TITANTALKS

AN ILLINOIS WESLEYAN UNIVERSITY WEBINAR SERIES

The Epidemiology of SARS-CoV2

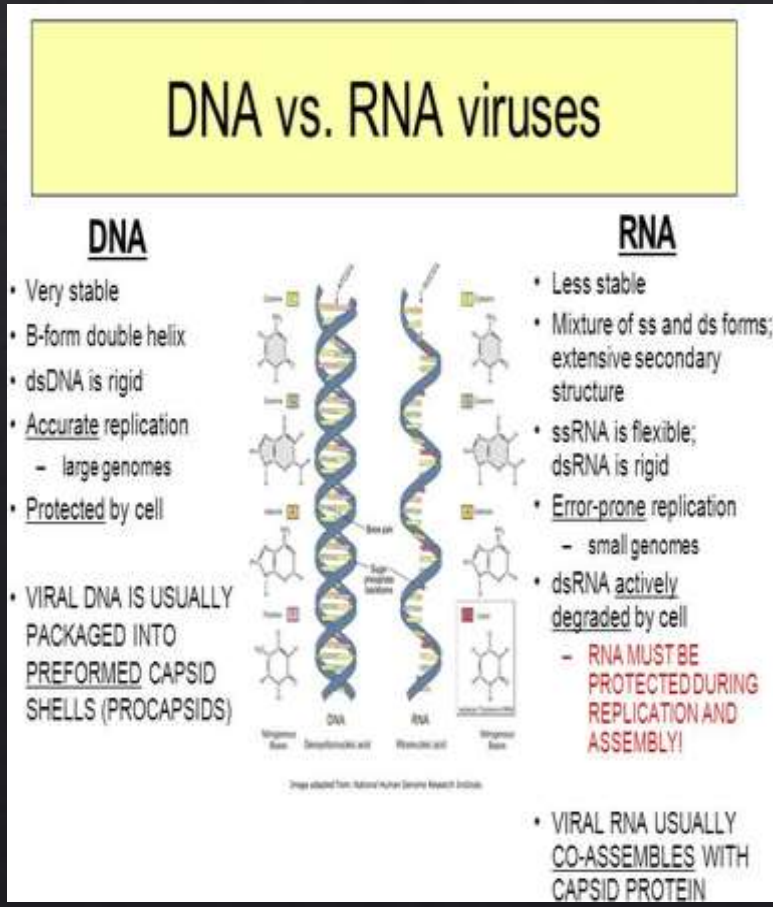
April 23 | 12 – 1 p.m. CDT

Dr. John Herrmann ’74

ILLINOIS WESLEYAN UNIVERSITY

Viruses

- A virus is a small cellular "parasite" that cannot reproduce by itself.
  - Once it infects a susceptible cell, however, a virus can direct the cell machinery to produce more viruses.
- Most viruses have either RNA or DNA as their genetic material.
  - The nucleic acid may be single- or double-stranded.
- The entire infectious virus particle, called a virion, consists of the nucleic acid and an outer shell of protein/lipid.
- The simplest viruses contain only enough RNA or DNA to encode four proteins. The most complex can encode 100 – 200 proteins.
  - https://www.ncbi.nlm.nih.gov/books/NBK21523/



