Trollen

Testing the Difference Between Proportions (p_1 - p_2)

BACKGROUND

VIAGRA® is a prescription medicine that is used to treat male impotence. To protect American consumers, the U. S. Food and Drug Administration requires drug manufacturers to conduct clinical trials to demonstrate a drug's safety and effectiveness. In applying for FDA approval for VIAGRA, Pfizer Pharmaceuticals, Inc. submitted the results of 21 separate clinical trials. The information below, obtained from the FDA web site[1,2], is part of the FDA's summary of those clinical trials. VIAGRA received FDA approval on March 27, 1998.

Review this material, including the footnotes and explanatory remarks. You'll perform a hypothesis test at the end of the document.

FDA SUMMARY

VIAGRA is used to treat impotence in men. VIAGRA increases the body's ability to achieve and maintain an erection during sexual stimulation. VIAGRA does not protect you from getting sexually transmitted diseases, including HIV.

In clinical studies, VIAGRA was assessed for its effect on the ability of men with erectile dysfunction (ED) to engage in sexual activity and in many cases specifically on the ability to achieve and maintain an erection sufficient for satisfactory sexual activity. VIAGRA was evaluated primarily at doses of 25 mg, 50 mg and 100 mg in 21 randomized[3], double-blind[4], placebo[5]-controlled trials of up to 6 months in duration, using a variety of study designs (fixed dose, titration, parallel, crossover). VIAGRA was administered to more than 3,000 patients aged 19 to 87 years, with ED of various etiologies[6] (organic, psychogenic, mixed) with a mean duration of 5 years. *VIAGRA demonstrated statistically significant improvement compared to placebo* in all 21 studies.

The frequency of patients reporting improvement of erections in four of the randomized, double-blind, parallel, placebo-controlled fixed dose studies (1797 patients) of 12 to 24 weeks duration is shown in Figure 4. Sixty-three percent, 74%, and 82% of the patients on 25 mg, 50 mg and 100 mg of VIAGRA, respectively, reported an improvement in their erections, compared to 24% on placebo.

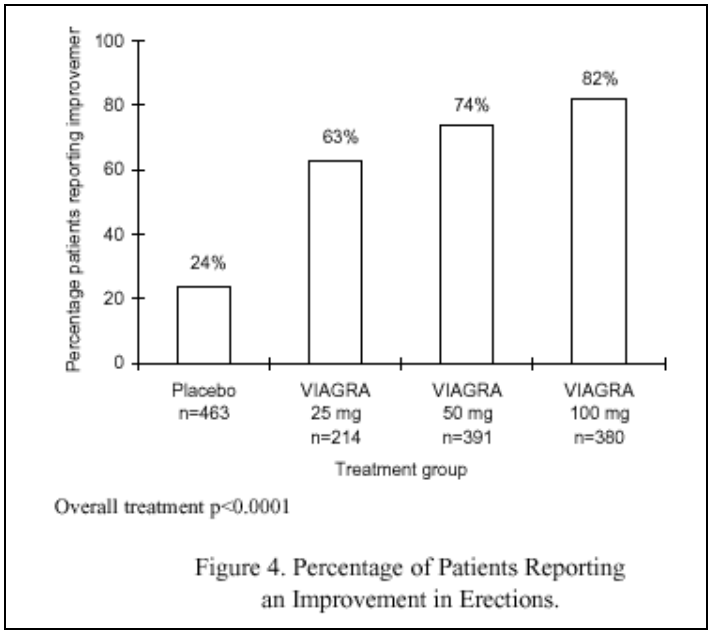

Figure 4. Percentage of Patients Reporting an Improvement in Erections.

[1] http://www.fda.gov/cder/foi/label/1998/viagralabel2.pdf
[2] http://www.fda.gov/cder/consumerinfo/druginfo/Viagra.htm
[3] This means patients were randomly assigned to one of the four treatment groups.
[4] This means that neither the patient nor the researcher knew whether the patient received Placebo or one of the three doses of VIAGRA.
[5] This means that some patients were given a pill with no active ingredients, the other patients were given one of the three doses of VIAGRA.
[6] The underlying cause of the patient's impotence.

EXPLANATORY NOTES

The chart cites the *percentage* of patients in each treatment group that reported improvement of erections. For convenience, the percentages were cited as whole numbers. For example, the chart cites the improvement percentage for Placebo as 24%. Since we know there were 463 in the Placebo group, we can obtain the *number* of men with improvement by multiplying the percentage by the number in the Placebo group. This calculates as 111.12 (.24*463). We can infer that there were 111 out of 463, which is actually .2397408, which was rounded to 24% for the chart. Since we need to use the sample proportion in calculations when we perform a hypothesis test, we'll use the more *precise* value .2397 rather than the *rounded* value. Similarly, the improvement rate for $VIAGRA_{25}$ was .6308, for $VIAGRA_{50}$ was .7391, and for $VIAGRA_{100}$ was .8211.

