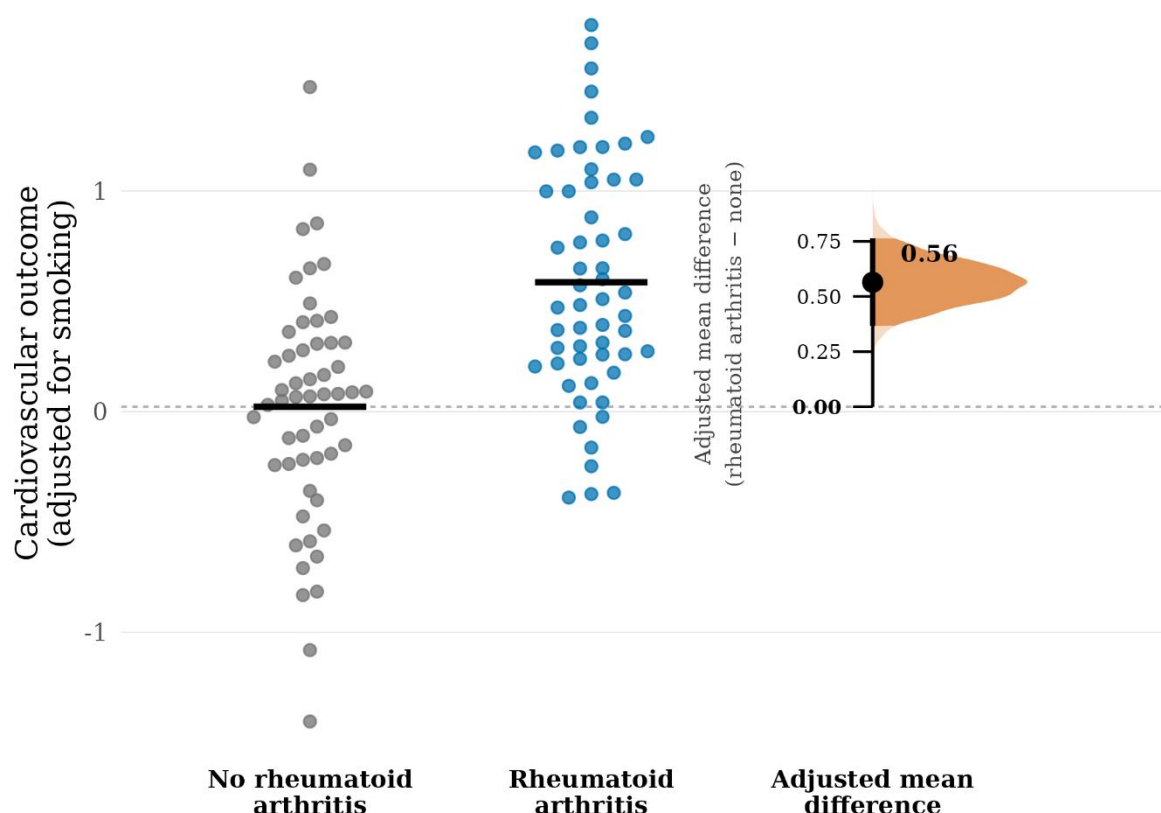


Fig. S1. Estimation graphic for the adjusted exposure effect (illustrative simulated data).



Note: The cardiovascular outcome, after adjustment for the confounder (smoking), is plotted for participants with and without rheumatoid arthritis, with horizontal bars marking the group means. The floating panel shows this adjusted mean difference as a point with its bootstrap sampling distribution; the vertical bar is the 95% confidence interval [CI] (adjusted difference 0.56; 95% CI 0.37–0.76). The outcome here is a continuous measure, so the adjusted effect is a mean difference; for a binary event outcome, the identical display shows the absolute risk difference. In keeping with the estimation-graphics approach,⁷ the interval is given here, and the effect is shown with its full uncertainty rather than reduced to a significance test.

For the citation, please refer to the REFERENCES section in the main article.

Appendix. R code for the simulation.

```
set.seed(1985)
n <- 5000

# Data-generating coefficients (worked example: Z = smoking, X = rheumatoid arthritis, Y =
# cardiovascular risk)
b_ZX <- 0.8 # Z -> X
b_XY <- 0.5 # X -> Y (target effect)
b_ZY <- 0.4 # Z -> Y (Z's direct effect)

# Generate data
Z <- rnorm(n)
X <- b_ZX * Z + rnorm(n)
Y <- b_XY * X + b_ZY * Z + rnorm(n)

dat <- data.frame(Y, X, Z)

# Adjusted model for the target X-to-Y effect (rheumatoid arthritis on cardiovascular risk).
# The Z (smoking) coefficient is conditional on X, so it estimates smoking's DIRECT effect on
# Y,
# not smoking's total effect.
fit_adjusted <- lm(Y ~ X + Z, data = dat)

# Separate model for smoking's (Z's) TOTAL effect on Y: regress Y on Z alone,
# omitting X, a mediator of smoking's effect. This answers a different causal question.
fit_total_Z <- lm(Y ~ Z, data = dat)

# Estimates with 95% confidence intervals.

library(broom)

adjusted_results <- tidy(fit_adjusted, conf.int = TRUE)
total_Z_results <- tidy(fit_total_Z, conf.int = TRUE)

adjusted_results
total_Z_results

# Expected output (set.seed(1985), n = 5000):
# Adjusted model (Y ~ X + Z): X = 0.51 (95% CI 0.48, 0.53); Z = 0.39 (0.35, 0.42)
# Total-Z model (Y ~ Z): Z = 0.79 (95% CI 0.76, 0.82)
```