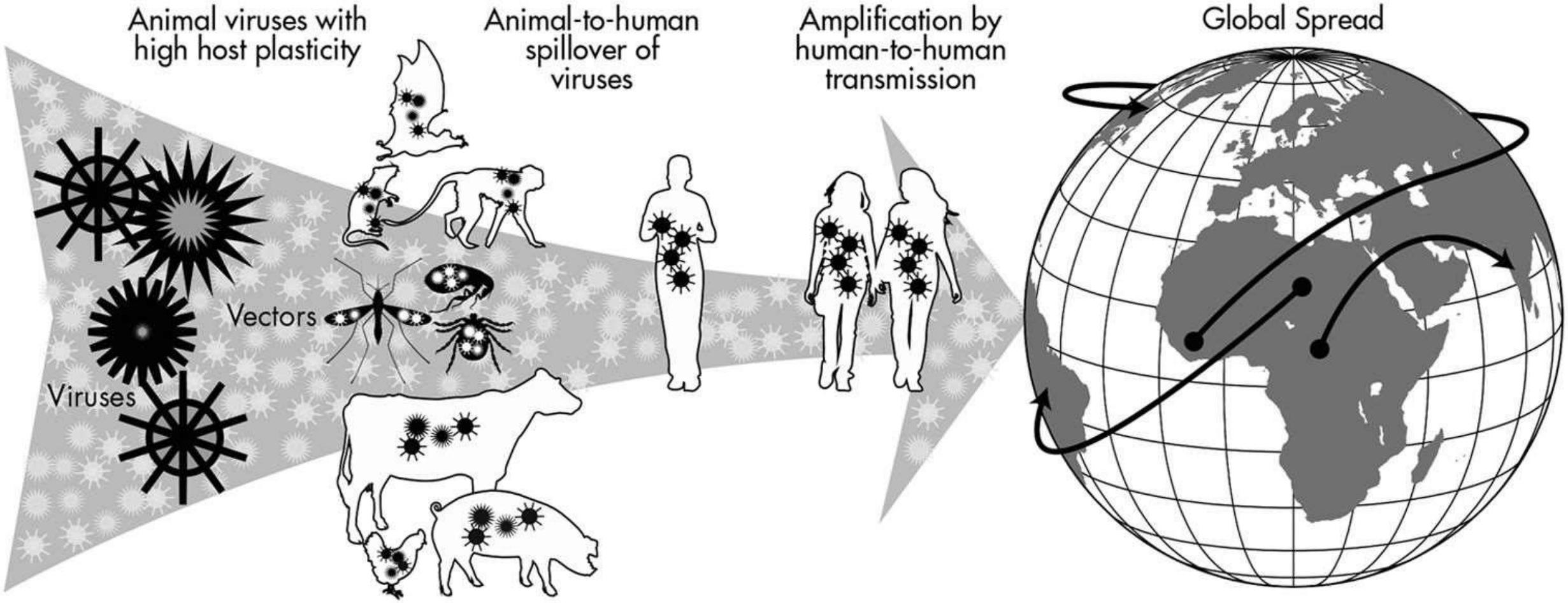
Coronaviruses

- Large family of viruses that usually cause mild to moderate upper-respiratory tract illnesses in humans, like the common cold.
- There are hundreds of coronaviruses, most of which circulate among domestic and wild animals (α, β, γ, δ)
  - Since 2003, three new (novel) coronaviruses have emerged from animal reservoirs to cause serious and widespread illness and death.
    - SARS (2002-3), MERS (2012+), SARS-CoV-2 (2019+)
      - https://www.niaid.nih.gov/diseases-conditions/coronaviruses
      - McIntosh K (1974), Kahn JS, McIntosh K (November 2005), Geller C, Varbanov M, Duval RE (November 2012)

Zoonoses and Spillover events

Zoonotic diseases: infectious diseases that are transmitted between animals and humans

Spillover events: occur when animal pathogens “spill over” into human populations


Animal viruses with high host plasticity
Animal-to-human spillover of viruses
Amplification by human-to-human transmission
Global Spread
Vectors
Viruses

Spillover events

Viral examples:

Filoviruses: Ebola virus disease, Marburg virus

Flaviviruses: Zika, West Nile, Dengue (all vector borne)

Coronaviruses: SARS, MERS, SARS-CoV-19, many in domestic animals

Henipaviruses: Nipah, Hendra

Lentiviruses: HIV

Estimated that 94% of zoonotic viruses are single strand RNA viruses; 91% from wild animals, 34% from domesticated animals (some = both)

Kreider Johnson C, Hitchens P, et al. Spillover and pandemic properties of zoonotic viruses with high host plasticity. *Nature*, 2015

Bacterial examples:

Borrelia burgdorferi – Lyme Disease

Francisella tularensis – Tularemia

Yersinia pestis – pneumonic and bubonic plague

***Brucella* spp.** – undulant fever, abortion,

Mycobacterium bovis – tuberculosis

Is SARS-CoV-2 a spillover event?

- Evidence of a spillover event
- Genomics suggest bats as the primary host species (88% genome homology)
- “The COVID-19 most likely developed from bat origin coronaviruses. Another piece of evidence that supports the COVID-19 is of bat origin is the existence of a high degree of homology of the ACE2 receptor from a diversity of animal species, thus implicating these animal species as possible intermediate hosts or animal models for COVID-19 infection.”
  - Rothan HA, Byrareddy, SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun. 2020 May;109:102433. doi: 10.1016/j.jaut.2020.102433. Epub 2020 Feb 26.

Is SARS-CoV-2 a spillover event?

- Evidence of a early human to human transmission?
  - SARS-CoV-2 from betacoronavirus genus
- Evidence of novel coronaviruses in North American bats?
  - Alphacoronavirus genus only?

