bijwerkingen centrumlareb

Overview of Bell's palsy associated with COVID-19 vaccines

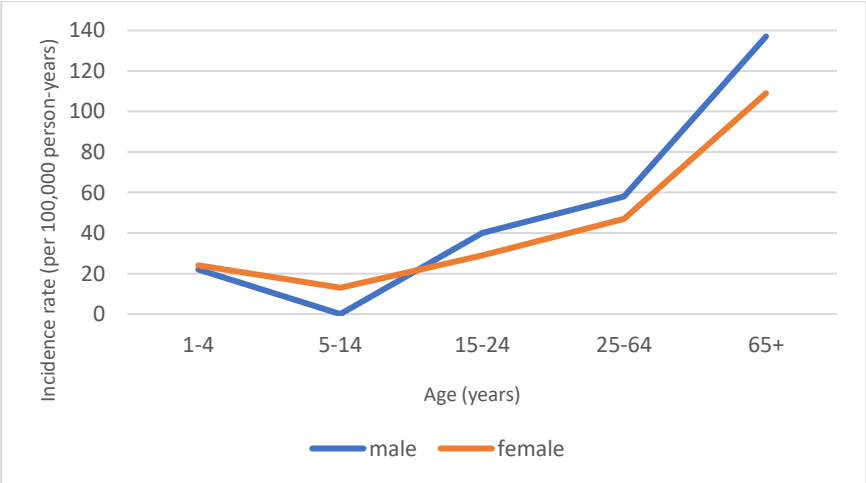
Introduction

Idiopathic peripheral facial paralysis or Bell's palsy has been acknowledged as rare adverse drug reaction (ADR) of the mRNA vaccines for active immunization against COVID-19 manufactured by Pfizer/BioNTech (Comirnaty) and Moderna (Spikevax), as well as the vector vaccine manufactured by AstraZeneca (Vaxzevria). The updated Summaries of Product Characteristics (SmPCs) of these vaccines mention the occurrence of Bell's palsy during the safety follow-up periods. For the Pfizer/BioNTech vaccine this concerned four participants in the vaccine group, and none in the placebo group [1]. Following vaccination with the AstraZeneca vaccine, five cases were reported and no cases in the group receiving a placebo [2]. After administration of the Moderna vaccine three participants in the vaccine group and one participant in the placebo group developed peripheral facial paralysis during the safety follow-up [3]. For the vector vaccine by Janssen (JCOVDEN) and the S-protein subunit vaccine by Novavax (Nuvaxovid), idiopathic facial paralysis, or Bell's palsy, is not labelled as an ADR [4, 5].

Bell's palsy is characterized as an acute unilateral paresis or paralysis of the face as a result of 7th cranial nerve dysfunction [6]. The clinical diagnosis is based on exclusion of other etiologies. It is however suggested that viral infections (e.g. Herpes Simplex, Herpes Zoster) or reactivation thereof may act as a trigger in part of the Bell's palsy cases [7]. Other potential causes of facial paralysis include trauma, autoimmune diseases, otitis media and malignancies [8].
The peak incidence is in the second to fifth decade of life [8]. The incidence rate of Bell's palsy in The Netherlands is about 20-30 per 100,000 person-years. Among children under 15 years the incidence is estimated at 2-3 per 100,000 person-years [9]. Figure 1 shows stratified background incidence rates in The Netherlands as registered in the Dutch healthcare data systems (i.e. hospitals, general practitioners) in 2019 [10].

This overview provides insight on characteristics of the spontaneous case reports of Bell's palsy in the Netherlands following COVID-19 vaccinations. A comparison of observed cases in relation to the expected background incidence rates is included, stratified per gender and age group in order to highlight the occurrence in different population subgroups including children and adolescents.

Figure 1. Background incidence rates of Bell's palsy in The Netherlands, in 2019. Data are based on PHARMO registration data from hospitals and general practitioners in 2019, stratified by age groups and sex (male/female) and counted per 100.000 person-years [10].



Reports

Until March 24th 2022, The Netherlands Pharmacovigilance Centre Lareb received 301 unique individual case safety reports of Bell's palsy, facial paralysis or facial paresis following vaccination with COVID-19 vaccines manufactured by Pfizer/BioNTech, Moderna, AstraZeneca and Janssen. These cases are all referred to as Bell's palsy in this overview. No cases following vaccination with Novavax were reported. In 10 reports the patient was diagnosed with transient ischemic attack or cerebrovascular accident. Since these

cases of facial paralysis were not considered of peripheral origin they were excluded from further analysis. Characteristics of the remaining 291 reports are summarized in Table 1.

	Total		Pfizer/BioNTech (Comirnaty)		Moderna (Spikevax)		AstraZeneca (Vaxzevria)		Janssen (JCOVDEN)	
Reports (N, %)	291	(100%)	191	(65.6%)	39	(13.4%)	21	(13.7%)	21	(7.2%)
Reported by (N, %)										
- Healthcare professionals	77	(26.5%)	47	(24.6%)	9	(23.1%)	12	(30.0%)	9	(42.9%)
- Consumers	214	(73.5%)	144	(75.4%)	30	(76.9%)	28	(70.0%)	12	(57.1%)
Serious* (N, %)	29	(10.0%)	17	(8.9%)	3	(7.7%)	7	(17.5%)	2	(9.5%)
Gender (N, %)										
- male	119	(40.9%)	74	(38.7%)	15	(38.5%)	16	(40.0%)	14	(66.7%)
- female	172	(59.1%)	117	(61.3%)	24	(61.5%)	24	(60.0%)	7	(33.3%)
Age, mean+range (years)										
- male	51.7	(12-94)	52.4	(12-94)	49.3	(22-73)	59.0	(38-63)	42.4	(18-61)
- female	51.6	(17-88)	53.5	(17-88)	44.3	(20-72)	50.6	(21-65)	47.7	(34-54)
Dose (N, %)										
- first	168	(57.7%)	104	(54.5%)	14	(35.9%)	29	(72.5%)	21	(100%)
- second	107	(36.8%)	79	(41.4%)	17	(43.6%)	11	(27.5%)	n.a.	
- third	16	(5.5%)	8	(4.2%)	8	(20.5%)	n.a.		n.a.	
Time to onset, mean+range (days)										
- first dose	11.4	(0-152.5)	8.7	(0-152.5)	8.5	(0-31)	16.5	(0-129)	20.1	(0-126)
- second dose	17.9	(0-190)	17.4	(0-190)	12.4	(0-68)	30.3	(0-180)	n.a.	
- third dose	8.0	(0.2-39)	7.3	(1-13)	8.7	(0.2-39)	n.a.		n.a.	
Time to onset, median+IQR (days)										
- first dose	5	(1-14.5)	3	(0.9-11)	2	(0.5-13.8)	10	(4-19)	13.5	(4-21.3)
- second dose	5	(1-20)	5	(1-20.5)	7	(2-14)	5	(1.3-17)	n.a.	
- third dose	6	(1.5-9)	7	(6-9)	2	(1-9.5)	n.a.		n.a.	
Medical history (N, %)										
- COVID-19**	35	(12.0%)	21	(7.2%)	8	(2.7%)	4	(1.4%)	2	(0.7%)
- infection ≤ 30 days prior***	13	(4.5%)	11	(3.8%)	1	(0.3%)	0		1	(0.3%)
- Bell's palsy	11	(3.8%)	9	(3.1%)	0		2	(0.7%)	0	
- after previous COVID-19 vaccination	2	(0.7%)	2	(0.7%)	0		0		0	

Table 1. Report characteristics of Bell's palsy associated with COVID-19 vaccines in The Netherlands. The selection of reports was based on MedDRA terminology including the Preferred Terms (PT) Bell's palsy, Facial paralysis and Facial paresis. * Seriousness based on CIOMS criteria, including hospitalization, life-threatening situation, death, disabling or invalidating, congenital anomaly, other medically important condition; ** Proven or suspected COVID-19 infection in medical history at any time before suspect vaccination; *** Patient had an infection ≤ 30 days prior to administration of suspect vaccine (i.e. Herpes simplex, Herpes zoster, otitis media, Lyme's disease or COVID-19).

The majority of reports concerned the Pfizer/BioNTech vaccine. This vaccine has been used most frequently in The Netherlands and is applied for all age groups. 27% of the reports were submitted by healthcare professionals. 10% of the reports were considered serious according to the CIOMS criteria, including hospitalization, disabling or other medically important condition.
Overall, more females than males developed Bell's palsy after vaccination (59%), however for the Janssen vaccine more males were affected (67%). The mean age of the patients who received the Janssen vaccine was lower as well (42.2 and 47.7 years for males and females, respectively) compared to the other vaccine brands, which is coherent with the use of this vaccine for younger age groups. The overall mean age of the patients for all vaccine brands was 51.7 years with a range of 12-94 years. Figure 2 illustrates the age distribution in males and females per vaccine brand.

The majority of reports concerned a first or second dose (58% and 37%, respectively), whereas few cases of Bell's palsy were reported after a third dose. The mean time to onset was 13.6 days with a wide range (0-190). The median was 5 days (IQR 1-15), indicating that the majority of times-to-onset had a relatively short latency within one or two weeks, whereas a limited number of reported cases had a latency of several weeks to months (Figure 3).

