UNDERSTANDING STATISTICS & EXPERIMENTAL DESIGN

Content

EPFL

1. Basic Probability Theory
2. Signal Detection Theory (SDT)
3. SDT and Statistics I and II
4. Statistics in a nutshell
5. Multiple Testing
6. ANOVA
7. Experimental Design & Statistics
8. Correlations & PCA
9. Meta-Statistics: Basics
10. Meta-Statistics: Too good to be true
11. Meta-Statistics: How big a problem is publication bias?
12. Meta-Statistics: What do we do now?

Part II
Multiple Comparisons

Problem 1: Independent tests

Multiple Comparisons

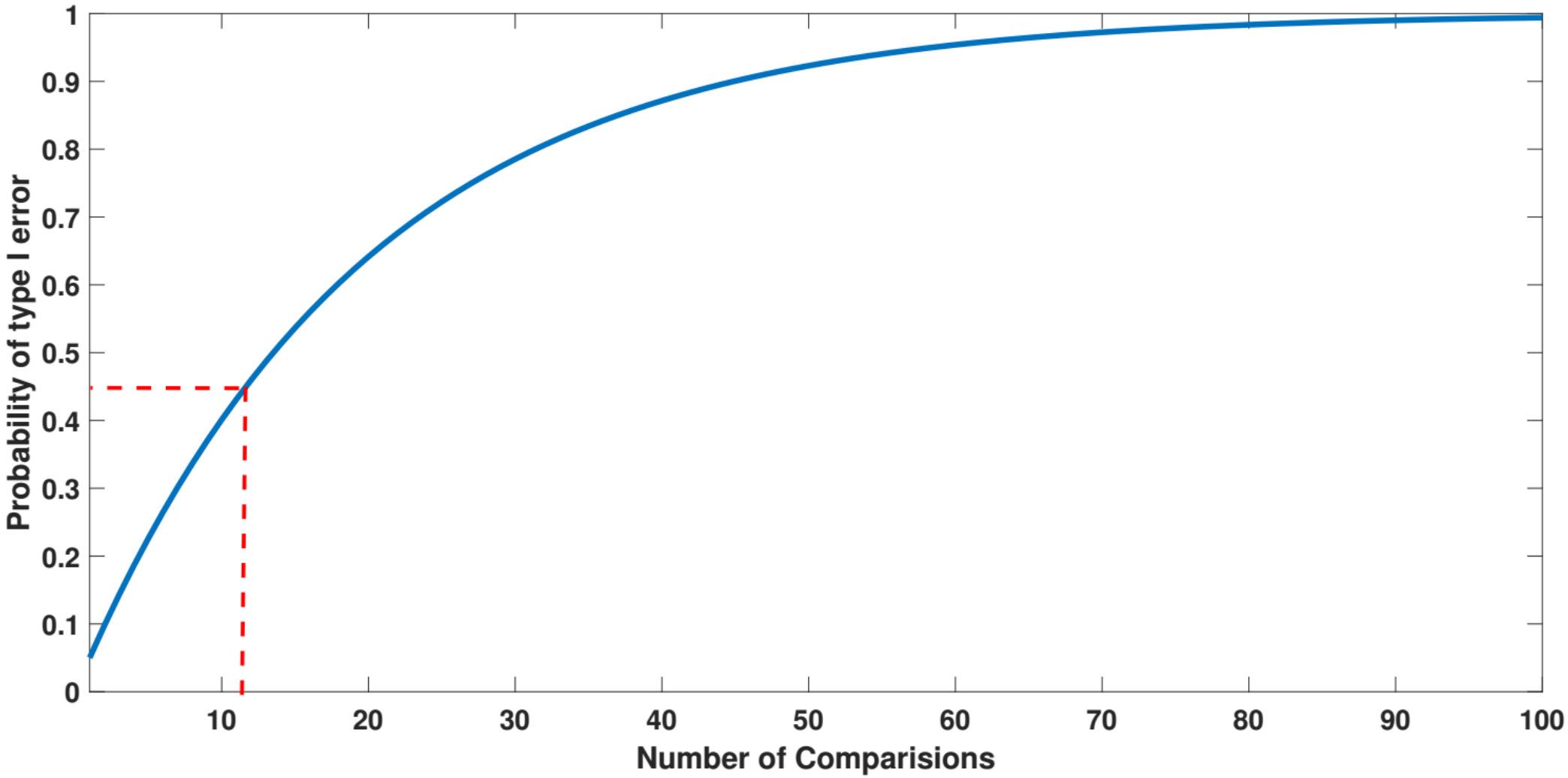
- A significance level of 0.05 means that your false positive rate for one test is 5%.
- If you run more than one test, your false positive rate will be higher than 5%.

