New Hampshire COVID-19 Healthcare Provider and Public Health Partner Call
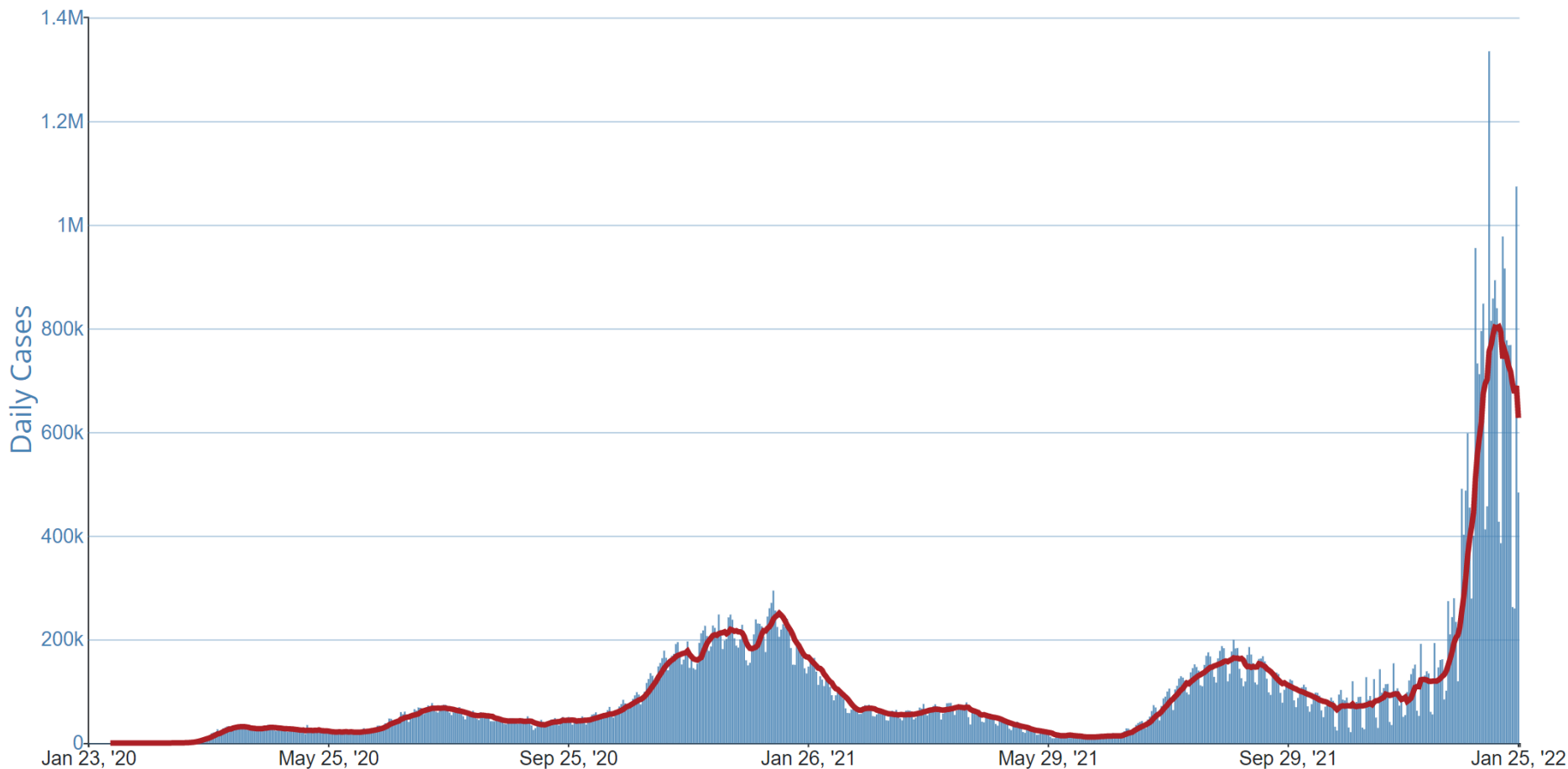
January 27, 2022

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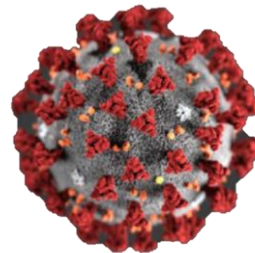
Epidemiology Update

