Infections transmitted via the respiratory route.

Christopher Whitty

Gresham College 2022

Route of transmission is key to understanding and combatting infectious diseases.

- Vector-borne (insects etc).
- Oral- food, water and other drink.
- Sexual (STI) & bloodborne.
- **Respiratory.**
- Touch.

- Usually one route dominant.
  Sometimes secondary routes.

NLM

The respiratory route has several advantages for the infection.

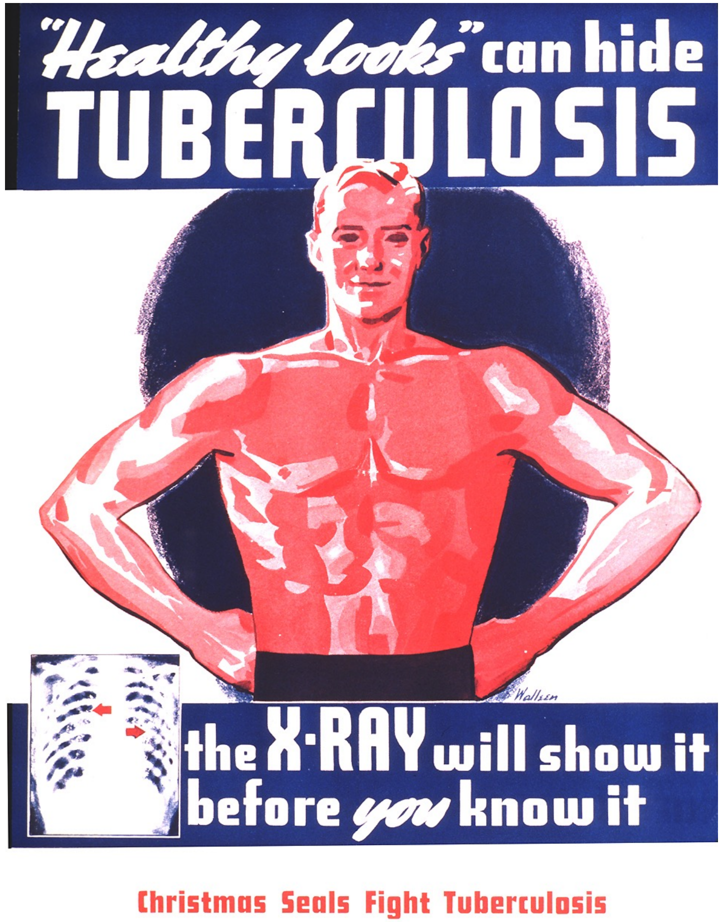
- Unlike some routes (eg oral, vector) it generally requires you to be near the infected person.
- But not necessarily at exactly the same time.
- You do not need to know them or touch them (eg sexual, touch)- a stranger in a crowded room can transmit to many others.
- This allows rapid spread through multiple households in one room.
- Transmission within households is even more efficient.
- The infection has to remain viable outside the host long enough to infect.

BBC

Several major infections have evolved to take advantage of the respiratory route of transmission.

Examples:

- Mycobacteria including tuberculosis.
- Bacteria including pneumococcus, meningococcus, plague (also vector).
- 'Atypical' bacteria such as legionella, chlamydia.
- **Many** viruses- include measles, 'flu, COVID-19, smallpox.
- Fungi acquired (but not transmitted) via the respiratory route.



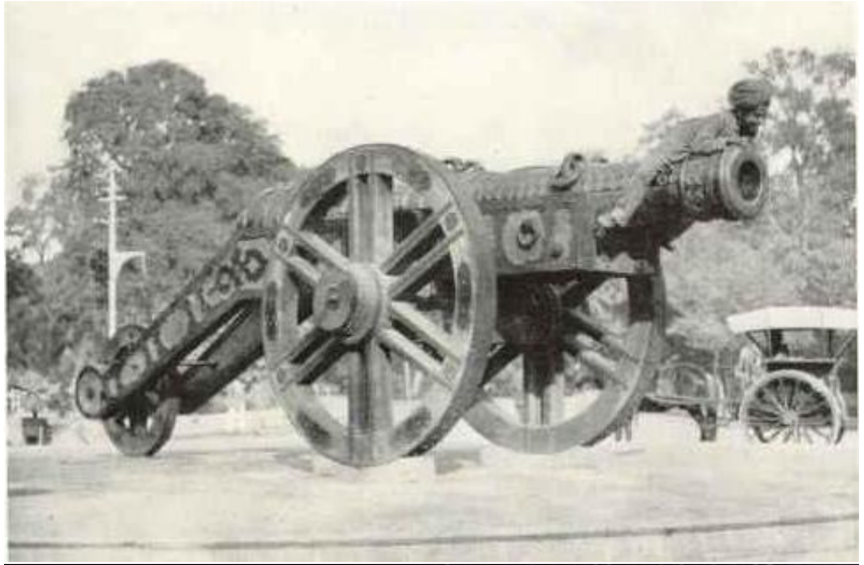
NLM

Respiratory route transmission.

- Droplets.
- Objects people touch and then touch their face. Hands, doorknobs etc. Can be persistent.
- Aerosols and true airborne infection.
- (Mouth-to-mouth- kissing).

A bit on ballistics.

- Large and medium sized droplets travel quite small distances (often 1-2m) before dropping to the ground/surface.
- Cough or sneeze may increase range, will increase number.
- May contaminate surfaces for some time.
- Very small droplets can be suspended in the air (aerosol) for some hours.



Zam-Zammeh, Lahore. CDC

Infections transmitted via the respiratory route cause damage throughout the body.

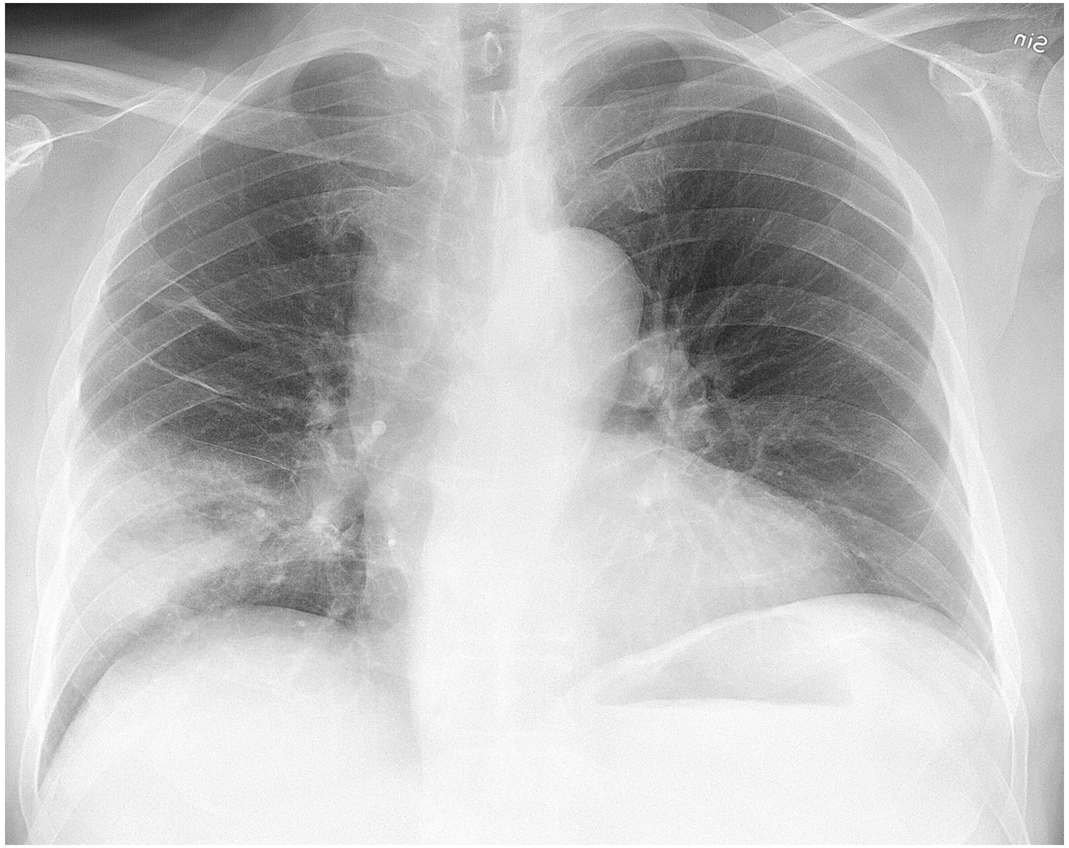
- Some infections transmitted via the respiratory route cause their main damage in the lungs, especially pneumonia.
- But many others cause most of their damage elsewhere in the body. Include:

- Several causes of meningitis.
- Sepsis and generalised inflammation.
- Diseases of the nerves including leprosy.
- Diseases of the heart including diphtheria.

Man with leprosy. JL Losting

Upper and lower respiratory tract infections.

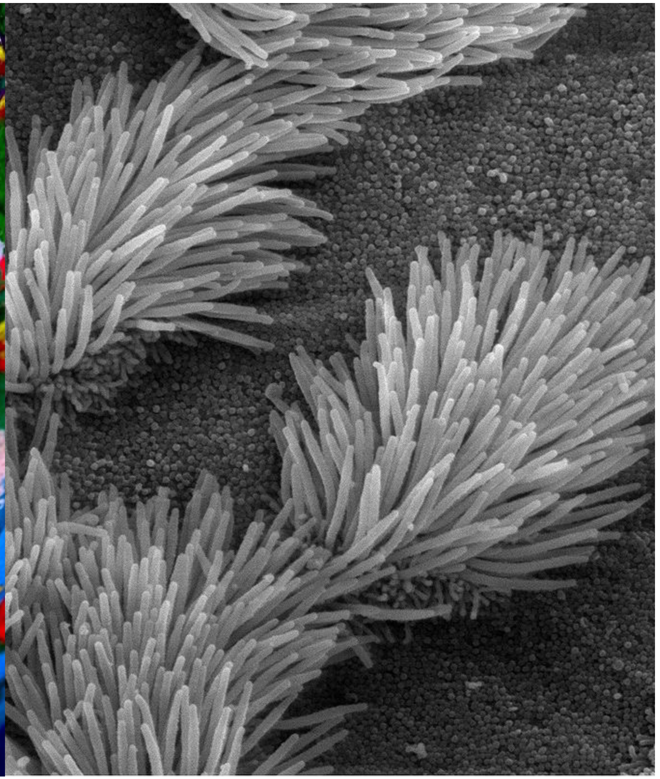
- Upper respiratory tract infections: nose, throat, upper airways.
- Many are trivial (coughs and colds).
- But the route of entry for many serious infections.
- Lower respiratory tract infections are lung infections, especially pneumonia.
- Many infections can be both including COVID-19.



Mikael Häggström

In praise of mucus (‘snot’) and other defences.

- Mucus very important. A physical barrier, constantly being excreted.
- Mucociliary escalator.
- Contains enzymes, antibodies (IgA).
- Behind this several other layers of immunological defence.
- Innate and adaptive immune system.



Bùi Linh Ngân, Charles Daghlian

Using the physical environment to reduce risk of respiratory transmission.

- The great outdoors.

-Rapid dilution of droplets, aerosols.

-Generally more spaced out.

-UV light.

- Improved ventilation indoors.

-‘Natural’ ventilation. Open windows….

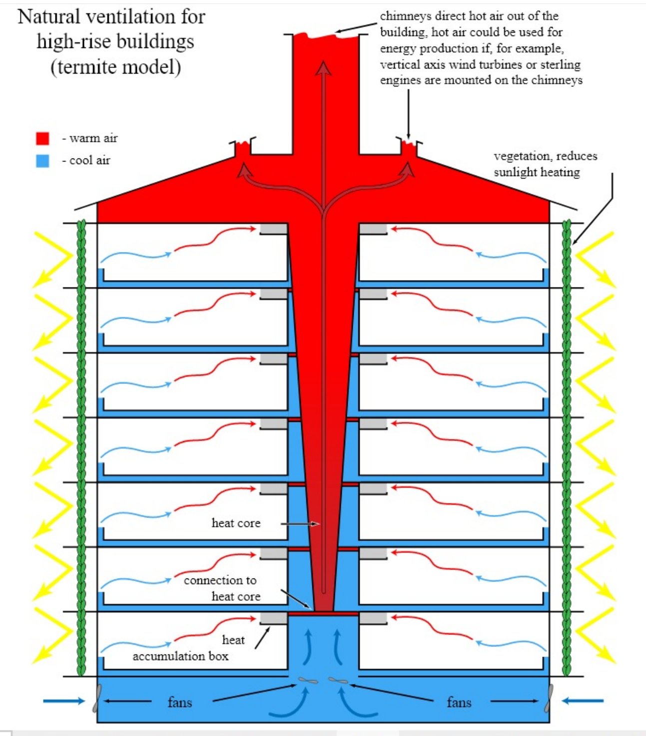
-Engineering in ventilation whilst keeping in heat.

