COVID-19 Vaccination – Study Data, Recommendations and Real World Experience

Lecture for pharmacy and medical students in Switzerland

23.2.2021

Prof. Dr. Ulrich Heininger

ulrich.heininger@ukbb.ch

UKBB
kompetent & menschlich

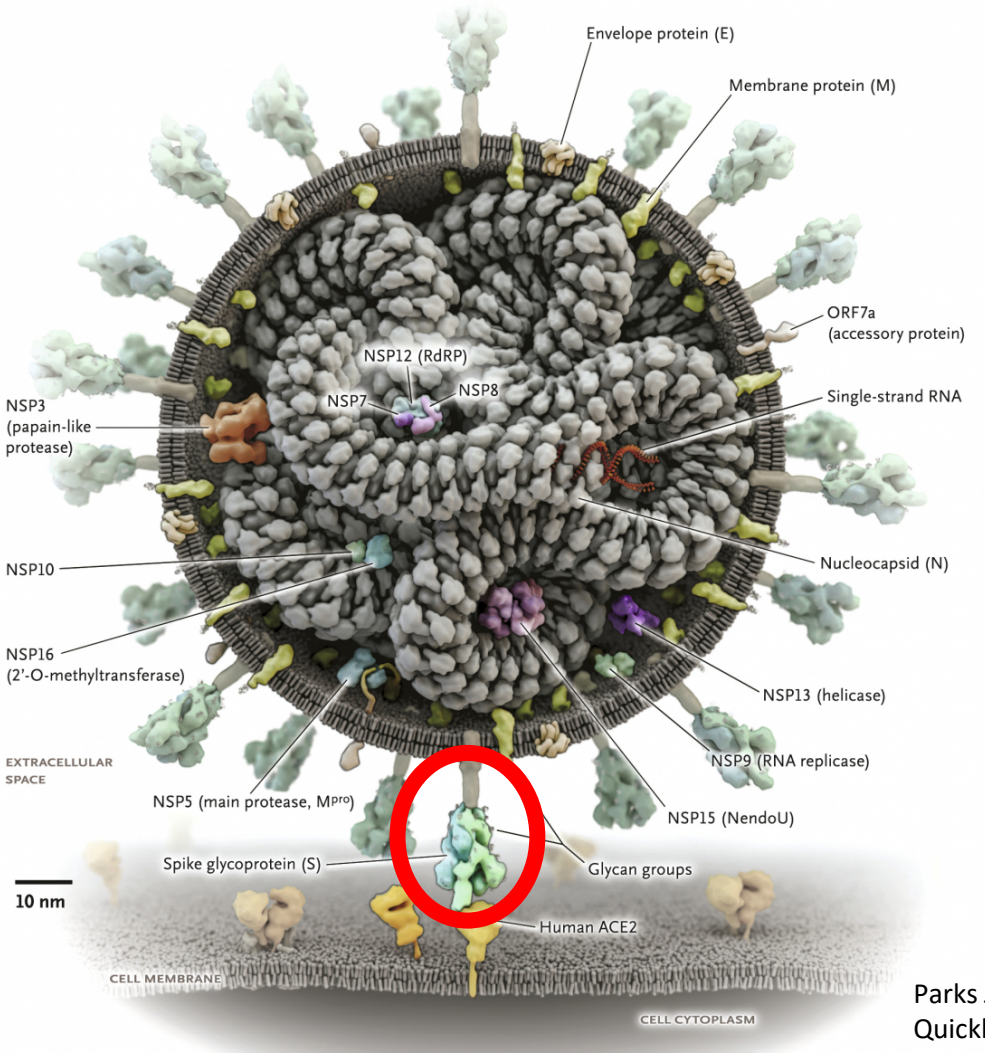
Universität Basel

COVID-19 Vaccination – Study Data, Recommendations and Real World Experience

1. Study data: BioNTech/Pfizer as an example
2. Recommendations: Switzerland
3. Real World Experience: INFOVAC experience

   (www.infovac.ch)

SARS-CoV-2, a single-stranded RNA-Virus



Parks JM, Smith JC. How to Discover Antiviral Drugs Quickly. N Engl J Med. 2020;382(23):2261–4.

COVID-19/SARS-CoV-2 Vaccines

© Hector Amezcua / AP Photo / picture alliance; Aerztezeitung 18.12.2020

UKBB
kompetent & menschlich

COVID-19/SARS-CoV-2 Vaccines

- >200 vaccines under development
- Different techniques: Protein subunit-, virus like particles-, mRNA-, DNA-Plasmid, replicating viral vector-, and live-attenuated
- 13 candidates in phase 3 studies
- Press releases and publication re preliminary efficacy available for 6 vaccines (mRNA-Vaccine BioNTech and Moderna, AdV-Vector-vaccines Astra Zeneca, Johnson&Johnson, Sputnik V, protein vaccine Novavax)
- Relative (!) safety is increasing…

https://www.who.int/blueprint/priority-diseases/key-action/WHO_Target_Product_Profiles_for_COVID-19_web.pdf?ua=1
https://www.who.int/blueprint/priority-diseases/key-action/Novel_Coronavirus_Landscape_nCoV_11April2020.PDF?ua=1
Heininger U Pediatr Infect Dis 2020;39(7):e123-e124; Yamey et al. Lancet 2020;395:1405-6

