

Emerging and re-emerging infectious diseases: A hearing health overview

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Outline

- Global perspective of hearing loss and the role of infectious disease
 - Why should/do we care?
- Overview of infectious agents
- Highlight: Endemic disease, Potential to re-emerge diseases, Emerging disease

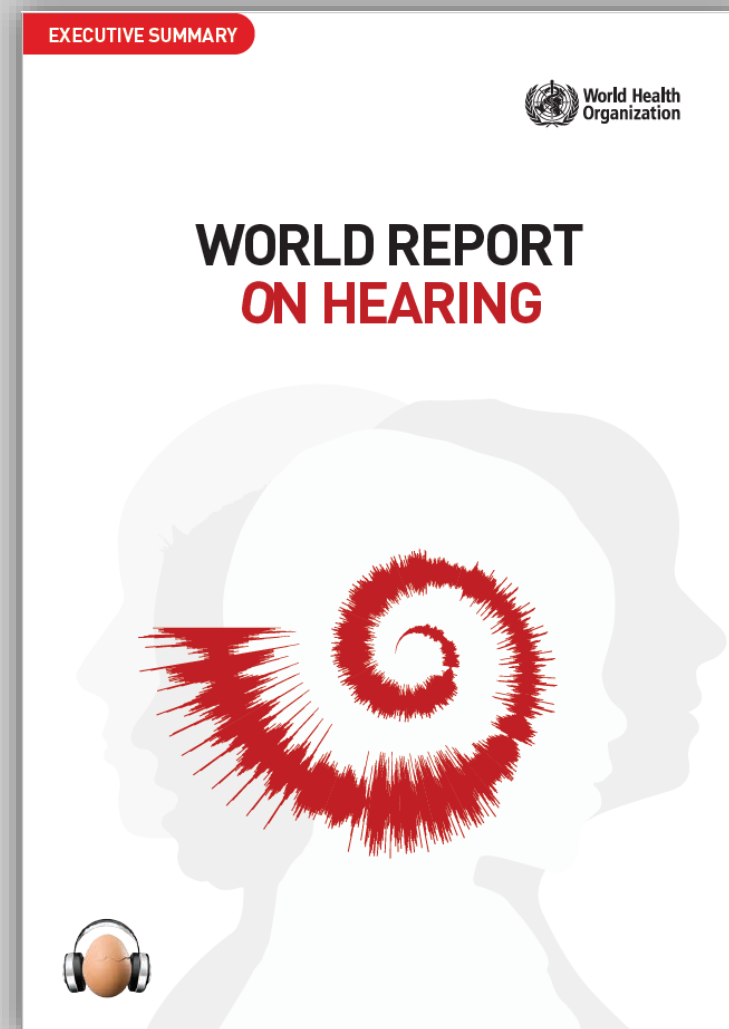
World Report on Hearing

First Ever World Report on Hearing

*released on World Hearing Day:
March 3rd, 2021*

In response to World Health Assembly resolution
(WHA70.13)

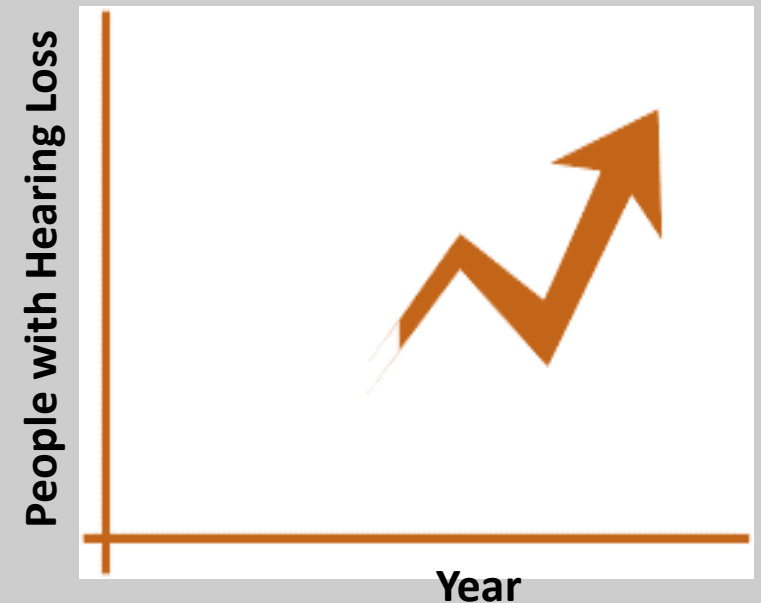
To provide guidance to WHO member states to integrate
ear and hearing care into national health plans



<https://www.who.int/publications/i/item/world-report-on-hearing>

Hearing loss (HL) as a Global Concern

- Estimated 430 million people with disabling hearing loss in 2019 (World Health Organization [WHO] 2021):
 - Adults (15 years and older): PTA > 40 dB
 - Children (0-14 years): PTA > 30 dB
- 5.5% of the world's population
- Expected to grow to 7.5% of the world's population by 2050
- **Unaddressed hearing loss global cost = \$980 billion annually (US dollars)**



World Health Organization (2021). "World Report on Hearing." Accessed from: <https://www.who.int/publications/i/item/world-report-on-hearing> (Accessed July 25, 2021).

Prevalence of Disabling HL by Income Group

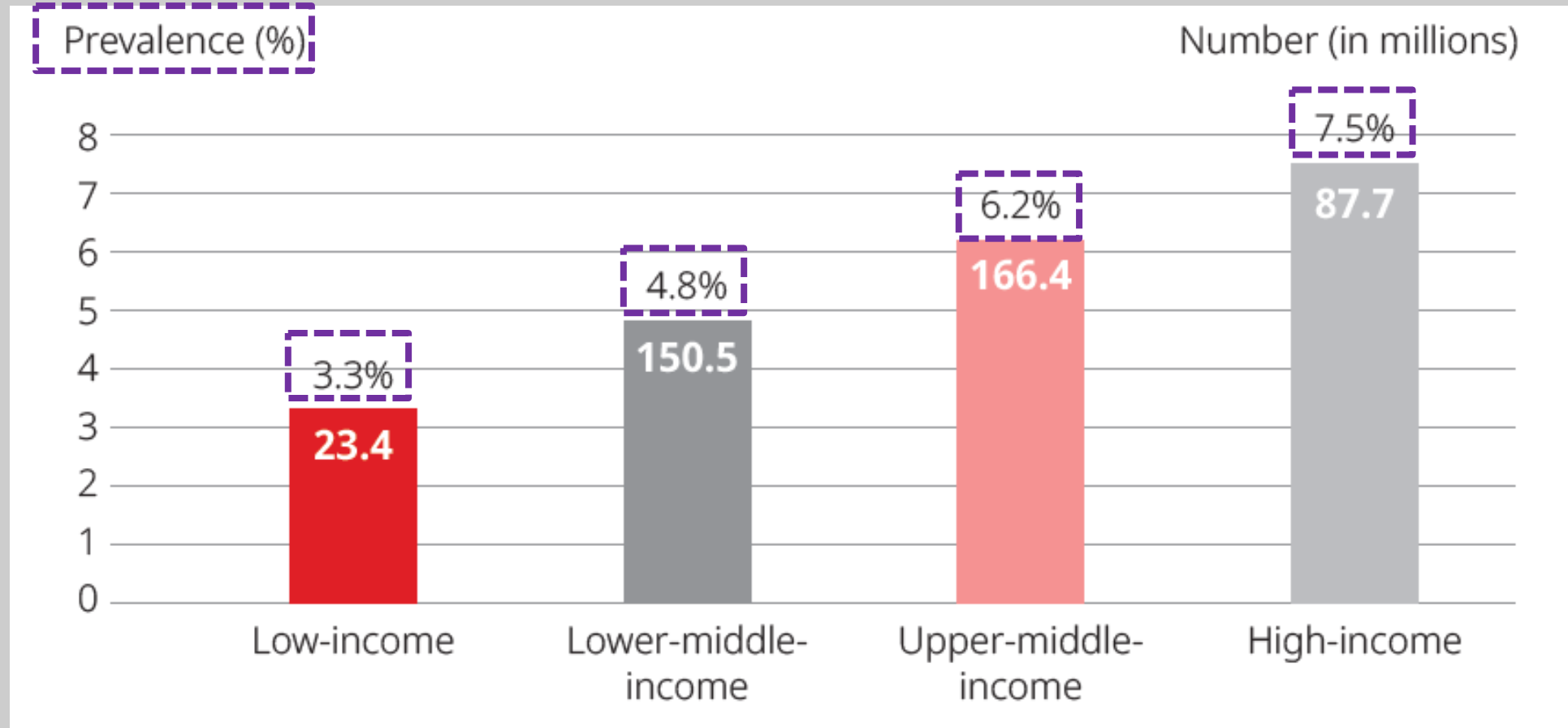


Figure 1. Prevalence of disabling hearing loss (PTA > 40 dB) by World Bank income group. (WHO, 2021)