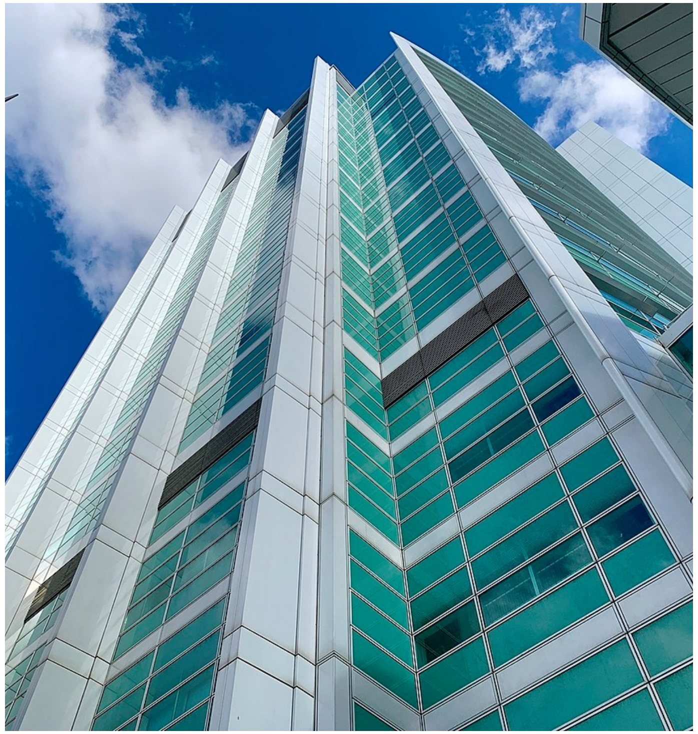
- Distance, or direction, or physical barriers. Most useful for droplet spread.

Jan Brueghel. Outdoor wedding dance.

Ventilation. Engineers (yet again) improve public health.

Include through drafts, hot air rising, mechanical ventilation +/- filters or UV.





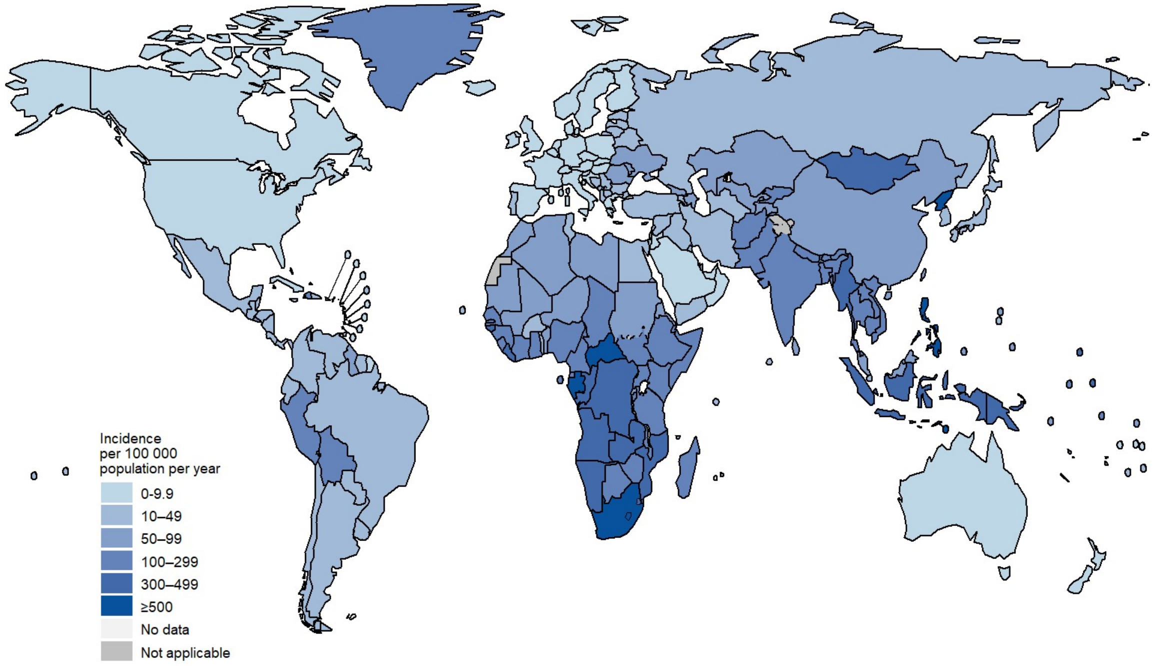
TB Sanitorium/ Fred the Oyster / Central Tower, Palace of Westminster/ UCLH Wiki

Personal behaviours which reduce the chances of passing on or acquiring respiratory infections.

- Stay at home and isolate when unwell with a seasonal respiratory infection.
- Maximise social time outdoors or with good ventilation.
- Cover mouth and nose when coughing or sneezing.
- Wash hands. Dispose of tissues.
- In periods of high transmission- eg epidemics- facemasks.

The important role of poverty and deprivation in respiratory infections.

- Strong correlation in many respiratory infections with poverty. Includes:
- Housing and crowding.
- Working conditions.
- Diet and malnutrition.
- Access to vaccines and curative medical services.
- As poverty has decreased, some infections have as well.



TB incidence, 2020. WHO

Smoking and respiratory infection.

- Clear evidence of increases of many respiratory infections in smokers.
- Includes tuberculosis, influenza, pneumococcal pneumonia.
- Damage to the lung’s defences.
- People with chronic obstructive airways disease vulnerable to respiratory infections.

Vincent Van Gogh

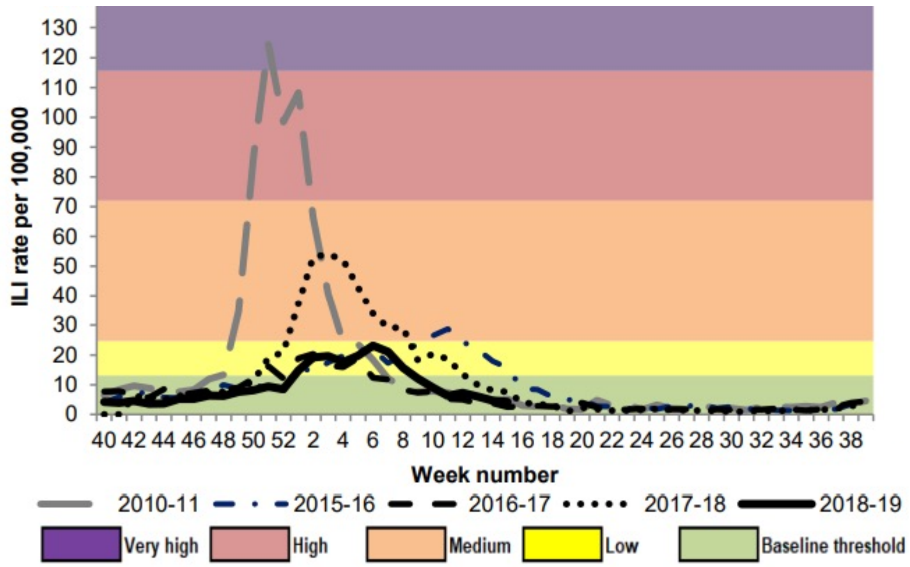
Some occupations increase the risk of respiratory infections.

- Close contact occupations- include healthcare workers, social care workers, taxi drivers.
- Some occupations damage the lung defences. Mining, some occupations that cause dust.
- Some occupations may increase risk of specific infections, for example farmers for fungal lung disease and zoonoses.

Jacob Elshin. Miners at work.

Seasonality of respiratory infections.

- Many respiratory infections are seasonal.
- Include infections where the level of population immunity is in rough balance with the infection.
- In winter several changes which advantage the infection including:
- More time together indoors, windows shut.
- Lower temperatures, changes in humidity.
- Lower UV light.



Influenza-like presentations to GP. PHE

Medical countermeasures.

- Drugs.

-Anti tuberculous drugs (TB).

-Antibiotics (bacterial).

-Antivirals.

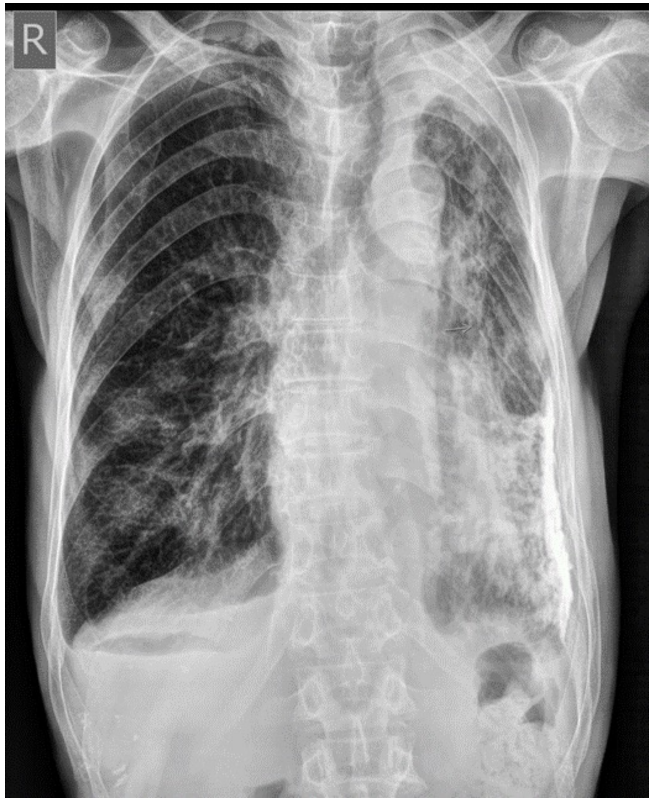
- Vaccines.

-We have effective vaccines for some, but not all, infections via the respiratory route.

-Some prevent infection, others more effective at preventing severe disease.

Tuberculosis (TB): still a leading cause of death worldwide.

- Was common everywhere, killing people in all walks of life including UK.
- In 2020, around 10 million people fell ill with TB, and 1.5 million died (WHO). Includes around 1 million children.
- Mainly spread by droplets via respiratory route.
- People can be chronically infected, and infectious over many years.
- Malnourished, immunosuppressed most at risk.

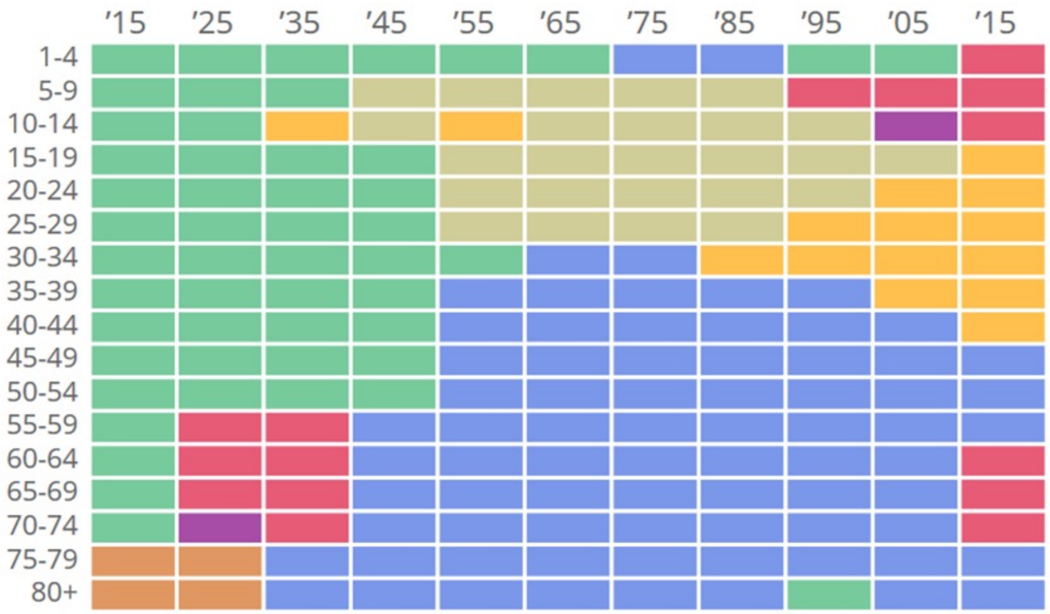


Mohammad Osama Yonso, Radiopedia

When NHS started a major cause of mortality. TB incidence, and even more mortality, in the UK has dropped sharply.

