Society of Hospital Medicine

Empowering hospitalists.
Transforming patient care.

SHM Clinical Rapid Updates COVID-19 mRNA Vaccines

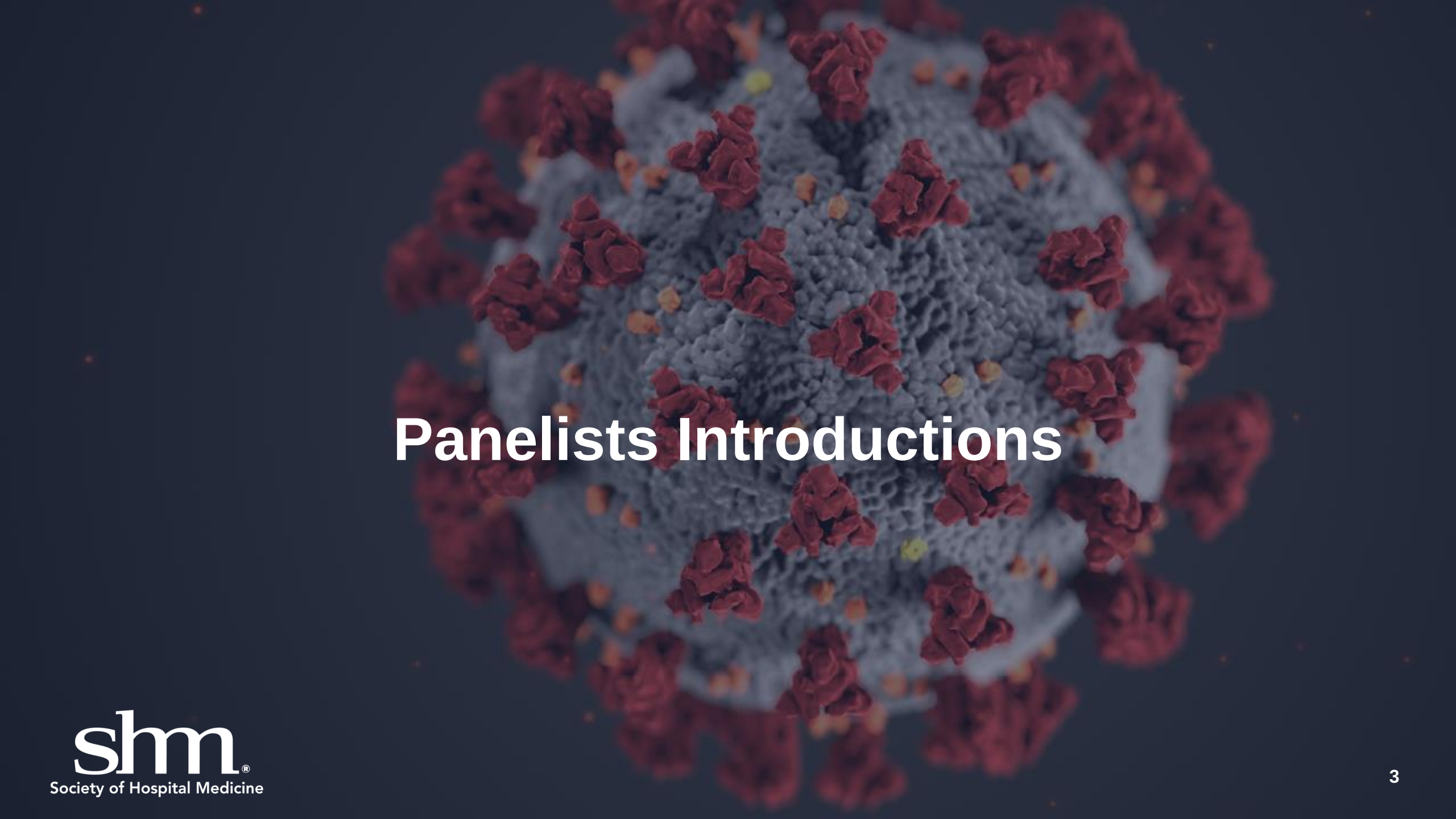
Moderated by Joseph Sweigart, MD
Derek W. Forster, MD | Fred Southwick, MD

February 23, 2021, 3 PM Eastern

Society of Hospital Medicine

Learning Objectives

- **Evaluate clinical features of current and future COVID-19 vaccines**
- **Explain the basic concepts of herd immunity and how vaccination, physical distancing, and masking may help reduce the spread of the Covid-19 pandemic.**



Panelists Introductions

Society of Hospital Medicine

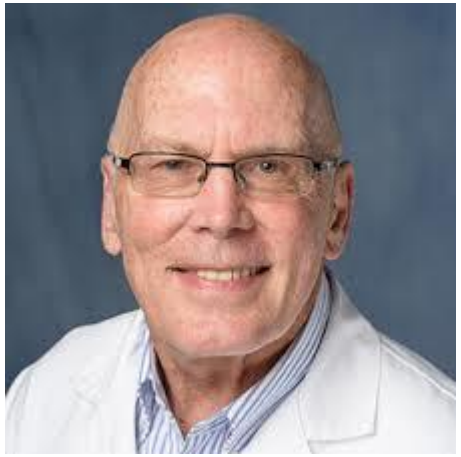
Dr. Derek W. Forster

- MD from University of Louisville School of Medicine
- IM Residency at University of Louisville
- ID Fellowship at Wake Forest University
- Associate Professor at the University of Kentucky
- Lead ID Physician for the VA MidSouth Health Care Network
- Provider with VA MidSouth Clinical Resource Hub

Society of Hospital Medicine

Dr. Frederick S. Southwick

- MD from Columbia University
- IM Residency at Boston City Hospital and Massachusetts General Hospital
- ID Fellowship at Massachusetts General Hospital
- Professor of Medicine at the University of Florida
- Former Chief of ID at the University of Florida
- Member of the Clinical Rapid Updates Team



shm
Society of Hospital Medicine

Society of Hospital Medicine

Case 1

Your hospital is offering vaccines to all front-line providers.

A 42 year old nurse approached you for advice about vaccination.

He has no medical problems and has never had any prior reaction to vaccines.

He expresses some concerns about exaggerated efficacy and unproven safety because of the speed at which these vaccines were created and brought to market.

Should he accept vaccination?

Case 1 – Should he pursue vaccination?

A) Yes, get vaccinated with whatever is available

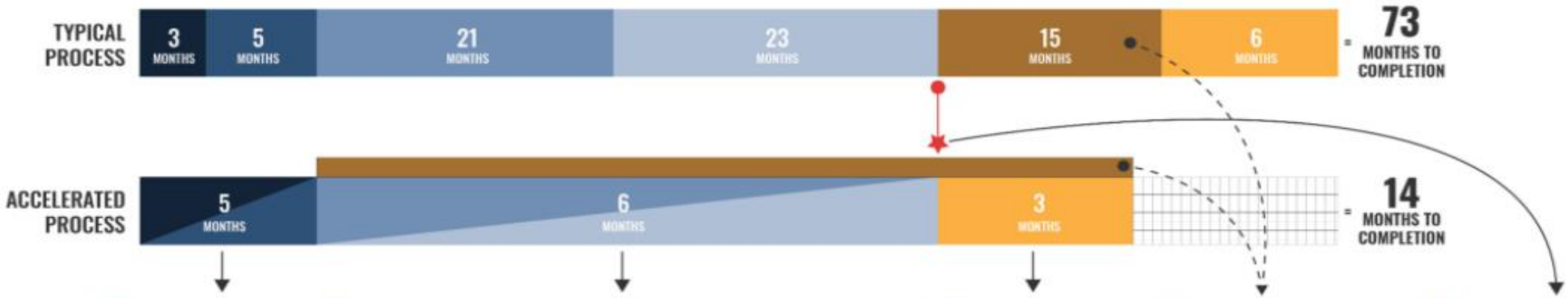
B) Yes, get vaccinated but pursue a specific brand of vaccine

C) No, delay vaccination until further evidence is available

D) No, do not allow microchip implantation under any circumstances

OPERATION WARP SPEED
ACCELERATED VACCINE PROCESS

MISSION: Deliver 300 million doses of safe and effective vaccine by 1 January 2021.



1

A typical 8-month process is accelerated by:

- Creating vaccine candidates immediately after viral genome sequence is available.
- Using vaccine platforms developed for other diseases.

2

A typical 42-month process is accelerated by:

- Large scale Phase III clinical trials of 30,000 volunteers allowing for rapid collection and earlier analysis of safety and efficacy data of demographically diverse populations by the FDA, reducing the typical 12-month approval process to three months.
- Two promising candidates began Phase III clinical trials in July, with others to follow quickly in coming months. Before beginning Phase III, candidates must show safety data from animal and human studies.
- The U.S. Government funding at-risk, large-scale manufacturing of the most promising vaccine candidates during Phase III clinical trials to ensure any vaccine proven to be safe and effective is available immediately upon FDA Emergency Use Authorization (EUA) approval or licensure.

4

A typical 6-month process is accelerated by:

- A tiered approach based on CDC recommended allocation methodology used as part of pandemic flu planning and the COVID-19 response will be used to determine vaccine distribution.

3

A typical 15-month process is accelerated by:

- Planning for infrastructure and distribution before the vaccines are approved or authorized.
- CDC leading distribution planning with DoD augmentation.

