UNIVERSITY OF LEEDS

# Why a fresher perspective is needed on childhood COVID-19

Prof Stephen Griffin

TAPAS International Seminar Series, 20<sup>th</sup> November 2023

Views expressed herein are my own





indie\_SAGE

### Synopsis

We remain amidst an ongoing SARS-CoV2 pandemic

Children ARE at risk from acute SARS-CoV2 infection

Children DO develop long COVID and other sequelae

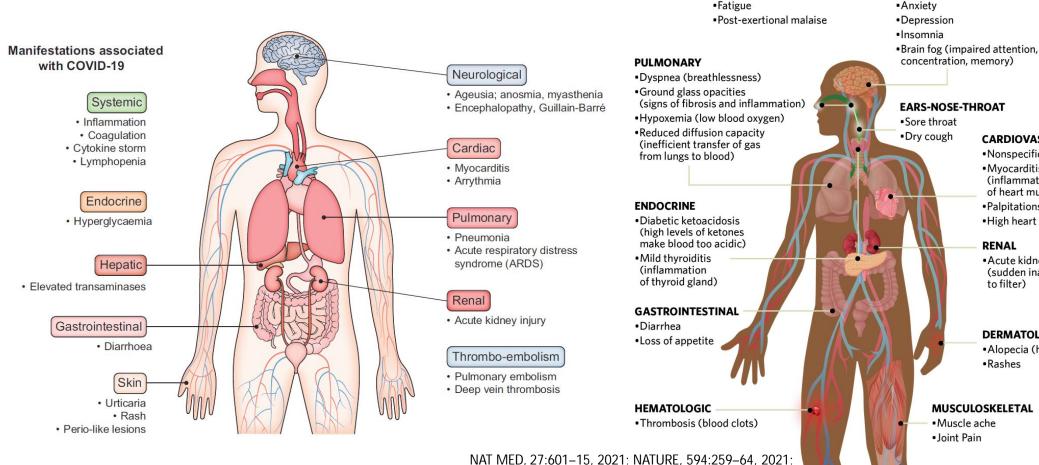
Vaccines are effective in adults and kids, but they are not perfect

Vaccination is particularly important for under 5s over the short and longer terms

The UK remains well behind the curve on children's vaccines

We need a "vaccines plus" strategy; combined immunisation and mitigation

## Coronavirus Disease 2019: the long and the short of it...



MEDRXIV, DOI:10.1101/2020.12.24.20248802 2021

Journal of Hepatology 2021 vol. 74 j 168-184

CARDIOVASCULAR

 Nonspecific chest pain Mvocarditis (inflammation of heart muscle) Palpitations High heart rate

RENAL

NEUROPSYCHIATRIC

SYSTEMIC

 Acute kidney injury (sudden inability to filter)

DERMATOLOGIC

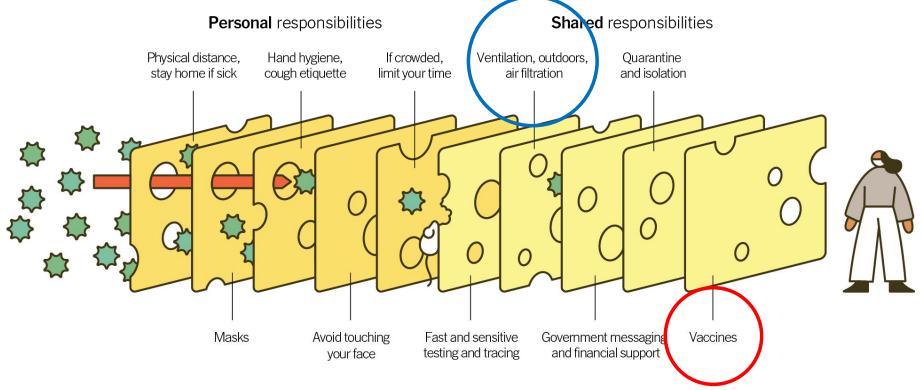
 Alopecia (hair loss) Rashes

#### MUSCULOSKELETAL

### We are running out of cheese...

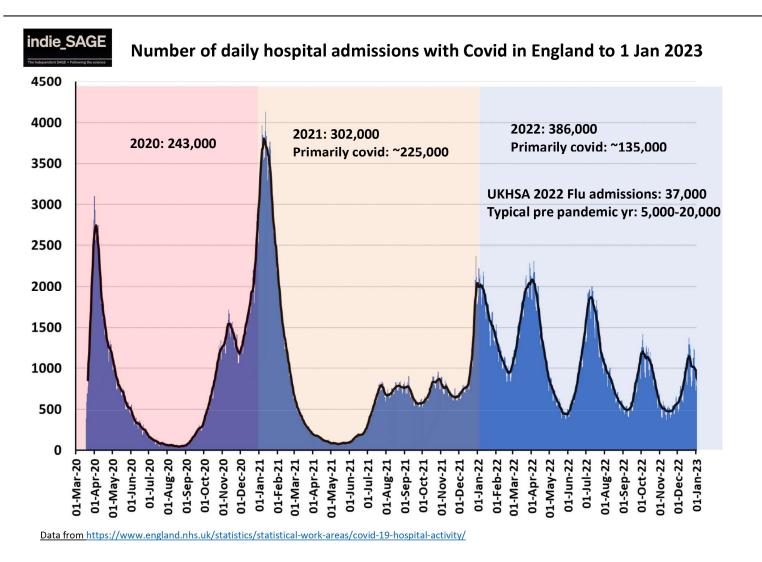
#### **Multiple Layers Improve Success**

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

## The ongoing SARS-CoV2 pandemic in the UK





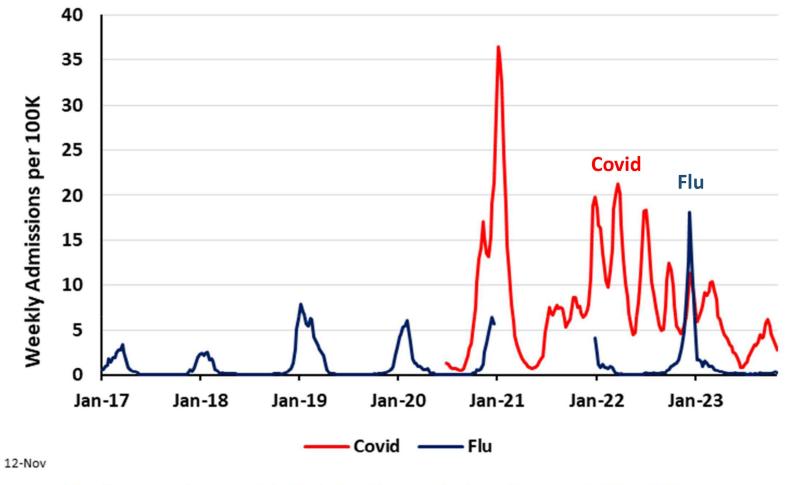
### 2023: 118479 up to 25<sup>th</sup> August

Independent SAGE slides H/T: Prof Christina Pagel Dr Kit Yates Dr Duncan Robertson Bob Hawkins



#### Weekly Influenza and Covid Hospital Admission Rate (per 100K) for England: Jan 1 2017 – Nov 12 2023

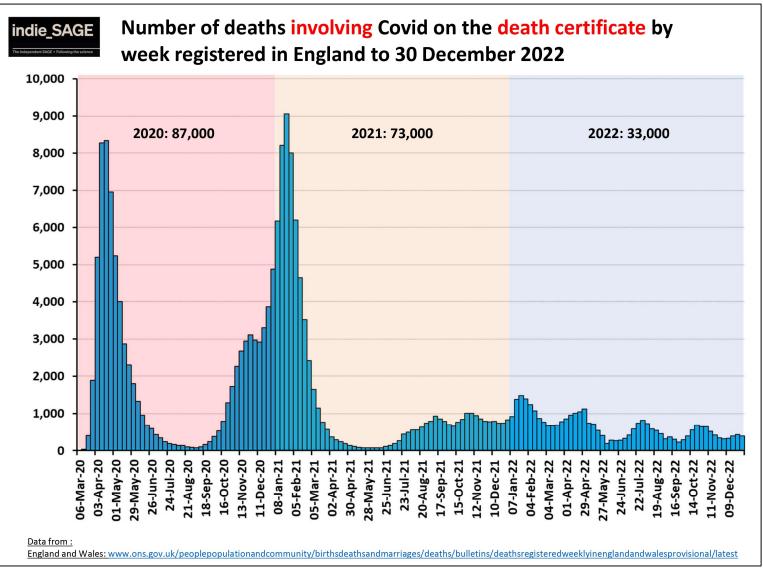
(Source: Weekly National Influenza and COVID-19 Surveillance Data Report)



https://www.gov.uk/government/statistics/national-flu-and-covid-19-surveillance-reports-2023-to-2024-season