A Primer on R_0

- Expected number of secondary cases caused by a single infected individual in a fully susceptible population
- R_e: Population is not fully susceptible (R_0 * %S)
- Herd Immunity = $1 - 1/R_0$

Estimates of R0	MINIMUM % Immune Needed
2.3 (cruise)	56.5%
2.35 (Wuhan)	57.4%
5.7 (China)	82.5%
15.4 (asymp)	93.5%

Quarantine Isolation & Social Distance

Vaccination (& Herd Immunity)

Hygiene & PPE

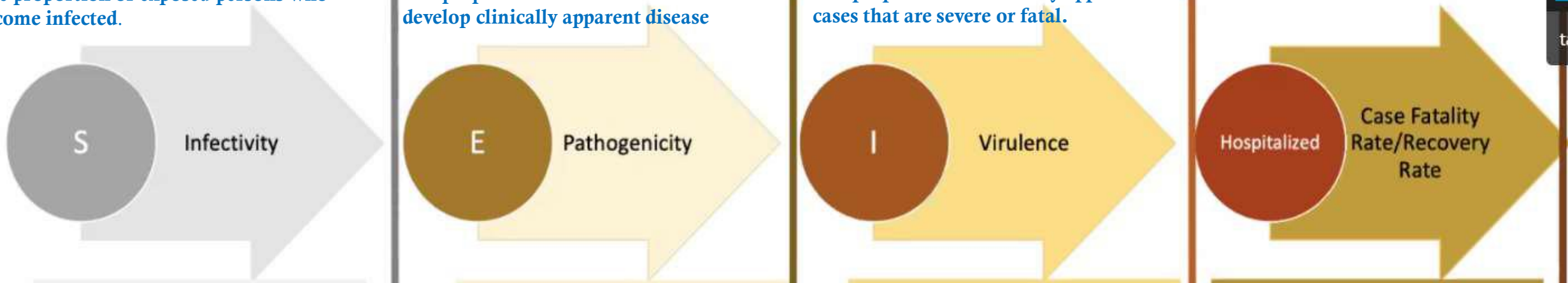
Treatment

Slide credit: Rebecca Smith DVM, PhD, UIUC CVM

The proportion of exposed persons who become infected.

The proportion of infected individuals who develop clinically apparent disease

The proportion of clinically apparent cases that are severe or fatal.



What we need:
- Serological data
- Household studies
- Contact tracing

What we need:
- Serological data
- Virological data
- Longitudinal studies

What we need:
- Virologic data
- Longitudinal studies

What we need:
- Longitudinal studies

Primary Prevention

How we can intervene:
- Decrease contacts
  - Social distancing
  - PPE
- Increase resistance
  - vaccination

Secondary Prevention

How we can intervene:
- Prophylaxis?

Tertiary Prevention

How we can intervene:
- Better therapies

How we can intervene:
- Hospital access
- Equipment and supplies
- HCWs

Slide credit: Rebecca Smith DVM, PhD, UIUC CVM

Epidemiology basics and the current pandemic

- **Brief history of the pandemic**
  - From December 18, 2019 through December 29, 2019, five patients were hospitalized in Wuhan, China with acute respiratory distress syndrome and one of these patients died
  - December 31, 2019 - China reports to WHO suspected SARS-like illnesses in Wuhan
  - January 7 – genome sequence identified and shared with WHO
  - January 17 – German diagnostic test validated and adopted by WHO
  - January 20 – first identified US case in Snohomish County, WA
  - January 28 – US develops own test; has trouble with consistent results
  - January 30 – WHO declares PHEIC
  - February 6 – first US death (CA)
  - February – due to test validation and lack of surge capacity, US testing < 100 samples per day for entire month at CDC Atlanta
  - March 5 – US allows private labs to use own tests and labs to process samples
  - March 11 – WHO declares a pandemic

Signs and symptoms

- Fever (83–99%)
- Cough (59–82%)
- Fatigue (44–70%)
- Anorexia (40–84%)
- Shortness of breath (31–40%)
- Loss of smell and taste (~50%?)
- Sputum production (28–33%)
- Myalgias (11–35%)

- The largest cohort of >44,000 persons with COVID-19 from China showed that illness severity can range from mild to critical:
  - Mild to moderate (mild symptoms up to mild pneumonia): 81%
  - Severe (dyspnea, hypoxia, or >50% lung involvement on imaging): 14%
  - Critical (respiratory failure, shock, or multiorgan system dysfunction): 5%
    - https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html

Signs and symptoms

- Additional possible complications:
  - Acute respiratory distress syndrome
  - Acute liver, kidney, or cardiac injury
  - Secondary infection
  - Septic shock
  - Disseminated intravascular coagulopathy
  - Rhabdomyolysis

