ENFORCE

Danish National Cohort Study of Effectiveness and Safety of SARS-CoV-2 Vaccines

Monthly Report

Report number: 2

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Report prepared by: the ENFORCE consortium

Approved by: the ENFORCE scientific steering committee

This report is an edited version of the confidential report generated for distribution and review to the Danish Medicines Agency only. Tables and figures with small numbers (<5 participants per cell) or very specific details and where there is the potential that individual participants could be identified or be able to identify themselves have been removed or edited to maintain participant confidentiality.

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Danish National Cohort Study of Effectiveness and Safety of SARS-CoV-2 vaccines

Contents

Summary of key changes from previous report

This is the first public report.

Methods

The data presented in this report are descriptive. A detailed statistical analysis plan will be developed prior to any formal analysis being conducted.

Data sources

The data used to generate this report are currently based only on the data stored in REDCap from the case report forms (CRF's) and online symptoms form. Data on serum antibody quantification using ELISA (Wantai) was provided by the SSI.

Results from the ELISA detection of total serum Ig to the Receptor Binding Domain (Wantai) were recorded as Negative (ratio <0.9), Positive (ratio >1.1), or inconclusive (ratio between 0.9-11). The ratio was calculated as the OD value/cut-off, where the cut-off= average of the negative controls+0.16. If the average is below 0.03 then the cut-off is set to 0.16 + 0.03. For manual execution the cut-off will almost always be 0.19.

Definitions

In this version of the report the type of vaccine received is based on self-reports from participants at enrollment into the study which occurs prior to them receiving their first vaccine. In subsequent reports this will be updated using data from the national vaccine registry as the gold standard when this data is available.

Enrollment

The section gives an overview of the current enrollment status of participants in the study. Table 1 outlines the number of participants currently enrolled in the study and reasons for exclusion.

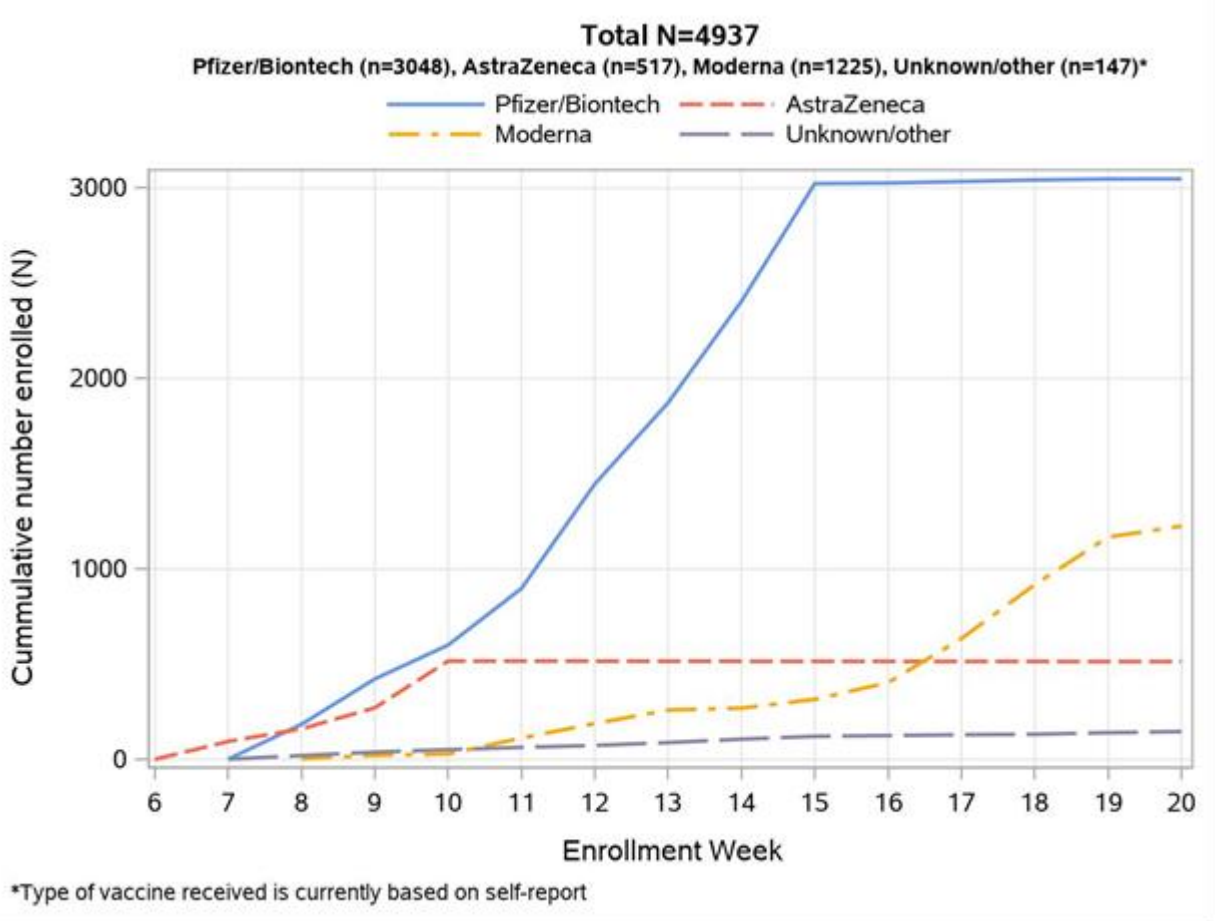
Table 1

Total included	*Reason for exclusion*
4950	All patients
4943	Consent withdrawn
4937	Provided informed consent
4937	Missing enrolment date
4937	Aged under 18
4937	Vaccine not recommended
4937	Vaccinated Previously
4937	Belongs to a vaccine target group
4937	Agrees to follow protocol

Figure 1 shows the cumulative number of participants enrolled by vaccine type. Enrollment began on the 13 February 2021 (Week 6) when the first patient was enrolled prior to receiving the AstraZeneca vaccine. The first participant enrolled prior to receiving the Pfizer/BionTech vaccination was on the 16th February 2021, followed by Moderna on the 24 February 2021 (week 8).

