CAHS Research Education Program Research Skills Seminar

Introductory Biostatistics

16th Feb 2024



Presented by

Michael Dymock Biostatistician, Telethon Kids Institute





Neonatology | Community Health | Mental Health | Perth Children's Hospital



© 2024 CAHS Research Education Program Child and Adolescent Health Service, Department of Research Department of Health, Government of Western Australia

Copyright to this material produced by the CAHS Research Education Program, Department of Research, Child and Adolescent Health Service, Western Australia, under the provisions of the Copyright Act 1968 (C'wth Australia). Apart from any fair dealing for personal, academic, research or non-commercial use, no part may be reproduced without written permission. The Department of Research is under no obligation to grant this permission. Please acknowledge the CAHS Research Education Program, Department of Research, Child and Adolescent Health Service when reproducing or quoting material from this source.

Perth Children's Hospital **Foundation**

Introductory Biostatistics

PRESENTATION SLIDES

CAHS Research Education Program Research Skills Seminar Series

 Image: ResearchEducationProgram@health.wa.gov.au

 Image: Cahs.health.wa.gov.au/ResearchEducationProgram

Perth Children's Hospital **Foundation**

















More formally... Biostatistics can be conceptualised as the methodology for the design, analysis and interpretation of studies using health, medical or biological data Study design is important to efficiently answer your question of interest, save resources and conduct ethical research Rigorous analysis and modelling is important to compute the "correct" results Appropriate interpretation of the results is important to draw justifiable conclusions









A generic problem

- Suppose that we are interested in testing if a new treatment improves some generic biological measure (e.g., blood pressure, survival time, infection status, hospital admission time, lung capacity)
 - Assume the measure is continuous and higher values are preferable
 - Denote the mean value without treatment as α
 - Denote the **mean** value with treatment as $\alpha + \beta$
 - Denote the **variance** of the response as σ^2
- We want find out:
 - What is my best guess for the value of β?
 - How certain/uncertain am I in this guess?
 - Once I have data, can I make statements with evidence about the value of β?







What could the output look like?

Parameter	Estimate	Standard Error	P-Value
α	30.2	4.3	??
β	5.7	1.1	??
σ	2.1	1.7	??

- For the control arm:
- For the treatment arm:

 $y_i \sim N(30.2, 2.1^2)$

 $y_i \sim N(35.9, 2.1^2)$

But how should I interpret the uncertainty in these estimates??



What do we mean by uncertainty?

- In frequentist statistics, parameters have unknown but fixed values
- Because they are **unknown**, we cannot be sure how close our guess/estimate is to the true **fixed** value
- But we can estimate our uncertainty in the estimation itself
- We usually do this using confidence intervals







What is a hypothesis test?

- We assess the claim of a hypothesis against the evidence
- Specifically, we assess the evidence that a **model parameter** takes on a certain value or lies within a certain range
- E.g., one may hypothesise that β > 0 (i.e., that the treatment has some positive benefit)
- We can test this claim using the two hypotheses:
 - Null hypothesis: $H_0: \beta = 0$
 - Alternative hypothesis: $H_1: \beta > 0$

Froof by contradiction Suggest Theory X Find a contradiction (or counter example) to Theory X Therefore, Theory X is false Scientific arguments or theories (rarely) can ever be proven Instead, we gather evidence to support or counter a theory With a hypothesis test, we aim to assess evidence that counters the claim of the null hypothesis, thus supporting the alternative hypothesis BUT the failure to find counter evidence does not prove the null hypothesis We do this with p-values!









Is this an issue?

- The significance level is also called type one error
- This is the probability that I will incorrectly reject the null hypothesis
- Things happen by chance!
- If I were to test a faulty claim over and over again with a significance level of 5% then 5% of the time I would **incorrectly** claim it to be true!



Why do we care about sample size?

Decreasing the sample size

- Save resources!
- Ethics??



Increasing the sample size

- Increase precision!
- Ethics??