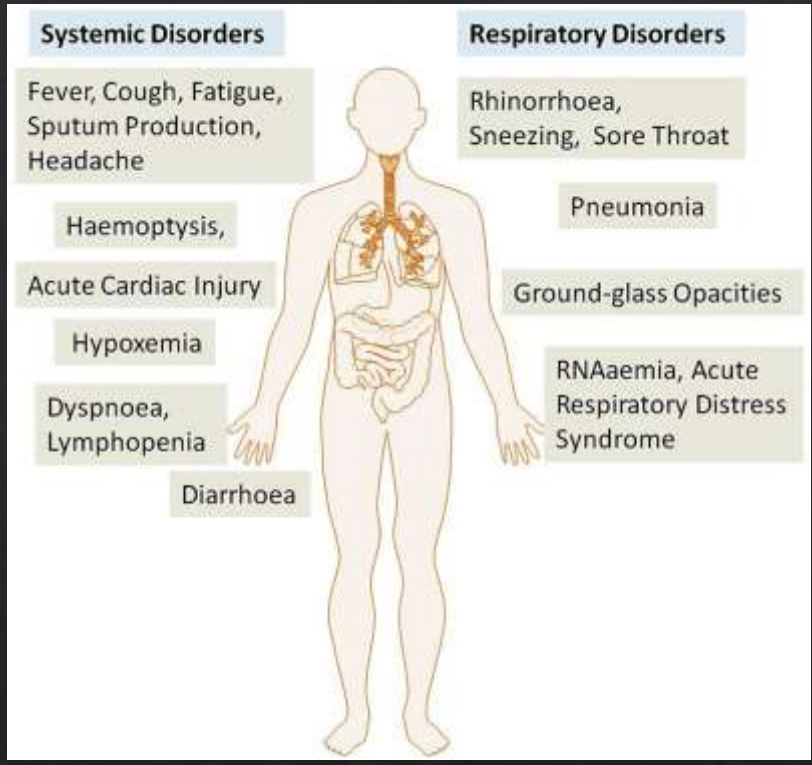


TABLE. Underlying conditions and symptoms among adults aged ≥18 years with coronavirus disease 2019 (COVID-19)–associated hospitalizations — COVID-NET, 14 states,* March 1–30, 2020†

