



Evaluating COVID-19 Vaccination in Children

Morbidity and Mortality Prevention

Eric Lofgren MSPH, PhD

Assistant Professor

Paul G. Allen School for Global Health

Washington State University



College of
Veterinary Medicine



Paul G. Allen School
for Global Health

Definitions

- Morbidity
 - The consequences and complications from a disease *other* than death
 - These can be long or short term
 - Also considering exacerbating already existing conditions
 - Even “mild” cases of COVID-19 (those not requiring hospitalization) can have long term impacts
- Mortality
 - Deaths
 - Deaths directly resulting from infection
 - Deaths resulting from infection exacerbating an already existing condition
- Relative Risk
 - The probability of something (i.e. a hospitalization) in one group divided by the probability of it happening in another. For example, a 10% chance of hospitalization in the unvaccinated and a 5% chance in the vaccinated would result in a relative risk of $0.10/0.05 = 2.0$
- Hazard Ratio
 - Like a relative risk, but considering the time in which an event occurs, not merely whether it does



Vaccine Effectiveness

- An expression of vaccine effectiveness is the percentage reduction in an outcome *as compared to those who are not vaccinated*
- For example, if 5% of unvaccinated individuals experience some outcome, and a vaccine is 90% effective, the percentage of vaccinated individuals experiencing that outcome is:
 - $0.05 \times (1 - 0.90) = 0.005$ or 0.5%

