

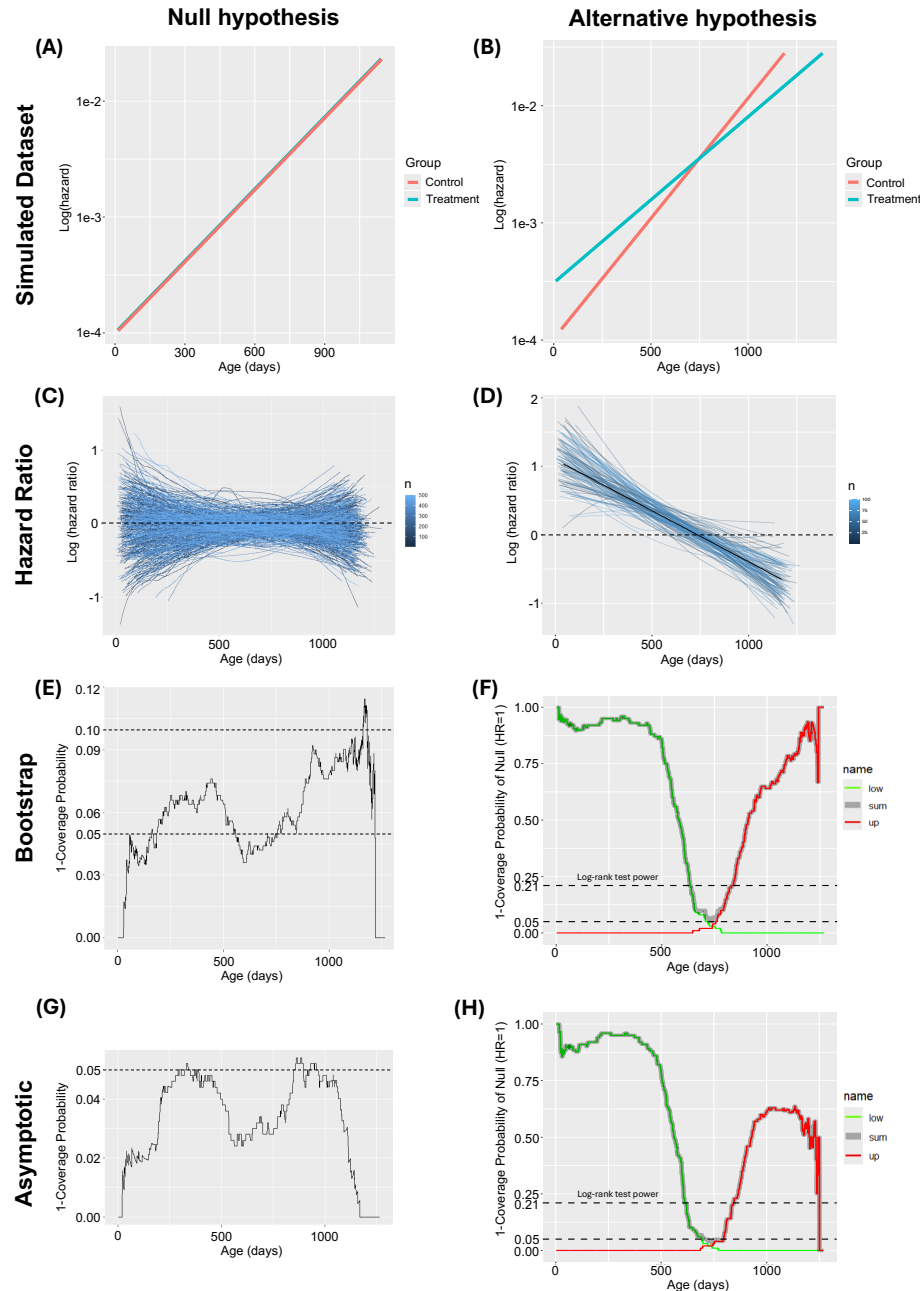


Figure S1. Evaluation of the performance of the asymptotic and bootstrap methods under null and alternative scenarios. (A) The Log mortality hazard for creating the 500 cases for null hypothesis scenario, the control and treatment group share the same age-specific mortality hazard; (B) The Log mortality hazard for creating the 100 cases for alternative hypothesis scenario, treatment group have high mortality hazard early in life, but lower mortality hazard later in life, which switch around the median lifespan; (C) Case specific Log hazard ratio of treatment to control under null-hypothesis. (D) Case specific Log hazard ratio of treatment to control under alternative hypothesis. (E) Summary of the performance of the bootstrap method under null hypothesis. (F) Summary of the performance of the bootstrap method under alternative hypothesis. (G) Summary of the performance of the asymptotic method under null hypothesis. (H) Summary of the performance of the asymptotic method under alternative hypothesis.

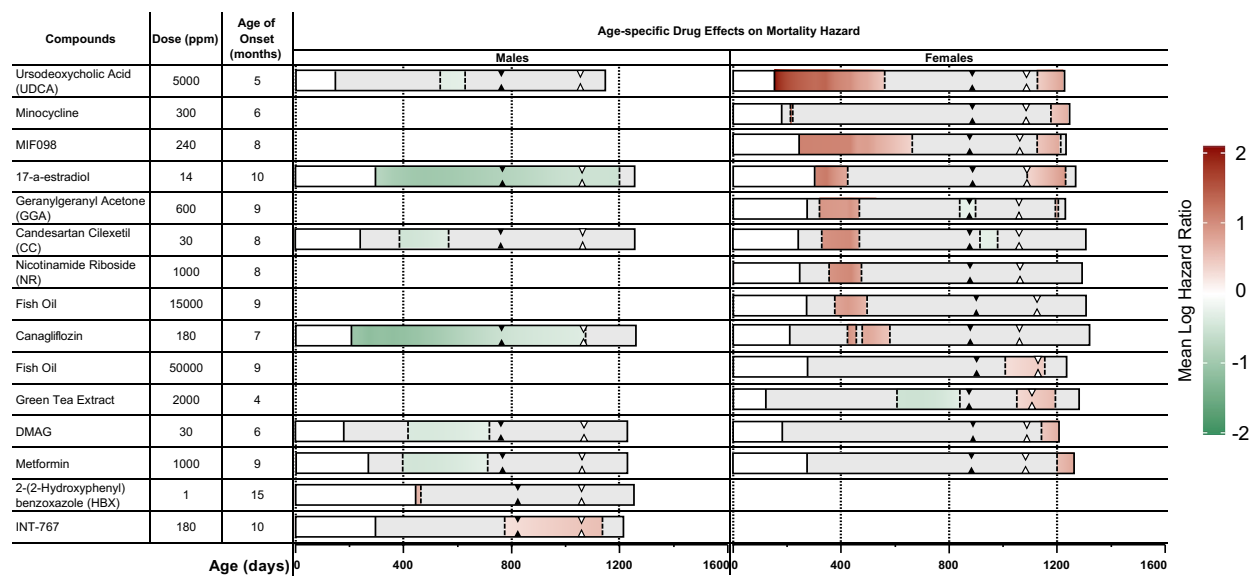


Figure S2. Life course heat maps of trials with drug-induced detrimental effects on mortality hazard. Only interventions confirmed by both bootstrap and asymptotic methods are displayed, with the asymptotic method results used as the representative data. These trials are shown ranked by the age when detrimental effects started in females (earliest to oldest), then by males. Other information is same as Figure 2. Source data are provided as a Source Data file.