1-3. We can illustrate these two methods of analysis (ITT and PP) through the following study on diabetes. People design a clinical trials about a new drug in the treatment A that may reduce the risk to develop diabetes. This study identified 350 patients as being at increased risk and randomly assigned them to treatment or placebo. Of the 170 patients randomized to the treatment A, 75 patients withdrew from the study, 95 completed it, and 10 developed diabetes. Among the 180 patients randomized to the placebo group, 70 withdrew from the study, 110 participated until delivery, and 15 patients developed diabetes.

Number	Study groups	
	New Drug	Placebo
Patients randomized	170	180
Patients who withdraw from the study	75	70
Patients who develop diabetes	10	15
Compliers who develop diabetes	4	8
Analysis Percentage of patients developing diabetes		
Intention-to-treat Analysis (ITT)		
Per protocol analysis (PP)		

1. Please use ITT and PP analyses to calculate the percentage of patients developing diabetes separately, complete the table, and use Z test to compare the treatment effects of ITT study and PP study. $\alpha = 0.01$

2. Compare ITT results with PP results, what's your conclusion?

3. Given $\alpha = 0.05$, please do odds ratio tests and confidence interval to compare the developing diabetes rate in treatment A with the developing diabetes rate in placebo for ITT and PP analysis separately.

$$ITT: \qquad H_0: \log(OR_{ITT}) = 0 \quad vs \quad H_a: \log(OR_{ITT}) \neq 0$$

$$PP: \qquad H_0: \log(OR_{PP}) = 0 \quad vs \quad H_a: \log(OR_{PP}) \neq 0$$

ITT:

	New Drug	Placebo
Diabetes	10	15
No diabetes	160	165

PP:

	New Drug	Placebo
Diabetes	4	8
No diabetes	95	110

Statistical issues	Tests or measurements	Null hypothesis	Test statistics	Confidence intervals
Estimate of the population proportion	One-sample Z-test	$H_0: \pi_1 = \pi_0$ π_1 is the population proportion for the drug group and π_0 is a fixed proportion	$Z = \frac{p_1 - \pi_0}{SE(p_1)}$ $SE(p_1 - p_2) = \sqrt{p_1(1 - p_1)/n_1}$	$p_1 \pm Z_{\alpha/2} SE(p_1)$
Comparison of two proportions	Chi-squared test	$H_0: \pi_1 = \pi_2$ π_1 and π_2 are the population proportions for the active drug and placebo groups, respectively	$\chi^2 = \sum \frac{(O - E)^2}{E}$ $df = 1$	Not available
	Z-test	$H_0: \pi_1 = \pi_2$	$Z = \frac{p_1 - p_2}{SE(p_1 - p_2)}$ $SE(p_1 - p_2) = \sqrt{(p[1 - p][1/n_1 + 1/n_2])}$ $p = \frac{(a + b)}{(n_1 + n_2)}$	$(p_1 - p_2) \pm Z_{\alpha/2} SE(p_1 - p_2)$
Assessment of the size of treatment effect	Risk difference	$H_0: \pi_1 = \pi_2$	The same as in the Z-test, above	The same as in the Z-test, above
	Risk ratio (RR)	$H_0: RR = 1$	$Z = \frac{\log RR}{SE(\log RR)}, RR = \frac{p_1}{p_2}$ $SE(\log RR) = \sqrt{1/a - 1/n_1 + 1/b - 1/n_2}$	95% CI(RR) = RR / EF to $RR \times EF$ $EF = \exp[1.96 \times SE(\log RR)]$
	Odds ratio (OR)	$H_0: OR = 1$	$Z = \frac{\log OR}{SE(\log OR)}, OR = \frac{a/c}{b/d}$ $SE(\log OR) = \sqrt{1/a + 1/b + 1/c + 1/d}$	95% CI(OR) = OR / EF to $RR \times EF$ $EF = \exp[1.96 \times SE(\log OR)]$
Comparison of $r \times c$ table	Chi-squared test	H_0: percentage distributions are the same among different groups	$\chi^2 = \sum \frac{(O - E)^2}{E}$, $df = (r - 1)(c - 1)$	Not available

Death	Treatment		Total
	Active drug	Placebo	
Yes	110 (a)	165 (b)	275 ($a + b$)
No	1935 (c)	1857 (d)	3792 ($c + d$)
Total	2045 (n_1)	2022 (n_2)	4067 ($n_1 + n_2$)
Proportion of deaths	5.38% ($p_1 = \frac{a}{n_1} \times 100$)	8.16% ($p_2 = \frac{b}{n_2} \times 100$)	6.76% ($p = \frac{a + b}{n} \times 100$)