Essential Statistical Concepts for Understanding the COVID-19 Pandemic

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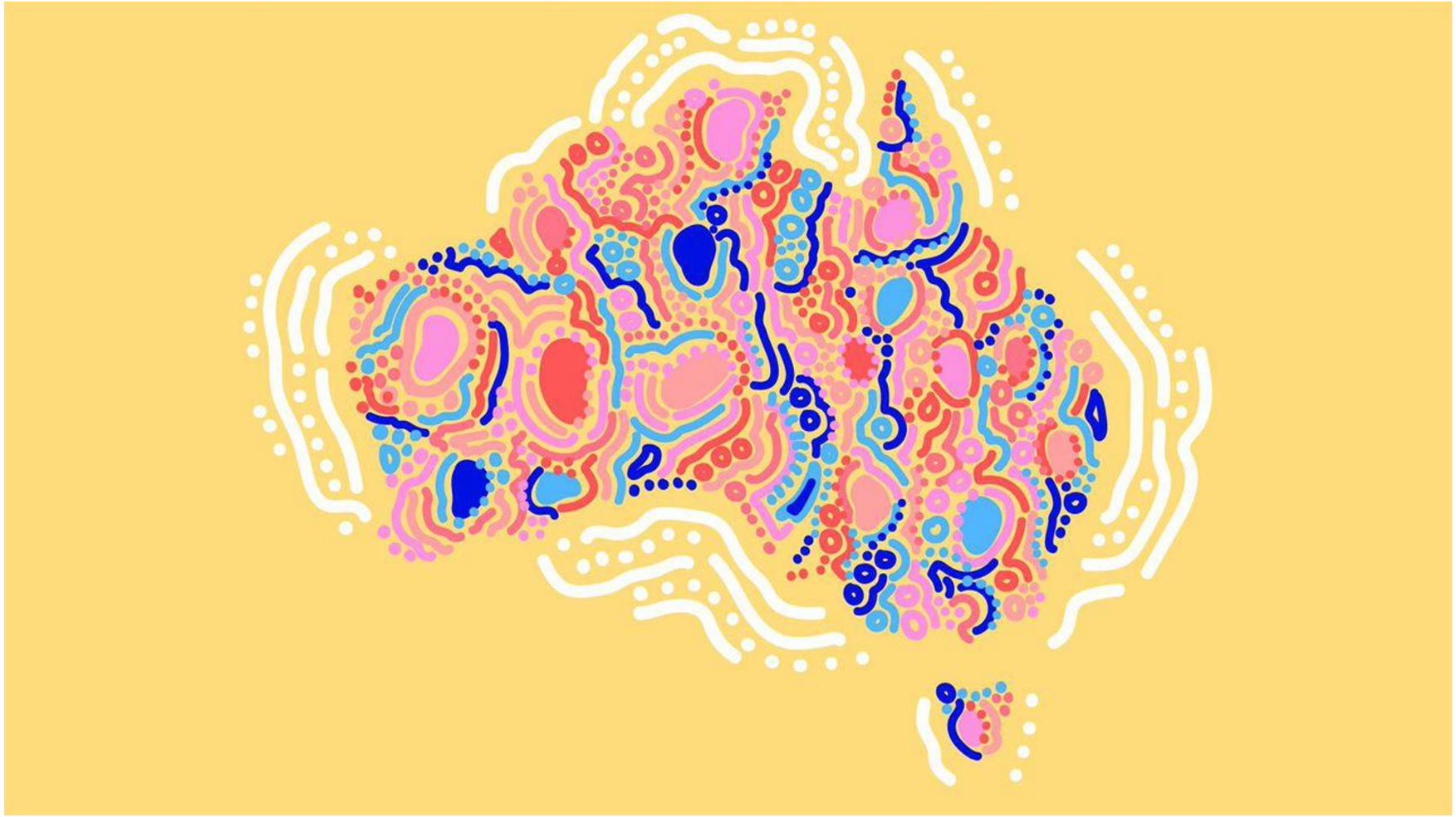
Acknowledgement of Country



Aim

Provide an entry-level glossary of statistical concepts that are frequently encountered in academic and popular literature on COVID-19.

Who am I?

- Freshly minted biostatistician
- Based at the Clinical Trials Enablement Platform WA (CTEP-WA) at Curtin University.
- Funded by Western Australian Health Translation Network (WAHTN) Biostatistician Fellowship.
- Not an expert in infectious disease modelling, epidemiology, or COVID-19!

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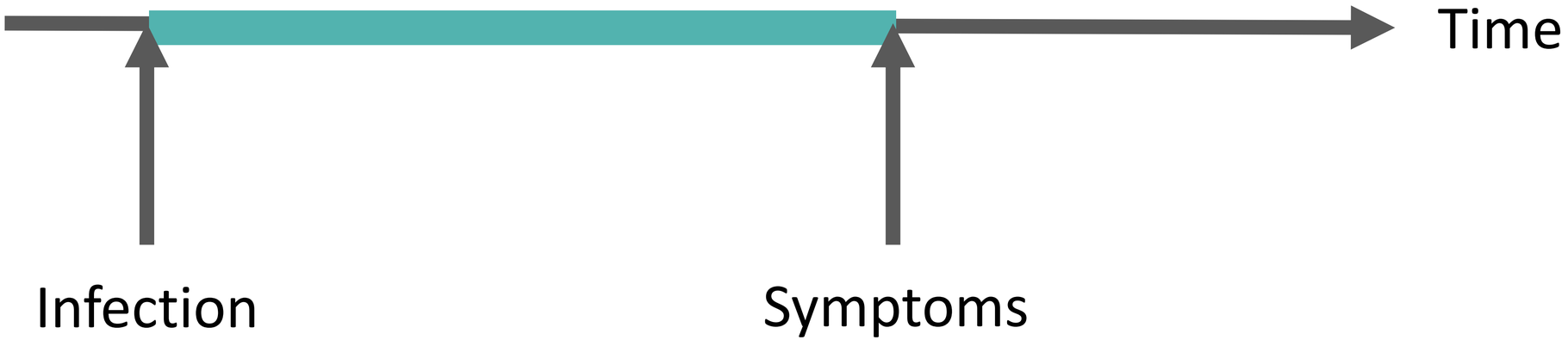
Outline

