

Measures of Effect & Precision: an Introduction

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Why is it important to measure effects & precision?

Trump steroid treatment for COVID-19 raises potential side effect risk

(Reuters) - U.S. President Donald Trump is being treated for COVID-19 with a steroid that is recommended for severe cases of the illness and that comes with risks of serious side effects, including mood swings, aggression and confusion.

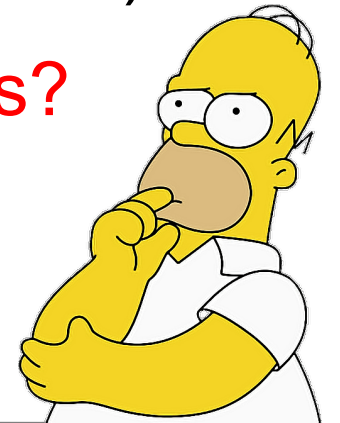


Why are measures of effects important?

In the dexamethasone group, the incidence of death was lower than that in the usual care group among patients receiving invasive mechanical ventilation (29.3% vs. 41.4%; rate ratio, 0.64; 95% CI, 0.51 to 0.81) and among those receiving oxygen without invasive mechanical ventilation (23.3% vs. 26.2%; rate ratio, 0.82; 95% CI, 0.72 to 0.94)

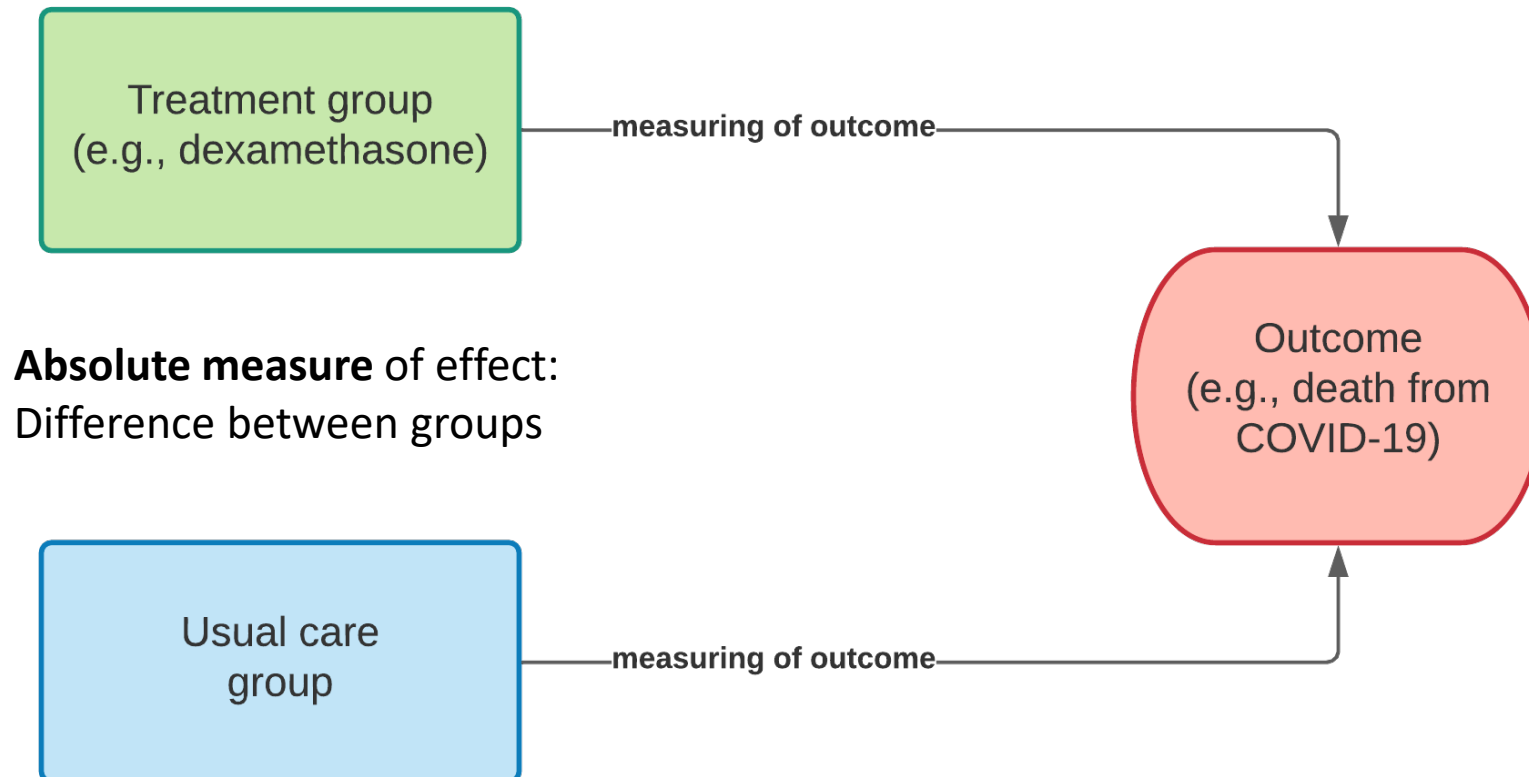
Mortality at Insel Group: ~7% at that time (~22% in 2nd wave)

➔ What is the effect of dexamethasone in our patients?

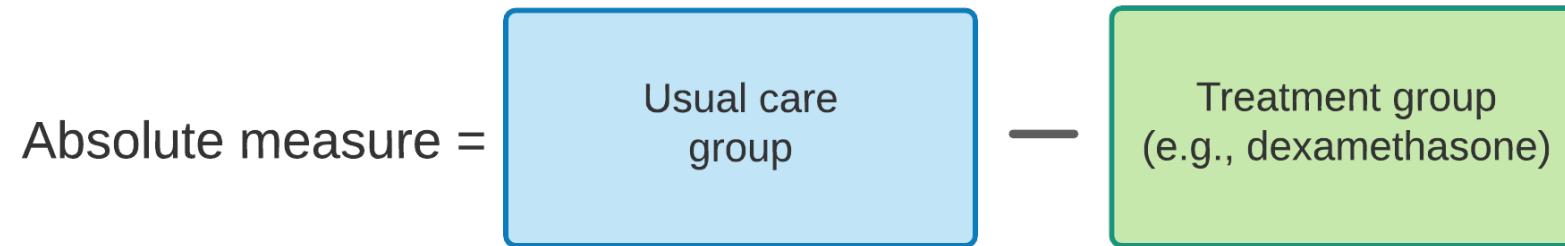


RECOVERY Collaborative Group. New England Journal of Medicine. 2020 Jul 17.

