1. Consider studies designed to compare the occurrence of a binary outcome between two populations: population A and population B. In general, which of the following statements best describes the relationship between the relative risk estimate (RR-hat) and the odds ratio estimate (OR_hat), both based on the same two samples from populations A and B?

- ○ RR_hat = OR_hat/(n1+n2) where n1 and n2 are the size of the samples from populations A and B, respectively.
- ◉ RR_hat and OR_hat may differ in value, but will show the same direction of association.
- ○ If RR_hat >1 then will OR_hat will be less than 1.
- ○ RR_hat and OR_hat will always be exactly the same in value.

2. How does the Kaplan-Meier approach to estimating the survival function utilize information from censored observations?

- ○ It does not. All censored observations are dropped from the data sample before the curve is estimated.
- ◉ The Kaplan-Meier approach uses the censored observations when considering who is "at risk" of an event at a given time in the follow-up period. All censored observations are considered "at risk" of an event until the time of censoring.
- ○ The Kaplan-Meier approach treats the censoring times as event times. (i.e., it ignores the fact that these observations are censored)
- ○ The Kaplan-Meier approach treats the event times as censoring times

3. A randomized prospective study is conducted to estimate the association between taking a drug and remission for patients with a specific type of cancer. The estimated incidence rate ratio of remission for the treatment group relative to the placebo is 1.35. What is the proper interpretation of this value?

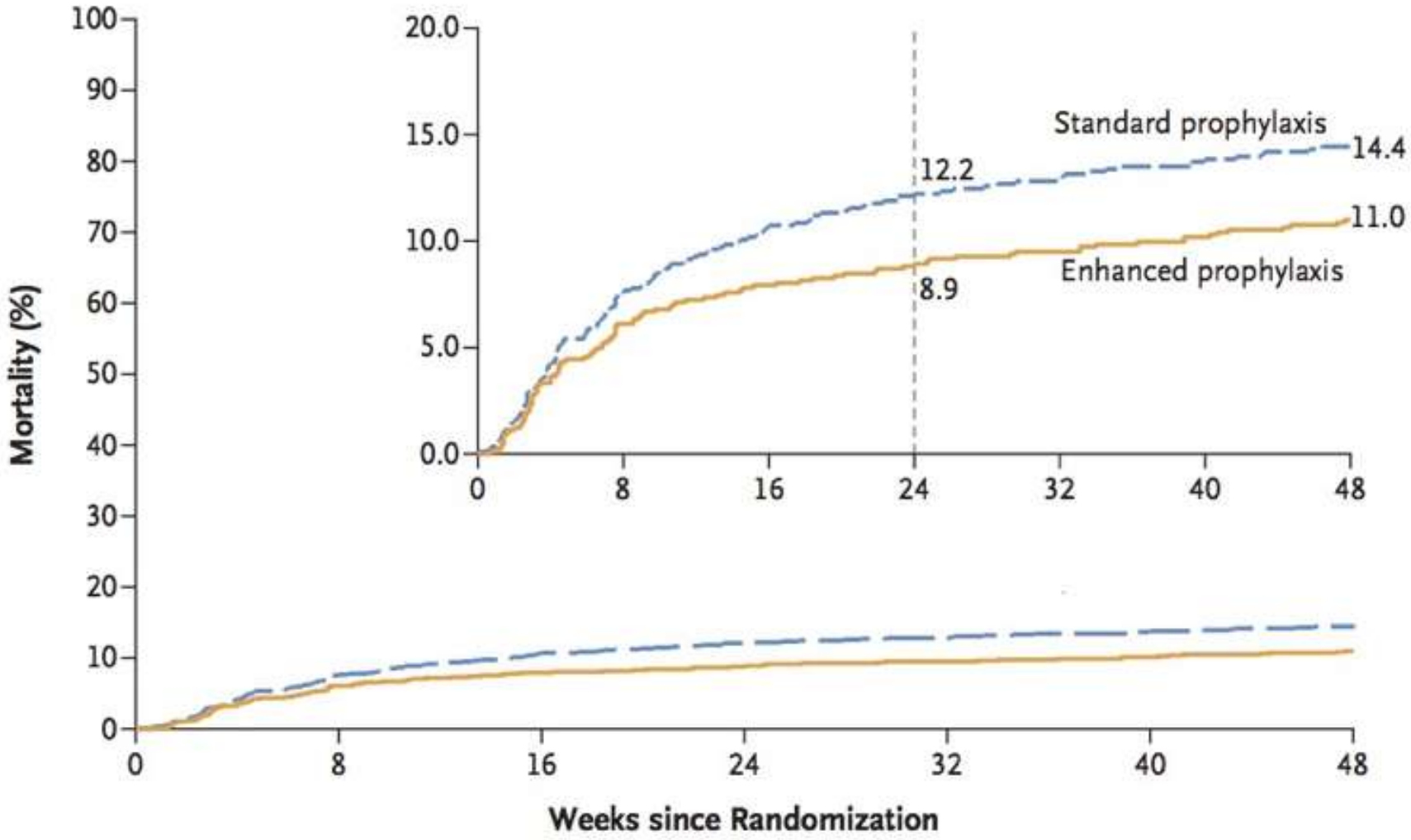
- ○ In a random sample of 1,000 persons from the same cancer population, there would be 350 more remissions if these 1,000 persons took the drug as compared to if they did not take the drug.
- ◉ An individual (from the same cancer population) who takes the drug is 35% more likely to go into remission as compared to an individual who has not taken the drug.
- ○ An individual (from the same cancer population) who does not take the drug is 35% less likely to go into remission as compared to an individual who has taken the drug.
- ○ In a random sample of 1,000 persons from the same cancer population, there would be 650 less remissions if these 1,000 persons took the drug as compared to if they did not take the drug.

