Risk factors for severe Covid-19 outcomes among vaccinated adults in the US

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Game plan

- Review a recent article on Covid-related outcomes among Covid-19 vaccinees, including hospitalizations and mortality risk (a report worth your time to read if you see patients or are just concerned about welfare of people you know with chronic conditions)
- Revisit my 'case family' in California for new developments
- We will consider some additional Covid study findings re: pre-prints and their potential (or real) pitfalls

Objectives

- Be able to list the major demographic and chronic disease-related conditions that are associated with severe Covid-19-related outcomes post vaccination
- Be able to state how you will use this information to counsel patients, friends, family members who have been vaccinated
- Be able to cite positive and negative examples of Covid-19 studies that have appeared before peer-review of the manuscripts and the data therein
- Pass a test at the end

Take home messages

- Among vaccinated adults, severe Covid-19 outcomes are rare
- Age is the strongest risk factor associated with severe outcomes
- Numerous other chronic diseases are associated with increased risk for severe outcomes
- Despite size and thorough analysis of these data, we could still benefit from population-based perspectives…including current circulating variants

First, the case family you have heard about before

- Four members, two middle aged adults, one twenty-something, one teen
- One fragile by most definitions, who remained uninfected during the time of my earlier reports
- All live active lives, not hiding from Covid but compliant with masking and home testing if any unusual symptoms or signs appear

Transmission event from earlier presentaion

23 yr old male, partied with PCR+ friend

Goes home to family

+, asymptomatic

Mom
55 yrs
+

Sister
15 yrs
-

Dad
72 yrs
-

Case family developments

- After asymptomatic son apparently infected mom (who became sick with typical symptoms and signs), daughter brought home infection and was also sick (two months ago)
- Dad (with multiple chronic disease issues) once again escaped infection despite lack of consistent isolation of daughter (variant not identified)
- Daughter recovered after prolonged cough and sore throat

Case family developments

- In past two months, all family members had been vaccinated and boosted with mRNA vaccine
- All continued to go about daily routines (23+ year old has office job, mom continues to work in close contact with hundreds of others weekly, 16 year-old goes to high school in person, retired dad in party mode 24/7)
- Two weeks ago, all developed URI-type symptoms and tested positive on antigen test and PCR test for SARS-CoV-2…presumably Omicron variant, not tested, tho. All tested at same time. (3/4 second infection)
- Mom developed mild renal failure with decreased estimated GFR resulting in renal work-up (expensive)..unknown time frame for this
- Following CDC isolation guidelines (the new set), they all headed back to their regular lives with little consequence (so far)

Introduction, Risk factor study

- Various estimates of the frequency of occurrence of Covid-19 post vaccination, including severe outcomes
- From a clinical management standpoint, and patient counselling viewpoint, knowing more about risks (and rates) of severe outcomes for Covid-19 post vaccination would be useful
- A population-based perspective on severe outcomes post vaccination would be useful and help guide public health messages and perhaps policy…this study is not population-based, but is multi-center and provides useful information

Yek C, et al. Risk factors for severe Covid-19 outcomes among persons aged >18 years who completed vaccination series. MMWR, Jan 7, 2022, 71(2), pg 19. https://www.cdc.gov/mmwr/volumes/71/wr/mm7101a4.htm

Methods, Risk factor study

- Admin dataset from 465 facilities in US
- All included had received primary series of one of the approved vaccines in US (an unknown proportion had been boosted)
- All diagnosed with Covid-19 after 14 days post second vaccine dose
- Severe outcomes: hospitalization with acute respiratory failure, need for non-invasive ventilation, admit to ICU (including ventilation mechanically), death (including discharge to hospice)
- No. of risk factors per person was collected and analyzed
- Logistic regression model to estimate odds for severe vs. non-severe outcomes with simultaneous adjustment for multiple risk factors for severe outcomes

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Key results

- 1,228,664 persons completed vaccination
- 2,246 developed Covid-19 (1.8%)
- 189 had severe outcome/36 deaths (thus, 8% of the Covid cases had severe outcomes)
- Strongest risks for severe outcome included age >65 years, immunosuppression, or having at least one of six other underlying conditions
- All persons with severe outcome had at least one risk factor
- 75% of those who died had four or more risk factors