5

A typical 12-month FDA review for EUA approval or licensure is accelerated by:

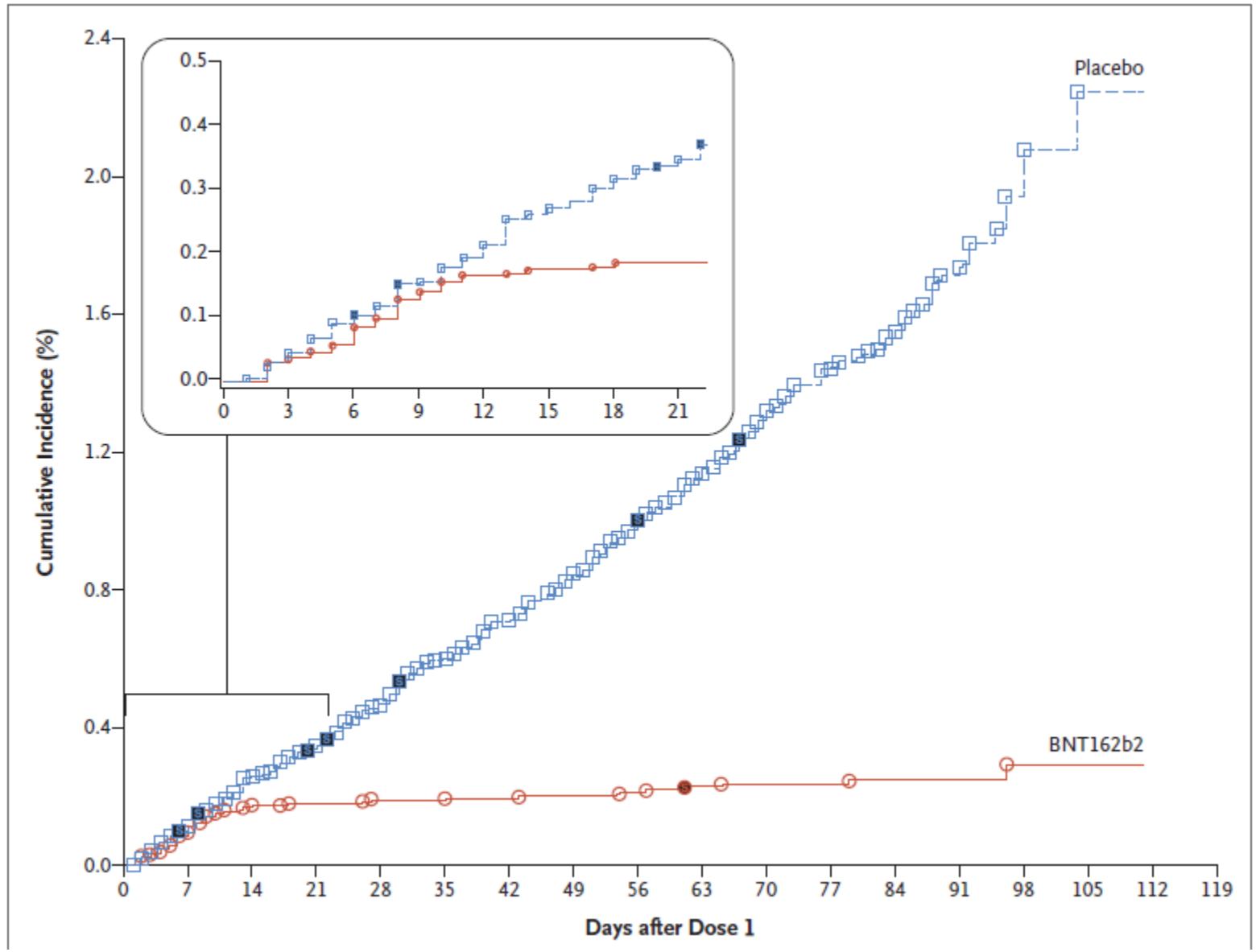
- Providing continuous safety and efficacy data collected in large Phase III clinical trials.

R&D + Preclinical Trials Vaccine Candidate/s Identified
Phase I Clinical Trials
Phase II Clinical Trials
Phase III Clinical Trials
Manufacturing
Distribution

Society of Hospital Medicine

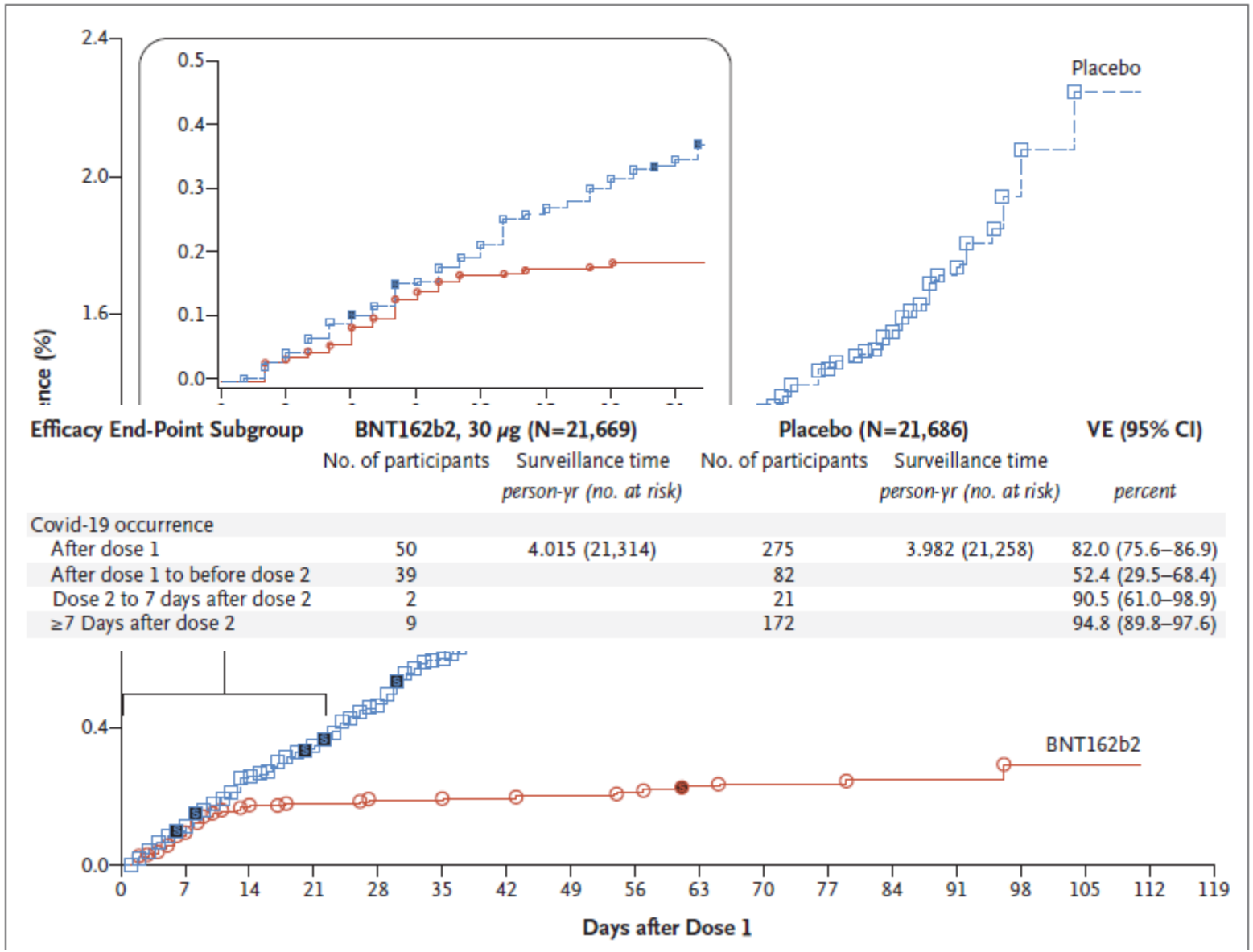
COVID-19 Vaccine Categories

- **mRNA**
  - BNT162.b.2 (Pfizer/BioNtec)
  - mRNA-1273 (Moderna)
- **Viral Vectored (adenovirus)**
  - Ad26.COV2.S (Janssen)
  - AZD1222 (AstraZeneca)
- **Protein Subunit**
  - NXV-CoV2373 (Novavax)



Society of Hospital Medicine

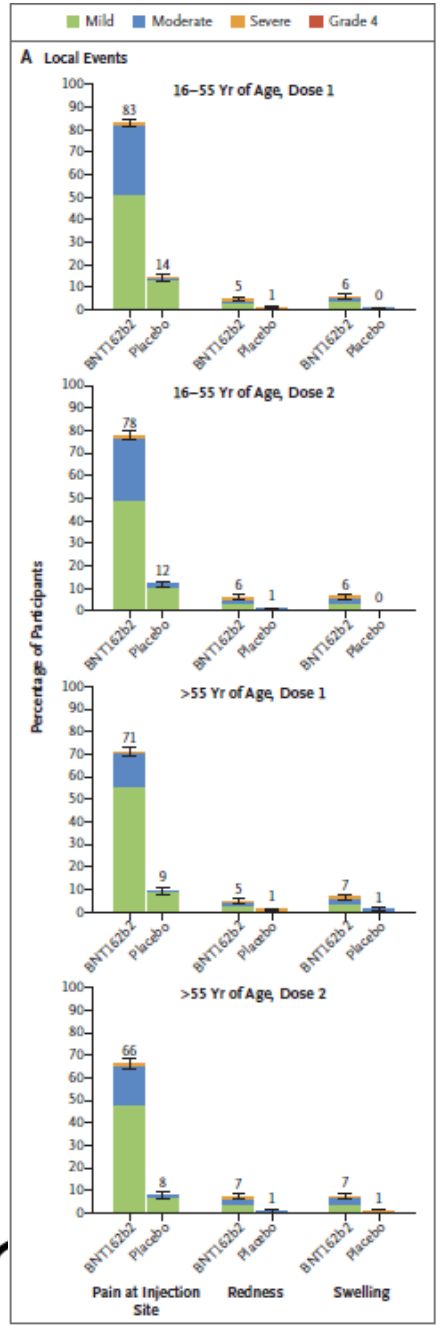
N Engl J Med 2020;383:2603-15.

