Anhang zur 23. Aktualisierung der STIKO-Empfehlung zur Impfung gegen COVID-19

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1.1 Studiencharakteristika

Tabelle 1: Demografische und klinische Merkmale der Teilnehmer in der Sicherheitspopulation bei Studienbeginn, stratifiziert nach Alterskohorte und Studiengruppenzuordnung

Merkmal	2-5-Jährige Kinder		6-23 Monate alte Kinder	
	BNT162b2, 3 μg (N = 1835)	Placebo (N = 915)	BNT162b2, 3 μg (N = 1178)	Placebo (N = 598)
Alter (Monate/Jahre)				
Mittel	3,1 Jahre (SD 0,79)	3,0 Jahre (0,79)	15,2 Monate (SD 4,97)	15,4 Monate (SD 5,06)
Median	3,0 Jahre	3,0 Jahre	16,0 Monate	16,0 Monate
Geschlecht				
Männlich	901 (49,1%)	471 (51,5%)	589 (50,0%)	291 (48,7%)
Weiblich	934 (50,9%)	444 (48,5%)	589 (50,0%)	307 (51,3%)
Adipositas – n (%)				
Ja	120 (6,5%)	16 (3,9%)	Nicht berichtet	Nicht berichtet
Nein	1712 (93,3%)	870 (95,1%)	Nicht berichtet	Nicht berichtet
Fehlende Daten	3 (0,2%)	0	Nicht berichtet	Nicht berichtet
Komorbiditäten – n (%)				
Ja	222 (12,1%)	130 (14,2%)	50 (4,2%	34 (5,7%)
Nein	1613 (87,9%)	785 (85,8%)	1128 (95,8%)	564 (94,3%)
Rasse/Ethnie – n (%)				
Weiß	1469 (80,1%)	720 (78,7%)	922 (78,3%)	480 (80,3%)
Schwarz oder Afro-Amerikanisch	94 (5,1%)	41 (4,5%)	42 (3,6%)	24 (4,0%)
Amerikanischer Indianer/ Alaska-Ureinwohner	3 (0,2%)	4 (0,4%)	3 (0,3%)	1 (0,2%)
Asiatisch	127 (6,9%)	76 (8,3%)	91 (7,7%)	40 (6,7%)
Gemischtrassig	131 (7,1%)	69 (7,5%)	117 (9,9%)	49 (8,2%)
Andere/nicht berichtet	11 (0,6%)	5 (0,5%)	3 (0,3%)	4 (0,7%)
Land – n (%)				
Brasilien	0	0	0	2 (0,3%)
Finnland	63 (3,4%)	30 (3,3%)	54 (4,6%)	26 (4,3%)
Polen	205 (11,2%)	103 (11,3%)	125 (10,6%)	63 (10,5%)
Spanien	73 (4,0%)	35 (3,8%)	42 (3,6%)	22 (3,7%)
USA	1494 (81,4%)	747 (81,6%)	957 (81,2%)	485 (81,1%)
SARS-CoV-2 Status – n (%)				
Negativ	1597 (87,0%)	783 (85,6%)	1078 (91,5%)	541 (90,5%)
Positiv	233 (12,7%)	125 (13,7%)	89 (7,6%)	44 (7,4%)
Fehlende Daten	5 (0,3%)	7 (0,8%)	11 (0,9%)	13 (2,2%)
Verabreichte Dosen vor Entblindung – n (%)				
Dosis 1	1835 (100%)	915 (100%	1178)100%)	598 (100%)
Dosis 2	1819 (99,1%)	907 (99,1%)	1166 (99,0%)	596 (99,7%)
Dosis 3	606 (33,0%)	280 (30,6%)	386 (32,8%)	184 (30,8%)

1.2 Risk of Bias-Bewertung

Tabelle 2: Risk of Bias assessment for pivotal trial of COVID-19 vaccination with Comirnaty in 6 months to 4 year old children