U.S. National Daily Incidence of COVID-19

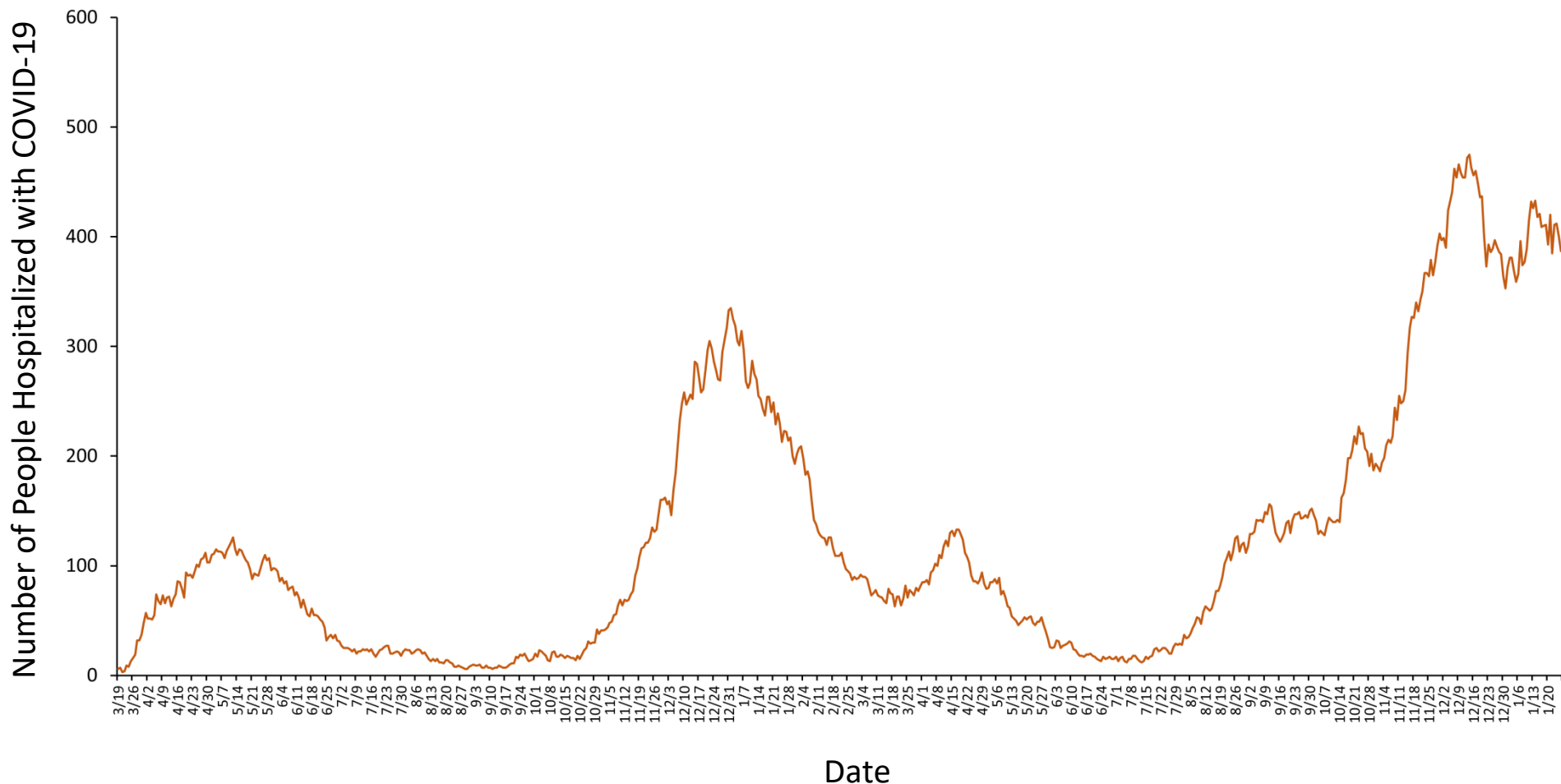Daily Trends in Number of COVID-19 Cases in The United States Reported to CDC

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Number of New COVID-19 Cases per Day in NH

Note: Case counts are incomplete for the last ~2 weeks due to surge in cases, so number of cases each day (and average) will increase

Number of Daily New Cases

5K
4K
3K
2K
1K
0K

Mar 1, 20   Jun 1, 20   Sep 1, 20   Dec 1, 20   Mar 1, 21   Jun 1, 21   Sep 1, 21   Dec 1, 21   Mar 1, 22