A total of 517 participants were enrolled in the AstraZeneca vaccine group prior to the pausing of AstraZeneca vaccination in week 10 (11th March 2021). Enrollment for those receiving Pfizer was paused in week 15, after the target of 2500 participants was reached, since then the majority of enrollment has been for participants scheduled to receive Moderna.

Figure 1 Cumulative number of participants enrolled by vaccine type



Demographics at enrollment

Table 2 gives an overview of the participant demographics at the time of enrollment into the study overall and by vaccine. Table 3 gives an overview of the number of participants with concomitant diseases at enrollment and the use of any medications in the 24 hours prior to enrollment.

Table 2 Participant demographics at study enrollment by vaccine

		Vaccine type			
	Total (N=4937)	*Pfizer/Biontech (N=3048)*	*AstraZeneca (N=517)*	*Moderna (N=1225)*	*Unknown/other (N=147)*
Number of persons (%)					
Gender					
Male	2252 (45.6)	1538 (50.5)	81 (15.7)	546 (44.6)	87 (59.2)
Female	2685 (54.4)	1510 (49.5)	436 (84.3)	679 (55.4)	60 (40.8)
Median (interquartile range, IQR)					
Age at enrolment (years)	69 (61, 77)	74 (63, 79)	45 (31, 56)	69 (64, 70)	71 (63, 79)
Enrolment date	MAR21 (MAR21, APR21)	MAR21 (MAR21, APR21)	MAR21 (FEB21, MAR21)	APR21 (APR21, MAY21)	MAR21 (MAR21, APR21)

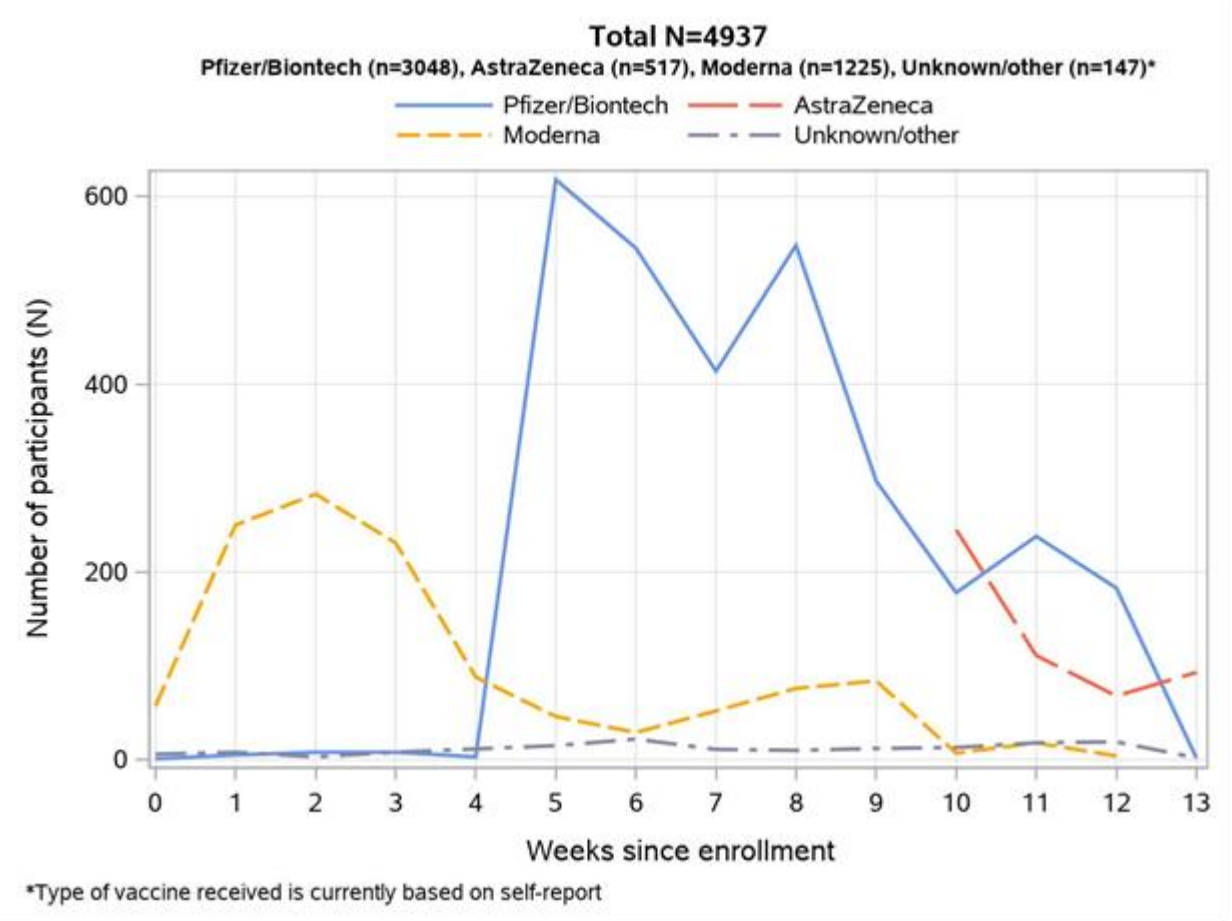
Table 3 Concomitant diseases and medications, overall and by vaccine

		Vaccine type			
	Total (N=4937)	*Pfizer/Biontech (N=3048)*	*AstraZeneca (N=517)*	*Moderna (N=1225)*	*Unknown/other (N=147)*
Any concomitant disease N (%)	3591 (72.7)	2464 (80.8)	173 (33.5)	846 (69.1)	108 (73.5)
Any medications taken in the last 24 hours N (%)	3795 (76.9)	2558 (83.9)	237 (45.8)	885 (72.2)	115 (78.2)

Enrolment Progress

Figure 2 shows the current status of participants in the study at the date of most recent data extract. The first participant was enrolled 13 weeks ago. The majority of participants in the Pfizer vaccine group have been under follow-up for at least 4 weeks, whereas most of those in the Moderna group have been under follow-up for less than 4 weeks.

