

Objectives

- * This presentation aims to present information on common errors in scientific research originating from bias and confounding.
- * At the end of this session, the participants are expected to;
 - * Discuss the different types of bias and their effect to study reporting
 - * Discuss confounding variables and their role in interpreting scientific studies.

Internal vs. External Validity

- * Internal: Did the study measure what it said it would?
- * External: Are the results applicable to your setting?

Bias

- * Bias may be defined as any systematic error in a study that results in an incorrect estimate of the association between exposure and risk of disease.
- * Selection Bias
- * Application Bias
- * Measurement Bias
- * Attrition Bias
- * Publication Bias

<https://methods.cochrane.org/bias/sites/methods.cochrane.org.bias/files/public/uploads/6.%20Assessing%20risk%20of%20bias%20in%20included%20studies%20v1.0%20Standard%20author%20slides.pdf>

Selection bias

- * Was the sampling random?
- * Was allocation concealed?
- * What about the non-respondents?

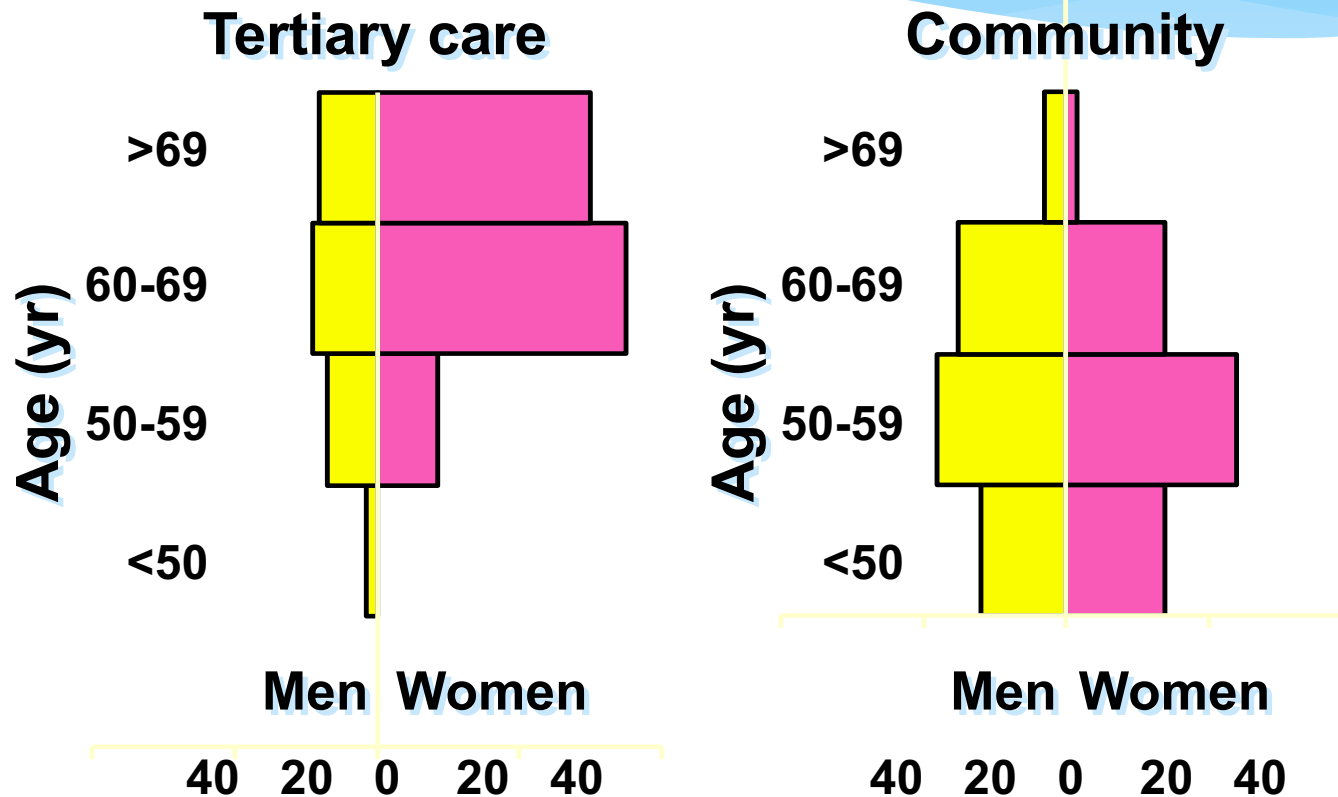
Selection Bias

- * Selection Bias occurs when recruitment processes lead to a sample that systematically differs from the target population in important characteristics
- * For example, you are studying the effect of cell phone towers on head/neck cancers
 - * Can you recruit patients based on cell phone numbers?

Selection Bias

- * Patients seen at a tertiary care center may differ from those seen in a primary care setting, and those will differ from the general population.

Studied Population



Participation Bias

Healthy Worker Effect

- * Mortality rate relative to general population by length of employment in vinyl chloride industry:
