

**Association of exercise with late mortality in adult survivors of childhood cancer: A
report from the Childhood Cancer Survivor Study**

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Background: Adult survivors of childhood cancer are at excess risk for late mortality compared to the general population. Whether exercise attenuates this risk is not known.

Methods: We examined the association between self-reported vigorous exercise [metabolic equivalent-hrs/week (MET-h/wk)] and cause-specific late mortality among 15,450 adult survivors participating in the Childhood Cancer Survivor Study using multivariable piecewise exponential regression analysis to estimate rate ratios (RR). Longitudinal change in vigorous exercise was evaluated among a subset of 5689 survivors.

Results: During a median follow-up of 10 years (interquartile range: 15 years), 1063 deaths (811 health-related, 120 recurrence/progression of primary cancer, 132 external/unknown causes) were documented. At 15 years the cumulative incidence of all-cause mortality was 11.7% (95% CI, 10.57-12.80) for 0 MET-h/wk, 8.6% (95% CI, 7.42-9.72) for 3 to 6 MET-h/wk, 7.4% (95% CI, 6.23-8.57) for 9-12 MET-h/wk, and 8.0% (95% CI, 6.50-9.45) for 15-21 MET-h/wk ($P < 0.001$). There was a significant inverse association across quartiles of exercise and all-cause mortality after adjusting for chronic health conditions and treatment exposures ($P_{\text{trend}} = 0.023$). Among a subset of 5689 survivors, increased exercise ($+7.9 \pm 4.4$ MET-h/wk) over an 8-year period was associated with a 40% reduction in all-cause mortality rate compared with maintenance of low exercise (RR=0.60; 95% CI, 0.44 to 0.82, $p=0.01$).

Conclusion: Vigorous exercise in early adulthood and increased exercise over eight years is associated with lower risk of late mortality in adult survivors of childhood cancer.