MA03.06
Respiratory Tract Malignancy-associated Mortality Attributable to Particulate Matter in South Asia from the Global Burden of Disease

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Introduction: There is strong evidence to suggest that fine particulate matter ($PM_{2.5}$) air pollution is associated with increased risk of incidence and mortality due to malignancies of the respiratory tract. With fine particulate matter in some of the region's most densely populated areas being almost 20 times, the WHO safe permissible limits, air pollution in South Asia region (SAR) is a matter of public health importance. We sought to investigate the temporal pattern of the contribution of $PM_{2.5}$ to the burden of respiratory tract malignancies (RTM) in the SAR from 1990 to 2019. **Methods:** We used the 1990-2019 global burden of disease methodology to calculate the total $PM_{2.5}$, ambient $PM_{2.5}$, and household $PM_{2.5}$-related deaths and YLL (years of life lost) due to RTM (tracheal, bronchus, and lung) in SAR (India, Pakistan, Bangladesh, Bhutan, and Nepal). State of the Global Air repository was used to obtain population-weighted ambient PM2.5 and household air pollution (HAP). **Results:** There has been an increase in the average annual population-weighted ambient $PM_{2.5}$ exposure in SAR from 68 μg/m3 [95% confidence interval (CI): 34.5-120] to 78.2 μg/m3 [95% CI: 71.9-85] from 1990 to 2019. This was despite a 41% reduction in HAP due to solid fuel sources over the same period. In 2019, $PM_{2.5}$ contributed to 31.81% (95% CI: 24.37-38.62%) of total RTM-deaths and 31.69% (95% CI: 24.28-37.69%) of YLLs due to RTM in the region. It is estimated that 15,252 (95% CI: 10,828-21,452) RTM-deaths in SAR were attributable to $PM_{2.5}$ in 2019, including 11,659 (95% CI: 7,440-17,852) and 3,593 (95% CI: 1,522-6,640) RTM-deaths due to HAP and ambient PM2.5 pollution, respectively. Age-standardized rate of RTM-deaths from 1990 to 2019 decreased by 54.26% and increased by 162.68% due to HAP and ambient $PM_{2.5}$ respectively. Similarly, the age-standardized rate of YLLs from RTM attributed to HAP decreased by 53.69%, while that attributed to ambient $PM_{2.5}$ increased by 168.69% from 1990 to 2019. **Conclusions:** A high exposure to $PM_{2.5}$ in SAR continues to have significant contribution to overall mortality due to RTM, accounting for one third of RTM deaths and YLLs over the past 3 decades. Despite an encouraging reduction in HAP, there continues to be a rise in ambient $PM_{2.5}$ exposure in SAR. Our analysis suggests there is a sense of urgency to inform policy in order to have stronger regulation of particulate matter exposure to protect health of populations in SAR.

Keywords: Respiratory tract malignancy, fine particulate matter, air pollution

Tables/Figures:

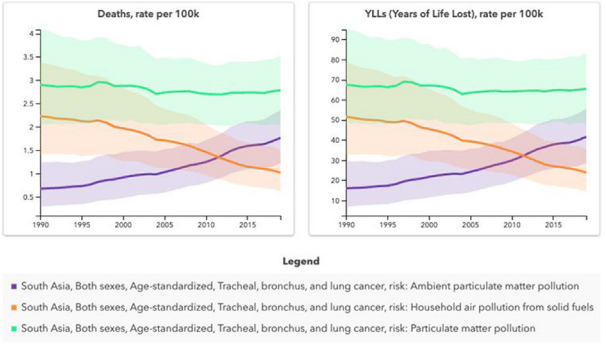

Figure 1: Age-standardized rate of respiratory tract malignancy-related deaths (A) and YLLs (B) per 100,000 from 1990 to 2019 attributed to total, ambient and household particulate matter in the South Asia region.

