
VECTOR

Vaccine effectiveness of COVID-19 in the population at risk



COVID-19 vaccination in the Netherlands



Vaccine effectiveness

Vaccine efficacy

- RCT, standardized conditions
- (pre-registration)

Vaccine effectiveness

- Real world performance
- Other outcomes of interest
- Subpopulations

	Vaccine	Vaccine efficacy
	Comirnaty (BioNTech/Pfizer)	95%
	Spikevax (Moderna)	94.1%
COVID-19 Vaccine Janssen (1 dose)		67%
	Vaxzevria (AstraZeneca)	58.5%



Objectives

Primary objective

To estimate the vaccine effectiveness (VE) against COVID-19 related hospital admission

Secondary objectives

1. To measure VE stratified for age, vaccination product, sex, risk-category.
2. To measure VE against more severe COVID-19 related outcomes (ICU-admission, death)
3. To measure VE stratified for circulating SARS-CoV-2 strains





Methods



Test-negative design

Study population

Patients hospitalized with a suspected respiratory infection

- *Cases (COVID-positives)*
- *Controls (COVID-negatives)*



Determinant

Vaccination against COVID-19



Data collection

- Retrospective
 - *Vaccination status*
 - *COVID-19 labresults*
 - *Clinical characteristics*
 - *Disease course*

- “COVID Vaccinatie Informatie Monitoringssystem” (CIMS)

- PCR-material for sequencing



Inclusion criteria

- Hospitalisation
- Suspected respiratory infection
- Respiratory sample is adequately tested on SARS-CoV-2 at admission on within 14 days prior to admission
- 18 years or older
- Eligible for vaccination

WHO SARI definition

- *Hospital admission AND*
- *Fever AND*
- *Cough AND*
- *Acute onset (<10 days)*

Exclusion criteria

- Readmission within 14 days of prior admission
- Referral from another hospital



Inclusion criteria

- Hospitalisation
- Suspected respiratory infection
- Respiratory sample is adequately tested on SARS-CoV-2 at admission on within 14 days prior to admission
- 18 years or older
- Eligible for vaccination

WHO SARI definition

- *Hospital admission AND*
- *Fever AND*
- *Cough and/or dyspnea AND*
- *Acute onset (<10 days)*

