The Moderna COVID-19 Vaccine’s Local Reactions, Systemic Reactions, Adverse Events, and Serious Adverse Events

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Persons Aged 6 Months – 5 Years

Local Reactions

Local reactions were reported by the majority of vaccine recipients and at higher rates than placebo recipients. Vaccine recipients reported higher rates of local reactions after dose 2 than dose 1. The frequency of local reactions was higher in the older age group (ages 2 to 5 years) than the younger age group (ages 6-23 months) (73.4% vs 54.4% after dose 2). Pain at the injection site was the most frequent and severe reported solicited local reaction among vaccine recipients. After dose 1, the older age group reported pain more frequently than the younger age group (61.4% vs 37.4%); a similar pattern was observed after dose 2 (71.4% vs 46.2%). Axillary (or groin) swelling or tenderness was the second most frequently reported local reaction. Axillary (or groin) swelling or tenderness was reported slightly more frequently in the younger age group than the older age group (9.3% vs 9.1% after dose 2). Injection site redness and swelling following either dose were reported less frequently. Redness and swelling were more common after dose 2. No grade 4 local reactions were reported. Overall, the median onset of local reactions in the vaccine group was 1 day after either dose, with a median duration of 2 days.

Table 1. Local reactions in persons ages 6-23 months, Moderna mRNA-1273 COVID-19 vaccine and placebo

	Dose 1		Dose 2	
	mRNA-1273 N=1746	**Placebo N=582**	**mRNA-1273 N=1596**	**Placebo N=526**
Redness[a], n (%)				
Any	150 (8.6)	24 (4.1)	215 (13.5)	20 (3.8)
Severe	5 (0.3)	2 (0.3)	13 (0.8)	0
Grade 4	0	0	0	0
Swelling[a] (hardness), n (%)				
Any	146 (8.4)	15 (2.6)	243 (15.2)	11 (2.1)
Severe	5 (0.3)	0	14 (0.9)	0
Grade 4	0	0	0	0
Pain at the injection site[b], n (%)				
Any	652 (37.4)	175 (30.1)	738 (46.2)	135 (25.7)
Severe	0	0	0	0
Grade 4	0	0	0	0
Axillary (or groin) swelling or tenderness[b], n (%)				
Any	102 (5.9)	26 (4.5)	148 (9.3)	28 (5.3)
Severe	0	0	0	0
Grade 4	0	0	0	0
Any local, n (%)				
Any	775 (44.4)	193 (33.2)	868 (54.4)	159 (30.2)
Severe	9 (0.5)	2 (0.3)	22 (1.4)	0
Grade 4	0	0	0	0

[a]severe: > 50 mm; Grade 4: necrosis or exfoliative dermatitis

[b]severe: prevents daily activity; Grade 4: emergency room visit or hospitalization

Table 2. Local reactions in persons ages 2 – 5 years, Moderna mRNA-1273 COVID-19 vaccine and placebo

	Dose 1		Dose 2	
	mRNA-1273 N=2957	Placebo N=970	mRNA-1273 N=2938	Placebo N=959
Redness[a], n (%)				
Any	164 (5.5)	14 (1.4)	259 (8.8)	15 (1.6)
Grade 3 or above	12 (0.4)	3 (0.3)	12 (0.4)	0
Swelling[a] (hardness), n (%)				
Any	134 (4.5)	17 (1.8)	240 (8.2)	11 (1.1)
Grade 3 or above	10 (0.3)	2 (0.2)	13 (0.4)	0
Pain at the injection site[b], n (%)				
Any	1813 (61.4)	382 (39.4)	2099 (71.4)	395 (41.2)
Grade 3 or above	4 (0.1)	0	11 (0.4)	0
Axillary (or groin) swelling or tenderness[b], n (%)				
Any	205 (6.9)	56 (5.8)	267 (9.1)	31 (3.2)
Grade 3 or above	0	0	1 (<0.1)	0
Any local, n (%)				
Any	1874 (63.4)	407 (42.0)	2157 (73.4)	404 (42.1)
Grade 3 or above	23 (0.8)	4 (0.4)	34 (1.2)	0

[a] Grade 3: > 100 mm; Grade 4: necrosis or exfoliative dermatitis

[b] Grade 3: prevents daily activity; Grade 4: emergency room visit or hospitalization for severe pain at the injection site.

Systemic Reactions

Solicited systemic adverse reactions were most common in the vaccine group than the placebo group and after dose 2 compared to dose 1. The most common solicited systemic adverse reactions after any dose were irritability/crying and fatigue for participants 6—36 months and 37 months—5 years, respectively. The majority of systemic events were mild or moderate in severity, but there was a higher occurrence of grade 3 or higher reactions in the vaccine group. Grade 4 solicited systemic adverse reactions were reported for fever (placebo: 1/585, 0.2%; vaccine: 4/1758, 0.2%) in the 6-23 months age group. There were 13 fever events >40°C reported: 11 (0.4%) participants in the vaccine group and 2 (0.2%) in the placebo group among the 2 to 5-year-old-age group. Upon further review, 3 of the 13 fever events were incorrectly reported as grade 4, given that none of these 3 participants recorded any elevated temperature resulting in 10 confirmed grade 4 fevers: 8 (0.3%) in the mRNA-1273 group and 2 (0.2%) in the placebo group in the 2-5 age group. The majority of reactions occurred within the first 2 days after dose 1 and dose 2, persisting for a median of 3 and 2 days for the 6-23 months and 2-5 age groups respectively.

