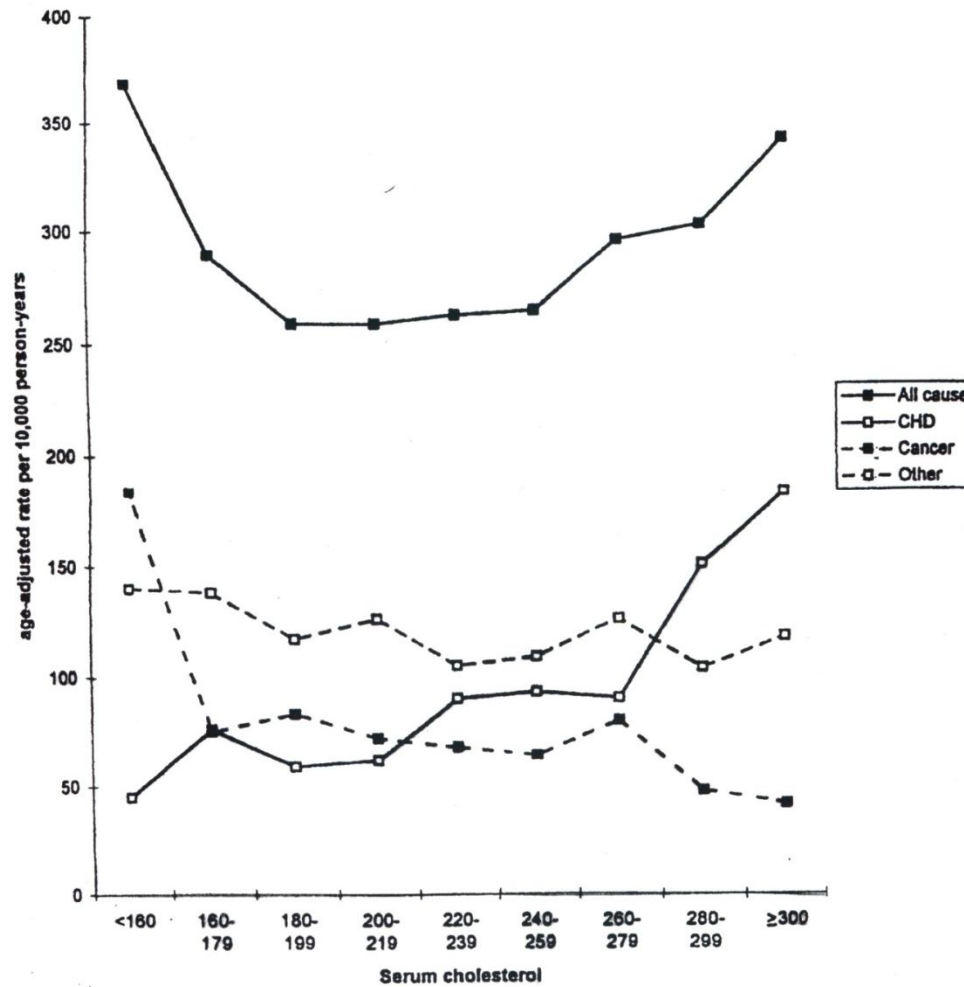
