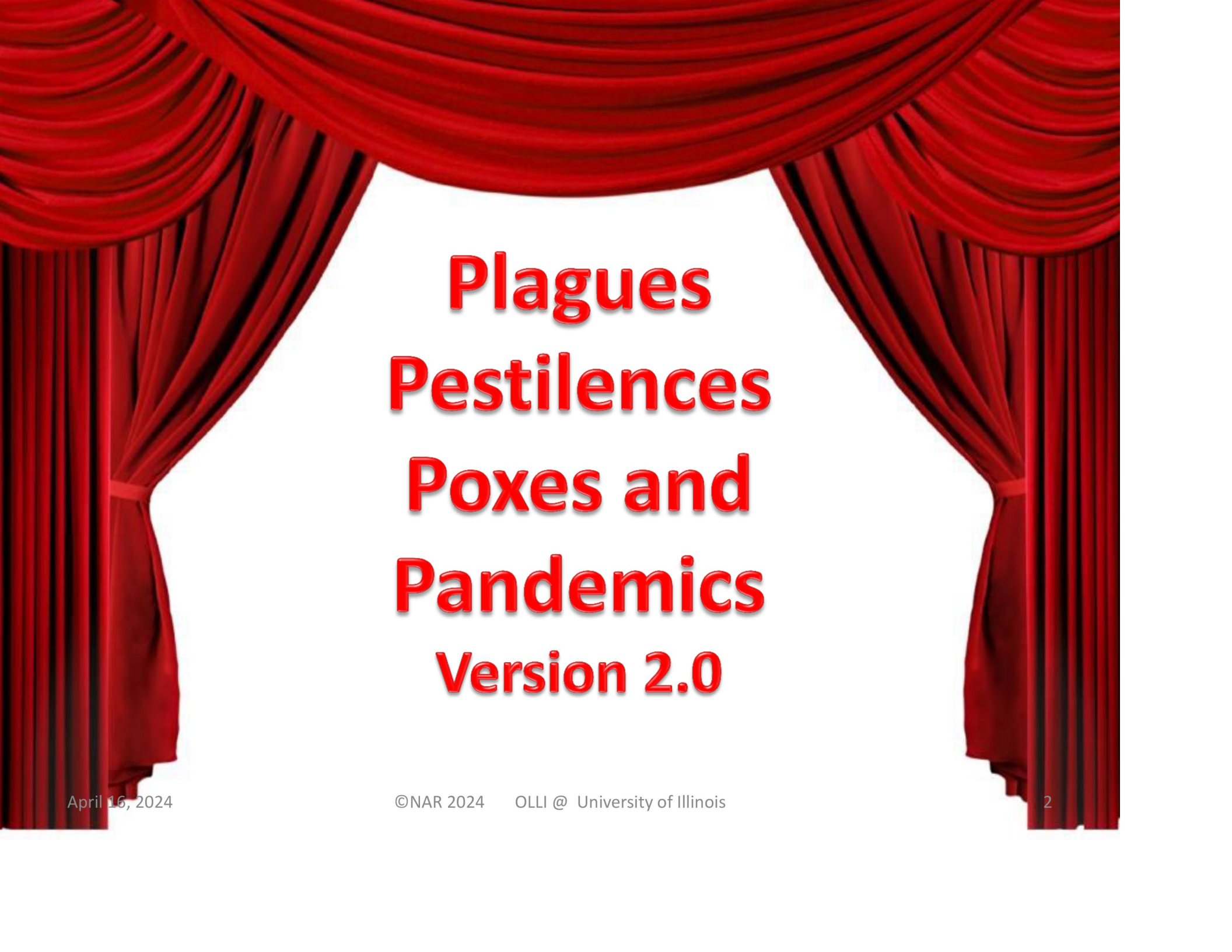


# Good Afternoon





**Plagues  
Pestilences  
Poxes and  
Pandemics  
Version 2.0**

April 16, 2024

©NAR 2024 OLLI @ University of Illinois

2



# Plagues, Pestilences Poxes and Pandemics

OLLI @ University of Illinois  
2024 Spring Semester

# Session 8

## Crystal Ball into the Future?

April 16, 2024

Néstor A. Ramírez, MD, MPH



# Course Overview

- Session 1 February 27: Definitions, Biblical Plagues.
- Session 2 March 5: The PLAGUE through time & place.
- Session 3 March 12: Other epidemic diseases.
- Session 4 March 19: The Columbian Exchange.
- Session 5 March 26: 20<sup>th</sup> Century Pandemics Past & Current
- Session 6 April 2: HIV/AIDS
- Session 7 April 9: 20<sup>th</sup> and 21<sup>st</sup> Century Viruses.
- **Session 8 April 16: Crystal Ball into the Future?**


# Purpose and Plan of this Program (Recap)

**Provide a peripatetic, panoramic perusal of the particulars of the past, present and potential plagues, pestilences, poxes and pandemics that produce pervasive panic and persistently put peoples' permanence on this planet at prolonged peril, plus presenting possible positive principles of prevention.**

Ramírez 2020

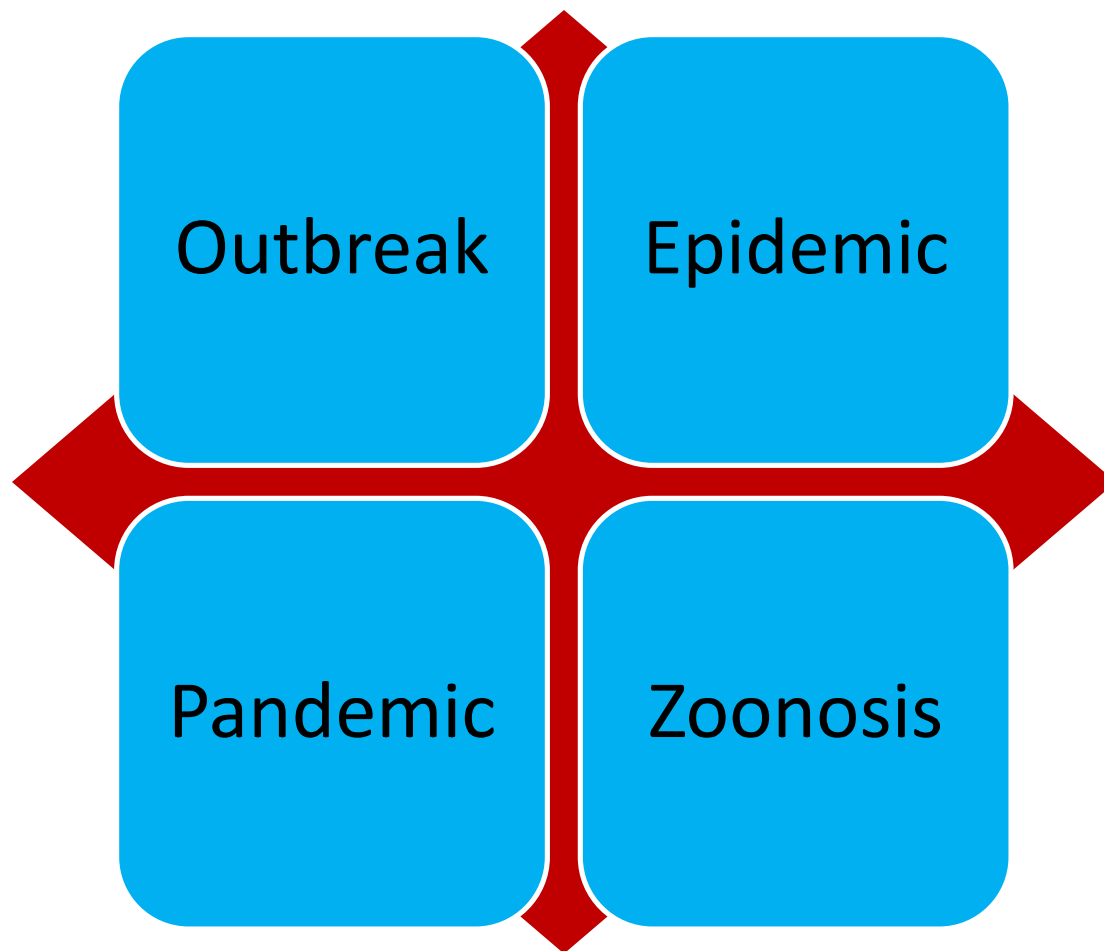


# Plan for the Session

- Disease in the Movies
- Mistakes in Covid-19 handling
- Old enemies returning
- New enemies
- Animals  Humans transmission
- The next pandemic
- Disease X
- What now?

# Definitions

(Reminder)





# Disease Attacks in Movies



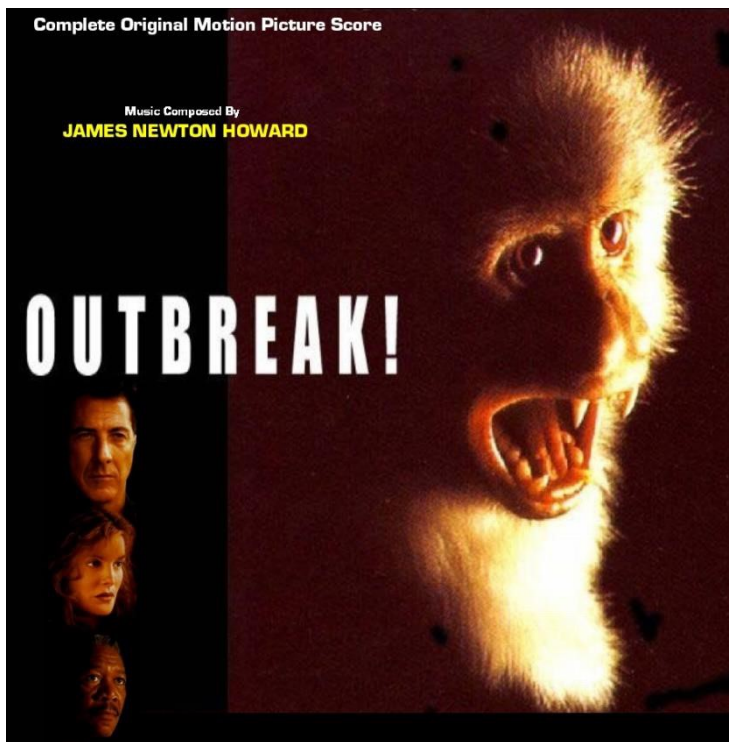
The sudden occurrence of a mysterious illness has always fascinated moviegoers.

Large numbers of sick and dead scare, amuse, and engage audiences worldwide.

Hollywood glamorizes health workers and embellishes their jobs.

Exaggeration, misrepresentation and distortion of actual facts often happen.

**The good guys always end up winning!**



April 16, 2024

©NAR 2024 OLLI @ University of Illinois

10

# Humans vs Animals

- For years, scientists have warned the next pandemic threat could be triggered by humans catching infections from animals.
- But now, a study suggests the opposite is actually more likely.
- Researchers from University College London said that Mankind passes on more viruses to animals than we catch from them,

# Humans vs. Animals

- Experts said “humans are as much a source as a sink” for viral health crises.
- UCL Professor Francois Balloux said: 'We should consider humans as one node in a vast network of hosts endlessly exchanging pathogens, rather than a sink for zoonotic bugs.’”

# Humans vs. Animals

- The study found that 64% (about 2/3) of the samples they analyzed were transmitted to animals by humans.
- The author warned that human-transmitted viruses could potentially pose a conservation threat to the human race.
- It may also impact food security if large numbers of livestock need to be culled to prevent an epidemic (H5N1 bird flu strain and cattle in last few years).



# Human vs Animals

- If a virus carried by humans infects a new animal species, the virus may continue to thrive even if eradicated among humans.
- It may even evolve new adaptations before it winds up infecting humans again.
- Understanding how and why viruses evolve to jump into different host species may help us figure out how new viral diseases emerge in humans and animals.

# **COVID-19 PANDEMIC ERRORS and FAILURES**

# Covid-19

- Estimates of the number of people infected by one person with COVID-19 (the  $R_0$ ) have varied.
- WHO's initial  $R_0$  estimates were 1.4–2.5 (average 1.95).
- In April 2020, estimate of the median  $R_0$  was 5.7
- $R_0$  without control measures can be as high as 8.9

# Covid-19 Weaknesses

- COVID-19 revealed weaknesses in global preparedness for, and in response to a pandemic:
  - the underfunding of pandemic preparedness
  - inadequate disease surveillance
  - initially slow response to an emerging pandemic
  - early challenges in procuring PPE
  - inequitable distribution of countermeasures (especially vaccines)
  - fragmented global response

# Lessons from CoVID-19

- We need to rapidly scale up testing
- We need to leverage data more effectively
- We need to seek out a diversity of voices
- We need to continue betting big on vaccines
- We need to actively crowd out bad information
- We need to infuse public health communication with vulnerability



# Lessons from CoVID-19

- We need to question whether we've learned our lessons (or did we just learn how and who to blame?).
- We need to fully accept the failures of the pandemic and ensure that we can learn from our mistakes.
- We need to **m**ourn, **m**emorialize and then **m**ove forward.
- We have to **m**ake **m**eaning out of things we've endured.

A. Acton 2022

# Covid-19 Lessons

- The COVID-19 pandemic is another reminder, that in a human-dominated world, where our activities represent aggressive, damaging, and unbalanced interactions with nature, we will increasingly provoke new disease emergences.
- We remain at risk for the foreseeable future.

# Covid-19 Lessons

- COVID-19 is among the most vivid wake-up calls in over a century.
- It should force us to start thinking collectively and in earnest about living in more thoughtful and creative harmony with nature, even as we plan for nature's inevitable, and always unexpected, surprises.

David M. Morens & Anthony S. Fauci 2020

# COVID-19 Update

January 1 to January 6, 2024

- In the United States:
  - Test Positivity: 12.7%
  - ER visits: 2.9% diagnosed as COVID-19
  - Hospital Admissions: 35,801
  - Total Deaths: 1,167,210
  - % of All Deaths in U.S. Due to COVID-19: 4.0%

To the tune of:  
“50 Ways to Leave Your Lover”  
by Paul Simon.

## **Fifty ways to beat COVID-19**

**Don't hop on the bus, Gus,  
Stay away from the pack, Jack,  
Sneeze into your sleeve, Steve,  
To keep virus free.**

**Stop touching your face, Grace,  
Stay back to six feet, Pete,  
Keep washing your hands, Stan,  
And heed CDC.**

**Don't visit your Gran, Jan,  
Wipe down every toy, Roy,  
Don't hoard all the food, dude,  
Please buy sensibly.**

**Just use some Purell, Mel,  
Keep wipes near at hand, man.  
Don't listen to John, Don -  
You don't need more TP!**

**This isn't Spring Break, Jake,  
Stay home if you're sick, Dick,  
Just follow the rules, fools,  
And stay virus free!**



# THE NEXT PANDEMIC

# The Next Pandemic

## 1. What Could It Be?

- Pandemics often arise from viruses that leap from animals to humans: in recent decades, this has been a common pattern.
- Identifying the specific pathogen for the next pandemic is challenging, but vigilance is crucial.
- Machine learning could play a role in predicting the next pandemic-causing pathogen.
- Climate modeling might inform strategies for managing infectious disease outbreaks.

# The Next Pandemic

## 2. How Might It Occur?

- The emergence of a new pandemic can happen in any place with close interactions between people and wild or domesticated animals.
- Historically, influenza pandemics have originated in southern China, making it a focal point for monitoring potential new strains of the influenza virus.

# The Next Pandemic

## 3. Where Could It Originate?

- hotspots where humans and animal species mingle are often the breeding grounds for diseases
- areas, such as rainforest edges and regions of high biodiversity, are potential sources of future pandemics
- to prevent and prepare for the next pandemic, scientific research, surveillance, and global cooperation remain essential

# **FACTORS AFFECTING PANDEMIC PROGRESSION**

# Factors that Affect Pandemic Progression

- 1. The Jump
- 2. Locomotion
- 3. Filth
- 4. Crowds
- 5. Corruption
- 6. Blame
- 7. The Cure

# Pandemic Progression

## 1. The Jump <sup>(1)</sup>

- Introduction and spread of a pathogen in a new host population, by jumping from one host species to another, with *spillover* or cross-species infection.
- Usually between species that share some DNA characteristics.
- HIV: humans and chimpanzees (***Pan troglodytes troglodytes***) share between 98% and 99% of their genomes.



# Pandemic Progression

## 1. The Jump <sup>(2)</sup>

- Emerging pathogens tend to share some common traits.
- **Simian Immunodeficiency Virus (SIV)** appears to have been present in monkeys in Africa for 100's of years.
- **SIV** jumped into humans and mutated to **Human Immunodeficiency Virus (HIV)**.
- Directly transmitted RNA viruses are most likely to jump between host species and mutate into new versions.

# Pandemic Progression

## 1. The Jump <sup>(3)</sup>

- SIV mutated in smaller monkeys who were eaten by the larger chimpanzees.
- In the 1910's, first jump into humans.
- “Cut Hunter hypothesis”: human infected by contact with sick ape's blood.

# Pandemic Progression

## 2. Locomotion

- To pass infection, the host species and/or the infecting species must mobilize and meet.
- ***P.t. troglodytes*** are very poor swimmers, so that rivers acted like walls, keeping them in.
- Humans, who are intrepid explorers invaded the chimp's environment and became exposed to the virus.
- Roads built, railroads laid, cities created, jungle destroyed.

# Pandemic Progression

## 3. Filth

- Bad sanitary conditions, water supply, poor protection against pests (rats, roaches, etc.).
- Risky behaviors, deficient health care and overcrowded living.
- Eating unrefrigerated meat from wild animals, including monkeys.

# Pandemic Progression

## 4. Crowds

- City growth brought in many laborers, with attendant numbers of sex workers.
- Workers from many countries, races, habits, and various immune history and exposures.
- Overcrowded living quarters.

# Pandemic Progression

## 5. Corruption

- 3<sup>rd</sup> World countries experience diversion of funds, fake medicines, erroneous supplies, repression, distortion and withholding of information.
- Disease control or its absence are often exploited for political gain and domination.
- Progress over a disease is denied for ethnic, political or economic reasons, mostly to gain or maintain power.

# Pandemic Progression

## 6. Blame

- Intrinsic, unavoidable part of pandemic progression.
- The scientific community, the people, the political establishment, and anyone who has an ox to gore or an axe to grind will find someone to blame for any aspect of the pandemic.
- Sometimes the finger-pointing produces positive results and effective actions, but more often not.

# Pandemic Progression

## 7. The Cure

- In many pandemics, no vaccine or cure is attained.
- In some, a therapy or treatment is found.
- The most valuable lesson is understanding the disease and learning how to prevent its spread.
- Societal change should be part of process.



# EMERGING DISEASES

## Emerging Infectious Diseases in History

Year	Name	Deaths	Comments
430 BCE	"Plague of Athens"	~100,000	First identified trans-regional pandemic
541	Justinian plague ( <i>Yersinia pestis</i> )	30–50 million	Pandemic; killed half of world population
1340s	"Black Death" ( <i>Yersinia pestis</i> )	~50 million	Pandemic; killed at least a quarter of world population
1494	Syphilis ( <i>Treponema pallidum</i> )	>50,000	Pandemic brought to Europe from the Americas
c. 1500	Tuberculosis	High millions	Ancient disease; became pandemic in Middle Ages
1520	<i>Hueyahuatl</i> ( <i>Variola major</i> )	3.5 million	Pandemic brought to New World by Europeans
1793–1798	"The American plague"	~25,000	Yellow fever terrorized colonial America
1832	2nd cholera pandemic (Paris)	18,402	Spread from India to Europe/Western Hemisphere
1918	"Spanish" influenza	~50 million	Led to additional pandemics in 1957, 1968, 2009
1976–2020	Ebola	15,258	First recognized in 1976; 29 regional epidemics to 2020
1981	Acute hemorrhagic conjunctivitis	rare deaths	First recognized in 1969; pandemic in 1981
1981	HIV/AIDS	~37 million	First recognized 1981; ongoing pandemic
2002	SARS	813	Near-pandemic
2009	H1N1 "swine flu"	284,000	5th influenza pandemic of century
2014	Chikungunya	uncommon	Pandemic, mosquito-borne
2015	Zika	~1,000?*	Pandemic, mosquito-borne

# Emerging Diseases

- Emerging and re-emerging infectious diseases are epiphenomena of human existence, our interactions with each other, and with nature.
- As human societies grow in size and complexity, we create an endless variety of opportunities for genetically unstable infectious agents to emerge into the unfilled ecologic niches we continue to create.
- There is nothing new about this situation, except that we now live in a human-dominated world in which our increasingly extreme alterations of the environment induce more extreme backlashes from nature.

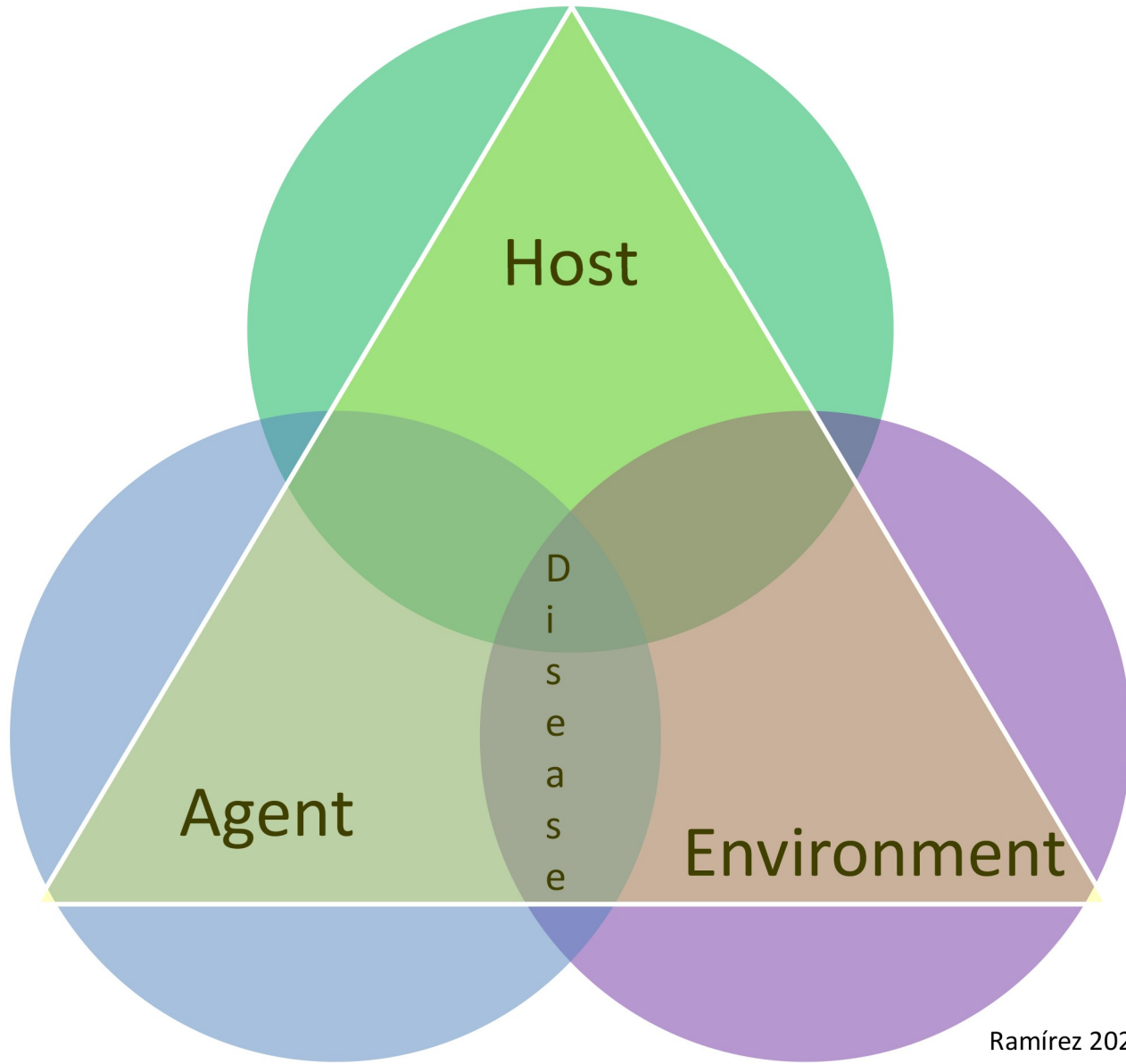
# Dual Strategies

## Immediate and Long-term control

- First, in the immediate sense, it is important to mitigate spread of infection, illness, and death.
- Second, it is critical to prevent the persistence of microbes that may lead to additional emergencies that are cumulatively as deadly, or more so, than the original emergencies .
- Viral genetic descendants of the 1918 influenza pandemic virus are still causing seasonal outbreaks throughout the world, and still killing cumulatively millions of people a century later.
- This is a powerful reminder that single disease emergencies can have consequences beyond immediate morbidity and mortality.