4. An article in the *New England Journal of Medicine* reports the results from a randomized study designed to evaluate the efficacy of enhanced prophylaxis treatment for affecting mortality in patients with advanced AIDS living in sub-Saharan Africa.

   As per the researchers, "A total of 1805 patients (1733 adults and 72 children or adolescents) underwent randomization to receive either enhanced prophylaxis (906 patients) or standard prophylaxis (899 patients) and were followed for 48 weeks (after start of treatment)". The primary outcome of interest was mortality (death) in the 48-week follow-up period after receiving the treatment.

   The following Kaplan-Meier curves shows the estimated mortality (percentage of deaths) over the follow-up period separately for the treatment (enhanced prophylaxis) and control (standard prophylaxis) samples:

A Overall Mortality



No. at Risk (no. of deaths)

Standard prophylaxis	899 (67)	816 (27)	786 (13)	768 (7)	754 (7)	739 (6)	637
Enhanced prophylaxis	906 (55)	839 (16)	817 (8)	807 (6)	797 (6)	787 (7)	689

(Approximately) what percentage of patients in the intervention (enhanced prophylaxis) group survived (lived) beyond 48 weeks after being randomized to this group?

(Reference: Hakim J, et al. Enhanced Prophylaxis plus Antiretroviral Therapy for Advanced HIV Infection in Africa. *New England Journal of Medicine* 2017;377:233-45)

- [x] 89%
- [ ] 14.4%
- [ ] 85.6%
- [ ] 11%

Which of the following statements is true about the incidence rate ratio of death (IRR_hat) in the 48 week follow-up period for the enhanced prophylaxis group compared to the standard prophylaxis group (based on the results in the Kaplan-Meier curve)?

- ○ IRR_hat > 1
- ◉ IRR_hat < 1
- ○ IRR_hat =1
- ○ IRR_hat should be “close” to 1, but there is no way to tell exactly how it will compare to 1.

6. An article in the *New England Journal of Medicine* reports the results from a randomized study designed to evaluate the efficacy of enhanced prophylaxis treatment for affecting mortality in patients with advanced AIDS living in sub-Saharan Africa.

As per the researchers, "A total of 1805 patients (1733 adults and 72 children or adolescents) underwent randomization to receive either enhanced prophylaxis (906 patients) or standard prophylaxis (899 patients) and were followed for 48 weeks (after start of treatment)". The primary outcome of interest was mortality (death) in the 48-week follow-up period after receiving the treatment.

In the article, the authors report an incidence rate of 2.3 deaths/1,000 person-weeks for patients randomized to the enhanced prohylaxis group. This incidence rate (IR1) was calculated using data on all patients in the enhanced prohylaxis group, including those who were censored. Suppose, instead, the authors computed this incidence rate, but only used the data on patients in the enhanced prohylaxis group who died while in the study (IR2). How would IR2 compare in value to this reported incidence rate, IR1, of 2.3 deaths/1,000 person-weeks?

IR2 will be similar in value to IR1, but there is no way to predict exactly how the two estimates will compare.

IR2 < IR1

IR2 > IR1

IR2 = IR1

7. An article in the November 20, 2008 edition of the *New England Journal of Medicine* reports the results from a large, randomized study designed to assess the relationship between statin treatment and cardiovascular disease (as indicated by having at least one of several clinical endpoints).

   The researchers randomized 17,800 healthy (without a history of cardiovascular disease) men and women with non-elevated LDL cholesterol levels to either 20 mg of statins daily, or placebo. Subjects were followed for up to 5 years. At the end of the follow-up period the study results included the following:

   Of the 8900 subjects randomized to the statins group, 142 developed cardiovascular disease. Of the 8900 subjects randomized to the placebo group, 251 developed cardiovascular disease.

   (Reference: Ridker P, et al. Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein. *New England Journal of Medicine*. (2008). 359;21)

   What is the estimated relative risk of developing cardiovascular disease for subjects in the statins group compared to subjects on placebo?