- Virus Transmission
- Mortality
- Testing
- Statistical Inference
- Q & R

Virus Transmission

Incubation Period

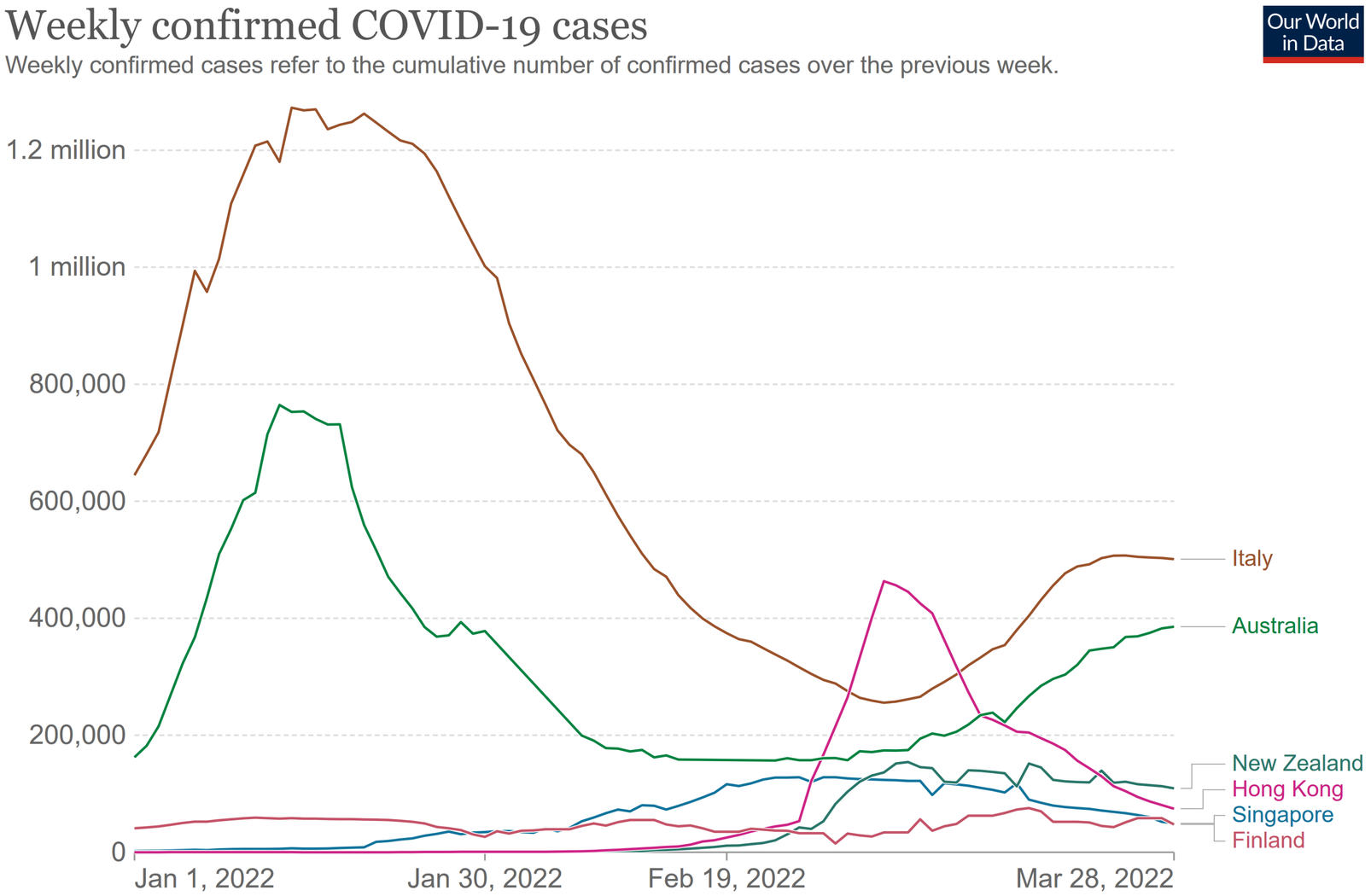
- Incubation period is the interval from receipt of infection to the time of onset of clinical illness, i.e., the onset of recognisable symptoms.
- Australia's national COVID-19 public health guidelines use a **14-day** incubation period to inform many public health measures, such as quarantine and isolation.



Epidemic Curve

- Epidemic curves depict the progression of an outbreak over time.
- Shows the distribution of the times of onset of disease (incubation period).
- Typically there is a delay between start of illness and reports to public health authorities.