Study	Outcome	Randomization Process	Deviations from intended interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the reported result	Overall Bias
Study	SARS-CoV-2 Infections	..	..	..	..	..	..
	Symptomatic COVID-19	Low	High[1]	Some concern[2]	Low[3]	Some concern [4]	High
	Severe COVID-19	Low	High[1]	Some concern[2]	Low[3]	Low	High
	Local reactions (dose 1&2)	Low	Low	Low	Some concern[5]	Low	Some concern
	Local reactions (dose 3)	Low	Low	Low	High[6]	Low	High
	Systemic reactions (dose 1&2)	Low	Low	Low	Some concern[5]	Low	Some concern
	Systemic reactions (dose 3)	Low	Low	Low	High[6]	Low	High
	AEs	Low	Low	Low	High[6]	Low	High
	SAEs	Low	Low	Low	Some concern[7]	Low	Some concern
	AESIs (Myocarditis)	Low	Low	Low	Low	Low	Low

1: >23% of participants in Comirnaty group (31.6% in 6-23 months olds and 23.7% in 2-4 year olds) were excluded from efficacy analysis due to unblinding before receipt of dose 3; in comparison, 0% of placebo-group-participants were unblinded/excluded due to unblinding. Also, >69% of 6-23 months old placebo recipients did not receive all interventions as randomized

2: few data missing, but also only few events reported. Therefore missing data might still have an impact on results

3: valid test applied; study personnel blinded; outcome assessment does not influence result

4: unclear why report is based on a data cutoff with fewer than the 21 events specified for efficacy analysis in study protocol

5: limited information on outcome measurement provided causing some concerns

6: limited information on outcome measurement provided and >20% unblinding before receipt of dose 3, thus outcome assessment (subjective reporting) might be biased through awareness of intervention

7: limited information on outcome measurement provided and >20% unblinding before receipt of dose 3, thus outcome assessment (subjective reporting) might be biased through awareness of intervention; however less severe than for AEs or reactogenicity outcomes as assessment of myocarditis is probably more objective

1.3 GRADE-Bewertung

Tabelle 3: GRADE profile on the effects of COVID-19 vaccination with Comirnaty in 6 to 23 months old children

Population: Children, aged 6-23 months
Intervention: Comirnaty, 3 doses à 3 µg (dose 1 and 2: 21 days apart; dose 2 and 3: min. 8 weeks apart)
Comparison: Placebo or no intervention
Setting: Community

Outcomes	Absolute effect with placebo/no vaccination	Absolute effect with vaccination	Relative effect (95% CI)	Timing of outcome measurement	No. of participants (studies)	Certainty of the evidence (GRADE)
Vaccine efficacy						
SARS-CoV-2 Infections	NA	NA	NA	NA	0	NA
Symptomatic COVID-19	11 per 1000	3 per 1000 (0 to 52)	VE 75.6% (-369.1 to 99.6)	≥ 7 days after dose 3 (median: 1,3 months)	555 (1)	⨁◯◯◯ VERY LOW[a,b]
Severe COVID-19	6 per 1000	0 per 1000 (0 to 23)	VE 84% (-289 to 99)	≥ 7 days after dose 2 (median: NR)	1510 (1)	⨁◯◯◯ VERY LOW[a,b]
Vaccine Safety						
Local Reactions (dose 1)	175 per 1000	238 per 1000 (194 to 177)	RR 1.36 (1.11 to 1.67)	≤ 7 days	1768 (1)	⨁⨁⨁◯ MODERATE[a]
Local Reactions (dose 2)	134 per 1000	217 per 1000 (172 to 273)	RR 1.62 (1.28 to 2.04)	≤ 7 days	1738 (1)	⨁⨁⨁◯ MODERATE[a]
Local Reactions (dose 3)	153 per 1000	534 per 1000 (183 to 1000)	RR 3.49 (1.85 to 6.59)	≤ 7 days	535 (1)	⨁⨁◯◯ LOW[a,c]
Systemic Reactions (dose 1)	582 per 1000	611 per 1000 (565 to 663)	RR 1.05 (0.97 to 1.14)	≤ 7 days	1768 (1)	⨁⨁◯◯ LOW[a,c]
Systemic Reactions (dose 2)	504 per 1000	559 per 1000 (509 to 615)	RR 1.11 (1.01 to 1.22)	≤ 7 days	1738 (1)	⨁⨁⨁◯ MODERATE[a]
Systemic Reactions (dose 3)	453 per 1000	516 per 1000 (426 to 625)	RR 1.14 (0.94 to 1.38)	≤ 7 days	535 (1)	⨁⨁◯◯ LOW[a,c]
Adverse Events	271 per 1000	301 per 1000 (257 to 352)	RR 1.11 (0.95 to 1.30)	Up to 1 month post dose 3	1776 (1)	⨁⨁◯◯ LOW[a,c]
Serious Adverse Events	23 per 1000	14 per 1000 (7 to 29)	RR 0.62 (0.31 to 1.24)	Up to data-cutoff or timepoint of unblinding	1776 (1)	⨁⨁◯◯ LOW[b]
Adverse Events of Special Interest (Myocarditis)	N.E., 0 Events observed	N.E., 0 Events observed	N.E.	Up to data-cutoff or timepoint of unblinding	1776 (1)	⨁◯◯◯ VERY LOW[d]