COVID 19 Vaccine study – BioNTech mRNA

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Fernando P. Polack, M.D., Stephen J. Thomas, M.D., Nicholas Kitchin, M.D., Judith Absalon, M.D., Alejandra Gurtman, M.D., Stephen Lockhart, D.M., John L. Perez, M.D., Gonzalo Pérez Marc, M.D., Edson D. Moreira, M.D., Cristiano Zerbini, M.D., Ruth Bailey, B.Sc., Kena A. Swanson, Ph.D., Satrajit Roychoudhury, Ph.D., Kenneth Koury, Ph.D., Ping Li, Ph.D., Warren V. Kalina, Ph.D., David Cooper, Ph.D., Robert W. Frenck, Jr., M.D., Laura L. Hammitt, M.D., Özlem Türeci, M.D., Haylene Nell, M.D., Axel Schaefer, M.D., Serhat Ünal, M.D., Dina B. Tresnan, D.V.M., Ph.D., Susan Mather, M.D., Philip R. Dormitzer, M.D., Ph.D., Uğur Şahin, M.D., Kathrin U. Jansen, Ph.D., and William C. Gruber, M.D., for the C4591001 Clinical Trial Group*

This article was published on December 10, 2020, at NEJM.org.

DOI: 10.1056/NEJMoa2034577

UKBB
kompetent & menschlich

Methods

- Placebo-controlled, observer blinded, multinational Phase 2/3-Study

  (USA, 130 centers; Argentina, 1; Brazil, 2; South-Africa, 4; Germany, 6; Turkey; 9)
- Individuals ≥16 years of age
- 2 doses each 30 ug mRNA ≥21d: N= 21,720
- 2 doses placebo ≥21d: N= 21,728
- Primary study endpoints:

  - Efficacy against lab-confirmed COVID-19 disease

  - Safety and reactogenicity

Pollack et al; NEJM, online Dec. 10, 2020

UKBB
kompetent & menschlich

Table 1. Demographic Characteristics of the Participants in the Main Safety Population.*

Characteristic	BNT162b2 (N=18,860)	Placebo (N=18,846)	Total (N=37,706)
Sex — no. (%)			
Male	9,639 (51.1)	9,436 (50.1)	19,075 (50.6)
Female	9,221 (48.9)	9,410 (49.9)	18,631 (49.4)
Race or ethnic group — no. (%)†			
White	15,636 (82.9)	15,630 (82.9)	31,266 (82.9)
Black or African American	1,729 (9.2)	1,763 (9.4)	3,492 (9.3)
Asian	801 (4.2)	807 (4.3)	1,608 (4.3)
Native American or Alaska Native	102 (0.5)	99 (0.5)	201 (0.5)
Native Hawaiian or other Pacific Islander	50 (0.3)	26 (0.1)	76 (0.2)
Multiracial	449 (2.4)	406 (2.2)	855 (2.3)
Not reported	93 (0.5)	115 (0.6)	208 (0.6)
Hispanic or Latinx	5,266 (27.9)	5,277 (28.0)	10,543 (28.0)
Country — no. (%)			
Argentina	2,883 (15.3)	2,881 (15.3)	5,764 (15.3)
Brazil	1,145 (6.1)	1,139 (6.0)	2,284 (6.1)
South Africa	372 (2.0)	372 (2.0)	744 (2.0)
United States	14,460 (76.7)	14,454 (76.7)	28,914 (76.7)

Table 1. Demographic Characteristics of the Participants in the Main Safety Population.*

Characteristic	BNT162b2 (N=18,860)	Placebo (N=18,846)	Total (N=37,706)
Age group — no. (%)			
16–55 yr	10,889 (57.7)	10,896 (57.8)	21,785 (57.8)
>55 yr	7,971 (42.3)	7,950 (42.2)	15,921 (42.2)
Age at vaccination — yr			
Median	52.0	52.0	52.0
Range	16–89	16–91	16–91
Body-mass index‡			
≥30.0: obese	6,556 (34.8)	6,662 (35.3)	13,218 (35.1)

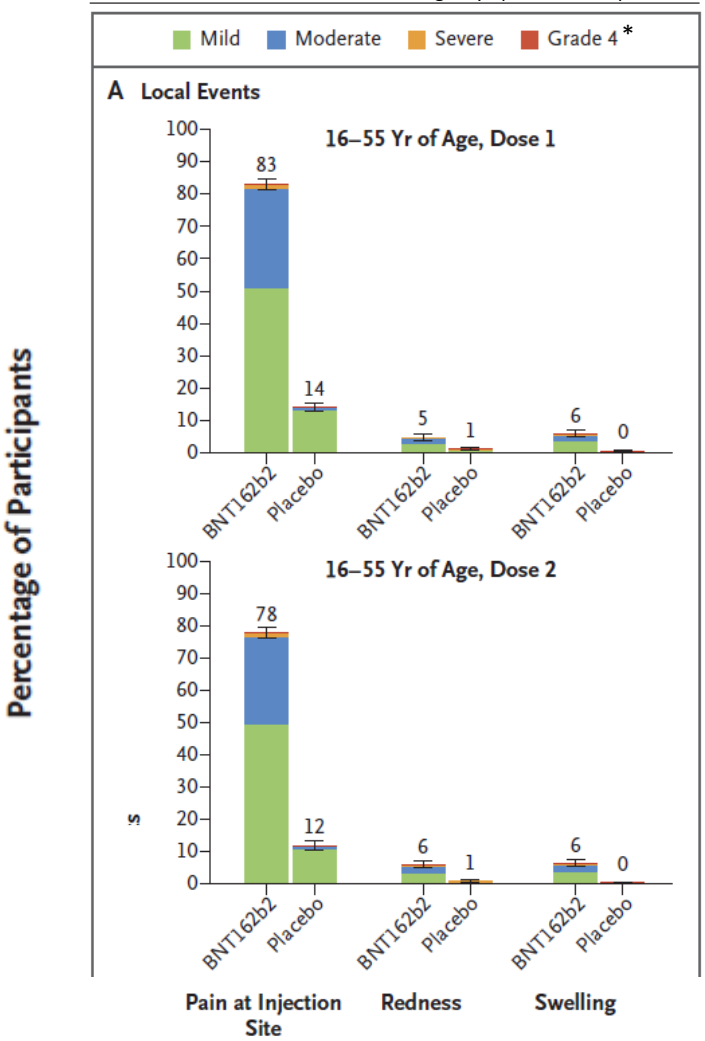
* Percentages may not total 100 because of rounding.
† Race or ethnic group was reported by the participants.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.