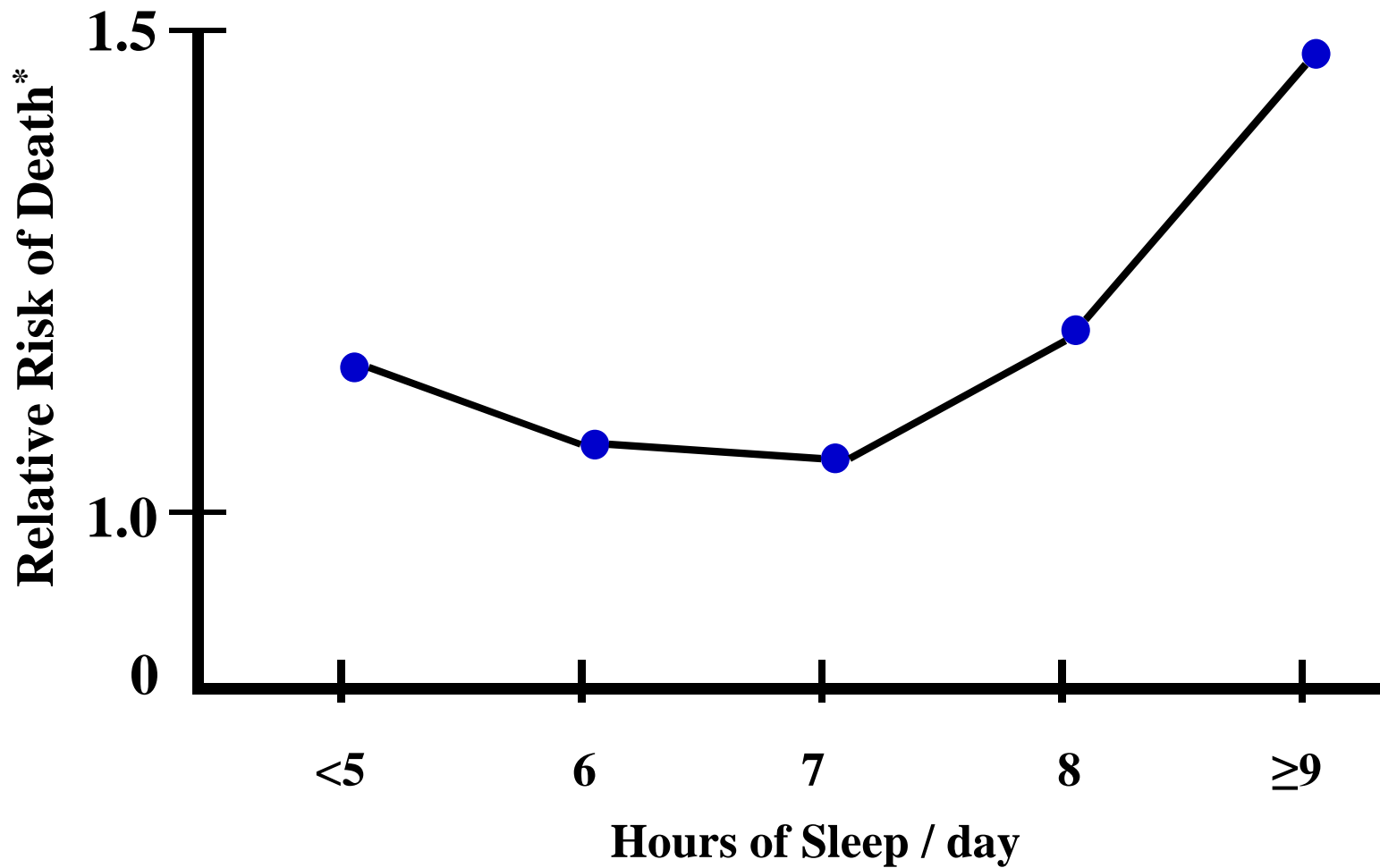


