

Association of Electronic Cigarette Use After Conventional Smoking Cessation With Lung Cancer Risk: A Nationwide Cohort Study

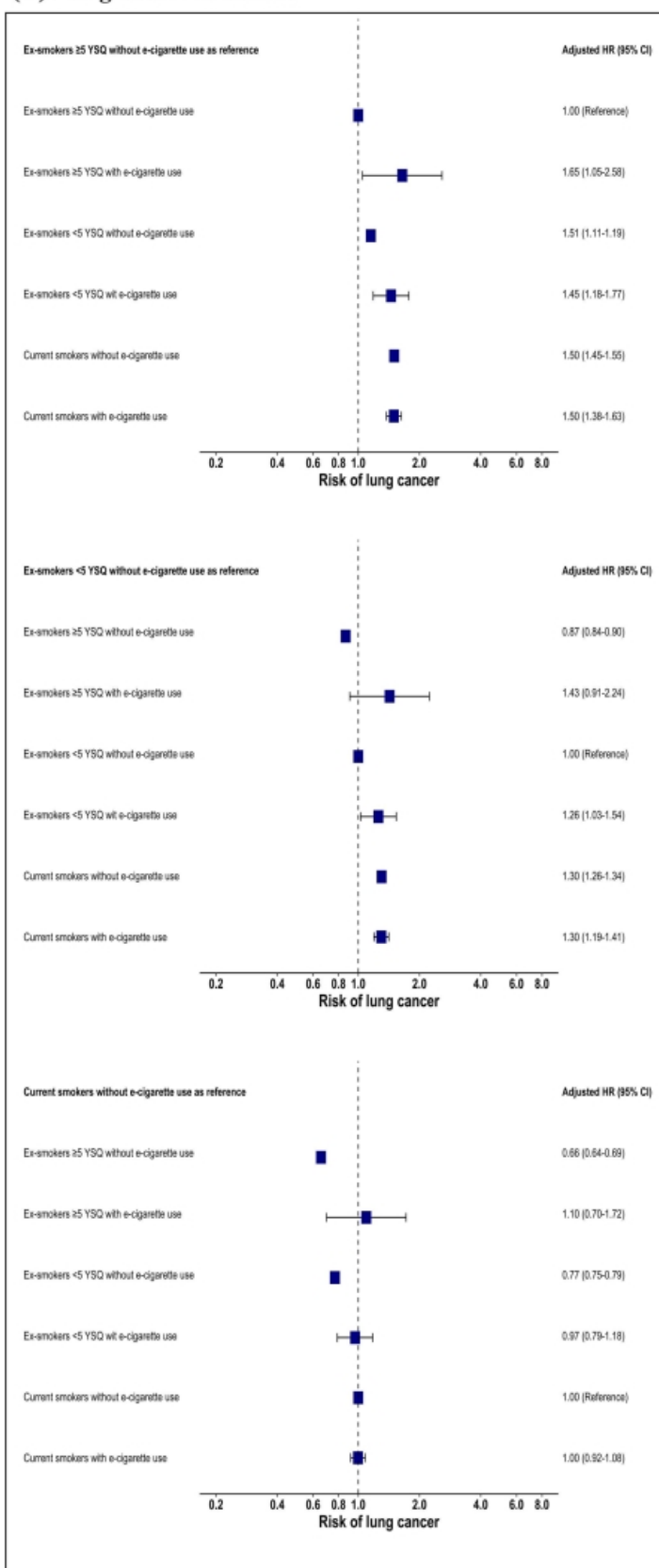
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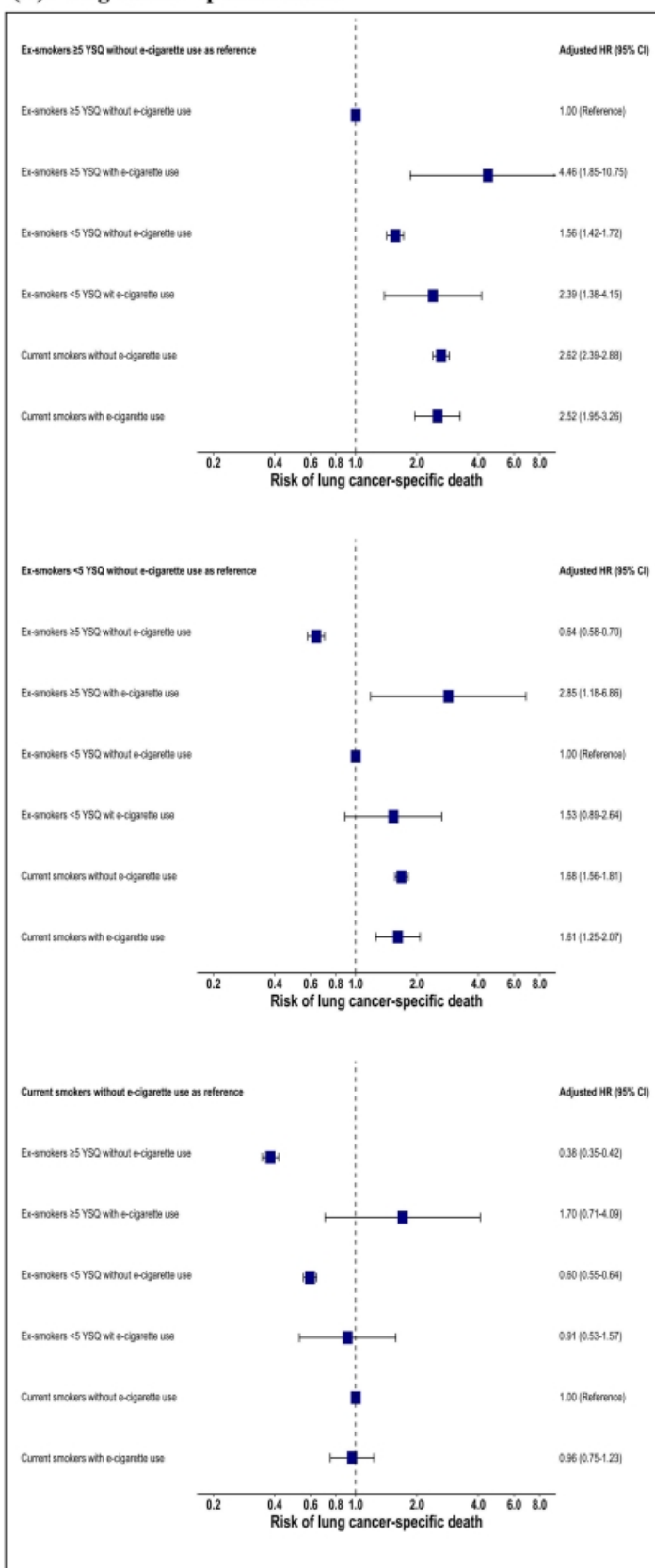
RATIONALE: Electronic cigarettes (e-cigarettes) have gained popularity as a less harmful alternative to conventional cigarette smoking. However, whether switching to e-cigarette use after conventional smoking cessation affects future lung cancer risk remains unclear. Therefore, we designed a nationwide population-based study to determine lung cancer risk and related mortality associated with smoking habit changes to e-cigarette use among those who smoked conventional cigarettes, further stratified by the length of smoking cessation. **METHODS:** We evaluated 4,329,288 individuals with a conventional smoking history who participated in the National Health Screening Program during the first (2012-2014) and second (2018) periods and followed up until December 2021. Participants were categorized into six groups according to their smoking history and habit change to e-cigarette use as follows: ex-smokers ≥ 5 years since quitting (YSQ) without e-cigarette use, ≥ 5 YSQ with e-cigarette use, < 5 YSQ without e-cigarette use, < 5 YSQ with e-cigarette use, and current smokers without and with e-cigarette use. The risk of lung cancer and lung cancer-specific death (LCSD) were assessed using cox-proportional hazards models with adjustments for potential confounders. Stratified analysis was performed for high-risk individuals aged 50-80 years with ≥ 20 PYs smoking history, likely recommended for lung cancer screening according to the USPSTF 2021 