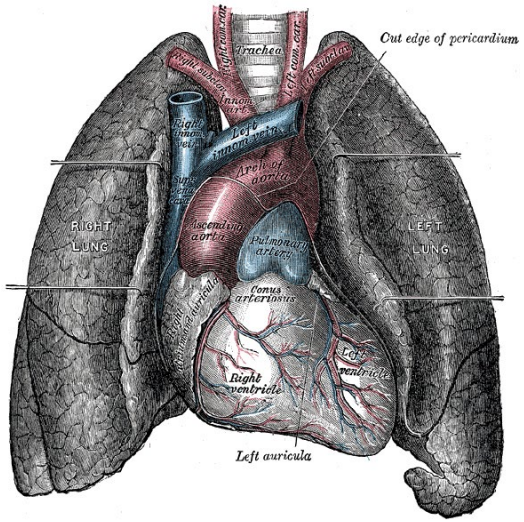
Infections of the lungs and heart.

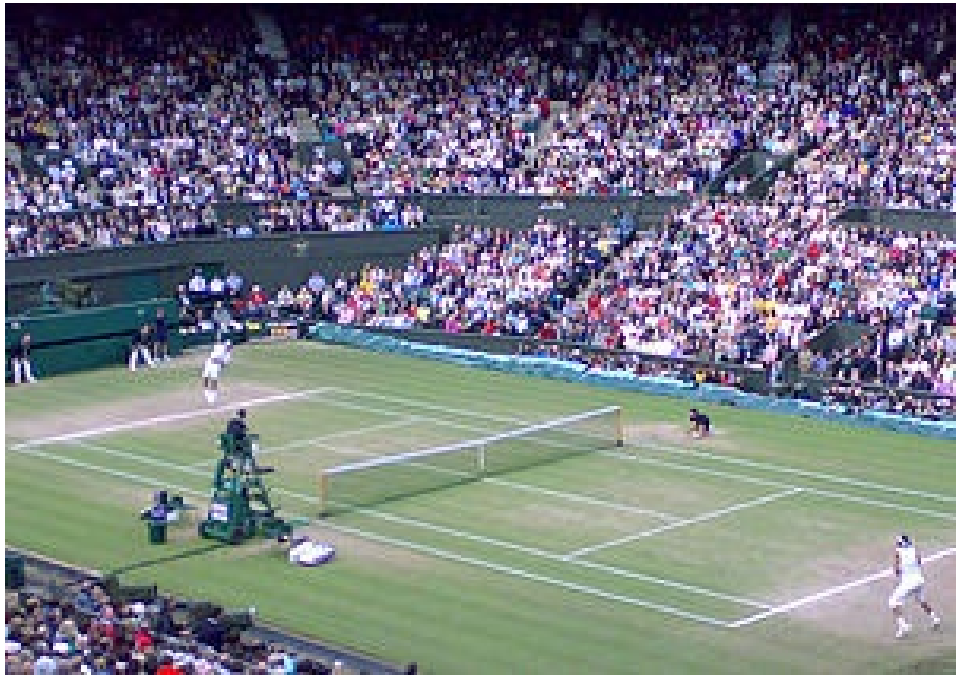


Christopher Whitty

Gresham College 2019

The main function of the lungs and heart is to get oxygen from the air to the tissues, and CO_2 out.

- 50-140 m^2 (up to a tennis court), over 200km of airways, inhale about 11,000 litres a day.
- At its base about 0.5–2 µm thick, folded into about 300 million alveoli.
- Infections can kill by stopping oxygen transfer, getting into the blood (sepsis).

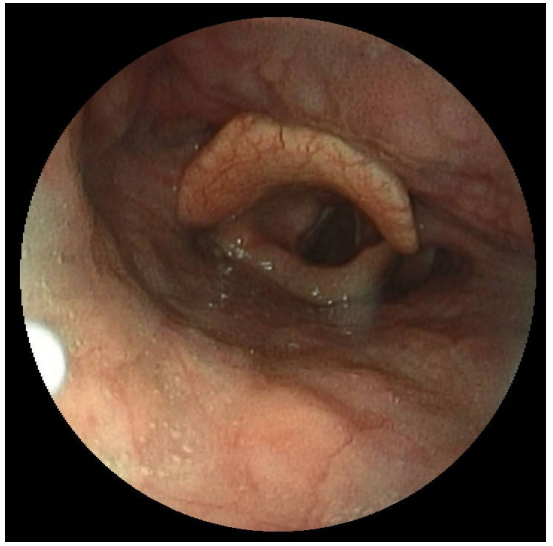


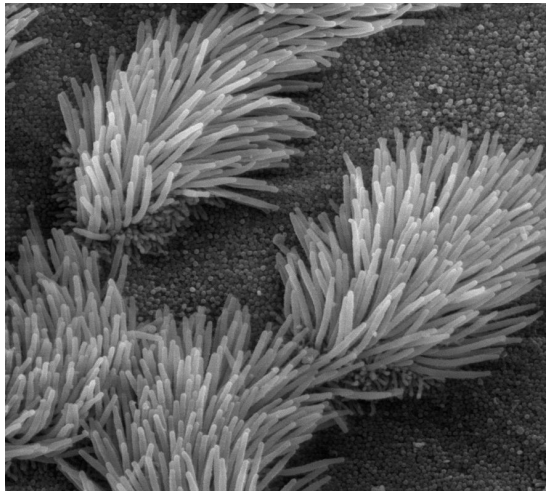
Federer v Nadal 2008.
David Underdown.

Multiple layers of defence for the lung.
But there has to be airflow.

Include

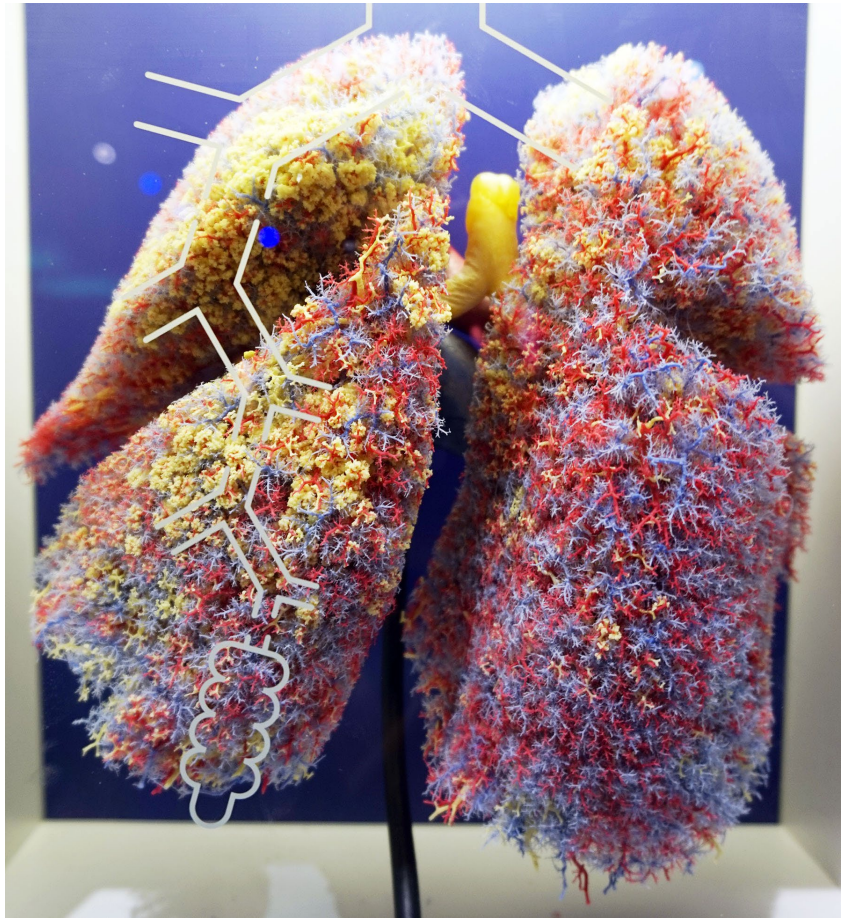
- Epiglottis.
- Cough reflex.
- Muco-ciliary escalator.
- Mucus secretion from goblet cells with defensins (proteins).
- Immunoglobulin A.
- Macrophages which engulf bacteria.
- Dendritic cells to present antigens to the adaptive immune system B- and T-cells.





Infections and the lung.

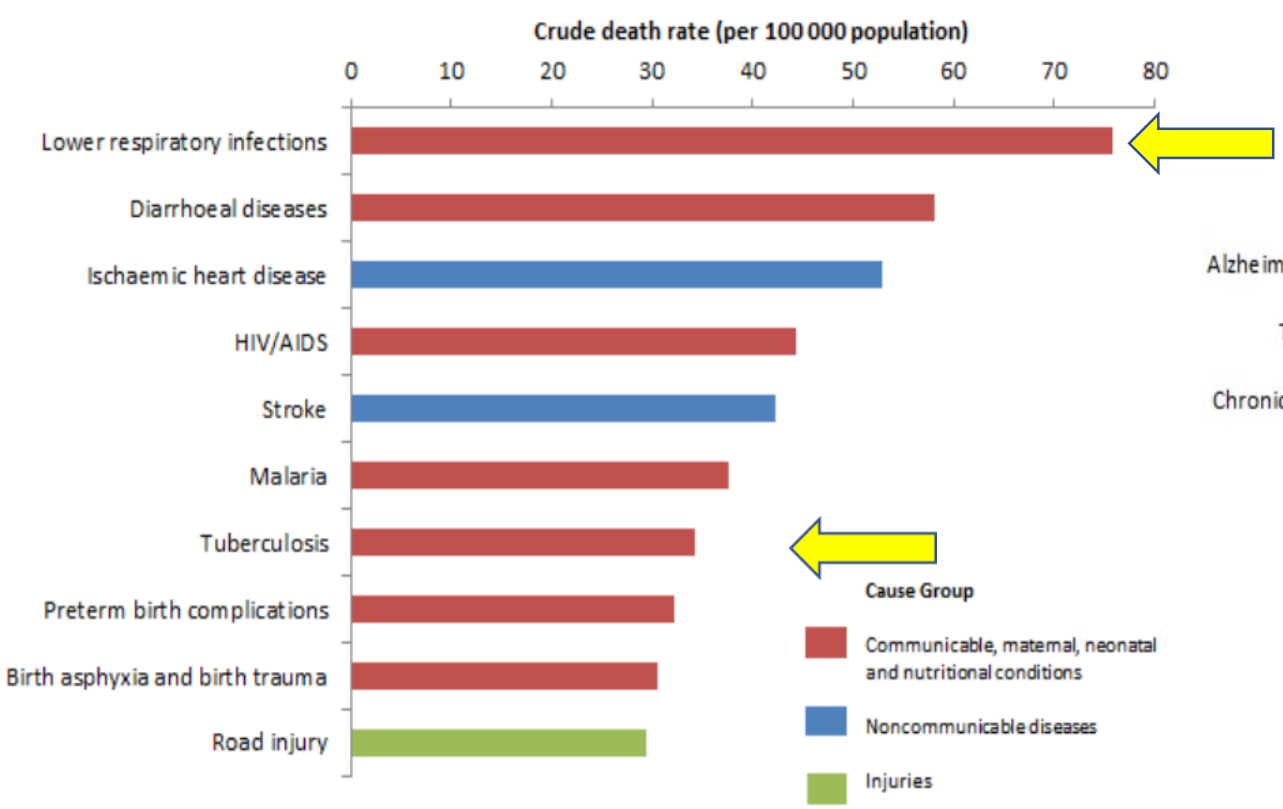
- Within the lung. Lower respiratory tract infection (LRTI, LRI), pneumonia, bronchitis.
- Between the lung and the chest wall- effusion.
- Affecting the chest wall / diaphragm ability to breathe- motor system.



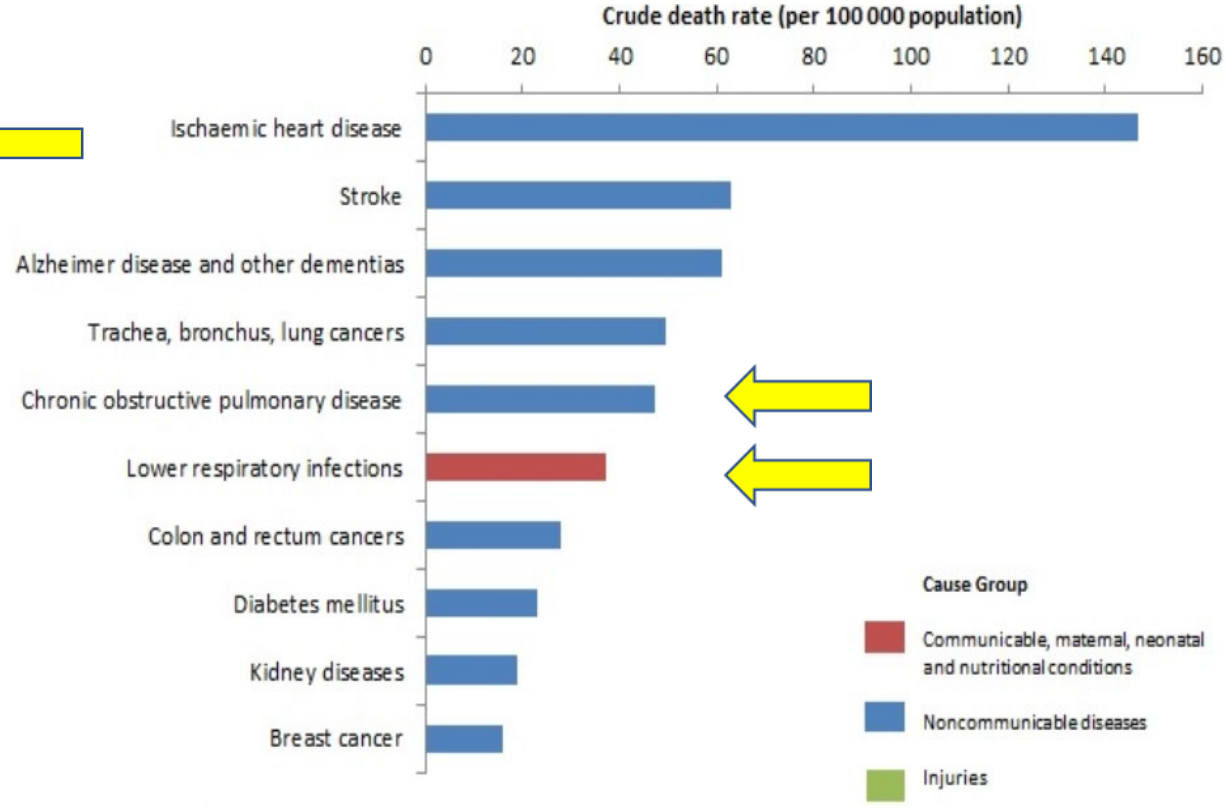
Tiia Monto, Wiki

Top 10 causes of death: WHO 2016 data.
3 million people a year die from lower respiratory infections.

Low income countries

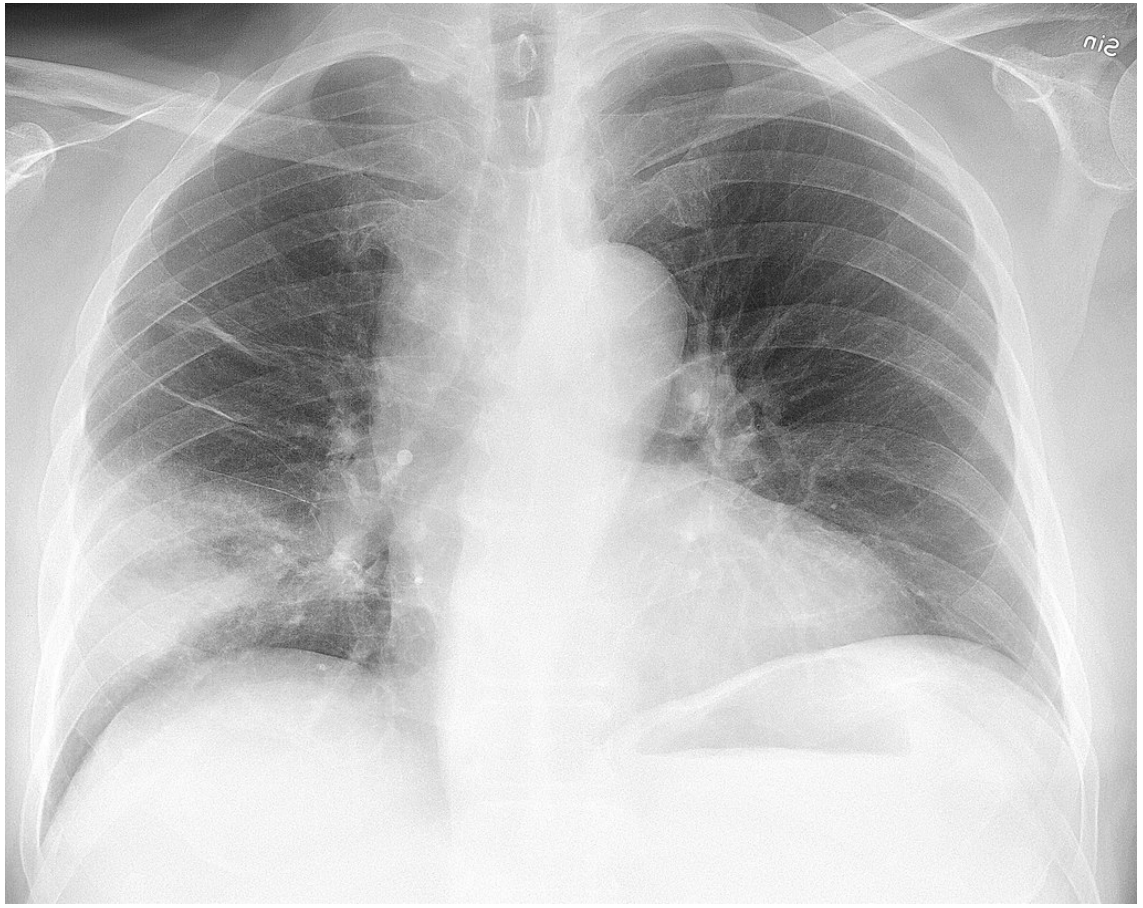


High income countries



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, the very poor and the immunosuppressed.



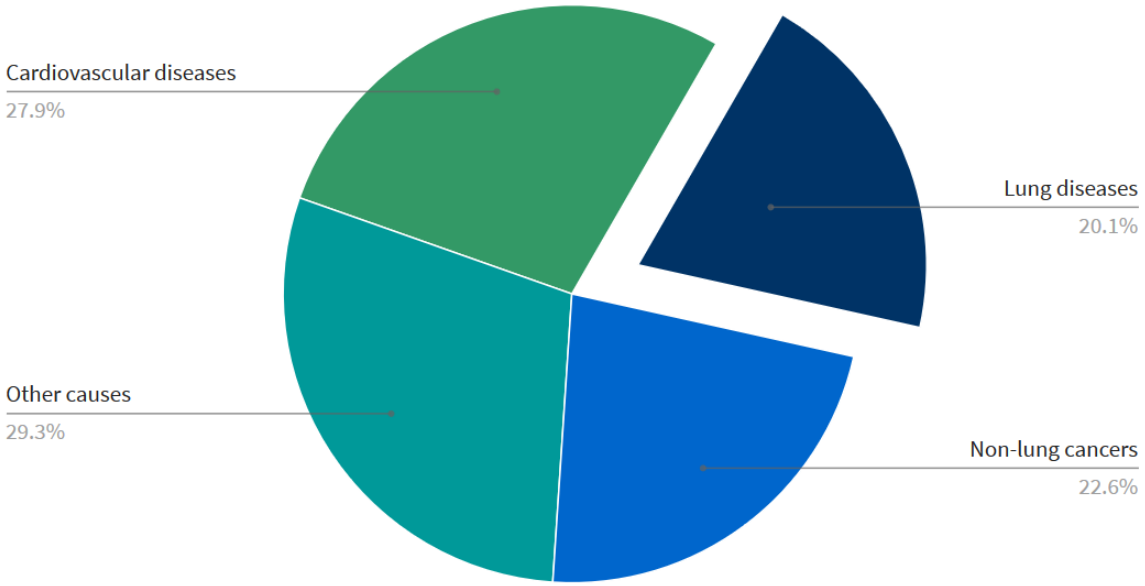
Mikael Häggström

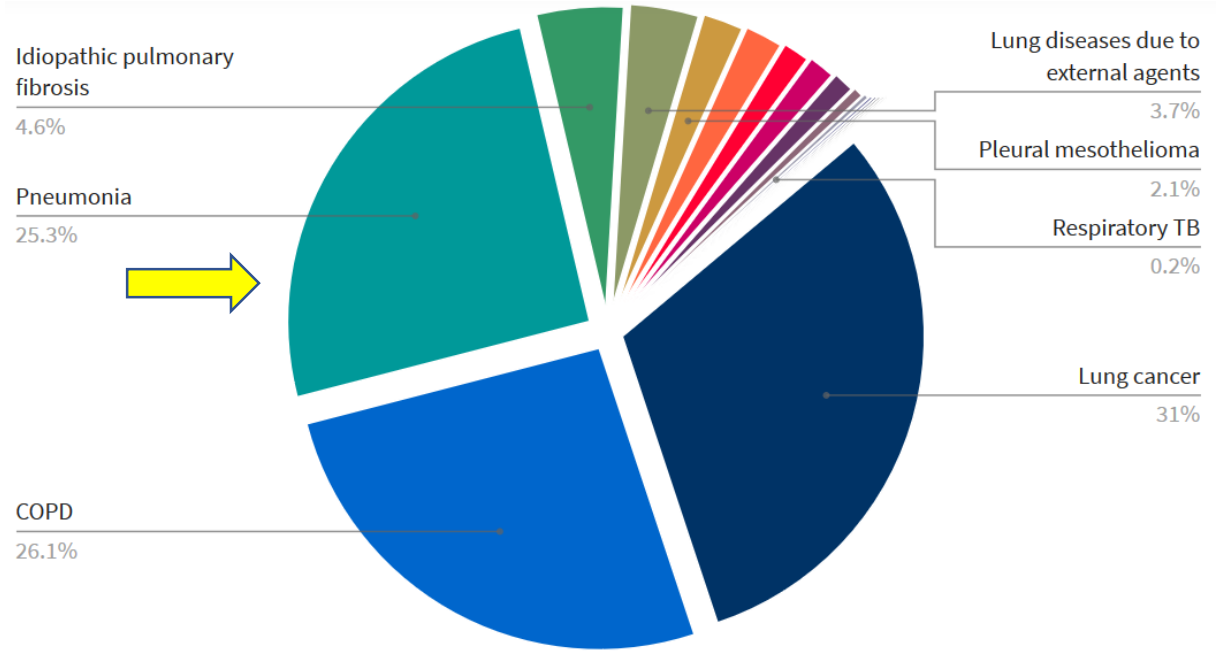
Other than age and poverty the risk factors for pneumonia:

- Smoking, active and passive (2-4x).
- Air pollution (esp. PMs).
- Other health conditions, including asthma, cystic fibrosis, or a heart, kidney or liver condition.
- A weakened immune system, e.g. as a result of a recent illness, advanced HIV, having chemotherapy, or medication following organ transplant.

