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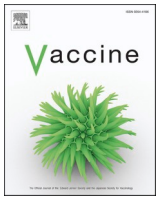

Short communication

# Local and systemic reactogenicity after mRNA and protein-based COVID-19 vaccines compared to meningococcal vaccine (MenACWY) in a UK blinded, randomized phase 2 trial (COV-BOOST)

Anthony M. Marchese [a], Hadi Beyhaghi [a], Matthew D. Rousculp [a], Vivian Huang [a], Xinxue Liu [b], Seth Toback [a,*], Saul N. Faust [c]

[a] Novavax, Inc., Gaithersburg, MD, USA
[b] Oxford Vaccine Group, Department of Paediatrics, University of Oxford, Oxford, UK
[c] NIHR Southampton Clinical Research Facility and Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust and University of Southampton, Southampton, UK

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ABSTRACT

Reactogenicity, the occurrence of vaccine side effects, can impact vaccine acceptance. There is limited data comparing the reactogenicity of COVID-19 vaccines to other routinely used vaccines, such as the meningococcal conjugate vaccine (MenACWY). In a trial of UK adults, participants received a third COVID-19 vaccine dose (NVX-CoV2373, BNT162b2, or mRNA1273) alongside MenACWY as an active control. Compared to MenACWY, we found that mRNA vaccines, particularly mRNA1273, showed the greatest relative increase in side effects, while protein-based NVX-CoV2373 generally elicited similar reactogenicity to MenACWY. These findings suggest that platform type can influence vaccine reactogenicity, and further research is needed to compare COVID-19 vaccines with other routinely administered vaccines.

## 1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection remains an ongoing health concern due to the continued emergence of new antigenically distant viral variants and the possibility of increased transmissibility and pathogenicity that could lead to an increased incidence of severe disease and death. Presently, COVID-19–associated hospitalizations and deaths have dropped considerably compared to the peak pandemic era levels. In the current COVID-19 landscape, numerous factors can impact an individual's decision to receive an additional COVID-19 vaccine dose (e.g., cost, accessibility, belief that one's risk for disease is low), and vaccine hesitancy has become a complex issue which will require multiple approaches to address. For some individuals, the potential for vaccine-associated side effects may be a concern, as studies have indicated a link between acceptance of vaccines and expectation of the occurrence of local and systemic reactogenic events [1–7]. For example, in several studies of healthcare workers, the side effects associated with mRNA COVID-19 vaccinations disrupted work activities, leading to workplace absenteeism [2,4,5] and reduced future willingness to receive booster vaccinations [2,8]. Among parents, vaccine safety signals and side effects were central concerns [9,10]. Those who refrain from vaccinating their children did so in part due to concern that side effects may cause missed school or exacerbate preexisting medical conditions. In addition, hesitancy rates were found to disproportionately affect different racial/ethnic groups [8,10,11].

An improved understanding of reactogenicity differences across COVID-19 vaccine platforms could potentially improve COVID-19 vaccination rates, which would be particularly beneficial to high-risk and low acceptance groups. COVID-19 vaccine platforms have included mRNA, adjuvanted protein-based, adenoviral vector, and inactivated platforms. In the US and Europe, updated JN.1 based mRNA and adjuvanted protein-based COVID-19 vaccines have been authorized/approved. Several studies, including systematic reviews and meta-analyses of COVID-19 vaccination, have suggested that the protein-based NVX-CoV2373 (Novavax, Inc.) COVID-19 vaccine induces a lower incidence and reduced severity of reactogenicity events than mRNA vaccines [12–17]. While direct comparison of reactogenicity profiles across different types of COVID-19 vaccines is important, comparing the reactogenicity profile of COVID-19 vaccines relative to

* Corresponding author at: Novavax, Inc., 700 Quince Orchard Rd, Gaithersburg, MD 02878, United States.
*E-mail address:* stoback@novavax.com (S. Toback).

