ESCP · PASCAR 2026
JOINT CONGRESS

July 31– August 2, 2026
Interluxury Hotel, Addis Ababa, Ethiopia

Statistical concepts for Clinicians

Dr Niveditha Devasenapathy
Head, Academic Clinical Trials Unit, George Institute for Global Health, India

ጤና ሚኒስቴር - ኢትዮጵያ
MINISTRY OF HEALTH-ETHIOPIA

1

Key topics

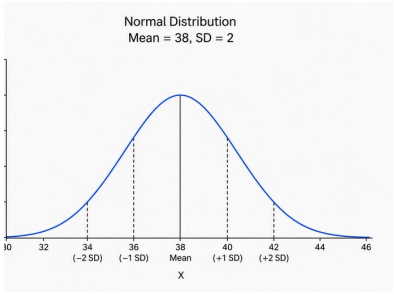
The George Institute for Global Health India

- Variability and uncertainty
- Absolute versus relative effect measures
- Clinically important difference
- Interpreting trial results

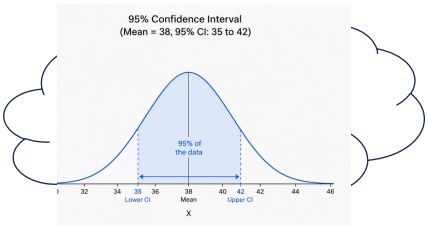
The George Institute for Global Health India

2

Data to information



Research question → Data → Describe the Sample data → Infer from the sample data about the population

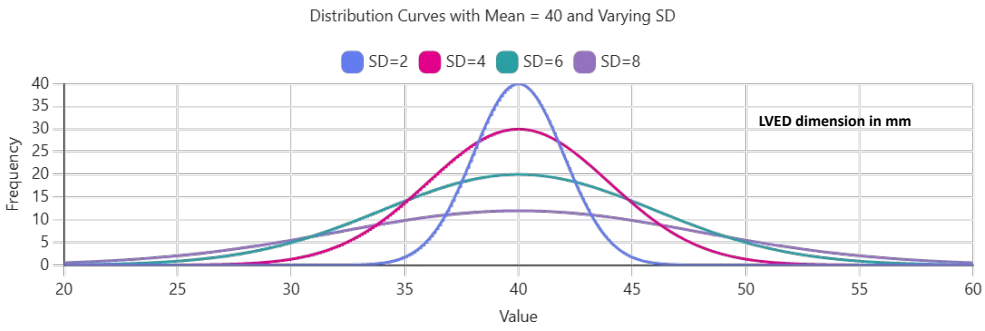


Sample

Sample should be representative and randomly drawn

3

Variability (Noise)



Variability of data for a particular parameter is function of

- Sample characteristics
- Measurement method
- Biological reasons

4

Common measures of variability

Standard deviation

$$SD = \sqrt{\frac{\sum_{i=1}^{n} (x_i - \bar{x})^2}{n-1}}$$

xi = each data value
x = mean of the data
n = number of data values

Absolute spread of data **around** the mean
Cannot compare SD across data with varying units
Measurement error and natural variation

Coefficient of variation

$$CV = \frac{SD}{Mean} \times 100\%$$

Relative spread of data **compared** to mean
Can compare across datasets with varying units
Operational consistency

Interpreting SD and CV

Group	Mean HR (bpm)	SD (bpm)	CV (%)
Healthy adults	60	6	10%
Heart failure patients	100	10	10%

