

# Hypothesis testing: one sample

# Is P53 gene expressed at a lower level in **cancer** patients than in **healthy** people?

- We are interested if a P53 gene expression is lowered in **population of cancer patients** compared to the **healthy population**.
- We know that mean gene expression in the **healthy population** is  $\mu_h = 50$  mRNAs/cell. We are interested in deciding whether or not the mean expression in **cancer population** is lower than in **healthy population**. It is called hypothesis  $H_1$ . Here  $H_1$  is one-sided.  
If we asked: cancer not equal healthy – two-sided hypothesis
- Assume we have a sample of **100 cancer patients** with **sample mean  $\bar{X} = 48$  mRNAs/cell** and **sample standard deviation  $S = 10$  mRNA/cell**
- **Based on this sample can we reject the “strawman” or null hypothesis  $H_0$ : **cancer** = **healthy** and accept alternative hypothesis  $H_1$  that P53 in cancer is lower than in healthy?**

# Two types of errors

		True State of Nature	
		$H_0$ is true	$H_a$ is true
Decision Made	Accept $H_0$	<b>Correct decision</b> Probability = $1 - \alpha$	<b>Type II error</b> Probability = $\beta$
	Reject $H_0$	<b>Type I error</b> Probability = $\alpha$ (significance level)	<b>Correct decision</b> Probability = $1 - \beta$ (power)

# P-Values of Hypothesis Tests

- **P-value**: what is the probability to get the observed sample mean of  $\bar{X} = 48$  mRNAs/cell (or even smaller) in a healthy population with  $\mu_h = 50$  mRNAs/cell
- If **P-value is small** – the null hypothesis is likely wrong and thus my **probability of making a type I error (incorrectly rejecting a null hypothesis)** is small
- P-value answers the question: if I reject a null hypothesis  $H_0$  based on the sample, what is the probability that I am making a type I error?



