Stats in the News

July 27, 2020

Audrey E. Hendricks, Associate Professor


In the time of COVID-19
University of Colorado
CU IN THE CITY

The use of statistics to make logical conclusions is everywhere. . .

Journal of Travel Medicine
International Society of Travel Medicine
Promoting healthy travel worldwide
Journal of Travel Medicine, 2020, 1–7
doi: 10.1093/jtm/taaa030
Advance Access Publication Date: 28 February 2020
Original Article

Original Article

COVID-19 outbreak on the Diamond Princess cruise ship: estimating the epidemic potential and effectiveness of public health countermeasures

J Rocklöv PhD[1,*], H Sjödin PhD[1], and A Wilder-Smith MD[2,3,4]

[1]Department of Public Health and Clinical Medicine, Section of ... Sweden,
[2]Department of Epidemiology and ... London School of H... Germany

No clinical benefit from use of hydroxychloroquine in hospitalised patients with COVID-19

5 June 2020

Statement from the Chief Investigators of the Randomised Evaluation of COVid-19 thERapY (RECOVERY) Trial on hydroxychloroquine, 5 June 2020

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, ... V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, ... N. Ohmagari, M. Oh, ... Atmar, ... rgess, ... Lane,

Health

CDC confirms six coronavirus symptoms showing up in patients over and over

RAPID COMMUNICATION

Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020

Kenji Mizumoto[1,2,3], Katsushi Kagaya[2,4], Alexander Zarebski[5], Gerardo Chowell[3]

1. Graduate School of Advanced Integrated Studies in Human Survivability, Kyoto University Yoshida-Nakaadachi-cho, Sakyo-ku, Kyoto, Japan
2. Hakubi Center for Advanced Research, Kyoto University, Yoshidahonmachi, Sakyo-ku, Kyoto, Japan
3. Department of Population Health Sciences, School of Public Health, Georgia State University, Atlanta, Georgia, United States
4. Seto Marine Biological Laboratory, Field Science, Education and Reseach Center, Kyoto University, Shirahama-cho, Nishimuro-gun, Wakayama, Japan
5. Department of Zoology, University of Oxford, Oxford, United Kingdom

Correspondence: Kenji Mizumoto (mizumoto.kenji.5a@kyoto-u.ac.jp)

Citation style for this article:
Mizumoto Kenji , Kagaya Katsushi , Zarebski Alexander , Chowell Gerardo . Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Euro Surveill. 2020;25(10):pii=2000180. https://doi.org/10.2807/1560-7917.ES.2020.25.10.2000180

Article submitted on 20 Feb 2020 / accepted on 12 Mar 2020 / published on 12 Mar 2020

CNN health Food Fitness Wellness Parenting Vital Signs • LIVE TV Edition

Study finds hydroxychloroquine may have boosted survival, but other researchers have doubts

By Maggie Fox, Andrea Kane, and Elizabeth Cohen, CNN

Updated 1:31 PM ET, Fri July 3, 2020

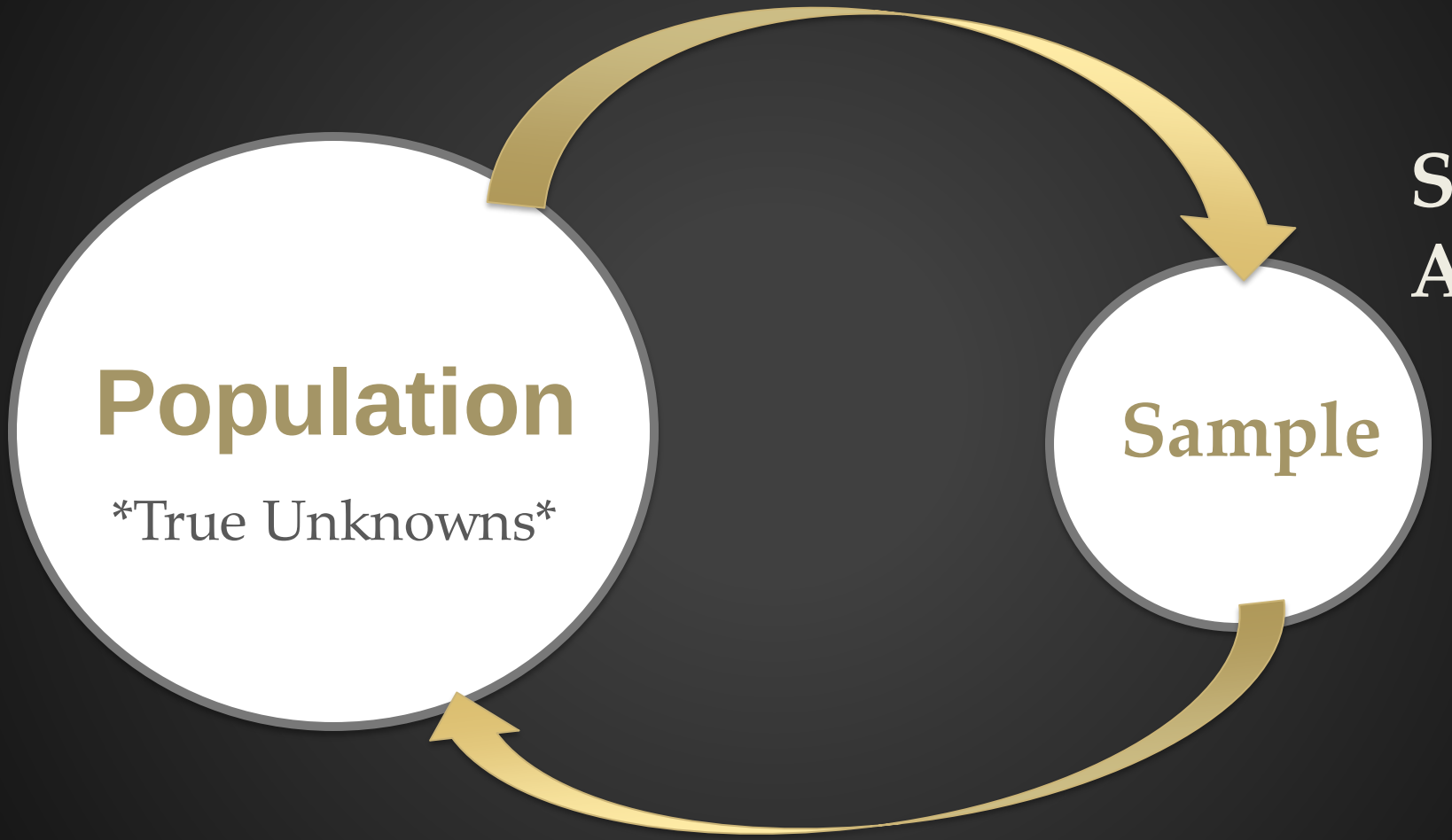
CORONAVIRUS

Remdesivir may work even better against COVID-19 than once thought

What is Statistics?

. . .

Statistics is:



