A Phase III dose-finding clinical trial in patients with pancreatic cancer was conducted to determine if at least one of two doses of a new experimental treatment has a beneficial effect on 1-year mortality. Occasionally, for serious illnesses such as pancreatic cancer, the FDA allows the sponsor to skip Phase II and go directly to a Phase III dose-finding study in order to expedite product testing and get the product on the market as soon as possible, especially when there is no current treatment for the disease being studied. However, the usual appropriate statistical rigor required for Phase III (i.e., control the probability of a false positive study at 0.05) needs to be applied.

	Died Within 1 Year of Randomization	
Treatment Group	**Yes**	**No**
Control	30	16
Low Dose	23	22
High Dose	13	31

H_0: $p_{low} = p_P$ The proportion of death is the same in the low experimental dose and placebo groups.
H_A: $p_{low} \neq p_P$ The proportion of death is not the same in the low experimental dose and placebo groups.

H_0: $p_{high} = p_P$ The proportion of death is the same in the low experimental dose and placebo groups.
H_A: $p_{high} \neq p_P$ The proportion of death is not the same in the low experimental dose and placebo groups.

2 tests will be performed, so the Bonferroni correction is $\frac{0.05}{2} = 0.025$.

Pairwise Comparison between Low Dose and Placebo

The FREQ Procedure

Frequency Row Pct	Table of trt by outcome		
	outcome(Death)		
trt	Alive	Died	Total
Low Dose	22 48.89	23 51.11	45
Placebo	16 34.78	30 65.22	46
Total	38	53	91

Pairwise Comparison between High Dose and Placebo

The FREQ Procedure

Frequency Row Pct	Table of trt by outcome		
	outcome(Death)		
trt	Alive	Died	Total
High Dose	31 70.45	13 29.55	44
Placebo	16 34.78	30 65.22	46
Total	47	43	90

There are 14.11% (95% CI: -37.06%, 8.84%,) fewer cases of death in the low dose group than in the placebo group. The risk of death in the low dose group is 78.36% (95% CI: 52.21%, 117.65%) of the risk in the placebo group.

There are 35.67% (95% CI: -57.70%, -13.64%) fewer cases of death in the high dose group than in the placebo group. The risk of death in the high dose group is 45.30% (95% CI: 25.49%, 80.50%) of the risk in the placebo group.

$$low\ dose\ vs\ placebo\ p-value\ =\ 0.1725$$
$$adjusted\ p-value\ =\ 2\times 0.1725\ =\ 0.3454$$

$$high\ dose\ vs\ placebo\ p-value\ =\ 0.0007$$
$$adjusted\ p-value\ =\ 2\times 0.0007\ =\ 0.0014$$

The low doses' adjusted p-value was 0.3454, which is greater than the α=0.05 significance level, while the high dose's adjusted p-value was 0.0014, which is less than the α=0.05 significance level. Only the null hypothesis of the proportion of death being the same as the placebo group can be rejected for the high dose comparison.

The low dose's 95% confidence interval for the risk difference contains 0 and the risk ratio contains 1, so those effects were not significant. On the other hand, the high dose's 95% confidence interval for the risk difference doesn't contain 0 and the risk ratio doesn't contain 1, so those effects are statistically significant. Since at least one dose, the high dose, was found to be significantly more effective than the control at reducing mortality, the study was found to be a success.

Persons who inject drugs (PWID) often experience stigma, which is defined as the social exclusion and dehumanization of individuals in an undesirable social category. A randomized controlled trial will be conducted to assess the effect of a stigma intervention targeted to help PWID cope with stigma. Patients will be recruited at 3 treatment addition clinics. They will be randomized 1:1 to either i) stigma intervention consisting of three 2-hour group sessions (stigma intervention), or ii) standard of care (control intervention). The primary outcome is overdose during the 12-month study period. The investigators expect that 15% of patients in the control group will experience an overdose in the 12 months following the intervention, but they hope that only 5% of patients in the stigma intervention group will experience an overdose event.

H_0: $p_A = p_P$ The proportion of overdose is the same in the stigma intervention group and control group.
H_A: $p_A \neq p_P$ The proportion of overdose is not the same in the stigma intervention group and control group.

The investigators are hoping to detect a 10% decrease in proportion of overdose in the stigma intervention group compared to the control group.

$$\frac{282}{1 - 0.15} = 332$$

A sample size of 282 total subjects, 141 per group, yields 80% power to detect a significant difference in proportion of overdoses of 10%, assuming risk of 15% in the control group and 5% in the stigma intervention group. To allow for 15% loss to follow-up, a total of 332 total subjects are needed.

$$\frac{297}{1 - 0.15} = 350$$

A sample size of 297 total subjects yields 80% power to detect a significant difference in proportion of overdoses of 10%, using a 2:1 allocation ratio while assuming risk of 15% in the control group and 5% in the stigma intervention group. To allow for 15% loss to follow-up, a total of 350 total subjects are needed.

H_0: $\mu_A = \mu_P$ The average change in stigma score from baseline to 12 months is the same in the stigma intervention group and control group.
H_A: $\mu_A \neq \mu_P$ The average change in stigma score from baseline to 12 months is not the same in the stigma intervention group and control group.

Using a sample of 350 subjects in a 2:1 allocation ratio to detect a significant difference in change in stigma score from baseline to 12 months of at least 3 units, 90.8% power will be yielded.