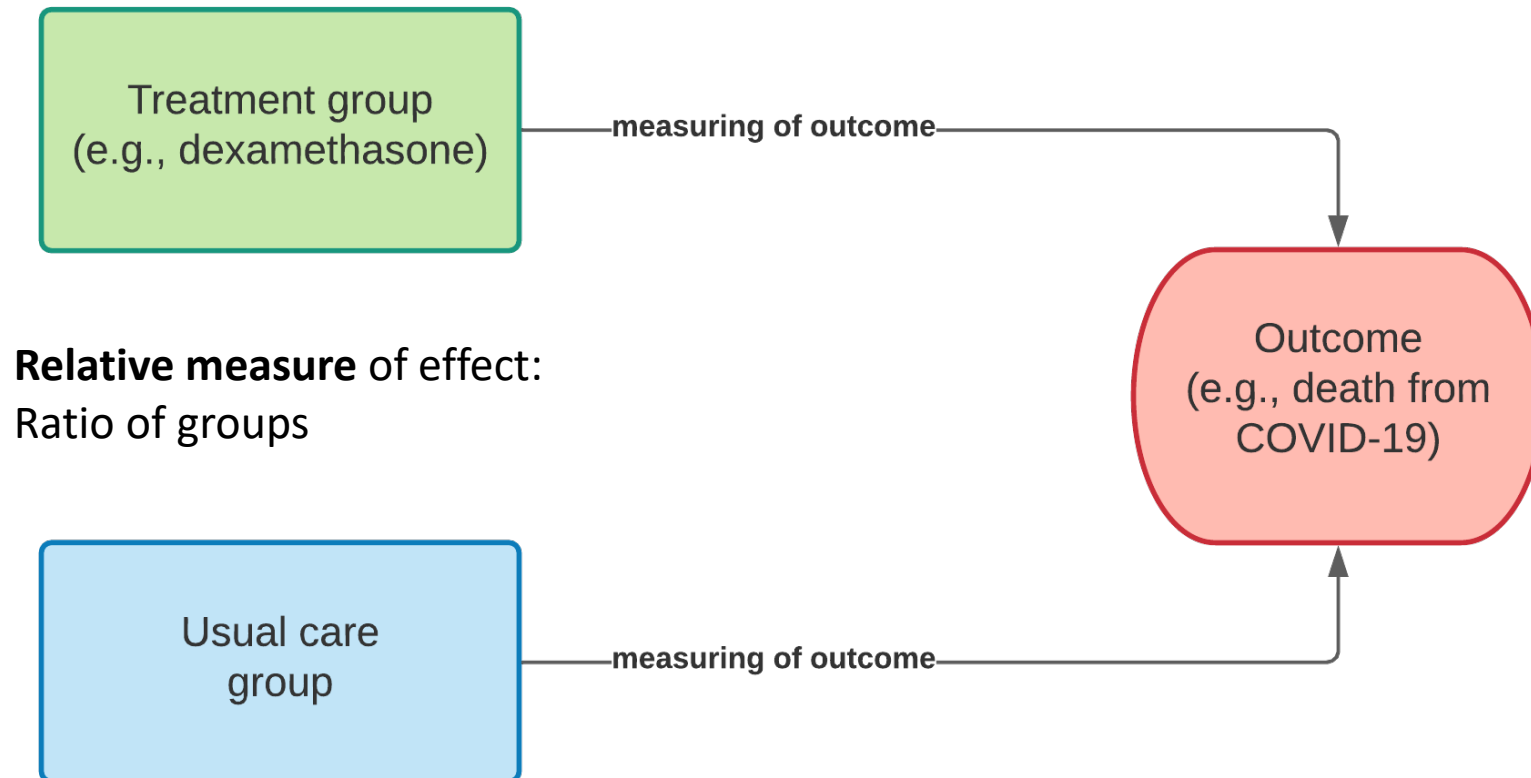
What are measures of effect?



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What are measures of effect?

Relative measure =
$$\frac{\text{Treatment group (e.g., dexamethasone)}}{\text{Usual care group}}$$

What are the absolute and relative measures?

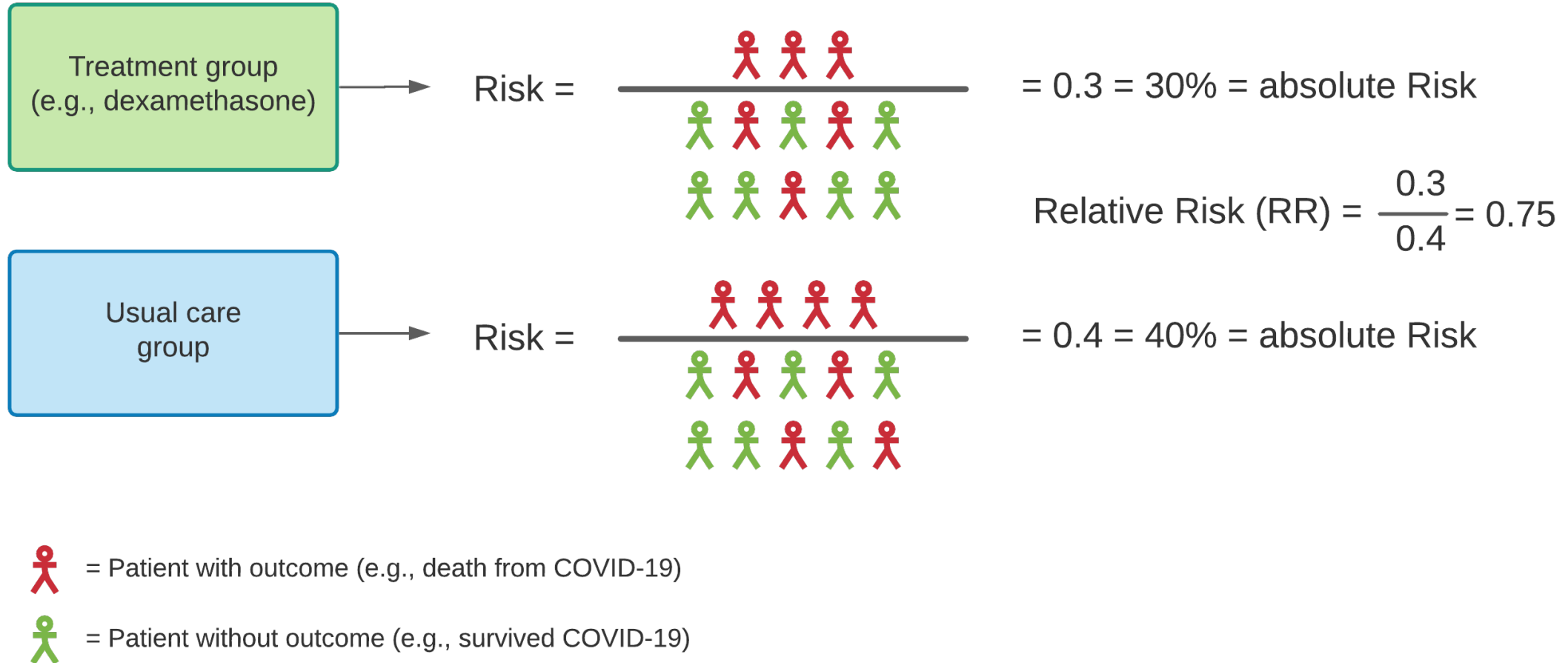
Absolute measures of effect

- Absolute Risk Reduction (ARR)
- Number Needed to Treat (NNT)

Relative measures of effect

- Relative Risk, Risk Ratio, Rate Ratio (RR)
- Relative Risk Reduction (RRR)
- Hazard Ratio (HR)
- Odds Ratio (OR)

What is a Relative Risk (RR)?