Simulate some data

- Let's simulate some observational data and see what happens
- Assume:
 - **Temperature** $t_i \sim \text{Bernoulli}(0.3)$
 - Ice-cream $x_i \sim \text{Bernoulli}(0.2 + 0.6t_i)$
 - Sunburn $s_i \sim \text{Bernoulli}(0.1 + 0.3t_i)$
- Run analyses with and without including temperature to assess the relationship between ice-cream consumption and sunburn for 200 participants

Without	temperature

Model: $s_i \sim \text{Bernoulli}^*(\alpha + \beta \times x_i)$ Output:

Parameter**	Estimate	Confidence Interval	P-Value
α	0.12	(0.05, 0.17)	
β	3.35	(0.05, 0.17)	<0.01

With temperature

Model: $s_i \sim \text{Bernoulli}^*(\alpha + \beta \times x_i + \gamma \times t_i)$ Output:

Parameter**	Estimate	Confidence Interval	P-Value		
α	0.10	(0.05, 0.17)			
β	1.36	(0.49, 3.66)	0.54		
γ	4.74	(1.79, 13.32)	<0.01		

*Using a logistic regression model (details omitted) **Interpret α as the intercept and β and γ as odds ratios

39

Hounding the confounding

- If we adjust for a confound in the analysis, then its effect disappears
- Without the adjustment it appears that ice-cream is incorrectly causally related to sunburn

J. H. H. H. K.

• However! It is still true to say that ice-cream and sunburn are **associated** as knowing one informs on the other

8880088

• Caveat: in complex phenomena it is not always correct to adjust ("control") for every variable – it depends on the causal structure!





Some examples

- Selection bias some designs only attract "healthy volunteers"
- Recall bias events are easier to remember events than non-events
- Efficacy bias if treatment is known the effect may be distorted (placebo)

- Survival bias outcomes are dependent on participants surviving
- Analysis bias adjusting for a "collider" may introduce bias



Why use randomisation?

- Randomisation breaks causal relationships
- What if we randomised participants to consume ice-cream (or not)?











Academic and a second second



What should I report?

- Estimated effect gives direction and magnitude
- Estimated uncertainty confidence intervals or analogous
- Evidence for conclusion p-values or analogous
- **Conclusion** e.g., treatment is beneficial

But interpret with caution!















<section-header><section-header><section-header><text><text><section-header><text><text>







Introductory Biostatistics

RESOURCE NOTES

CAHS Research Education Program Research Skills Seminar Series

 Image: ResearchEducationProgram@health.wa.gov.au

 Image: Cahs.health.wa.gov.au/ResearchEducationProgram

Perth Children's Hospital **Foundation**

Table of Contents

1.	Additional websites	38
2.	Bradford-Hill criteria for causality	38
3.	Statistical support contacts	38
	3.1. Perth Children's Hospital	38
	3.2. Telethon Kids Institute	38
	3.3. University of Western Australia	38
	3.4. WAHTN Clinical Trial and Data Management Centre	39
4.	Reporting guidelines	39
6.	Textbook: 'Basic Statistics'	41
7.	Article: 'Scientific method: Statistical errors'	41

1. Additional websites

John Hopkins University – Data Science Specialization
 https://www.coursera.org/specializations/jhu-data-science

2. Bradford-Hill criteria for causality

- a) Temporal relationship
- b) Strength of relationship
- c) Dose-response
- d) Consistency
- e) Plausibility
- f) Consideration of alternative explanations
- g) Experiment
- h) Specificity
- i) Coherence

3. Statistical support contacts

3.1. Perth Children's Hospital

Telethon Clinical Research Centre (TCRC)

Department of Research, Child and Adolescent Health Service

 Phone:
 (08) 6456 0124

 Email:
 CAHS.TCRC@health.wa.gov.au

 Website:
 https://cahs.health.wa.gov.au/Research/For-researchers/Research-suites-at-Perth-Childrens-Hospital

Biostatistics and Data Management Support through TCRC

https://cahshealthpoint.hdwa.health.wa.gov.au/directory/research/researchers/Pages/ Biostatistics.aspx (WA Health employees only)

- 3.2. Telethon Kids Institute **Consultancy Service** Email: Biometrics@telethonkids.org.au
- 3.3. University of Western Australia
 The Centre for Applied Statistics
 Offers free advice for UWA postgraduate research students
 Email: consulting-cas@uwa.edu.au
 - **CAHS Research Education Program Research Skills Seminar Series**

ResearchEducationProgram@health.wa.gov.au

Cahs.health.wa.gov.au/ResearchEducationProgram

3.4. WAHTN Clinical Trial and Data Management Centre

The Clinical Trial and Data Management Centre is a WAHTN enabling platform which aims to enhance clinical trials and related data management in Western Australia. The platform is a WAHTN-wide entity sharing expertise in clinical trial study design (including novel designs), clinical trial conduct, data management, data-linkage, analytical techniques for clinical trial datasets, bio-repository techniques and clinical registry datasets. It facilitates the pursuit of large-scale clinical trials and translational healthcare research in WA.