Table 3. Systemic reactions in persons ages 6–23 months, Moderna mRNA-1273 COVID-19 vaccine and placebo

	Dose 1 6-23 Months		Dose 2 6-23 Months	
	mRNA-1273	Placebo	mRNA-1273	Placebo

	N=1746	N=582	N=1596	N=526
Fever[a], n (%)				
Any	191 (11.0)	49 (8.4)	232 (14.6)	44 (8.4)
Grade 3 or higher	12 (0.7)	4 (0.7)	10 (0.6)	6 (1.1)
Irritability/crying[b], n (%)				
Any	1175 (67.6)	361 (62.1)	1021 (64.3)	307 (58.5)
Grade 3 or higher	24 (1.4)	6 (1.0)	25 (1.6)	5 (1.0)
Sleepiness[b], n (%)				
Any	645 (37.1)	217 (37.3)	558 (35.1)	175 (33.3)
Grade 3 or higher	4 (0.2)	1 (0.2)	1 (<0.1)	1 (0.2)
Loss of appetite[b], n (%)				
Any	524 (30.2)	152 (26.2)	510 (32.1)	132 (25.1)
Grade 3 or higher	10 (0.6)	1 (0.2)	16 (1.0)	2 (0.4)
Any systemic event				
Any	1334 (76.4)	421 (72.3)	1174 (73.6)	350 (66.5)
Grade 3 or higher	46 (2.6)	11 (1.9)	47 (2.9)	12 (2.3)

[a]Grade for fever: Any ≥38.0°C; grade 3=39.6-40.0°C; grade 4=> 40.0°C.

[b]Grade 3: prevents daily activity; Grade 4: emergency room visit or hospitalization for severe pain at the injection site.

Table 4. Systemic reactions in persons ages 24 – 36 months, Moderna mRNA-1273 COVID-19 vaccine and placebo

	Dose 1 24-36 months		Dose 2 24-36 months	
	mRNA-1273 N=944	Placebo N=320	mRNA-1273 N=963	Placebo N=330
Fever[a], n (%)				
Any	106 (11.3)	25 (7.8)	182 (18.9)	35 (10.6)
Grade 3 or higher	6 (0.6)	4 (1.3)	15 (1.6)	0
Irritability/crying[b], n (%)				
Any	513 (54.5)	163 (51.1)	523 (54.3)	148 (44.8)
Grade 3 or higher	12 (1.3)	6 (1.9)	10 (1.0)	2 (0.6)
Sleepiness[b], n (%)				
Any	285 (30.3)	92 (28.8)	347 (36.0)	89 (27.0)
Grade 3 or higher	2 (0.2)	0	1 (0.1)	0
Loss of appetite[b], n (%)				
Any	225 (23.9)	71 (22.3)	294 (30.5)	69 (20.9)
Grade 3 or higher	7 (0.7)	1 (0.3)	8 (0.8)	0
Any systemic event				
Any	612 (65.0)	198 (61.9)	651 (67.6)	194 (58.8)
Grade 3 or higher	21 (2.2)	10 (3.1)	31 (3.2)	2 (0.6)

[a]Grade for fever: grade 3=39.6-40.0°C; grade 4=> 40.0°C.

[b]Grade 3: prevents daily activity; Grade 4: emergency room visit or hospitalization for severe pain at the injection site.

Table 5. Systemic reactions in children ages 37 months – 5 years, Moderna mRNA-1273 COVID-19 vaccine and placebo

	Dose 1		Dose 2	
	mRNA-1273 N=2013	Placebo N=650	mRNA-1273 N=1975	Placebo N=629
Fever[a], n (%)				
Any	155 (7.7)	33 (5.1)	316 (16.0)	28 (4.5)
Grade 3 or higher	24 (1.2)	5 (0.8)	62 (3.1)	2 (0.3)
Headache[b], n (%)				
Any	232 (11.5)	78 (12.0)	310 (15.7)	51 (8.1)
Grade 3 or higher	5 (0.2)	2 (0.3)	8 (0.4)	1 (0.2)
Fatigue[b], n (%)				
Any	807 (40.1)	236 (36.3)	956 (48.4)	185 (29.4)
Grade 3 or higher	21 (1.0)	11 (1.7)	45 (2.3)	8 (1.3)
New or worsening muscle pain[b], n (%)				
Any	200 (9.9)	60 (9.2)	310 (15.7)	47 (7.5)
Grade 3 or higher	5 (0.2)	2 (0.3)	9 (0.5)	3 (0.5)
New or worsening joint pain[b], n (%)				
Any	124 (6.2)	32 (4.9)	168 (8.5)	28 (4.5)
Grade 3 or higher	2 (<0.1)	1 (0.2)	3 (0.2)	0
Nausea/vomiting[b], n (%)				
Any	137 (6.8)	50 (7.7)	194 (9.8)	30 (4.8)
Grade 3 or higher	7 (0.3)	2 (0.3)	6 (0.3)	0
Chills[b], n (%)				
Any	129 (6.4)	40 (6.2)	245 (12.4)	31 (4.9)
Grade 3 or higher	1 (<0.1)	0	10 (1.0)	2 (0.3)
Any systemic event				
Any	983 (48.8)	290 (44.6)	1163 (58.9)	234 (37.2)
Grade 3 or higher	48 (2.4)	15 (2.3)	104 (5.3)	11 (1.7)

[a]Grade for fever: grade 3=39-40.0°C; grade 4=> 40.0°C.