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that of familiar, routinely used vaccines provides additional insights that can help to inform individuals' vaccine-related decisions. Here, we strengthen the limited evidence that exists on the reactogenicity of COVID-19 vaccines compared to other routinely administered vaccines, by investigating the incidence and severity of reactogenicity events associated with protein-based and mRNA COVID-19 vaccines compared to the widely administered conjugate quadrivalent meningococcal vaccine (MenACWY).

## 2. Methods

COV-BOOST (ISRCTN 73765130) is a multicenter, blinded, randomized, phase 2 clinical study aimed to assess the safety, reactogenicity, and immunogenicity of homologous and heterologous COVID-19 boosters in ≥30-year-old UK adults [15]. The study was not powered to make comparisons between vaccines, but all vaccine arms were compared to the active control, MenACWY (Pfizer, Inc.) vaccine, separated into groups A, B, and C (Tables 1 and 2). In the present study, we further analyzed the reactogenicity data from COV-BOOST. Participants aged 30 years and older were randomly assigned to one of three study groups with equal probability within groups A–C. Group A received NVX-CoV2373 (protein-based, Novavax, Inc., 5 μg rS + 50 μg Matrix-M™), or control MenACWY. Group B received BNT162b2 (mRNA, Pfizer, Inc., 30 μg) or MenACWY. Group C received mRNA-1273 (mRNA, Moderna, Inc., 100 μg, twice the currently approved dosage) or MenACWY. Each cohort (A, B, and C) had their own control group and recruited two separate populations, those receiving primary series ChAdOx1 nCoV vaccine (viral vector, AstraZeneca, not included in the present analysis) and those receiving BNT162b2. Each group included approximately 40–45% participants aged 70 years or greater, and median ages ranged from 61.9 to 68.1 years. Detailed study design and demographic information has been published as part of the primary study analysis, Munro et al., 2021 [15]. The occurrence of solicited reactogenicity events following the third vaccination was recorded in participant electronic diaries were recorded daily for 7 days. The percentage of participants who reported local events (pain, warmth, redness, itch, swelling, and/or hardness) and systemic events (malaise, muscle ache, fatigue, headache, joint pain, fever, feverishness, diarrhea, and/or nausea) after vaccination were measured. Feverishness was defined as feeling unwell/shivery but not always associated with measurable fever. Grade 3 events were considered severe, and defined as "marked limitation in activity, some assistance usually required; medical intervention/therapy required" [15]. Grade 4 events were considered to be potentially life-threatening, and were defined as "requires assessment in A&E or hospitalization" [15]. The difference in percentage of events following COVID-19 vaccination compared to the percentage of events following MenACWY vaccination with 95% confidence intervals (CI) were calculated.

## 3. Results

Among groups A, B, and C, any grade pain was the most common local symptom, ranging from 20.7% to 32.1% in the active control recipients, and 50.5% in NVX-CoV2373, 76.6% in BNT162b2, and 89.0% in mRNA-1273 vaccine groups (Table 1). The proportion of participants with local symptoms following mRNA-1273 (100 μg) were generally higher than those of BNT162b2 (30 μg), most likely related to the difference in concentration, though both mRNA vaccines elicited higher frequencies of events than protein-based NVX-CoV2373 (Table 1). The highest absolute difference among COVID-19 vaccine–associated local reactions to those of MenACWY was in injection site pain: 68.3% (95% CI: 58.9 to 77.7), mRNA-1273; 44.6% (95% CI: 32.5 to 56.5), BNT162b2; and 22.0% (95% CI: 9.6 to 34.6), NVX-CoV2373 (Fig. 1A). NVX-CoV2373 was similar to MenACWY, as the differences for redness (−0.7, 95% CI: −5.1 to 3.9), warmth (3.5, 95% CI: −5.5 to 12.5), swelling (−2.5, 95% CI: −6.3 to 1.3), hardness (−2.5, 95% CI: −7 to 2) and itch (0.4, 95% CI: −5.9 to 6.7) were each less than 4%. Although rare, Grade 3+ local symptoms were more frequently reported after mRNA-1273 vaccine administration (Table 1 and Fig. 2).