Figure 2 Current status of participants



Outcomes

Primary outcome – only data from the SSI available

Until the threshold for MPNAT has been established we will present the results from both the ELISA (Wantai) and the multiantigen serological test including the Receptor Binding Domain (RBD), and the complete Spike(S) protein. Data from the ELISA (wantai) are presented as negative, positive and inconclusive (see methods for categorization) and from the multiantigen serological tests the geometric mean and 95% confidence intervals (CI) for the neutralizing antibody titer (NAb) levels at each study visit will be reported in future reports.

Table 4 Presence of antibodies at study visit, ELISA (Wantai) from SSI

		Vaccine type			
	Total (N=4937)	*Pfizer/Biontech (N=3048)*	*AstraZeneca (N=517)*	*Moderna (N=1225)*	*Unknown/other (N=147)*
Number of persons with antibody data at enrollment (% of total)	3392 (68.7)	2476 (81.2)	503 (97.3)	302 (24.7)	111 (75.5)
Wantia result at enrollment					
Negative	3246 (95.7)	2399 (96.9)	449 (89.3)	291 (96.4)	107 (96.4)
Positive	145 (4.3)	76 (3.1)	54 (10.7)	11 (3.6)	4 (3.6)
Inconclusive	1 (0.0)	1 (0.0)	0	0	0

Secondary outcome – data not yet available will be included in future reports

The secondary outcome, of breakthrough infections is monitored in two different ways. The number of participants testing positive for SARS-CoV-19, as reported via MiBa, and by serological monitoring (detection of SARS-CoV-2 nucleocapsid antibodies). The number of participants experiencing these outcomes will be reported in table 5.

Table 5 Number of participants experiencing break through infection and hospitalisation due to COVID-19

	Overall	**Pfizer/BionTech**	**Moderna**	**AstraZeneca**	**Other**
	N (%)	N (%)	N (%)	N (%)	N (%)
Number of participants with break through infection					
Number testing positive for SARS-CoV-2 reported via M					
Number with SARS_CoV-2 nucleocapis					

antibodies detected					
Time to breakthrough infection (median, IQR)					
Age group					
<65					
65-74					
75-79					
80-84					
≥85					
Sex					
Male					
Female					
Number admitted to hospital due to COVID-19					
Time to hospitalisation (median, IQR)					
Age group					
<65					
65-74					
75-79					
80-84					
≥85					
Sex					
Male					
Female					

Safety Monitoring

Local and systemic reactions

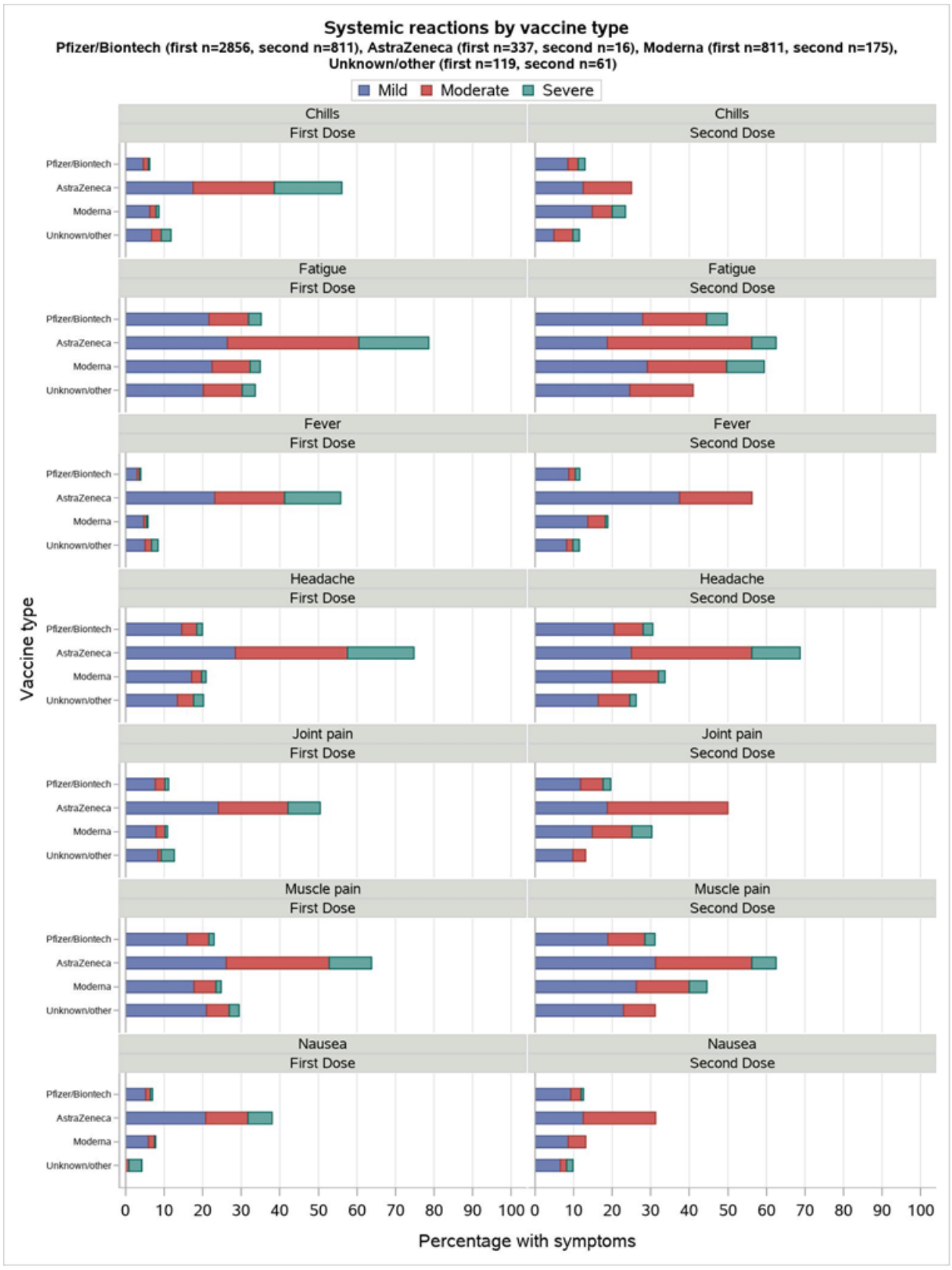
Table 6 outlines the number of participants reporting any local or systemic reactions within 7 days of vaccination. Note that participants can report multiple symptoms. The percentages are out of the total number of participants who had completed the symptoms form at the time of data extraction. All participants are encouraged to complete the form even if they experience no symptoms.