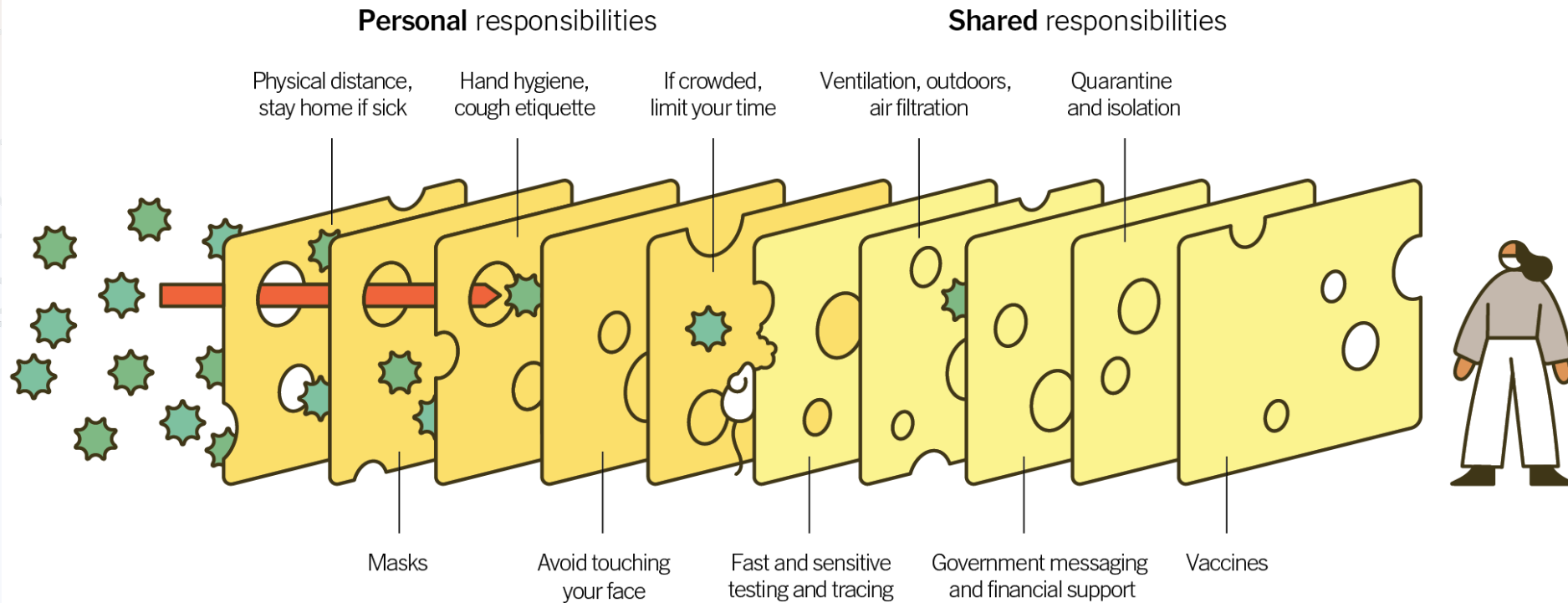
Why Consider These Endpoints

- Immediately measurable
 - Morbidity and mortality arising from infections are readily measurable, observable and generally occur on short time-frames post infection
- Important from a public health standpoint
 - The goal of public health is to save lives and prevent disease
 - Blocking transmission is one aspect of that, but preventing adverse outcomes represents a direct reduction in the health impact of a disease
 - The results are achievable even when we have not, or are unlikely to, reach herd immunity
- Represents direct benefits to the vaccinated
 - Individuals assume risk from being vaccinated for both individual and societal level benefits
 - Reductions in morbidity and mortality are individual-level benefits

The Swiss Cheese Model

Multiple Layers Improve Success

The Swiss Cheese Respiratory Pandemic Defense recognizes that no single intervention is perfect at preventing the spread of the coronavirus. Each intervention (layer) has holes.



Source: Adapted from Ian M. Mackay (virologydownunder.com) and James T. Reason. Illustration by Rose Wong

