people (45%) reported a high-risk allergy history, of whom 43 (47%) reported immediate hypersensitivity reactions to the first dose of a COVID-19 vaccine. Thirty-six (39%) reported PEG/PS80/Trometamol allergies. Additionally, 13 people (14%) reported a history of idiopathic anaphylaxis or mastocytosis (Fig. 1A). All 92 high-risk vaccines were vaccinated with the most appropriate vaccine following the risk assessment. Eighty-three (90.2%) received Janssen and nine (9.8%) received Comirnaty (Pfizer BioNTech) (Fig. 2).

One hundred and fourteen people (55%) were not considered high risk. Forty-six people (40%) reported single/multiple drug allergy, nine (8%) reported a combined drug and food allergy and nine (8%) reported a food allergy history alone but sought supervised vaccination. Nineteen people (17%) reported a mild non-allergic reaction and eight people (7%) self-reported a severe non-allergic reaction to the first COVID-19 vaccine. Twenty-three people (20%) reported a history of vaccine anxiety/other (Fig. 1B). Eighty-nine people (78%) from this cohort received the Janssen and 25 (22%) received Comirnaty (Pfizer BioNTech) (Fig. 2).

In total, 34 people (17%) received Comirnaty (Pfizer-BioNTech) and 172 (83%) received Janssen vaccine (Fig. 3).

Four people (2%) met the criteria for adverse drug reactions in the monitoring period. Three people developed limb or chest urticaria and were treated with an oral antihistamine, which induced recovery and they were discharged home; one of these also developed a transient tachycardia which self-resolved within the monitoring period. All had received the Janssen vaccine. One person with a known history of non-epileptic seizures developed a pseudoseizure following the Comirnaty (Pfizer-BioNTech) vaccine and remained haemodynamically stable. No acute management was required and the patient was transferred to the hospital for a full review.

Separate to this cohort of 206 people, there were an additional two people referred during this time period who declined vaccination despite pre-vaccination risk stratification

Table 2: demographic variables of people stratified by high- or low-risk allergy histories

	All (%)	High risk (%)	Low risk (%)
Gender			
Female	78	48	52
Male	22	33	67
Age			
18–29	13	7	18
30–49	50	60	42
50–64	28	24	31
65+	9	9	9

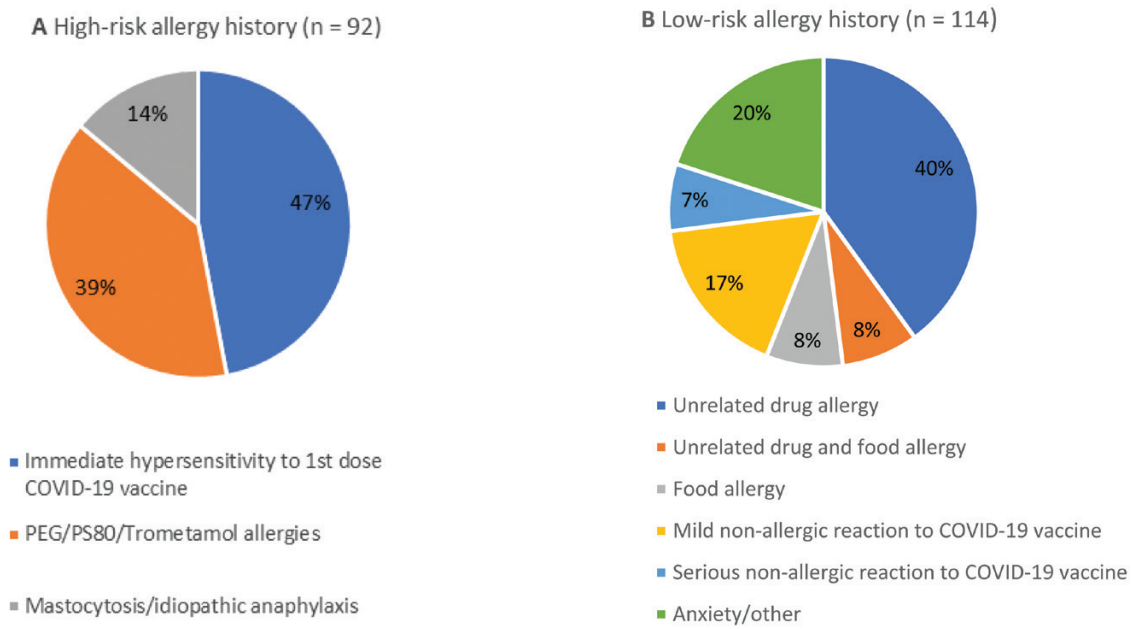

Figure 1: percentage of people reporting (A) high- or (B) low-risk allergy histories