MMWR / April 8, 2020 / Vol. 69

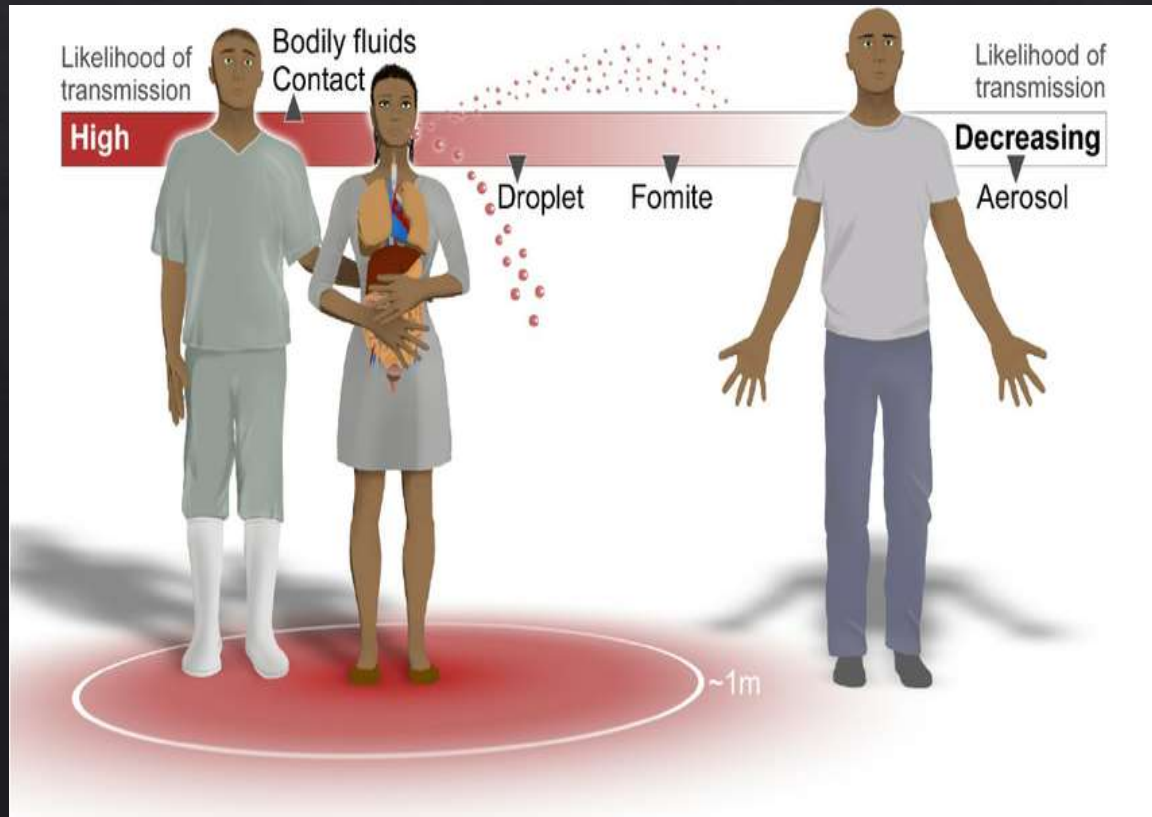
Underlying condition	Overall	Age group (yrs), no./total no. (%) 18–49	50–64	≥65 years
Any underlying condition	159/178 (89.3)	41/48 (85.4)	51/59 (86.4)	67/71 (94.4)
Hypertension	79/159 (49.7)	7/40 (17.5)	27/57 (47.4)	45/62 (72.6)
Obesity§	73/151 (48.3)	23/39 (59.0)	25/51 (49.0)	25/61 (41.0)
Chronic metabolic disease¶	60/166 (36.1)	10/46 (21.7)	21/56 (37.5)	29/64 (45.3)
Diabetes mellitus	47/166 (28.3)	9/46 (19.6)	18/56 (32.1)	20/64 (31.3)
Chronic lung disease	55/159 (34.6)	16/44 (36.4)	15/53 (28.3)	24/62 (38.7)
Asthma	27/159 (17.0)	12/44 (27.3)	7/53 (13.2)	8/62 (12.9)
Chronic obstructive pulmonary disease	17/159 (10.7)	0/44 (0.0)	3/53 (5.7)	14/62 (22.6)
Cardiovascular disease**	45/162 (27.8)	2/43 (4.7)	11/56 (19.6)	32/63 (50.8)
Coronary artery disease	23/162 (14.2)	0/43 (0.0)	7/56 (12.5)	16/63 (25.4)
Congestive heart failure	11/162 (6.8)	2/43 (4.7)	3/56 (5.4)	6/63 (9.5)
Neurologic disease	22/157 (14.0)	4/42 (9.5)	4/55 (7.3)	14/60 (23.3)
Renal disease	20/153 (13.1)	3/41 (7.3)	2/53 (3.8)	15/59 (25.4)
Immunosuppressive condition	15/156 (9.6)	5/43 (11.6)	4/54 (7.4)	6/59 (10.2)
Gastrointestinal/Liver disease	10/152 (6.6)	4/42 (9.5)	0/54 (0.0)	6/56 (10.7)
Blood disorder	9/156 (5.8)	1/43 (2.3)	1/55 (1.8)	7/58 (12.1)
Rheumatologic/Autoimmune disease	3/154 (1.9)	1/42 (2.4)	0/54 (0.0)	2/58 (3.4)
Pregnancy††	3/33 (9.1)	3/33 (9.1)	N/A	N/A
Symptom§§				
Cough	155/180 (86.1)	43/47 (91.5)	54/60 (90.0)	58/73 (79.5)
Fever/Chills	153/180 (85.0)	38/47 (80.9)	53/60 (88.3)	62/73 (84.9)
Shortness of breath	144/180 (80.0)	40/47 (85.1)	50/60 (83.3)	54/73 (74.0)
Myalgia	62/180 (34.4)	20/47 (42.6)	23/60 (38.3)	19/73 (26.0)
Diarrhea	48/180 (26.7)	10/47 (21.3)	17/60 (28.3)	21/73 (28.8)
Nausea/Vomiting	44/180 (24.4)	12/47 (25.5)	17/60 (28.3)	15/73 (20.5)
Sore throat	32/180 (17.8)	8/47 (17.0)	13/60 (21.7)	11/73 (15.1)
Headache	29/180 (16.1)	10/47 (21.3)	12/60 (20.0)	7/73 (9.6)
Nasal congestion/Rhinorrhea	29/180 (16.1)	8/47 (17.0)	13/60 (21.7)	8/73 (11.0)
Chest pain	27/180 (15.0)	9/47 (19.1)	13/60 (21.7)	5/73 (6.8)
Abdominal pain	15/180 (8.3)	6/47 (12.8)	6/60 (10.0)	3/73 (4.1)
Wheezing	12/180 (6.7)	3/47 (6.4)	2/60 (3.3)	7/73 (9.6)
Altered mental status/Confusion	11/180 (6.1)	3/47 (6.4)	2/60 (3.3)	6/73 (8.2)

Abbreviations: COVID-NET = Coronavirus Disease 2019–Associated Hospitalization Surveillance Network; N/A = not applicable.

* Counties included in COVID-NET surveillance: California (Alameda, Contra Costa, and San Francisco counties); Colorado (Adams, Arapahoe, Denver, Douglas, and Jefferson counties); Connecticut (New Haven and Middlesex counties); Georgia (Clayton, Cobb, DeKalb, Douglas, Fulton, Gwinnett, Newton, and Rockdale counties);

Transmission

- Contact (fomites) up to 72 hrs?
  - Touching face, especially nose and eyes
- Aerosol – up to 6 feet? For how long?
  - Coughing
  - Sneezing
  - Talking/breathing?



Transmission

Contact tracing in the early stages at various locations suggested that most secondary infections were among household contacts, with a secondary attack rate of up to 10 percent

Burke RM, Midgley CM, Dratch A, et al. Active Monitoring of Persons Exposed to Patients with Confirmed COVID-19 - United States, January-February 2020. MMWR Morb Mortal Wkly Rep 2020; 69:245.