Thanks to Bob Hawkins for the slide

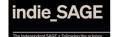
## The ongoing SARS-CoV2 pandemic in the UK



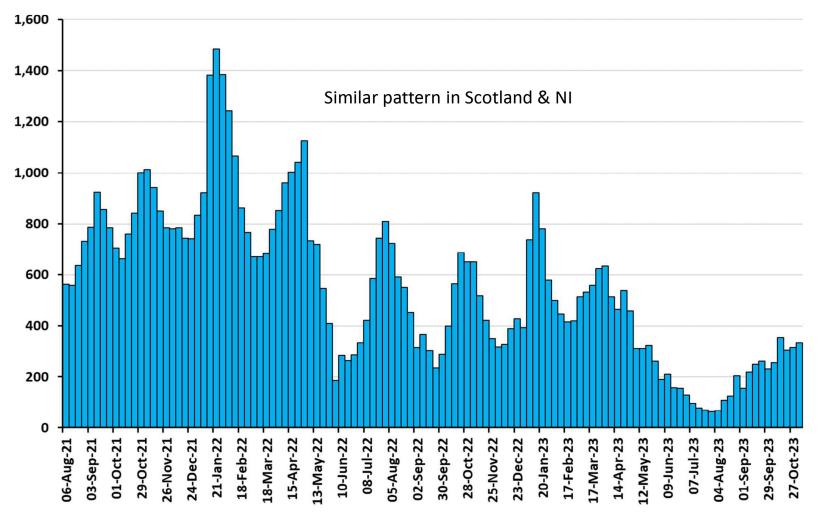


2023: >16K up to 1<sup>st</sup> November

60-70% have COVID as main underlying cause



## Number of deaths with Covid on the death certificate by week registered in England and Wales July 2021 to 3 Nov 2023

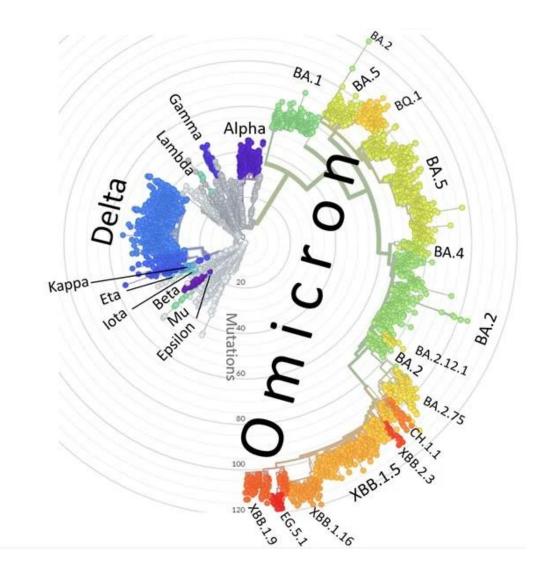


Data from :

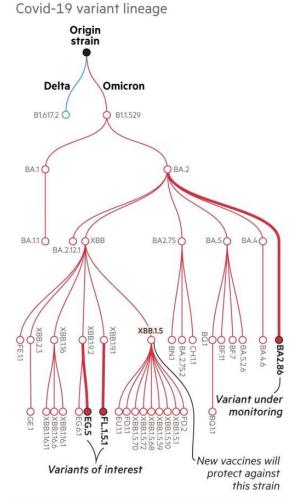
England and Wales: www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsregisteredweeklyinenglandandwalesprovisional/latest

#### The <u>ongoing</u> SARS-CoV2 pandemic in the UK Number of People Living with Self-Reported Long Covid 12 Weeks after Infection in the UK by Age: Feb 5 - Mar 5, 2023 (Source: ONS Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK Reports) 800,000 674,000 700,000 At least 17mn people in Europe have had long Women twice as likely as men to suffer condition associated with cognitive problems and 600,000 Covid, says WHO 508,000 500,000 fatigue, modelling shows 400,000 300,000 216,000 196,000 200,000 81,000 100,000 37,000 22,000 Independent SAGE slides H/T: **Prof Christina Pagel** Dr Kit Yates Dr Duncan Robertson 2 to 11 12 to 16 25 to 34 35 to 49 17 to 24 70+ 50 to 69 12 Wk Bob Hawkins

## SARS-CoV2 evolution and variants



The US is monitoring several new subvariants of Omicron



Sources: Centers for Disease Control and Prevention; FT research  $\circledast\mbox{\it FT}$ 

National Influenza and COVID-19 Report: week 46 report (up to week 45 data)

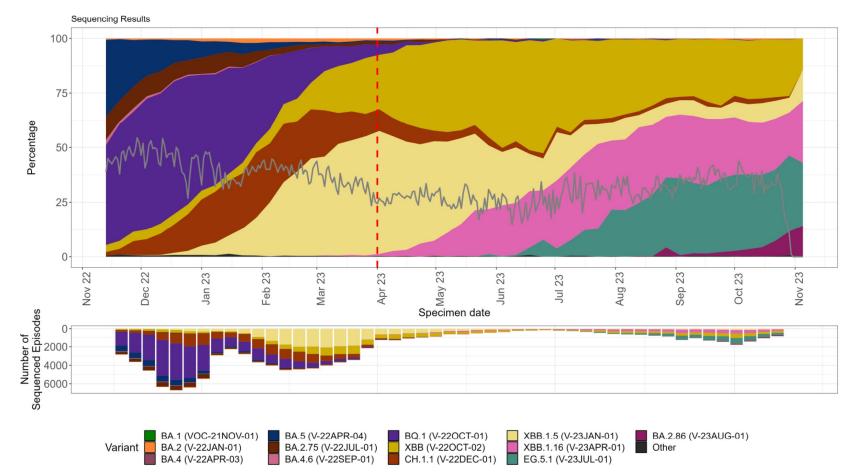


Figure 13: Prevalence of SARS-CoV-2 variants amongst available sequences cases for England from 7 November 2022 to 12 November 2023

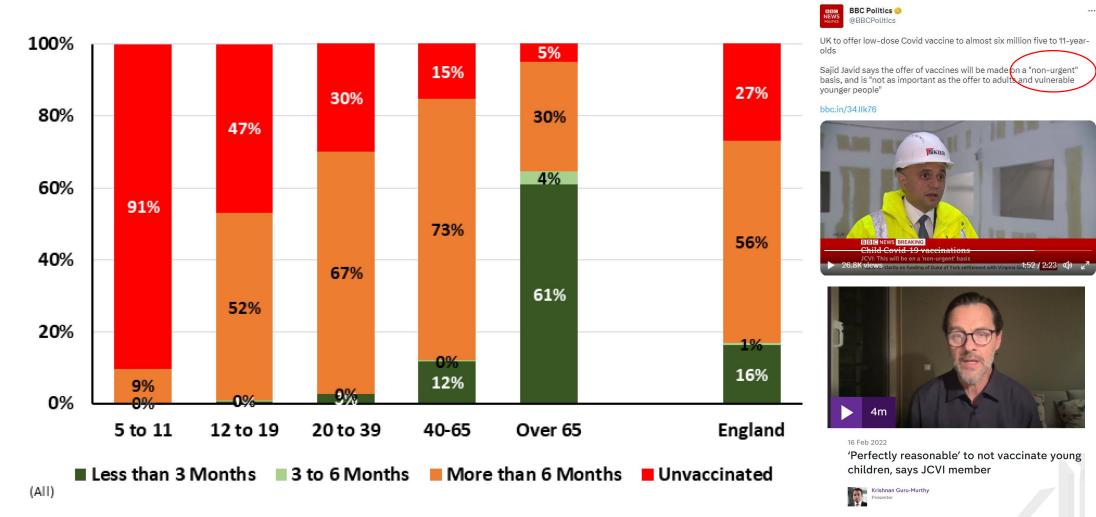
The grey line indicates proportion of cases sequenced.

The vertical dashed line (red) in April 2023 denotes changes in PCR testing in social care and hospital settings.