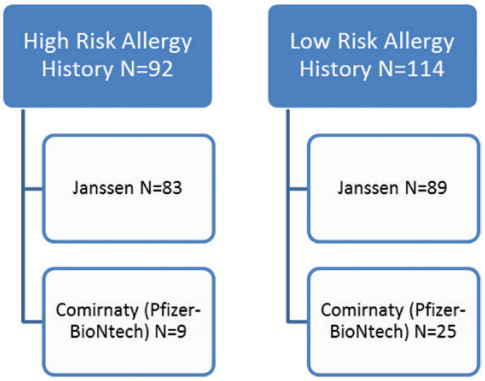

Figure 2: vaccine type is chosen based on risk classification

with a clinical immunologist, citing a personal preference for declining vaccination.

Discussion

All people with high-risk allergy histories attending our vaccine clinic were vaccinated following face-to-face screening by an Immunologist. Only three people developed mild and manageable adverse events and one person was transferred to the hospital with a pseudoseizure. No patient had an anaphylactic reaction. This data highlights the poor predictive value of a history of drug allergies for vaccine-related adverse events [8]. Additionally, these data are reassuring for medical professionals involved in COVID-19 vaccination, as they support the safety of these vaccinations. Notably, several people in the examined cohort were referred to the specialized clinic with a food allergy alone, which may reflect a lack of knowledge with regard to allergy in the community. We can only report those subjects referred for review and vaccination. We cannot estimate the number of people who chose not to be vaccinated at all due to their personal beliefs about vaccine safety or real or suspected allergies to drugs and excipients. Most vaccination centres in Ireland are not linked with an immunology service. Suitable people living far from this site were not offered the opportunity to attend their local site for such evaluation pre-vaccination. Subjects who attended this service must have been extremely motivated to overcome their own fears or to seek second opinions about the COVID-19 vaccination. For continuity and prescribing safety reasons, Comirnaty (Pfizer-BioNTech) and Janssen were the only vaccines used at this specialist clinic. Comirnaty (Pfizer-BioNTech) was the most widely used vaccine in ROI during the study period at a mean of 82.5% of all vaccines administered compared to 5% for Janssen [2]. However, the majority of vaccinees (83%) in this specialist clinic received Janssen. One of the main aims of this clinic was to provide safe and timely vaccination in a cohort of the population who, because of reported allergy history, may not have otherwise received full protection against COVID-19. It was also imperative to ensure maximum population coverage and protection of public health in the setting of high national COVID-19 infection rates at the time. Janssen provided an alternative vaccine choice for those deemed to be at risk of reaction to or previously reacted to an mRNA vaccine. Also, even for those deemed low risk following immunologist assessment, it was hypothesized that the use of a one-shot vaccine would not only allow for the swift completion of the vaccination schedule ensuring adequate protection against COVID-19 but would also remove the risk of persons not attending for the second dose of Comirnaty (Pfizer-BioNTech). This approach was in line with the National Immunisation Advisory Committee (NIAC) advice during the study period, where Janssen was deemed suitable in a wider age range of the population in cases where a two-dose vaccine was not feasible, in the setting of high COVID-19 infection rates or where early protection was paramount, following an informed decision by the vaccinee [9]. The Janssen vaccine remains licensed for use in the ROI and is still available in this specialist clinic as required.