Phone:	(08) 9266 1970
Email:	CTDMC@curtin.edu.au
Website:	https://wahtn.org/platforms/clinical-trials-data-centre/

4. Reporting guidelines

Estimating intervention effects:	CONSORT (randomised clinical trial) TREND (non-randomised study)
Assessing causes & prognosis:	STROBE (observational studies)
Quantifying accuracy of diagnosis &	STARD (diagnostic studies)
prognosis tools:	REMARK (tumour markers prognostic studies)
Testing genetic association:	STREGA (genetic observational studies)
Aggregating evidence: systematic reviews & meta-analyses	PRISMA (previously known as QUOROM) [MOOSE, IOM]

CONSORT (CONsolidated Standards Of Reporting Trials)

Moher D, Hopewell S, Schulz KF, Montori V, Gotzsche PC, Devereux PJ, et al. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c869.

TREND (Transparent Reporting of Evaluations with Non-randomised Designs) Des Jarlais DC, Lyles C, Crepaz N, TREND Group. Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: the TREND statement. Am J Public Health 2004;94:361-6. **STROBE** (STrengthening the Reporting of OBservational studies in Epidemiology) Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, et al; STROBE Initiative. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. PLoS Med 2007;4:1628-54.

STARD (STAndards for the Reporting of Diagnostic accuracy studies) Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. BMJ2003;326:41-4.

REMARK (REporting recommendations for tumour MARKer prognostic studies) McShane LM, Altman DG, Sauerbrei W, Taube SE, Gion M, Clark GM. REporting recommendations for tumour MARKer prognostic studies (REMARK). Br J Cancer 2005;93:387-91.

STREGA (STrengthening the REporting of Genetic Associations) Little J, Higgins JP, Ioannidis JP, Moher D, Gagnon F, von Elm E, et al. Strengthening the reporting of genetic association studies (STREGA): an extension of the STROBE statement. Eur J Epidemiol2009;24:37-55.

PRISMA (preferred reporting items for systematic reviews and meta-analyses) Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med2009;6:e1000097. [Previously known as Quality of Reporting of Meta-analyses or QUOROM]

MOOSE Meta-analysis Of Observational Studies in Epidemiology <u>http://www.consortstatement.org/Media/Default/Downloads/Other%20Instruments/MOOSE%</u> <u>20Statement%202000.pdf</u>

IOM Institutes of Medicine Standards for Systematic Reviews Finding What Works in Health Care - NCBI Bookshelf (nih.gov)

5. Textbook: 'Basic Statistics'

De Veaux, R.D., Velleman, P.F., and Bock, D. (2012) "Stats: Data And Models (3rd Edition)" Pearson Education, Boston. Textbook excerpt; *Quick Guide to Inference*. The pages that follow are from "Stats: Data And Models (2nd Edition)" and provide a great

overview of common (basic) statistical formulas, methods and associated assumptions.

6. Article: 'Scientific method: Statistical errors'

Scientific method: Statistical errors

P values, the 'gold standard' of statistical validity, are not as reliable as many scientists assume.

Regina Nuzzo 12 February 2014

https://www.nature.com/news/scientific-method-statistical-errors-1.14700?WT.mc_id=FBK_NPG_1402_NatureNews **CAHS** Research Education Program



REDCap Workshop 1: Basic Walkthrough

27th February 2024 2.30 - 4.30pm

An introduction to project set-up

Workshops aim to directly build user skills in a guided environment, with time to ask questions and work on your own project.

This workshop offers an introduction to building databases in REDCap and covers basic concepts and best practices to equip researchers in building a database for their research project.

Workshop 1 is most useful to anyone building a new project in REDCap and those who have been tasked with managing an existing database. Open to DoH and TKI staff only.