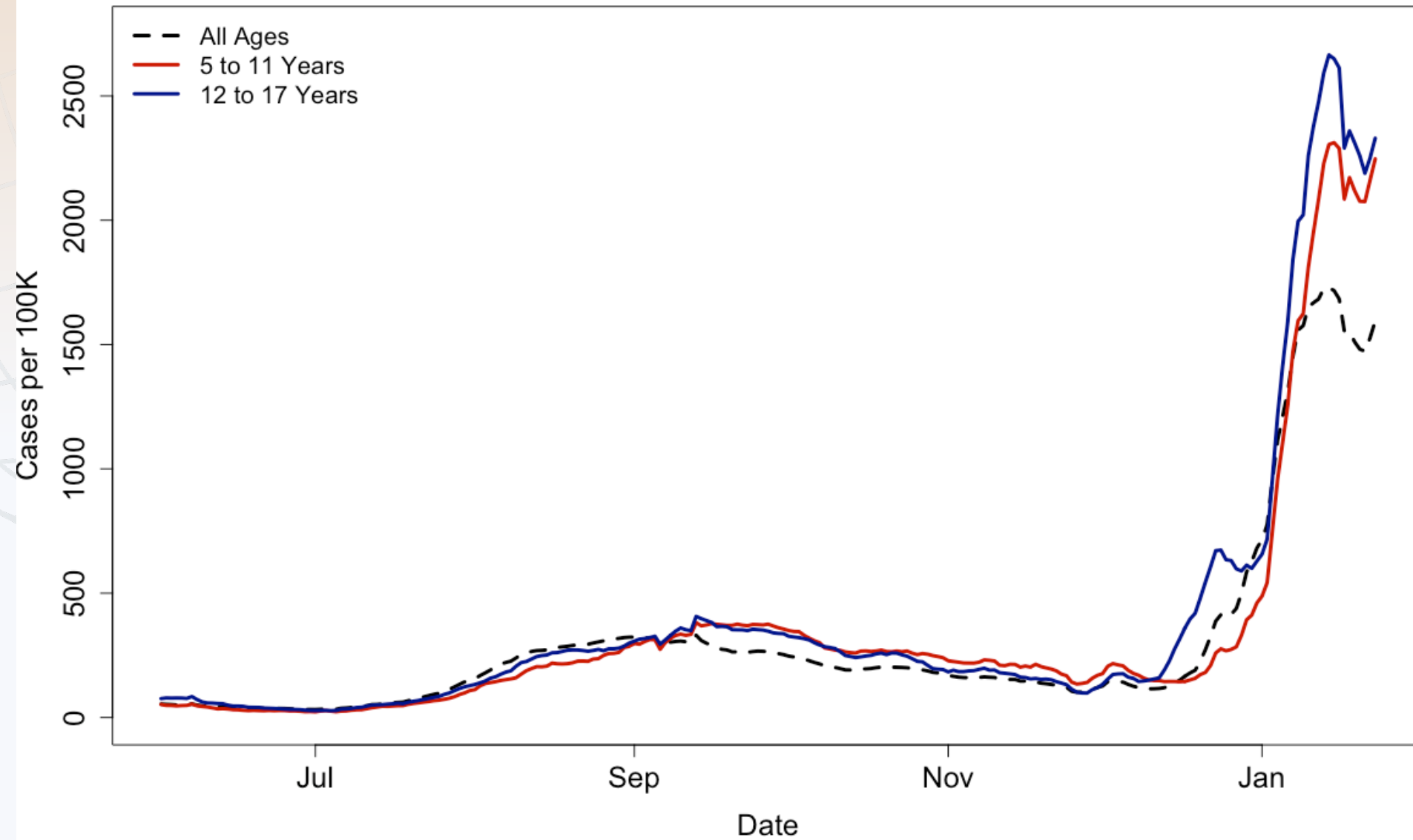
Source: NYT



Overall Cases

- School-aged children (5-17) currently have the highest 7-Day case rate of any age groups in Washington State
 - 2161.4 cases/100,000 children for 5-11 year olds
 - 2250.8 cases/100,000 children for 12-17 year olds
- These groups have been higher than the statewide average case rate since roughly halfway through the Delta wave

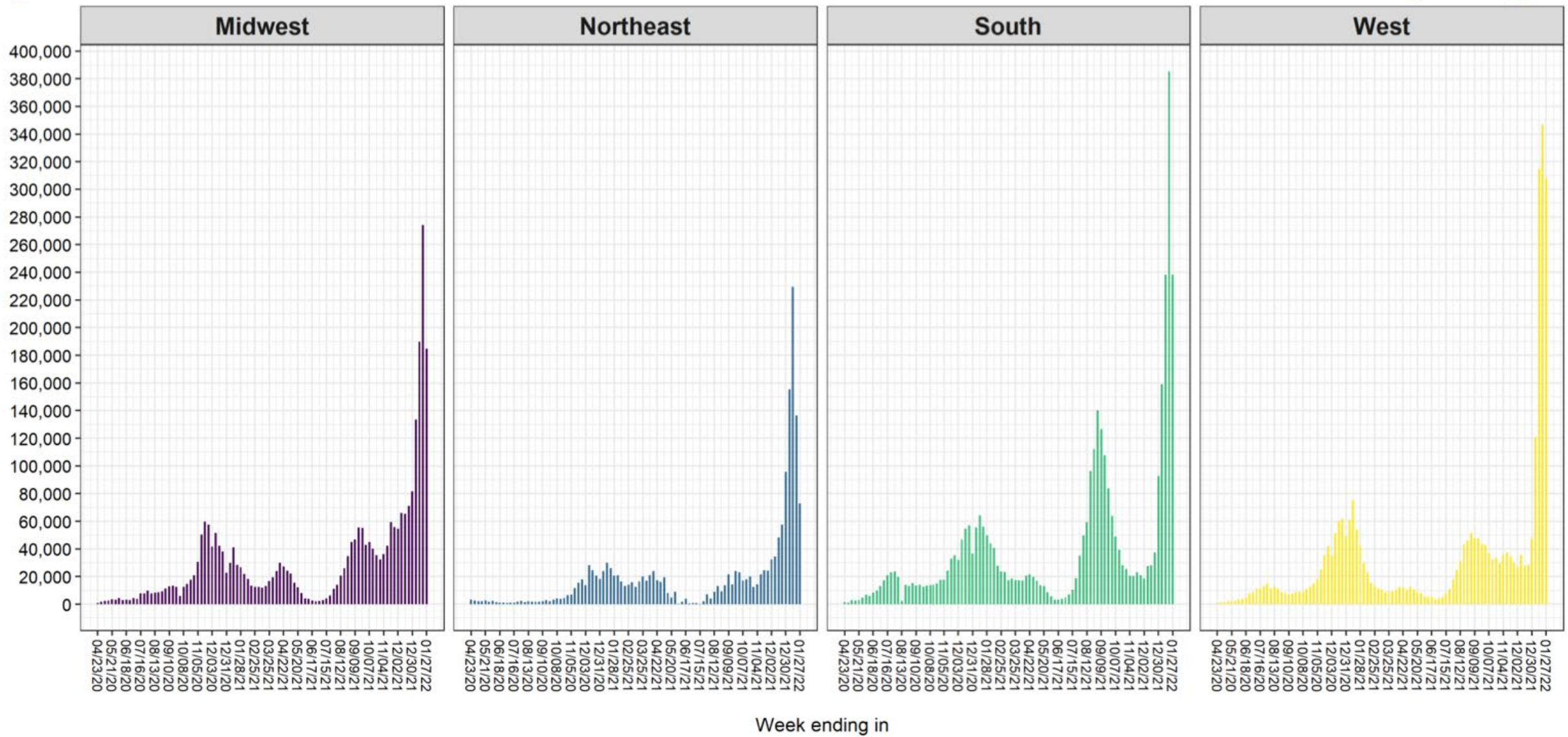
COVID-19 Cases in School Aged Children from 6/1/2021 to 1/23/2022 in Washington



