1.1 Case study: using stents to prevent strokes

We start with a case study and we consider the following questions:

- Does the use of stents reduce the risk of stroke?
- How do researchers collect data to answer this question?
- What do they do with the data once it is collected?
- How different must the risk of stroke be in each group before there is sufficient evidence that it's a real difference and not just random variation?

Learning objectives

1. Understand the four steps of a statistical investigation (identify a question, collect data, analyze data, form a conclusion) in the context of a real-world example.
2. Consider the concept of statistical significance.

1.1.1 Case study

Section 1.1 introduces a classic challenge in statistics: evaluating the efficacy of a medical treatment. Terms in this section, and indeed much of this chapter, will all be revisited later in the text. The plan for now is simply to get a sense of the role statistics can play in practice.

In this section we will consider an experiment that studies effectiveness of stents in treating patients at risk of stroke.[1] Stents are devices put inside blood vessels that assist in patient recovery after cardiac events and reduce the risk of an additional heart attack or death. Many doctors have hoped that there would be similar benefits for patients at risk of stroke. We start by writing the principal question the researchers hope to answer:

> Does the use of stents reduce the risk of stroke?

The researchers who asked this question collected data on 451 at-risk patients. Each volunteer patient was randomly assigned to one of two groups:

> **Treatment group**. Patients in the treatment group received a stent and medical management. The medical management included medications, management of risk factors, and help in lifestyle modification.
>
> **Control group**. Patients in the control group received the same medical management as the treatment group, but they did not receive stents.

Researchers randomly assigned 224 patients to the treatment group and 227 to the control group. In this study, the control group provides a reference point against which we can measure the medical impact of stents in the treatment group.

[1] Chimowitz MI, Lynn MJ, Derdeyn CP, et al. 2011. Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis. New England Journal of Medicine 365:993-1003. www.nejm.org/doi/full/10.1056/NEJMoa1105335. NY Times article reporting on the study: www.nytimes.com/2011/09/08/health/research/08stent.html.

Researchers studied the effect of stents at two time points: 30 days after enrollment and 365 days after enrollment. The results of 5 patients are summarized in Figure 1.1. Patient outcomes are recorded as "stroke" or "no event", representing whether or not the patient had a stroke at the end of a time period.

Patient	group	0-30 days	0-365 days
1	treatment	no event	no event
2	treatment	stroke	stroke
3	treatment	no event	no event
⋮	⋮	⋮	
450	control	no event	no event
451	control	no event	no event

Figure 1.1: Results for five patients from the stent study.

Considering data from each patient individually would be a long, cumbersome path towards answering the original research question. Instead, performing a statistical data analysis allows us to consider all of the data at once. Figure 1.2 summarizes the raw data in a more helpful way. In this table, we can quickly see what happened over the entire study. For instance, to identify the number of patients in the treatment group who had a stroke within 30 days, we look on the left-side of the table at the intersection of the treatment and stroke: 33.

	0-30 days		0-365 days	
	stroke	no event	stroke	no event
treatment	33	191	45	179
control	13	214	28	199
Total	46	405	73	378

Figure 1.2: Descriptive statistics for the stent study.

GUIDED PRACTICE 1.1

G What proportion of the patients in the treatment group had no stroke within the first 30 days of the study? (Please note: answers to all Guided Practice exercises are provided using footnotes.)[2]

We can compute summary statistics from the table. A **summary statistic** is a single number summarizing a large amount of data.[3] For instance, the primary results of the study after 1 year could be described by two summary statistics: the proportion of people who had a stroke in the treatment and control groups.

Proportion who had a stroke in the treatment (stent) group: $45/224 = 0.20 = 20\%$.

Proportion who had a stroke in the control group: $28/227 = 0.12 = 12\%$.

These two summary statistics are useful in looking for differences in the groups, and we are in for a surprise: an additional 8% of patients in the treatment group had a stroke! This is important for two reasons. First, it is contrary to what doctors expected, which was that stents would *reduce* the rate of strokes. Second, it leads to a statistical question: do the data show a "real" difference between the groups?

This second question is subtle. Suppose you flip a coin 100 times. While the chance a coin lands heads in any given coin flip is 50%, we probably won't observe exactly 50 heads. This type of fluctuation is part of almost any type of data generating process. It is possible that the 8% difference in the stent study is due to this natural variation. However, the larger the difference we observe (for a particular sample size), the less believable it is that the difference is due to chance. So what we are really asking is whether the difference is **statistically significant**, that is, whether the difference so large that we should reject the notion that it was due to chance.