12% of all patients had a proven or suspected COVID-19 infection at any time before the suspect vaccination. An active infection or infection within 30 days prior to administration of the vaccine was reported in 13 cases. These infections included Herpes simplex, Herpes zoster, otitis media, Lyme's disease and COVID-19. Furthermore, 1 patient had a schwannoma as a possible confounding factor.
11 patients had Bell's palsy in their medical history, 2 of whom as an adverse event of a prior COVID-19 vaccination.

Figure 2. Age distribution of Bell's palsy reports for males and females per COVID-19 vaccine.

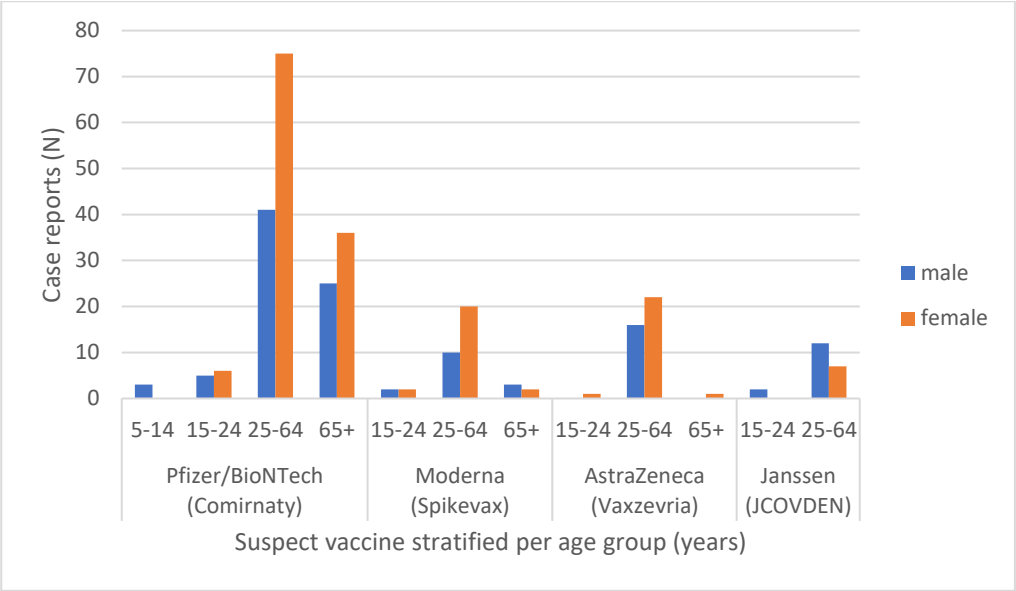
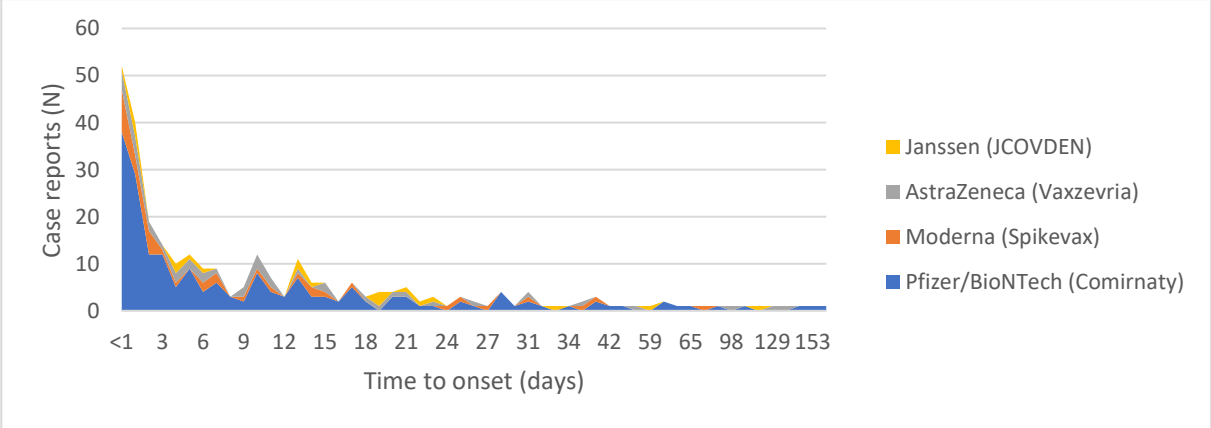


Figure 3. Distribution of times to onset of Bell's palsy reports per COVID-19 vaccine.



Comparison with background incidence

For calculating observed-over-expected ratios, the SMR (standardized morbidity rate) was used, which uses reported cases as observed (O) and background incidence rates applied to a certain vaccinated population as expected cases (E). Background incidence rates of Bell's palsy were determined by PHARMO, based on hospital and general practitioners' registration data from 2019 (Figure 1).

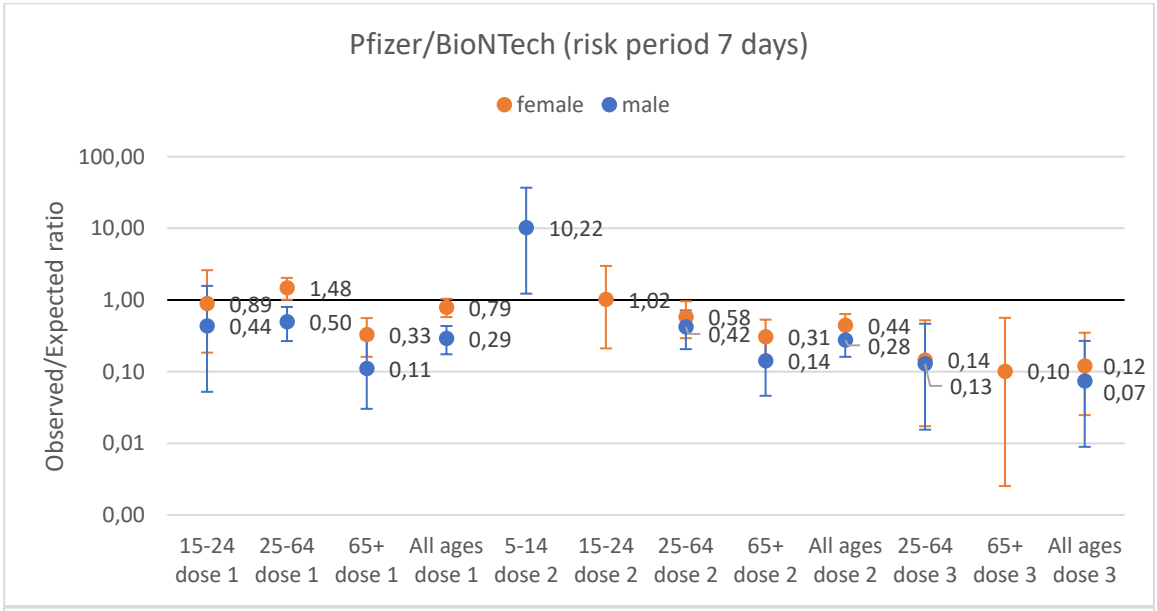
Stratified vaccine exposure data until March 7th 2022 were obtained from the CIMS database of RIVM for men and women per vaccine, dose and age [11]. For the calculations, reports received until March 24th with vaccination dates until March 10th (for risk period of 14 days) and March 17th (for risk period of 7 days) were taken into account, as well as times to onset up to 7 and 14 days respectively. Hence, cases with longer latencies were not included. A minor difference in vaccine exposures for the period between March 7th and

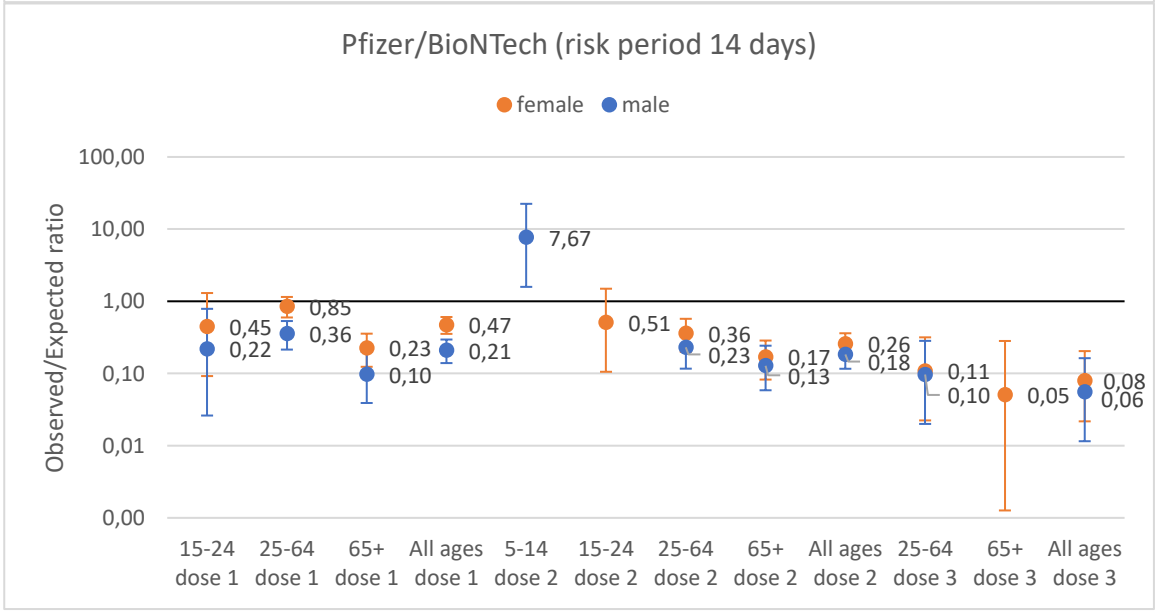
March 17th was considered acceptable, since the vaccination campaign was coming to an end and the number of administered vaccines was low [12].
The following formulas were used in calculating SMRs:

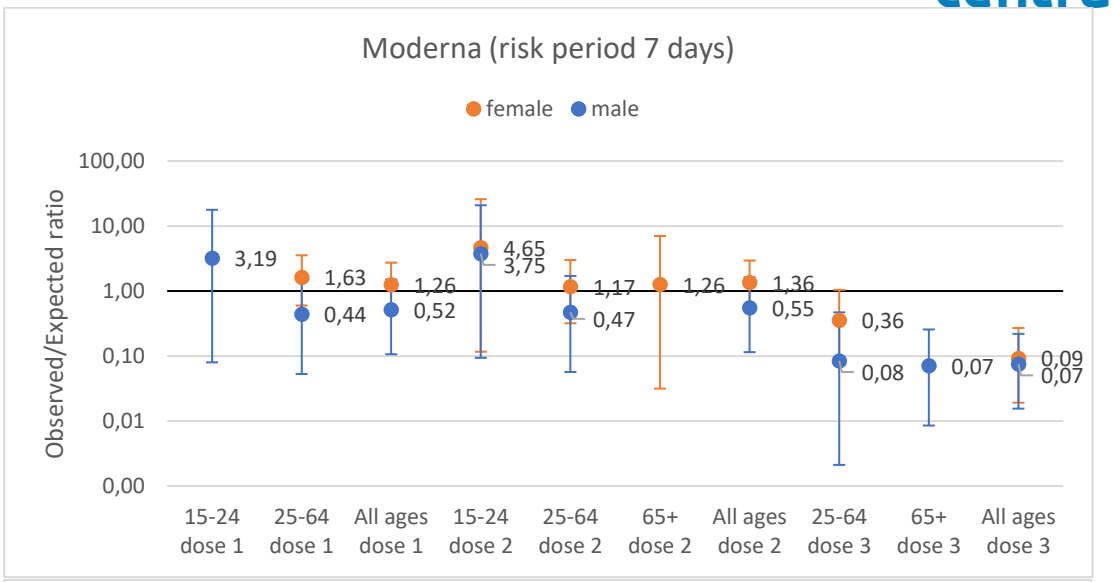
- E = ($N_{events\ in\ PHARMO}$ / $N_{person\ years\ in\ PHARMO}$)*(risk period (days)/365)*$N_{vaccine\ exposure}$
- SMR = O / E
- 95% confidence intervals: $\sqrt{((\sum(O -/+1)^2)}$ / $\sum E$; using Poisson distribution tables for low numbers of O (<10)

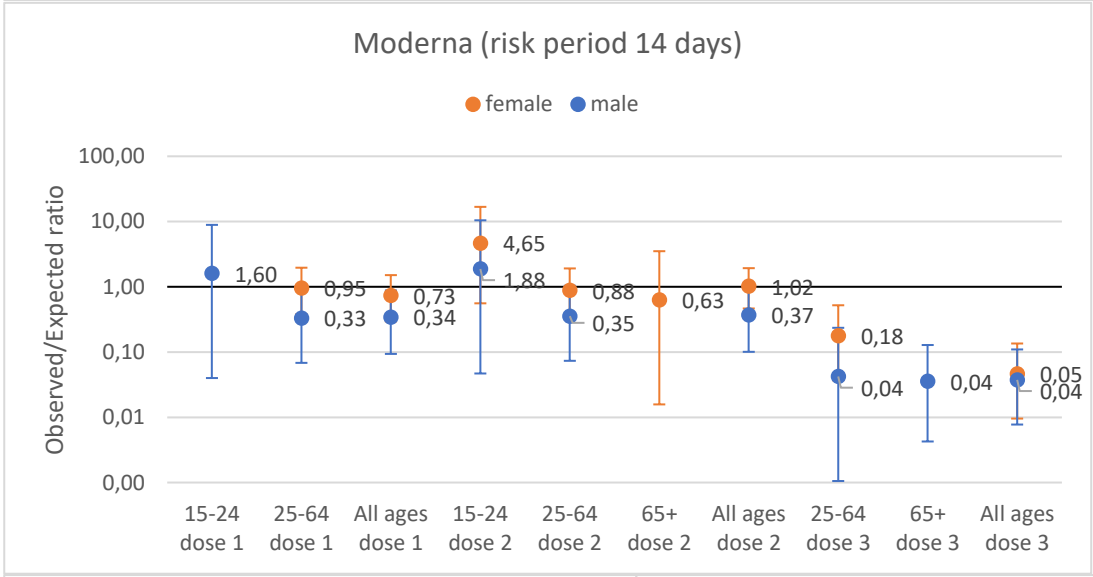
The results are summarized in Figure 4.

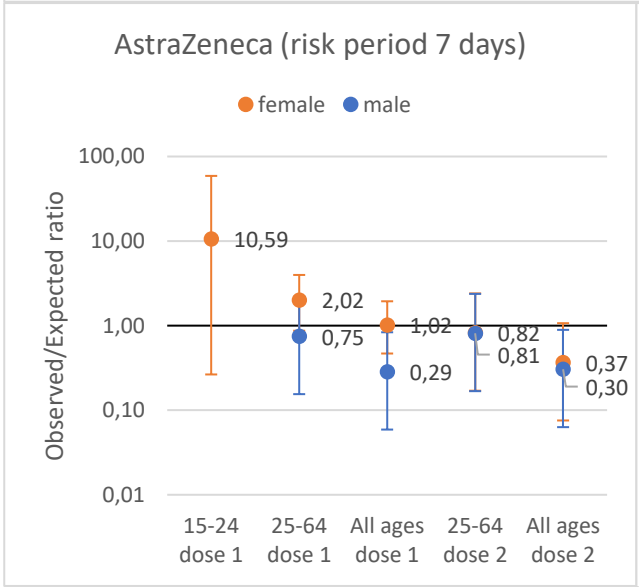
Figure 4: Observed over expected ratios (OE) of Bell's palsy reports per COVID-19 vaccine for risk periods 7 and 14 days, stratified per dose and age group for men and women. The scale is semi-logarithmic. Data points are not shown if there are no cases in a subgroup (OE = 0). If OE ratio > 1, the number of reported cases exceeds the expected number based on background incidence. The error bars show the range of the lower and upper limits of the 95% confidence intervals. More details are available in Appendix A.

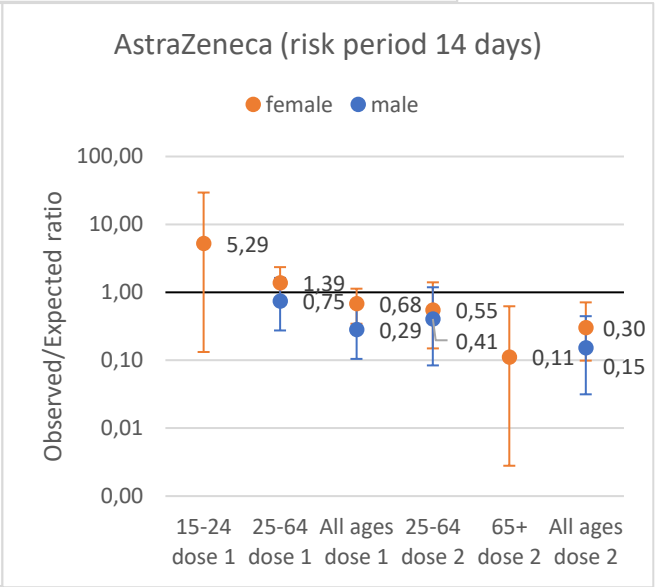


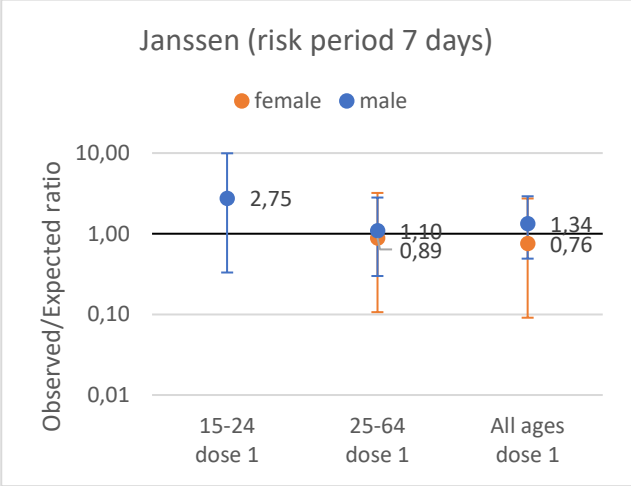


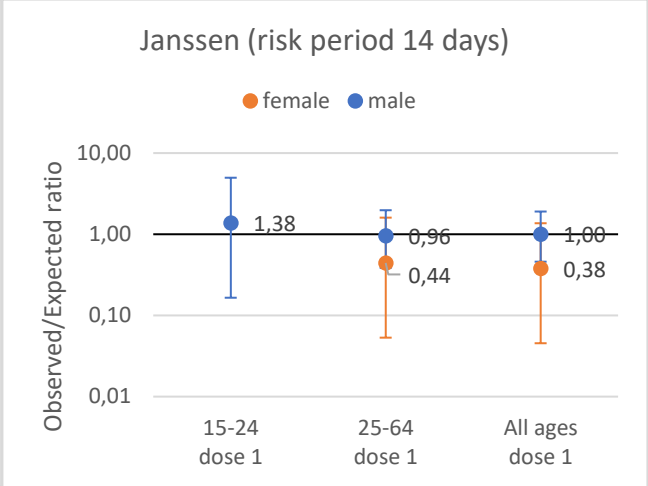

Moderna (risk period 7 days)
female
male
Observed/Expected ratio
100,00
10,00
1,00
0,10
0,01
0,00
3,19
1,63
0,44
1,26
0,52
4,65
3,75
1,17
0,47
1,26
1,36
0,55
0,36
0,08
0,07
0,09
0,07
15-24 dose 1
25-64 dose 1
All ages dose 1
15-24 dose 2
25-64 dose 2
65+ dose 2
All ages dose 2
25-64 dose 3
65+ dose 3
All ages dose 3