Dr Giulia Peacock

CAHS Research Education Program Research Fellow

Giulia graduated medical school from the University of Notre Dame Fremantle in 2014. She supplements her clinical work as an Advanced Paediatric Trainee by conducting and publishing research in paediatric cardiology and through active involvement in medical education.

She is currently completing her Masters in Clinical Science, Child Health Research at the University of Western Australia. She hopes to ensure easy accessibility to research education and support, to create best outcomes for all patients.

PCH, TKI Level 5 Seminar Room



Accessible via the yellow or pink lifts



Places are capped at 40. Laptops are available if required



Government of Western Australia Child and Adolescent Health Service Perth Children's Hospital **Foundation**

researcheducationprogram@health.wa.gov.au



The CAHS Research Education Program REDCap Workshops are proudly supported by the Perth Children's Hospital Foundation and Telethon Kids Institute.

(08) 6456 0514



Research Skills Seminar Series

A free, open-access resource designed to upskill busy clinical staff and students and improve research quality and impact.

Using Social Media in Research

8th March 2024

12.30 -1.30pm

Building and maintaining your 'brand'



As a researcher, it is difficult to reach the public and broadcast your work. Building and maintaining your "brand" will help set you apart. This seminar provides the tools to connect with other researchers, build your network, and in the long run, effectively translate your research to a wider audience.

Meet the presenter



Dr Amy Page Senior Lecturer – School of Allied Health, UWA

Dr Amy Page is a registered consultant pharmacist and qualified biostatistician. Her vision is to reduce medicines-related harm while balancing symptom control to align with individualised treatment goals for older people to improve well-being. She undertakes knowledge creation and translation through implementation, practitioner development, communication and media, engagement with professional bodies and policy for sustained impact on pharmacy practice.

Perth Children's Hospital Auditorium

Level 5, 15 Hospital Ave Nedlands Accessible via pink or yellow lifts or

Access online via Teams or Avaya or Watch from a hosted video-conferencing site

- Fiona Stanley Hospital
- Lions Eye Institute
- Pathways in Shenton Park

(08) 6456 0514

Royal Perth Hospital





Government of Western Australia Child and Adolescent Health Service



A light lunch is provided for our in-person attendees. Bookings are essential.

The CAHS Research Education Program is proudly supported by the Perth Children's Hospital Foundation.





Interactive in pdf format

Last updated 13/2/24

CAHS Research Education Program

Research Skills Seminar Series

A free, open-access resource designed to upskill busy clinical staff and students and improve research quality and impact.

2024 Seminar Schedule

#	DATE	ТОРІС	PRESENTER	ENROL	WATCH
1	9 Feb	Research Fundamentals	Dr Kenneth Lee, UWA	REGISTER	<u>2023</u>
2	16 Feb	Introductory Biostatistics	Michael Dymock, TKI	REGISTER	<u>2023</u>
3	8 Mar	Social Media in Research	Dr Amy Page, UWA	<u>REGISTER</u>	<u>2023</u>
4	22 Mar	Introduction to Good Clinical Practice	Alexandra Robertson, CAHS	REGISTER	<u>2023</u>
5	19 Apr	Research Governance	Dr Natalie Giles and Tracy Chapman CAHS	REGISTER	<u>2023</u>
6	3 May	Scientific Writing	A/Prof Tony Kemp, UWA	REGISTER	<u>2023</u>
7	17 May	Project Management	Melanie Wright, SMHS	REGISTER	<u>2023</u>
Mon	20 May	World Clinical Trials Day Workshop	Dr Charlie McLeod, CAHS	REGISTER	<u>2023</u>
8	24 May	Getting the Most out of Research Supervision	A/Prof Sunalene Devadason, UWA/CAHS	REGISTER	<u>2022</u>
9	7 Jun	Research Impact	Dr Tamika Heiden, Vic	REGISTER	<u>2023</u>
10	21 Jun	REDCap for Data Capture and Management	Dr Giulia Peacock, CAHS	REGISTER	<u>2023</u>
11	19 Jul	Consumer & Community Involvement in Research	Belinda Frank, TKI	REGISTER	<u>2023</u>
12	26 Jul	Oral Presentation of Research Results	Dr Giulia Peacock, CAHS	REGISTER	2023
13	2 Aug	Sample Size Calculations	Michael Dymock, TKI	REGISTER	<u>2023</u>
14	9 Aug	Rapid Critical Appraisal of Scientific Literature	Dr Natalie Strobel, ECU	REGISTER	<u>2023</u>
15	16 Aug	Media and Communications in Research	Peta O'Sullivan, CAHS	REGISTER	<u>2023</u>
16	23 Aug	Knowledge Translation	Prof Fenella Gill, Curtin/CAHS	REGISTER	<u>2023</u>
17	30 Aug	Conducting Systematic Reviews	Prof Sonya Girdler, Curtin Uni	REGISTER	<u>2023</u>
18	6 Sep	Involving Aboriginal Communities in Research	Cheryl Bridge, TKI and co.	REGISTER	<u>2023</u>
19	11 Oct	Data Collection and Management	Dr Giulia Peacock, CAHS	REGISTER	<u>2023</u>
20	18 Oct	Grant Applications and Finding Funding	Dr Tegan McNab, TKI	REGISTER	<u>2023</u>
21	25 Oct	Statistical Tips for Interpreting Scientific Claims	Michael Dymock, TKI	REGISTER	<u>2023</u>
22	1 Nov	Survey Design & Techniques	Dr Giulia Peacock. CAHS	REGISTER	<u>2023</u>
23	15 Nov	Ethics Processes for Clinical Research in WA	Dr Natalie Giles, CAHS	REGISTER	2023
24	22 Nov	Qualitative Research Methods	Dr Lorna Davin, Notre Dame	REGISTER	2023
25	29 Nov	Innovation and Commercialisation	Dr Helga Mikkelsen (Brandon BioCatalyst) & Asbley Schoof (TKI)	REGISTER	2022