Example: Epidemic Curve



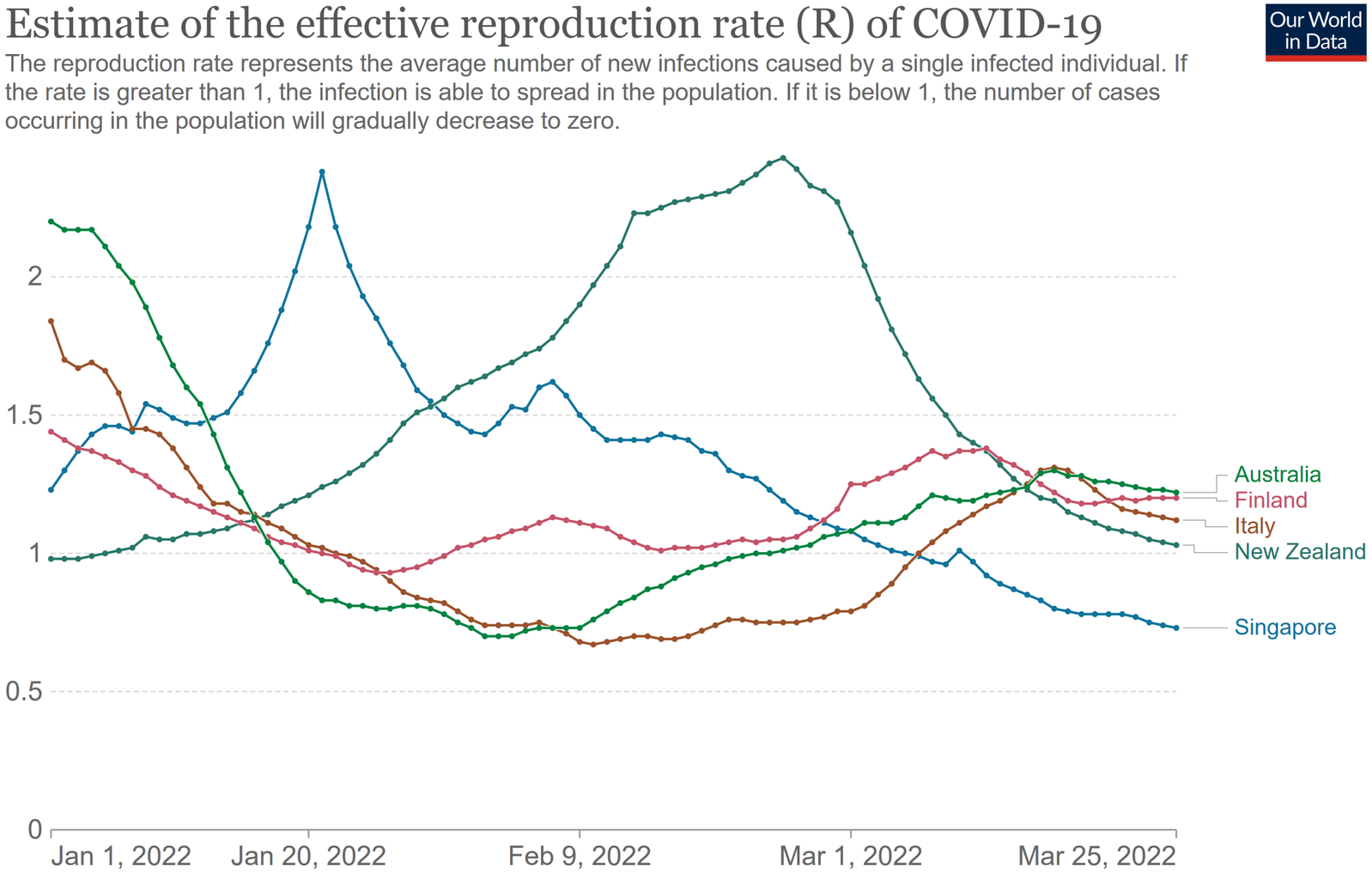
Basic Reproductive Number (R_0)

Expected number of additional cases that one case will generate, on average, over the course of its infectious period in an otherwise uninfected population.

- Until this number falls below 1.0, it is likely that an outbreak will continue to spread.
- In January 2020 the R_0 for COVID-19 was estimated to be 2.2 (Li, Guan, Wu, et al. 2020).

Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel Coronavirus-infected pneumonia. N Engl J Med. 2020;382:1199–1207. DOI: 10.1056/NEJMoa2001316

Example: R_0



Source: Arroyo-Marioli F, Bullano F, Kucinskas S, Rondón-Moreno C (2021) Tracking R of COVID-19: A new real-time estimation using the Kalman filter. CC BY

Mortality

Mortality Risk

Q: If someone is infected with COVID-19,
how likely are they going to die from it?

Crude Mortality Rate

$$\text{Crude Mortality Rate} = \frac{\text{Number who have died from COVID}-19}{\text{Total population}}$$

e.g., if in a population of 10,000 people 200 people die from COVID-19, then the crude mortality rate = 2%.

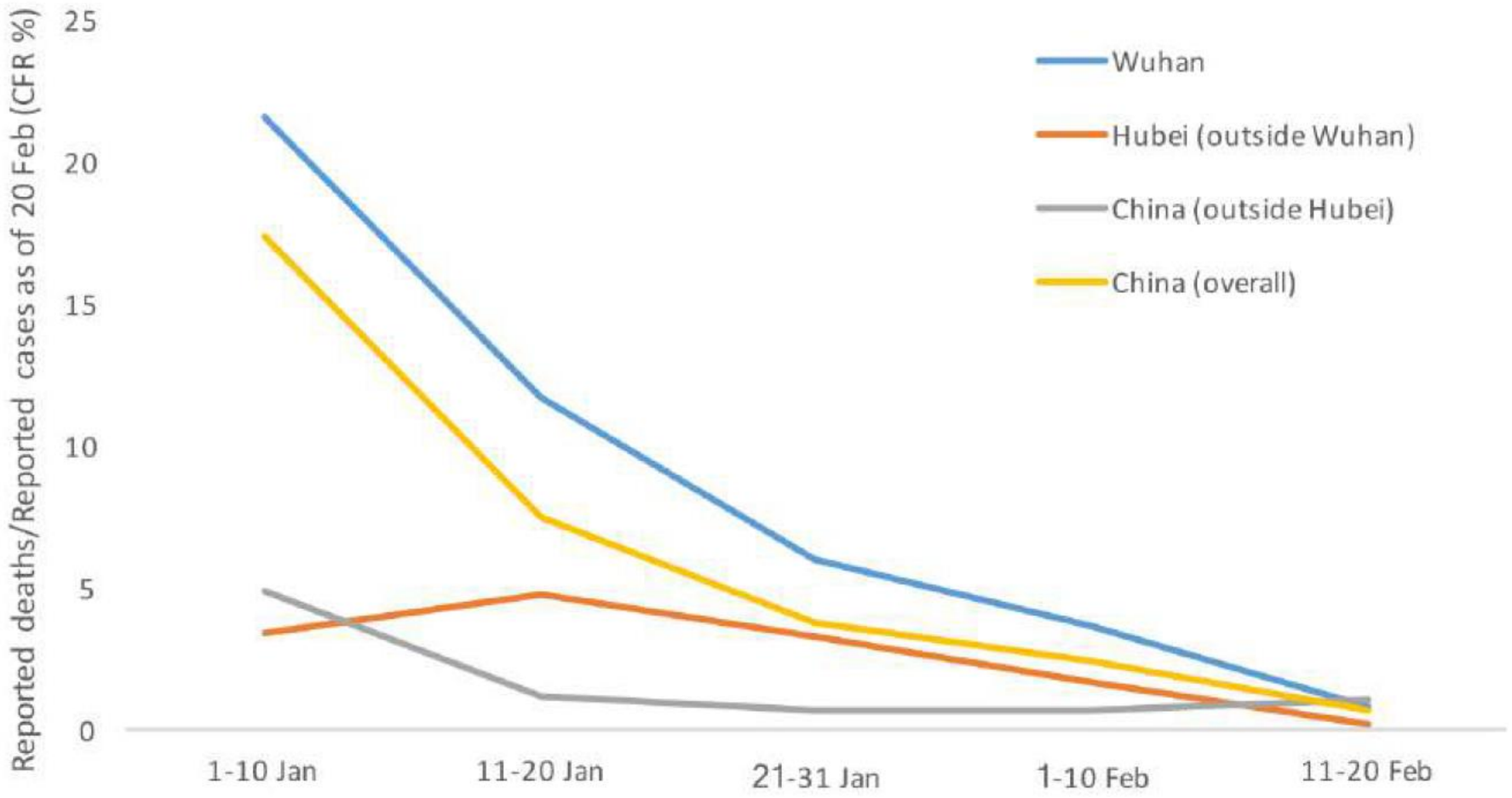
- NOT a measure of the true risk of death of someone who has COVID-19 since the denominator includes those without COVID-19.
- Often confused with the Case Fatality Rate (CFR).