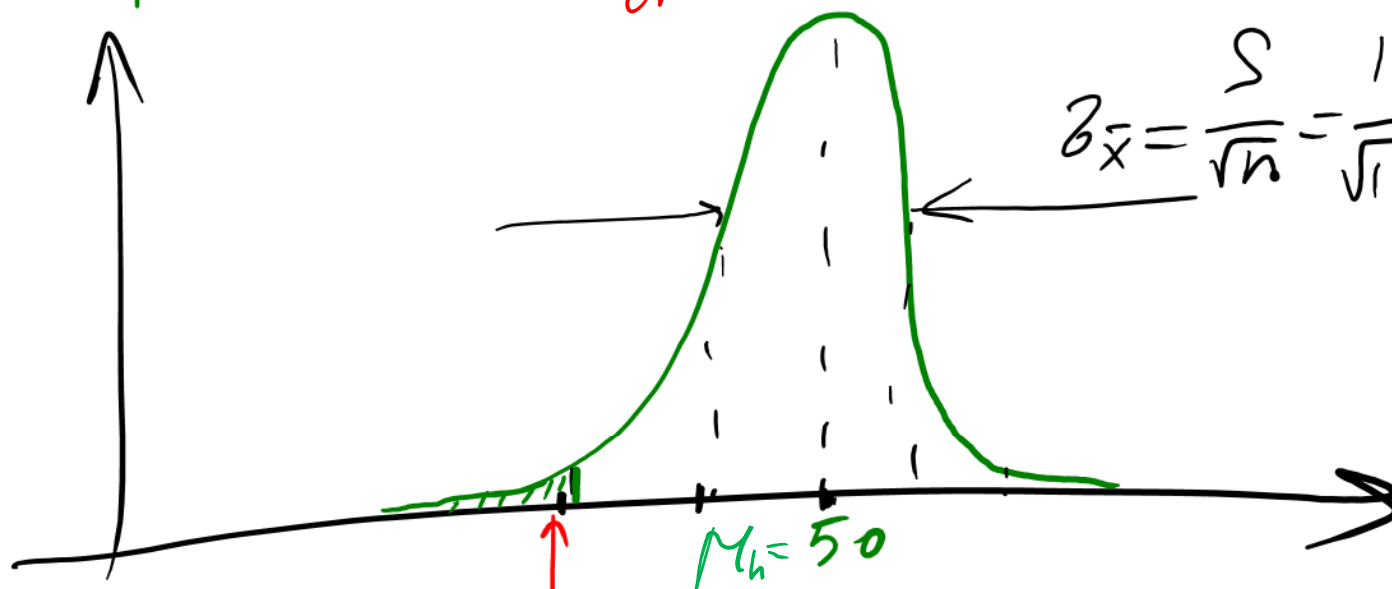
$$\mu_h = 50$$

$$H_0: \mu_c = \mu_h$$

$$n=100, \bar{X}=48, S=10$$

$$\text{One-sided hypothesis } H_1: \mu_c < \mu_h$$

$$z_{\bar{X}} = \frac{S}{\sqrt{n}} = \frac{10}{\sqrt{100}} = 1$$



$$\text{P-value}(\bar{X}=48 \mid H_0: \mu_c = \mu_h) = \text{Prob}(\bar{X} \leq 48) \approx 2.5\% = 0.025$$

If  $H_1: \mu_c \neq \mu_h$  :  $\text{p-value} = \text{Prob}(\bar{X} \leq 48) + \text{Prob}(\bar{X} \geq 52) = 0.05$

