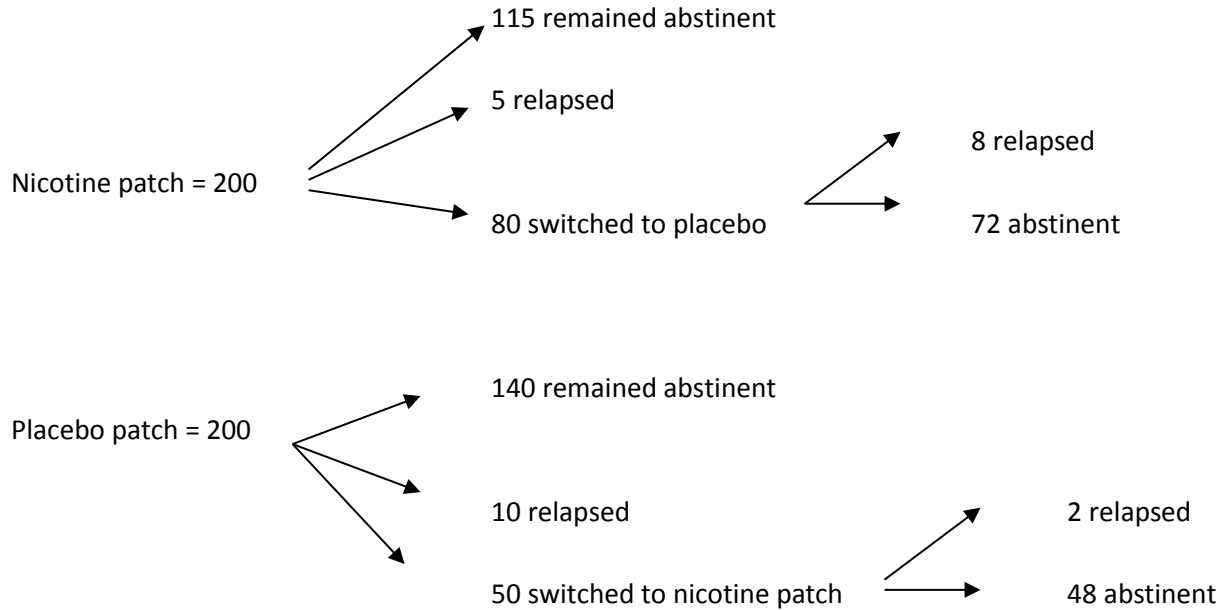


Chapter 10 Exercises

1. Intent-to-treat analysis: Example 1

In a randomized controlled trial to determine whether the nicotine patch reduces the risk of relapse among smokers who have committed to quit, 200 ex-smokers who recently quit were assigned to either a nicotine patch (the “exposed”) or a placebo patch (the “unexposed”). After six months, investigators assessed participants’ smoking status and whether or not they were using the patch.



a. Fill out the 2x2 table below.

	Relapsed	Remained abstinent	Total
Nicotine patch			
Placebo patch			
Total			

b. Calculate and interpret the risk ratio and risk difference for relapse using the final group membership (i.e., those who ended up in the nicotine patch and placebo group at the end of the study), along with their 95% confidence intervals:

c. Fill out the 2x2 table below using intent-to-treat analysis.

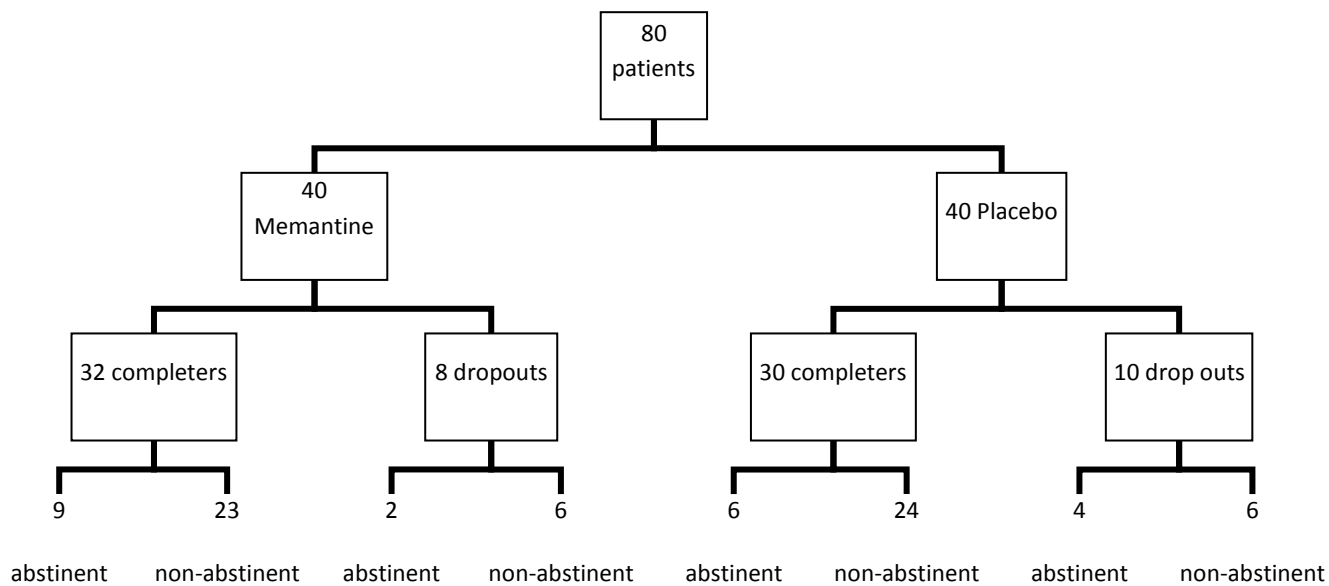
	Relapsed	Remained abstinent	Total
Nicotine patch			
Placebo patch			
Total			

d. Calculate and interpret the risk ratio and risk difference with 95% confidence intervals using intent-to-treat analysis:

e. Which risk ratio should you report? Why?