[b]Grade 3: prevents daily activity; Grade 4: emergency room visit or hospitalization for severe pain at the injection site.

Unsolicited Adverse Events

The overall incidence of unsolicited adverse events up to 28 days after any dose were similar in the vaccine group (40.0%) and the placebo group (37.5%) for participants ages 2 – 5 years. Adverse events in the vaccine group were similar in nature and incidence to those in the placebo group, with the exception of higher incidence of injection site erythema in the vaccine group compared to the placebo group (1.3% vs 0.2%) and COVID-19 in the placebo group compared to the vaccine group (5.5% vs 3.1%).

The overall incidence of unsolicited adverse events up to 28 days after any dose were similar in the vaccine group (49.3%) and the placebo group (48.2%) for participants ages 5—23 months. In general, unsolicited adverse events experienced in the vaccine group were similar in nature and incidence to those in the placebo group. The following unsolicited adverse events were higher in the vaccine group compared with the placebo group by at least 1%: injection site lymphadenopathy (1.4% vs 0.2%); croup (1.3% vs 0.3%); diarrhea (3.2% vs 2.2%). The following were higher in the placebo group compared with the vaccine group by at least 1%: upper respiratory tract infection (12.2% vs 10.3%), COVID-19 (4.9% vs 3.5%), and otitis media (3.7% vs 2.6%).

Serious Adverse Events

Serious adverse events were defined as any untoward medical occurrence that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, or resulted in persistent disability or incapacity. The proportions of participants who reported at least one serious adverse event were 0.5% in the vaccine group and 0.2% in the placebo group. In the younger age group, the most common serious adverse event occurring at higher rates in the vaccine group than the placebo group was febrile seizure (3 cases in vaccine group vs. 0 cases in placebo group). Other serious adverse events in the vaccine group included dehydration, metapneumovirus, foreign body respiratory tract infection, mastoiditis, bronchiolitis, pyrexia, rhinovirus, asthma, adenovirus infection, erythema multiforme, croup infectious, viral gastroenteritis, and 1 participant with Type 1 diabetes and diabetic ketoacidosis. In the placebo group there was 1 participant with bronchiolitis, rhinovirus and acute respiratory failure.

In the older age group, the most common serious adverse event occurring at higher rates in the vaccine group than the placebo group was pneumonias (2 cases in vaccine group vs. 0 cases in placebo group). Other serious adverse events in the vaccine group were bronchial hyperactivity, respiratory distress, adenovirus infection, seizure, rhinovirus infection (bronchiolitis due to rhinovirus), Epstein-Barr infection, urinary tract infection, and humerus fracture. In the placebo group serious adverse events, 1 participant experienced an abdominal wall abscess and 1 participant with rhinovirus infection and asthma. Two serious adverse events in one participant were determined by the Food and Drug Administration (FDA) as potentially related to the vaccination. No specific safety concerns were identified among vaccine recipients aged 6 months–5 years.

Persons Aged 6 – 11 Years

Local Reactions

Local reactions were reported by the majority of vaccine recipients and at higher rates than placebo recipients. Vaccine recipients reported higher rates of local reactions after dose 2 than dose 1. Local reactions in both groups were mostly grade mild or moderate; however, severe reactions were more frequent in the vaccine group than in the placebo group. There were no grade 4 local reactions reported. Pain at the injection site was the most frequent and severe reported solicited local reaction among vaccine recipients. Pain at the injection site was more common post Dose 2 (94.8%) than Dose 1 (93.1%). Injection site redness was the second most frequently reported local reaction. Injection site redness was more common after Dose 2 (18.7%) than Dose 1 (11.6%). Axillary (or groin) swelling or tenderness and injection site swelling following either dose were reported less frequently and were more common after dose 2. There were no grade 4 local reactions reported. The majority of solicited local reactions occurred within the first 2 days after any dose, persisting for a median of 3.0 days.

Table 6. Local reactions in persons aged 6-11 years, Moderna mRNA-1273 COVID-19 vaccine and placebo

	Dose 1		Dose 2	
	mRNA-1273 N=3004	**Placebo N=993**	**mRNA-1273 N=2988**	**Placebo N=969**
Redness[a], n (%)				
Any	349 (11.6)	13 (1.3)	559 (18.7)	10 (1.0)
Severe	16 (0.5)	1 (0.1)	33 (1.1)	1 (0.1)
Grade 4	0	0	0	0
Swelling[a], n (%)				
Any	354 (11.8)	12 (1.2)	507 (17.0)	12 (1.2)
Severe	19 (0.6)	1 (0.1)	20 (0.7)	0
Grade 4	0	0	0	0
Pain at the injection site[b], n (%)				
Any	2796 (93.1)	465 (46.8)	2832 (94.8)	480 (49.5)
Severe	28 (0.9)	0	81 (2.7)	2 (0.2)
Grade 4	0	0	0	0
Axillary (or groin) swelling or tenderness[b], n (%)				
Any	465 (15.5)	84 (8.5)	537 (18.0)	65 (6.7)
Severe	3 (< 0.1)	1 (0.1)	3 (0.1)	2 (0.2)
Grade 4	0	0	0	0
Any local adverse reaction (n%)				
Any	2814 (93.7)	480 (48.3)	2849 (95.3)	490 (50.6)
Severe	54 (1.8)	3 (0.3)	122 (4.1)	5 (0.5)
Grade 4	0	0	0	0

[a] mild: 25-50 mm; moderate: 51-100 mm; severe: >100 mm; Grade 4=necrosis or exfoliative dermatitis.