UKBB
kompetent & menschlich

Pollack et al; NEJM, online Dec. 10, 2020

Results – Reactogenicity (Days 0-7)

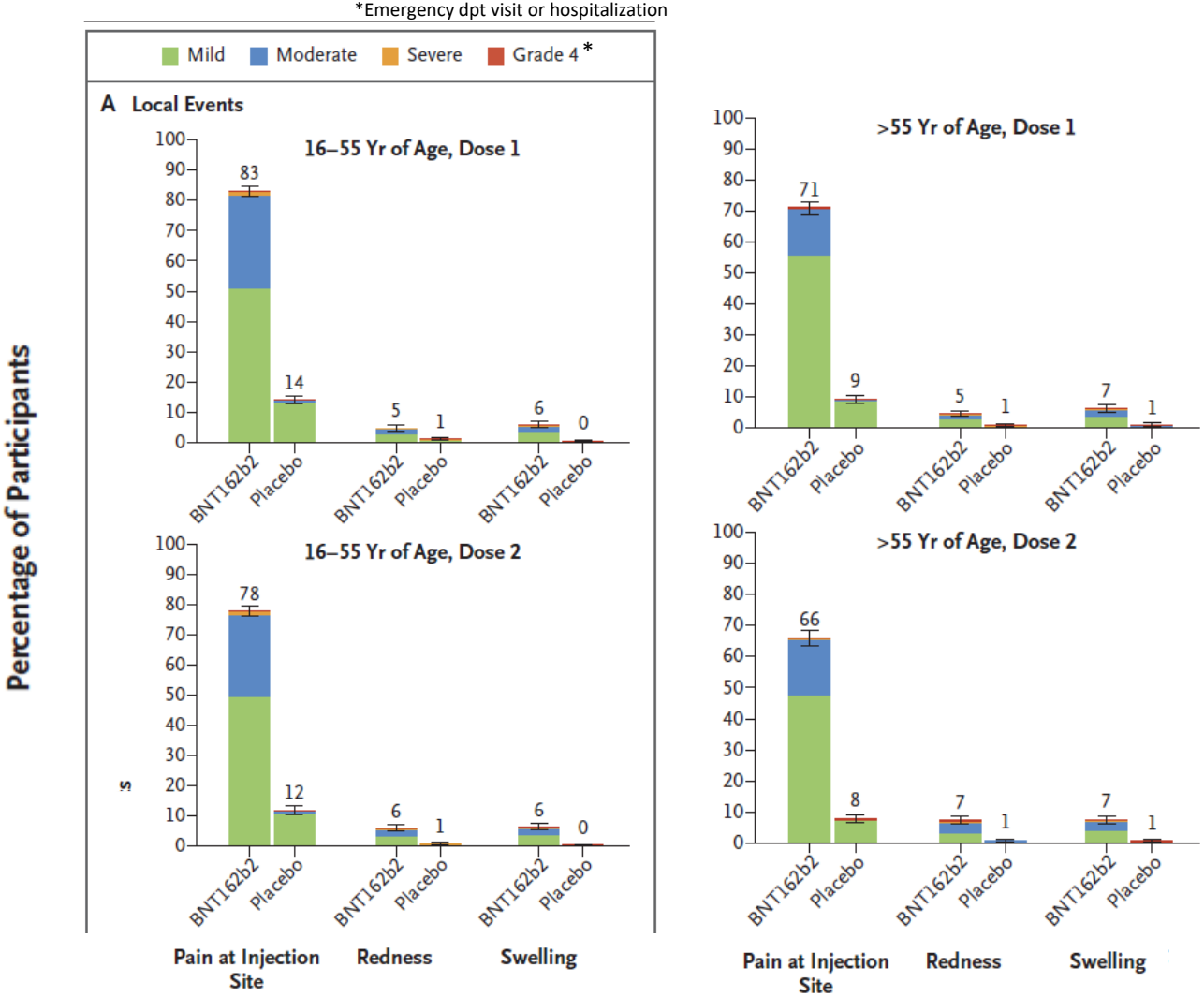