Case Fatality Rate (CFR)

$$\text{CFR} = \frac{\text{Number of } \textit{confirmed} \text{ deaths from COVID}-19}{\text{Number of } \textit{confirmed} \text{ cases of COVID}-19}$$

- Again, cannot be interpreted as the risk of death for an infected person.
- *Confirmed* cases are those verified by a lab test result; but many cases go undiagnosed.
- May vary over time, between locations, by characteristics of infected population.

Example: CFR



World Health Organization (2020). Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19).

Infection Fatality Rate (IFR)

$$\text{IFR} = \frac{\text{Number of } \textit{actual} \text{ deaths from COVID}-19}{\text{Number of } \textit{actual} \text{ cases of COVID}-19}$$

e.g., if 10,000 people have COVID-19 and 200 die from it, then IFR = 2%.

- Number of *actual* cases is difficult to ascertain – relies upon testing coverage.
- A lot of literature describing how to estimate actual cases from samples.

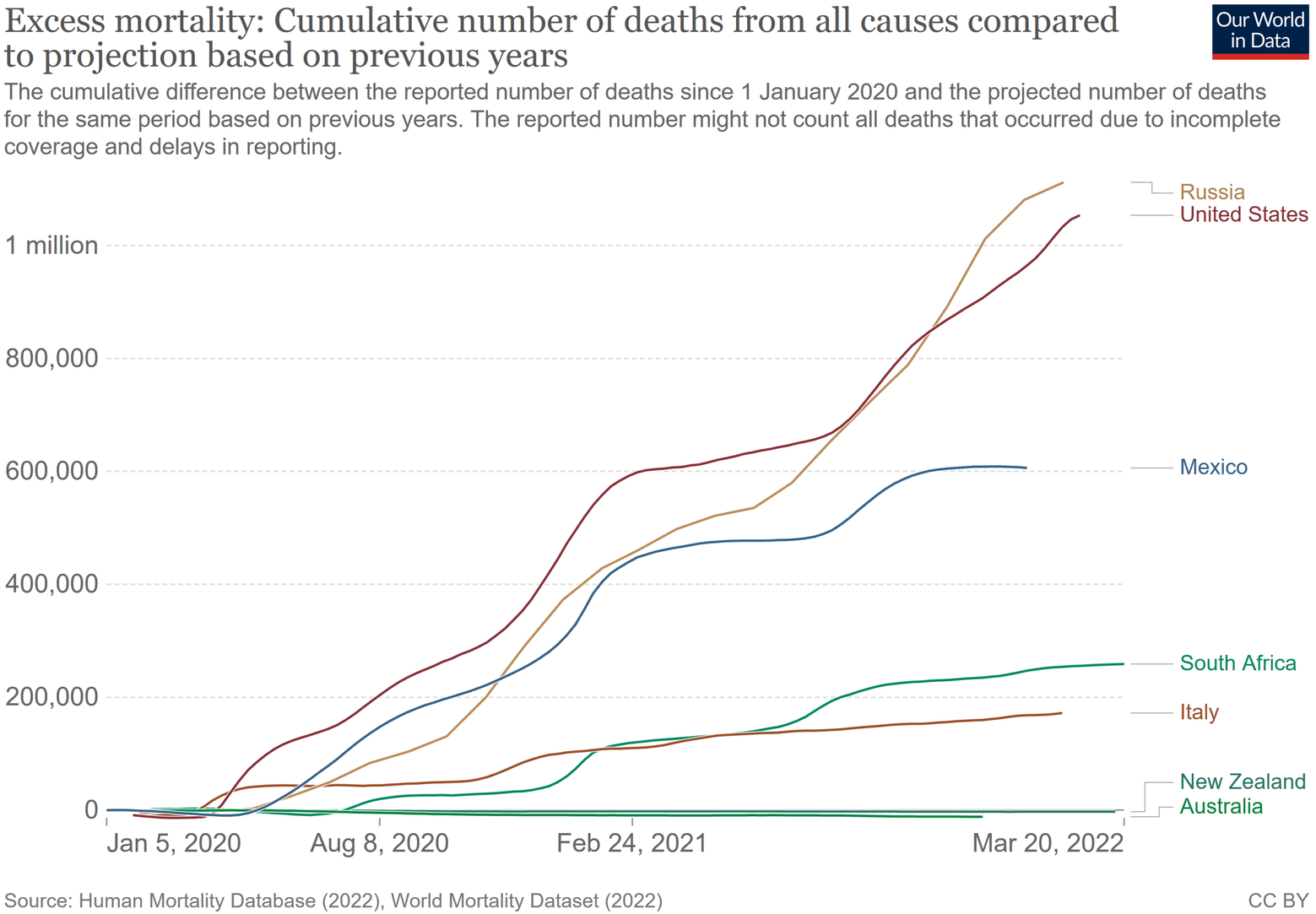
Excess Mortality

Excess mortality is measured as the difference between the reported number of deaths in a period and an estimate of the expected deaths for that same period had the COVID-19 pandemic not occurred.

$$\text{Excess Deaths} = \text{Reported Deaths} - \text{Expected Deaths}$$

- Looks at All-Cause Mortality, not just COVID-19.
- Measures the *total* impact of the pandemic on deaths.
- Expected deaths is estimated using historical data.