Figure 3 three shows the proportion reporting mild, moderate or severe symptoms by vaccine type. To further illustrate the symptoms reported by participant demographics Figures 4- 6 show the proportion reporting mild, moderate or severe symptoms by each vaccine separately stratified by age group (<55years, 55-65 years and >65 years) and Figures 7-9 stratified by gender.

Table 6 Number & percent reporting local/systemic reactions within 7 days post vaccination overall all and by vaccination

	Total		*Pfizer/Biontech*		*AstraZeneca*		*Moderna*		*Unknown/Other*	
	First (N=4123)	*Second (N=2021)*	*First (N=2856)*	*Second (N=1769)*	*First (N=337)*	*Second (N=16)*	*First (N=811)*	*Second (N=175)*	*First (N=119)*	*Second (N=61)*
Number of persons (%)										
Any clinical symptoms	2249 (54.5)	1271 (62.9)	1439 (50.4)	1096 (62.0)	307 (91.1)	12 (75.0)	434 (53.5)	128 (73.1)	69 (58.0)	35 (57.4)
Any local symptoms at injection site	3020 (73.2)	1464 (72.4)	1978 (69.3)	1257 (71.1)	305 (90.5)	13 (81.3)	655 (80.8)	145 (82.9)	82 (68.9)	49 (80.3)

*Figure 3 Percentage of participants reporting systemic and local symptoms following **1st dose and 2nd dose** of the vaccine, by vaccine type*