*Emergency dpt visit or hospitalization



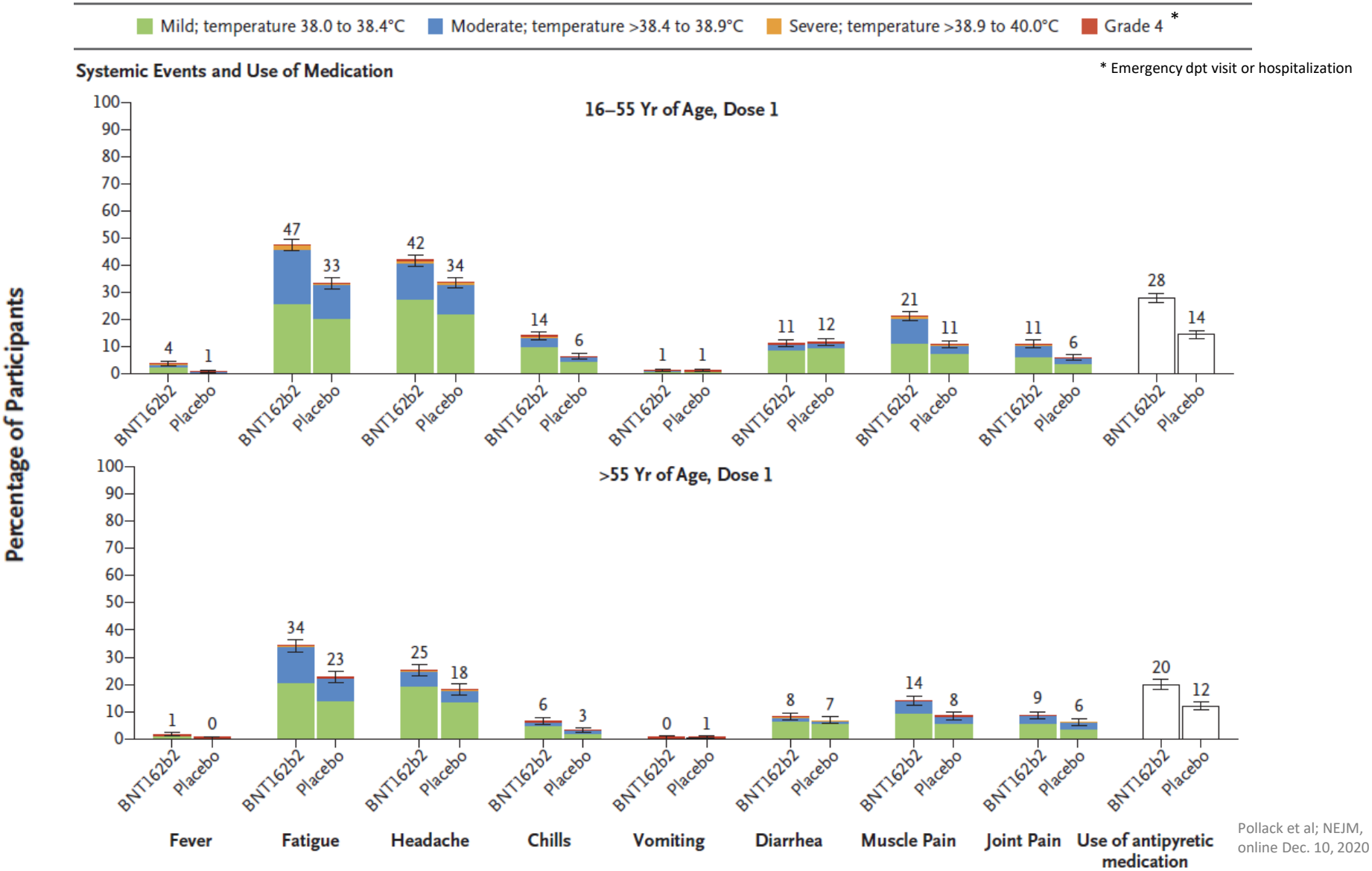
Pollack et al; NEJM, online Dec. 10, 2020

Results – Reactogenicity (Days 0-7)