[b] mild: no interference with activity; moderate: some interference with activity; severe: prevents daily activity; Grade 4: emergency room visit or hospitalization

Systemic Reactions

Systemic reactions were reported by the majority of vaccine recipients and at higher rates than placebo recipients. The frequency and severity of systemic reactions was higher after dose 2 than dose 1 (78.1% vs 57.9%). Headache and fatigue were the most common systemic reactions. The majority of systemic reactions were mild or moderate in severity, after both doses. Fever was more common after the second dose (23.9%) compared to the first dose (3.3%). The majority of solicited systemic reactions occurred within the first 2 days after each, persisting for a median of 2 days. One grade 4 fever was erroneously reported in the placebo group after dose 1. There were no other systemic grade 4 reactions reported. (Table 7)

Table 7. Systemic reactions in persons aged 6–11 years, Moderna mRNA-1273 COVID-19 vaccine and placebo

	Dose 1 6-11 Years		Dose 2 6-11 Years	
	mRNA-1273 N=3004	Placebo N=993	mRNA-1273 N=2988	Placebo N=969
Fever, n (%)				
Any	99 (3.3)	15 (1.5)	714 (23.9)	19 (2.0)
Severe	17 (0.6)	2 (0.2)	113 (3.8)	2 (0.2)
Grade 4	0	1* (0.1)	0	0
Fatigue[a], n (%)				
Any	1298 (43.2)	334 (33.6)	1925 (64.5)	335 (34.6)
Severe	31 (1.0)	8 (0.8)	191 (6.4)	8 (0.8)
Grade 4	0	0	0	0
Headache[a], n (%)				
Any	938 (31.2)	306 (30.8)	1622 (54.3)	275 (28.4)
Severe	18 (0.6)	4 (0.4)	119 (4.0)	8 (0.8)
Grade 4	0	0	0	0
Chills[a], n (%)				
Any	309 (10.3)	67 (6.7)	904 (30.3)	74 (7.6)
Severe	3 (< 0.1)	0	19 (0.6)	0
Grade 4	0	0	0	0
Nausea/vomiting[a], n (%)				
Any	325 (10.8)	107 (10.8)	716 (24.0)	97 (10.0)
Severe	5 (0.2)	0	19 (0.6)	0
Grade 4	0	0	0	0
New or worsening muscle pain[a], n (%)				
Any	438 (14.6)	96 (9.7)	843 (28.2)	105 (10.8)
Severe	11 (0.4)	1 (0.1)	71 (2.4)	1 (0.1)
Grade 4	0	0	0	0
New or worsening joint pain[a], n (%)				
Any	260 (8.7)	75 (7.6)	482 (16.1)	84 (8.7)
Severe	3 (< 0.1)	1 (0.1)	25 (0.8)	0
Grade 4	0	0	0	0
Any systemic event				
Any	1740 (57.9)	518 (52.2)	2335 (78.1)	485 (50.1)
Severe	53 (1.8)	12 (1.2)	364 (12.2)	14 (1.4)
Grade 4	0	1 (0.1)	0	0

[a] Any: ≥38.0°C; Severe: 39°C to 40.0°C; Grade 4: >40.0°C

[b] Severe: prevents daily activity; Grade 4: emergency room visit or hospitalization

* Grade 4 event reported due to error in eDiary data entry, event was actually grade 0 (100.0°F).

Unsolicited Adverse Events

Unsolicited adverse events were collected during the 28 days after each dose. A higher frequency of unsolicited adverse events was reported in the vaccine group compared to the placebo group (29.6% vs 25.1%). The main imbalances between the vaccine and placebo groups were general disorders and administration site conditions, consistent with the known reactogenicity profile of the vaccine. An increase in the incidence of injection site conditions were seen in the vaccine group (9.8%) compared to the placebo group (4.1%). An imbalance of unsolicited adverse events in the skin and subcutaneous tissue disorders was also observed between the vaccine group (2.4%) and placebo group (1.0%). An increase in the incidence of the adverse event of COVID-19 was seen in the placebo group (2.2%) compared to the vaccine group (0.4%).

Serious Adverse Events

Serious adverse events were defined as any untoward medical occurrence that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, or resulted in persistent disability or incapacity. The proportions of participants who reported at least one serious adverse event were 0.2% in the vaccine group and 0.2% in the placebo group. There were 7 SAEs among 6 participants in the vaccine group (appendicitis, cellulitis, cellulitis orbital, type 1 diabetes mellitus, appendicitis, pyelonephritis and urosepsis). There were 2 SAEs among 2 participants in the placebo group (affective disorder and COVID-19). No serious adverse events during the blinded randomized control trial were considered by the FDA as related to vaccine. In a review of additional SAEs accrued during open-label phase through data cutoff of February 21, 2022, one SAE of ileus in a participant with complex medical history was considered possibly related to vaccine.

Persons Aged 12 – 17 Years

Local Reactions

Local reactions were reported by the majority of vaccine recipients and at higher rates than placebo recipients. Pain at the injection site was the most common and severe local reaction among vaccine recipients. Pain at the injection site was reported more frequently after dose 1 (93.1%) than after dose 2 (92.4%). Axillary swelling or tenderness was the second most frequently reported local reaction. Axillary swelling or tenderness was reported more frequently post dose 1 (23.2%) than dose 2 (21.0%). Injection site redness and swelling following either dose was reported slightly less frequently and was more common after dose 2 than dose 1. There were no grade 4 local reactions reported. The majority of solicited local adverse reactions in vaccine recipients occurred within the first 1 to 2 days after each dose and generally persisted for a median of 3 days (Table 8).