Two-sided hypothesis



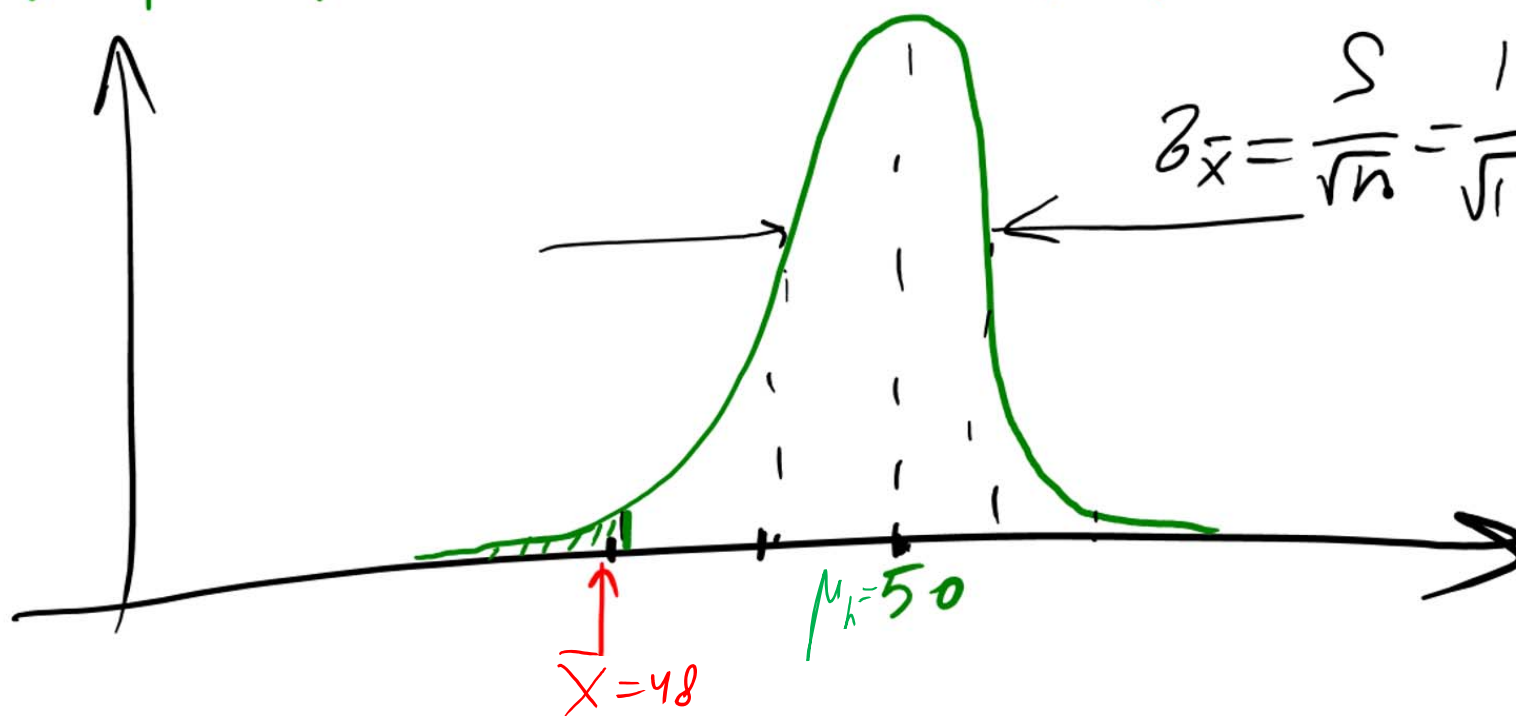
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