 - * 0-4 years: 0.37
 - * 5-9 years: 0.63
 - * 10-14 years: 0.75
 - * 15+ years: 0.94
 - * Overall: 0.75

Application Bias

- * How was the study applied?
- * Blinding?
 - * Single
 - * Double
- * Placebo, positive control?

Exposure Assessment

- * Particular problem in case control studies.
- * Recall may be different because of knowledge of disease.
- * Attitude and knowledge may change after having a diagnosis.

Measurement Bias

- * Was the measurement precise?
 - * Example: arterial blood pressure measurement
- * Was the psychometric instrument validated
 - * Reliability-Validity?
- * Did you have blinding on measurement?
- * Self-reported or researcher-collected data?
- * What about the memory factor?

Measurement Bias: Outcome Assessment

- * Assessment of outcome may differ because of:
 - * Knowledge of exposure
 - * Knowledge of hypothesis
 - * Conflict of interest?

Recall Bias

- * Birth defects and prenatal EtOH exposure
- * Who is more likely to remember that one glass of wine during the first trimester?
 - * Mom with normal, healthy baby?
 - * Mom with baby with cleft palate?

Measurement Bias

- * Measurement bias occurs when characteristics of measurements systematically lead to differences in the study sample as compared to true characteristics in the target population
- * You are studying blood pressure, and you use a standard blood pressure cuff for all patients.

Hawthorne Effect

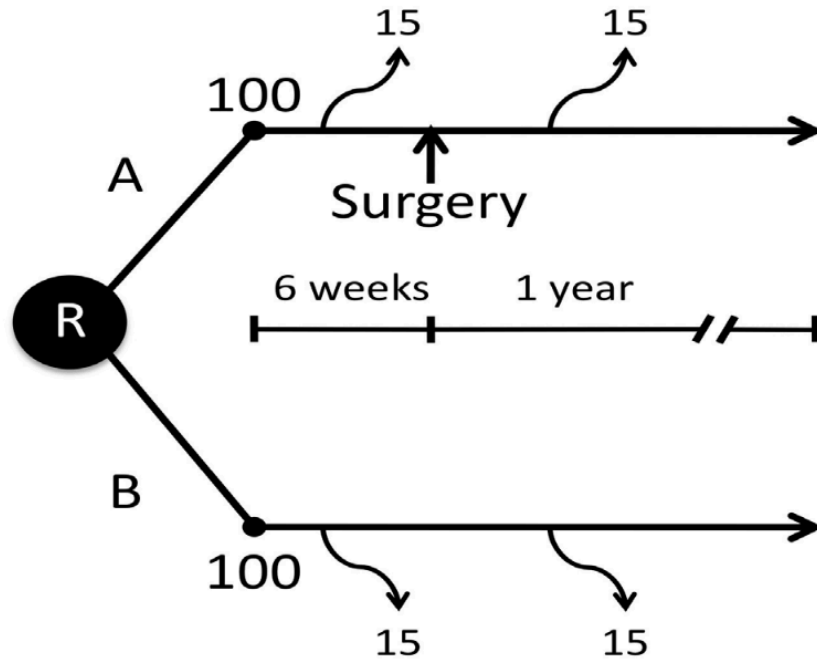
- * The Hawthorne effect refers to a type of reactivity in which individuals modify an aspect of their behavior in response to their awareness of being observed.
- * The response of participants may change once they know people are concerned about them.