Example: Excess Mortality



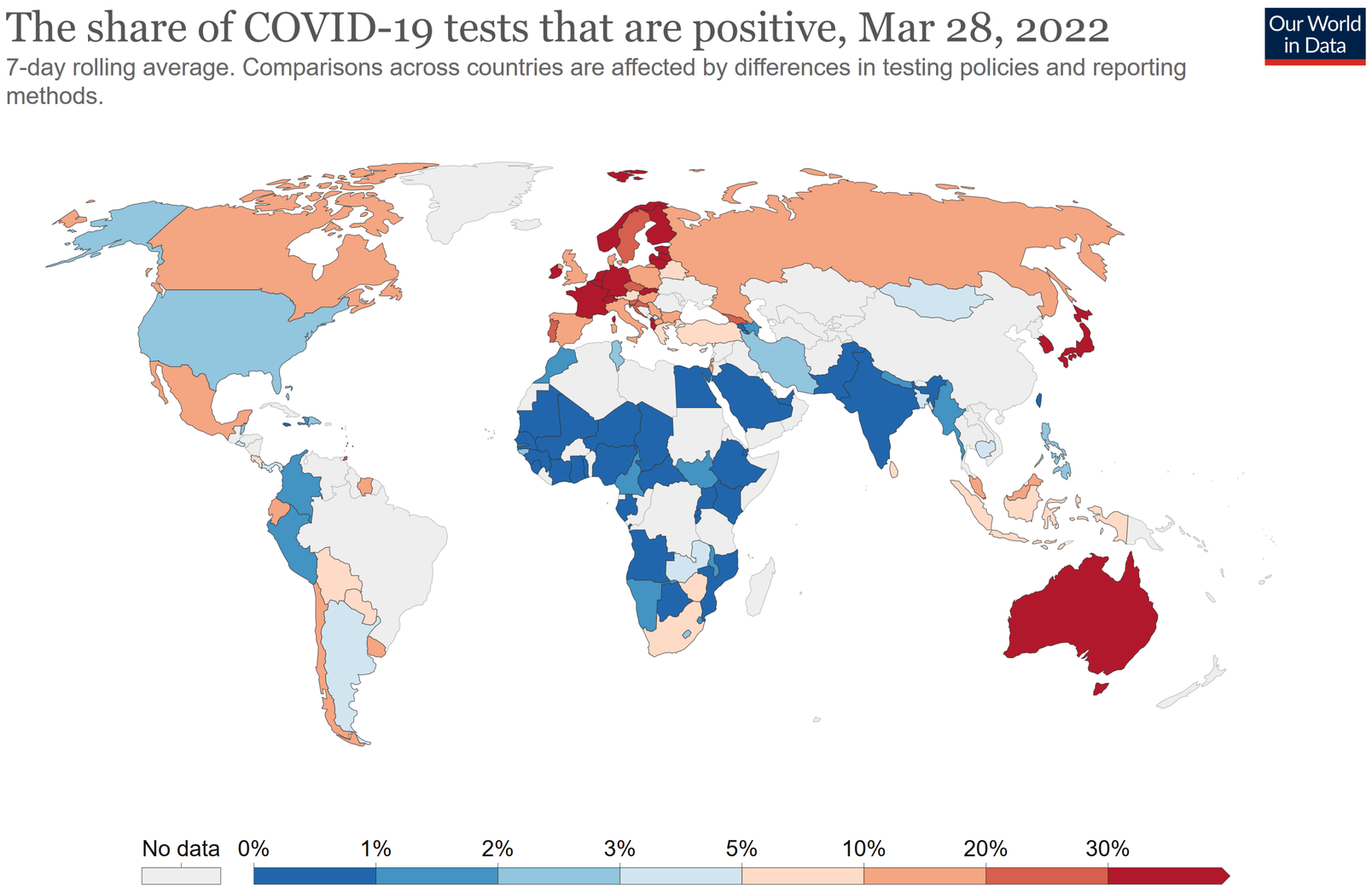
Testing:
Without testing there is no data

Positive Rate

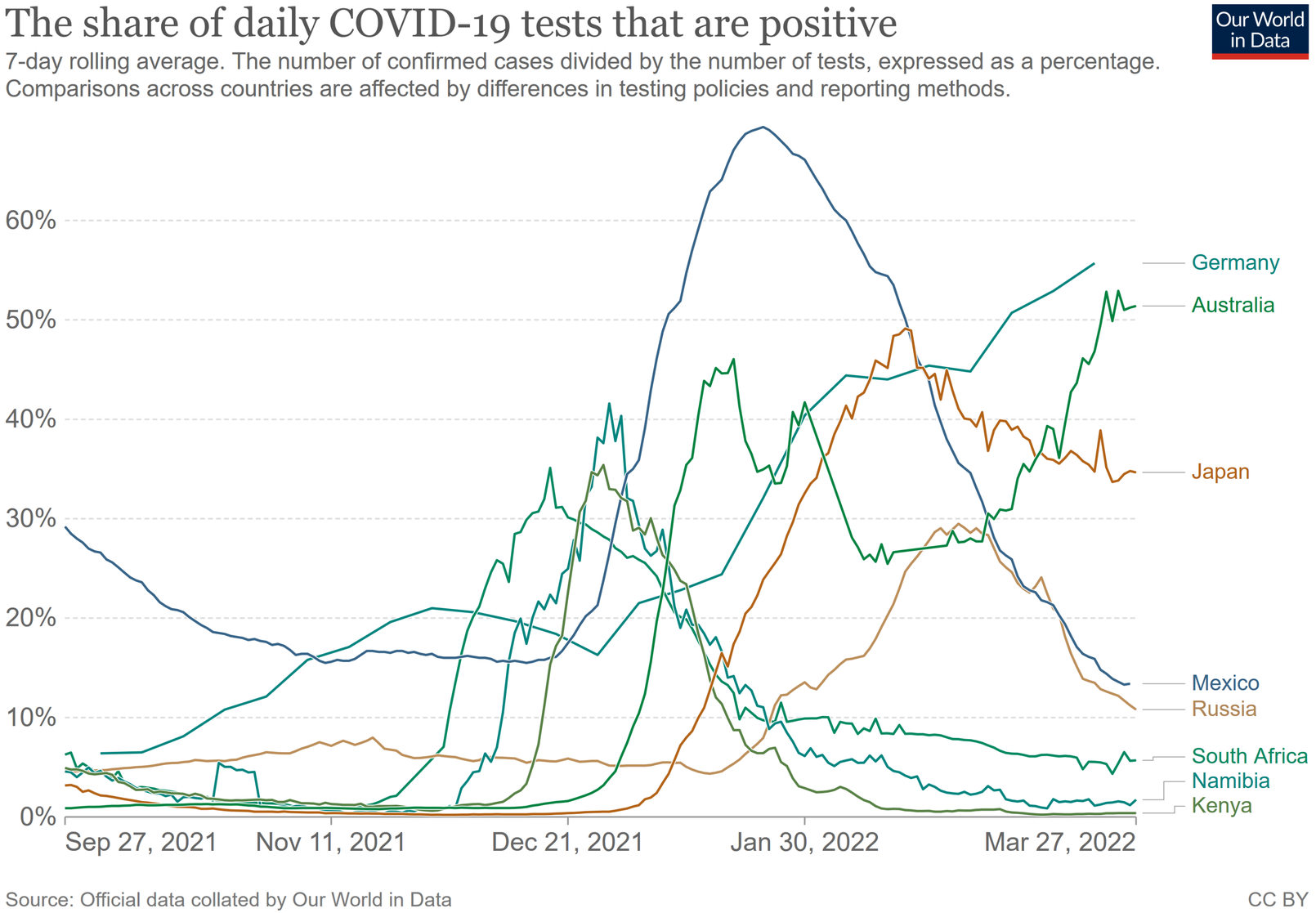
$$\text{Positive Rate} = \text{Proportion of tests returning positive}$$