criteria. **RESULTS:** During the follow-up, 53,354 individuals developed lung cancer, and 6,351 LCSD events occurred. Compared with ex-smokers ≥ 5 YSQ without e-cigarette use, ex-smokers ≥ 5 YSQ with e-cigarette use demonstrated an increased risk of LCSD (aHR=2.69, 95% CI=1.12-6.46). Ex-smokers < 5 YSQ with e-cigarette use demonstrated a higher risk of lung cancer development (aHR=1.23, 95% CI=1.09-1.39) and LCSD (aHR=1.71, 95% CI=1.10-2.66) than those < 5 YSQ without e-cigarette use. Stratified analysis for individuals aged 50-80 with a smoking history of ≥ 20 PY revealed that ex-smokers ≥ 5 YSQ with e-cigarette use reported higher risk of lung cancer (aHR=1.65, 95% CI=1.05-2.58) and LCSD (aHR=4.46, 95% CI=1.85-10.75) than those ≥ 5 YSQ without e-cigarette use, respectively. Similarly, ex-smokers < 5 YSQ with e-cigarette use reported a higher risk of lung cancer (aHR=1.26, 95% CI=1.03-1.54) than those < 5 YSQ without e-cigarette use. **CONCLUSIONS:** Switching to e-cigarette use after conventional smoking cessation was associated with a higher risk of lung cancer and related mortality, particularly in high-risk individuals who are likely recommended for low-dose CT-based screening. Clinicians must highlight the potential harmful effects of alternative e-cigarette use when integrating smoking cessation interventions to reduce lung cancer risk.

Figure. Forest plots for adjusted hazard ratios of (A) lung cancer incidence and (B) lung cancer-specific death according to smoking habit change to e-cigarette use among individuals aged 50-80 years with a cigarette smoking intensity of ≥ 20 pack-years

(A) Lung cancer incidence



(B) Lung cancer-specific death



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