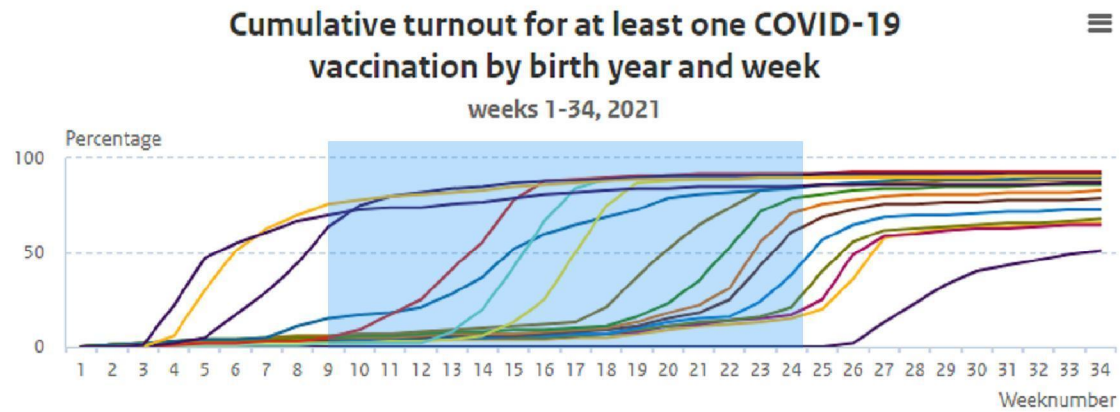
Exclusion criteria

- Readmission within 14 days of prior admission
- Referral from another hospital

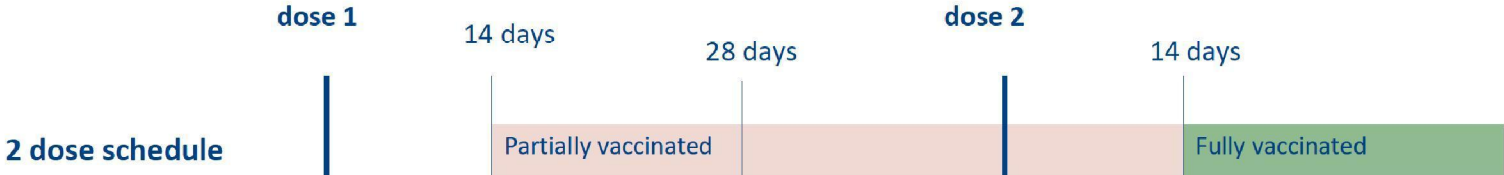


Inclusion procedure

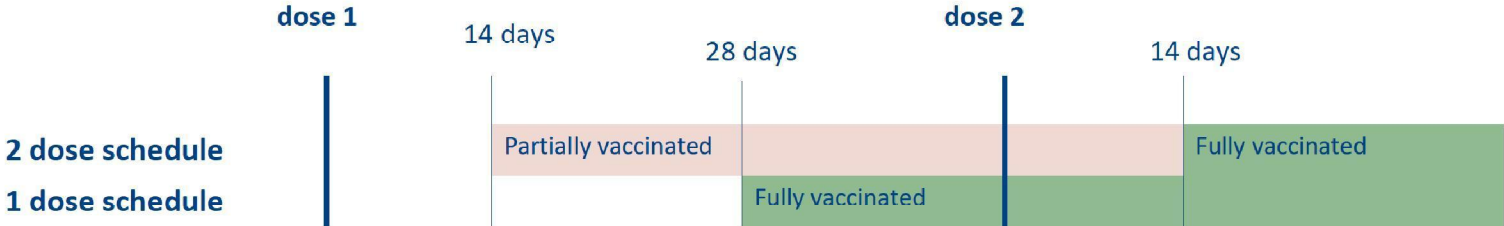
- Max. 700 inclusions
- Evenly distributed over time
 - Phase 1: 230 patients of 75+
 - Phase 2: 230 patients of 60-74
 - Phase 3: 230 patients of 18-59