Frederick William Fairholt

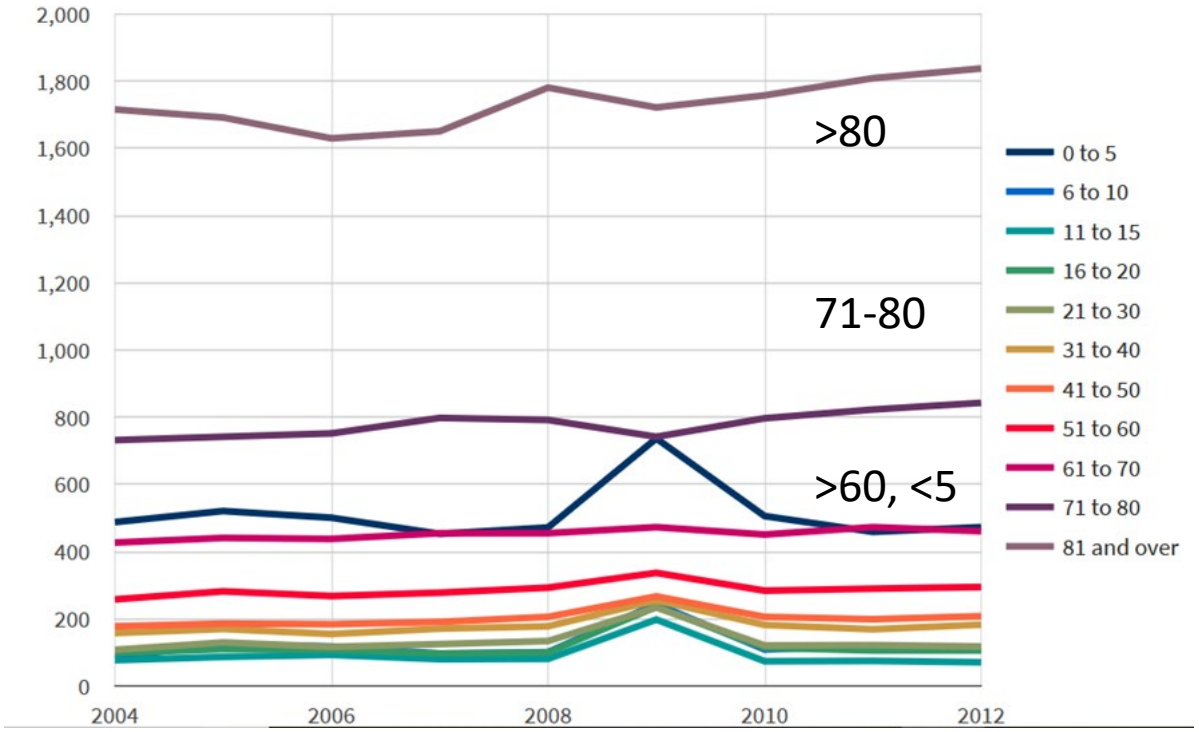
Around a quarter of lung related deaths in the UK pneumonia. In high income countries most are in adults.



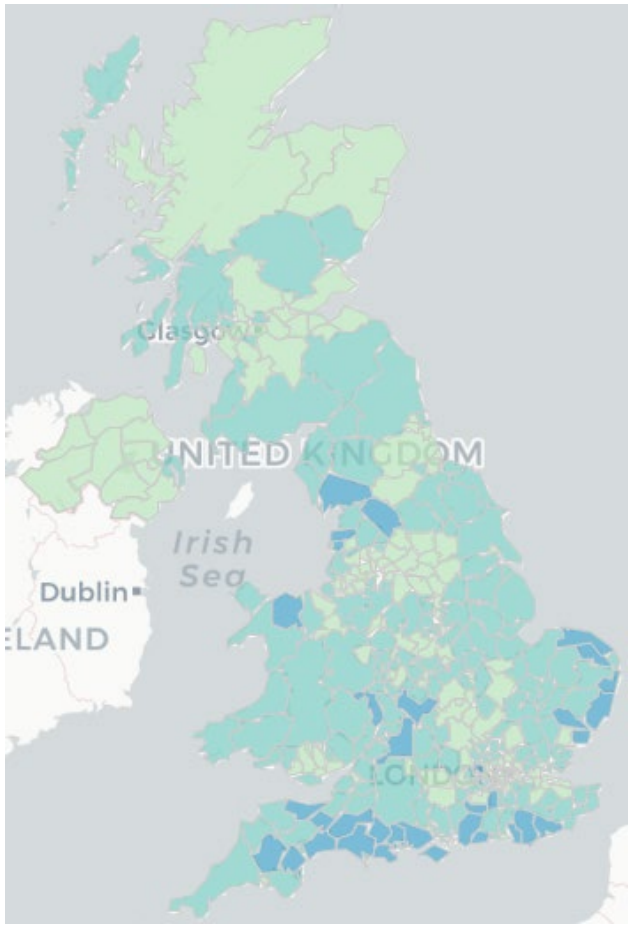


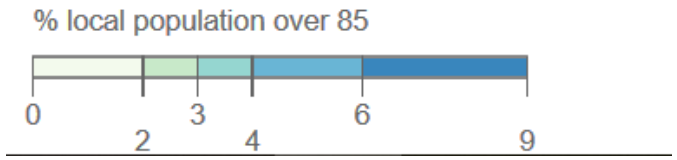
British Lung Foundation mortality data.

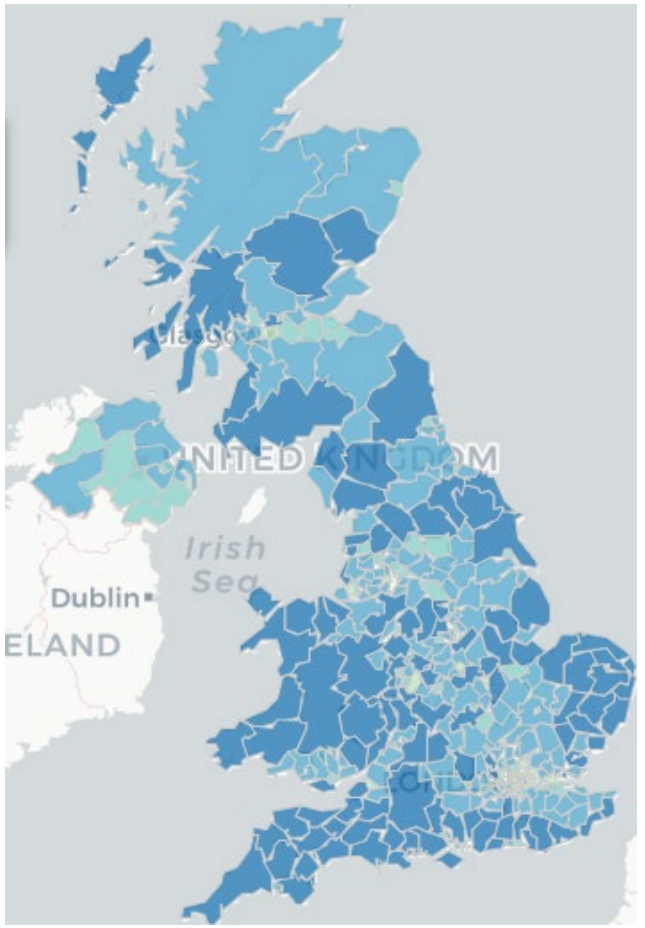
Pneumonia and age.



People/100,000 pneumonia. BLF.



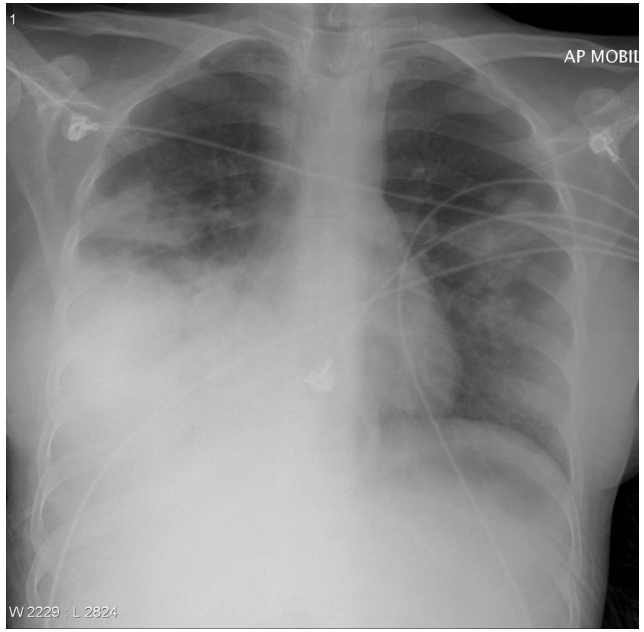


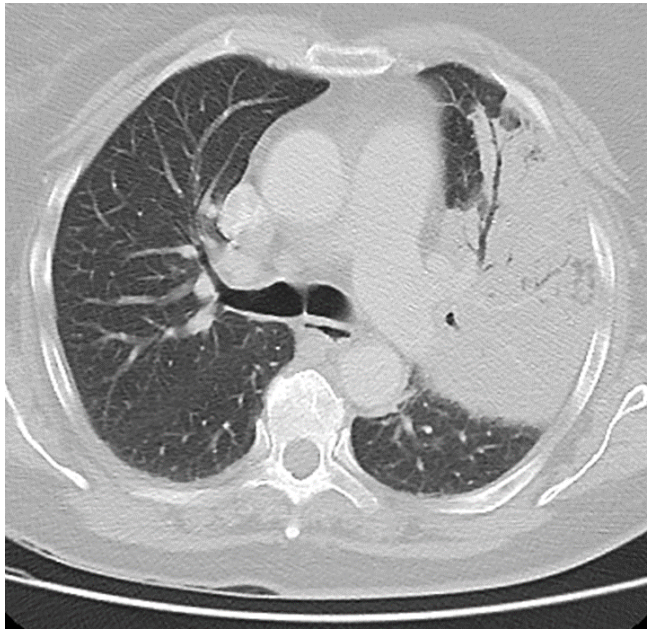


Population >85 2016-2036. ONS

The most common bacterial cause is pneumococcal pneumonia.

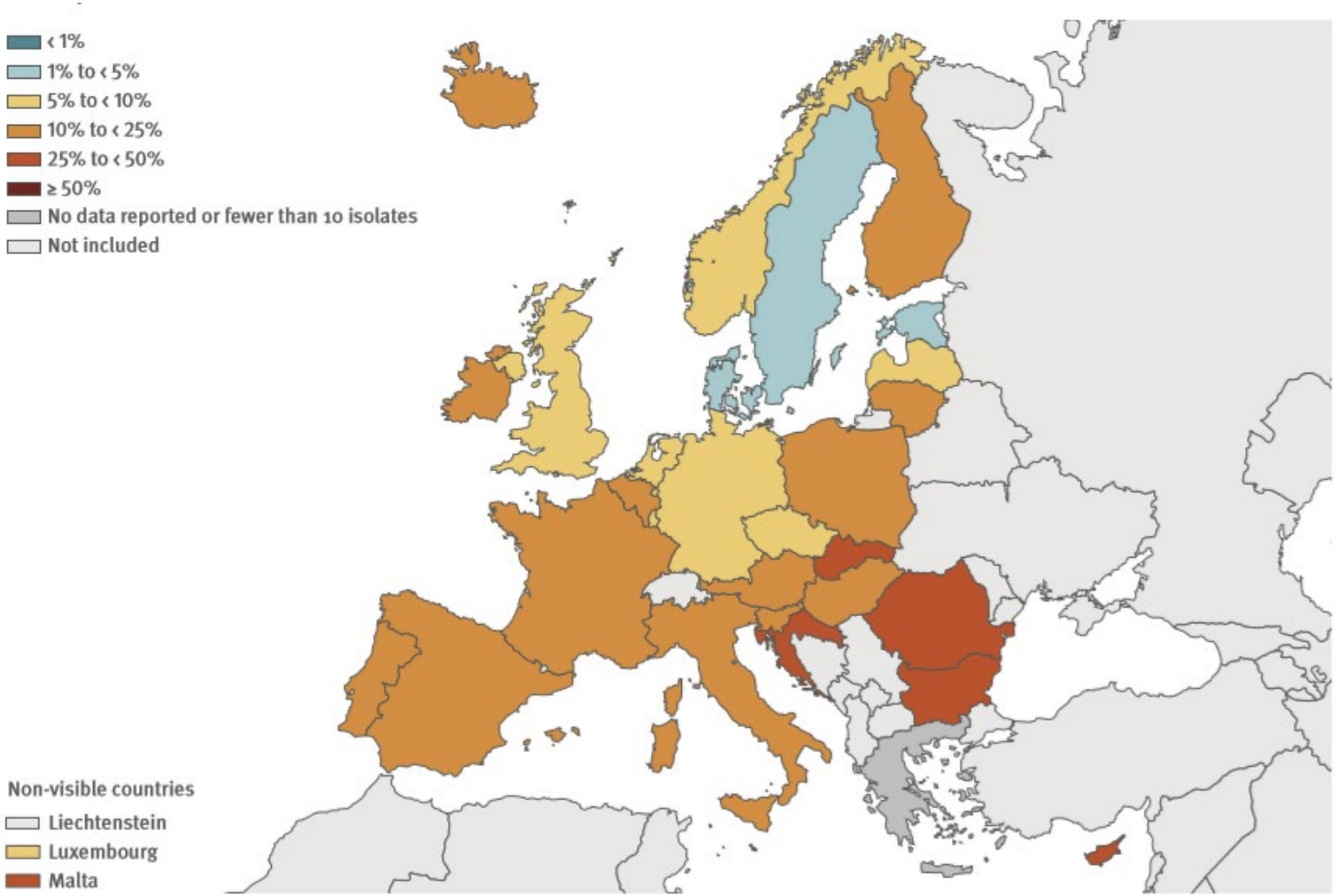
- *Streptococcus pneumoniae* pneumonia. Usually lobar.
- In adults this is the most common cause overall.
- Most common cause of mortality in adults and children.
- Treatment antibiotics.





Jack Ren (L), Chris O'Donnell Radiopaedia.

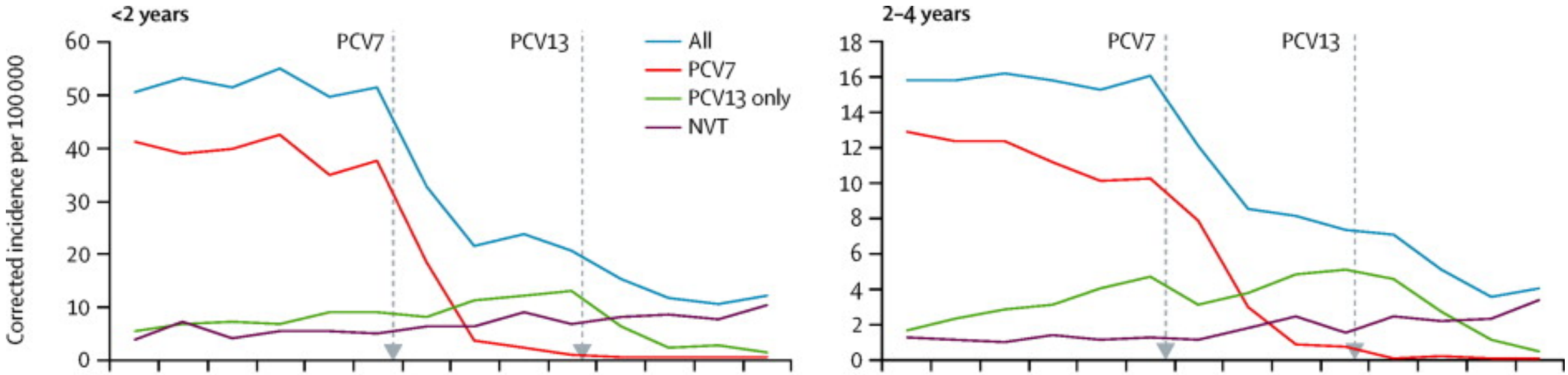
Antibiotic resistance a clear and present danger.
Macrolide resistance to pneumococcus- ECDC 2017 data.
Penicillin resistance varies from <1% to 45%. UK 5%.



Pneumococcal conjugate vaccine.

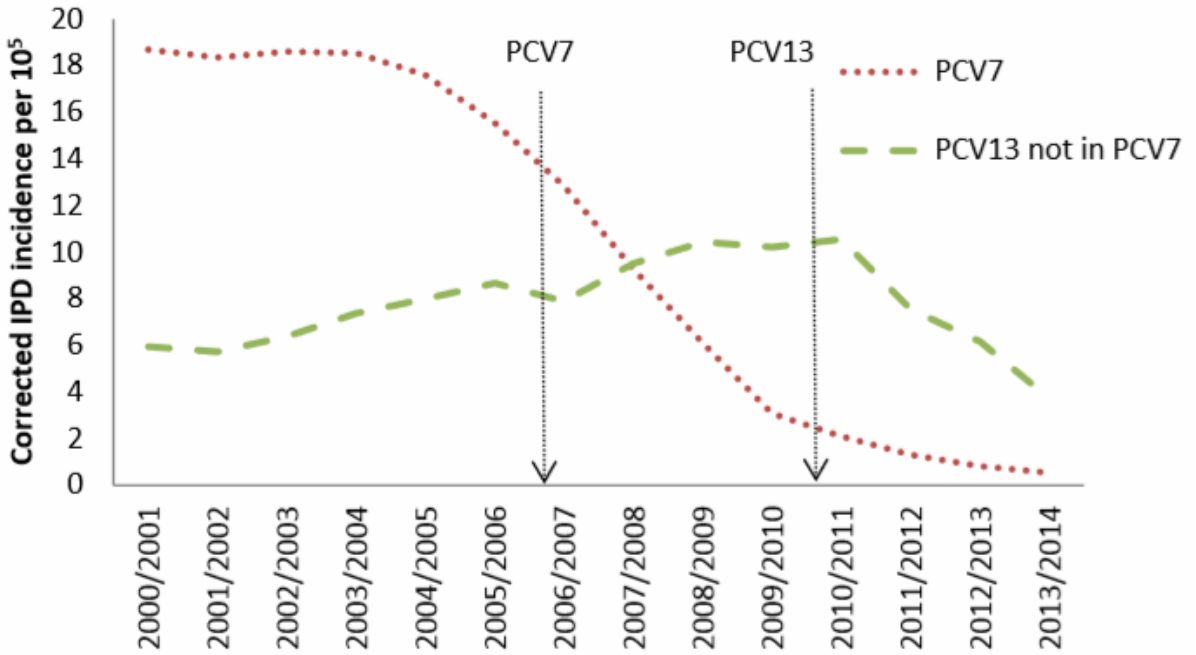
(PHE E&W data- *Waight P et al Lancet ID 2015*).