Moderna (risk period 14 days)
female
male
Observed/Expected ratio
100,00
10,00
1,00
0,10
0,01
0,00
1,60
0,95
0,33
0,73
0,34
4,65
1,88
0,88
0,35
0,63
1,02
0,37
0,18
0,04
0,04
0,05
0,04
15-24 dose 1
25-64 dose 1
All ages dose 1
15-24 dose 2
25-64 dose 2
65+ dose 2
All ages dose 2
25-64 dose 3
65+ dose 3
All ages dose 3


AstraZeneca (risk period 7 days)
female
male
Observed/Expected ratio
100,00
10,00
1,00
0,10
0,01
10,59
2,02
0,75
1,02
0,29
0,82
0,81
0,37
0,30
15-24 dose 1
25-64 dose 1
All ages dose 1
25-64 dose 2
All ages dose 2


AstraZeneca (risk period 14 days)
female
male
Observed/Expected ratio
100,00
10,00
1,00
0,10
0,01
0,00
5,29
1,39
0,75
0,68
0,29
0,55
0,41
0,11
0,30
0,15
15-24 dose 1
25-64 dose 1
All ages dose 1
25-64 dose 2
65+ dose 2
All ages dose 2





Overall, high numbers of reports on Bell's palsy were received regarding administration of all four COVID-19 vaccines. Stratified by age, the observed number of reports of boys of 5-14 years after receiving a second dose of Pfizer/BioNTech was higher than expected with a OE ratio of 10.22 (1.23-36.90) and 7.67 (1.58-22.41) for risk periods of 7 and 14 days respectively. In addition, the observed over expected ratio for this vaccine in women aged 15-24 years was 1.02 (0.21-2.99) after dose 2, and 1.48 (1.01-2.04) in women aged 25-64 years after dose 1 (risk periods 7 days) (Figure 4; Appendix A).

Despite the low absolute number of reports in some strata, it is notable that when weighed for all ages in a population, high SMRs were observed, in several cases exceeding 1. Regarding the Moderna vaccine, women of 15-24 and 25-64 developed Bell's palsy more often than expected, with weighed SMRs of 1.26 (0.46-2.73) and 1.36 (0.50-2.95) after the first and second dose, respectively, when a risk period of 7 days was applied. For AstraZeneca the observed reports in both men and women were high in the ages of 25-64. The weighed SMR for all women after the first dose was 1.02 (0.47-1.94; risk period 7 days). Furthermore, men of ages 15-24 and 25-64 who received the Janssen vaccine had high observed over expected ratios, with weighed SMRs of 1.34 (0.49-2.91) and 1.00 (0.46-1.90) for all men for risk periods of 7 and 14 days, respectively.

Other sources of information

Literature

A population-based observed over expected study conducted in Israel suggested an increased risk for developing Bell's palsy after administration of the Pfizer/BioNTech vaccine. The incidence rates were highest in older age groups (45-64 and ≥65 years) after the first and second doses, especially in women of these ages. The OE rate in ages 16-44 were 1.06 (0.68-1.57) for men and 1.22 (0.80-2.10) for females after the first dose, with a weighed SMR for all ages and sexes of 1.36 (1.14-1.61) after dose 1. Risk periods of 21 days were applied. A varying distribution of times to onset was observed when including latencies up to 21 days after the first dose. Latencies after the second dose were similar, with slightly more cases in the first week. Furthermore, it was suggested that there is a higher risk of developing Bell's palsy after the first vaccine dose [13].

A self-reporting database study in the USA conducted by VAERS indicated a significantly high reporting rate of facial nerve palsy in individuals ≥ age 18 years after administration of COVID-19 mRNA vaccines with reporting odds ratios (RORs) of 1.84 (95% CI 1.65-2.06) and 1.54 (95% CI 1.39-1.70) for the Pfizer/BioNTech and Moderna vaccines, respectively [14]. A 2-month case control study at the emergency department of a tertiary referral center in Israel did not observe an association between recent Pfizer/BioNTech vaccination and risk of facial nerve palsy. As the inclusion of patients was however dependent on referral patterns, a possible bias exists [15].

Multiple case studies indicating a potential causal relationship between Bell's palsy and COVID-19 vaccines have been reported. After administration of the Pfizer/BioNTech vaccine this concerned, among others, 1) a 37-year-old male developing idiopathic facial palsy 5 days after the first dose [16], 2) a 21-year-old female diagnosed with Bell's palsy 2 days after the first dose [17], 3) sequential facial nerve palsies after the first and second doses in a 61-year old male [18], and 4) a 50-year-old male with no relevant medical history, 9

days after the first dose [19]. For Moderna, case reports have been published of Bell's palsy in 1) a 34-year-old woman with a previous episode of Bell's palsy during pregnancy, 2 days after vaccination [20], and 2) a 36-year-old male 24 hours after receiving the second dose [21]. In addition, a case report of Bell's palsy in a 62-year-old female 20 days after administration of the Janssen vaccine was published [22].

Aside from the latter case report regarding the Janssen vaccine, literature on Bell's palsy associated with COVID-19 vaccines other than the mRNA vaccines is rather scarce. However, in addition to the association with COVID-19 vaccines, multiple case reports and literature reviews indicate an association with other vaccines as well, including influenza and meningococcal conjugate vaccines [23, 24]. It is implied that Bell's palsy could be a potential AEFI for vaccines in general [25].

Mechanism

In addition to the temporal relationship (outliers excluded) in the onset of Bell's palsy indicating an association with COVID-19 vaccination, a mechanism is proposed by which the vaccines could induce this reaction. This involves the elicited type 1 interferon production as a result of activation of the innate immune response [26]. In many vaccines, including the adenovector vaccines, presence of additive adjuvants are responsible for initiating this immunomodulatory response, however, in the mRNA vaccines lacking adjuvants it is thought that the combined effect of mRNA and lipids induce interferon production [15].

Several arguments are made to support the plausibility of the role of type 1 interferon in the pathogenesis of vaccine-induced Bell's palsy. First, type 1 interferons regulate lymphocyte recirculation and can thereby cause transient lymphopenia [27]. It has been recognized in phase 1 clinical trials that mRNA vaccines can induce transient lymphopenia, while decreased CD3 and CD4 lymphocyte levels have been reported during the acute stage of Bell's palsy as well [26, 28]. In addition, facial nerve palsy has been reported as potential rare complication of interferon-α therapy (a type 1 interferon). It is suggested that interferon-α causes decreased tolerance towards myelin sheath antigens, resulting in neuropathy [26, 29]. Meanwhile, other sources also proposed that an autoimmune reaction against a myelin sheath protein could be involved in the pathogenesis of Bell's palsy [30]. Considering the role of autoimmune phenomena in the onset of Bell's palsy, several other mechanisms by which vaccines can act as a trigger have been suggested, including molecular mimicry of host molecules and bystander activation of dormant autoreactive T-cells [24].

Discussion and conclusions

Report characteristics

Considering the pandemic, a previously experienced COVID-19 infection among patients was possible. 12% of the patients reported to have had a suspected or proven previous COVID-19 infection at any time before vaccination, however asymptomatic infections could have been overlooked. Although the questionnaire explicitly informed on whether the patient had a previous COVID-19 infection, the presence of any other infection may not have been reported in all cases and can therefore not be ruled out. 13 patients indicated to have had an infection either simultaneously or shortly (≤ 30 days) before the vaccination, concerning Herpes simplex, Herpes zoster, Lyme's disease, otitis media or COVID-19 infections. Although infections have been suggested as potential trigger for Bell's palsy, there is no definite consensus, hence presence of an infection was not considered an exclusion criterium for this study. With regard to patients' medical history, potential comorbidities such as diabetes or hypertension are mentioned in the literature [31], however presence of these specific medical conditions were not asked for in the questionnaire and were therefore not always known in our case reports. While selecting for Bell's palsy cases, all reports of PT Bell's palsy as well as facial paresis and facial paralysis were included in the analysis. Whereas Bell's palsy per definition has a peripheral cause, facial paresis or paralysis can have both a central and peripheral origin. Cases in which cerebral vascular accidents were co-reported were therefore excluded from this overview.