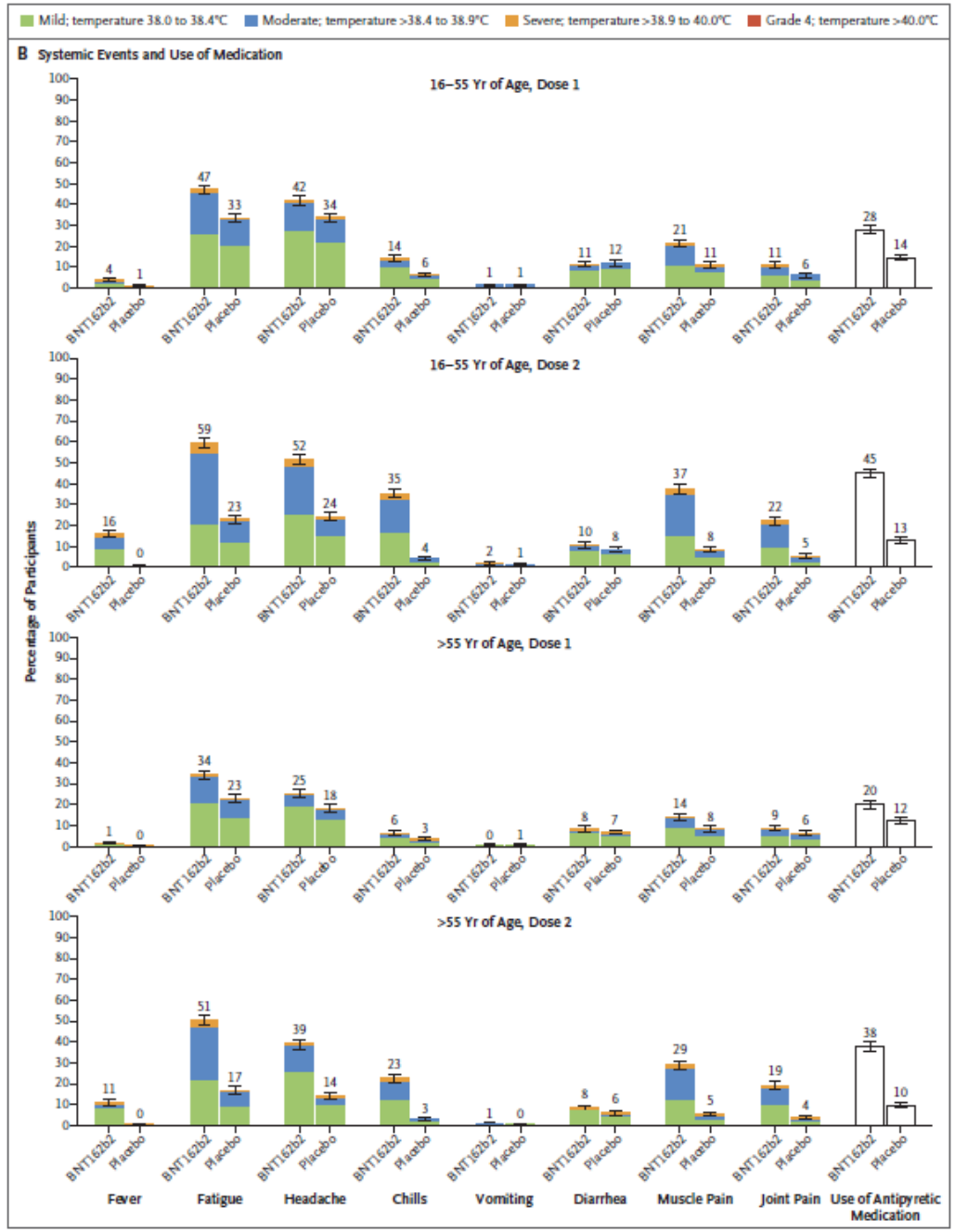


Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669)		Placebo (N=21,686)		VE (95% CI)
	No. of participants	Surveillance time *person-yr (no. at risk)*	No. of participants	Surveillance time *person-yr (no. at risk)*	*percent*
Covid-19 occurrence					
After dose 1	50	4.015 (21,314)	275	3.982 (21,258)	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)

Society of Hospital Medicine

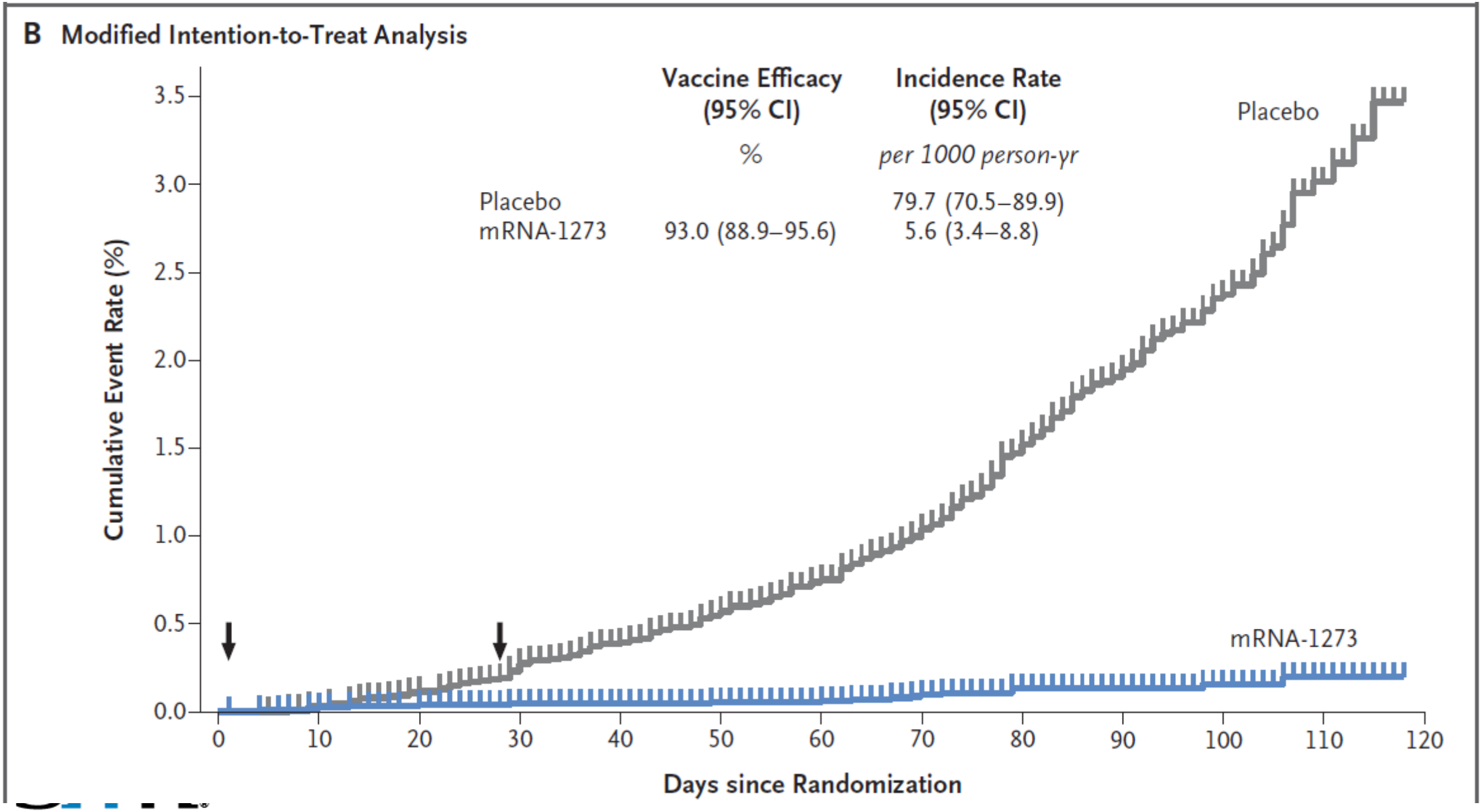
N Engl J Med 2020;383:2603-15.





Society of Hospital Medicine
N Engl J Med 2020;383:2603-15.