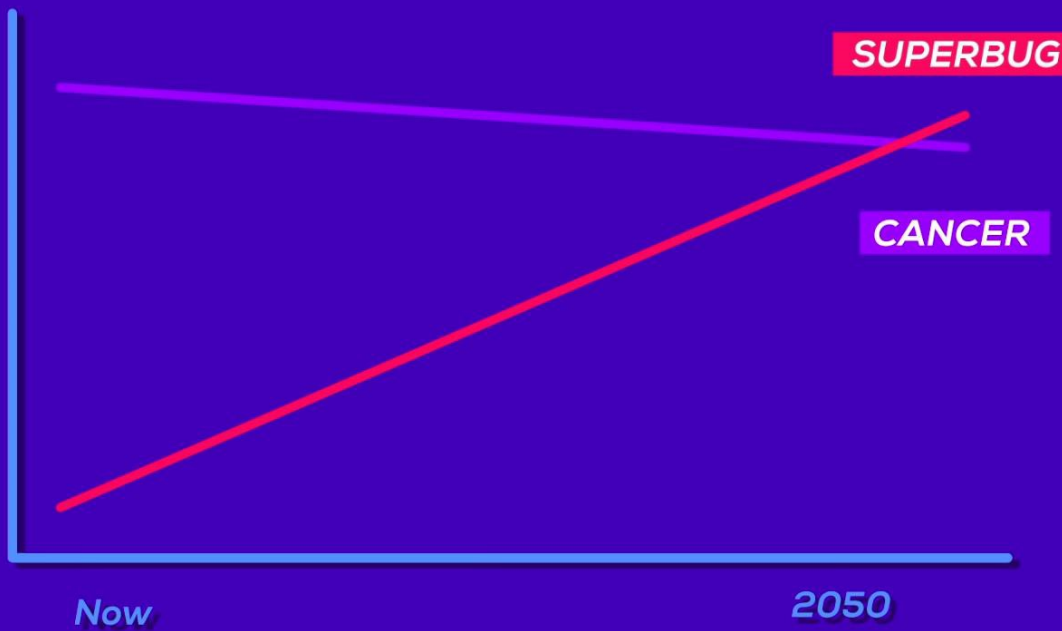
# Emerging Diseases

- newly emerging
- re-emerging
- deliberately emerging (bioterrorism)
- accidentally emerging (human-generated)
- de-emerging: eliminated or eradicated or in the process of elimination and/or eradication

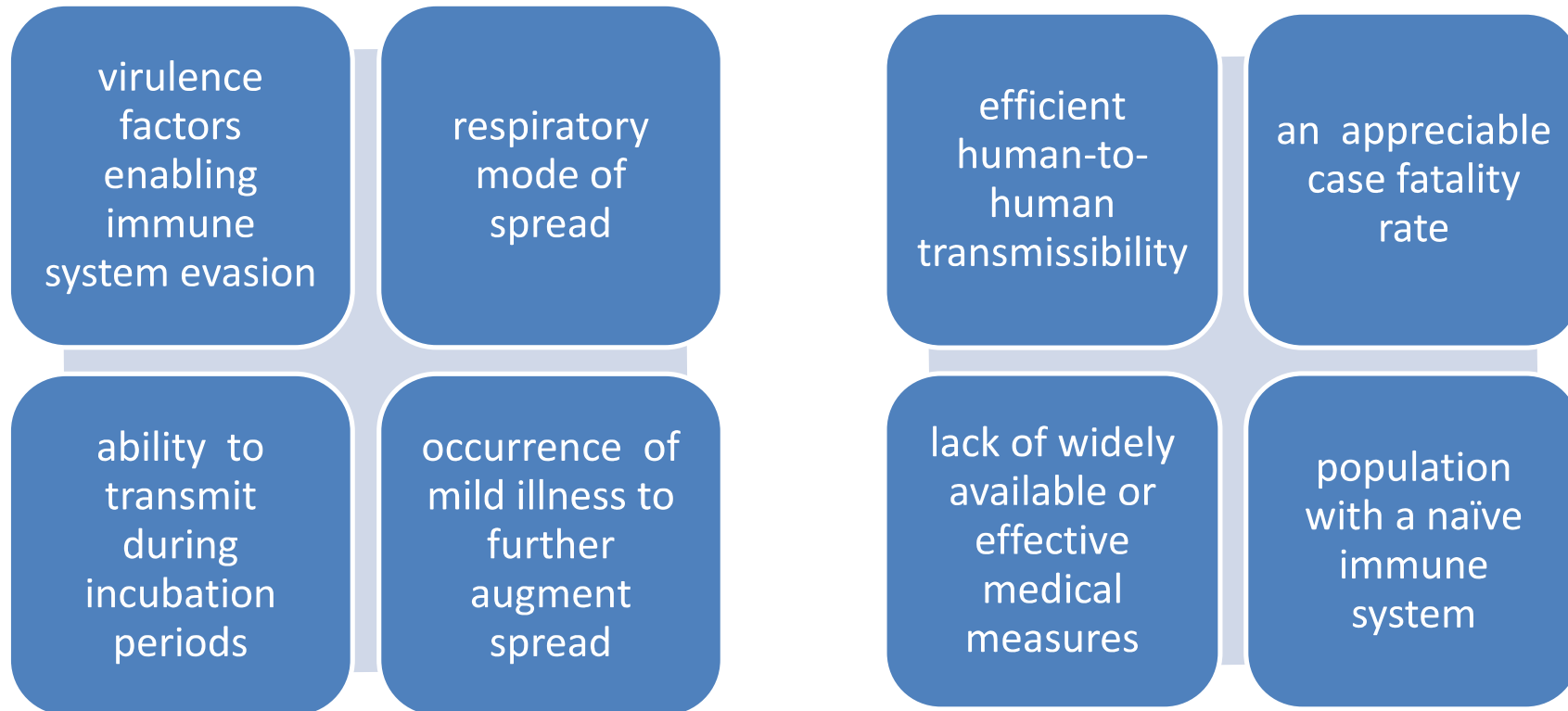


Ramírez 2024

## Causes of Death



# Essential Components of any **GCBR** pathogen (**Global Catastrophic Biological Risk**)







Measles

Whooping Cough

Syphillis

Leprosy

# **RE-EMERGENCE of DISEASES**

# Measles in US

- As of April 11, 2024, the USA has experienced a surge in measles cases, threatening measles elimination status
- Total Measles cases: 121 cases have been reported across 18 jurisdictions, including AZ, CA, FL, GA, IL, IN, LA, MD, MI, MN, MO, NJ, NYC, NY, OH, PA, VA, and WA.
- Outbreaks: there have been 7 outbreaks (3 or more related cases) in 2024, accounting for 71% of all cases (86 / 121).
- For comparison, in 2023, there were 4 outbreaks, with 48% of cases being outbreak-associated.

# Measles in US 2024

## (April 11)

Age in years	Cases	Hospitalization
<5	57 (47%)	37 (65 %)
5-19	27 (22%)	10 (37 %)
20+	37 (31%)	21 (57 %)
TOTAL	121 (100 %)	68 (56 %)

Vaccines	None or Unknown	One dose MMR	Two doses MMR
	99 (82 %)	16 (13 %)	6 (5 %)

# Measles in Florida

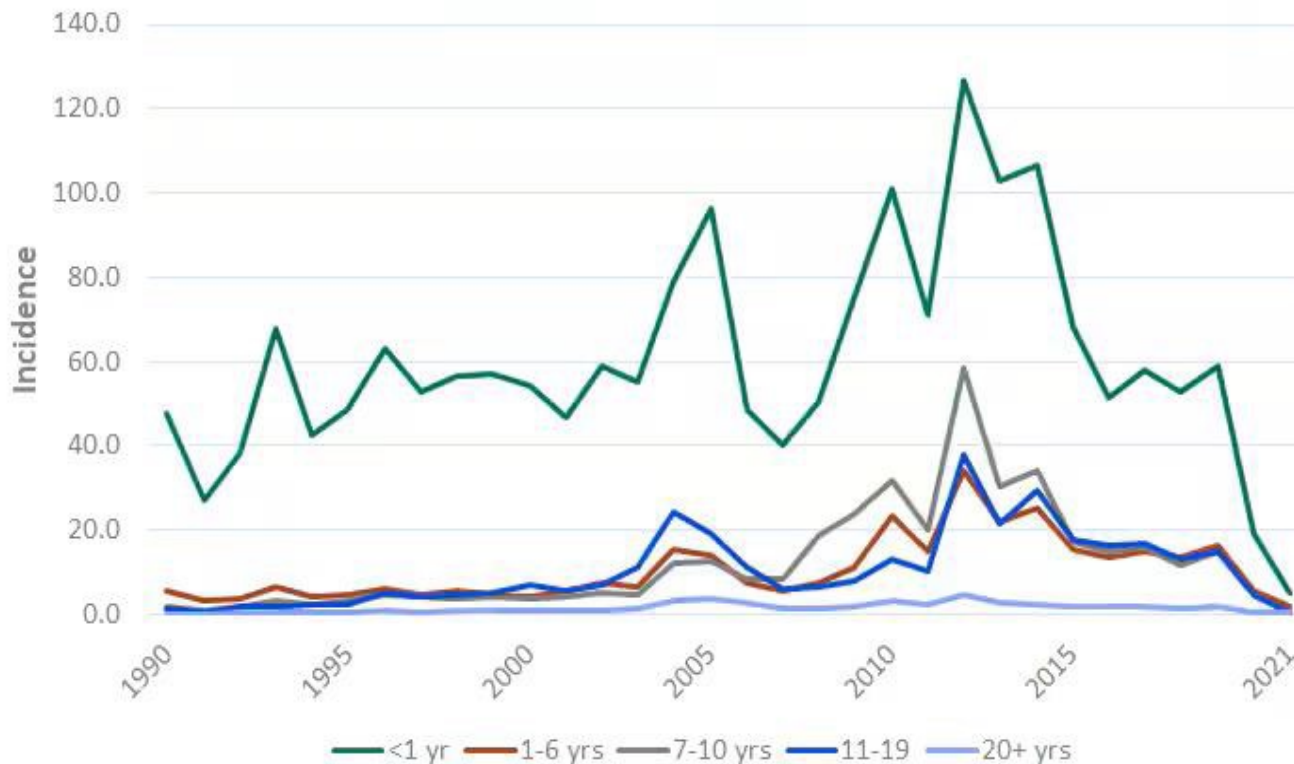
- From February 1 to February 25, there have been nine confirmed cases in Florida:
  - eight cases are in Broward County
  - one case is in Polk County (attributed to travel)
- The CDC recommends that unvaccinated children exposed to measles be isolated for 3 weeks.
- The vaccination rate for measles in Florida is approximately 91%, but vaccination coverage among U.S. kindergartners has dropped:
  - during the 2019–2020 school year, coverage was 95.2%
  - in the 2022–2023 school year, it decreased to 93.1%
  - this leaves about 250,000 kindergartners at risk each year.

# **WHOOPING COUGH**

## **PERTUSSIS**

# Whooping Cough

## Reported pertussis incidence by age group: 1990-2021



SOURCE: CDC, National Notifiable Diseases Surveillance System

# Whooping Cough

- Pertussis, can be fatal, especially in children and babies.
- 13 deaths were reported in China in the first two months of 2024, with 32,380 cases reported, more than 20X higher than a year earlier.
- The Philippines said infection figures were 34 times higher than last year, with 54 deaths recorded in the first three months of 2024.



# Whooping Cough

- By the first decade of the 21st century, pertussis outbreaks had started to increase: California has been slammed with two major outbreaks: one in 2010 that hit 9,120 people, with 10 infants dead, and one in 2014 that involved 7,503 cases and 3 infants dead.
- As a result of the waning immunity of the acellular vaccine, U.S. preteens now receive an additional inoculation, at age 11 or 12 years.
- The first 5 shots, given from infancy through age 4 to 6 years, are in a formulation known as DTaP.
- The 6<sup>th</sup> shot, the preteen booster, is referred to as the Tdap.

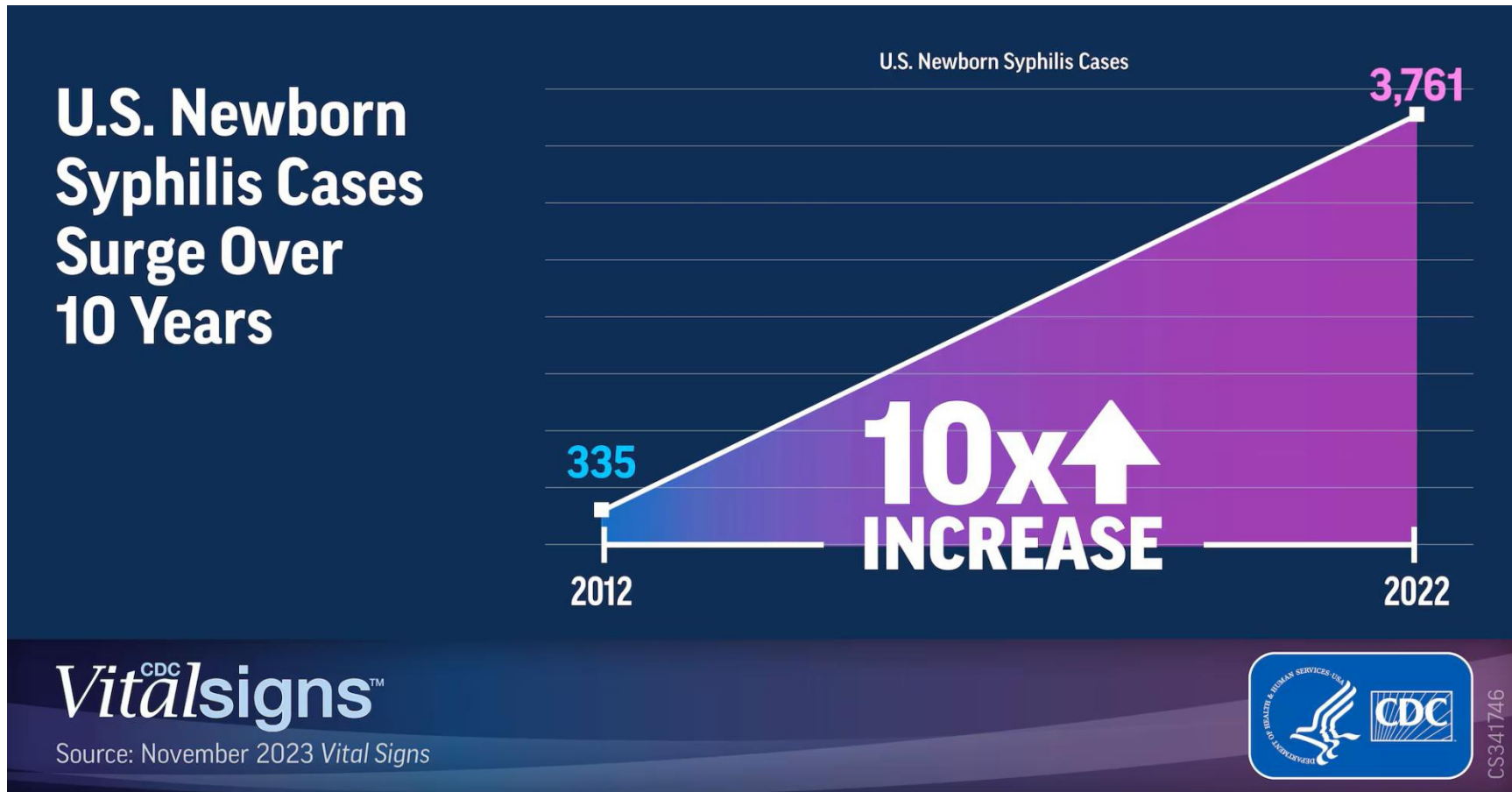
# **SYPHILLIS**

**“THE GREAT IMITATOR”**

# Syphilis

- Between 2018 and 2022, syphilis cases in the US increased by 80%, with a total of 207,255 reported cases of primary and secondary syphilis in 2022.
- Even more alarming is the rise in congenital syphilis, which saw a 183% increase since 2018, totaling 3,755 cases in 2022.

# Syphilis



# LEPROSY

# Leprosy

- In recent years, the U.S. has seen about 180 cases of leprosy annually.
- While this represents an increase from fewer than 100 cases in 1999 and 2000, the disease remains rare in the country.
- Florida has experienced a leprosy outbreak, leading researchers to believe that the infection is endemic to the region.

# Leprosy

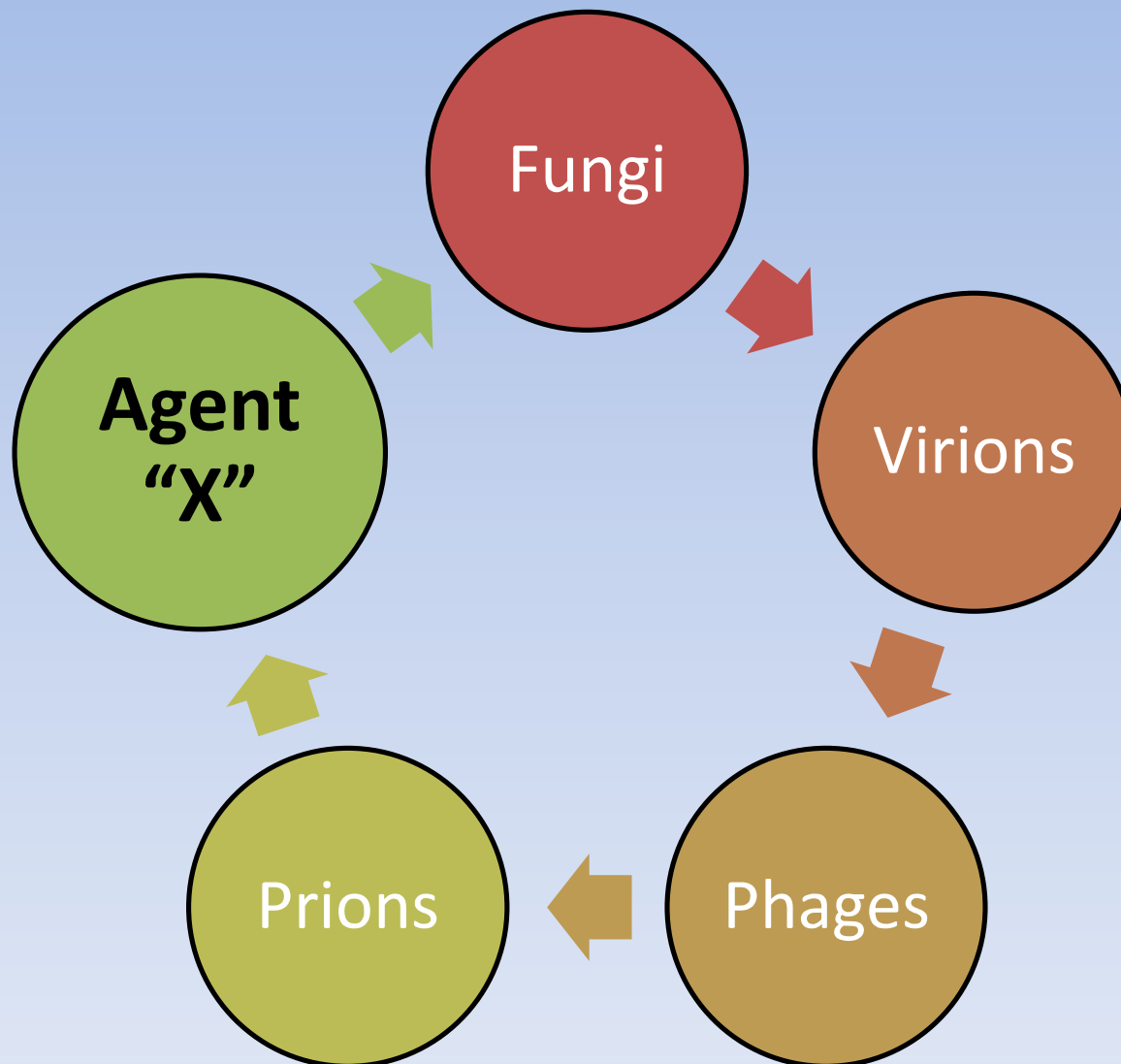
- National cases dropped from 173 to 159 from 2011 to 2020, but cases in the southeast more than doubled over the last decade.
- Central Florida saw the most uptick in cases, making up 81% of all cases in Florida and one-fifth of all cases across the country.
- Other states that account for a combined 69% of new leprosy cases are Texas, Hawaii, California, New York and Louisiana, according to the US Department of Health and Human Services data.
- About 66% of cases are from people who immigrated from leprosy endemic countries, but 34% were locally acquired, and the cause unknown because there's no clear evidence of animal transmission or other "traditionally known risk factors.

# Questions? 1





# Other Infectious Agents



# FUNGAL DISEASE

# Fungal Disease

- Fungal pathogens are becoming increasingly common and resistant to treatment with the only 4 classes of antifungal medicines currently available.
- Most fungal pathogens lack rapid and sensitive diagnostics and those that exist are not widely available or affordable globally.
- People at greatest risk of invasive fungal infections are those with cancer, HIV/AIDS, organ transplants, chronic respiratory disease, and post-primary TB infection.

# Fungal Disease

- Critically ill patients in an intensive care unit (ICU), patients undergoing invasive medical procedures and receiving broad-spectrum antibiotics, and those taking immune-suppressing medicines are also at risk.
- Evidence indicates that both the incidence and geographic range of fungal diseases are expanding due to global warming and the increase in international travel and trade.

# Fungal Disease

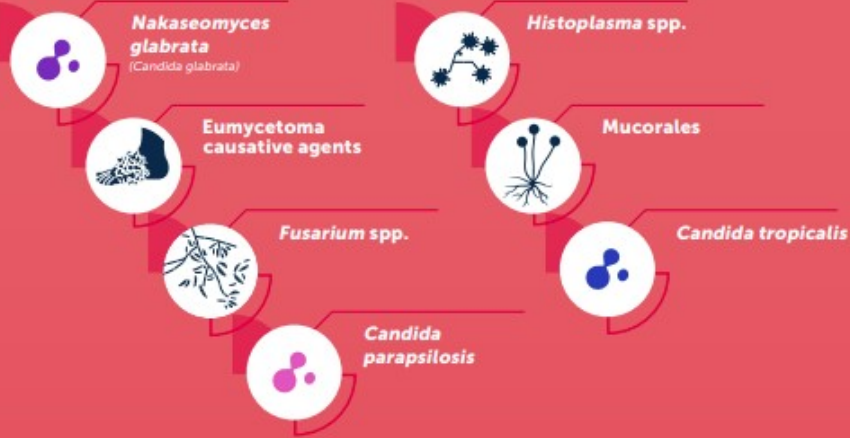
- On 25 October 2022, WHO published the first ever list of fungal "priority pathogens" – a catalogue of the 19 fungi that represent the greatest threat to public health.
- The WHO **fungal priority pathogens list (FPPL)** is the first global effort to systematically prioritize fungal pathogens,

### Critical Priority Group



Current outbreaks

### High Priority Group



### Medium Priority Group



# WHO Fungal Priority Pathogens List 2022

PCP in AIDS

Illinois

# Candida Auris

- *C. auris* can cause infections in different parts of the body, and symptoms may be similar to an infection caused by bacteria.
- People can get *C. auris* on their skin and other body sites without getting sick or having an infection; this is called colonization.
- Someone who is colonized can still transmit *C. auris* onto surfaces or objects that they contact, which can then spread it to other patients.

# *Candida Auris*

- *Candida auris* (C. auris) is a type of yeast that can cause severe illness and spreads easily among patients in healthcare facilities.
- US cases nearly doubled in 2021 - from 756 to 1,471, the CDC reports.
- It is often resistant to antifungal treatments, so the medications that are designed to kill fungus and stop infections do not work.



# VIRIONS

# Virions (2)

- A complete, entire virus particle that has an RNA or DNA core with an external protein shell (capsid).
- The core confers infectivity and the capsid provides specificity to the *virion*.
- It is the extracellular manifestation of the intracellular virus which is actively infecting.
- It is not dormant, it is more of a ready, potentially infectious, cocked and loaded particle.

# Virions

- Single viral particle that is released from an infected cell and is capable of infecting other cells of the same type.
- It is a complete virus that does not have to be inside the cell to be infective.
- Not to be confused with:
  - *Viroid*: RNA without capsid, infects only plants
  - *Virusoid*: requires “helper” virus to replicate

# Virions

- All virions are viruses, but not all viruses are in the virion state.
- Virions are the active, contagious form of viruses that mediate infection, whereas viruses encompass the entire lifecycle, including intracellular replication

# Virion infections

- 1. Common Colds: caused by various viruses, such as rhinoviruses.
- 2. Influenza (Flu)
- 3. COVID-19: SARS-CoV-2 coronavirus caused the ongoing pandemic.
- 4. Respiratory Syncytial Virus (RSV)
- 5. Chickenpox (Varicella): varicella-zoster virus.
- 6. Measles (Rubeola): highly contagious.
- 7. HIV/AIDS: weakens the immune system, making the body susceptible to various infections and cancers.

# Corny old joke

Question: Why do elephants have fleas?

Answer: Because fleas can't have elephants!

Question: Why do bacteria have viruses?

Answer: Because viruses can't have bacteria!

# BACTERIOPHAGES

# Bacteriophages

Phages are a form of viruses that attach to bacteria and inject viral genome into the cell.

The viral genome replaces the bacterial genome, and thus stops the bacterial infection.

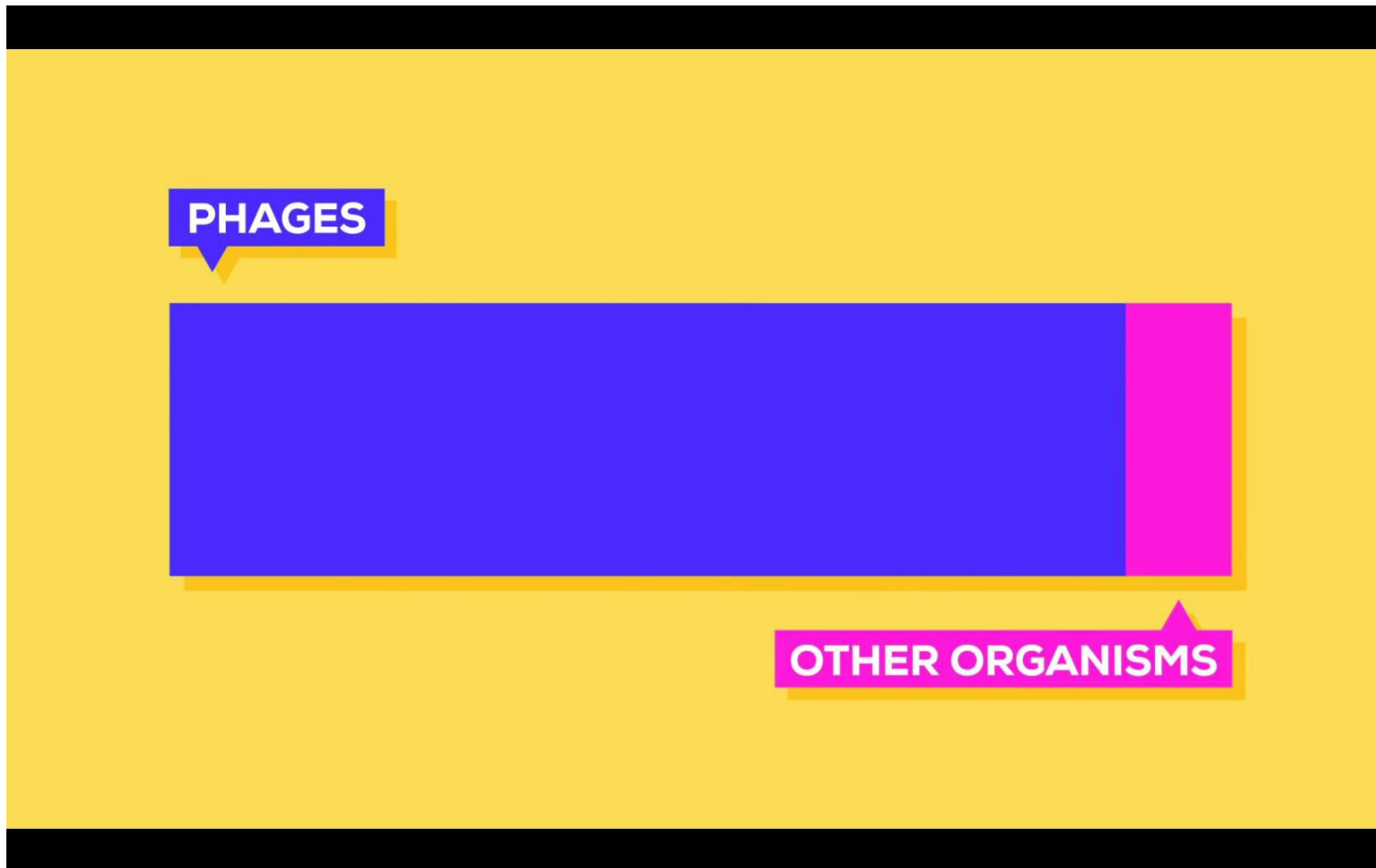
More specific than antibiotics, harmless to the host organism and the gut microbiota, reducing chances of opportunistic infections.

A phage will kill a bacterium only if it matches the specific strain, so phage mixtures ("cocktails") are often used to improve the chances of success.

