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Histology-specific meta-analysis of physical activity and lung cancer: the modifying role of gender across subtypes

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Backgrounds

Physical activity is an established protective factor for several cancers, but whether its association with lung cancer differs by histological subtype and sex remains unclear. Clarifying these differences is essential for precision prevention.

Objective

To examine associations between physical activity and lung cancer risk across major histological subtypes—adenocarcinoma (LUAD), squamous cell carcinoma (LUSC), and small-cell lung cancer (SCLC)—and to assess sex-specific patterns.

Methods

PubMed and Embase were searched from January 1990 through September 4, 2025. Observational cohort or case-control studies evaluating prediagnostic physical activity and reporting subtype-specific lung cancer risk estimates were included. Eight studies met eligibility criteria. Two reviewers independently extracted study characteristics and maximally adjusted risk estimates. Random-effects models pooled relative risks (RRs) comparing the highest versus lowest physical activity categories. Sex-stratified analyses were performed.

Results

Eight studies were included (five cohorts: 1,094,095 participants; three case-control studies: 3,951 cases and 7,423 controls). Higher physical activity was associated with lower risk across all subtypes: LUAD (RR, 0.80; 95% CI, 0.73–0.88), LUSC (RR, 0.83; 95% CI, 0.73–0.94), and SCLC (RR, 0.78; 95% CI, 0.68–0.91). Sex-stratified analyses revealed subtype-specific heterogeneity. For SCLC, men showed a strong inverse association (RR, 0.66; 95% CI, 0.49–0.88), whereas the association in women was weaker and non-significant (RR, 0.82; 95% CI, 0.58–1.16). In contrast, for LUSC, women demonstrated the strongest protective association (RR, 0.73; 95% CI, 0.56–0.96), while associations in men were minimal (RR, 0.92; 95% CI, 0.74–1.15). Associations for LUAD were similar between sexes.

Conclusions

Physical activity was associated with reduced risk across major lung cancer subtypes, with effect magnitude varying by histology and sex. These findings suggest multiple, subtype-specific preventive pathways and support incorporating physical activity into precision lung cancer prevention strategies.

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Exercise Medicine, Lung Cancer Histology, Small Cell Lung Cancer, Lung Squamous Cell Carcinoma

Conflict of Interest & Ethical Approval

yes

Abstract submitters declaration

yes

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