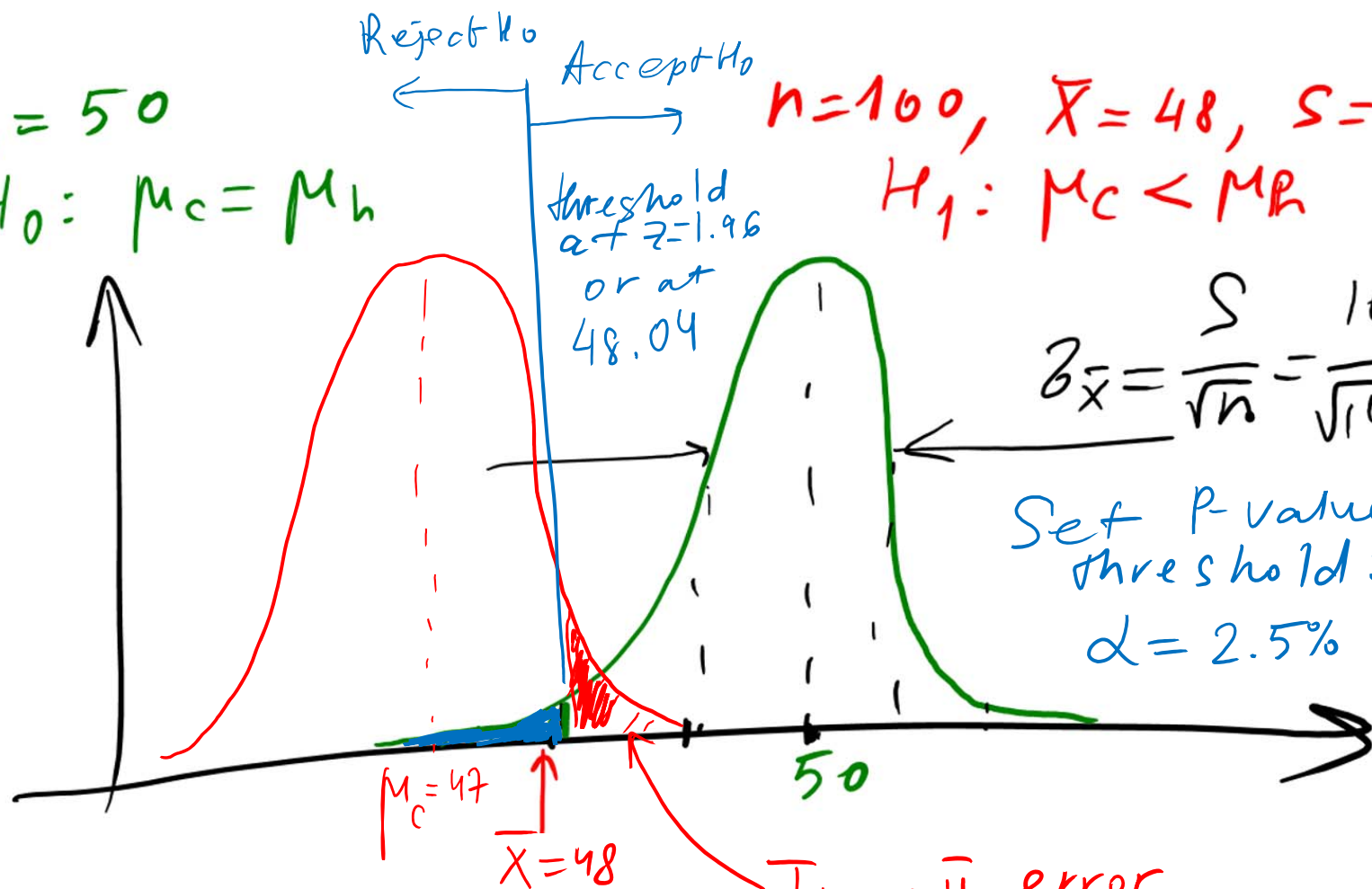
$$H_0: \mu_c = \mu_h$$

