COVID-19 Vaccines
A Harm Benefit Analysis

Dr. Joseph Fraiman

Early COVID-19 Pandemic Experience in the Emergency Room

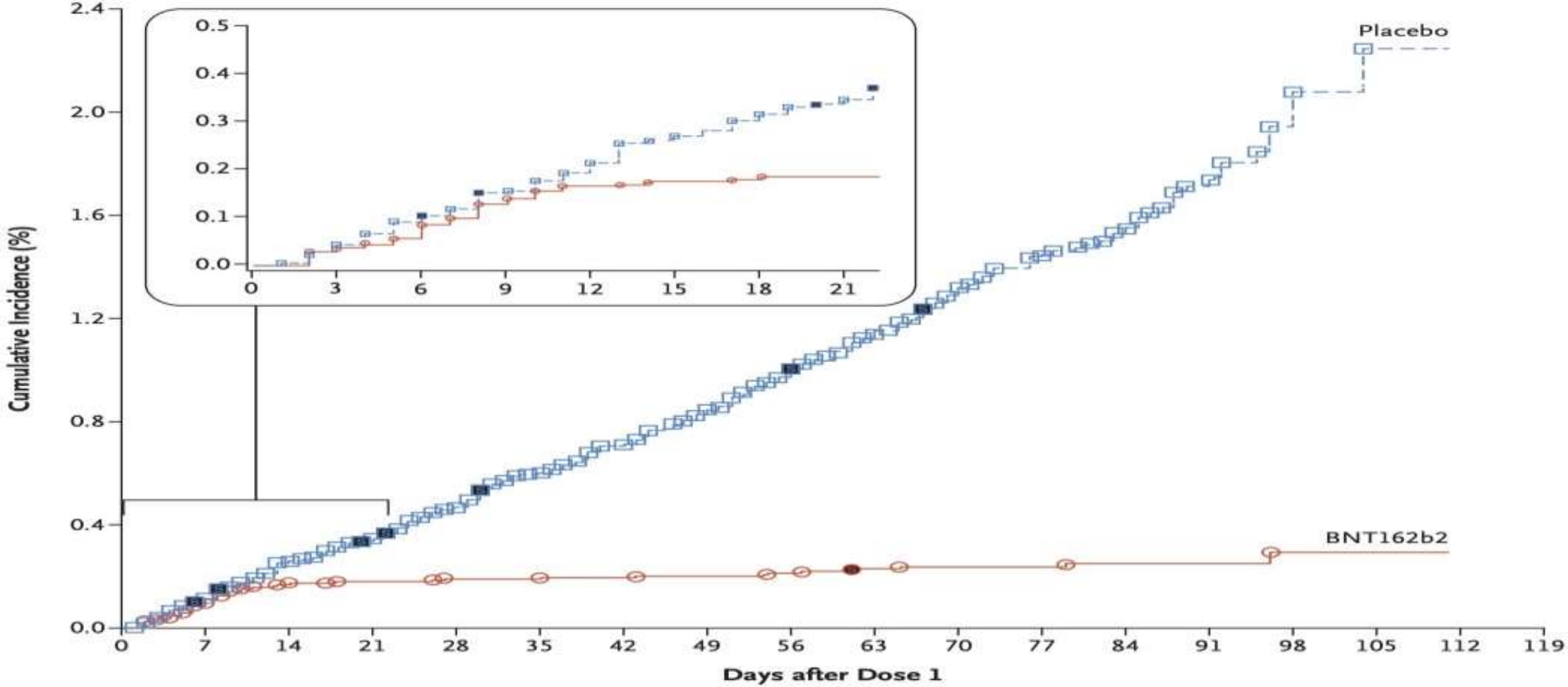
Pfizer
mRNA COVID-19 Vaccine
Randomized Controlled Trial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 31, 2020 VOL. 383 NO. 27