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TABLE. Characteristics of persons with COVID-19 after completing a primary COVID-19 vaccination series, overall and by disease outcome, and adjusted odds ratios for severe COVID-19 outcomes — 465 health care facilities, United States, December 2020–October 2021

Characteristic	No. (%) with COVID-19 after primary vaccination			
	Total (N = 2,246)	Nonsevere outcome (n = 2,057)	Severe outcome (n = 189)	aOR of severe versus nonsevere COVID-19 outcome (95% CI)
Disposition				
Outpatient	**1,360 (60.6)**	NA	NA	NA
ED/Observation	**559 (24.9)**	NA	NA	NA
Hospitalization	**327 (14.6)**	NA	NA	NA
Severe outcome				
Any severe outcome	**189 (8.4)**	NA	NA	NA
Death	**36 (1.6)**	NA	NA	NA
Survivors admitted to ICU*	**24 (1.1)**	NA	NA	NA
Survivors with respiratory failure,† without ICU admission or death	**129 (5.7)**	NA	NA	NA

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Underlying medical conditions				
Overweight/Obesity	**609 (27.1)**	532 (25.9)	77 (40.7)	1.28 (0.97–1.7)
Diabetes mellitus	**633 (28.2)**	535 (26.0)	98 (51.9)	1.47 (1.14–1.89)
Immunosuppression	**446 (19.9)**	360 (17.5)	86 (45.5)	1.91 (1.37–2.66)
Chronic kidney disease	**353 (15.7)**	271 (13.2)	82 (43.4)	1.61 (1.19–2.19)
Chronic neurologic disease	**301 (13.4)**	242 (11.8)	59 (31.2)	1.54 (1.06–2.25)
Chronic cardiac disease	**753 (33.5)**	624 (30.4)	129 (68.3)	1.44 (1.01–2.06)
Chronic pulmonary disease	**889 (39.6)**	752 (36.6)	137 (72.5)	1.69 (1.31–2.18)
Chronic liver disease	**124 (5.5)**	103 (5.0)	21 (11.1)	1.68 (1.12–2.52)
Previous COVID-19 illness	**68 (3.0)**	67 (3.3)	1 (0.5)	0.27 (0.09–0.84)

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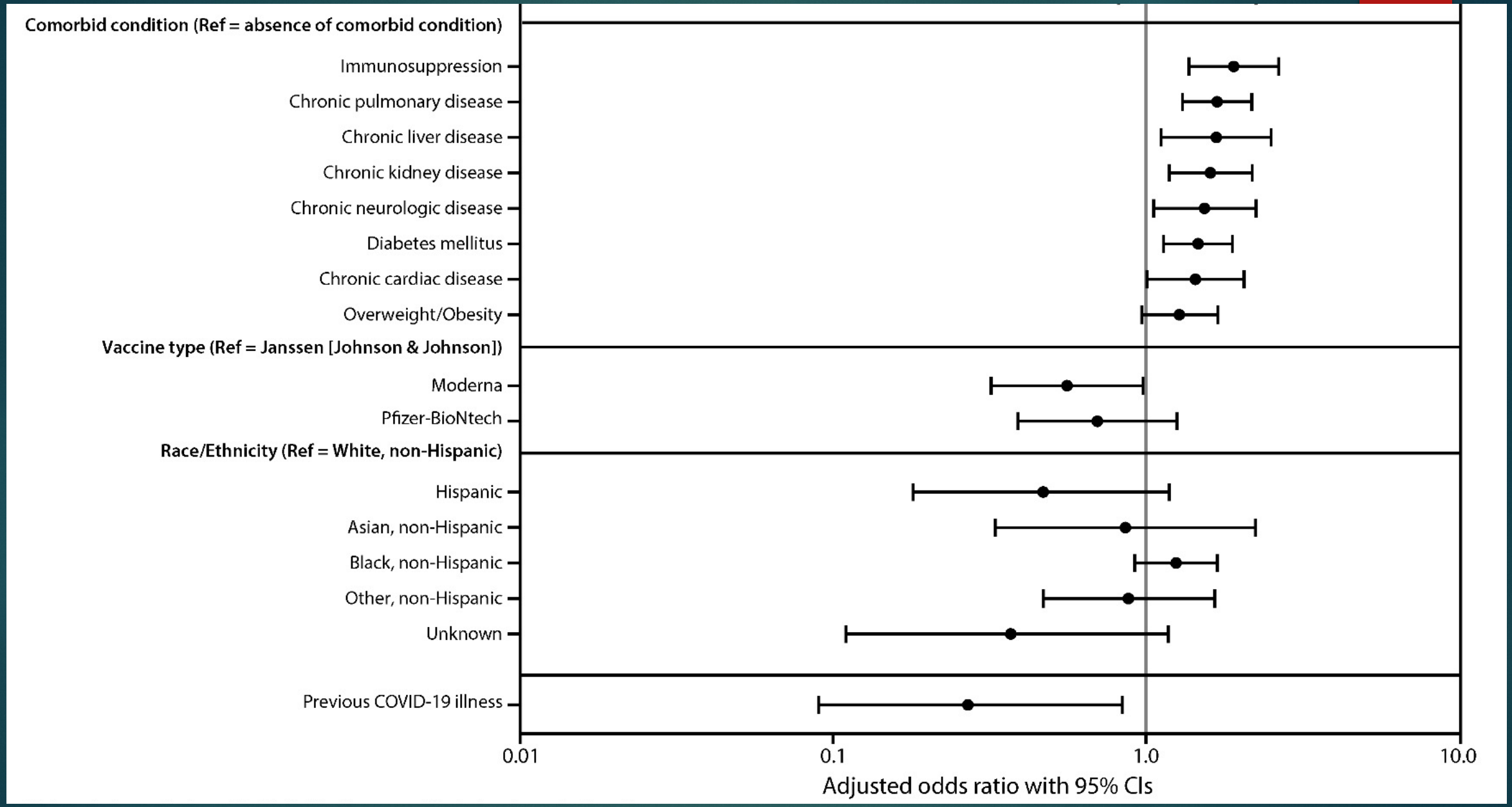

