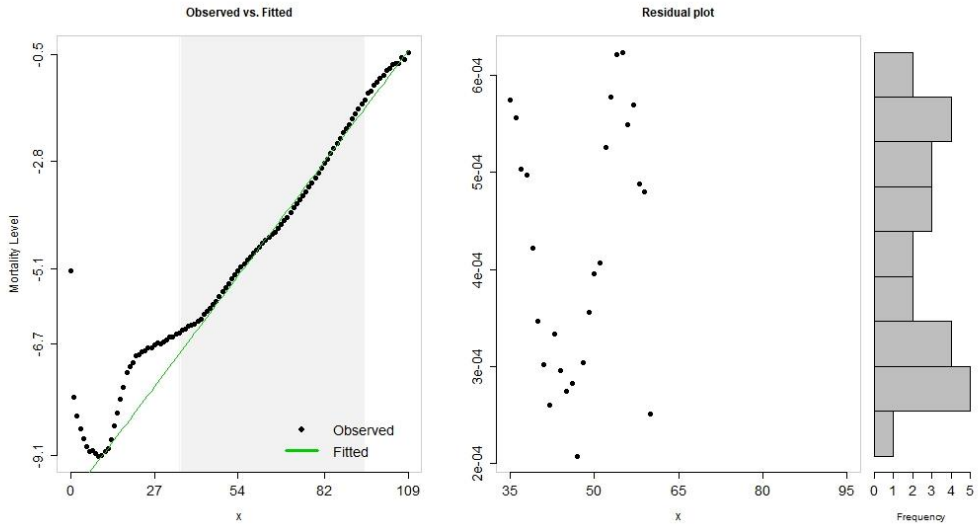
Supplemental Material

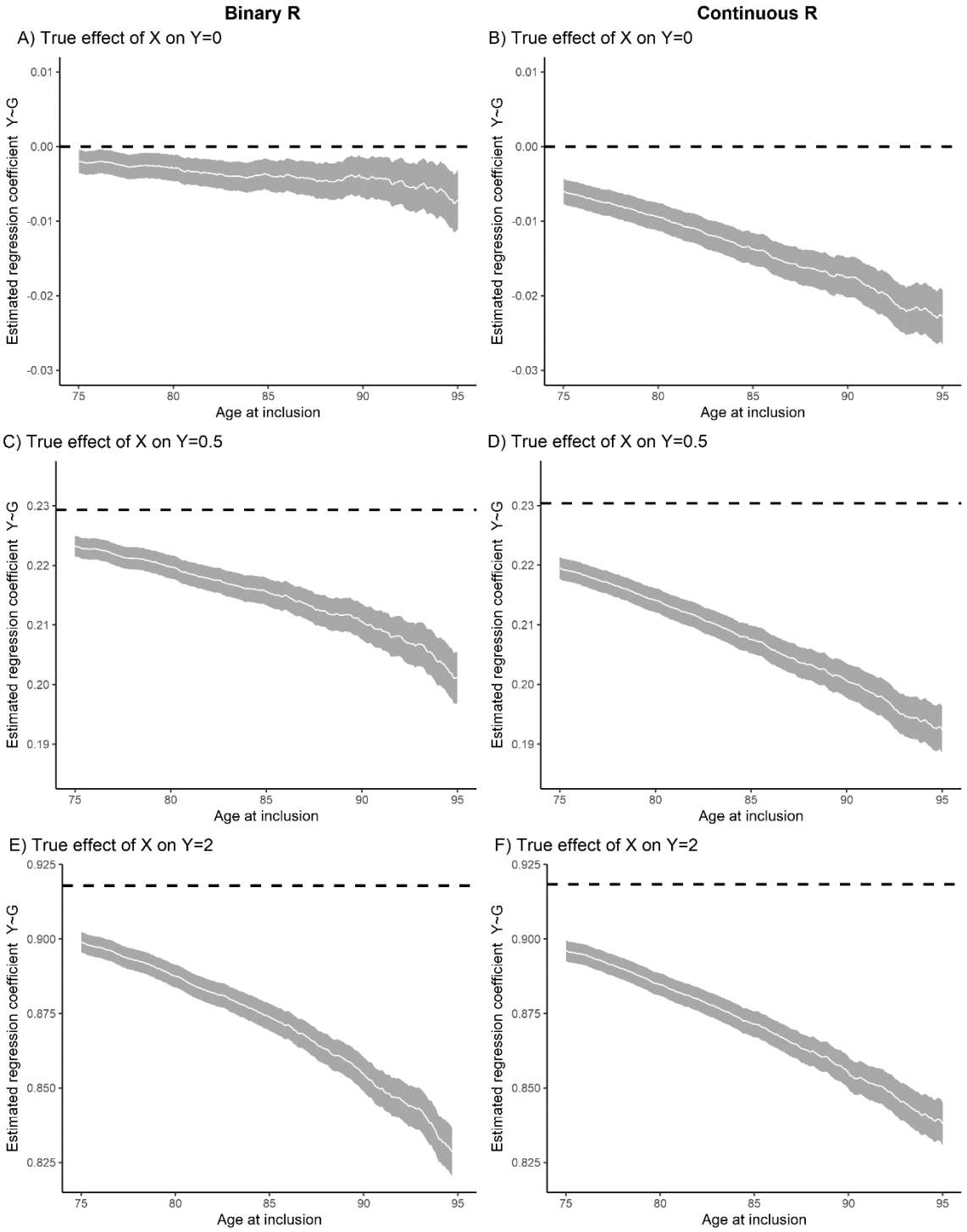


eFigure 1. Results from fitting the Gompertz-model ($a*e^{b*age}$) onto the 2016 mortality data of the United States (age range 35-95) obtained from the Human Mortality Database (www.mortality.org), using the *MortalityLaws* R-package. Estimated model parameters: a, 0.0000459053; b, 0.0876978320.

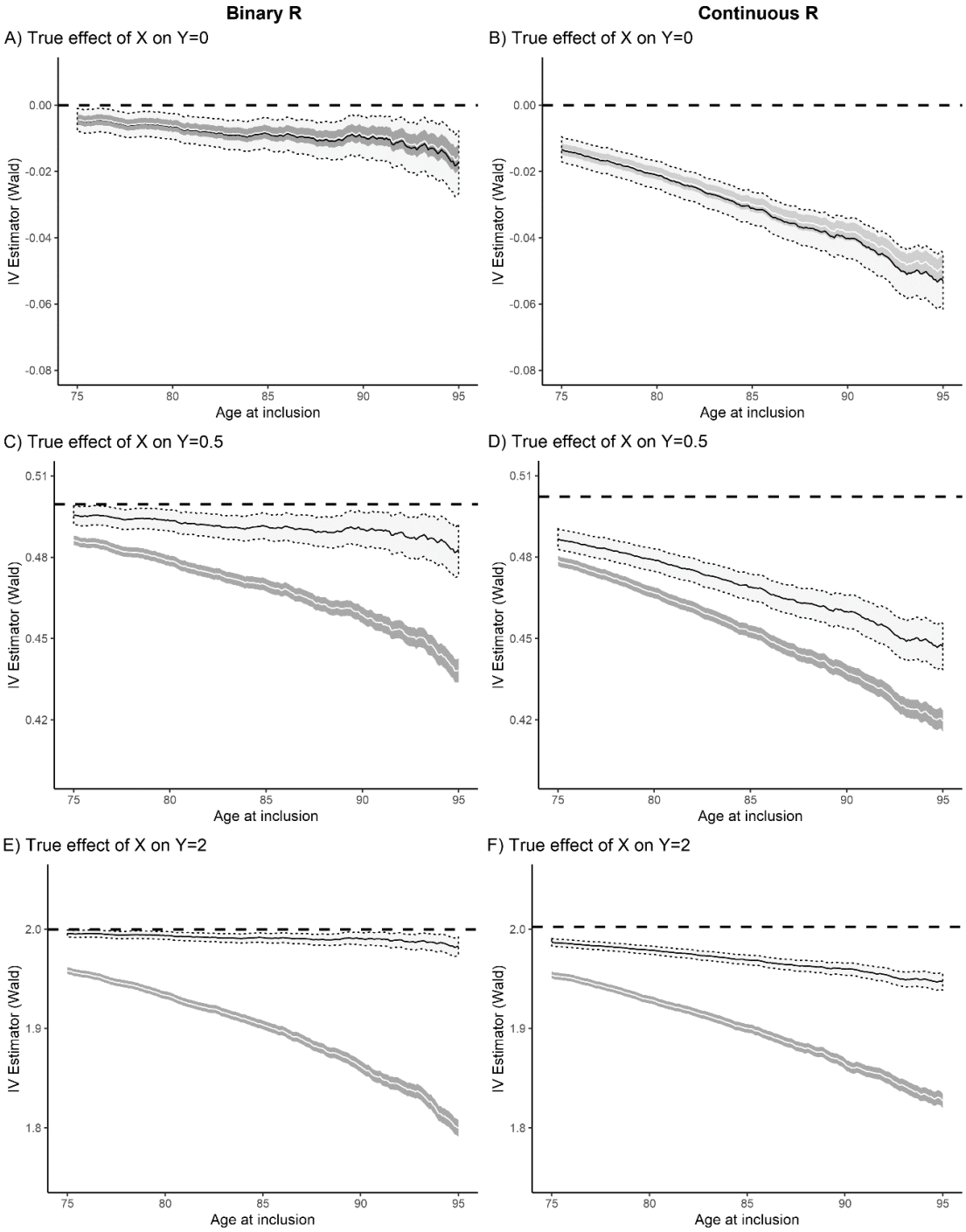