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*



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)

mRNA COVID-19 Vaccine Efficacy COVID-19 Hospitalization

Pfizer

Emergency Use Authorization (EUA) for an Unapproved Product
Review Memorandum

Identifying Information

Application Type	EUA (Event-driven EUA request)
Application Number	27034
Sponsor	Pfizer, Inc., on behalf of Pfizer and BioNTech
Submission Date	November 20, 2020
Receipt Date	November 20, 2020
Signatory Authority	Marion F. Gruber, Ph.D., Director, CBER/OVRR
Review Team	Ramachandra Naik, Ph.D., Chair, OVRR/DVRPA; CAPT Michael Smith, Ph.D., Regulatory Project Manager, OVRR/DVRPA; Susan Wollersheim, M.D., Clinical reviewer, OVRR/DVRPA; Nabil Al-Humadi, Ph.D., Toxicology reviewer, OVRR/DVRPA; Lei Huang, Ph.D., Biostatistics reviewer, OBE/DB; Haruhiko Murata, Ph.D., CMC/Product reviewer, OVRR/DVP; Xiao Wang, Ph.D., CMC/Product reviewer, OVRR/DVP; Laura Fontan, Ph.D., CMC/Facility reviewer; OCBQ/DMPQ; Kathleen Jones, Ph.D., CMC/Facility reviewer, OCBQ/DMPQ; Kerry Welsh, M.D., Pharmacovigilance reviewer, OBE/DE; Narayan Nair, M.D., Pharmacovigilance reviewer, OBE/DE; Brenda Baldwin, Ph.D., Data Integrity reviewer, OVRR/DVRPA; Bhanumathi Kannan, Ph.D., BIMO reviewer, OCBQ/DIS/BMB; Oluchi Elekwachi, Ph.D., Labeling reviewer, OCBQ/DCM/APLB
Review Completion Date	December 11, 2020
Established Name/Other names used during development	Pfizer-BioNTech COVID-19 Vaccine/ BNT162b2
Dosage Forms/Strengths and Route of Administration	A 0.3 mL Suspension for intramuscular injection
Intended Use for EUA	Active immunization to prevent coronavirus disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)
Intended Population	Individuals 16 years of age and older

Moderna

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med 2021;384:403-16. DOI: 10.1056/NEJMoa2035389

(PDF updated January 21, 2021.)

Pfizer
Vaccine Efficacy
COVID-19 Hospitalizations

Vaccine	Placebo
0	5

Hospital Reduction
2.3 per 10,000 Participants

Moderna
Vaccine Efficacy
COVID-19 Hospitalizations

Vaccine	Placebo
0	9

Hospital Reduction
6.4 per 10,000 Participants

Pfizer
Vaccine Efficacy
COVID-19 Death Reduction

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine through 6 Months

S.J. Thomas, E.D. Moreira, Jr., N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, J.L. Perez, G. Pérez Marc, F.P. Polack, C. Zerbini, R. Bailey, K.A. Swanson, X. Xu, S. Roychoudhury, K. Koury, S. Bouguermouh, W.V. Kalina, D. Cooper, R.W. Frenck, Jr., L.L. Hammitt, Ö. Türeci, H. Nell, A. Schaefer, S. Ünal, Q. Yang, P. Liberator, D.B. Tresnan, S. Mather, P.R. Dormitzer, U. Şahin, W.C. Gruber, and K.U. Jansen, for the C4591001 Clinical Trial Group*

Pfizer mRNA COVID-19 Vaccine Efficacy
COVID-19 All-Cause Death

Reported Cause of Death[a]	BNT162b2 (N=21,926) n	Placebo (N=21,921) n
Deaths	15	14
Acute respiratory failure	0	1
Aortic rupture	0	1
Arteriosclerosis	2	0
Biliary cancer metastatic	0	1
COVID-19	0	2
COVID-19 pneumonia	1	0
Cardiac arrest	4	1
Cardiac failure congestive	1	0
Cardiorespiratory arrest	1	1
Chronic obstructive pulmonary disease	1	0
Death	0	1
Dementia	0	1
Emphysematous cholecystitis	1	0
Hemorrhagic stroke	0	1
Hypertensive heart disease	1	0
Lung cancer metastatic	1	0
Metastases to liver	0	1
Missing	0	1
Multiple organ dysfunction syndrome	0	2
Myocardial infarction	0	2
Overdose	0	1
Pneumonia	0	2
Sepsis	1	0
Septic shock	1	0
Shigella sepsis	1	0
Unevaluable event	1	0

Table S4 | Causes of Death from Dose 1 to Unblinding (Safety Population, ≥16 Years Old). a. Multiple causes of death could be reported for each participant. There were no deaths among 12–15-year-old participants.