A: Downgraded one level for serious study limitations/ B: Downgraded two levels for very serious imprecision/ C: Downgraded one level for serious imprecision

D: Downgraded three levels for critical imprecision

Tabelle 4: GRADE profile on the effects of COVID-19 vaccination with Comirnaty in 2 to 4 year old children

Population: Children, aged 2-4 years
Intervention: Comirnaty, 3 doses à 3 µg (dose 1 and 2: 21 days apart; dose 2 and 3: min. 8 weeks apart)
Comparison: Placebo or no intervention
Setting: Community

Outcomes	Absolute effect with placebo/no vaccination	Absolute effect with vaccination	Relative effect (95% CI)	Timing of outcome measurement	No. of participants (studies)	Certainty of the evidence (GRADE)
Vaccine efficacy						
SARS-CoV-2 Infections	NA	NA	NA	NA	0	NA
Symptomatic COVID-19	18 per 1000	3 per 1000 (0 to 19)	VE 82.4% (-7.6 to 98.3)	≥ 7 days after dose 3 (median: 1,4 months)	860 (1)	⨁◯◯◯ VERY LOW[a,b]
Severe COVID-19	N.E., 0 Events observed	N.E., 0 Events observed	N.E.	≥ 7 days after dose 3 (median: 1,4 months)	860 (1)	⨁◯◯◯ VERY LOW[a,c]
Vaccine Safety						
Local Reactions (dose 1)	252 per 1000	355 per 1000 (312 to 403)	RR 1.41 (1.24 to 1.60)	≤ 7 days	2734 (1)	⨁⨁⨁◯ MODERATE[a]
Local Reactions (dose 2)	233 per 1000	361 per 1000 (317 to 415)	RR 1.55 (1.36 to 1.78)	≤ 7 days	2657 (1)	⨁⨁⨁◯ MODERATE[a]
Local Reactions (dose 3)	156 per 1000	314 per 1000 (231 to 427)	RR 2.01 (1.48 to 2.74)	≤ 7 days	814 (1)	⨁⨁◯◯ LOW[a,d]
Systemic Reactions (dose 1)	389 per 1000	381 per 1000 (342 to 420)	RR 0.98 (0.88 to 1.08)	≤ 7 days	2734 (1)	⨁⨁⨁◯ MODERATE[a]
Systemic Reactions (dose 2)	322 per 1000	335 per 1000 (299 to 377)	RR 1.04 (0.93 to 1.17)	≤ 7 days	2657 (1)	⨁⨁⨁◯ MODERATE[a]
Systemic Reactions (dose 3)	294 per 1000	309 per 1000 (247 to 385)	RR 1.05 (0.84 to 1.31)	≤ 7 days	814 (1)	⨁⨁◯◯ LOW[a,d]
Adverse Events	187 per 1000	187 per 1000 (159 to 221)	RR 1.00 (0.85 to 1.18)	Up to 1 month post dose 3	2750 (1)	⨁⨁⨁◯ MODERATE[a]
Serious Adverse Events	9 per 1000	7 per 1000 (3 to 11)	RR 0.75 (0.31 to 1.18)	Up to data-cutoff or timepoint of unblinding	2750 (1)	⨁⨁◯◯ LOW[b]
Adverse Events of Special Interest (Myocarditis)	N.E., 0 Events observed	N.E., 0 Events observed	N.E.	Up to data-cutoff or timepoint of unblinding	2750 (1)	⨁◯◯◯ VERY LOW[c]