What is a Relative Risk Reduction (RRR)?


Treatment group
(e.g., dexamethasone)


Risk = $\frac{\text{3 red stick figures}}{\text{10 stick figures (3 red, 7 green)}}$ = 0.3 = 30% = absolute Risk

Relative Risk Reduction (RRR) =
1 - RR = 1 - 0.75 = 0.25 = 25%

Usual care
group

Risk = $\frac{\text{4 red stick figures}}{\text{10 stick figures (4 red, 6 green)}}$ = 0.4 = 40% = absolute Risk

 = Patient with outcome (e.g., death from COVID-19)

 = Patient without outcome (e.g., survived COVID-19)

What is the Absolute Risk Reduction (ARR)?


Treatment group
(e.g., dexamethasone)


Risk = $\frac{\text{3 red stick figures}}{\text{10 stick figures (3 red, 7 green)}} = 0.3 = 30\% = \text{absolute Risk}$

Absolute Risk Reduction (ARR) = $0.4 - 0.3 = 0.1 = 10\%$

Usual care group

Risk = $\frac{\text{4 red stick figures}}{\text{10 stick figures (4 red, 6 green)}} = 0.4 = 40\% = \text{absolute Risk}$

 = Patient with outcome (e.g., death from COVID-19)

 = Patient without outcome (e.g., survived COVID-19)

What is the Number Needed to Treat?

Treatment group
(e.g., dexamethasone)


Risk = $\frac{\begin{matrix} \text{Red} & \text{Red} & \text{Red} \\ \text{Green} & \text{Red} & \text{Green} & \text{Red} & \text{Green} \\ \text{Green} & \text{Green} & \text{Red} & \text{Green} & \text{Green} \end{matrix}}{10} = 0.3 = 30\% = \text{absolute Risk}$


$$\text{Number Needed to Treat (NNT)} = \frac{1}{\text{ARR}}$$

$$= \frac{100\%}{10\%} = 10$$

Usual care group

Risk = $\frac{\begin{matrix} \text{Red} & \text{Red} & \text{Red} & \text{Red} \\ \text{Green} & \text{Red} & \text{Green} & \text{Red} & \text{Green} \\ \text{Green} & \text{Green} & \text{Red} & \text{Green} & \text{Red} \end{matrix}}{10} = 0.4 = 40\% = \text{absolute Risk}$

 = Patient with outcome (e.g., death from COVID-19)

 = Patient without outcome (e.g., survived COVID-19)

What are the Odds and their Ratio?


Treatment group
(e.g., dexamethasone)


$$\text{Odds} = \frac{\begin{array}{c} \text{👤} \text{👤} \text{👤} \\ \hline \text{👤} \text{👤} \text{👤} \\ \text{👤} \text{👤} \text{👤} \text{👤} \end{array}}{=} 0.43$$

Usual care
group

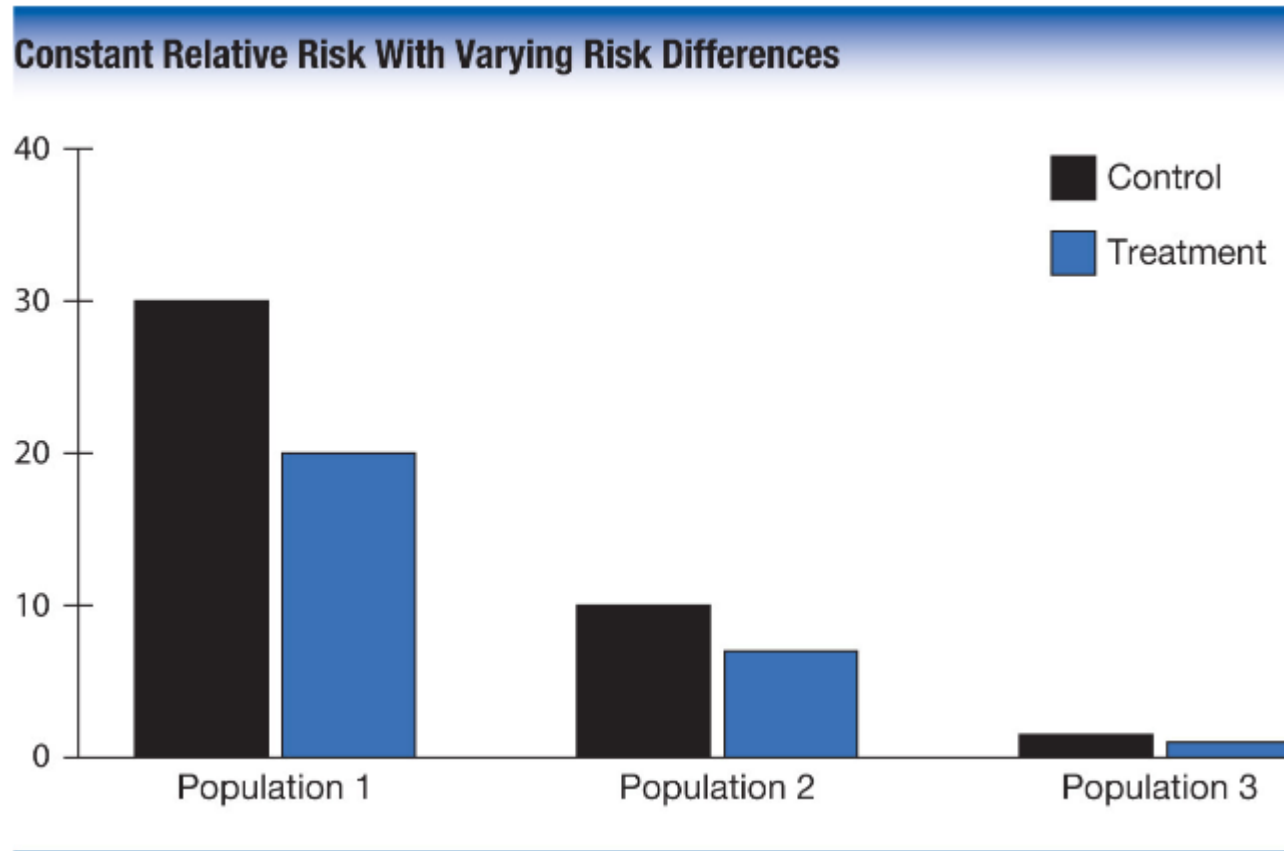
$$\text{Odds} = \frac{\begin{array}{c} \text{👤} \text{👤} \text{👤} \text{👤} \\ \hline \text{👤} \text{👤} \text{👤} \\ \text{👤} \text{👤} \text{👤} \end{array}}{=} 0.67$$

$$\text{Odds Ratio (OR)} = \frac{0.43}{0.67} = 0.64$$

 = Patient with outcome (e.g., death from COVID-19)