Among systemic symptoms, any-grade malaise, headache, muscle ache, and fatigue were most commonly reported. The frequency of malaise ranged from 12.6% to 19.8% (average per group) in the active control recipients, and 10.1% in NVX-CoV2373, 22.4% in BNT162b2, and 48.6% in mRNA-1273 vaccine groups (Table 2). Similarly, muscle ache ranged from 17.1% to 26.4% in active control recipients, and 17.4% in NVX-CoV2373, 31.8% in BNT162b2, and 52.3% in mRNA-1273 vaccinees, and fatigue ranged from 38.7% to 43.1% in the active control recipients, and 42.2% in NVX-CoV2373, 44.9% in BNT162b2, and 71.6% in mRNA-1273 vaccinees (Table 2). Systemic reactions to mRNA-1273 and BNT162b2 followed the trend of local reactions compared to the MenACWY vaccine in each group. One hundred micrograms of mRNA-1273 elicited the highest frequency of symptoms, though both mRNA vaccines showed generally higher reactogenicity than NVX-CoV2373. As an exception, among COVID-19 vaccines, BNT162b2 had the lowest incidences of diarrhea (3.7%), compared to NVX-CoV2373 (7.3%) and mRNA-1273 (9.2%) (Table 2) when each was compared to MenACWY. The absolute difference of systemic reactogenicity events was highest after mRNA-1273 followed by BNT162b2 and NVX-CoV2373: malaise: 36.0% (95% CI: 24.8 to 47.2) mRNA-1273; 2.6% BNT162b2 (95% CI: −8.4 to 13.6); and − 2.8% (95% CI: −11.1 to 5.5) NVX-CoV2373 (Fig. 1B). The systemic reactogenicity profile of NVX-CoV2373 was similar to MenACWY, as the differences for chills

**Table 1**
Local Symptoms.

| Local Symptom | | MenACWY (Control-A) | | NVX-CoV2373 | | MenACWY (Control-B) | | BNT162b2 [30 μg] | | MenACWY (Control-C) | | mRNA-1273 [100 μg] | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total, $N = 658$ | $N = 116$ | | $N = 109$ | | $N = 106$ | | $N = 107$ | | $N = 111$ | | N = 109 | |
| | | events | (%) | events | (%) | events | (%) | events | (%) | events | (%) | events | (%) |
| **Hardness** | Any Grade | 5 | (4.3) | 2 | (1.8) | 3 | (2.8) | 3 | (2.8) | 1 | (0.9) | 13 | (11.9) |
| | Grade 3+ | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.9) | 1 | (0.9) |
| **Itch** | Any Grade | 7 | (6.0) | 7 | (6.4) | 5 | (4.7) | 10 | (9.3) | 6 | (5.4) | 19 | (17.4) |
| | Grade 3+ | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| **Pain** | Any Grade | 33 | (28.4) | 55 | (50.5) | 34 | (32.1) | 82 | (76.6) | 23 | (20.7) | 97 | (89.0) |
| | Grade 3+ | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (3.7) |
| **Redness** | Any Grade | 4 | (3.4) | 3 | (2.8) | 0 | (0.0) | 5 | (4.7) | 1 | (0.9) | 21 | (19.3) |
| | Grade 3+ | 1 | (0.9) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.9) | 5 | (4.6) |
| **Swelling** | Any Grade | 4 | (3.4) | 1 | (0.9) | 2 | (1.9) | 6 | (5.6) | 0 | (0.0) | 13 | (11.9) |
| | Grade 3+ | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 3 | (2.8) |
| **Warmth** | Any Grade | 14 | (12.1) | 17 | (15.6) | 10 | (9.4) | 22 | (20.6) | 8 | (7.2) | 47 | (43.1) |
| | Grade 3+ | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.9) |

* All doses received after previous administration of two-dose (2x) BNT162b2. Abbreviations: BNT162b2, Pfizer Inc.; MenACWY, Pfizer Inc.; mRNA-1273, Moderna Inc.; NVX-CoV2373, Novavax Inc.