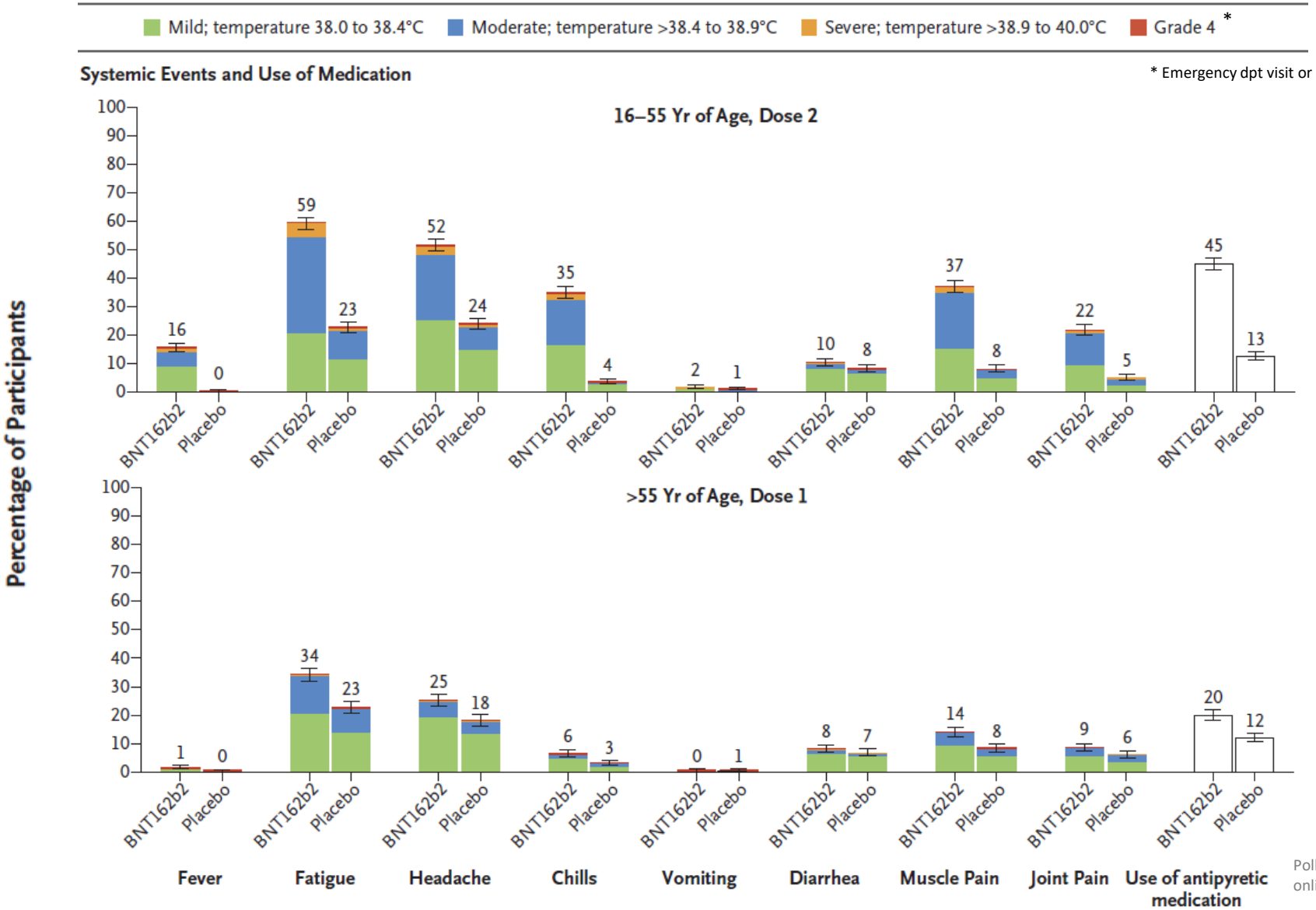
*Emergency dpt visit or hospitalization



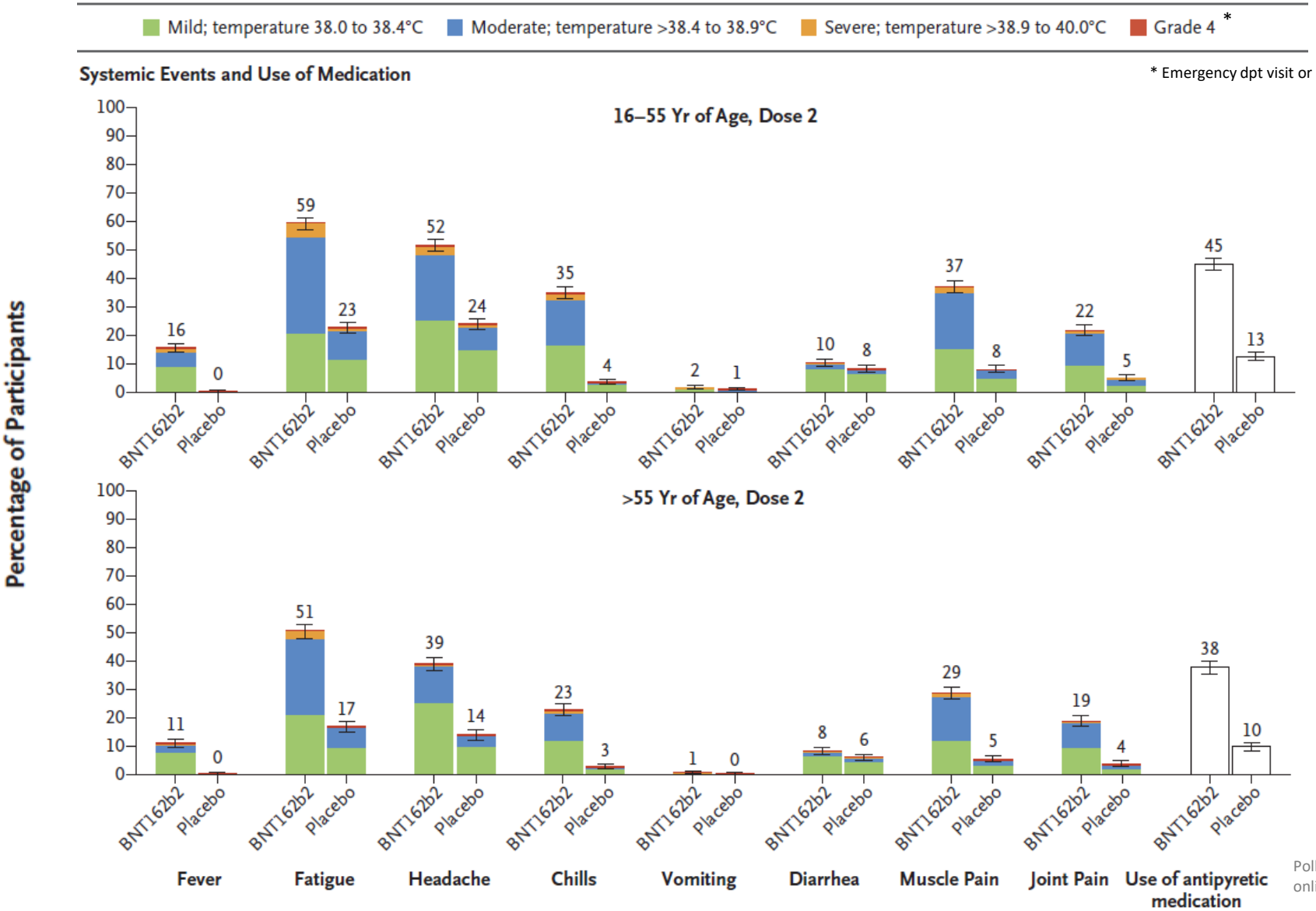
Pollack et al; NEJM, online Dec. 10, 2020