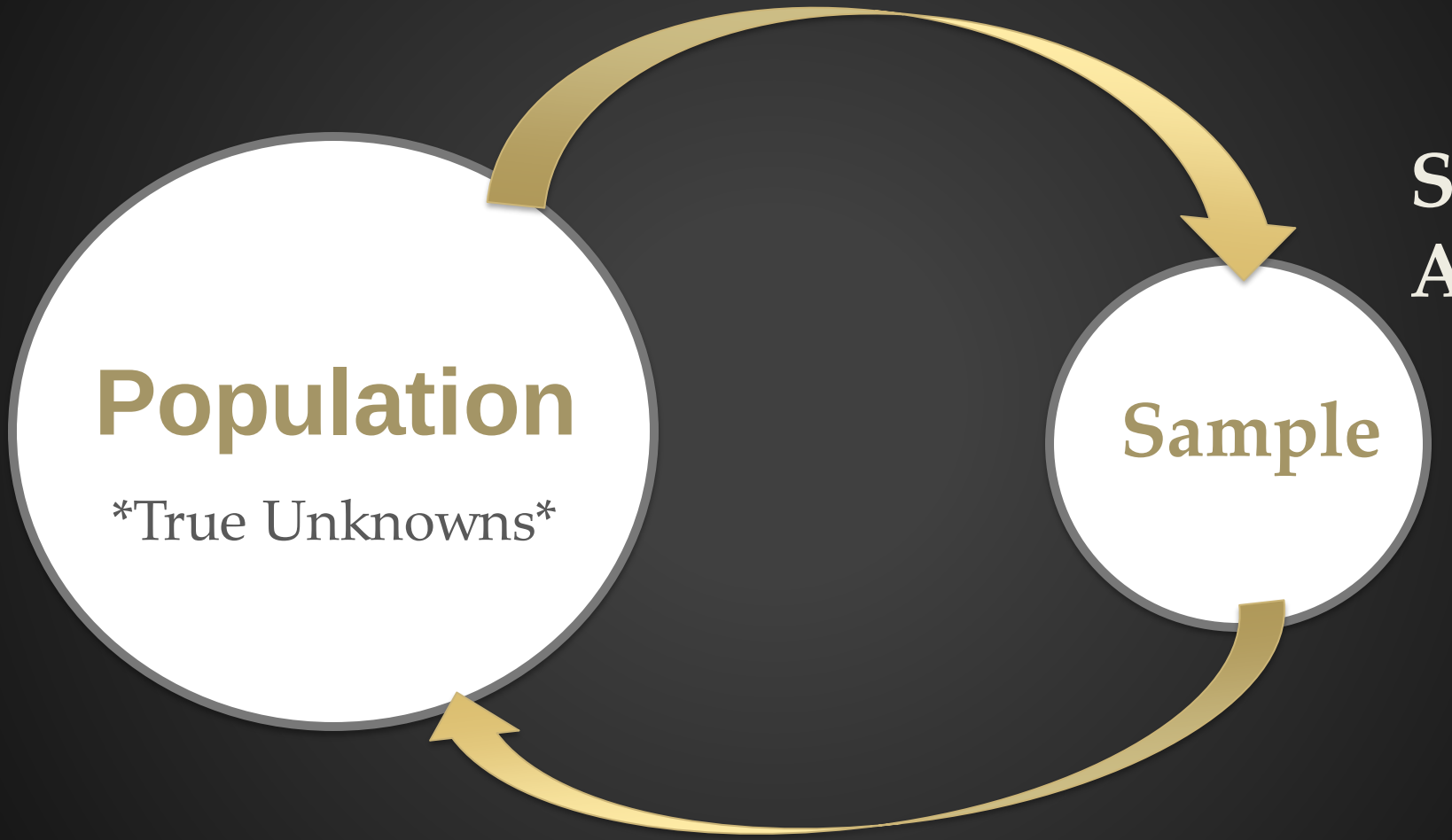
Summarize
Analyze

Inference (logical conclusion)

Inference

- A logical conclusion
- We can even get an idea of (i.e. quantify) the uncertainty of our inference!
- The way data are collected is very important
  - Will influence what logical conclusions we can make about the population using our sample
    - Cause and effect
    - To whom can we generalize

Data Science is:



Summarize
Analyze

Inference (logical conclusion)

Machine Learning is:

Summarize
Analyze

Inference (logical conclusion)

Inference

- **Cause and effect**
  - Drawing a cause and effect relationship between two variables (e.g. traits, features, attributes)
  - e.g. putting my hand on a hot stove ***caused*** me to feel pain
  - e.g. exposure to COVID-19 caused me to get sick

- **Generalizability**
  - e.g. the conclusions from this study extend to
    - All people with COVID-19 in the world?
    - The people with COVID-19 that are hospitalized?
    - Race, ethnicity, SES, biological sex, adult/child, those with “minor” or “major” responses

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JAMA Network | Open™

Original Investigation | Infectious Diseases

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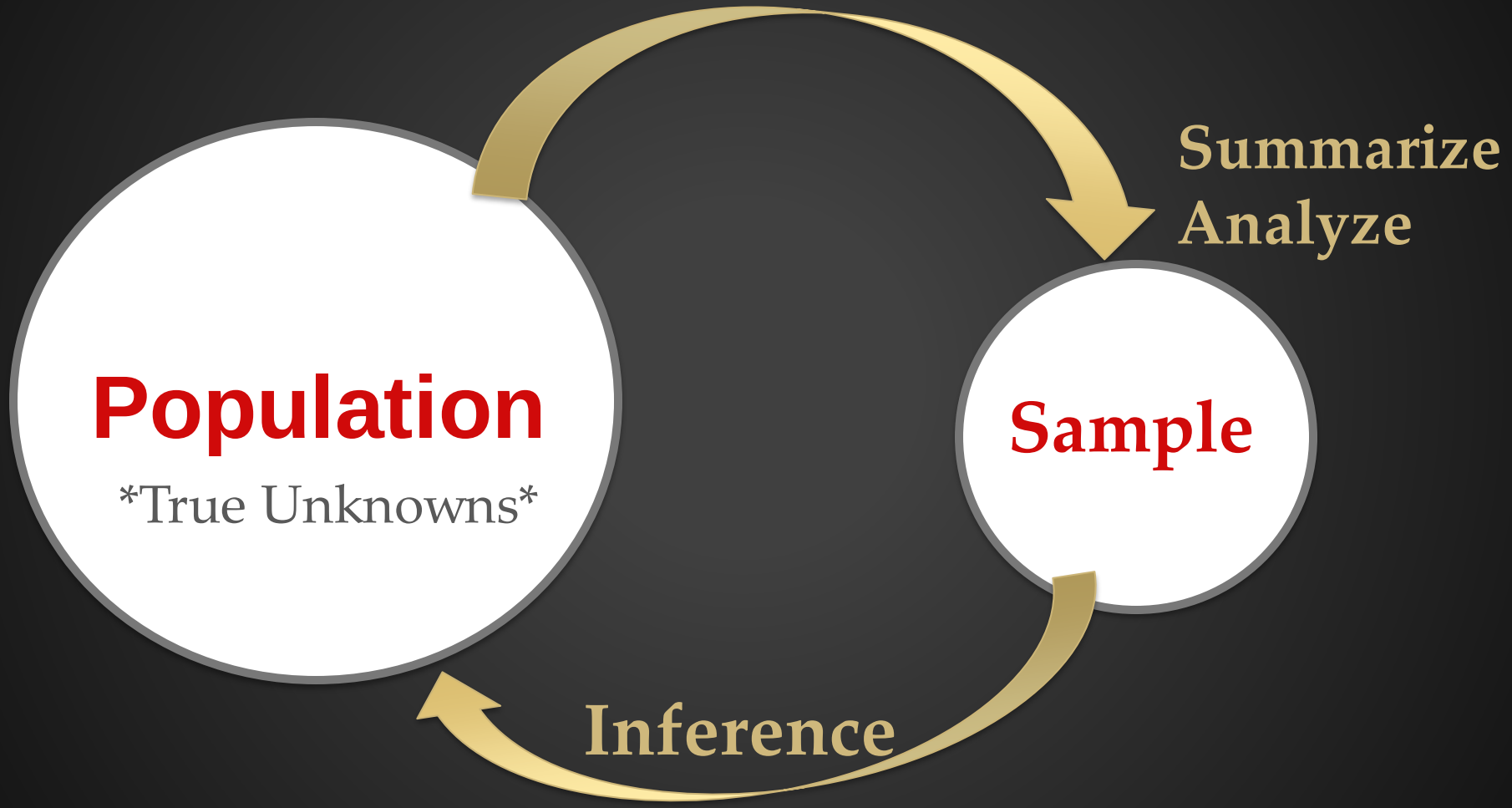
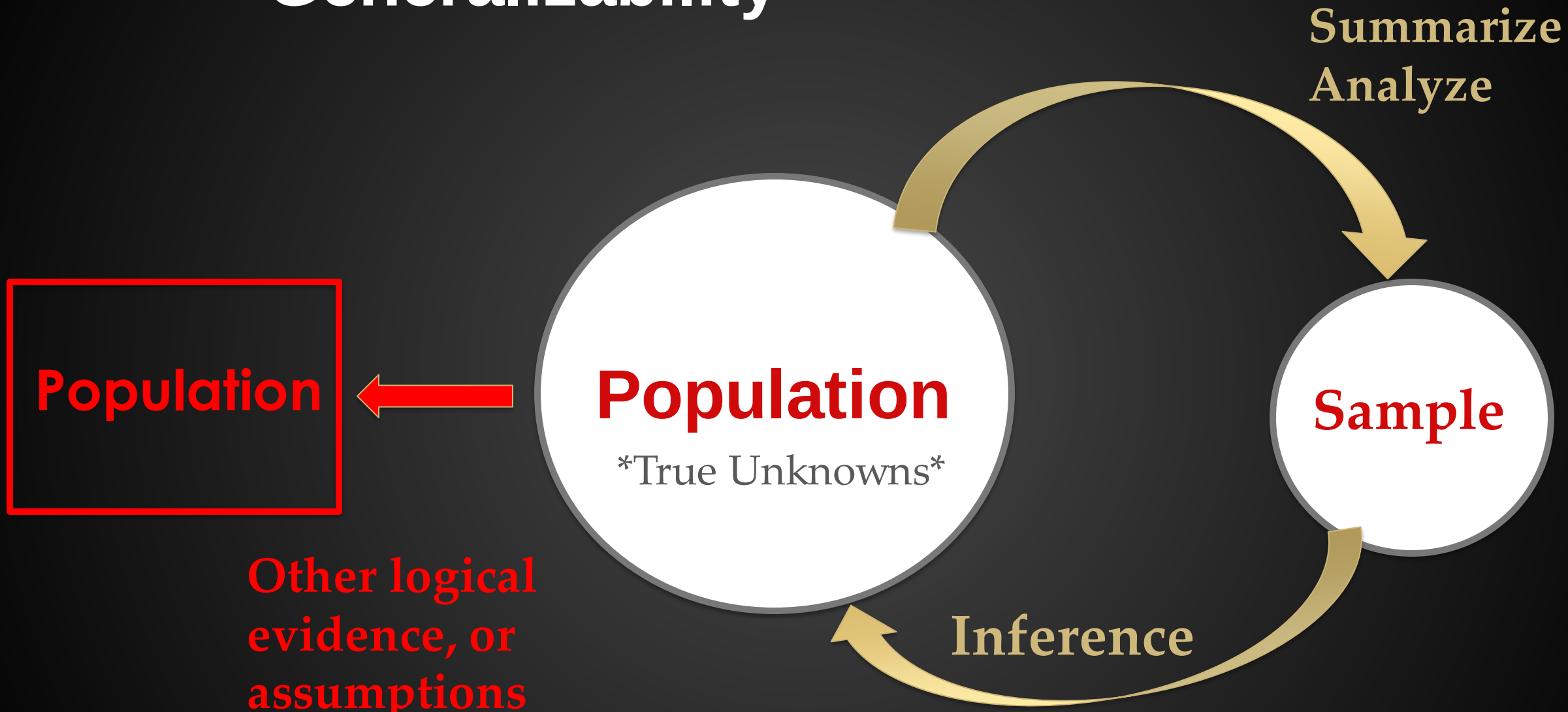
Generalizability