**Table 2**
Systemic Symptoms.

| Systemic Symptom | | MenACWY (Control-A) | | NVX-CoV2373 | | MenACWY (Control-B) | | BNT162b2 [30 µg] | | MenACWY (Control-C) | | mRNA-1273 [100 µg] | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total, N = 658 | N = 116 | | N = 109 | | N = 106 | | N = 107 | | N = 111 | | N = 109 | |
| | | Events | (%) | events | (%) | events | (%) | events | (%) | events | (%) | events | (%) |
| **Chills** | Any Grade | 3 | (2.6) | 6 | (5.5) | 14 | (13.2) | 10 | (9.3) | 6 | (5.4) | 35 | (32.1) |
| | Grade 3+ | 0 | (0.0) | 0 | (0.0) | 1 | (0.9) | 0 | (0.0) | 0 | (0.0) | 3 | (2.8) |
| **Fatigue** | Any Grade | 50 | (43.1) | 46 | (42.2) | 41 | (38.7) | 48 | (44.9) | 46 | (41.4) | 78 | (71.6) |
| | Grade 3+ | 1 | (0.9) | 1 | (0.9) | 2 | (1.9) | 1 | (0.9) | 0 | (0.0) | 4 | (3.7) |
| **Fever** | Any Grade | 0 | (0.0) | 1 | (0.9) | 2 | (1.9) | 2 | (1.9) | 0 | (0.0) | 8 | (7.3) |
| | Grade 3+ | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| **Feverishness** | Any Grade | 9 | (7.8) | 10 | (9.2) | 10 | (9.4) | 11 | (10.3) | 8 | (7.2) | 33 | (30.3) |
| | Grade 3+ | 0 | (0.0) | 0 | (0.0) | 2 | (1.9) | 0 | (0.0) | 0 | (0.0) | 3 | (2.8) |
| **Headache** | Any Grade | 35 | (30.2) | 36 | (33.0) | 28 | (26.4) | 40 | (37.4) | 34 | (30.6) | 58 | (53.2) |
| | Grade 3+ | 1 | (0.9) | 0 | (0.0) | 1 | (0.9) | 0 | (0.0) | 0 | (0.0) | 3 | (2.8) |
| **Joint Pain** | Any Grade | 12 | (10.3) | 12 | (11.0) | 12 | (11.3) | 19 | (17.8) | 9 | (8.1) | 30 | (27.5) |
| | Grade 3+ | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (1.8) |
| **Malaise** | Any Grade | 15 | (12.9) | 11 | (10.1) | 21 | (19.8) | 24 | (22.4) | 14 | (12.6) | 53 | (48.6) |
| | Grade 3+ | 1 | (0.9) | 0 | (0.0) | 1 | (0.9) | 0 | (0.0) | 0 | (0.0) | 6 | (5.5) |
| **Muscle Ache** | Any Grade | 20 | (17.2) | 19 | (17.4) | 28 | (26.4) | 34 | (31.8) | 19 | (17.1) | 57 | (52.3) |
| | Grade 3+ | 0 | (0.0) | 0 | (0.0) | 1 | (0.9) | 0 | (0.0) | 1 | (0.9) | 4 | (3.7) |
| **Nausea** | Any Grade | 13 | (11.2) | 10 | (9.2) | 9 | (8.5) | 13 | (12.1) | 12 | (10.8) | 19 | (17.4) |
| | Grade 3+ | 1 | (0.9) | 0 | (0.0) | 0 | (0.0) | 1 | (0.9) | 1 | (0.9) | 1 | (0.9) |
| **Vomiting** | Any Grade | 1 | (0.9) | 1 | (0.9) | 0 | (0.0) | 0 | (0.0) | 1 | (0.9) | 0 | (0.0) |
| | Grade 3+ | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.9) | 0 | (0.0) |
| **Diarrhea** | Any Grade | 8 | (6.9) | 8 | (7.3) | 11 | (10.4) | 4 | (3.7) | 6 | (5.4) | 10 | (9.2) |
| | Grade 3+ | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |

* All doses received after previous administration of two-dose (2x) BNT162b2. Abbreviations: BNT162b2, Pfizer Inc.; MenACWY, Pfizer Inc.; mRNA-1273, Moderna, Inc.; NVX-CoV2373, Novavax, Inc. Note: Feverishness was defined as feeling unwell/shivery but not always associated with measurable fever.