Date

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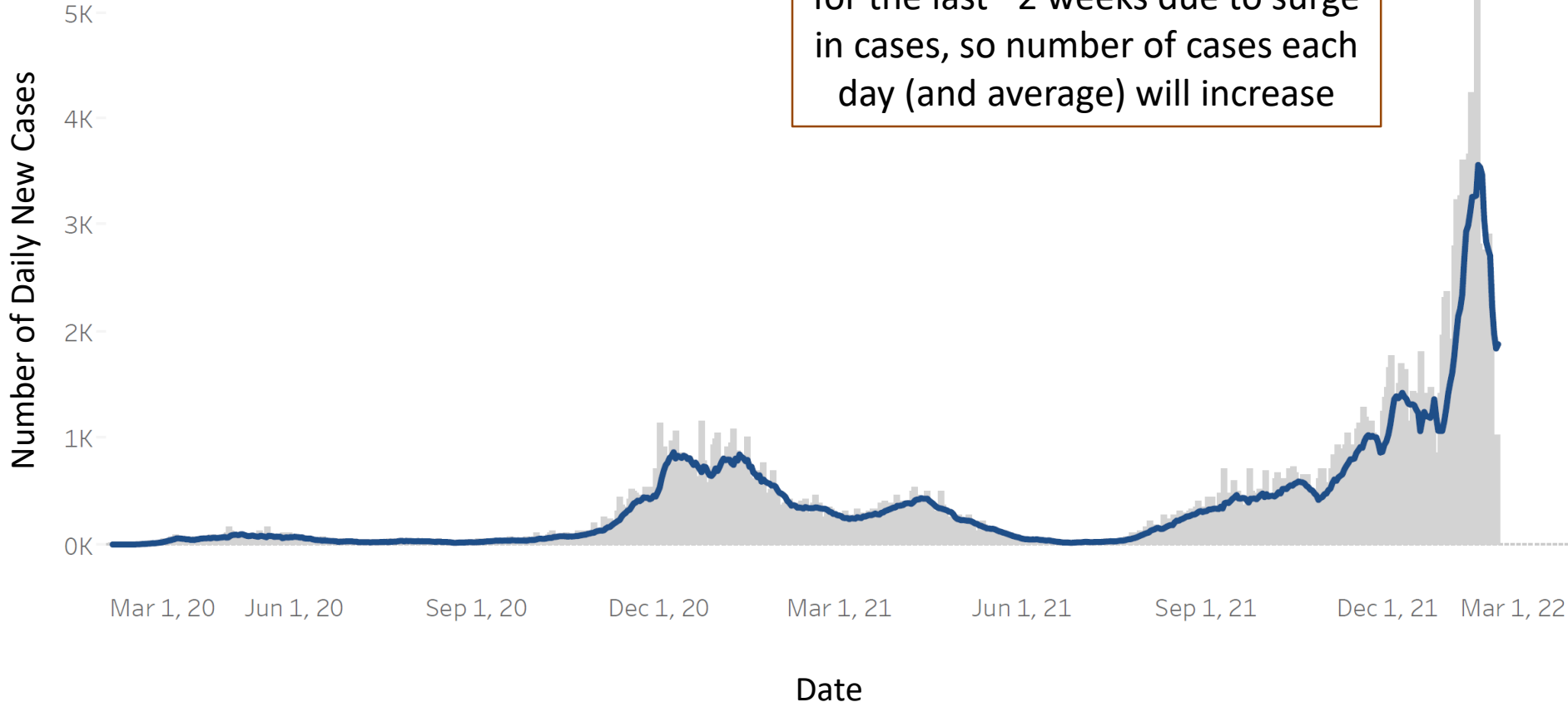
Number of People Hospitalized with COVID-19 Each Day in NH (Hospital Census)

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Average Number of COVID-19 Deaths per Day in NH (Based on Date of Death)

In the last week there have been 65 new COVID-19 related deaths identified (average of ~9 deaths/day)

