Biostatistics Refresher

Douglas Whitaker, Ph.D.
Mount Saint Vincent University

ISANS IEP/IMG Bridging
2019-05-09

Topics

- Core Ideas: Prevalence & Incidence
- Types of Studies
- Measures of Risk
- Statistical Inference
- Measures for Screening and Diagnostic Tests

Notes

- Biostatistics & Epidemiology are *big* topics
- The measures and approaches discussed here are the core ideas
- Many studies use more sophisticated techniques and/or adjustments
- Trying to reproduce results from a paper?
  - Sophisticated techniques or adjustments might prevent this
  - Rounding might make numbers 'a little' off
- Proportions vs. Percentages
  - Proportions are more suitable for calculations; between 0 and 1
  - Percentages are often reported; between 0% and 100%

Incidence and Prevalence

- **Prevalence**: the *proportion* of a population with the disease (overall)

$$\text{Prevalence} = \frac{\text{Number of subjects with the disease}}{\text{Total number of subjects in the population}}$$

- **Incidence**: measures new cases of a disease in a population in a specific time period
  - Reported as *incidence rate* or *incidence proportion* (also called *incidence risk* or *cumulative incidence*)

Incidence

$$\text{Incidence Proportion} = \frac{\text{number of new cases of disease over time}}{\text{population without disease at baseline}}$$

$$\text{Incidence Rate} = \frac{\text{number of new cases of disease over time}}{\text{person-time at risk}}$$

Example 2.3 Investigators seek to determine the incidence of influenza among nurses at three local hospitals. They identify 500 nurses who do not have influenza as of December 1, 2010, and follow them for the development of influenza over the next 3 months. They find that ten of the study nurses develop influenza during follow-up. What is the incidence proportion of influenza?

Example 2.3 from Kestenbaum B. *Epidemiology and Biostatistics: An Introduction to Clinical Research*. Second edition. (Weiss NS, Shoben A, eds.). Cham: Springer; 2019.

Incidence

Detour: Instead of all 500 nurses, consider these 6.

What is the incidence rate for these 6 individuals?

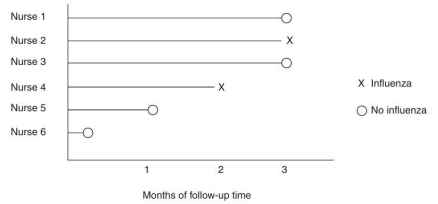

Fig. 2.1 Diagram of individual risk times and disease status

Table 2.1 List of individual risk times and disease status

	Develops influenza	Person-time	Reason for discontinuation
Nurse 1	No	3 months	Study ended
Nurse 2	Yes	3 months	Developed influenza
Nurse 3	No	3 months	Study ended
Nurse 4	Yes	2 months	Developed influenza
Nurse 5	No	1.25 months	Dropped out
Nurse 6	No	0.25 months	Dropped out
Total	2 cases	12.5 months	

Example 2.3 from Kestenbaum B. *Epidemiology and Biostatistics: An Introduction to Clinical Research*. Second edition. (Weiss NS, Shoben A, eds.). Cham: Springer; 2019.

Incidence

Example 2.3 Investigators seek to determine the incidence of influenza among nurses at three local hospitals. They identify 500 nurses who do not have influenza as of December 1, 2010, and follow them for the development of influenza over the next 3 months. They find that ten of the study nurses develop influenza during follow-up.

What is the incidence rate of influenza?

Need to know person-time at risk. Suppose it is 1200 months.

Example 2.3 from Kestenbaum B. *Epidemiology and Biostatistics: An Introduction to Clinical Research*. Second edition. (Weiss NS, Shoben A, eds.). Cham: Springer; 2019.

Incidence

- Incidence proportions: more interpretable
- Incidence rates: used for comparisons of disease among different groups
- Incidence rate is often multiplied by a factor (e.g. 10 or 1000) to make it more easily interpretable.