A: Downgraded one level for serious study limitations/ B: Downgraded two levels for very serious imprecision/ C: Downgraded three levels for critical imprecision /D: Downgraded one level for serious imprecision

2. Zulassungsstudie Spikevax zur COVID-19 Impfung von Kindern im Alter von 6 Monaten bis 4 Jahren

2.1 Studiencharakteristika

Tabelle 5: Demografische und klinische Merkmale der Teilnehmer in der Sicherheitspopulation bei Studienbeginn, stratifiziert nach Alterskohorte und Studiengruppenzuordnung

Merkmal	2-5-Jährige Kinder		6-23 Monate alte Kinder	
	mRNA-1273, 25 µg (N = 3031)	Placebo (N = 1007)	mRNA-1273, 25 µg (N = 1761)	Placebo (N = 589)
Alter (Monate/Jahre)				
Mean (±SD)	3,0±0,9	3,0±0,9	15,8±5,0	15,9±4,5
Median (IQR)	3,0 (2,0–4,0)	3,0 (2,0–4,0)	16,0 (12,0–20,0)	16,0 (13,0–20,0)
Altersgruppen – n (%)				
≥6 bis <12 Monate	-	-	375 (21,3)	124 (21,1)
≥12 bis <24 Monate	-	-	1373 (78,0)	462 (78,4)
≥24 Monate	-	-	13 (0,7)	3 (0,5)
<2 Jahre	24 (0,8)	12 (1,2)	-	-
≥2 bis <4 Jahre	2057 (67,9)	655 (65,0)	-	-
≥4 bis <6 Jahre	950 (31,3)	340 (33,8)	-	-
≥24 bis <37 Monate	999 (33,0)	345 (34,3)	-	-
≥37 Monte bis <6 Jahre	2032 (67,0)	662 (65,7)	-	-
Geschlecht				
Männlich	1543 (50,9)	510 (50,6)	910 (51,7)	290 (49,2)
Weiblich	1488 (49,1)	497 (49,4)	851 (48,3)	299 (50,8)
Rasse/Ethnie – n (%)				
Weiß	2297 (75,8)	792 (78,6)	1390 (78,9)	466 (79,1)
Schwarz	142 (4,7)	38 (3,8)	57 (3,2)	16 (2,7)
Asiatisch	191 (6,3)	51 (5,1)	79 (4,5)	35 (5,9)
Amerikanischer Indianer/ Alaska-Ureinwohner	12 (0,4)	3 (0,3)	4 (0,2)	0
Ureinwohner Hawaiis/ pazifischer Insulaner	7 (0,2)	4 (0,4)	0	0
Gemischtrassig	322 (10,6)	99 (9,8)	186 (10,6)	64 (10,9)
Andere/nicht berichtet	56 (1,8)	20 (2,0)	40 (2,3)	7 (1,2)
Unbekannt	4 (0,1)	0	5 (0.3)	1 (0,2)
Lateinamerikanisch oder Latinx – n (%)				
Ja	433 (14,3)	142 (14,1)	227 (12,9)	84 (14,3)
Nein	2579 (85,1)	856 (85,0)	1517 (86,1)	498 (84,6)
Nicht berichtet	14 (0,5)	8 (0,8)	15 (0,9)	6 (1,0)
Unbekannt	5 (0,2)	1 (0,1)	2 (0,1)	1 (0,2)
Rasse und ethnische Gruppe – n (%)				
Weiß nicht-hispanisch	1975 (65,2)	678 (67,3)	1221 (69,3)	393 (66,7)
Farbige Gemeinschaften	1054 (34,8)	327 (32,5)	538 (30,6)	194 (32,9)
Fehlende Daten	2 (<0,1)	2 (0,2)	2 (0,1)	2 (0,3)
Gewicht – kg				
Mean (±SD)	16,1±3,2	16,0±3,0	10,9±2,1	10,9±2,1
Median (IQR)	15,7 (14,1–17,7)	15,6 (14,1–17,6)	10,8 (9,6–12,1)	10,8 (9,6–12,1)
SARS-CoV-2 Status – n (%)				
Negativ	2695 (88,9)	898 (89,2)	1575 (89,4)	530 (90,0)
Positiv	266 (8,8)	82 (8,1)	106 (6,0)	38 (6,5)
Fehlende Daten	70 (2,3)	27 (2,7)	80 (4,5)	21 (3,6)