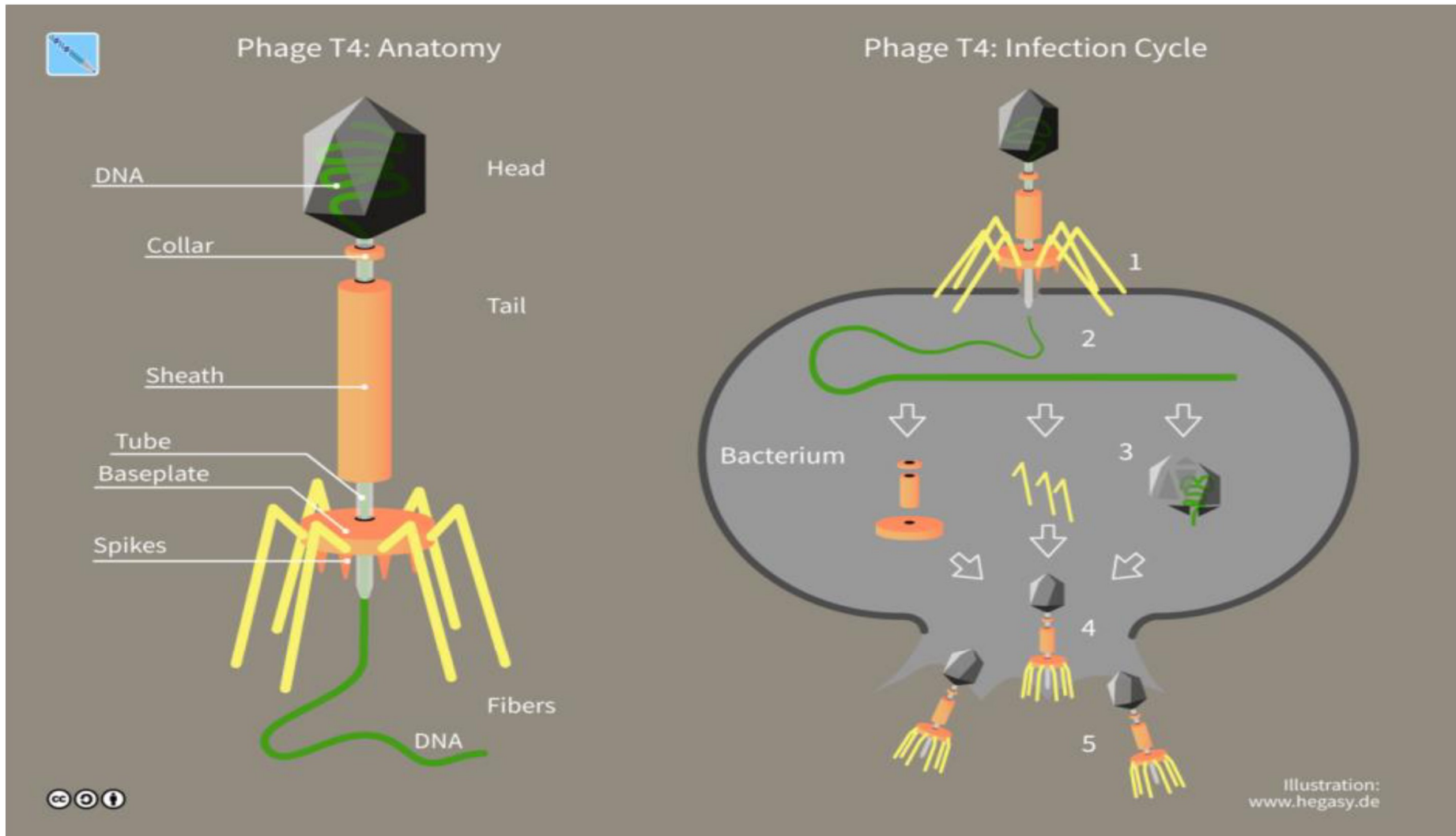
Samples from recovering patients may contain appropriate phages that can be grown to cure other patients infected with the same strain.



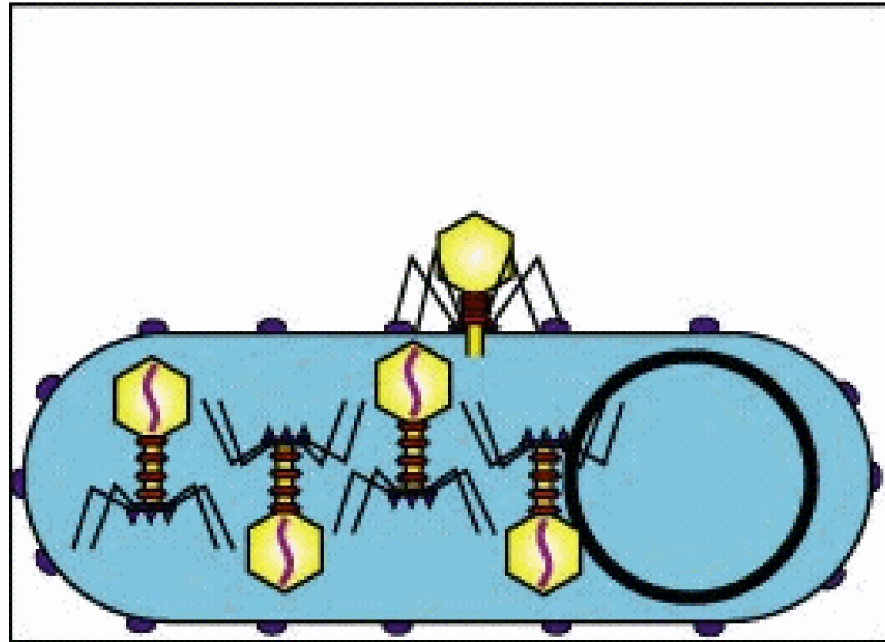
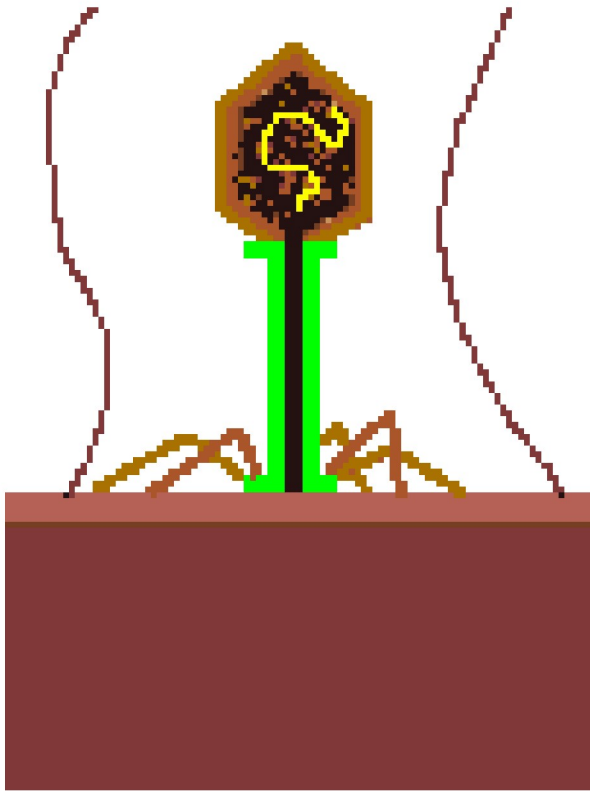
# Phages and all other organisms



# How Phages Work



# Bacteriophages



# If They're So Good...

It has long been known that there are specific phages for *M. tuberculosis* but not for *C. difficile*.

Phage therapy in humans has not been approved in most Western countries.

The negative public perception of viruses may play a role in the reluctance to embrace phage therapy.

Washington and Oregon law allows naturopathic physicians to use any therapy that is legal any place in the world on an experimental basis.

In Texas, phages are considered natural substances and can be used in addition to (but not as a replacement for) traditional therapy.





# PRIONS (1)



April 16, 2024

©NAR 2024 OLLI @ University of Illinois

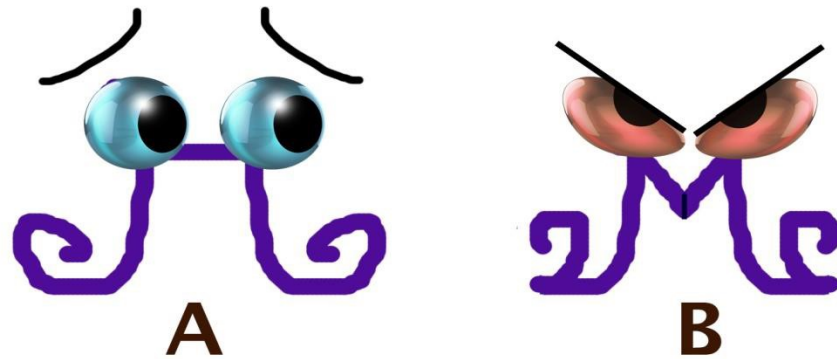
84

# Prions <sup>(2)</sup>

- *Prion*: union of **protein** and **infection**.
- A proteinaceous infectious particle *without* genetic material.
- Can *self-propagate* and transmit its misfolded shape conformation to normal proteins of its same variety.

# Prions <sup>(3)</sup>

- It is not known what causes a normal protein to spontaneously misfold.
- The abnormal 3-D structure confers infectious properties, collapsing nearby protein molecules into the same shape.





# Prions (4)

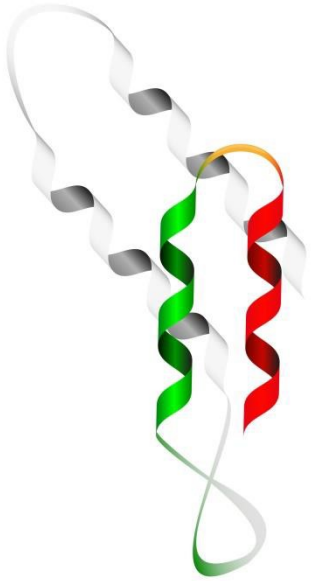
- All known infectious agents contain nucleic acids (DNA, RNA or both), while prions are just misfolded proteins.
- Cause **Transmissible Spongiform Encephalopathies (TSEs)**:
  - scrapie in sheep
  - **chronic wasting disease (CWD)** in deer
  - **bovine spongiform encephalopathy (BSE)** in cattle (mad cow disease)
  - *Creutzfeldt–Jakob* disease (**CJD**) in humans
- All known prion diseases in mammals:
  - affect the structure of the brain
  - are progressive
  - have no known effective treatment
  - are **always** fatal

# Prions (5)

- PrP<sup>c</sup> = cellular Prion Protein, is the normal form of the protein ( $\alpha$  helix) which exists in the uninfected host.
- PrP<sup>sc</sup> = scrapie Prion Protein, is the infectious form of the protein ( $\beta$  sheet) which can convert the normal cellular prion protein into more PrP<sup>sc</sup>, perpetuating the infection.

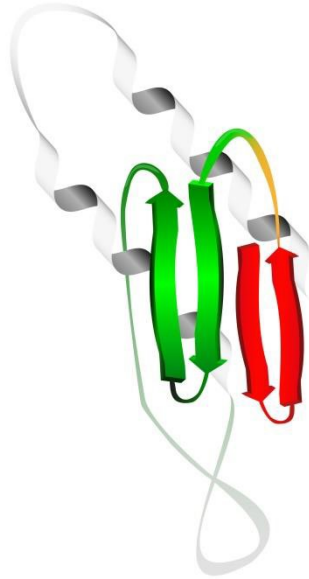
# Prions (6)

**PrP<sup>C</sup>**  
is a normal protein



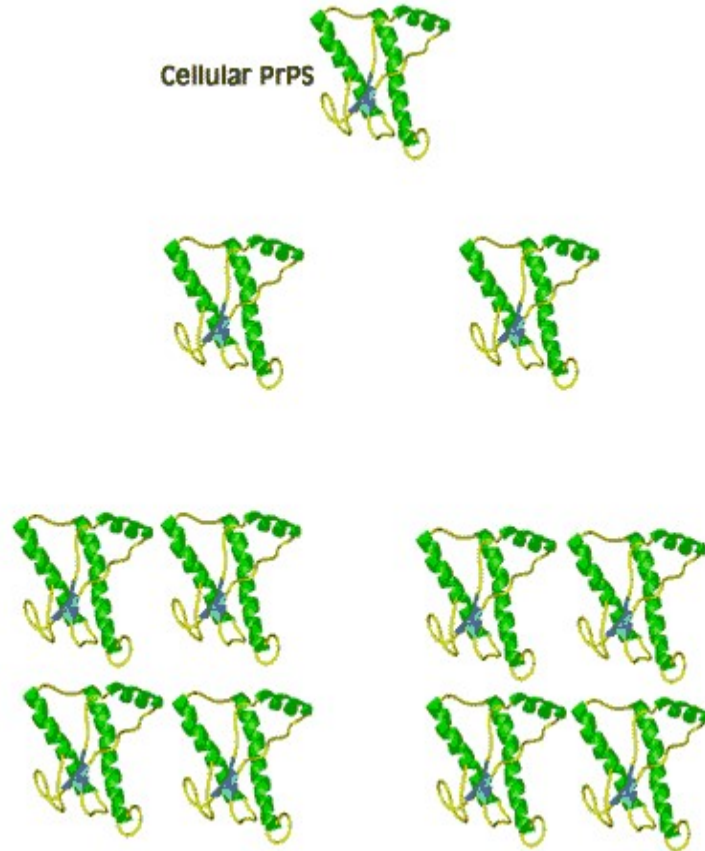
$\alpha$  helix

**PrP<sup>Sc</sup>**  
the disease-causing form of the  
prion protein

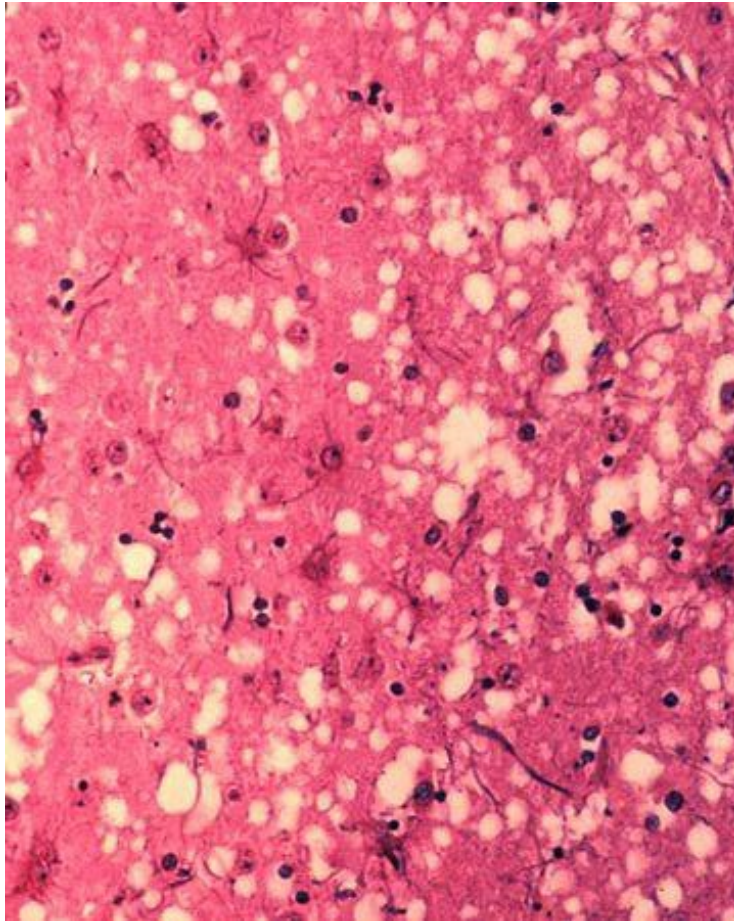


$\beta$  sheet

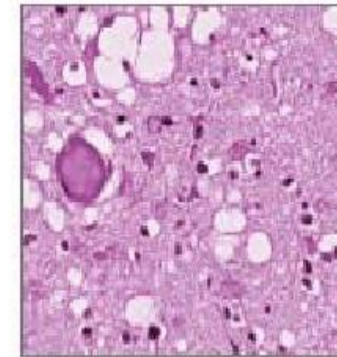
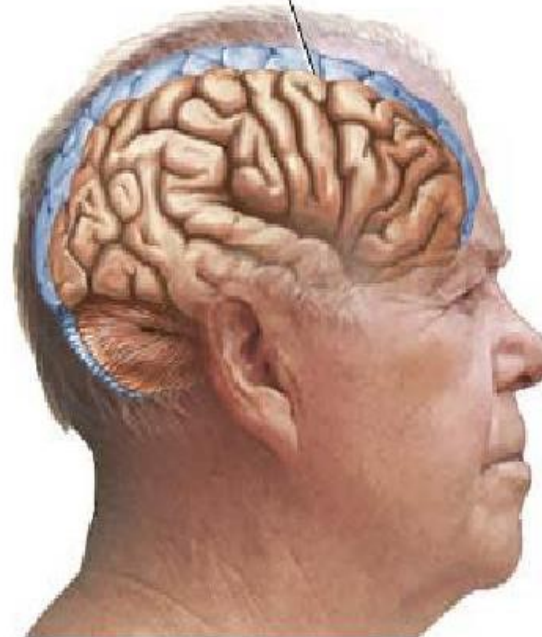
Cellular PrP<sup>S</sup>



# Spongiform Brain



Brain shrinkage and deterioration occurs rapidly



Brain section showing spongiform pathology characteristic of Creutzfeldt-Jakob

Spongiform = sponge-like

# Acquired Prion Diseases

- Iatrogenic CJD (*iCJD*): Caused by exposure to infected tissue during medical procedures (e.g., cornea transplant).
- Variant CJD (*vCJD*): Linked to "mad cow disease" (BSE); eating contaminated meat may cause *vCJD* in humans.
- Kuru: Historically associated with ritualistic cannibalism in Papua, New Guinea.

# **WHO PRIORITY DISEASES and DISEASE X**

# Your Tax Dollars at work

- CDC ➡ *Preparedness 101: Zombie Apocalypse.*
- 2011: Tips on preparing to survive a *zombie invasion.*
- Store water, food, medical supplies, & other needs to *prepare* for any and all potential disasters:
  - hurricanes
  - earthquakes
  - tornadoes
  - floods
  - or **“hordes of ravenous brain-devouring undead!”**

# WHO Priority Diseases

- COVID-19
- Crimean-Congo hemorrhagic fever
- Ebola virus & Marburg virus diseases
- Lassa fever

- MERS-CoV & SARS CoV
- Nipah & Henipaviral diseases
- Rift Valley fever
- Zika
- **“Disease X”**



- “**Disease X**” represents the knowledge that a serious international epidemic could be caused by a pathogen that is currently unknown.
- The WHO R&D Blueprint seeks to enable early cross-cutting R&D preparedness that is also relevant for an unknown “**Disease X**”.



# Disease X

## “Agent X”

- Name adopted by the WHO in February 2018 to represent a hypothetical, unknown pathogen that could cause a future epidemic.
- The WHO adopted the name to ensure that their planning was sufficiently flexible to adapt to an unknown pathogen (e.g., broader vaccines and manufacturing facilities).
- The Disease X concept would encourage WHO projects to focus their research on entire classes of viruses (instead of just individual strains) improving WHO capability to respond to unforeseen strains.
- In 2020, experts speculated that COVID-19 met the requirements to be the first Disease X.

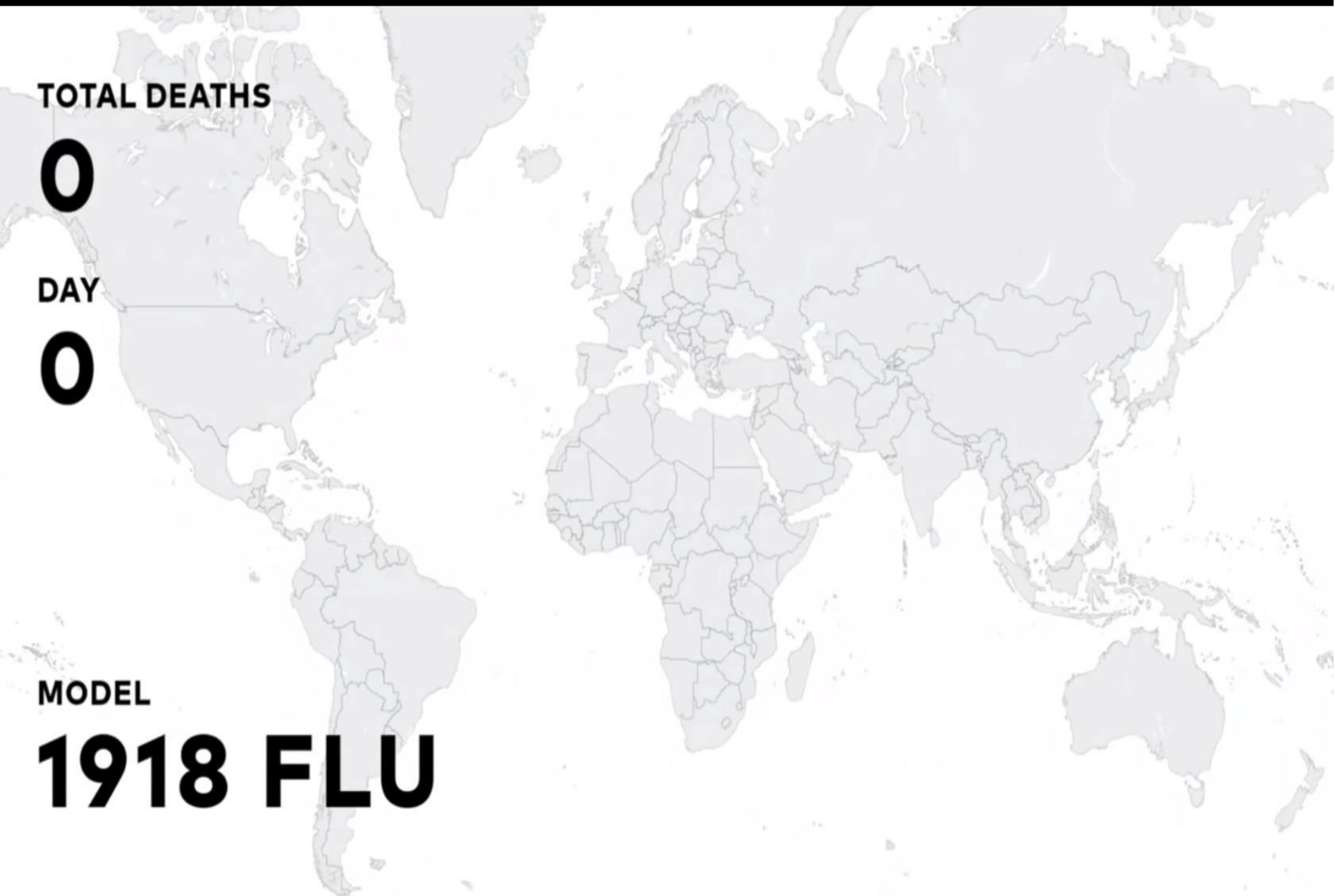
# Summary

Agent	Infectious	Epidemic potential	Morbidity
Prions	GI tract	Low	Mostly fatal
Virions	Highly	Very high	Very high
Fungi	High	Low	High
Phages	No	No	Protective
Agent "X"	Yes (respiratory?)	Extremely high ?	Massive mortality