Definition vaccination status



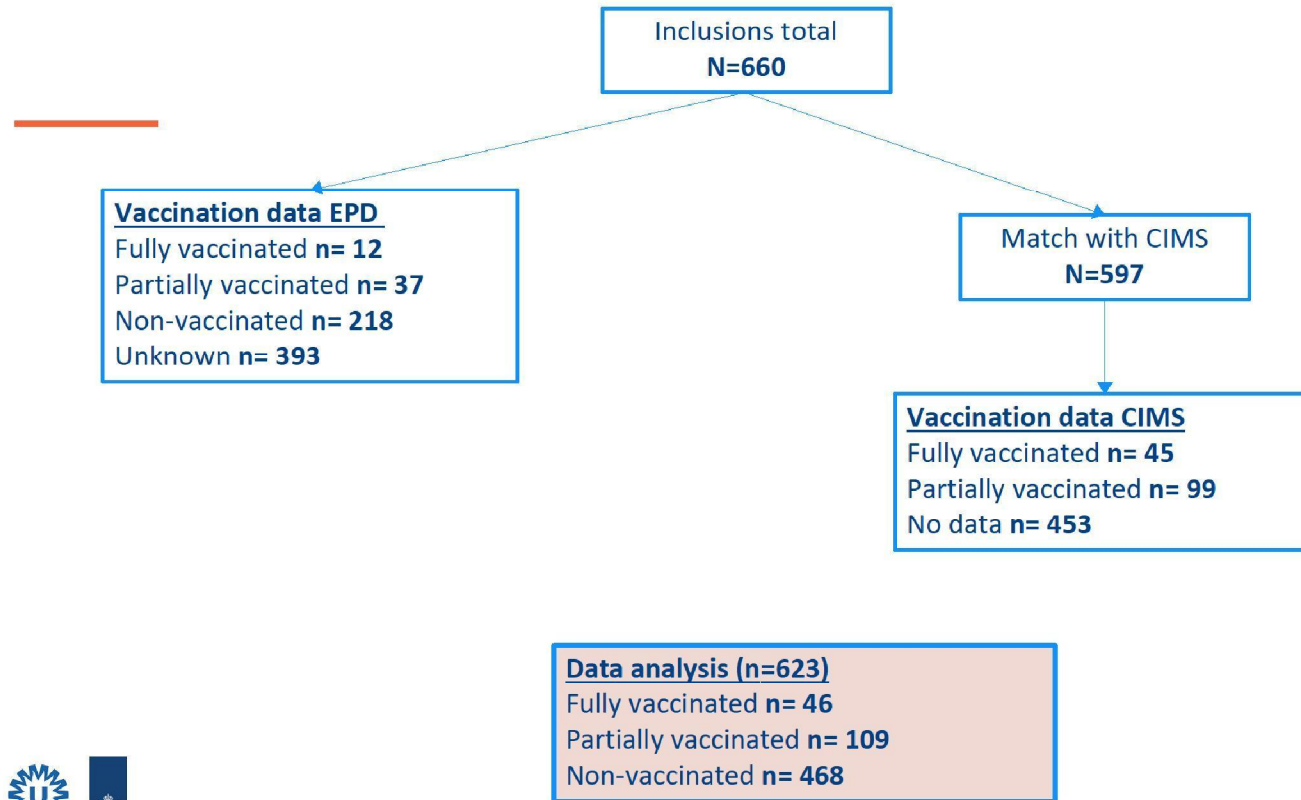
Definition vaccination status





Results





Patient characteristics

	Controls	Cases	p
n	254	369	
Age median (IQR)	70.50 [60.00, 83.00]	65.00 [55.00, 76.00]	<0.001
Age-group			<0.001
75+	112 (44.1)	102 (27.6)	
61-74	77 (30.3)	132 (35.8)	
18-60	65 (25.6)	135 (36.6)	
Male Sex	135 (53.1)	223 (60.4)	0.085
Residency status			0.038
Nursing home	13 (5.1)	8 (2.2)	
Non-institutional	233 (91.7)	356 (96.5)	
Unknown	8 (3.1)	5 (1.4)	
BMI (mean, SD)	26.79 (5.43)	29.38 (5.65)	<0.001
Chronic pulmonary disease	119 (46.9)	97 (26.3)	<0.001
Immune deficiency	40 (15.7)	23 (6.2)	<0.001
Chronic cardiac disease	87 (34.3)	80 (21.7)	0.001
Malignancy	47 (18.5)	31 (8.4)	<0.001
Obesity	58 (22.8)	137 (37.1)	<0.001
Diabetes	45 (17.7)	103 (27.9)	0.004
Hypertension	88 (34.6)	120 (32.5)	0.641
Severe renal insufficiency	6 (2.4)	1 (0.3)	0.041
Other comorbidity	157 (61.8)	206 (55.8)	0.160
No comorbidity	22 (8.7)	48 (13.0)	0.119



Disease presentation

	Controls	Cases	p
n	254	369	
Fever	107 (42.1)	234 (63.4)	<0.001
Cough	169 (66.5)	290 (78.6)	0.001
Shortness of breath	230 (90.6)	327 (88.6)	0.523
Loss of smell	3 (1.2)	39 (10.6)	<0.001
Loss of taste	8 (3.1)	50 (13.6)	<0.001
Other cold symptoms	15 (5.9)	37 (10.0)	0.093
Headache	20 (7.9)	72 (19.5)	<0.001
Myalgia	15 (5.9)	66 (17.9)	<0.001
General malaise	78 (30.7)	162 (43.9)	0.001
Gastro-intestinal symptoms	53 (20.9)	127 (34.4)	<0.001
Chills	25 (9.8)	30 (8.1)	0.551
Palpitations	5 (2.0)	5 (1.4)	0.784
Chestpain	39 (15.4)	59 (16.0)	0.919
Dizziness	11 (4.3)	12 (3.3)	0.627
Skin rash	1 (0.4)	1 (0.3)	1.000
Disorientation	16 (6.3)	28 (7.6)	0.647
CRP (median, IQR)	59.00 [16.50, 141.00]	99.00 [50.00, 153.75]	<0.001
Leuko's (median, IQR)	12.00 [8.70, 14.70]	6.60 [4.80, 9.30]	<0.001



Primary outcome

	Controls	Cases
Non-vaccinated	144	324
Partially vaccinated	70	39
Fully vaccinated	40	6