Morbidity and Mortality

- **Morbidity** refers to *illness* – not death
- **Mortality** refers to *death*

Prevalence measures morbidity in a population
Mortality rate measures deaths in the population

Types of Studies: Overview

- Case Reports
- Cross-Sectional Studies
- Cohort Studies
- Case-Control Studies
- Randomized Trials

Types of Studies: Case Reports

- Observational study
- Describes experiences of individuals with a disease or condition

- **Good for**: new diseases, generating hypotheses, raising awareness
- **Limitations**:
  - Cannot calculate incidence
  - No comparison group
  - Often describe individuals that are *not typical*
  - Often small sample sizes – lots of variability

Types of Studies: Cross-Sectional

- Measure the outcome of interest and exposures/factors *at the same time* from a group of interest.

Good for: establishing associations between exposures/factors and disease prevalence

Limitations: cannot establish a temporal link (though if only one direction of a link is plausible you may still be able to justify a temporal link)

Types of Studies: Cohort

Observational study that follows a group over time:

1. Exclude individuals with the disease
2. Define cohorts by measuring exposures
3. Follow over time to determine incidence

- **Good for**:
  - Temporal relationships
  - Studying multiple outcomes
- **Limitations**:
  - Confounding & bias
  - Not always efficient (rare or long latency)
- **Analysis**:
  - Relative risk
  - Attributable risk, population attributable risk

Types of Studies: Case-Control

Observational study that compares groups of individuals

1. Identify individuals **with** the condition of interest
2. Separately, identify another group of individuals **without** the condition of interest.
3. Work backward to determine what factors may be influencing having the condition of interest.

- **Good for**:
  - Studying rare diseases
  - Efficiency (using few participants)
  - Multiple risk factors
- **Limitations**:
  - Confounding & bias
  - Retrospective
  - **Cannot** calculate incidence
- **Analysis:**
  - **Cannot** use Relative Risk
  - Odds Ratio

Types of Studies: Randomized Trials

- Experimental, prospective study to compare treatments with controls
- Participants are *assigned* to an experimental condition (contrast with observational studies)
- **Good for**:
  - Establishing cause and effect (e.g. does a treatment perform better than control?)
- **Limitations**:
  - External validity issues (realism, monitored clinical environment, many exclusion criteria)

Risk

- Risk
- Absolute Risk Reduction (ARR)
- Number Needed to Treat (NNT)
- Number Needed to Harm (NNH)
- Relative Risk (RR)
- Relative Risk Reduction (RRR)
- Odds Ratio (OR)

		Event Occurred	
		Yes	No
Group	Treatment	a	b
	Control	c	d

These labels are arbitrary. Often exposed/unexposed is used. There is no firm rule about which variable is *rows* and which is *columns*. A description of the data and study design is key.

Risk

- Risk means the *proportion* of people for which an event occurs during the study.
  - This is sometimes called the *incidence proportion* (different from the *incidence rate*).
- The proportion in each group for which the Event did occur (Yes):

$$p_{\text{Treatment}} = \frac{a}{a+b}$$

$$p_{\text{Control}} = \frac{c}{c+d}$$

		Event Occurred	
		Yes	No
Group	Treatment	a	b
	Control	c	d

Risk and Study Design

- Note that the study design is deeply connected to the types of analyses that can be done with a 2x2 table.
- Example: In a **Cohort Study**, the *Exposed* group and *Unexposed* group belong to a single cohort. The cohort is followed to determine *Status*.

		Status	
		Disease	Not
Group	Exposed	a	b
	Unexposed	c	d

- Note these sums have meanings:
  - $a+b$ is the number of people in the *Exposed* group with the *Disease*
  - $a+c$ is the number of people in the Cohort with the *Disease*

These values can be used to estimate the prevalence of the *Disease*,

$$\frac{a+c}{a+c+b+d}$$

Risk and Study Design

- Note that the study design is deeply connected to the types of analyses that can be done with a 2x2 table.
- Example: In a **Case Control Study**, participants are recruited because they have the *Disease* and or because they do *Not* it.

