QUESTION 2

Refer to the article A CONTROLLED TRIAL OF A HUMAN PAPILLOMAVIRUS TYPE 16 VACCINE

a. The study employed a fixed-numbers of events design" (1st sentence Statistical Analysis section).

Why this design rather than a "fixed number of woman-years-of-followup" design?

b. With I denoting incidence, v denoting the vaccinated and u the unvaccinated, Efficacy (E) is defined here as a percentage

$$E = 100 \times (I_u - I_v) / I_u = 100 \times (1 - I_v / I_u)$$

Consider a very large rct (so random variation is not an issue), with 1/2 receiving the vaccine and 1/2 the placebo, and concentrate on the ***total number of cases*** (of persistent infection).

What is the relation between the proportion (P) of these cases that would be in the vaccinated group (i.e. what fraction of cases would be 'exposed' cases) and the vaccine efficacy E?

To answer, calculate for every 1 case in the unvaccinated, how many cases there would be in the vaccinated; then express the #v as a proportion of (#u + #v).

E (%)	0	25	50	75	80	90
# u cases	1	1	1	1	1	1
# v cases	___	___	___	___	___	___
P=proportion of cases that received v	___	___	___	___	___	___

c. Suppose that in the actual (finite) study, subject as it was to random variations, the authors had analyzed the data when the total number of cases was 31, i.e. when the observed proportion of cases that had been vaccinated was p=0/31 i.e., when the point estimate for P was p=0.0. This point estimate translates into an 'exact' 95% 2-sided CI for P of 0.0 to 0.11.

From this CI, and interpolation in the table you constructed in part b, find 'exact' 95% limits for E.