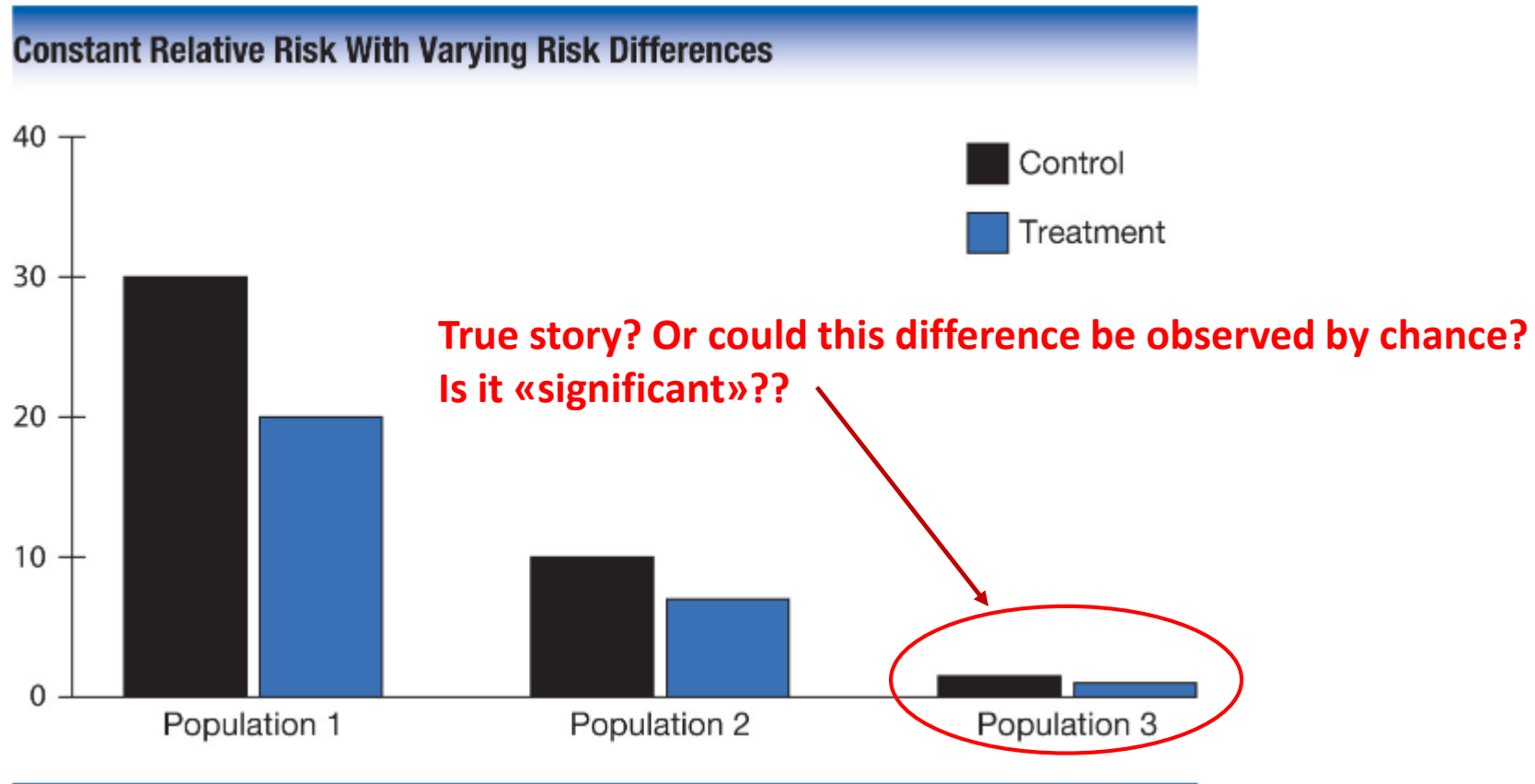
 = Patient without outcome (e.g., survived COVID-19)

Importance of knowing absolute and relative risk



Guyatt GH, et al., JAMA, 2000

Should we measure the precision of our effect?



Guyatt GH, et al., JAMA, 2000

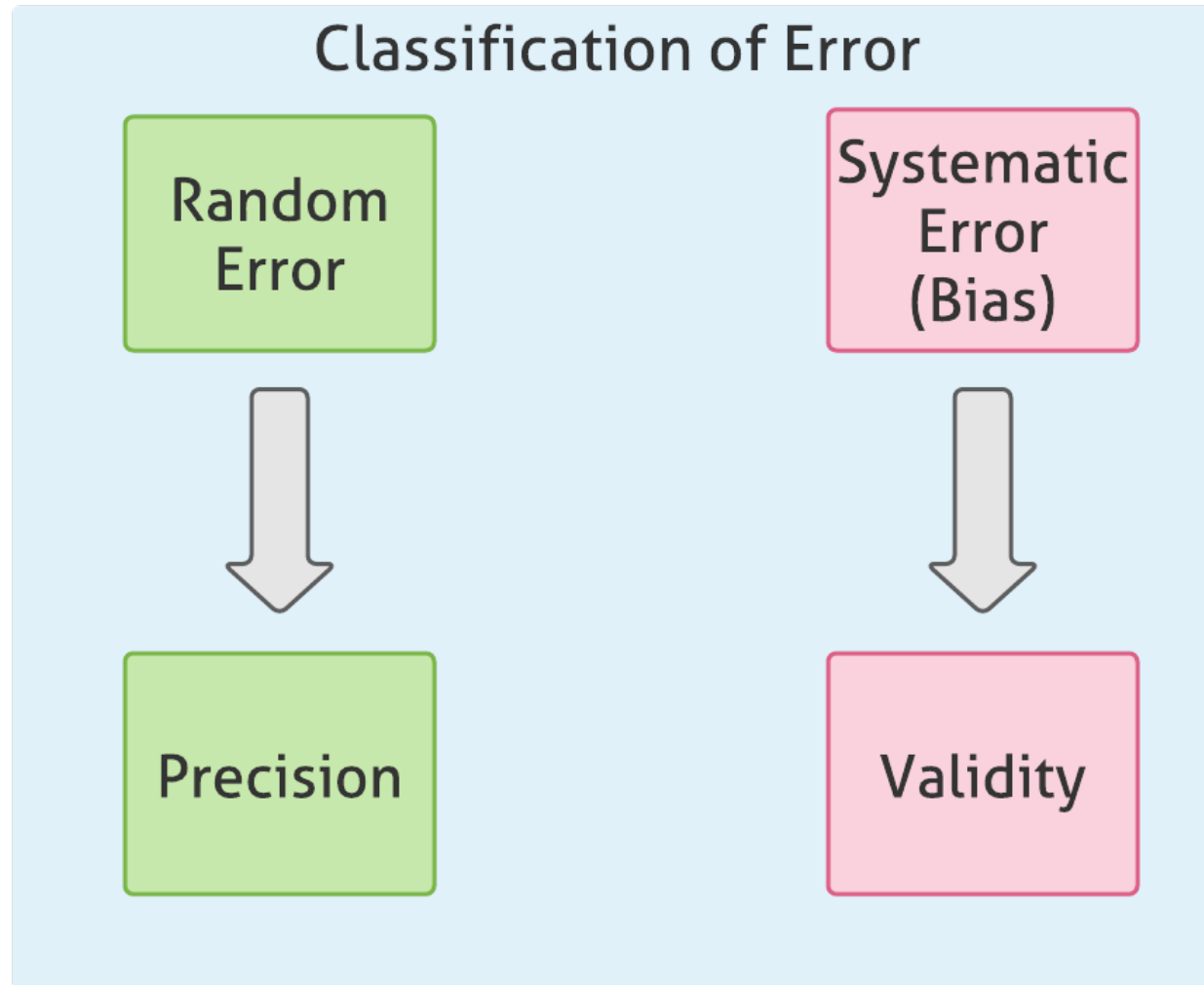
Why are measures of precision important?