https://en.wikipedia.org/wiki/Hawthorne_effect

Attrition Bias (Incomplete outcome data)

- * loss to follow up, withdrawals, other missing data
- * exclusions –some available data not included in report
- * how much data is missing from each group?
- * why is it missing?
- * how were the data analysed? (ITT)

ITT



	<u>Intention-to-treat</u>	<u>Per-protocol</u>
	$30/100 = 0.3$	$15/85 = 0.18$
	$RR = 1$	$RR = 0.59$
	$RRR = 0$	$RRR = 0.41$
	$30/100 = 0.3$	$30/100 = 0.3$
	No effect (true)	Apparent effect (untrue)

A = medical management + surgery

B = medical management only

Figure. Hypothetical prospective randomized controlled trial evaluating effectiveness of intervention (A = medical management + surgery) vs. control (B = medical management only) in patients with cardiovascular disease.

R, randomization; RR, relative risk; RRR, relative risk reduction.

Publication Bias

- * Statistically significant results more likely to be reported
- * Journals with impact factors had a 100% increased probability of publishing a statistically significant result compared with journals with no impact factor (odds ratio [OR], 1.99; 95% CI, 1.19-3.31).

<https://pubmed.ncbi.nlm.nih.gov/19892276/>

Other sources of bias

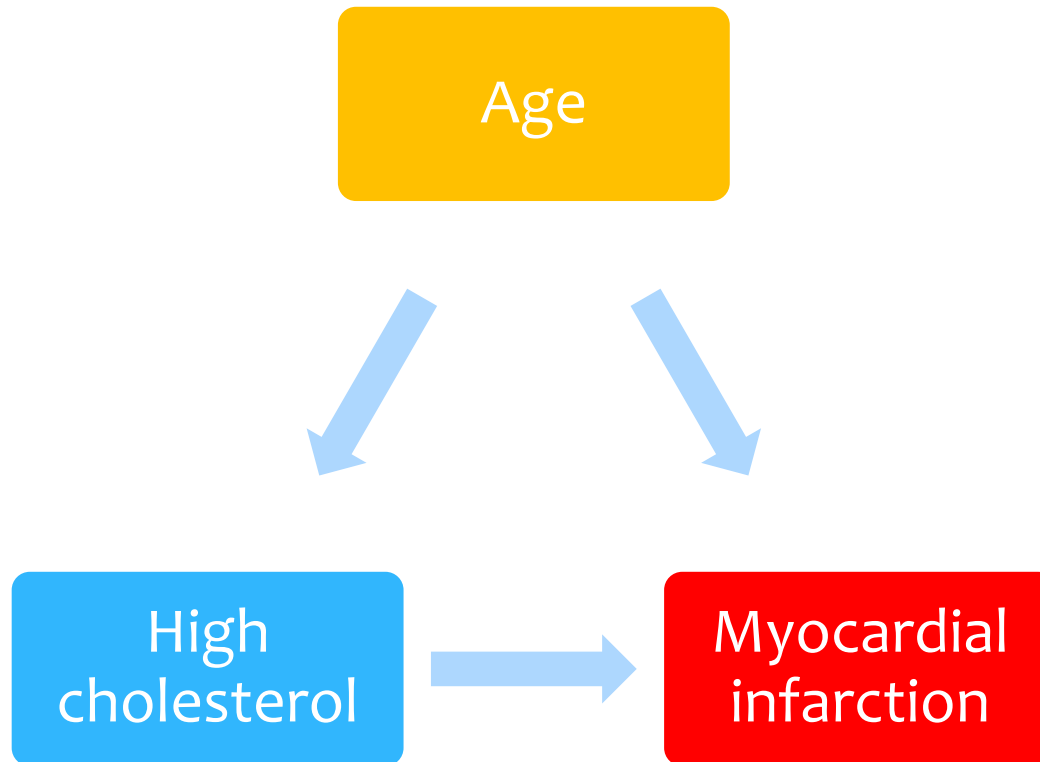
- * Imprecision
 - * Small sample size
- * Diversity
 - * Inadequate dose,
 - * Unusual population
- * Other measures of quality
 - * Ethics approval,
 - * Funding

