INTRODUCTION TO BIOSTATISTICS
Hypothesis Testing

Perform the following steps in any test of hypotheses:

1. Determine the null hypothesis $H_0$.
2. Determine the alternative hypothesis $H_a$.
3. Choose the level of significance of the test ($\alpha$-level).
4. Follow the appropriate decision rule (see below).

1 Single sample hypothesis tests

1.1 Hypothesis tests involving the mean $\mu$ of a population

1.1.1 $\sigma$ known

Compute $z = \frac{\bar{x} - \mu_0}{\sigma / \sqrt{n}}$, where $\bar{x} = \frac{1}{n} \sum_{i=1}^{n} x_i$.

- Two-sided test hypotheses
  $H_0: \mu = \mu_0$
  $H_a: \mu \neq \mu_0$

  **Decision Rule:** Reject if $z \leq -z_{\alpha/2}$, or if $z \geq z_{\alpha/2}$

- One-sided test of hypotheses
  - $H_0: \mu \geq \mu_0$
    $H_a: \mu < \mu_0$

    **Decision Rule:** Reject if $z \leq -z_\alpha$

  - $H_0: \mu \leq \mu_0$
    $H_a: \mu > \mu_0$

    **Decision Rule:** Reject if $z \geq z_\alpha$

1.1.2 $\sigma$ unknown

Compute $t = \frac{\bar{x} - \mu_0}{s / \sqrt{n}}$, where $s = \sqrt{\frac{1}{n-1} \sum_{i=1}^{n} (x_i - \bar{x})^2}$ and $\bar{x} = \frac{1}{n} \sum_{i=1}^{n} x_i$.

- Two-sided test hypotheses
  $H_0: \mu = \mu_0$
  $H_a: \mu \neq \mu_0$

  **Decision Rule:** Reject if $t \leq -t_{n-1; \alpha/2}$, or if $t \geq t_{n-1; \alpha/2}$

- One-sided test of hypotheses
  - $H_0: \mu \geq \mu_0$
    $H_a: \mu < \mu_0$

    **Decision Rule:** Reject if $t \leq -t_{n-1; \alpha}$

  - $H_0: \mu \leq \mu_0$
    $H_a: \mu > \mu_0$

    **Decision Rule:** Reject if $t \geq t_{n-1; \alpha}$

\[ a P(Z \geq z_{\alpha/2}) = \frac{\alpha}{2} \text{ (the tail of the normal density to the right of } z_{\alpha/2}). \]

\[ b P(T \geq t_{n-1; \alpha}^*) = \frac{\alpha}{2} \text{ (the tail of the } t \text{ density with } n-1 \text{ degrees of freedom to the right of } t_{n-1; \alpha}). \]
1.2 Hypothesis tests involving the proportion $p$ of a characteristic of interest (successes) in a population

Compute $z = \frac{\hat{p} - p_0}{\sqrt{\frac{p_0(1-p_0)}{n}}}$, where $\hat{p} = \frac{x}{n}$ that is the number of “successes” $x$ out of the number of “trials” (sample size) $n$.

- **Two-sided test hypotheses**
  
  $H_0: p = p_0$
  
  $H_a: p \neq p_0$

  **Decision Rule:** Reject if $z \leq -z_{\frac{\alpha}{2}}$, or if $z \geq z_{\frac{\alpha}{2}}$

- **One-sided test of hypotheses**

  - $H_0: p \geq p_0$
    
    $H_a: p < p_0$

    **Decision Rule:** Reject if $z \leq -z_\alpha$

  - $H_0: p \leq p_0$
    
    $H_a: p > p_0$

    **Decision Rule:** Reject if $z \geq z_\alpha$

Notice that when dealing with proportions, we do not have the case where $\sigma$ is unknown. This is because the distribution of sample proportions is approximately normal with mean $p$ and standard deviation $\sqrt{\frac{p(1-p)}{n}}$. By making the assumption (null hypothesis) that $p = p_0$ we also made the assumption that $\sigma = \sqrt{\frac{p_0(1-p_0)}{n}}$. 
2 Two-sample Tests

When comparing the means of two populations, the following assumptions are made:

1. The populations are normal, with means $\mu_1$ and $\mu_2$ respectively, and
2. Both populations have the same (unknown) variance $\sigma^2$.

2.1 Hypothesis tests involving the means of the populations

When comparing two population means we are confronted with the following scenarios:

2.1.1 Independent samples

A typical example of such a case is a trial with two distinct samples of sizes $n_1$ and $n_2$ respectively, that are gathered from each population (e.g. a control and a active treatment group). These two groups are independent and similar in all other characteristics but the one of interest (usually a great deal of effort goes into the design of the clinical trial to achieve this), with means $\mu_1$ and $\mu_2$. We derive the following pooled estimate of the unknown common variance, using the samples that are collected from both populations:

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

$$
= \sqrt{\frac{\sum_{i=1}^{n_1}(x_{i1} - \bar{x}_1)^2 + \sum_{j=1}^{n_2}(x_{j2} - \bar{x}_2)^2}{n_1 + n_2 - 2}}
$$

where $\bar{x}_1$ and $\bar{x}_2$ are the sample means of the two groups. The following tests are based on the statistic

$$
t = \frac{\bar{x}_1 - \bar{x}_2 - (\mu_1 - \mu_2)}{SP \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}}
$$

- Two-sided test of hypotheses
  
  $H_0: \mu_1 = \mu_2$
  
  $H_a: \mu_1 \neq \mu_2$

  **Decision Rule:** Reject if $t \leq -t_{n_1+n_2-2}; \frac{\alpha}{2}$, or if $t \geq t_{n_1+n_2-2}; \frac{\alpha}{2}$. In this and the following cases, $t = \frac{\bar{x}_1 - \bar{x}_2}{SP \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}}$, since $\mu_1 - \mu_2 = 0$ according to the null hypothesis.

- One-sided test of hypotheses

  - $H_0: \mu_1 \geq \mu_2$
  
    $H_a: \mu_1 < \mu_2$

    **Decision Rule:** Reject if $t \leq -t_{n_1+n_2-2}; \alpha$

  - $H_0: \mu_1 \leq \mu_2$
  
    $H_a: \mu_1 > \mu_2$

    **Decision Rule:** Reject if $t \geq t_{n_1+n_2-2}; \alpha$

\[c\text{Refer to section 11.2.2 in your textbook for the situation, where the two variances are unequal}\]
2.1.2 Paired samples

This situation typically involves multiple measurements taken on the same subject. For example, a before treatment (baseline) measurement and a on treatment measurement. These measurements are not independent and the methods of the previous section do not apply. Instead, the tests are based on the difference \( \bar{d} = \bar{X}_1 - \bar{X}_2 \) of the sample means of the \( n \) (paired) measurements. Compute

\[
t = \frac{\bar{d} - d_o}{s_d / \sqrt{n}}
\]

where \( s_d = \sqrt{\frac{1}{n-1} \sum_{i=1}^{n} (d_i - \bar{d})^2} \), \( d_i = (x_{i1} - x_{i2}) \) and \( \bar{d} = \frac{1}{n} \sum_{i=1}^{n} d_i \) is the sample mean difference. Note that in the case where the difference is zero under \( H_o \), \( t = \frac{\bar{d}}{s_d / \sqrt{n}} \). All tests proceed along the same lines as in subsection 1.1.2.

- **Two-sided test hypotheses**
  - \( H_o : d = 0 \)
  - \( H_a : d \neq 0 \)
  - **Decision Rule:** Reject if \( t \leq -t_{n-1; \frac{\alpha}{2}} \), or if \( t \geq t_{n-1; \frac{\alpha}{2}} \)

- **One-sided test of hypotheses**
  - \( H_o : d \geq 0 \)
  - \( H_a : d < 0 \)
  - **Decision Rule:** Reject if \( t \leq -t_{n-1; \alpha} \)
  - \( H_o : d \leq 0 \)
  - \( H_a : d > 0 \)
  - **Decision Rule:** Reject if \( t \geq t_{n-1; \alpha} \)

2.2 Comparison of two proportions

When comparing two proportions \( p_1 \) and \( p_2 \) from two independent samples, we proceed in a similar fashion as in subsection 2.1.1. If \( x_1 \) subjects out of \( n_1 \) in the first sample and \( x_2 \) out of \( n_2 \) in the second exhibit the characteristic of interest (death, development of AIDS, cancer remission, etc.) all tests are based on the sample proportions \( \hat{p}_1 = \frac{x_1}{n_1} \) and \( \hat{p}_2 = \frac{x_2}{n_2} \).

Compute \( \hat{p} = \frac{n_1 \hat{p}_1 + n_2 \hat{p}_2}{n_1 + n_2} = \frac{x_1 + x_2}{n_1 + n_2} \). Now compute the statistic,

\[
z = \frac{(\hat{p}_1 - \hat{p}_2) - (p_1 - p_2)}{\sqrt{\hat{p}(1 - \hat{p}) \left( \frac{1}{n_1} + \frac{1}{n_2} \right)}}
\]

- **Two-sided test of hypotheses**
  - \( H_o : p_1 = p_2 \)
  - \( H_a : p_1 \neq p_2 \)
  - **Decision Rule:** Reject if \( z \leq -z_{\frac{\alpha}{2}} \), or if \( z \geq z_{\frac{\alpha}{2}} \). In this and the following cases, \( z = \frac{\hat{p}_1 - \hat{p}_2}{\sqrt{\hat{p}(1 - \hat{p}) \left( \frac{1}{n_1} + \frac{1}{n_2} \right)}} \), since \( p_1 - p_2 = 0 \) according to the null hypothesis.

- **One-sided test of hypotheses**
  - \( H_o : p_1 \geq p_2 \)
    - \( H_a : p_1 < p_2 \)
    - **Decision Rule:** Reject if \( z \leq -z_{\alpha} \)
  - \( H_o : p_1 \leq p_2 \)
    - \( H_a : p_1 > p_2 \)
    - **Decision Rule:** Reject if \( z \geq z_{\alpha} \)