Pfizer mRNA COVID-19 Vaccine Efficacy
COVID-19 Death

Reported Cause of Death[a]	BNT162b2 (N=21,926) n	Placebo (N=21,921) n
Deaths	15	14
Acute respiratory failure	0	1
Aortic rupture	0	1
Arteriosclerosis	2	0
Biliary cancer metastatic	0	1
COVID-19	0	2
COVID-19 pneumonia	1	0
Cardiac arrest	4	1

Observational Data of Vaccine Efficacy

THE LANCET

Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data

Eric J Haas, MD • Frederick J Angulo, PhD • John M McLaughlin, PhD • Emilia Anis, MD • Shepherd R Singer, MD • Farid Khan, MPH • Nati Brooks, MA • Meir Smaja, BA • Gabriel Mircus, PhD • Kaijie Pan, MS • Jo Southern, PhD • David L Swerdlow, MD • Luis Jodar, PhD • Yeheskel Levy, MD • Sharon Alroy-Preis, MD • Show less

Published: May 05, 2021 • DOI: https://doi.org/10.1016/S0140-6736(21)00947-8 •

Observational Data of Vaccine Efficacy

Table 3 Estimated effectiveness of two doses of BNT162b2 (≥7 days after the second dose) against laboratory-confirmed SARS-CoV-2 outcomes in the oldest age groups (Jan 24 to April 3, 2021)

	Vaccine effectiveness*		
	Age ≥65 years	Age ≥75 years	Age ≥85 years
SARS-CoV-2 infection†	94·8% (93·9–95·5)	95·1% (93·9–96·0)	94·1% (91·9–95·7)
Asymptomatic SARS-CoV-2 infection	88·5% (86·4–90·3)	87·5% (84·2–90·1)	83·2% (76·3–88·1)
Symptomatic COVID-19	96·4% (95·9–97·0)	96·7% (95·9–97·4)	96·6% (95·2–97·6)
COVID-19-related hospitalisation	96·8% (96·2–97·3)	97·0% (96·2–97·7)	96·9% (95·5–97·9)
Severe or critical COVID-19-related hospitalisation	97·3% (96·8–97·8)	97·6% (96·8–98·1)	97·4% (95·9–98·3)
COVID-19-related death	96·9% (96·0–97·6)	97·1% (96·0–97·9)	97·0% (94·9–98·3)

COVID-19 Emergency Room Experience Post-Vaccine

Circulation Research
Volume 128, Issue 9, 30 April 2021; Pages 1323-1326
https://doi.org/10.1161/CIRCRESAHA.121.318902

American Heart Association.

RESEARCH LETTERS

SARS-CoV-2 Spike Protein Impairs Endothelial Function via Downregulation of ACE 2

Meet the First Author, see p 1239

Yuyang Lei†, Jiao Zhang†, Cara R. Schiavon, Ming He, Lili Chen, Hui Shen, Yichi Zhang, Qian Yin, Yoshitake Cho, Leonardo Andrade, Gerald S. Shadel, Mark Hepokoski, Ting Lei, Hongliang Wang, Jin Zhang, Jason X.-J. Yuan, Atul Malhotra, Uri Manor, Shengpeng Wang, Zu-Yi Yuan, and John Y-J. Shyy

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Randomized Controlled Trials

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Vaccine 40 (2022) 5798–5805

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journal homepage: www.elsevier.com/locate/vaccine

Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults

Joseph Fraiman [a], Juan Erviti [b], Mark Jones [c], Sander Greenland [d], Patrick Whelan [e], Robert M. Kaplan [f], Peter Doshi [g,*]

Serious Adverse Event (SAE) Definition

An SAE is defined as any untoward medical occurrence that, at any dose:
a. Results in death
b. Is life-threatening
c. Requires inpatient hospitalization or prolongation of existing hospitalization
d. Results in persistent disability/incapacity
e. Is a congenital anomaly/birth defect
f. Other situations: • Medical or scientific judgment should be exercised in deciding whether SAE reporting is appropriate in other situations such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events should usually be considered serious.