CONCLUSIONS AND RELEVANCE Among patients with moderate COVID-19, those randomized to a 10-day course of remdesivir did not have a statistically significant difference in clinical status compared with standard care at 11 days after initiation of treatment. Patients randomized to a 5-day course of remdesivir had a statistically significant difference in clinical status compared with standard care, but the difference was of uncertain clinical importance.

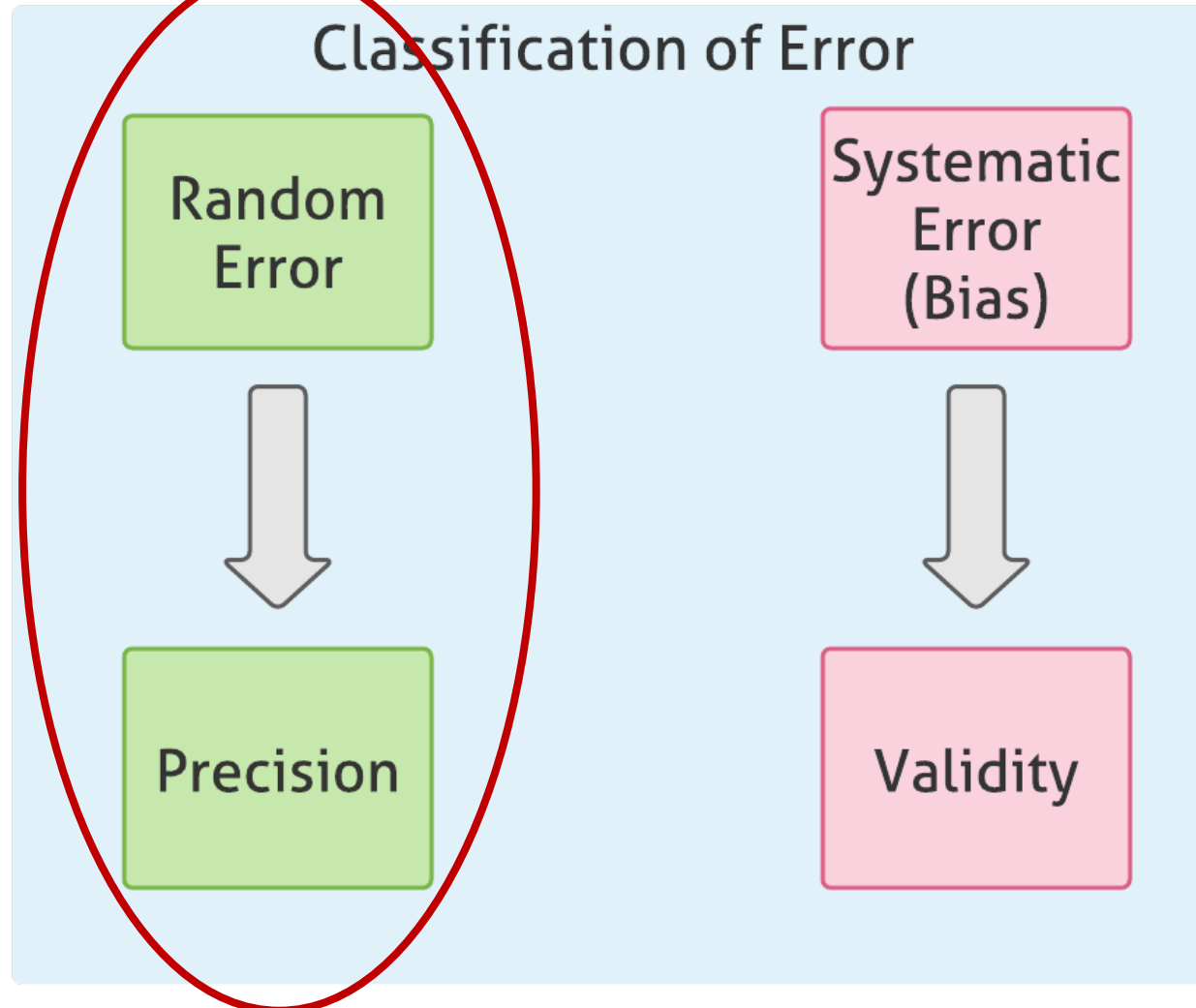
➔ If significance = good, then $5 > 10$ days?



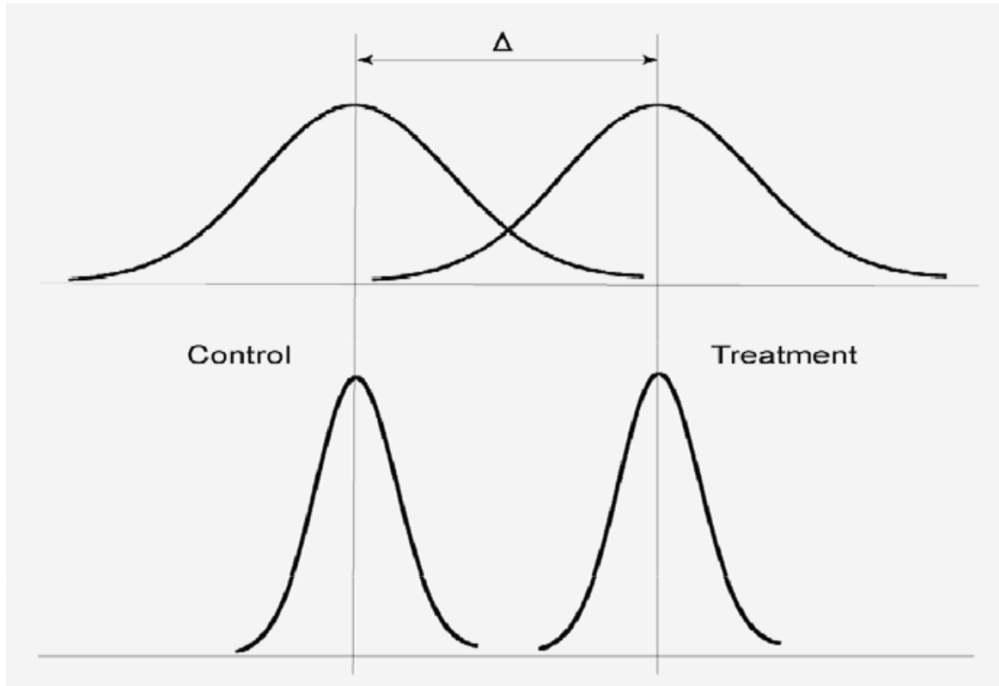
What is Precision?