Table 8. Local reactions in persons aged 12-17 years, Moderna mRNA-1273 COVID-19 vaccine and placebo

	Dose 1		Dose 2	
	mRNA-1273 N = 2,482	**Placebo N = 1,238**	**mRNA-1273 N = 2,478**	**Placebo N = 1,220**
Redness[a], n (%)				
Any	334 (13.5)	8 (0.6)	484 (19.5)	11 (0.9)

Severe	21 (0.8)	0	72 (2.9)	0
Grade 4	0	0	0	0
Swelling[a], n (%)				
Any	403 (16.2)	12 (1.0)	509 (20.5)	12 (1.0)
Severe	27 (1.1)	0	56 (2.3)	0
Grade 4	0	0	0	0
Pain at the injection site[b], n (%)				
Any	2,310 (93.1)	431 (34.8)	2,290 (92.4)	370 (30.3)
Severe	133 (5.4)	1 (<0.1)	126 (5.1)	3 (0.2)
Grade 4	0	0	0	0
Axillary swelling or tenderness[b], (n%)				
Any	578 (23.3)	101 (8.2)	519 (21.0)	61 (5.0)
Severe	10 (0.4)	0	7 (0.3)	0
Grade 4	0	0	0	0
Any local adverse reaction, n (%)				
Any	2,339 (94.2)	455 (36.8)	2,314 (93.4)	398 (32.6)
Severe	170 (6.8)	1 (<0.1)	220	3 (0.2)
Grade 4	0	0	0	0

[a]severe: >10 cm; Grade 4: necrosis (redness and swelling categories) or exfoliative dermatitis (redness category only).

[b]severe: any use of prescription pain reliever/prevents daily activity; Grade 4: emergency room visit or hospitalization for severe pain at the injection site.

Systemic Reactions

Systemic reactions were reported by the majority of vaccine recipients and at higher rates than placebo recipients. The frequency and severity of systemic reactions was higher after dose 2 than dose 1 (86.1% vs 68.5%). Headache and fatigue were the most common reactions. The majority of systemic reactions were mild or moderate in severity, after both doses. Fever was more common after the second dose (12.1%) compared to the first dose (2.5%). The majority of reactions occurred within the first 1 to 2 days after each dose and persisted for a median of 2 days. Grade 4 fever (>40.0°C) was reported by one vaccine recipient after dose 2 and one placebo recipient after dose 2. There was one report of grade 4 headache and one report of grade 4 nausea/vomiting, both after dose 2. No other systemic grade 4 reactions were reported. (Table 9)

Table 9. Systemic reactions in persons aged 12-17 years, Moderna mRNA-1273 COVID-19 vaccine and placebo

	Dose 1		**Dose 2**	
	mRNA-1273 N = 2,482	**Placebo N = 1,238**	**mRNA-1273 N = 2,478**	**Placebo N = 1,220**
Fever, n (%)				
≥38.0°C	63 (2.5)	12 (1.0)	302 (12.2)	12 (1.0)
38.0°C to 38.4°C	36 (1.5)	9 (0.7)	162 (6.5)	6 (0.5)

38.5°C to 38.9°C	18 (0.7)	2 (0.2)	93 (3.8)	4 (0.3)
39°C to 40.0°C	9 (0.4)	1 (<0.1)	46 (1.9)	1 (<0.1)
>40.0°C	0	0	1 (<0.1)	1 (<0.1)
Fatigue[a], n (%)				
Any	1,188 (47.9)	453 (36.6)	1,679 (67.8)	353 (28.9)
Severe	33 (1.3)	18 (1.5)	188 (7.6)	10 (0.8)
Grade 4	0	0	0	0
Headache[b], n (%)				
Any	1,106 (44.6)	477 (38.5)	1,739 (70.2)	370 (30.3)
Severe	56 (2.3)	17 (1.4)	112 (4.5)	14 (1.1)
Grade 4	0	0	1 (<0.1)	0
Chills[c], n (%)				
Any	456 (18.4)	138 (11.1)	1,066 (43.0)	97 (8.0)
Severe	4 (0.2)	1 (<0.1)	11 (0.4)	0
Grade 4	0	0	0	0
Nausea/vomiting[d], n (%)				
Any	281 (11.3)	110 (8.9)	591 (23.9)	106 (8.7)
Severe	2 (<0.1)	0	2 (<0.1)	0
Grade 4	0	0	1 (<0.1)	0
New or worsening muscle pain[a], n (%)				
Any	668 (26.9)	205 (16.6)	1154 (46.6)	153 (12.5)
Severe	24 (1.0)	10 (0.8)	129 (5.2)	3 (0.2)
Grade 4	0	0	0	0
New or worsening joint pain[a], n (%)				
Any	371 (15.0)	143 (11.6)	716 (28.9)	113 (9.3)
Severe	15 (0.6)	5 (0.4)	57 (2.3)	2 (0.2)
Grade 4	0	0	0	0
Any systemic event				
Any	1,701 (68.5)	687 (55.5)	2,134 (86.1)	561 (46.0)
Severe	108 (4.4)	36 (2.9)	340 (13.7)	25 (2.0)
Grade 4	0	0	3 (0.1)	1 (<0.1)
Use of antipyretic or pain medication, n (%)	748 (30.1)	118 (9.5)	1,242 (50.1)	108 (8.9)

[a] Severe: prevents daily activity; Grade 4: emergency room visit or hospitalization

[b] Severe: any use of prescription pain reliever or prevents daily activity; Grade 4: emergency room visit or hospitalization

[c] Severe: prevents daily activity and requires medical intervention; Grade 4: emergency room visit or hospitalization

[d] Severe: prevents daily activity, requires intravenous hydration; Grade 4: emergency room visit or hospitalization for hypotensive shock.