Generalizability



Generalizability

- But I want to generalize beyond
  - Not based on the statistical model
  - Must be based on other logic or **assumptions**

  - Sometimes likely ok
    - How to sharpen skates
      - Canadian expert skaters → amateur skaters
    - Human to human transmission in Europe and Asia → Human to human transmission in US

  - Sometimes not
    - Clinical trials on heart disease
      - white men → women or different ethnicities or ancestries
    - Vaccine trials for COVID-19 of young, healthy people → older, more at risk populations

Inference

- **Cause and effect**
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Two Main Types of Studies

- **Experimental Studies**

- **Observational Studies**

Two Main Types of Studies

- **Experimental Studies**
  - Studies where we manipulate/change something (e.g. vaccine, treatment) to try to **cause** an effect on another variable (e.g. COVID-19 diagnosis)
  - **Randomized Experiment**
    - Study objects (e.g. people, animals, beer batches, etc.) randomly assigned to treatment groups

Randomized experiments

- Randomized clinical trial
- Causal conclusions can be made
  - Randomization mixes up subjects with different features (i.e., confounding variables) among treatment groups
  - But even random groups can have patterns (i.e. other differences exist between groups)
    - Can be incorporated into statistical analysis

A side note on one of my favorite words

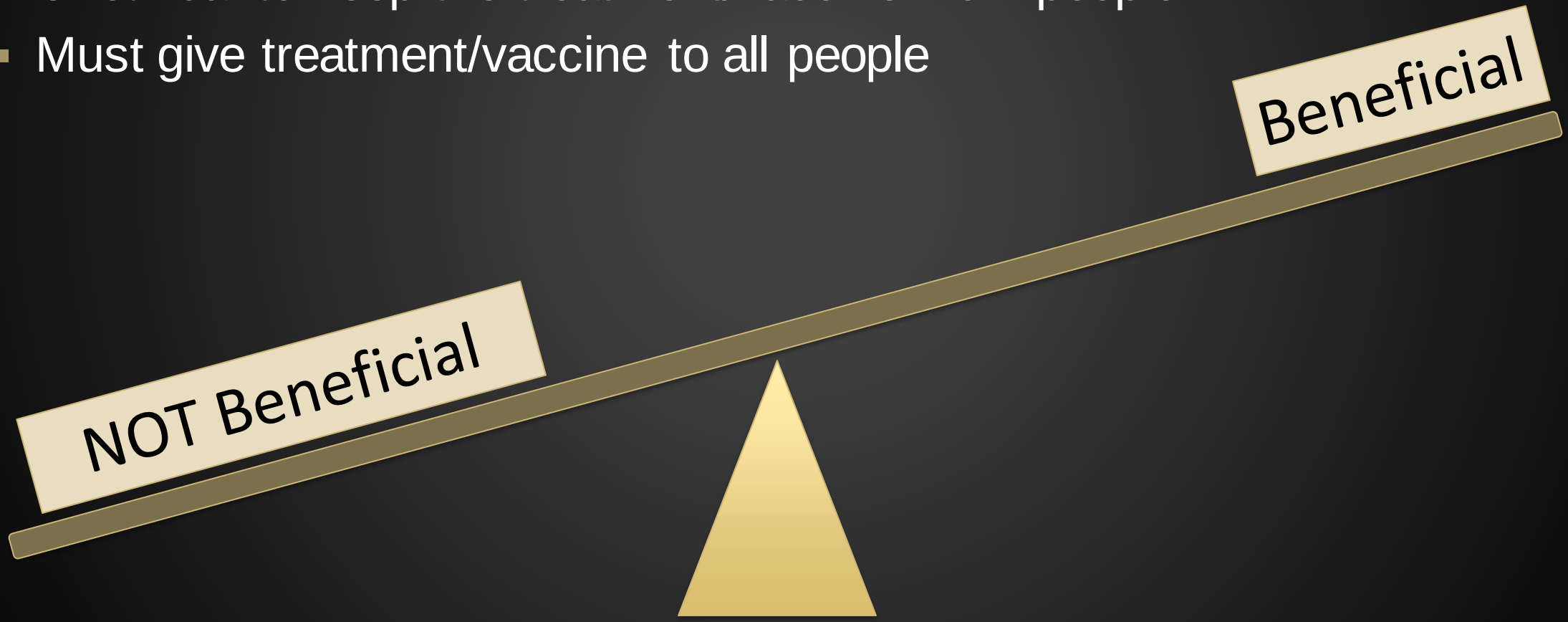
. . .