$$n=100, \bar{X}=48, S=10$$

$$H_1: \mu_c < \mu_h$$

$$\sigma_{\bar{X}} = \frac{S}{\sqrt{n}} = \frac{10}{\sqrt{100}} = 1$$

Set P-value threshold:  
 $\alpha = 2.5\%$

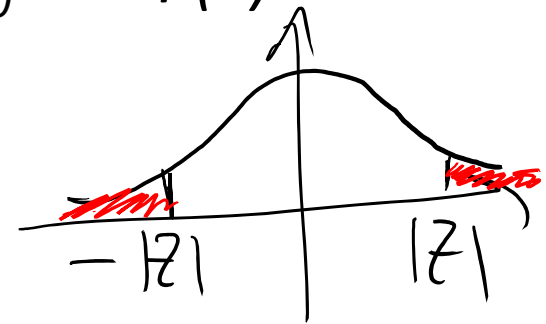


$$\beta = P(\text{Accept } H_0 \mid H_1 \text{ is true}) = \int_{48.04}^{\infty} \frac{1}{\sqrt{2\pi}} \exp\left(-\frac{(x-47)^2}{2}\right) dx = 1 - \Phi(1.04) = 15\%$$

$$\alpha = 1 - \Phi(1.96) = 2.5\%$$

# Generalizations

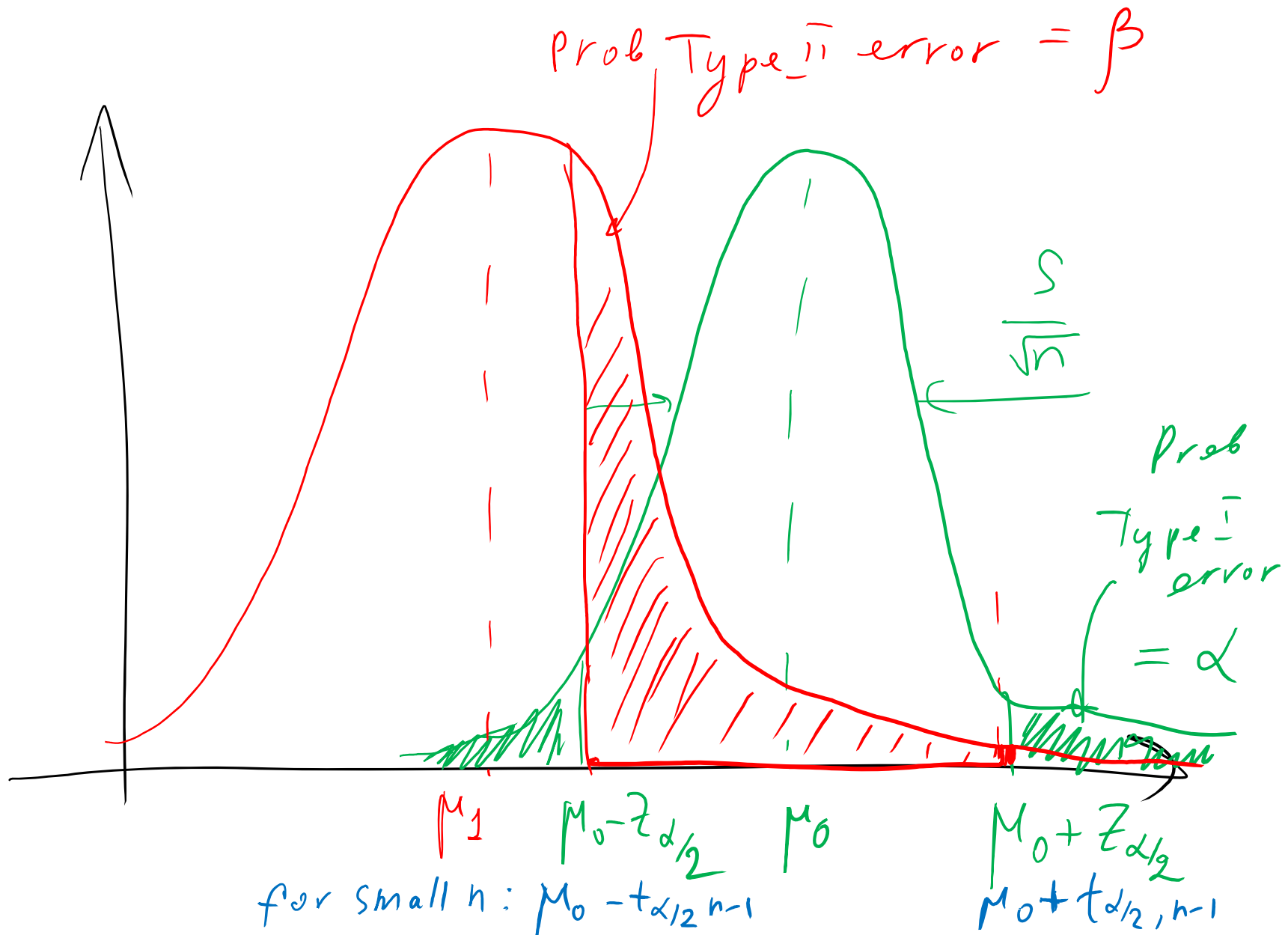
- What if  $H_1$  is a two-sided hypothesis?
- A: P-value is  $2(1-\Phi(|Z|))$ , where  $Z=(\bar{X}-\mu_0)/[S/\sqrt{n}]$   
 Compare to: For one sided  $\mu_1 > \mu_0$  it is  $1-\Phi(Z)$   
 For one sided  $\mu_1 < \mu_0$  it is  $\Phi(Z)$
- If  $\alpha$  is given use  $\mu_0 \pm z_{\alpha/2}$  as thresholds to reject the null hypothesis



- What if the sample size  $n$  is small (say  $n < 10$ ):
- A: Use t-distribution with  $n-1$  degrees of freedom for 2-sided  $P\text{-value} = 2(1 - \text{CDF\_Tdist}(|T|))$   
 where  $T=(\bar{X}-\mu_0)/[S/\sqrt{n}]$ .
- For given  $\alpha$  use  $\mu_0 \pm t_{\alpha/2, n-1}$  to reject the null hypothesis