# Relationship Between Serum Cholesterol and Mortality in Men



Smith et al, *JAMA* 1992

# Relationship Between Sleep Duration and Mortality in 82,000 Nurses



\*Adjusted for age, smoking, alcohol, physical activity, depression, snoring, BMI, history of cancer and cardiovascular disease,

Patel et al, *Sleep* 2004

# U-Shaped Relationship Between Blood Glucose and Adverse Outcome After Heart Attack

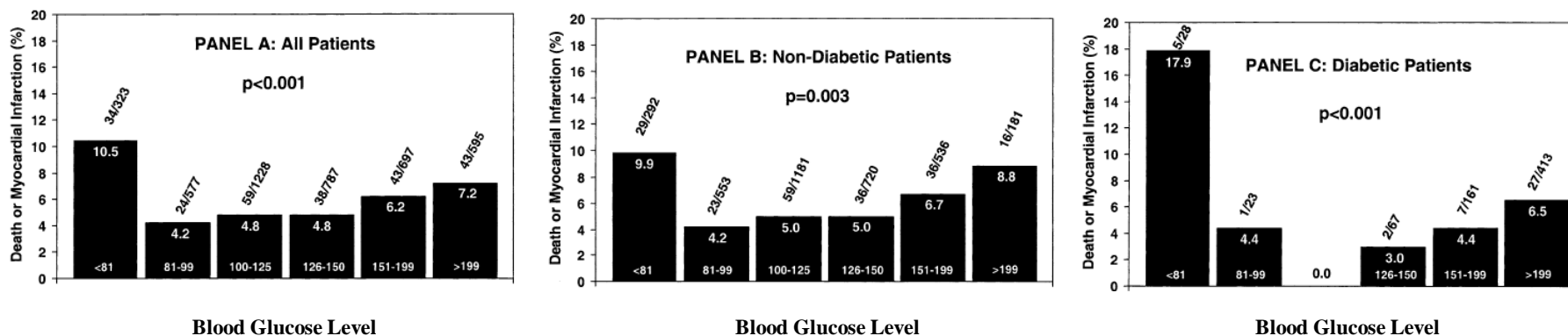


Figure 1. U-shaped association of admission blood glucose level with death or recurrent myocardial infarction at 30 days in the overall population (n = 4,227) (A), non diabetic patients (n = 3,463) (B), and diabetic patients (n = 738) (C).