Methods to Eliminate Bias

- * RCTs allow limiting biases
- * Design
 - * Randomization
 - * Restriction
 - * Matching
- * Measurement
 - * Masking
- * Analysis
 - * Stratification
 - * Modeling

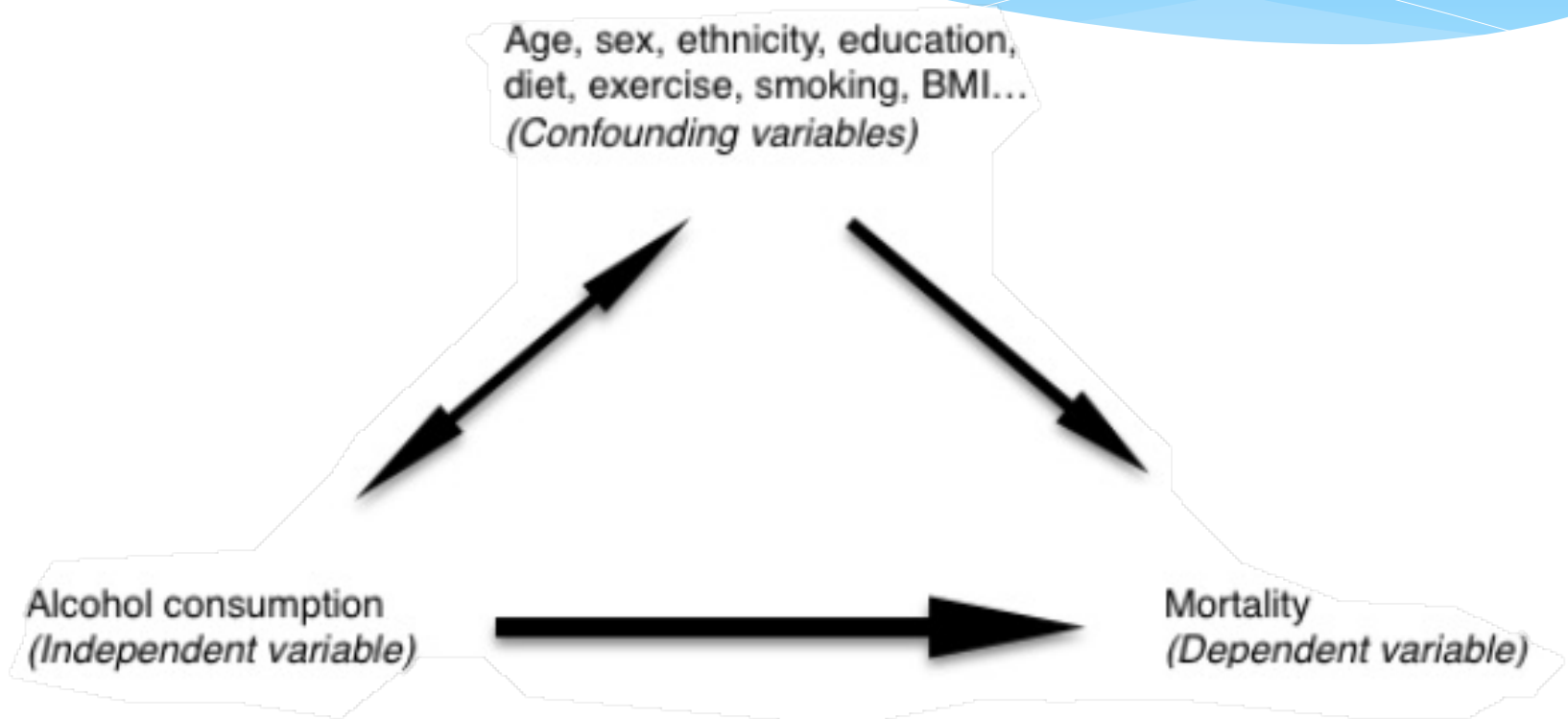
Confounders

- * Confounders are factors affecting both input and outcome variables.



- * **In order for a variable to be considered as a confounder:**
- * 1. The variable must be independently associated with the outcome (i.e. be a risk factor).