Greater absolute variability
Relative variability same

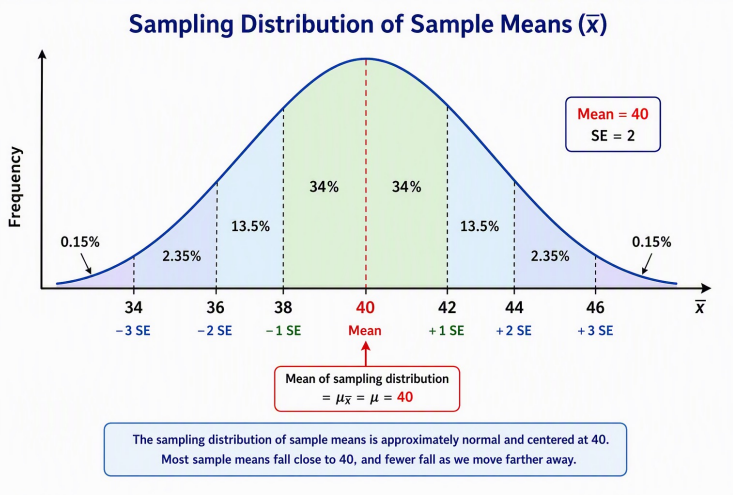
Parameter	Mean %	SD	CV
Left ventricular ejection fraction (LVEF)	60%	3%	5%
NT-proBNP (pg/mL)	2000	400	20%

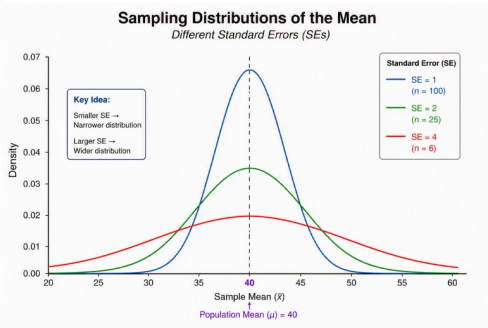
SDs cannot be directly compared
NT-proBNP is proportionally much more variable than LVEF

Site	Mean SBP (mmHg)	SD	CV
Site A	120	12	10%
Site B	180	12	6.7%

Which site is more consistent with the BP measurements ?

Uncertainty around the mean

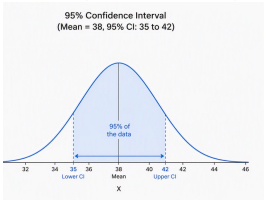




In search of the true mean .....

	Standard Deviation (SD)	Standard Error (SE)	95% Confidence Interval (CI)
Formula	$SD = \sqrt{\frac{\sum(x_i - x)^2}{n-1}}$	$SE = \frac{SD}{\sqrt{n}}$	$Mean \pm 1.96 \times SE$
Interpretation	Measures the **spread of individual observations values** around the mean. Larger sample stabilises the SD	Measures the **precision of the sample mean**. Larger samples give smaller SEs.	Gives the range of values likely to contain the **true population mean**. Larger samples give narrower intervals
Example	Mean diff = 10mmHg SD = 5 mmHg n = 25	SE = 5/5=1	10 ± (1.96×1) = 8 to 12

Interpreting confidence intervals



Sample 1 [---38---] ✓

Sample 2 [----42----] ✓

Sample 3 [------40------] ✓

Sample 4 [---] ✗

Sample 5 [-----41-----] ✓

...

True mean is 40 (which we do not know)

The 95%CI 35 to 42 means……

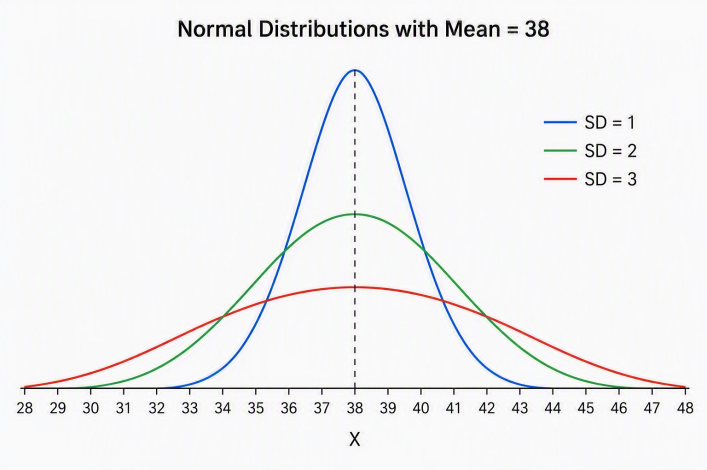
Which means of 100 repeated sampling experiments, 5 of the experiments may not contain the true 40.