Prevalence of Disabling HL by Income Group

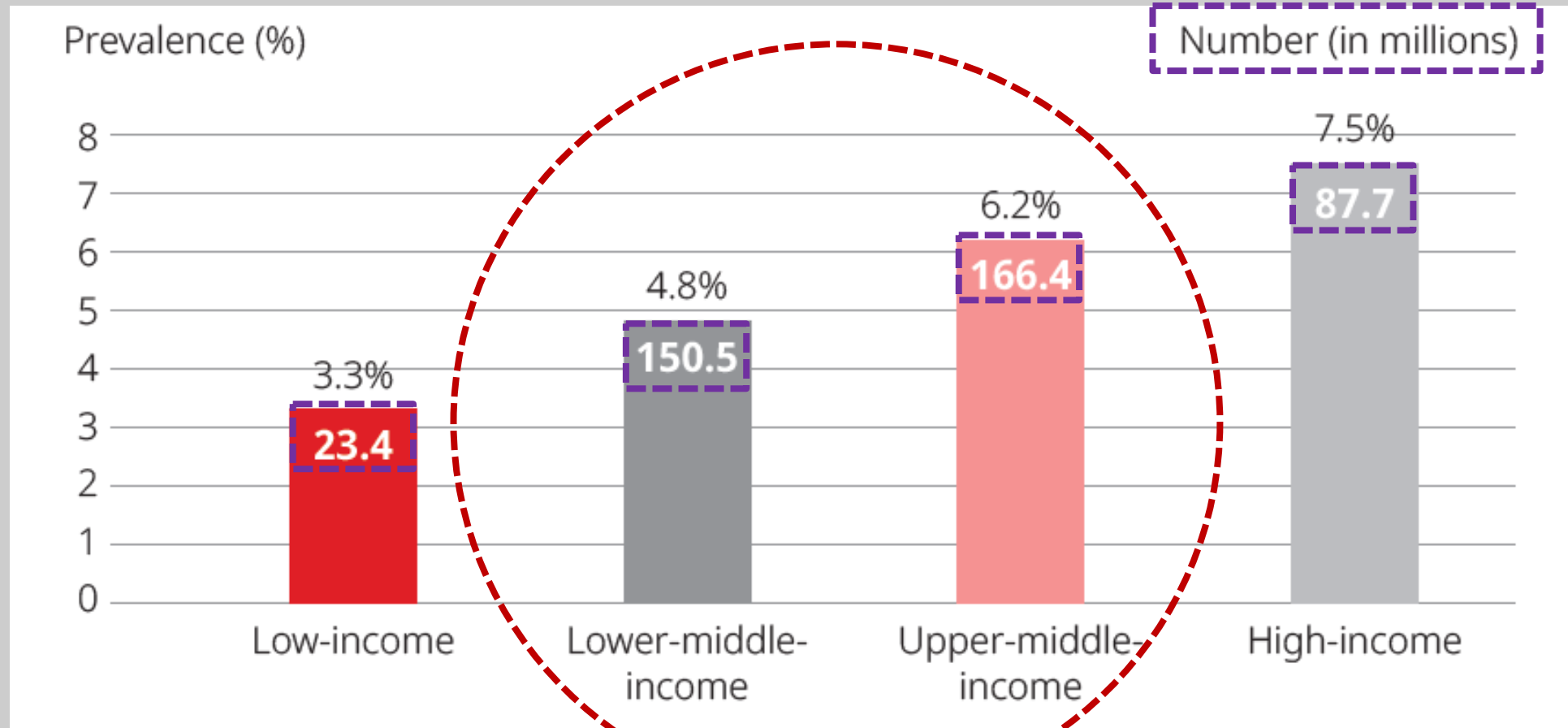


Figure 1. Prevalence of disabling hearing loss (PTA > 40 dB) by World Bank income group. (WHO, 2021)

Prevalence of Disabling HL by Income Group

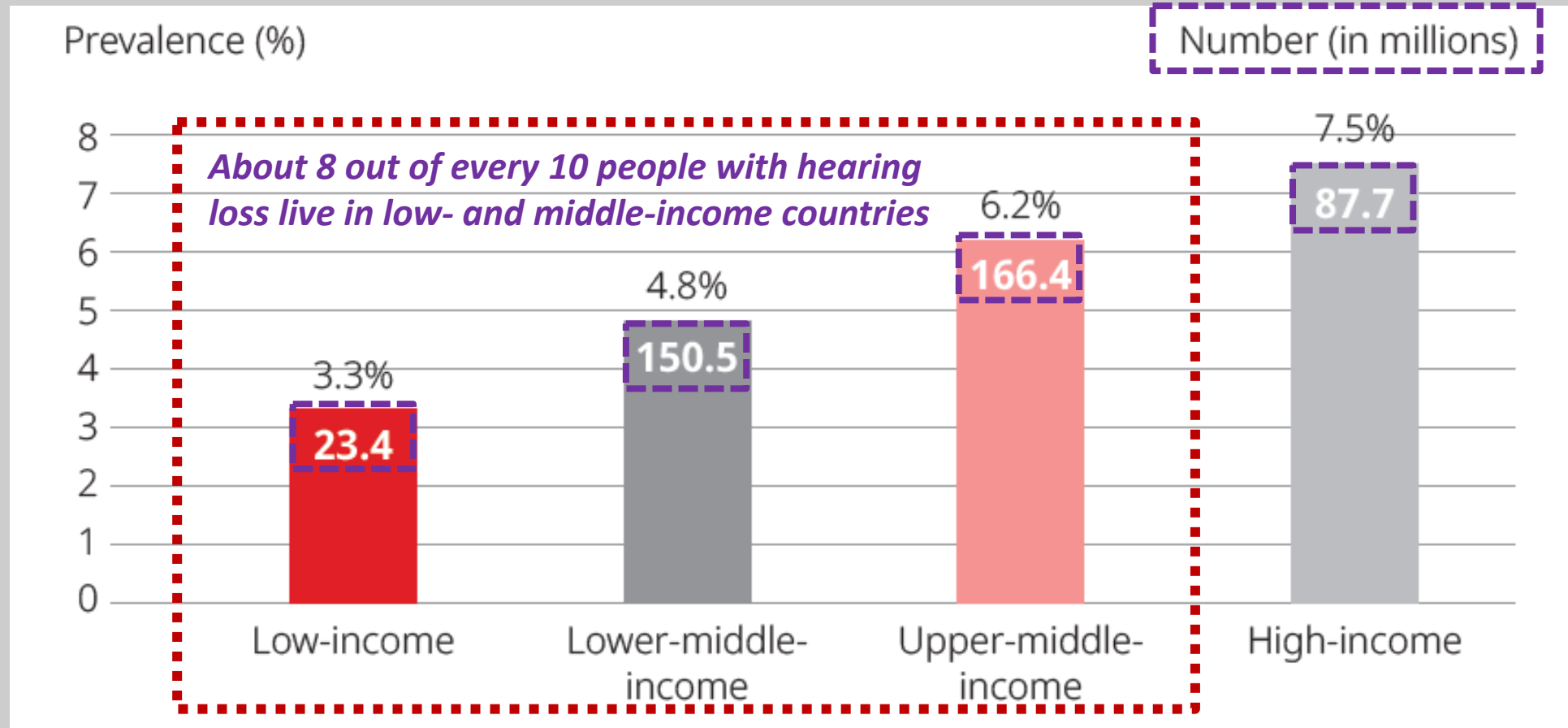
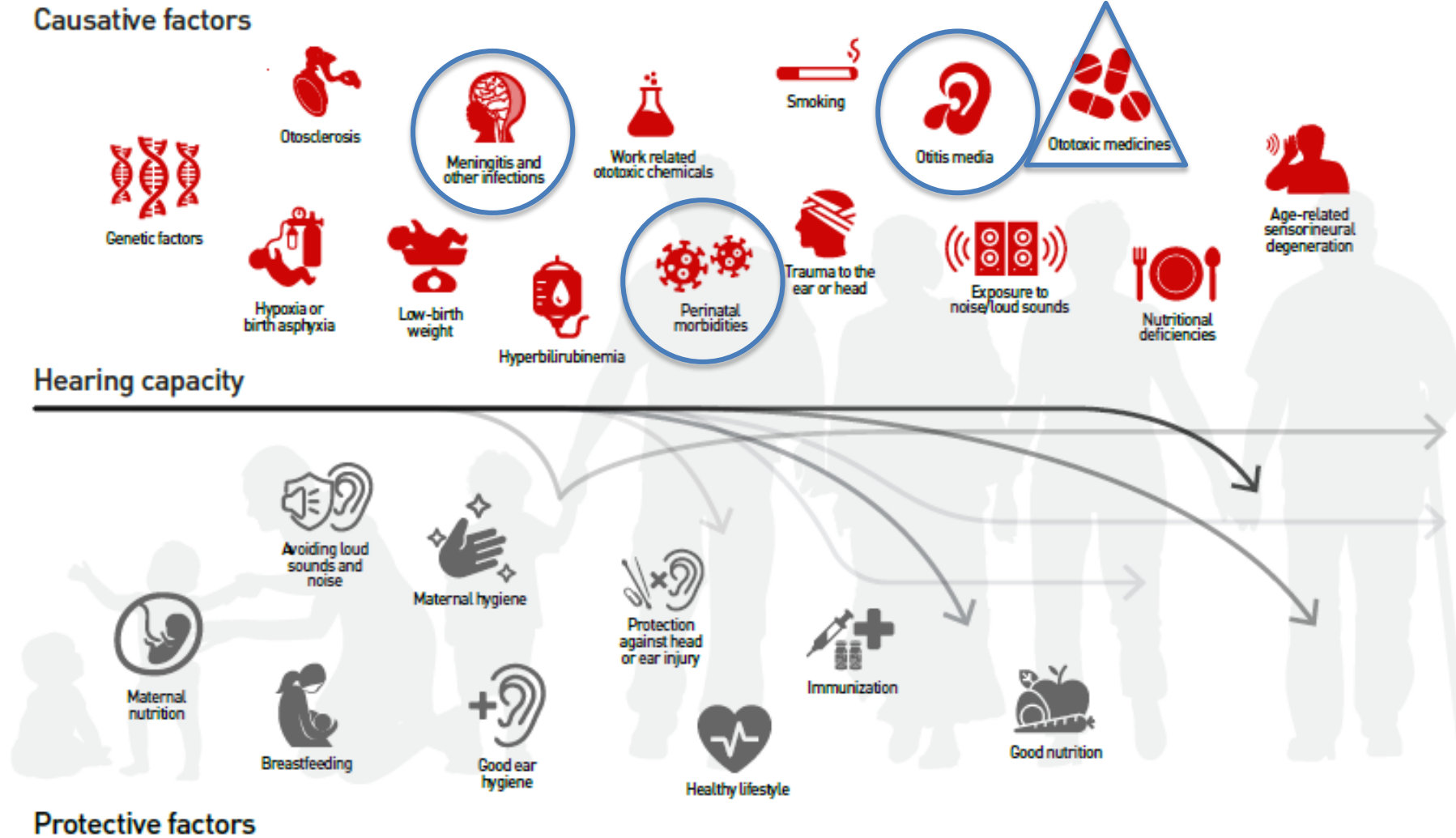