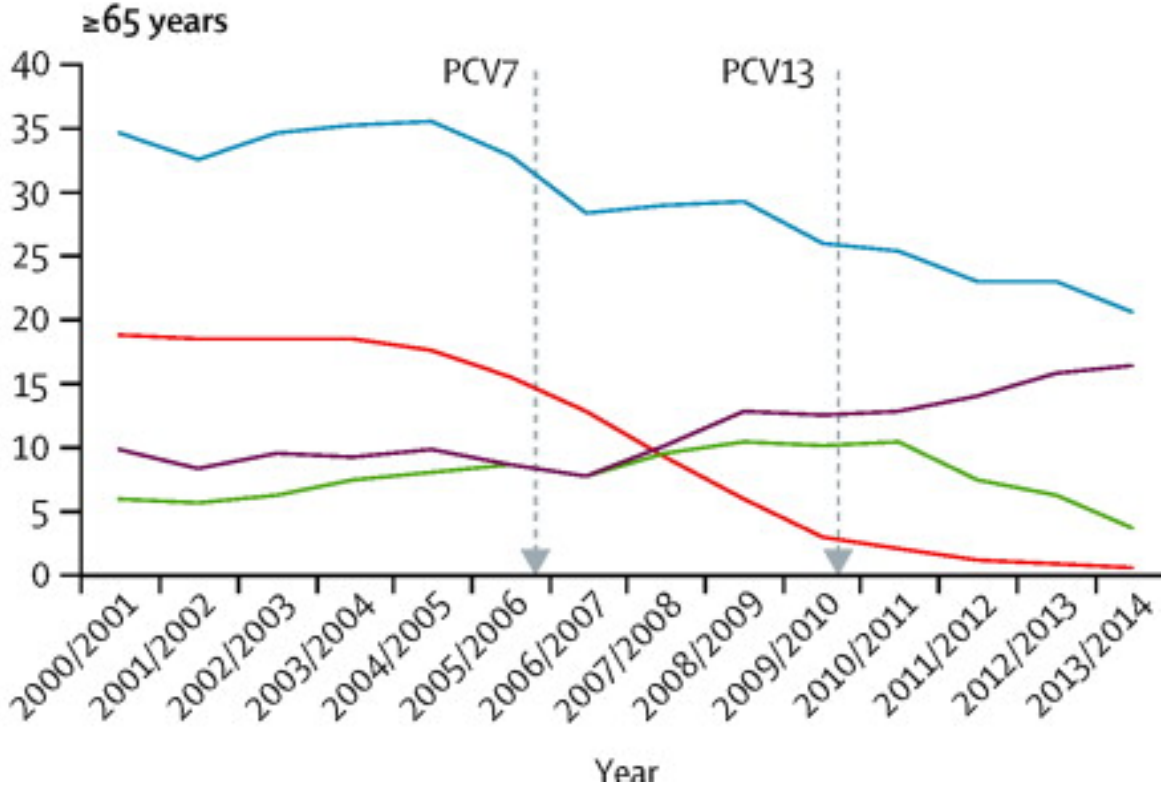
- PCV7 (7-valent) introduced UK 2006.
- Vaccine-type invasive pneumococcal disease decreased 86%.
- Significant increase in non-PCV7 disease.
- PCV13 replaced PCV7 in April, 2010. Further 32% reduction.
- Compared with pre-PCV7 baseline, there was a 56% overall decrease.



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

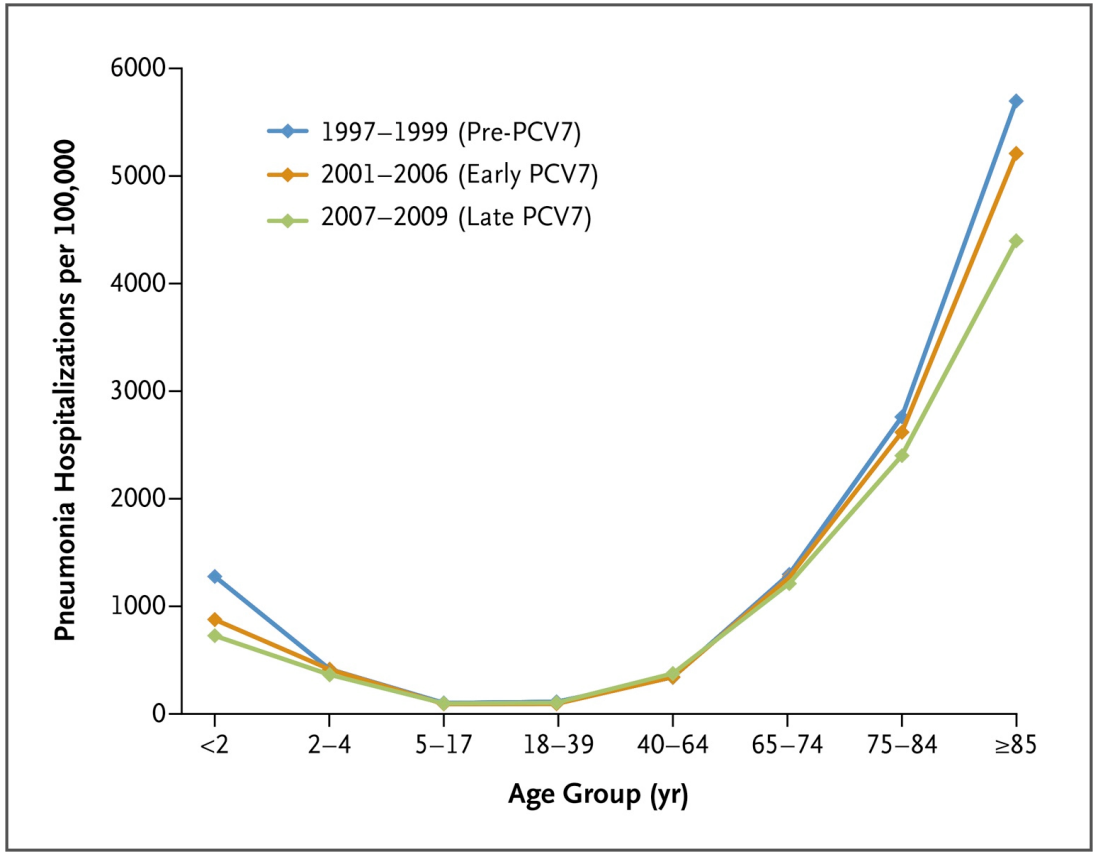
Adults over 65 get pneumococcal polysaccharide vaccine (PPV23) since 2003.

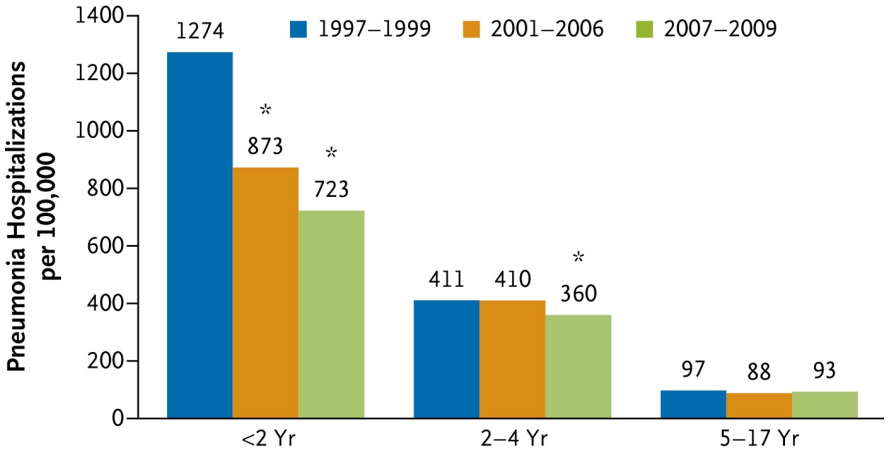


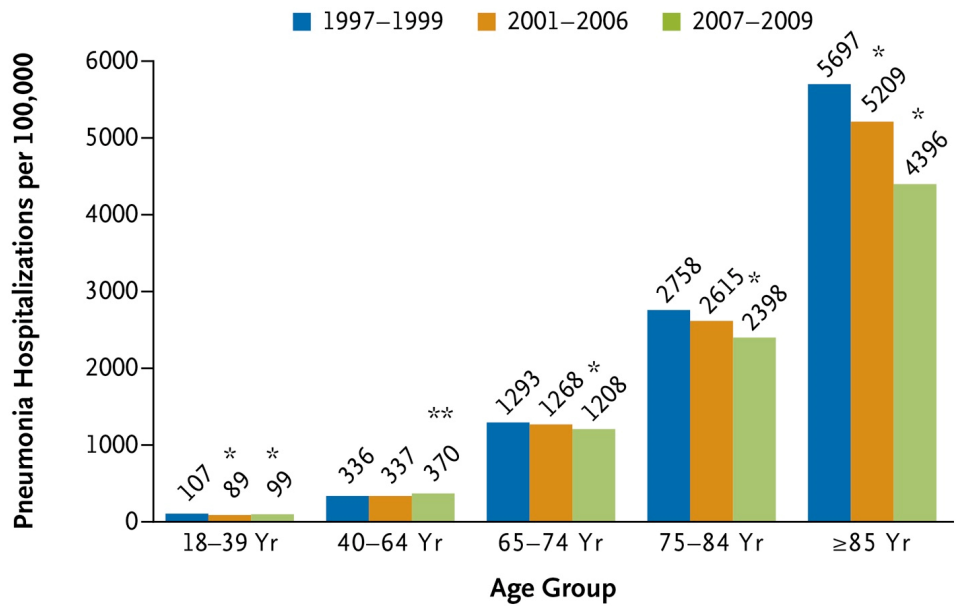


Hospitalisations for pneumonia following PCV7 in USA, by age.

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

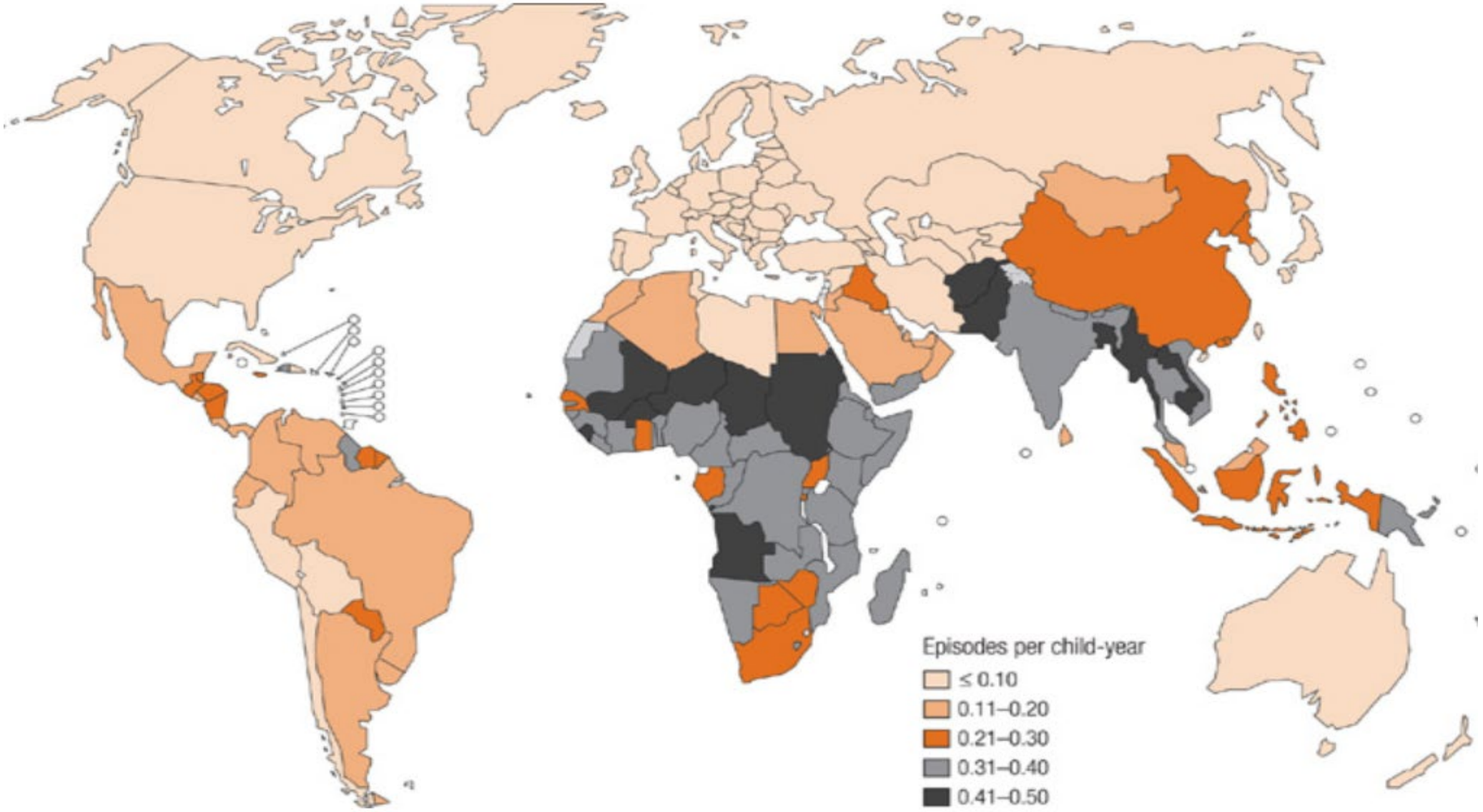






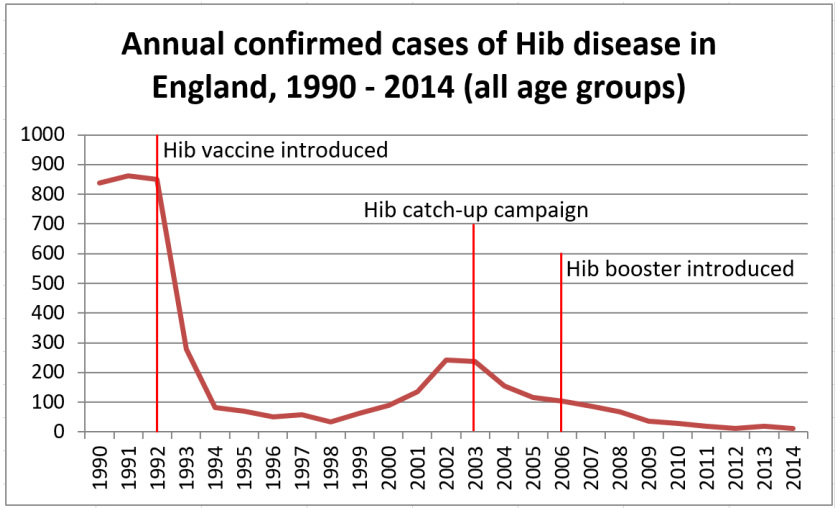
Griffin M et al NEJM 2013.

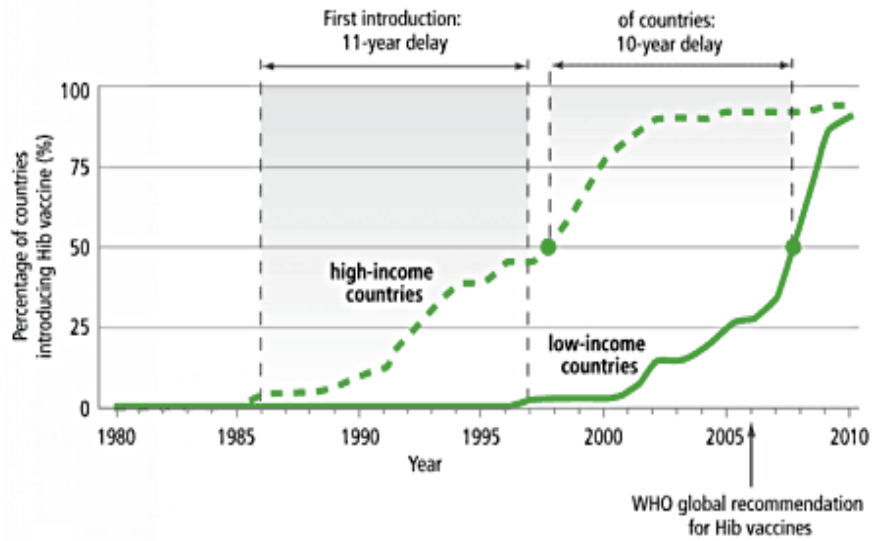
Around 700,000 deaths from pneumonia in children <5 globally.
Incidence of pneumonia in children <5 (WHO).



Vaccine preventable pneumonia deaths in children: pneumococcus and Hib.

- Pneumococcal pneumonia contributes around 56% of these deaths.
- *Haemophilus influenzae* type b (Hib) bacteria around 8% (not common in adults). Vaccine highly effective.
- Pentavalent vaccine against five major infections: Hib, diphtheria, tetanus, pertussis (whooping cough), hepatitis B.
- Deployed globally since 2014 (GAVI).
- In UK has reduced from over 800 to around 20 Hib cases a year.



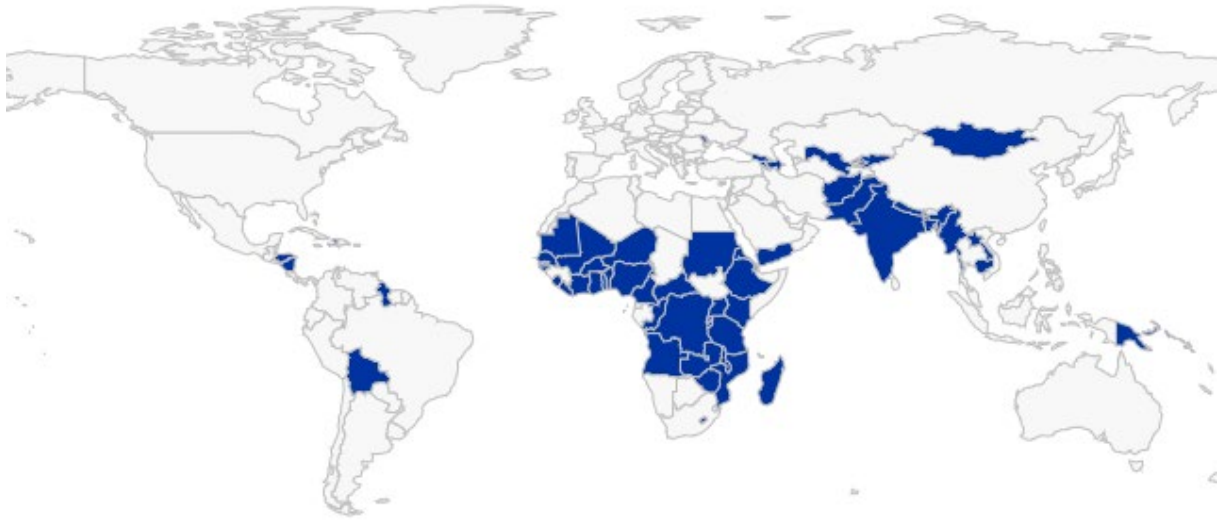


PHE/GAVI

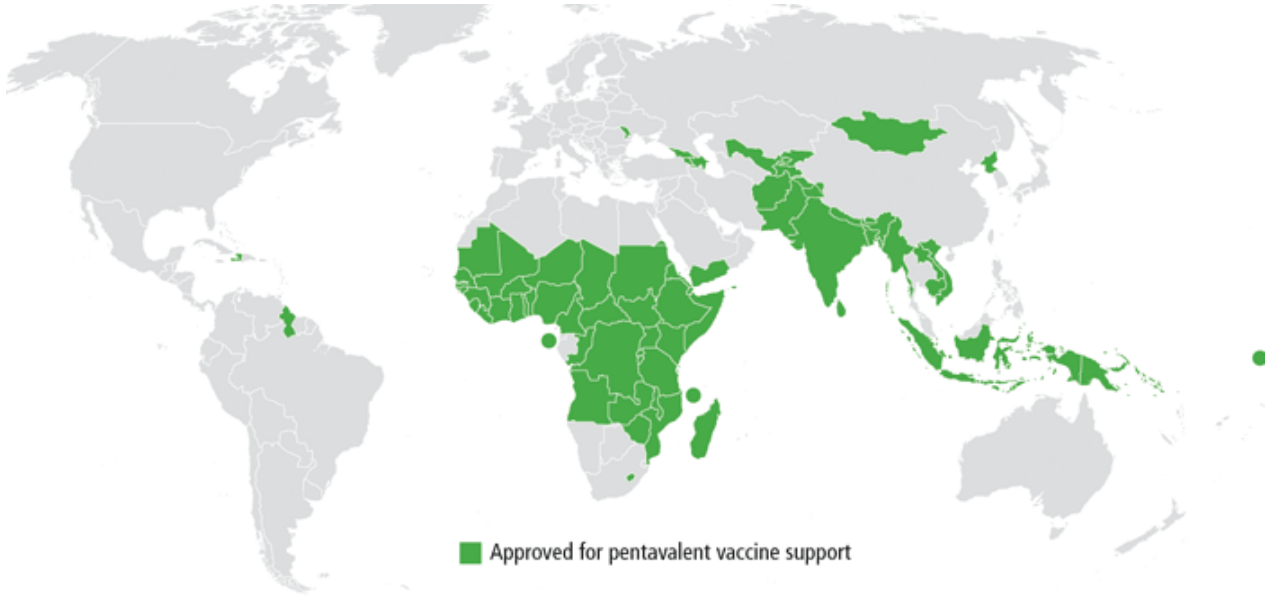
GAVI Alliance support for vaccines against LRTI.

UK one of the largest supporters.