PFIZER-BIONTECH COVID-19 VACCINE (BNT162, PF-07302048)

VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE

BRIEFING DOCUMENT

MEETING DATE: 10 December 2020

https://www.fda.gov/media/144246/download

Appendix 4. Supplemental Tables

Table 23. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – ~38000 Subjects for Phase 2/3 Analysis – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N=18801)		Placebo (N=18785)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	103 (0.5)	(0.4, 0.7)	81 (0.4)	(0.3, 0.5)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Lymphadenopathy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Neutropenia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Thrombocytopenia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
CARDIAC DISORDERS	14 (0.1)	(0.0, 0.1)	12 (0.1)	(0.0, 0.1)
Atrial fibrillation	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Acute myocardial infarction	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Acute coronary syndrome	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cardiac failure congestive	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Myocardial infarction	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Angina pectoris	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Angina unstable	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Aortic valve incompetence	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Arrhythmia supraventricular	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Arteriospasm coronary	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Bradycardia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Coronary artery disease	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Coronary artery dissection	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Coronary artery occlusion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tachyarrhythmia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tachycardia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Ventricular arrhythmia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Heart disease congenital	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
EAR AND LABYRINTH DISORDERS	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Vertigo	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
EYE DISORDERS	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Choroidal neovascularisation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Diplopia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Retinal artery occlusion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
GASTROINTESTINAL DISORDERS	8 (0.0)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Small intestinal obstruction	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Abdominal adhesions	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 23. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – ~38000 Subjects for Phase 2/3 Analysis – Safety Population

System Organ Class Preferred Term	Vaccine Group (as Administered)			
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BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Lymphadenopathy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Neutropenia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Thrombocytopenia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
CARDIAC DISORDERS	14 (0.1)	(0.0, 0.1)	12 (0.1)	(0.0, 0.1)
Atrial fibrillation	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Acute myocardial infarction	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Acute coronary syndrome	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cardiac failure congestive	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Myocardial infarction	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Angina pectoris	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Angina unstable	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

COVID-19 mRNA Vaccines
Number of Serious Adverse Events

Table 2

Serious adverse events.

Trial	Total events (events per 10,000 participants)[a] Vaccine	Placebo	Risk difference per 10,000 participants (95 % CI)[e]	Risk ratio (95 % CI)[e]
Serious adverse events				
Pfizer[b]	127 (67.5)	93 (49.5)	18.0 (1.2 to 34.9)	1.36 (1.02 to 1.83)
Moderna[c,d]	206 (135.7)	195 (128.6)	7.1 (−23.2 to 37.4)	1.06 (0.84 to 1.33)
Combined[f]	333 (98.0)	288 (84.8)	13.2 (-3.2 to 29.6)	1.16 (0.97 to 1.39)
Serious adverse events of special interest				

COVID-19 mRNA Vaccines
Number of Serious Adverse Events

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Combined[f]	333 (98.0)	288 (84.8)	13.2 (-3.2 to 29.6)	1.16 (0.97 to 1.39)
Serious adverse events of special interest				

COVID-19 Vaccine Pfizer Clinical Trials
Number of Serious Adverse Events

Risk Increase in Vaccine group (95% CI)	
Risk difference	Risk Ratio
18 Per 10,000 (1.2-34.9)	1.36 (1.02-1.83)

Pfizer mRNA COVID-19 Vaccine Serious Adverse Events

36%

Higher risk of SAE

in vaccine group

Pfizer
mRNA COVID-19 Vaccine
Serious Adverse Events

1 in 555

Additional SAE

in vaccine group

What Type of Serious Harms?

Adverse Events of Special Interest (AESI)

Brighton collaboration | A program of THE TASK FORCE FOR GLOBAL HEALTH

vaccine safety net

Country: United States of America **VSN member since: 2020**

Website language: English

Seek reliable information from trusted sources on vaccine safety

World Health Organization

Table 3
Serious AESIs, Pfizer trial.