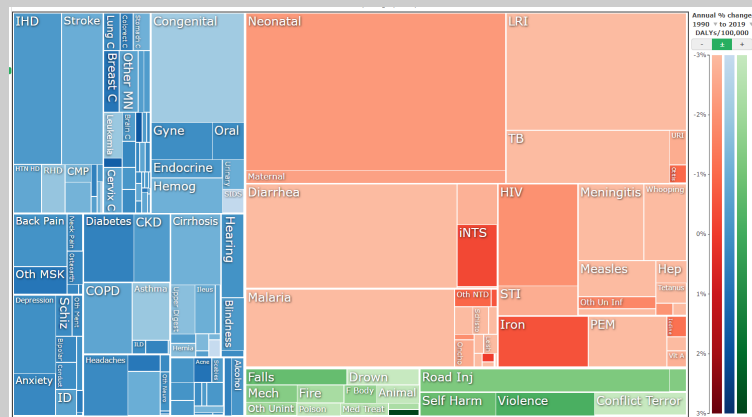
Figure 1. Prevalence of disabling hearing loss (PTA > 40 dB) by World Bank income group. (WHO, 2021)

Figure 1.1 Hearing across the life course

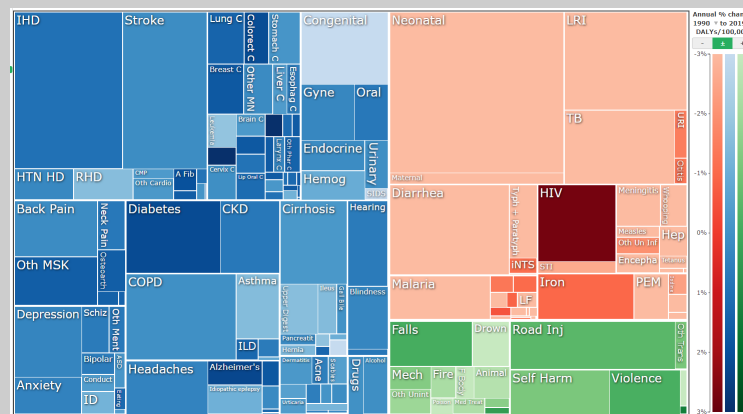


Disability Adjusted Life Years by Cause

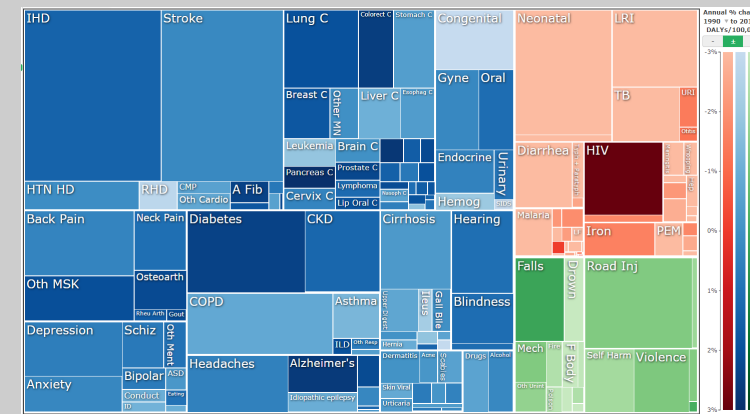
Low Income



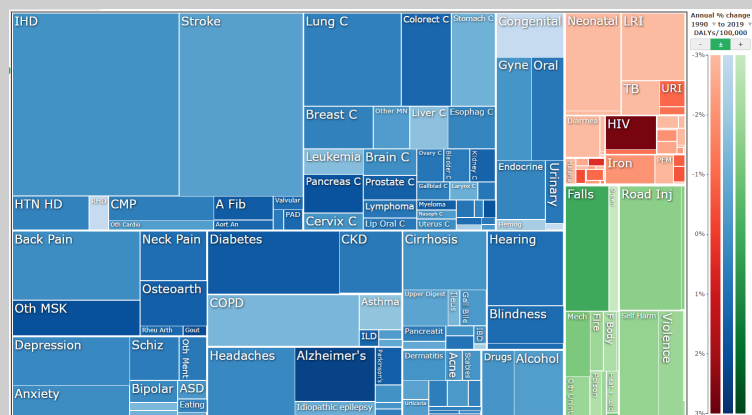
Low-Middle Income



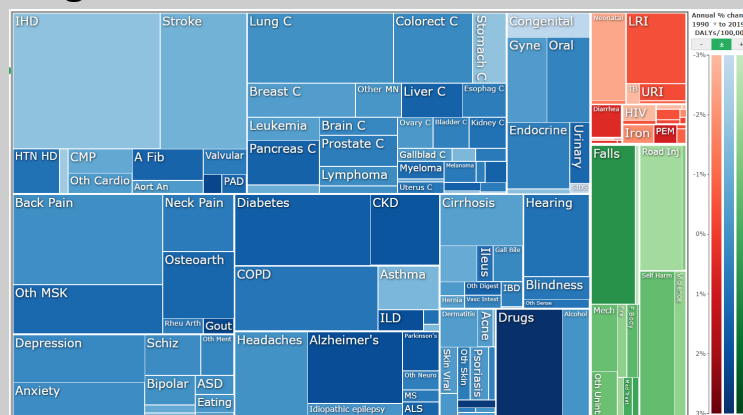
Middle Income



High-Middle Income



High Income



Blue: Non-communicable disease
Red: Communicable disease
Green: Injury

Costs of Infection-related HL

- Viral infections account for ~40% of non-genetic congenital HL
- Infectious-related hearing loss comes with staggering costs
 - Health sector, educational support, loss productivity, societal costs, reduced income
 - Cytomegalovirus economic burden > \$2 billion annually

Costs of Infection-related HL

- Some viral infections can be prevented with robust vaccination programs
- WHO estimates **nearly 20% of childhood hearing loss** can be avoid through rubella and meningitis vaccination programs

Reducing the Burden: Prevention

- Primary
 - Avert the adverse condition
 - Implementation at the community (population) level
 - Usually relatively inexpensive
- Secondary
 - Detect the condition early and treat promptly
 - More expensive
- Tertiary
 - Reduce the impact of an established condition
 - The most expensive
 - Requires robust specialized workforce

*Where audiologists
need to spend more
time*

*Where audiologists
usually spend their time*

Global Perspective – Why should we care?

- Migration: Main source of infectious disease transmission throughout history
 - In US, ~45 million immigrants
 - Individuals bring along a history of exposure to infections often not present in the host country
 - Disease patterns and access to vaccinations in the country of origin to inform

Global Perspective – Why should we care?