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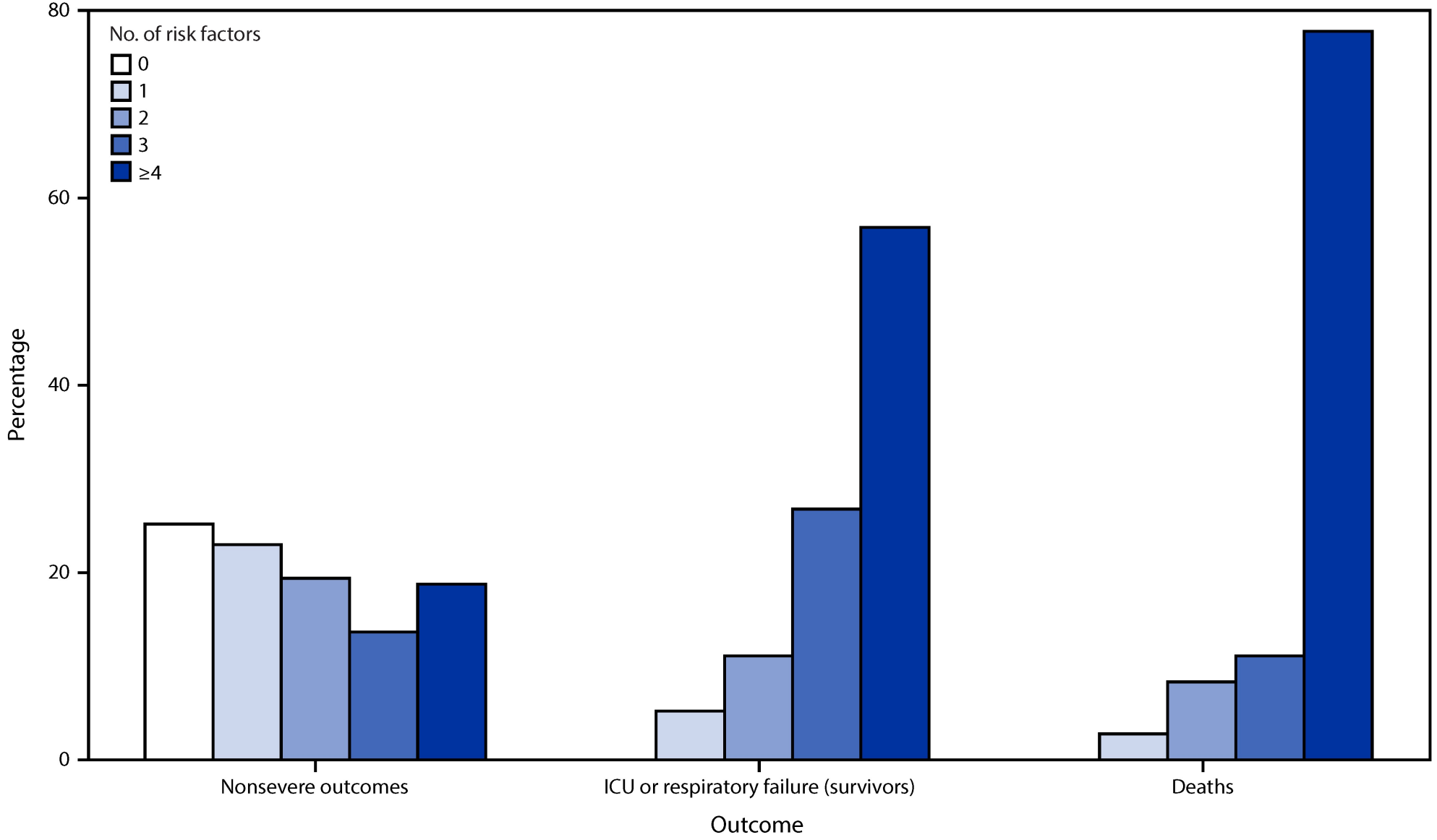
FIGURE 2. Frequency of risk factors in persons with COVID-19 after completion of a primary vaccination series, by outcome*,† — 465 health care facilities, United States, December 2020–October 2021