Unsolicited Adverse Events

Unsolicited AEs were collected during the 28 days after each dose. A higher frequency of unsolicited adverse events after any dose was reported in the vaccine group (20.5%) compared to the placebo group (15.9%). The most commonly reported unsolicited adverse events after any vaccine dose were injection site lymphadenopathy (4.3%) and headache (2.2%). Imbalances in unsolicited adverse events in the vaccine group compared to the placebo group were observed and were primarily attributable to local injection site reactions including events of lymphadenopathy, erythema, induration, pain, pruritis, hypersensitivity, and urticaria. Incidence of lymphadenopathy was higher in the vaccine group (0.7%) than the placebo group (<0.1%). The majority of these events of lymphadenopathy occurred in the arm and neck region. An imbalance of unsolicited adverse events in the skin and subcutaneous tissue disorders was also observed between the vaccine group (1.1%) and placebo group (0.6%). The unsolicited adverse event of COVID-19 within 28 days of any dose was more frequently reported in the placebo group (1.0%) than the vaccine group (0.2%).

Serious Adverse Events

Serious adverse events were defined as any untoward medical occurrence that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, or resulted in persistent disability or incapacity. The proportions of participants who reported at least one serious adverse event were 0.2% in the vaccine group and 0.2% in the placebo group. There were 9 SAEs among 6 vaccine recipients (appendicitis, diarrhea, vomiting, drug-induced liver injury, pectus excavatum, post-procedural fever, suicidal ideation [2], depression suicidal). There were 2 SAEs among 2 recipients (obstructive nephropathy and suicide attempt). No serious adverse events were considered by the FDA as related to vaccine.

Persons Aged ≥ 18 Years

Local Reactions

Local reactions were reported by the majority of vaccine recipients and at higher rates than placebo recipients. Vaccine recipients reported higher rates of local reactions after dose 2 than dose 1. The frequency of local reactions was higher in the younger age group (aged 18 to 64 years) than the older age group (aged ≥65 years) (90.5% vs 83.9% after dose 2). Pain at the injection site was the most frequent and severe reported solicited local reaction among vaccine recipients. After dose 1, the younger age group reported pain more frequently than the older age group (86.9% vs 74.0%); a similar pattern was observed after dose 2 (90.1% vs 83.4%). Axillary swelling or tenderness was the second most frequently reported local reaction. Axillary swelling or tenderness was reported more frequently in the younger age group than the older age group (16.0% vs 8.4% after dose 2). Injection site redness and swelling following either dose were reported less frequently. Redness and swelling were slightly more common after dose 2. No grade 4 local reactions were reported. Overall, the median onset of local reactions in the vaccine group was 1 day after either dose, with a median duration between 2 and 3 days. (Table 10, Table 11)

Table 10. Local reactions in persons aged 18-64 years, Moderna COVID-19 vaccine and placebo

	Dose 1		Dose 2	
	Moderna Vaccine N=11401	**Placebo N=11404**	**Moderna Vaccine N=10357**	**Placebo N=10317**
Any Local, n (%)				
Any	9960 (87.4)	2432 (21.3)	9371 (90.5)	2134 (20.7)

Grade 3	452 (4.0)	39 (0.3)	766 (7.4)	41 (0.4)
Pain[a], n (%)				
Any	9908 (86.9)	2179 (19.1)	9335 (90.1)	1942 (18.8)
Grade 3	367 (3.2)	23 (0.2)	479 (4.6)	21 (0.2)
Redness[a], n (%)				
Any	345 (3.0)	46 (0.4)	928 (9.0)	42 (0.4)
Severe	34 (0.3)	11 (<0.1)	206 (2.0)	12 (0.1)
Swelling[b], n (%)				
Any	768 (6.7)	33 (0.3)	1309 (12.6)	35 (0.3)
Grade 3	62 (0.5)	3 (<0.1)	176 (1.7)	4 (<0.1)
Axillary Swelling/Tenderness[c], n (%)				
Any	1322 (11.6)	567 (5.0)	1654 (16.0)	444 (4.3)
Grade 3	36 (0.3)	13 (0.1)	45 (0.4)	10 (<0.1)

[a] Pain grade 3: any use of prescription pain reliever or prevented daily activity; grade 4: required emergency room visit or hospitalization.

[b] Swelling grade 3: >100mm/>10cm; grade 4: necrosis/exfoliative dermatitis.

[c] Axillary swelling or tenderness was collected as a solicited local adverse reaction (i.e., lymphadenopathy: localized axillary swelling or tenderness ipsilateral to the vaccination arm); grade 3: any use of prescription pain reliever or prevented daily activity; grade 4: required emergency room visit or hospitalization.

Note: No grade 4 local reactions were reported.