- Travel – we are more connected now than ever before
 - 1970: 165.8 million international arrivals
 - 2018: 1.47 billion international arrivals
 - Infectious agents that survive in human hosts can be carried to any part of the world

Sick cities: how pandemics spread

By: Dirk Brockmann (Theoretical physicist)

<https://www.theguardian.com/cities/video/2014/feb/26/sick-cities-pandemic-spread-video>



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Global Perspective – Why should we care?

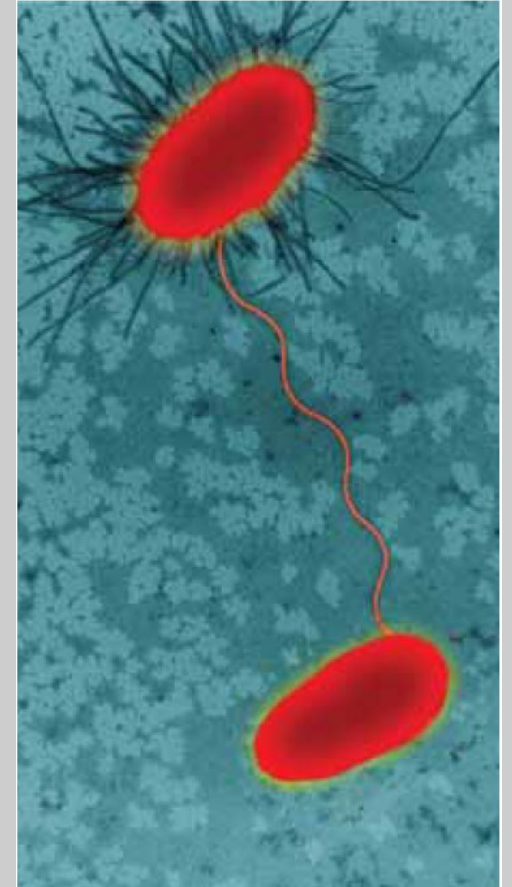
- Climate Change
 - Many infectious agents are influenced and constrained by environmental factors such as temperature, rainfall, and humidity (Thomas, 2020)
 - Affect infectious disease patterns, increasing the prevalence of infectious disease in some areas while decreasing the prevalence of disease in others
 - Contribute to human population migration (for example flooding, food insecurities, droughts, catastrophic weather systems, etc...)

Types of Infectious Agents

- Bacteria
- Viruses
- Fungi
- Protozoa/Helminths (parasites)
- Prions

Bacteria

- One-cell organisms
- Live and reproduce on its own
- Quick to adapt and acquire new genetic material from other bacteria, viruses, yeasts, etc...
- Transmission:
 - Between people
 - Pregnant person to fetus (vertical transmission)
 - Primary infection or Reactivation of prior infection
 - Primary infection during pregnancy associated with more severe disease
 - Animal to person (zoonotic)
 - Indirectly through insect
- Treated with antibiotics – can become resistant to treatment



Virus

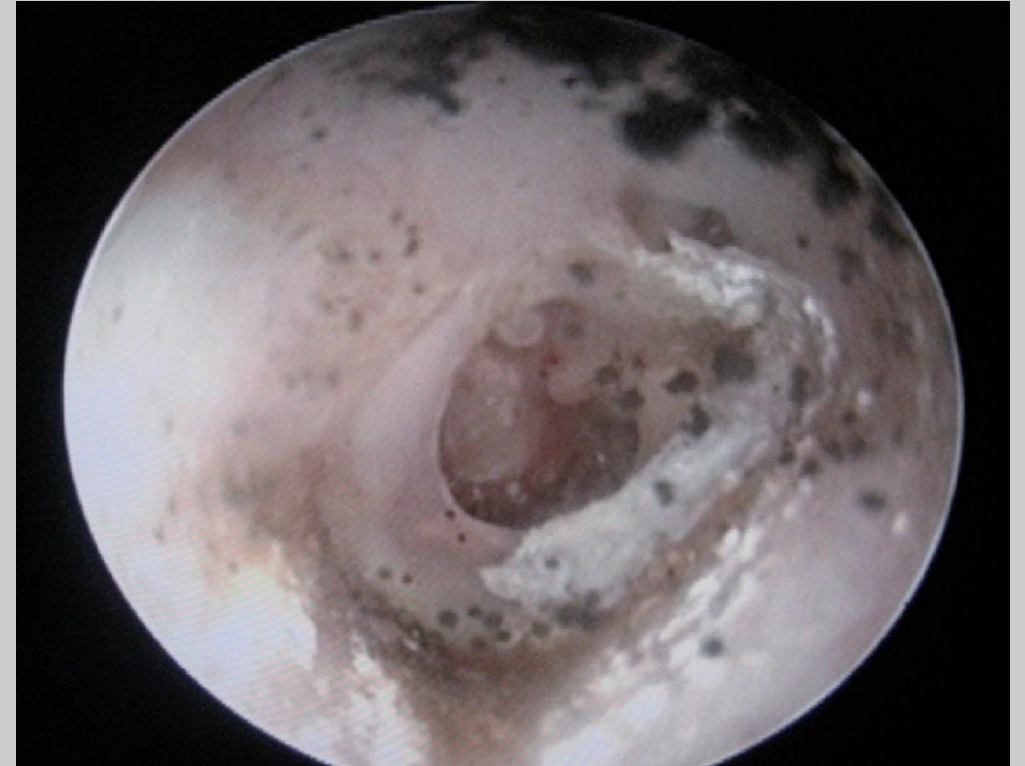
- Packets of nucleic acid (DNA or RNA) surrounded by a protein shell
- Smaller than bacteria and cannot reproduce without a host
- Transmission:
 - Between people
 - Pregnant person to fetus (vertical transmission)
 - Primary infection or Reactivation of prior infection
 - Primary infection during pregnancy associated with more severe disease
 - Animal to person (zoonotic)
 - Indirectly through insect
- Responsible for illness such as the common cold and influenza (flu).



An electron micrograph of an influenza virus particle (Drexler 2010)

Fungi

- Spore-forming organisms
- In healthy individuals, fungi exposure usually results in no or mild disease
- In immune-compromised individuals, fungal infections are more common and severe



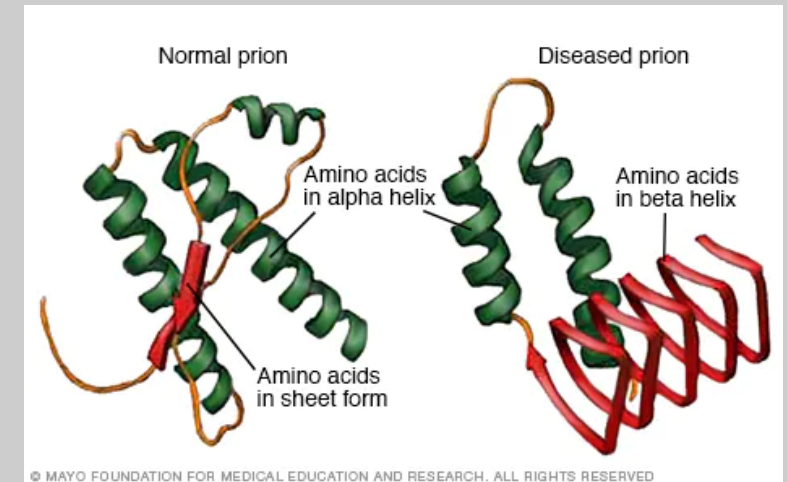
Otomycosis – Outer ear fungal infection (Dundar & İynen, 2019)

Protozoa and Helminths

- Class of parasites (responsible for malaria, toxoplasmosis and others)
- Organisms that live on/in a host and feeds off the host
- Multiply easily in humans
- Transmission:
 - Fecal-oral
 - Insect vector
 - Consuming contaminated water or food (undercooked meat)
- Infection is usually asymptomatic, but the parasite can cause tissue damage or indirectly via immune response

Prions

- Protein found in the brain that becomes an abnormal shape, causing neurologic disease
- Creutzfeldt-Jakob disease associated with bilateral moderate or worse retrocochlear hearing loss, dizziness, and gait disturbances along with cognitive decline
- Can occur sporadically, be inherited, or acquired (infectious)
 - Transmission – eating diseased meat
 - Variant Creutzfeldt-Jakob disease
 - Same agent responsible for bovine spongiform encephalopathy (mad-cow)
- Disease is always fatal



[Creutzfeldt-Jakob disease - Symptoms and causes - Mayo Clinic](#)

Infectious disease that are endemic or have potential to (re)emerge in the US

Endemic in the US

- Toxoplasmosis (congenital)
- Cytomegalovirus (congenital)
- HIV (congenital/acquired)
- HSV (congenital)
- Syphilis (congenital/acquired)
- Varicella-zoster (acquired)
- Meningitis (congenital/acquired)