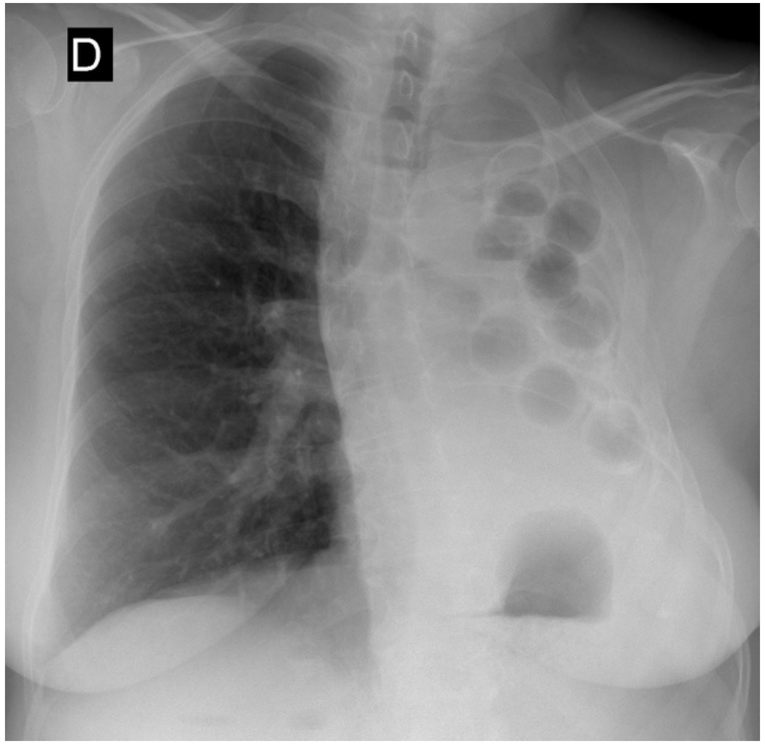
TB incidence and mortality, E&W 1913-2017 (Log scale)

Principle cause of male mortality in England by decade. Infection, heart disease.



Treated and untreated TB in pre-drug pre-HIV era.

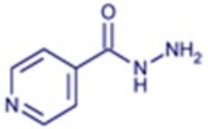
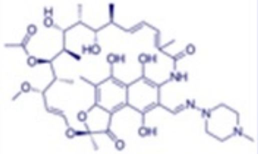
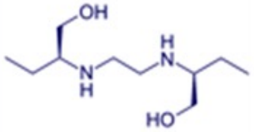
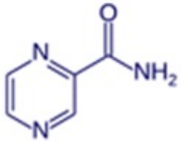
- Without treatment smear-positive TB had a mortality of around 70% (30-80%) over 10 years.
- Smear-negative mortality around 20%.
- Pre-drug era treatment included collapsing a lung, plombage.
- First effective drug 1946 (streptomycin).
- Now highly effective treatments.



David Clemo Steel, Radiopaedia

The key to preventing spread of pulmonary TB is early diagnosis, then 6 months of (directly observed) multi-drug treatment.

The Four Principal First-Line TB Drugs

Drug Name	Formulation	Chemical Structure
Isoniazid		
Rifampin		
Ethambutol		
Pyrazinamide		

TB a respiratory transmitted disease but not just a lung disease.

- ‘Consumption’ with lung disease killed many in pre-treatment era.
- TB meningitis.
- Generalised TB (‘miliary’).
- TB around the heart.
- TB of the spine and bones.
- TB of the kidneys and glands.
- TB of the lymph nodes.

Dr Hani Makky Al Salam, Radiopaedia.org

Tuberculosis vaccination (BCG). Helps prevent severe disease but limited impact on transmission.

- BCG vaccine remains one of the most widely used.
- Effective at preventing severe TB in children, but:

-Less effective in adults.

-Less effective in low-income settings.

-Less effective in lung TB.

- Various new vaccines, so far none have improved significantly on BCG.

Tuberculosis. Opportunity and threat.

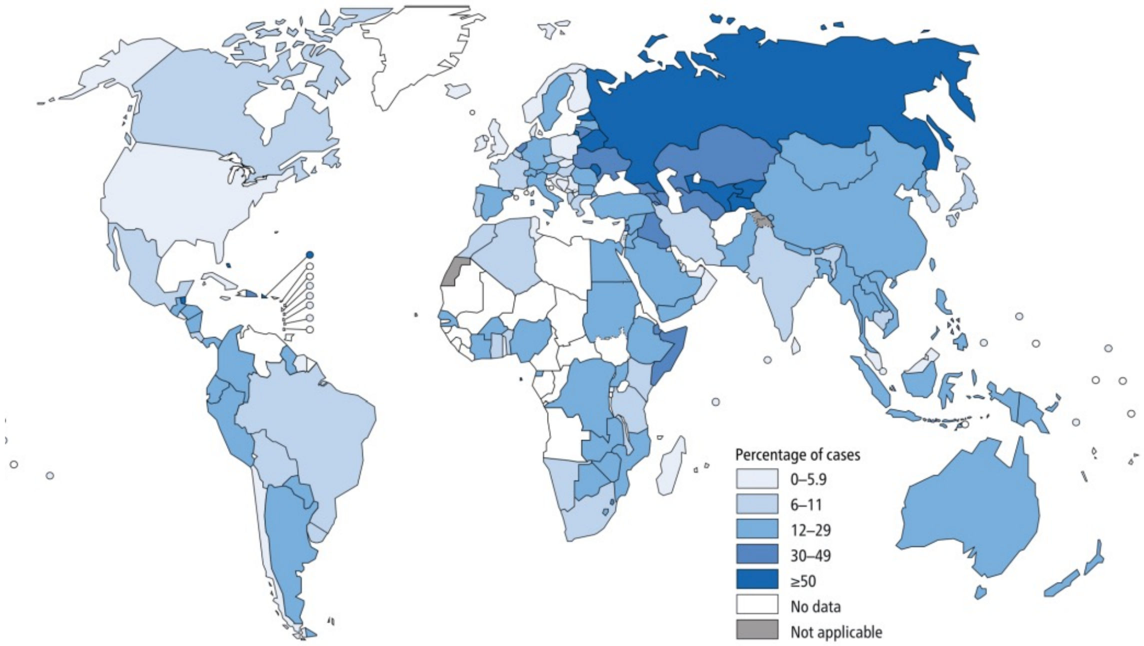
Opportunity

- International development with reduction in global poverty.
- Improved diagnosis and treatment.
- Treatment and prevention of HIV.

Threat

- Multi-drug resistant TB.

% MDR/RR-TB in previously treated TB cases



WHO

Leprosy. *Mycobacterium leprae.*

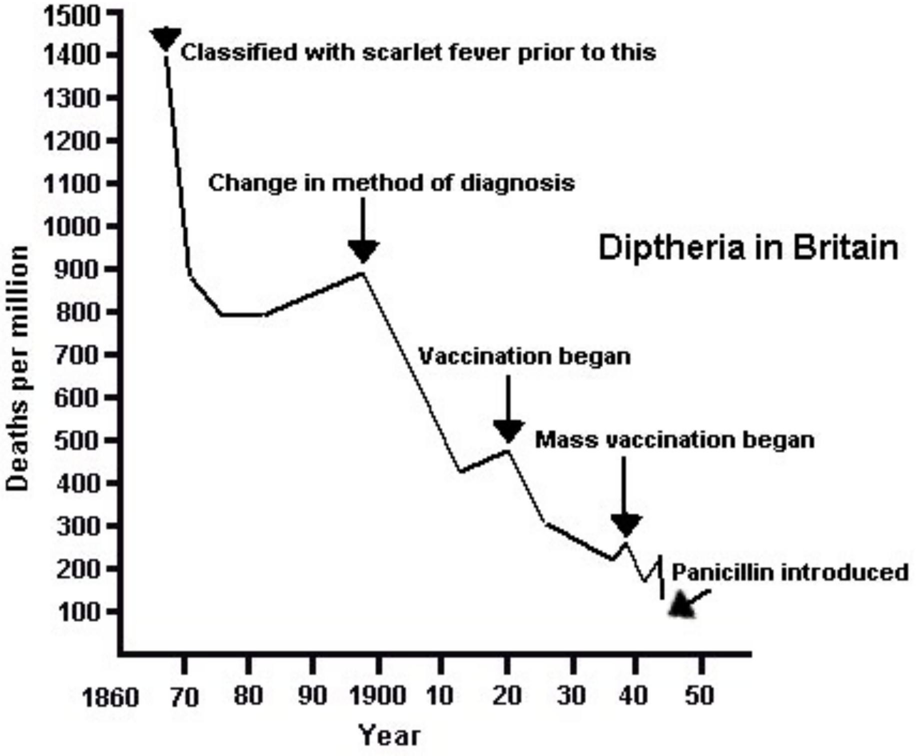
- One of the most feared and stigmatised diseases, historically of great importance.
- Transmission probably through droplets from nose and mouth.
- Transmission needs close prolonged contact and stops after treatment starts.
- Destroys nerves, eyes.
- Effective multi-drug treatment.
- BCG fairly effective vaccine.
- 10s of millions as late as 1960s. Now globally < 150,000 new cases reported annually.

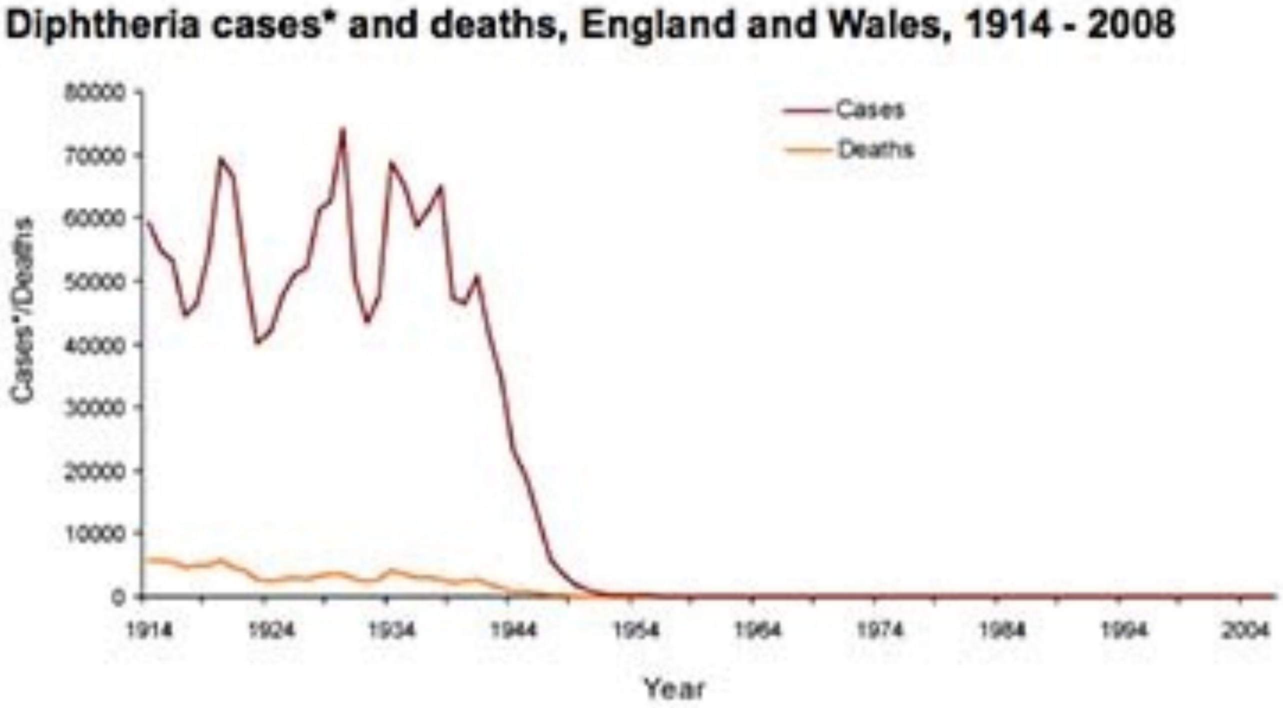
Diphtheria.

- Used to be a major cause of death, especially in children. Over 1m cases before 1980s.
- Mainly transmitted by droplets.
- Colonises the throat. The damage is caused by toxins.
- Local effect- massive swelling compress the throat.
- Can cause heart block.
- Peripheral nerve damage.

Dileepunnikri

Diphtheria in the UK. Improved living conditions, antibiotics, vaccination (95% effective).





Rheumatic fever.

- From streptococcal sore throat.
- Droplet spread.
- Caused joint pains.
- Was a major cause of permanent heart valve damage.
- Also affects brain and skin.
- Immunological reaction to the infection.
- Was very common- now very rare.

J. Heilman

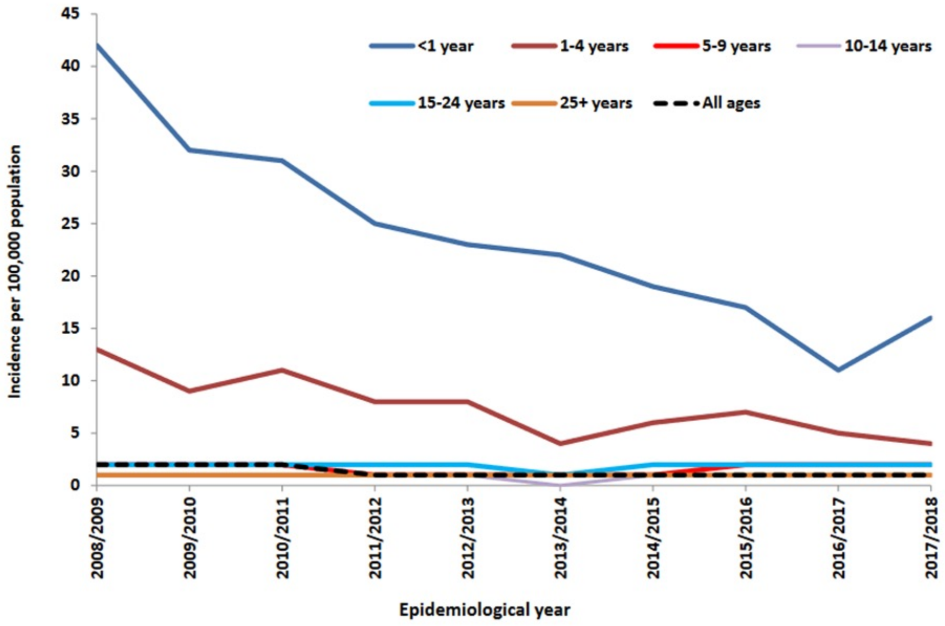
Bacterial meningitis and septicaemia. Meningococcus.