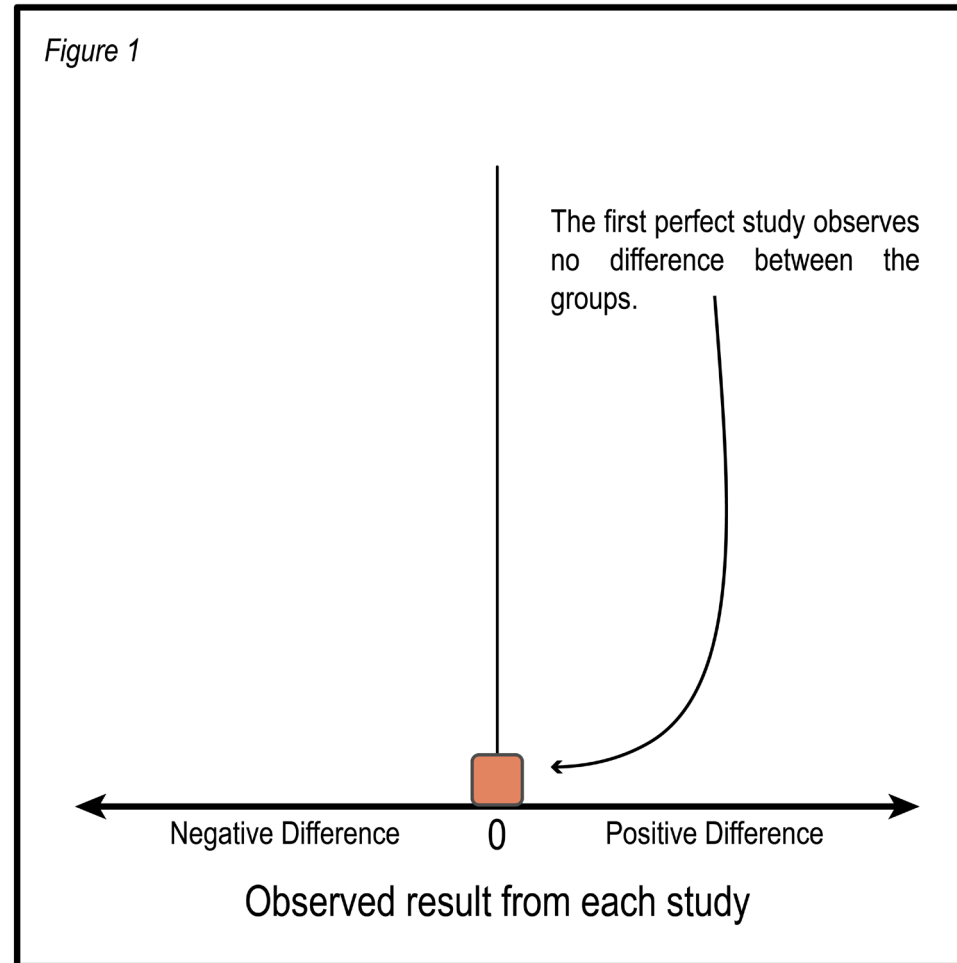
What is Precision?



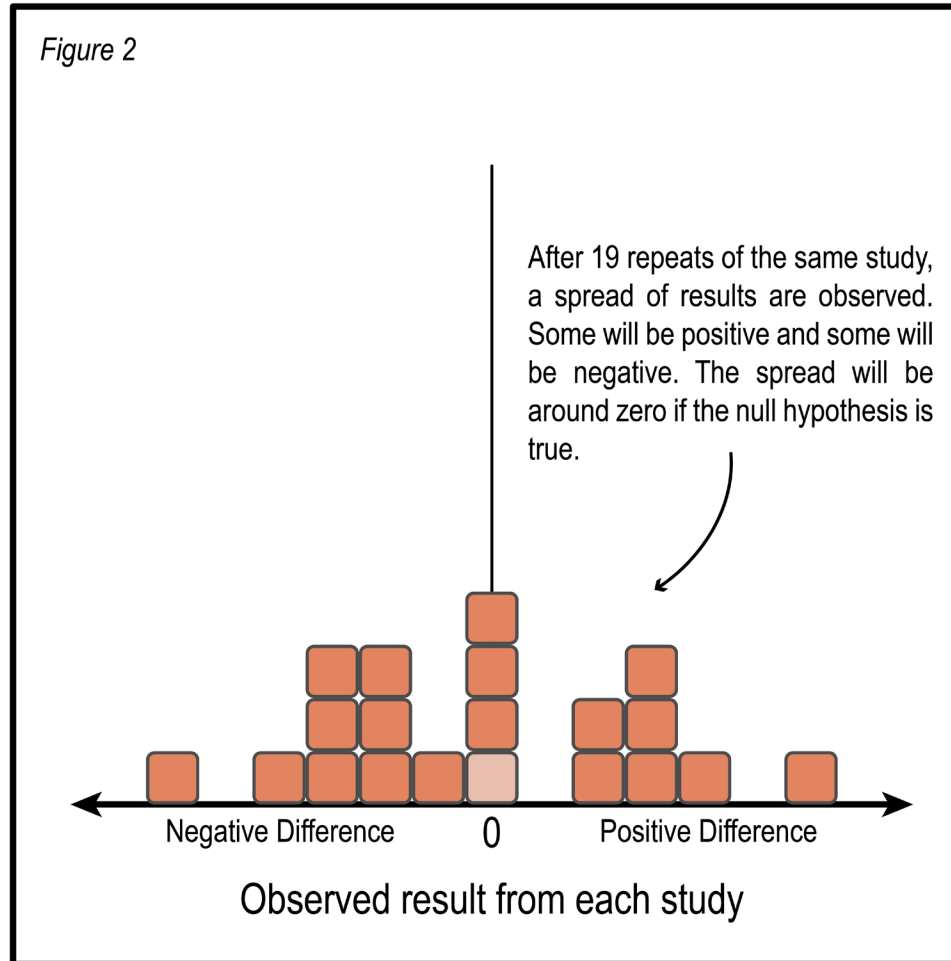
What is Precision?