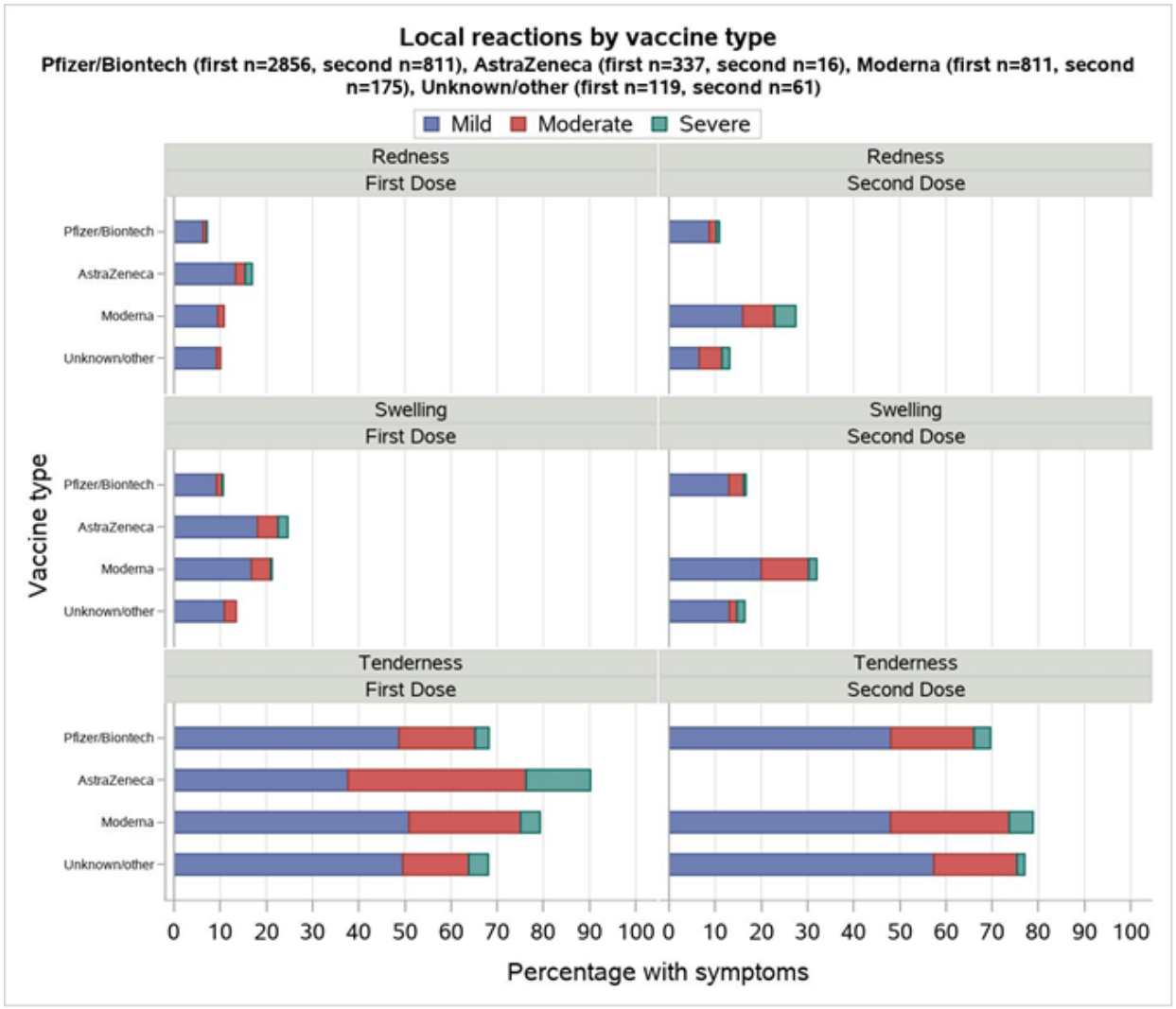

Local reactions by vaccine type
Pfizer/Biontech (first n=2856, second n=811), AstraZeneca (first n=337, second n=16), Moderna (first n=811, second n=175), Unknown/other (first n=119, second n=61)
Mild
Moderate
Severe
Redness
First Dose
Redness
Second Dose
Swelling
First Dose
Swelling
Second Dose
Tenderness
First Dose
Tenderness
Second Dose
Vaccine type
Pfizer/Biontech
AstraZeneca
Moderna
Unknown/other
0 10 20 30 40 50 60 70 80 90 100
Percentage with symptoms

*Figure 4 Percentage of participants reporting systemic and local symptoms following **1st and 2nd dose** of Pfizer/Biontech, by age group*

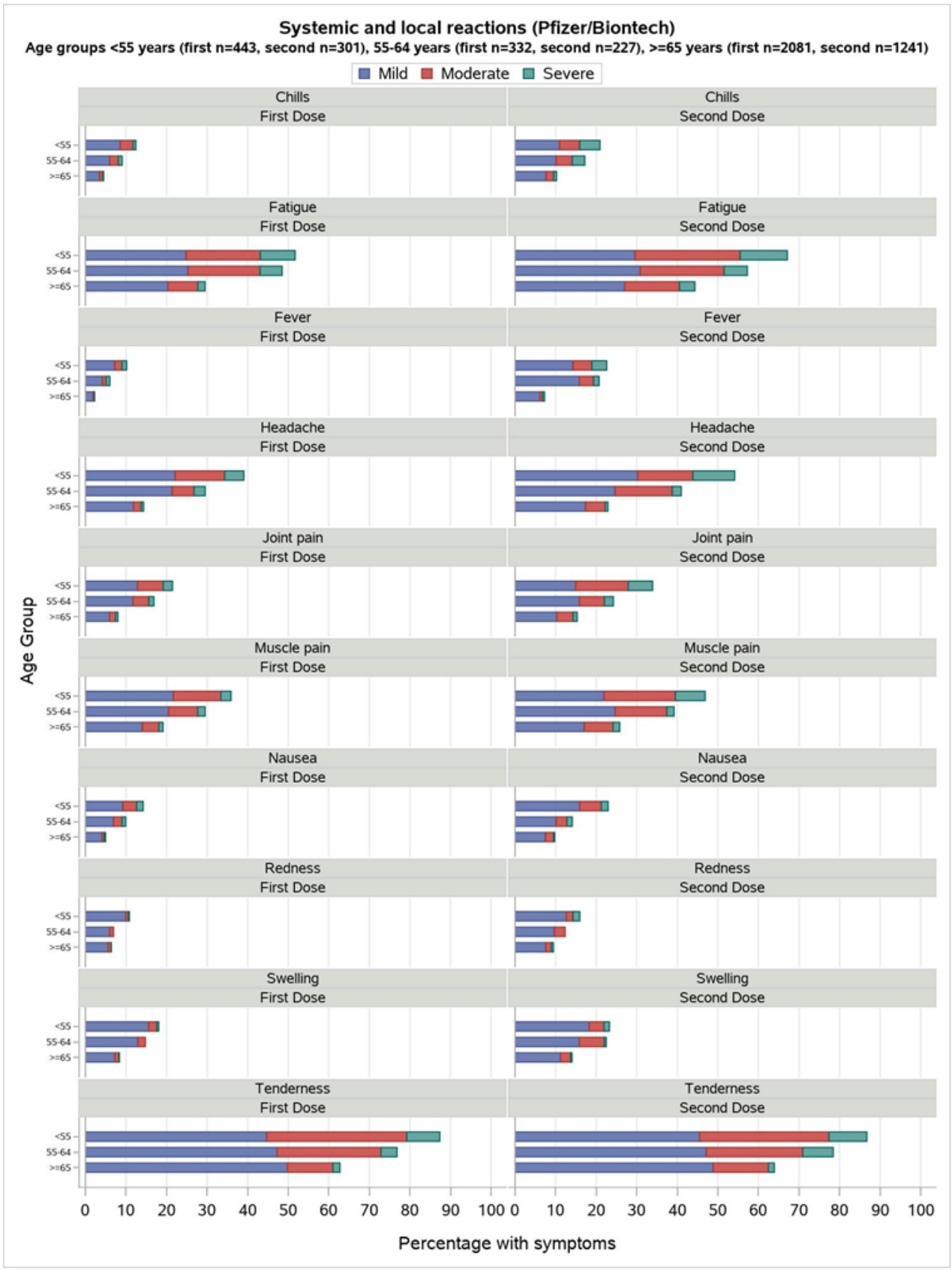


*Figure 5 Percentage of participants reporting systemic and local symptoms following **1st & 2nd dose** of AstraZeneca, by age group. Data not shown due to the small numbers in some age groups.*

Figure 6 Percentage of participants reporting systemic and local symptoms following 1st dose & 2nd dose of Moderna, by age group.