The time to onset of Bell's palsy following vaccination in literature case reports varies, however latencies of several days have been mentioned often. The times to onset in our reports are relatively short as well, especially considering that in some cases the time of diagnosis rather than the time of onset of the first symptoms may have been reported and furthermore, time may have passed to exclude alternative etiologies prior to the diagnosis. A limited number of reported cases had a latency of multiple weeks to months. As the latency increases, causality with the vaccine becomes more questionable. With a median time to onset of 5 days (IQR 1-15), the latencies in our received reports differ from the cases mentioned in the SmPCs of the vaccines for which Bell's palsy is labelled as adverse event. As such, the SmPC of the Moderna vaccine describes that the cases of facial paralysis observed during the safety follow-up period had an onset of 22, 28, and 32 days after dose 2 [3]. During the safety follow-up of the Pfizer/BioNTech vaccine, peripheral

facial paralysis occurred on day 37 after dose 1 and days 3, 9, and 48 after dose 2 [1]. Following the AstraZeneca vaccine participants developed facial paralysis with an onset of 8 and 15 days after the first dose and 4, 17, and 25 days after the second dose [2]. Our overview thereby provides novel insight on the temporal course of development of Bell's palsy following COVID-19 vaccination.

Contrary to the suggestion in literature regarding a higher risk to develop Bell's Palsy after the first dose [13], our reports did not indicate a clear distinction in the numbers of cases after either the first or second dose. The number of cases following the Pfizer/BioNTech and AstraZeneca vaccines was slightly higher after the first dose compared to the second dose, whereas for Moderna a few more reports were received after the second dose. A relatively small number of reports concerned a third or booster vaccine. Two cases of sequential recurrence of Bell's palsy after COVID-19 vaccination were reported, a phenomenon which has been described in a literature case report as well [18].

Considerations regarding the Observed over Expected method

In the calculations of the observed over expected ratios and SMRs, the background incidence and vaccine exposure were corrected for. Considering that in the majority of received reports the event occurred within the first weeks, risk periods of 7 and 14 days after each vaccine dose were applied. Thereby, reports with longer latencies were excluded from the calculations. Applying a risk period of 30 days provided a similar pattern of outcomes, however with lower OE ratios due to a minimal change in the number of observed reports, whereas the exposure increased to a larger extent. Hence, these data are not included in this overview. Furthermore, using a broader risk period is prone to underreporting as patients or health care professionals are less likely to associate the event with the vaccine as the latency increases. The occurrence of underreporting is nonetheless inevitable in a spontaneous reporting system and cannot be corrected for in observed over expected calculations. It is therefore likely that the number of observed cases is underestimated.

Since infections are a potential cause of Bell's palsy as well, the COVID-19 pandemic may have influenced the incidence. As a consequence, the used background incidence rates from 2019 may differ from subsequent years. The low absolute number of reports, partly due to the age stratification, reduced statistical certainty for some age groups. Considering the weighed SMR for all ages however, a ratio of 1 was still exceeded in several populations (male or female) for Moderna, AstraZeneca and Janssen.

The results of the observed over expected analysis show that Bell's palsy has been reported more frequently than expected in several subgroups of patients for all four COVID-19 vaccines (Pfizer/BioNTech, Moderna, AstraZeneca and Janssen), including children and adolescents. Among children a high OE ratio was found for boys aged 5-14 years after receiving the Pfizer/BioNTech vaccine (this was the only brand appointed for this age group in The Netherlands), while the general incidence in young children is very low [9]. Regarding adolescents and young adults, women aged 15-24 years receiving Pfizer/BioNTech and Moderna, and men aged 15-24 years receiving Janssen developed Bell's palsy more often than expected. Furthermore, OE ratios were high for the age groups 25-64, regarding females receiving Pfizer, Moderna and AstraZeneca and males receiving Janssen. As Bell's palsy has not been labelled as adverse event for the Janssen vaccine, the results on this vaccine brand are especially noteworthy. Whereas an Israeli study described high numbers of reports in particularly older age groups (45-64 and ≥65 years) [13], the absolute number of received reports as well as the OE ratios in our results for the subgroups aged 65+ were less pronounced. Although the results imply a potential association of Bell's palsy with all four COVID-19 vaccines, the causality cannot be entirely confirmed nor ruled out using merely data from a spontaneous case reporting system. Additional research is needed to elucidate the risks with more certainty. The association between the Janssen vaccine and Bell's palsy warrants further investigation.

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This signal has been raised on July 11, 2022. It is possible that in the meantime other information became available. For the latest information, including the official SmPC's, please refer to website of the MEB www.cbg-meb.nl

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Supplements

Appendix A: Detailed observed-over-expected (SMR) calculations for Bell's palsy per COVID-19 vaccine and risk period (7 and 14 days).

Risk period / TTO 7 days	N reports Observed	N persons vaccine exposed	N Events - 1 yr PHARMO	N pyrs PHARMO	Expected	Obs/Exp (# O > E=0)	SMR	LL 95%CI (* O<10 with poisson table)	UL 95%CI (* O<10 with poisson table)	
PFIZER/BIONTECH										
Female 1-4 (dose 1)	0	0	3	12,304	0.00					
Female 5-14 (dose 1)	0	143,955	5	38,434	0.36					
Female 15-24 (dose 1)	3	609,223	13	45,112	3.37	0.89		0.18	2.60	*
Female 25-64 (dose 1)	33	2,502,377	97	208,425	22.33	1.48		1.01	2.04	
Female 65+ (dose 1)	11	1,598,403	97	89,232	33.32	0.33		0.16	0.56	
Female total (dose 1)	**47**	**4,853,958**	**215**	**393,507**	**59.38**		**0.79**	**0.58**	**1.04**	
Male 1-4 (dose 1)	0	0	3	13,402	0.00					
Male 5-14 (dose 1)	0	155,749	4	40,975	0.29					
Male 15-24 (dose 1)	2	602,360	17	42,803	4.59	0.44		0.05	1.57	*
Male 25-64 (dose 1)	14	2,512,235	114	195,419	28.11	0.50		0.27	0.80	
Male 65+ (dose 1)	4	1,374,299	106	77,596	36.00	0.11		0.03	0.28	*
Male total (dose 1)	**20**	**4,644,643**	**244**	**370,195**	**68.99**		**0.29**	**0.17**	**0.43**	
Male/Female 1-4 (dose 1)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 1)	0	299,704	9	79,409	0.65					
Male/Female 15-24 (dose 1)	5	1,211,583	30	87,915	7.93	0.63		0.20	1.47	*
Male/Female 25-64 (dose 1)	47	5,014,612	211	403,844	50.25	0.94		0.68	1.23	
Male/Female 65+ (dose 1)	15	2,972,702	203	166,828	69.37	0.22		0.12	0.34	
Male/Female total (dose 1)	**67**	**9,498,601**	**459**	**763,702**	**128.20**		**0.52**	**0.40**	**0.66**	
Female 1-4 (dose 2)	0	0	3	12,304	0.00					
Female 5-14 (dose 2)	0	96,791	5	38,434	0.24					
Female 15-24 (dose 2)	3	531,047	13	45,112	2.93	1.02		0.21	2.99	*
Female 25-64 (dose 2)	12	2,323,720	97	208,425	20.74	0.58		0.29	0.96	
Female 65+ (dose 2)	10	1,562,689	97	89,232	32.58	0.31		0.14	0.53	
Female total (dose 2)	**25**	**4,514,247**	**215**	**393,507**	**56.49**		**0.44**	**0.28**	**0.64**	
Male 1-4 (dose 2)	0	0	3	13,402	0.00					
Male 5-14 (dose 2)	2	104,506	4	40,975	0.20	10.22		1.23	36.90	*
Male 15-24 (dose 2)	0	519,372	17	42,803	3.96					
Male 25-64 (dose 2)	11	2,325,885	114	195,419	26.02	0.42		0.21	0.72	
Male 65+ (dose 2)	5	1,343,013	106	77,596	35.18	0.14		0.05	0.33	*
Male total (dose 2)	**18**	**4,292,776**	**244**	**370,195**	**65.36**		**0.28**	**0.16**	**0.42**	
Male/Female 1-4 (dose 2)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 2)	2	201,297	9	79,409	0.44	4.57		0.55	16.50	*
Male/Female 15-24 (dose 2)	3	1,050,419	30	87,915	6.87	0.44		0.09	1.28	*
Male/Female 25-64 (dose 2)	23	4,649,605	211	403,844	46.59	0.49		0.31	0.72	
Male/Female 65+ (dose 2)	15	2,905,702	203	166,828	67.81	0.22		0.12	0.35	
Male/Female total (dose 2)	**43**	**8,807,023**	**459**	**763,702**	**121.71**		**0.35**	**0.25**	**0.47**	
Female 1-4 (dose 3)	0	0	3	12,304	0.00					
Female 5-14 (dose 3)	0	0	5	38,434	0.00					
Female 15-24 (dose 3)	0	246,297	13	45,112	1.36					
Female 25-64 (dose 3)	2	1,551,080	97	208,425	13.84	0.14		0.02	0.52	*
Female 65+ (dose 3)	1	473,415	97	89,232	9.87	0.10		0.00	0.56	*
Female total (dose 3)	**3**	**2,270,792**	**215**	**393,507**	**25.07**		**0.12**	**0.02**	**0.35**	*
Male 1-4 (dose 3)	0	0	3	13,402	0.00					
Male 5-14 (dose 3)	0	0	4	40,975	0.00					
Male 15-24 (dose 3)	0	224,610	17	42,803	1.71					
Male 25-64 (dose 3)	2	1,384,530	114	195,419	15.49	0.13		0.02	0.47	*
Male 65+ (dose 3)	0	370,116	106	77,596	9.70					
Male total (dose 3)	**2**	**1,979,256**	**244**	**370,195**	**26.90**		**0.07**	**0.01**	**0.27**	*
Male/Female 1-4 (dose 3)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 3)	0	0	9	79,409	0.00					
Male/Female 15-24 (dose 3)	0	470,907	30	87,915	3.08					
Male/Female 25-64 (dose 3)	4	2,935,610	211	403,844	29.42	0.14		0.04	0.35	*
Male/Female 65+ (dose 3)	1	843,531	203	166,828	19.68	0.05		0.00	0.28	*
Male/Female total (dose 3)	**5**	**4,250,048**	**459**	**763,702**	**52.18**		**0.10**	**0.03**	**0.22**	*