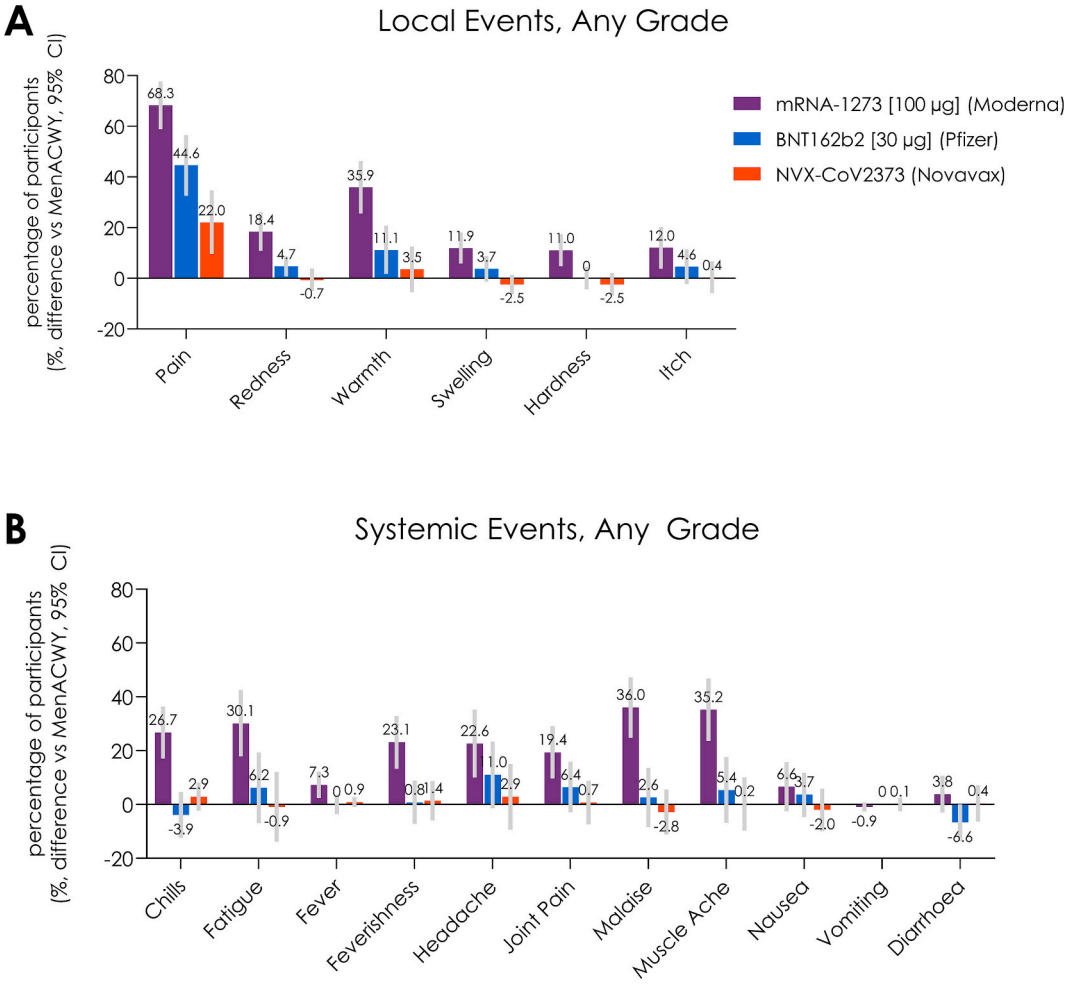


**Fig. 1.** Difference in any grade local and systemic reactogenicity of COVID-19 vaccine booster doses compared to MenACWY.