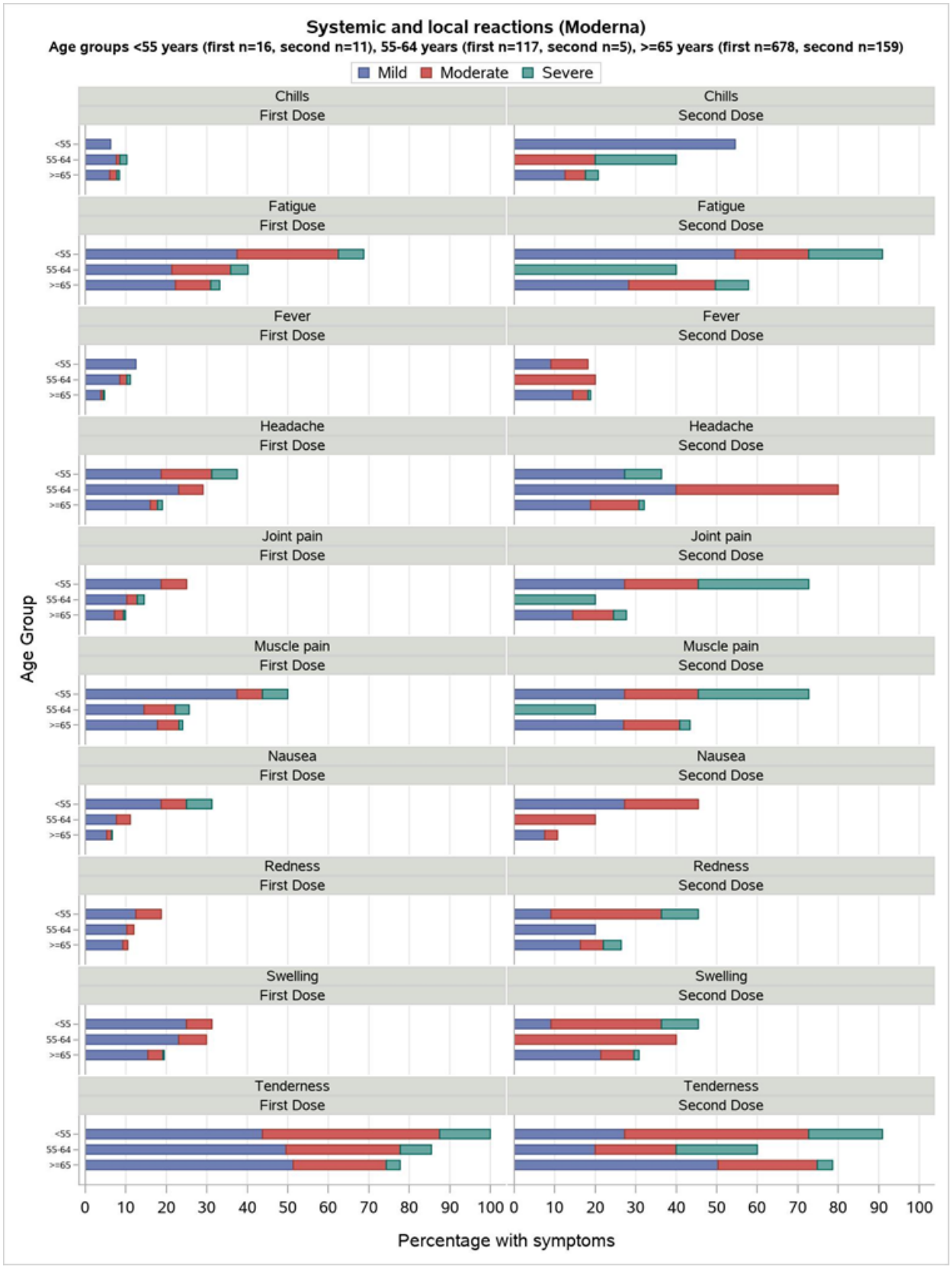


*Figure 7 Percentage of participants reporting systemic and local symptoms following **1st & 2nd dose** of Pfizer/Biontech, by gender*