Potential to Re-emerge in the US

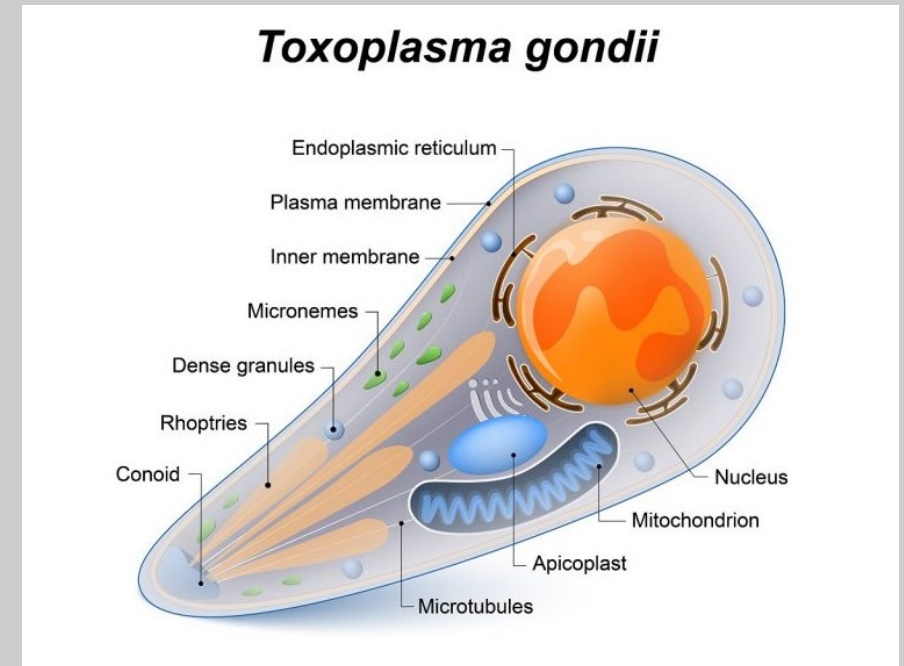
- Mumps (acquired)
- Measles (acquired)
- Rubella (congenital)

Emerging

- SARs-CoV-2 (acquired)
- Zika (congenital)

Endemic: Toxoplasmosis

- Worldwide disease
- First human case described in 1923
- Only natural hosts are members of the feline family
- Infects ~800,000 persons/year in the US
 - 11% of the US Population > 6 y.o.
 - Generally infected for life
- Transmission:
 - Consuming contaminated food/drink
 - Contact with cat feces
 - Vertical transmission (primary infection)
 - 300-4,000 cases per year



[List of Parasites of Humans | STD.GOV Blog \(std.gov.org\)](https://std.gov/blog/list-of-parasites-of-humans/)

Congenital Toxoplasmosis

- Incidence of in the US is 1-10 per 10,000 live births (Lopez et al., 2000)
 - Higher in Brazil 6-13 per 10,000 live births (de Andrade et al., 2008)
- Parasites reach the brain and all other organs through the bloodstream
- Pathology often limited to the central nervous system including inflammation of the brain and brainstem
- Mastoid, middle ear, and inner ear (stria vascularis) have shown parasites and lesions and was considered to be the cause of HL historically (Kelemen, 1958).
 - Bilateral and unilateral

Congenital Toxoplasmosis

- Several studies in the US and Norway suggest anti-parasitic treatment in the first year significantly reduces the risk of HL
- Conflicting results observed in Brazil
 - 56.6% normal hearing
 - 12.3% had conductive HL
 - 27.4% SNHL
 - 27.4% central hearing dysfunction
- Considering effects of *T. gondii* on the central nervous system – primary effects on the auditory system may be neuromaturational lag
- May be related to the strain *T. gondii*

Potential to Re-emerge: Rubella

- Recognized since the 18th century
- Humans are the only natural host
- Transmission:
 - Droplets from respiratory secretions
 - Vertical transmission
 - Significant transmission among those who are asymptomatic
- Serious health problems if primary infection occurs just before conception or early in pregnancy (< 16 weeks gestation)
- Congenital rubella infection may be as high as 80-90% during first trimester and declines with increasing gestational age