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Limitations, Yek study

- Pre-Omicron variant data collection and analysis (only)
- A small proportion had booster dose
- Time period split Delta surge…not complete info on that
- Administrative data set, not set up for research per se
- Underlying conditions may not have been completely captured
- Uncontrolled chronic diseases could be a result of 'hiding from Covid'…exacerbating severe outcomes in patients with co-morbidities
- This reporting system is a convenience sample of health care facilities, therefore, limiting generalizability to the entire US

Applying this information…

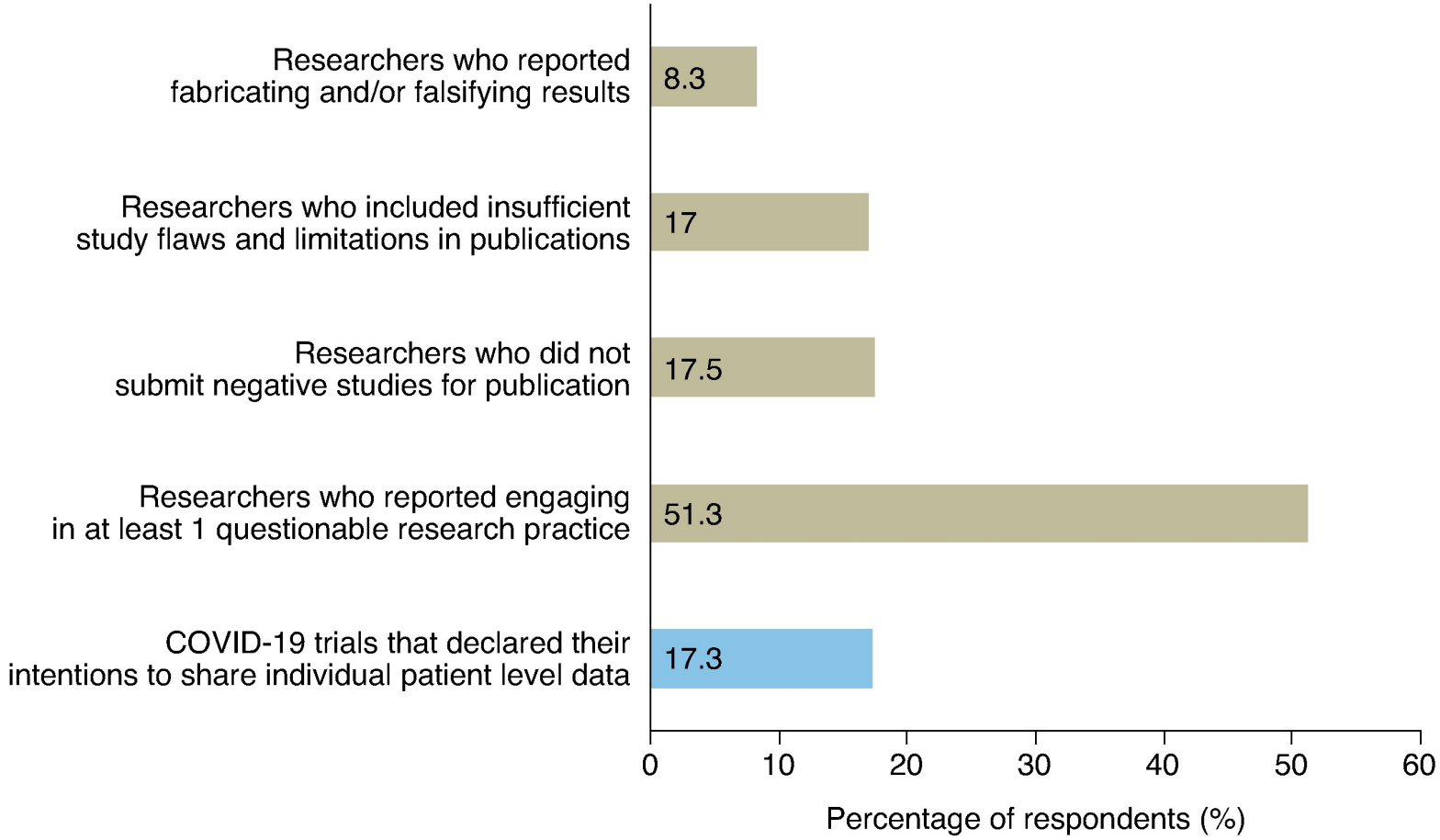
- Even with vaccination completed, control of chronic disease is important to your patients' health
- Continue to exercise precautions re: exposures esp among those with chronic conditions
- Booster doses of vaccine
- Effective pharmacologic therapy as indicated to reduce risk for severe Covid outcomes
- Continue to encourage vaccine uptake…tho this will be hard
- Note to patients that findings from this study did not include current circulating variants…or, of course, future variants. Perhaps some findings would be altered if included.