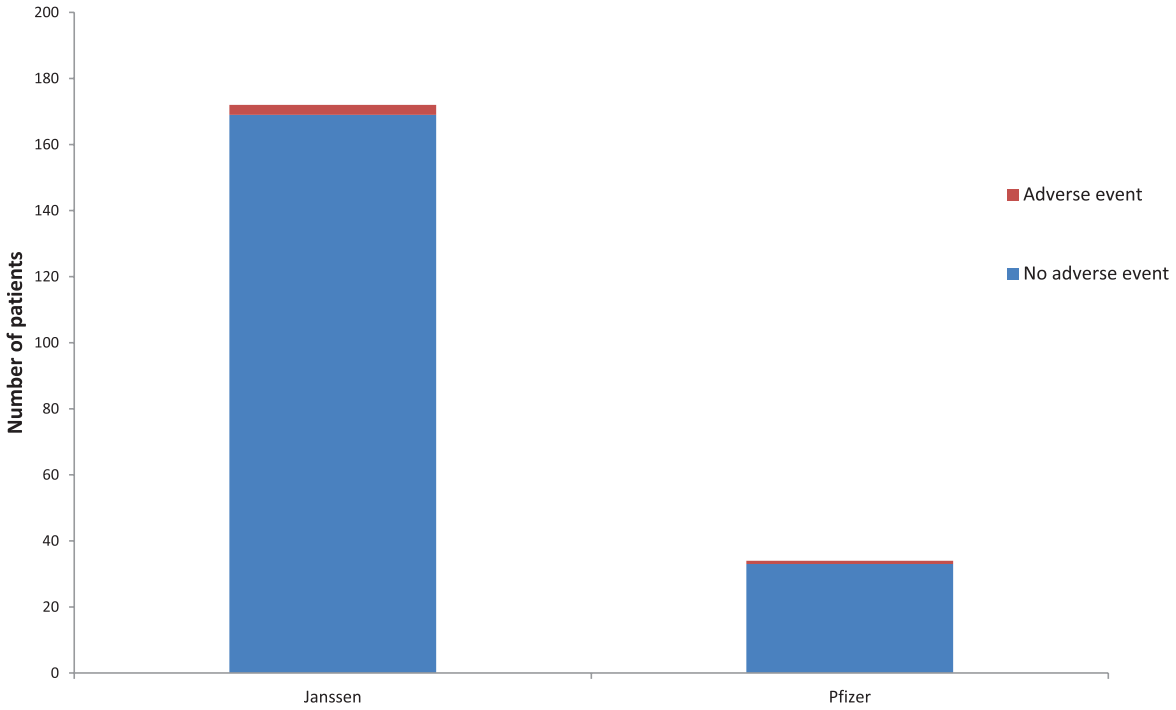

Figure 3: proportion of people vaccinated with Janssen or Comirnaty (Pfizer-BioNTech) vaccines and observed immediate adverse events.