# Type II error for two-sided hypothesis

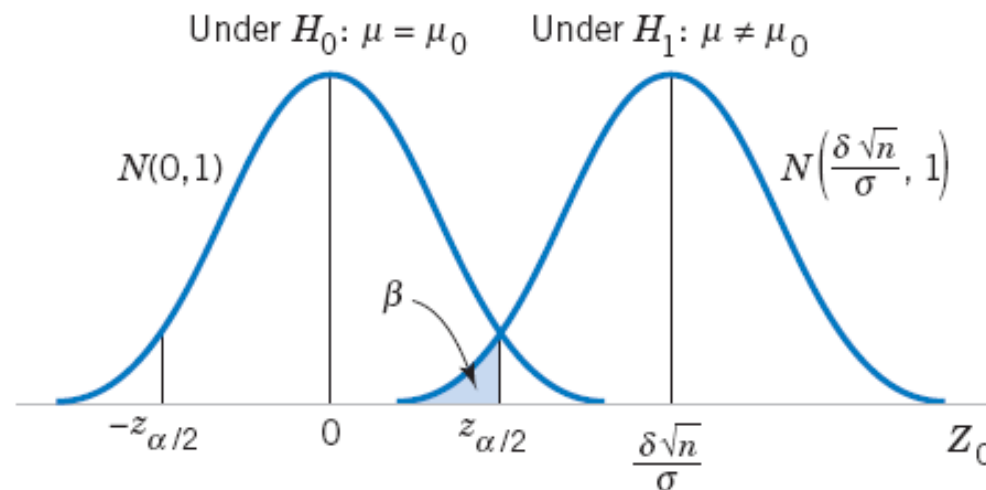


# Type II Error and Choice of Sample Size

Assume you know the minimum  $\delta = |\mu_1 - \mu_0|$  that you care about.

What is the minimal sample you should use to separate  $H_0$  and  $H_1$  hypotheses if your tolerance to type I and type II errors is  $\alpha$  and  $\beta$  ?

**Figure 9-9** The distribution of  $Z_0$  under  $H_0$  and  $H_1$ .



$$\frac{\delta\sqrt{n}}{\sigma} = z_{\alpha/2} + z_{\beta}$$

$$n \simeq \frac{(z_{\alpha/2} + z_{\beta})^2 \sigma^2}{\delta^2} \quad \text{where} \quad \delta = \mu - \mu_0 \quad (9-22)$$

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# P-value vs $\alpha$

- P-value gives the result of accept/reject the null hypothesis at all values of  $\alpha$

Table 11.1: A commonly adopted convention for reporting  $p$  values: in many places it is conventional to report one of four different things (e.g.,  $p < .05$ ) as shown below. I've included the "significance stars" notation (i.e., a \* indicates  $p < .05$ ) because you sometimes see this notation produced by statistical software. It's also worth noting that some people will write *n.s.* (not significant) rather than  $p > .05$ .

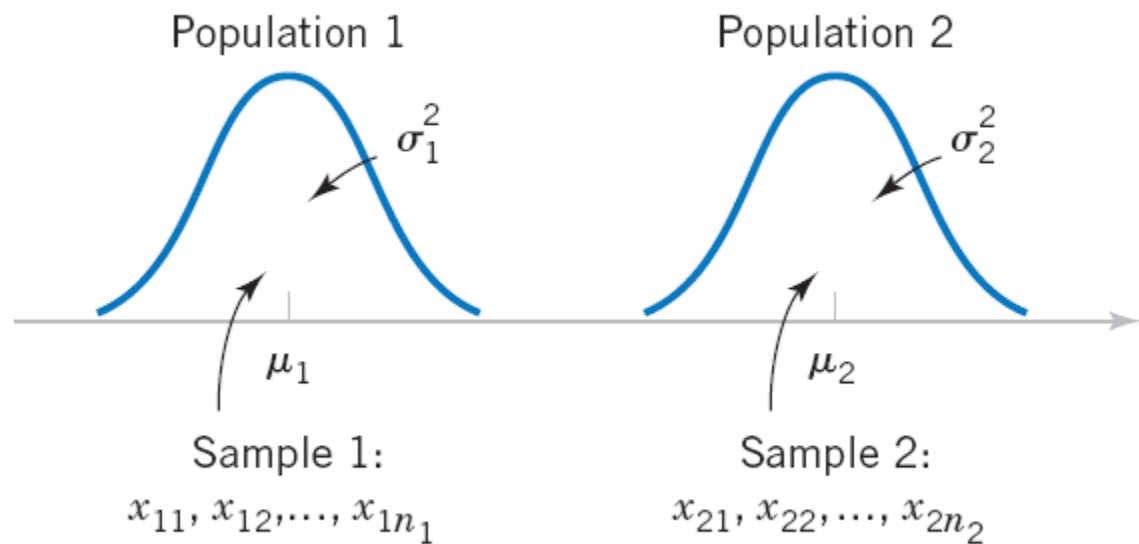
Usual notation	Signif. stars	English translation	The null is...
$p > .05$		The test wasn't significant	Retained
$p < .05$	*	The test was significant at $\alpha = .05$ but not at $\alpha = .01$ or $\alpha = .001$ .	Rejected
$p < .01$	**	The test was significant at $\alpha = .05$ and $\alpha = .01$ but not at $\alpha = .001$ .	Rejected
$p < .001$	***	The test was significant at all levels	Rejected

.....