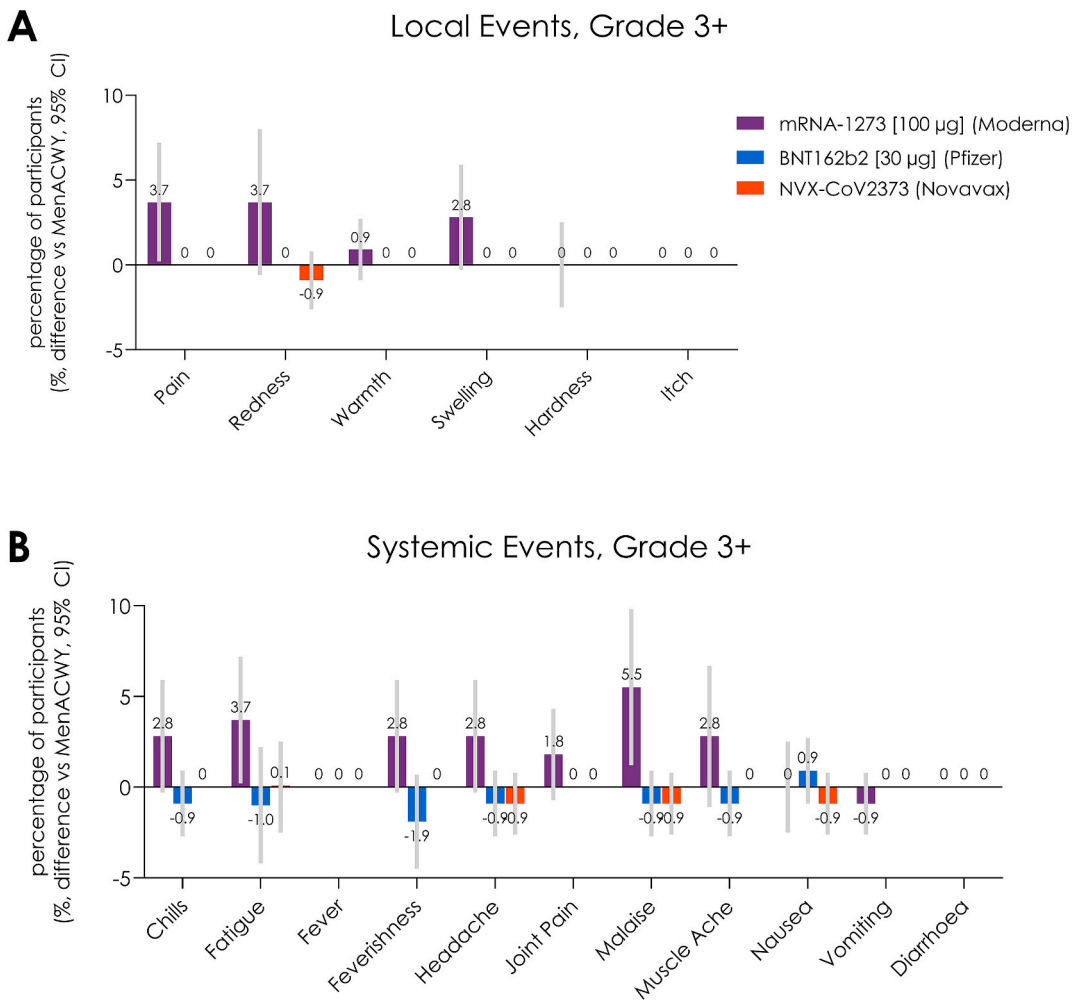


**Fig. 2.** Difference in grade 3+ local and systemic reactogenicity of COVID-19 vaccine booster doses compared to MenACWY.

(2.9, 95% CI: −2.3 to 8.1), fatigue (−0.9, 95% CI: −13.8 to 12.0), fever (0.9, 95% CI: −0.9 to 2.7), feverishness (1.4, 95% CI: −5.9 to 8.7), headache (2.9, 95% CI: −9.4 to 15.0), joint pain (0.7, 95% CI: −7.4 to 8.8), malaise (−2.8, 95% CI: −11.1 to 5.5), muscle ache (0.2, 95% CI: −9.7 to 10.1), nausea (−2.0, 95% CI: −9.9 to 5.9), vomiting (0.1, 95% CI: −2.5 to 2.5), and diarrhea (0.4, 95% CI: −6.3 to 7.1) were each comparatively lower or were no higher than 3%. For any grade diarrhea, BNT162b had a lower incidence (Fig. 1B **and** Table 2**)**.