The improvement rates plotted in the chart *seem* to indicate that VIAGRA was more effective than Placebo, and was even more effective at higher doses (50 and 100 mg). But recall that these are *sample* results, which may be biased. Although the sample improvement rate for $VIAGRA_{25}$ was .6308, the *true* improvement rate could actually be higher or lower. Similarly, Placebo's *sample* improvement rate was .2397, which could either overestimate or underestimate the *true* Placebo improvement rate.

Notice the text below the chart that says "Overall treatment $p<0.0001$." Based partially on this small p-value, the FDA researchers concluded *"VIAGRA demonstrated statistically significant improvement compared to placebo*."

In order to verify the FDA's conclusion regarding VIAGRA's effectiveness, we can perform hypothesis tests to determine whether the difference between the improvement rate for Placebo and for VIAGRA is *significantly different* (i.e., unlikely to be caused by sampling error). We can also perform tests to determine whether higher doses of VIAGRA have significantly higher improvement rates than lower doses. We'll focus on three hypothesis tests:

- Is the improvement rate for $VIAGRA_{25}$ significantly different from the rate for Placebo?
- Is the improvement rate for $VIAGRA_{50}$ significantly different from the rate for $VIAGRA_{25}$?
- Is the improvement rate for $VIAGRA_{100}$ significantly different from the rate for $VIAGRA_{50}$?

Suppose we perform the first hypothesis test and find a *significant difference* between the improvement rates for $VIAGRA_{25}$ and for Placebo. This would mean it is unlikely that sampling error could cause this large a difference (.2397 and .6308) if the *true* improvement rates for these two treatments were the same. We'd conclude that $VIAGRA_{25}$ has a *higher* improvement rate and is more effective than Placebo.

On the other hand, suppose we perform the first hypothesis test and find that the rates *aren't significantly different*. This would mean that it is possible that the improvement rate for $VIAGRA_{25}$ and for Placebo are the same value (eg: .4555) and that sampling error caused the $VIAGRA_{25}$ improvement rate to be too high (.6308) and caused the Placebo improvement rate to be too low (.2397). We'd conclude that $VIAGRA_{25}$ is not more effective than Placebo.

ASSIGNMENT

Although there are three hypothesis tests to do, perform the one assigned to you based on your Student ID (Social Security number) as described in the table below.

Perform this test…	**…if the *last* two digits of your StudentId are**
Is the improvement rate for $VIAGRA_{25}$ significantly different from the improvement rate for Placebo?	00-32
Is the improvement rate for $VIAGRA_{50}$ significantly different from the improvement rate for $VIAGRA_{25}$?	33-66
Is the improvement rate for $VIAGRA_{100}$ significantly different from the improvement rate for $VIAGRA_{50}$?	67-99

Perform your assigned test in the space provided on the attached worksheet, showing all calculations. In step 5, use *your choice* of either method I or method II, and also calculate the p-value. Use the *precise* improvement rates of: Placebo = .2397, $VIAGRA_{25}$ = .6308, $VIAGRA_{50}$ = .7391, and $VIAGRA_{100}$ = .8211.

NAME _____ STUDENT ID_____

Is the improvement rate for VIAGRA$_{25}$ significantly different from the improvement rate for Placebo?

1) H_o: $p_{Viagra25} - p_{Placebo} = 0$ (no difference in rates)
   H_a: $p_{Viagra25} - p_{Placebo} \neq 0$ (is a difference in rates)
2) $\alpha = .01$
3) Test statistic: _____ whose sampling distribution follows the ____ distribution.
4) Critical value(s) _____
5) Analyze sample results

p-value

6) The researcher [can | cannot] reject H_o and should conclude

Is the improvement rate for VIAGRA$_{50}$ significantly different from the improvement rate for VIAGRA$_{25}$?

1) H_o: $p_{Viagra50} - p_{Viagra25} = 0$ (no difference in rates)
   H_a: $p_{Viagra50} - p_{Viagra25} \neq 0$ (is a difference in rates)
2) $\alpha = .01$
3) Test statistic: _____ whose sampling distribution follows the ____ distribution.
4) Critical value(s) _____
5) Analyze sample results

p-value

6) The researcher [can | cannot] reject H_o and should conclude

Is the improvement rate for VIAGRA$_{100}$ significantly different from the improvement rate for VIAGRA$_{50}$?

1) H_o: $p_{Viagra100} - p_{Viagra50} = 0$ (no difference in rates)
   H_a: $p_{Viagra100} - p_{Viagra50} \neq 0$ (is a difference in rates)
2) $\alpha = .01$
3) Test statistic: _____ whose sampling distribution follows the ____ distribution.
4) Critical value(s) _____
5) Analyze sample results

p-value

6) The researcher [can | cannot] reject H_o and should conclude