Table. Parameters values and details of data generation

Parameter (scale)	**Data generation**
G (binary)	Prevalence of 50%
X (continuous)	Normally distributed with mean 0 and var(X|G)=1
Variance of X explained by G	5% of X
U (continuous)	Normally distributed with mean 0 and var=1
R (binary)	Prevalence of 25%
R (continuous)	Normally distributed with mean 0 and var=1
Age of death (continuous)	Gompertz distributed with baseline parameters $a=4.59053\times10^{-5}$ and $b=8.76978320\times10^{-2}$, with (additional) contribution of X and R
Effects of X on age of death	HR of 1.25 per one unit increase in X
Effects of R on age of death	HR of 1.5 per one unit increase in R
S (binary)	Indicates whether age of death is larger than age at inclusion
Y (continuous)	Normally distributed with mean 0 and variance(Y|X,R)=1, with fixed contribution of R and varying contribution of X
Effects of X on Y	Increase of 0, 0.5, or 2 per one unit increase in X
Effects of R on Y	Increase of 0.5 per unit increase in R
Effect of U on X and Y	Increase of 0.5 per one unit increase in U
Number of observations	10.000.000
Interaction between X and R on age of death	HR of -2, -1.5, none, 1.5, or 2

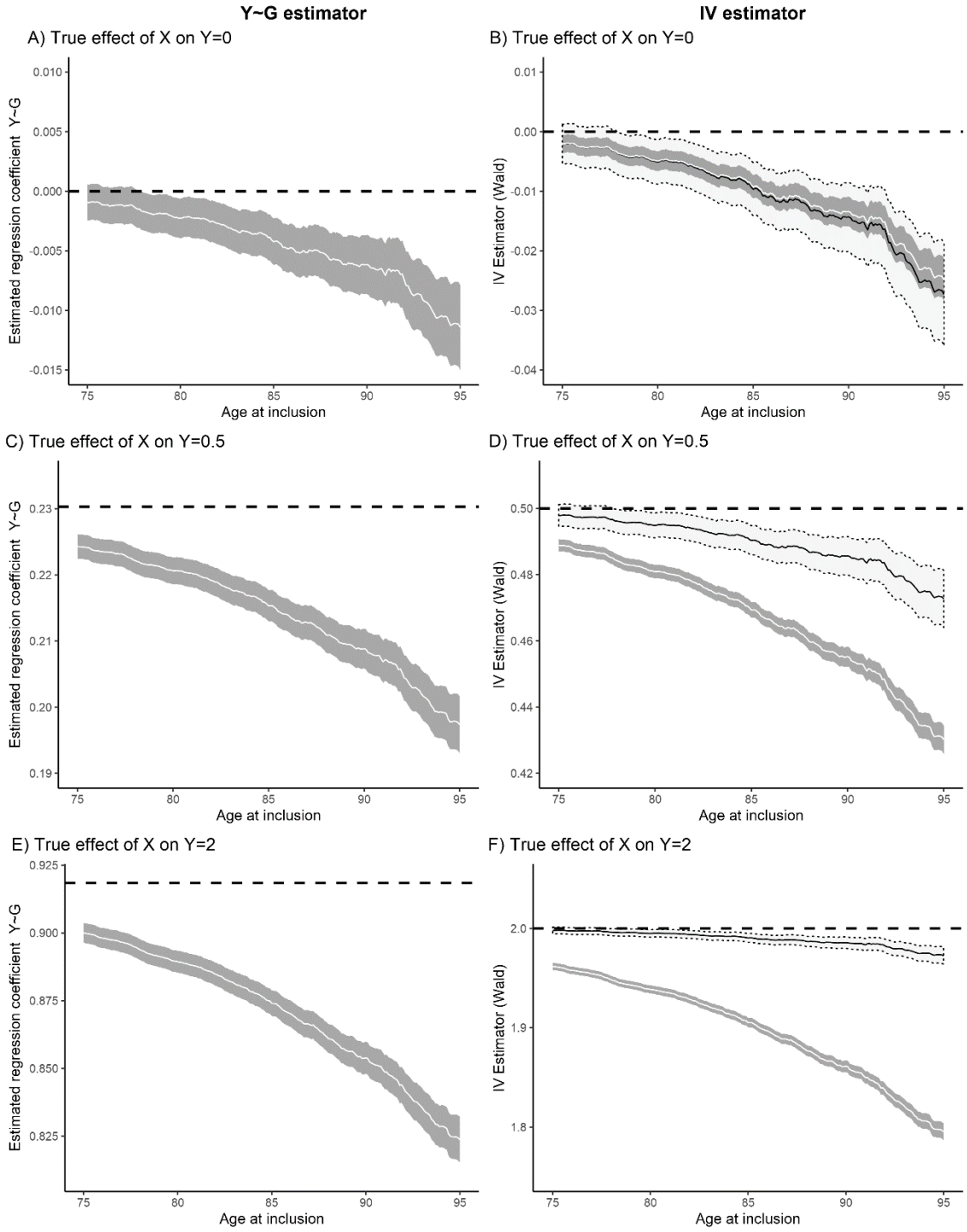
S.D. denotes standard deviation; HR: Hazard ratio



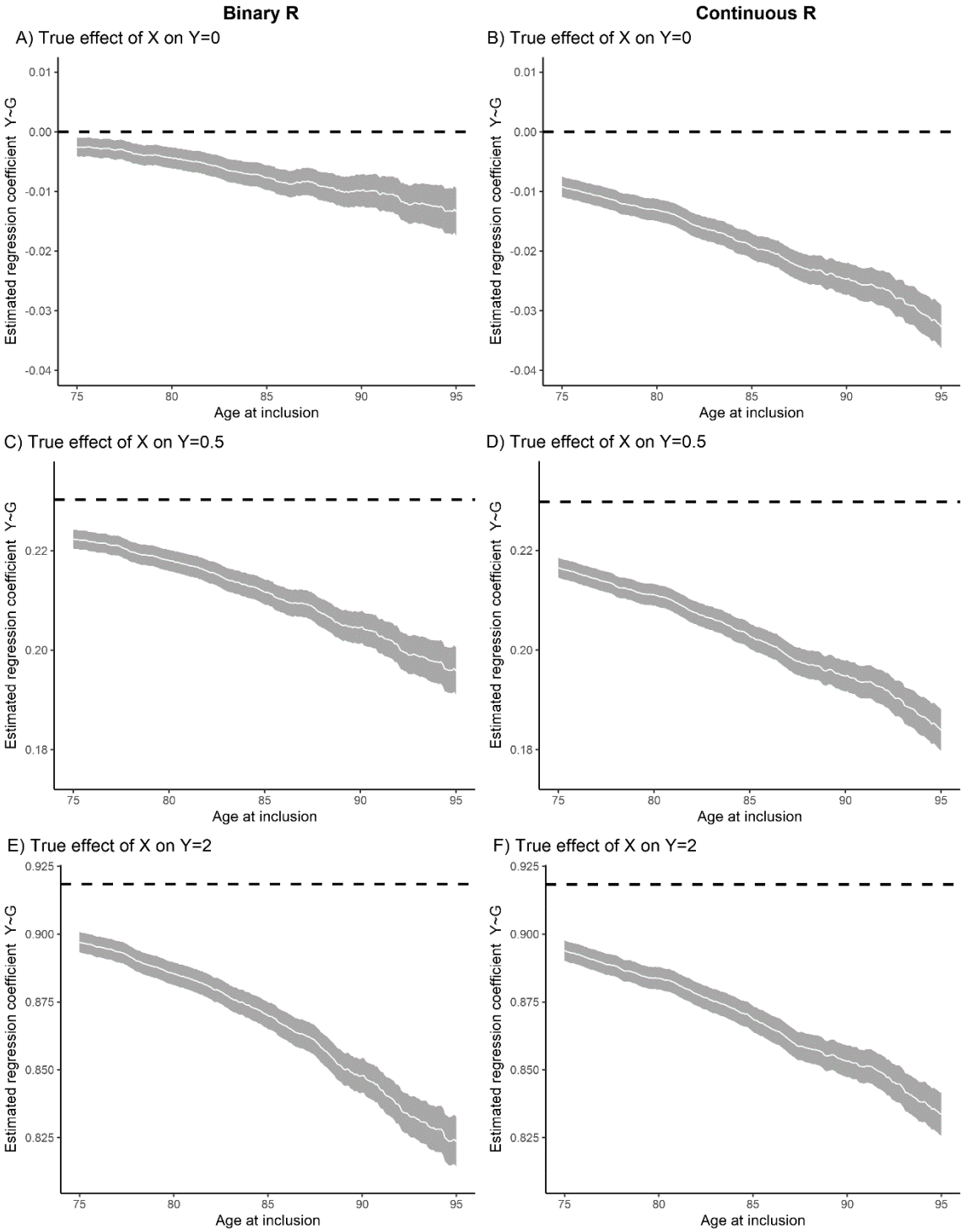
eFigure 2. Effect of survival bias on the association between the genetic instrument *G* and the outcome of interest *Y*, for different true effects of exposure *X* on *Y*. Data are presented as regression coefficients (95% CI) estimated with linear regression. The true (i.e. unselected) regression coefficient for *G* on *Y* is shown as a dashed line in each plot. Shown for binary (left column) and continuously (right column) distributed *R*.