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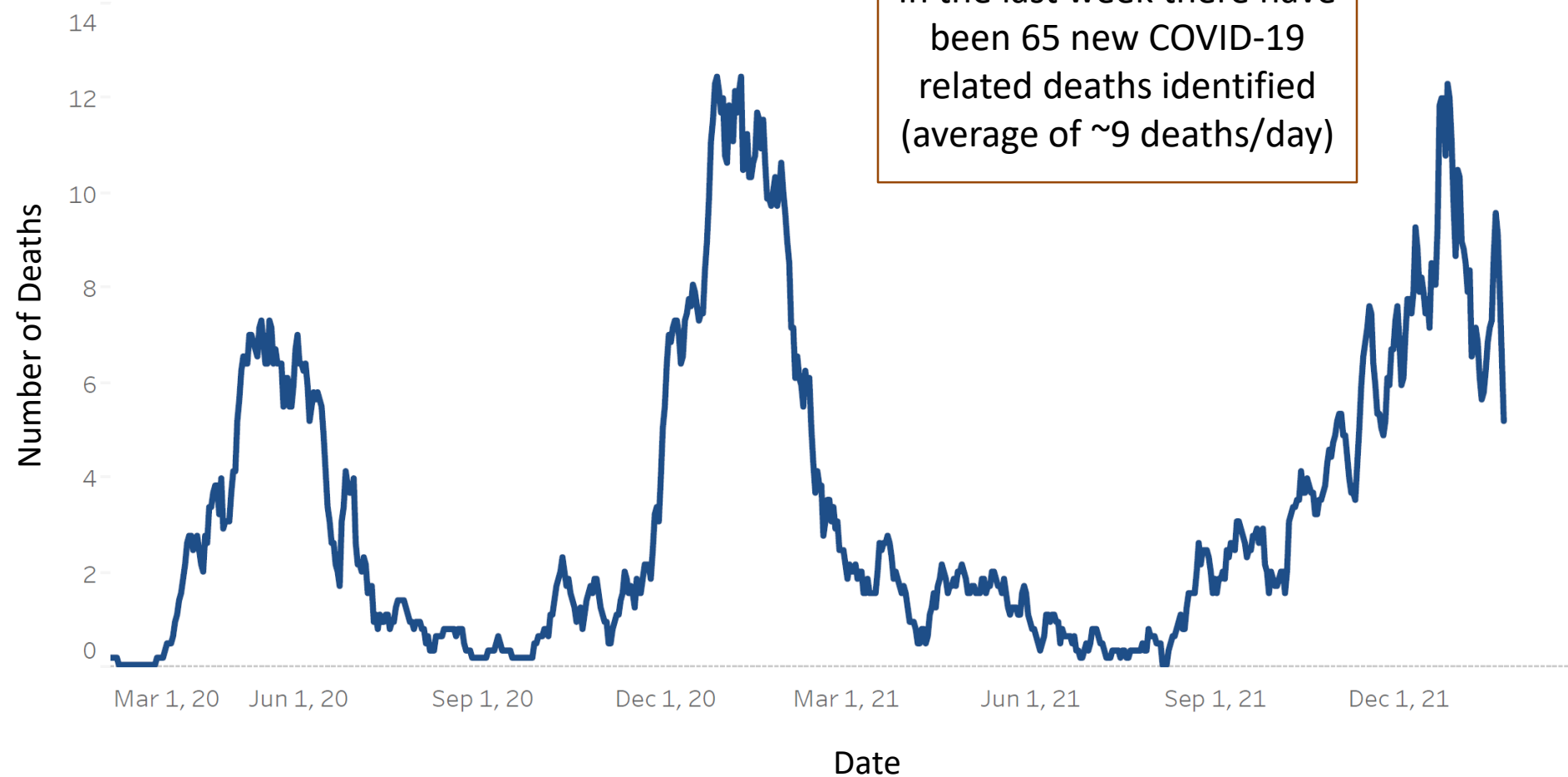
Ivermectin to Treat COVID-19

Medical Recommendations

- ## National Institutes of Health (NIH):

  "There is insufficient evidence for the COVID-19 Treatment Guidelines Panel to Recommend either for or against the use of ivermectin for the treatment of COVID-19. Results from adequately powered, well-designed, and well-conducted clinical trials are needed to provide more specific evidence-based guidance on the role of ivermectin in the treatment of COVID-19."

- ## Infectious Disease Society of America (IDSA):

  "In hospitalized patients with COVID-19, the IDSA panel suggests against ivermectin outside of the context of a clinical trial... In ambulatory persons with COVID-19, the IDSA panel suggests against ivermectin outside of the context of a clinical trial. (very low certainty of evidence)"

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Ivermectin for COVID-19: Addressing Potential Bias and Medical Fraud

Andrew Hill,[1] Manya Mirchandani,[2] and Victoria Pilkington[3]

[1]Department of Pharmacology and Therapeutics, University of Liverpool, Liverpool, UK, [2]Faculty of Medicine, Imperial College London, London, UK, and [3]Oxford University Clinical Academic Graduate School, University of Oxford, Oxford, UK

- Authors present a subgroup meta-analysis to assess the effects of stratifying study results by quality of study (specifically evaluating ivermectin on survival)

- Some studies and meta-analyses evaluating ivermectin have been retracted because of fraud (authors of the current study published a meta-analysis in July 2021 and subsequently retracted once fraudulent studies were identified that had been included in the meta-analysis)

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Meta-Analyses 101

- Meta-analyses are conducted to pool data from multiple different studies into a single larger analysis to assess clinical efficacy

- Meta-analyses need to be conducted carefully and with very clear study inclusion criteria to ensure individual studies (methods and outcomes) are comparable and appropriate to be combined into a meta-analysis

- There needs to be an assessment of bias for each study before inclusion (bias in one or a few studies can erroneously impact the meta-analysis and lead to incorrect conclusions)