BioCatalyst) & Ashley Schoot (TKI)



Register via Trybooking.com

 \bigcirc

View recorded seminars online

(08) 6456 0514

researcheducationprogram@health.wa.gov.au

Subscribe to our mailing list

cahs.health.wa.gov.au/Research/For-researchers/Research-Education-Program

Seminars are held from 12:30-1:30pm at Perth Children's Hospital Auditorium and are broadcast live online through Avaya and Teams. Seminars are recorded and uploaded to our website within a week of presentation. Topics are subject to change with appropriate email notice provided. Handouts are revised and updated regularly. Attendance certificates are available on request.



Research Skills Seminar Series

A free, open-access resource designed to upskill busy clinical staff and students and improve research quality and impact.

Introductory Biostatistics

Thank you for your interest in this seminar

Please complete this 1-minute evaluation. Your feedback will help guide future presentations and educational activities.

How did you attend the seminar?

O Live seminar at Perth Children's Hospital

- \bigcirc Hosted video-conference on-site (e.g. FSH, Lions Eye, RPH etc.)
- Online via Avaya or Teams
- \bigcirc Viewed online recording

Please rate your agreement with the following statements:

	N/A	Strongly Disagree	Disagree	Neither	Agree	Strongly Agree	
The aims and objectives were clear	\bigcirc	\bigcirc	\bigcirc	\bigcirc	\bigcirc	\bigcirc	
The session was well structured	\bigcirc	\bigcirc	\bigcirc	\bigcirc	\bigcirc	0	
Presentation style retained my interest	\bigcirc	\bigcirc	\bigcirc	\bigcirc	\bigcirc	0	
The speaker communicated clearly	\bigcirc	\bigcirc	\bigcirc	\bigcirc	\bigcirc	0	
The material extended my knowledge	\bigcirc	\bigcirc	\bigcirc	\bigcirc	\bigcirc	0	
The additional resources were helpful	\bigcirc	\bigcirc	\bigcirc	\bigcirc	\bigcirc	\bigcirc	

What were the best aspects of the seminar?

What changes or improvements would you suggest?

How did you hear about the seminar?

(you can select multiple answer)

- Email invitation from Research Education Program
- CAHS Newsletters e.g. The Headlines, The View, CAHS Research Newsletter
- □ "Health Happenings" E-News
- Healthpoint Intranet Upcoming Events
- Collegiate lounge screen or other posted promotional material
- Telethon Kids Institute screen or other posted promotional material
- Telethon Kids Institute Newsletter

Other

cahs.health.wa.gov.au/ResearchEducationProgram

