A: Spread: variability of observations: sample variance:  $s^2 = \sum (X_i - \overline{X})^2 / (n-1)$ why  $(n-1)$ ? Data used twice: to compute  $\overline{X}$  and then to compute  $s^2$ account for this by adjusting the sample size called "degrees of freedom" or df. More later standard deviation:  $s = \sqrt{\text{Variance}}$ coefficient of variation, cv:  $s/\overline{X}$ , measures relative variation.

B: Inference: two types: Confidence interval, hypothesis test

Spoiler: multiple opinions and lots of controversy.

Lots of tricky epistemological and practical issues.

I give the traditional approach

Some perspectives in the refeences to extra material section of the non-canvas web site

C: Hypothesis test and p-values:

Assume something (null hypothesis) is correct, ask whether observations are unusual If so, either a fluke happened or the null hypothesis assumption is probably wrong p-value: probability of observing data or something more extreme given null hypothesis

Scale of evidence: Display 2.12, applied to difference of two group means

Null hypothesis is no difference in means  $\Leftrightarrow$  equal means

 $p > 0.10$ : no evidence of a difference

not: "null is true", e.g., not: "X has no effect", not "Two groups have the same mean"

 $0.05 < p < 0.10$ : weak evidence of a difference

 $0.01 < p < 0.05$ : evidence of a difference

 $0.001 < p < 0.01$ : strong evidence of a difference

p < 0.001: very strong evidence of a difference

Mis-interpretations of p-values:

Frequently mis-interpreted, leading many to reject any use of p-values

Does not prove null hypothesis (even if p-value large)

Does not show that alternative more likely than null.

Limited knowledge: small p only tells you parameter not zero (for most frequent H0).

D: Randomization test: design-based inference

randomly reassign labels, compute  $S =$  statistic of interest

e.g., difference in means or absolute value of difference in means:  $|\overline{Y}_A - \overline{Y}_B|$  $p = P[obs S$  more extreme than random  $S]$ , e.g., (two-sided hypothesis)  $P[ | \overline{Y}_A - \overline{Y}_B | \geq \text{random} | \overline{Y}_A - \overline{Y}_B | ]$ 

One- and two-sided null hypotheses: Notation:  $\delta$  = population difference in the means  $d =$  sample estimated difference in averages two-sided: H<sub>0</sub>:  $\delta = 0$ , H<sub>a</sub>:  $\delta \neq 0$ reject H<sub>0</sub> when d sufficient large  $(d > 0)$  or sufficiently small  $(d < 0)$ one-sided: two possibilities, depending on which "side" H<sub>0</sub>:  $\delta \leq 0$ , H<sub>a</sub>:  $\delta > 0$ reject H<sub>0</sub> when d sufficient large  $(d > 0)$ H<sub>0</sub>:  $\delta \geq 0$ , H<sub>a</sub>:  $\delta < 0$ reject H<sub>0</sub> when d sufficient small  $(d < 0)$ p-value for two-sided test "counts" both tails Twice the smaller one-sided p-value Two-sided tests much more common, even when only one-side is interesting Less opportunity to "fudge" the result Can't pick the side after seeing the data Two very similar versions of a randomization test: permutation test: enumerate all possible treatment arrangements randomization test: randomly sample from all possible treatment arrangements want/need to sample when too many possibilities: creativity:  $>16,123,800,000,000$  arrangements Calculating the p-value from a permutation or randomization test: need to know: R: number of as or more extreme randomizations, N: number of randomizations permutation: observed arrangement is one of the possibilities:  $p = R/N$ randomization: observed arrangement is one more possibility:  $p = (R+1)/(N+1)$ which is why commonly see 999 or 9999 randomizations Randomization/Permutation tests can be very useful, especially for simple studies: logic is clear no model, few assumptions. key assumptions: random assignment of treatments to each unit observations are independent ⇔ treatment assigned separately to each observation applicable when standard models aren't easy: e.g., inference on difference of medians or ratio of means But can be (very) hard to implement for non-simple (most) studies

E: How precise are estimates? standard deviation: estimated variability in observations does not get systematically smaller with larger sample sizes standard error: estimated precision of a statistic (e.g., mean) for simple random sample:  $se_{average} = s/\sqrt{n}$ Generally smaller with larger sample sizes Can use se to determine number of replicates to use in a study Spoiler: sd and se can be defined in multiple ways. My use focuses on the "endpoints". you might see "standard deviation of the mean": se, but with known sd, not estimated Which should you report? My suggestion: what do you want to describe? variability in observations: report sd precision of the average (or other statistic): report se Correctly say which statistic you are reporting

editor's note on Med diet retraction:

reviewed 934 manuscripts in NEJM

found 11 with curious results.

5 of those were because se was incorrectly reported as sd or vice-versa

When reporting an average, should you report 106.4 or 106.3867190? Kelley's rule: Science 60:524 (1924)

report a statistic (e.g., an average) to the leading digit of  $\frac{\text{se}}{3}$ 



F: Model based inference: T-test

$$
T = \frac{\text{statistic} - \text{H}_0 \text{ parameter}}{\text{se of statistic}}
$$

Many T distributions: which depends on (error) degrees of freedom  $T > 2$  or  $\lt -2 \Rightarrow$  two-sided p  $\lt 0.05$  (approximately, unless df small) Need to know se of various statistics se for mean from a single population: se =  $s/\sqrt{n}$ 

Now, need to know se for a difference of two means

## SE of a difference of two means

Two independent samples: statistic is difference in averages

se = 
$$
\sqrt{\frac{\sigma_1^2}{n_1} + \frac{\sigma_2^2}{n_2}}
$$
, when variances unequal  
\n=  $\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}$   
\nse =  $\sigma \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}$ , when variances equal  
\n=  $s_p \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}$ , estimated pooled variance

Pooled error variance:

$$
s_p^2 = \frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2}{n_1 + n_2 - 2}
$$

Degrees of freedom: how much information used to estimate a variance (or sd) n observations in a group minus number of estimates one group: need to estimate mean (1 parameter), so  $n-1$  for one group  $n_1 + n_2 - 2$  for two groups (estimate two means)

G: Paired data:

compute difference for each subject (pair).

compute mean difference and sd of differences (across subjects) compute n<br>se =  $s/\sqrt{n}$  $df = n - 1$ 

Hypothesis test really doesn't tell you much

if p small, parameter is not zero.

even though p values are all over the scientific literature

H: Confidence interval: tells you both location and precision of a statistic. a 95% interval includes all parameters for which p-value  $> 0.05$ Many statistics: estimate  $\pm T_{quantile} \times$  se  $T_{quantile}$  approx 2 for 95% interval unless df small 95% interval includes  $0 \Rightarrow$  p-value for test of  $0 > 0.05$ 95% interval does not include  $0 \Rightarrow$  p-value for test of  $0 < 0.05$ 

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