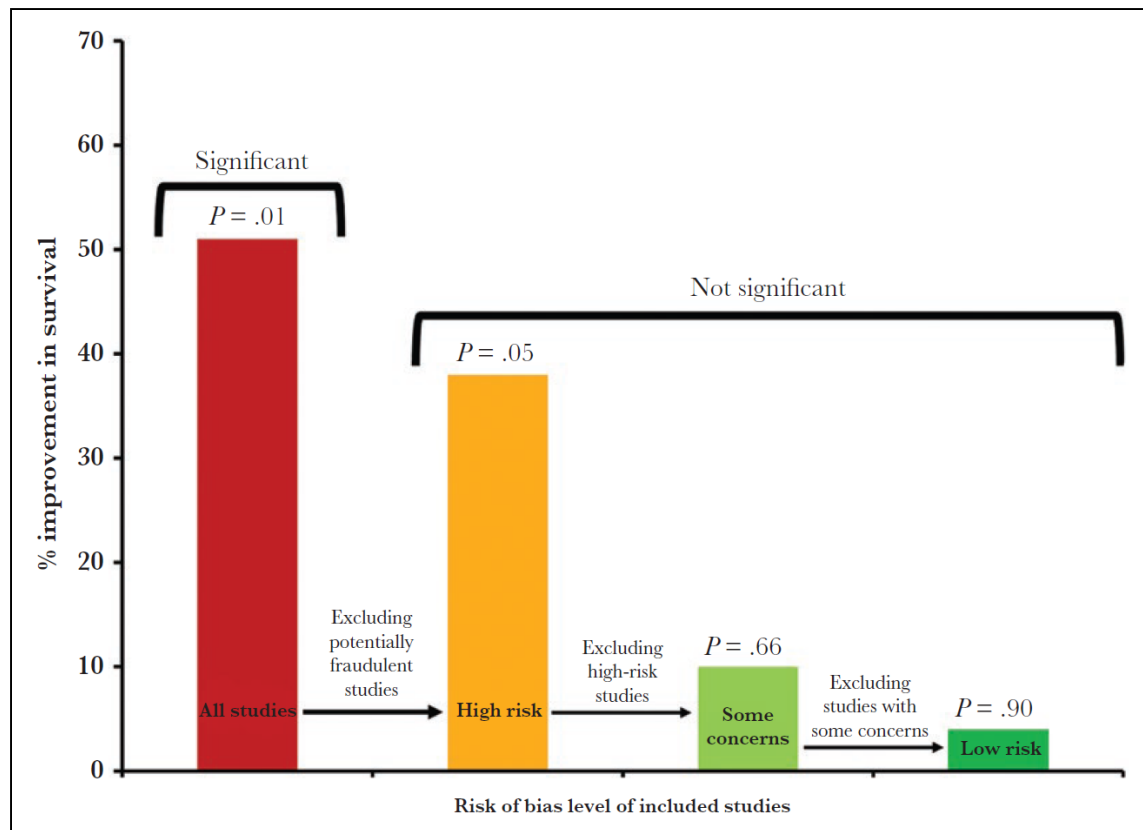**Table 1. Studies Included in the Survival Analysis [4]**

Study	Risk of Bias Level	Sample Size	Ivermectin Arm	Control Arm
Lopez-Medina et al.	Low risk	398	0/200	1/198
Fonseca et al.	Low risk	168	12/53	25/115
Zoni et al.	Low risk	501	4/250	3/251
Kirti et al.	Low risk	112	0/55	4/57
Rezai et al.	Some concerns	69	1/35	0/34
Abd-Elsalam et al.	Some concerns	164	3/82	4/82
Gonzalez et al.	Some concerns	73	5/36	6/37
Mahmud et al.	Some concerns	363	0/183	3/180
Niaee et al.	High risk	180	4/120	11/60
Hashim et al.	High risk	140	2/70	6/70
Okumus et al.	High risk	60	6/30	9/30
Elgazzar et al.	Apparent fraud	400	2/200	24/200
Total		2628	39/1314	96/1314

- Potential Sources of Bias:

  – Poor randomization of treatment groups

  – Differences in baseline characteristics between treatment groups

  – Lack of treatment allocation concealment or lack of blinding of participants/investigators

  – Publication bias impacts meta-analyses by skewing results to positive/significant findings (which are more likely to be reported and published)

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Risk of Bias Impact on Meta-Analysis Findings

- The significant effect of ivermectin on survival was dependent on inclusion of studies in the meta-analysis with a high risk of bias or potential medical fraud

