There is increasing interest in applying a precision medicine approach to understanding exercise as a potential treatment for cancer. We aimed to inform this new approach by appraising epidemiologic literature relating post-diagnosis physical activity to cancer outcomes overall and by molecular/genetic subgroups. Across 26 studies of breast, colorectal and prostate cancer patients, there was a 37% reduction in risk of cancer-specific mortality, comparing the most versus the least active patients (pooled relative risk=0.63, 95% confidence interval: 0.54-0.73). Risks of recurrence or recurrence/cancer-specific death (combined outcome) were also reduced based on fewer studies. We identified ten studies of associations between physical activity and cancer outcomes by molecular or genetic markers. Two studies showed statistically significant risk reductions in breast cancer mortality/recurrence for the most (versus least) physically active ER+PR+ patients, while others showed risk reductions among ER-PR- and triple-negative patients. In colorectal cancer, four studies showed statistically significant risk reductions in cancer-specific mortality for patients with high (versus low) physical activity and P21 expression, P27 expression, nuclear CTNNB1-, PTGS2 (COX-2)+, or IRS1 low/negative status. One prostate cancer study showed effect modification by Gleason score. To enhance this evidence, there is need for future observational studies that measure physical activity objectively before and after diagnosis, use standardized definitions for outcomes, control for competing risks, assess non-linear dose-response relations and consider reverse causality. Ultimately, randomized controlled trials with clinical cancer outcomes and a correlative component will provide the best evidence of causality, relating exercise to cancer outcomes, overall and for molecular and genetic subgroups.