Brighton category	Vaccine	Placebo	Vaccine events per 10,000	Placebo events per 10,000	Difference in events per 10,000	Risk ratio
Association with immunization in general						
Anaphylaxis	1	1	0.5	0.5	0.0	1.00
Association with specific vaccine platform(s)						
Encephalitis/encephalomyelitis	0	2	0.0	1.1	−1.1	0.00
Seen with COVID-19						
Acute kidney injury	2	0	1.1	0.0	1.1	N/A
Acute liver injury	0	1	0.0	0.5	−0.5	0.00
Acute respiratory distress syndrome	2	1	1.1	0.5	0.5	2.00
Coagulation disorder	16	10	8.5	5.3	3.2	1.60
Myocarditis/pericarditis	2	1	1.1	0.5	0.5	2.00
Other forms of acute cardiac injury	16	12	8.5	6.4	2.1	1.33
Subtotal	39	28	20.7	14.9	5.8	1.39
Brighton list of 29 clinical diagnoses seen with COVID-19						
Abscess	4	1	2.1	0.5	1.6	4.00
Cholecystitis	4	2	2.1	1.1	1.1	2.00
Colitis/Enteritis	1	1	0.5	0.5	0.0	1.00
Diarrhea	1	0	0.5	0.0	0.5	N/A
Hyperglycemia	1	1	0.5	0.5	0.0	1.00
Pancreatitis	1	0	0.5	0.0	0.5	N/A
Psychosis	1	0	0.5	0.0	0.5	N/A
Subtotal	13	5	6.9	2.7	4.3	2.60
Total	**52**	**33**	**27.7**	**17.6**	**10.1**	**1.57**

Table 3
Serious AESIs, Pfizer trial.

Brighton category	Vaccine	Placebo	Vaccine events per 10,000	Placebo events per 10,000	Difference in events per 10,000	Risk ratio
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Anaphylaxis	1	1	0.5	0.5	0.0	1.00
Association with specific vaccine platform(s)						
Encephalitis/encephalomyelitis	0	2	0.0	1.1	−1.1	0.00
Seen with COVID-19						
Acute kidney injury	2	0	1.1	0.0	1.1	N/A
Acute liver injury	0	1	0.0	0.5	−0.5	0.00
Acute respiratory distress syndrome	2	1	1.1	0.5	0.5	2.00
Coagulation disorder	16	10	8.5	5.3	3.2	1.60
Myocarditis/pericarditis	2	1	1.1	0.5	0.5	2.00
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Cholecystitis	4	2	2.1	1.1	1.1	2.00
Colitis/Enteritis	1	1	0.5	0.5	0.0	1.00
Diarrhea	1	0	0.5	0.0	0.5	N/A
Hyperglycemia	1	1	0.5	0.5	0.0	1.00
Pancreatitis	1	0	0.5	0.0	0.5	N/A
Psychosis	1	0	0.5	0.0	0.5	N/A
Subtotal	13	5	6.9	2.7	4.3	2.60
Total	**52**	**33**	**27.7**	**17.6**	**10.1**	**1.57**

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Serious AESIs, Pfizer trial.

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Association with specific vaccine platform(s)			
Encephalitis/encephalomyelitis	0	2	−1.1
Seen with COVID-19			
Acute kidney injury	2	0	1.1
Acute liver injury	0	1	−0.5
Acute respiratory distress syndrome	2	1	0.5
Coagulation disorder	16	10	3.2
Myocarditis/pericarditis	2	1	0.5
Other forms of acute cardiac injury	16	12	2.1
Subtotal	39	28	5.8
Brighton list of 29 clinical diagnoses seen with COVID-19			
Abscess	4	1	1.6
Cholecystitis	4	2	1.1
Colitis/Enteritis	1	1	0.0
Diarrhea	1	0	0.5
Hyperglycemia	1	1	0.0
Pancreatitis	1	0	0.5
Psychosis	1	0	0.5
Subtotal	13	5	4.3
Total	**52**	**33**	**10.1**

Multiple Rare Serious Harms Add Up

COVID-19 mRNA Vaccines and Serious AESIs

Table 2
Serious adverse events.

Trial	Total events (events per 10,000 participants)[a] Vaccine	Placebo	Risk difference per 10,000 participants (95 % CI)[e]	Risk ratio (95 % CI)[e]
Serious adverse events of special interest				
Pfizer	52 (27.7)	33 (17.6)	10.1 (-0.4 to 20.6)	1.57 (0.98 to 2.54)
Moderna	87 (57.3)	64 (42.2)	15.1 (-3.6 to 33.8)	1.36 (0.93 to 1.99)
Combined[f]	139 (40.9)	97 (28.6)	12.5 (2.1 to 22.9)	1.43 (1.07 to 1.92)

COVID-19 mRNA Vaccines and Serious AESIs

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Harms and Benefits:
How can they be compared?

mRNA COVID-19 Vaccine
Clinical Trials
All-Cause Hospitalization

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 31, 2020 VOL. 383 NO. 27

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*

Harms and Benefits:
How can they be compared?