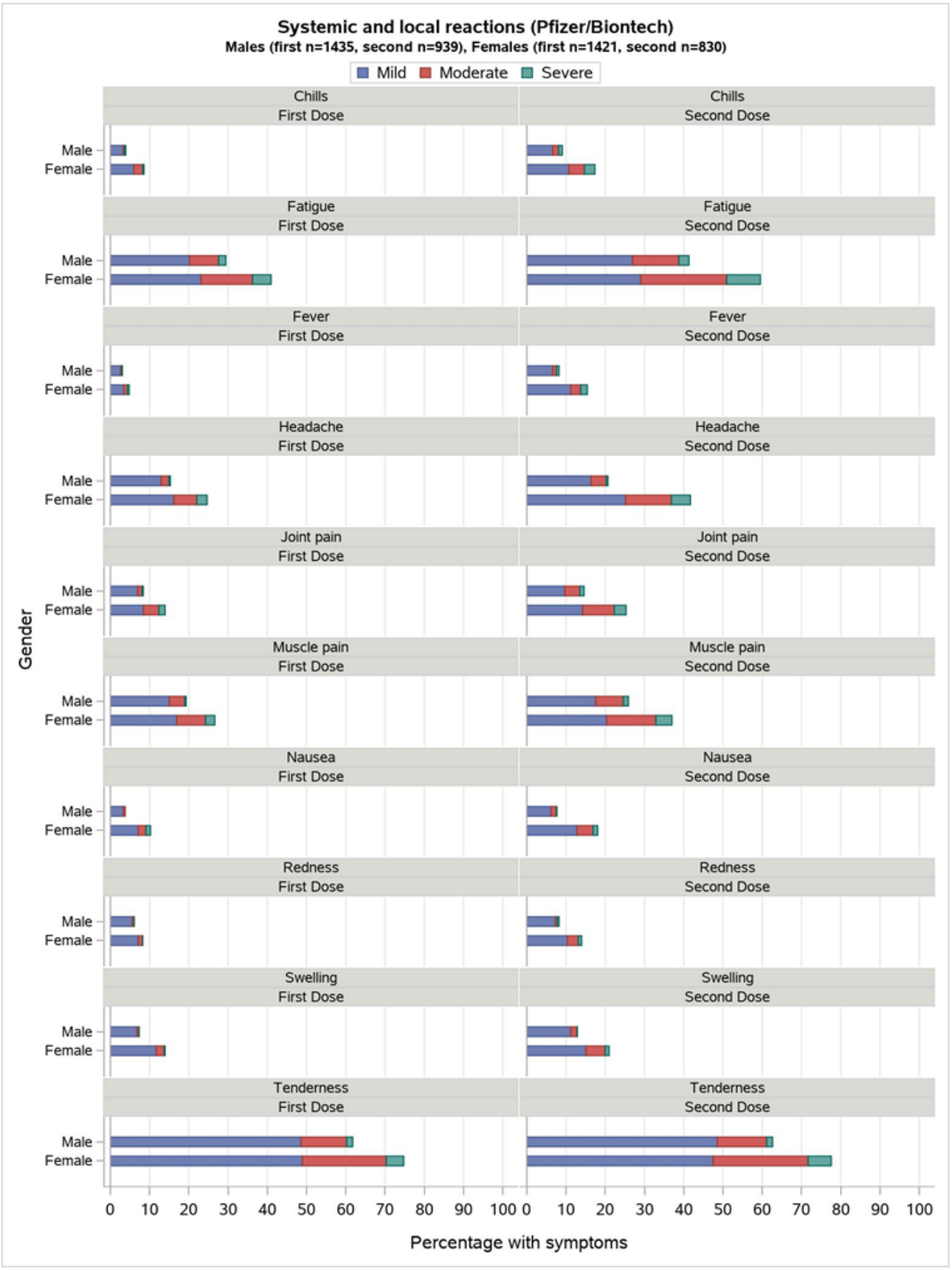


*Figure 8 Percentage of participants reporting systemic and local symptoms following **1st dose** of AstraZeneca, by gender. Data on second dose not shown due to the small numbers*