	Status	
	Disease	Not
Exposed	a	b
Unexposed	c	d

- Note these sums have meanings:
  - $a+c$ is the number of people in the study with the *Disease* (i.e. selected in the *Disease* group)
  - $a+b$ is NOT the number of people in the *Exposed* group… there wasn't an exposure group!

Because the participants were selected based on outcome (*Disease* then *Not*), we **cannot** get an estimate of the prevalence.

Risk Difference

- Also known as:
  - Attributable Risk
  - Absolute Risk Increase (ARI)
  - Absolute Risk Reduction (ARR) (context)
- Compare the risks using *subtraction*

$$\text{Attributable Risk} = \text{Risk}_{\text{Control}} - \text{Risk}_{\text{Treatment}}$$

$$\text{Risk Difference} = p_{\text{Control}} - p_{\text{Treatment}}$$

- Be careful with order and context – usually structured so that the value is *positive*

		Event Occurred	
		Yes	No
Group	Treatment	a	b
	Control	c	d

Number Needed to Treat (NNT)

- Also known as Number Needed to Harm (NNH), depending on context
- Estimates the number of people who need to receive the treatment/intervention to prevent or cause one instance of the outcome
- Note the value should be positive and is usually rounded

$$NNT = \frac{1}{\text{Attributable Risk}} = \frac{1}{\text{Risk}_{\text{Control}} - \text{Risk}_{\text{Treatment}}}$$

$$NNT = \frac{1}{p_{\text{Control}} - p_{\text{Treatment}}}$$

Relative Risk

The **relative risk (RR)** is an *incidence ratio*.

$$RR = \frac{\text{Risk for } \mathbf{Treatment} \text{ Group}}{\text{Risk for } \mathbf{Control} \text{ Group}}$$

$$\text{RR} = \frac{\text{"Yes" proportion for } \mathbf{Treatment} \text{ Group}}{\text{"Yes" proportion for } \mathbf{Control} \text{ Group}}$$

$$RR = \frac{a/(a+b)}{c/(c+d)}$$

		Event Occurred	
		Yes	No
Group	Treatment	a	b
	Control	c	d

Possible values for RR and their meaning:
- $RR > 1$: The Treatment group has a *higher* risk than the Control group
- $RR = 1$: The Treatment group has the *same* risk as the Control group
- $RR < 1$: The Treatment group has a *lower* risk than the Control group

Cannot be calculated from case-control studies

Relative Risk

A study of patients presenting GeoSentinel clinics following rabies exposure for rabies post-exposure provalaxis (RPEP) examined the relationship between receiving rabies immunoglobin (RIG) and where RPEP was started (in country of exposure or not). (Gautret et al., 2018)

		RIG given in country of exposure	
		Yes	No
Country of Exposure	Thailand	43	44
	Other	78	139

		RIG given in country of exposure	
		Yes	No
Country of Exposure	Indonesia	5	82
	Other	42	175

Relative Risk

		RIG given in country of exposure	
		Yes	No
Country of Exposure	Thailand	43	44
	Other	78	139

The relative risk for receiving RIG in the country of exposure for Thailand is 1.38. Reasonable interpretations of 1.38 include:

- Exposure to rabies in Thailand is associated with 1.38 times greater chance of receiving RIG compared with exposure in other countries.
- Exposure to rabies in Thailand is associated with a 38% greater chance of receiving RIG compared with exposure in other countries.

Relative Risk

		RIG given in country of exposure	
		Yes	No
Country of Exposure	Indonesia	5	82
	Other	42	175

The relative risk for receiving RIG in the country of exposure for Indonesia is 0.30. Reasonable interpretations of 0.30 include:

- Exposure to rabies in Indonesia is associated with a 70% lower chance of receiving RIG compared with exposure in other countries.
- Exposure to rabies in a country *other than* Indonesia is associated with a 3.33 times greater chance of receiving RIG compared with exposure in Indonesia.