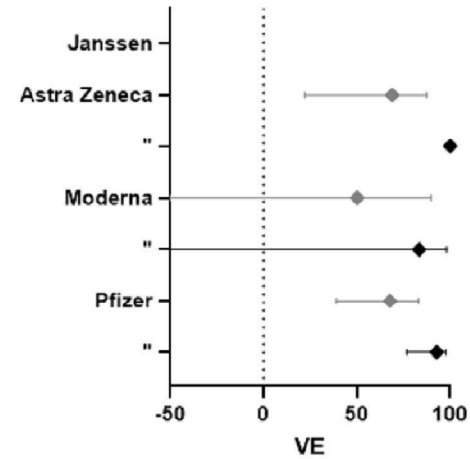
	Adjusted for week and agegroup		Adjusted for age, sex, week, comorbidity*, nursing home residency	
	VE	95% CI	VE	95% CI
Partial vaccination	58.7	(19.0 - 79.0)	67.2	(45.2 - 80.3)
Full vaccination	93.3	(75.9 - 98.2)	90.3	(74.6 - 96.3)

*Comorbidities adjusted for: chronic pulmonary disease, chronic cardiac disease, immunodeficiency, severe renal insufficiency, diabetes, malignancy, obesity



Product specific VE

		Cases vaccinated	Controls vaccinated	VE	95% CI
Janssen		1	1	-82	(-198 --15)
AstraZeneca	1 dose	11	14	67	(22-86)
	2 doses	1	0		
Moderna	1 dose	5	6	64	(-39-91)
	2 doses	1	7	83	(-51-98)
Pfizer	1 dose	22	46	78	(59-88)
	2 doses	4	30	93	(77-98)



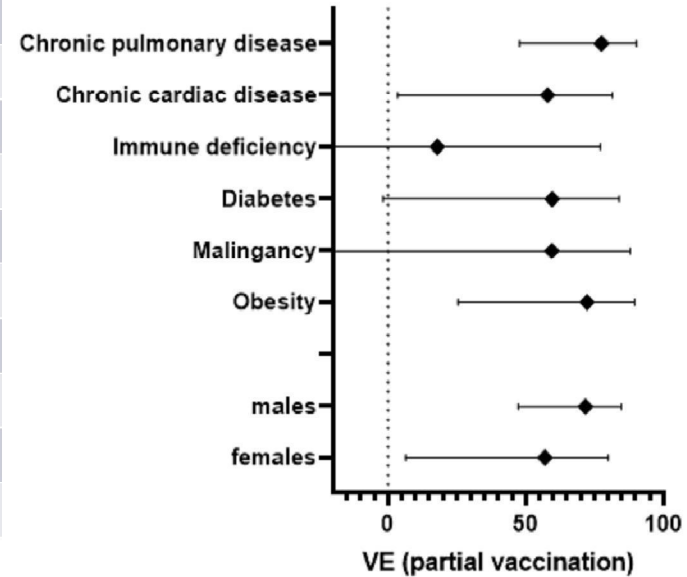
Subgroup analysis (age)

		Number vaccinated		VE adjusted for week	
		cases	controls	VE	95% CI
75+	partial	19	31	59	(19-79)
	Full	3	25	94	(79-99)
61-74	partial	15	26	72	(36-88)
	Full	0	8		
18-60	partial	5	13	75	(11-93)
	Full	3	7	58	(-116-92)



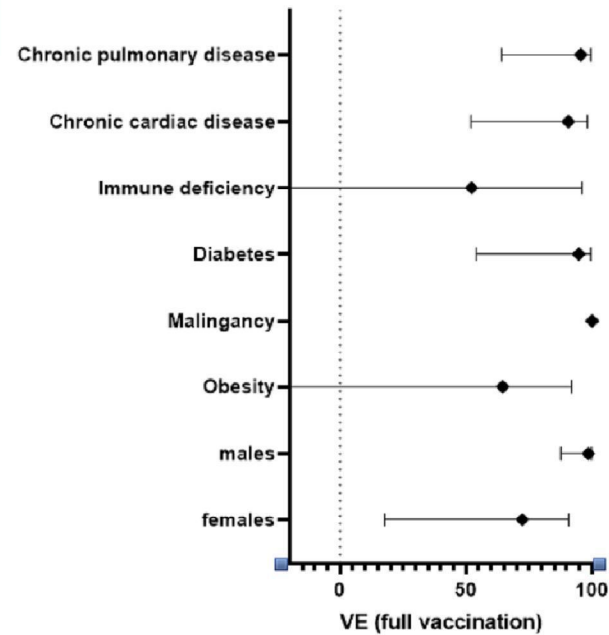
Subgroup analysis (partial vaccination)