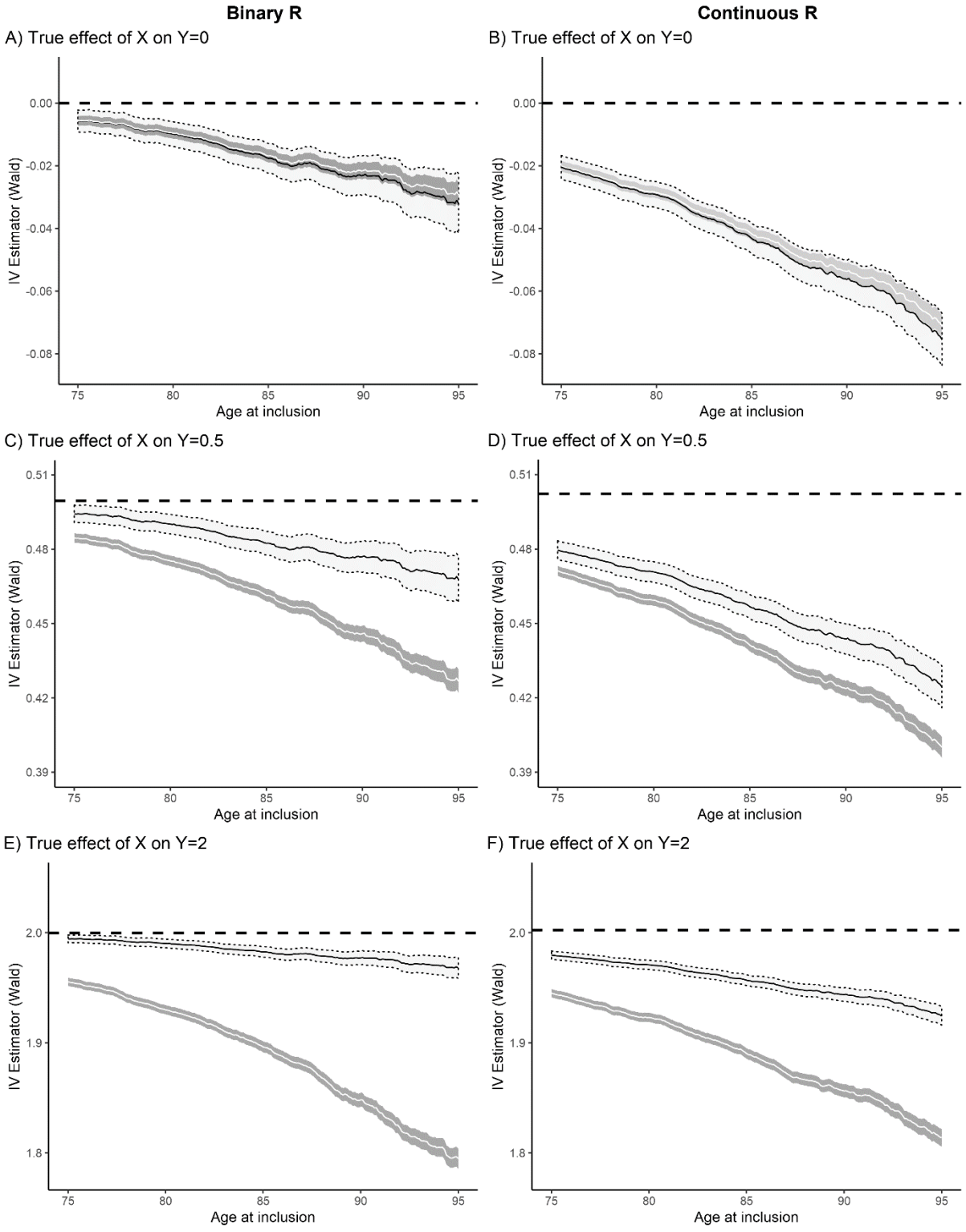
eFigure 3. Wald ratios (95% CI) based on internally (white ribbon) versus externally (grey ribbon) estimated association between exposure *X* and the outcome *Y*, for different true effects of exposure *X* on *Y*. Shown for binary (left column) and continuously (right column) distributed *R*. Dashed lines denote the true (i.e. unselected) Wald ratio, which equals the true causal effect of *X* on *Y*. Panels A, C, E mirror those shown in Figure 2 in the manuscript.