Ramírez 2023

# **THEORETICAL SPREAD OF A RESPIRATORY VIRAL DISEASE**

Model: 1918 Flu Pandemic



TOTAL DEATHS

0

DAY

0

MODEL

1918 FLU

TOTAL DEATHS

**2,642**

DAY

**7**

MODEL

**1918 FLU**

TOTAL DEATHS

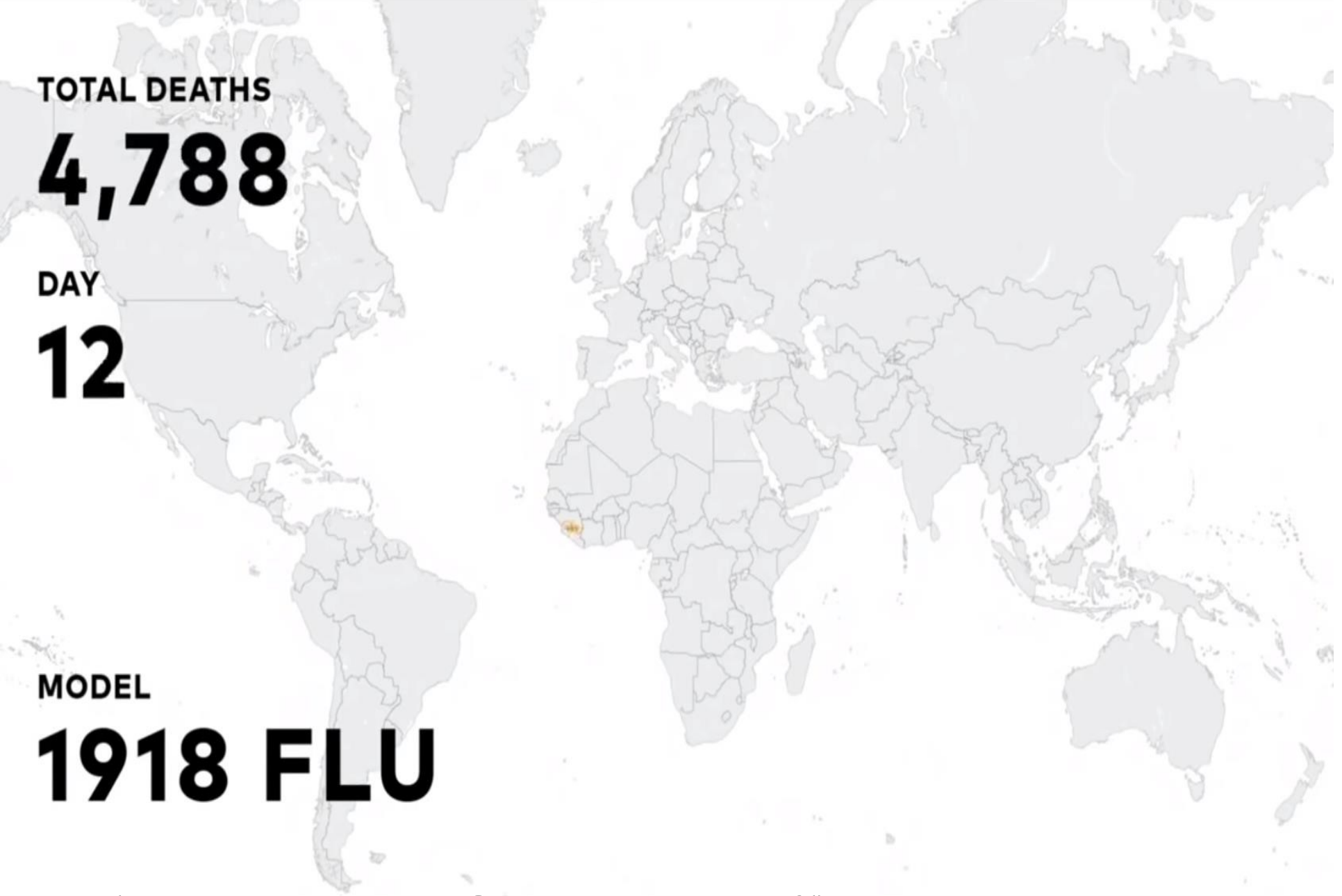
**4,788**

DAY

**12**

MODEL

**1918 FLU**



TOTAL DEATHS

**15,010**

DAY

**28**

MODEL

**1918 FLU**





TOTAL DEATHS

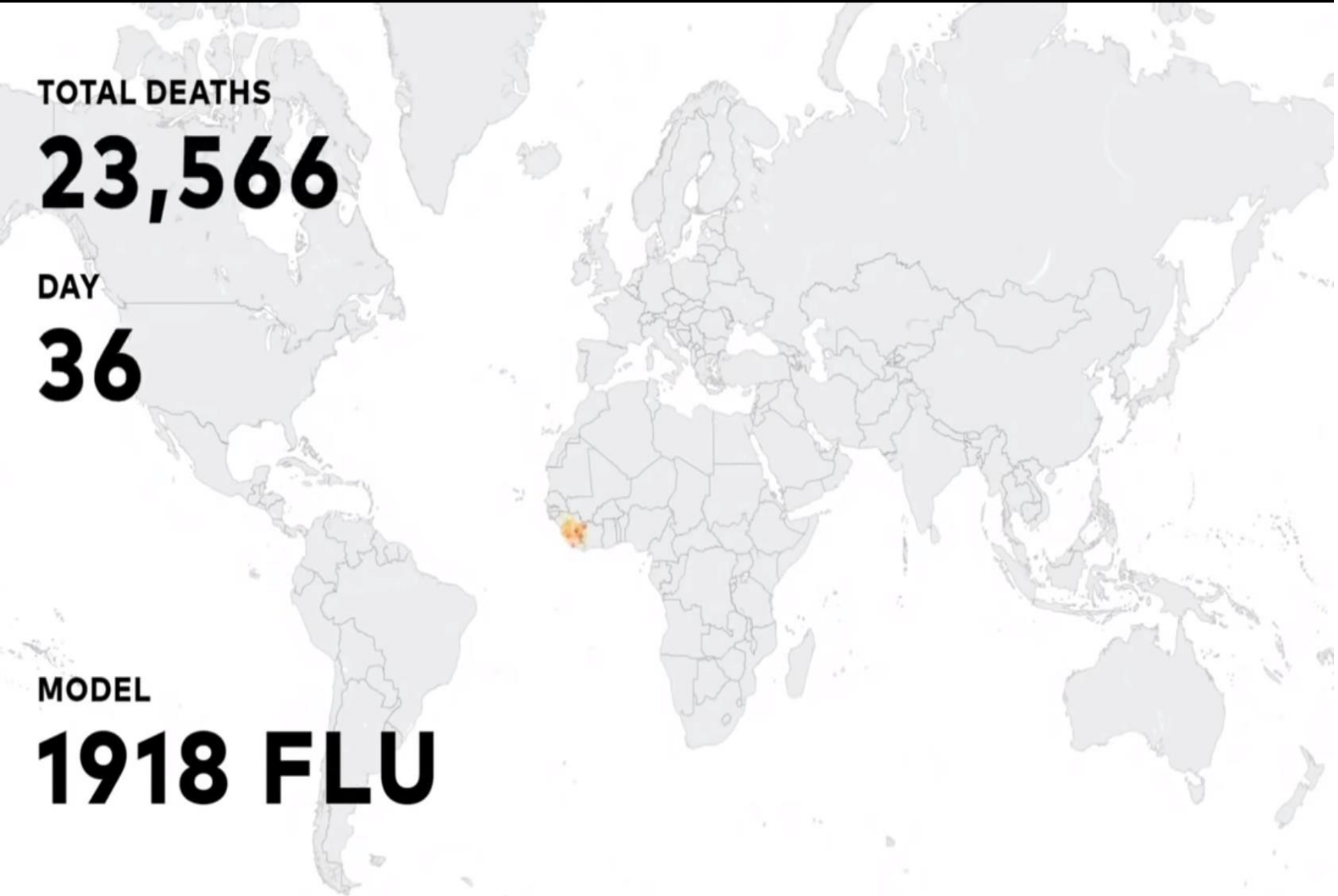
**23,566**

DAY

**36**

MODEL

**1918 FLU**



TOTAL DEATHS

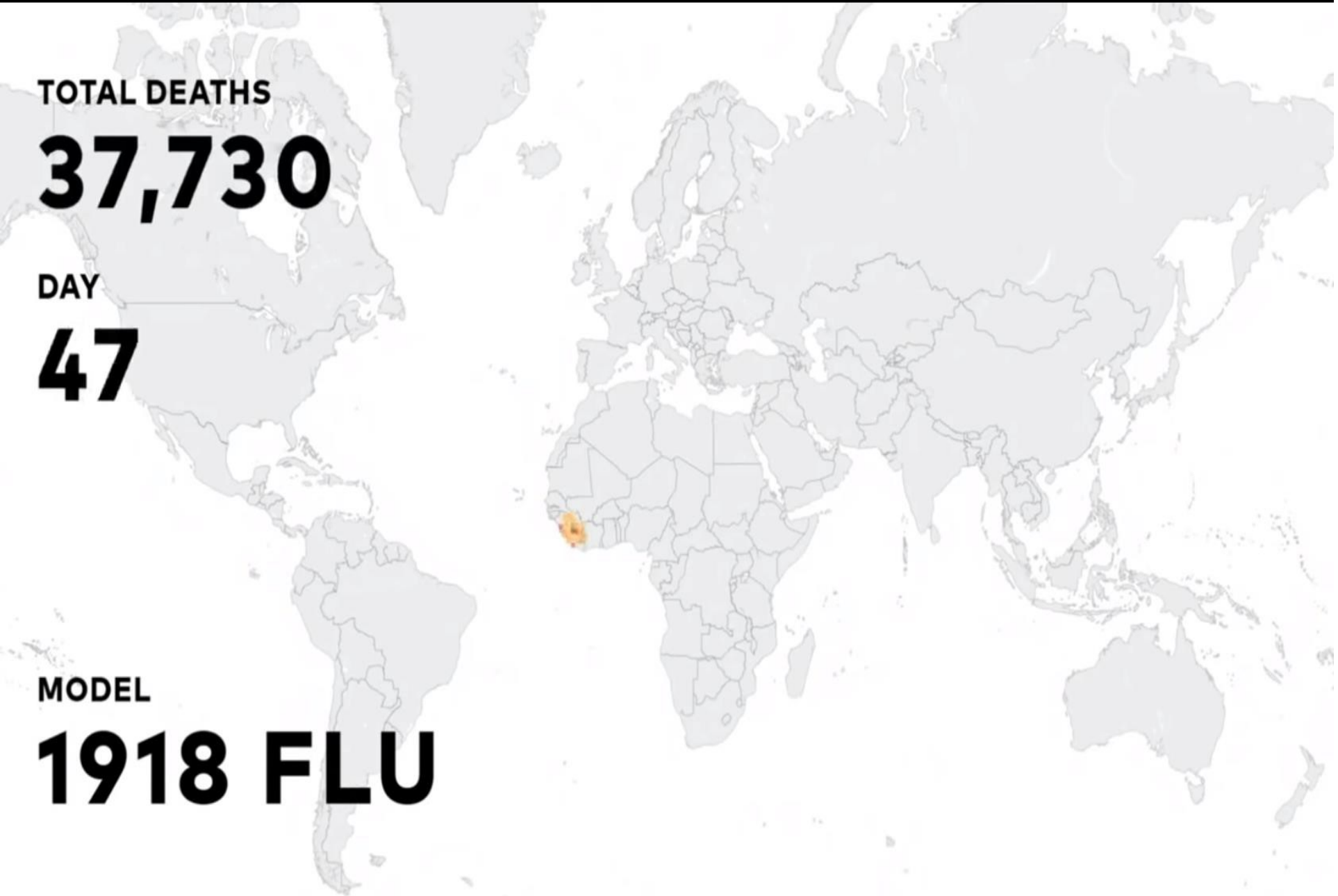
**37,730**

DAY

**47**

MODEL

**1918 FLU**



TOTAL DEATHS

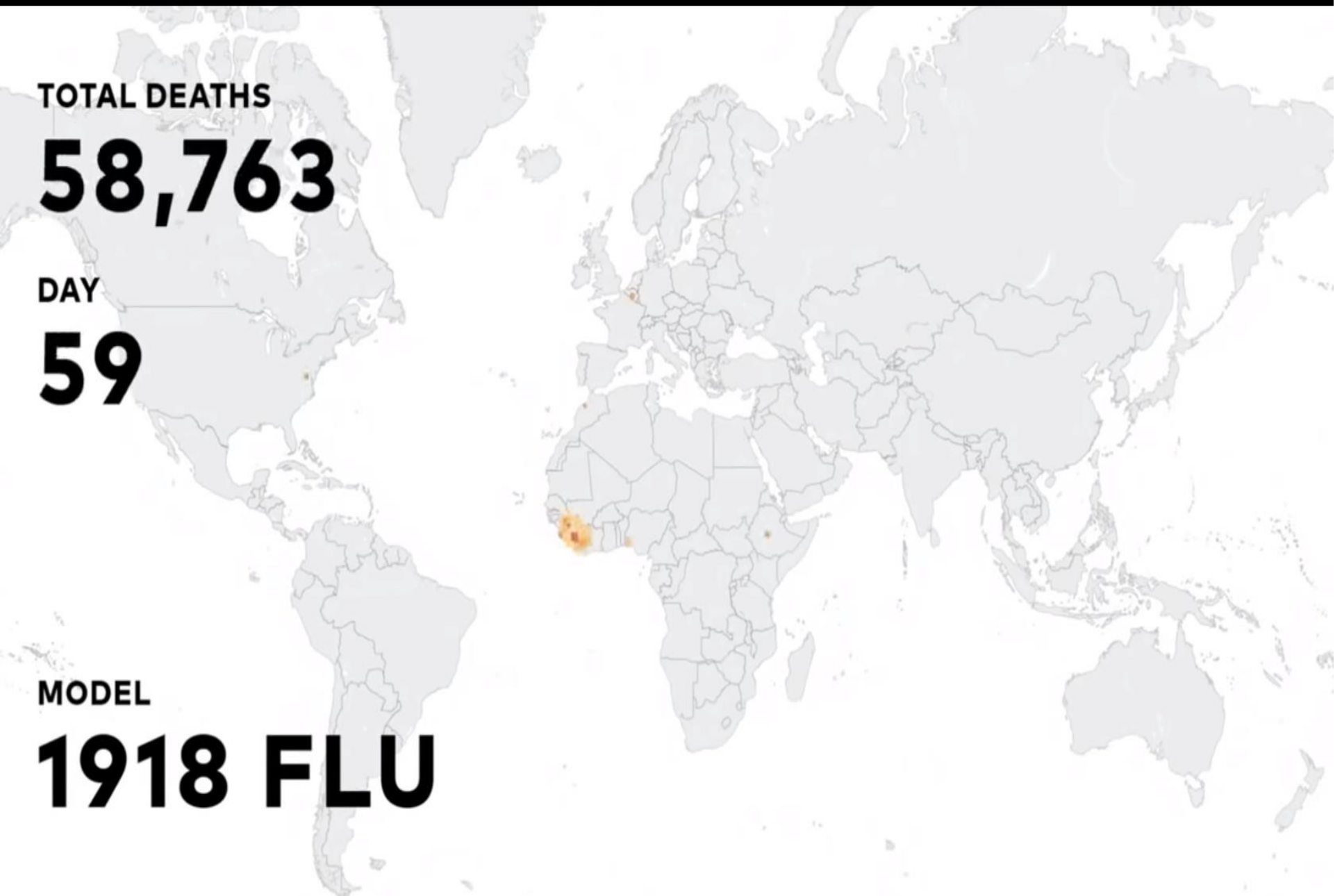
**58,763**

DAY

**59**

MODEL

**1918 FLU**



TOTAL DEATHS

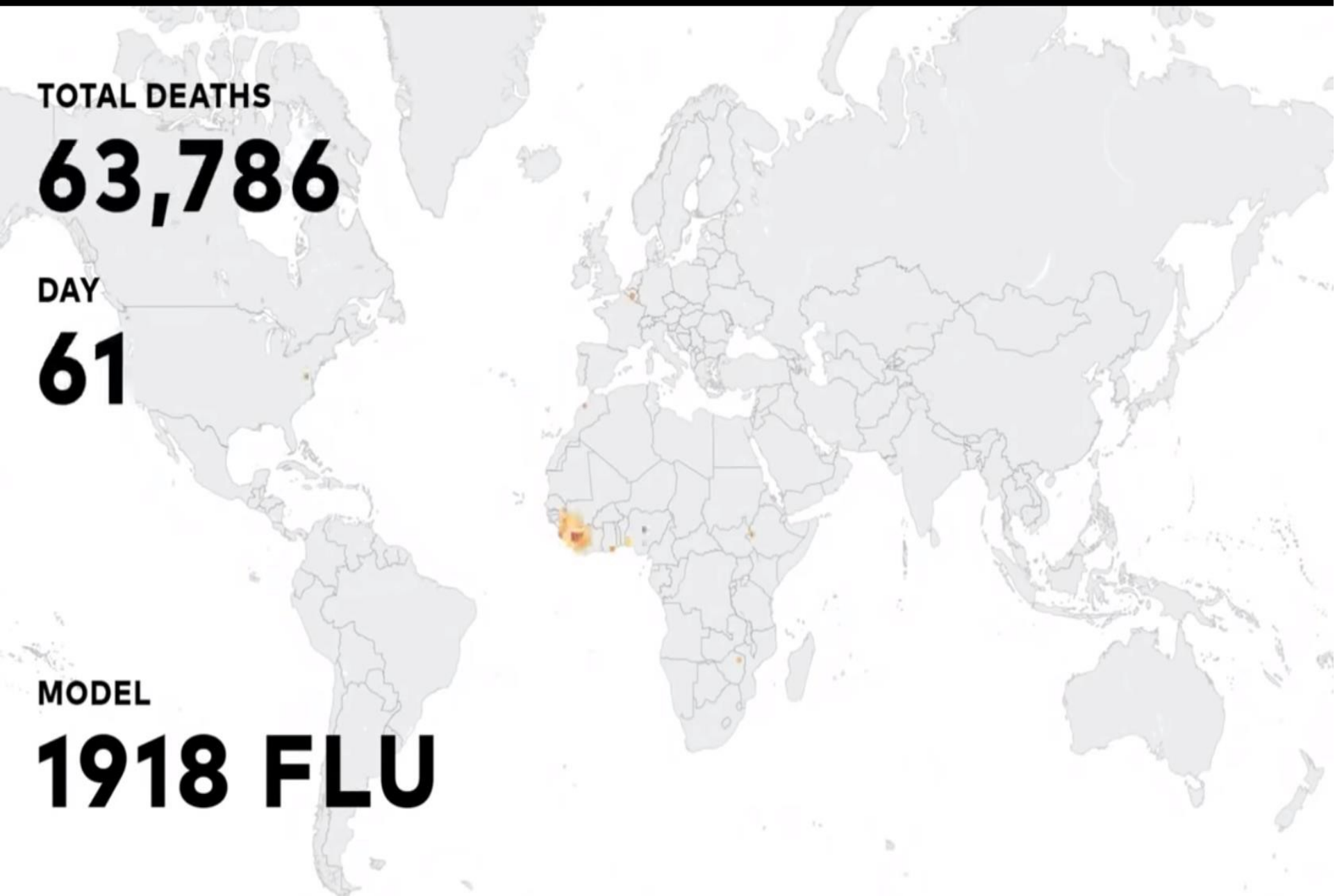
**63,786**

DAY

**61**

MODEL

**1918 FLU**



TOTAL DEATHS

**124,803**

DAY

**76**

MODEL

**1918 FLU**



TOTAL DEATHS

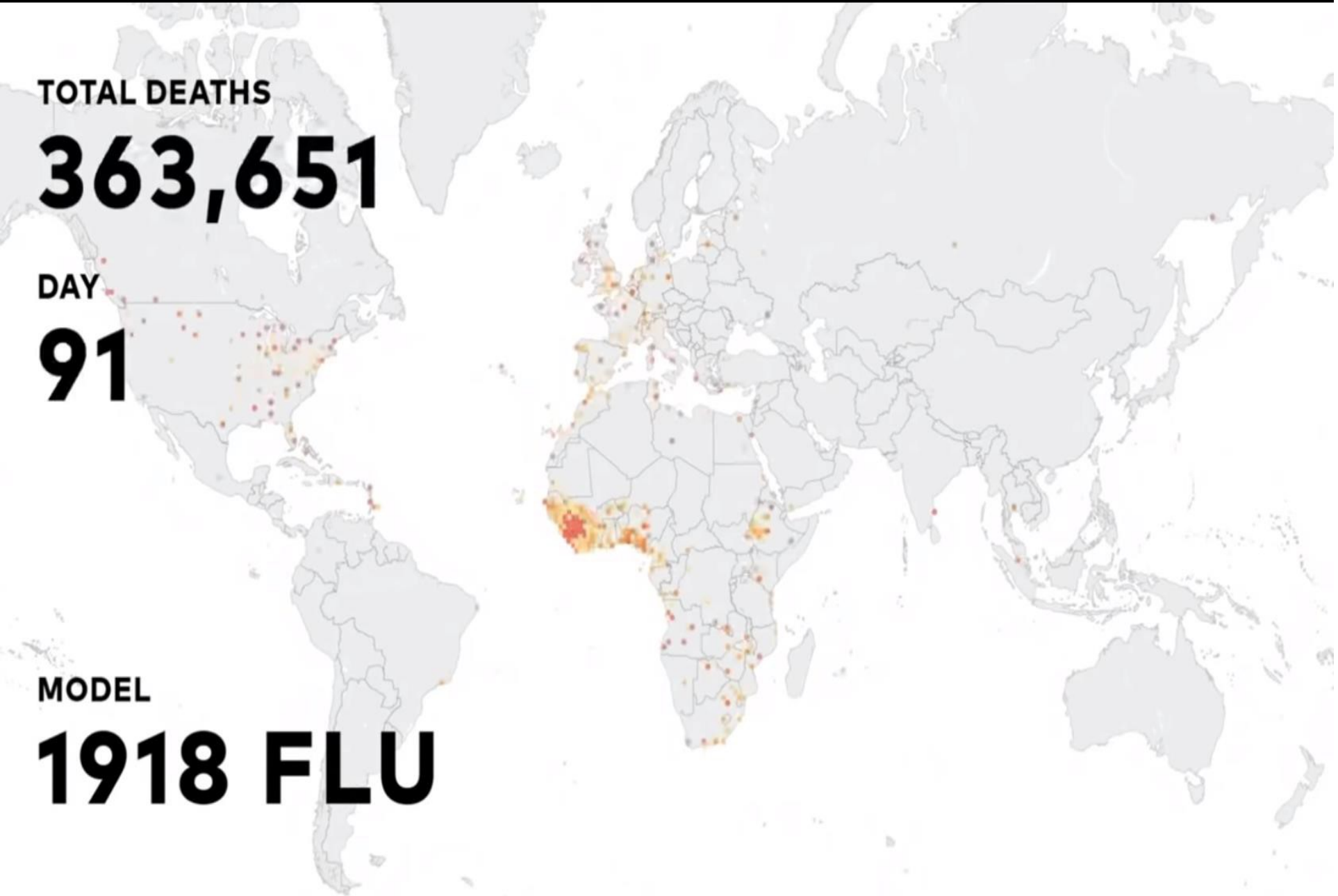
**363,651**

DAY

**91**

MODEL

**1918 FLU**





TOTAL DEATHS

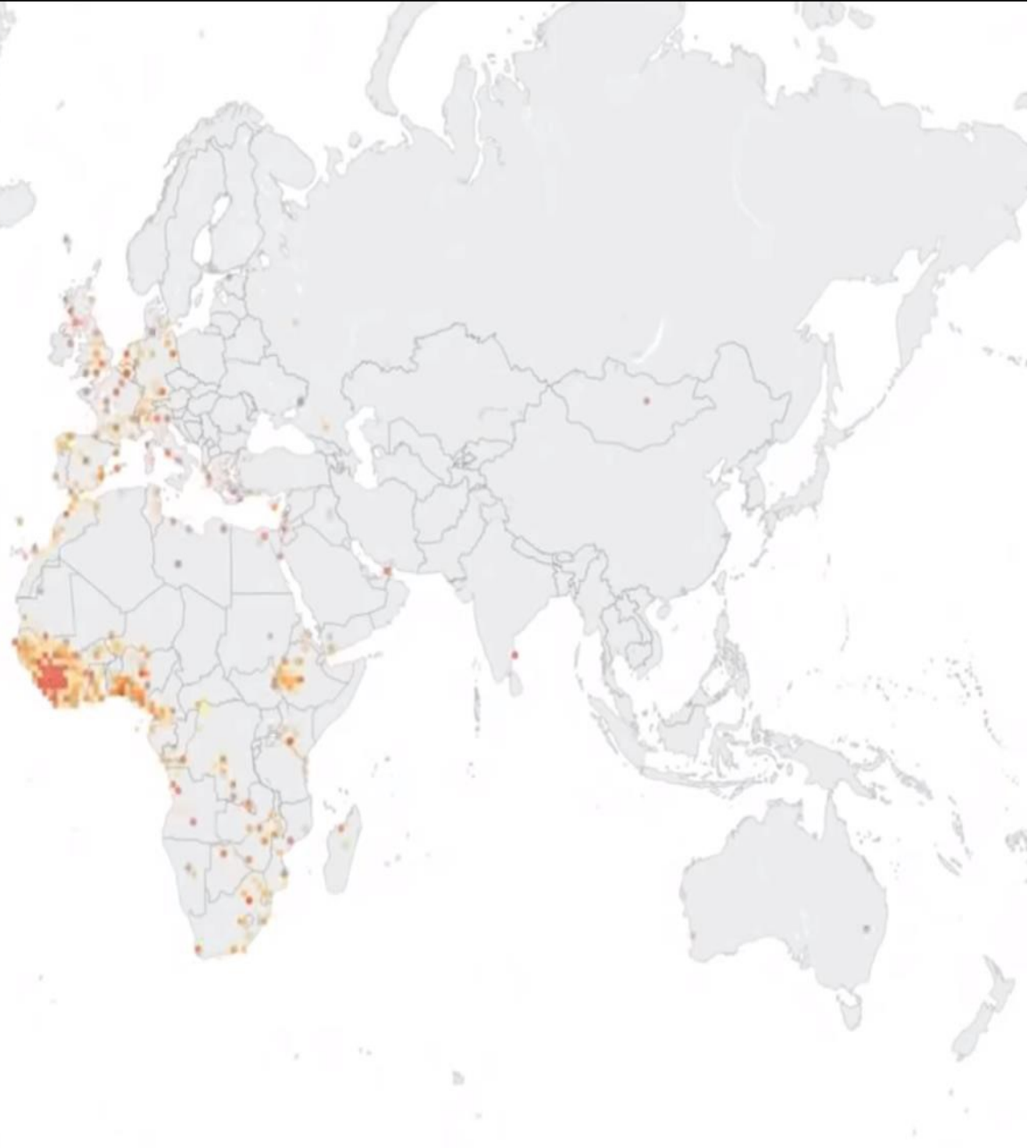
**509,070**

DAY

**95**

MODEL

**1918 FLU**



TOTAL DEATHS

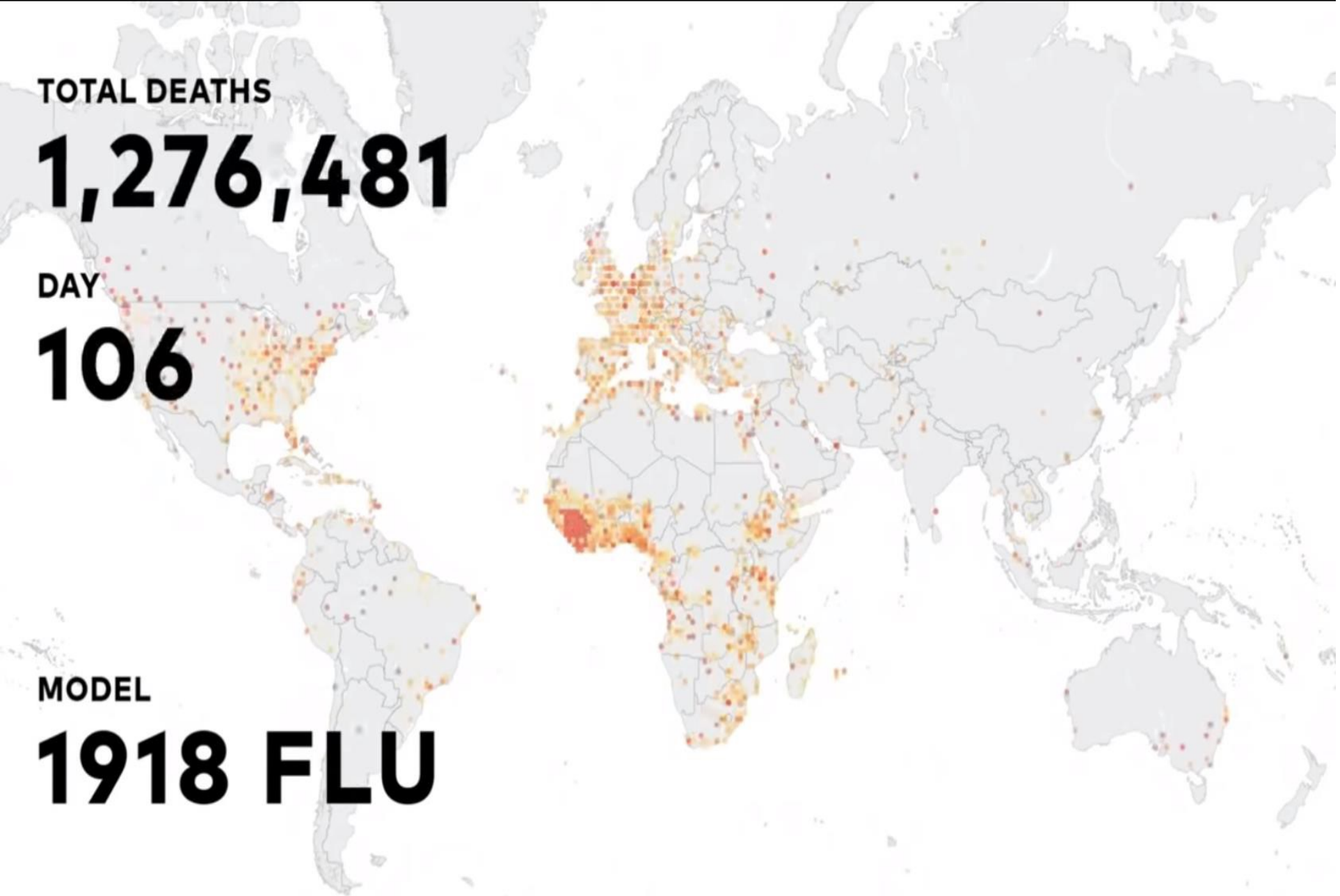
**1,276,481**

DAY

**106**

MODEL

**1918 FLU**





TOTAL DEATHS

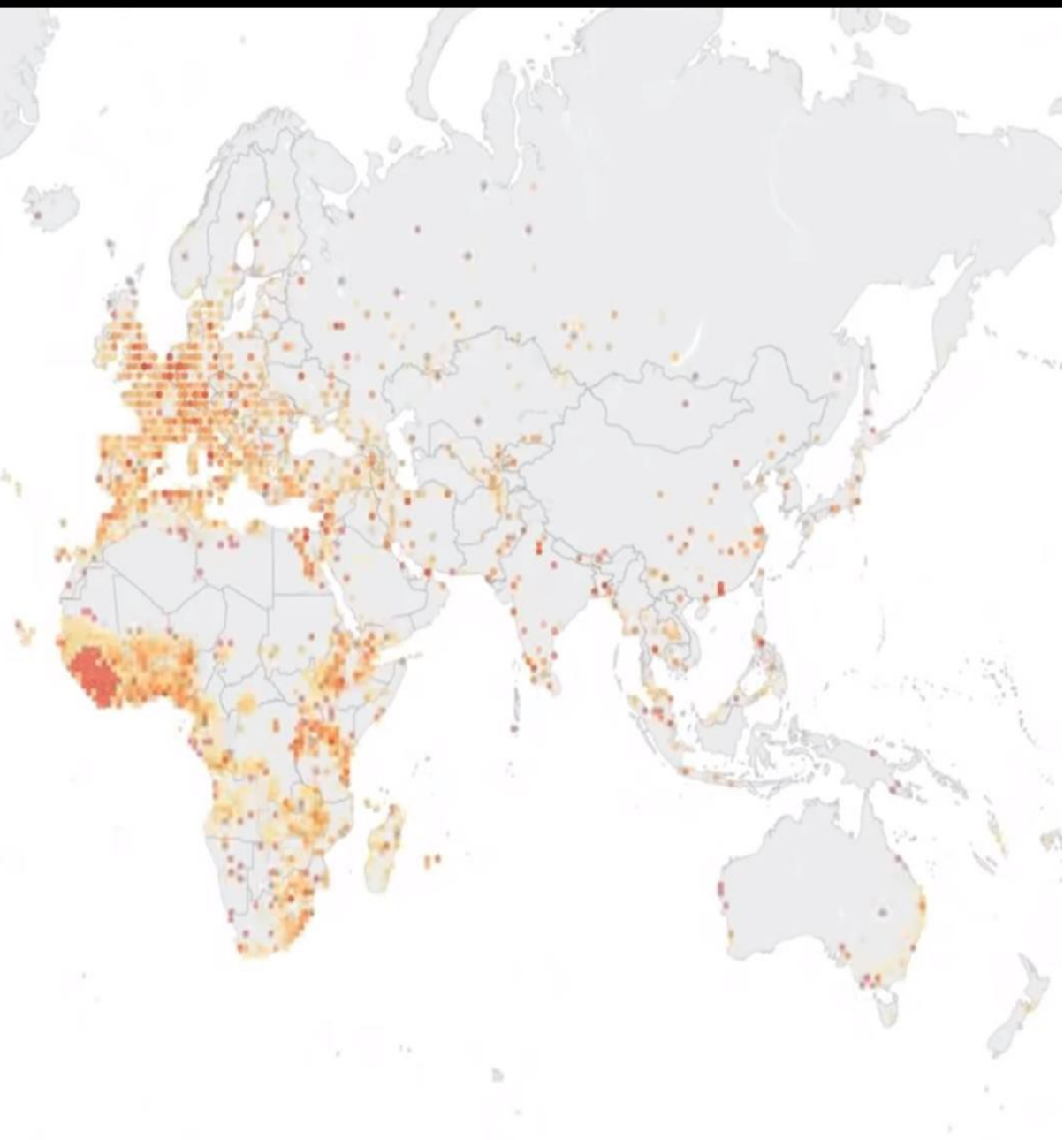
**3,342,117**

DAY

**118**

MODEL

**1918 FLU**



TOTAL DEATHS

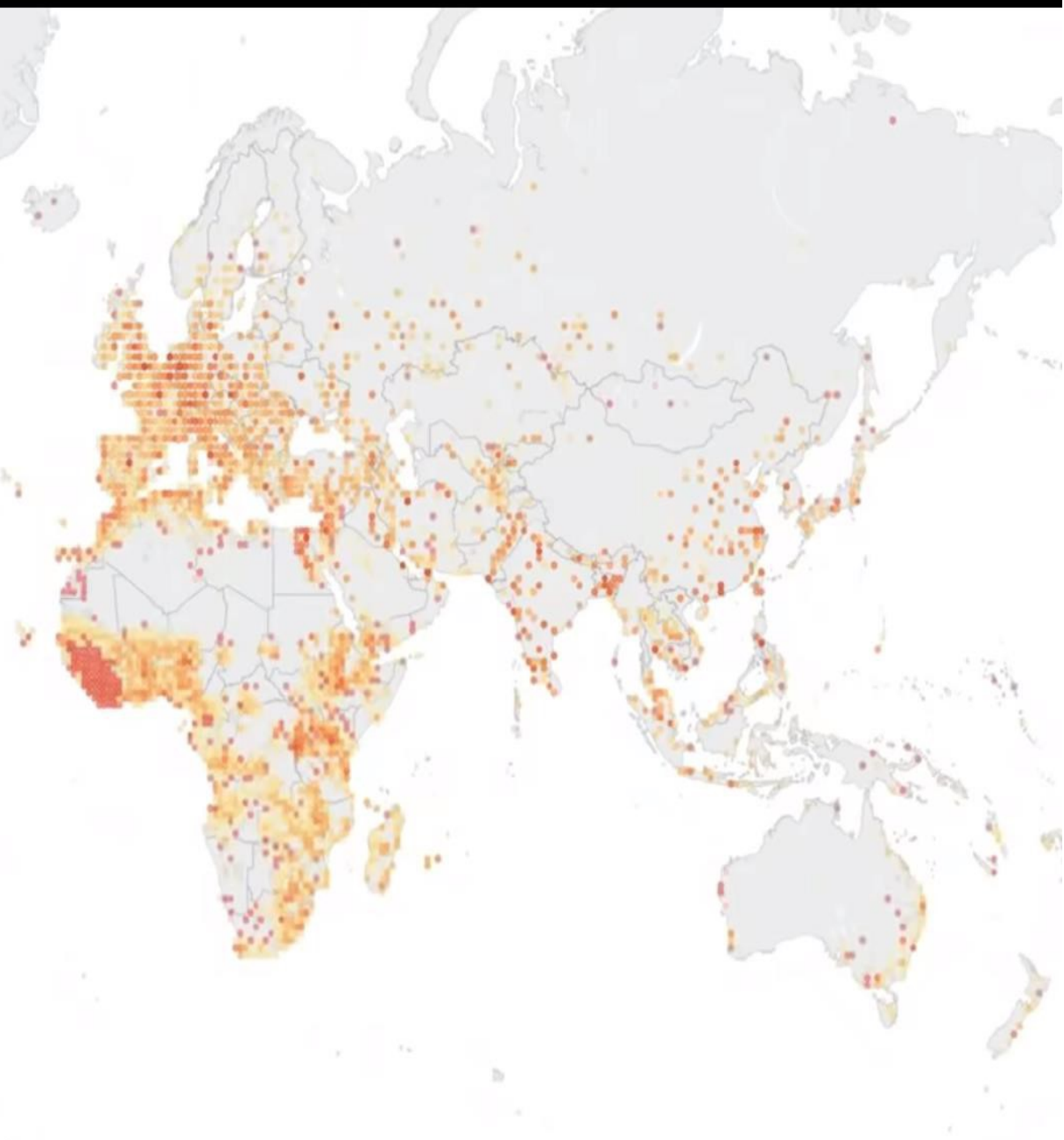
**5,842,842**

DAY

**126**

MODEL

**1918 FLU**



TOTAL DEATHS

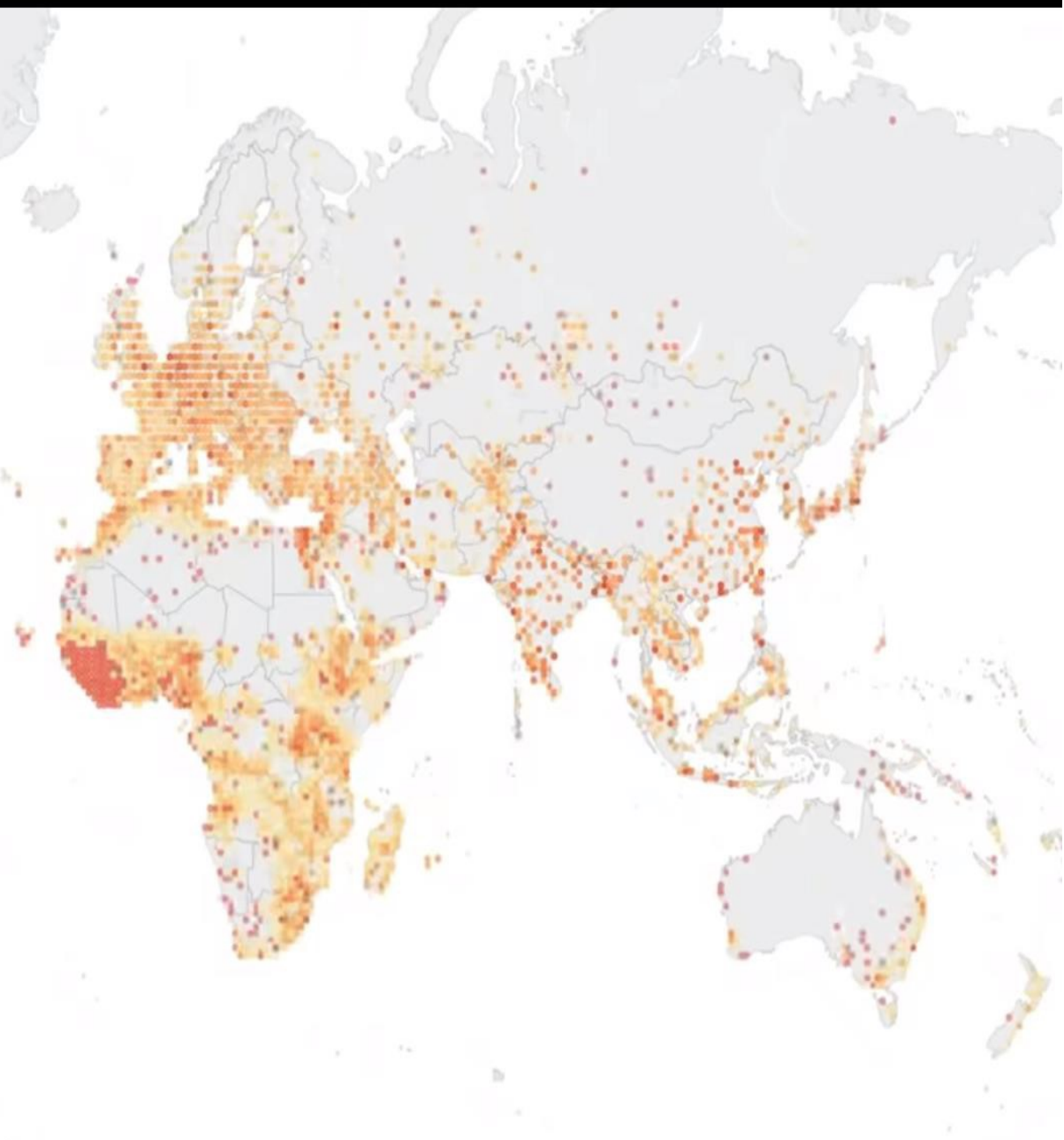
**8,691,088**

DAY

**133**

MODEL

**1918 FLU**





TOTAL DEATHS

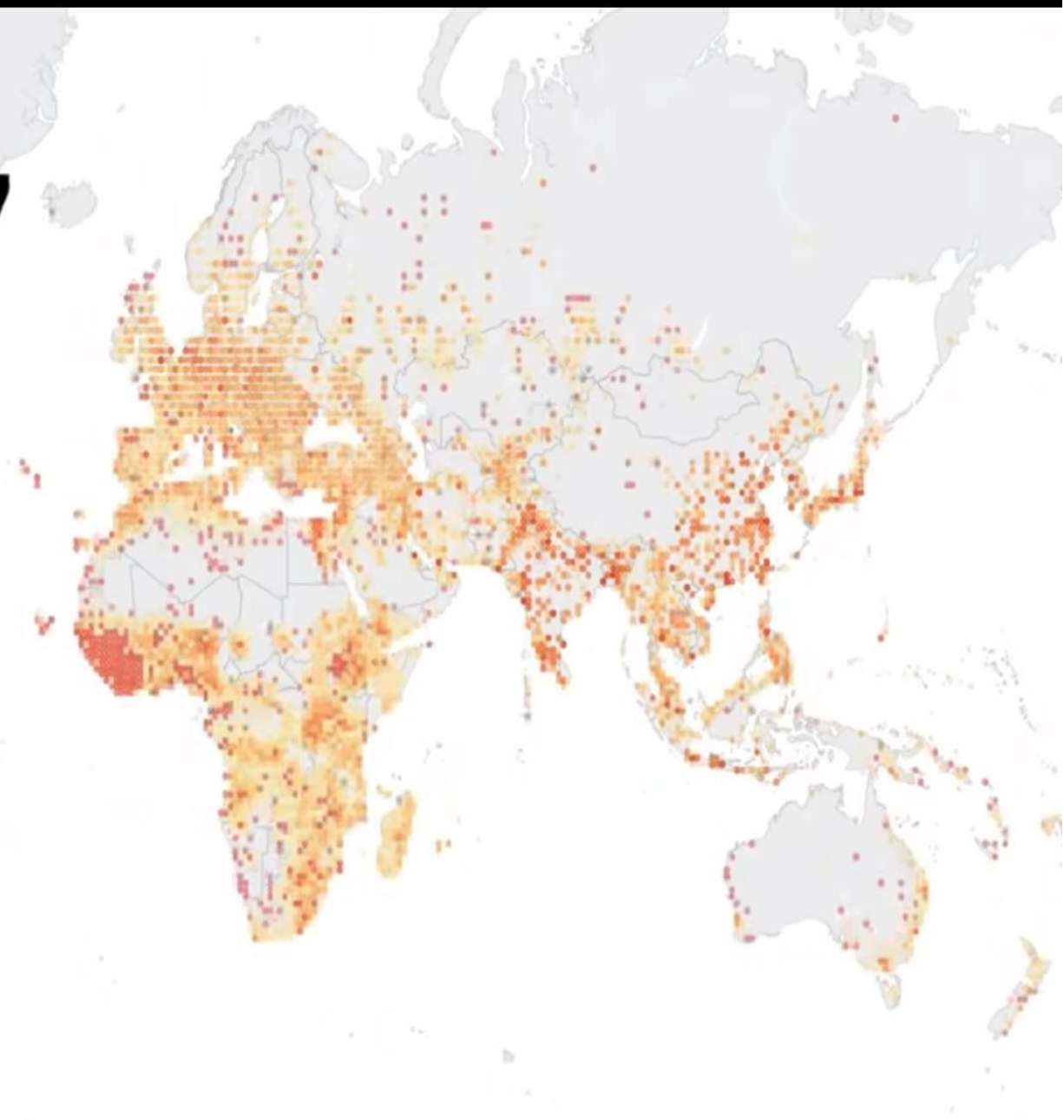
**12,105,187**

DAY

**140**

MODEL

**1918 FLU**



TOTAL DEATHS

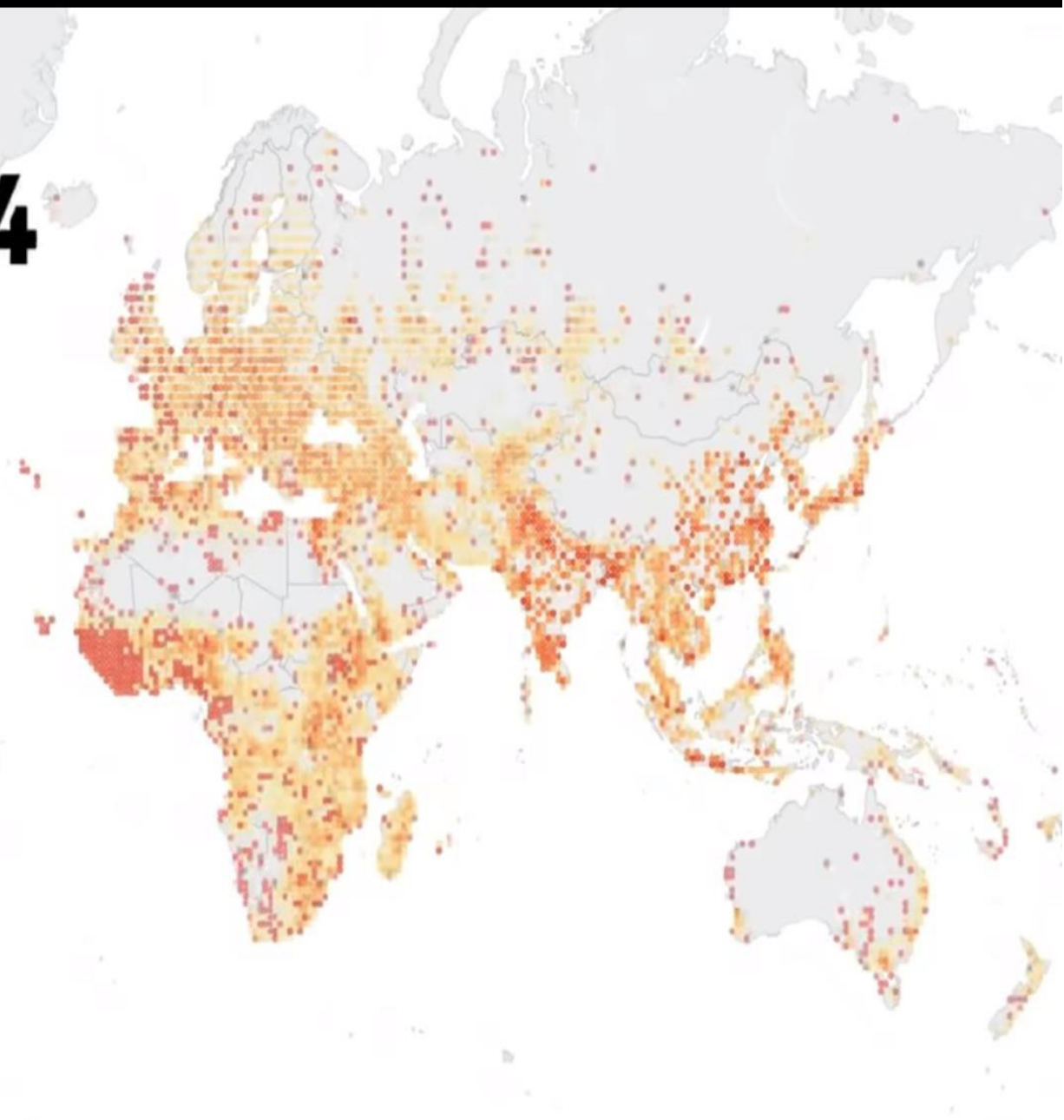
**15,910,784**

DAY

**147**

MODEL

**1918 FLU**



TOTAL DEATHS

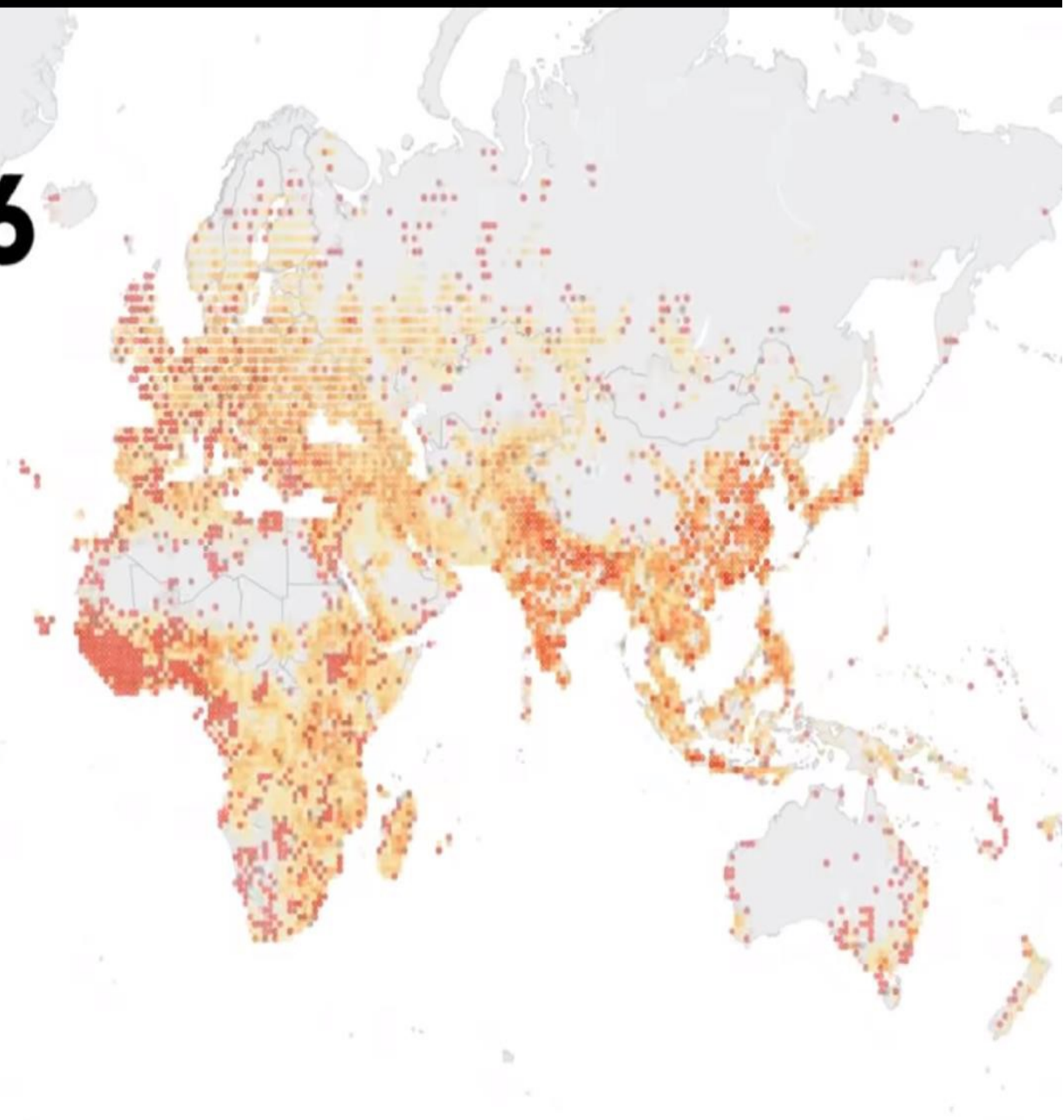
**19,180,566**

DAY

**153**

MODEL

**1918 FLU**





TOTAL DEATHS

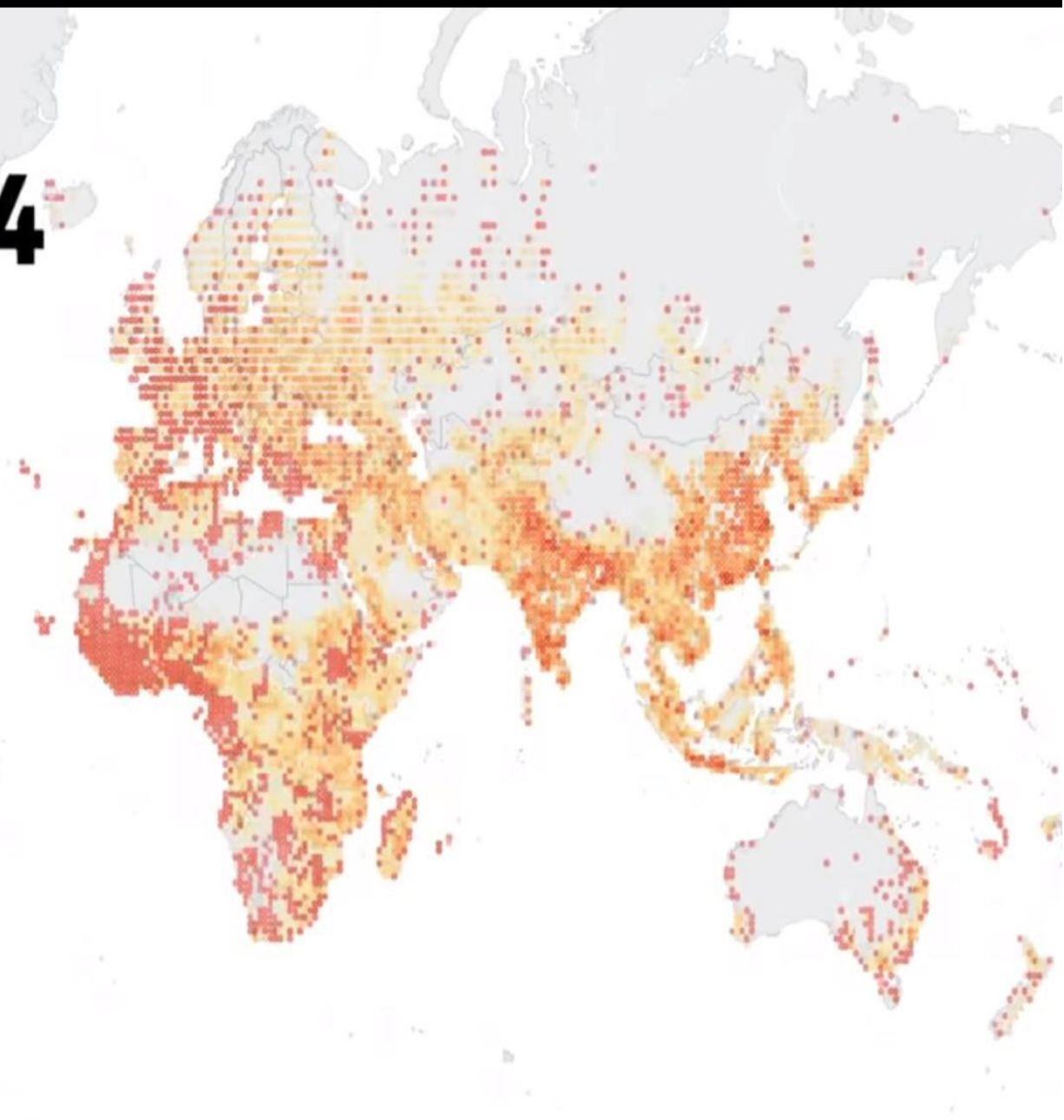
**22,165,564**

DAY

**159**

MODEL

**1918 FLU**



TOTAL DEATHS

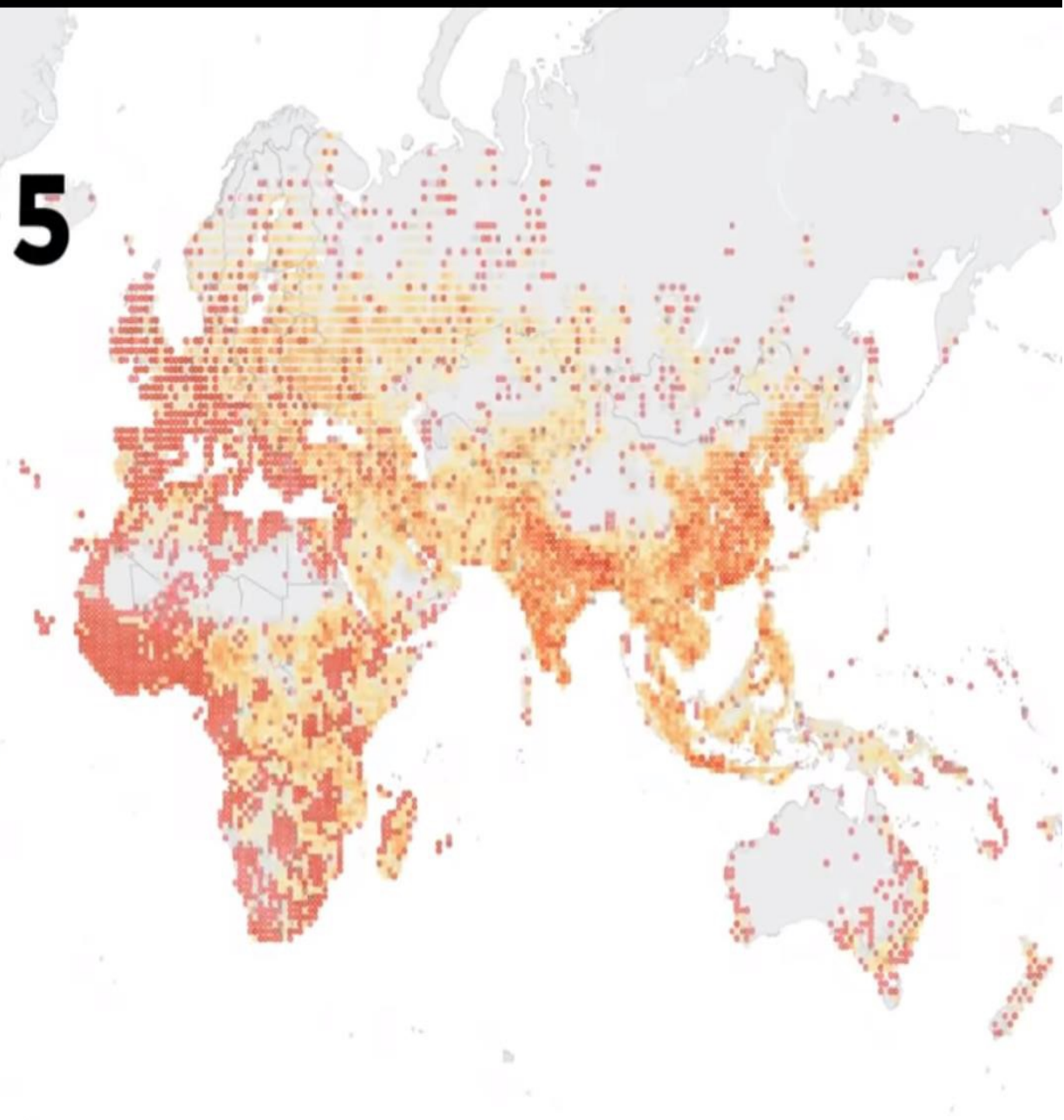
**24,816,805**

DAY

**165**

MODEL

**1918 FLU**





TOTAL DEATHS

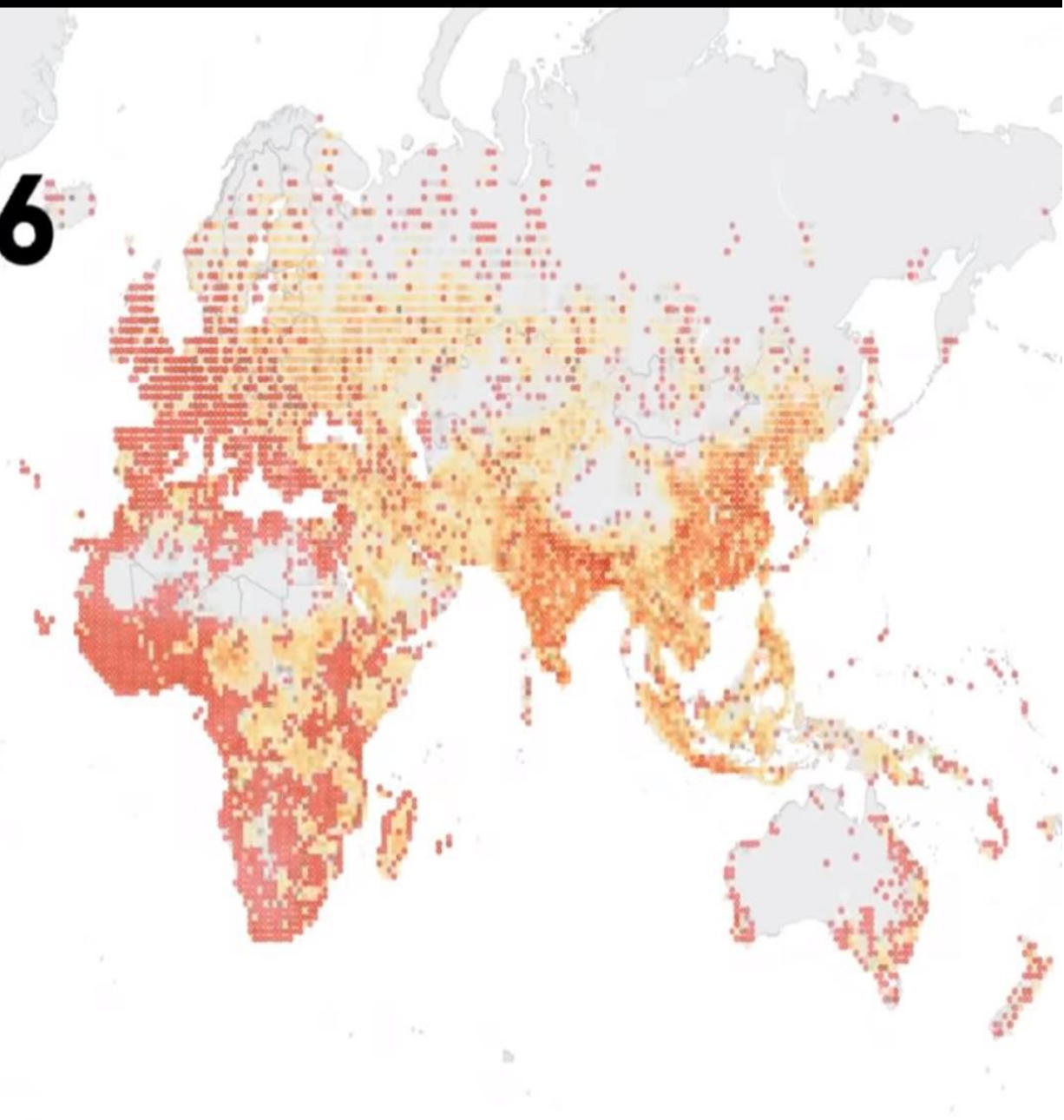
**26,857,226**

DAY

**170**

MODEL

**1918 FLU**



TOTAL DEATHS

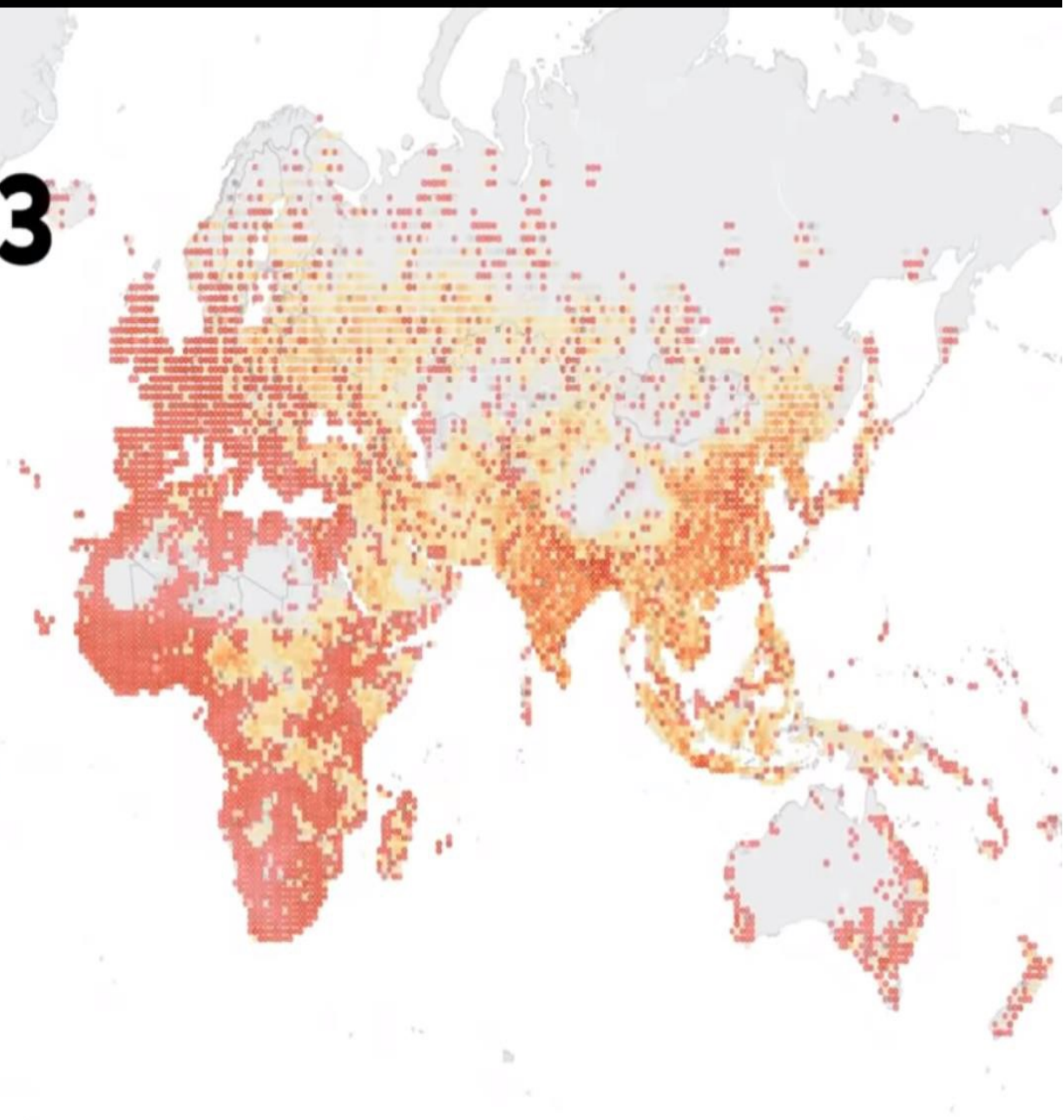
**29,013,643**

DAY

**176**

MODEL

**1918 FLU**





TOTAL DEATHS

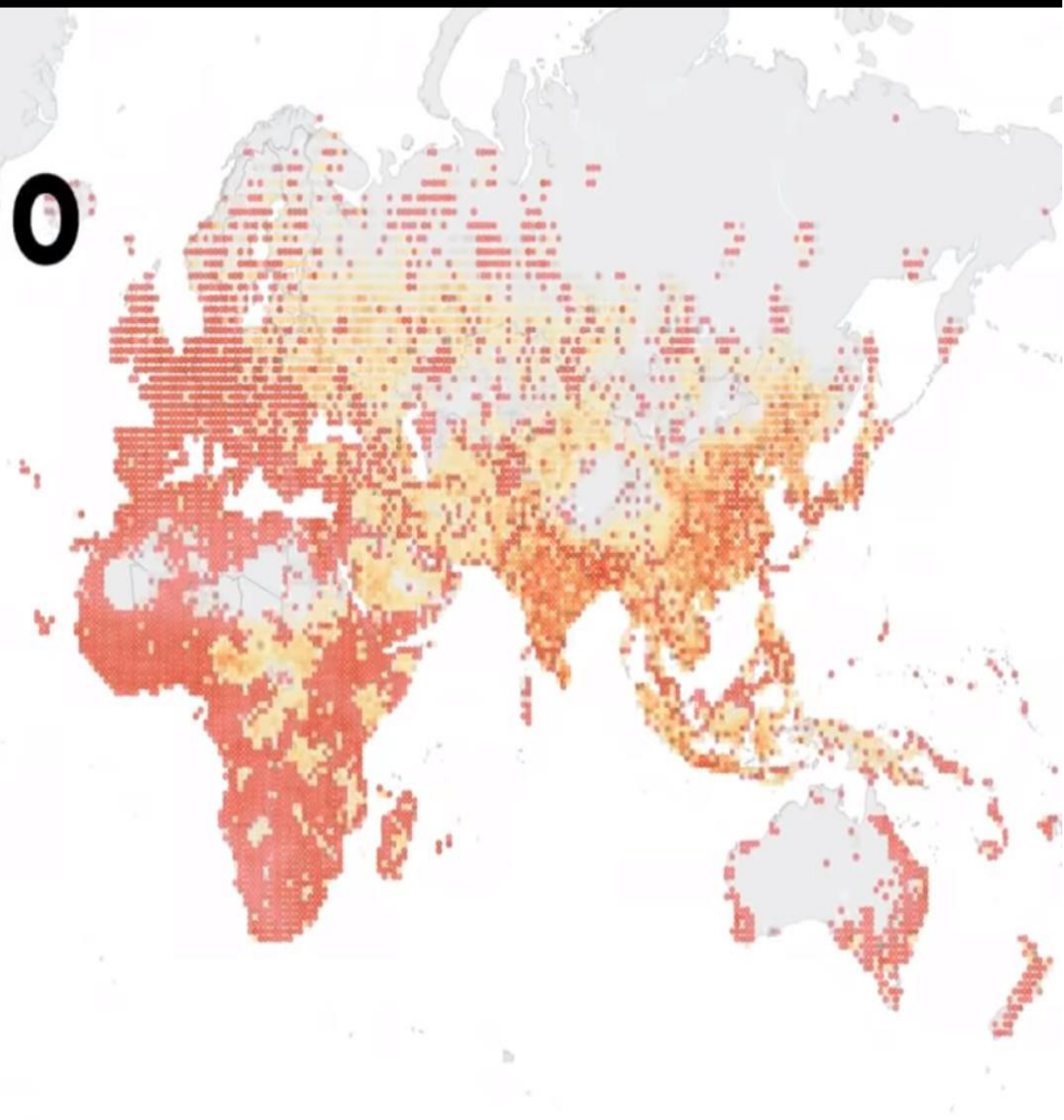
**30,525,790**

DAY

**181**

MODEL

**1918 FLU**



TOTAL DEATHS

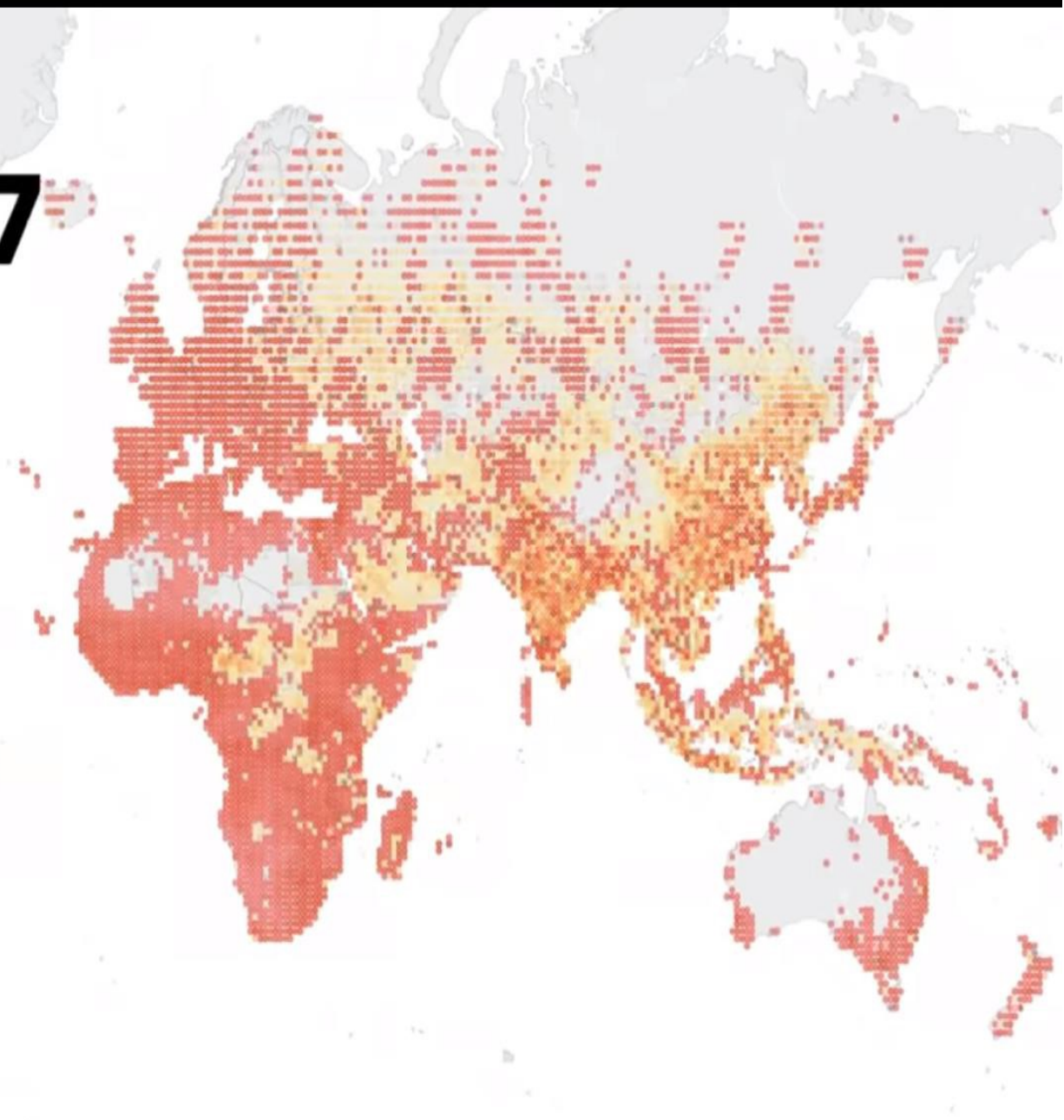
**31,993,647**

DAY

**188**

MODEL

**1918 FLU**





TOTAL DEATHS

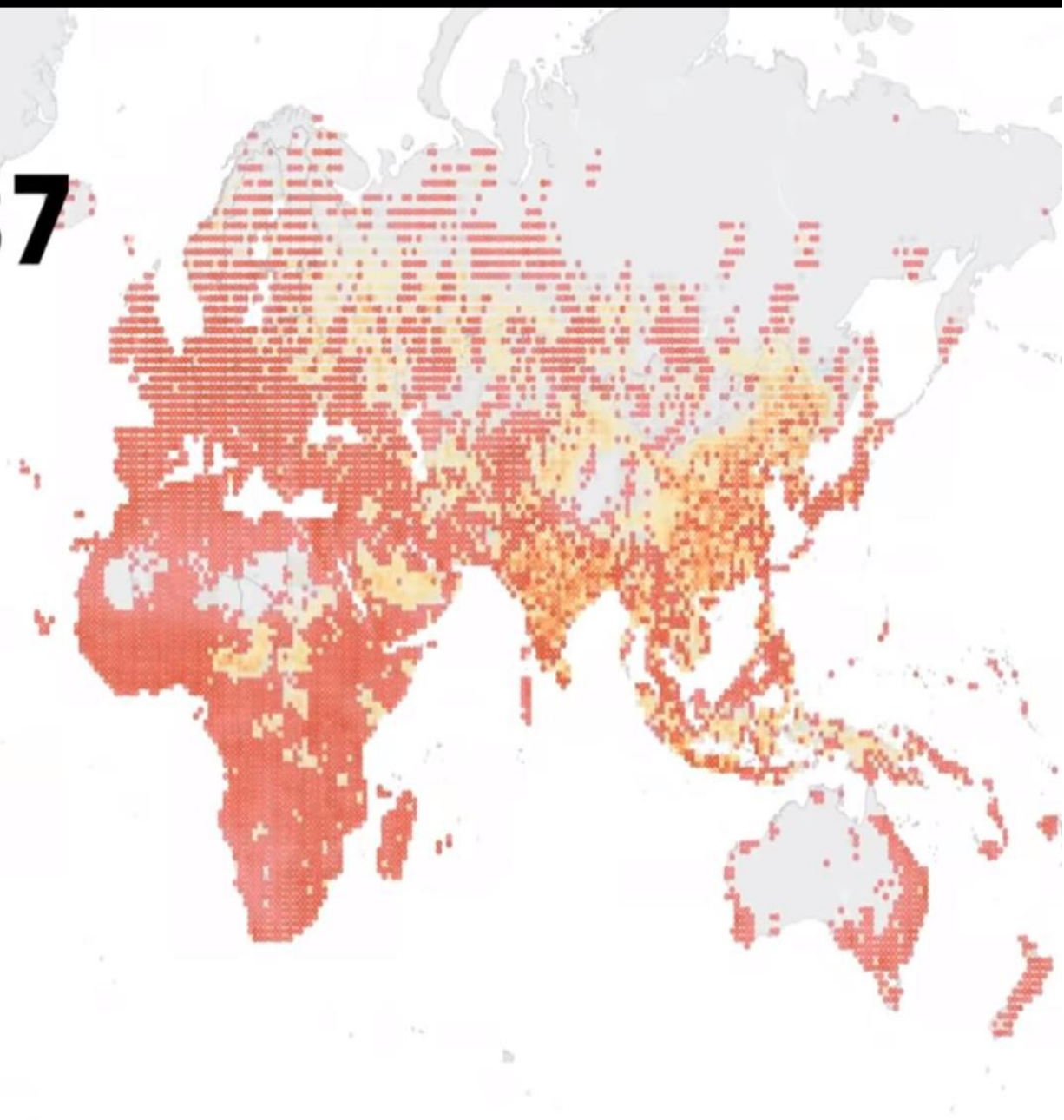
**32,603,537**

DAY

**193**

MODEL

**1918 FLU**



TOTAL DEATHS

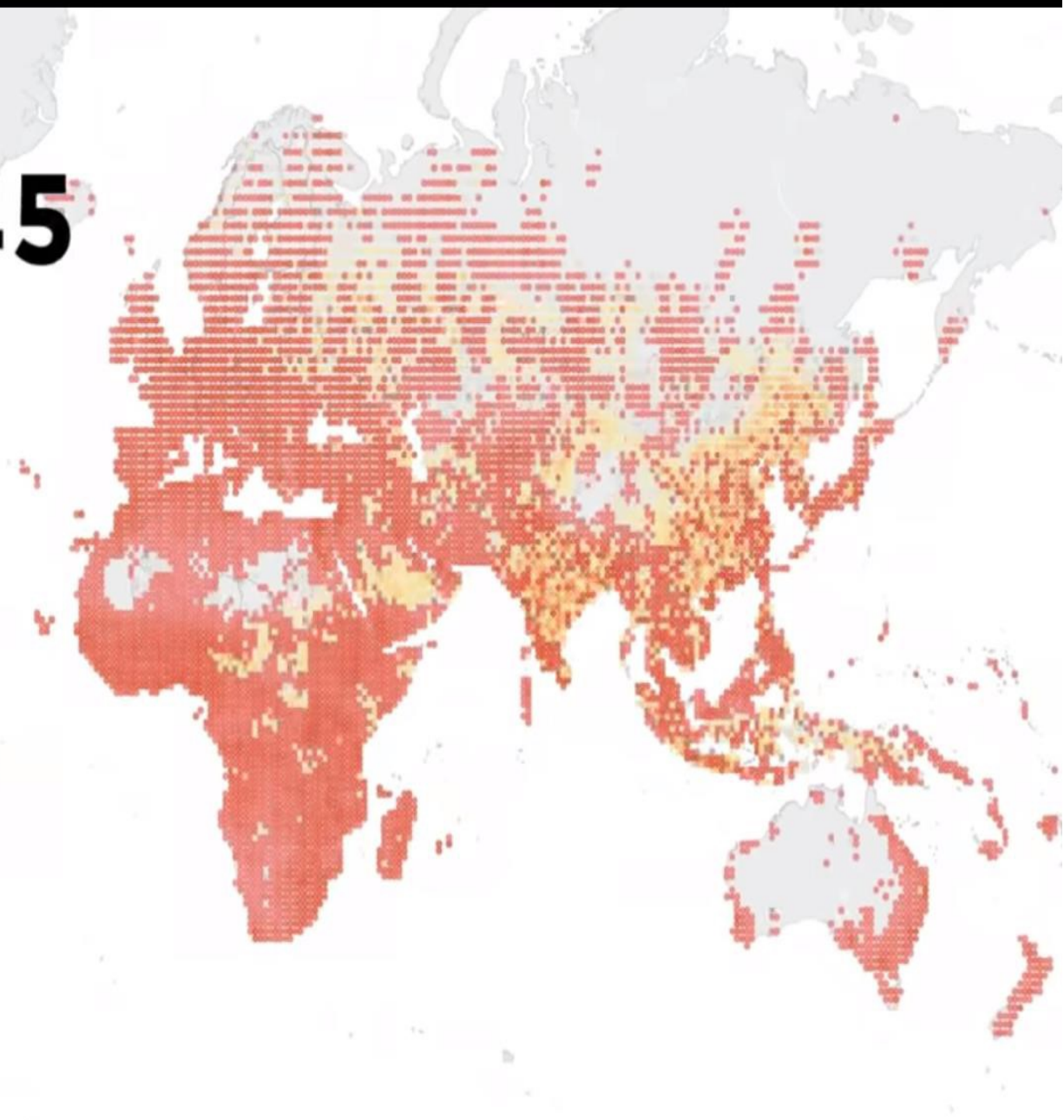
**33,007,245**

DAY

**199**

MODEL

**1918 FLU**





TOTAL DEATHS

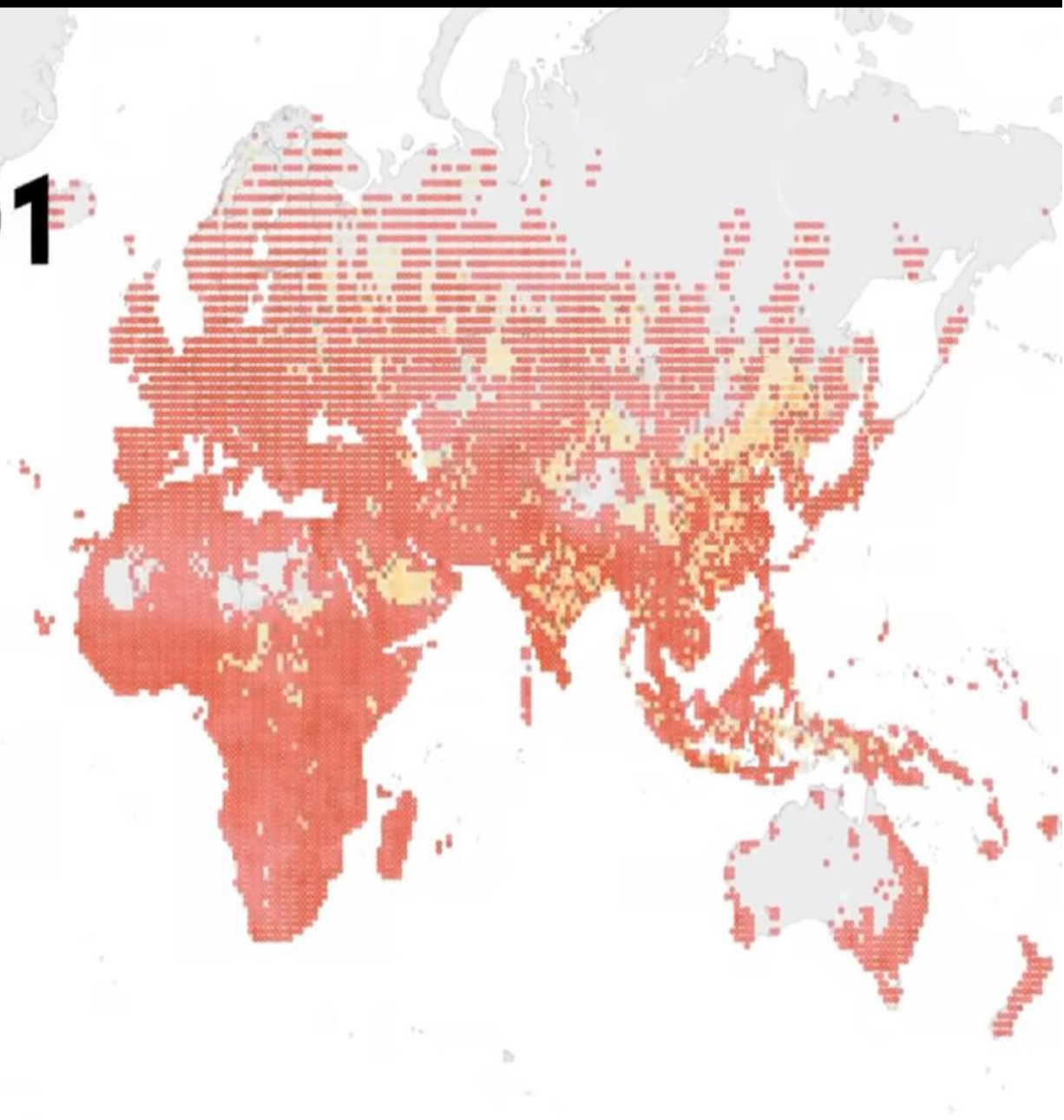
**33,236,301**

DAY

**207**

MODEL

**1918 FLU**



TOTAL DEATHS

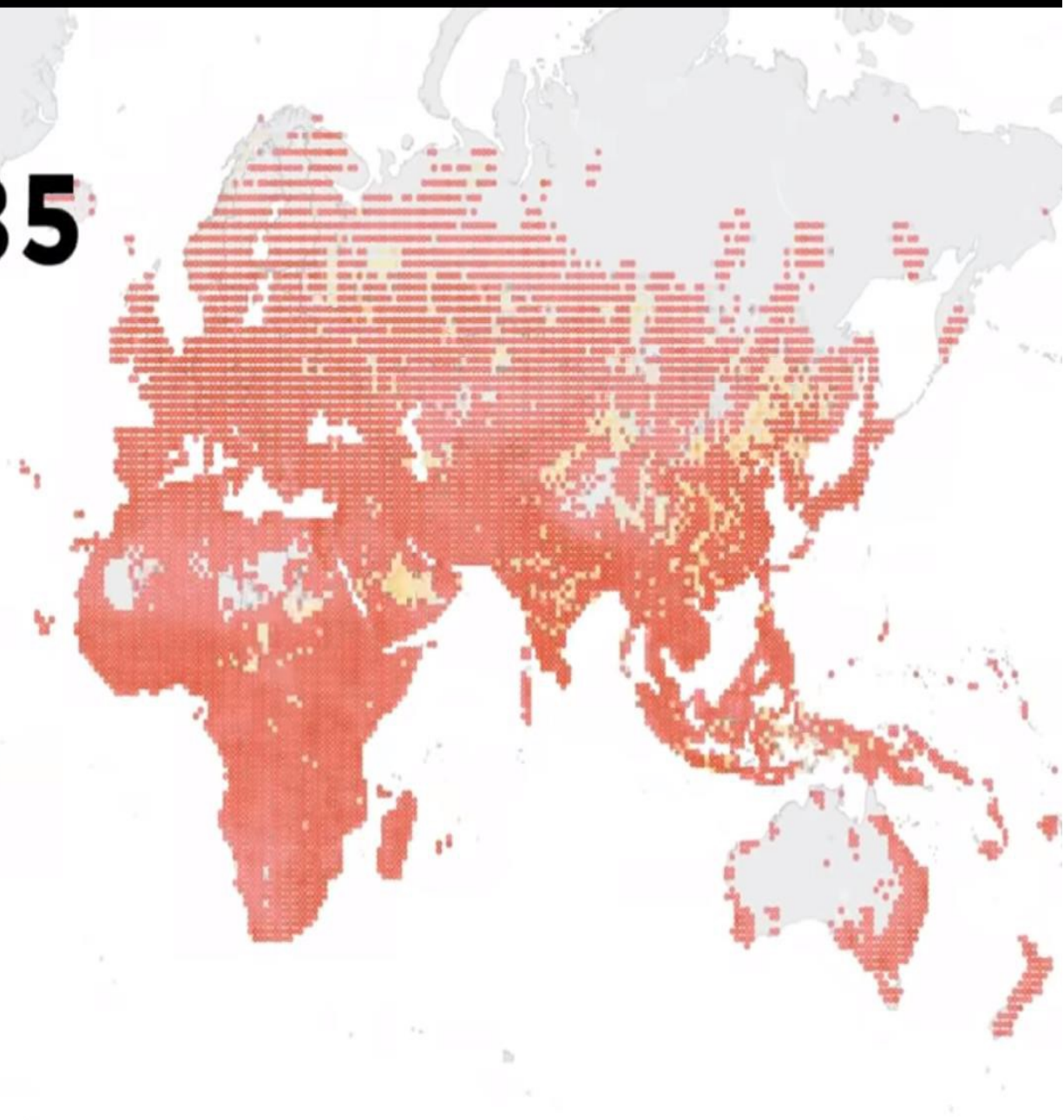
**33,306,585**

DAY

**213**

MODEL

**1918 FLU**





TOTAL DEATHS

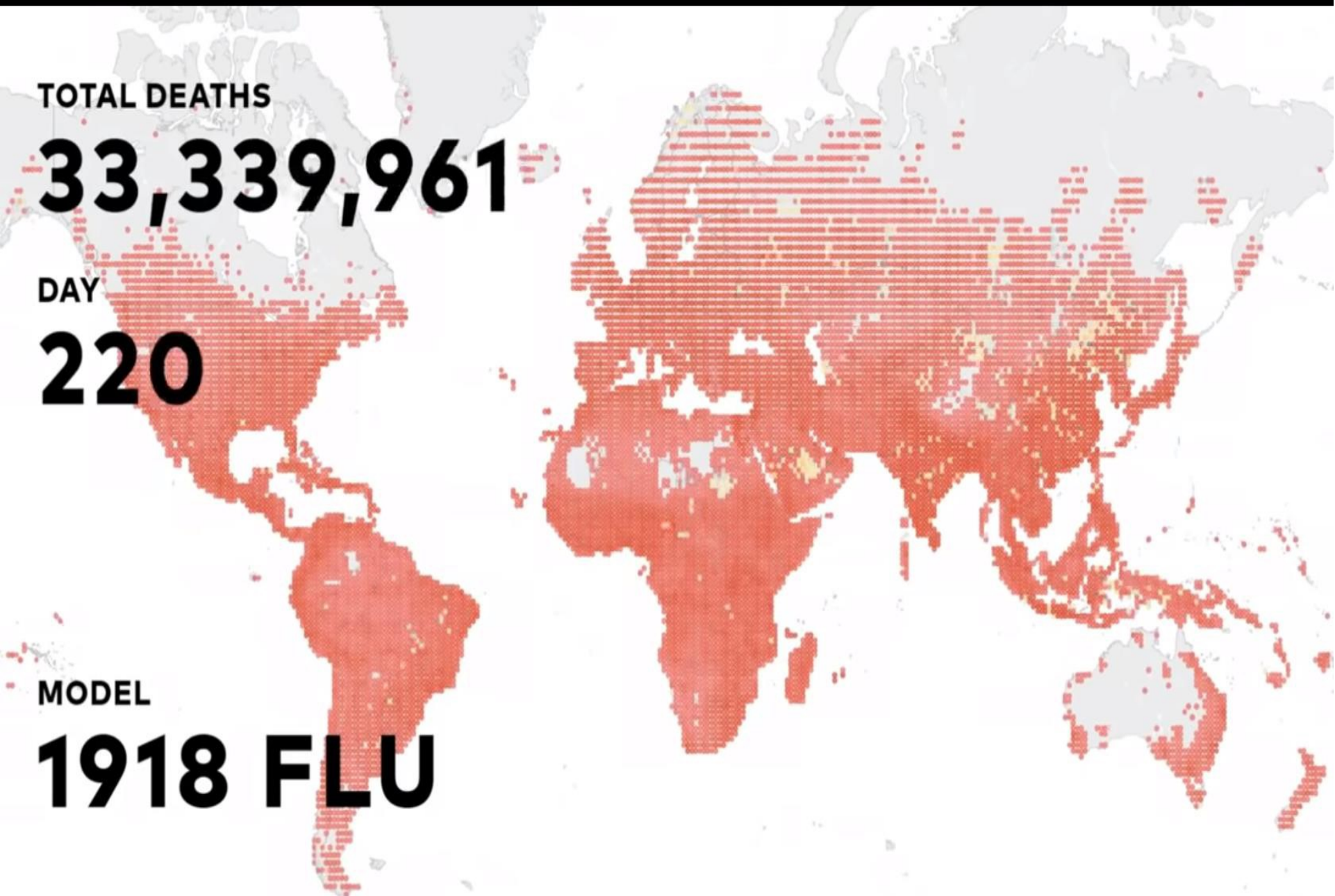
**33,339,961**

DAY

**220**

MODEL

**1918 FLU**



TOTAL DEATHS

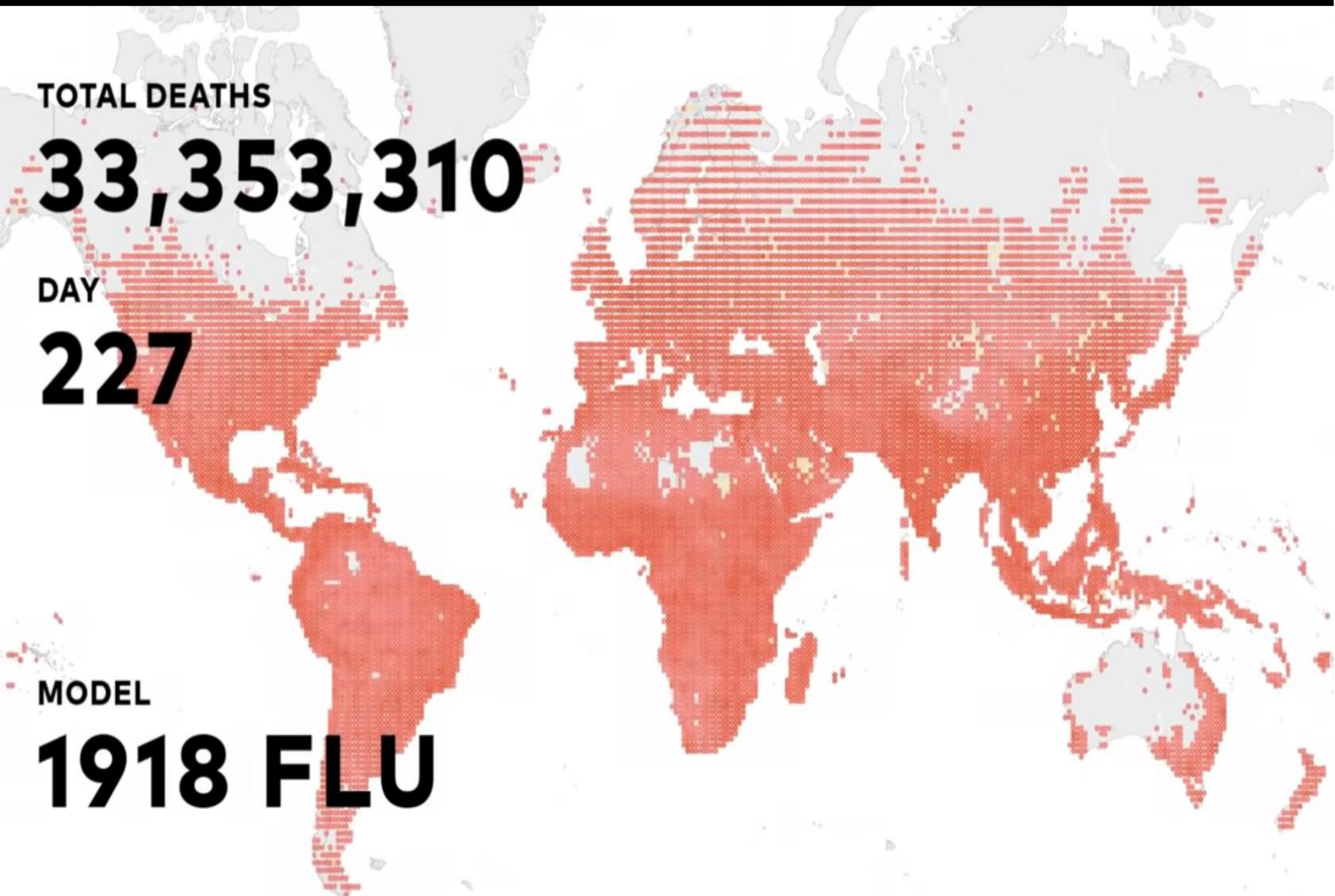
**33,353,310**

DAY

**227**

MODEL

**1918 FLU**





TOTAL DEATHS

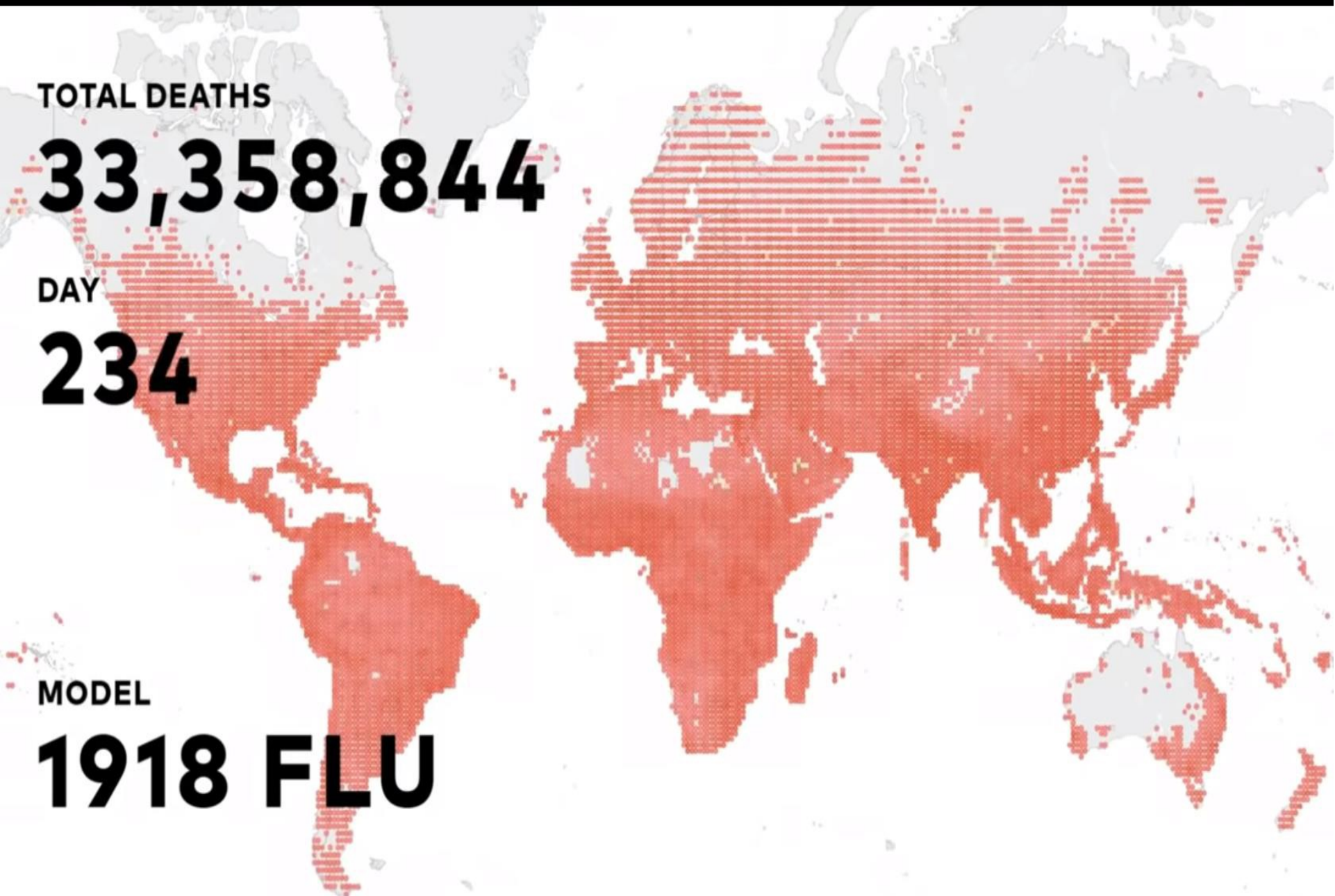
**33,358,844**

DAY

**234**

MODEL

**1918 FLU**



TOTAL DEATHS

**33,361,734**

DAY

**241**

MODEL

**1918 FLU**



TOTAL DEATHS