	Number vaccinated		VE adjusted for week and agegroup	
	cases	controls	VE	95% CI
Chronic pulmonary disease	9	37	78	(48-90)
Chronic cardiac disease	13	27	58	(4-82)
Immune deficiency	7	16	18	(-194-77)
Diabetes	16	14	60	(-2-84)
Malignancy	5	12	60	(-37-88)
Obesity	9	16	72	(26-90)
Males	26	44	72	(47-85)
Females	13	26	57	(6-80)



Subgroup analysis (full vaccination)

	Number vaccinated		VE adjusted for week and agegroup	
	cases	controls	VE	95% CI
Chronic pulmonary disease	1	19	96	(64-99)
Chronic cardiac disease	2	15	91	(52-98)
Immune deficiency	1	7	52	(-477-96)
Diabetes	1	10	95	(54-99)
Malignancy	0	8		
Obesity	4	6	64	(-54-92)
Males	1	21	98	(88-100)
Females	5	19	72	(18-91)



Subgroup analysis (full vaccination)

	Cases vaccinated		Controls vaccinated		VE adjusted for week and agegroup		Adjusted for age, sex, week, comorbidity*, nursing home residency	
	n		n		VE	95% CI	VE	95% CI
Males	1	0.4%	21	15.6%	98	88-100	98	85-100
Females	5	3.4%	19	16.0%	72	18-91	77	24-93



Subgroup analysis (full vaccination)

	Cases vaccinated		Controls vaccinated		VE adjusted for week and agegroup		Adjusted for age, sex, week, comorbidity*, nursing home residency	
	n		n		VE	95% CI	VE	95% CI
Males	1	0.4%	21	15.6%	98	88-100	98	85-100
Females	5	3.4%	19	16.0%	72	18-91	77	24-93
Males	26	11.7%	44	32.6%	72	47-85	71	42-85
Females	13	8.9%	26	21.8%	57	6-80	68	25-87



Vaccine failures

	Fully vaccinated	Partially vaccinated	Unvaccinated
n	6	39	324
Age median (IQR)	72.50 [59.25, 85.75]	74.00 [63.50, 84.00]	64.50 [54.00, 74.00]
Age-group			
75+	3 (50.0)	19 (48.7)	80 (24.7)
61-74	0 (0.0)	15 (38.5)	117 (36.1)
18-60	3 (50.0)	5 (12.8)	127 (39.2)
Male Sex	1 (16.7)	26 (66.7)	196 (60.5)
Residency status			
Nursing home	2 (33.3)	0 (0.0)	6 (1.9)
Non-institutional	4 (66.7)	38 (97.4)	314 (96.9)
Unkwnown	0 (0.0)	1 (2.6)	4 (1.2)
BMI (mean, SD)	33.45 (5.39)	28.62 (5.94)	29.41 (5.61)
Chronic pulmonary disease	1 (16.7)	9 (23.1)	87 (26.9)
Immune deficiency	1 (16.7)	7 (17.9)	15 (4.6)
Chronische_hartaandoening.	2 (33.3)	13 (33.3)	65 (20.1)
Malignancy	0 (0.0)	5 (12.8)	26 (8.0)
Obesity	4 (66.7)	9 (23.1)	124 (38.3)
Diabetes	1 (16.7)	16 (41.0)	86 (26.5)
Hypertension	2 (33.3)	12 (30.8)	106 (32.7)
Severe renal insufficiency	0 (0.0)	0 (0.0)	1 (0.3)
Other comorbidity	4 (66.7)	21 (53.8)	181 (55.9)
No comorbidity	0 (0.0)	2 (5.1)	46 (14.2)



Secondary outcomes

ICU admission and in-hospital mortality among cases

	Fully vaccinated N=6	Partially vaccinated N=39	Unvaccinated N=324
ICU admission	0 (0.0)	5 (12.8)	64 (19.8)
In-hospital mortality	0 (0.0)	9 (23.1)	33 (10.2)