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Medical Recommendations

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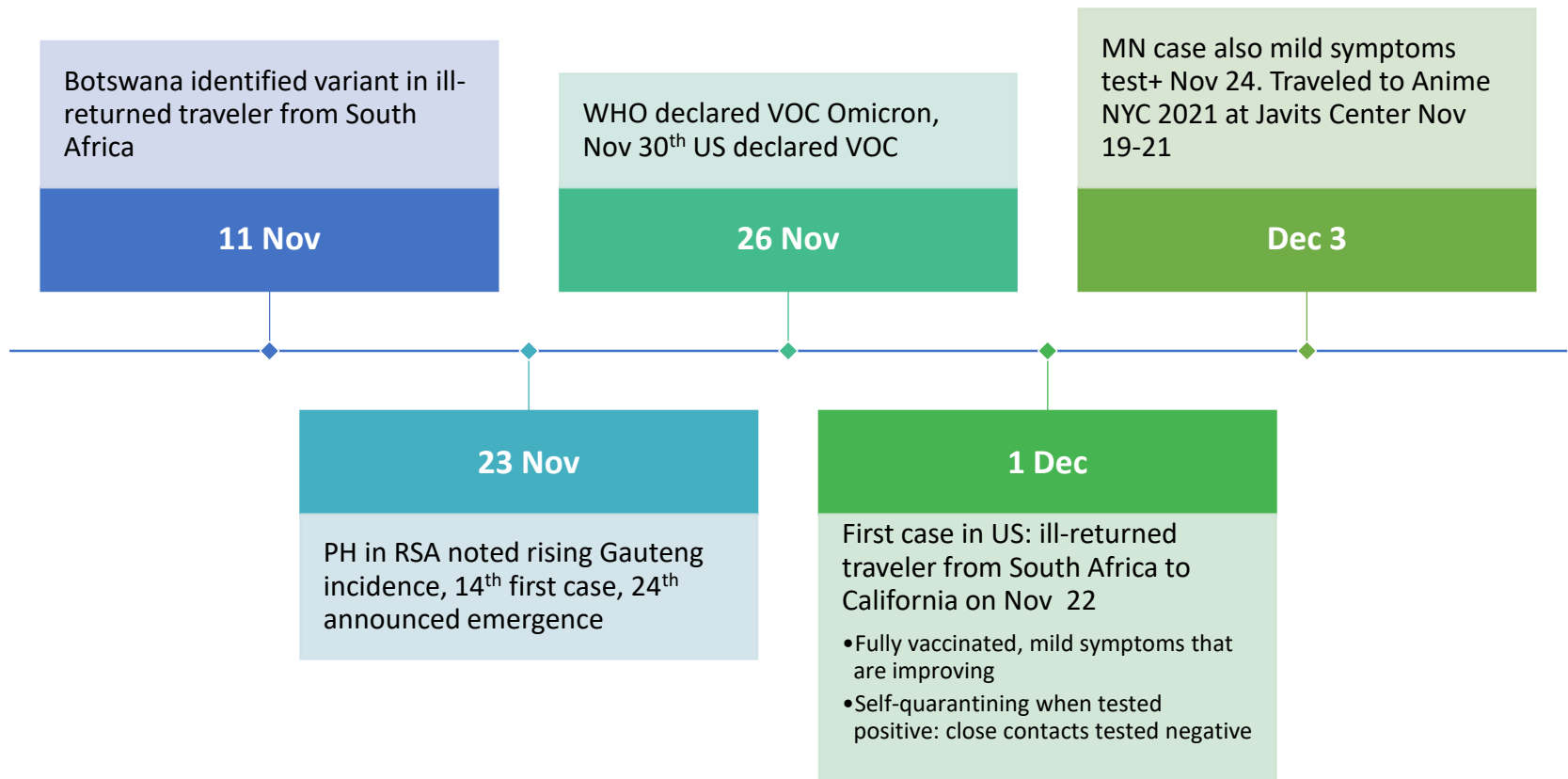
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Omicron Update

Association Between COVID-19 and New-Onset Diabetes

Omicron (B.1.1.529) 5th VOC
Now the "Omicron Lineage"

Botswana identified variant in ill-returned traveler from South Africa

11 Nov

WHO declared VOC Omicron, Nov 30th US declared VOC

26 Nov

MN case also mild symptoms test+ Nov 24. Traveled to Anime NYC 2021 at Javits Center Nov 19-21

Dec 3

23 Nov

PH in RSA noted rising Gauteng incidence, 14th first case, 24th announced emergence

1 Dec

First case in US: ill-returned traveler from South Africa to California on Nov 22

- Fully vaccinated, mild symptoms that are improving
- Self-quarantining when tested positive: close contacts tested negative

Jan 15 ECDC Update re Omicron Severity

- Data 12/20/21 – 1/20/22 from 23 countries with Omicron proportion 69.4% (5.7-99.9%)

- Median age 30y, 7% $\geq$ 60yo

- Among 111,946 (72%) Omicron with complete data, 76% symptomatic and 24% asymptomatic

- Only 2% of Omicron cases had associated vaccination status: 79% any vaccine, 11% UTD

Among Omicron Cases with Known Outcomes

- Status of COVID-19 outcomes was known for
  - 77,233 (50%) hospitalization: 1.14%
  - 76,744 (49%) ICU/resp support: 0.16%
  - 81,912 (53%) for death: 0.06%
- Incomplete reporting of these variables is expected for recent cases, but consistent with reports from Canada, Texas, California, and Denmark in which RR for hospitalization ranged half to two-thirds reduced c/w Delta, depending on vaccination status