**33,363,402**

DAY

**249**

MODEL

**1918 FLU**

TOTAL DEATHS

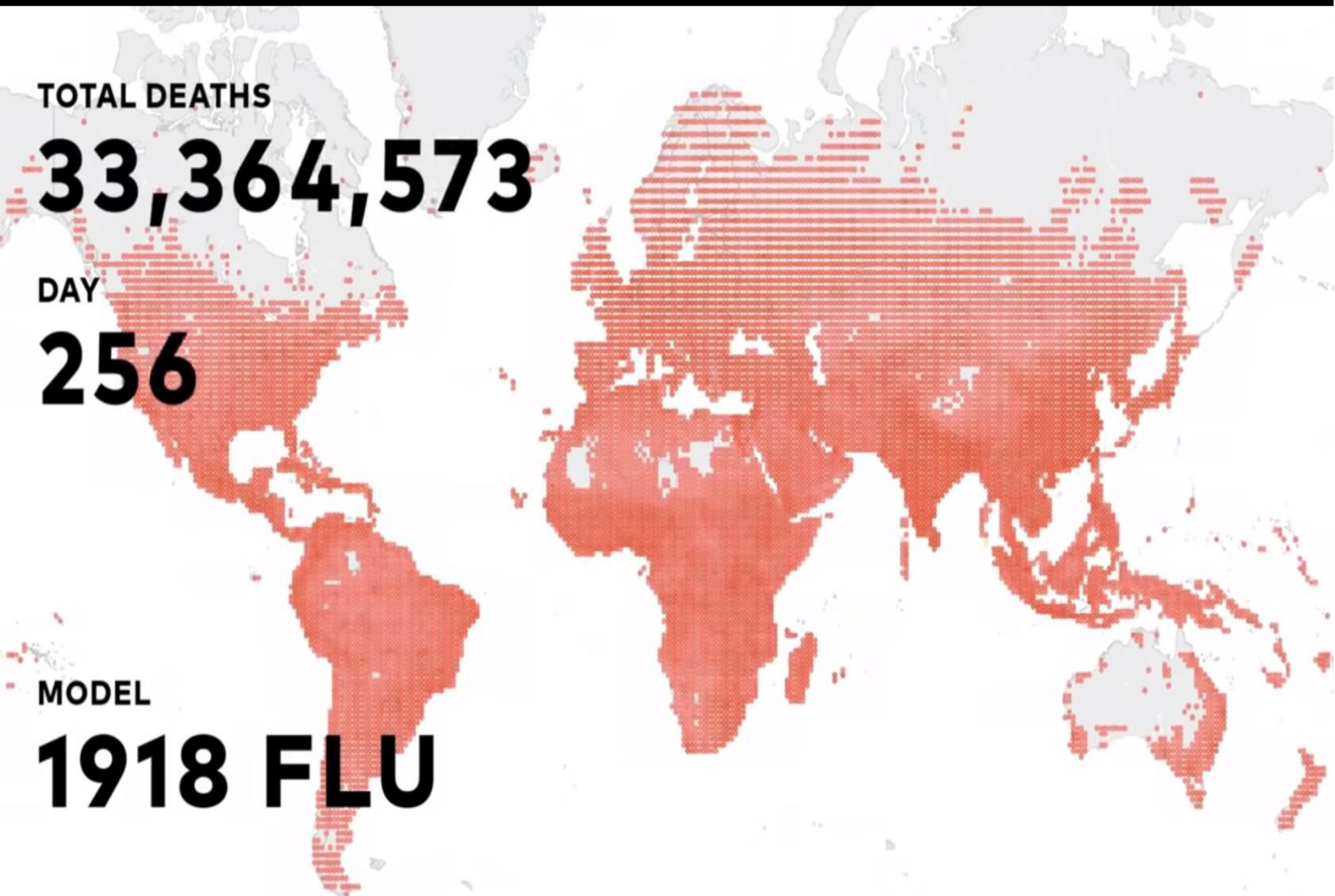
**33,364,573**

DAY

**256**

MODEL

**1918 FLU**





TOTAL DEATHS

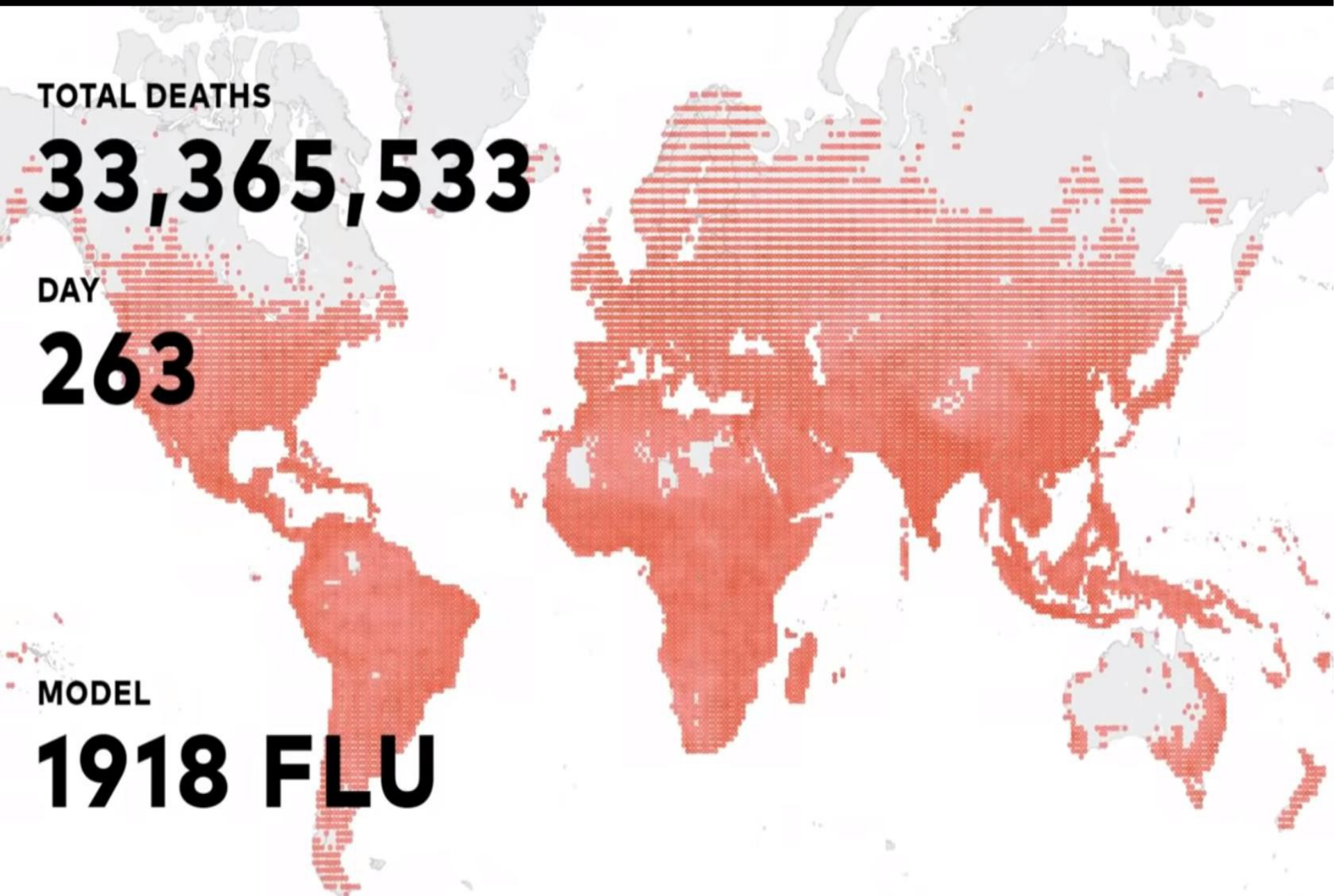
**33,365,533**

DAY

**263**

MODEL

**1918 FLU**



TOTAL DEATHS

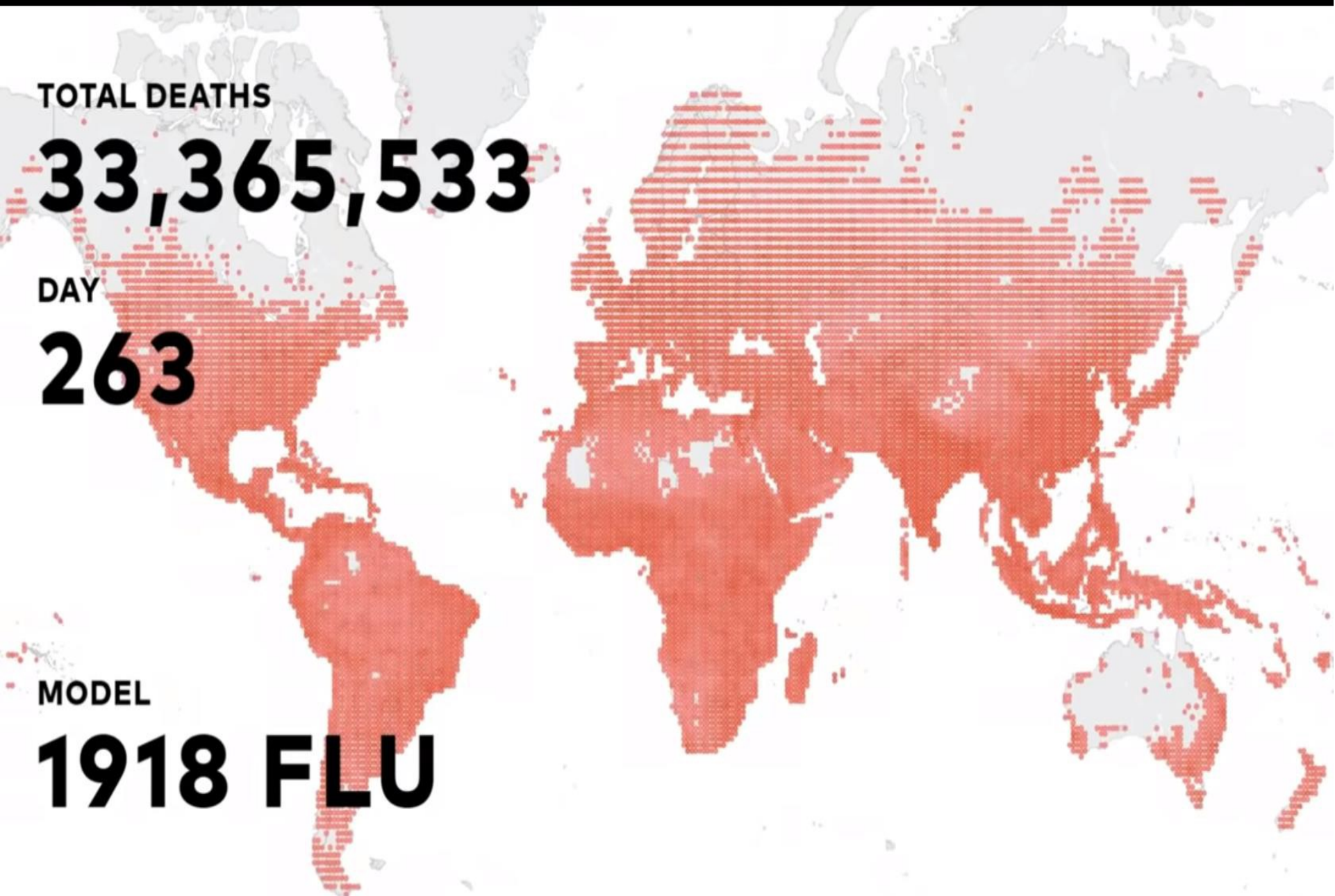
**33,365,533**

DAY

**263**

MODEL

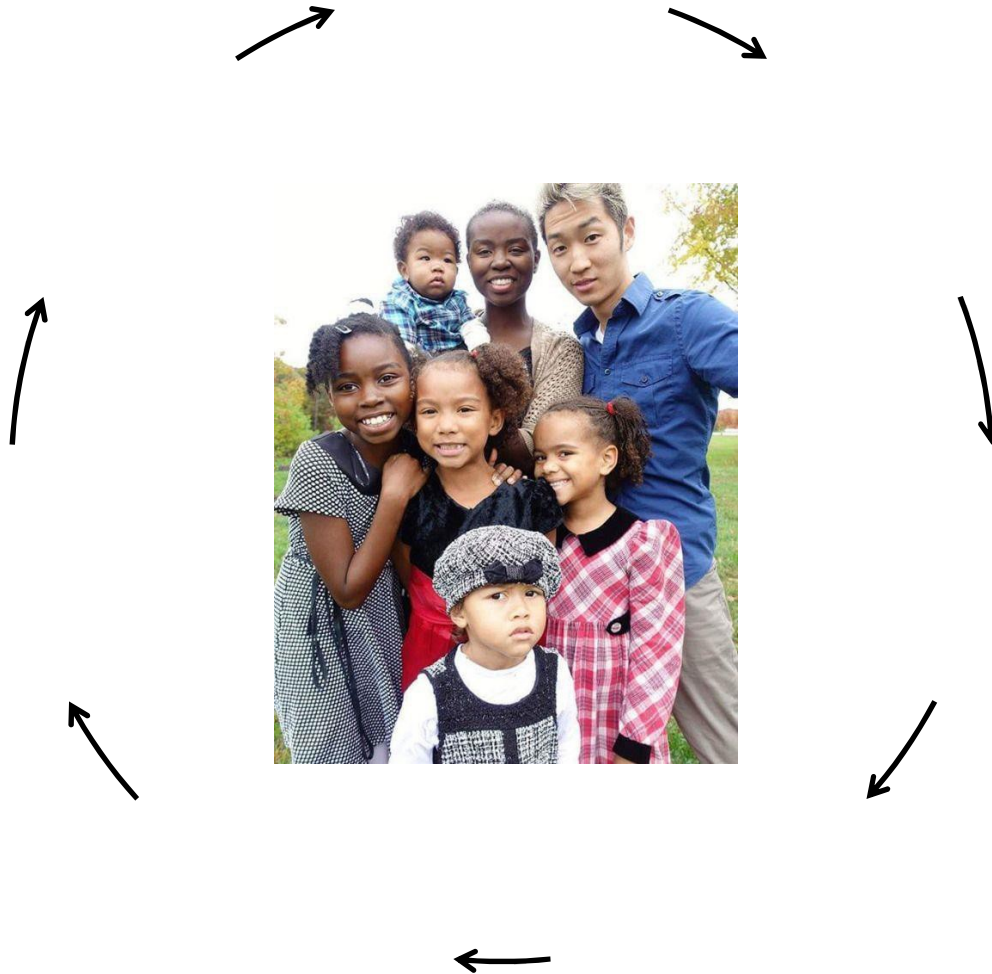
**1918 FLU**





# ZOONOTIC SPILLOVERS

# Zoonoses Around Us



# Spillover (1)

Most new human pathogens originate in the bodies of other animals.

>60% of new pathogens come from animals around us, with 70% of them from wild animals.

142 viruses are known to have spilled over into people.

Host species are mostly domesticated species or wildlife that have adapted to the way we've changed their landscape.

# Spillover <sup>(2)</sup>

- Viruses jump species when there is close contact between an infected animal and a **susceptible** person.
- Animals share viruses through feces, urine, blood, or respiratory droplets.
- Domesticated animals, like livestock, have been the largest source of virus spillover.
- This is due to their large numbers and our frequent close interaction with them.

# Spillover <sup>(3)</sup>

- Wild animals that have adapted to environments where humans dominate are another significant source of spillovers.
- Human encroachments on wildlife habitats increase opportunities and risks for animal-human interactions and spillover.
- Exploitation of wildlife like hunting and the wildlife trade have also led to transmission of zoonotic viruses.

# Wet Markets

- Animals and people mix in high density & close contact, creating the perfect opportunity for host jumping.
- Most of these species would not have normally come together in the natural world.
- Nearly 1/3 of all vertebrate species are threatened or endangered, as wildlife shift their distributions in response to human activities that modify their landscape.





# Spillover

- Wildlife markets are a petri dish for the next pandemic.
- The wildlife trade can be deadly for the wild animals involved and for people throughout the world.
- >200 organizations from across the world sent a letter to WHO urging them to endorse a permanent ban on the wildlife trade, including for food, medicine, fur, pets and other reasons.
- Governments must also help the traders involved to find new livelihoods as quickly as possible.

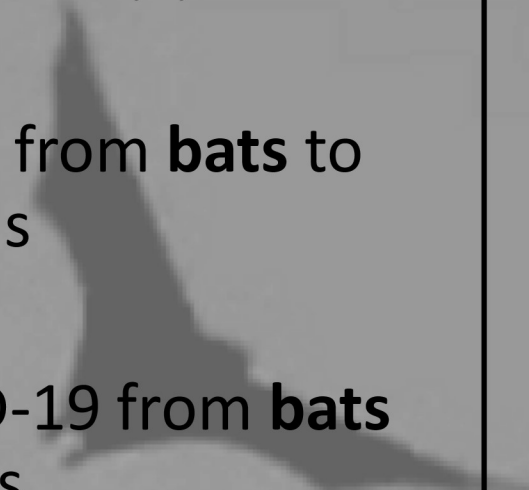
# Bats



- Bats are host to a higher proportion of zoonoses than all other mammalian orders.
- Bats are not affected by the viruses they carry due to their special immune systems.
- Interaction with livestock, pets, accidental encounters, and scavenging bat carcasses, increase risk of transmission.
- The novel coronavirus comes from a group of viruses that originate or spread in bats.



# Some Spillovers

- 
- SARS from **bats** to pangolins (?) to civets
  - MERS from **bats** to camels
  - CoVID-19 from **bats** to pigs
  - EBOLA from **bats** to monkeys to deer

- NIPAH virus from **bats**, pigs and fruit
- HENDRA virus from **bats** to horses to humans
- MARBURG virus from **bats** to monkeys
- HIV from chimpanzees to humans

Example of Spillover

# PSITTACOSIS

# Psittacosis

parrot fever

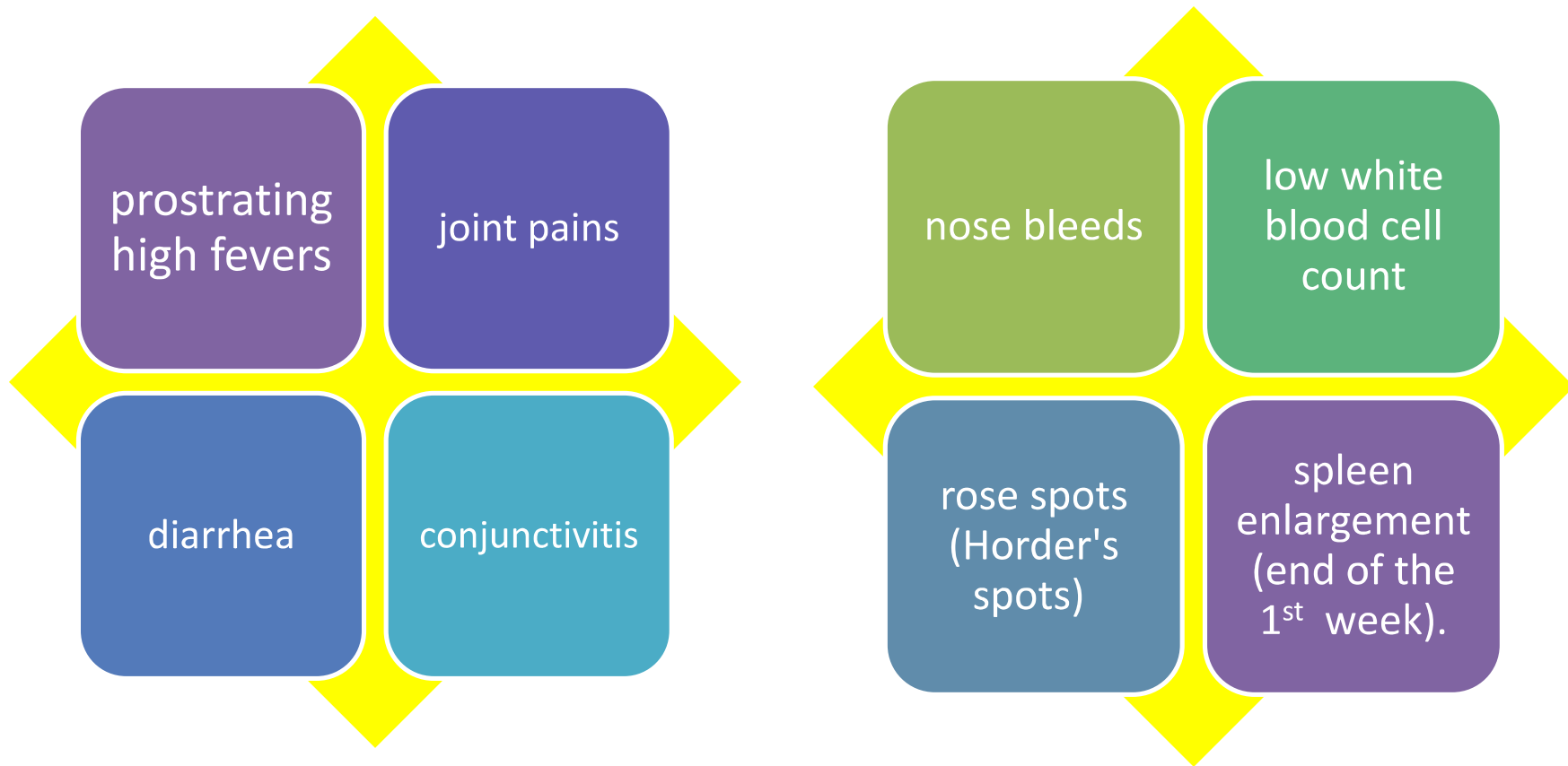