The Omicron Variant

- Much of the science for COVID-19 is fast moving due to different variants as well as improvements in our understanding of how to treat COVID-19
- The Omicron variant is generally milder, but *much* more transmissible
 - Lower risks but occurring in more children is still cause for concern
- Omicron is causing considerably more cases in children
 - Nationally, 20.7% of *all* COVID-19 cases in children occurred between 1/13/2022 and 1/27/2022 according to an American Academy of Pediatrics analysis
 - This trend is more severe in the U.S. West census region, of which Washington is a part

Cases added in past week



Source: AAP. **Children and COVID-19: State Data Report.** Version: 1/27/22



Hospitalizations

- Hospitalizations are increasing in WA state in all age groups
- School-aged children still have the lowest hospitalization rate, but these rates have risen dramatically as cases have risen
- “The Denominator Problem” – a small number multiplied by a large number can be a large number



COVID-19 Hospitalizations in Context

Age Group	RSV per 100,000*	Influenza per 100,000*	COVID-19 per 100,000 (Last 7 Days – WA)
5-6 Years Old	1.39	0.77	3.5
7-11 Years Old	0.70	0.44	
12-17 Years Old	0.75	0.34	6.0

All expressed as weekly rates

* Goldstein *et al.*, 2019



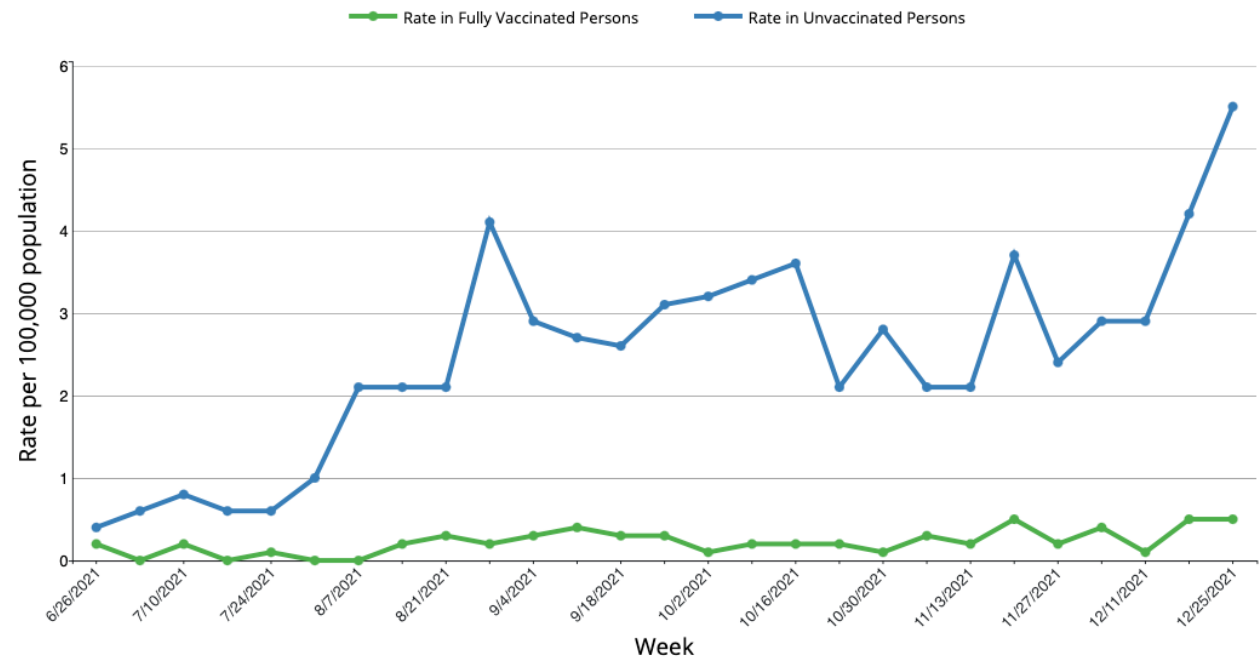
Consequences of Hospitalization

- CDC study from COVID-NET by Delahoy *et al.*
 - 3116 hospitalized children (pre-Delta)
 - 26.5% admitted to the ICU, 6.1% required ventilation
 - 164 hospitalized children (Delta)
 - 23.2% were admitted to the ICU, 9.5% required ventilation
- National study in six hospitals by Wanga *et al.* from July-August 2021
 - In 5-11 year olds, 25.9% were admitted to the ICU, 18% required ventilation
 - In 12-17 year olds, 39.7% were admitted to the ICU, 14.7% required ventilation
- Recent preprints on Omicron:
 - Kaiser study in southern CA: Hazard ratio of 0.94 (0.26,3.42) for hospitalization in patients 0-17 compared to pre-Omicron
 - Study based on national EHR data:
 - Relative risk of 0.29 (0.21-0.39) for 5-11 year olds and 0.16 (0.11-0.24) for 12-17 year olds for ED visit
 - Relative risk 0.53 (0.25-1.13) for 5-11 year olds and 0.63 (0.33-1.19) for 12-17 year olds for Hospitalization

Vaccination's Impact on Hospitalization

- Delahoy *et al.* COVID-NET study:
 - Rate ratio of 10.1 (3.7-27.9) for hospitalization comparing unvaccinated adolescents to vaccinated adolescents
- This difference has been climbing in adolescences over time based on CDC COVID-NET data
- Study by Olson *et al.* estimates a vaccine effectiveness against hospitalization of 93% (83%-97%)

Rates of COVID-19-Associated Hospitalizations by Vaccination Status in Adolescents Ages 12–17 Years, June–December 2021



Source: CDC



MIS-C