Equipoise

- An ethical balance
- Necessary for a randomized clinical trial
- Uncertainty whether a treatment or a vaccine will be beneficial

Equipoise

- Once treatment/vaccine proven beneficial
  - Unethical to keep the treatment/vaccine from people
  - Must give treatment/vaccine to all people



Equipoise

- Once treatment/vaccine proven NOT beneficial
  - Unethical to give the treatment/vaccine to people
  - Must stop giving treatment/vaccine to all people

Randomized clinical trial

- Randomized clinical trial
  - Can be used to conclude that a vaccine or treatment causes an outcome
    - e.g. vaccine causes people to be less likely to become sick from COVID-19
  - Equipoise is necessary to start and continue randomized clinical trial

Two Main Types of Studies

- **Experimental Studies**
  - Studies where we manipulate/change something (e.g. explanatory variables, treatments) to try to **cause** an effect on another variable
  - **Randomized Experiment**
    - Study objects (e.g. people, animals, beer batches, etc.) randomly assigned to treatment groups

- **Observational Studies**
  - Data are measured by observing the world
  - Grouping is not assigned
    - e.g. COVID-19 + and COVID-19 -, fever vs. not fever, people who go to college vs. those who do not

Observational studies

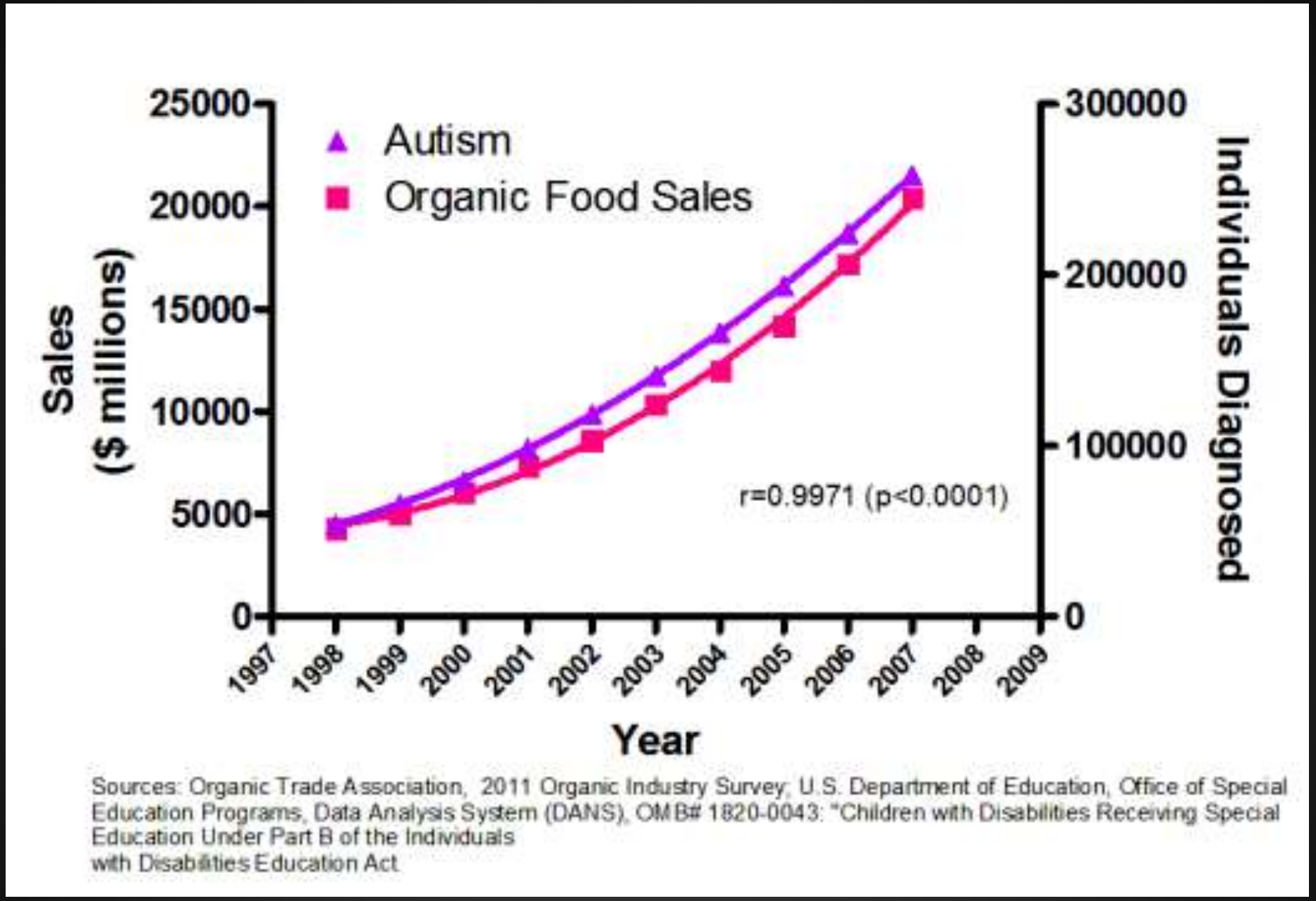
- Causal conclusions are not possible *
  - *field of causal inference – advanced statistical techniques to provide more or less evidence of possible causality

- We don't know the direction or even if there is a causal relationship at all!
- e.g. a correlation between treatment and survival from COVID-19

- **Confounding Variable**
  - Is related to both variables
  - Can make a relationship appear or disappear (i.e. confounds relationship/association)

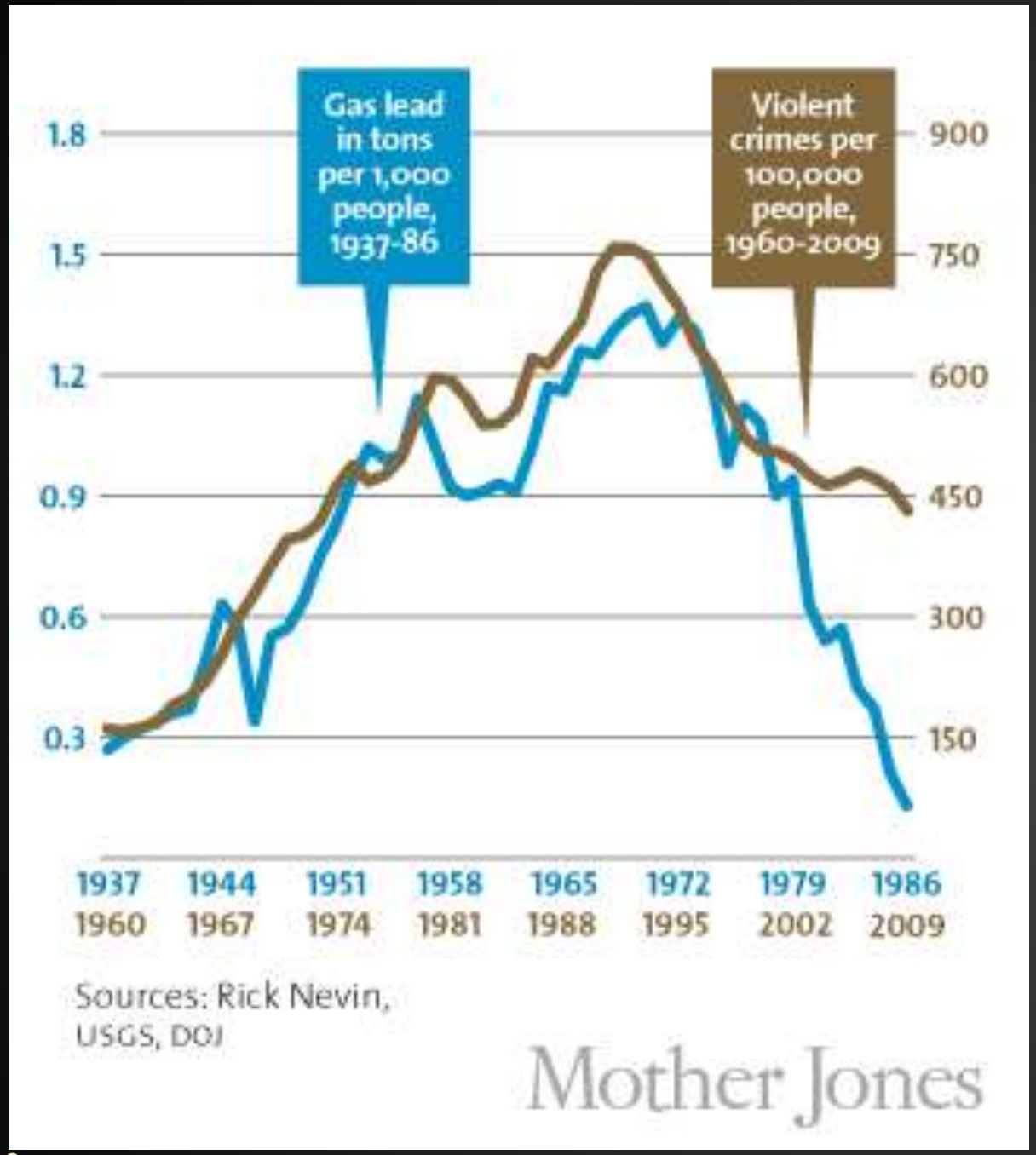
confounding

confounding



https://mathcoachblog.files.wordpress.com/2014/11/correlation-does-not-imply-causation.png

But what about something not obviously silly. . .