- Zoonosis caused by *Chlamydia psittaci*.
- Bacterium from infected parrots, macaws, budgies, cockatiels, pigeons, sparrows, ducks, hens, gulls and many other species of birds.
- The incidence of infection in canaries and finches is believed to be lower than in psittacine birds.
- Also known as ornithosis when referring to other birds.

# Psittacosis

parrot fever

- Incubation period of 5–19 days in humans (longest 54 days).
- Stages of disease progression:
  - flu-like symptoms w/o X-ray abnormalities
  - mild to moderate pneumonia
  - severe pneumonia
  - acute respiratory failure
  - sepsis, septic shock
  - death in older or immunocompromised patients

# In the 1st week, symptoms mimic typhoid fever:



Ramírez 2023

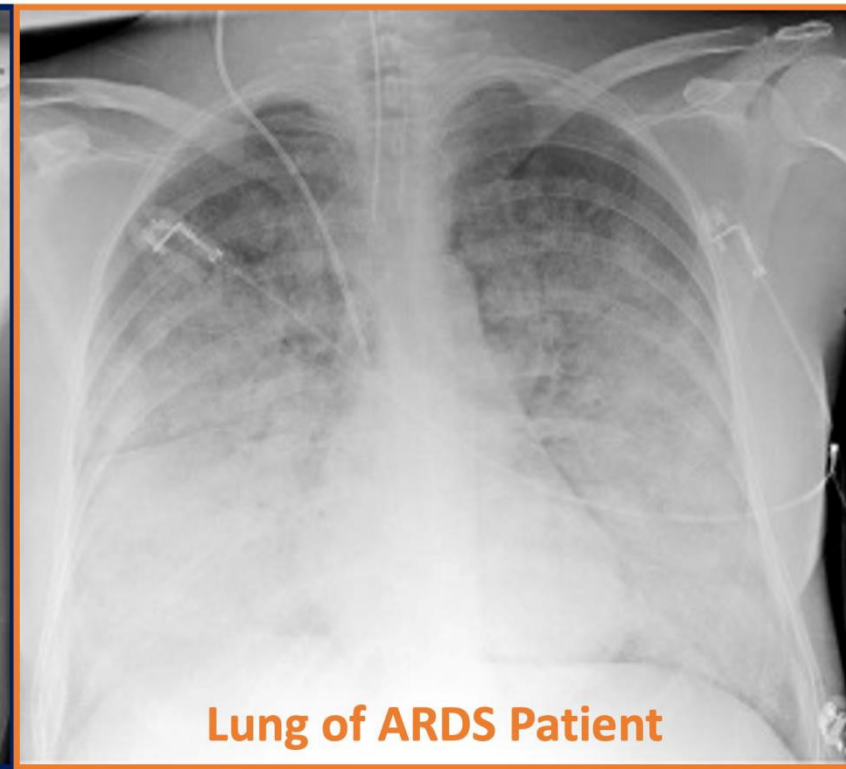
# Psittacosis

parrot fever

- Severe respiratory infection associated with splenomegaly and/or epistaxis.
- Severe headache and nuchal rigidity suggesting meningitis are not unusual.
- In severe cases, towards the end of the 1<sup>st</sup> week, stupor or coma can result.
- 2<sup>nd</sup> week is like acute pneumococcal pneumonia with high fevers, headaches, cough, and dyspnea.

# Pneumonia with White-out

X-rays with patchy infiltrates and diffuse whiteout of lung fields.



**ARDS = Acute Respiratory Distress Syndrome**



# Psittacosis

parrot fever

- *Chlamydia psittaci* bacterium transmitted by:
  - mouth-to-beak contact
  - airborne inhalation of feather dust
  - inhalation of dried feces
  - respiratory secretions of infected birds
  - person-to-person transmission is rare
  
- Human mortality is less than 1%.

# Psittacosis

## parrot fever

- *Chlamydia psittaci* infection (avian chlamydiosis) first reported in Europe in 1879.
- Signs in birds include inflamed eyes, difficulty breathing, watery droppings, and green urines.
- *C. psittaci* infections can be mild, severe, acute, or chronic with intermittent shedding.
- Infected birds shed the bacteria in feces and nasal discharges, and can remain infectious for several months.

# Psittacosis

parrot fever

- Outbreak in the US in 1929-1930, largest up to then: 5,000 birds, 169 humans, 33 dead.
- Led to the establishment of the National Institutes of Health (NIH).
- From 2002 through 2009, 66 human cases were reported to the CDC.
- Most resulted from exposure to infected pet birds, usually cockatiels, parakeets, and macaws.

# Psittacosis

parrot fever

- A risk: bird owners, veterinarians, employees of pet shops, and zookeepers.
- Outbreaks of psittacosis in plants that process poultry have been reported.
- Birds are highly mobile vectors for chlamydial infection because they feed on the detritus of infected animals of all sorts.

# Psittacosis

parrot fever

## Prevention in birds

keep  
cages  
clean

clean  
food and  
water  
bowls  
daily

place cages  
to prevent  
food,  
feathers,  
and  
droppings  
spreading

avoid  
over-  
crowding

isolate  
and treat  
infected  
birds

maintain  
a healthy  
pet diet

# Psittacosis

parrot fever

Treatment

- **In birds:** *doxycycline*, (a *tetracycline* drug) for 45 days to treat the disease through all stages
- **In humans:**
  - Patient isolation and prophylaxis of contacts usually not indicated, as person-to-person transmission is rare.