Risk period / TTO 14 days	N reports Observed	N persons vaccine exposed	N Events - 1 yr PHARMO	N pyrs PHARMO	Expected	Obs/Exp (# O > E=0)	SMR	LL 95%CI (* O<10 with poisson table)	UL 95%CI (* O<10 with poisson table)	
PFIZER/BIONTECH										
Female 1-4 (dose 1)	0	0	3	12,304	0.00					
Female 5-14 (dose 1)	0	143,955	5	38,434	0.72					
Female 15-24 (dose 1)	3	609,223	13	45,112	6.73	0.45		0.09	1.30	*
Female 25-64 (dose 1)	38	2,502,377	97	208,425	44.67	0.85		0.60	1.15	
Female 65+ (dose 1)	15	1,598,403	97	89,232	66.65	0.23		0.12	0.36	
Female total (dose 1)	**56**	**4,853,958**	**215**	**393,507**	**118.77**		**0.47**	**0.35**	**0.61**	
Male 1-4 (dose 1)	0	0	3	13,402	0.00					
Male 5-14 (dose 1)	0	155,749	4	40,975	0.58					
Male 15-24 (dose 1)	2	602,360	17	42,803	9.18	0.22		0.03	0.79	*
Male 25-64 (dose 1)	20	2,512,235	114	195,419	56.21	0.36		0.21	0.53	
Male 65+ (dose 1)	7	1,374,299	106	77,596	72.01	0.10		0.04	0.20	*
Male total (dose 1)	**29**	**4,644,643**	**244**	**370,195**	**137.98**		**0.21**	**0.14**	**0.30**	
Male/Female 1-4 (dose 1)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 1)	0	299,704	9	79,409	1.30					
Male/Female 15-24 (dose 1)	5	1,211,583	30	87,915	15.86	0.32		0.10	0.74	*
Male/Female 25-64 (dose 1)	58	5,014,612	211	403,844	100.49	0.58		0.44	0.74	
Male/Female 65+ (dose 1)	22	2,972,702	203	166,828	138.74	0.16		0.10	0.23	
Male/Female total (dose 1)	**85**	**9,498,601**	**459**	**763,702**	**256.40**		**0.33**	**0.26**	**0.41**	
Female 1-4 (dose 2)	0	0	3	12,304	0.00					
Female 5-14 (dose 2)	0	96,791	5	38,434	0.48					
Female 15-24 (dose 2)	3	531,047	13	45,112	5.87	0.51		0.11	1.49	*
Female 25-64 (dose 2)	15	2,323,720	97	208,425	41.48	0.36		0.20	0.57	
Female 65+ (dose 2)	11	1,562,689	97	89,232	65.16	0.17		0.08	0.29	
Female total (dose 2)	**29**	**4,514,247**	**215**	**393,507**	**112.99**		**0.26**	**0.17**	**0.36**	
Male 1-4 (dose 2)	0	0	3	13,402	0.00					
Male 5-14 (dose 2)	3	104,506	4	40,975	0.39	7.67		1.58	22.41	*
Male 15-24 (dose 2)	0	519,372	17	42,803	7.91					
Male 25-64 (dose 2)	12	2,325,885	114	195,419	52.04	0.23		0.12	0.38	
Male 65+ (dose 2)	9	1,343,013	106	77,596	70.37	0.13		0.06	0.24	*
Male total (dose 2)	**24**	**4,292,776**	**244**	**370,195**	**130.72**		**0.18**	**0.12**	**0.27**	
Male/Female 1-4 (dose 2)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 2)	3	201,297	9	79,409	0.88	3.43		0.71	10.02	*
Male/Female 15-24 (dose 2)	3	1,050,419	30	87,915	13.75	0.22		0.05	0.64	*
Male/Female 25-64 (dose 2)	27	4,649,605	211	403,844	93.18	0.29		0.19	0.41	
Male/Female 65+ (dose 2)	20	2,905,702	203	166,828	135.62	0.15		0.09	0.22	
Male/Female total (dose 2)	**53**	**8,807,023**	**459**	**763,702**	**243.42**		**0.22**	**0.16**	**0.28**	
Female 1-4 (dose 3)	0	0	3	12,304	0.00					
Female 5-14 (dose 3)	0	0	5	38,434	0.00					
Female 15-24 (dose 3)	0	246,297	13	45,112	2.72					
Female 25-64 (dose 3)	3	1,551,080	97	208,425	27.69	0.11		0.02	0.32	*
Female 65+ (dose 3)	1	473,415	97	89,232	19.74	0.05		0.00	0.28	*
Female total (dose 3)	**4**	**2,270,792**	**215**	**393,507**	**50.15**		**0.08**	**0.02**	**0.20**	*
Male 1-4 (dose 3)	0	0	3	13,402	0.00					
Male 5-14 (dose 3)	0	0	4	40,975	0.00					
Male 15-24 (dose 3)	0	224,610	17	42,803	3.42					
Male 25-64 (dose 3)	3	1,384,530	114	195,419	30.98	0.10		0.02	0.28	*
Male 65+ (dose 3)	0	370,116	106	77,596	19.39					
Male total (dose 3)	**3**	**1,979,256**	**244**	**370,195**	**53.79**		**0.06**	**0.01**	**0.16**	*
Male/Female 1-4 (dose 3)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 3)	0	0	9	79,409	0.00					
Male/Female 15-24 (dose 3)	0	470,907	30	87,915	6.16					
Male/Female 25-64 (dose 3)	6	2,935,610	211	403,844	58.83	0.10		0.04	0.22	*
Male/Female 65+ (dose 3)	1	843,531	203	166,828	39.37	0.03		0.00	0.14	*
Male/Female total (dose 3)	**7**	**4,250,048**	**459**	**763,702**	**104.36**		**0.07**	**0.03**	**0.14**	*

Risk period / TTO 7 days	N reports Observed	N persons vaccine exposed	N Events - 1 yr PHARMO	N pyrs PHARMO	Expected	Obs/Exp (# O > E=0)	SMR	LL 95%CI (* O<10 with poisson table)	UL 95%CI (* O<10 with poisson table)	
MODERNA										
Female 1-4 (dose 1)	0	0	3	12,304	0.00					
Female 5-14 (dose 1)	0	12	5	38,434	0.00					
Female 15-24 (dose 1)	0	44,463	13	45,112	0.25					
Female 25-64 (dose 1)	6	412,036	97	208,425	3.68	1.63		0.60	3.55	*
Female 65+ (dose 1)	0	40,940	97	89,232	0.85					
Female total (dose 1)	**6**	**497,451**	**215**	**393,507**	**4.78**		**1.26**	**0.46**	**2.73**	*
Male 1-4 (dose 1)	0	0	3	13,402	0.00					
Male 5-14 (dose 1)	0	16	4	40,975	0.00					
Male 15-24 (dose 1)	1	41,101	17	42,803	0.31	3.19		0.08	17.79	*
Male 25-64 (dose 1)	2	406,003	114	195,419	4.54	0.44		0.05	1.59	*
Male 65+ (dose 1)	0	36,898	106	77,596	0.97					
Male total (dose 1)	**3**	**484,018**	**244**	**370,195**	**5.82**		**0.52**	**0.11**	**1.51**	*
Male/Female 1-4 (dose 1)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 1)	0	28	9	79,409	0.00					
Male/Female 15-24 (dose 1)	1	85,564	30	87,915	0.56	1.79		0.04	9.95	*
Male/Female 25-64 (dose 1)	8	818,039	211	403,844	8.20	0.98		0.42	1.92	*
Male/Female 65+ (dose 1)	0	77,838	203	166,828	1.82					
Male/Female total (dose 1)	**9**	**981,469**	**459**	**763,702**	**10.57**		**0.85**	**0.39**	**1.62**	*
Female 1-4 (dose 2)	0	0	3	12,304	0.00					
Female 5-14 (dose 2)	0	22	5	38,434	0.00					
Female 15-24 (dose 2)	1	38,901	13	45,112	0.21	4.65		0.12	25.91	*
Female 25-64 (dose 2)	4	382,894	97	208,425	3.42	1.17		0.32	3.00	*
Female 65+ (dose 2)	1	38,054	97	89,232	0.79	1.26		0.03	7.02	*
Female total (dose 2)	**6**	**459,871**	**215**	**393,507**	**4.43**		**1.36**	**0.50**	**2.95**	*
Male 1-4 (dose 2)	0	0	3	13,402	0.00					
Male 5-14 (dose 2)	0	16	4	40,975	0.00					
Male 15-24 (dose 2)	1	34,991	17	42,803	0.27	3.75		0.09	20.90	*
Male 25-64 (dose 2)	2	377,813	114	195,419	4.23	0.47		0.06	1.71	*
Male 65+ (dose 2)	0	34,861	106	77,596	0.91					
Male total (dose 2)	**3**	**447,681**	**244**	**370,195**	**5.41**		**0.55**	**0.11**	**1.62**	*
Male/Female 1-4 (dose 2)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 2)	0	38	9	79,409	0.00					
Male/Female 15-24 (dose 2)	2	73,892	30	87,915	0.48	4.14		0.50	14.93	*
Male/Female 25-64 (dose 2)	6	760,707	211	403,844	7.62	0.79		0.29	1.71	*
Male/Female 65+ (dose 2)	1	72,915	203	166,828	1.70	0.59		0.01	3.27	*
Male/Female total (dose 2)	**9**	**907,552**	**459**	**763,702**	**9.81**		**0.92**	**0.42**	**1.74**	*
Female 1-4 (dose 3)	0	0	3	12,304	0.00					
Female 5-14 (dose 3)	0	0	5	38,434	0.00					
Female 15-24 (dose 3)	0	471	13	45,112	0.00					
Female 25-64 (dose 3)	3	943,647	97	208,425	8.42	0.36		0.07	1.04	*
Female 65+ (dose 3)	0	1,151,921	97	89,232	24.01					
Female total (dose 3)	**3**	**2,096,039**	**215**	**393,507**	**32.44**		**0.09**	**0.02**	**0.27**	*
Male 1-4 (dose 3)	0	0	3	13,402	0.00					
Male 5-14 (dose 3)	0	0	4	40,975	0.00					
Male 15-24 (dose 3)	0	446	17	42,803	0.00					
Male 25-64 (dose 3)	1	1,058,977	114	195,419	11.85	0.08		0.00	0.47	*
Male 65+ (dose 3)	2	1,075,790	106	77,596	28.18	0.07		0.01	0.26	*
Male total (dose 3)	**3**	**2,135,213**	**244**	**370,195**	**40.03**		**0.07**	**0.02**	**0.22**	*
Male/Female 1-4 (dose 3)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 3)	0	0	9	79,409	0.00					
Male/Female 15-24 (dose 3)	0	917	30	87,915	0.01					
Male/Female 25-64 (dose 3)	4	2,002,624	211	403,844	20.07	0.20		0.05	0.51	*
Male/Female 65+ (dose 3)	2	2,227,711	203	166,828	51.99	0.04		0.00	0.14	*
Male/Female total (dose 3)	**6**	**4,231,252**	**459**	**763,702**	**72.06**		**0.08**	**0.03**	**0.18**	*