- Reflects how adequately countries are testing relative to the size of the outbreak
  - Limited testing means many cases are missed → small Positive Rate
- A rising Positive Rate suggests COVID-19 is spreading faster than the growth in the observed confirmed cases.

Example: Positive Rate



Example: Positive Rate



Testing

Q: How “accurate” are COVID-19 tests?

Sensitivity & Specificity

PERFORMANCE CHARACTERISTICS

Clinical performance

A clinical evaluation was conducted comparing the results obtained using the SARS-CoV-2 Antigen Rapid Test with RT-PCR test result. The clinical trial included 841 nasal swab specimens. The results demonstrated 99.4% specificity and 95.9% sensitivity with an overall accuracy of 98.0%.

	PCR confirmed sample number	Correct identified	Rate
Positive sample	341	327	95.9% (Sensitivity)
Negative sample	500	497	99.4% (Specificity)
Total	841	824	98.0% (Total Accuracy)

95.9% Sensitivity: In total 341 PCR confirmed positive samples: 327 PCR confirmed positive samples were correctly detected by SARS-CoV-2 Antigen Rapid Test. There are 14 false negative cases. 99.4% Specificity: In total 500 PCR confirmed negative samples: 497 PCR confirmed negative samples were correctly detected by SARS-CoV-2 Antigen Rapid Test. There are only 3 false positive cases. 98.0% Accuracy: In total 841 PCR confirmed samples: 824 PCR confirmed samples were correctly detected by SARS-CoV-2 Antigen Rapid Test.

Sensitivity

$$\text{Sensitivity} = \frac{\text{True Positives}}{\text{True Positives} + \text{False Negatives}}$$

Correctly returning a *positive* result for someone who *does* have COVID-19.

Reduced when someone is incorrectly identified as *NOT* having COVID-19 when the they actually *do* (False Negative).

Specificity

$$\text{Specificity} = \frac{\text{True Negatives}}{\text{True Negatives} + \text{False Positives}}$$

Correctly returning a *negative* result for someone who *does not* have COVID-19.

Reduced when someone is incorrectly identified as *having* COVID-19 when the they actually *do not* (False Positive).

Example

Test Result	Actual Disease Status: Infected	Actual Disease Status: Not Infected
Positive	True Positive **327**	False Positive **3**
Negative	False Negative **14**	True Negative **497**

$$\text{Sensitivity} = \frac{327}{327 + 14} = 95.9\%$$

$$\text{Specificity} = \frac{497}{497 + 3} = 99.4\%$$

$$\text{Accuracy} = \frac{327 + 497}{841} = 98.0\%$$

Positive Predictive Value (PPV)

$$\text{PPV} = P(\text{Have COVID}-19 \mid \text{Tested Positive}) = \frac{\text{TP}}{\text{TP} + \text{FP}}$$

- Answers the question: If test results are positive in a patient, what is the probability that they have COVID-19?
- More influenced by Specificity than Sensitivity of test if cases are few (i.e., low prevalence) since most of the population is negative for the disease.

$$\text{PPV} = \frac{327}{327 + 3} = 99.1\%$$

Inferential Statistics

Inferential Statistics

- By statistical inference we mean going beyond just describing the state or distribution of our sample data and rather make conclusions about the target population.
- Any conclusions are therefore subject to some uncertainty, not least due to the variability in our data sampling.
- In Classical statistics, one framework for making this inductive leap from sample to population is *Null Hypothesis Significance Testing* (NHST).

Hypothesis Testing

From our research question we formulate two hypotheses, typically:

- **H_0**: A treatment or intervention has zero effect (Null).
- **H_1**: A treatment or intervention has a non-zero effect (Alternative).

We then proceed to collect data and depending on how much our sample appears compatible with the assumption that H_0 is true, we may reject or fail to reject H_0 in favour of H_1.

p-values

A p-value is the probability, assuming that the **null hypothesis is true**, of observing a test statistic that is the same or more extreme than that observed in the collected data.

- It is NOT the probability that the null hypothesis is true!
- Consider it a measure of your surprise at seeing your sample when all along you've assumed that H_0 was true.
  - The smaller the p-value the less compatible the data seems with H_0 and the more plausible to reject it.
- But how small is small?

Type I and Type II Errors

Under the NHST framework, it is possible to make an error with respect to deciding between H_0 and H_1:

- **Type I Error** ("False Positive")
  - incorrectly rejecting H_0, i.e., deciding that there is a real effect when in reality there is none.
- **Type II Error** ("False Negative")
  - incorrectly failing to reject H_0, i.e., deciding that no real effect was observed when in reality there is one.