Informal interpretation: "We are 95% confident that the true mean lies between 35 and 42"

The George Institute for Global Health India

9

Variability may not be always random



10

The George Institute for Global Health India

10

One person's noise is another person's signal

- Why was clopidogrel less effective in some groups ?
  - Stent thrombosis with Clopidogrel (CYP2C19 loss-of-function variants)
- Why do patients with apparently similar heart failure respond so differently to treatments?
  - HFrEF and HFpEF

- Treat variability as noise and try to reduce it
- Examine the remaining unexplained variability
- Discover hidden patient subgroups, mechanisms, or biomarkers

Key topics

- Variability and uncertainty
- Absolute versus relative effect measures
- Clinically important difference
- Interpreting trial results

Effect measures

Measure	Simple Formula	Interpretation
Mean Difference (MD)	$Mean_t - Mean_c$	Absolute difference in average outcome between treatment and control groups.
Cohen's d	$(Mean_t - Mean_c)$ / Pooled SD	Expresses difference in SD units. Rough guide: 0.2 = small, 0.5 = moderate, 0.8 = large effect.

13

Effect measures

Measure	Simple Formula	Interpretation
Mean Difference (MD)	$Mean_t - Mean_c$	Absolute difference in average outcome between treatment and control groups.
Cohen's d	$(Mean_t - Mean_c)$ / Pooled SD	Expresses difference in SD units. Rough guide: 0.2 = small, 0.5 = moderate, 0.8 = large effect.
Relative Risk (RR)	$Risk_t / Risk_c$	How many times more (or less) likely an event is in the treatment group compared with control. RR = 1 means no difference.
Absolute Risk Reduction (ARR)	$Risk_c - Risk_t$	Absolute decrease in event rate due to treatment.
Relative Risk Reduction (RRR)	$(Risk_c - Risk_t) / Risk_c$	Percentage reduction in risk relative to the control group.
Odds Ratio (OR)	$Odds_t / Odds_c$	Ratio of odds of an event between groups. OR = 1 means no association.
Number Needed to Treat (NNT)	1 / ARR	Number of patients who need treatment to prevent one additional adverse event. Lower is better.

14

Effect measures

Measure	Simple Formula	Interpretation
Mean Difference (MD)	$Mean_t - Mean_c$	Absolute difference in average outcome between treatment and control groups.
Cohen's d	$(Mean_t - Mean_c)$ / Pooled SD	Expresses difference in SD units. Rough guide: 0.2 = small, 0.5 = moderate, 0.8 = large effect.
Relative Risk (RR)	$Risk_t$ / $Risk_c$	How many times more (or less) likely an event is in the treatment group compared with control. RR = 1 means no difference.
Absolute Risk Reduction (ARR)	$Risk_c - Risk_t$	Absolute decrease in event rate due to treatment.
Relative Risk Reduction (RRR)	$(Risk_c - Risk_t)$ / $Risk_c$	Percentage reduction in risk relative to the control group.
Odds Ratio (OR)	$Odds_t$ / $Odds_c$	Ratio of odds of an event between groups. OR = 1 means no association.
Number Needed to Treat (NNT)	1 / ARR	Number of patients who need treatment to prevent one additional adverse event. Lower is better.
Hazard Ratio (HR)	$Hazard_t$ / $Hazard_c$	Relative rate at which events occur over time. HR = 0.80 suggests a 20% lower event rate at any point in time.
Win Ratio (WR)	Number of $Wins_t$ / Number of $Wins_c$	Compares paired patient outcomes using a hierarchy of clinical importance. WR > 1 favors treatment.
Restricted Mean Survival Time Difference (RMST Difference)	$RMST_t - RMST_c$	Difference in average event-free survival time up to a specified time horizon.