Relative Risk Reduction (RRR)

- This measure is a blend of two:
  - Relative Risk
  - Risk Difference (Attributable Risk)
- The *risk difference* is compared to the *risk for the control* group using division:

$$RRR = \frac{\text{Attributable Risk}}{\text{Risk for } \mathbf{Control} \text{ Group}}$$

$$RRR = \frac{\text{Risk}_{\text{Control}} - \text{Risk}_{\text{Treated}}}{\text{Risk}_{\text{Control}}} = \frac{p_{\text{Control}} - p_{\text{Treatment}}}{p_{\text{Control}}}$$

Odds Ratio

The **odds ratio (OR)** compares *odds* for two groups.

Odds is a technical term for $\frac{p_{success}}{p_{failure}}$ and NOT a synonym for "probability."

The odds ratio is more difficult to interpret then the relative risk.

$$OR = \frac{a/b}{c/d} = \frac{ad}{bc}$$

Can be calculated from case-control studies… often a good estimate for relative risk.

$$OR = RR \times \left(\frac{1 - p_{\text{Treatment}}}{1 - p_{\text{Control}}}\right)$$

		Event Occurred	
		Yes	No
Group	Treatment	a	b
	Control	c	d

Possible values for RR and their meaning:

$OR > 1$: The Treatment group has a *higher* odds than the Control group

$OR = 1$: The Treatment group has the *same* odds as the Control group

$OR < 1$: The Treatment group has a *lower* odds than the Control group

Can be calculated from case-control studies

Relative Risk and Odds Ratio

- OR is more difficult to interpret… but we often want to (and can) interpret it *like* a RR
- Note that for both measures the reciprocal is also a valid value.
- That is, $\frac{1}{RR}$ is a relative risk, and $\frac{1}{OR}$ is an odds ratio.
- The relationship (less than, greater than) 1 will change.
- This might make the value easier or harder to interpret.
- Neither RR nor OR are symmetric about 1 (e.g. 1.5 vs. 0.67)
- Exposed group usually in the numerator (convention).

Statistical Inference

Statistical Inference

Use data from a small group (sample) …

… to draw conclusions about a larger group (population).

Statistical Inference

Two major approaches:

- Hypothesis testing (p-values)
  - "Which of two descriptions of the population is better-supported by the data?"
- Confidence Intervals (CIs)
  - "Based on the data, what are plausible values for an unknown population value?"

- Underlying logic of statistical inference is *sophisticated and subtle* – be careful when reporting/documenting statistics (see NHST)

Hypothesis Testing

- Null hypothesis (H_0): usually "no effect" (or equivalent)
- Alternative hypothesis (H_A): usually "there is some effect"

- Critical idea:
  - We **assume that the null hypothesis is true** and collect evidence *against it*.
  - If we collect *enough* evidence against the null hypothesis to think it is wrong…
  - Then we think the alternative hypothesis is a better description of reality.
  - We do **NOT** *accept* or *prove* the null hypothesis true.
  - *At best* we "fail to reject" the null hypothesis.

Hypothesis Testing

A p-value quantifies the strength of the evidence against the null hypothesis.

A p-value answers this question:

- If the null hypothesis is true,
- what is the probability
- we would observe a test statistic as extreme
- (or more extreme)
- than the test statistic we actually did observe?

Hypothesis Testing

A p-value quantifies the strength of the evidence against the null hypothesis.

A p-value answers this question:

- If the null hypothesis is true, what is the probability we would observe a test statistic as extreme (or more extreme) than the test statistic we actually did observe?

  A *small* p-value is *strong evidence against* the null hypothesis.

  A BIG p-value is *weak evidence against* the null hypothesis.

- Caution: This feels *counterintuitive* to many people at first.

Hypothesis Testing

- Cut-offs/guidelines for p-values depend on the context, but one set you might consider is

p−value	Strength of Evidence
$\text{p}-\text{value} > 0.10$	Almost no evidence for H_A
$0.05 < \text{p}-\text{value} \leq 0.10$	Weak evidence for H_A
$0.01 < \text{p}-\text{value} \leq 0.05$	Good evidence for H_A
$\text{p}-\text{value} \leq 0.01$	Very good evidence for H_A

- Note that these cutoffs reflect a continuum of evidence *against the null hypothesis,* H_0.