COVID-19 National Emergency Response Center, Epidemiology and Case Management Team, Korea Centers for Disease Control and Prevention. Coronavirus Disease-19: Summary of 2,370 Contact Investigations of the First 30 Cases in the Republic of Korea. Osong Public Health Res Perspect 2020; 11:81.

SYMPTOMATIC SECONDARY ATTACK RATE	Close contacts	Household members
U.S. Study (n = 445)	0.45%	10.5%
South Korea (n = 2370)	0.55%	7.6%

Transmission

- Asymptomatic carriers?
  - Estimates = 25% ??? (WHO 4/1/20)
    - "However, it is notable that the infection appears to have been transmitted during the incubation period of the index patient, in whom the illness was brief and nonspecific."
    - Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. March 5, 2020, *N Engl J Med* 2020; 382:970-971
  - Incubation period ~2-14 days
  - Duration of viral shedding –
    - Study 1 - 90% no virus after 10 days (n =21)
    - Study 2 - range of shedding range = 8 to 37 days (dependent on severity of illness; n = 137)
    - ***detection of virus doesn't mean recovery of infectious virus

Transmission

- Environmental contamination
  - **The frequency and the relative importance of this type of transmission remain unclear.**
  - It is unknown how long SARS-CoV-2 can persist on surfaces.
  - Other coronaviruses have been tested and may survive on inanimate surfaces for up to six to nine days without disinfection. However, in a systematic review of similar studies, various disinfectants inactivated a number of coronaviruses related to SARS-CoV-2 within one minute.
  - Based on data concerning other coronaviruses, duration of viral persistence on surfaces also likely depends on the ambient temperature, relative humidity, and the size of the initial inoculum.
  - It may be more likely to be a potential source of infection in settings where there is heavy viral contamination (eg, in an infected individual's household or in health care settings).
    - McIntosh, K. https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-epidemiology-virology-clinical-features-diagnosis-and-prevention

Transmission

- Animals and SARS-CoV-2
  - Cats and ferrets – showed viral replication and recovery after intranasal inoculation
  - Dogs, pigs, chickens – seroconverted but no viral replication or recovery
    - Shi J, Wen Z, Zhong G, et al. Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS-coronavirus 2. Science 2020.
  - Bronx Zoo – Tiger tested (+) April 5, 2020

Immunity

- Preliminary evidence suggests that some of these antibodies are protective, but this remains to be definitively established.
  - Moreover, it is unknown whether all infected patients mount a protective immune response and how long any protective effect will last.
- Antibodies to the receptor-binding domain of the spike protein and the nucleocapsid protein were detected by enzyme-linked immunosorbent assay (ELISA) in most patients by 14 days following the onset of symptoms (n = 23); ELISA antibody titers correlated with neutralizing activity
  - To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis 2020.

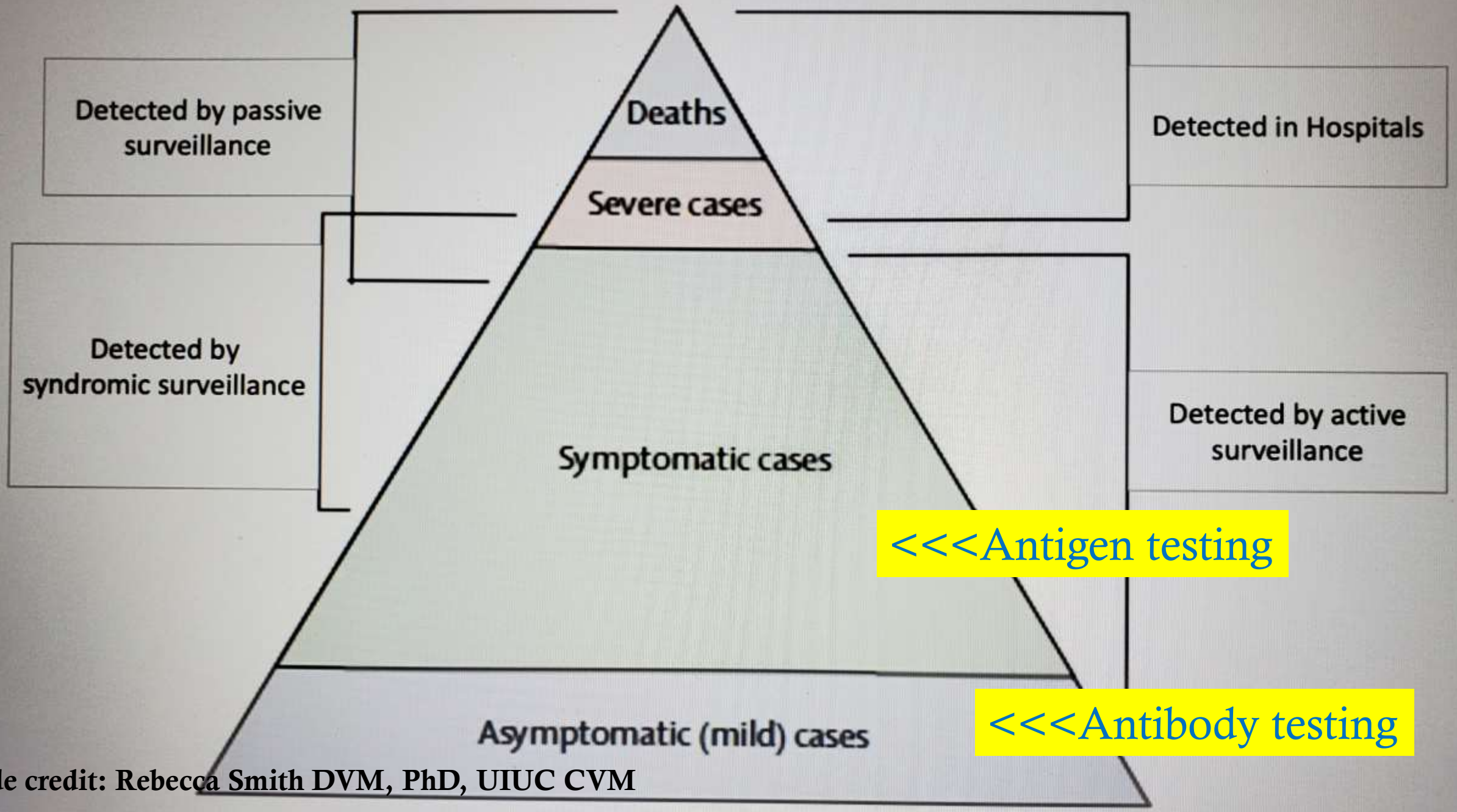
Epidemiology basics and the current pandemic