Multiple Hypothesis Testing

If the Null hypothesis is true:

- For one test the chances of *not* making a type I error are: $P = 1 - \alpha = 0.95$
- For two *independent* tests: $P = (1- \alpha)^2 = 0.90$
- For three *independent* tests: $P = (1 - \alpha)^3 = 0.86$
- For 12 *independent* tests: $P = (1 - \alpha)^{12} = 0.53$

Multiple Comparisons



How to avoid false discovery?

For *m* independent statistical tests with the α significance level, the probability of at least one false discovery is:

$$1 - (1 - \alpha)^m < 0.05$$

$$\alpha = 1 - (1 - 0.05)^{1/m} \approx \frac{0.05}{m}$$

Bonferroni correction: for *m* independent statistic tests only those results are significant, for which

$$p < \frac{0.05}{m}$$

Bonferroni Correction

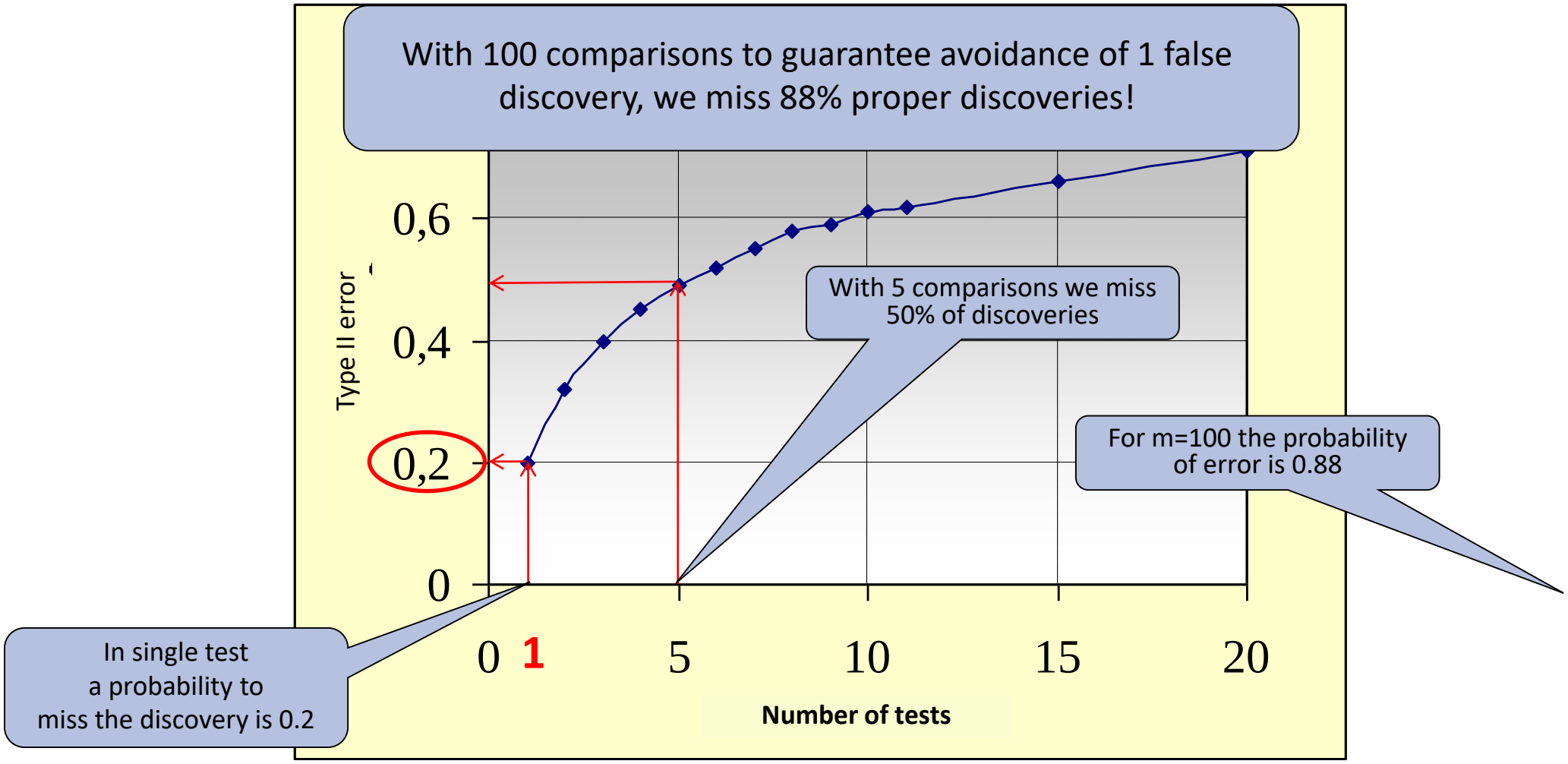
Bonferroni method creates more problems than it solves