#### indie\_SAGE

#### Percent Vaccinated by Age Group in the Last 3 Months, 3 to 6 Months, More than 6 Months, and Unvaccinated: England – Oct 29, 2023

(Source: National Influenza and COVID-19 Surveillance Data Report based on NIMS Population Estimates)



We're joined by Professor Adam Finn, who is on the

Government's Joint Committee on Vaccination and Immunisation

https://www.gov.uk/government/statistics/national-flu-and-covid-19-surveillance-reports-2023-to-2024-season

## SARS-CoV2 infection of CYP

Deaths remain highest for those aged 85 years and over

#### Deaths by age

#### Deaths Deaths involving COVID-19 registered by week, England Latest week 85 and over 85 and over 75 to 84 75 to 84 65 to 74 65 to 74-55 to 64 55 to 64 45 to 54 45 to 54 25 to 44 25 to 44 15 to 24 15 to 24 1 to 14 1 to 14-Under 1 year Under 1 year 0 100 200 300 w/e 23/09/2022 w/e 17/03/2023 Number of people

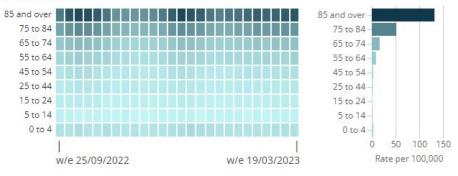
Source: Deaths registered weekly from the Office for National Statistics

Hospital admissions remain highest for those aged 85 years and

over

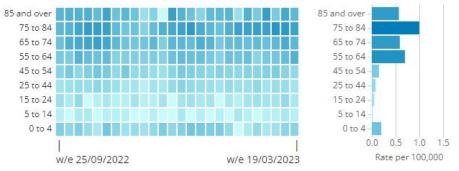
#### **Overall hospital admissions**

Weekly COVID-19 positive hospital admission rates per 100,000 Latest week people, England



### Intensive care unit (ICU) and high dependency unit (HDU) admissions

Weekly COVID-19 positive ICU/HDU admission rates per 100,000 people, England



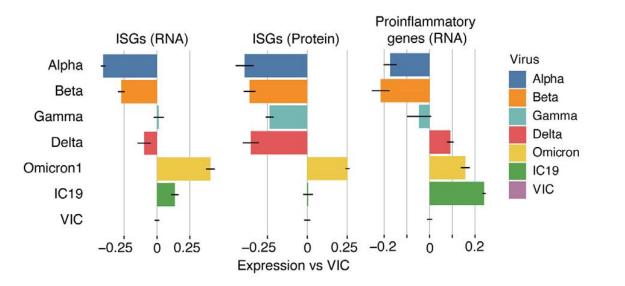
Latest week

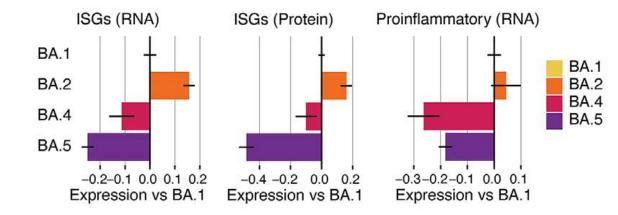
Source: Severe Acute Respiratory Infection Watch surveillance system from the UK Health Security Agency

# Why is SARS-CoV2 infection of CYP usually less severe vs adults?

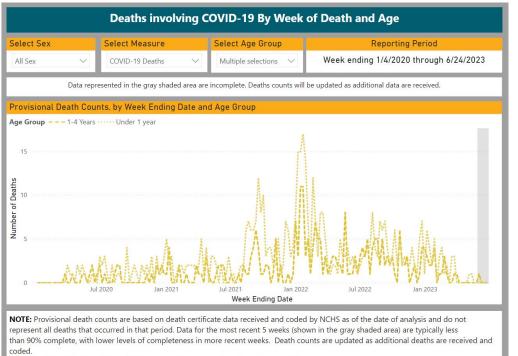
- <u>No differences</u> in household transmission, ACE2 expression, antibodies vs other CoVs, or viral load compared to adults
- Hospitalised kids tend to have less robust memory T cell responses, lower neutralising/Fc-γ-receptor activating antibodies
- Age-dependent decrease in interferon  $\gamma$  and IL-17 production
- Stronger mucosal innate (and adaptive memory post-vaccine) responses, confirmed by comparative RNA Seq/cytokine measurement vs adults
- Possibly a narrower, less cytotoxic, adaptive response post-seroconversion (doesn't always follow infection)
- Vaccines effective and protect vs. MIS-C (PIMS-TS)

## Will CYP innate responses remain protective?



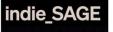


## SARS-CoV2 infection of CYP, globally...(data up to Sep'22)



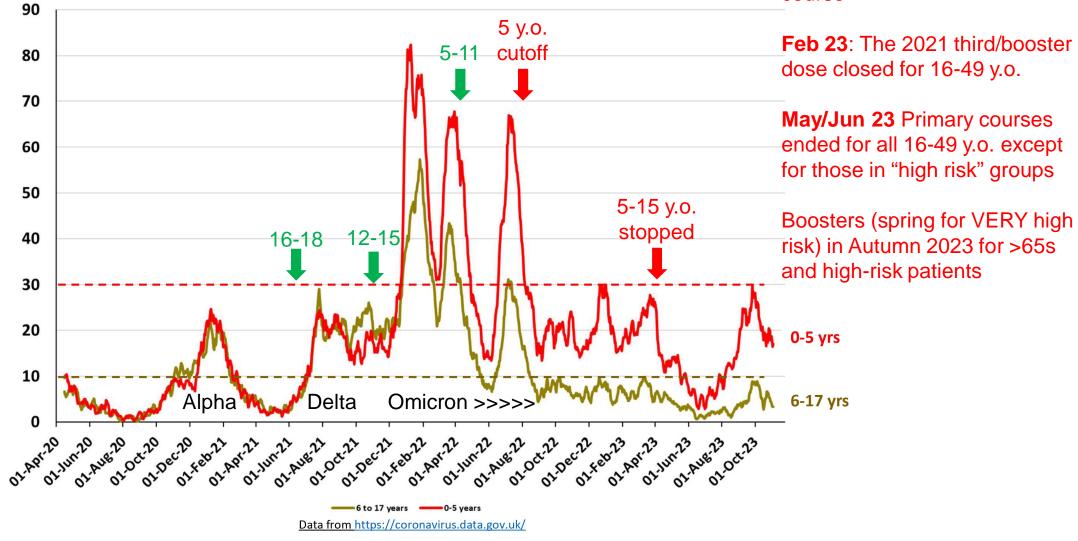
SOURCE: NCHS, National Vital Statistics System. Estimates are based on provisional data.

- US >1200 CYP had lost their lives due to COVID, ~same as annual deaths from all other vaccine-preventable deaths (~300/yr)
- UNICEF estimated ~17000 lives lost, half in under 10s
- WHO estimates based upon prevalence and COVID excess deaths up to 60,000 deaths in CYP
- Hence, COVID equivalent to Hib meningitis and almost as high as measles



7-day average of Covid hospital admissions in England per million population since Dec 2020 for under 18s

Aug 22: kids turning 5 no longer eligible for primary vaccine course

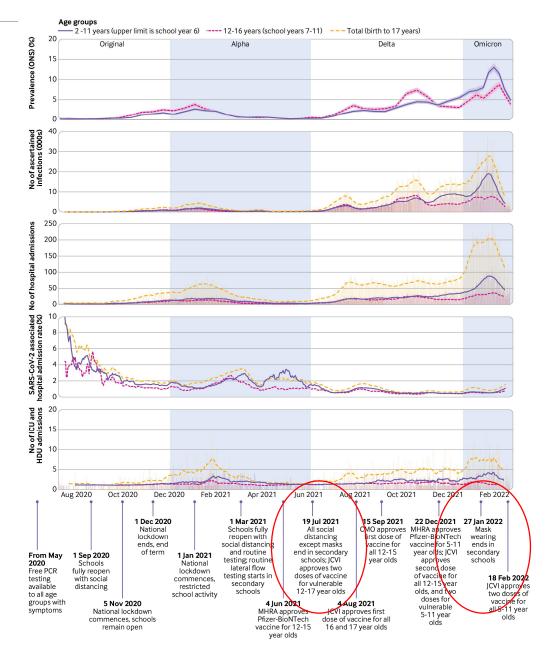


#### Hospital admissions linked to SARS-CoV-2 infection in children and adolescents: cohort study of 3.2 million first ascertained infections in England