# Response of Worms to Heat Shock

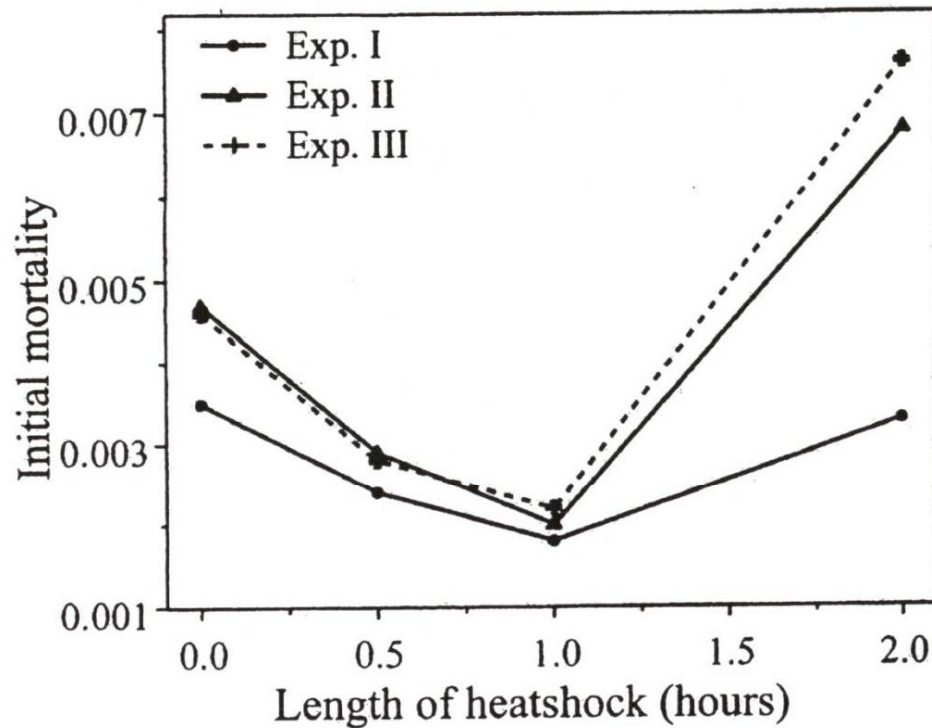
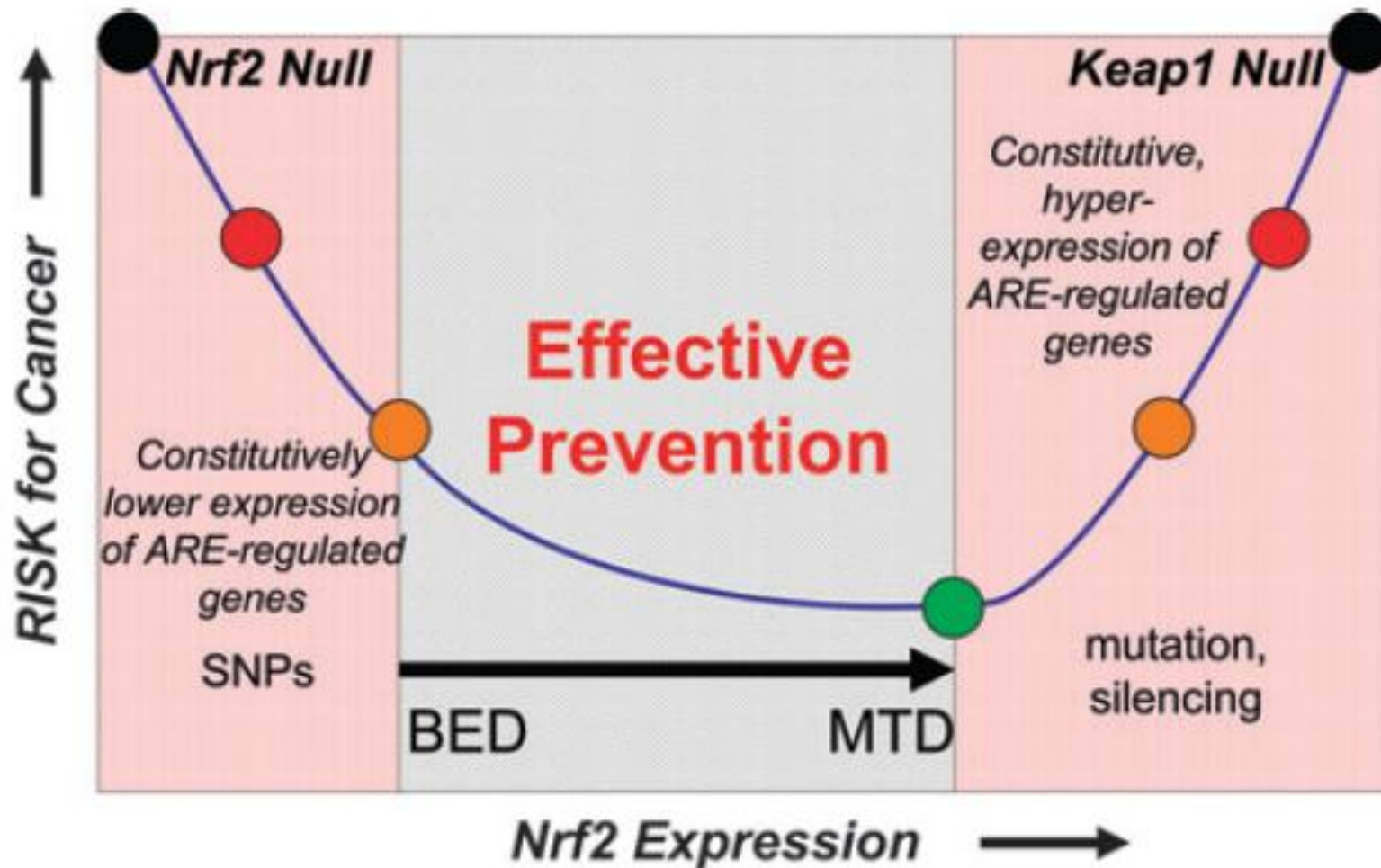


Figure 4. The U-shape of the initial mortality of the control, the 0.5-hour-heated population, the first subpopulation of the 1-hour-heated population, and the first subpopulation of the 2-hour-heated population in each experiment. The rates of increase in mortality of the four populations (subpopulations) are the same.



U-Shaped modulation of cancer risk through the KEAP1–NRF2 pathway. Optimal activation of the pathway lies in a pharmacological range between the biologically effective dose (BED) that minimally activates the pathway and a maximal-tolerated dose (MTD) that not only activates the pathway but also may produce dose-limiting ‘off target’ toxicities as well. Single-nucleotide polymorphisms (SNPs) in the Nrf2 promoter may diminish constitutive or inducible capacity of the pathway, whereas mutations or epigenetic silencing of Keap1 leads to sustained hyperactivation.