MA03.08
Regular Use of Pharmaceutical Opioids and Subsequent Risk of Lung Cancer

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Introduction: Opium consumption was recently classified as "carcinogenic to humans" by the International Agency for Research on Cancer for cancers of the lung, larynx, and bladder. We investigated whether regular use of pharmaceutical opioids, which are either derived from opium or synthesized to mimic its structure and effects, is associated with lung cancer risk. **Methods:** We analyzed 473,067 participants in the UK Biobank study who were recruited during 2006-2010, cancer-free at baseline, and followed through April 2021. Participants reported medications they took regularly, including opioids, on the baseline questionnaire. To account for underlying health conditions, we created a propensity score for taking opioids based on history of chronic pain, musculoskeletal disorders, diabetes, hypertension, coronary heart diseases, stroke, reflux, inflammatory bowel diseases, and chronic kidney disease. We estimated hazard ratios for incident lung cancer associated with opioid use using adjusted Cox regression. To assess the potential causality of this relationship, we further performed a two-sample Mendelian randomization (MR) analysis using summary statistics from genome-wide association studies (GWAS). The genetic instrument included 34 SNPs, based on a GWAS of medication use in UK Biobank, and the outcome was based on a GWAS of 29,266 lung cancer cases and 56,450 controls. **Results:** During follow-up, 3,480 participants developed lung cancer. At baseline, 27,856 (6%) participants reported regular opioid use. After adjustment for potential confounders, regular opioid use was associated with increased lung cancer risk (HR=1.32, 95%CI 1.20-1.47) (Figure 1). Lung cancer risk increased in a dose-

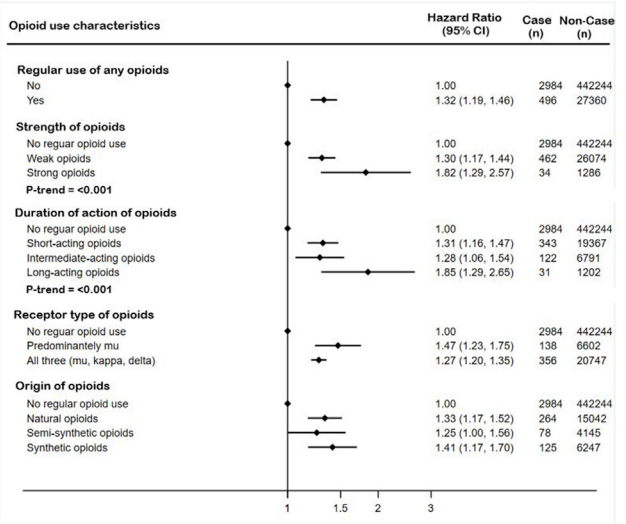

Figure 1. Association between opioid use and risk of incident lung cancer in the UK Biobank study. Hazard ratios were estimated using Cox regression models adjusted for age, sex, education, Townsend deprivation index, body mass index, alcohol drinking status, smoking status, pack-years of smoked cigarettes, and the propensity score for chronic health conditions.

dependent manner with higher strength and longer duration of action of opioids used (both p-trend<0.001), reaching more than 80% higher risk among participants using strong (HR=1.82, 95%CI 1.29-2.57) and long-acting (HR=1.85, 95%CI 1.29-2.64) opioids compared with those not regularly using opioids. In the MR analysis, genetic predisposition to using opioids was associated with increased risk for lung cancer (odds ratio=1.16, 95%CI 1.05-1.28). Results were comparable across strata of sex, chronic pain, smoking, alcohol use, and socioeconomic status (all p-interaction>0.25). **Conclusions:** Our findings suggest that regular use of pharmaceutical opioids may increase the risk of developing lung cancer. Given the widespread use of opioid medications, further research is needed to evaluate this association and understand potential underlying mechanisms linking opioid use to lung cancer risk.
Keywords: Analgesics, Opioids, Risk factor

MA03.09
Embedding Smoking Cessation into a Potential Lung Cancer Screening Program: Australian Tobacco Control Expert Perspectives