Pollack et al; NEJM, online Dec. 10, 2020

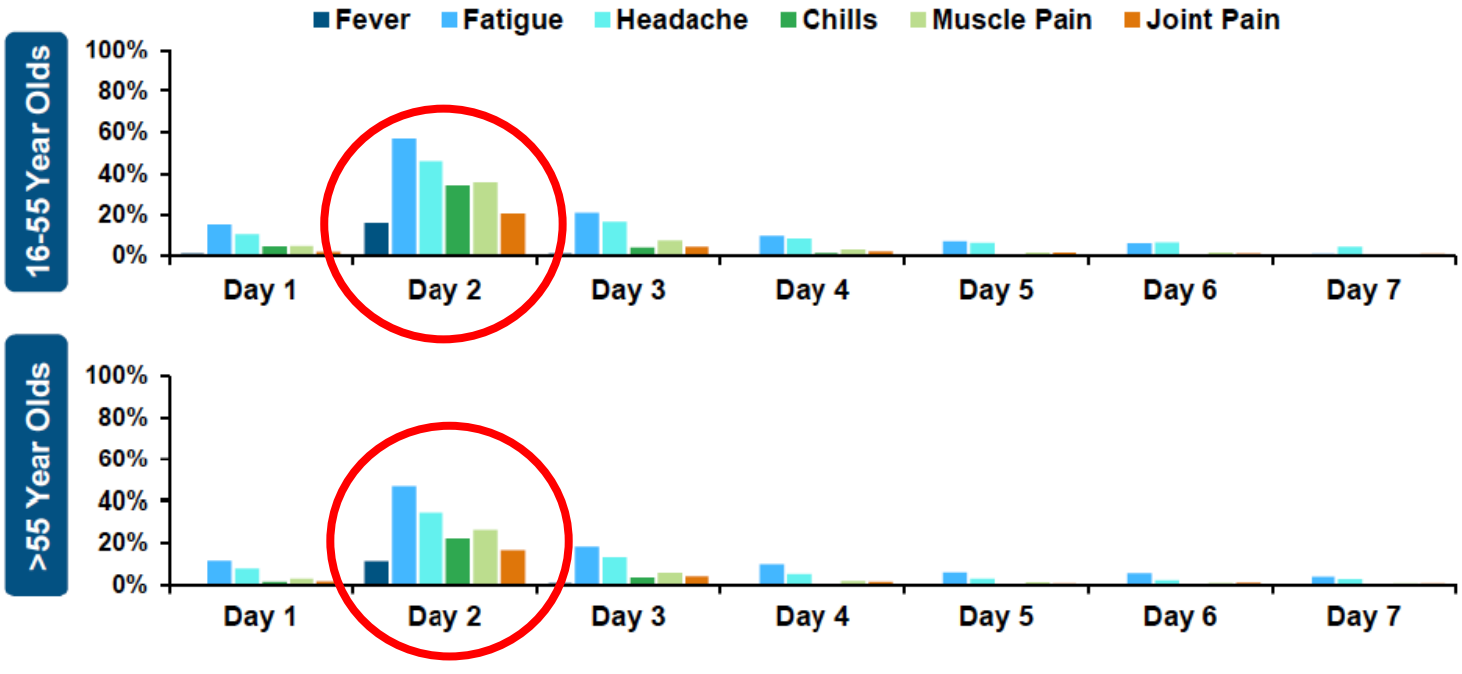


Pollack et al; NEJM, online Dec. 10, 2020



Pollack et al; NEJM, online Dec. 10, 2020

eDiary: Systemic Events Each Day From Dose 2 in 16-55 and >55 Year Olds (N=8,183) BNT162b2