Can we assume that a change in gas lead levels caused a change in violent crimes 23 years later?

http://www.forbes.com/sites/alexknapp/2012/02/how-lead-caused-americas-violent-crime-epidemic/#1d43f9a63b27

Accumulate & Combine Evidence

- Combine Evidence
  - Observational studies in human children
  - Experimental studies in model organisms (laboratory)
  - Extremely bad outcomes for children with high blood lead levels (seizures, etc.)
  - Etc.
- Accumulate lots of evidence over time
- Statistical, experimental methods exist that can add support to a causal relationship
  - Psuedo-experimental studies
  - Causal inference analyses
  - Etc.

4 Examples of Generalizability and Causal Inference

In the time of COVID-19…

Ex. 1: Who do we test for COVID-19?

- In early days of COVID-19, only tested people with
  - Contact with COVID-19 + test
  - Certain symptoms: Cough, fever, shortness of breath
- Thus, prevalence of those symptoms seen at a higher rate
- End of April CDC added chills, repeated shaking with chills, muscle pain, headache, sore throat, loss of taste or smell
- Now include fatigue, congestion or runny nose, nausea or vomiting, diarrhea

Ex. 1: Who do we test for COVID-19?

JAMA Network | Open™

Original Investigation | Infectious Diseases

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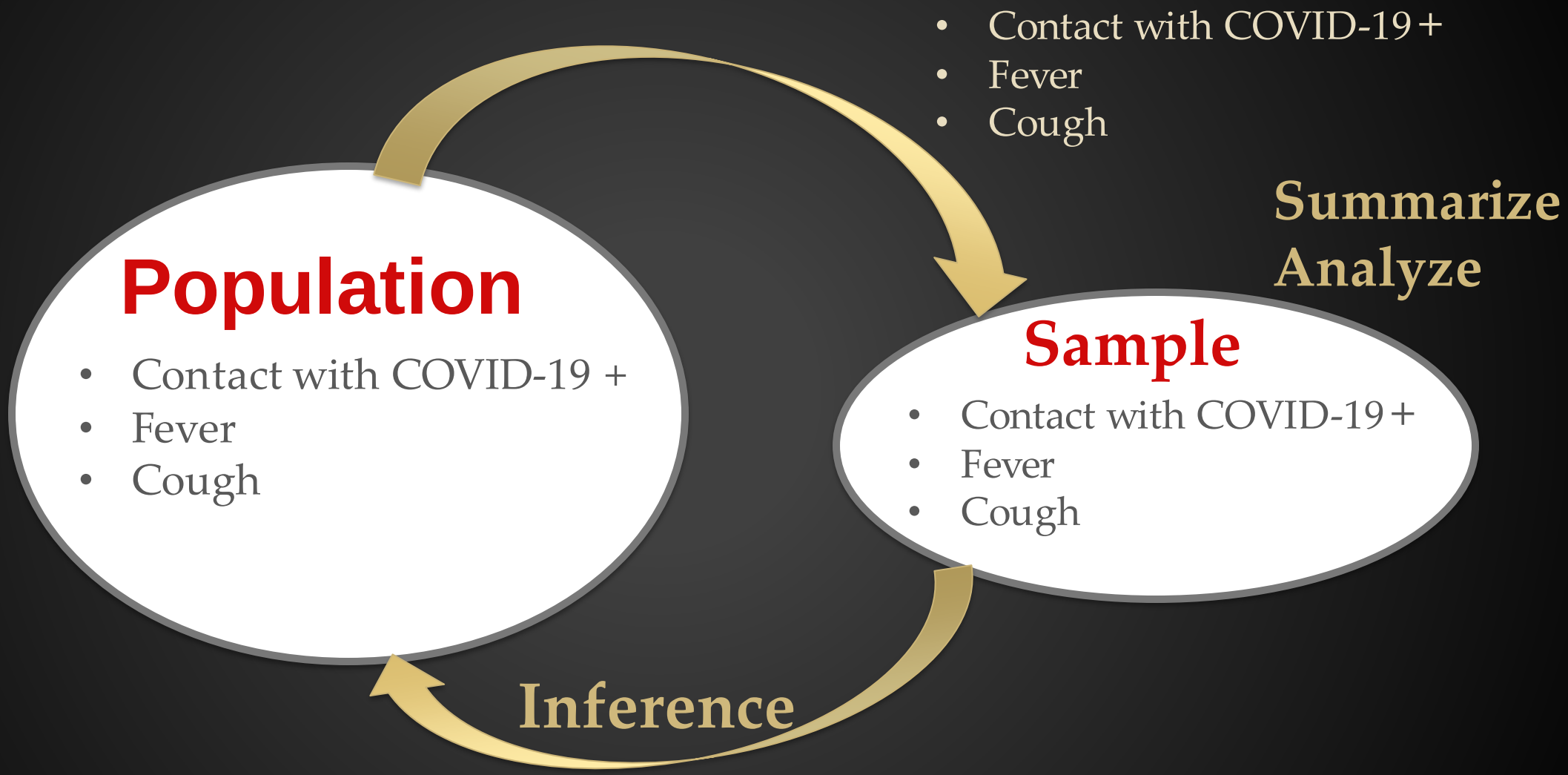
Ex. 2

RESULTS Of 9705 HCWs employed (1722 male [18%]), 1353 (14%) reported fever or respiratory symptoms and were tested. Of those, 86 HCWs (6%) were infected with severe acute respiratory syndrome coronavirus 2 (median age, 49 years [range, 22-66 years]; 15 [17%] male), representing 1% of all HCWs employed. Most HCWs experienced mild disease, and only 46 (53%) reported fever. Eighty HCWs (93%) met a case definition of fever and/or coughing and/or shortness of breath. Only 3 (3%) of the HCWs identified through the screening had a history of travel to China or northern Italy, and 3 (3%) reported having been exposed to an inpatient with a known diagnosis of COVID-19 before the onset of symptoms.

- Generalizable
  - Hospital workers
  - With fever or respiratory symptoms
- 93% of sample had fever, cough, or shortness of breath

Ex. 1: Who do we test for COVID-19?



Ex. 2 Hydroxychloroquine

No clinical benefit from use of hydroxychloroquine in hospitalised patients with COVID-19

5 June 2020

Statement from the Chief Investigators of the Randomised Evaluation of COVid-19 t
hydroxychloroquine, 5 June 2020

INTERNATIONAL JOURNAL OF INFECTIOUS DISEASES

INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

Log in Regist

FULL LENGTH ARTICLE | VOLUME 97, P396-403, AUGUST 01, 2020

PDF [797 KB] Figures Save Sh

Treatment with hydroxychloroquine, azithromycin, and combination in patients hospitalized with COVID-19

Samia Arshad • Paul Kilgore • Zohra S. Chaudhry • ... William O'Neill • Marcus Zervos

Henry Ford COVID-19 Task Force [1] • Show all authors • Show footnotes

Open Access • Published: July 01, 2020 • DOI: https://doi.org/10.1016/j.ijid.2020.06.099

Check for updates

CNN health Food Fitness Wellness Parenting Vital Signs

Study finds hydroxychloroquine may have boosted survival, but other researchers have doubts