- Carried by around 10% of adults in nose or throat.
- Transmitted by close contact- coughing, kissing. Not casual contact.
- Can cause meningitis, septicaemia, or both.
- Rapid onset (hours).
- Untreated very high mortality (~ 50%).
- Antibiotic sensitive.
- Meningococcus A, B, C, W, X, Y.
- Incidence varies by age and geography.
- Effective vaccines available.

Charlotte Cleverley-Bisman- survived with many disabilities. Her family campaigned to increase vaccine uptake.

Globally the most important Meningococcus A, B, C. Now have effective vaccines for all of them.

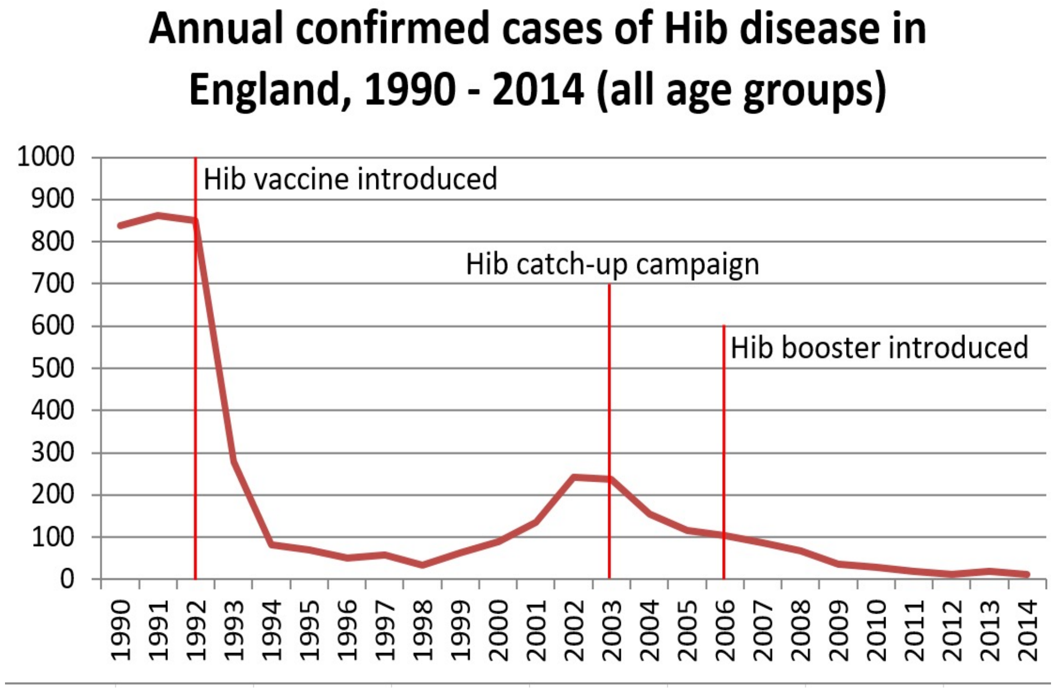
- Used to be massive epidemics in West Africa- Meningococcus A.
- Meningococcus A outbreaks have been virtually eliminated by introduction of vaccine- 71% decline in meningitis cases.
- UK reduction in invasive meningococcal disease from 2,595 (1999/2000) to 755 (2017/18).
- Men C vaccines available UK and Ireland since around 2000. Reduced by 96%. Men B since 2015.



Incidence of invasive meningococcal disease England, 2008-2018. PHE.

Bacterial meningitis in children- *Haemophilus influenzae* b (Hib).

- Was the commonest cause of meningitis in children <4.
- Passed on by droplets- coughing and sneezing.
- 1:20 died, 1:5 left with serious neurological disability.
- Hib vaccine introduced in UK and Ireland 1992. Reduced incidence >90%.



PHE data.

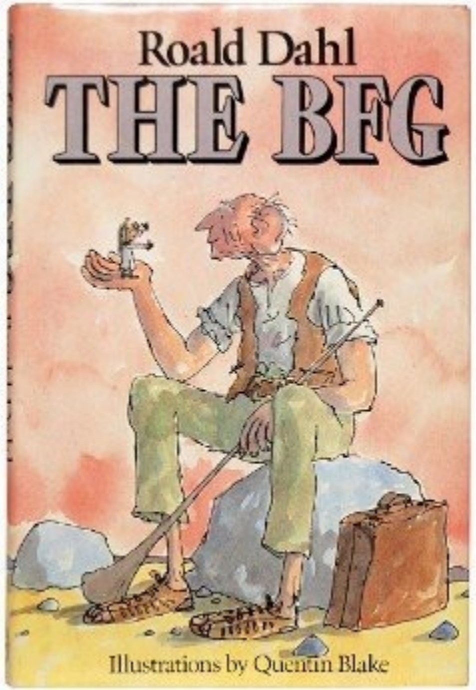
Measles.

- Spread by coughs and sneezes.
- Up to 90% of immune naïve children near an infected person will catch it. Can be in air for up to 2 hours.
- In epidemics in areas of poor nutrition (esp. Vitamin A) mortality 5-10%.
- Highly effective vaccine giving lifelong protection.

NHS

Measles encephalitis.

- 1-3 in 1,000 children will develop encephalitis with measles. 10–15% of these will die, a further 25% will be left with permanent neurological damage.
- 1 in 1,000 children with measles will develop post-infectious encephalitis.
- 1 in 25,000 children will develop subacute sclerosing panencephalitis (SSPE), up to years later (usually fatal).
- 1-2 in 1,000,000 children will develop encephalitis from measles vaccination (less than the incidence of all types of encephalitis).



Dedicated to Olivia who died of measles encephalitis.

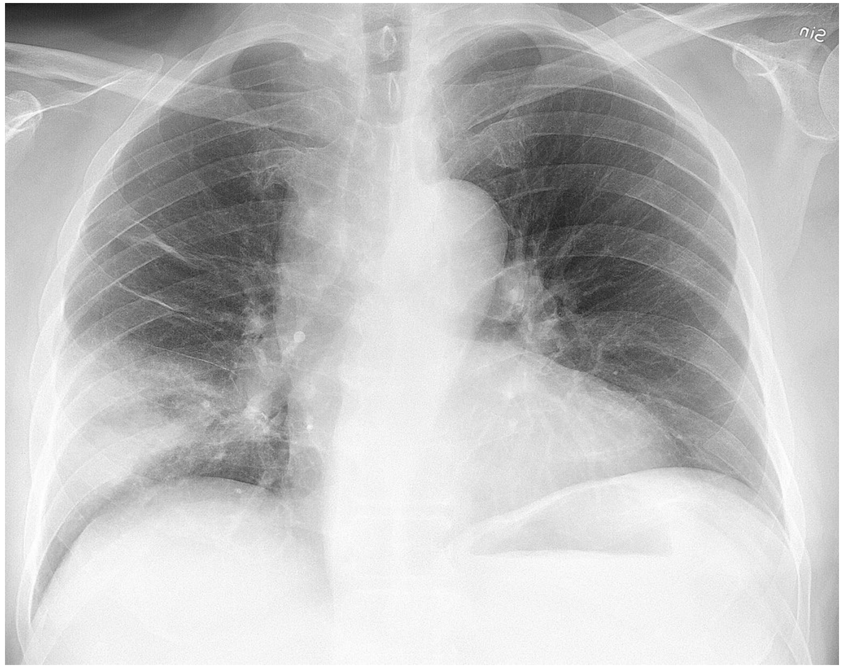
Mumps, rubella. Both vaccine preventable.

- Around 1:4 cases of viral meningitis in children were mumps prior to MMR.
- Mumps passed on by direct saliva and droplets.
- Rubella, a significant risk for miscarriage, stillbirth and foetal abnormalities if women catch it in early pregnancy.
- Passed on by droplets.

Child with mumps. NHS

Pneumonia.

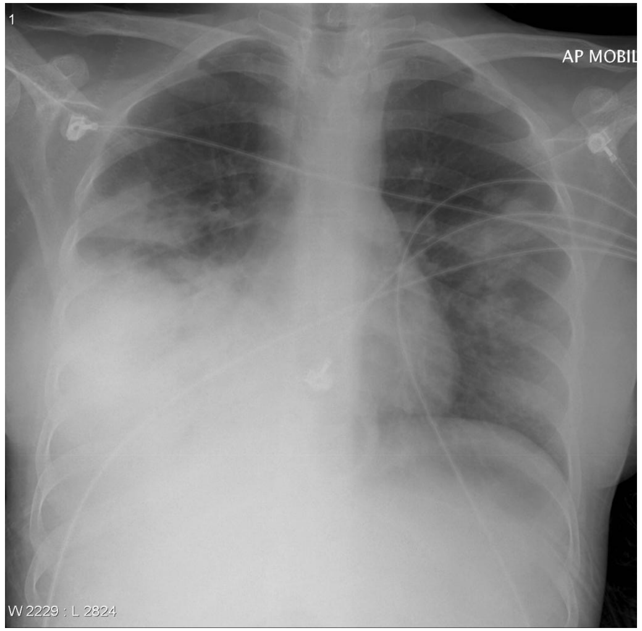
- Bacteria, viruses, occasionally fungi.
- Very common- up to 450 million cases a year globally.
- In pre-antibiotic era killed people throughout their lives.
- Now deaths tend to occur in the very young, the very old, those living in less wealthy countries and the immunosuppressed.
- Often the commonest cause of mortality in low income settings, especially children.
- Among leading causes of mortality in UK, mainly older adults.



Mikael Häggström

The most common bacterial cause is pneumococcal pneumonia.

- Pneumococcus carried in throats of many adults, over half of pre-school children.
- Transmission by droplets, secretions.
- *Streptococcus pneumoniae* pneumonia.
- In adults this is the most common cause of pneumonia overall.
- Treatment antibiotics.



Jack Ren Radiopaedia.

Pneumococcal meningitis and sepsis.

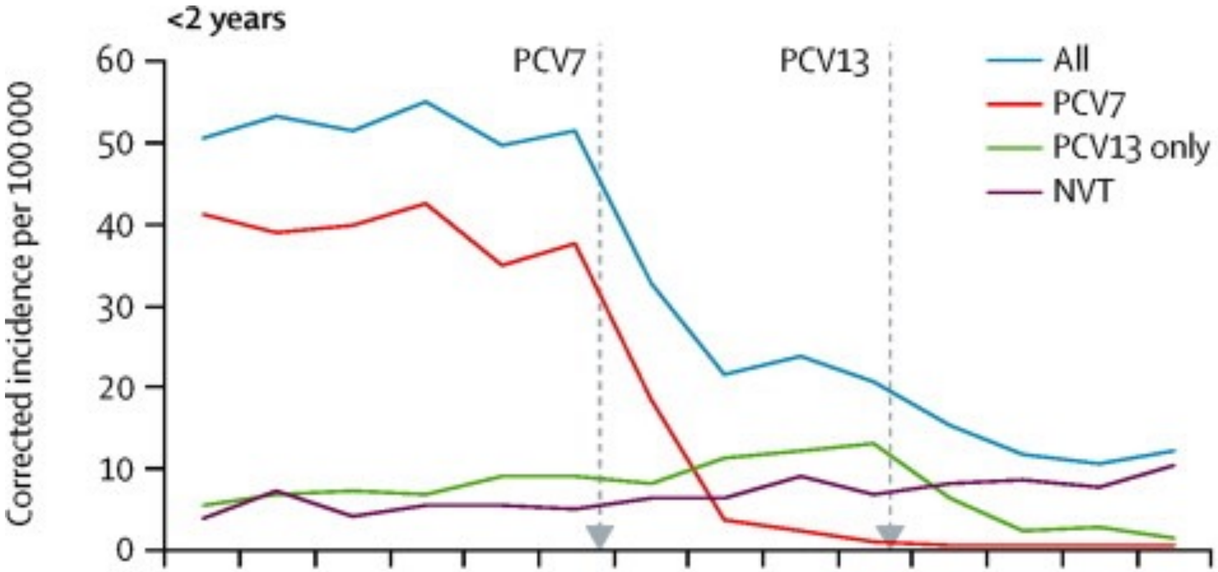
- Young children (<2) and >65 years.
- High mortality for untreated pneumococcal meningitis, and around 1:5 survivors have significant disability.
- Routine immunisation for 13 most common strains in infants. Vaccine for over-65s.