Hypothesis Testing

- A study compared healthcare costs for patients prescribed a High Dose of gabapentin to those prescribed a Low Dose. (Fleet et al., 2018)

Table 5. Average per person adjusted cost in 30-day follow-up period.

All Patients	Gabapentin	Emergency Visit
High Dose	$64.75	$103.70
Low Dose	$33.53	$90.30
Average Cost Differential	$31.22	$13.41
P-value	<0.0001	<0.0001

- If there was really no difference in average cost for Emergency Visits, the probability we would see an average difference of $13.41 (or greater) is less than 0.0001.

Hypothesis Testing

- Consider this excerpt of Table 3 from the rabies study earlier (Gautret et al., 2018)

Characteristic		RIG given in country of exposure (N = 87)	RIG not given in country of exposure (N = 217)	Relative risk of receiving RIG in the country of exposure (95% CI)	*P* value
Countries of exposure n (%)	Thailand	43 (49.4)	78 (39.5)	1.38 (1.0–1.8)	0.02
	Indonesia	5 (5.8)	42 (19.4)	0.30 (0.1–0.7)	0.01
	India	3 (3.4)	13 (6.0)	0.58 (0.2–2.0)	0.38
	China	1 (1.2)	12 (5.5)	0.21 (0.0–1.6)	0.13
	Algeria	6 (6.9)	7 (3.2)	2.14 (0.7–6.2)	0.16
	Philippines	8 (9.2)	1 (0.5)	19.95 (2.5–157.2)	0.01
	Sri Lanka	8 (9.2)	5 (2.3)	3.99 (1.3–11.9)	0.013

- For which countries have a RR significantly different from 1?

Type I and Type II Errors

- If we reject H_0 when H_0 is true, we have committed a **Type I error**.
- If we fail to reject H_0 when H_0 is false, we have committed a **Type II error**.

		Truth about the population	
		H_0 true	H_0 false (H_a true)
Conclusion based on sample	Reject H_0	**Type I error**	*Correct conclusion*
	Fail to reject H_0	*Correct conclusion*	**Type II error**

Type I and Type II Errors

- If we reject H_0 when H_0 is true, we have committed a **Type I error**.
- If we fail to reject H_0 when H_0 is false, we have committed a **Type II error**.

		Actual Truth	
Conclusion of trial	*Guilty* Reject H_0		
	Not Guilty Fail to reject H_0		

Type I and Type II Errors

- How can we reduce the chances that we *send an innocent person to jail*?
  - How can we lower the chances of a **Type I Error**?
- What are the consequences of this?

		Actual Truth	
		Innocent H_0 true	*Committed Crime* H_0 false (H_a true)
Conclusion of trial	*Guilty* Reject H_0	**Type I error**	*Correct conclusion*
	Not Guilty Fail to reject H_0	*Correct conclusion*	**Type II error**

Type I and Type II Errors

- How can we reduce the chances that we *let a guilty person go free*?
  - How can we lower the chances of a **Type II Error**?
- What are the consequences of this?

		Actual Truth	
		Innocent H_0 true	*Committed Crime* H_0 false (H_a true)
Conclusion of trial	*Guilty* Reject H_0	**Type I error**	*Correct conclusion*
	Not Guilty Fail to reject H_0	*Correct conclusion*	**Type II error**

Type I and Type II Errors

- Replication studies and meta-analyses are important
- Importance of Type I & Type II Errors strongly depend on context
- Need to know statistical hypotheses (may not be explicitly written, but usually standard – consult references)
- **Power** is the ability to correctly reject the null hypothesis

$$\text{Power} = 1 - \text{P(Type II Error)}$$

Confidence Intervals

- Provide an interval of values that are all *plausible* for a true, unknown population value based on the data
- A confidence level is specified (often 95%)

- Want to be more confident (e.g. 95% -> 99%)?
- Interval gets w i d e r .