Serious AESI vs Hospitalization Reduction

Pfizer
Vaccine Efficacy
COVID-19 Hospitalizations

Vaccine	Placebo
0	5

Hospital Reduction
2.3 per 10,000 Participants

Pfizer
Harm-Benefit Analysis
AESI vs Hospitalization

Serious AESI risk

10.1

Per 10,000
Participants

Hospitalization Reduction

2.3

Per 10,000
Participants

Moderna
Harm-Benefit Analysis
AESI vs Hospitalization

Serious AESI risk

15.1

Per 10,000

Participants

Hospitalization Reduction

6.4

Per 10,000

Participants

Harm Benefit Analysis Limitations

https://doi.org/10.5281/zenodo.6564402

COVID-19 Emergency Room Omicron Experience

Incidental COVID-19 Hospitalization During Omicron

Incidental COVID-19 Hospitalization During Omicron

SURVEILLANCE

COVID-19 mortality attenuated during widespread Omicron transmission, Denmark, 2020 to 2022

Nikolaj U Friis[1] , Tomas Martin-Bertelsen[1] , Rasmus K Pedersen[2] , Jens Nielsen[1] , Tyra G Krause[1] , Viggo Andreasen[2] , Lasse S Vestergaard[1]

1. Epidemiological Infectious Disease Preparedness, Statens Serum Institut, Copenhagen, Denmark
2. PandemiX Center, Department of Science and Environment, Roskilde University, Roskilde, Denmark

"**The share of deaths of COVID-19 (as opposed to with COVID-19)** fell from 60–75% before week 1/2022 to **25–35%** in the following months."

Protection from Prior Infection

THE LANCET

ARTICLES | VOLUME 401, ISSUE 10379, P833-842, MARCH 11, 2023

Past SARS-CoV-2 infection protection against re-infection: a systematic review and meta-analysis

COVID-19 Forecasting Team † • Show footnotes

Open Access • Published: February 16, 2023 • DOI: https://doi.org/10.1016/S0140-6736(22)02465-5 •

"**protection against severe disease** remained high for all variants, with 90·2% (69·7–97·5) for ancestral, alpha, and delta variants, and **88·9% (84·7–90·9) for omicron BA.1 at 40 weeks**."

Omicron Hospitalizations

nature medicine

ARTICLES

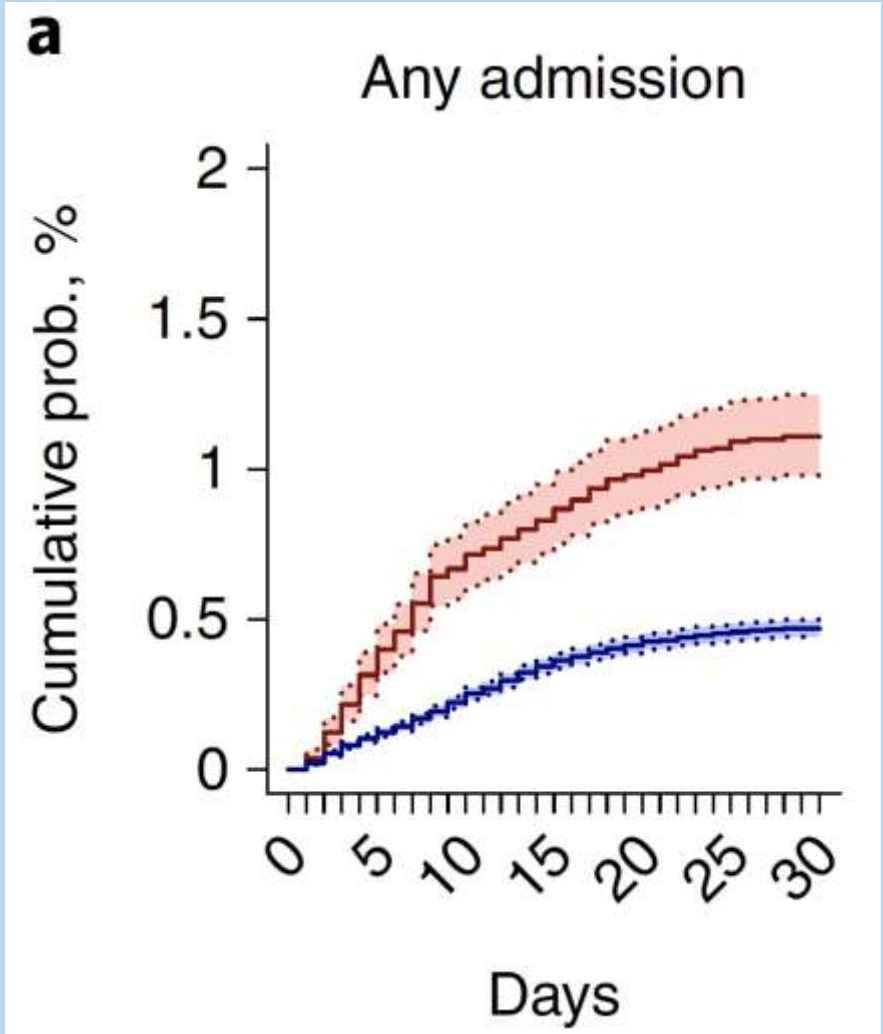
https://doi.org/10.1038/s41591-022-01887-z