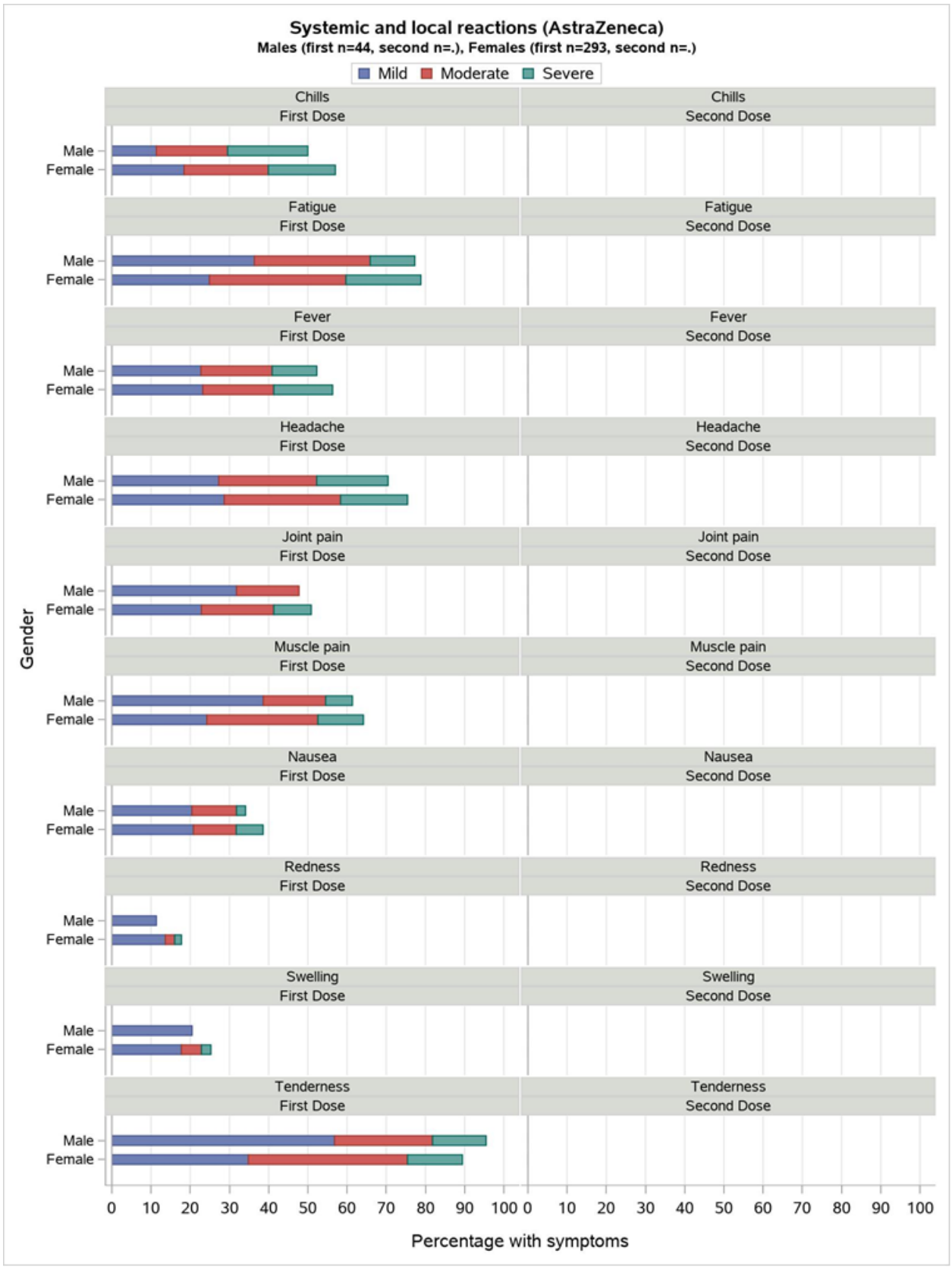
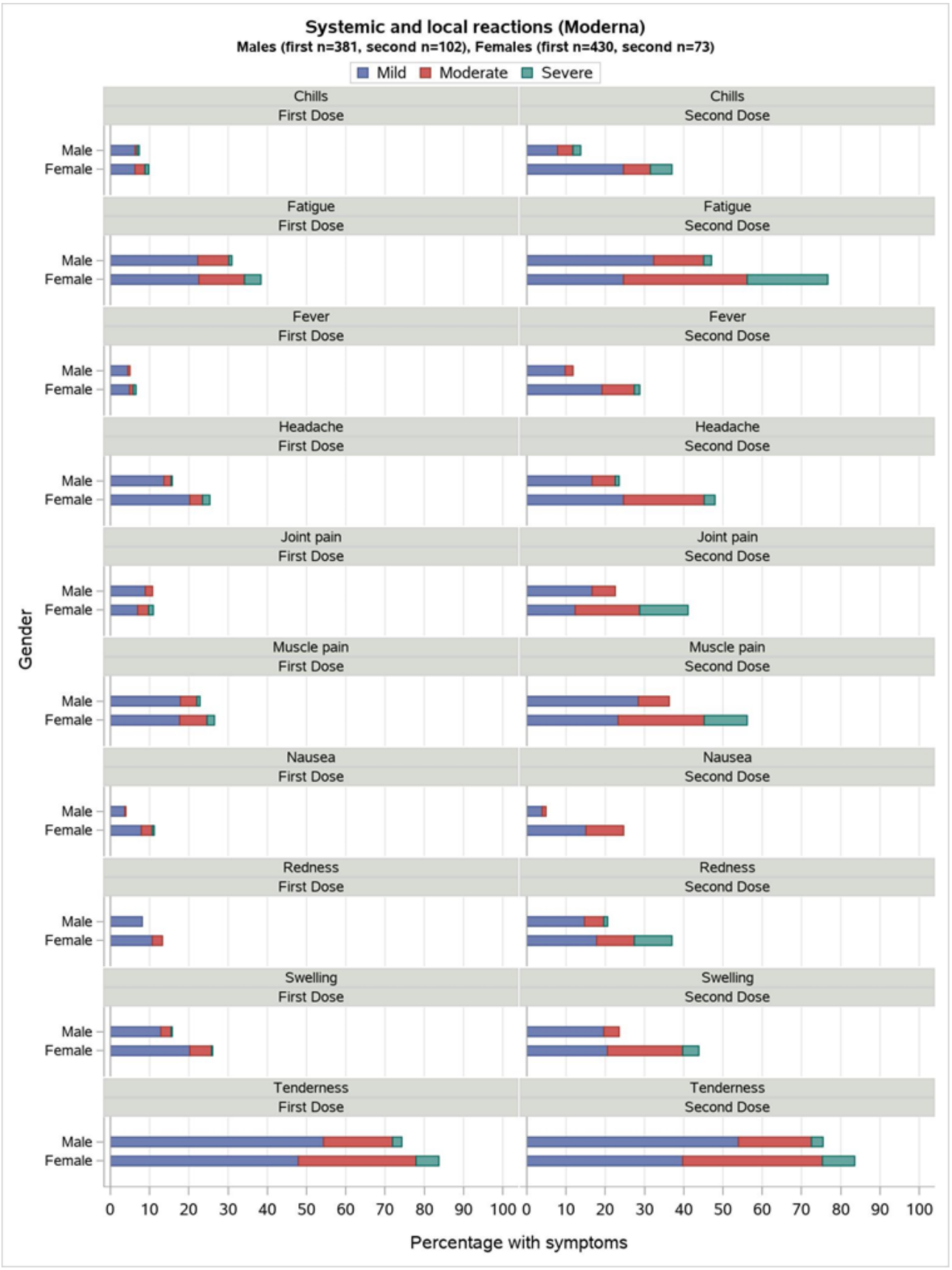


*Figure 9 Percentage of participants reporting systemic and local symptoms following **1st dose and 2nd dose** of Moderna, by gender.*



Adverse and Serious Adverse Events

This section gives an overview of the AE (table 7) and SAE (table 8) reported in the study thus far. The data are first shown overall and by vaccine type

Table 7 Overview of AE (grade 3 and 4) reported by vaccine

		Vaccine type			
	Total (N=4937)	*Pfizer/Biontech (N=3048)*	*AstraZeneca (N=517)*	*Moderna (N=1225)*	*Unknown/other (N=147)*
At least one Adverse Event reported (N, % of total)	141 (2.9)	110 (3.6)	13 (2.5)	12 (1.0)	6 (4.1)
Total number of AE reported (N, % of AE)	173 (100)	134 (100)	16 (100)	12 (100)	11(100)

Table 8 Overview of SAEs reported by vaccine

		Vaccine type			
	Total (N=4937)	*Pfizer/Biontech (N=3048)*	*AstraZeneca (N=517)*	*Moderna (N=1225)*	*Unknown/other (N=147)*
Total number of participants reporting any SAE (N, %)	26 (0.5)	20 (0.7)	<5*	<5*	<5*
Total number of SAE reported (N, % of SAE)	31 (100)	24 (100)	<5*	<5*	<5*

*Exact numbers not shown due to small numbers

Deaths

There have been <5 deaths reported in the study thus far and none had a reasonable probability of relatedness to vaccination.