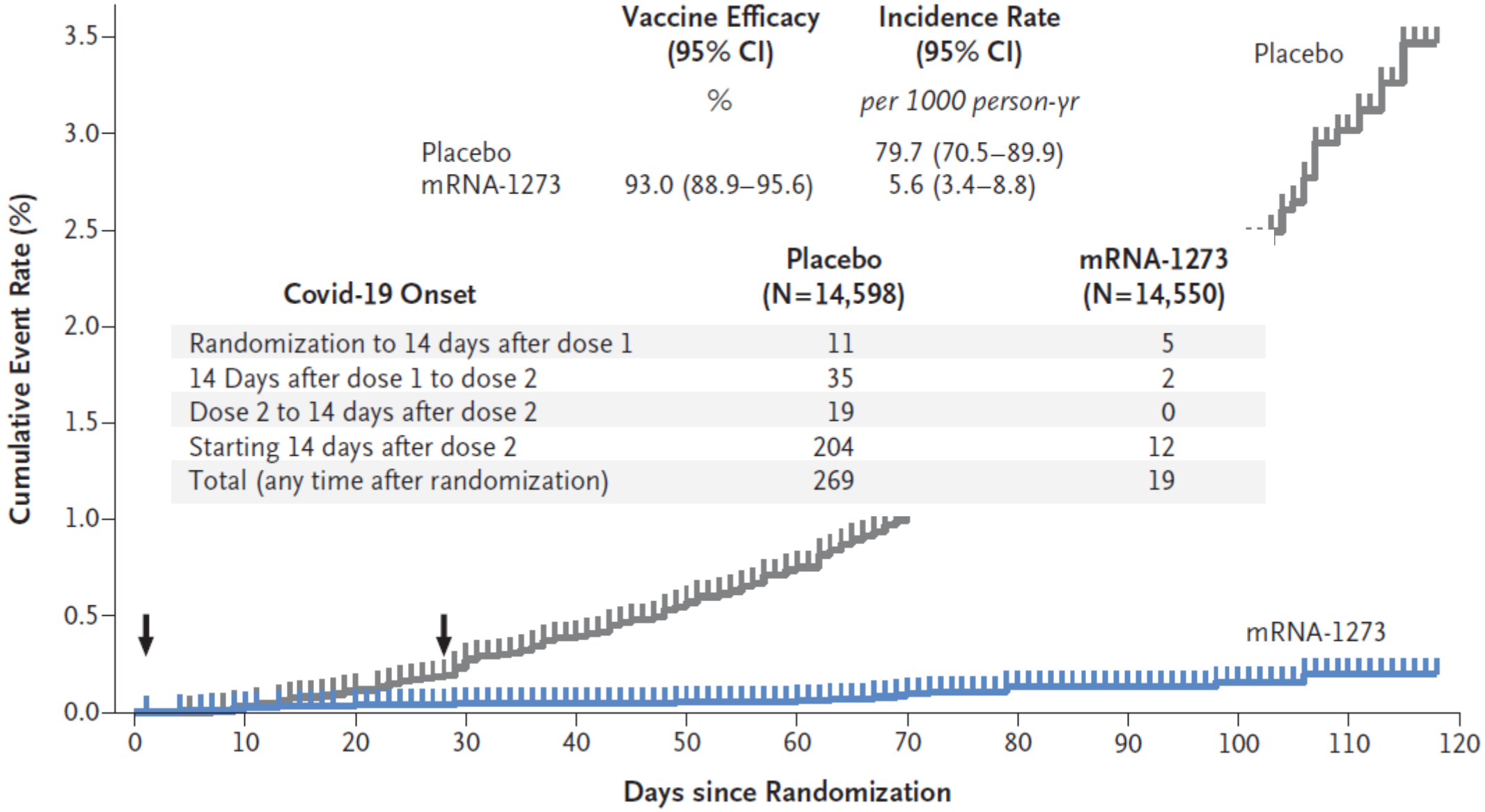
B Modified Intention-to-Treat Analysis



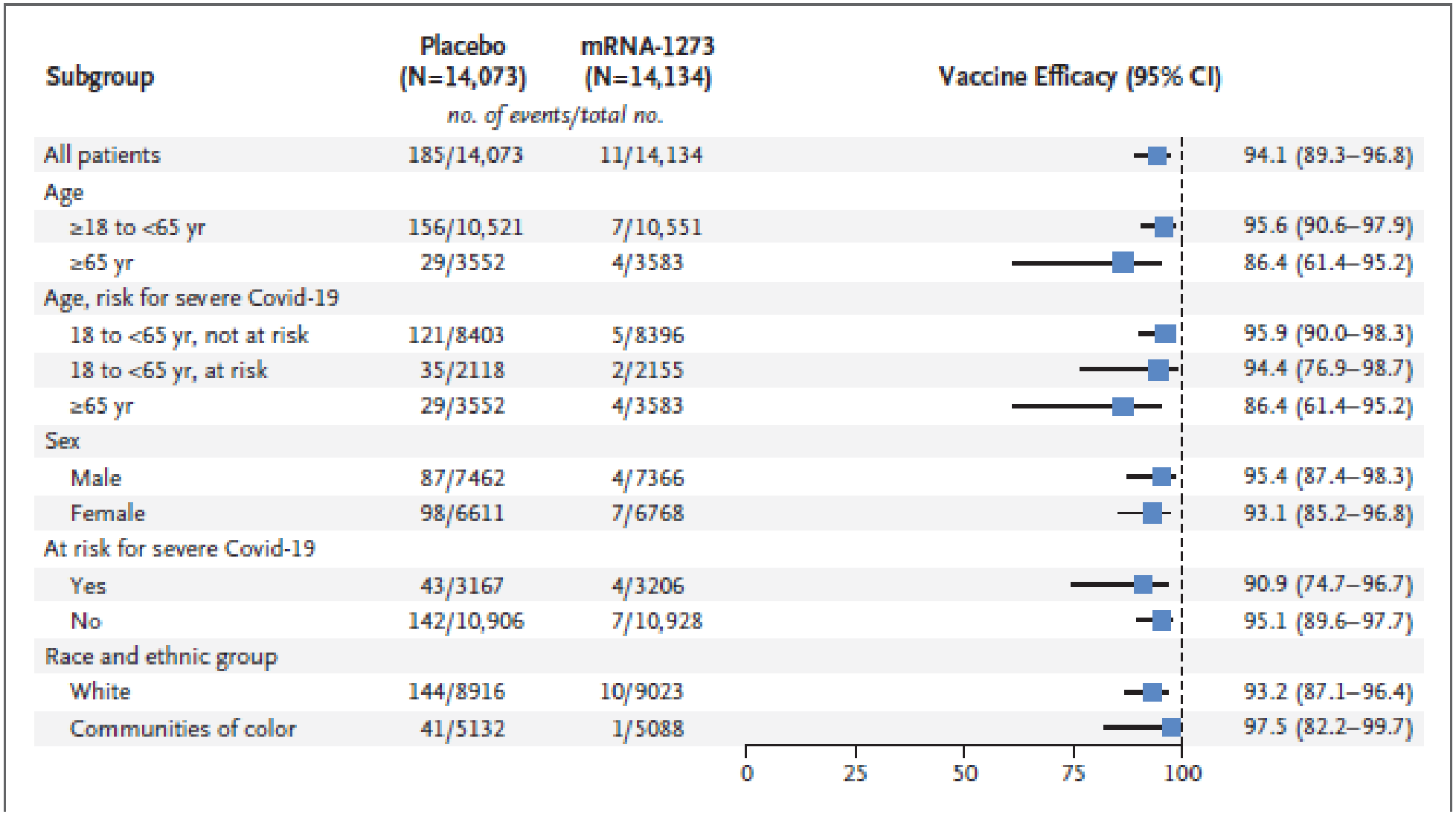
B Modified Intention-to-Treat Analysis

	Vaccine Efficacy (95% CI)	Incidence Rate (95% CI)
	%	*per 1000 person-yr*
Placebo		79.7 (70.5–89.9)
mRNA-1273	93.0 (88.9–95.6)	5.6 (3.4–8.8)

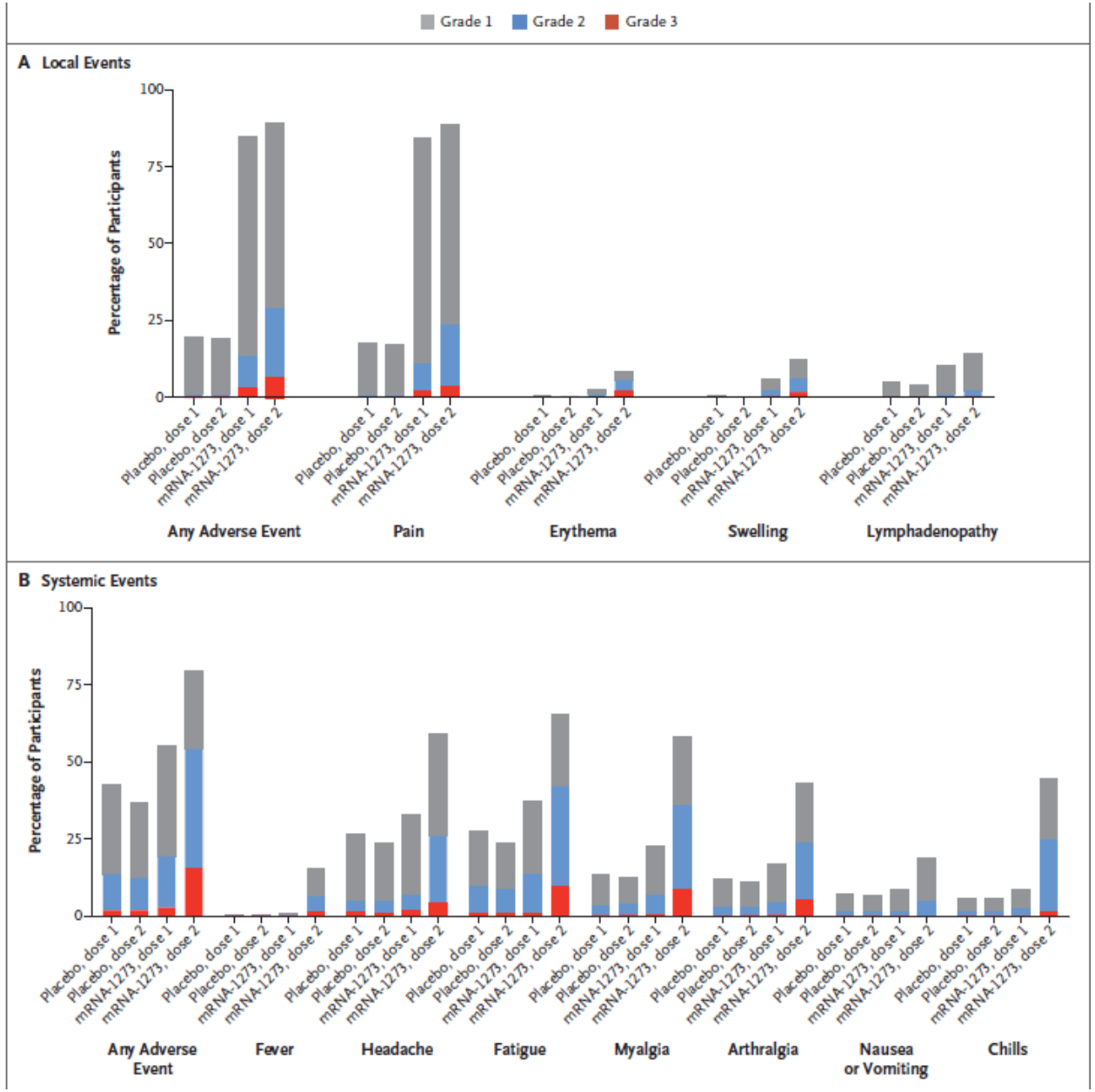
Covid-19 Onset	Placebo (N=14,598)	mRNA-1273 (N=14,550)
Randomization to 14 days after dose 1	11	5
14 Days after dose 1 to dose 2	35	2
Dose 2 to 14 days after dose 2	19	0
Starting 14 days after dose 2	204	12
Total (any time after randomization)	269	19



N Engl J Med 2021;384:403-16.



N Engl J Med 2021;384:403-16.


Grade 1
Grade 2
Grade 3
A Local Events
Percentage of Participants
100
75
50
25
0
Placebo, dose 1
Placebo, dose 2
mRNA-1273, dose 1
mRNA-1273, dose 2
Any Adverse Event
Pain
Erythema
Swelling
Lymphadenopathy
B Systemic Events
Percentage of Participants
Any Adverse Event
Fever
Headache
Fatigue
Myalgia
Arthralgia
Nausea or Vomiting
Chills

Reports of Anaphylaxis After Receipt of mRNA COVID-19 Vaccines in the US—December 14, 2020-January 18, 2021

Table. Characteristics of Reported Cases of Anaphylaxis Following Receipt of Pfizer-BioNTech (9 943 247 Doses) and Moderna (7 581 429 Doses) COVID-19 Vaccines—Vaccine Adverse Events Reporting System (VAERS), US, December 14, 2020-January 18, 2021

Characteristics	No. (%) of cases	
	Pfizer-BioNTech (n = 47)	Moderna (n = 19)
Age, median (range), y	39 (27-63)[a]	41 (24-63)
Female sex	44 (94)	19 (100)
Minutes to symptom onset, median (range)	10 (<1-1140 [19 h])[b]	10 (1-45)
Symptom onset, min		
≤15	34 (76)[b]	16 (84)
≤30	40 (89)[b]	17 (89)
Reported history[c]		
Allergies or allergic reactions	36 (77)	16 (84)
Prior anaphylaxis	16 (34)	5 (26)
Vaccine dose		
First	37	17
Second	4	1
Unknown	6	1
Brighton Collaboration case definition level[d]		
1	21 (45)	10 (52)
2	23 (49)	8 (43)
3	3 (6)	1 (5)
Anaphylaxis reporting rate (cases per million doses administered)	4.7	2.5

JAMA Published online February 12, 2021

Society of Hospital Medicine

What about other vaccines?