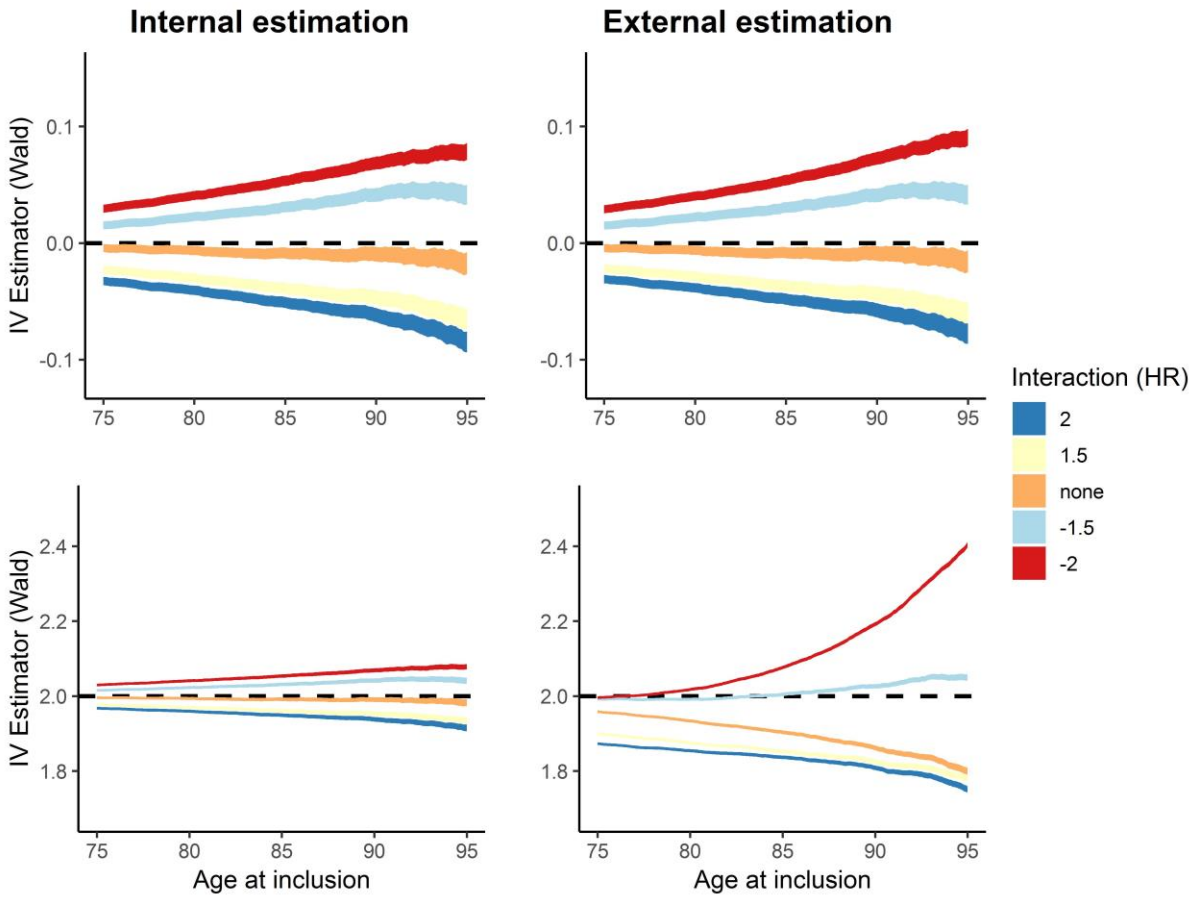
eFigure 4. Effect of survival bias on the association between the genetic instrument G and the outcome of interest *Y* (left panels), and on the Wald ratio IV-estimator (right panels), for different true effects of exposure *X* on *Y*. The true (i.e. unselected) regression coefficient for *G* on *Y*, and of true (i.e. unselected) Wald ratio, are shown as a dashed line in each plot.



eFigure 5. Effect of survival bias on the association between the genetic instrument G and the outcome of interest *Y*, for different true effects of exposure *X* on *Y*. Data are presented as regression coefficients (95% CI) estimated with linear regression. The true (i.e. unselected) regression coefficient for *G* on *Y* is shown as a dashed line in each plot. Shown for binary (left column) and continuously (right column) distributed *R*.



eFigure 6. Wald ratios (95% CI) based on internally (white ribbon) versus externally (grey ribbon) estimated association between exposure *X* and the outcome *Y*, for different true effects of exposure *X* on *Y*. Shown for binary (left column) and continuously (right column) distributed *R*. Dashed lines denote the true (i.e. unselected) Wald ratio, which equals the true causal effect of *X* on *Y*.



eFigure 7. Wald ratio (95% CI shown) when interaction exists between *X* and *R* on age of death. Shown for internally (left column) and externally (right column) estimated Wald ratio (see methods). Dashed lines denote the true (i.e. unselected) Wald ratio, which equals the true causal effect of *X* on *Y*. HR denotes Hazard ratio.