Harrison Wilde,<sup>1,2</sup> Christopher Tomlinson,<sup>2,3,4</sup> Bilal A Mateen,<sup>2,4,5</sup> David Selby,<sup>6,7</sup> Hari Krishnan Kanthimathinathan,<sup>8</sup> Padmanabhan Ramnarayan,<sup>9</sup> Pascale Du Pre,<sup>10</sup> Mae Johnson,<sup>10</sup> Nazima Pathan,<sup>11</sup> Arturo Gonzalez-Izquierdo,<sup>2</sup> Alvina G Lai,<sup>2</sup> Deepti Gurdasani,<sup>12,13</sup> Christina Pagel,<sup>14</sup> Spiros Denaxas,<sup>2,4</sup> Sebastian Vollmer,<sup>6,7</sup> Katherine Brown,<sup>15,10</sup> on behalf of the CVD-COVID-UK/COVID-IMPACT consortium



Removal of mitigations coincided with emergence of Omicron (BA.1, BA.2) and before 5-11 permitted to be vaccinated

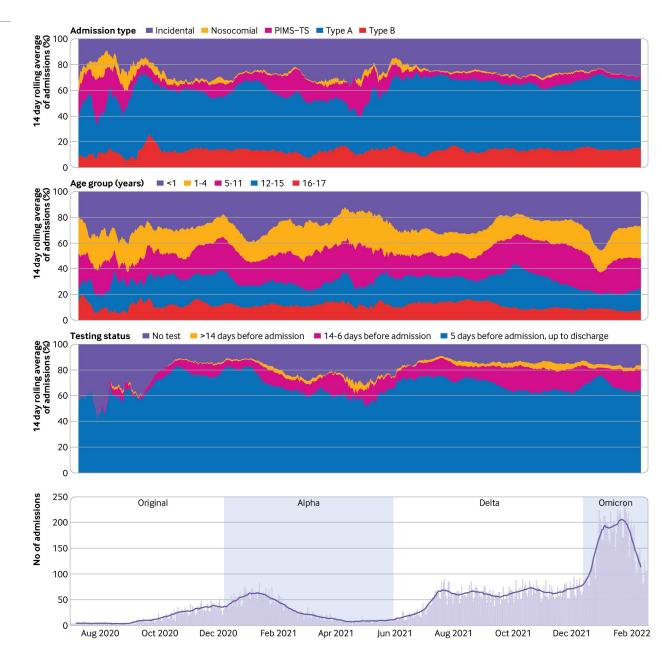


#### Hospital admissions linked to SARS-CoV-2 infection in children and adolescents: cohort study of 3.2 million first ascertained infections in England

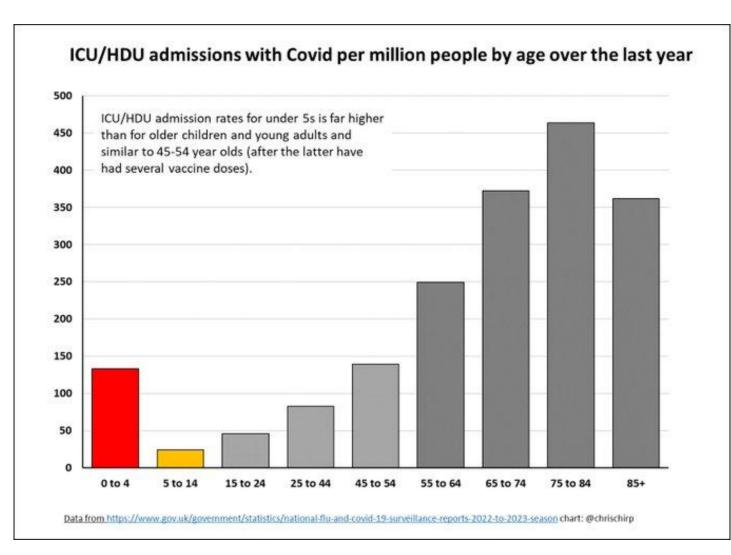
Harrison Wilde,<sup>1,2</sup> Christopher Tomlinson,<sup>2,3,4</sup> Bilal A Mateen,<sup>2,4,5</sup> David Selby,<sup>6,7</sup> Hari Krishnan Kanthimathinathan,<sup>8</sup> Padmanabhan Ramnarayan,<sup>9</sup> Pascale Du Pre,<sup>10</sup> Mae Johnson,<sup>10</sup> Nazima Pathan,<sup>11</sup> Arturo Gonzalez-Izquierdo,<sup>2</sup> Alvina G Lai,<sup>2</sup> Deepti Gurdasani,<sup>12,13</sup> Christina Pagel,<sup>14</sup> Spiros Denaxas,<sup>2,4</sup> Sebastian Vollmer,<sup>6,7</sup> Katherine Brown,<sup>15,10</sup> on behalf of the CVD-COVID-UK/COVID-IMPACT consortium



Around half of admissions in under 5's, incidental COVID minor component



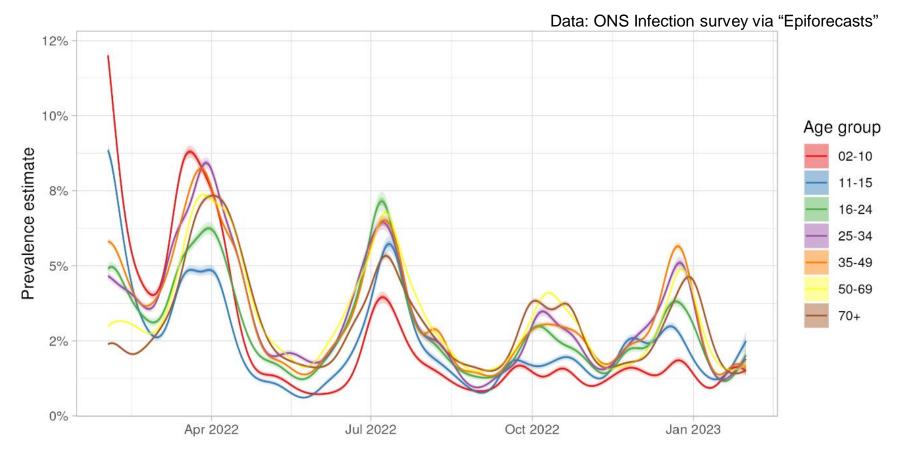
## A U-shaped curve of clinical risk for COVID





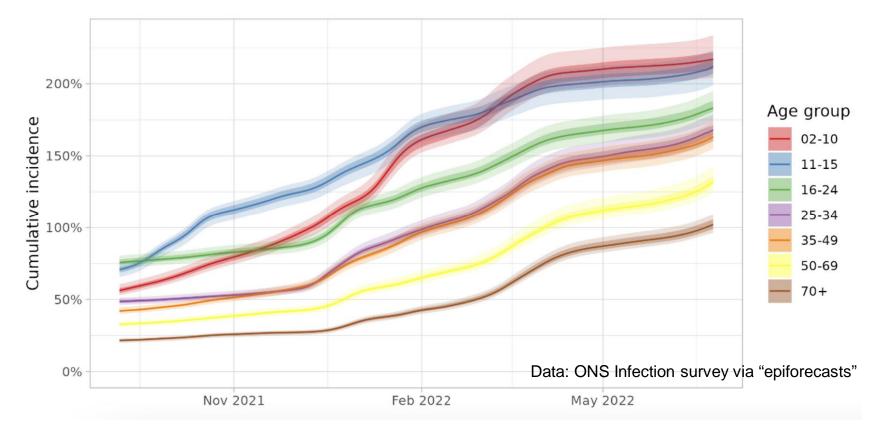
A small % of a very large number (~15M CYP) is still a large number!!!

## What does this mean in terms of children being exposed to infection?



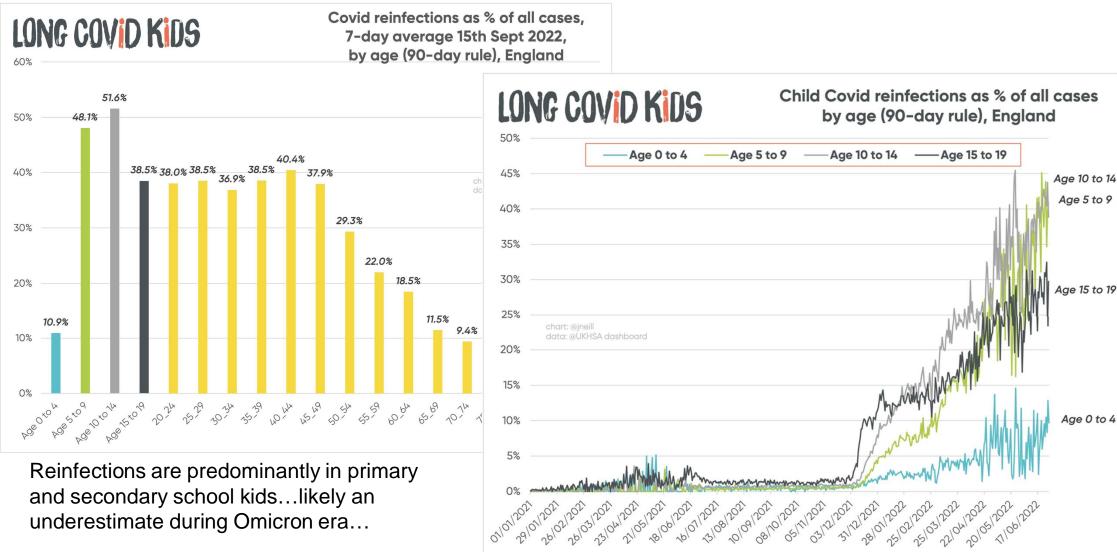
Infections in younger age groups falling with successive Omicron waves...infectioninduced immunity? What would Jenner say?!