AstraZeneca/Oxford (adenoviral vector)[1]

Overall efficacy 62.3% and was well tolerated

Janssen(adenoviral vector)[2]

66% overall efficacy

- **72% in US**; 66% in Latin America; 57% in South Africa
  - 95% of cases in South Africa due to SARS CoV-2 variant from B.1.351 lineage
- 85% efficacy in preventing severe disease

Novavax (adjuvanted protein subunit)[3]

89.3% efficacy in the UK

- 50% of cases due to UK variant

60% efficacy in South Africa

- 90% of cases due to variant from B.1.351 lineage

Society of Hospital Medicine

1. *Lancet* 2021; 397: 99-11
2. Johnson and Johnson Press Release – Jan 29, 2021 Johnson & Johnson Announces Single-Shot Janssen COVID-19 Vaccine Candidate Met Primary Endpoints in Interim Analysis of its Phase 3 ENSEMBLE Trial | Johnson & Johnson (jnj.com)
3. Novavax Press Release – Jan 28, 2021 Novavax COVID-19 Vaccine Demonstrates 89.3% Efficacy in UK Phase 3 Trial | Novavax Inc. - IR Site

Vaccine Efficacy Summary

Vaccine	Type	Overall Efficacy	Efficacy for Preventing Hospitalization and Death
Pfizer-BioNTech	mRNA	95%	100%
Moderna	mRNA	94%	100%
AztraZeneca/Oxford	Adenovirus vector	62%	100%
Janssen (J+J)	Adenovirus vector	66% (72% in US; 66% in LA; 57% in South Africa)	100%
Novavax	Adjuvanted protein subunit	89.3% in UK; 60% in South Africa	100%

Society of Hospital Medicine

Case 1 – Should he pursue vaccination?

A) Yes, get vaccinated with whatever is available

B) Yes, get vaccinated but pursue a specific brand of vaccine

C) No, delay vaccination until further evidence is available

D) No, do not allow microchip implantation under any circumstances

Society of Hospital Medicine

Case 2

65 year-old female with no significant medical problems has agreed had her first round of vaccination.

She tolerated the vaccine well.

She approaches you about when and in what ways she can “get back to normal” now that vaccinations are more widely available in her state.

She specifically asks about:

-how close we are to herd immunity

-whether she should be concerned about mutants wreaking havoc.

Case 2 Question 1
How close are we to herd immunity?

A) We're there, Baby!

B) Unclear so far, but achieving it will require rapid and widespread vaccination

C) Unclear so far, but it's probably fine to stop physically distancing and stop masking in public

D) Herd immunity is #FakeNews and totally unachievable

Society of Hospital Medicine

Society of Hospital Medicine

Case 2 Question 2
What about the mutants?

A) Mutant strains are unlikely to reach the US

B) Current vaccines are expected to offer no protection against mutant strains

C) Current vaccines are expected to offer 100% protection against mutant strains

D) Current vaccines are likely to offer some protection against mutants

E) The mutants will likely fight each other to the death and our problems will be solved

What is herd immunity?

Resistance to the spread of an infectious disease within a population that is based on pre-existing immunity of a high proportion of individuals as a result of previous infection or vaccination.

"the level of vaccination needed to achieve herd immunity varies by disease but ranges from 83 to 94 percent"

Flickr Alachua County

Society of Hospital Medicine

How do we achieve herd immunity?

Two Strategies:

1. **Allow the virus to spread unchecked through the less vulnerable population (Sweden)**

- **Advantages –**

Government does nothing
Infection control practices ignored
Business as usual

- **Problems**

Overwhelm our health systems
Millions of unnecessary deaths (can't prevent spread to the vulnerable)
Variable Immunity - depends on the severity of disease

- Mild disease poor antibody response that may be short lived
- Severe disease likely to confer long term immunity

Society of Hospital Medicine

Flickr Memroid

The price of herd immunity U.S.

0.8 x 326 million = 260. 8 M infected

Hospitalization rate 6-10% = 15.6-26.8 M hospitalized
0.924 million beds

17-29 x bed capacity

Death rate = 1.76% in U.S. = 4.6 million deaths

12-22-20

Sweden

787 deaths per 1 million

4.5 -10 X higher than Denmark, Finland or Norway.

U.S

1,041 deaths per million

How do we achieve herd immunity?

2. Vaccinate the entire world

Advantages

- A controlled approach
- Decreased hospitalizations
- Decreased deaths
- Potential to confer long term immunity for everyone
- Historically a safe and effective approach (Polio, Smallpox)

Society of Hospital Medicine

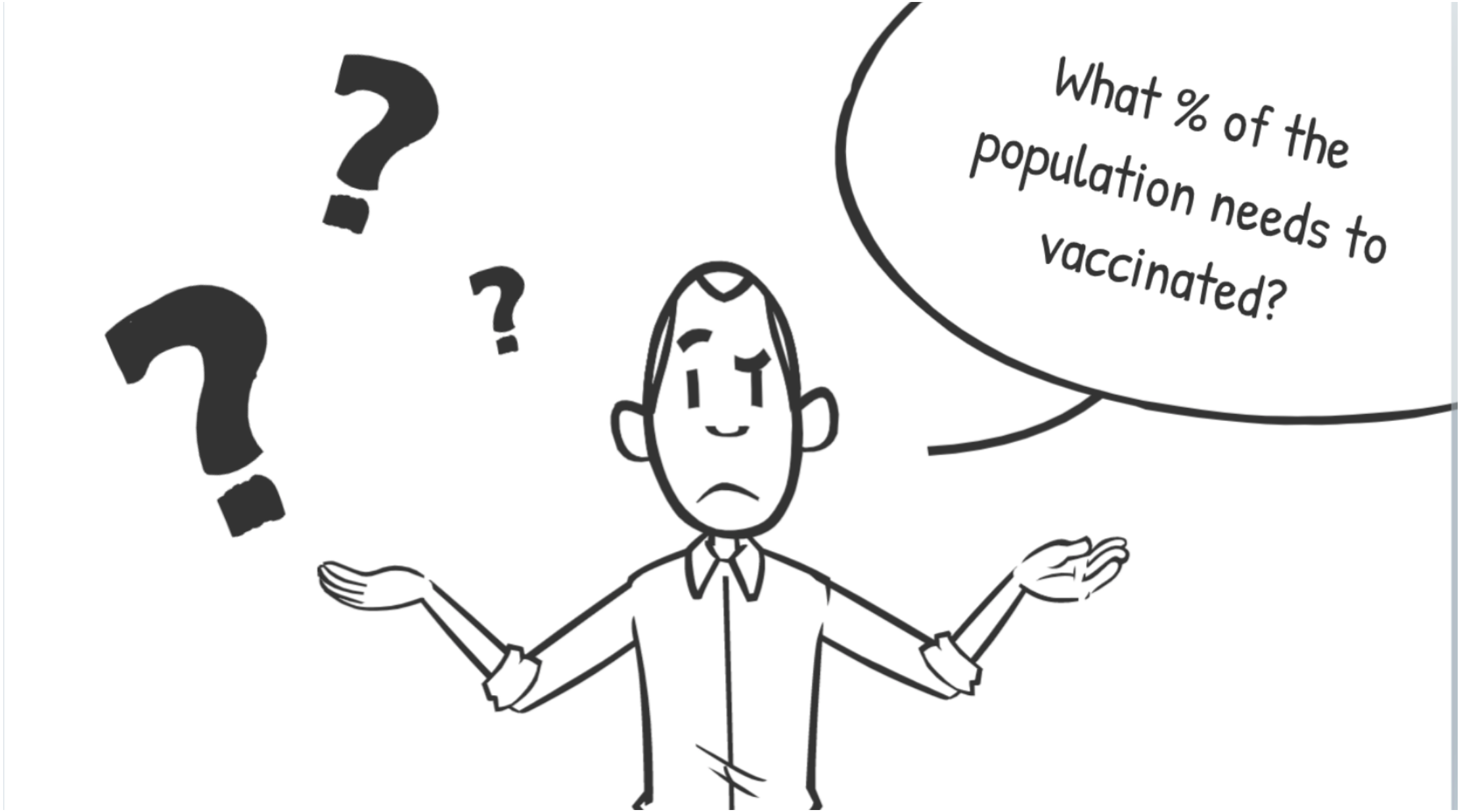
How do we achieve herd immunity?