Clinical outcomes associated with SARS-CoV-2 Omicron (B.1.1.529) variant and BA.1/BA.1.1 or BA.2 subvariant infection in Southern California

Joseph A. Lewnard[1,2,3] ✉, Vennis X. Hong[4], Manish M. Patel[5], Rebecca Kahn[5], Marc Lipsitch[5] and Sara Y. Tartof[4,6] ✉

NATURE MEDICINE

Comparison of Delta and Omicron variant detections, 15 December 2021 to 17 January 2022



NATURE MEDICINE

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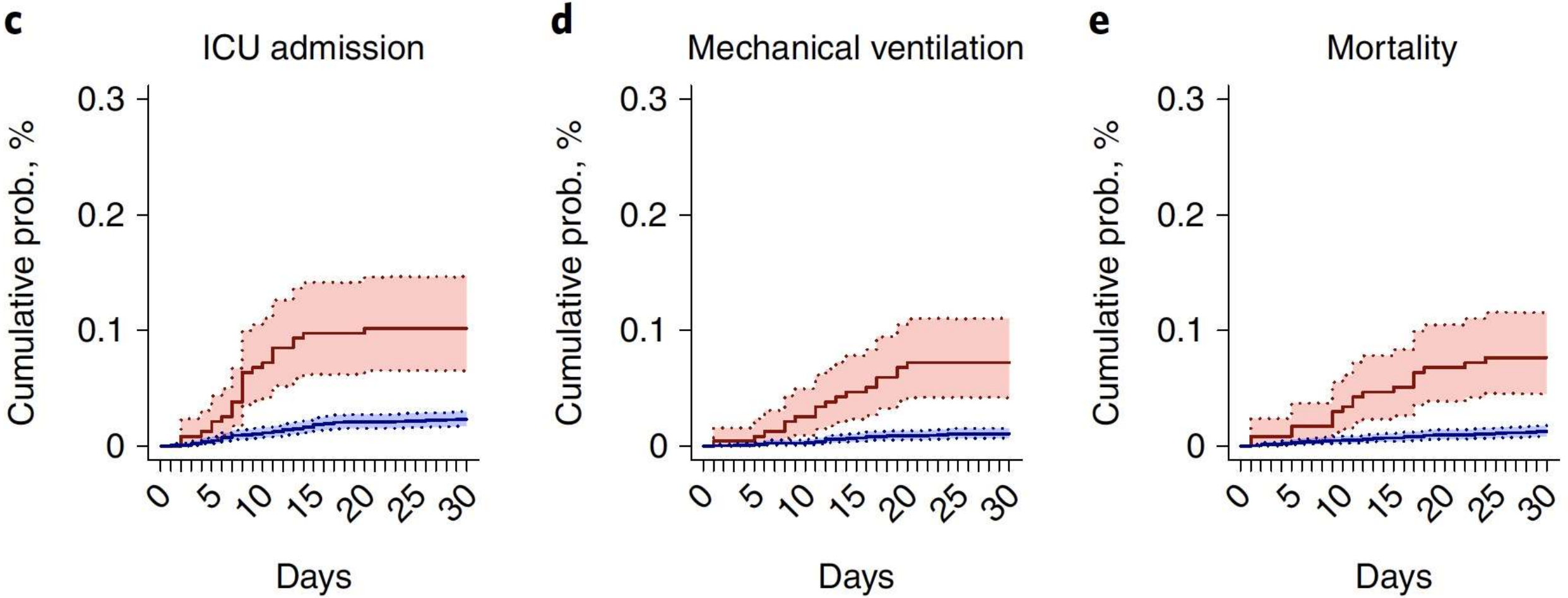