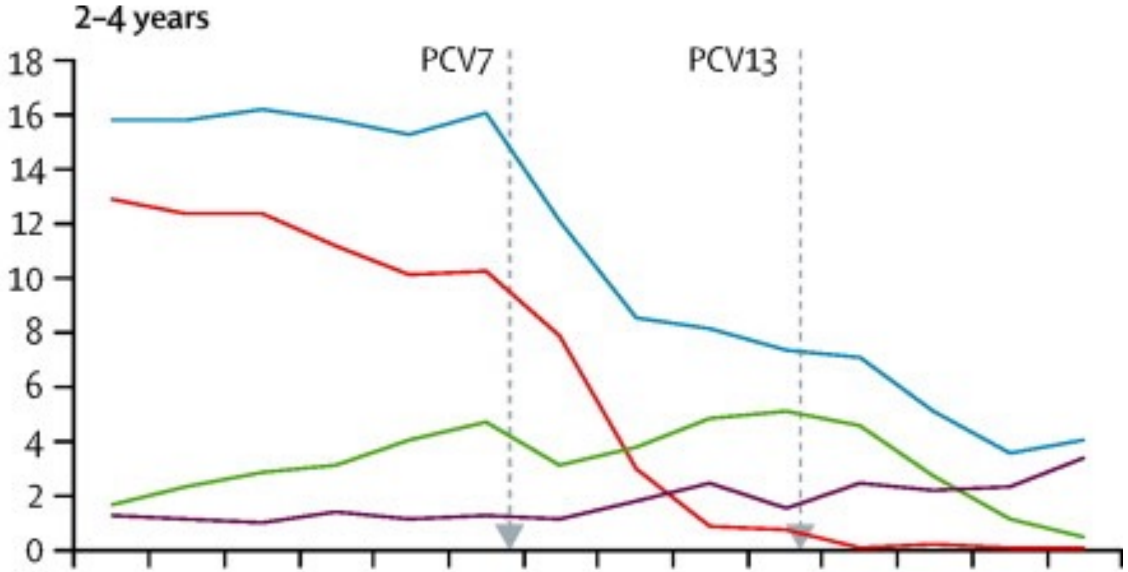
The Favorite Georgios Jakobides (1890)

Pneumococcal conjugate vaccine in children.

(PHE E&W data- *Waight P et al Lancet ID 2015*).

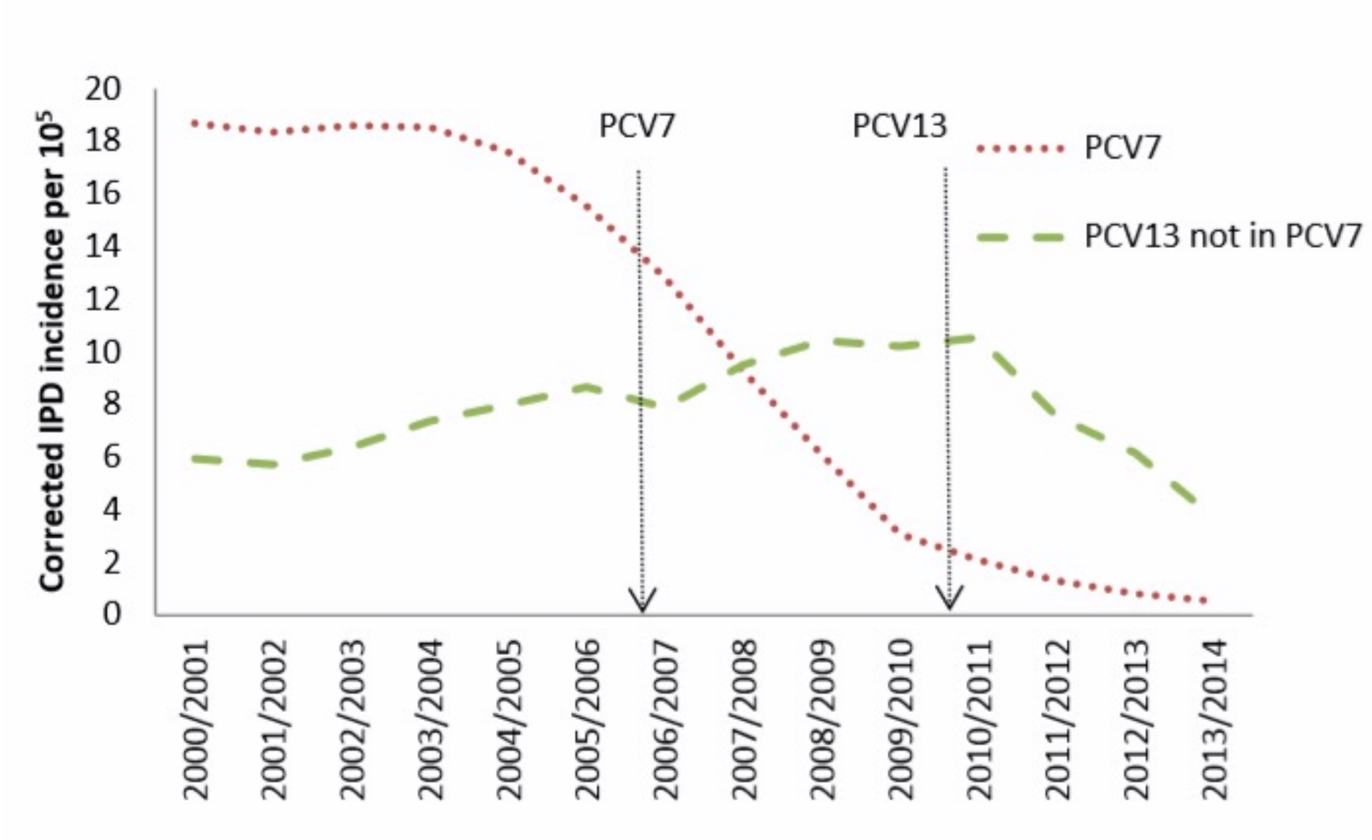
- PCV7 (7-valent) introduced UK 2006.
- Vaccine-type invasive pneumococcal disease decreased 86%.
- Significant increase in non-PCV7 disease.
- PCV13 replaced PCV7 in April, 2010. Further 32% reduction.
- Compared with pre-PCV7 baseline, there was a 56% overall decrease.





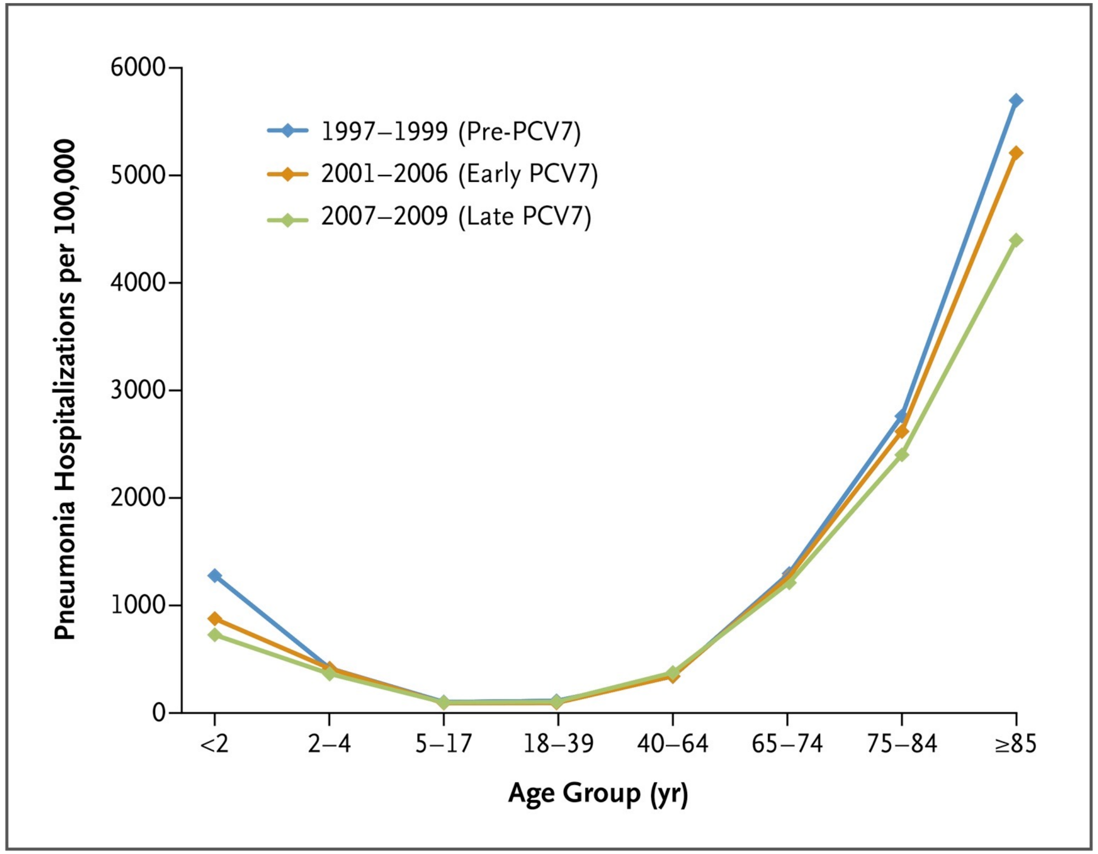
Effect of vaccine in adults >65, UK (PHE).

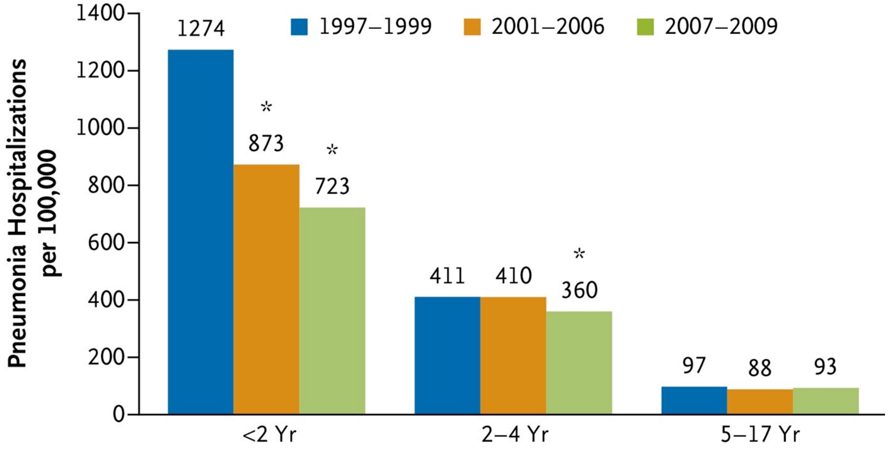
Adults over 65 get pneumococcal polysaccharide vaccine (PPV23) since 2003.

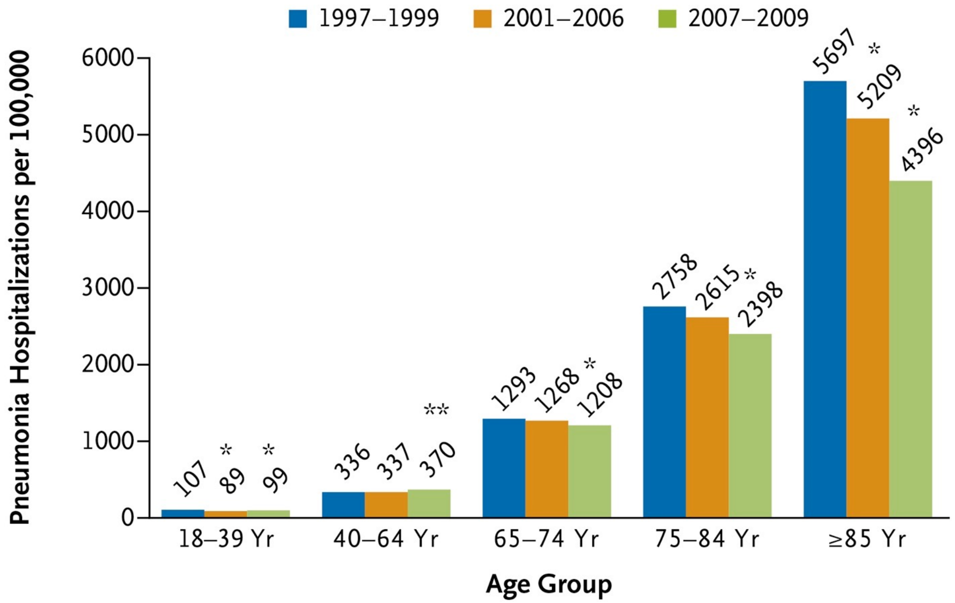


Hospitalisations for pneumonia following PCV7 in USA, by age.

Age <2, 47,000; age >85 73,000 fewer hospitalizations annually.

