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Risks and burden of lung cancer incidence for residential petrochemical industrial complexes: A meta-analysis and application

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ABSTRACT

Background: Lung cancer is one of the most common cancers in the world. Higher incidence of lung cancer may be associated with residential proximity to a petrochemical industrial complex (PIC) due to exposure to various carcinogens, although results from previous epidemiologic studies remain inconclusive. Because disease burden due to residential inequality is a public health and societal concern, this study analyzed published data to estimate lung cancer incidence in association with residential proximity to PICs.

Methods: We performed a meta-analysis on selected epidemiologic studies that met the following criteria: lung cancer incidence was coded by the International Classification of Diseases; exposure groups were clearly defined as residents living near PICs; and confidence intervals were available or calculable from original articles. We further applied a population attributable factor (PAF) method to estimate disease burden attributable to living near PICs in 22 European Union (EU) countries.

Results: Meta-analysis included six studies with a total of 466,066 residents living near PICs in six countries. Residents living near PICs had a 19% higher risk of lung cancer compared to those who lived farther away (95% CI = 1.06–1.32). By sex, risks were higher and more significant for females (RR = 1.29; 95% CI = 1.09–1.54; $P = 0.004$) than males (RR = 1.12; 95% CI = 0.95–1.33; $P = 0.173$). By location, only groups in Europe had a significantly greater risk of lung cancer with exposure to PICs (95% CI = 1.03–1.33; $P = 0.019$), although groups in other locations showed similar trends. By bona fide observation, observation of residents for at least seven years provided sufficient latency to estimate risk (RR = 1.25; 95% CI = 1.17–1.34; $P < 0.001$). Regarding burden of lung cancer in 22 EU countries, 494 males and 478 females were attributed to living in the vicinity of a PIC annually.

Conclusions: Lung cancer incidence is significantly higher in individuals living near PICs. This result provides strong epidemiologic evidence for further policy to regulate potential pollutants near PICs.

Highlights: Higher incident rates of lung cancer for residents living close to petrochemical industry complex

1. Introduction

Industrial development, which generally refers to chemical production and consumption, is associated with the emergence of environmental risk factors due to industrial release of hazardous chemicals into the environment (Elliott et al., 2004; Zhang et al., 2010). Estimating health risks associated with environmental exposure is important for residential justice and to identify strategies to reduce disease burden and health inequality (Elliott et al., 2004; Solomon et al., 2016).

Since the mid-1970s, there has been growing concern over excessive cancer cases among residents living in coastal counties in the United States (U.S.) (Blot and Fraumeni, 1976). One major concern is the impact of rapid development of petrochemical industrial complexes

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(PICs)—defined as clusters of industries that manufacture petroleum and chemical products (United Nations Statistics Division (UNSD), 2008)—on the long-term health of residents in the vicinity of these areas (Lin et al., 2017; Lopez-Navarro et al., 2013; Nadal et al., 2011). Industrial PIC manufacturing processes are diverse and usually involve toxic chemicals, such as volatile organic compounds, polycyclic aromatic hydrocarbons, polychlorinated biphenyls, ethylene, propane, polyvinyl chloride, benzene, and heavy metals (Axelsson et al., 2010; Beccaloni et al., 2014; Li et al., 2009; Cetin et al., 2003). Exposure to these toxicants among residents living close to PICs can increase their risk of cancers, particularly respiratory cancers such as lung cancer (Kaldor et al., 1984).

As one of the most common cancers worldwide, lung cancer has global incidence rates of 36.75 and 17.41 per 100,000 males and females, respectively, contributing to around 682,000 cases globally in 2016 (Global Burden of Disease Collaborative Network, 2016). Apart from well-known behavioral risk factors, such as smoking, and naturally occurring environmental carcinogens, such as radon, other environmental determinants also contribute to lung cancer (Li et al., 2009; International Energy Agency, 2017; Tirmarche et al., 2010).

Due to public health concerns, several studies have attempted to address whether there is an increased risk of lung cancer in residents living near PICs, but results have varied across countries and study periods. In the 1980s, Kaldor and colleagues found a higher risk of lung cancer among males living close to PICs (Kaldor et al., 1984). Some U.S. studies also have reported consistent findings of an association between lung cancer risk and residential exposure to PICs (Simonsen et al., 2010; Gottlieb et al., 1982). However, Anna-Karin and colleagues' study in Ecuador reported statistical non-significance of the relative risks of lung cancer with residential exposure to PICs (Hurtig and San Sebastian, 2002). One Italian study even reported a protective effect of residential PIC exposure for females in Melilli and Priolo, although the results were not statistically significant (Fazzo et al., 2016).