Tabelle 6: Disposition der Teilnehmenden in den Sicherheitspopulationen

Disposition	2-5-Jährige Kinder		6-23 Monate alte Kinder	
	mRNA-1273 25 µg	Placebo	mRNA-1273 25 µg	Placebo
Randomisiert	N=3040	N=1008	N=1762	N=593
≥1 Dosis erhalten	3031 (99,7)	1007 (99,9)	1760 (99,9)	590 (99,5)
2 Dosen erhalten	2960 (97,4)	970 (96,2)	1600 (90,8)	529 (89,2)
Abbruch der Intervention	20 (0,7)	21 (2,1)	4 (0,2)	5 (0,8)
Abbruch der Studienteilnahme	57 (1,9)	31 (3,1)	19 (1,1)	15 (2,5)
Sicherheitspopulation – n (%)	N=3031	N=1007	N=1761	N=589
Anzahl der entblindeten Teilnehmenden – n (%)	89 (2,9)	51 (5,1)	1 (<0,1)	1 (0,2)

Tabelle 7: Subgruppenanlyse – Vakzineeffektivität gegen COVID-19 bei 6-23 Monate alten Teilnehmenden, 14 Tage nach erhalt der 2. Impfdosis

Charakteristika	**mRNA-1273 25 µg Fälle/N (%) Inzidenz Rate pro 1.000 Personenjahren (95% KI)**	**Placebo Fälle/N (%) Inzidenz Rate pro 1.000 Personenjahren (95% KI)**	**VE (95% CI)**
Geschlecht			
Männlich	22/780 (2,8) 115,8 (72,5 – 175,3)	15/256 (5,9) 244,959 (137,102 – 404.022)	52,7% (2,1 – 76,6)
Weiblich	29/731 (4,0) 162,1 (108,6 – 232,8)	19/257 (7,4) 315,2 (189,8 – 492,3)	48,6% (2,9 – 72,1)
Rasse			
Schwarz oder Afroamerikanisch	6/49 (12,2) 470,4 (172,6 – 1023,8)	2/13 (15,4) 545,6 (66,1 – 1970,7)	13,8% (-773,5 – 84,6)
Weiß	42/1189 (3,5) 146,0 (105,2 – 197,3)	28/408 (6,9) 291,9 (194,0 – 421,9)	50,0% (16,2 – 69,7)
Andere	3/273 (1,1) 43,8 (9,0 – 128,1)	4/92 (4,3) 182,4 (49,7 – 467,1)	76,0% (-42,0 – 96,5)
Ethnie			
Hispanoamerikanisch oder Latino	9/188 (4,8) 186,3 (85,2 – 353,7)	6/70 (8,6) 339,0 (124,4 – 737,9)	45,0% (-87,7 – 81,3)
Nicht-Hispanoamerikanisch oder Latino	42/1323 (3,2) 131,0 (94,4 – 177,1)	28/443 (6,3) 269,7 (179,2 – 389,8)	51,4% (18,6 – 70,6)
Rasse und Ethnie			
Weiß & Nicht-Hispanoamerikanisch	34/1051 (3,2) 134,7 (93,3 – 188,3)	24/348 (6.9) 298.4 (191.2, 444.1)	54.9% (20.4, 74.0)
Farbige Gemeinschaften	17/458 (3,7) 146,4 (85,3 – 234,4)	10/164 (6,1) 245,4 (117,7 – 451,3)	40,3% (-45,8 – 74,2)
Adipositas-Status			
Adipös	13/330 (3,9) 160,5 (85,4 – 274,4)	4/118 (3,4) 151,9 (41,4 – 388,9)	-5,6% (-344,8 – 67,4)
Nicht-adipös	38/1179 (3,2) 132,2 (93,6 – 181,5)	30/394 (7,6) 316,2 (213,3 – 451,4)	58,2% (30,1 – 74,8)