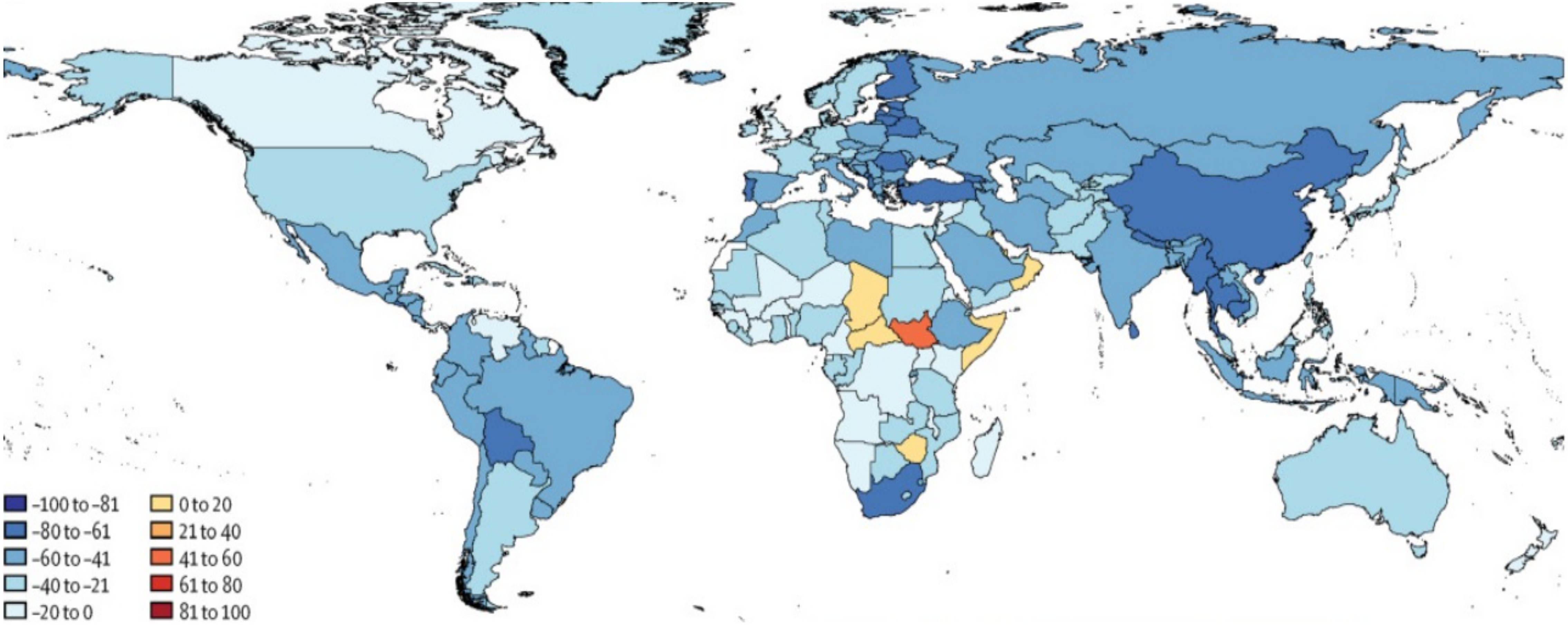






Griffin M et al NEJM 2013.

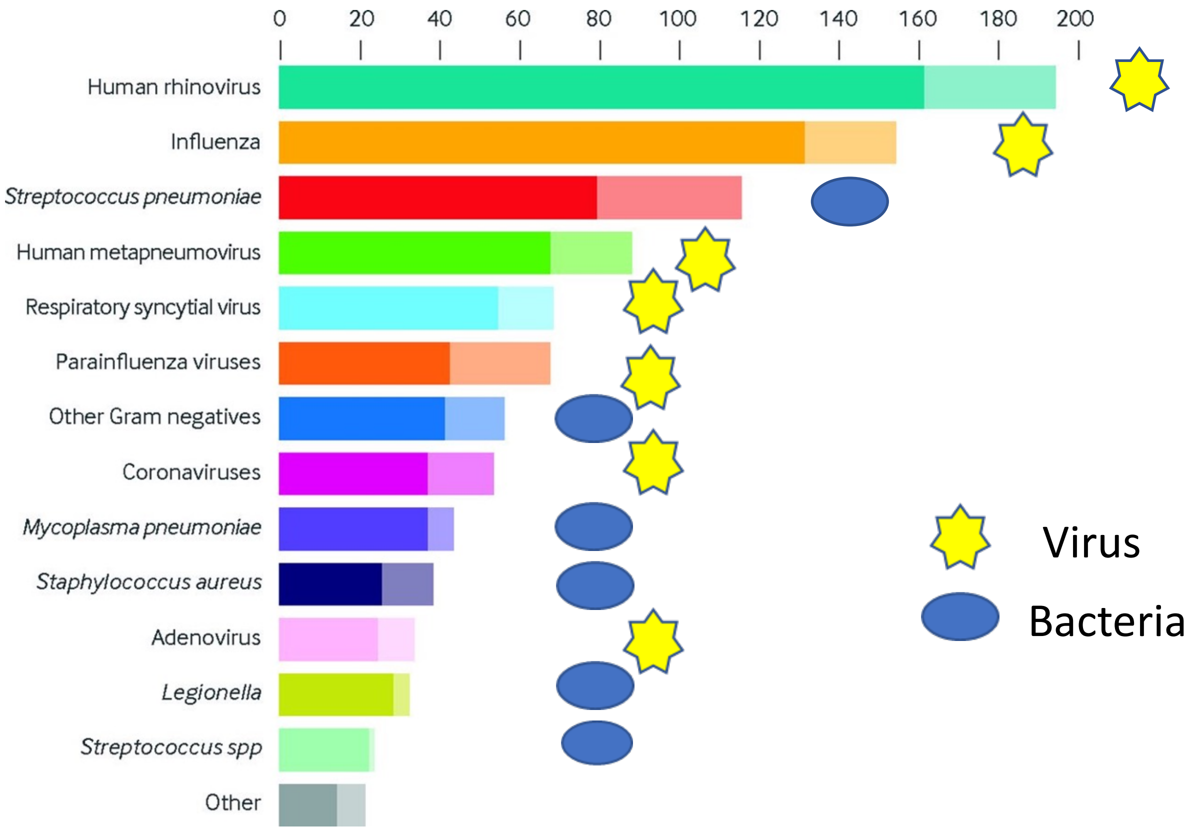
Under-5 deaths due to LRTI decreased by estimated 37% 2005-2015.



Global Burden of Disease LRTI Collaborators.
Lancet 2017

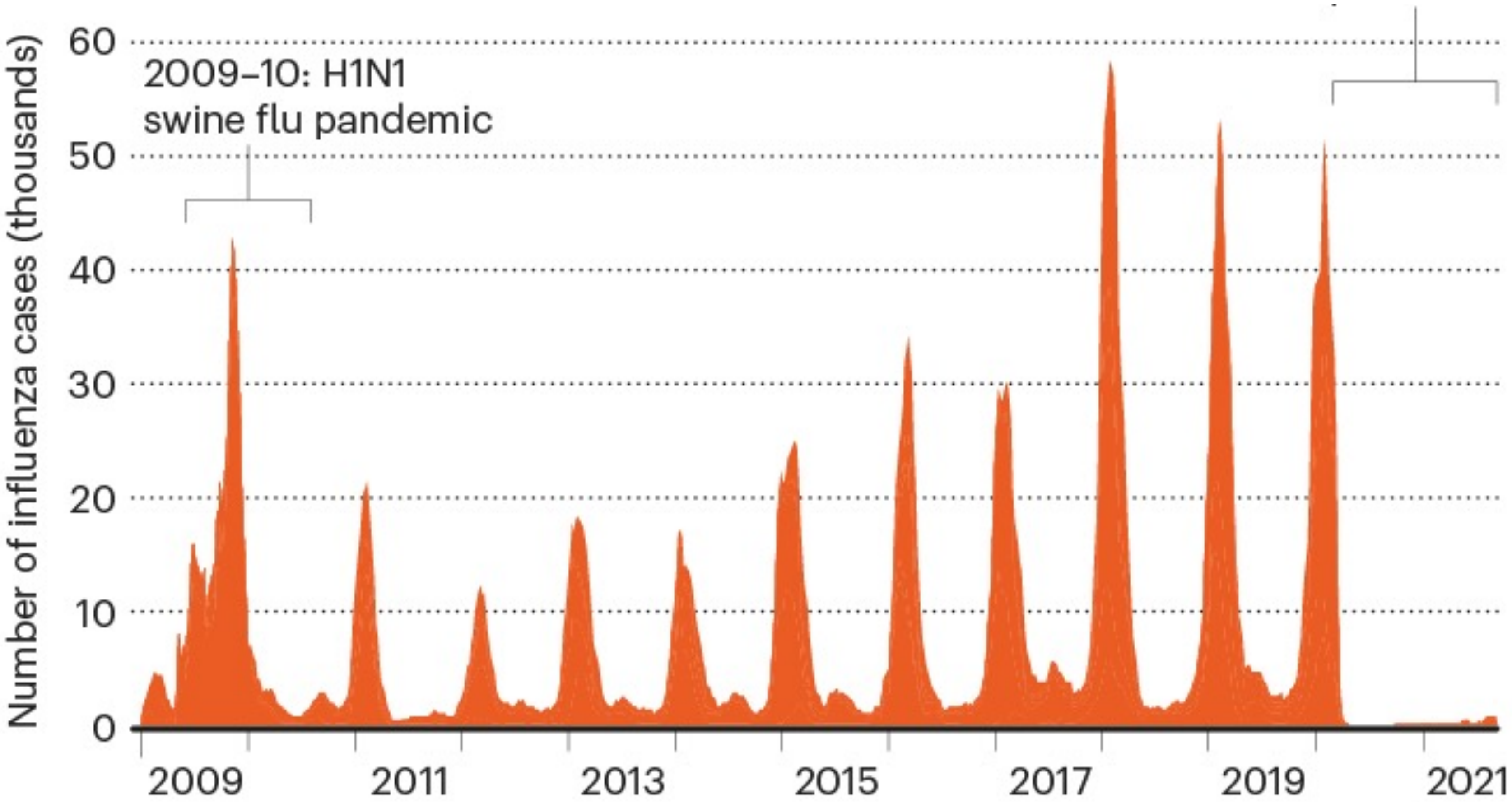
Viruses make up a large proportion of pneumonia, a much smaller proportion of deaths pre COVID-19.

- Respiratory syncytial virus (RSV) the most important for childhood mortality- 5-7% globally. Currently no vaccine.
- Influenza varies by season and year. Typically <2% of deaths, but can be much higher.