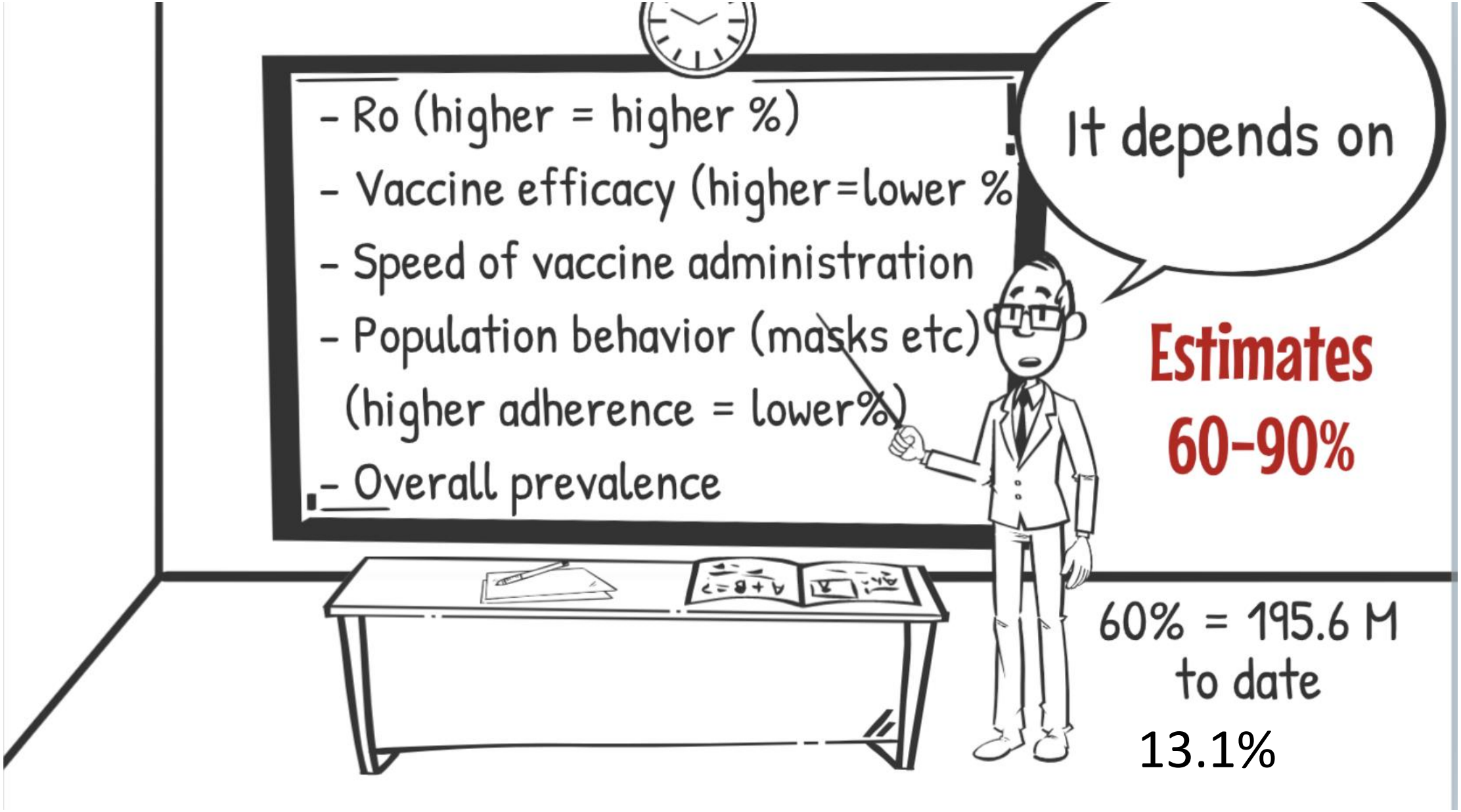
2. Vaccinate the entire world

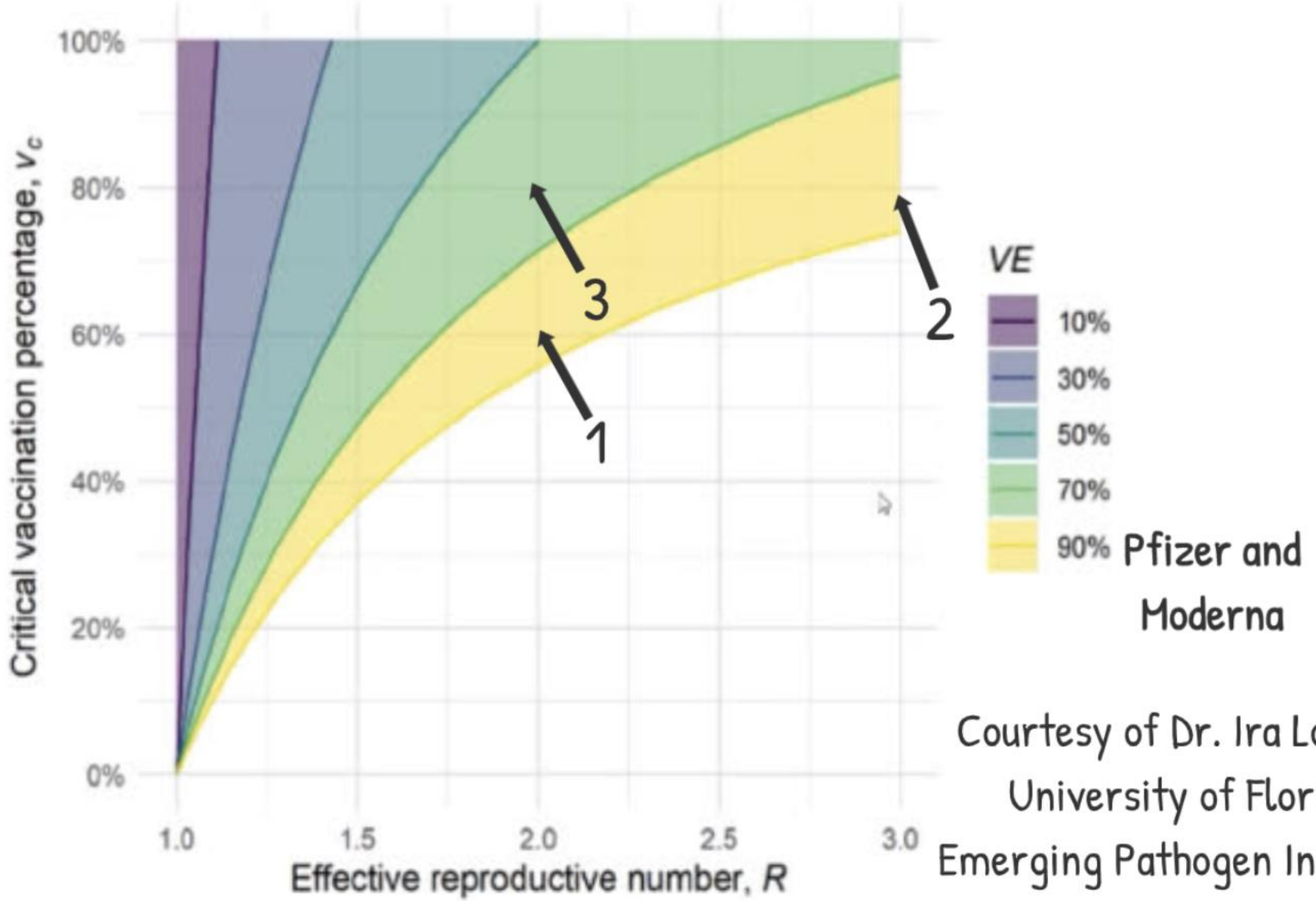
Potential Problems

- **Immune enhancement syndrom**e (Dengue Fever)
- **Hypersensitivity reactions**
- **Unexpected toxicities** (Guillan Barre Syndrome, other autoimmune diseases)
- **Low efficacy – mutant viruses**
- Failure long term immunity
- **Anti-vaccine groups**
- Expensive, but very cost-effective
- **Supply chain challenges**
- **Inequity** - lower socioeconomic groups and developing countries could be last in line

Society of Hospital Medicine


What % of the population needs to vaccinated?


- Ro (higher = higher %)
- Vaccine efficacy (higher=lower %
- Speed of vaccine administration
- Population behavior (masks etc)
(higher adherence = lower%)
- Overall prevalence
It depends on
Estimates
60-90%
60% = 195.6 M
to date
13.1%



Courtesy of Dr. Ira Longini, University of Florida, Emerging Pathogen Institute.

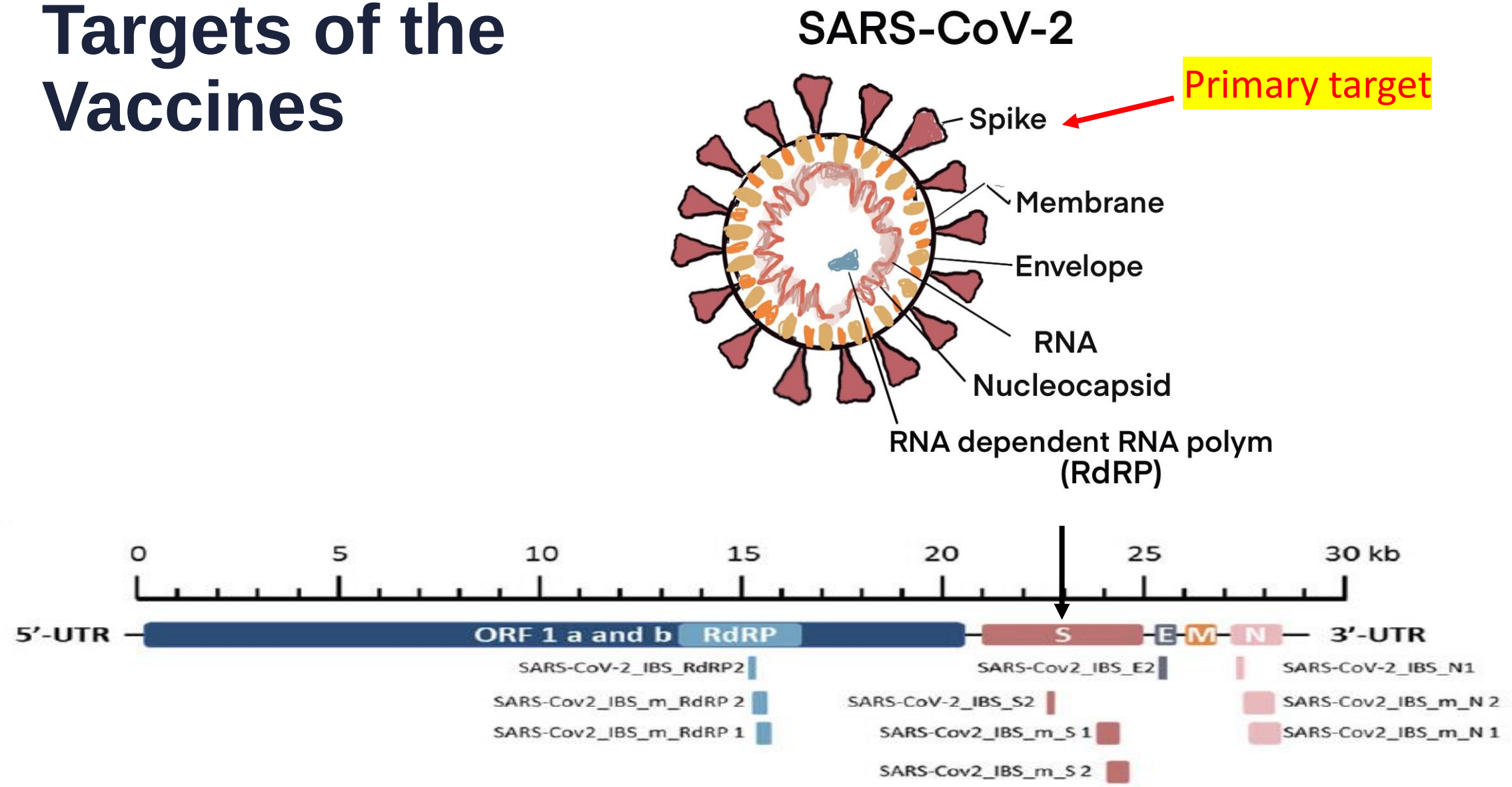
Summary

- Vaccination the only safe way to achieve herd immunity
- Serious side effects not observed
- Antivaxers prevent herd immunity
- Inequity a concern
- % Vaccination needed depends on: Ro, Vaccine efficacy, speed of vaccination

Can the virus mutant escape the vaccines?