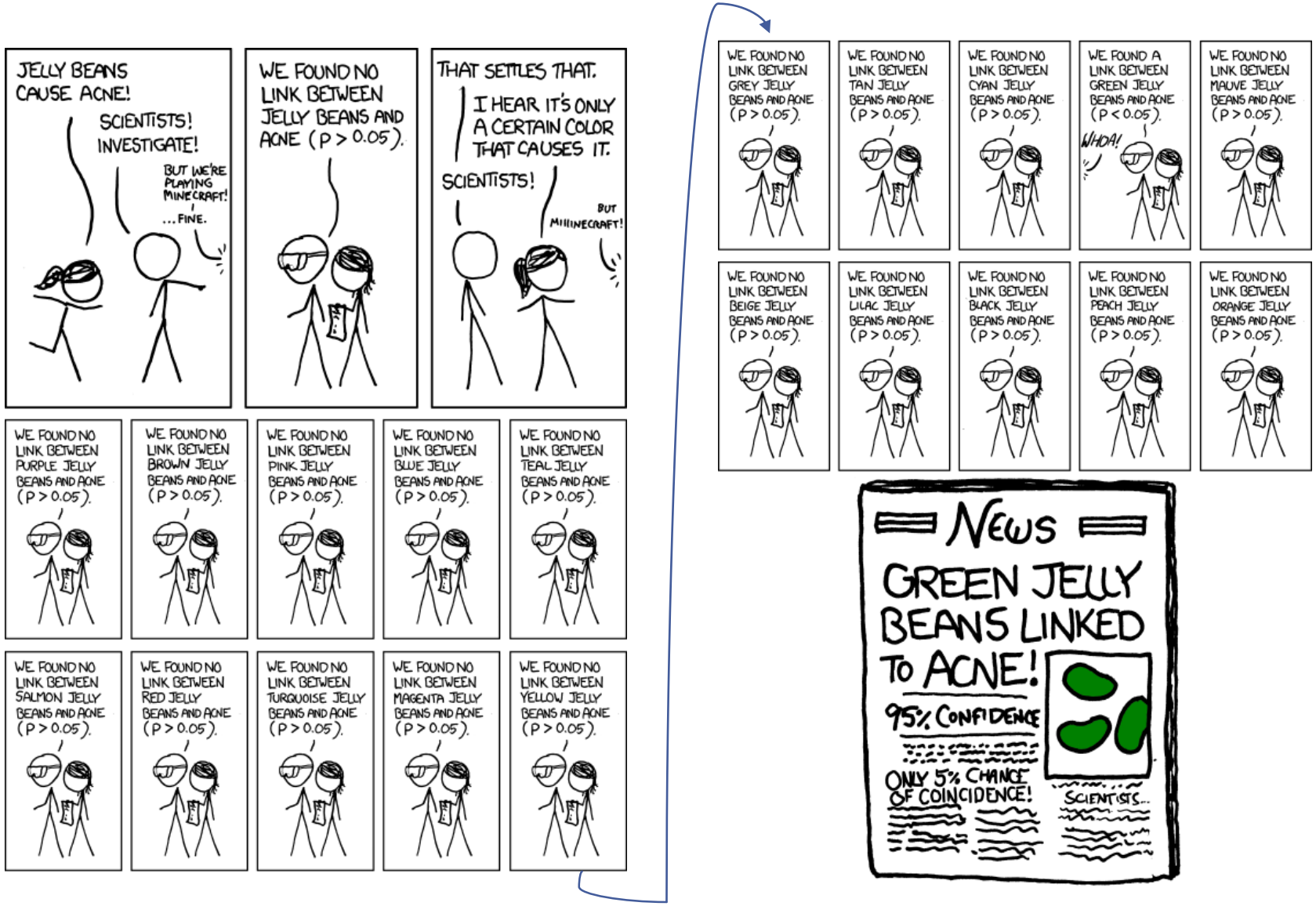
(Thomas Perneger, 1998):