By Maggie Fox, Andrea Kane, and Elizabeth Cohen, CNN

Updated 1:31 PM ET, Fri July 3, 2020

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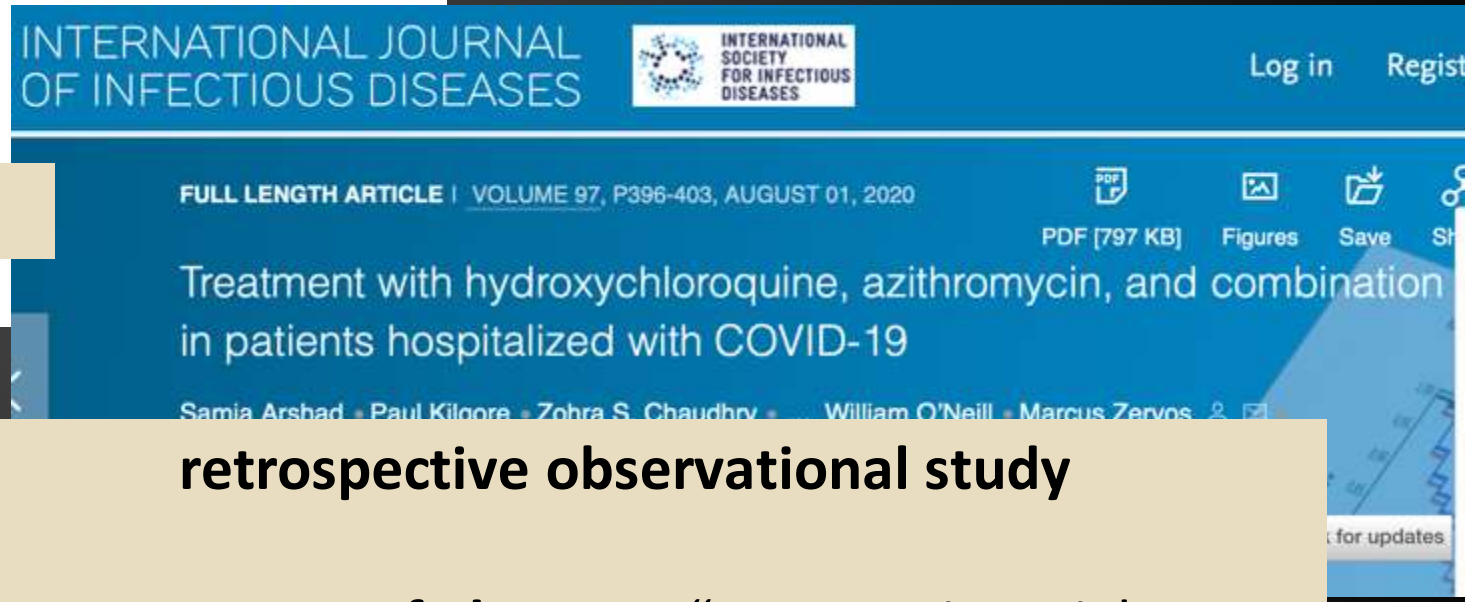
Randomized clinical trial

hydroxychloroquine, 5 June 2020



retrospective observational study

Last sentence of abstract: "prospective trials are needed to examine this impact."

CNN health Food Fitness Wellness Parenting Vital Signs

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By Maggie Fox, Andrea Kane, and Elizabeth Cohen, CNN

Updated 1:31 PM ET, Fri July 3, 2020

Ex 3. A Treatment

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

METHODS

We conducted a double-blind, randomized, placebo-controlled trial of intravenous remdesivir in adults hospitalized with Covid-19 with evidence of lower respiratory tract involvement. Patients were randomly assigned to receive either remdesivir (200 mg loading dose on day 1, followed by 100 mg daily for up to 9 additional days) or placebo for up to 10 days. The primary outcome was the time to recovery, defined by either discharge from the hospital or hospitalization for infection-control purposes only.

- Generalizability
  - Adults hospitalized with Covid-19
  - Time to recovery
    - defined by hospitalization no longer needed

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- Causality
  - Double-blind: neither doctors nor patients know treatment group
  - Randomized: subjects randomly assigned to treatment group
  - Placebo-controlled: subjects are assigned to drug or placebo group

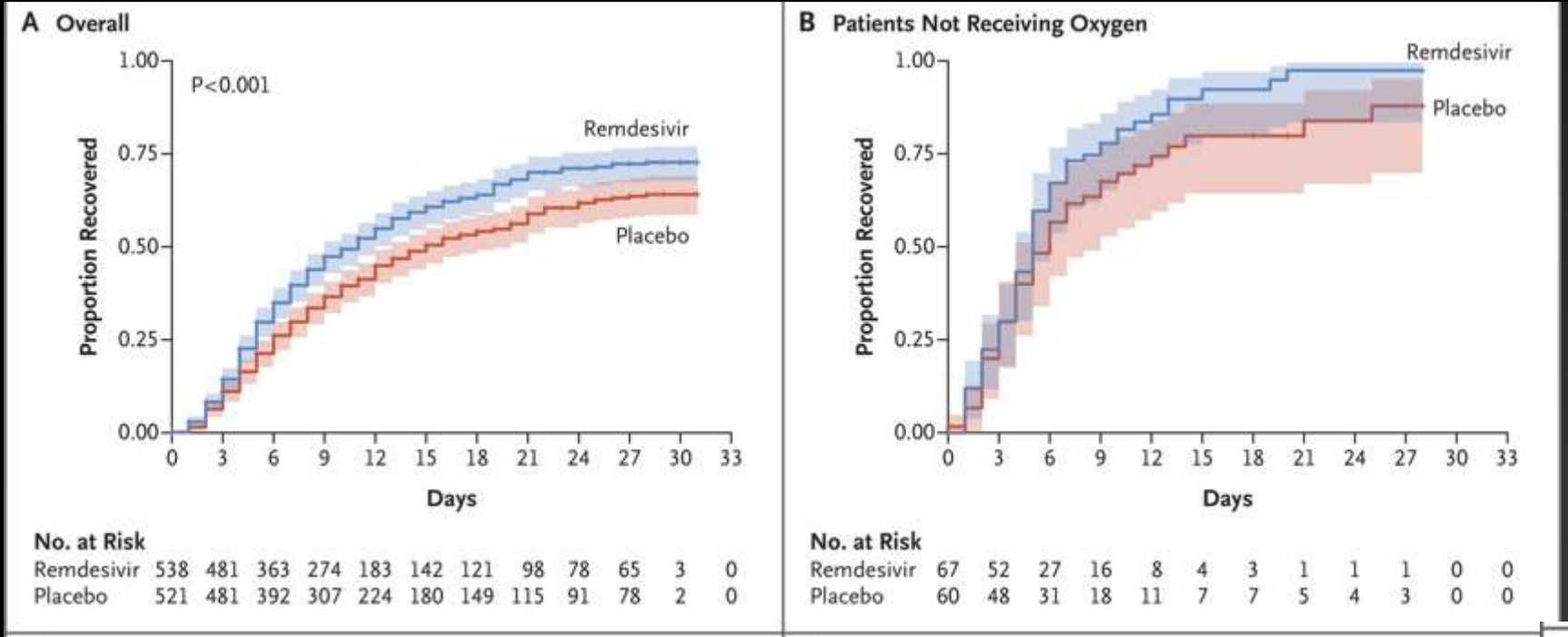
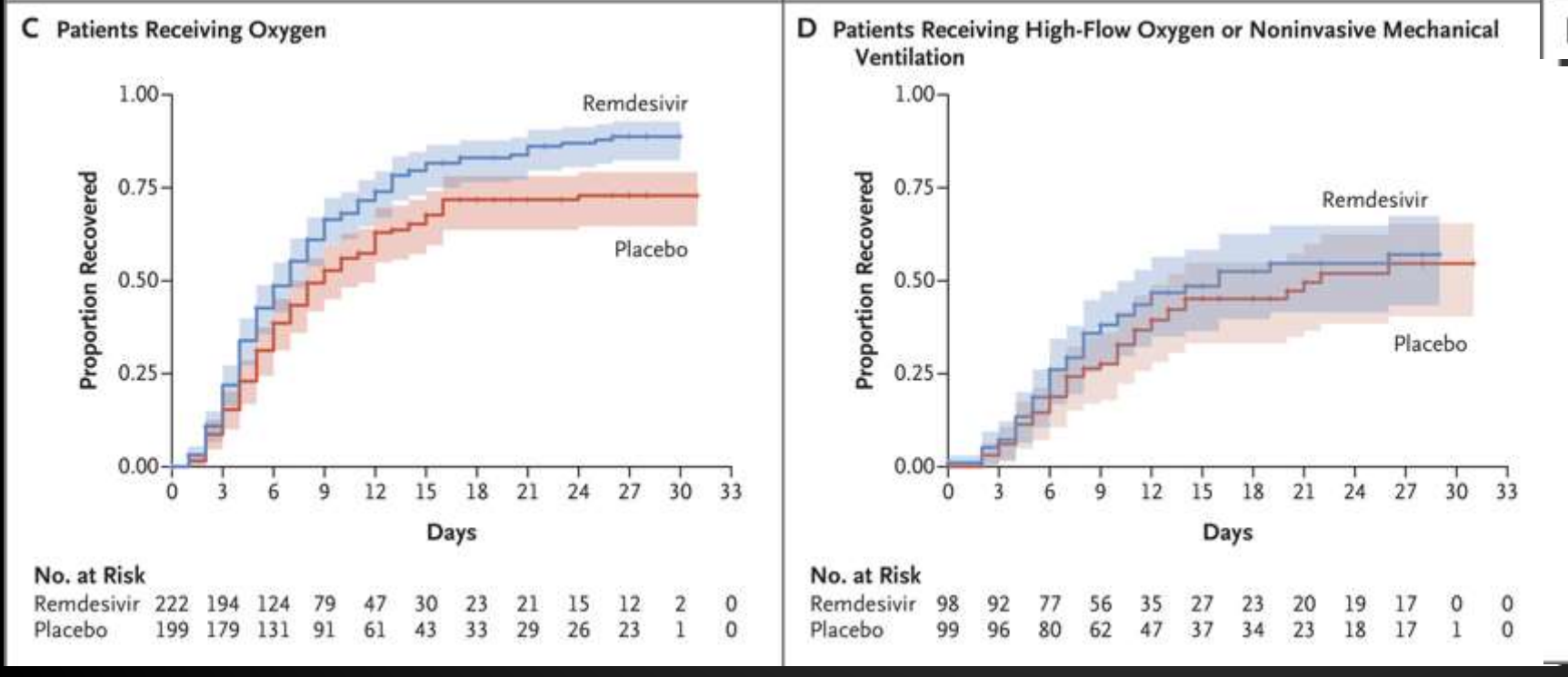
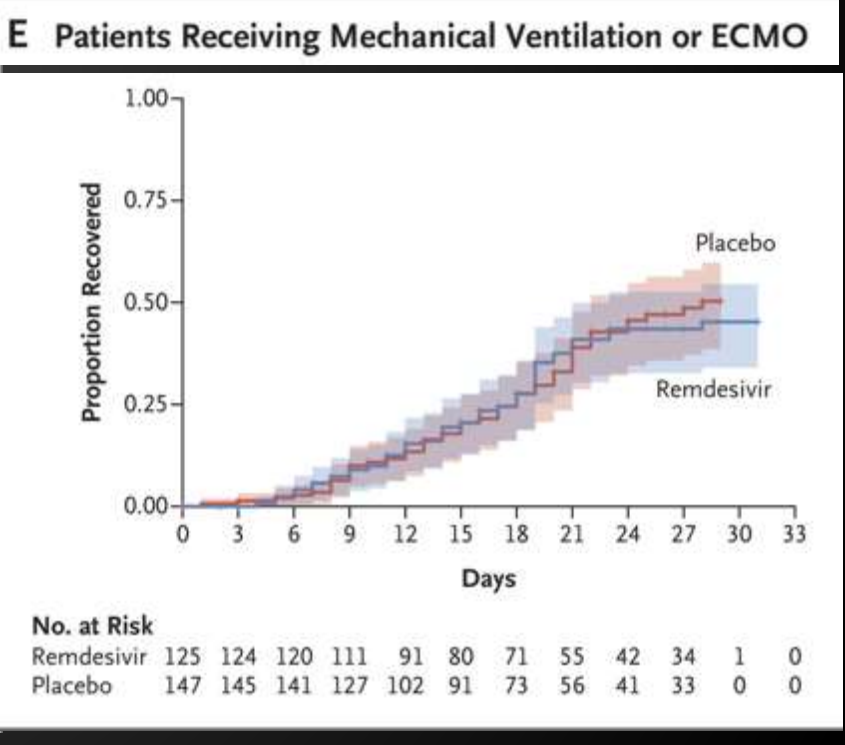