ven-day moving average number of COVID-19 cases, emergency department visits, hospital admissions cember 1, 2020–January 15, 2022
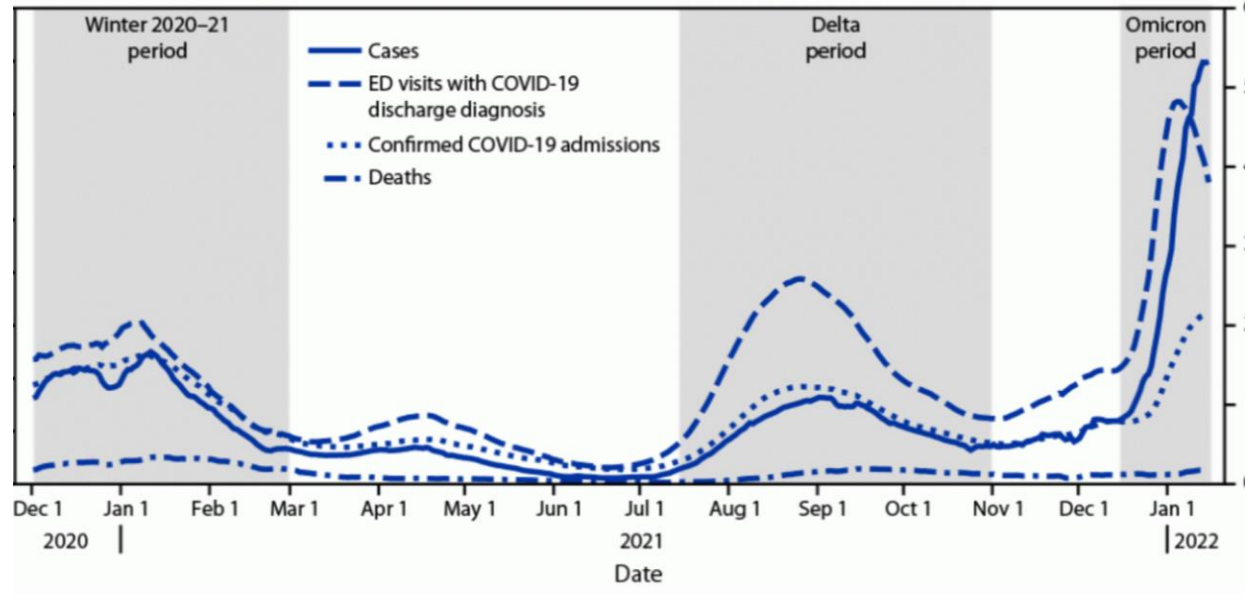
[CDC Trends of Disease Severity and Healthcare Utilization](link)

- CDC compared 6w timeframe with cases and outcomes from Dec 1, 2020, through Feb 28, 2021 (wild-type strain), and Jul 15 to Oct 31, 2021 (Delta), with Omicron to-date

- Highest numbers of cases and hospitalizations during Omicron but ratio of peak ED visits, hospital admissions, and deaths to case were lower in Omicron than other variants

Among hospitalized patients from 199 U.S. hospitals, mean LOS and percentages admitted to ICU, received invasive mechanical ventilation, and died were lower during the Omicron era

Per 1,000 cases	ED visits	Hospital adm	Deaths
Wildtype	92	68	16
Delta	167	78	13
Omicron	87	27	9

Among children <18y, LOS was similar and ICU adm was lower during Omicron era
High relative increases in ED visits and hospitalizations were observed, ?related to lower vaccination rates

Appropriate Messaging

- Evidence from a variety of settings suggests that infections with Omicron have less severe clinical presentation than those due to Delta: cases and admission rates were high and increasing, while death and ICU admission rates remained stable

- Vaccines may be less effective against Omicron infection, but still provide protection against hospitalization and severe disease

- True risk of severe infection for Omicron may be underestimated because these populations younger, prior immunity from natural infection, vaccination including booster dose, and improved treatment options that contributed to less severe outcomes

"Although disease severity appears lower with the Omicron variant, the high volume of hospitalizations can strain local health care systems and the average daily number of deaths remains substantial. This underscores the importance of national emergency preparedness, specifically, hospital surge capacity and the ability to adequately staff local health care systems. In addition, being up to date on vaccinations and following other recommended prevention strategies are critical to preventing infections, severe illness, or death from COVID-19."

Tracking SARS-CoV-2
variants

Omicron Specific Vaccine?

- Current vaccines offer protection against severe COVID and death from Omicron, but need better

- Pfizer/BioNTech study of mRNA against Omicron in 1,420 healthy 15-55yos
  - Third shot (first booster)
  - Fourth shot (second booster)
  - Primary series

- Expect to apply end March in case endemic strain
  - Omicron waning and new VOCs expected: BA.2 outcompeting Omicron in India, Sweden and Denmark and detected in UK and US

**Table. Patient Characteristics During the Year of the COVID-19 Pandemic[a] Compared With Prior Years**

Characteristic	COVID-19 Year[a]	Pre-COVID-19 by 5 years[a]	P value
Total children, No.	187	641	NA
Age, mean (SD), y	9.6 (4.2)	9.7 (4.2)	.82
HbA$_{1c}$ at presentation, mean (SD), %	11.6 (1.8)	11.7 (1.9)	.52
Body mass index z score, mean (SD)	−0.4 (1.8)	−0.4 (1.6)	.72
Children requiring insulin infusion, % (95% CI)	49.7 (42.6-56.8)	40.7[b]	.01
Children requiring PICU admission, % (95% CI)	8.6 (5.3-13.4)	6.4[b]	.39