Bonferroni correction leads to a very high probability to miss proper associations!

Dependence of type ii error on number of tests using the Bonferroni correction

Probability to miss gene with OR=2.7 with sample sizes 100 (case) and 100 (control)




JELLY BEANS CAUSE ACNE!
SCIENTISTS! INVESTIGATE!
BUT WE'RE PLAYING MINECRAFT!
... FINE.
WE FOUND NO LINK BETWEEN JELLY BEANS AND ACNE (P > 0.05).
THAT SETTLES THAT.
I HEAR IT'S ONLY A CERTAIN COLOR THAT CAUSES IT.
SCIENTISTS!
BUT MIIIINECRAFT!
WE FOUND NO LINK BETWEEN PURPLE JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN BROWN JELLY BEANS AND ACNE (P > 0.05).
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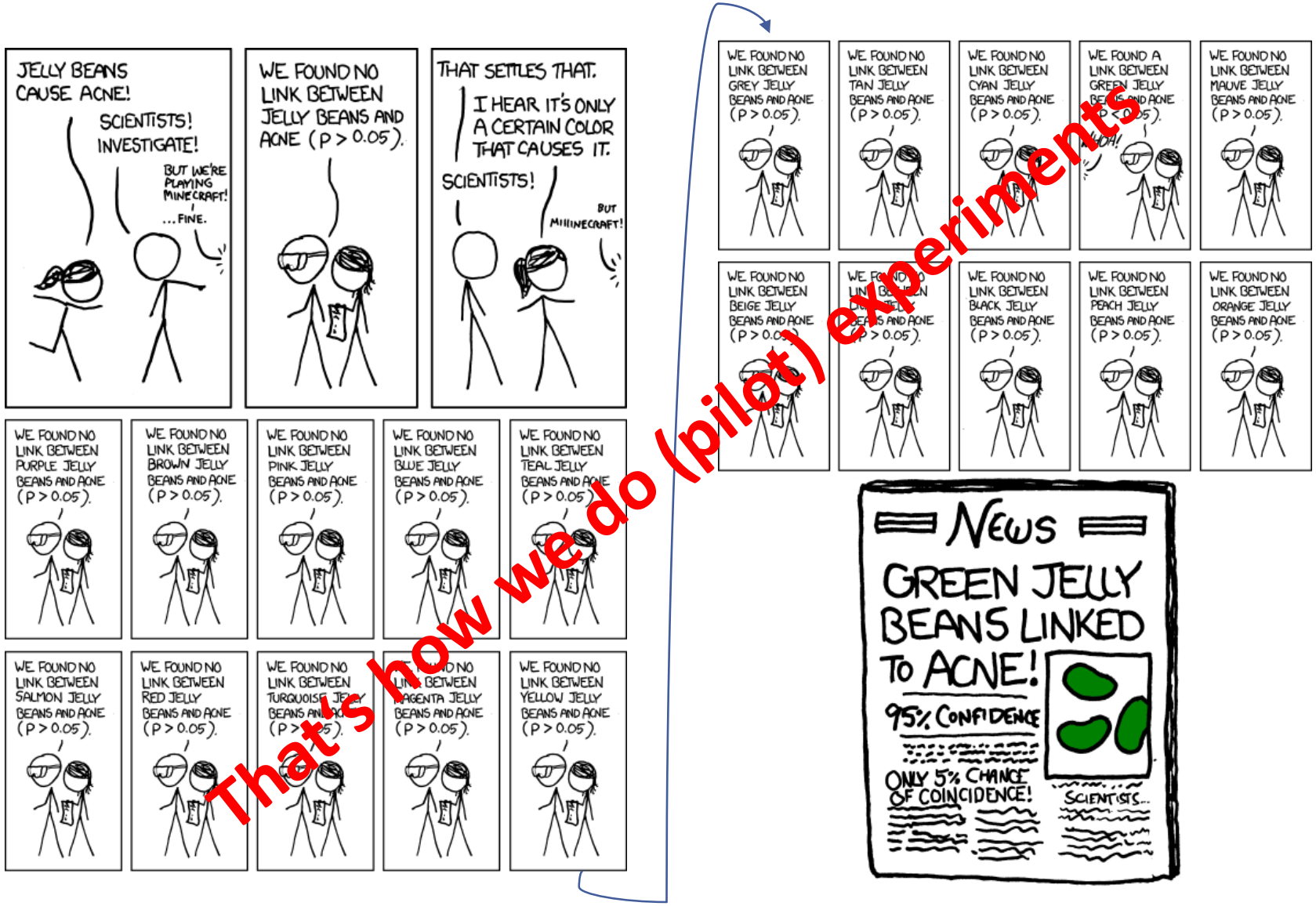
WE FOUND NO LINK BETWEEN TURQUOISE JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN MAGENTA JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN YELLOW JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN GREY JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN TAN JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN CYAN JELLY BEANS AND ACNE (P > 0.05).
WE FOUND A LINK BETWEEN GREEN JELLY BEANS AND ACNE (P < 0.05).
WHOA!
WE FOUND NO LINK BETWEEN MAUVE JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN BEIGE JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN LILAC JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN BLACK JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN PEACH JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN ORANGE JELLY BEANS AND ACNE (P > 0.05).
NEWS
GREEN JELLY BEANS LINKED TO ACNE!
95% CONFIDENCE
ONLY 5% CHANCE OF COINCIDENCE!
SCIENTISTS...