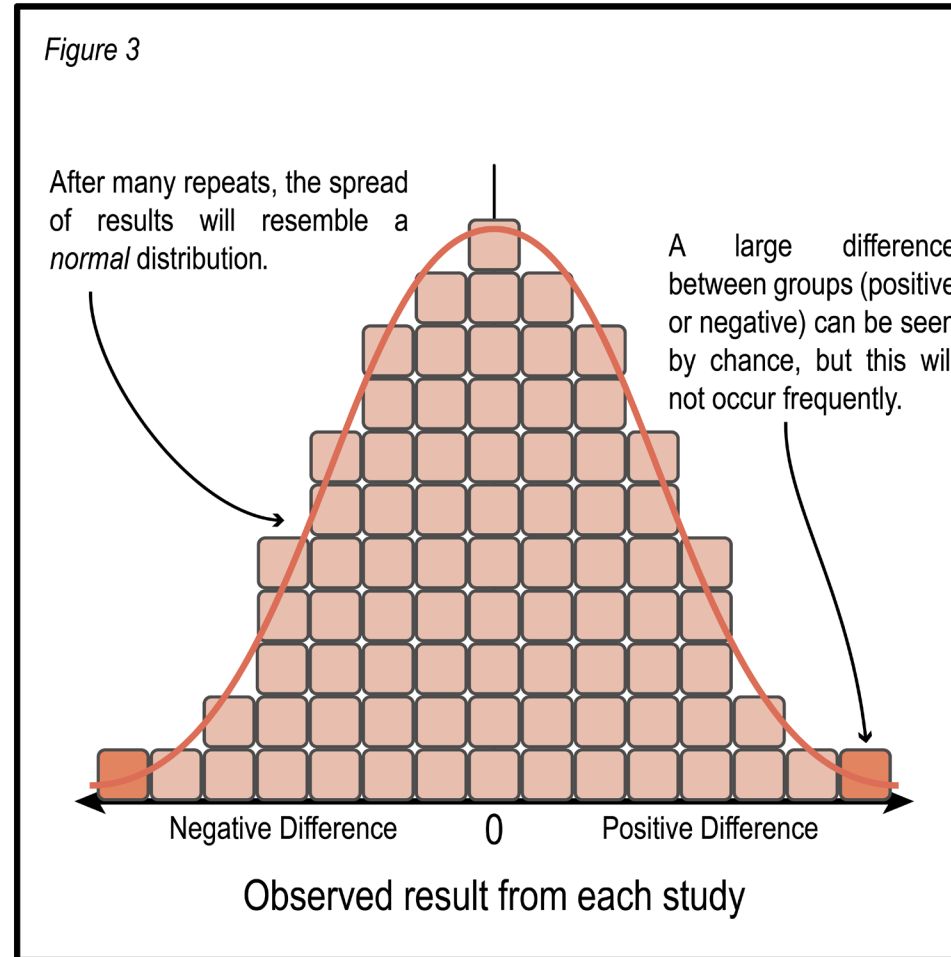
If the null hypothesis was true and we did a study?



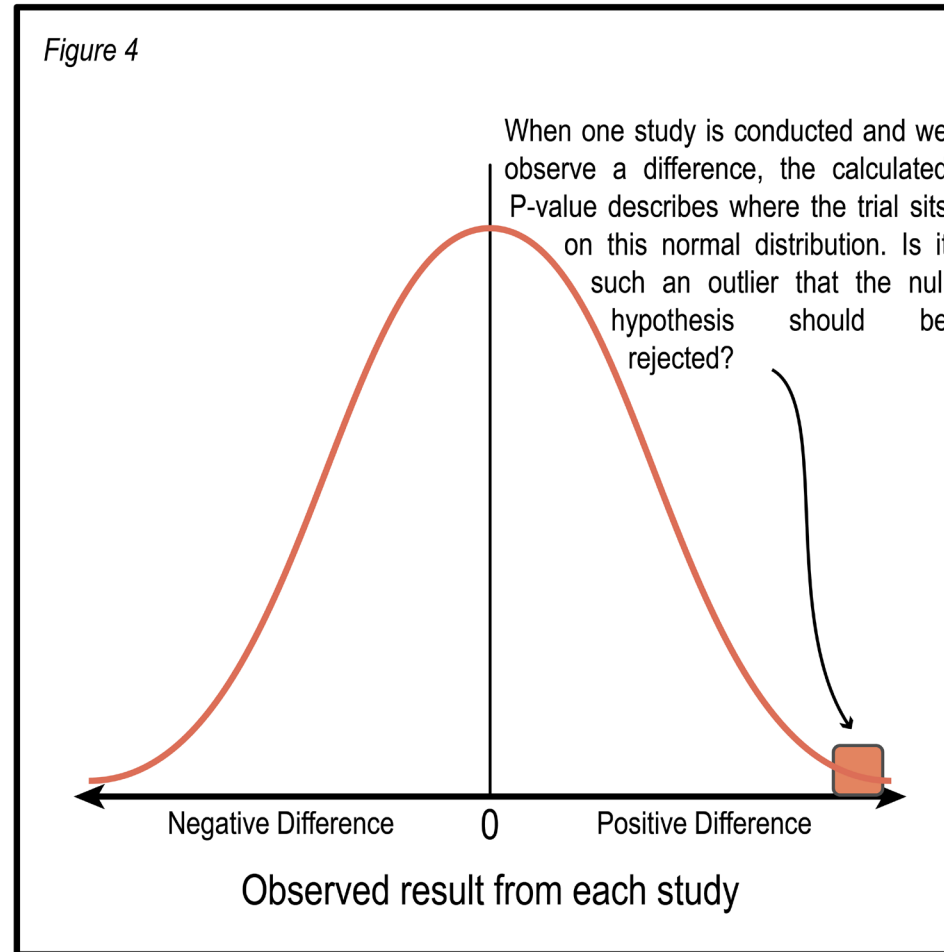
If the null hypothesis was true and we did a study?



If the null hypothesis was true and we did a study?



If the null hypothesis was true and we did a study?