- Multisystem inflammatory syndrome in children (MIS-C) causes inflammation of organs including the heart, lungs, brain, kidneys and GI tract
- Associated with COVID-19 infection
- 93 reported cases in WA State as of Dec. 2021
 - 35 from 2020, 58 from 2021
- Median age of 8 years, roughly 60/40 split between 0-9 year olds and 10-20 year olds

Vaccination's Impact on MIS-C

- Study in MMWR looking at children 12-18 years of age nationwide, July-December 2021 examining two doses of Pfizer-BioNTech vaccine
 - Focused on 12-18 year olds as children 5-11 were not yet authorized to receive the Pfizer-BioNTech vaccine
 - Estimated vaccine effectiveness against MIS-C of 91% (78%-97%)
 - 39% of unvaccinated MIS-C patients required respiratory or cardiovascular life support, 0% of vaccinated patients did
- Study from France estimated a hazard ratio of 0.09 (0.04,0.21) for developing MIS-C for children with one dose of vaccine (primarily Pfizer-BioNTech) vs. unvaccinated children 12-18 years of age



Long COVID

- The evidence base for Long COVID in children is still developing
- A study by Magnusson *et al.* in Norway in 1.3 million children and adolescents found an increase in primary care use after COVID-19 infection, primarily for respiratory and non-specific conditions
 - In children 6-15 years, elevated use of primary care up to 12 weeks after infection, and 4 weeks after infection for children 16-19 years



Long COVID Cont.

- In the UK, a national sample of 11-17 year old children as part of the CLoCk Study found elevated rates of self-reported symptoms 3 months post-testing in children who tested positive (66.5%) vs. those who tested negative (53.3%)
- 30.3% of test positives reported 3+ symptoms, while 16.2% of test negatives did so
 - These children were more like to be female, older, and those with worse pre-test physical and mental health
- A study of children in Switzerland of 1355 children found that 4% of children that were seropositive for COVID-19 reported symptoms vs. 2% of children who were seronegative lasting beyond 12 weeks

Vaccination's Impact on Long COVID

- Again, very little data here, especially in the U.S.
- Study by Antonelli *et al.* in UK adults reported an odds ratio of 0.51 (0.32, 0.82) for long-duration (>28 days) symptoms following two doses of vaccine

Deaths

- Death is, thankfully, a rare outcome in children with COVID-19 infections
- There have been 13 total deaths in children in WA state reported from Jan. 1, 2021 to Jan 23, 2022 in the most recent WA DoH report “COVID-19 Cases Among Children and Youth in Washington”
- It is important, however, to remember that deaths in children are rare generally. Based on a Kaiser Family Foundation analysis, in November and December 2021, COVID-19 was the 7th leading cause of death in those 5-14, and the 4th leading cause of death in those 15-24

