

LONDON  
SCHOOL of  
HYGIENE  
& TROPICAL  
MEDICINE



LSHTM Research Online

Suthar, AB; Lawn, SD; del Amo, J; Getahun, H; Dye, C; Sculier, D; Sterling, TR; Chaisson, RE; Williams, BG; Harries, AD; +1 more... Granich, RM; (2012) Antiretroviral Therapy for Prevention of Tuberculosis in Adults with HIV: A Systematic Review and Meta-Analysis. PLoS medicine, 9 (7). ISSN 1549-1277 DOI: <https://doi.org/10.1371/journal.pmed.1001270>

Downloaded from: <http://researchonline.lshtm.ac.uk/251164/>

DOI: <https://doi.org/10.1371/journal.pmed.1001270>

**Usage Guidelines:**

Please refer to usage guidelines at <https://researchonline.lshtm.ac.uk/policies.html> or alternatively contact [researchonline@lshtm.ac.uk](mailto:researchonline@lshtm.ac.uk).

Available under license: <http://creativecommons.org/licenses/by/2.5/>

<https://researchonline.lshtm.ac.uk>

**Text S2.** Calculation of incidence rate ratios and 95% confidence intervals

Reference for all calculations: Rothman KJ, Greenland S. Modern epidemiology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2008.

**Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, et al. (2011) Prevention of HIV-1 Infection with Early Antiretroviral Therapy. N Engl J Med 365: 493-505.**

An effect estimate and 95% confidence interval was not reported in this study. However, the data necessary to calculate a rate ratio has been provided in the supplementary appendix. First, we must calculate the point estimate:

$$\hat{IR} = \frac{A_1/T_1}{A_0/T_0}$$

A1 = 17 = tuberculosis cases in immediate ART arm

T1 = 1661.9 = person-years at risk of a clinical event in immediate ART arm

A0 = 33 = tuberculosis cases in deferred ART arm

T0 = 1641.8 = person-time at risk of a clinical event in deferred ART arm

$$IR = (17/1661.9) / (33/1641.8) = 0.5089$$

Next, we must calculate the standard deviation of the log rate ratio:

$$\widehat{SD}[\ln(\hat{IR})] = \left( \frac{1}{A_1} + \frac{1}{A_0} \right)^{1/2}$$

$$SD[\ln(IR)] = (1/17 + 1/33)^{0.5} = 0.2985$$

Finally, we can calculate the lower and upper limits of the rate ratio:

$$\begin{aligned} \underline{IR}, \overline{IR} &= \exp\{\ln(\hat{IR}) \pm Z_{\gamma} \widehat{SD}[\ln(\hat{IR})]\} \\ &= \exp[\ln(0.5089) \pm 1.96(0.2985)] = 0.2835, 0.9136 \end{aligned}$$

Therefore the rate ratio and its 95% confidence interval is: 0.51 (0.28 to 0.91).

**Lannoy LH, Cortez-Escalante JJ, Evangelista Mdo S, Romero GA (2008)  
Tuberculosis incidence and risk factors among patients living with HIV/AIDS in public health service institutions in Brasilia, Federal District. Rev Soc Bras Med Trop 41: 549-555.**

An effect estimate and 95% confidence interval was not reported in participants with baseline CD4 counts < 200 cells/ $\mu$ L. However, the data necessary to calculate a rate ratio has been provided. In order to calculate the tuberculosis rate ratio for people with CD4 counts < 200 cells/ $\mu$ L we must use the incidence rates and their 95% confidence intervals.

The incidence rate in people who started ART with baseline CD4 counts < 200 cells/ $\mu$ L was 0.60 cases / 100 person-years of observation (95% CI, 0.15 to 2.37). Given

$$\widehat{SD}[\ln(\widehat{IR})] = \frac{1}{A^{1/2}}$$

we can solve for the  $(1/A^{0.5})$ , i.e. the standard deviation of the log incidence rate, using the lower 95% confidence interval:

$$\underline{IR}, \overline{IR} = \exp[\ln(\widehat{IR}) \pm Z_y(1/A^{1/2})]$$

$$\ln(95\% \text{ IR Lower Limit, LL}) = \ln(IR) - Z_y \text{SD}[\ln(IR)]$$

$$(\ln(LL) - \ln(IR)) / -Z_y = \text{SD}[\ln(IR)]$$

$$\text{SD}[\ln(IR)] = (\ln(0.15) - \ln(0.60)) / -1.96 = 0.7073$$

Given  $\text{SD}[\ln(IR)]$  we can now calculate  $A_1$ , or the number of events in the stratum on ART:

$$\widehat{SD}[\ln(\widehat{IR})] = \frac{1}{A^{1/2}}$$

$$0.7073 = 1/(A_1^{0.5})$$

$$1 = 0.7073*(A_1^{0.5})$$

$$1 / 0.7073 = (A_1^{0.5})$$

$$1.4138 = (A_1^{0.5})$$

$$1.9989 = A_1$$

$A_1 \sim 2$  cases of tuberculosis

The incidence rate in people off ART with baseline CD4 counts < 200 cells/ $\mu$ L was 5.47 cases / 100 person-years of observation (95% CI, 2.73 to 10.94). Given

$$\widehat{SD}[\ln(\widehat{IR})] = \frac{1}{A^{1/2}}$$

we can solve for the  $(1/A^{0.5})$ , i.e. the standard deviation of the log incidence rate, using the lower 95% confidence interval:

$$\underline{IR}, \overline{IR} = \exp[\ln(\widehat{IR}) \pm Z_y(1/A^{1/2})]$$

$$\ln(95\% \text{ IR Lower Limit, LL}) = \ln(IR) - Z_y SD[\ln(IR)]$$

$$(\ln(LL) - \ln(IR)) / -Z_y = SD[\ln(IR)]$$

$$SD[\ln(IR)] = (\ln(2.73) - \ln(5.47)) / -1.96 = 0.3546$$

Given  $SD[\ln(IR)]$  we can now calculate  $A_0$ , or the number of events in the stratum off ART:

$$\widehat{SD}[\ln(\widehat{IR})] = \frac{1}{A^{1/2}}$$

$$0.3546 = 1/(A_0^{0.5})$$

$$1 = 0.3546(A_0^{0.5})$$

$$1 / 0.3546 = (A_0^{0.5})$$

$$2.8202 = (A_0^{0.5})$$

$$7.9537 = A_0$$

$A_0 \sim 8$  cases of tuberculosis

Since we have calculated the number of cases in both study arms, we can now calculate the rate ratio and its 95% confidence interval. First, we must calculate the point estimate:

$$\widehat{IR} = \frac{A_1/T_1}{A_0/T_0}$$

$$IR = (0.60/100) / (5.47/100) = 0.1097$$

Next we must calculate the standard deviation of the log rate ratio:

$$\widehat{SD}[\ln(\widehat{IR})] = \left( \frac{1}{A_1} + \frac{1}{A_0} \right)^{1/2}$$

$$SD[\ln(IR)] = (1/2 + 1/8)^{0.5} = 0.7912$$

Finally, we can calculate the 95% limits of the rate ratio:

$$\begin{aligned} \underline{IR}, \overline{IR} &= \exp\{\ln(\widehat{IR}) \pm Z_y \widehat{SD}[\ln(\widehat{IR})]\} \\ &= \exp[\ln(0.1097) \pm 1.96(0.7912)] = 0.0233, 0.5172 \end{aligned}$$

Therefore the rate ratio and its 95% confidence interval is: 0.11 (0.02 to 0.52).