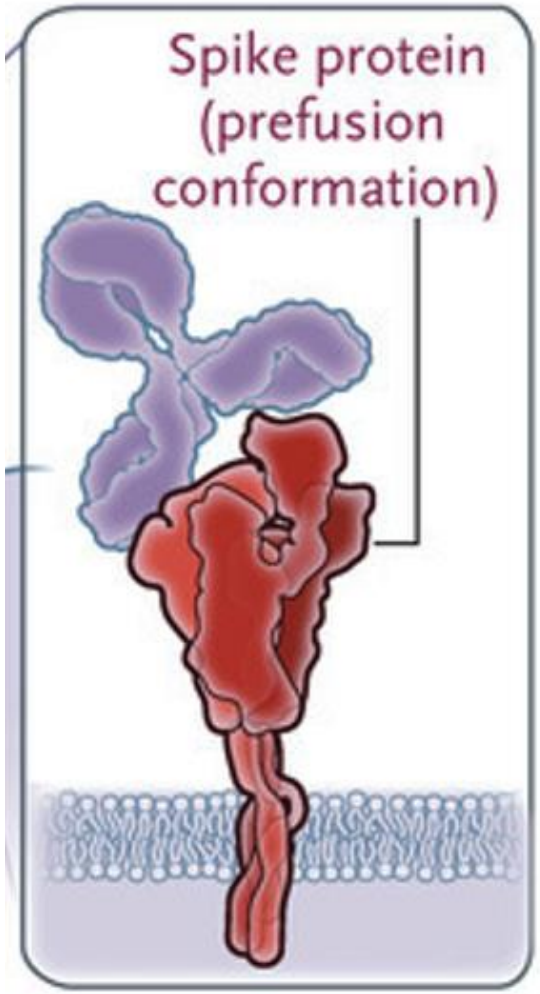
Society of Hospital Medicine

Targets of the Vaccines



Can the virus escape the vaccine?

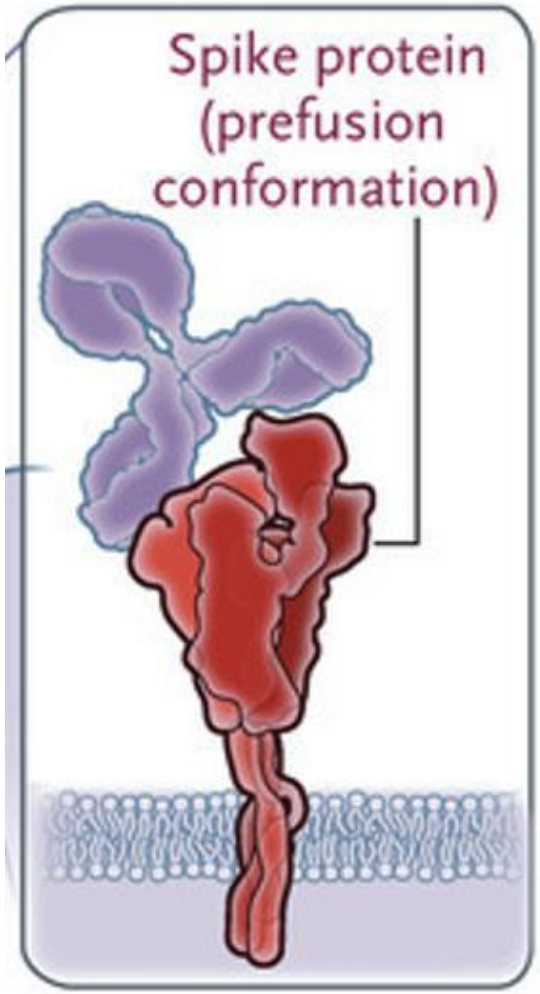
- **United Kingdom Variant = Mutant VUI – 202012/01 or B1.1.17)**
- **One mutation in the Spike Protein N (Asparagine) to Y (tyrosine) 501 mutant**
  - Higher affinity for ACE2 receptor
  - Spreads 50-70% more efficiently.
- **Vaccines use the full-length spike protein multiple sites for Ab production.**
- **Abs directed against the S2 binding domain block viral entry.**
- **No evidence for reduced vaccine efficacy**
- **RNA virus have poor proof reading and commonly mutate, changes are expected**
- **The longer the pandemic the higher the risk of escape mutants**



Society of Hospital Medicine

Can the virus escape the vaccine?

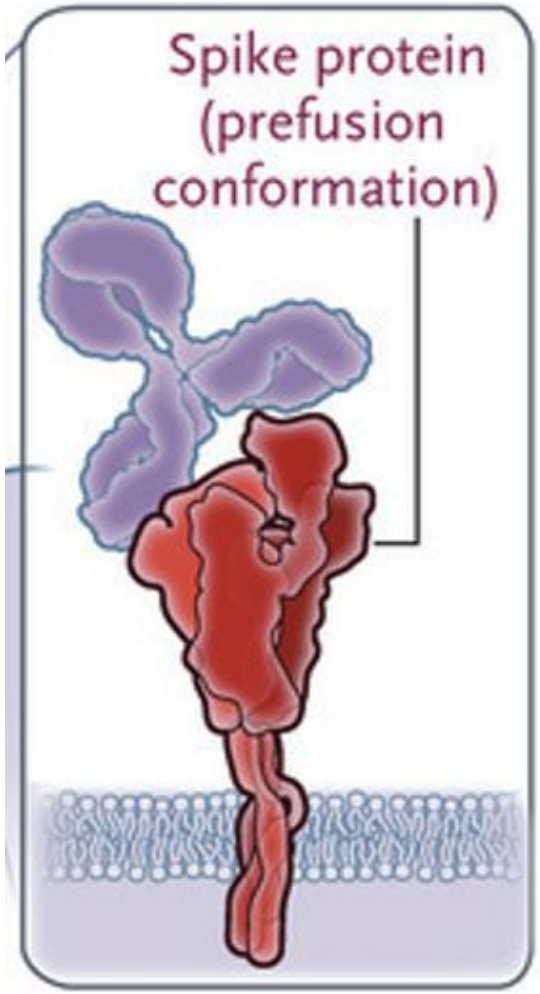
- **South African Variant B.1.351**
- **3 mutations** in the Spike Protein
  N (Asparagine) to Y (tyrosine) 501 mutant
  K (Lysine) to N (Asparagine) 417
  E (Glutamate) to K (Lysine) 484
- **Evidence of decreased efficacy for Astra Zeneca 66 to 22%**
  J&J vaccines 72 to 57%
  Moderna - decrease neutralizing Ab
  no evidence for reduced protection



Society of Hospital Medicine

Can the virus escape the vaccine?

- **Brazilian Variant P 1**
- **10 mutations** in the Spike Protein
  N (Asparagine) to Y (tyrosine) 501 mutant
  K (Lysine) to N (Asparagine) 417
  E (Glutamate) to K (Lysine) 484
  7 other mutations
- **Expect decreased efficacy for Astra Zeneca and J&J vaccines Possibly Moderna and Pfizer**



Society of Hospital Medicine

Society of Hospital Medicine

Conclusions

- Vaccination will be critical for generating herd immunity (60-90%) and ending pandemic
- Majority of vaccines are directed against the spike protein
- Mutations are expected with any RNA virus and the longer the pandemic continues the more mutations will be selected
- Darwin's survival of the fittest is taking place before our eyes
- The longer it takes to achieve herd immunity the greater the risk of mutants that will escape the vaccine
- Importance of continued masks, distancing and avoiding crowds and closed spaces

Society of Hospital Medicine

Case 2 Question 1
How close are we to herd immunity?

A) We're there, Baby!

B) Unclear so far, but achieving it will require rapid and widespread vaccination

C) Unclear so far, but it's probably fine to stop physically distancing and stop masking in public

D) Herd immunity is #FakeNews and totally unachievable

Society of Hospital Medicine

Case 2 Question 2
What about the mutants?

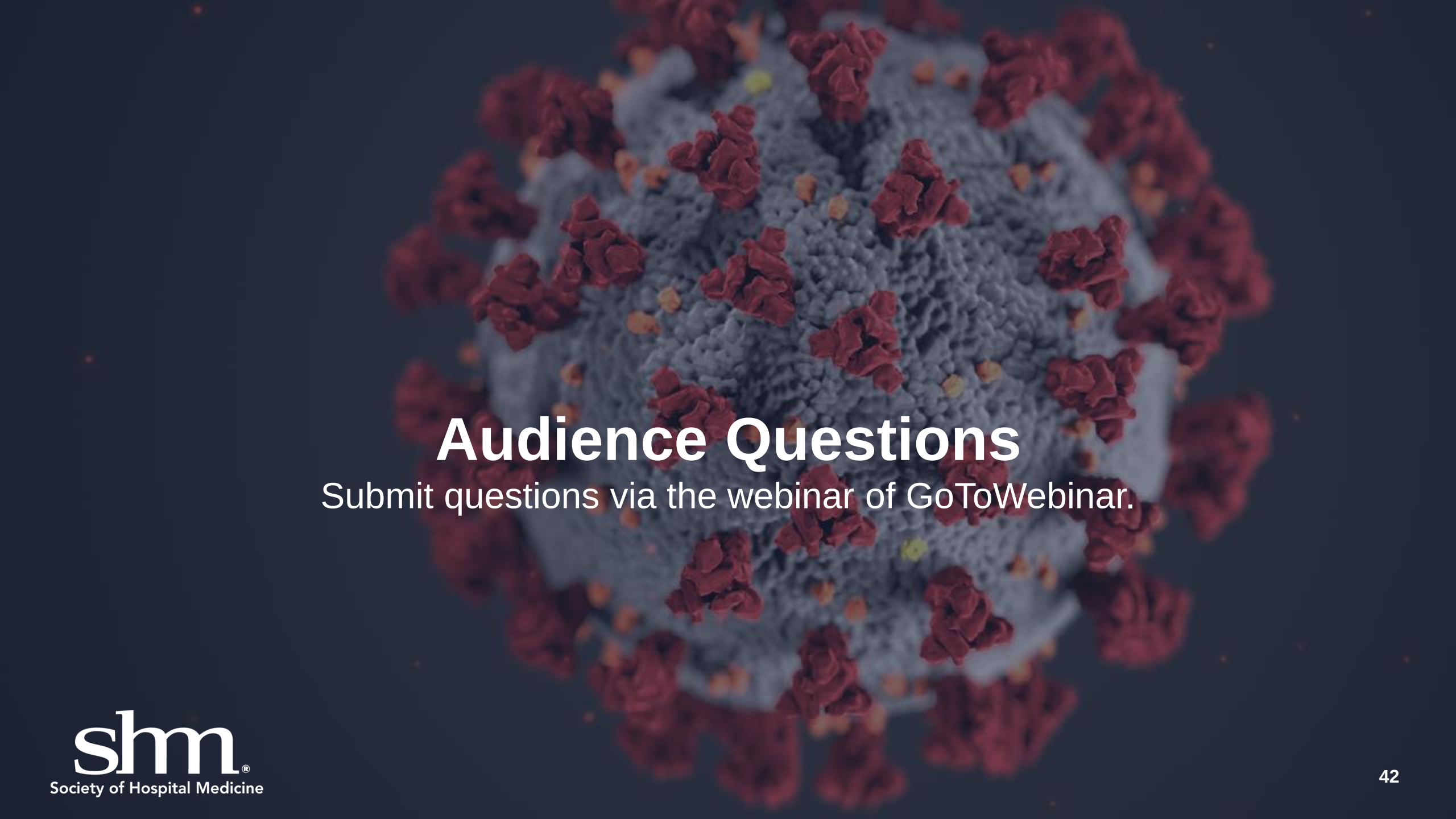
A) Mutant strains are unlikely to reach the US