Impacts of Vaccination on Mortality

- Difficult to have good data on what is an extremely rare outcome
- A recent study by Olson *et al.* studied 445 case patients and 777 controls at 31 hospitals in 23 states
 - Estimated 98% vaccine effectiveness against ICU admission and 98% against receipt of life support
 - Of the 7 patients who died in the study, none were vaccinated

Vaccine Side Effects

- MISC
 - Preprint from Ouldali *et al.* in France: 1.1 cases per 1,000,000 doses for vaccinated children vs. 113 cases per 1,000,000 12-17 year old children with a COVID-19 infection. Higher in males vs. females, and less severe short-term outcomes
- CDC review of the Vaccine Adverse Event Reporting System (VAERS) with followup and v-safe, a smartphone-based surveillance system from November 3 to December 19, 2021
 - 8.7 million doses of the Pfizer-BioNTech vaccine were administered to children 5-11 during this period
 - 100 “serious event” reports in VAERS
 - Median age was 9 years of age, 61% of reports were among males
 - Fever (29%), vomiting (21%) and increased troponin (15%) – potentially an indicator of myocardial damage, seizures (12%)
 - V-safe data: ~1% of parents reported seeking medical care in the week after vaccination, 0.02% received care at a hospital.

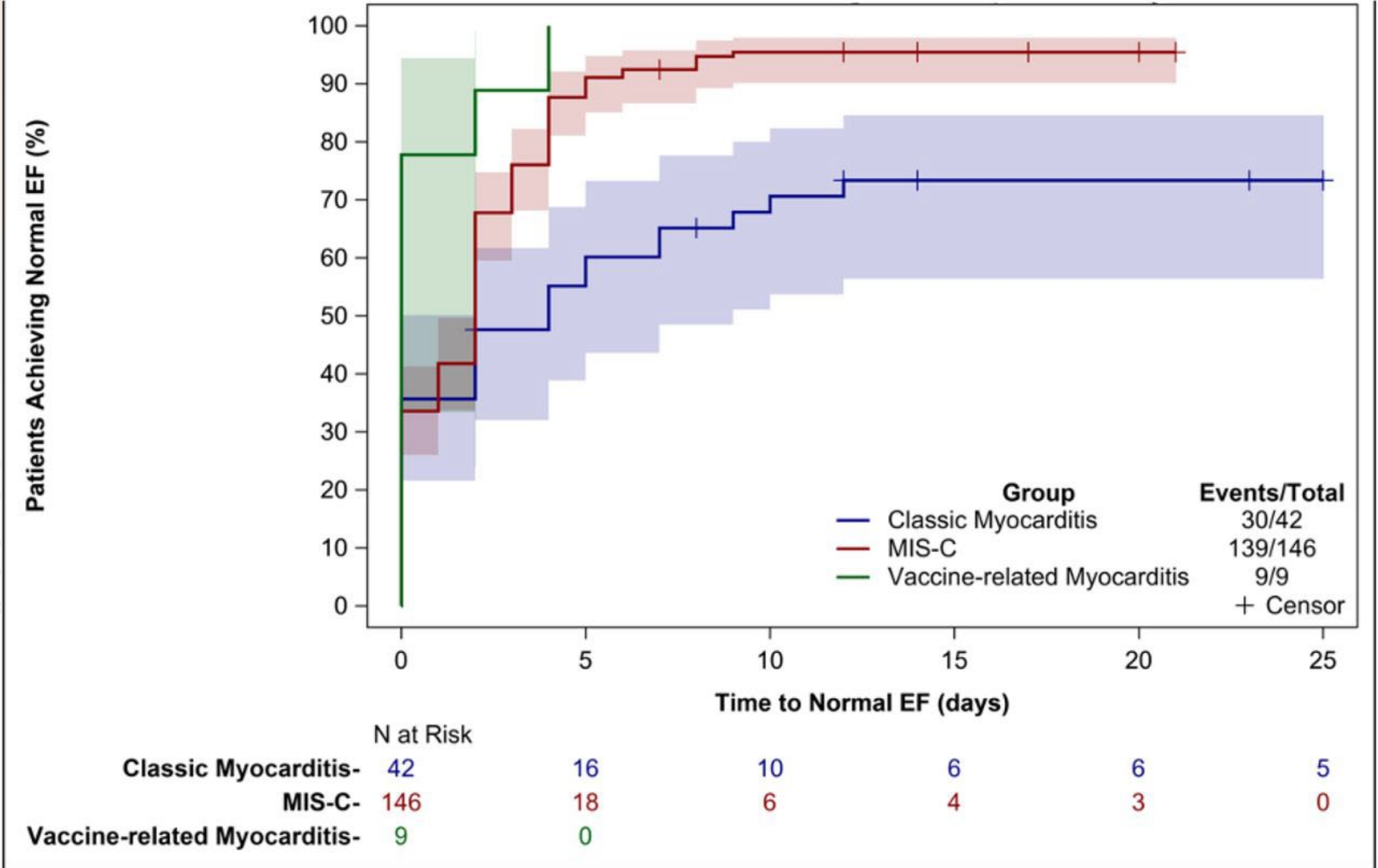


Myocarditis

- Myocarditis is the most serious adverse event of concern for COVID-19 vaccination in the school-aged group
- Recent study by Oster *et al.* from Dec. 2020 to August 2021 found that rates were elevated after the second dose of Pfizer-BioNTech vaccine in adolescent males
 - 12-15: 70.7 per million doses
 - 16-17: 105.9 per million doses
- Males comprise 82% of myocarditis cases
- Nearly all appeared within 4 days of being vaccinated
- In 826 cases with detailed clinical information and younger than 30
 - 96.4% were hospitalized
 - 0.3% were placed on mechanical ventilation
 - 98% were discharged from the hospital at the time the study reviewed their records
 - 0 had died
- A study of 63 patients in adolescents by Jain *et al.* noted “The hospital course is mild, with quick clinical recovery and excellent short-term outcomes”.

COVID-19 Induced Myocarditis

- FDA risk:benefit analysis looked at several scenarios for 5 to 11 year olds, varying the risk of myocarditis, COVID-19 case rates, and the effectiveness of the vaccine