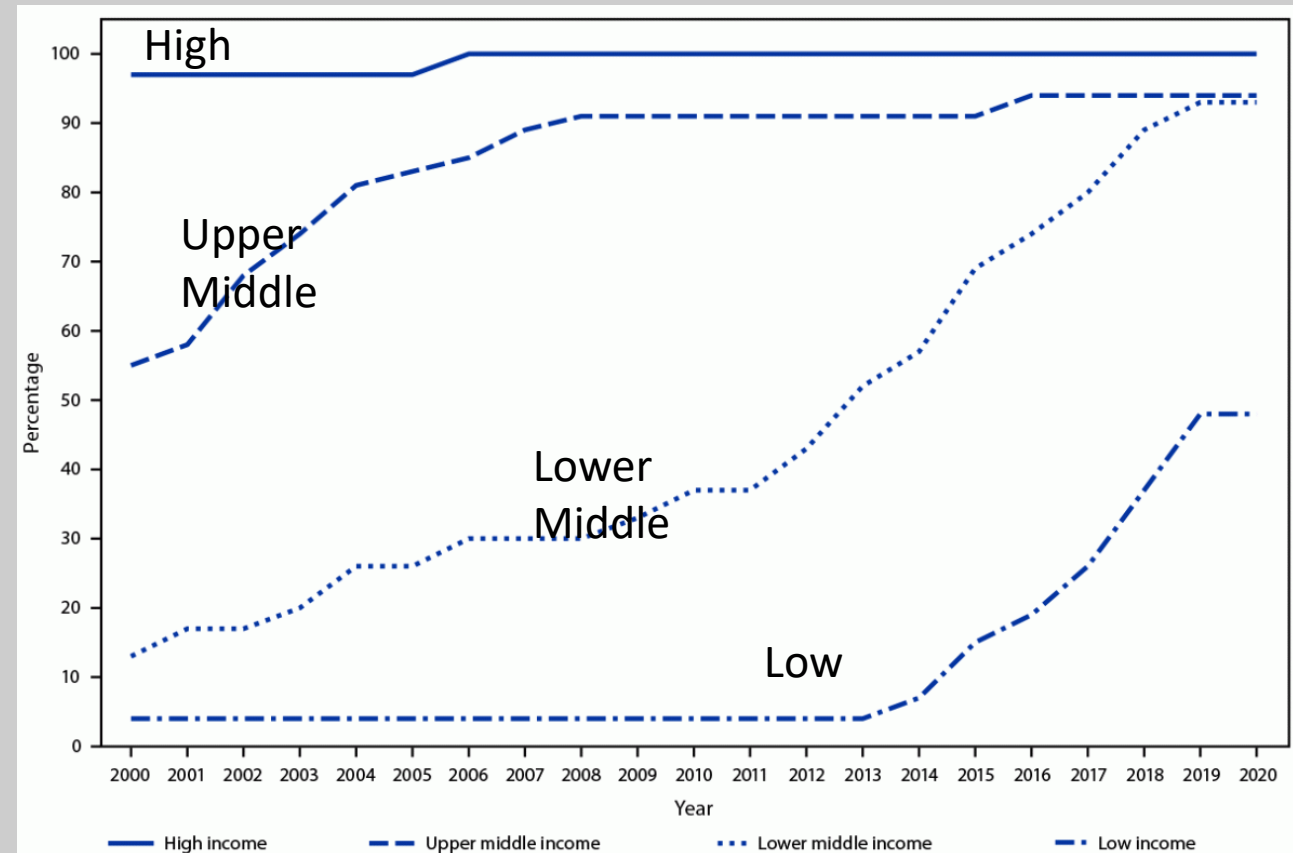


Rubella

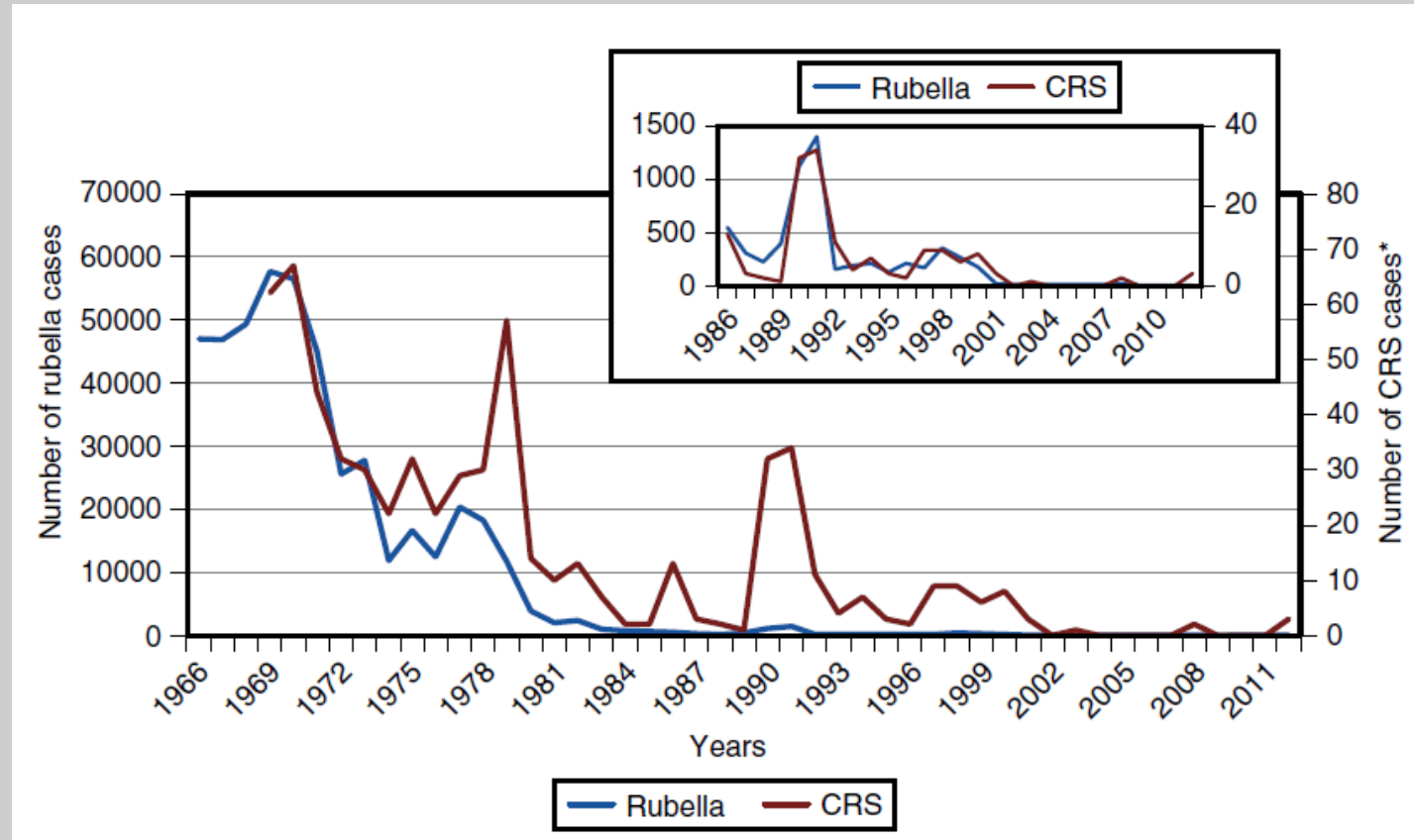
- Congenital Rubella Syndrome (CRS)
 - Ocular abnormalities
 - Sensorineural hearing loss (SNHL)
 - Heart/brain abnormalities
- CRS highest < 11 weeks gestation – near 90%
 - Declines with gestational age
 - SNHL as late as week 20
- HL is usually severe, relatively flat 250-8000 Hz, bilateral, and unchanging
- 1964 Epidemic in US – 20,000 infants were born with CRS
- 1969 US introduced a rubella vaccine – MMR 1971

Rubella: Worldwide vaccination rates

- Eliminated in the US and most of the Americas with widespread vaccination efforts
- Vaccination remains lowest in WHO African and South-East Asian regions



Rubella Vaccination



Reported rubella and congenital rubella syndrome—United States, 1966-2012. *Year of birth (Reef & Plotkin, 2013)

Emerging: SARS-CoV-2 (COVID-19)

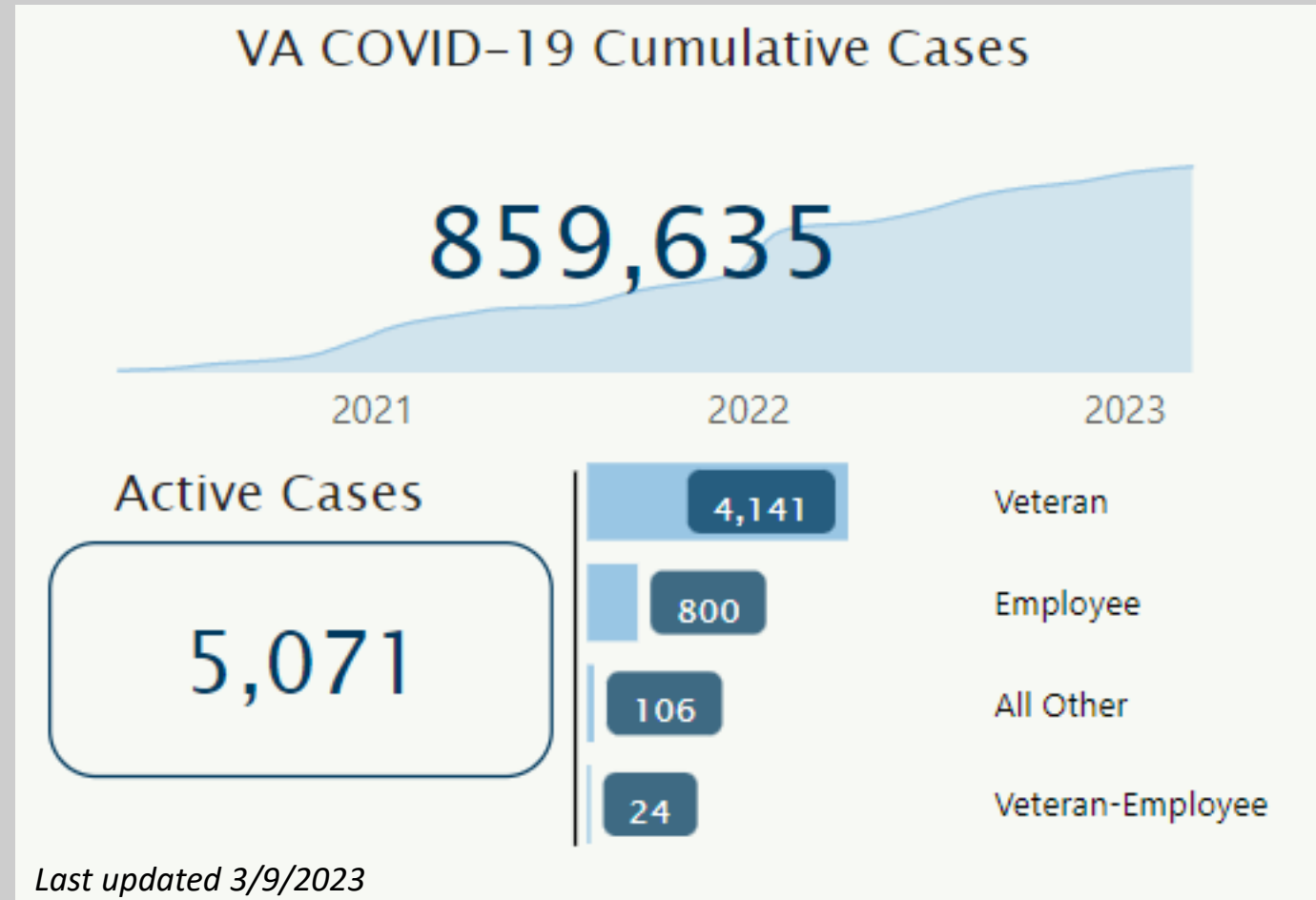
- Novel coronavirus identified in late 2019
- Hosts in mammals and birds
- Transmission:
 - direct contact
 - droplets from respiratory secretions
 - Aerosolized respiratory droplets
- Worldwide, over 759 million cases and 6.8 million deaths
 - Mortality rate 0.9% or 904 per 100,000 cases
 - Flu/pneumonia mortality 12.6 per 100,000