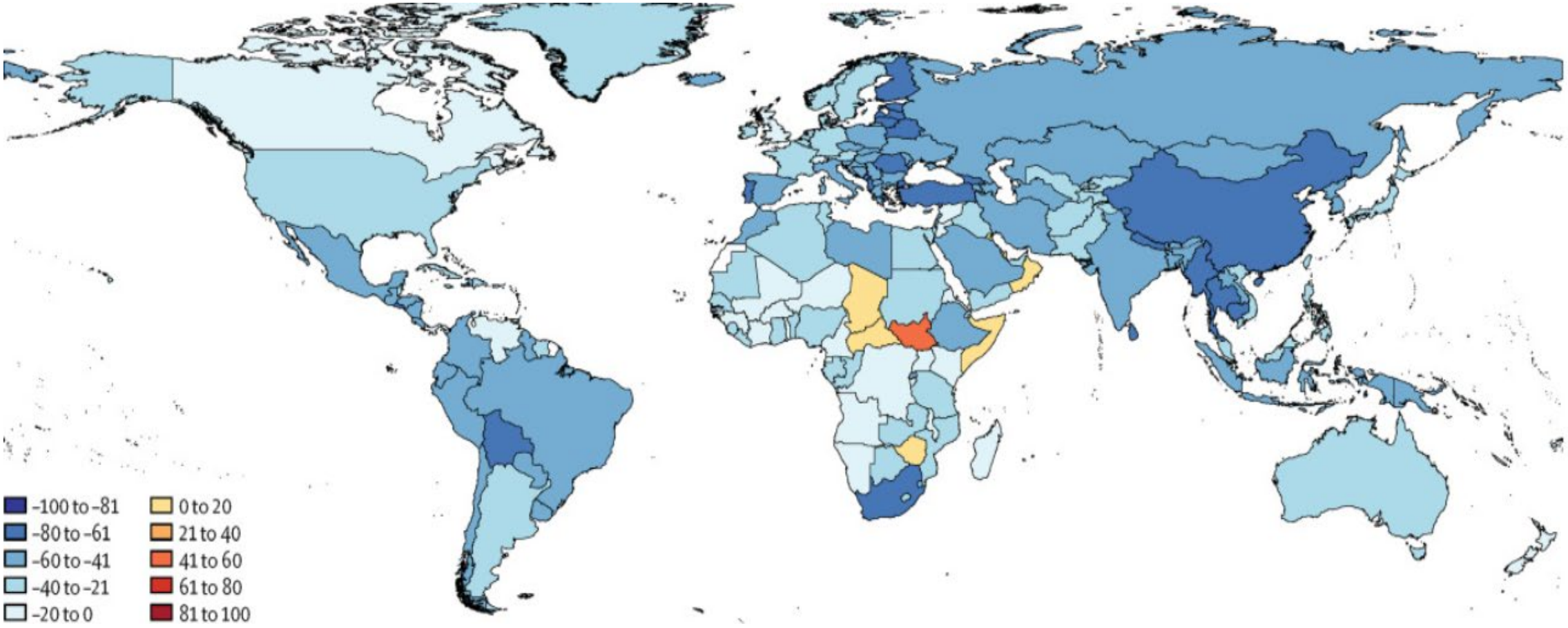
Pneumococcal vaccine support.



Pentavalent vaccine support (Hib).



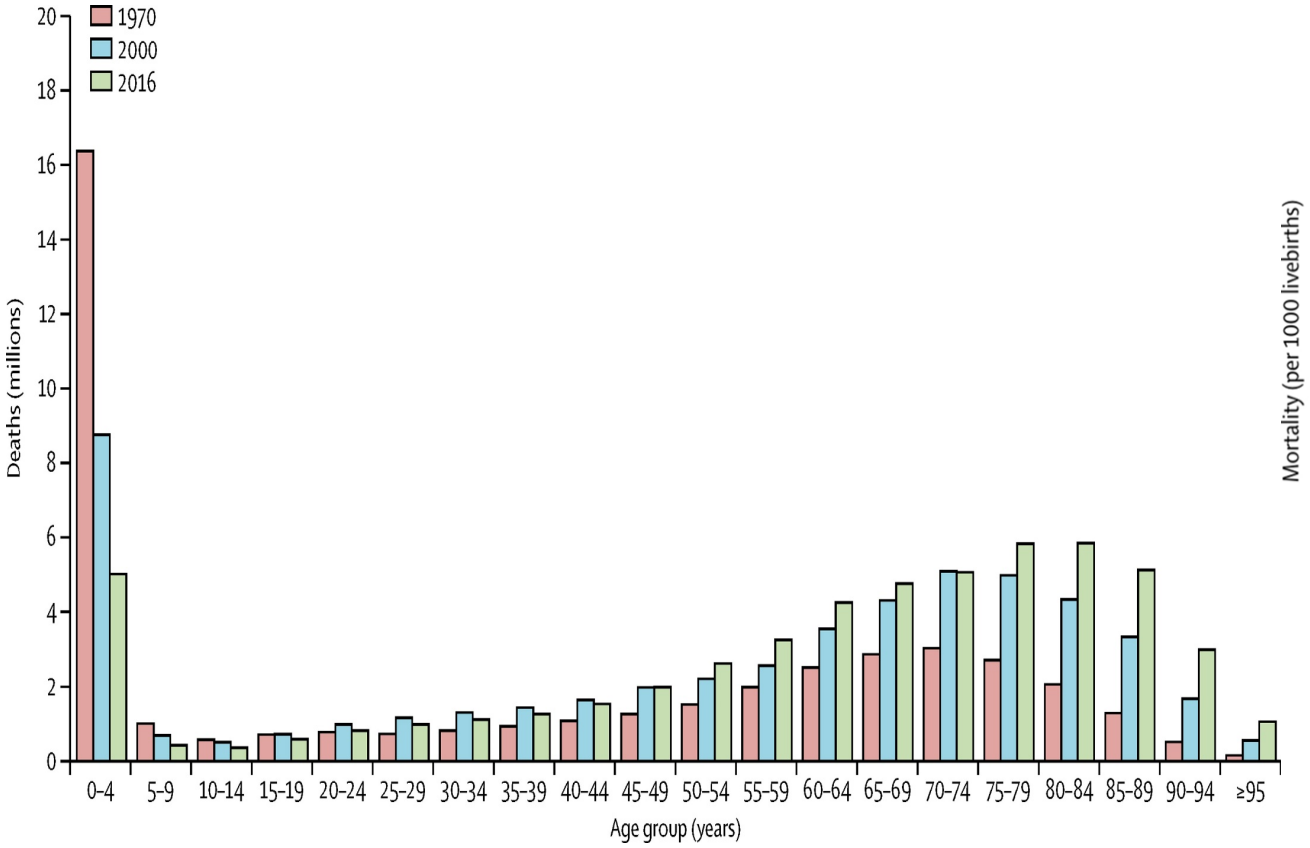
Under-5 deaths due to LRTI decreased by estimated 37% 2005-2015.

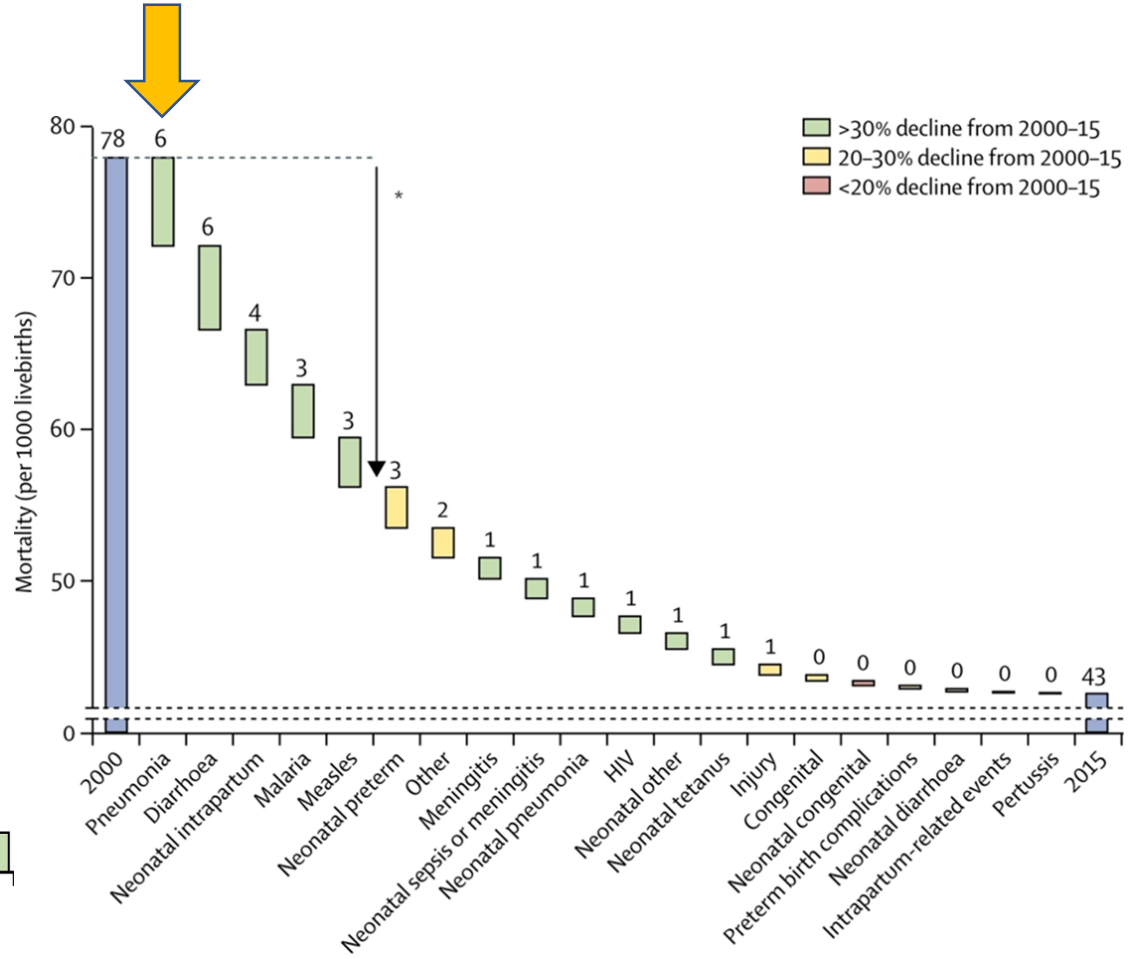


Global Burden of Disease LRTI Collaborators.
Lancet 2017

Reduction in child deaths (absolute) by age globally- reduction in pneumonia a major contribution.

(*Global Burden of Disease Study (GBD), Lancet 2017, Liu et al Lancet 2016.*)

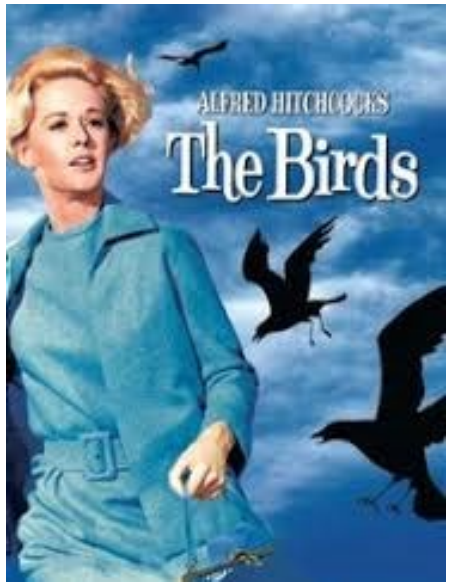




‘Atypical’ bacterial pneumonia.

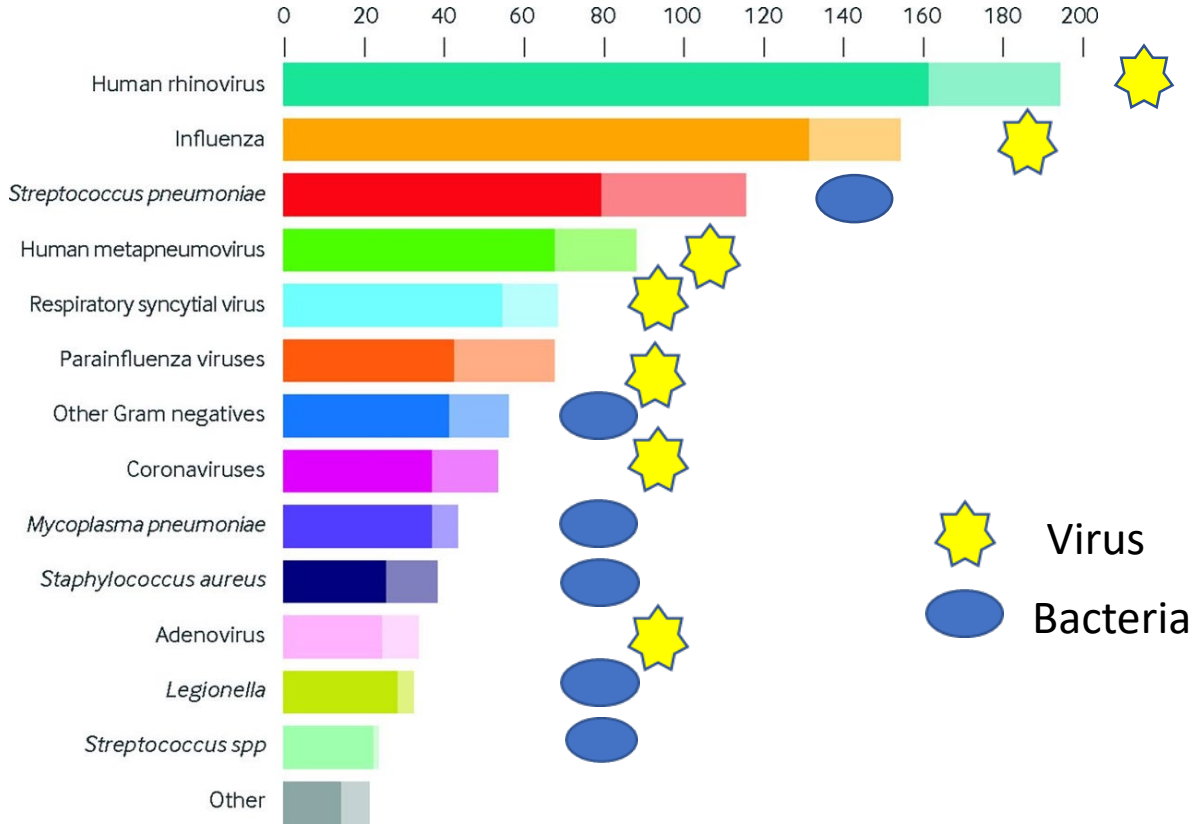
- *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, *Legionella pneumophila* most common.
- Can have other affects on the body- eg gastrointestinal upset, rash.
- Different antibiotics used.
- Legionnaires disease- hotel water supplies, hot tubs, spa pools.
- Psittacosis. Parrots, budgerigars, pigeons, wild birds.
- No deployable vaccines.

Roberto Schubert Radiopaedia.



Viruses make up a large proportion of pneumonia, a much smaller proportion of deaths.

- 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.



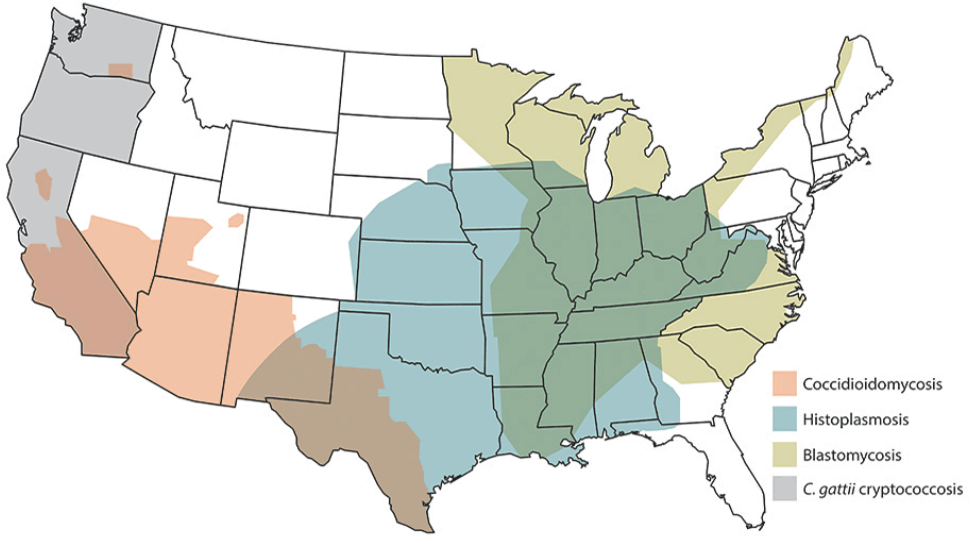
Wunderink R et al 2017 BMJ

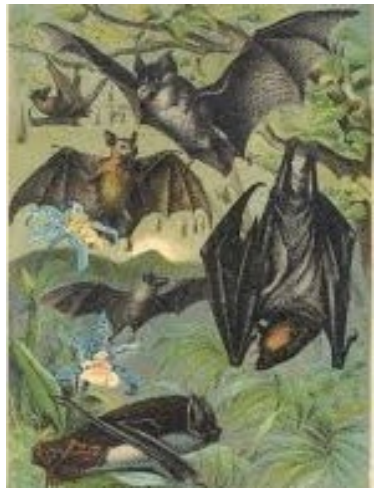
Influenza pandemic 1918 probably killed 50-100 million people globally. Primary and secondary pneumonia.

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

Fungal lung infections.

- Most common as a significant pneumonia in immunosuppressed people.
- Others catch them but generally self-cure.
- Some fungi which cause lung disease have a particular geographical range.
- Others are associated with particular activities including exotic (caving with bats) and common (composting).

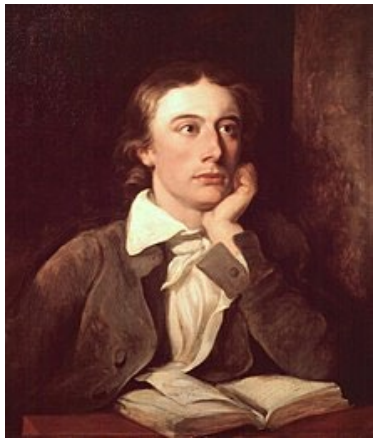




CDC/Wiki

Tuberculosis (TB): still one of the top 10 causes of death worldwide.

- Was common everywhere, killing people in all walks of life.
- Associated with art, and artists. *La bohème*, *La traviata, Moulin Rouge* examples where the heroine dies of TB.
- In 2017, around 10 million people caught TB, and 1.6 million died (WHO).
- In 2017, an estimated 1 million children became ill with TB and 230 000 died.