[2]There were 191 patients in the treatment group that had no stroke in the first 30 days. There were $33 + 191 = 224$ total patients in the treatment group, so the proportion is $191/224 = 0.85$.

[3]Formally, a summary statistic is a value computed from the data. Some summary statistics are more useful than others.

While we don't yet have the statistical tools to fully address this question on our own, we can comprehend the conclusions of the published analysis: there was compelling evidence of harm by stents in this study of stroke patients.

Be careful: do not generalize the results of this study to all patients and all stents. This study looked at patients with very specific characteristics who volunteered to be a part of this study and who may not be representative of all stroke patients. In addition, there are many types of stents and this study only considered the self-expanding Wingspan stent (Boston Scientific). However, this study does leave us with an important lesson: we should keep our eyes open for surprises.

Section summary

- To test the effectiveness of a treatment, researchers often carry out an experiment in which they randomly assign patients to a **treatment group** or a **control group**.
- Researchers compare the relevant **summary statistics** to get a sense of whether the treatment group did better, on average, than the control group.
- Ultimately, researchers want to know whether the difference between the two groups is **significant**, that is, larger than what would be expected by chance alone.

Exercises

1.1 Migraine and acupuncture, Part 1. A migraine is a particularly painful type of headache, which patients sometimes wish to treat with acupuncture. To determine whether acupuncture relieves migraine pain, researchers conducted a randomized controlled study where 89 females diagnosed with migraine headaches were randomly assigned to one of two groups: treatment or control. 43 patients in the treatment group received acupuncture that is specifically designed to treat migraines. 46 patients in the control group received placebo acupuncture (needle insertion at non-acupoint locations). 24 hours after patients received acupuncture, they were asked if they were pain free. Results are summarized in the contingency table below.[4]

		Pain free		
		Yes	No	Total
Group	Treatment	10	33	43
	Control	2	44	46
	Total	12	77	89

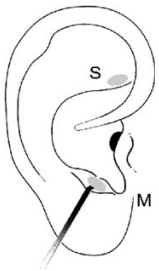

Figure from the original paper displaying the appropriate area (M) versus the inappropriate area (S) used in the treatment of migraine attacks.

(a) What percent of patients in the treatment group were pain free 24 hours after receiving acupuncture?

(b) What percent were pain free in the control group?

(c) In which group did a higher percent of patients become pain free 24 hours after receiving acupuncture?

(d) Your findings so far might suggest that acupuncture is an effective treatment for migraines for all people who suffer from migraines. However this is not the only possible conclusion that can be drawn based on your findings so far. What is one other possible explanation for the observed difference between the percentages of patients that are pain free 24 hours after receiving acupuncture in the two groups?

1.2 Sinusitis and antibiotics, Part 1. Researchers studying the effect of antibiotic treatment for acute sinusitis compared to symptomatic treatments randomly assigned 166 adults diagnosed with acute sinusitis to one of two groups: treatment or control. Study participants received either a 10-day course of amoxicillin (an antibiotic) or a placebo similar in appearance and taste. The placebo consisted of symptomatic treatments such as acetaminophen, nasal decongestants, etc. At the end of the 10-day period, patients were asked if they experienced improvement in symptoms. The distribution of responses is summarized below.[5]

		Self-reported improvement in symptoms		
		Yes	No	Total
Group	Treatment	66	19	85
	Control	65	16	81
	Total	131	35	166

(a) What percent of patients in the treatment group experienced improvement in symptoms?

(b) What percent experienced improvement in symptoms in the control group?

(c) In which group did a higher percentage of patients experience improvement in symptoms?

(d) Your findings so far might suggest a real difference in effectiveness of antibiotic and placebo treatments for improving symptoms of sinusitis. However, this is not the only possible conclusion that can be drawn based on your findings so far. What is one other possible explanation for the observed difference between the percentages of patients in the antibiotic and placebo treatment groups that experience improvement in symptoms of sinusitis?

[4] G. Allais et al. "Ear acupuncture in the treatment of migraine attacks: a randomized trial on the efficacy of appropriate versus inappropriate acupoints". In: *Neurological Sci.* 32.1 (2011), pp. 173–175.

[5] J.M. Garbutt et al. "Amoxicillin for Acute Rhinosinusitis: A Randomized Controlled Trial". In: *JAMA: The Journal of the American Medical Association* 307.7 (2012), pp. 685–692.