- Diagnostic Testing
  - Reverse Transcriptase- Polymerase Chain Reaction (RT-PCR)
  - Sensitivity
    - "In a series of 51 patients with chest CT and RT-PCR assay performed within 3 days, the sensitivity of CT for COVID-19 infection was 98% compared to RT-PCR sensitivity of 71% ($p<.001$)."
      - Fang Y, Zhang H, Xie J, et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiology. Published online Feb 19 2020; https://doi.org/10.1148/radiol.2020200432. Accessed April 2, 2020.
      - West CP, Montori VM, Sampathkumar P. COVID-19 testing: the threat of false-negative results [published online ahead of print April 9, 2020]. Mayo Clin Proc. [https//doi.org/10.1016/j.mayocp.2020.04.004].
- **If current test have a Sn of 90%, we are missing 10% of cases.**
- **The results from viral genome testing is only good <u>for that point in time.</u>**

All | Europe | North America | Asia | South America | Africa | Oceania

www.worldometer.com 4/22/20

Country, Other	Total Cases	New Cases	Total Deaths	New Deaths	Total Recovered	Active Cases	Serious, Critical	Tot Cases/ 1M pop	Deaths/ 1M pop	Total Tests	Tests/ 1M pop
World	2,629,951	+74,191	183,723	+6,264	716,731	1,729,497	56,678	337	23.6		
USA	844,992	+26,248	47,430	+2,112	83,910	713,652	14,014	2,553	143	4,307,429	13,013
Spain	208,389	+4,211	21,717	+435	85,915	100,757	7,705	4,457	464	930,230	19,896
Italy	187,327	+3,370	25,085	+437	54,543	107,699	2,384	3,098	415	1,513,251	25,028
France	159,877	+1,827	21,340	+544	40,657	97,880	5,218	2,449	327	463,662	7,103
Germany	150,062	+1,609	5,250	+164	99,400	45,412	2,908	1,791	63	2,072,669	24,738
UK	133,495	+4,451	18,100	+763	N/A	115,051	1,559	1,966	267	559,935	8,248
Turkey	98,674	+3,083	2,376	+117	16,477	79,821	1,814	1,170	28	750,944	8,904
Iran	85,996	+1,194	5,391	+94	63,113	17,492	3,311	1,024	64	377,396	4,493
China	82,788	+30	4,632		77,151	1,005	78	58	3		
Russia	57,999	+5,236	513	+57	4,420	53,066	700	397	4	2,250,000	15,418
Brazil	45,757	+2,678	2,906	+165	25,318	17,533	8,318	215	14	291,922	1,373
Belgium	41,889	+933	6,262	+264	9,433	26,194	1,020	3,614	540	171,400	14,789