Risk period / TTO 14 days	N reports Observed	N persons vaccine exposed	N Events - 1 yr PHARMO	N pyrs PHARMO	Expected	Obs/Exp (# O > E=0)	SMR	LL 95%CI (* O<10 with poisson table)	UL 95%CI (* O<10 with poisson table)	
MODERNA										
Female 1-4 (dose 1)	0	0	3	12,304	0.00					
Female 5-14 (dose 1)	0	12	5	38,434	0.00					
Female 15-24 (dose 1)	0	44,463	13	45,112	0.49					
Female 25-64 (dose 1)	7	412,036	97	208,425	7.36	0.95		0.38	1.96	*
Female 65+ (dose 1)	0	40,940	97	89,232	1.71					
Female total (dose 1)	**7**	**497,451**	**215**	**393,507**	**9.55**		**0.73**	**0.29**	**1.51**	*
Male 1-4 (dose 1)	0	0	3	13,402	0.00					
Male 5-14 (dose 1)	0	16	4	40,975	0.00					
Male 15-24 (dose 1)	1	41,101	17	42,803	0.63	1.60		0.04	8.90	*
Male 25-64 (dose 1)	3	406,003	114	195,419	9.08	0.33		0.07	0.97	*
Male 65+ (dose 1)	0	36,898	106	77,596	1.93					
Male total (dose 1)	**4**	**484,018**	**244**	**370,195**	**11.64**		**0.34**	**0.09**	**0.88**	*
Male/Female 1-4 (dose 1)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 1)	0	28	9	79,409	0.00					
Male/Female 15-24 (dose 1)	1	85,564	30	87,915	1.12	0.89		0.02	4.97	*
Male/Female 25-64 (dose 1)	10	818,039	211	403,844	16.39	0.61		0.29	1.06	
Male/Female 65+ (dose 1)	0	77,838	203	166,828	3.63					
Male/Female total (dose 1)	**11**	**981,469**	**459**	**763,702**	**21.15**		**0.52**	**0.25**	**0.88**	
Female 1-4 (dose 2)	0	0	3	12,304	0.00					
Female 5-14 (dose 2)	0	22	5	38,434	0.00					
Female 15-24 (dose 2)	2	38,901	13	45,112	0.43	4.65		0.56	16.79	*
Female 25-64 (dose 2)	6	382,894	97	208,425	6.83	0.88		0.32	1.91	*
Female 65+ (dose 2)	1	38,054	97	89,232	1.59	0.63		0.02	3.51	*
Female total (dose 2)	**9**	**459,871**	**215**	**393,507**	**8.85**		**1.02**	**0.47**	**1.93**	*
Male 1-4 (dose 2)	0	0	3	13,402	0.00					
Male 5-14 (dose 2)	0	16	4	40,975	0.00					
Male 15-24 (dose 2)	1	34,991	17	42,803	0.53	1.88		0.05	10.45	*
Male 25-64 (dose 2)	3	377,813	114	195,419	8.45	0.35		0.07	1.04	*
Male 65+ (dose 2)	0	34,861	106	77,596	1.83					
Male total (dose 2)	**4**	**447,681**	**244**	**370,195**	**10.81**		**0.37**	**0.10**	**0.95**	*
Male/Female 1-4 (dose 2)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 2)	0	38	9	79,409	0.00					
Male/Female 15-24 (dose 2)	3	73,892	30	87,915	0.97	3.10		0.64	9.07	*
Male/Female 25-64 (dose 2)	9	760,707	211	403,844	15.24	0.59		0.27	1.12	*
Male/Female 65+ (dose 2)	1	72,915	203	166,828	3.40	0.29		0.01	1.64	*
Male/Female total (dose 2)	**13**	**907,552**	**459**	**763,702**	**19.62**		**0.66**	**0.35**	**1.08**	
Female 1-4 (dose 3)	0	0	3	12,304	0.00					
Female 5-14 (dose 3)	0	0	5	38,434	0.00					
Female 15-24 (dose 3)	0	471	13	45,112	0.01					
Female 25-64 (dose 3)	3	943,647	97	208,425	16.84	0.18		0.04	0.52	*
Female 65+ (dose 3)	0	1,151,921	97	89,232	48.03					
Female total (dose 3)	**3**	**2,096,039**	**215**	**393,507**	**64.88**		**0.05**	**0.01**	**0.14**	*
Male 1-4 (dose 3)	0	0	3	13,402	0.00					
Male 5-14 (dose 3)	0	0	4	40,975	0.00					
Male 15-24 (dose 3)	0	446	17	42,803	0.01					
Male 25-64 (dose 3)	1	1,058,977	114	195,419	23.70	0.04		0.00	0.24	*
Male 65+ (dose 3)	2	1,075,790	106	77,596	56.37	0.04		0.00	0.13	*
Male total (dose 3)	**3**	**2,135,213**	**244**	**370,195**	**80.07**		**0.04**	**0.01**	**0.11**	*
Male/Female 1-4 (dose 3)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 3)	0	0	9	79,409	0.00					
Male/Female 15-24 (dose 3)	0	917	30	87,915	0.01					
Male/Female 25-64 (dose 3)	4	2,002,624	211	403,844	40.13	0.10		0.03	0.26	*
Male/Female 65+ (dose 3)	2	2,227,711	203	166,828	103.97	0.02		0.00	0.07	*
Male/Female total (dose 3)	**6**	**4,231,252**	**459**	**763,702**	**144.12**		**0.04**	**0.02**	**0.09**	*

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Risk period / TTO 7 days	N reports Observed	N persons vaccine exposed	N Events - 1 yr PHARMO	N pyrs PHARMO	Expected	Obs/Exp (# O > E=0)	SMR	LL 95%CI (* O<10 with poisson table)	UL 95%CI (* O<10 with poisson table)	
ASTRAZENECA										
Female 1-4 (dose 1)	0	0	3	12,304	0.00					
Female 5-14 (dose 1)	0	9	5	38,434	0.00					
Female 15-24 (dose 1)	1	17,089	13	45,112	0.09	10.59		0.26	58.98	*
Female 25-64 (dose 1)	8	444,069	97	208,425	3.96	2.02		0.87	3.98	*
Female 65+ (dose 1)	0	227,558	97	89,232	4.74					
Female total (dose 1)	**9**	**688,725**	**215**	**393,507**	**8.80**		**1.02**	**0.47**	**1.94**	*
Male 1-4 (dose 1)	0	0	3	13,402	0.00					
Male 5-14 (dose 1)	0	3	4	40,975	0.00					
Male 15-24 (dose 1)	0	6,007	17	42,803	0.05					
Male 25-64 (dose 1)	3	358,030	114	195,419	4.01	0.75		0.15	2.19	*
Male 65+ (dose 1)	0	246,442	106	77,596	6.46					
Male total (dose 1)	**3**	**610,482**	**244**	**370,195**	**10.51**		**0.29**	**0.06**	**0.83**	*
Male/Female 1-4 (dose 1)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 1)	0	12	9	79,409	0.00					
Male/Female 15-24 (dose 1)	1	23,096	30	87,915	0.15	6.62		0.17	36.85	*
Male/Female 25-64 (dose 1)	11	802,099	211	403,844	8.04	1.37		0.67	2.32	
Male/Female 65+ (dose 1)	0	474,000	203	166,828	11.06					
Male/Female total (dose 1)	**12**	**1,299,207**	**459**	**763,702**	**19.25**		**0.62**	**0.32**	**1.04**	
Female 1-4 (dose 2)	0	0	3	12,304	0.00					
Female 5-14 (dose 2)	0	8	5	38,434	0.00					
Female 15-24 (dose 2)	0	15,796	13	45,112	0.09					
Female 25-64 (dose 2)	3	408,611	97	208,425	3.65	0.82		0.17	2.40	*
Female 65+ (dose 2)	0	214,243	97	89,232	4.47					
Female total (dose 2)	**3**	**638,658**	**215**	**393,507**	**8.20**		**0.37**	**0.08**	**1.07**	*
Male 1-4 (dose 2)	0	0	3	13,402	0.00					
Male 5-14 (dose 2)	0	2	4	40,975	0.00					
Male 15-24 (dose 2)	0	5,446	17	42,803	0.04					
Male 25-64 (dose 2)	3	330,010	114	195,419	3.69	0.81		0.17	2.38	*
Male 65+ (dose 2)	0	233,009	106	77,596	6.10					
Male total (dose 2)	**3**	**568,467**	**244**	**370,195**	**9.84**		**0.30**	**0.06**	**0.89**	*
Male/Female 1-4 (dose 2)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 2)	0	10	9	79,409	0.00					
Male/Female 15-24 (dose 2)	0	21,242	30	87,915	0.14					
Male/Female 25-64 (dose 2)	6	738,621	211	403,844	7.40	0.81		0.30	1.76	*
Male/Female 65+ (dose 2)	0	447,252	203	166,828	10.44					
Male/Female total (dose 2)	**6**	**1,207,125**	**459**	**763,702**	**17.98**		**0.33**	**0.12**	**0.73**	*