Significance Level $\alpha = 0.05$

- We don't know for a particular statistical test whether we've made a Type I error or Type II error or neither.
- But we can control our *long-run* Type I Error Rate by making decisions based on a threshold α ("alpha"):
  - p-value below $\alpha \rightarrow$ decide to reject H_0,
  - p-value above $\alpha \rightarrow$ decide in favour of H_0.
- This threshold P(Type I Error) = α is by convention often set at 5%,

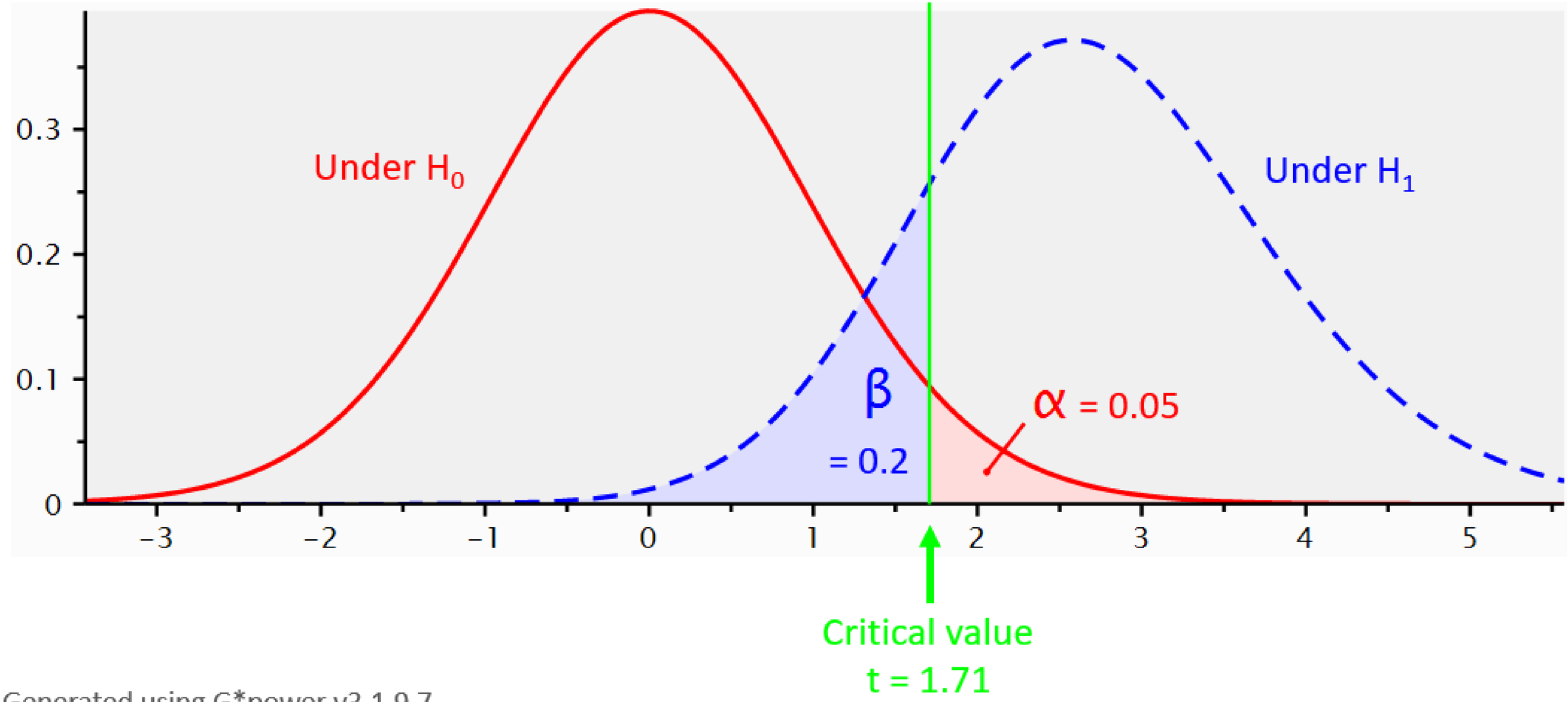
  i.e., if we were to repeat our experiment 100 times we'd expect to erroneously reject H_0 only 5 times.
- What about Type II errors?

Statistical Power (1 – β)

- The probability of making a Type II Error is denoted β (“beta”).
- The complement of β, known as **statistical power,** is the probability of correctly rejecting a false H_0,

  e.g., correctly concluding that a treatment has an effect when in reality it does.
- Underpowered studies, assuming that H_0 is false, may overlook real treatment effects that are very small.
- This leads into Power Analysis and sample size calculation.

Example: Independent sample t-test



Generated using G*power v3.1.9.7

Effect Size

- p-values provide no indication of the magnitude of the effect of a treatment, whether “statistically significant” or not.
- It is common to report “standardised effect sizes” which have been scaled so that they are unitless and more easily compared between studies.
  - Pearson correlation, r
  - Cohen’s d
  - Odds ratio
  - Relative Risk
- Cohen (1988) suggested some conventions for what constitutes small, medium, and large effect sizes.

Example: Cohen's d

$$d = \frac{\text{mean}(\text{Treatment Group}) - \text{mean}(\text{Comparator Group})}{\text{SD}(\text{Pooled Sample})}$$

- Standardised mean differences, e.g., d = 1 indicates two groups' means differ by 1 standard deviation.

Effect Size	Cohen's d
"Small"	0.20
"Medium"	0.50
"Large"	0.80

Sample Size

- For a statistical test the following factors are inter-related:
  - Level of significance, α = P(Type I error)
  - Statistical power, $(1 - \beta) = 1 -$ P(Type II error)
  - Sample size, n
  - Minimal effect size of interest
- Knowing three of the above lets you compute the fourth.