Table 11. Local reactions in persons aged ≥65 years, Moderna COVID-19 vaccine and placebo

	Dose 1		**Dose 2**	
	Moderna Vaccine N=3762	**Placebo N=3746**	**Moderna Vaccine N=3587**	**Placebo N=3549**
Any Local, n (%)				
Any	2805 (74.6)	566 (15.1)	3010 (83.9)	473 (13.3)
Grade 3	77 (2.0)	39 (1.0)	212 (5.9)	29 (0.8)
Pain[a], n (%)				
Any	2782 (74.0)	481(12.8)	2990 (83.4)	421 (11.9)
Grade 3	50 (1.3)	32 (0.9)	96 (2.7)	17 (0.5)
Redness[a], n (%)				
Any	86 (2.3)	19 (0.5)	265 (7.4)	13 (0.4)
Grade 3	8 (0.2)	2 (<0.1)	75 (2.1)	3 (<0.1)
Swelling[b], n (%)				
Any	166 (4.4)	19 (0.5)	386 (10.8)	13 (0.4)
Grade 3	20 (0.5)	3 (<0.1)	69 (1.9)	7 (0.2)

Axillary Swelling/Tenderness[c], n (%)				
Any	231 (6.1)	155 (4.1)	302 (8.4)	90 (2.5)
Grade 3	12 (0.3)	14 (0.4)	21 (0.6)	8 (0.2)

[a] Pain grade 3: any use of prescription pain reliever or prevented daily activity; grade 4: required emergency room visit or hospitalization.

[b] Swelling grade 3: >100mm/>10cm; grade 4: necrosis/exfoliative dermatitis.

[c] Axillary swelling or tenderness was collected as a solicited local adverse reaction (i.e. lymphadenopathy: localized axillary swelling or tenderness ipsilateral to the vaccination arm); grade 3: any use of prescription pain reliever or prevented daily activity; grade 4: required emergency room visit or hospitalization.

Note: No grade 4 local reactions were reported.

Systemic Reactions

Systemic reactions were reported by the majority of vaccine recipients and at higher rates than placebo recipients. The frequency of systemic reactions was higher in the younger age group than the older age group (81.9% vs 71.9% after dose 2). Within each age group, the frequency and severity of systemic reactions was higher after dose 2 than dose 1. For both age groups, fatigue, headache and myalgia were the most common. The majority of systemic reactions were mild or moderate in severity, after both doses and in both age groups. Fever was more common after the second dose and in the younger group (17.6%) compared to the older group (10.2%). Among vaccine recipients, the median onset of systemic reactions was 1 to 2 days after either dose, with a median duration of 2 days. Grade 4 fever (>40.0°C) was reported by four vaccine recipients after dose 1 and 11 vaccine recipients after dose 2. There was one report of grade 4 fatigue and one report of grade 4 arthralgia, both in the younger age group after dose 1. In the older age group, there was one report of grade 4 nausea or vomiting after dose 2. No other systemic grade 4 reactions were reported. (Table 3, Table 4)

Table 12. Systemic reactions in persons aged 18-64 years, Moderna COVID-19 vaccine and placebo

	Dose 1		Dose 2	
	Moderna Vaccine N=11405	**Placebo N=11406**	**Moderna Vaccine N=10358**	**Placebo N=10320**
Any systemic, n (%)				
Any	6503 (57.0)	5063 (44.4)	8484 (81.9)	3967 (38.4)
Grade 3	363 (3.2)	248 (2.2)	1801 (17.4)	215 (2.1)
Grade 4	5 (<0.1)	4 (<0.1)	10 (<0.1)	2 (<0.1)
Fever[a], n (%)				
Any	105 (0.9)	39 (0.3)	1806 (17.4)	38 (0.4)
Grade 3	10 (<0.1)	1 (<0.1)	168 (1.6)	1 (<0.1)
Grade 4	4 (<0.1)	4 (<0.1)	10 (<0.1)	1 (<0.1)
Headache[b], n (%)				
Any	4031(35.4)	3303 (29.0)	6500 (62.8)	2617 (25.4)
Grade 3	219 (1.9)	162 (1.4)	515 (5.0)	124 (1.2)
Fatigue[c], n (%)				

Any	4384 (38.5)	3282 (28.8)	7002 (67.6)	2530 (24.5)
Grade 3	120 (1.1)	83 (0.7)	1099 (10.6)	81 (0.8)
Grade 4	1 (<0.1)	0 (0)	0 (0)	0 (0)
Myalgia[c], n (%)				
Any	2698 (23.7)	1626 (14.3)	6353 (61.3)	1312 (12.7)
Grade 3	73 (0.6)	38 (0.3)	1032 (10.0)	39 (0.4)
Arthralgia[c], n (%)				
Any	1892 (16.6)	1327 (11.6)	4685 (45.2)	1087 (10.5)
Grade 3	47 (0.4)	29 (0.3)	603 (5.8)	36 (0.3)
Grade 4	1 (<0.1)	0 (0)	0 (0)	0 (0)
Nausea/Vomiting[d], n (%)				
Any	1069 (9.3)	908 (8.0)	2209 (21.3)	754 (7.3)
Grade 3	6 (<0.1)	8 (<0.1)	8 (<0.1)	8 (<0.1)
Chills[e], n (%)				
Any	1051 (9.2)	730 (6.4)	5001 (48.3)	611 (5.9)
Grade 3	17 (0.1)	8 (<0.1)	151 (1.5)	14 (0.1)

[a] Fever – Grade 3: ≥39.0 – ≤40.0°C or ≥102.1 – ≤104.0°F; Grade 4: >40.0°C or >104.0°F
[b] Headache – Grade 3: significant; any use of prescription pain reliever or prevented daily activity; Grade 4: required emergency room visit or hospitalization.
[c] Fatigue, Myalgia, Arthralgia – Grade 3: significant; prevented daily activity; Grade 4: required emergency room visit or hospitalization.
[d] Nausea/Vomiting – Grade 3: prevented daily activity, required outpatient intravenous hydration; Grade 4: required emergency room visit or hospitalization for hypotensive shock.
[e] Chills – Grade 3: prevented daily activity and required medical intervention; Grade 4: required emergency room visit or hospitalization.