Figure 2. Kaplan–Meier Estimates of Cumulative Recoveries.

Beigel, 2020 NEJM





Ex. 4: A Vaccine!

- Clinical Trials
  - Randomized experimental placebo-controlled trials
    - Volunteers randomized to receive vaccine or a placebo

Ex. 4: A Vaccine!

- Clinical Trials
  - Phase 1: small; assesses safety and dosage in healthy volunteers
    - Is vaccine safe?
    - Does safety vary at different dosages?
  - Phase 2: moderately sizes; assesses potential benefit & side effects
    - Does vaccine elicit immune system/antibody response?
    - Any severe side effects?
  - Phase 3: large; assesses benefit, effectiveness, and side effects
    - COVID-19 vaccine trials will likely have >10,000 volunteers

Won't it take forever to conduct a trial on >10,000 people?

COVID-19 human challenge studies: ethical issues

...ik, Michael J Selgelid

Lancet Infect Dis 2020
Published Online
May 29, 2020

...ses an extraordinary threat to global public health and an effective vaccine could provide a key means of ...is crisis. Human challenge studies involve the intentional infection of research participants and can ...evelopment by rapidly providing estimates of vaccine safety and efficacy. Human

The New York Times

Researchers Debate Infecting People on Purpose to Test Coronavirus Vaccines

The technique, called a human challenge trial, has been used to evaluate other vaccines.

An experimental vaccine for the coronavirus at Sinovac Biotech in Beijing earlier this year. Nicolas Asfouri/Agence France-Presse — Getty Images

By Denise Grady

STAT

FIRST OPINION

Human challenge trials with live coronavirus aren't the answer to a Covid-19 vaccine

By MICHAEL ROSENBLATT / JUNE 23, 2020

Reprints

Moderna coronavirus vaccine trial set to launch at UCHealth University of Colorado Hospital

The phase 3 trial of Moderna's mRNA vaccine candidate for COVID-19 will enroll 1,000 at University of Colorado Hospital, 30,000 nationwide.

By: **Todd Neff, for UCHealth** | July 9th, 2020 Share

Ex. 4: A Vaccine!

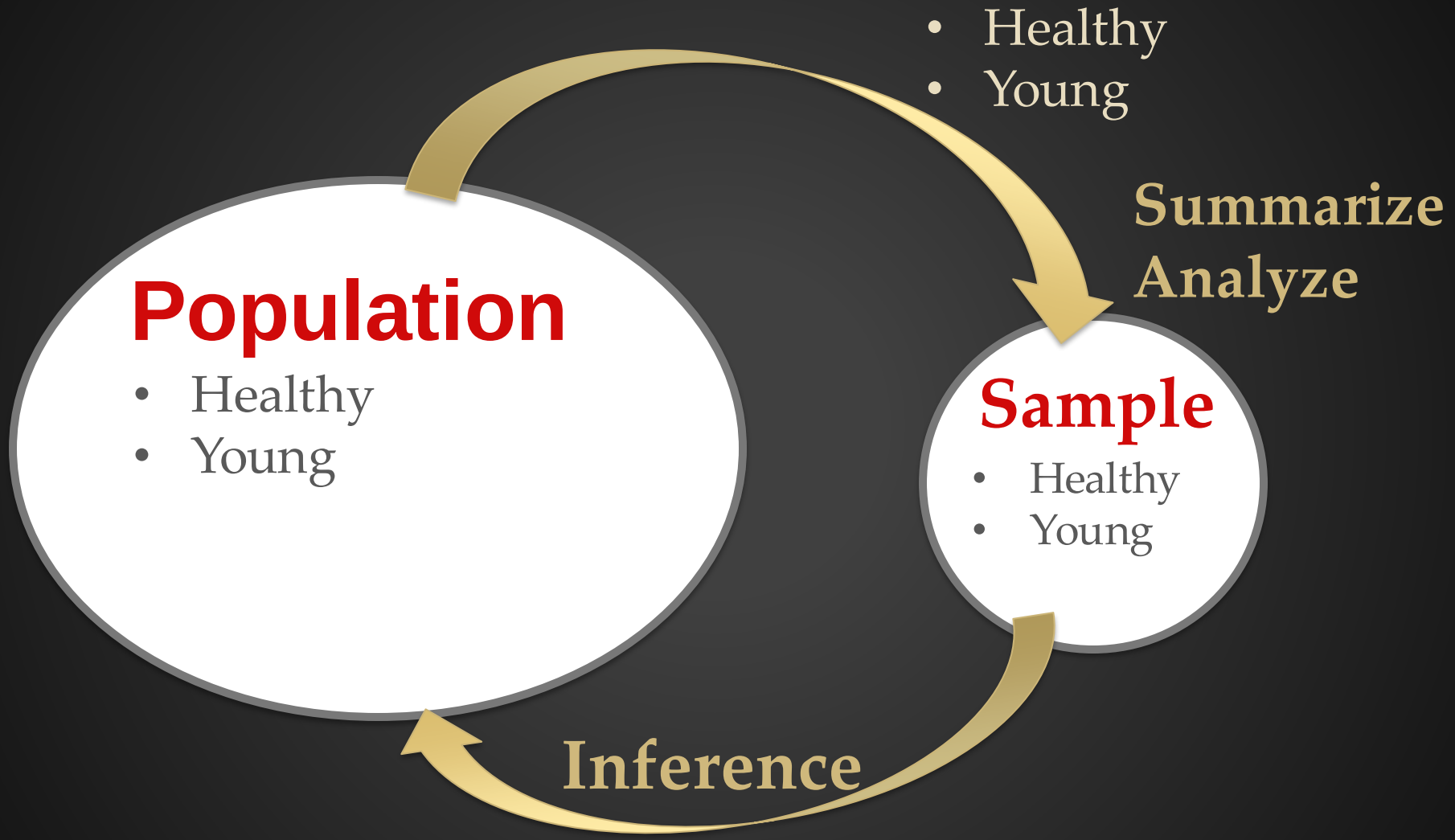
So, what about a Human Challenge Trial?