In all groups, local events occurred more frequently than systemic events, and grade 3+ events were rare in occurrence ranging from 0% to 4.6% for local events and 0% to 5.5% for systemic events (Tables 1 and 2, and Fig. 2**)**. The general observed trend shows that the highest incidence of local and systemic symptoms was reported following vaccination with mRNA-1273 and were lower in BNT162b2, followed by NVX-CoV2373 and MenACWY, although a few exceptions were observed. Overall, protein-based NVX-CoV2373 booster vaccination reactogenicity profile was most like MenACWY, with a comparable or lower incidence of most local and systemic reactogenicity events **(**Tables 1 and 2**, and** Fig. 1**).**

## 4. Discussion

These findings offer new insights on COVID-19 vaccine reactogenicity side effects as they relate to a routinely used meningococcal vaccine (MenACWY). Consistent with previous studies, this study suggests that the NVX-CoV2373 COVID-19 vaccine may be associated with a lower incidence and severity of reactogenicity symptoms than mRNA COVID-19 vaccines [12–17]. Importantly, the NVX-CoV2373 vaccine elicited comparable reactogenicity symptoms to MenACWY. All NVX-CoV2373 reported symptoms were lower or at most 3% higher than MenACWY, except for injection site pain (+22%, 95% CI: 9.6 to 34.6) and warmth (+3.5%, 95% CI: −5.5 to 12.5). In contrast, the higher incidence of mRNA vaccine–associated side effects, after both 100 mg mRNA-1273 and 30 mg BNT162b2, represents a potentially clinically meaningful elevation when compared with MenACWY-associated symptoms. It is important to highlight that the study concentration of mRNA-1273 was 100 µg, which is notably higher than the currently used 50 µg adult updated JN.1 vaccine dose concentration [18]. The inclusion of this study arm in the present analysis is useful as COVID-19 mRNA vaccines may be altered during expected annual formulation changes, and novel investigational mRNA vaccines are being evaluated for use against other diseases at varying concentrations. These findings provide additional new evidence that the reactogenicity symptoms a vaccine recipient may experience can be impacted by the type of the COVID-19 vaccine platform they receive. Collectively, evidence indicates mRNA COVID-19 vaccines eliciting greater levels of local and systemic side effects than routinely used vaccines, while the NVX-CoV2373 COVID-19 vaccine has been demonstrated to be similar to influenza and meningococcal vaccine-associated symptoms [19]. Previous studies included both mRNA COVID-19 vaccines and seasonal influenza comparators, permitting a descriptive analysis of reactogenicity differences [20,21]. In a comparative observational cohort study, more participants who received mRNA-1273 (Moderna, Inc.) and BNT162b2 (Pfizer Inc.) were found to report at least one local, systemic, or unsolicited reaction than

those in the comparator cohort of either influenza, pneumococcus, tick-borne encephalitis (TBE), tetanus and diphtheria (Td) vaccinations, with or without pertussis and poliomyelitis (TdaP and TdaP-IPV), or herpes zoster vaccines [21]. Related, in a sub-study of a phase 3 randomized controlled trial, the NVX-CoV2373 COVID-19 vaccine–associated reactogenicity appeared to induce slightly higher local and comparable systemic symptoms to that of the Flucelvax® Quadrivalent (Seqirus, for those aged 18–64 years) and Fluad® (Seqirus, for those ≥65 years old) influenza vaccines [19].