# Hypothesis testing: two samples

## 10-2: Inference for a Difference in Means of Two Normal Distributions, Variances Known

**Figure 10-1** Two independent populations.



**Figure 10-1** Two independent populations.

## 10-2: Inference for a Difference in Means of Two Normal Distributions, Variances Known

### Assumptions

1.  $X_{11}, X_{12}, \dots, X_{1n_1}$  is a random sample from population 1.
2.  $X_{21}, X_{22}, \dots, X_{2n_2}$  is a random sample from population 2.
3. The two populations represented by  $X_1$  and  $X_2$  are independent.
4. Both populations are normal.

$$E(\bar{X}_1 - \bar{X}_2) = E(\bar{X}_1) - E(\bar{X}_2) = \mu_1 - \mu_2$$

$$V(\bar{X}_1 - \bar{X}_2) = V(\bar{X}_1) + V(\bar{X}_2) = \frac{\sigma_1^2}{n_1} + \frac{\sigma_2^2}{n_2}$$

## 10-2: Inference for a Difference in Means of Two Normal Distributions, Variances Known

The quantity

$$Z = \frac{\bar{X}_1 - \bar{X}_2 - (\mu_1 - \mu_2)}{\sqrt{\frac{\sigma_1^2}{n_1} + \frac{\sigma_2^2}{n_2}}} \quad (10-1)$$

has a  $N(0, 1)$  distribution.

## 10-2: Inference for a Difference in Means of Two Normal Distributions, Variances Known

### 10-2.1 Hypothesis Tests for a Difference in Means, Variances Known

Null hypothesis:  $H_0: \mu_1 - \mu_2 = \Delta_0$

Test statistic: 
$$Z_0 = \frac{\bar{X}_1 - \bar{X}_2 - \Delta_0}{\sqrt{\frac{\sigma_1^2}{n_1} + \frac{\sigma_2^2}{n_2}}} \quad (10-2)$$

Alternative Hypotheses	P-Value	Rejection Criterion For for Fixed-Level Tests
$H_1: \mu_1 - \mu_2 \neq \Delta_0$	Probability above $ z_0 $ and probability below $- z_0 $ , $P = 2[1 - \Phi( z_0 )]$	$z_0 > z_{\alpha/2}$ or $z_0 < -z_{\alpha/2}$
$H_1: \mu_1 - \mu_2 > \Delta_0$	Probability above $z_0$ , $P = 1 - \Phi(z_0)$	$z_0 > z_\alpha$
$H_1: \mu_1 - \mu_2 < \Delta_0$	Probability below $z_0$ , $P = \Phi(z_0)$	$z_0 < -z_\alpha$

## 10-2.1 Hypotheses Tests on the Difference in Means, Variances Unknown

**Case 2:**  $\sigma_1^2 \neq \sigma_2^2$

If  $H_0: \mu_1 - \mu_2 = \Delta_0$  is true, the statistic

$$T_0^* = \frac{\bar{X}_1 - \bar{X}_2 - \Delta_0}{\sqrt{\frac{S_1^2}{n_1} + \frac{S_2^2}{n_2}}} \quad (10-15)$$

is distributed as **t-distribution** with degrees of freedom given by

$$v = n_1 + n_2 - 2,$$

or more generally

# Let's do a sweet exercise #1

424

## Example 10-7

### Chocolate and Cardiovascular Health

An article in *Nature* (2003, Vol. 424, p. 1013) described an

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## Plasma antioxidants from chocolate

Dark chocolate may offer its consumers health benefits the milk variety cannot match.