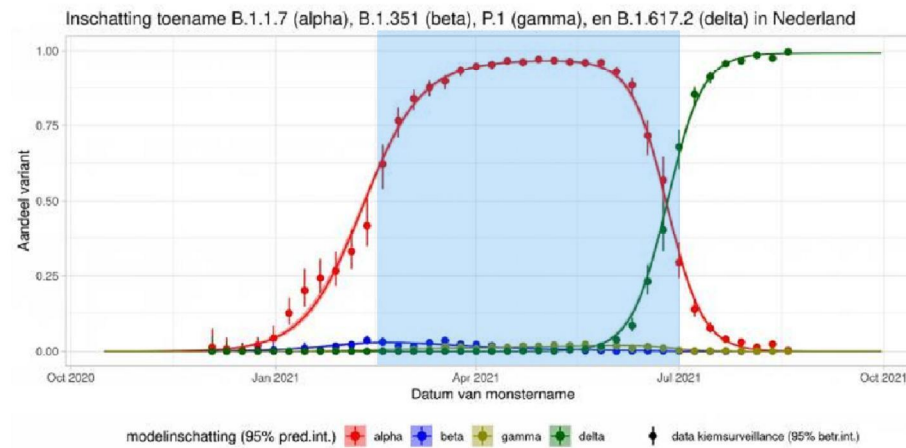
Conclusion

- Significant overall vaccine effectiveness
 - (Partial vaccination + full vaccination)
- Vaccine effectiveness is lower in females
- No VE differences within risk groups



Limitations

- Alfa-variant was dominant during study period



Limitations

- Only representative for alfa-variant
- Prior COVID-19 infection not taken into account
- Representativeness of controls



Future plans

Continuation of data collection as surveillance

- Comparison with alfa variant
- Effect of time since vaccination on VE

Analysis of molecular data



Acknowledgements

Study team



Researches involved (RIVM/UMCU)



Comparison with other VE-estimates

	Time period	VE partial		VE full	
NICE-CIMS linkage	April 4th – may 29th	79%	(76-81)	93%	91-94
Screening method (OISIRS)					



Resultaten

Sensitiviteitsanalyse 1
Vaccinatiestatus onbekend = niet gevaccineerd

	Controls	Cases
Niet-gevaccineerd	104	111
Gedeeltelijk gevaccineerd	9	9
Volledig gevaccineerd	6	1

	N	OR	95% CI	VE
1x gevaccineerd	18	0.908	(0.340– 2.420)	0.092
2x gevaccineerd	7	0.136	(0.007 – 0.935)	0.849

Overige geplande sensitiviteitsanalyses

- Officiële SARI case-definitie
- Als gevaccineerd beschouwen na 7 dagen

Sensitivity analysis

SARI-patients
(with reported fever)

	Controls	Cases
Niet-gevaccineerd	19	60
Gedeeltelijk gevaccineerd	7	8
Volledig gevaccineerd	3	2

	N	OR	95% CI	VE
1x gevaccineerd		0.342	(0.101– 1.147)	65.8%
2x gevaccineerd		0.187	(0.021 – 1.338)	81.3%

Vaccination status
unknown
= non-vaccinated

	Controls	Cases
Niet-gevaccineerd	174	239
Gedeeltelijk gevaccineerd	15	12
Volledig gevaccineerd	8	2

	N	OR	95% CI	VE
1x gevaccineerd		0.728	(0.322– 1.618)	27.2%
2x gevaccineerd		0.278	(0.041– 1.176)	72.2%

Age 60-75

zkh	inclusies	cases	controls	gevaccineerd	Niet gevaccineerd	Vaccinatiestatus onbekend
CWZ	34	20	14	11	4	19
Sint Antonius	13	7	6	2	3	8
Martini	2	1	1	1	0	1
OLVG	6	5	1	0	0	6
Catharina zkh	42	25	17	11	13	18
Totaal	97	58	39	25	20	52

Age 18-60

zkh	inclusies	cases	controls	gevaccineerd	Niet gevaccineerd	Vaccinatiestatus onbekend
CWZ	34	14	19	9	9	15
Sint Antonius	16	15	1	1	0	15
Catharina zkh	27	20	7	3	14	10
Totaal	77	49	27	13	23	40