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Introduction: Tobacco smoking prevalence in Australia has been substantially reduced through evidence-based tobacco control policy. Nevertheless, smoking remains the leading cause of premature mortality and over the next two decades an estimated 62% of all smoking-attributable Australian cancer deaths will be from lung cancer. A national program of lung cancer screening (LCS) via low-dose computed tomography is being explored, including smoking cessation support for participants. Various approaches to providing smoking cessation support (e.g., wholly embedded, wholly external, or hybrid) have been implemented within LCS settings. We aimed to explore the perspectives of tobacco control experts on how smoking cessation interventions can be optimally embedded into an organised LCS program in the Australian context. **Methods:** In 2022, individual/group interviews were conducted with practitioners, researchers, or policymakers recognised as experts in tobacco control and/or smoking cessation. National recruitment was via maximum variation purposive and snowball sampling, plus invitation of two participants from Aotearoa New Zealand. After piloting, the interview schedule included a structured evidence summary about international LCS trials and covered: factors to enhance acceptability and feasibility; LCS participant-, provider- and system-level barriers and facilitators for implementation, and; potential delivery models and implementation strategies. An analytical framework was developed for application through a collaborative process of transcript coding by six researcher and consumer advocate authors. **Results:** Experts (N=30) generally advocated for a 'hybrid' pathway of smoking cessation support. Using this pathway, some dedicated services will be embedded within the LCS program and other services may require external clinical and community-based referral, to maximise cost-effectiveness and available cessation supports. In contrast, wholly external cessation services alone were considered insufficient to engage participants for uptake, and wholly embedded services were considered resource-intensive and therefore to have lower feasibility. Experts noted that many smoking cessation resources were already in use, and wanted to avoid unnecessary duplication, thus placing priority on implementation efforts. It was suggested that LCS presents an opportunity to leverage broader tobacco control initiatives (e.g., anti-tobacco mass media) and reinforce existing prevention strategies, which could normalise routine offers of cessation support. Experts described a range of system-level barriers (particularly time pressures) to providing support in existing clinical settings, and the importance of countering perceived stigma to maximise engagement. Specialised training on cessation intervention delivery for program staff, role clarity, and buy-in from all levels of leadership (with funding commitments) were emphasised as workforce requirements. **Conclusions:** This study builds on recent Australian recommendations to improve embedded smoking cessation support across the entire healthcare system. It also emphasises policy opportunities to assist patient groups with heavy smoking histories (e.g., the accessibility of subsidised combination nicotine replacement therapy, supported by a clinical workforce with dedicated smoking cessation training). Efforts are now required to identify, evaluate, and adapt smoking cessation resources with LCS-eligible consumers that can be offered most effectively in the context of a potential Australian program. These findings will also support other ongoing work including a national (Australian) consensus workshop to seek further input across the sector about embedding smoking cessation into LCS.
Keywords: smoking cessation interventions, qualitative research, implementation science

MA03.10
The Interim Analysis of Can-Prevent-Lung Trial: Canakinumab for The Prevention of Lung Cancer

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Introduction: Tumor promoting inflammation plays important roles during initiation and progression of lung cancers. Our recent work has demonstrated anti-inflammation by blocking interleukin-1beta (IL-1B) pathway can delay the progression of precancers into invasive lung cancers. Canakinumab, a humanized anti-ILB antibody has been demonstrated to decrease lung cancer incidence by ~70% in CANTOS trial. This single arm Phase II trial aims to test whether canakinumab can increase regression rate of persistent high-risk lung nodules and prevent lung cancer. **Methods:** Patients with persistent pulmonary nodules (at least 2 CT scans, 3 months apart showing no evidence of regression) with predicted risk (by Brock model) >10% in patients with no personal history of lung cancer; or >5% in patients with localized lung cancer who completed standard of care therapy receive canakinumab subcutaneously every 3 weeks for up to 8 doses. CT scans after 2 doses, 4 doses and 8 doses are performed. Therapeutic response and growth trajectory before and after canakinumab therapy were assessed using modified RECISIT criteria (mRECISIT, measuring both solid and ground-glass opacity components), 3D volumetric analysis and radiomics analysis. A control group of patients identified by propensity matching were analyzed in the same way. **Results:** At the data lock for the planned interim analysis, 15 patients have received at least one dose of canakinumab; 11 patients have completed treatment and safety follow up. Canakinumab has been overall well tolerated with no ≥grade 3 drug-related toxicities. The most common toxicity was grade 2 neutropenia (n= 4) leading to treatment disruption or