Slide credit: Rebecca Smith DVM, PhD, UIUC CVM

Case fatality rate vs. Mortality rate

Case Fatality Rate

- This is not a rate, this is a proportion
- Proportion of deaths from a specific illness

$$\text{Case Fatality Rate} = \frac{a}{N}$$

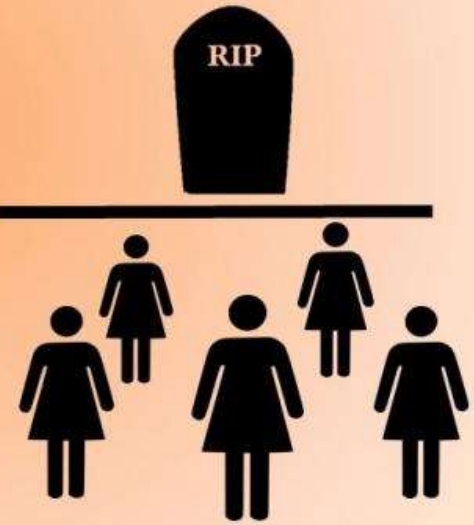
Where:
a = Number of deaths from an illness
N = Number of people with that illness

What percentage of people diagnosed as having a disease die within a certain time after diagnosis?

Mortality: Deaths per a population

Numerator: Deaths

Denominator: Population



Population Research Institute: pop.org

Also cause specific mortality, age specific, etc. and proportionate mortality

Illinois Data 4/22/2020

- Population 12,659,682
  - Assume 4% prevalence = 506, 387 cases
- Tested 164,346 (55.5% F)
- Cases 35,108 (50.3% F)
- Deaths 1565 (41.3% F)
- Case Fatality Rate 4.46%

AGE	CASES %	DEATHS (n)
< 20	2.7	2
20-29	12.6	5
30-39	15.4	27
40-49	18.3	59
50-59	19.8	141
60-69	14.6	281
70-79	8.9	406
>80	7.7	644

85%

67%

Illinois Data 4/22/2020

*Numbers do not equal 100% due to missing data – 50% tested did not specify RE group

	White	Black	LatinX
TESTED	38415	21670	9958
CASES	8573 (22.3% tested) (24.4% of total)	8504 (39.2% tested) (24.2% of total)	6195 (62.2% tested) (17.6% of total)
DEATHS (CFR)	621 (7.2%)	596 (7%)	181 (2.9%)
% ILLINOIS POPULATION	60.9%	13.8%	17.3%
% OF DEATHS	39.7%	38.1%	11.6%

Wearing masks in a community setting

- WHO (4/4/20)
  - "Wide use of masks by healthy people in the community setting is not supported by current evidence…"
    - https://www.who.int/publications-detail/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak

- Annals of Internal Medicine (4/6/20)
  - "In conclusion, both surgical and cotton masks seem to be ineffective in preventing the dissemination of SARS–CoV-2 from the coughs of patients with COVID-19 to the environment and external mask surface."
    - https://annals.org/aim/fullarticle/2764367/effectiveness-surgical-cotton-masks-blocking-sars-cov-2-controlled-comparison

Social distancing

- Slipstream effect - NYT article 4/17/20
  - “A droplet that is small enough to float in air for a while also is unlikely to deposit on clothing because of aerodynamics. The best way to describe it is that they follow the streamlines, or air flow, around a person, because we move relatively slowly. It’s kind of like small insects and dust particles flowing in the streamlines around a car at slow speed but potentially slamming into the windshield if the car is going fast enough,”
  - “As we move, we push air out of the way, and most of the droplets and particles get pushed out of the way, too. Someone would have to spray large droplets through talking — a spit talker — coughing or sneezing for them to land on our clothes. The droplets have to be large enough that they don’t follow the streamlines.”
    - Dr. Linsey Marr, Aerosol Scientist at Va. Tech

- Virus on packages, hair, clothes, etc.
  - “When you go through the string of events that must occur, such an extended number of things have to happen just right. That makes it a very low risk.”
    - Dr. Andrew Janowski, Pediatrician at Washington University Hospitals St. Louis Children’s Hospital
    - https://www.nytimes.com/2020/04/17/well/live/coronavirus-contagion-spead-clothes-shoes-hair-newspaper-packages-mail-infectious.html?algo=top_conversion&fellback=false&imp_id=558018451&imp_id=857904272&action=click&module=Most%20Popular&pgtype=Homepage

The current SARS-CoV-2 pandemic

- The way forward…
- Sero-surveillance
  - Testing for antibody acute (IgM) and convalescent (IgG)
- Trace backs (active case finding and contact tracing)
- Vaccine – 2021?
- Therapeutics – so we can say that if you take xyz, you'll recover; take load off of ICUs, ventilators, etc.
- Potentiate your immune system!
  - Eat, sleep, exercise well!
  - Extracellular superoxide dismutase (EcSOD)
    - https://eurekalert.org/pub_releases/2020-04/uovh-cem041520.php

TITAN TALKS

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Thank you for joining today's webinar!

Save the date for our next webinar:

May 6 | 12 – 1 p.m. CDT

Speaker: President Georgia Nugent

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