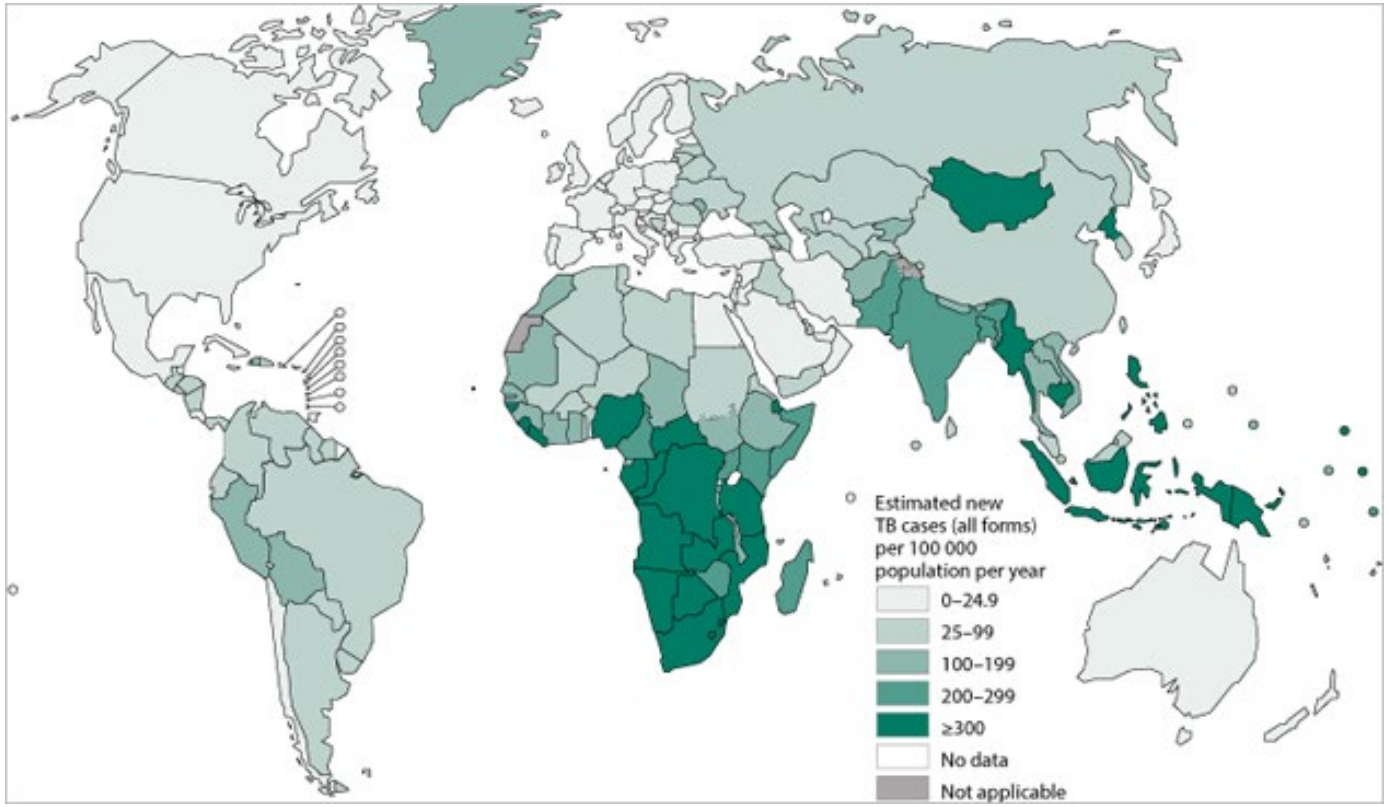


Keats, DH Lawrence, Emily Brontë, Orwell

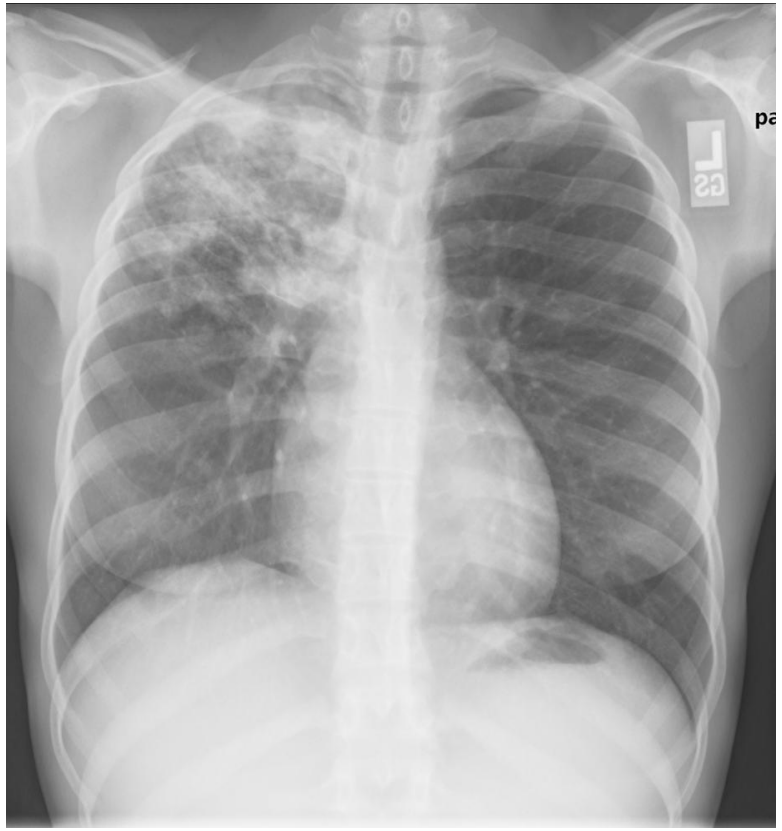
Tuberculosis distribution (WHO).

- Three major drivers:

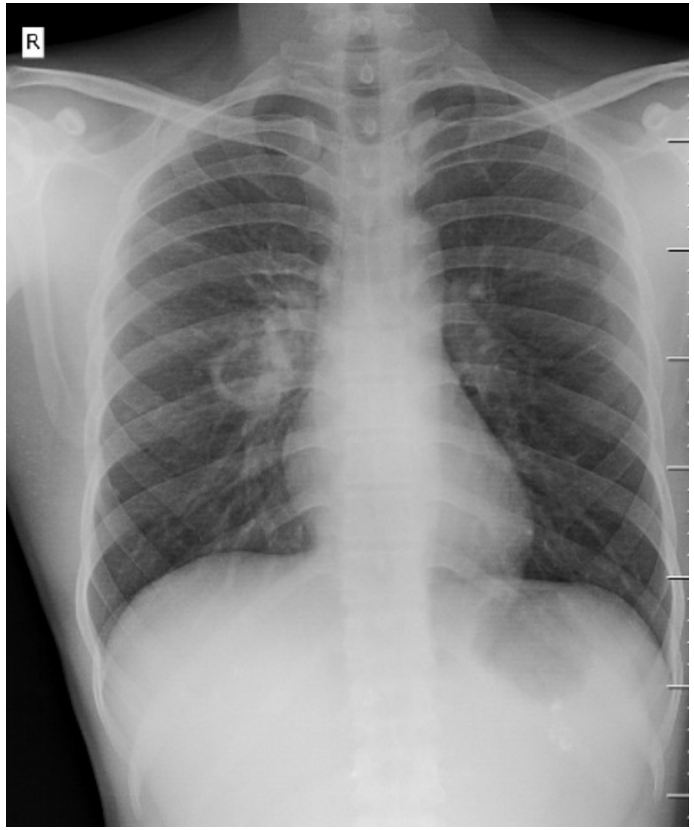
- Poverty (malnutrition, crowding, limited health services).
- HIV (20-30x more likely).
- Drug resistance (MDR, XDR).
- (Prisons, mining).



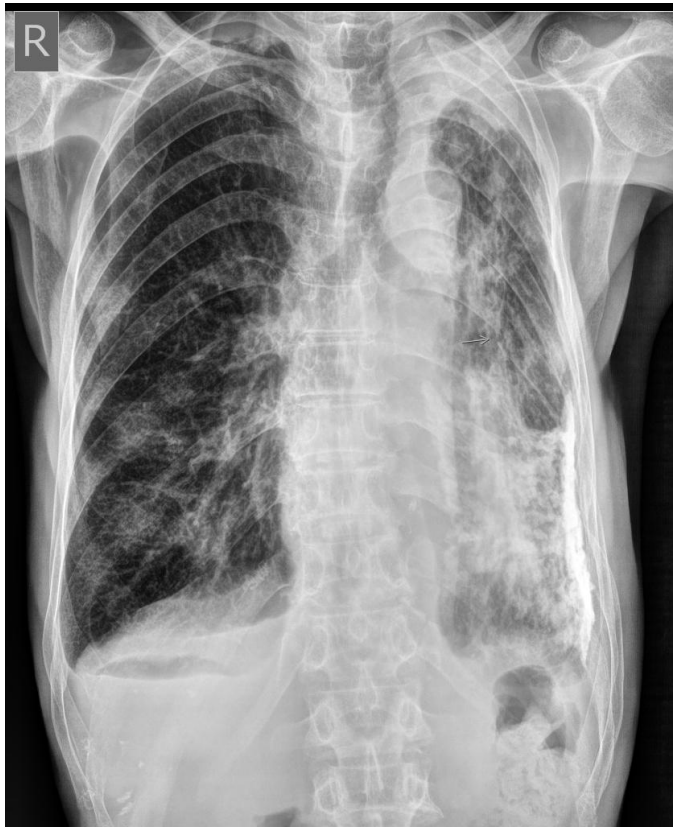
Pulmonary tuberculosis- 85-90% of cases, almost all transmission.



Frank Gaillard. Radiopaedia.



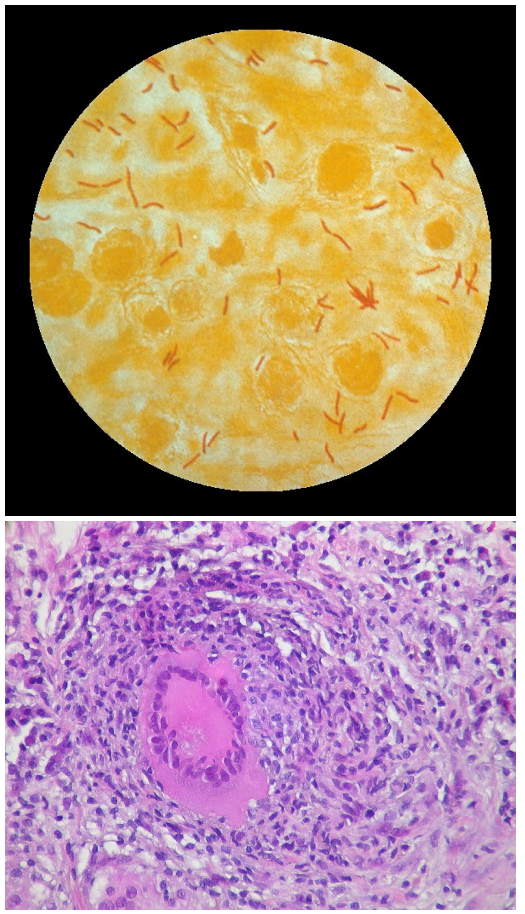
Aditya Shetty.



Mohammad Osama Yonso.

Pulmonary TB

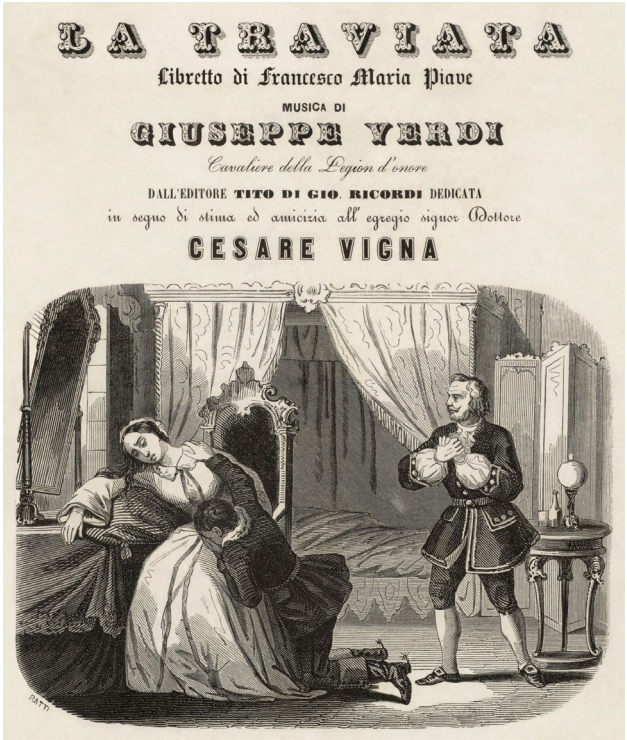
- After infection reaches alveoli in most cases macrophages surround the mycobacteria, and wall it off- granuloma.
- Latent TB- maybe a quarter of worlds population.
- Without treatment (or HIV), around 5% will develop disease in the first couple of years, 5% develop disease later in life.
- Immune health, malnutrition, age relevant.
- ‘Open’ TB- mycobacteria seen in sputum- smear positive. Much more infectious.
- Culture- or lab-proven TB without mycobacteria seen: smear-negative.

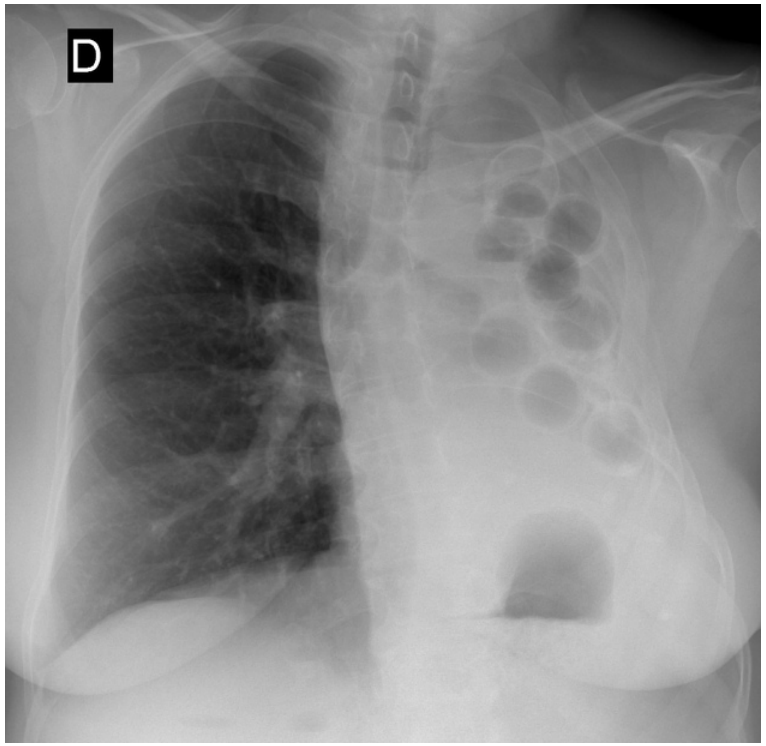


CDC/Yale Rosen

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, mountain and cave air.

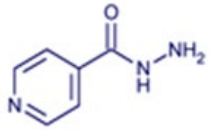
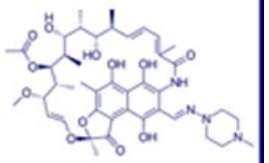
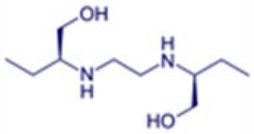
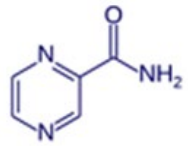




David Clemo Steel, Radiopaedia

The key to pulmonary TB is early diagnosis, then 6 months of (directly observed) multi-drug treatment. First drug, streptomycin, 1946.

The Four Principal First-Line TB Drugs

Drug Name	Formulation	Chemical Structure
Isoniazid		
Rifampin		
Ethambutol		
Pyrazinamide		

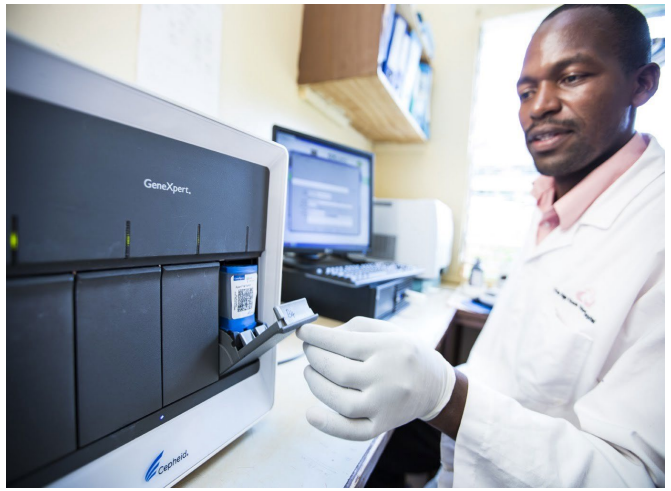
WHO/TBP/Gary Hampton

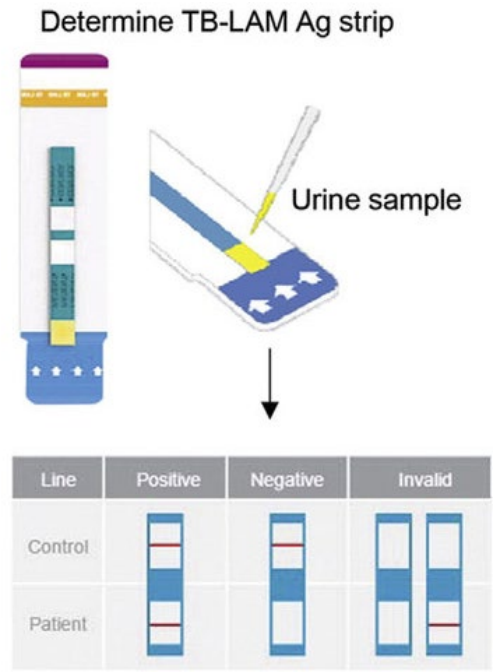
Better diagnosis of pulmonary TB.

- Microscopy low sensitivity. Culture 6-8 weeks.
- Several new methods of diagnosing TB more quickly.
- New gene-based approaches to rapid diagnosis of drug resistance.

But…

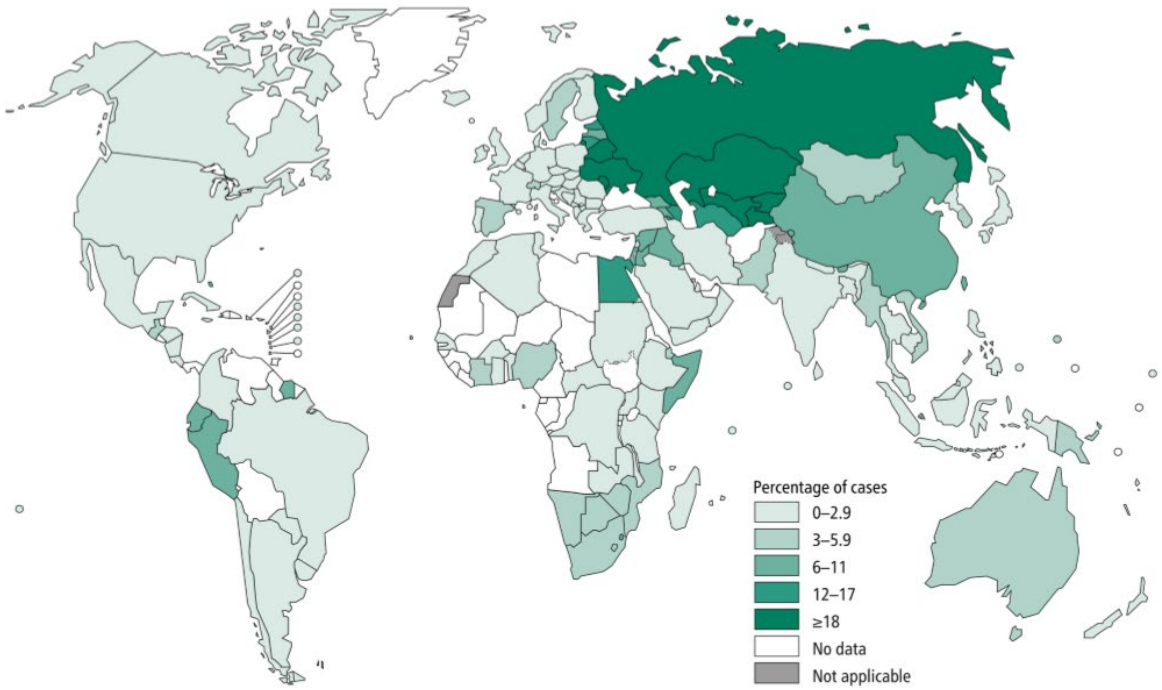
- Where much of the TB is the new diagnostic tests are not yet available.

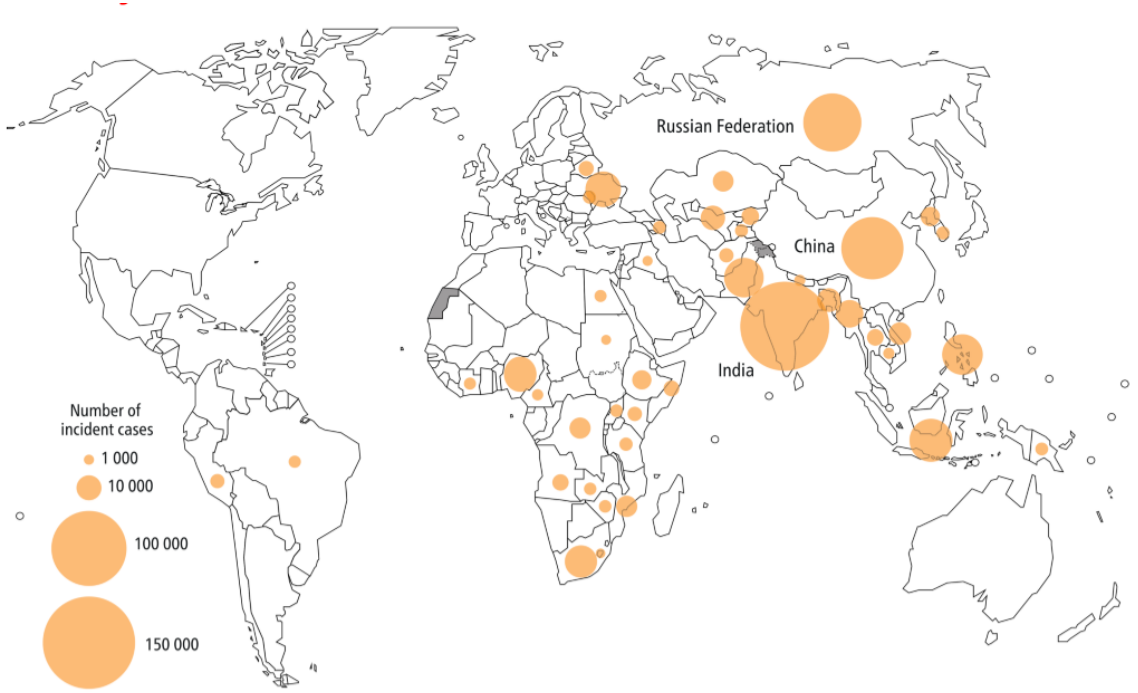




©FIND/John Rae. Kenya.

Drug resistant tuberculosis. Proportion of drug-resistant cases at first presentation, (L) and number (R). WHO.