The rise of the pre-print

- In the first 4 months of the pandemic, 20,000 articles appeared…not all 'passing muster' from a transparency standpoint
- Pre-print examples of harmful effects of poor science (or fabrication) related to therapy: ivermectin, hydroxychloroquine
- Positive benefits of quick publication via pre-prints: asymptomatic transmission (that affected contact tracing), and dexamethasone for intubated ICU patients in respiratory failure
- Even Lancet and New England Journal had to withdraw articles that contained faked data…and these WERE peer reviewed

Questionable research

A survey of 6813 researchers at Dutch institutes found that many admitted to engaging in questionable research practices, as did data sharing statements from 924 registered COVID-19 trials.



Sources: G. Gopalakrishna et al. MetaArXiv, 6 July 2021; R. Li et al. Trials 22, 153 (2021)

"Rise of the preprint: how rapid data sharing during COVID-19 has changed science forever," Watson, C. News feature in *Nature Medicine*. https://www.nature.com/articles/s41591-021-01654-6

Take home test

- What proportion of US adults has at least one chronic disease that increases their risk for serve COVID-19 outcome?
- If you wanted to calculate actual incidence rates of severe outcomes of Covid-19 within one year after vaccination, what type of study design would you choose?
- What is the definition of 'risk' in epidemiologic terms? (or vernacular, that is ok, too)
- How do we measure risk in epi studies?
- What key information from the Yek study will you use to counsel patients you may see…or family or friends whom you may advise?
- What is your solution to improving publication of non-fraudulent research, and, excluding poorly done or fraudulent studies?
- True or false: behavioral health issues, including anxiety, depression, substance use disorder, and suicide are likely to increase the further we progress into the Covid-19 pandemic. (from one of my earlier quizzes months ago)

Bradford-Hill criteria for causation…did they disappear?

- Timing of exposure and outcomes (exposure happens first)
- Biologic plausibility
- Consistency of findings (for pre-prints, this is missing)
- Multiple lines of evidence (lab, epi studies, etc)
- Human experimental data (almost always missing)
- Specificity
- Strength of association
- Dose response
- Other criteria

References

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