- 2. The variable must be associated with the exposure under study in the source population.
- 3. It should not lie on the causal pathway between exposure and disease.

Other examples of confounders



<https://s4be.cochrane.org/blog/2018/10/01/a-beginners-guide-to-confounding/>

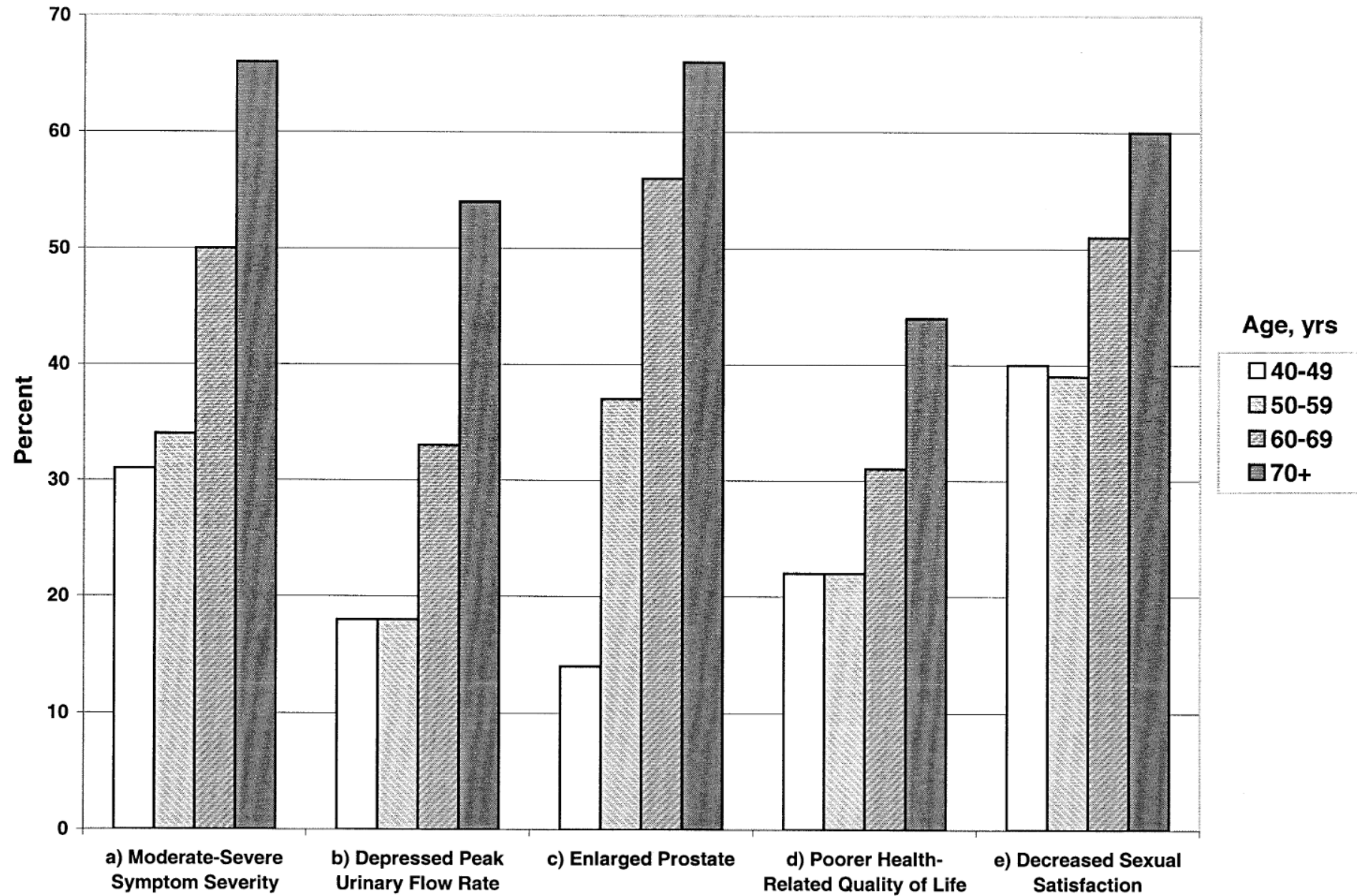
Frequency of sexual activity and prostatic health: fact or fairy tale?