- Volunteers for a vaccine trial are injected with the virus

- **Pro**: much faster trial than waiting for volunteers to be exposed to COVID-19 on own
- **Con**: non-trivial risk of death and co-morbidities (e.g. lasting lung damage)

- Modifications to make safer
  - Only complete trial in healthy, young adults

Ex. 4: A Vaccine!



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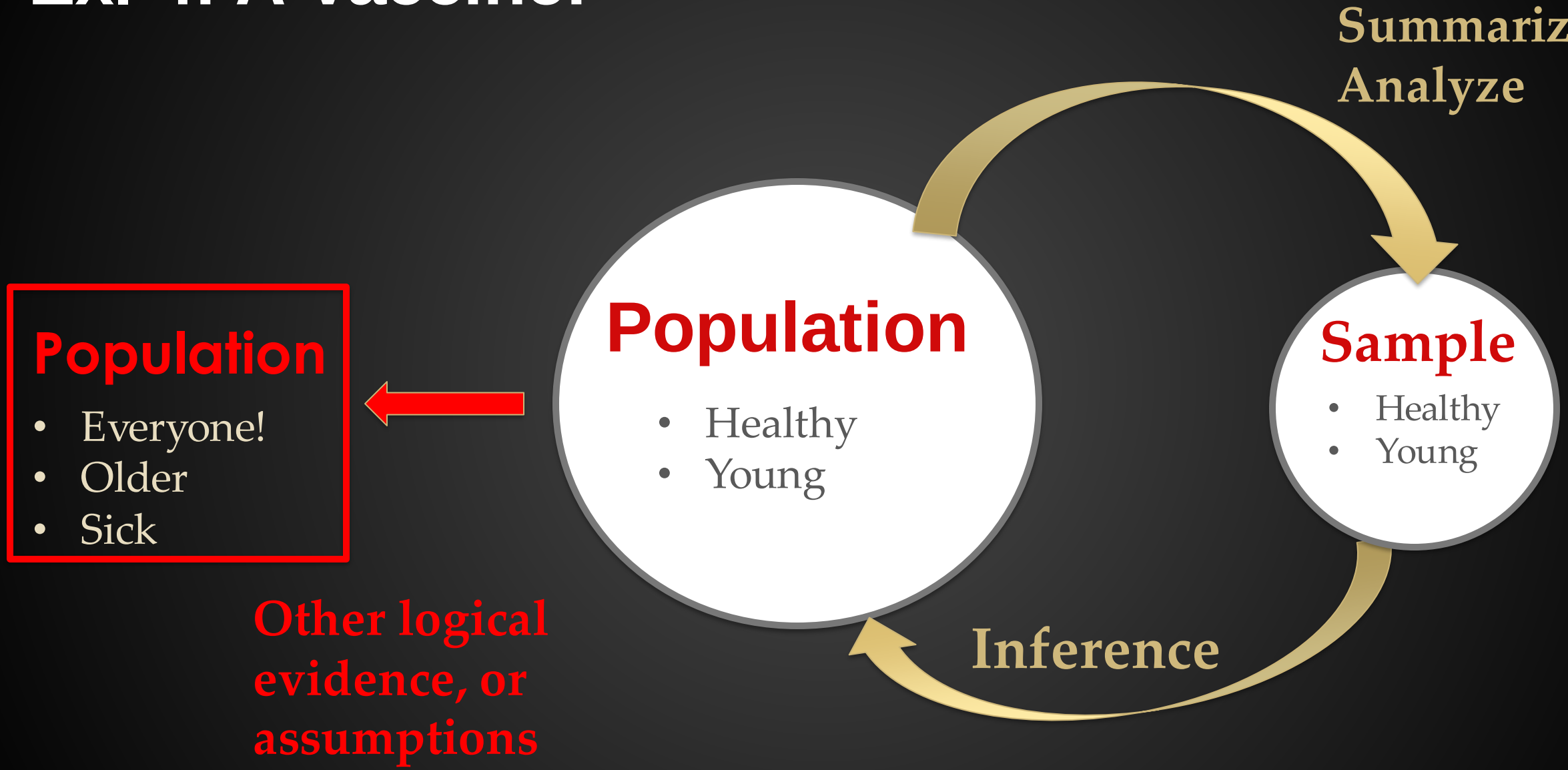

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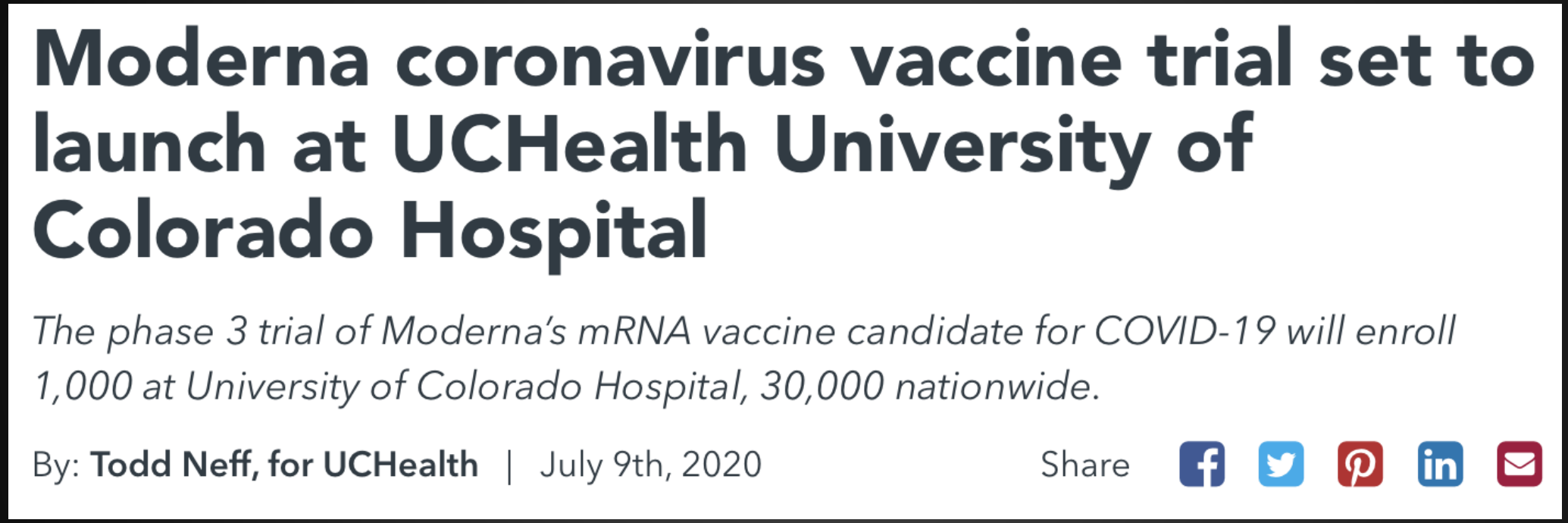

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- Will not be human challenge

In Summary

- Always ask
  - Can I conclude causality?
    - (correlation does not imply causation)
    - Experimental studies are useful here when possible
  - To whom can I generalize?
- Stay safe and wear a mask

Thank you!