2.2 Risk of Bias-Bewertung

Tabelle 8: Risk of Bias assessment for pivotal trial of COVID-19 vaccination with Spikevax in 6 months to 5 year old children

Study	Outcome	Randomization Process	Deviations from intended interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the reported result	Overall Bias
Study	SARS-CoV-2 Infections	Low	Low	Low	Low	Low	Low
	Symptomatic COVID-19	Low	Low	Low	Low	Low	Low
	Severe COVID-19	Low	Low	Low	Low	Low	Low
	Local reactions (dose 1&2)	Low	Low	Low	Some concern[1]	Low	Some concern
	Systemic reactions (dose 1&2)	Low	Low	Low	Some concern[1]	Low	Some concern
	AEs	Low	Low	Low	Low	Low	Low
	SAEs	Low	Low	Low	Some concern[1]	Low	Some concern
	AESIs (Myocarditis)	Low	Low	Low	Some concern[1]	Low	Some concern

AEs: adverse events, SAEs: serious adverse events, AESIs: adverse events of special interest

[1]Limited information on outcome measurement provided causing some concerns

2.3 GRADE-Bewertung

Tabelle 9: GRADE profile on the effects of COVID-19 vaccination with Spikevax in 6 to 23 months old children

Population: Children, aged 6-23 months
Intervention: Spikevax, 2 doses à 25 µg 28 days apart
Comparison: Placebo
Setting: Community

Outcomes	Absolute effect with placebo	Absolute effect with vaccination	Relative effect (95% CI)	Timing of outcome measurement	No. of participants (studies)	Certainty of the evidence (GRADE)
Vaccine efficacy						
SARS-CoV-2 Infections	88 per 1000	52 per 1000 (36 to 77)	VE 40.5% (12.3 – 59.2)	14 days after dose 2 (median 68 days)	2024 (1)	⨁⨁⨁◯ MODERATE[a]
Symptomatic COVID-19 (seronegative only)	66 per 1000	33 per 1000 (26 to 52)	VE 50.6% (21.4 – 68.6)	14 days after dose 2 (median 68 days)	2024 (1)	⨁⨁⨁◯ MODERATE[a]
Symptomatic COVID-19 (seropositive included)	N.E., Cases and number of participants not reported	N.E., Cases and number of participants not reported	VE 52.1% (24.3 – 69.3)	14 days after dose 2 (median 68 days)	N.R. (1)	⨁⨁⨁◯ MODERATE[a]
Severe COVID-19	N.E., 0 Events observed	N.E., 0 Events observed	N.E.	14 days after dose 2 (median 68 days)	2024 (1)	⨁◯◯◯ VERY LOW[b]
Vaccine Safety						
Local Reactions (dose 1)	332 per 1000	445 per 1000 (392 to 505)	RR 1.34 (1.18 – 1.52)	≤ 7 days	2328 (1)	⨁⨁⨁◯ MODERATE[c]
Local Reactions (dose 2)	302 per 1000	544 per 1000 (474 to 622)	RR 1.8 (1.57 – 2.06)	≤ 7 days	2122 (1)	⨁⨁⨁◯ MODERATE[c]
Systemic Reactions (dose 1)	723 per 1000	766 per 1000 (723 to 810)	RR 1.06 (1.0 – 1.12)	≤ 7 days	2328 (1)	⨁⨁⨁◯ MODERATE[c]
Systemic Reactions (dose 2)	504 per 1000	559 per 1000 (509 to 615)	RR 1.11 (1.01 – 1.22)	≤ 7 days	1738 (1)	⨁⨁⨁◯ MODERATE[c]
Adverse Events	482 per 1000	492 per 1000 (448 to 545)	RR 1.02 (0.93 – 1.13)	Up to 28 days post dose 2	2350 (1)	⨁⨁◯◯ LOW[a, c]
Serious Adverse Events	2 per 1000	10 per 1000 (3 to 76)	RR 5.02 (0.66 – 37.9)	Up to data-cutoff	2350 (1)	⨁⨁◯◯ LOW[d]
Adverse Events of Special Interest (Myocarditis)	N.E., 0 Events observed	N.E., 0 Events observed	N.E.	Up to data-cutoff	2350 (1)	⨁◯◯◯ VERY LOW[b]