 - Only a scenario with COVID-19 cases at the level of June 2021 (i.e. extremely low) suggested the benefits of vaccinations did not outweigh the risks
- A study by Boehmer *et al.*, using hospital based administrative data in the U.S. from March 2020 to January 2021 found that in 3.7 million individuals under 16 years of age, that 0.133% of COVID-19 patients had myocarditis, compare with 0.004% of patients without COVID-19, for a risk ratio of 36.8 (25.0, 48.6)



Source: Patel *et al.* Preprint. EF = Ejection Fraction



Predicted cases prevented vs. myocarditis cases for every million second dose vaccinations over 120 days

Females 12–17 Years



8,500 COVID-19 cases prevented



183 hospitalizations prevented



38 ICU admissions prevented

1 death prevented

8–10 myocarditis cases



Males 12–17 Years



5,700 COVID-19 cases prevented



215 hospitalizations prevented



71 ICU admissions prevented

2 deaths prevented

56–69 myocarditis cases



Source: Katelyn Jetelina, Sept. 2021



Looking Beyond Omicron

- Moderate levels of vaccination combined with high levels of COVID-19 transmission provide many opportunities for new variants
- This is compounded by low vaccination rates in much of the world providing ample opportunities for new variants to arise
 - Thus far, travel restrictions have been ineffective at preventing new variants from reaching the United States
- Especially in children, who are currently one of the least vaccinated groups
- There is no guarantee that a new variant will be mild or less transmissible

Placing Things In Context

Other vaccine preventable diseases: Deaths per year prior to recommended vaccines

	Hepatitis A ¹	Meningococcal (ACWY) ²	Varicella ³	Rubella ⁴	Rotavirus ⁵	COVID-19
Age	<20 years	11–18 years	5–9 years	All ages	<5 years	5–11 years
Time period	1990–1995	2000–2004	1990–1994	1966–1968	1985–1991	Oct 2020–Oct 2021
Average deaths per year	3	8	16	17	20	66

Other pediatric vaccine preventable diseases: Hospitalizations per year prior to recommended vaccines

	Hepatitis A ¹	Varicella ² (Chickenpox)	Influenza ³	COVID-19
Age	5–14 years	<20 years	5–17 years	5–11 years
Time period	2005	1988–1995	2003–2007	Oct 2020–Oct 2021
Hospitalization Burden (per 100,000 population)	<1	4-31	30-80	25

Source: CDC Advisory Committee on Immunization Practices (ACIP), Nov. Meeting

Thank You



College of
Veterinary Medicine



Paul G. Allen School
for Global Health