## What does this mean in terms of children being exposed to infection?



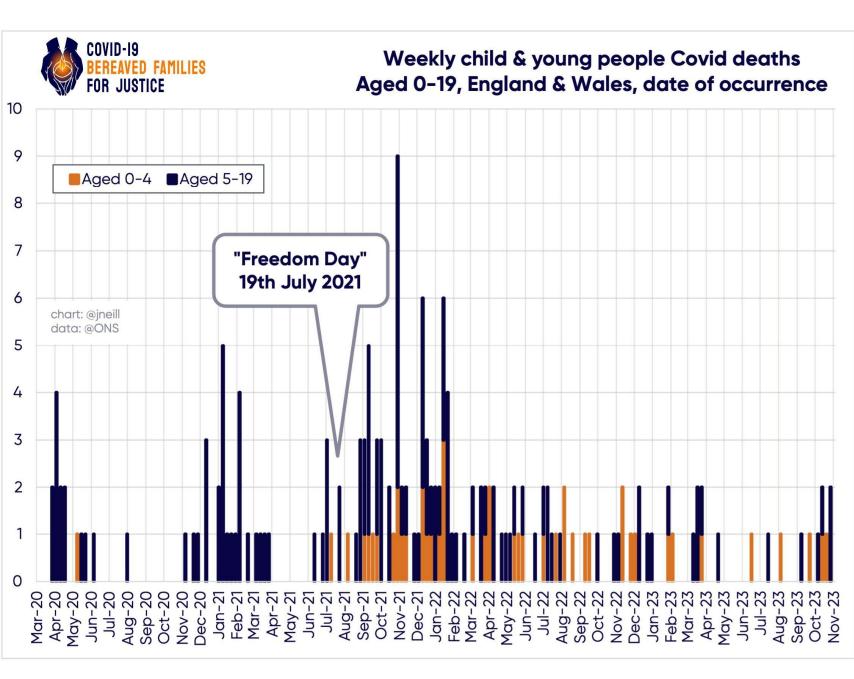
Younger age groups have accumulated enough infections for all to have had COVID twice, compared to once for >70s. Jenner would be fuming...

## Which children are being infected more than once?



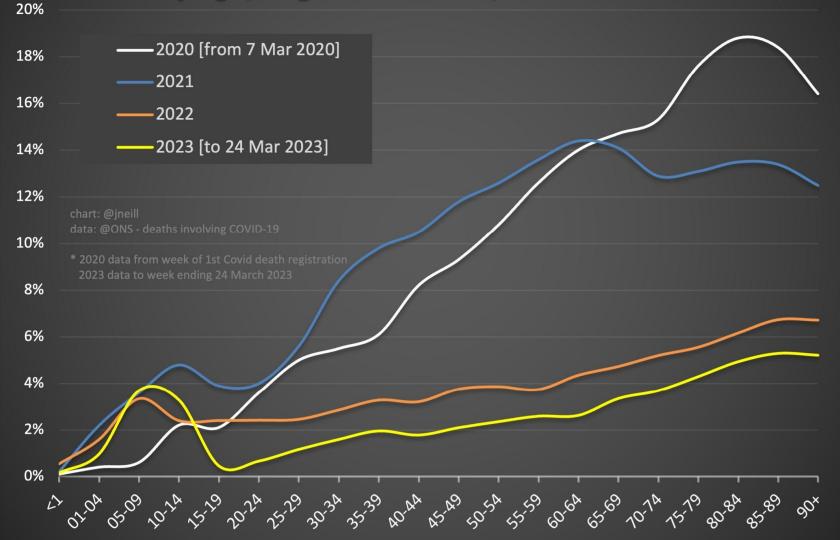
25/02/2022

and secondary school kids...likely an underestimate during Omicron era...

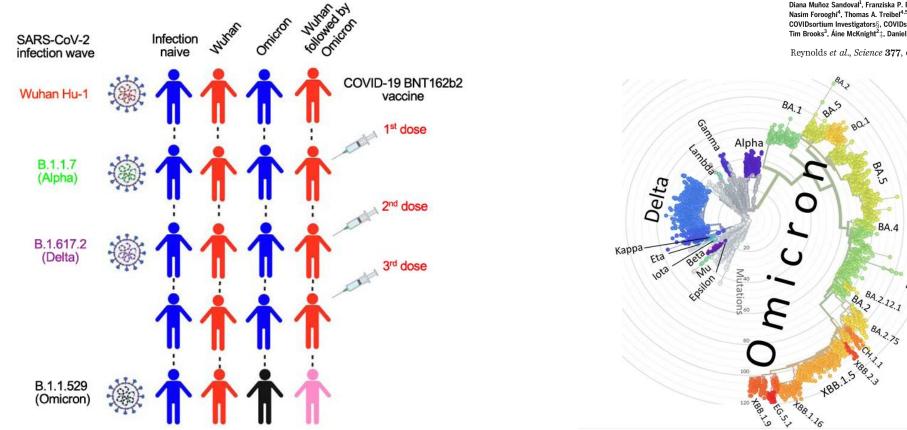


- Children & young people rarely die
- ONS listed COVID as 5th highest cause of death for females aged 5-19 in 2022
- Most child COVID-19 deaths during the Delta & Omicron waves
- 170 certificated deaths registered by ONS in the UK since 2020, ~70% underlying cause
- Lag as child deaths are subject to coroner's inquiry
- 72% do <u>NOT</u> involve "underlying conditions"
- ~18 children/year die from flu (ONS Nomis age 0-19 to 2020). We vaccinate children against influenza

### Covid deaths as % of total deaths By age, England & Wales, 2020 - 2023\*



## But, if kids have been infected, they're protected, right?



Omicron is <u>similar enough</u> to previous viruses that it triggers existing vaccine/infection induced antibody responses, yet it is also <u>different enough</u> that those responses don't work well...This is known as *"original antigenic sin"*, or *"immune imprinting"*...hence, infection-induced "herd immunity" has not, and will not happen while prevalence and diversity exists as it does now...

#### **RESEARCH ARTICLE**

#### CORONAVIRUS

#### Immune boosting by B.1.1.529 (Omicron) depends on previous SARS-CoV-2 exposure

Catherine J. Reynolds<sup>1</sup>†, Corinna Pade<sup>2</sup>†, Joseph M. Gibbons<sup>2</sup>†, Ashley D. Otter<sup>3</sup>†, Kai-Min Lin<sup>1</sup>, Diana Muñoz Sandoval<sup>1</sup>, Franziska P. Pieper<sup>1</sup>, David K. Butle<sup>2</sup>, Siyi Liu<sup>1</sup>, George Joy<sup>4</sup>, Nasim Forooghi<sup>4</sup>, Thomas A. Treibel<sup>4,5</sup>, Charlotte Manisty<sup>4,5</sup>, James C. Moon<sup>4,5</sup>, COVIDsortium Investigators<sup>5</sup>, COVIDsortium Immune Correlates Network<sup>5</sup>, Annada Semper<sup>3</sup>, Tim Brooks<sup>3</sup>, Áine McKnight<sup>2</sup>‡, Daniel M. Altmann<sup>6</sup>‡, Rosemary J. Boyton<sup>17,a</sup>‡

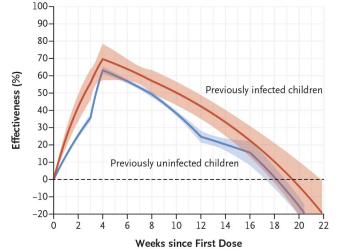
Reynolds et al., Science 377, eabq1841 (2022) 15 July 2022