There is some speculation that dietary flavonoids from chocolate, in particular (–)epicatechin, may promote cardiovascular health as a result of direct antioxidant effects or through antithrombotic mechanisms<sup>1–3</sup>. Here we show that consumption of plain, dark chocolate (Fig. 1) results in an increase in both the total antioxidant capacity and the (–)epicatechin content of blood plasma, but that these effects are markedly reduced when the chocolate is consumed with milk or if milk is incorporated as milk chocolate. Our findings indicate that milk may interfere with the absorption of antioxidants from chocolate *in vivo* and may therefore negate the potential health benefits that can be derived from eating moderate amounts of dark chocolate.

To determine the antioxidant content of different chocolate varieties, we took dark chocolate and milk chocolate prepared from the same batch of cocoa beans and defatted them twice with *n*-hexane before extracting them with a mixture of water, acetone and acetic acid (70.0:29.8:0.2 by volume). We measured their *in vitro* total antioxidant capacities using the ferric-reducing antioxidant potential (FRAP) assay<sup>4</sup>; FRAP

reduced iron per 100 g for dark and milk chocolate, respectively. Volunteers must therefore consume twice as much milk chocolate as dark chocolate to receive a similar intake of antioxidants.

We recruited 12 healthy volunteers (7 women and 5 men with an average age of  $32.2 \pm 1.0$  years (range, 25–35 years). Subjects were non-smokers, had normal blood lipid levels, were taking no drugs or vitamin supplements, and had an average weight of  $65.8 \pm 3.1$  kg (range, 46.0–86.0 kg) and body-mass index of  $21.9 \pm 0.4$  kg m<sup>–2</sup> (range, 18.6–23.6 kg m<sup>–2</sup>). On different days, following a crossover experimental design, subjects consumed 100 g dark chocolate, 100 g dark chocolate with 200 ml full-fat milk, or 200 g milk chocolate (containing the equivalent of up to 40 ml milk).

One hour after subjects had ingested the chocolate, or chocolate and milk, we measured the total antioxidant capacity of their plasma by FRAP assay. Plasma antioxidant levels increased significantly after consumption of dark chocolate alone, from  $100 \pm 3.5\%$  to  $118.4 \pm 3.5\%$  (*t*-test,  $P < 0.001$ ), returning to baseline values ( $95.4 \pm 3.6\%$ ) after 4 h (Fig. 2a). There was



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†Plant Products and Human Nutrition Group, Graham Kerr Building, Division of Biochemistry and Molecular Biology, Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow G12 8QQ, UK

**Figure 1** Stack of benefits? Unlike its milky counterpart, dark chocolate may provide more than just a treat for the tastebuds.

could be due to the formation of secondary bonds between chocolate flavonoids and milk proteins<sup>6,7</sup>, which would reduce the biological accessibility of the flavonoids and therefore the chocolate's potential antioxidant properties *in vivo*.

Our findings highlight the possibility

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Vol. 424

# Sweet matlab exercise #1

- **dark=[118.8 122.6 115.6 113.6 119.5 115.9  
115.8 115.1 116.9 115.4 115.6 107.9];**
- **milk=[102.1 105.8 99.6 102.7 98.8 100.9 102.8  
98.7 94.7 97.8 99.7 98.6]**
- You can download it at the course website
- Calculate **P-value** of the null hypothesis  **$H_0$**  that **milk = dark** against  **$H_1$**  that **dark > milk**

# Sweet matlab exercise #1

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- `milk=[102.1 105.8 99.6 102.7 98.8 100.9 102.8 98.7 94.7 97.8 99.7 98.6]`
- `x_dark=mean(dark) % sample mean dark chocolate`
- `x_milk=mean(milk) % sample mean milk chocolate`
- `s_dark=std(dark) % sample std dark chocolate`
- `s_milk=std(milk) % sample std milk chocolate`
- `n=12 % % sample size of both dark and milk`
- `std_xdiff=sqrt(s_dark.^2./2+s_milk.^2./n) % std diff x`
- `z_stat=(x_dark-x_milk)./std_xdiff % z-statistic`
- `P_value_z=erfc (z_stat./sqrt(2))./2 %P-value null true`

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WHY IS SPACE BLACK  
WHY IS OUTER SPACE SO COLD  
WHY ARE THERE PYRAMIDS ON THE MOON  
WHY IS NASA SHUTTING DOWN



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