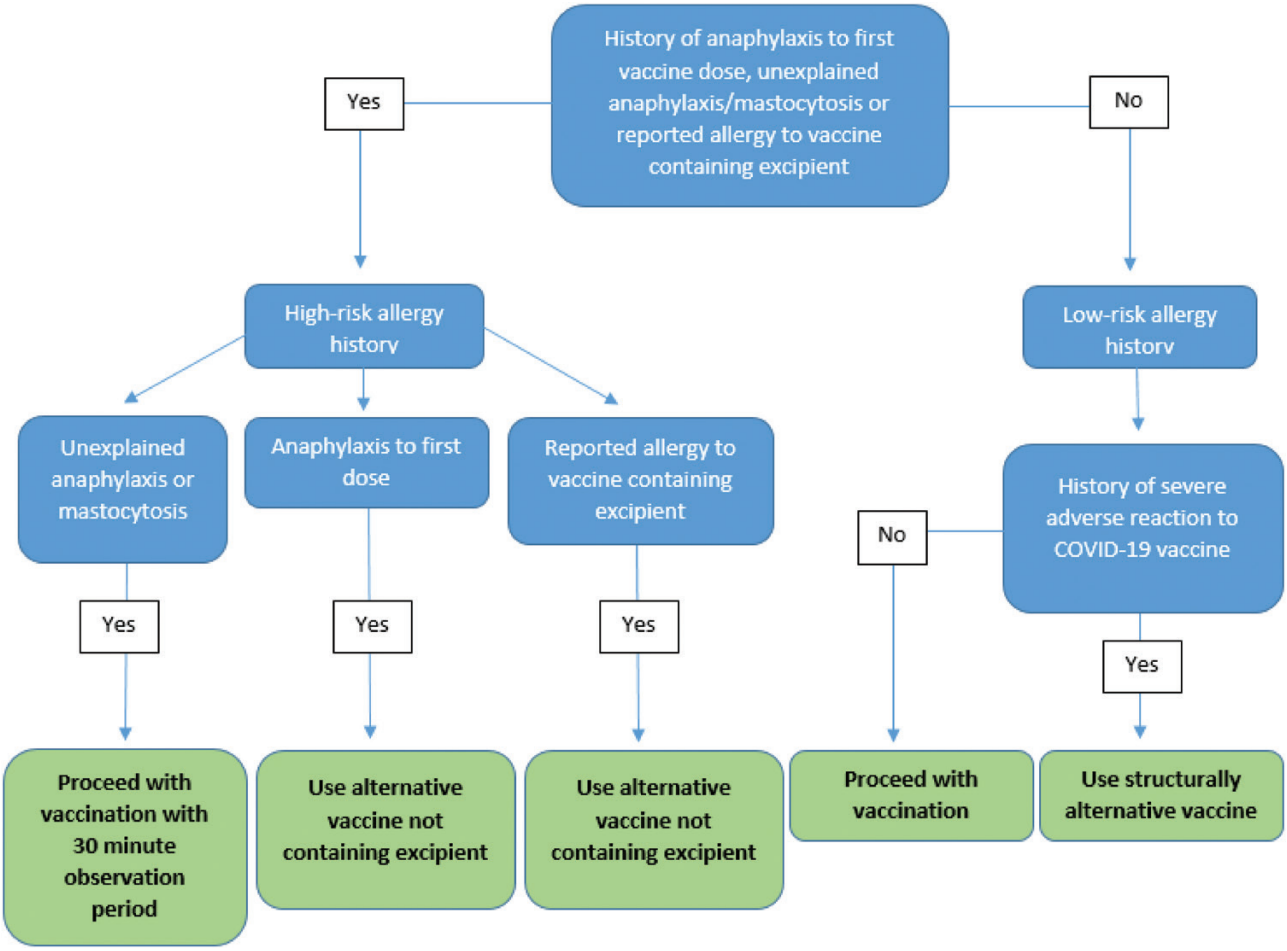

Figure 4: modified algorithm of the standard decision process followed to screen people in the clinic.

The recommendation for use of formal allergological investigation in persons reporting anaphylaxis to prior COVID-19 vaccines has been described [10–12]. Low positivity rates to skin testing have been noted and vaccination schedules have therefore been largely completed [11–13].

In Ireland, there are limited adult Clinical Immunology and Allergy services with six Immunology consultants in total. Therefore, it would not have been time or resource efficient to test people with a history of anaphylaxis to the first dose or reported excipient allergy before vaccination as is currently recommended by the BSACI [14] and detailed in the ENDA/EAACI position paper on allergy and COVID-19 vaccines [15]. Based on these limitations it was also not possible at the time to provide an onward referral for formal excipient allergy investigation to local clinical immunology departments. However, through this real-life experience, we were able to design a modified decision algorithm to guide the safe administration of COVID-19 vaccines in people with a high-risk allergy history, where alternative vaccines can be used where indicated (Fig. 4).

It is important to note that there was a high level of anxiety and vaccine-hesitancy regarding the vaccination of people referred to the clinic. Each healthcare professional present at these clinics had a role in assuaging this anxiety through accurate history taking, clear communication, and reassurance of the safety of vaccination for each individual. Employing appropriately trained staff may be useful and improve vaccine uptake. The need to vaccinate the maximum amount of people for overall community protection against COVID-19 is paramount in this pandemic response. For the first time, our data show evidence that even persons with a high-risk drug allergy can be vaccinated safely in a community setting, under expert review but without the need for hospital capacity or referral for excipient skin testing. As the clinic is now accommodating people receiving additional/booster vaccines further research is needed on this cohort. Overall, it is hoped this study will contribute to the current risk management of the administration of COVID-19 vaccines and act as reassurance of the safety of COVID-19 vaccination to reduce unnecessary referrals to immunology clinics and resultant delays in vaccination.

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Conflict of interests

None to declare.

Note: Dr Hourihane provides advice, without remuneration, to Ireland's Health Products Regulatory Authority and the National Immunisation Advisory Council.

Authorship contributions

Conceptualization: N.C., M.K., K.K., C.F., J.O.B.H., J.D.M.E. Data curation: S.H., K.K., C.F., J.D.M.E. Formal analysis: D.L., C.M., S.A., K.K., J.D.M.E. Funding acquisition: N.C., M.K., K.K., C.F., J.O.B.H., J.D.M.E. Investigation: D.L., C.M., S.H., J.S., S.A., K.K., C.F., M.C., J.D.M.E. Methodology: D.L., C.M., S.H., J.S., S.A., K.K., C.F., M.C., J.D.M.E. Project administration: K.K., J.D.M.E., C.F. Resources: S.H., S.A., K.K., J.D.M.E., C.F. Software: D.L., C.M., S.A., J.S., K.K., M.C., C.F., J.D.M.E. Supervision: K.K., C.F., J.D.M.E. Validation: K.K., C.F., J.D.M.E. Visualization: D.L., C.M. Writing—original draft: D.L., C.M. Writing—reviewing and editing: All authors.

Ethical approval

This study conducted was a service evaluation only. It was approved by the COVID Vaccination Centre clinical governance committee (Citywest, Dublin, Ireland) and confirmed as GDPR compliant and as such did not require full ethical approval.

Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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