COVID-19 Cases in the VA

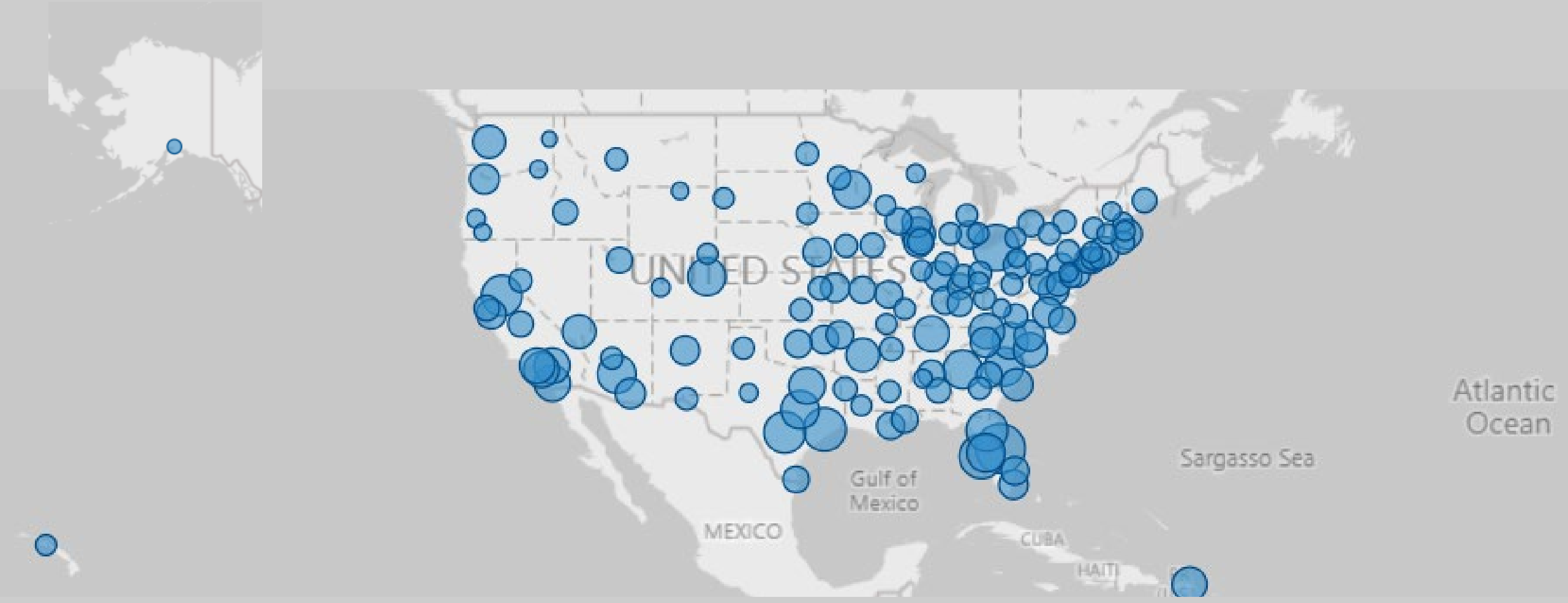
*First Veteran case:
March 2nd, 2020*

*Mortality Rate: 2.8%
(2,830 per 100,000 cases)*

*3x the mortality rate of the
general population*



Distribution of COVID-19 Cases in the VA



VA



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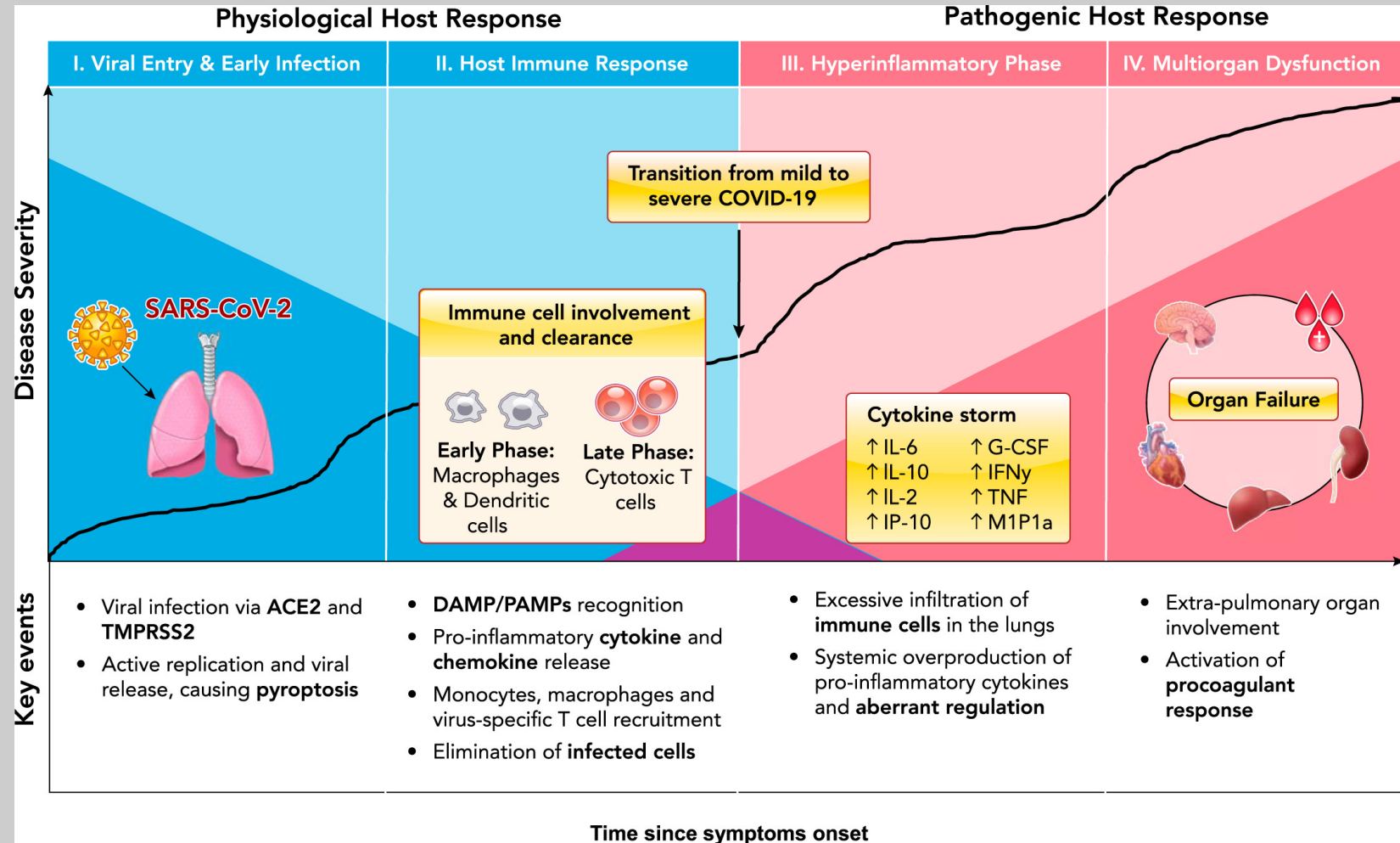
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[COVID-19 National Summary | Veterans Affairs \(va.gov\)](https://www.va.gov/covid-19-national-summary/)

COVID-19 Pathophysiology

- Angiotensin converting enzyme 2 (ACE2) as an entry receptor for SARS-CoV-2
 - Respiratory tract epithelial cells serve as a gateway to systemic infection
 - ACE2 receptors are abundant in the body including in the brain and temporal lobe
 - ACE2 receptors are also abundant in the walls of blood vessels
 - Inner ear expresses ACE2 receptor (Jeong et al 2021)
- SARS-CoV-2 prevents the receptors from performing their normal function, subsequently allowing inflammation and injury to multiple organs in the body

COVID-19 Pathophysiological Progression



The dark blue shading indicates physiological viral host response over time, and the dark red shading indicates pathogenic hyperinflammatory host response over time. <https://journals.physiology.org/doi/full/10.1152/physiol.00019.2020>

Current Research COVID-19→HL

- Several case studies/series highlighting sudden hearing loss with infection
- Detected in the middle ear cadavers
- Survey of individuals (n=121) with COVID and hospitalized: 13% reported change in hearing/tinnitus
- Survey of individuals (n=95) with tinnitus and COVID-19 symptoms, 40% reported worsening tinnitus
- Decreased hearing sensitivity and OAEs in those with vs without COVID-19
- Minimal to no vertical transmission and no reported associations between COVID-19 during pregnancy and congenital HL in offspring

Current Research COVID-19→HL

- Meta-Analysis reported event rates (Jafari et al 2021):
 - 3.1% (1.0-9.0%) hearing loss
 - 4.5% (1.2-15.3%) tinnitus
 - 12.2% (7.0-20.4%) dizziness

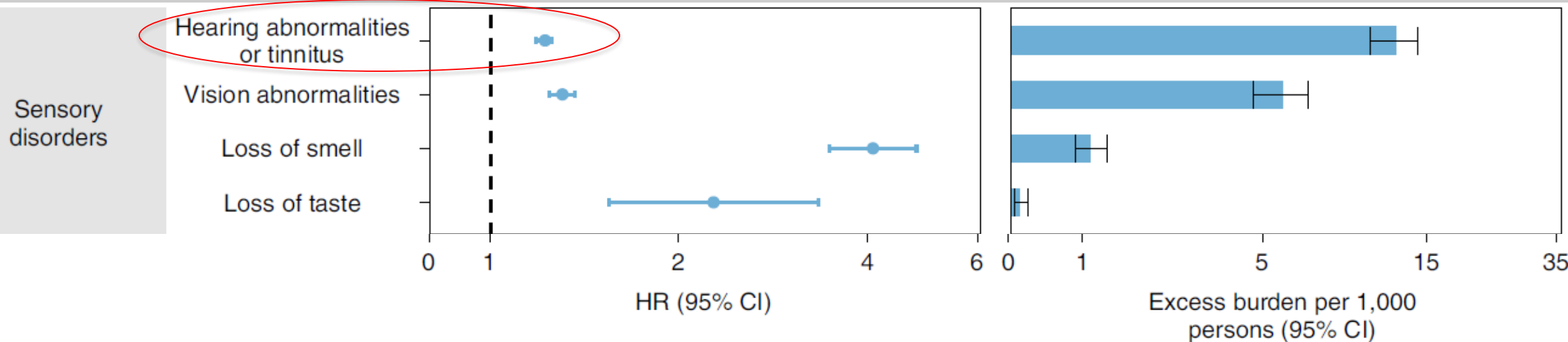
Caution: Insufficient evidence and
heterogeneity among studies