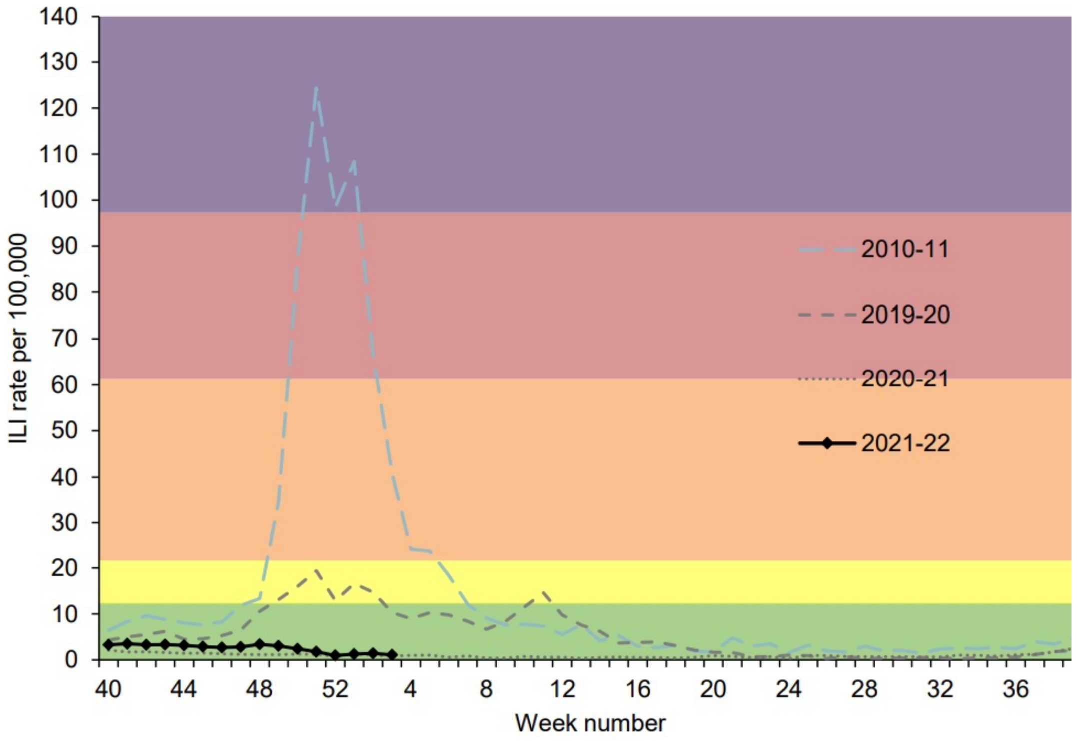
Wunderink R et al 2017 BMJ

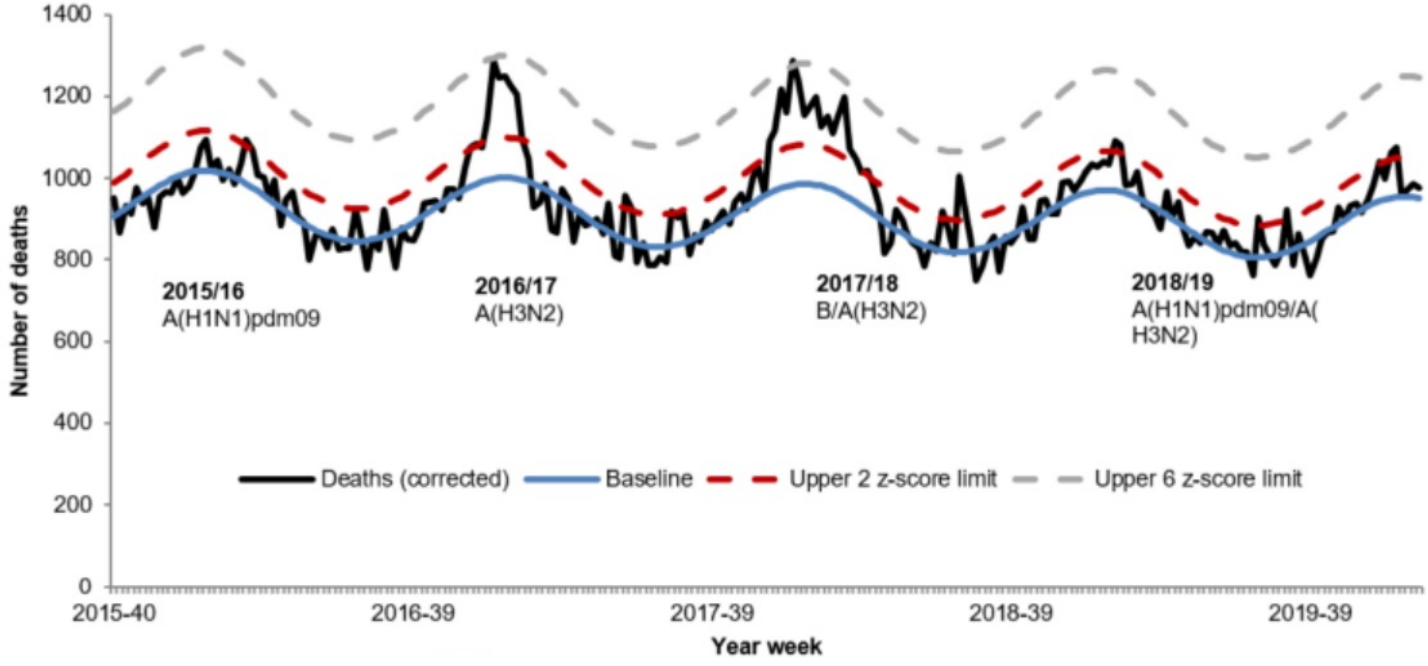
Global influenza annually since 2009-10 H1N1 (swine flu) pandemic.



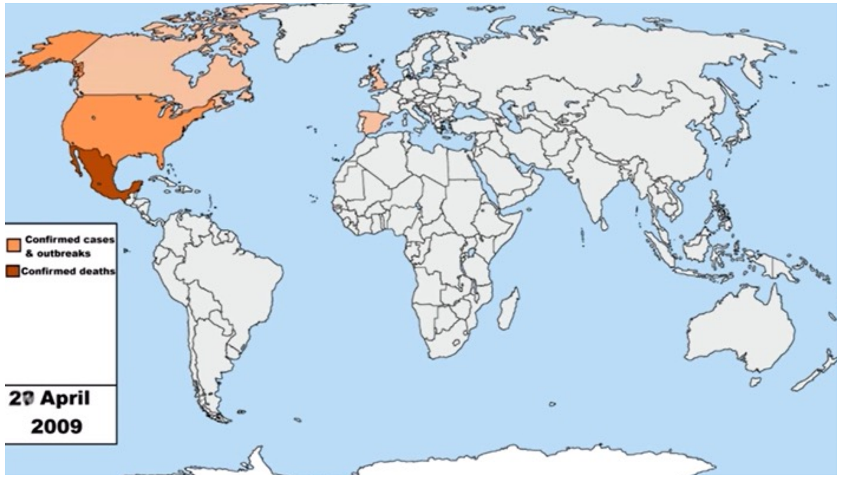
WHO / N Jones Nature 2021

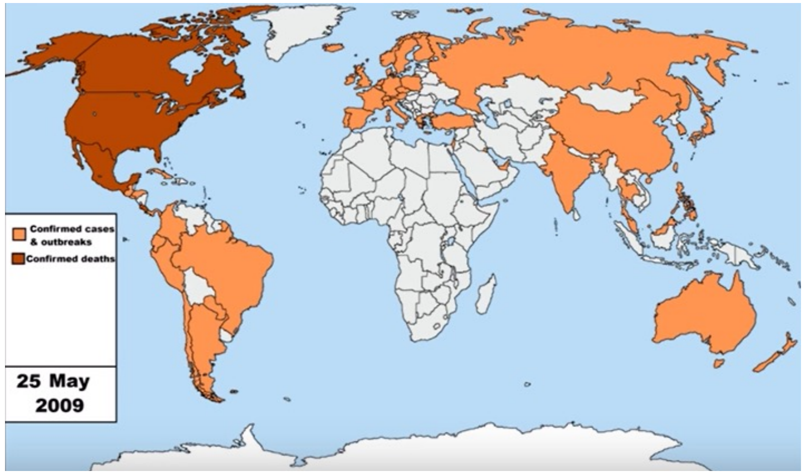
Influenza-like GP consultations in England (L); all cause excess mortality by year for London (R).

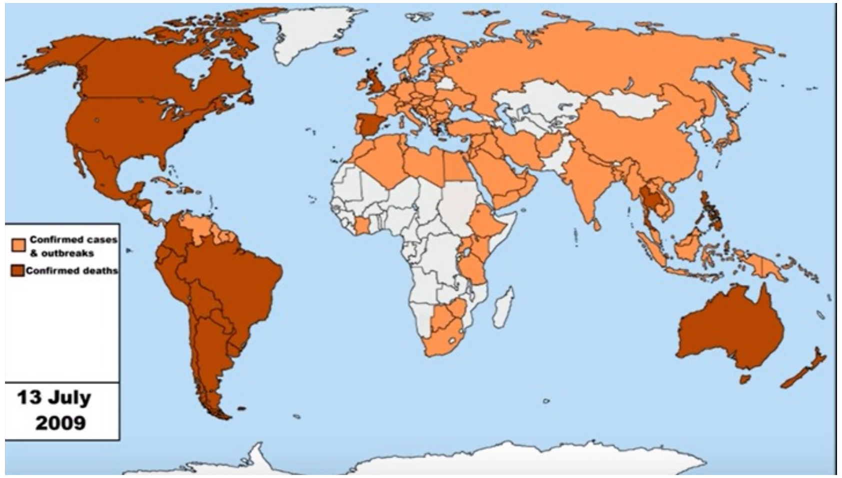




H1N1 2009. Officially 457 deaths in UK. 2 waves.







43-89 million cases 2009-10 (CDC)

8-18 thousand deaths (CDC)

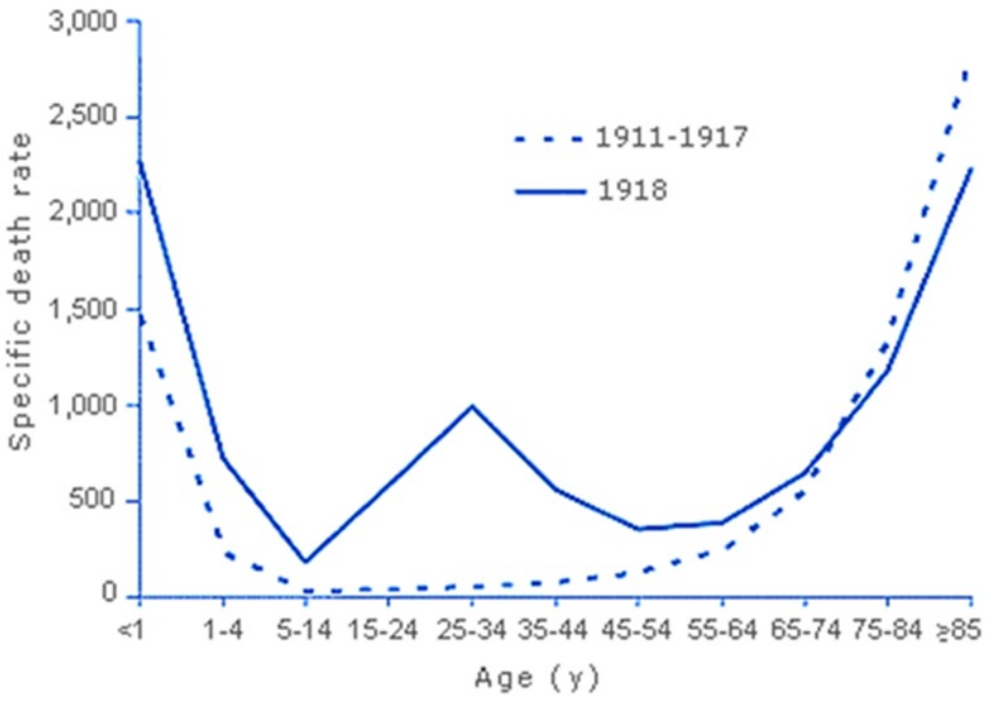
Wide estimates on numbers.

Mark Honigsbaum

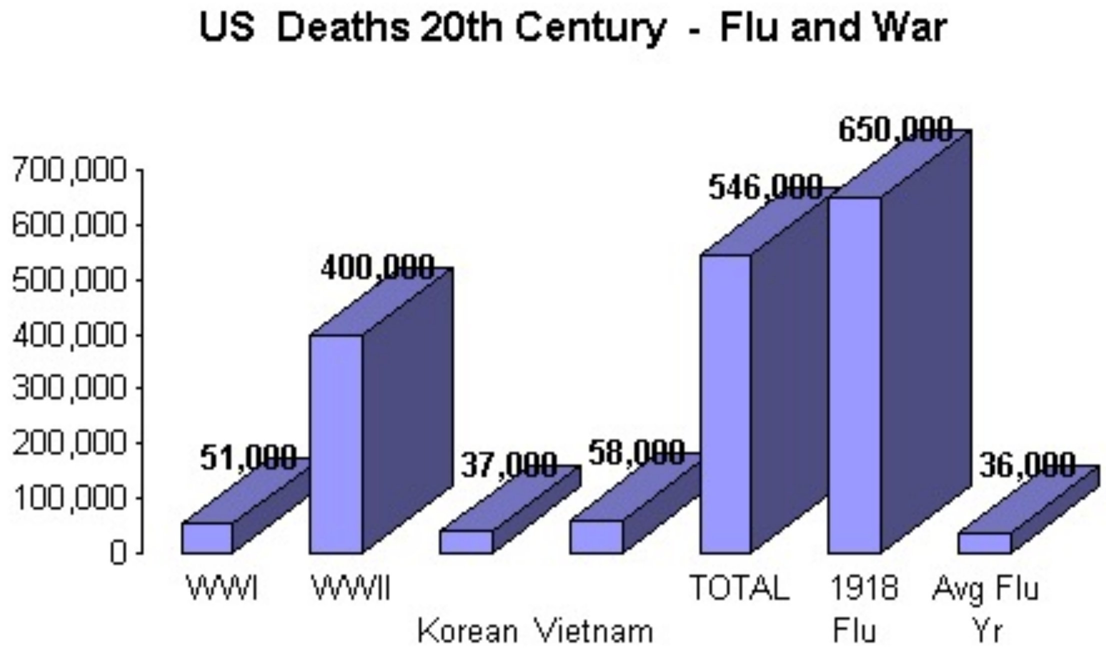
Influenza pandemic 1918 probably killed 50-100 million people globally. Primary and secondary pneumonia.

- People died of primary viral pneumonia.
- Secondary bacterial pneumonia killed a substantial proportion- possibly the majority.
- This was the pre-antibiotic era.