BA

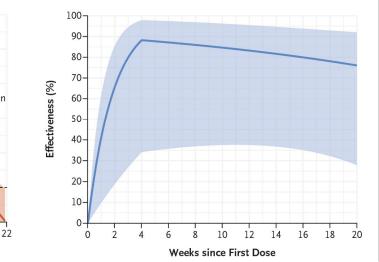
## Vaccine versus infection-induced immunity in children

#### 5-11 y.o. +/- 1 or 2 doses (paediatric) of Pfizer vaccine

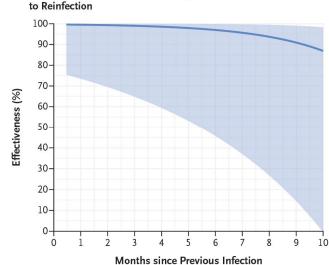
B Effectiveness of BNT162b2 against Infection, According to Previous Infection Status



E Effectiveness of BNT162b2 against Hospitalization



Th NEW ENGLAND JOURNAL of MEDICINE CORRESPONDENCE Effects of Vaccination and Previous Infection on Omicron Infections in Children



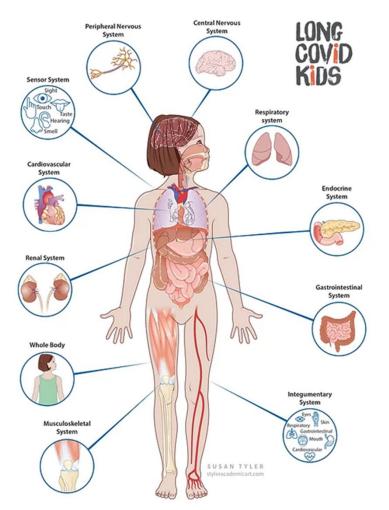
So, infection is better, right?!

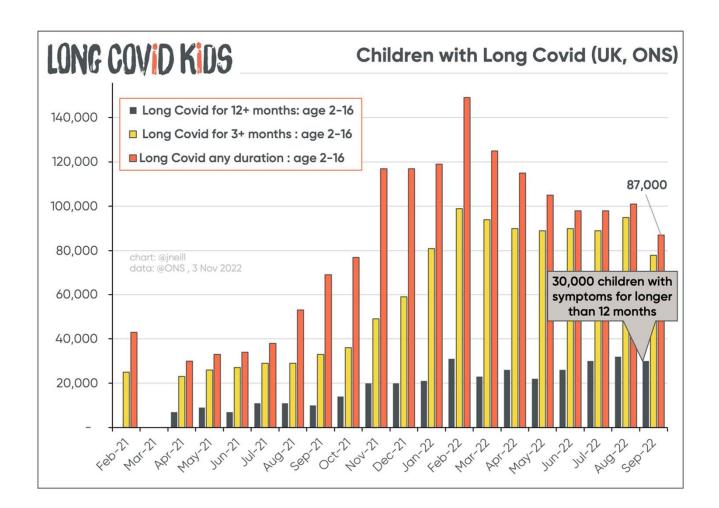
#### Wrong:

- > 193K infections, 309 hospitalised, 7 died
- 273k vaccinees, 15 hospitalised, 0 died
- Lower kids dose, 3 needed for max protection in adults
- Protection vs severe disease better than vs infection
- Omicron is highly antibody evasive...

"The rapid decline in protection against omicron infection that was conferred by vaccination and previous infection provides support for booster vaccination."

## LONG COVID KIDS





## LONG COVID KIDS





LONG COVID: THE ELEPHANT IN THE ROOM. HOW DO CHILDREN DESCRIBE THEIR LONG COVID? www.longcovidkids.org



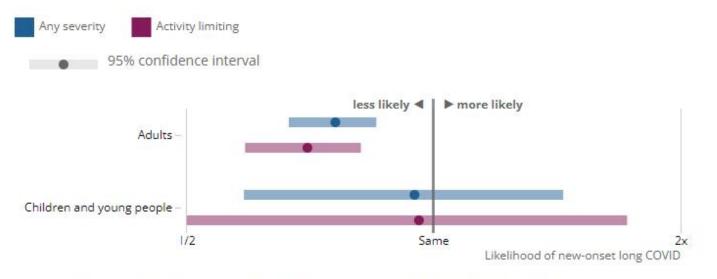
- Extreme exhaustion
- Dizziness
- Rashes
- Cognitive Issues
- Headaches / Sickness or nausea
- Pain
- Stomach pain or upset
- PESE
- Mood changes
- Tics
- Neuropsychiatric symptoms (altered mood, regression, OCD, anxiety)
- Muscle and joint pain or swelling
- Breathlessness



## Impact of reinfections on Long COVID...

Figure 1: The adjusted odds of new-onset, self-reported long COVID were 28% lower in adults following a second coronavirus (COVID-19) infection, compared with a first infection

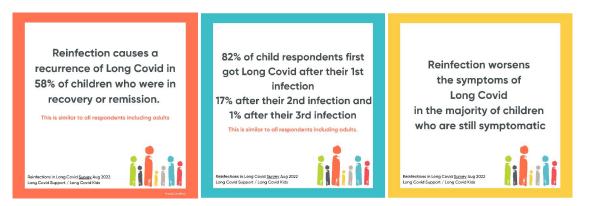
Adjusted odds ratios for new-onset, self-reported long COVID 12 to 20 weeks after a second COVID-19 infection, compared with a first infection, in adults (aged 16 years and over) and children and young people (aged 2 to 15 years), UK: 1 November 2021 to 8 October 2022



Source: Office for National Statistics - Coronavirus (COVID-19) Infection Survey

## Impact of reinfections on Long COVID...

## LONG COVID KIDS



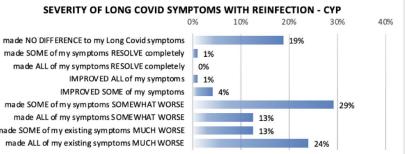


#### New survey suggests reinfection worsens Long COVID

e behind COVID-19 Research summary COVID-19 Explainer

Survey indicates that getting reinfected worsens symptoms of Long COVID or triggers a recurrence of symptoms in people who have recovered.

15 September 2022 • 2 min read • by Priva Joi



made SOME of my symptoms SOMEWHAT WORSE made ALL of my symptoms SOMEWHAT WORSE

made SOME of my existing symptoms MUCH WORSE made ALL of my existing symptoms MUCH WORSE

## LONG COVID KIDS Impact of vaccination on Long COVID...

### **PLOS MEDICINE**

RESEARCH ARTICLE

Post-COVID-19-associated morbid children, adolescents, and adults: cohort study including more than individuals with COVID-19 in Germ

OPEN ACCESS	ORIG
<b>bmj</b> medicine Oneck for updates	Effect of covid-19 vaccination on long covid: syster review
	Oyungerel Byambasuren 🐵 ,¹ Paulina Stehlik 💿 ,¹ Justin Clark 💿 ,¹ Kylie A Paul Glasziou 💿 ¹
OPEN ACCESS	ORIG
hmimedicine	Efficacy of first dosp of covid-19 vaccing vorsus no

#### Conclusions

In this retrospective matched cohort study, we observed significant new onset morbidity in children, adolescents, and adults across 13 prespecified diagnosis/symptom complexes, following COVID-19 infection. These findings expand the existing available evidence on post-COVID-19 conditions in younger age groups and confirm previous findings in adults.

**CONCLUSIONS** Current studies suggest that covid-19 vaccines might have protective and therapeutic effects on long covid. More robust comparative observational studies and trials are needed, however, to clearly determine the effectiveness of vaccines in preventing and treating long covid.

#### RIGINAL RESEARCH

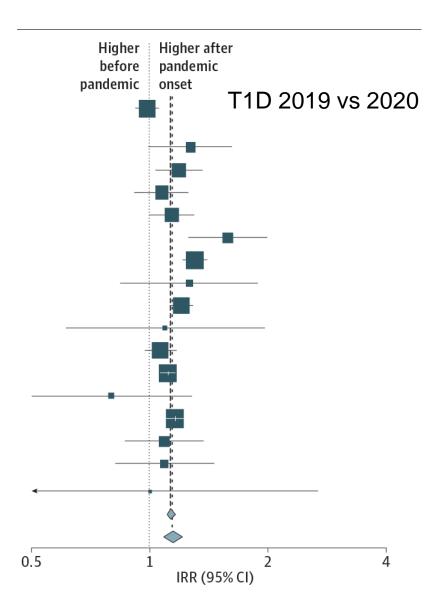
**bmj**medicine

Check for updates

Efficacy of first dose of covid-19 vaccine versus no on symptoms of patients with long covid: target tr based on ComPaRe e-cohort

Viet-Thi Tran <sup>(0)</sup>,<sup>1,2</sup> Elodie Perrodeau,<sup>2</sup> Julia Saldanha,<sup>3</sup> Isabelle Pane,<sup>2</sup> Phil

**CONCLUSION** In this study, covid-19 vaccination reduced the severity of symptoms and the effect of long covid on patients' social, professional, and family lives at 120 days in those with persistent symptoms of infection.