VE: vaccine effectiveness, RR: risk ratio, N.E.: not estimated, N.R.: not reported/ [a] Downgraded one level for serious imprecision/ [b] Downgraded three levels for critical imprecision/ [c] Downgraded one level for serious study limitations/ [d] Downgraded two levels for very serious imprecision

Tabelle 10: GRADE profile on the effects of COVID-19 vaccination with Spikevax in 2 to 5 year old children

Population: Children, aged 2-5 years
Intervention: Spikevax, 2 doses à 25 µg 28 days apart
Comparison: Placebo
Setting: Community

Outcomes	Absolute effect with placebo	Absolute effect with vaccination	Relative effect (95% CI)	Timing of outcome measurement	No. of participants (studies)	Certainty of the evidence (GRADE)
Vaccine efficacy						
SARS-CoV-2 Infections	108 per 1000	74 per 1000 (39 to 66)	VE 31.5% (11.4 – 46.7)	14 days after dose 2 (median 71 days)	3452 (1)	⊕⊕⊕◯ MODERATE[a]
Symptomatic COVID-19 (seronegative only)	71 per 1000	45 per 1000 (33 to 62)	VE 36.8% (12.5 – 54.0)	14 days after dose 2 (median 71 days)	3452 (1)	⊕⊕⊕◯ MODERATE[a]
Symptomatic COVID-19 (seropositive included)	N.E., Cases and number of participants not reported	N.E., Cases and number of participants not reported	VE 34.5% (9.8 – 52.0)	14 days after dose 2 (median 71 days)	N.R. (1)	⊕⊕⊕◯ MODERATE[a]
Severe COVID-19	N.E., 0 Events observed	N.E., 0 Events observed	N.E.	14 days after dose 2 (median 71 days)	3452 (1)	⊕◯◯◯ VERY LOW[b]
Vaccine Safety						
Local Reactions (dose 1)	420 per 1000	534 per 1000 (584 to 685)	RR 1.51 (1.39 – 1.63)	≤ 7 days	3926 (1)	⊕⊕⊕◯ MODERATE[c]
Local Reactions (dose 2)	421 per 1000	733 per 1000 (678 to 791)	RR 1.74 (1.61 – 1.88)	≤ 7 days	3897 (1)	⊕⊕⊕◯ MODERATE[c]
Systemic Reactions (dose 1)	503 per 1000	538 per 1000 (503 to 578)	RR 1.07 (1.0 – 1.15)	≤ 7 days	3925 (1)	⊕⊕⊕◯ MODERATE[c]
Systemic Reactions (dose 2)	446 per 1000	615 per 1000 (571 to 665)	RR 1.38 (1.28 – 1.49)	≤ 7 days	3897 (1)	⊕⊕⊕◯ MODERATE[c]
Adverse Events	375 per 1000	401 per 1000 (364 to 439)	RR 1.07 (0.97 – 1.17)	Up to 28 days post dose 2	4038 (1)	⊕⊕◯◯ LOW[a, c]
Serious Adverse Events	2 per 1000	3 per 1000 (1 to 14)	RR 1.5 (0.32 – 6.91)	Up to data-cutoff	4038 (1)	⊕⊕◯◯ LOW[d]
Adverse Events of Special Interest (Myocarditis)	N.E., 0 Events observed	N.E., 0 Events observed	N.E.	Up to data-cutoff	4038 (1)	⊕◯◯◯ VERY LOW[b]

VE: vaccine effectiveness, RR: risk ratio, N.E.: not estimated, N.R.: not reported

[a] Downgraded one level for serious imprecision/ [b] Downgraded three levels for critical imprecision/ [c] Downgraded one level for serious study limitations

[d] Downgraded two levels for very serious imprecision