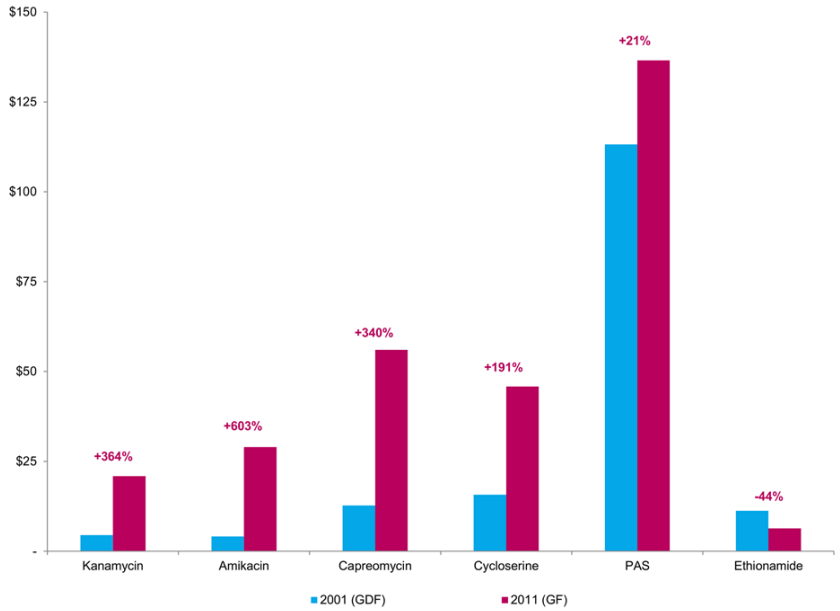


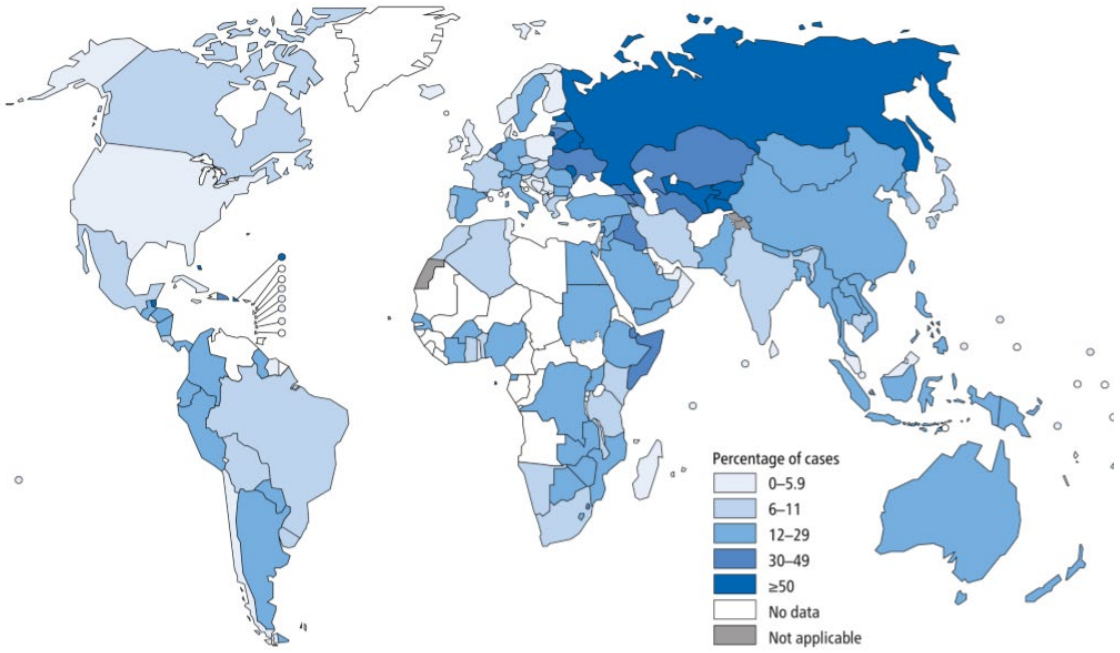


MDR TB even higher in those retreated. MDR/RR.

Cost of MDR Rx about 200x that for drug sensitive TB and rising.

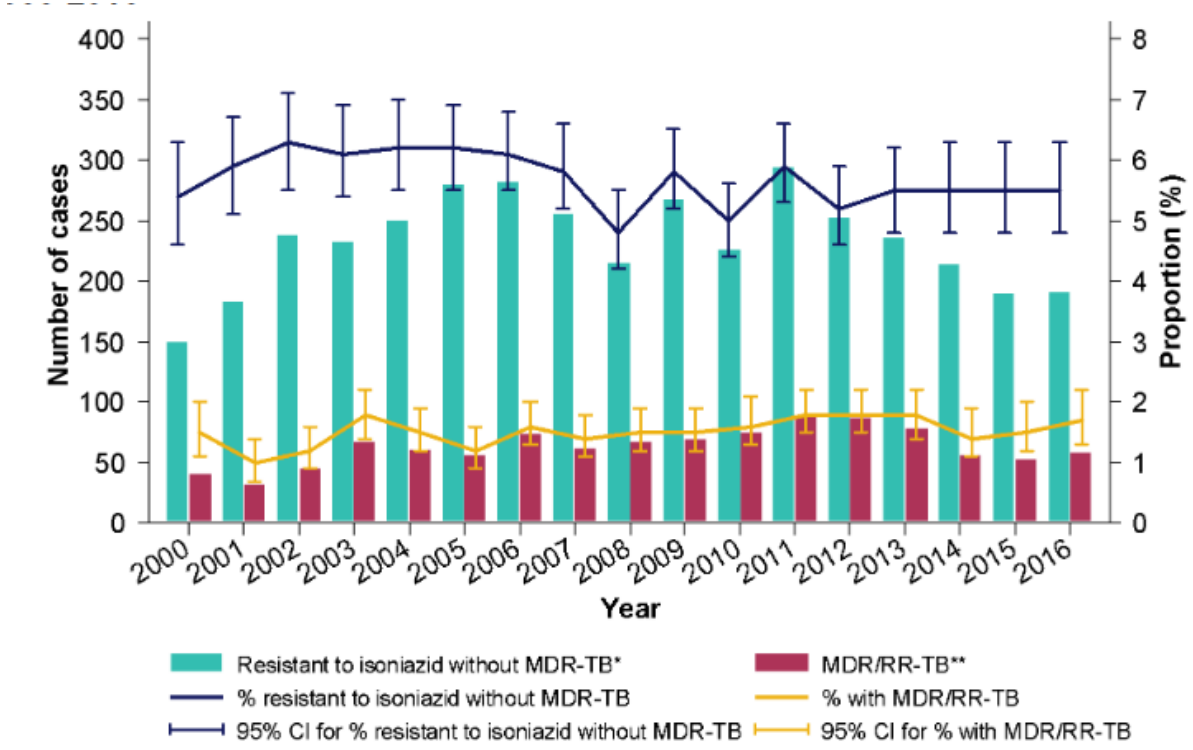
Direct USA costs averaged $134,000 per MDR TB, $430,000 per XDR TB patient; non-MDR TB $17,000.





Price for a month's treatment of second-line TB agents in 2001-11 (constant 2011 dollars). *Hwang et al 2014.*

It is not an inevitability that the proportion of MDR TB must increase. But it is likely to globally.



- Good progress in some parts of Eastern Europe.
- Stable in UK (data L proportion with MDR from PHE 2017).
- 38% drop in new TB diagnoses from the peak in 2011 to 2017 (from 8,280 to 5,102), with a 9% fall in diagnoses between 2016 and 2017 alone (PHE).

Tuberculosis vaccination.

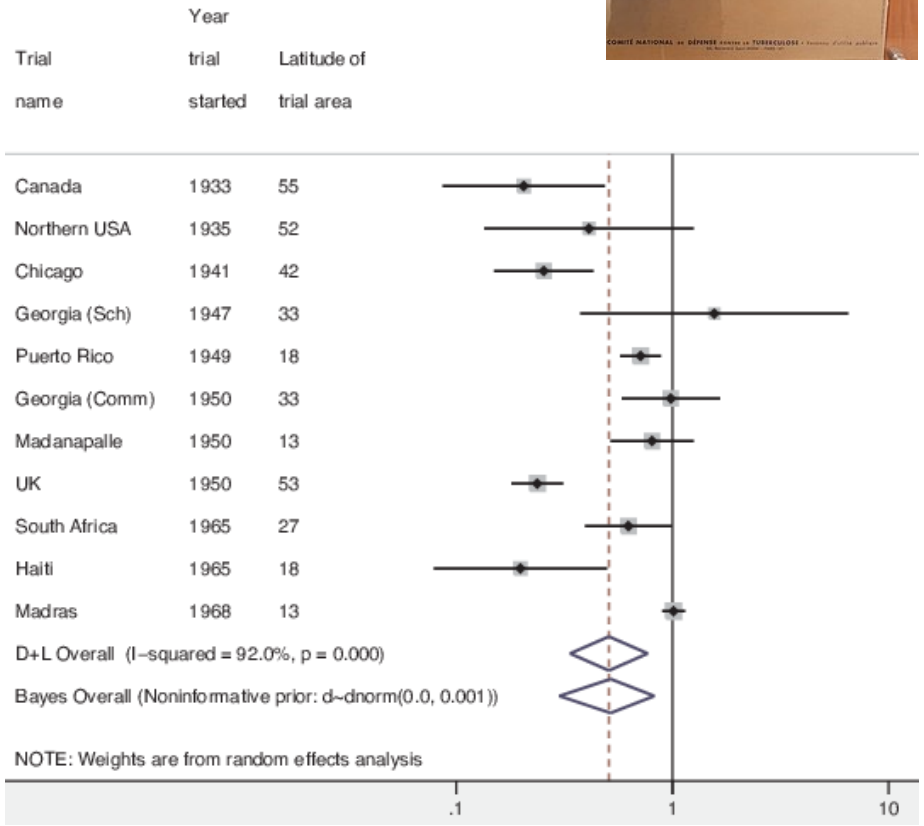
- BCG vaccine remains one of the most widely used.
- Effective at preventing severe TB in children, but:

-Less effective in adults.

-Less effective in low-income settings.

-Less effective in lung TB.

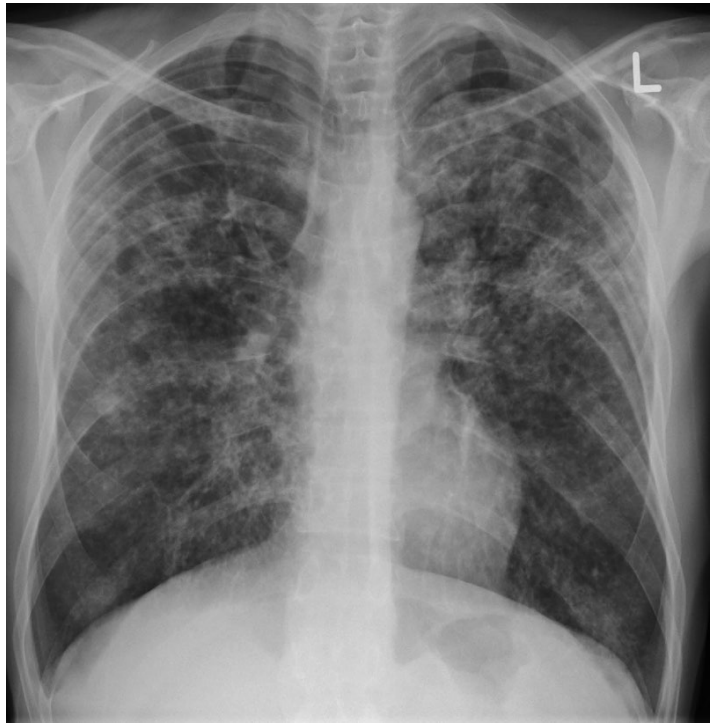
- Various new vaccines, so far none have improved significantly on BCG.

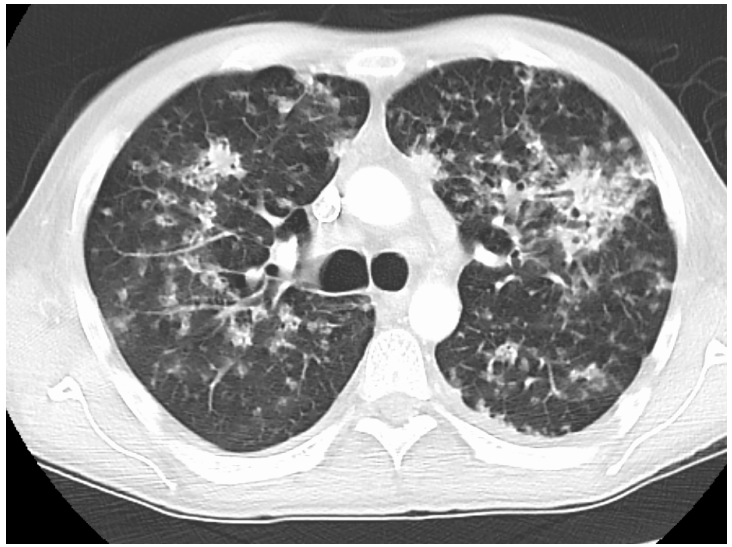


Harris R et al. BCG vaccination.

Miliary tuberculosis.

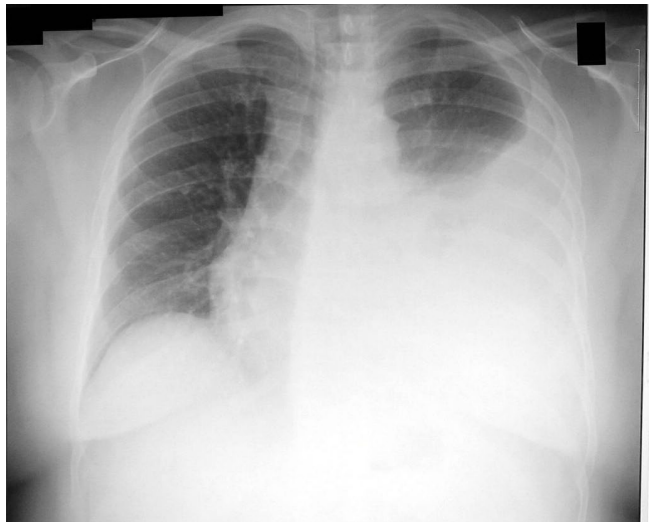
- About 2% of TB.
- Widely disseminated TB- the immune system not confining it.
- Mortality untreated almost 100%.
- Can be over 30% in low-resource settings or 2% with high-intensity care.





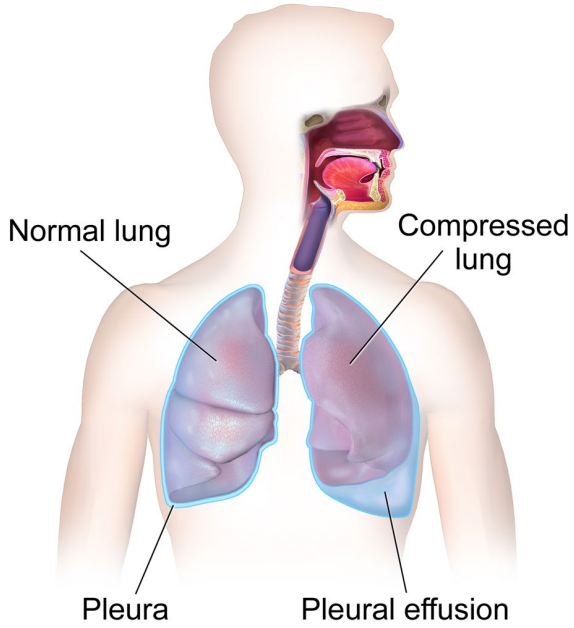
J. Heilman, Wiki

Pleural effusion.



- Fluid collecting between the lung and the chest wall/diaphragm.
- Most common infectious cause TB.
- 5-20% of non-HIV TB, up to 38% of HIV associated TB.
- Generally relatively easy to treat.

- Occasionally pneumonia can cause it.
- Pus (empyema)- may need drainage.

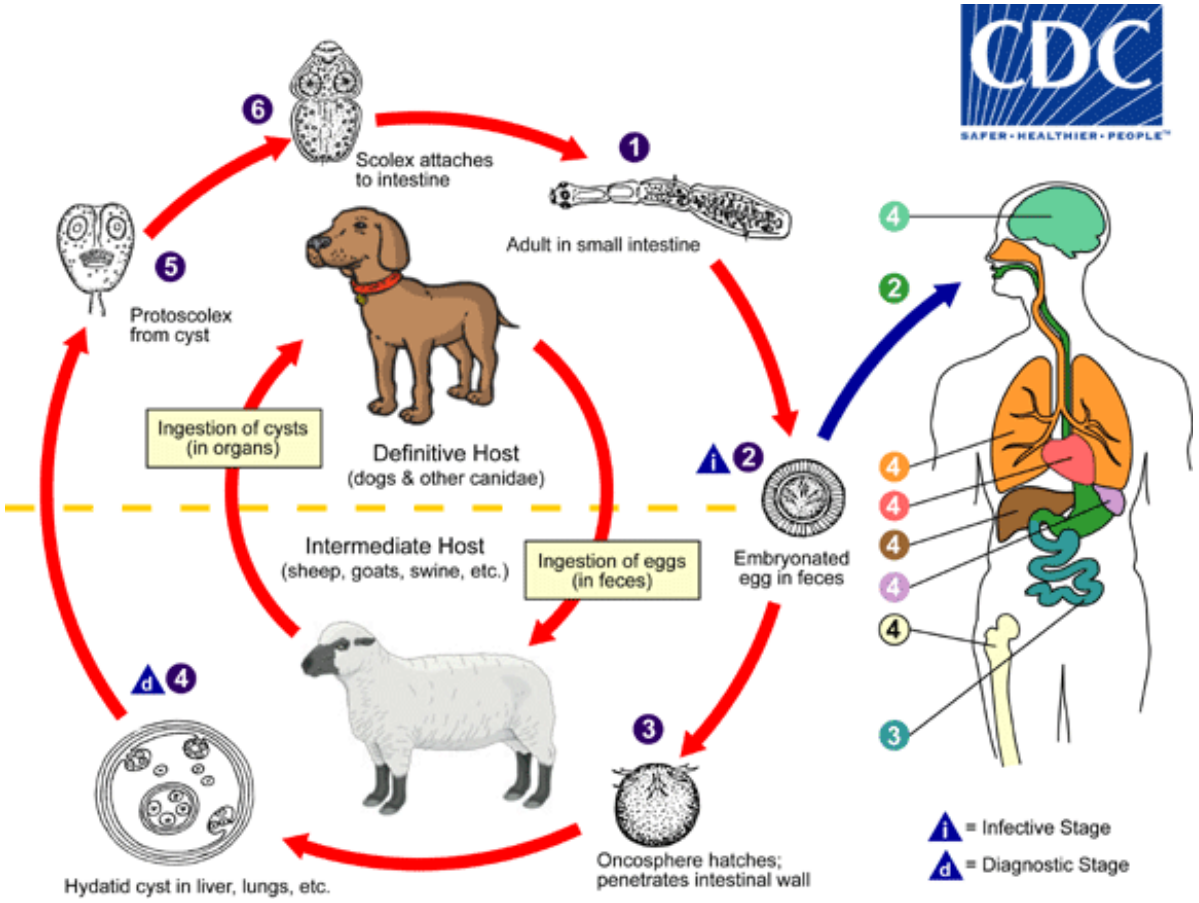


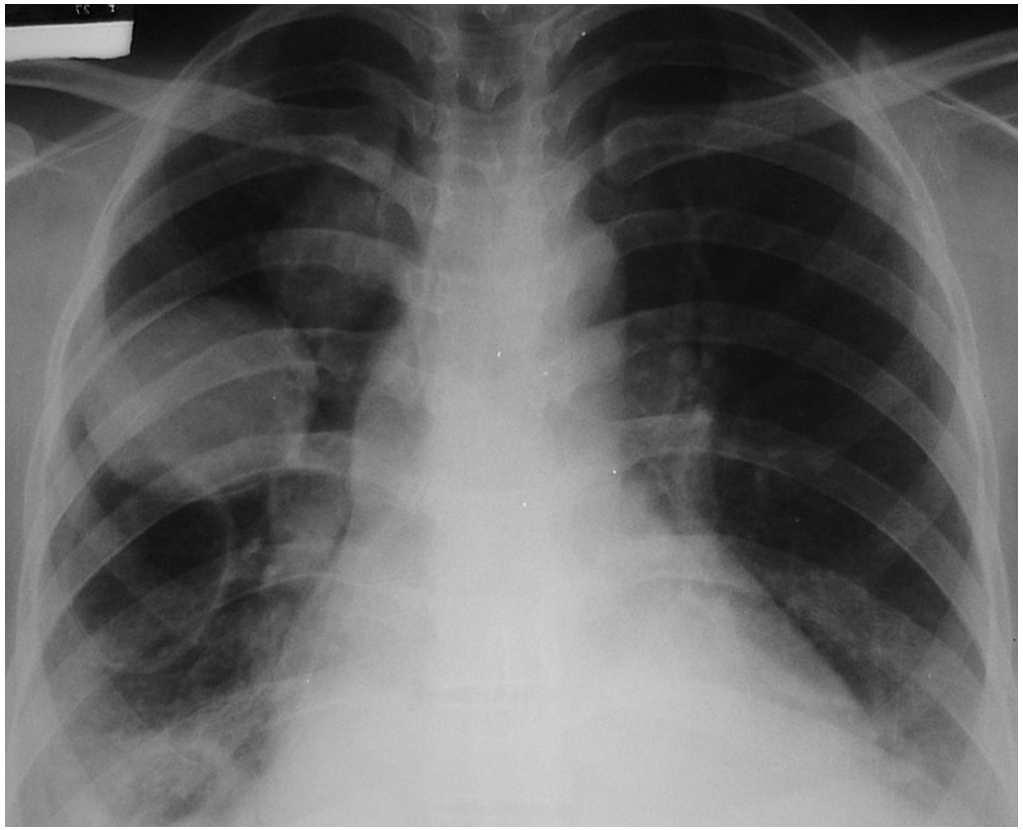
Infections affecting the motor nerves can stop breathing: polio, tetanus, botulinum, Guillain-Barré syndrome.