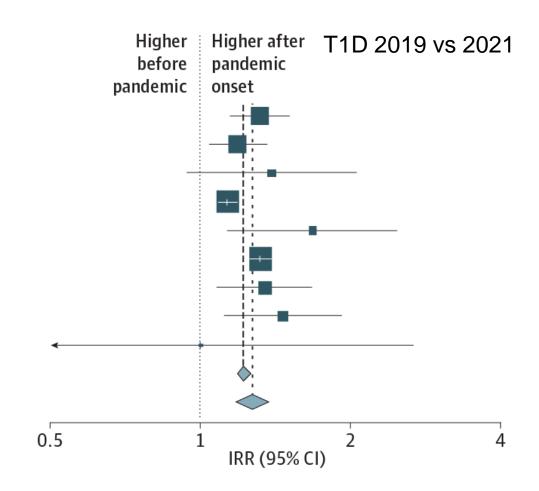




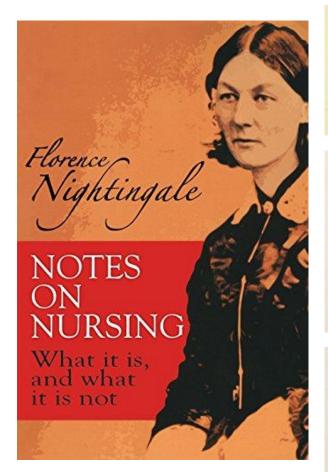
Original Investigation | Pediatrics

Incidence of Diabetes in Children and Adolescents During the COVID-19 Pandemic A Systematic Review and Meta-Analysis

Daniel D'Souza, BHSc; Jessica Empringham, MD; Petros Pechlivanoglou, PhD; Elizabeth M. Uleryk, MLS; Eyal Cohen, MD, MSc; Rayzel Shulman, MD, PhD



## We should NOT need a pandemic to reinforce the importance of cleaning the air...



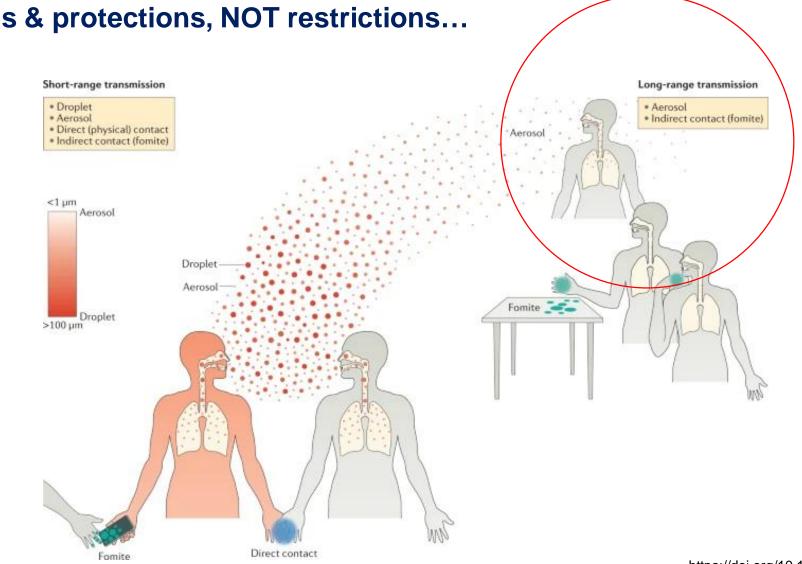
It is quite necessary, nevertheless, to lay down such a principle, because the actual mortality *in* hospitals, especially in those of large crowded cities, is very much higher than any calculation founded on the mortality of the same class of diseases among patients treated *out of* hospital would lead us to expect. The

### I. VENTILATION AND WARMING.

The very first canon of nursing, the first and the last thing upon which a nurse's attention must be fixed, the first essential to the patient, without which all the rest you can do for him is as nothing, with which I had almost said you may leave all the rest alone, is this: TO KEEP THE AIR HE BREATHES AS PURE AS THE EXTERNAL AIR, WITHOUT CHILLING HIM. Yet what is so little attended to? Even

water-closet, or even, as I myself have had sorrowful experience, from open sewers loaded with filth; and with this the patient's room or ward is aired, as it is called—poisoned, it should rather be said. Always air from the air without, and that, too, through those windows, through which the air comes freshest. From a closed

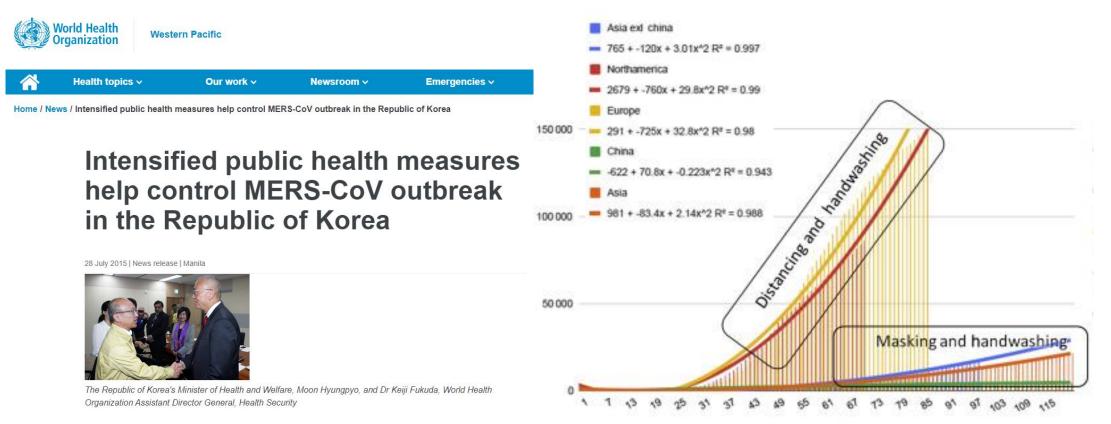
First rule of nursing, to keep the air within as pure as the air without.



### Mitigations & protections, NOT restrictions...

https://doi.org/10.1038/s41579-021-00535-6

### We know what to do, but it isn't "normal"



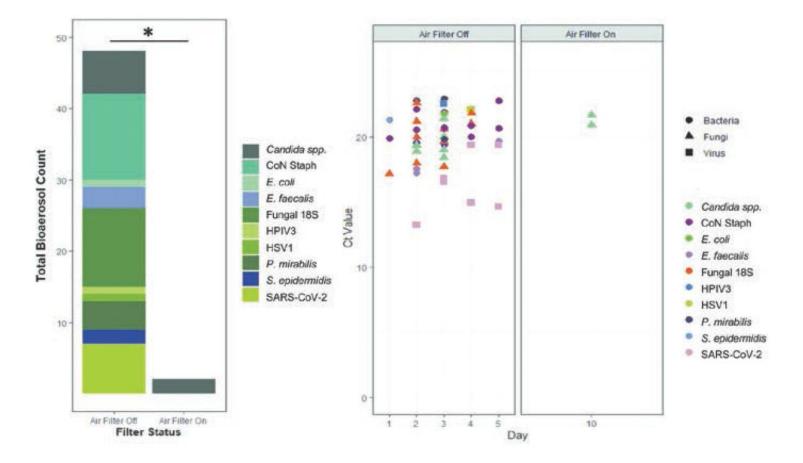
Day since the first case

### Mitigations & protections, NOT restrictions...

BRIEF REPORT The Removal of Airborne Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Other Microbial Bioaerosols by Air Filtration on Coronavirus Disease 2019 (COVID-19) Surge Units