- Want a narrower (more precise) interval?
- Lower confidence level (e.g. 95% -> 90%)

Confidence Intervals

- The confidence level (e.g. 95%) is a statement about the confidence in *the method* and not a statement of confidence about the specific interval calculated!
- That is, if you commit to making 95% confidence intervals over and over and over, about 95% of them will contain the true (unknown) value you want to identify.
- And therefore about 5% will *not* contain the true (unknown) value you want to identify. (That is, they will be wrong.)
- No way of knowing which are right and which are wrong.
- (Confidence in the *method!*)

Confidence Intervals

- Confidence Intervals can be used in a way analogous to Hypothesis Testing.
- In Hypothesis Testing, there is often a single value in the null hypothesis.
  - Difference in values? Usually null hypothesis is "0"
  - Ratio of values? Usually null hypothesis is "1"
- Examine the CI:
  - if this value is *in* the CI, then it is plausible…
  - if it is plausible, that is *not* evidence against the null hypothesis…
  - "fail to reject" the null hypothesis
- If the value is *not* in the CI, it is not plausible, go with the alternative hypothesis

Hypothesis Testing

- Consider this excerpt of Table 3 from the rabies study earlier (Gautret et al., 2018)

Characteristic		RIG given in country of exposure (N = 87)	RIG not given in country of exposure (N = 217)	Relative risk of receiving RIG in the country of exposure (95% CI)	*P* value
Countries of exposure n (%)	Thailand	43 (49.4)	78 (39.5)	1.38 (1.0–1.8)	0.02
	Indonesia	5 (5.8)	42 (19.4)	0.30 (0.1–0.7)	0.01
	India	3 (3.4)	13 (6.0)	0.58 (0.2–2.0)	0.38
	China	1 (1.2)	12 (5.5)	0.21 (0.0–1.6)	0.13
	Algeria	6 (6.9)	7 (3.2)	2.14 (0.7–6.2)	0.16
	Philippines	8 (9.2)	1 (0.5)	19.95 (2.5–157.2)	0.01
	Sri Lanka	8 (9.2)	5 (2.3)	3.99 (1.3–11.9)	0.013

- For which countries have a RR significantly different from 1?

Sensitivity and Specificity

- Screening diseases – need a gold standard
- "Accuracy" of a test is not good enough
- The **sensitivity** of a test is its ability to correctly identify patients who have the condition being tested for
  - Correct positives
- The **specificity** of a test is its ability to correctly identify patients who do not have the condition being tested for
  - Correct negatives

Sensitivity and Specificity

TP = True Positive
TN = True Negative
FN = False Negative
FP = False Positive

		True Disease Status	
		Yes	No
Screening Result	Positive	TP	FP
	Negative	FN	TN

$$\text{Sensitivity} = \frac{\text{True Positives}}{\text{All Yes Disease}} = \frac{\text{TP}}{\text{TP} + \text{FN}}$$

$$\text{Specificity} = \frac{\text{True Negatives}}{\text{All No Disease}} = \frac{\text{TN}}{\text{TN} + \text{FP}}$$

$$\text{False Positive Error Rate} = \frac{\text{False Positives}}{\text{All No Disease}} = \frac{\text{FP}}{\text{TN} + \text{FP}}$$

The rate at which true No disease patients are incorrectly flagged Positive.

$$\text{False Negative Error Rate} = \frac{\text{False Negatives}}{\text{All Yes Disease}} = \frac{\text{FN}}{\text{TP} + \text{FN}}$$

The rate at which true Yes disease patients are incorrectly flagged Negative.

Sensitivity and Specificity

TP = True Positive
TN = True Negative
FN = False Negative
FP = False Positive

		True Disease Status	
		Yes	No
Screening Result	Positive	TP	FP
	Negative	FN	TN

$$\text{Positive Predictive Value(PPV)} = \frac{\text{True Positives}}{\text{All Positives}} = \frac{\text{TP}}{\text{TP} + \text{FP}}$$

The proportion of patients with *Positive* results who *Yes* had the disease

$$\text{Negative Predictive Value(NPV)} = \frac{\text{True Negatives}}{\text{All Negatives}} = \frac{\text{TN}}{\text{TN} + \text{FN}}$$

The proportion of patients with *Negative* results who *No,* did not have the disease

$$\text{Likelihood Ratio Positive (LR+)} = \frac{\text{Sensitivity}}{1 - \text{Specificity}}$$

The higher this value is, the better a test is. (Should be much larger than 1.)

$$\text{Likelihood Ratio Negative (LR−)} = \frac{1 - \text{Sensitivity}}{\text{Specificity}}$$

The lower this value is, the better a test is. (Should be as close to 0 as possible.)