TABLE 1. Cross-sectional association between frequency of ejaculation and urologic measures

Ejaculations/mo	IPSS		Qmax (mL/s)		Prostate Volume (cm ³)	
	≤7	>7	≥12	<12	≤30	>30
0–4	381 (50.5)	374 (49.5)	113 (63.8)	64 (36.2)	74 (49.0)	77 (51.0)
>4	588 (62.2)	357 (37.8)	194 (78.9)	52 (21.1)	141 (64.7)	77 (35.3)
Odds ratio (95% CI)	0.62 (0.51–0.75)		0.47 (0.31–0.73)		0.53 (0.34–0.80)	

KEY: IPSS = International Prostate Symptom Score; Qmax = peak urinary flow rate.
Data presented as number of patients, with the percentage in parentheses, unless otherwise noted.

[https://www.goldjournal.net/article/S0090-4295\(02\)02265-3/fulltext](https://www.goldjournal.net/article/S0090-4295(02)02265-3/fulltext)



Ejaculation Frequency Decreases with Age

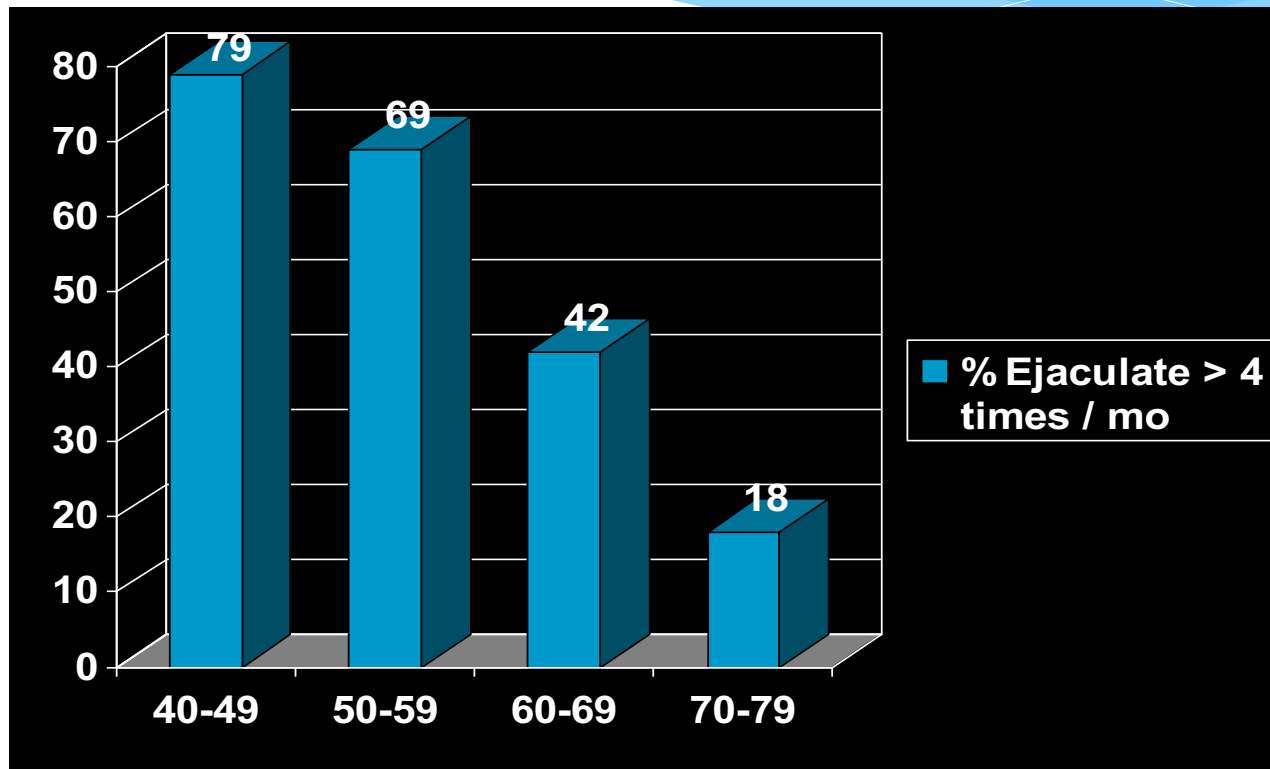


TABLE II. Dose-response relationship between frequency of ejaculation and urologic and quality-of-life measures

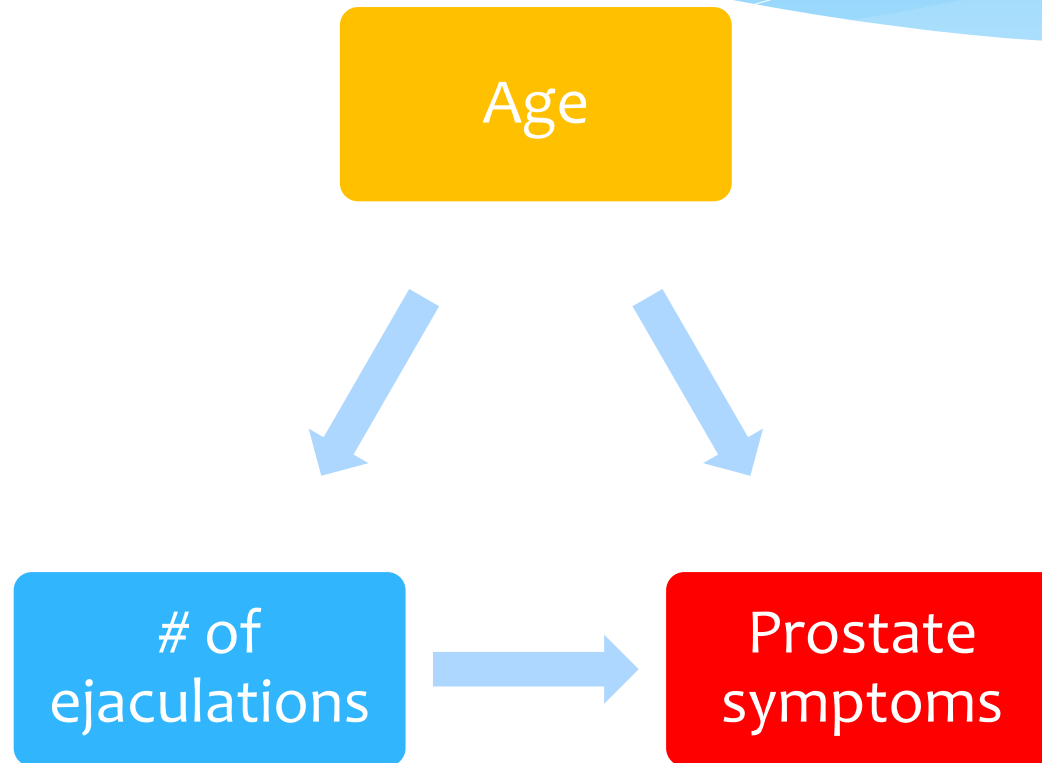
Ejaculations/ mo	IPSS (>7 vs. ≤7)	Qmax (≤12 vs. >12 mL/s)	Prostate Volume (>30 vs. ≤30 cm ³)	Health-Related Quality of Life (Excellent, Very Good vs. Good, Fair, Poor)	Sexual Satisfaction (Satisfied vs. Neutral, Dissatisfied)
0	1.0*	1.0*	1.0*	1.0*	1.0*
1–4	0.78 (0.58–1.06)	1.40 (0.70–2.80)	0.72 (0.35–1.46)	1.93 (1.42–2.63)	2.18 (1.54–3.08)
5–12	0.57 (0.43–0.76)	0.64 (0.33–1.27)	0.40 (0.21–0.80)	4.00 (2.95–5.42)	7.91 (5.65–11.06)
>12	0.38 (0.26–0.57)	0.48 (0.19–1.18)	0.45 (0.20–1.03)	3.72 (2.44–5.67)	11.04 (7.09–17.18)
<i>P</i> for trend	0.001	0.004	0.005	0.001	0.001