15

The George Institute for Global Health India

15

Effect measures (Absolute and relative)

Measure	Simple Formula	Interpretation
Mean Difference (MD)	$Mean_t - Mean_c$	Absolute difference in average outcome between treatment and control groups.
Cohen's d	$(Mean_t - Mean_c)$ / Pooled SD	Expresses difference in SD units. Rough guide: 0.2 = small, 0.5 = moderate, 0.8 = large effect.
Relative Risk (RR)	$Risk_t$ / $Risk_c$	How many times more (or less) likely an event is in the treatment group compared with control. RR = 1 means no difference.
Absolute Risk Reduction (ARR)	$Risk_c - Risk_t$	Absolute decrease in event rate due to treatment.
Relative Risk Reduction (RRR)	$(Risk_c - Risk_t)$ / $Risk_c$	Percentage reduction in risk relative to the control group.
Odds Ratio (OR)	$Odds_t$ / $Odds_c$	Ratio of odds of an event between groups. OR = 1 means no association.
Number Needed to Treat (NNT)	1 / ARR	Number of patients who need treatment to prevent one additional adverse event. Lower is better.
Hazard Ratio (HR)	$Hazard_t$ / $Hazard_c$	Relative rate at which events occur over time. HR = 0.80 suggests a 20% lower event rate at any point in time.
Win Ratio (WR)	Number of $Wins_t$ / Number of $Wins_c$	Compares paired patient outcomes using a hierarchy of clinical importance. WR > 1 favors treatment.
Restricted Mean Survival Time Difference (RMST Difference)	$RMST_t - RMST_c$	Difference in average event-free survival time up to a specified time horizon.

16

The George Institute for Global Health India

16

Absolute and (not or) relative effects

Low risk population
- Event rate in Control = 10%
- Event rate in Treatment = 7%

Measure	Calculation	Result
ARR	10% – 7%	3%
RR	7% / 10%	**0.70**
RRR	(10%–7%)/10%	**30%**
NNT	1/0.03	33

High risk population
- Event rate in Control = 40%
- Event rate in Treatment = 30%

Measure	Calculation	Result
ARR	40% – 30%	10%
RR	30% / 40%	**0.75**
RRR	(40%–30%)/40%	**25%**
NNT	1/0.01	10

The **relative reduction is identical, but absolute benefit is three times larger** in the high-risk group.

"Relative risk informs biology; absolute risk informs clinical decision making."

Certainty and sample size

Trial	HR	95% CI	Sample size	Interpretation	Impact
A	0.80	0.65-0.98	300	Likely beneficial	Need a larger trial for change in practice
B	0.80	0.50-1.28	100	Very uncertain	Uninformative, larger trial needed
C	0.80	0.78-0.82	1000	Highly precise (benefit)	Confirmatory findings

Need for further investigation and ability to change practice depends on the certainty of the results.

Clinically important difference

The smallest treatment effect that would matter enough to patients, clinicians, or policymakers to justify changing practice.

Trial	Primary Outcome	Effect Measure	Result (95% CI)	Statistically Significant?	Clinical Significance
FOURIER	MACE composite	HR	HR 0.85 (0.79-0.92)	Yes	Benefit is real but absolute effect modest (ARR 1.5%, NNT≈67)
REDUCE LAP-HF I	Exercise pulmonary capillary wedge pressure	Mean Difference	≈ -3.5 mmHg (-6.4 to -0.6)	Yes	Questioned because surrogate endpoint did not clearly translate into patient benefit

19

Sample size estimation

$$\text{Sample size} \propto \left(\frac{\text{Noise}}{\text{Signal}}\right)^2$$

- Expected magnitude of the signal
  - Smallest signal that will be clinically beneficial
- Estimate of the noise
  - Standard deviation observed in control group
- How much error (false positive) you are willing to make (type 1 error)
  - Alpha, two sided 5%,one sided 2.5%
- How sure you want your experiment to pick up the signal
  - Beta (1-beta) or power 80%, 85%, 90%

20

Summary

- Variability of measurements can be random or informative
- Random variability can be minimized by adequate sample
- Relative and absolute effects are important for interpretation
- Statistical significance does not always mean clinical significance

Resources (sample size)

- https://www.sealedenvelope.com/
  - For sample size for trials and randomisation sequence generation
- https://www.openepi.com/Menu/OE_Menu.htm
  - For sample size calculation for various study designs and statistical analyses
- https://www.psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower
  - Very good tool for sample size and power grpahs for various designs and analyses
  - https://pmc.ncbi.nlm.nih.gov/articles/PMC8441096/

Thank you!

ndevasenapathy@georgeinstitute.org.in

Golconda fort, 11th Century, Hyderabad, India