Definition of the p-value

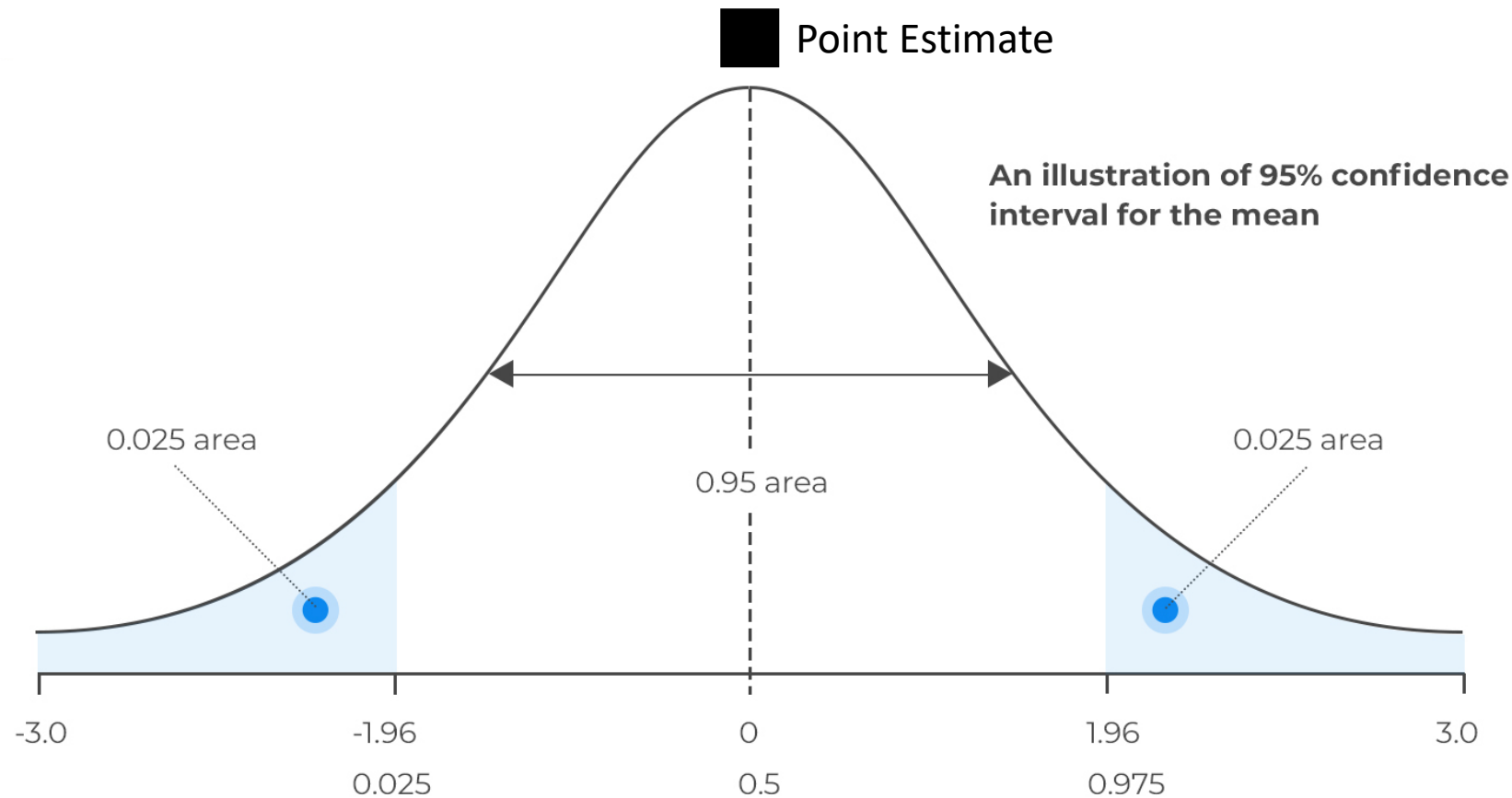
The probability (**p**) of obtaining a result equal to, or “more extreme” than, that actually observed, under the assumption that the null hypothesis (there is no difference between specified groups/populations) is correct.

Confidence Intervals: better than the p-value?

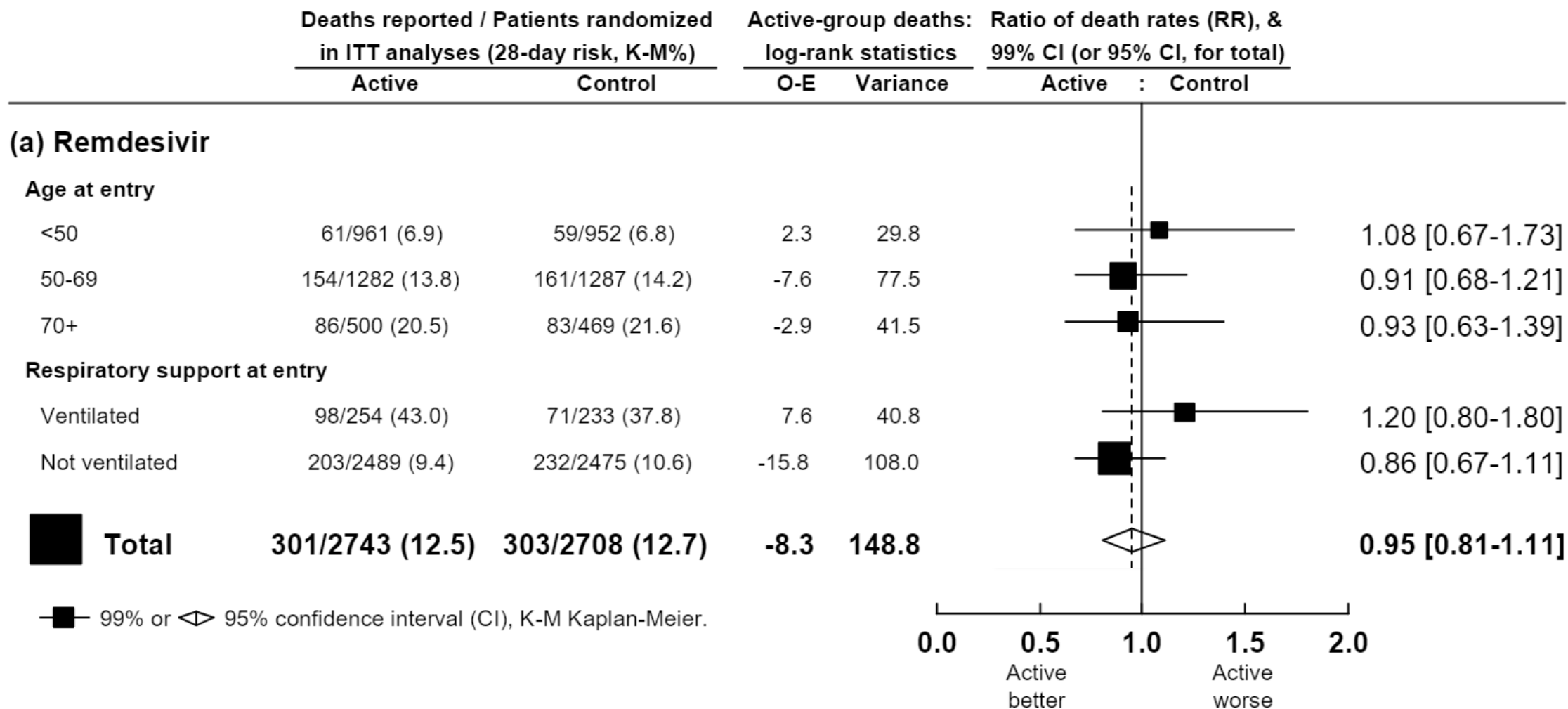
95% confidence interval (**CI**): the range that would include the values of 95% of study repeats, if the study was repeated many times.

Or easier: we can be 95% confident, that the true effect lies within the interval given by the 95% CI (in the absence of bias).

Confidence Intervals: better than the p-value?



Confidence Intervals: better than the p-value?



Take Home Message

Measures of Effect

- Absolute measures
 - Absolute risk reduction (ARR): the difference in absolute risk between groups
 - Number needed to treat (NTT): the number of patients that need to be treated to prevent one outcome (can be calculated as $1 / \text{ARR}$ or $100 / \text{ARR}\%$)
- Relative measures
 - Relative risk (RR): the relative change of risk to experience the outcome between the two groups (usually intervention and control)
 - Relative risk reduction: the reduction in risk from administering the intervention (compared to control)
 - Odds ratio (OR): the relative change of odds to experience the outcome between the two groups (usually intervention and control)

Measures of Precision

- P-value: probability of observing a difference by chance alone
- 95% confidence interval: range of values that we can be 95% confident would include the true effect