   - ○ The estimated relative risk is approximately 0.012.
   - ◉ The estimated relative risk is approximately 0.57.
   - ○ The estimated relative risk is approximately - 0.012.
   - ○ The estimated relative risk is approximately 1.77

8. An article in the November 20, 2008 edition of the *New England Journal of Medicine* reports the results from a large, randomized study designed to assess the relationship between statin treatment and cardiovascular disease (as indicated by having at least one of several clinical endpoints).

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   Of the 8900 subjects randomized to the statins group, 142 developed cardiovascular disease. Of the 8900 subjects randomized to the placebo group, 251 developed cardiovascular disease.

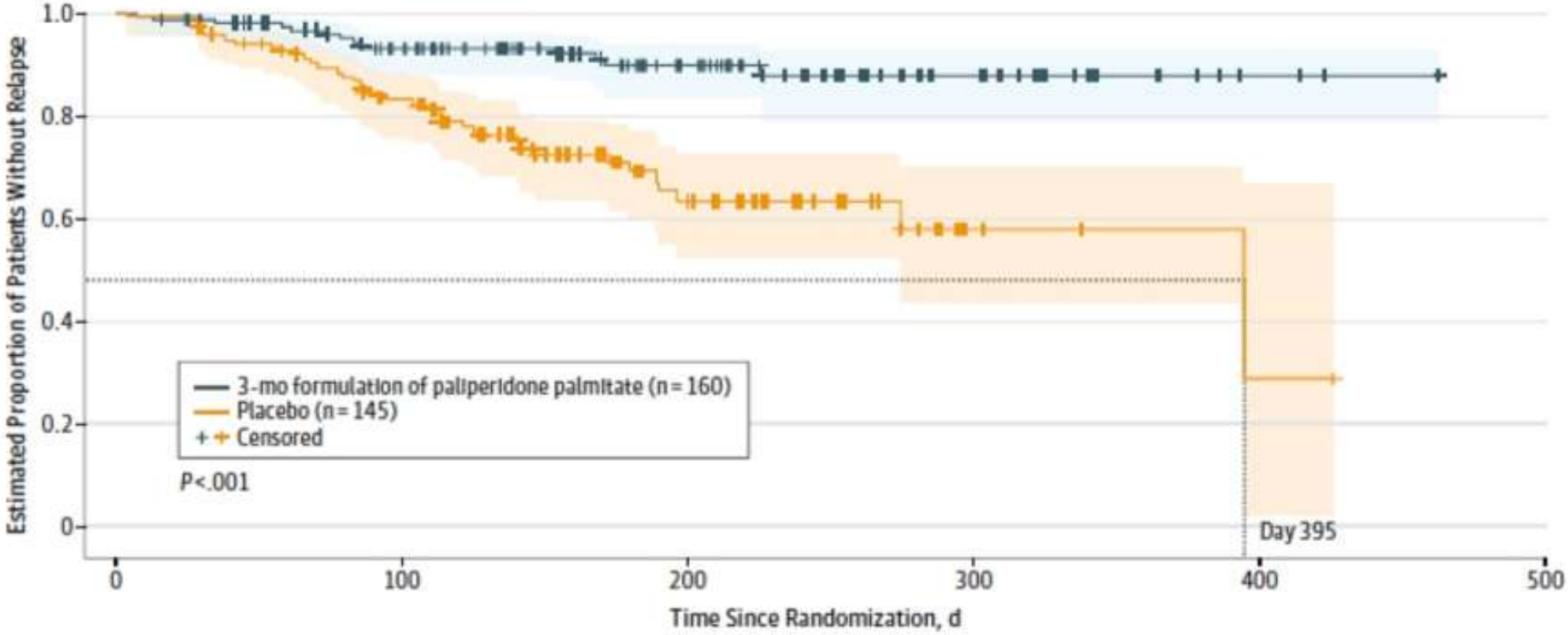
   Suppose a group of 200,000 healthy persons from the same population as the study sample were given 20 mg of statins daily. Approximately how many CVD cases would be prevented in the 5 years following the start of statin usage, as compared to had the 200,000 healthy persons not been given statins?

- ○ 218
- ○ 1,140
- ○ less than 200
- ◉ 2,400

Based on the Kaplan-Meier curve, what is the approximate 20th percentile of the time-to-relapse distribution for subjects randomized to the placebo group?

- ○ 20 days
- ○ 400 days
- ◉ 110 days
- ○ Percentiles cannot be estimated from a Kaplan-Meier curve

B Final analysis



Time, d	0	30	60	90	120	150	180	210	240	270	300	330	360	390	420	450

In the Kaplan-Meier graph, why are the estimated curves for both groups (Treatment and Placebo) at 1 (100%) when time since randomization (the follow-up period) is 0 months?

- ○ Because 100% of the subjects were censored by the end of the study.
- ○ Because the follow-up period is less than 2 years.
- ○ Because 100% of the subjects relapsed at 0 months of follow-up.
- ◉ Because all subjects followed in this study were event free (had not yet relapsed) at the beginning of the study