Lung fluke- paragonimus.

- Snail to crab or crayfish, to human.
- (or tiger, pig, dog, mongoose).
- Mimics TB- coughing up blood.
- Prevention: cook crabs or crayfish.

Hydatid disease of the lung: sheep/dog cycle.



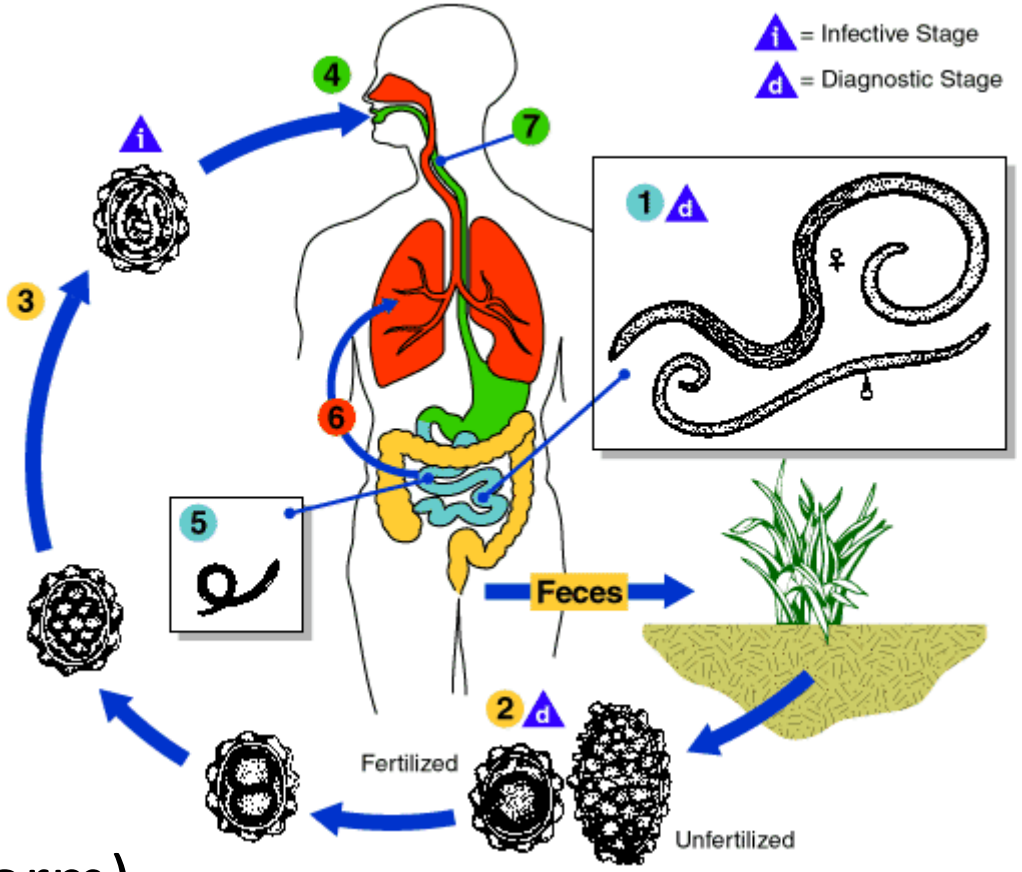


Courtesy of Dr FM Ebouda, Radiopaedia.org

Several worms pass through the lungs as part of their lifecycle.

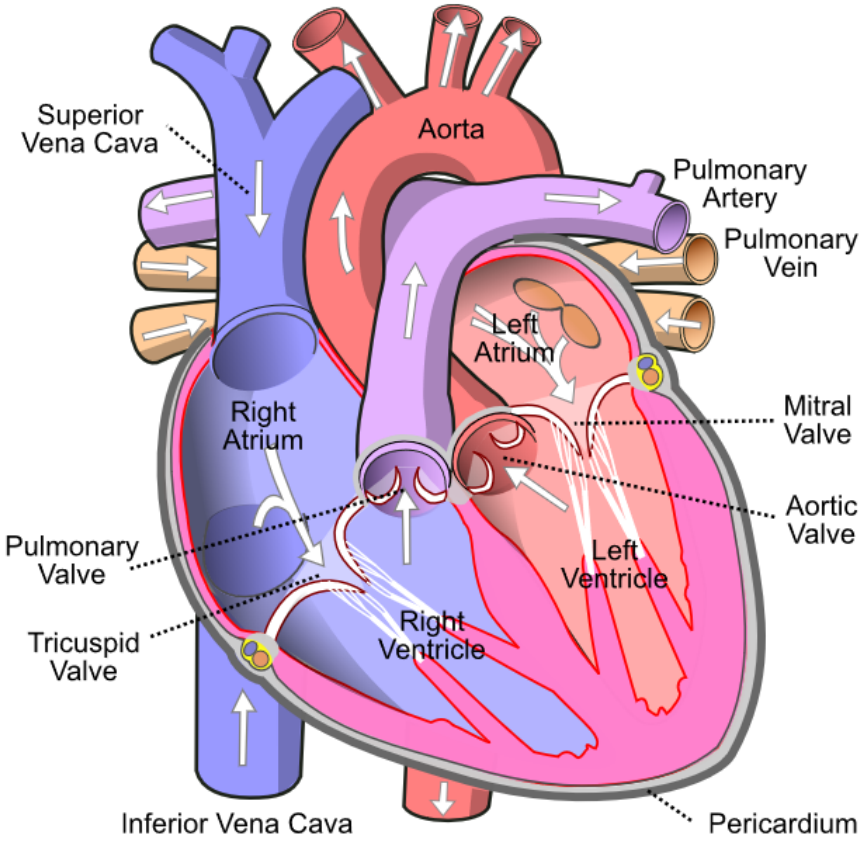
Hookworm

Ascaris (roundworm)



The heart and infections.

- Infections of the heart valves (endocarditis).
- Infections affecting the heart muscle (myocarditis).
- Infections causing changes in heart rhythm (heart block).
- Infections in the pericardial sac (pericarditis, pericardial effusion).
- Infections causing myocardial infarction (heart attack).
- Infection of the aortic arch (aortitis).



Bacterial and fungal endocarditis.

- Around 1:30,000 get endocarditis.
- Risk factors:

Heart structural abnormalities.

-Artificial valve.

-Congenital heart abnormality.

-Hypertrophic cardiomyopathy.

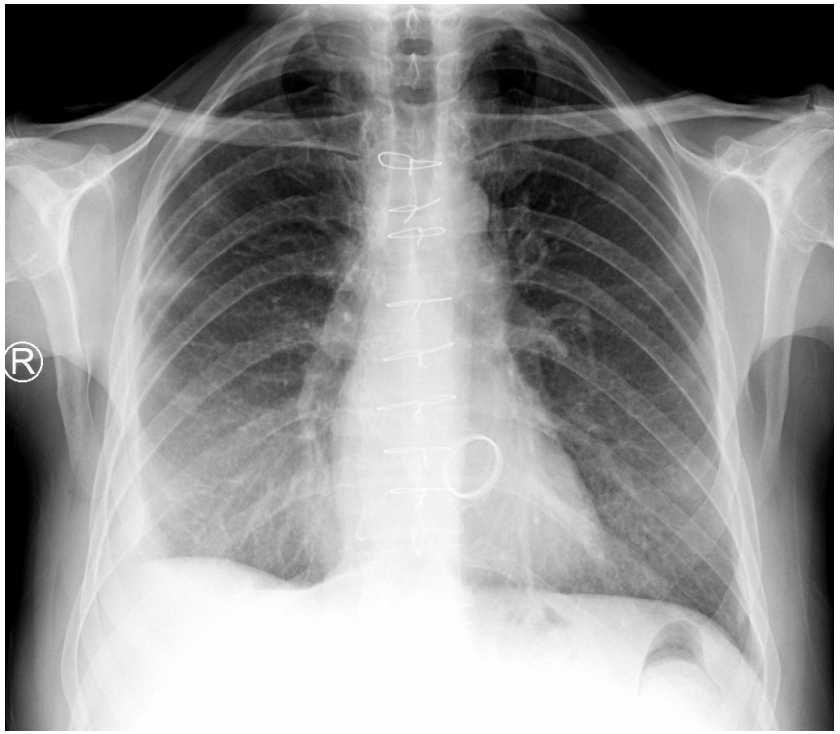
Risks for bacteria getting into blood.

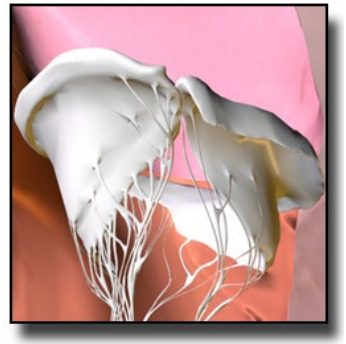
-Intravenous lines in hospital.

-Intravenous drug use.

-Dentistry / poor dentition.

-Surgery.





Dr Henry Knipe radiopedia (mitral); Bruce Blaus.

What bug, and treatment, depends on setting.

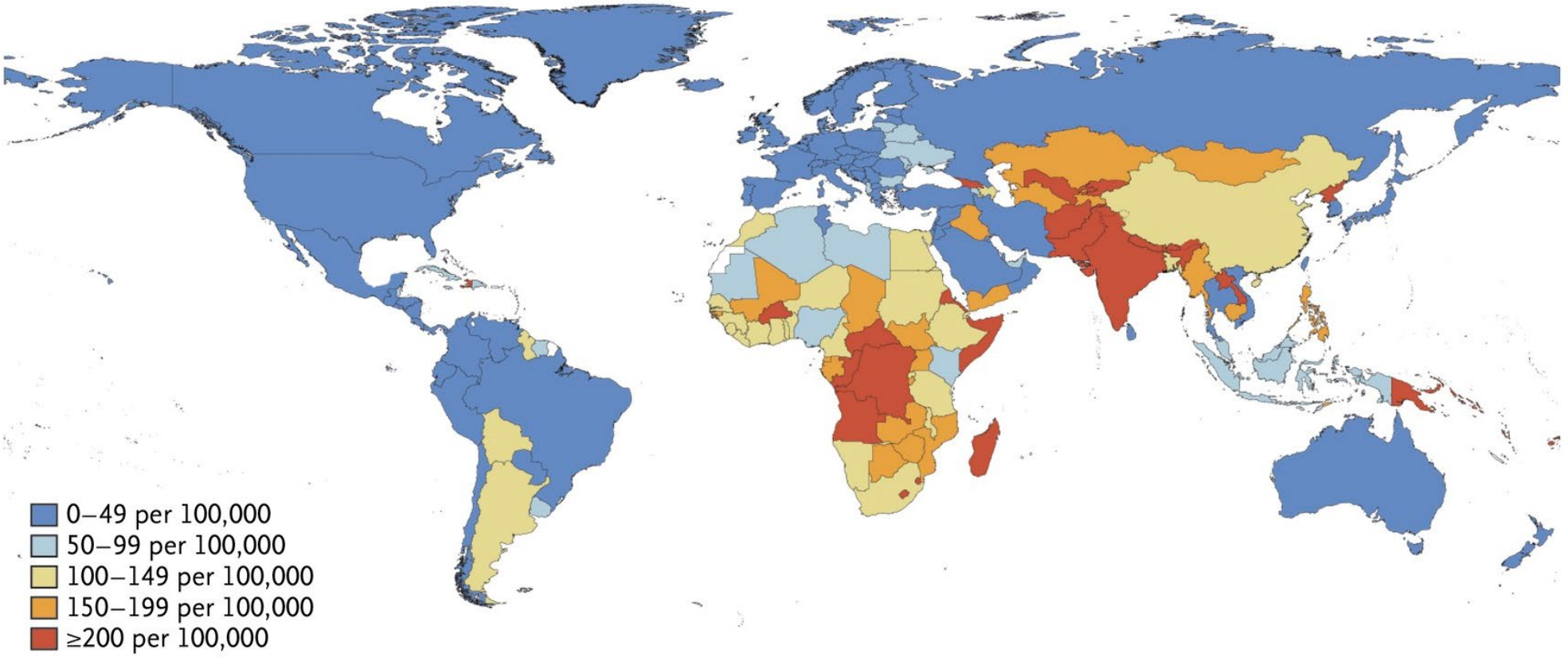
- Endocarditis can cause just fever, or emboli can flick off. Can cause strokes.
- When cause in hospital usually skin- Staphylococcus.
- In the community often dental- *Streptococcus viridans* group.
- From gut- *Streptococcus bovis.*
- Immunosuppressed- fungal (Candida).
- Treatment prolonged antibiotics, 20% surgery.

Rheumatic heart disease.

- Rheumatic fever follows a Group A streptococcal throat or skin infection. Around 3% of untreated.
- Was very common in UK. Chorea 2nd/4th most common cause for admission at Great Ormand St. in 1880s.
- Immunological reaction.
- Effects throughout body (esp. joints).
- Early heart inflammation, up to 60% have long term heart problems.
- Damage to mitral heart valve.
- Heart failure, atrial fibrillation.

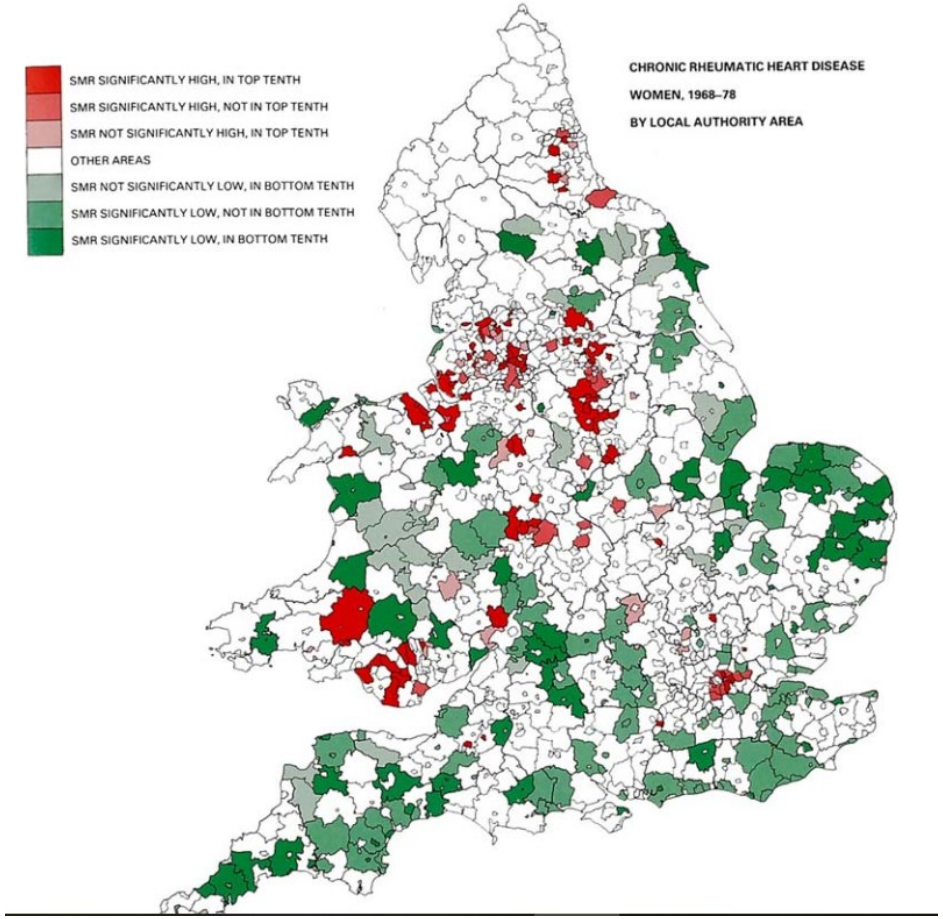
St. Vitus's Dance / Sydenham's chorea

About 30 million affected by rheumatic heart disease globally, around 300,000 deaths p.a. (WHO). Strong link to poverty.



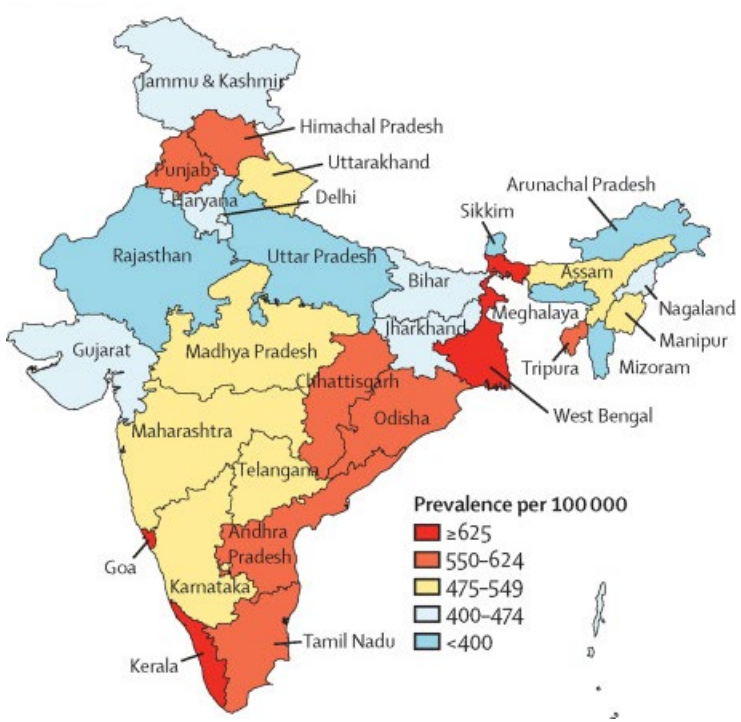
Age-Standardized Disability-Adjusted Life-Years Due to Rheumatic Heart Disease per 100,000 Population, 2015.
Watkins D et al NEJM 2017, GBDS.

Geographically tends to cluster in urban poorer areas. Stroke follows. UK RF 1970s, India 2010s.

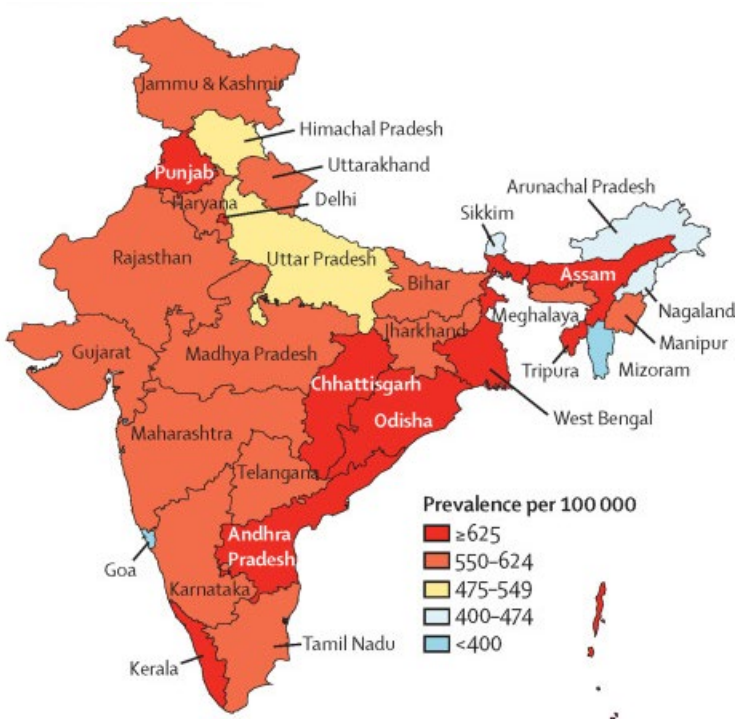


Philips 2014. Women.