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Risk period / TTO 14 days	N reports Observed	N persons vaccine exposed	N Events - 1 yr PHARMO	N pyrs PHARMO	Expected	Obs/Exp (# O > E=0)	SMR	LL 95%CI (* O<10 with poisson table)	UL 95%CI (* O<10 with poisson table)	
ASTRAZENECA										
Female 1-4 (dose 1)	0	0	3	12,304	0.00					
Female 5-14 (dose 1)	0	9	5	38,434	0.00					
Female 15-24 (dose 1)	1	17,089	13	45,112	0.19	5.29		0.13	29.49	*
Female 25-64 (dose 1)	11	444,069	97	208,425	7.93	1.39		0.68	2.35	
Female 65+ (dose 1)	0	227,558	97	89,232	9.49					
Female total (dose 1)	**12**	**688,725**	**215**	**393,507**	**17.60**		**0.68**	**0.34**	**1.13**	
Male 1-4 (dose 1)	0	0	3	13,402	0.00					
Male 5-14 (dose 1)	0	3	4	40,975	0.00					
Male 15-24 (dose 1)	0	6,007	17	42,803	0.09					
Male 25-64 (dose 1)	6	358,030	114	195,419	8.01	0.75		0.27	1.63	*
Male 65+ (dose 1)	0	246,442	106	77,596	12.91					
Male total (dose 1)	**6**	**610,482**	**244**	**370,195**	**21.02**		**0.29**	**0.10**	**0.62**	*
Male/Female 1-4 (dose 1)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 1)	0	12	9	79,409	0.00					
Male/Female 15-24 (dose 1)	1	23,096	30	87,915	0.30	3.31		0.08	18.43	*
Male/Female 25-64 (dose 1)	17	802,099	211	403,844	16.07	1.06		0.61	1.63	
Male/Female 65+ (dose 1)	0	474,000	203	166,828	22.12					
Male/Female total (dose 1)	**18**	**1,299,207**	**459**	**763,702**	**38.50**		**0.47**	**0.27**	**0.71**	
Female 1-4 (dose 2)	0	0	3	12,304	0.00					
Female 5-14 (dose 2)	0	8	5	38,434	0.00					
Female 15-24 (dose 2)	0	15,796	13	45,112	0.17					
Female 25-64 (dose 2)	4	408,611	97	208,425	7.29	0.55		0.15	1.40	*
Female 65+ (dose 2)	1	214,243	97	89,232	8.93	0.11		0.00	0.62	*
Female total (dose 2)	**5**	**638,658**	**215**	**393,507**	**16.40**		**0.30**	**0.10**	**0.71**	*
Male 1-4 (dose 2)	0	0	3	13,402	0.00					
Male 5-14 (dose 2)	0	2	4	40,975	0.00					
Male 15-24 (dose 2)	0	5,446	17	42,803	0.08					
Male 25-64 (dose 2)	3	330,010	114	195,419	7.38	0.41		0.08	1.19	*
Male 65+ (dose 2)	0	233,009	106	77,596	12.21					
Male total (dose 2)	**3**	**568,467**	**244**	**370,195**	**19.68**		**0.15**	**0.03**	**0.45**	*
Male/Female 1-4 (dose 2)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 2)	0	10	9	79,409	0.00					
Male/Female 15-24 (dose 2)	0	21,242	30	87,915	0.28					
Male/Female 25-64 (dose 2)	7	738,621	211	403,844	14.80	0.47		0.19	0.97	*
Male/Female 65+ (dose 2)	1	447,252	203	166,828	20.87	0.05		0.00	0.27	*
Male/Female total (dose 2)	**8**	**1,207,125**	**459**	**763,702**	**35.95**		**0.22**	**0.10**	**0.44**	*

Risk period / TTO 7 days	N reports Observed	N persons vaccine exposed	N Events - 1 yr PHARMO	N pyrs PHARMO	Expected	Obs/Exp (# O > E=0)	SMR	LL 95%CI (* O<10 with poisson table)	UL 95%CI (* O<10 with poisson table)	
JANSSEN										
Female 1-4 (dose 1)	0	0	3	12,304	0.00					
Female 5-14 (dose 1)	0	6	5	38,434	0.00					
Female 15-24 (dose 1)	0	58,136	13	45,112	0.32					
Female 25-64 (dose 1)	2	252,550	97	208,425	2.25	0.89		0.11	3.20	*
Female 65+ (dose 1)	0	3,166	97	89,232	0.07					
Female total (dose 1)	**2**	**313,858**	**215**	**393,507**	**2.64**		**0.76**	**0.09**	**2.73**	*
Male 1-4 (dose 1)	0	0	3	13,402	0.00					
Male 5-14 (dose 1)	0	9	4	40,975	0.00					
Male 15-24 (dose 1)	2	95,369	17	42,803	0.73	2.75		0.33	9.94	*
Male 25-64 (dose 1)	4	325,994	114	195,419	3.65	1.10		0.30	2.81	*
Male 65+ (dose 1)	0	4,220	106	77,596	0.11					
Male total (dose 1)	**6**	**425,592**	**244**	**370,195**	**4.48**		**1.34**	**0.49**	**2.91**	*
Male/Female 1-4 (dose 1)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 1)	0	15	9	79,409	0.00					
Male/Female 15-24 (dose 1)	2	153,505	30	87,915	1.00	1.99		0.24	7.19	*
Male/Female 25-64 (dose 1)	6	578,544	211	403,844	5.80	1.04		0.38	2.25	*
Male/Female 65+ (dose 1)	0	7,386	203	166,828	0.17					
Male/Female total (dose 1)	**8**	**739,450**	**459**	**763,702**	**6.97**		**1.15**	**0.49**	**2.26**	*

Risk period / TTO 14 days	N reports Observed	N persons vaccine exposed	N Events - 1 yr PHARMO	N pyrs PHARMO	Expected	Obs/Exp (# O > E=0)	SMR	LL 95%CI (* O<10 with poisson table)	UL 95%CI (* O<10 with poisson table)	
JANSSEN										
Female 1-4 (dose 1)	0	0	3	12,304	0.00					
Female 5-14 (dose 1)	0	6	5	38,434	0.00					
Female 15-24 (dose 1)	0	58,136	13	45,112	0.64					
Female 25-64 (dose 1)	2	252,550	97	208,425	4.51	0.44		0.05	1.60	*
Female 65+ (dose 1)	0	3,166	97	89,232	0.13					
Female total (dose 1)	**2**	**313,858**	**215**	**393,507**	**5.28**		**0.38**	**0.05**	**1.37**	*
Male 1-4 (dose 1)	0	0	3	13,402	0.00					
Male 5-14 (dose 1)	0	9	4	40,975	0.00					
Male 15-24 (dose 1)	2	95,369	17	42,803	1.45	1.38		0.17	4.97	*
Male 25-64 (dose 1)	7	325,994	114	195,419	7.29	0.96		0.39	1.98	*
Male 65+ (dose 1)	0	4,220	106	77,596	0.22					
Male total (dose 1)	**9**	**425,592**	**244**	**370,195**	**8.97**		**1.00**	**0.46**	**1.90**	*
Male/Female 1-4 (dose 1)	0	0	6	25,706	0.00					
Male/Female 5-14 (dose 1)	0	15	9	79,409	0.00					
Male/Female 15-24 (dose 1)	2	153,505	30	87,915	2.01	1.00		0.12	3.59	*
Male/Female 25-64 (dose 1)	9	578,544	211	403,844	11.59	0.78		0.36	1.47	*
Male/Female 65+ (dose 1)	0	7,386	203	166,828	0.34					
Male/Female total (dose 1)	**11**	**739,450**	**459**	**763,702**	**13.95**		**0.79**	**0.38**	**1.34**	