JELLY BEANS CAUSE ACNE!
SCIENTISTS! INVESTIGATE!
BUT WE'RE PLAYING MINECRAFT!
... FINE.
WE FOUND NO LINK BETWEEN JELLY BEANS AND ACNE (P > 0.05).
THAT SETTLES THAT.
I HEAR IT'S ONLY A CERTAIN COLOR THAT CAUSES IT.
SCIENTISTS!
BUT MIIIINECRAFT!
WE FOUND NO LINK BETWEEN PURPLE JELLY BEANS AND ACNE (P > 0.05).
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WE FOUND NO LINK BETWEEN RED JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN TURQUOISE JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN MAGENTA JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN YELLOW JELLY BEANS AND ACNE (P > 0.05).
That's how we do (pilot) experiments
WE FOUND NO LINK BETWEEN GREY JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN TAN JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN CYAN JELLY BEANS AND ACNE (P > 0.05).
WE FOUND A LINK BETWEEN GREEN JELLY BEANS AND ACNE (P < 0.05).
HUH!
WE FOUND NO LINK BETWEEN MAUVE JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN BEIGE JELLY BEANS AND ACNE (P > 0.05).
WE FOUND NO LINK BETWEEN BLACK JELLY BEANS AND ACNE (P > 0.05).
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NEWS
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Alternative Methods

FDR-control

False Discovery Rate Control: Benjamin, Hochberg (1995)

Problem 2: Not independent tests

FISH Example

1. Test for goldfish fin > silverfish fin ($p < 0.05$)
2. Test for goldfish tail > silverfish tail ($p < 0.05$)
3. .....

FISH Example

What if they are all correlated and you got a „bad“ sample?
Tests are not (necessarily) independent

Comment: It is not true that 5% of all science results are wrong because α is 0.05.
This would be true only if the Null Hypothesis were always true.

Take home messages

Take Home Messages

1. You can only ask one question for a set of data. Otherwise you need to account for multiple comparisons.
2. Keep your designs as simple as possible.
3. If you cannot keep your design simple and have more than one group comparison, read the next chapter.

END Class 5