The present analysis had several limitations. The population included a primarily seronegative cohort of mostly White people ≥30 years of age. The grouped study design did not permit randomization of all vaccines simultaneously. Instead, each COVID-19 vaccine arm included a MenACWY active control group. Hence, the frequency of the reported reactogenicity symptoms might vary partially due to population differences in different groups. Additionally, the dose concentration of the mRNA-1273 vaccine used at the time of this study (100 μg) was twice the subsequently approved dose concentration for adults receiving their third vaccine dose. The trial was not powered to directly compare reactogenicity, therefore, the descriptive evidence should be thought of as hypothesis-generating. Study participants had no history of laboratory-confirmed SARS-CoV-2 infection. It is likely that previous infection with SARS-CoV-2 prior to receiving a vaccine dose would impact reactogenicity. The incidence of symptoms among the different age groups was not stratified in the present analysis.

It would be valuable to continue to explore how COVID-19 vaccine reactogenicity compares to other frequently administered vaccines with high global uptake, such as the seasonal influenza vaccines. Although individuals may experience side effects from COVID-19 vaccines, these symptoms are generally short-lived and are outweighed by the long-term benefits, particularly among at-risk groups, of vaccination. Studying how healthcare providers can utilize this information, and how hesitant individuals are impacted by it, is warranted as it could inform future immunization initiatives and best practices for providers. If appropriately communicated, it could benefit healthcare providers and their patients to have a better understanding of COVID-19 vaccine side effects as they relate to routinely used vaccines with high familiarity among potential vaccinees. Future studies will be needed to demonstrate that this information could positively impact vaccination rates. Additionally, it would be valuable to study COVID-19 vaccine reactogenicity in the context of vaccine co-administration, as providers often offer co-administration to maximize the opportunity to protect patients during a single visit. Potential association of COVID-19 vaccines to reactogenicity could impact willingness to receive other routinely administered options such as influenza or RSV vaccines. To overcome low vaccination rates, we must be willing to address the valid concerns of hesitant individuals and leverage diverse sources of data capable of increasing trust and acceptance.

## CRediT authorship contribution statement

**Anthony M. Marchese:** Writing – review & editing, Writing – original draft, Visualization, Software, Resources, Project administration, Formal analysis, Conceptualization. **Hadi Beyhaghi:** Writing – review & editing, Writing – original draft, Project administration, Formal analysis, Conceptualization. **Matthew D. Rousculp:** Writing – review & editing, Formal analysis, Conceptualization. **Vivian Huang:** Writing – review & editing, Project administration. **Xinxue Liu:** Writing – review & editing, Methodology, Formal analysis, Data curation, Conceptualization. **Seth Toback:** Writing – review & editing, Supervision, Formal analysis, Conceptualization. **Saul N. Faust:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Anthony M. Marchese, Hadi Beyhaghi, Matthew D. Rousculp, Vivian Huan, and Seth Toback are employees and stockholders of Novavax, Inc. Saul N. Faust acts on behalf of University Hospital Southampton National Health Service (NHS) Foundation Trust as an investigator or providing consultative advice, or both, on clinical trials and studies of COVID-19 and other vaccines funded or sponsored by vaccine manufacturers including Janssen, Pfizer, AstraZeneca, GlaxoSmithKline, Novavax, Seqirus, Sanofi, Medimmune, Merck, and Valneva. He receives no personal financial payment for this work. Xinxue Liu has no conflicts of interest to declare.

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*Ethics approval*

Per the primary study publication, the trial was reviewed and approved by the South-Central Berkshire Research Ethics Committee, University Hospital Southampton, and the Medicines and Healthcare Products Regulatory Agency (EudraCT 2021–002175–19, IRAS 299180, REC reference 21/SC/0171) [15]. The study protocol is provided by Munro, et al., 2021 [15].

*Disclosures/conflicts of interest*

AMM, HB, MDR, VH, and ST are employees and stockholders of Novavax, Inc. SNF acts on behalf of University Hospital Southampton National Health Service (NHS) Foundation Trust as an investigator or providing consultative advice, or both, on clinical trials and studies of COVID-19 and other vaccines funded or sponsored by vaccine manufacturers including Janssen, Pfizer, AstraZeneca, GlaxoSmithKline, Novavax, Seqirus, Sanofi, Medimmune, Merck, and Valneva. He receives no personal financial payment for this work. XL has no conflicts of interest to declare.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2024.126569.

## Data availability

Data requests will be considered. Please refer to the original publication for details on the process.

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