  - *Tetracyclines* are generally avoided in children aged <8 years, and *macrolides* are the drug of choice for children.\*
  - People with more severe presentation should be treated with *doxycycline* right away if psittacosis is suspected.
  - Antibiotic treatment for 10-14 days after fever subsides

# **EBOLA HEMORRHAGIC FEVER**



# Ebola

- Around 2006 a bat virus started spilling over into humans.
- Ebola hemorrhagic fever can kill 90%.
- The 10<sup>th</sup> outbreak began in 2018 and ended in 2020 after infecting 3,470 people and killing 2,287 (a 65% fatality rate).
- The 2014 West African outbreak, led to more than 28,000 cases and 11,000 deaths (39%).

# Ebola Outbreak 2014





# Ebola Outbreak 2014



# Ebola Outbreak 2014





# Ebola Outbreak 2014



# Ebola Outbreak 2014





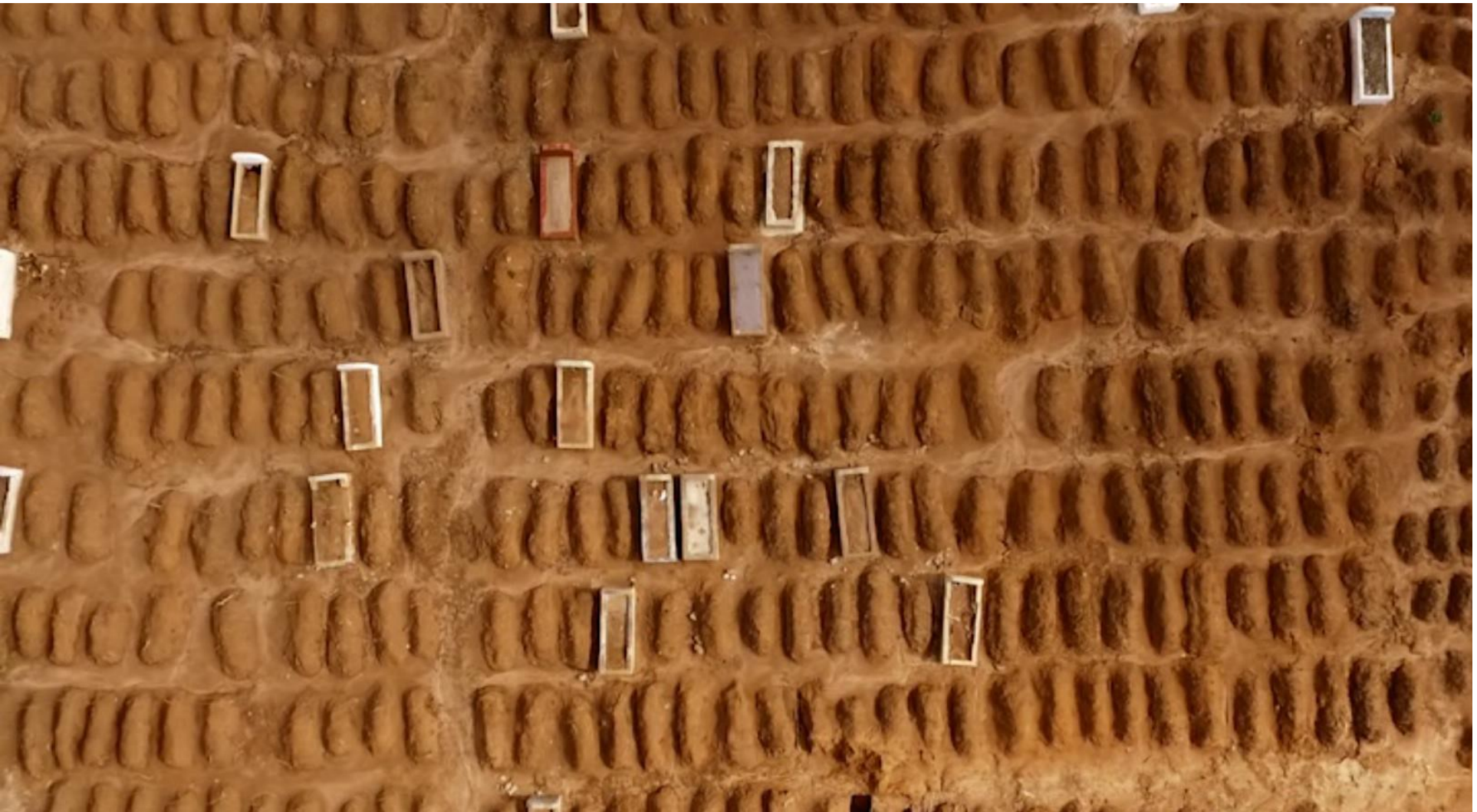
# Ebola Outbreak 2014







# Ebola Graves (Sierra Leone 2014)



# WHAT NOW?

# What do we do now? <sup>(1)</sup>

- Evaluate the immunological, social, ecological, social and behavioral factors that control the emergence and spread of novel pathogens.
- The latest data on spillovers could help authorities prepare for pandemics and prevent future outbreaks of disease.
- We should shift our thinking from pandemic response to pandemic prevention

# What do we do now? <sup>(2)</sup>

- We must get rid of the medical, social and financial hubris that currently dominates science, economics and politics.
- We are ALL potential victims, we still have a lot to learn, a lot more to do, and need to create much more fairness towards everyone.
- The social determinants of health (SDH) must be considered as inherent and inseparable from all levels of present and future planning.

Pandemic risk does not exist in isolation, and modeling efforts must take into account the range of risks that exist, including social determinants of health and disparities within countries. (Ali Mokdad, 2023)



# Social Determinants of Health

Economic Stability	Healthcare	Neighborhood & Environment	Education	Social & Community Context
Economic Harmony	Availability	Housing	Literacy	Community Resources
Concentrated Poverty	Accessibility	Parks & Playgrounds	Funding	Recreation & Leisure Activities
Job Training & Availability	Affordability	Ambulatory Ability and Ease	Elementary Education	Transportation Options/Costs
Availability of Food	Health Literacy	Segregation, Discrimination	Higher Education	Incarceration
Safe Housing	Insurance	Social Norms and Support	Libraries	Safety
Poverty Stresses	Provider Adequacy	Worksites	Technology	Trash, Toxins, Hazards

Ramírez 2019, from WHO

# What do we do now? <sup>(3)</sup>

- Even the experts now recognize the limits of their prognostication.
- Repeatedly we give microbes a helping hand:
  - we assist them in occupying new ecological niches
  - we empower them to spread to new places
  - we facilitate their infecting us in new ways
- Global interconnectivity, travel and commerce make it easy for viruses and their vectors to reach anywhere in the globe within 72 hours.
- Misuse of our miracle drugs has caused emergence of multi-drug resistance illnesses (PHAGES?).