JAMA Pediatrics. Jan 24, 2022. doi:10.1001/jamapediatrics.2021.5801

Incidence of New-Onset Type 1 Diabetes Among US Children During the COVID-19 Global Pandemic

- Four studies higher rate of presenting with T1D in DKA during pandemic, reflective of delayed health-seeking

- San Diego Children's Hospital observed increase in T1D, conducted 6y retrospective incidence review
    - T1D Ab, HA1c, +/- DKA, +/- PICU adm, COVID test

- Mar 2020-2021, 57% increase in T1D; inc DKA
    - Only 4 had active COVID by PCR (no Ab)

Figure. Autoregressive Integrated Moving Average (ARIMA) Forecast and Quarterly Moving Average (MA) of New Type 1 Diabetes (T1D) Cases
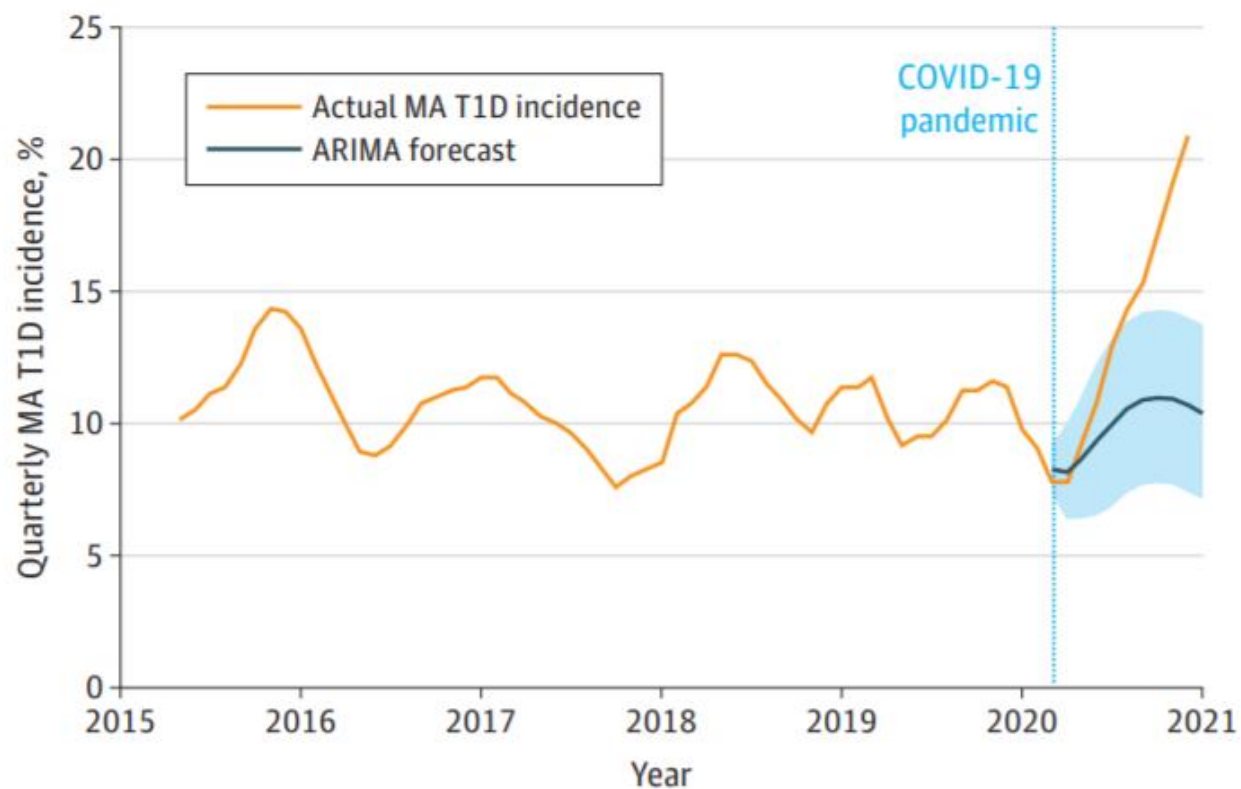
Another reason to vaccinate young children?

Vaccine Effectiveness Against Omicron

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Vaccine Effectiveness Against <u>Omicron</u>

	Primary Series (No Booster)	Primary Series + Booster
Infection*	64%	80%
ED/UC Visit**	52% → 38%	82%
Hospitalization**	81% → 57%	90%

ED: Emergency Department
UC: Urgent Care

- Preliminary estimates are based on U.S. data from December 2021-January 2022 with limited follow-up

- Vaccine Effectiveness: comparing vaccinated persons to unvaccinated reference population

- "→" indicates decline in vaccine effectiveness within 6 months after vaccination to 6+ months after vaccination

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Q&A