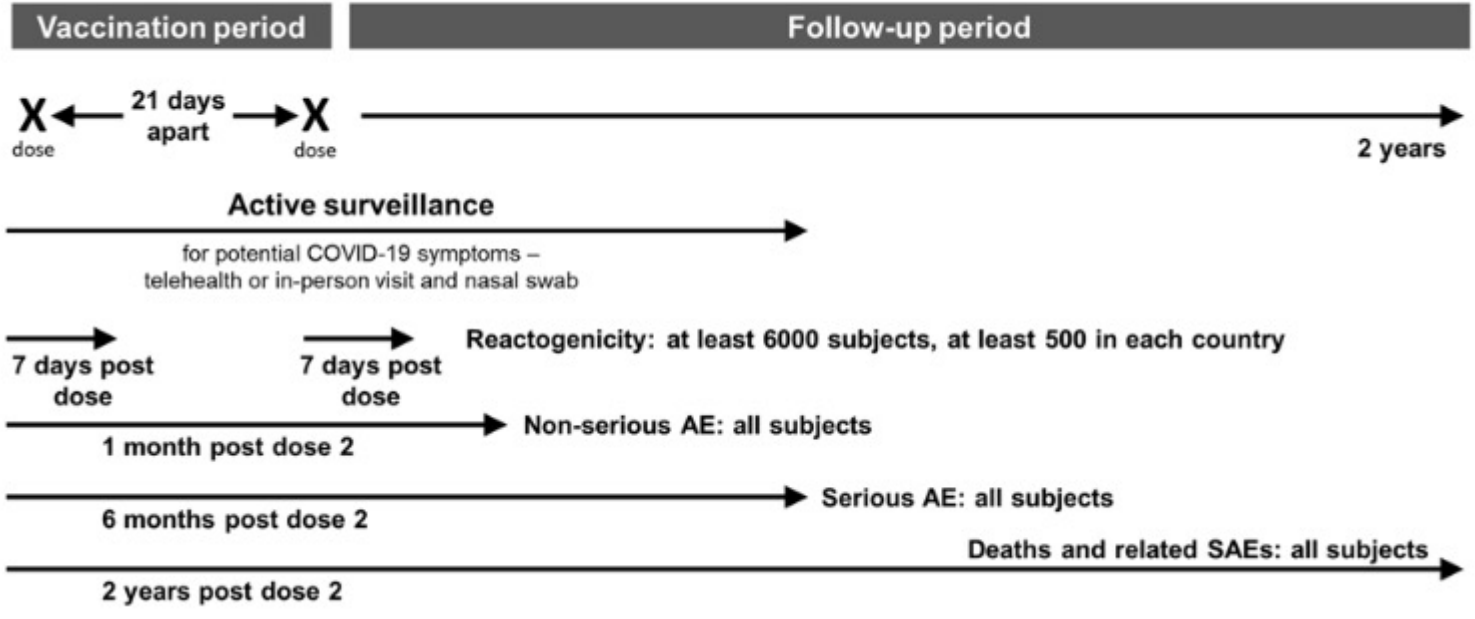


CC-31

Präsentation an FDA, Dezember 2020

UKBB
kompetent & menschlich

Figure 1. Safety Evaluation Follow-Up Periods in Study C4591001



Results – Efficacy

- ≥7 days after dose 2 (primary endpoint)
- Between doses 1 and 2 (secondary endpoint)

Pollack et al; NEJM, online Dec. 10, 2020

UKBB
kompetent & menschlich

Table 2. Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
	(N=18,198)		(N=18,325)			
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (1,7411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999

* The total population without baseline infection was 36,523; total population including those with and those without prior evidence of infection was 40,137.
† The surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from 7 days after the second dose to the end of the surveillance period.
‡ The credible interval for vaccine efficacy was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.
§ Posterior probability was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.

Table 2. Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

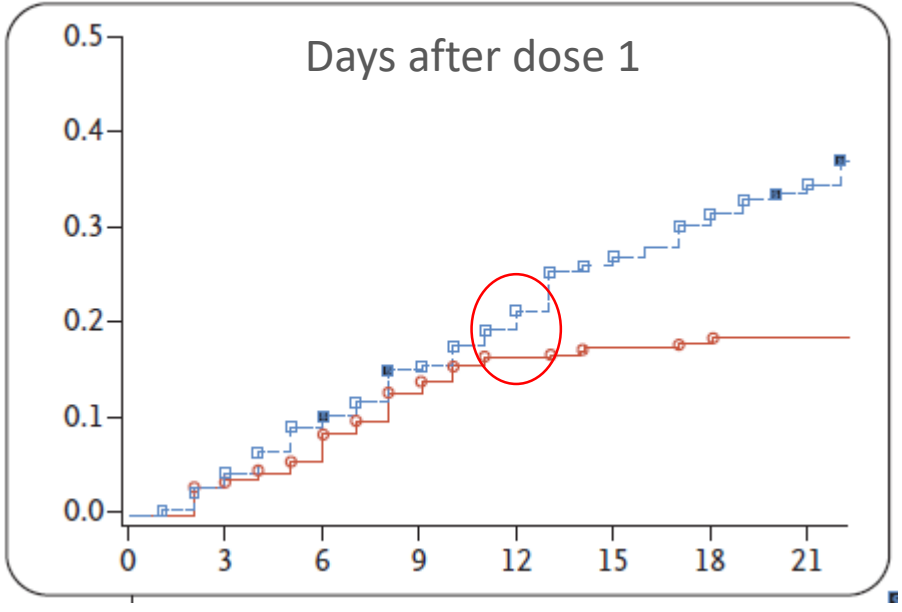
Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
		(N=18,198)		(N=18,325)		
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (1,7411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999
		(N=19,965)		(N=20,172)		
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2.332 (18,559)	169	2.345 (18,708)	94.6 (89.9–97.3)	>0.9999