# What do we do now?

**As we know, there are known knowns; these are things we know we know.**

**We also know there are known unknowns; that is to say we know there are some things we do not know.**

**But there are also unknown unknowns—the ones we don't know that we don't know.**

**And if one looks throughout the history of our country and other free countries, it is the latter category that tend to be the difficult ones.**

Donald Rumsfeld 2002



# My Thanks

- Thank you for participating in my OLLI course.
- I appreciate your support and cooperation.
- I hope that that I have been able to give you interesting information and motivated you to do extra research on the topics presented.





**Babies  
Rule!!**



# Thank you. Goodbye!



# Outbreak

- Sudden increase in occurrences of a disease in a particular time and place.
- Small, localized group or an entire country or continent.
- Four linked cases of a *rare* infectious disease may be considered an outbreak.

# Zoonosis <sup>(1)</sup>

(plural zoonoses)

- Infectious disease by an agent (virus, bacteria, prion or parasite) that has *jumped* from animal to human.
- First infected human transmits the infectious agent to at least one other human, who then infects others.
- Of 1,415 human pathogens, **61%** are zoonotic.

# Zoonosis (2)

- Diseases that routinely involve animal to human transmission, such as rabies, are considered *direct zoonosis*.
- In *direct zoonosis* the disease is transmitted from animals to humans through media such as air (influenza) or through bites and saliva (rabies).

# Zoonosis <sup>(3)</sup>

- In *indirect zoonosis* transmission occurs via an intermediate species (vector), which carries the disease pathogen without getting sick.
- When humans infect animals, it is called reverse zoonosis, zooanthroponosis, or anthroponosis

SARS-CoV-1

MERS-CoV

COVID-19

# **CORONA VIRUSES**



# SARS <sup>(1)</sup>

- Severe acute respiratory syndrome (SARS) is a zoonotic origin virus called SARS-CoV or SARS-CoV-1.
- Caused the 2002–2004 SARS outbreak.
- In 2017, Chinese traced the virus through Asian palm civets to cave-dwelling horseshoe bats in Yunnan.
- At end of the epidemic in June 2003, the incidence was 8,422 cases with a case fatality rate (CFR) of 11%.

# SARS (2)

- Started in ecologically unprecedented conglomeration of wild animals.
- Bats live in caves, palm civets in trees, and neither would normally contact humans.
- The civets were very sensitive to bat virus.
- Virus amplified its numbers, increased replication, and thus the chances to mutate and evolve.

# SARS <sup>(3)</sup>

- In wet markets, vendors display and sell live captured wild animals to consumers who slaughter and consume them at home
- A virus from horseshoe bats spread into raccoon dogs, ferret badgers, snakes, and palm civets.
- As the virus spread, it mutated, and in November 2003, a new mutant began infecting people.

# SARS <sup>(4)</sup>

- The virus disrupted cell immune response in lungs and produced pneumonia, pulmonary edema and deprived person's body of oxygen.
- >8,000 sick, 774 died over next 6 months.
- Disappeared soon. ***Killed people too quickly to spread any farther.***
- No cases of SARS-CoV-1 reported since 2004.

# OTHER CORONAS

# MERS CoV

- **Middle East Respiratory Syndrome virus.**
- MERS-CoV from camels to humans (how?).
- WHO strongly advises:
  - avoid contact with camels
  - eat only fully cooked camel meat
  - drink only pasteurized camel milk
  - avoid drinking camel urine