B) Current vaccines are expected to offer no protection against mutant strains

C) Current vaccines are expected to offer 100% protection against mutant strains

D) Current vaccines are likely to offer some protection against mutants

E) The mutants will likely fight each other to the death and our problems will be solved



Audience Questions

Submit questions via the webinar of GoToWebinar.

Society of Hospital Medicine

Society of Hospital Medicine

Empowering hospitalists.
Transforming patient care.

SHM Clinical Rapid Updates COVID mRNA Vaccines

Thank you:

Derek W. Forster, MD

Derek.Forster@uky.edu

Fred Southwick, MD

SouthF@epi.ufl.edu

Society of Hospital Medicine

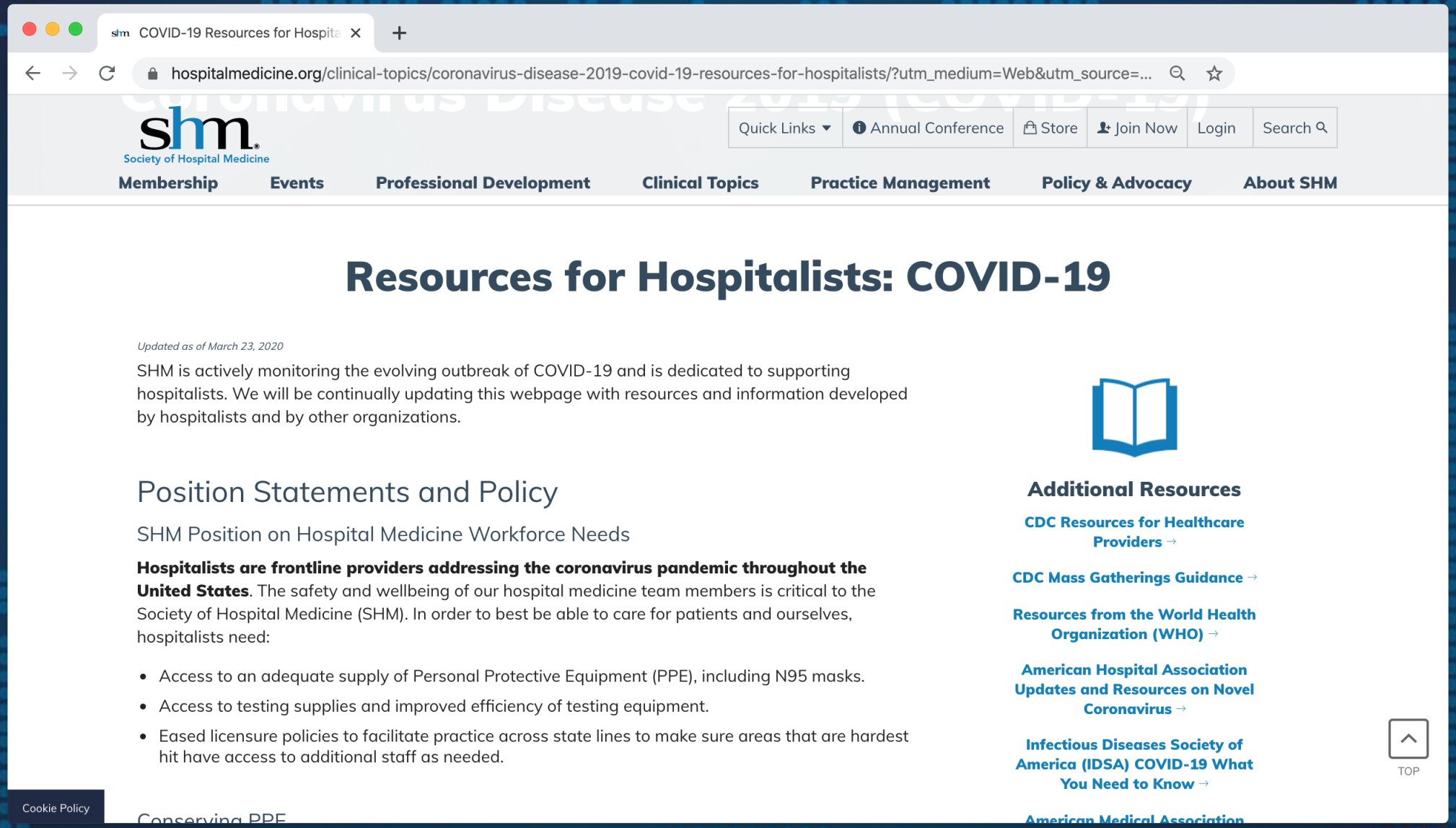
To Claim CME:

Please go to:
https://www.shmlearningportal.org/content/rapid-clinical-updates-covid-19-mrna-vaccines-and-hospital-medicine

The Society of Hospital Medicine designates this live activity, for a maximum of 1 *AMA PRA Category 1 Credits™.* Physicians should only claim credit commensurate with the extent of their participation in this activity

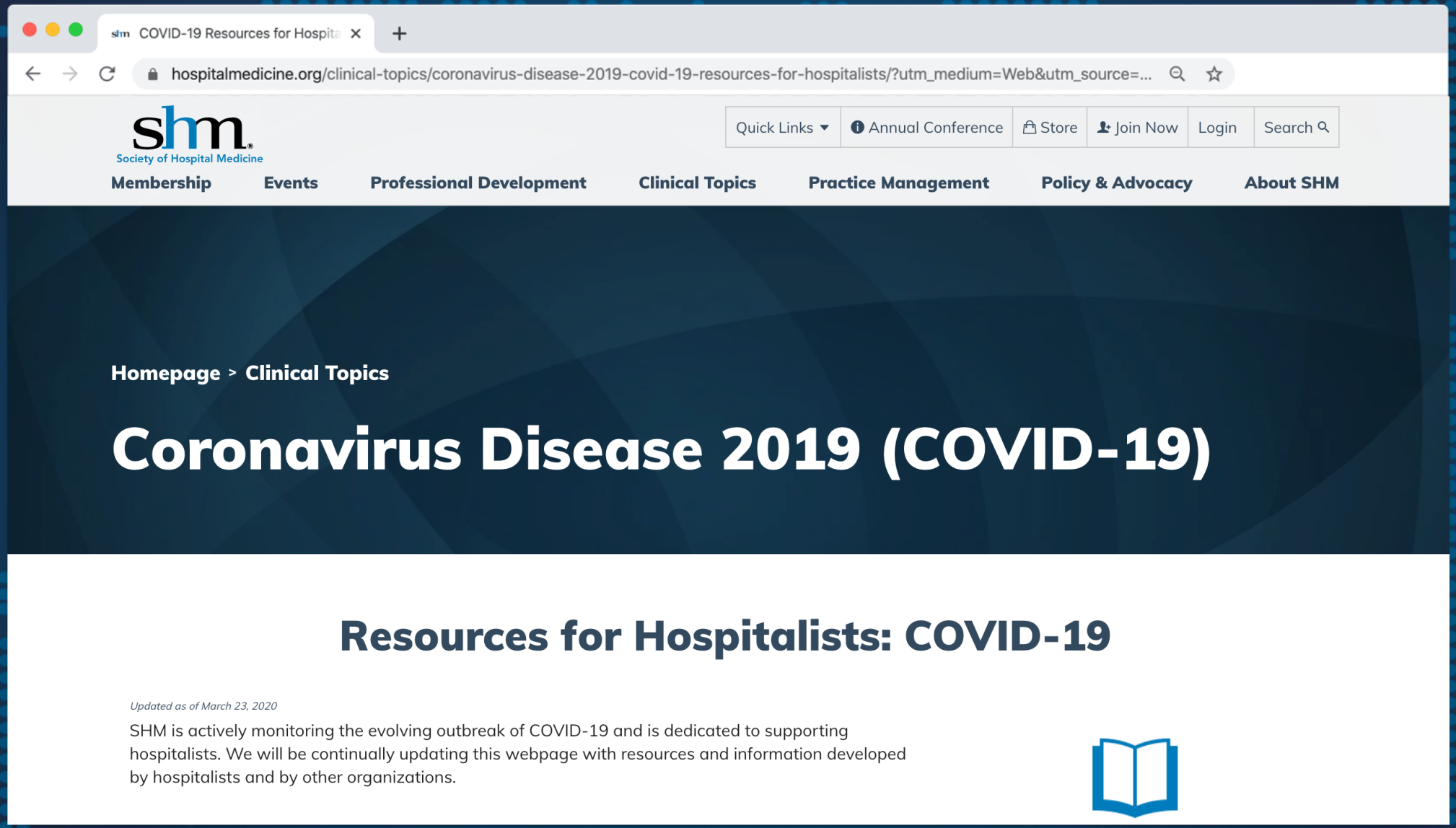
The Society of Hospital Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provider continuing medical education for physicians.

SHM is dedicated to promoting the highest quality care for all hospitalized patients. SHM is committed to promoting excellence in the practice of hospital medicine through education, advocacy and research.



hospitalmedicine.org

Society of Hospital Medicine



hospitalmedicine.org

shm
Society of Hospital Medicine