References

- Katz DL, Elmore JG, Wild DMG, Lucan SC, eds. *Jekel's Epidemiology, Biostatistics, Preventive Medicine, and Public Health*. 4th ed. Philadelphia, Pa. ; London: Saunders; 2014.
- Kestenbaum B. *Epidemiology and Biostatistics: An Introduction to Clinical Research*. Second edition. (Weiss NS, Shoben A, eds.). Cham: Springer; 2019.
- Noordzij M, Dekker FW, Zoccali C, Jager KJ. Measures of Disease Frequency: Prevalence and Incidence. *Nephron Clin Pract*. 2010;115(1):c17-c20. doi:10.1159/000286345
- Porta MS, Greenland S, Hernán M, Silva I dos S, Last JM, International Epidemiological Association, eds. *A Dictionary of Epidemiology*. Six edition. Oxford: Oxford University Press; 2014.
- Shapiro K, Brown SA. *RxPrep Course Book: A Comprehensive Course for the NAPLEX® and CPJE*. RxPrep, Inc.; 2015.

Examples

- Christiansen SC, Næss IA, Cannegieter SC, Hammerstrøm J, Rosendaal FR, Reitsma PH. Inflammatory Cytokines as Risk Factors for a First Venous Thrombosis: A Prospective Population-Based Study. Greaves M, ed. *PLoS Med*. 2006;3(8):e334. doi:10.1371/journal.pmed.0030334
- Fleet JL, Dixon SN, Kuwornu PJ, et al. Gabapentin dose and the 30-day risk of altered mental status in older adults: A retrospective population-based study. Wu P-H, ed. *PLOS ONE*. 2018;13(3):e0193134. doi:10.1371/journal.pone.0193134
- Galappaththi-Arachchige HN, Holmen S, Koukounari A, et al. Evaluating diagnostic indicators of urogenital Schistosoma haematobium infection in young women: A cross sectional study in rural South Africa. Knight M, ed. *PLOS ONE*. 2018;13(2):e0191459. doi:10.1371/journal.pone.0191459
- Gautret P, Angelo KM, Asgeirsson H, et al. Rabies post-exposure prophylaxis started during or after travel: A GeoSentinel analysis. Gilbert AT, ed. *PLoS Negl Trop Dis*. 2018;12(11):e0006951. doi:10.1371/journal.pntd.0006951
- Genton B, D'Acremont V, Rare L, et al. Plasmodium vivax and Mixed Infections Are Associated with Severe Malaria in Children: A Prospective Cohort Study from Papua New Guinea. Rogerson S, ed. *PLoS Med*. 2008;5(6):e127. doi:10.1371/journal.pmed.0050127
- Goarant C, Bourhy P, D'Ortenzio E, et al. Sensitivity and Specificity of a New Vertical Flow Rapid Diagnostic Test for the Serodiagnosis of Human Leptospirosis. Büscher P, ed. *PLoS Negl Trop Dis*. 2013;7(6):e2289. doi:10.1371/journal.pntd.0002289
- Zeidan AM, Long JB, Wang R, et al. Risk of myeloid neoplasms after radiotherapy among older women with localized breast cancer: A population-based study. Hills RK, ed. *PLOS ONE*. 2017;12(9):e0184747. doi:10.1371/journal.pone.0184747

Resources

- *The Little Handbook of Statistical Practice*
  - **StatisticalPractice.com** redirects to http://www.jerrydallal.com/LHSP/LHSP.HTM
  - Old but good