Correlation

$$r = \frac{\text{Covariance}(X, Y)}{\text{SD}(X) \times \text{SD}(Y)}$$

- Ranges between -1 and +1.
- Measure of the strength of *linear association* between two variables

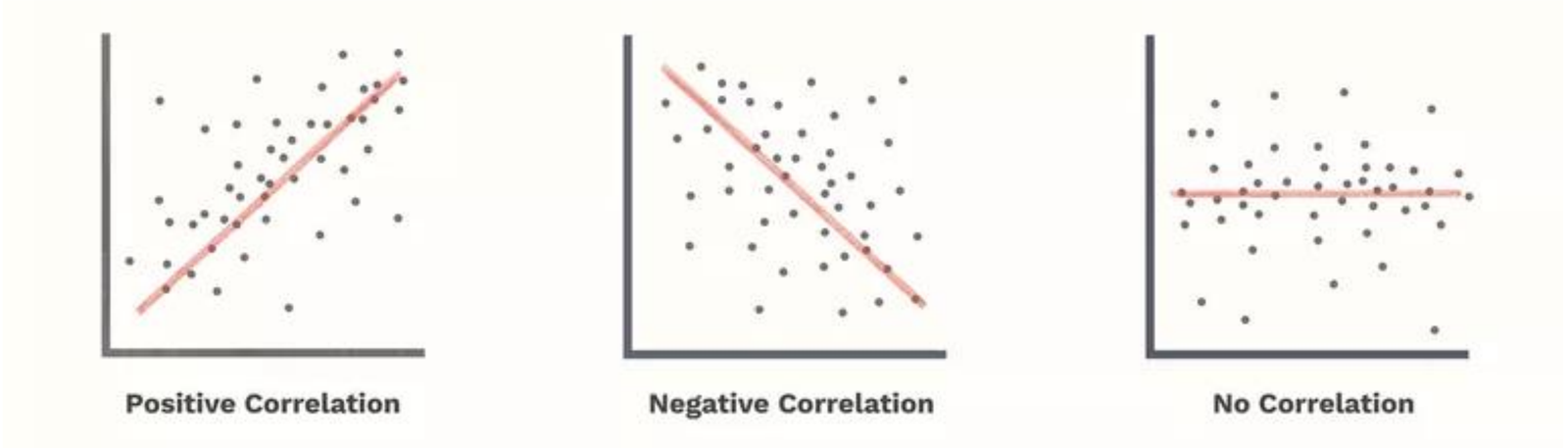
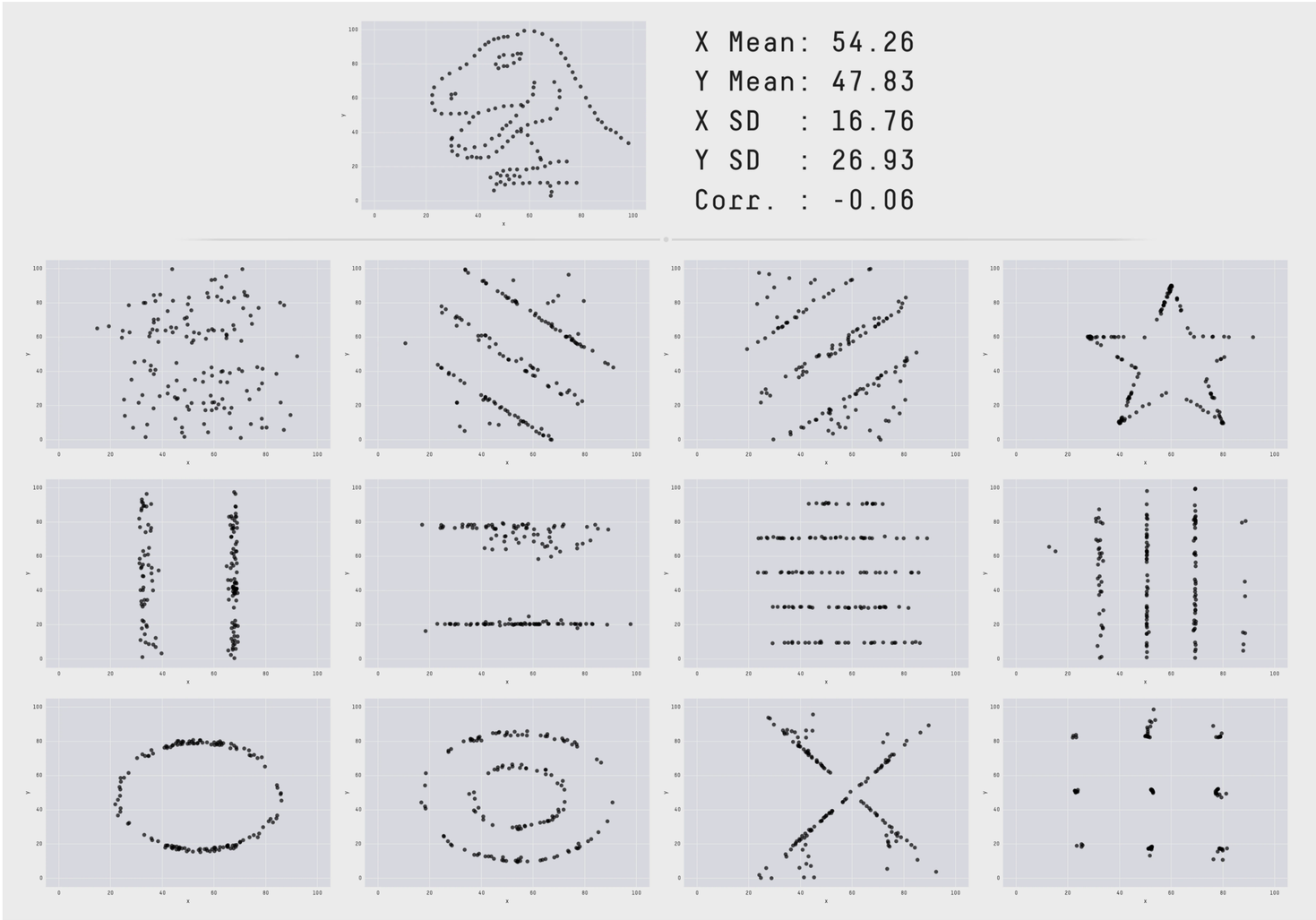


Illustration by Hugo Lin. ThoughtCo.

Example: The Datasaurus Dozen



Justin Matejka and George Fitzmaurice. 2017. Same Stats, Different Graphs: Generating Datasets with Varied Appearance and Identical Statistics through Simulated Annealing. DOI: https://doi.org/10.1145/3025453.3025912

What is CTEP-WA?

- Formerly called Clinical Trials and Data Management Centre (CTDMC)
- Expertise in clinical trial study design, clinical trial conduct, data management, data linkage, analytical techniques for clinical trial datasets, bio-repository techniques, and clinical registry datasets.
- Biostatistical consultation service to clients conducting clinical research.
- CTEP-WA also offers an Auditing and Monitoring Service for Investigator-Initiated clinical trials.

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Thank you

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