bis zu 7 Tage nach Dosis 2

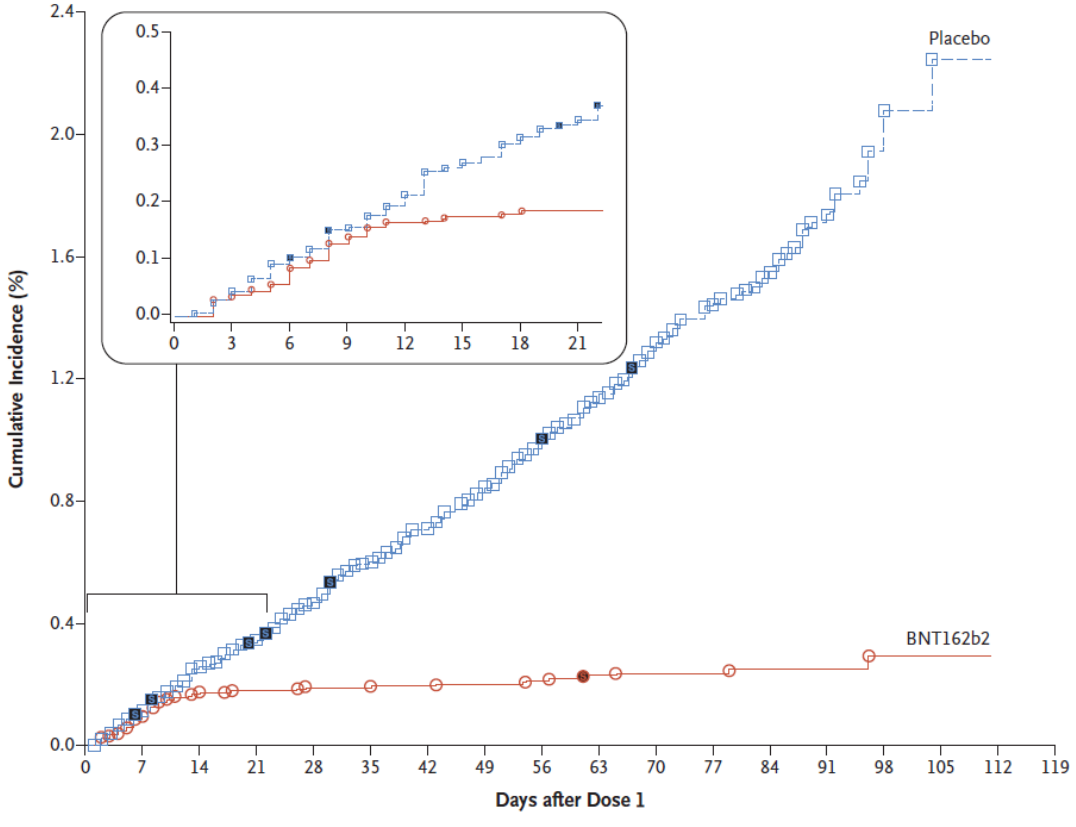
* The total population without baseline infection was 36,523; total population including those with and those without prior evidence of infection was 40,137.
† The surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from 7 days after the second dose to the end of the surveillance period.
‡ The credible interval for vaccine efficacy was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.
§ Posterior probability was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.

Results – Efficacy

- ≥7 days after dose 2 (primary endpoint) 95% (95%VB: 90.3-97.6)
- Between doses 1 and 2 (secondary endpoint) 52% (95%VB: 29.5-68.4)



Pollack et al; NEJM, online Dec. 10, 2020



Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669)		Placebo (N=21,686)		VE (95% CI)
	No. of participants	Surveillance time *person-yr (no. at risk)*	No. of participants	Surveillance time *person-yr (no. at risk)*	*percent*
Covid-19 occurrence					
After dose 1	50	4.015 (21,314)	275	3.982 (21,258)	82.0 (75.6–86.9)
After dose 1 to before dose 2	39		82		52.4 (29.5–68.4)
Dose 2 to 7 days after dose 2	2		21		90.5 (61.0–98.9)
≥7 Days after dose 2	9		172		94.8 (89.8–97.6)

Swiss NITAG («EKIF») Recommendations
Who should be immunized when?

Target group 1: especially vulnerable people

The following people are being given access to vaccinations first:

- People age 75 years and over
- People with chronic diseases of the highest risk, regardless of their age
- People who live in a retirement or care home. Staff who are in contact with residents of retirement and care homes also have the option of being vaccinated at the same time.

Then:

- People aged between 65 and 74 years
- People under 65 years with other chronic diseases

https://www.bag.admin.ch/bag/en/home/krankheiten/ausbrueche-epidemien-pandemien/aktuelle-ausbrueche-epidemien/novel-cov/impfen.html

Swiss NITAG («EKIF») Recommendations
Who should be immunized when?

Target group 2: Healthcare professionals with patient contact/carers for people at especially high risk

Target group 3: Close contacts (household members or relatives providing care) of people at especially high risk

Target group 4: People in communal facilities with an increased risk of infection and outbreaks (for example homes for the handicapped).

Once sufficient vaccine is available, adults who are not in target groups 1 to 4 mentioned as described above will also be able to have the vaccination.

https://www.bag.admin.ch/bag/en/home/krankheiten/ausbrueche-epidemien-pandemien/aktuelle-ausbrueche-epidemien/novel-cov/impfen.html

Swiss NITAG («EKIF») Recommendations
Who should be immunized when?

What about children?

Currently it is not planned to vaccinate children. Study data for the relevant age groups is not yet available.

https://www.bag.admin.ch/bag/en/home/krankheiten/ausbrueche-epidemien-pandemien/aktuelle-ausbrueche-epidemien/novel-cov/impfen.html

UKBB
kompetent & menschlich

Frequent Reports about late Reactions incl. Urticaria (www.infovac.ch)

34 year old health care professional;
Day 7 after 1st dose of mRNA vaccine.

Severe itching, regredient after 2 days and local Dimetindenmaleat

COVID-19 Vaccines – a Scientific Triumph (?)

"That the mRNA-1273 Covid-19 and the BNT162b2 Covid-19 vaccines protect with near identical 94 to 95% vaccine efficacies — and that both vaccines were developed and tested in less than a year — are extraordinary scientific and medical triumphs."

Haynes; A New Vaccine to Battle Covid-19; NEJM 2021

UKBB
kompetent & menschlich