STAT 206: Mr. Neyman's Confidence Intervals With a Continuous Outcome Variable: A Case Study

(medicine) Hypertension is a medical condition in which a person's blood pressure is chronically elevated. (A reminder: blood pressure is measured with two numbers called *systolic* (higher) and *diastolic* (lower), in a deeply anachronistic scale called mmHg (millimeters of mercury); blood pressures are stored as data in the form "systolic over diastolic" [i.e., 115 over 75 or 115/75; and ideal blood pressures range from 90/60 to 120/80.) Persistent hypertension is one of the risk factors for strokes, heart attacks, heart failure and arterial aneurysm, and is a leading cause of chronic renal failure; as of 1999, it was estimated that 29% of American adults were hypertensive. A U.S. public health goal in 2000 was to lower this rate to 16% by 2010, but thing have actually gotten worse since then: the *American Heart Association* estimated in 2018 that *46%* of all U.S. adults are hypertensive (although part of the increase is due to a change in the definition of high blood pressure from (above 140 systolic) to (above 130 systolic)). Diet and exercise can go a long way to lower blood pressure, but drugs are also sometimes needed (particularly given how hard it is to get Americans to exercise and eat in a healthier way :-) .

The online reference *Wikipedia* notes that "*Captopril* is an angiotensin-converting enzyme (ACE) inhibitor used for the treatment of hypertension and some types of congestive heart failure. Captopril was the first ACE inhibitor developed and was considered a breakthrough both because of its novel mechanism of action and also because of the revolutionary development process. ... The development of Captopril was among the earliest successes of the revolutionary concept of *structure-based drug design*. The renin-angiotensin-aldosterone system (a hormone system that helps regulate long-term blood pressure and blood volume in the body) had been extensively studied in the mid-20th century, and it had been decided that this system presented several opportune targets in the development of novel treatments for hypertension."

Captopril was developed in the mid 1970s; MacGregor et al. (1979, *British Medical Journal*) published the results of a clinical trial on its effects. Systolic blood pressures (in mmHg) were measured for $n = 12$ representatively-chosen hypertensive patients, before and after taking Captopril for a long enough time period for the drug to work. Before any data had been gathered, let (B_i, A_i) be a pair of random variables signifying the before and after blood pressure readings for person i in the study (as i runs from 1 to n), and define $D_i = (B_i - A_i)$ and $\bar{D}_n = \frac{1}{n}\sum_{i=1}^{n} D_i$; the realized values of these random variables are given in Table 1.

Subject	1	2	3	4	5	6	7	8	9	10	11	12	Mean	SD
Before	200	174	198	170	179	182	193	209	185	155	169	210	185.3	17.1
After	191	170	177	167	159	151	176	183	159	145	146	177	166.8	14.9
Difference	+9	+4	+21	+3	+20	+31	+17	+26	+26	+10	+23	+33	18.6	10.1

Table 1: *Before and after results for $n = 12$ hypertensive patients treated with Captopril.*

Estimate the average effect Δ of Captopril in the population to which you believe it's appropriate to generalize here, and explicitly identify that population. Is this estimated effect large in clinical terms? Attach a standard error to your estimated effect, and construct an approximate 99.9% confidence interval for Δ, explicitly identifying all assumptions you're making. Is the estimated effect statistically significant? What do you conclude about Captopril's usefulness in treating hypertension? Explain briefly.