Clinical Infectious Diseases

Andrew Conway Morris,<sup>12,a</sup> Katherine Sharrocks,<sup>3,a</sup> Rachel Bousfield,<sup>34,a</sup> Leanne Kermack,<sup>5,a</sup> Mailis Maes,<sup>5</sup> Ellen Higginson,<sup>5</sup> Sally Forrest,<sup>5</sup> Joana Pereira-Dias,<sup>5</sup> Claire Cormie,<sup>5</sup> Tim Old,<sup>2</sup> Sophie Brooks,<sup>3</sup> Islam Hamed,<sup>1</sup> Alicia Koenig,<sup>1</sup> Andrew Turner,<sup>6</sup> Paul White,<sup>6,7</sup> R. Andres Floto,<sup>8,9</sup> Gordon Dougan,<sup>5</sup> Effrossyni Gkrania-Klotsas,<sup>3,4</sup> Theodore Gouliouris,<sup>34,b</sup> Stephen Baker,<sup>5</sup> and Vilas Navapurkar<sup>1,®</sup>

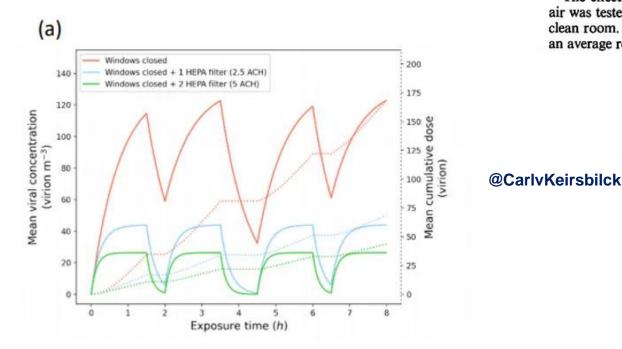


DOI https://doi.org/10.4414/SMW.2022.w30178

Cite this as: Swiss Med Wkly. 2022;152:w30178

## SARS-CoV-2 aerosol transmission in schools: the effectiveness of different interventions

Jennifer Villers<sup>a\*</sup>, Andre Henriques<sup>b\*</sup>, Serafina Calarco<sup>c</sup>, Markus Rognlien<sup>d</sup>, Nicolas Mounet<sup>b</sup>, James Devine<sup>b</sup>, Gabriella Azzopardi<sup>b</sup>, Philip Elson<sup>b</sup>, Marco Andreini<sup>b</sup>, Nicola Tarocco<sup>b</sup>, Claudia Vassella<sup>e</sup>, Olivia Keiser<sup>f</sup>



https://medium.com/@carlvank/luchtreiniging-air-purification-hepa-5dd2c728ef8f

Vol. 16, No. 10 Printed in U.S.A.

### Evaluation of a Commercial Air Filter for Removal of Viruses from the Air

P. ROELANTS, B. BOON, AND W. LHOEST

Recherche et Industrie Thérapeutiques, R.I.T., Rixensart, Belgium

Received for publication 14 June 1968

The effectiveness of a commercial absolute air filter for removal of viruses from air was tested with an actinophage, under the usual conditions of a laminar airflow clean room. A new method of dry phage dispersion is described. The filter showed an average reduction of 99.996% of airborne actinophage.

32 micron infective and antigenic material. Electrostatic or high efficiency particulate air (HEPA) filters are recommended for uhome use. The HEPA filtration of all fresh air will protect ric of against effects of air pollution and pollen induced bronchospasm. The HEPA filtration of all recirculated air is of the epidemiological key to halting acrosol transmission of viral uia by induced infection, allergy, and asthma among human hosts sharing a closed environment. The use of HEPA filters in de buses, trains, airplanes, and automobiles is suggested. )x 13.-151 1972 tic 100 Air Pollution Abstracts, Volume 4, Nrs 7–12, Environmental Protection Agency (US). Air Pollution Control Office. AIR POLLUTION ABSTRACTS, NOVEMBER The photochemical smog episode of the Moriguchi Junior High School in Ostohan 1072 man investigated by aliginations

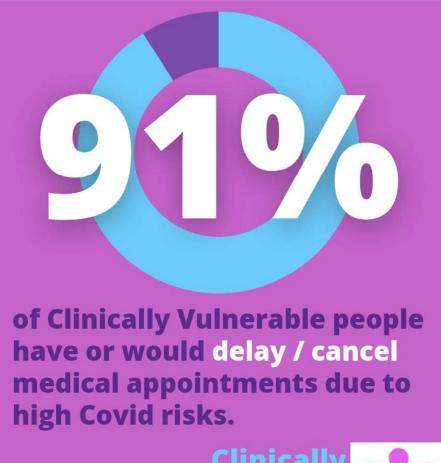
### A lack of mitigations in healthcare settings...

#### BBC Sor you Overall - Percentage HAI by day for English Acute Trusts combined **NEWS** 40.0% Home | Israel-Gaza war | Cost of Living | War in Ukraine | Climate | UK | World | Business | Politics | Culture England Local News Regions Shropshire Shropshire NHS trust criticised for 30.0% no Covid testing letter () 11 October Percentage HAI %0.02 Coronavirus 10.0% 0.0% 2021 2022 Date

## 

Impact on health care access

(Source: Clinically Vulnerable Families, Survey Oct 2022)



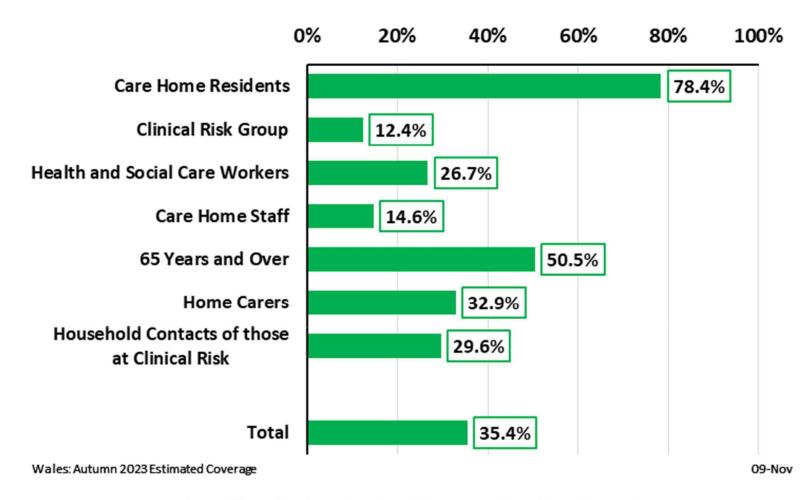
[Poll of 450 Clinically Vulnerable people October 2022]





#### Autumn 2023 Vaccine Coverage of Eligible Cohorts Wales: 9 Nov 2023

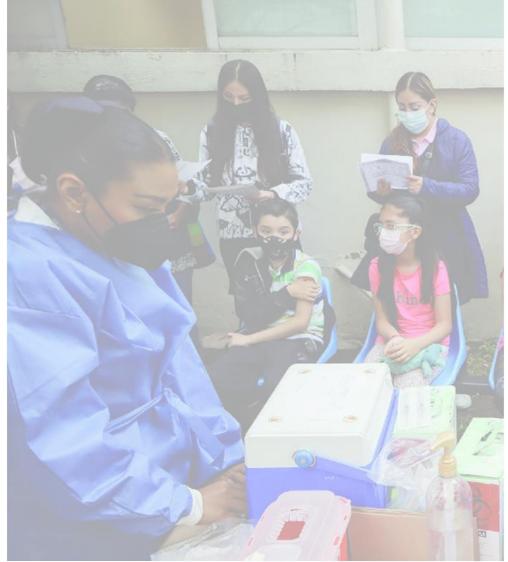
(Source: Wales Weekly Covid Vaccination Surveillance Report)



https://www2.nphs.wales.nhs.uk/CommunitySurveillanceDocs.nsf

Thanks to Bob Hawkins for the slide

## Summary – We must vaccinate children and mitigate risks



- The pandemic may continue for years, ignoring this fact has an ongoing human cost
- Children remain a major source of transmission, but also are themselves vulnerable to COVID
- We cannot predict SARS-CoV2 evolution...pi???
- The highest risk from acute infection is usually (not always) the first
- Under 5's are exposed to a lesser extent compared to primary & secondary pupils
- > Vaccines are safe and effective <u>at the population level</u>
- Vaccines protect against long COVID, sequelae?
- Future vaccines may
  - Provide pan-variant protection
  - > Be better at preventing transmission

Thank you...

# indie\_SAGE







Prof Christina Pagel

Dr Kit Yates







Sammie McFarland

Nathalie Pearson

**James Neill** 

**Bob Hawkins** 

## LONG COVID KIDS

- Created by parents and professionals whose children are living with Long Covid the Support Guide is a comprehensive pack containing evidence-based resources and information for parents, families, children, young people, school staff, education, health and social care professionals.
- Free to download from www.longcovidkids.org
- Available to by in our online shop