Stroke

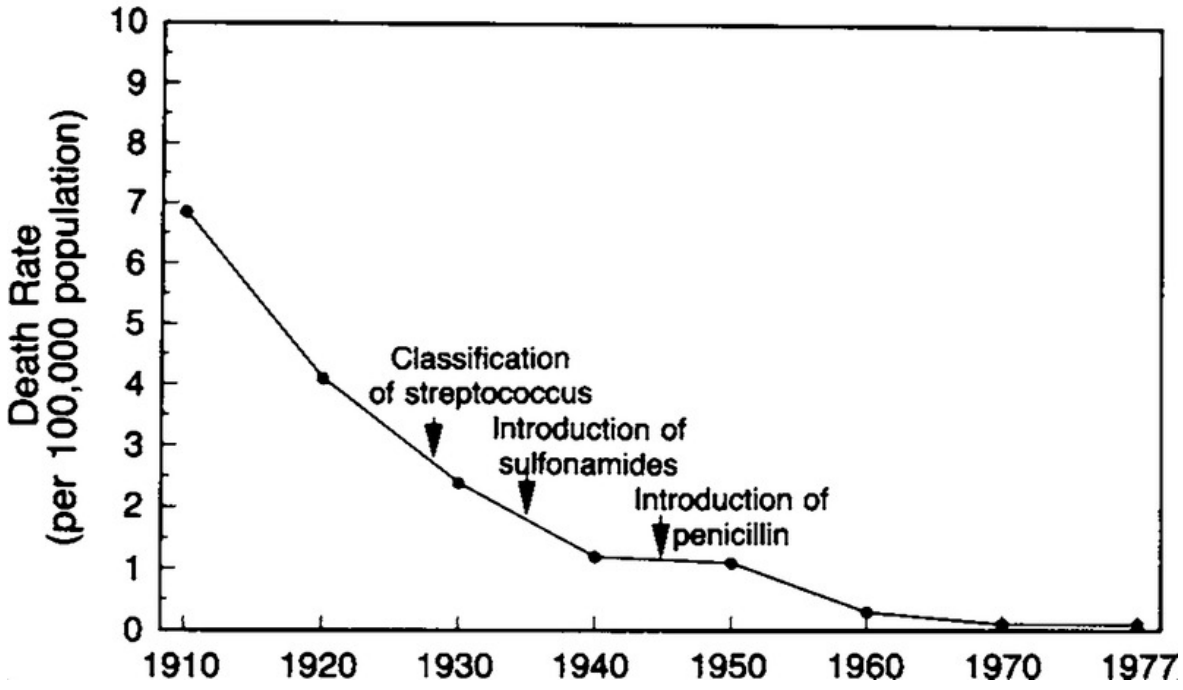


Rheumatic fever

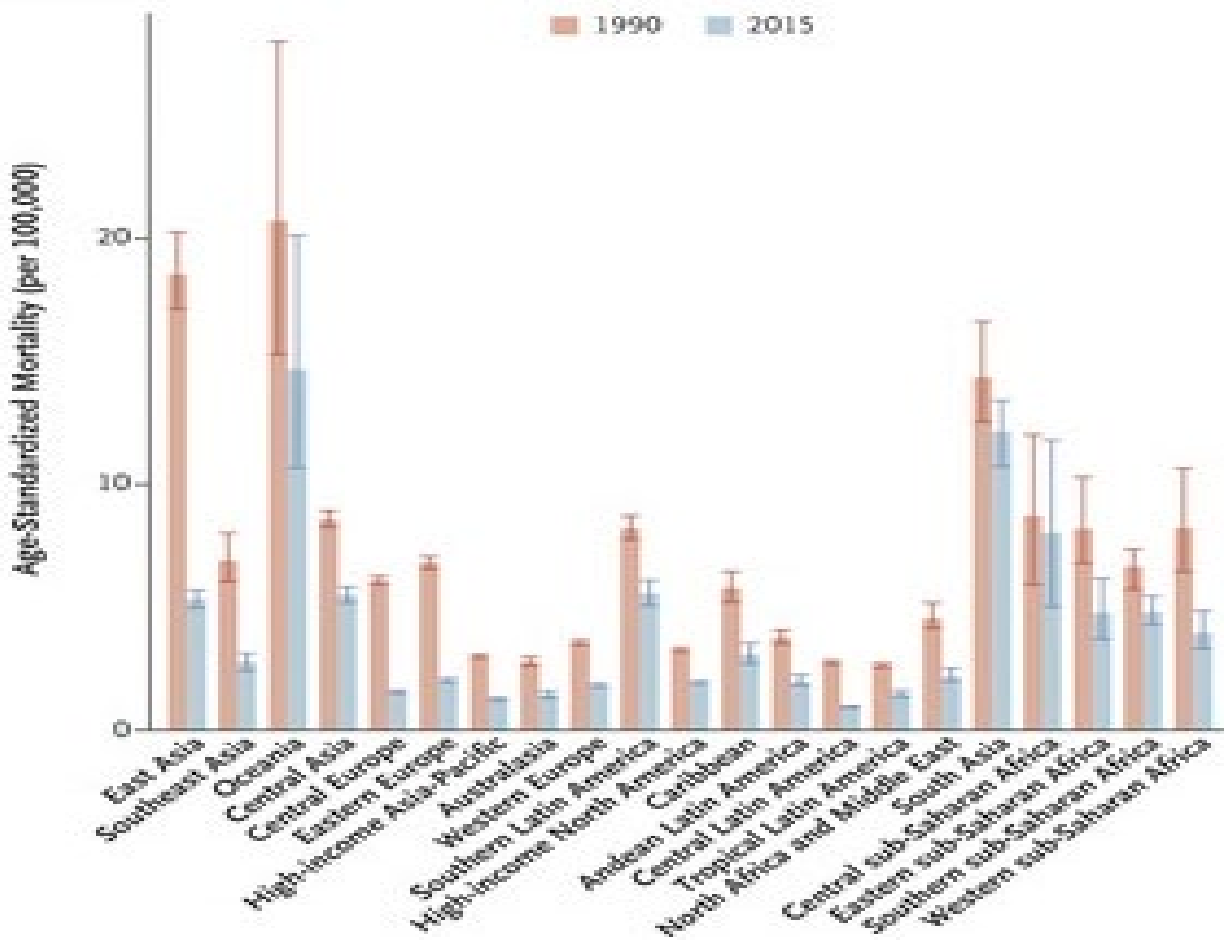


India State-Level Disease Burden Initiative CVD Collaborators, Lancet 2018

Deaths /100,000 from rheumatic heart disease over time.
USA (L) 1910-1980, global 1990-2015. 1990 2015

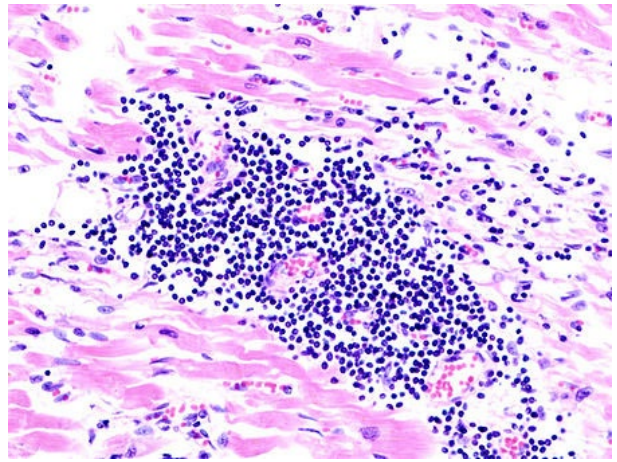


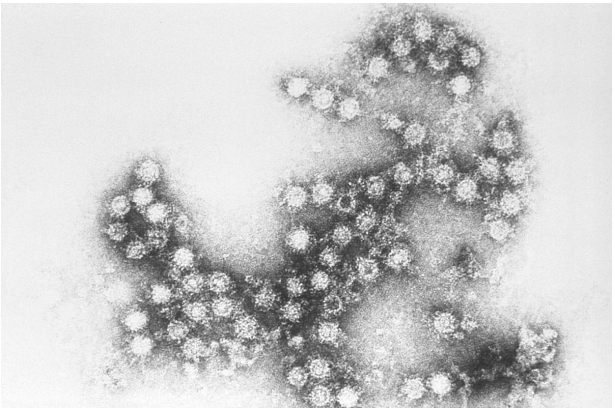
Gordis L; Watkins D et al



Viral and bacterial myocarditis.

- Around 1.5 million cases of acute myocarditis a year: around 20/100,000.
- Most recover. Important cause of heart disease in young adults, children; occasional sudden deaths (up to 20%).
- Viral most common.
- Viruses include Coxsackie B, Parvovirus B19, HHV6, HIV, Hepatitis C.
- Bacteria include Haemophilus, legionella, mycoplasma, brucellosis, Q-fever, typhus.
- Initial inflammation due to infection, then in some a second immune inflammation.

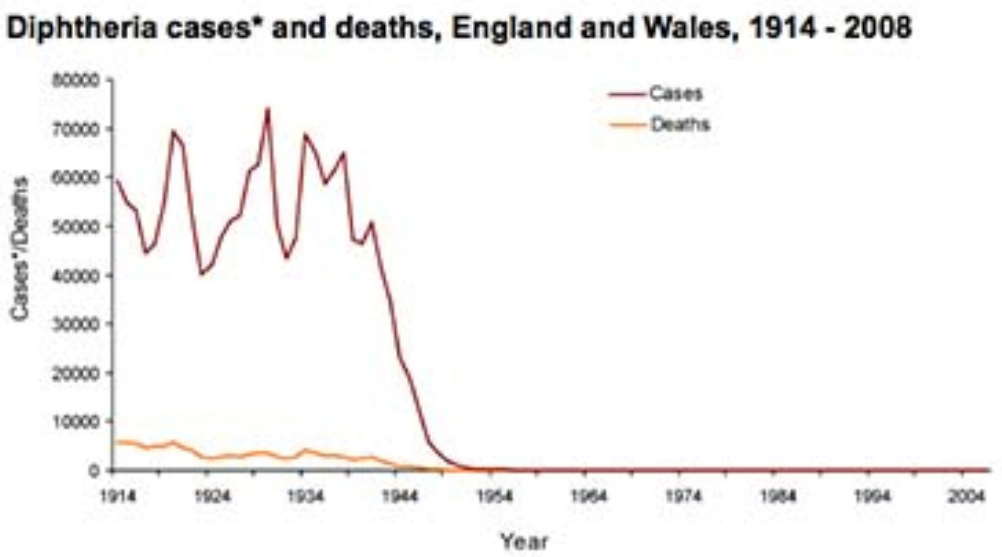




Heart inflammation; coxsackie virus. Wiki.

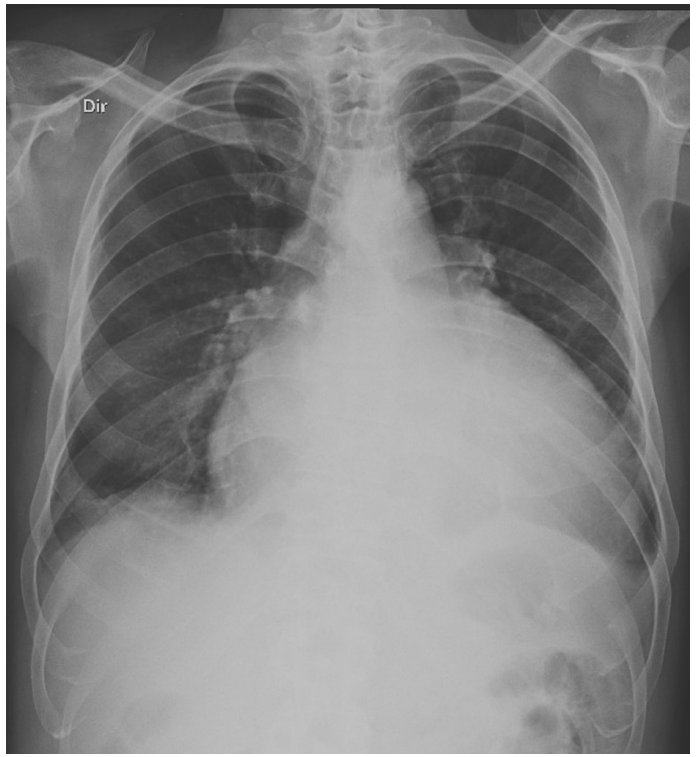
Diphtheria and the heart- toxin meditated myocarditis.

- Used to be a major cause of death, especially in children.
- The toxins of diphtheria cause myocarditis.
- Can cause heart block.
- Diphtheria now rare; better living conditions, antibiotics, vaccination.
- In 2015, 4,500 cases were officially reported worldwide; over 1m before 1980s. Fatal in 5-10%.

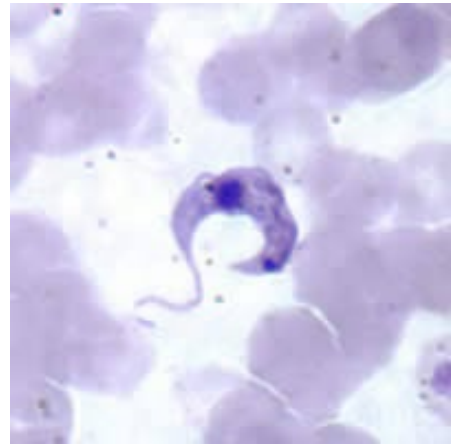


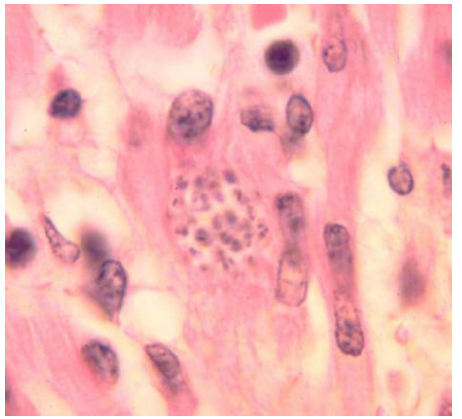
Chagas cardiomyopathy.

- Chagas disease is endemic in large areas of rural Latin America.
- A trypanosome parasite passed on by 15 species of reduviid bugs.
- Zoonosis- many mammals.
- The most common cause of non-ischaemic cardiomyopathy in Latin America.
- 5.7 million people in 21 countries have Chagas (WHO); 20-30% will get cardiomyopathy and heart failure in 20 years.
- Substantial reduction in new cases.



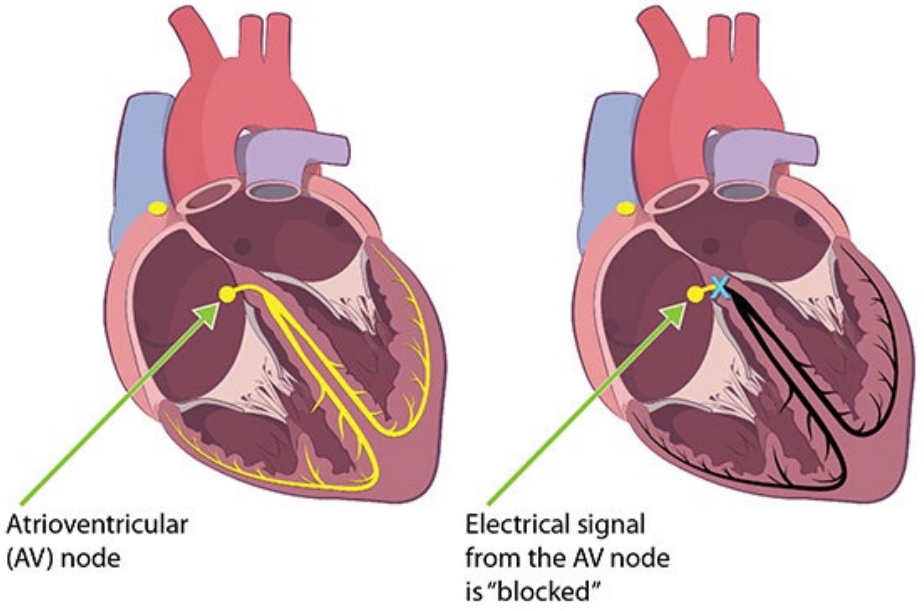
Dr Bruno Di Muzio, Radiopaedia.org: Wiki





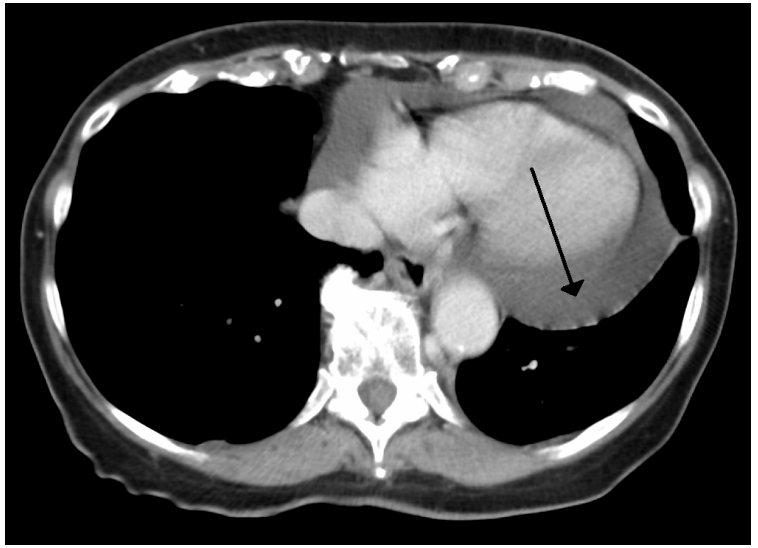
Infections causing rhythm disturbance- Lyme disease.

- Lyme- tick-borne bacterial zoonotic infection.
- About 1% of proven Lyme disease causes carditis (CDC).
- Can lead to heart-block. If treated with antibiotics recover in about 6 weeks.
- May need a temporary pacemaker.



Pericardial effusion.

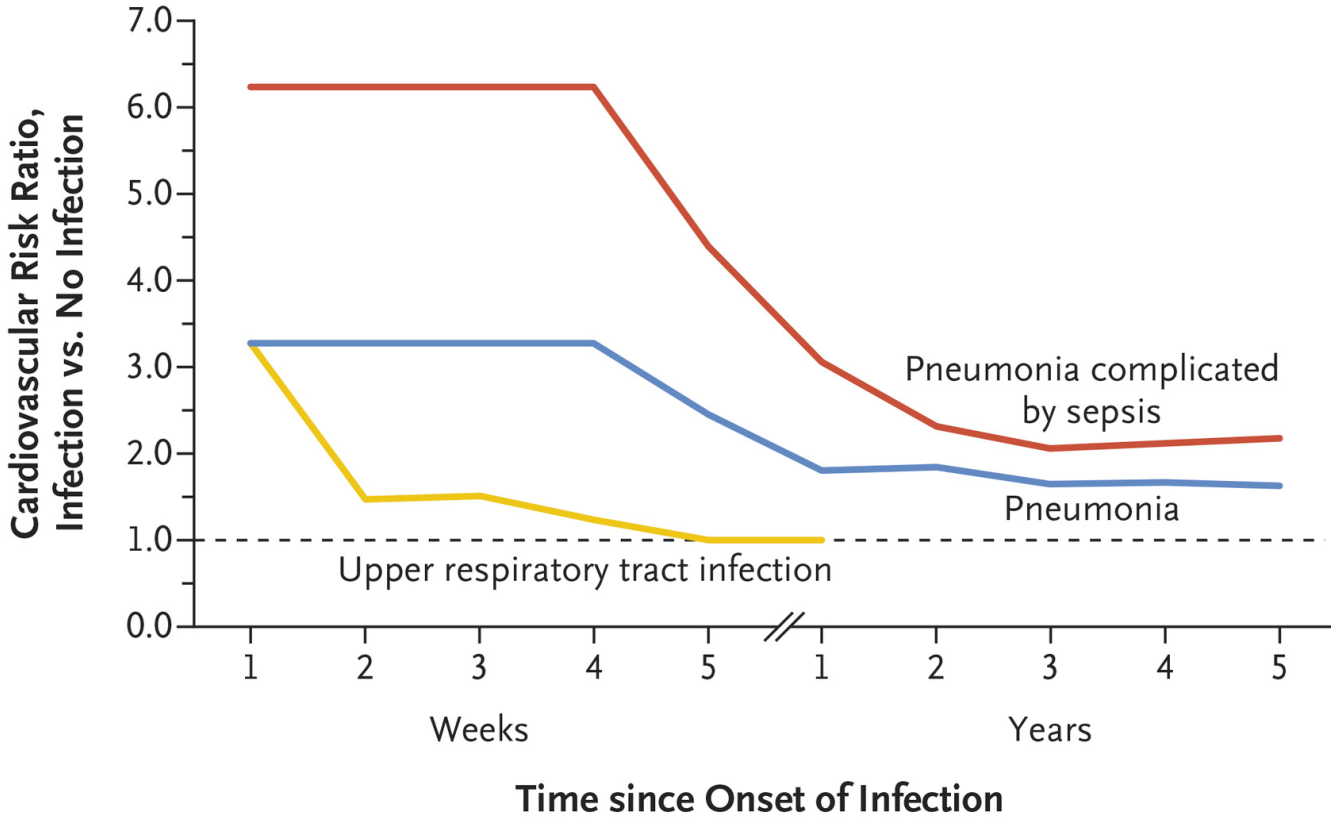
- Many infections can cause a small pericardial effusion.
- The classical cause of a massive pericardial effusion is tuberculosis (TB).
- Can squeeze the heart (tamponade).
- Treat with TB drugs and steroids to prevent constriction.



J Heilman Wiki.

Pneumococcal pneumonia increases the risk of heart attack (MI).

- "Among patients who are hospitalized for pneumococcal pneumonia, the incidence of myocardial infarction is 7 to 8%."
- There is also evidence of increased risks of myocardial infection and stroke after other lung infections.



D. Musher et al NEJM 2019

We are making substantial progress against diseases of the lung and heart.

- Rapid reductions in bacterial pneumonia in the young.
- Gradual reduction in TB globally- but drug resistance a risk.
- Many old enemies such as diphtheria, rheumatic heart disease, Chagas largely gone or going.

- Pneumonia will remain a significant risk in the elderly.
- Heart infections will remain rare but serious hazards.