KEY: IPSS = International Prostate Symptom Score; Qmax = peak urinary flow rate.

Data presented as the odds ratio, with the 95% confidence interval in parentheses.

*Reference category.

Confounders



- * Is symptom severity an effect of sex or an effect of age?
- * Both seem to have an impact.
- * Once corrected for age, does sex still have an effect on symptom severity?

TABLE III. Cross-sectional age-specific and age-adjusted associations between frequency of ejaculation* and urologic and quality-of-life measures

Age (yr)	IPSS (>7 vs. ≤7)	Qmax (≤12 vs. >12 mL/s)	Prostate Volume (>30 vs. ≤30 cm ³)	Health-Related Quality of Life (Excellent, Very Good vs. Good, Fair, Poor)	Sexual Satisfaction (Satisfied vs. Neutral, Dissatisfied)
40–49	0.93 (0.57–1.54)	1.30 (0.34–4.96)	1.35 (0.27–6.73)	2.10 (1.26–3.52)	4.02 (2.45–6.60)
50–59	0.79 (0.54–1.14)	0.75 (0.28–2.01)	0.61 (0.26–1.42)	1.90 (1.25–2.87)	7.20 (4.81–10.78)
60–69	1.21 (0.82–1.80)	0.89 (0.39–2.03)	1.60 (0.72–3.57)	2.43 (1.54–3.83)	4.65 (3.04–7.10)
70+	1.12 (0.56–2.23)	1.88 (0.41–8.77)	1.54 (0.27–8.89)	2.52 (1.24–5.14)	3.78 (1.92–7.48)
Age-adjusted	0.99 (0.79–1.24)	0.95 (0.56–1.61)	1.10 (0.66–1.84)	2.13 (1.67–2.72)	5.08 (4.06–6.36)


KEY: IPSS = International Prostate Symptom Score; Qmax = peak urinary flow rate.

Data presented as the odds ratio, with the 95% confidence interval in parentheses.

* Ejaculation frequency <1 per week vs. ≥1 per week.

Conclusion

- * There is a cross-sectional inverse association between frequency of ejaculation and IPSS
- * However, this appears to be the result of the confounding effect of age

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- * These cross-sectional data suggest that the frequency of ejaculation has no effect on lower urinary tract symptoms, peak urinary flow rates, or prostate volume; the apparent protective association appears to be an artifact caused by the confounding effects of age.

Summary

- * Which types of bias exist? Please explain and give examples on how they may affect the interpretation of studies.
- * What are confounding variables, and how do they interfere in interpreting scientific studies?