Long-term sensory disorder outcomes in COVID-19: Veteran Cohort

- Veteran health care users
 - COVID-19 n=154,068
 - Non-exposed COVID-19 n=5,638,795
 - Historical non-exposed cohort n=5,859,621
- Electronic medical record abstraction
- Followed for ~12 months for incident disease/outcomes

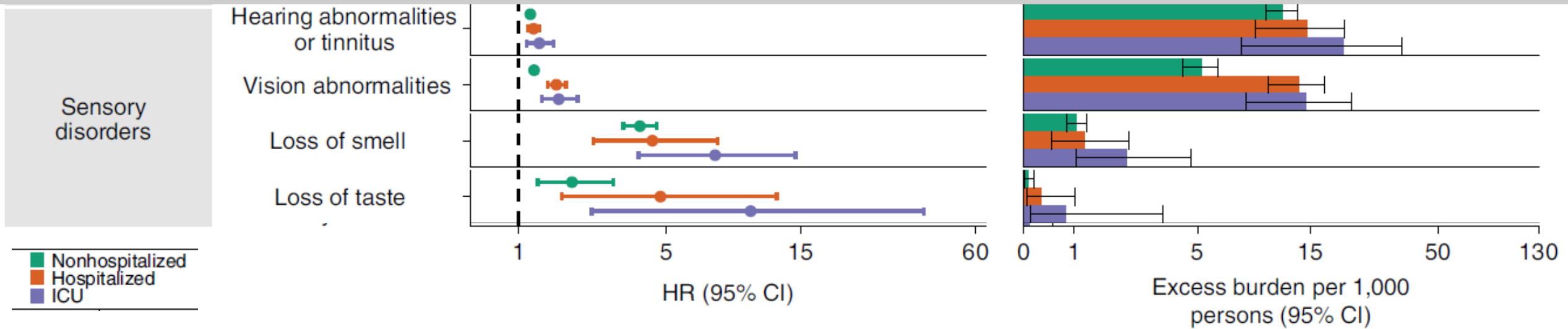


Long-term sensory disorder outcomes in COVID-19 – Veteran Cohort



Hearing abnormalities or tinnitus: **HR 1.22 (1.18, 1.25)** and **burden 11.87 (10.05, 13.75)**
Burdens are presented per 1,000 persons at 12 months of follow up – COVID-19 added about 10,000 cases of hearing loss/tinnitus

Long-term sensory disorder outcomes in COVID-19 – Veteran Cohort



Long-term sensory disorder outcomes in COVID-19 – Veteran Cohort

- Limitations
 - Diagnostic codes for incident disease that is insidious
 - Hearing loss progresses 7-10 years before someone seeks intervention

Auditory Rehabilitation Needs in COVID-19 Survivors

- 2-year Small Project Award (December 2021)
- Goal: Evaluate the prevalence of adverse auditory sequelae and assess the rehabilitation needs among COVID-19 survivors to assist the VA in supporting this population of Veterans
- Design: Mixed-methods study
 - Quantitative data regarding COVID-19 auditory sequelae will be gathered via patient surveys and review of the VA electronic health record.
 - Qualitative data will be gathered via semi-structured interviews with COVID-19 survivors.

Auditory Rehabilitation Needs in COVID-19 Survivors: Methods

Study Design:

- Retrospective cohort.

Data Source:

- VA electronic health records from the VA Corporate Data Warehouse (CDW) extracted between March 2020 and October 2022.
- VA COVID-19 Shared Data Resource provided information relevant to COVID-19.

Participants:

- Veterans who were tested for SARS-Cov-2 and were free from a history of sudden hearing loss at the time of the first test.

Auditory Rehabilitation Needs in COVID-19 Survivors: Methods

Exposure:

- Veterans were classified as either having:
 - a negative test result (n=1,392,578).
 - a positive test result without hospitalization within 30 days of the test date (n=548,908).
 - a positive test result with hospitalization within 30 days of the test date (n=72,818).

Outcome:

- International Classification of Disease – 10th ed. (ICD-10) diagnostic codes for sudden hearing loss (SHL): H91.20, H91.21, H91.22, or H91.23.

Statistical Analysis:

- Incidence rate ratios (aIRR) and 95% confidence intervals (CI) were estimated using binary logistic regression – adjusted for age, sex, race, and ethnicity.

Auditory Rehabilitation Needs in COVID-19 Survivors: Results

Table 3. Risk of sudden hearing loss diagnosis among those with a positive COVID-19 test in the VA health care record.

COVID-19 Test Result	# of SHL Events	Follow-up time (person-years)	Rate per 100,000 person-years	Rate Ratio	Adjusted* Rate Ratio (95% CI)
Negative	1099	2,412,118	45.56	[1]	[1]
Positive, Not hospitalized	269	649,273	41.43	0.91 (0.80 - 1.04)	0.95 (0.84 - 1.09)
Positive, Hospitalized	54	77,097	70.04	1.54 (1.17 - 2.02)	1.40 (1.07 - 1.84)
Total	1422	3,138,489	45.31	--	--

*Adjusted for age, sex, race, and ethnicity.

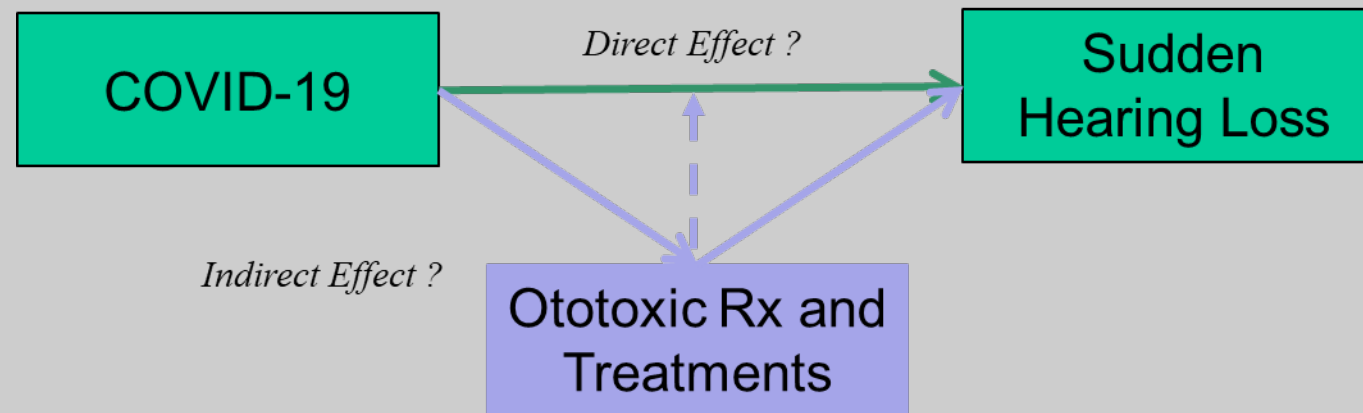


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Reavis KM, McMillan GP, Phillips R, Steyger P, Messer W, Hullar T, Pigott K, Carlson KF. *Association between COVID-19 and sudden hearing loss in military Veterans*. Poster presentation at the American Auditory Society, Scottsdale, AZ, March 2023

Auditory Rehabilitation Needs in COVID-19 Survivors: Discussion

- **Sudden hearing loss is a rare event** with a rate of about 45.3 cases per 100,000 person-years.
 - Previous reports place the incidence of SHL between 11-77 per 100,000 people per year (Alexander & Harris, 2013).
- Veterans **with COVID-19 and hospitalized** within 30 days of a positive test **have a 40% increased risk** of sudden hearing loss compared to individuals without COVID-19.
- Mechanisms behind the increased risk remain unclear.



Auditory Rehabilitation Needs in COVID-19 Survivors: Next Steps

- Investigate mechanisms
- Chart review 1422 – treatments, recovery
- Address selection bias (loss to follow-up)
- Incorporate results from survey
- Conduct interviews

Summary

- Infectious diseases are a significant cause of hearing loss around the world, and their impact can be profound
- Hearing loss may be permanent and can have significant impacts on the affected individuals' quality of life
- Important to prioritize measures to prevent and control infectious diseases including vaccination and appropriate treatment, to reduce the incidence of hearing loss and its associated complications.
- Efforts to improve access to hearing screening and intervention services can help individuals affected by infectious diseases to receive timely and appropriate care
- Some infectious agents can lead to multiple comorbidities and result in various clinical manifestations.
- This complexity necessitates interprofessional care to address the multiple problems associated with the infection.

Book Chapter *Coming*

Infectious Agents and Auditory Dysfunction

By:

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Thank you

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