Our previous research reported a higher risk of lung cancer mortality among residents living near PICs, although these results also were not statistically significant (Lin et al., 2017). To our best knowledge, it is the only study to focus on lung cancer mortality. Further, no studies have systematically combined previous data to quantitatively examine the risk of lung cancer incidence among residents living near PICs. Therefore, using a random-effects model in meta-analysis, we aimed to examine heterogeneity among previous studies and estimate the pooled risk of lung cancer incidence among residents living near PICs, including both environmental exposure and co-exposure from occupation. Since most studied groups were from European countries, and PIC data from the European Union (EU) are most accessible, we further estimated the burden of lung cancer attributable to PICs in 22 EU countries.

2. Methods

2.1. Literature review and study assessment

Two authors (RT Lin and YT Hsu) independently searched published studies available before October 16, 2017, from PubMed, Web of Science, Cochrane Library, ScienceDirect, and other sources. Search terms were: "(lung cancer OR lung neoplasm) AND (refinery OR petroleum OR petrochemical OR oil and gas industry)." The authors screened articles and included studies that met the following criteria: (1) original article available in English and full-text; and (2) title and abstract related to the study of interest.

We included studies in our analysis if they: (1) reported data on lung cancer incidence (as the outcome variable); (2) defined exposure group as residents living in the vicinity of PICs (with the definition of PIC exposure); and (3) did not contain populations overlapping with other studies. Studies were excluded if they focused only on occupational exposure or if point estimates and/or confidence intervals (CI) were not extractable or calculable.

We then applied the Newcastle-Ottawa Quality Assessment Scale (NOQAS) to assess study quality and possible risk of bias. NOQAS rates eight items in three categories—selection, comparability, and outcome—with nine stars to semi-quantitatively evaluate study quality (Wells et al., n.d.). We reviewed study quality independently and assigned stars (N-O score) for each item.

2.2. Data combination and synthesis

Four types of point estimates were reported in the selected studies: odds ratio (OR), relative risk (RR), standardized incidence ratio (SIR), and age-standardized rate ratio (ASRR). SIR or ASRR represent a comparison of the observed incidence in a studied group to the expected incidence in an age- and sex-adjusted standard population (Axelsson et al., 2010; Fazzo et al., 2016; Zusman et al., 2012). OR, ASRR, and SIR can be interpreted and analyzed as approximates of RR (Symons and Taulbee, 1981).

For studies that did not report either 95% CI or standard error (SE) (Kaldor et al., 1984; Zusman et al., 2012; Fares and Masri, 2012), we estimated variances and SE of *lnRR* using the following equation:

$$Var(lnRR) = Var(lnR_1) + Var(lnR_0) \approx \left(\frac{1}{R_1}\right)^2 \times \frac{R_1(1-R_1)}{N_1} + \left(\frac{1}{R_0}\right)^2 \times \frac{R_0(1-R_0)}{N_0} \quad (1)$$

where $Var(\ln RR)$ represents the variance of natural log of *RR*; R_1 and R_0 represent incidence rates of the studied group and reference group, respectively; and N_1 and N_0 represent populations of the studied group and reference group, respectively.

For studies that only provided upper and lower limits of 95% CI (Axelsson et al., 2010; Simonsen et al., 2010; Hurtig and San Sebastian, 2002; Fazzo et al., 2016), we estimated SE of natural log of RR using the following equation:

$$SE(lnRR) = \frac{1}{2} \times \left(\frac{\ln(RR_{upper}) - \ln(RR_{est})}{1.96} + \frac{\ln(RR_{est}) - \ln(RR_{lower})}{1.96}\right) \quad (2)$$

where $\ln(RR_{upper})$, $\ln(RR_{est})$, and $\ln(RR_{lower})$ represent the natural logs of upper limit, point estimate, and lower limit of RR, respectively.

2.3. Statistical analysis

Pooled point estimates with 95% CI were analyzed by a random effect model. We applied the I^2 test to address possible heterogeneity within and between studies by defining 10% as no heterogeneity, 10%–30% as low heterogeneity, 30%–60% as moderate heterogeneity, and > 60% as high heterogeneity (Zhao, 2013). Subgroup analysis was also performed to examine the effects among groups stratified by characteristics, including sex, location, and bona fide observation, which was defined as a study period of < 7 or ≥7 years after 20 years of PIC operation. Exposures to volatile organic compounds (VOC), polycyclic aromatic hydrocarbon (PAH), benzene, benzo-a-pyrene (BAP), heavy metal, and polychlorinated biphenyls (PCB) well documented from original researches were extracted for subgroup analysis.

We applied meta-regressions to investigate possible factors of heterogeneity, including latency of study period, starting year of study, ending year of study, published year, and starting year of PIC operation. By continually adding one estimate to the pooled estimate in order of starting year of study, we provided another approach for sensitivity analysis. Finally, we used a funnel plot to examine whether there was publication bias and used Begg's and Egger's regressions to test whether there was bias due to a small-study effect.