2. Intent-to-treat analysis: Example 2

Below is a randomized controlled trial that studies the effects of memantine on cocaine use among treatment seekers with cocaine dependence. The trial is 12 weeks long, but some patients drop out before the end of the study. The sample is composed of 80 patients—40 randomized to memantine and 40 randomized to placebo. The primary outcome is abstinence defined as any occurrence of three consecutive weeks of no use. (Note: abstinence status for dropouts is based on their last recorded observation).



a. Calculate and interpret the risk ratio and risk difference with 95% confidence intervals for abstinence based on final group membership:

b. Calculate and interpret the risk ratio and risk difference with 95% confidence intervals using intent-to-treat analysis:

3. For discussion: What are the advantages and limitations of RCTs?

4. Matched pair analysis

In a study of maternal praise and children's attention, 100 five-year-olds with attention-deficit hyperactivity disorder (ADHD) were matched on sex with 100 five-year-olds without ADHD, as ADHD is more common in boys and it has been shown that mothers interact differently with children based on their sex. Frequency of maternal praise was then assessed by an observer in a session where the mother was assigned to teach the child how to do a difficult puzzle. The results were as follows:

		Non-ADHD control		
	Exposure status	High praise	Low praise	Total
ADHD case	High praise	44 pair: 30 M, 14 F	15 pair: 10 M, 5 F	59 pair: 40 M, 19 F
	Low praise	24 pair: 15 M, 9 F	17 pair: 9 M, 8 F	41 pair: 24 M, 17 F
	Total	68 pair: 45 M, 23 F	32 pair: 19 M, 13 F	100 pair: 64 M, 36 F

Calculate and interpret the matched pair odds ratio and 95% confidence interval

5. Stratification: Example 1

Oral Contraceptive (OC) use is hypothesized to increase the risk of stroke. Assume that oral contraceptive use is inversely associated with age (*younger* women are more likely to use OCs compared to *older* women), and that age is positively associated with stroke (*older* women are more likely to have a stroke compared to *younger* women).

a. Is age associated with the exposure? The outcome? Is it in the causal pathway of interest?

b. Calculate the crude OR

	Stroke	No stroke	Total
OC use	86	683	769
No OC use	93	959	1052
Total	179	1642	1821

c. Stratify by the potential confounder, and calculate stratum-specific OR's

Stratified by age

	Ages 20-39		Ages 40-49		Ages 50-54	
	Stroke	No stroke	Stroke	No stroke	Stroke	No stroke
OC Use	13	51	31	301	42	331
No OC Use	46	285	30	463	17	211
Total	59	336	61	764	59	542

Odds ratio (age 20-39) =

Odds ratio (age 40-49) =

Odds ratio (age 50-54) =

Summary (age-adjusted) odds ratio* = 1.57

* The summary OR was calculated using a statistical procedure known as the Mantel-Haenszel weighted odds ratio. You will learn about this measure in future epidemiology and biostatistics classes.

d. Compare the crude odds ratio with the adjusted odds ratio. Do you think that age was a confounder in the association between OC use and stroke? Why or why not?

e. As the investigator, which measure of effect (crude or adjusted) would you choose to report to your audience?

6. Stratification: Example 2

The Boston Area Health Case-Control Study looked at the association between inactivity and myocardial infarction (MI). Information on smoking was collected. It has been shown in previous studies that smoking increases the risk for MI and that people who smoke are more likely to be inactive. Furthermore, it is hypothesized that smoking is not on the causal pathway between inactivity and MI.

Based on this information, the investigators considered smoking status to be a *potential* confounder of the inactivity-MI relationship. Therefore, they stratified on smoking status and obtained the following tables.

Never smoker

	M.I. (Case)	No M.I. (Control)
Inactive (E+)	39	52
Active (E-)	41	84

Ex-Smoker 10+ years

	M.I. (Case)	No M.I. (Control)
Inactive (E+)	31	39
Active (E-)	41	80

Ex-Smoker < 10 years

	M.I. (Case)	No M.I. (Control)
Inactive (E+)	27	26
Active (E-)	22	34

Current Smoker

	M.I. (Case)	No M.I. (Control)
Inactive (E+)	79	40
Active (E-)	86	68

Based on these data, determine if smoking status was in fact a confounder in this study. Use the following steps:

- a. Calculate the crude odds ratio and 95% confidence interval using the information provided in the above 2x2 tables:

	MI (Case)	No MI (Control)	Total
Inactive (E+)			
Active (E-)			
Total			

- b. Calculate the stratum-specific odds ratios for the relationship between exercise and MI:

Odds ratio (never smokers) =

Odds ratio (ex-smoker 10+ years) =

Odds ratio (ex-smoker < 10 years)=

Odds ratio (current smokers) =

Summary (smoking-adjusted) odds ratio* = 1.55

* calculated using Mantel-Haenszel weighted odds ratio

- c. Compare the crude odds ratio with the adjusted adjusted. Do you think that smoking was a confounder of the association between inactivity and MI? Why or why not?
- d. As the investigator, which measure of effect (crude or adjusted) would you choose to report to your audience?

7. Which study design offers the best opportunity to control for non-comparability between exposed and unexposed: randomized clinical trial, cohort or case-control study? Explain your reasoning.