Table 13. Systemic reactions in persons aged ≥65 years, Moderna COVID-19 vaccine and placebo

	Dose 1		Dose 2	
	Moderna Vaccine N=3761	**Placebo N=3748**	**Moderna Vaccine N=3589**	**Placebo N=3549**
Any systemic, n (%)				
Any	1818 (48.3)	1335 (35.6)	2580 (71.9)	1102 (31.1)
Grade 3	84 (2.2)	63 (1.7)	387 (10.8)	58 (1.6)
Grade 4	0 (0)	0 (0)	2 (<0.1)	1 (<0.1)
Fever[a], n (%)				
Any	10 (0.3)	7 (0.2)	366 (10.2)	5 (0.1)
Grade 3	1 (<0.1)	1 (<0.1)	18 (0.5)	0 (0)
Grade 4	0 (0)	2 (<0.1)	1 (<0.1)	1 (<0.1)
Headache[b], n (%)				
Any	921 (33.3)	443 (11.8)	1665 (46.4)	635 (17.9)

Grade 3	30 (0.8)	34 (0.9)	107 (3.0)	32 (0.9)
Fatigue[c], n (%)				
Any	1251 (38.5)	851 (22.7)	2094 (58.4)	695 (19.6)
Grade 3	120 (1.1)	23 (0.6)	248 (6.9)	20 (0.6)
Myalgia[c], n (%)				
Any	743 (19.8)	443 (11.8)	1683 (46.9)	385 (10.8)
Grade 3	17 (0.5)	9 (0.3)	201 (5.6)	10 (0.3)
Arthralgia[c], n (%)				
Any	618 (16.4)	456 (12.2)	1252 (34.9)	381 (10.7)
Grade 3	13 (0.3)	8 (0.2)	122 (3.4)	7 (0.2)
Nausea/Vomiting[d], n (%)				
Any	194 (5.2)	166 (4.4)	425 (11.8)	129 (3.6)
Grade 3	4 (0.1)	4 (0.1)	10 (0.3)	3 (<0.1)
Grade 4	0 (0)	0 (0)	1 (<0.1)	0 (0)
Chills[e], n (%)				
Any	202 (5.4)	148 (4.0)	1099 (30.6)	144 (4.1)
Grade 3	7 (0.2)	6 (0.2)	27 (0.8)	2 (<0.1)

[a] Fever – Grade 3: ≥39.0 – ≤40.0°C or ≥102.1 – ≤104.0°F; Grade 4: >40.0°C or >104.0°F
[b] Headache – Grade 3: significant; any use of prescription pain reliever or prevented daily activity; Grade 4: requires emergency room visit or hospitalization.
[c] Fatigue, Myalgia, Arthralgia – Grade 3: significant; prevented daily activity; Grade 4: required emergency room visit or hospitalization.
[d] Nausea/Vomiting – Grade 3: prevented daily activity, required outpatient intravenous hydration; Grade 4: Requires emergency room visit or hospitalization for hypotensive shock.
[e] Chills – Grade 3: prevented daily activity and required medical intervention; Grade 4: required emergency room visit or hospitalization.

Unsolicited Adverse Events

A higher frequency of unsolicited adverse events was reported in the vaccine group compared to the placebo group and was primarily attributed to local and systemic reactogenicity following vaccination. Reports of lymphadenopathy were imbalanced with 1.1 % of persons in the vaccine group and 0.6% in the placebo group reporting such events; lymphadenopathy is plausibly related to the vaccine. Lymphadenopathy occurred in the arm and neck region and was reported within 2 to 4 days after vaccination. The median duration of lymphadenopathy was 1 to 2 days. Bell's palsy was reported by three vaccine recipients and one placebo recipient. One case of Bell's palsy in the vaccine group was considered a serious adverse event. Currently available information is insufficient to determine a causal relationship with the vaccine.

Serious Adverse Events

Serious adverse events were defined as any untoward medical occurrence that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, or resulted in persistent disability or incapacity. The proportions of participants who reported at least one serious adverse event were 1% in the vaccine group and 1% in the placebo group. The most common serious adverse events occurring at higher rates in the vaccine group than the placebo group were myocardial infarction (5 cases in vaccine group vs. 3 cases in placebo group), cholecystitis (3

vs. 0), and nephrolithiasis (3 vs. 0). Three serious adverse events were considered by the U.S. Food and Drug Administration (FDA) as possibly related to vaccine: the one report of intractable nausea/vomiting and two reports of facial swelling in persons who had a previous history of cosmetic filler injections. The possibility that the vaccine contributed to the serious adverse event reports of rheumatoid arthritis (n=1), peripheral edema/dyspnea with exertion (n=1), and autonomic dysfunction (n=1) cannot be excluded.

Data source: FDA briefing document

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