Vaccine Efficacy
COVID-19 Hospitalization Reduction
Omicron

Vaccine Efficacy During Omicron COVID-19 Hospitalization Reduction

ELSEVIER

The Lancet Regional Health - Europe

Volume 25, February 2023, 100552

Effectiveness of BNT162b2 COVID-19 vaccination in prevention of hospitalisations and severe disease in adults with SARS-CoV-2 Delta (B.1.617.2) and Omicron (B.1.1.529) variant between June 2021 and July 2022: a prospective test negative case–control study

Anastasia Chatzilena,[a,e] Catherine Hyams,[b,c,e] Rob Challen,[a] Robin Marlow,[b] Jade King,[d] David Adegbite,[b] Jane Kinney,[b] Madeleine Clout,[b] Nick Maskell,[c] Jennifer Oliver,[b] Leon Danon,[a,] and Adam Finn,[b] On behalf of the Avon CAP Research Group*

Vaccine Efficacy During Omicron COVID-19 Hospitalization Reduction

Table 3: Vaccine effectiveness for three doses of BNT162b2 against the Omicron (B.1.1.529) variant.

Characteristic	All adults		
	VE (95% CI)	OR (95% CI)	*P*-value
1. Hospitalisation			
Unadjusted vaccine effectiveness			
Three doses	28.4 (7.1–44.8)	0.716 (0.552–0.929)	0.012
Adjusted vaccine effectiveness - Logistic regression model			
Three doses	30.9 (5.9–49.3)	0.691 (0.507–0.941)	0.019

Vaccine Efficacy During Omicron COVID-19 Hospitalization Reduction

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Morbidity and Mortality Weekly Report (*MMWR*)

Effectiveness of Monovalent mRNA Vaccines Against COVID-19–Associated Hospitalization Among Immunocompetent Adults During BA.1/BA.2 and BA.4/BA.5 Predominant Periods of SARS-CoV-2 Omicron Variant in the United States — IVY Network, 18 States, December 26, 2021–August 31, 2022

Weekly / October 21, 2022 / 71(42);1327–1334

CDC Estimate
Vaccine Efficacy During Omicron

TABLE 2. Effectiveness of monovalent mRNA vaccines against COVID-19–associated hospitalization during the BA.1/BA.2 and BA.4/BA.5 predominant periods of SARS-CoV-2 Omicron variant circulation* among immunocompetent adults — IVY Network, 21 hospitals in 18 U.S. states,† December 26, 2021–August 31, 2022

Return

Group/No. of doses	Interval from last vaccine dose to illness onset, days§	Median interval (IQR) from last vaccine dose to illness, days	Vaccinated case-patients, no./total no. (%)	Vaccinated control-patients, no./total no. (%)	Adjusted VE, % (95% CI)¶
BA.4/BA.5 period					
2	≥14	428 (324–468)	131/317 (41)	181/336 (54)	41 (17–57)
	14–150	102 (77–123)	3/189 (2)	13/168 (8)	83 (35–96)
	>150	430 (329–471)	128/314 (41)	168/323 (52)	37 (12–55)
3	≥7	233 (196–267)	232/418 (56)	232/387 (60)	31 (7–49)
	7–120	74 (33–110)	13/199 (7)	24/179 (13)	60 (12–81)
	>120	237 (204–269)	219/405 (54)	208/363 (57)	29 (3–48)

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COVID-19 mRNA Vaccine Omicron Hospitalization Reduction Is Uncertain

COVID-19 Vaccines can cause serious harm

How can we be confident COVID-19 Vaccines benefits outweigh the Harms?

Double Blind Randomized Clinical Trials (RCT) for All-Cause Hospitalization

Questions?