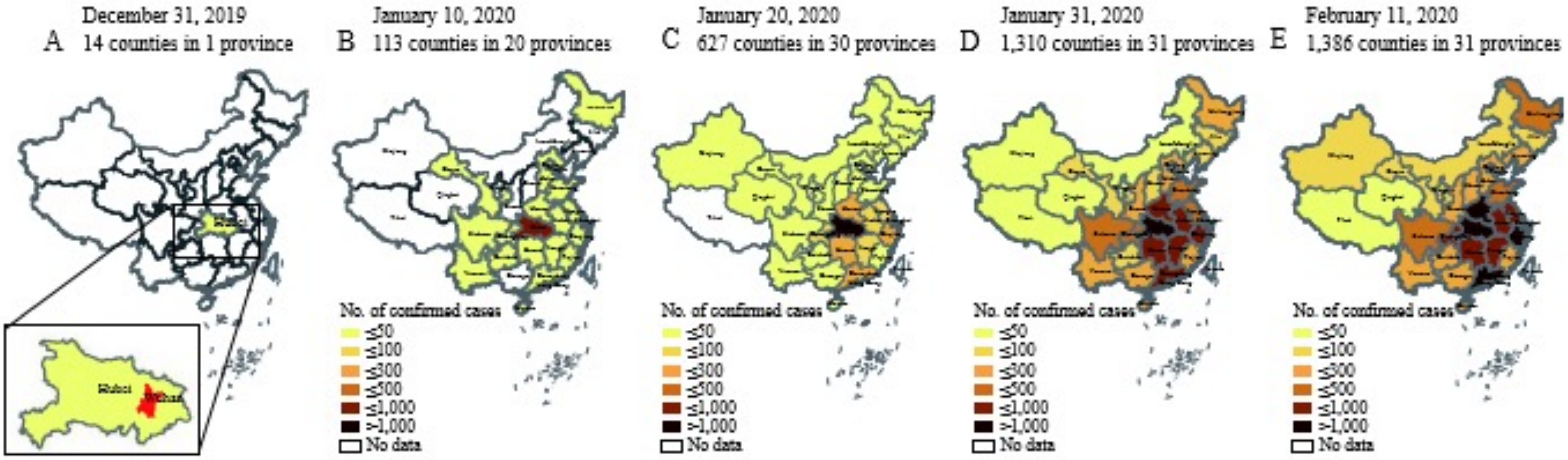
Influenza pandemic 1918. USA data.



CDC



COVID-19. China CDC Dec 31st-Feb 11th.



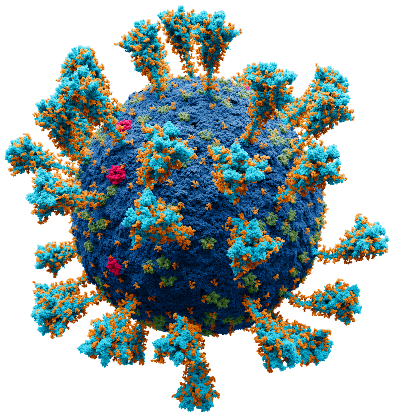
MERS-CoV, SARS and previous human coronaviruses.

- Four human coronaviruses 229E, NL63, OC43, HKU1.
- Generally cause colds, sore throats. Common, rarely serious.
- MERS-CoV from dromedaries to humans, and some human-to-human. 35% case fatality rate (CFR).
- One significant outbreak in South Korea 2015 (185 confirmed cases) brought under control.
- SARS 2002-3. Coronavirus from bats.
- Around 8422 cases, 774 deaths. 11-15% CFR.

Frederick Goodall 1880

COVID-19 in the UK. Steady move from social to medical countermeasures in each wave.

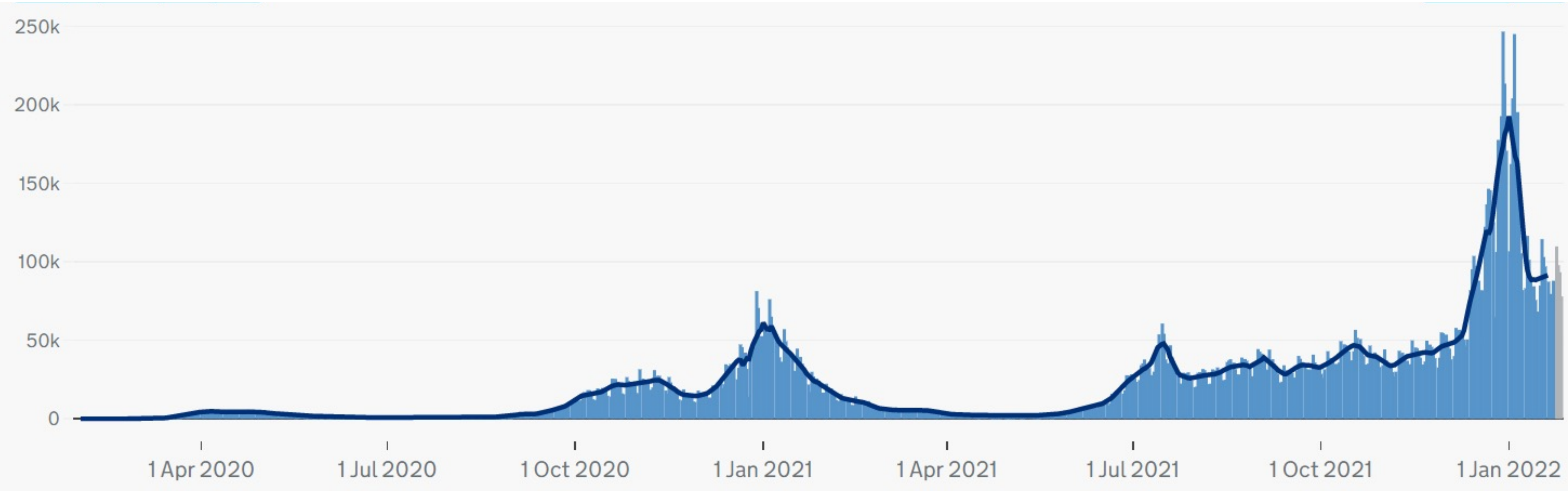
- Wave 1 very limited diagnostic tests, no treatment, no vaccine, no population immunity.
- Therefore **entirely** dependent on social measures to limit damage cases, hospitalisations, deaths.
- Alpha wave. Good diagnostic tests, better in-hospital treatment, only early vaccine rollout, no anti-virals. Still heavily dependent on social measures.
- Delta wave. Vaccines rolled out, so high population immunity. More limited need for social measures.
- Omicron wave. Vaccine plus booster. Some antivirals. Less severe variant (but still substantial hospitalisation).



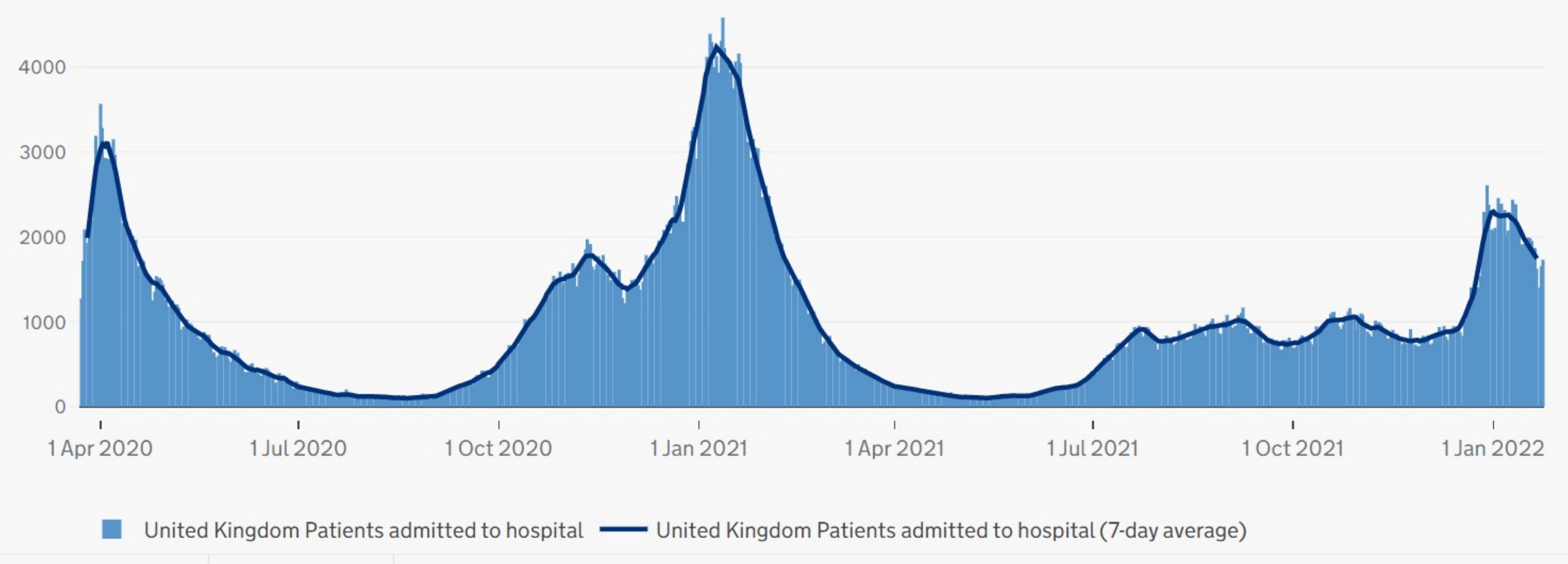
A. Solodovnikov, V. Arkhipova

COVID-19 cases over time, UK.

In wave 1 testing capacity was much smaller, so an underestimate. UKHSA

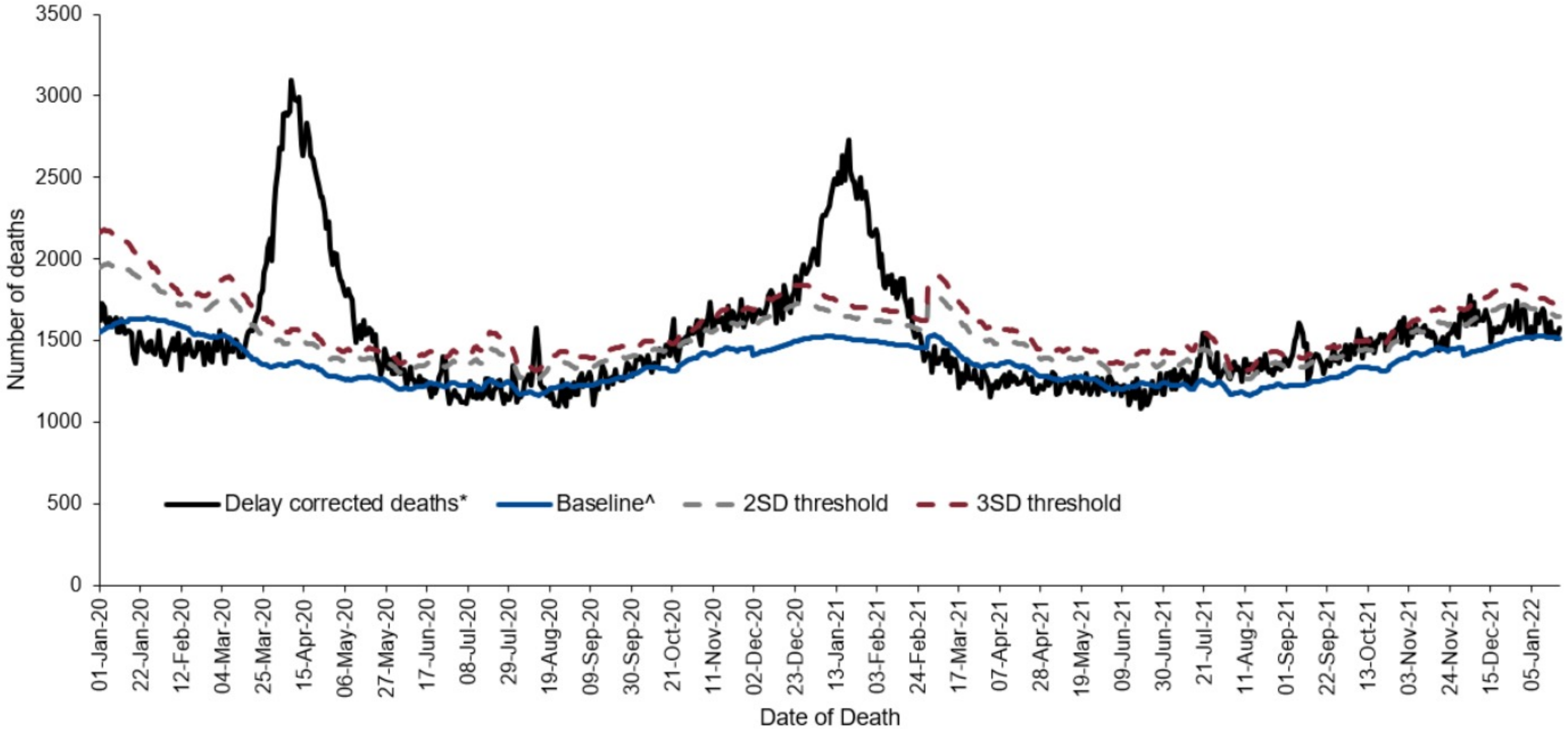


Patients admitted to hospital with COVID-19. 4/20-1/22. UKHSA.



Daily excess all-cause deaths, all ages. 1/1/20-19/1/22.
176,813 deaths due to COVID-19 on death certificate to date.

UKHSA/ONS.



Infections transmitted via the respiratory route.

- An effective route of transmission, can affect all part of the body.
- Medical countermeasures- drugs, vaccines and diagnostics- have substantially reduced the impact of many infections via this route.
- Simple social measures and ventilation can reduce transmission.
- They will remain a major cause of hospitalisation and mortality.

CDC