Environmental and occupational determinants of lung cancer

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Abstract: Lung cancer has become a global problem, from a rare disease to an emerging public health issue. The current data of GLOBOCAN 2018, indicates that this disease has recorded highest mortality among all types of cancer. The etiological factors of lung cancer have become more multiplex because of increasing industrialization and environmental pollution around the world, especially in India. There is a rise in incidence of lung cancer among non-smokers and this can be attributed to environmental and occupational exposure to various kinds of hazardous substances. Target mutations are high in Lung cancer among non-smokers when compared to smokers. Some developed countries have guidelines and policies for prevention and control of risk factors focusing on these issues. Intervention aiming for primary prevention can be an important and cost-effective tool in developing countries to deal with increasing incidence of lung cancer. There is a need to define high risk group among non-smokers after taking into account environmental and occupational determinants as important risk factors. Research on etiology of lung cancer and prevention provides evidence to work on global incidence and prevalence of lung cancer, and for designing cost effective lung cancer prevention strategies. Research in the area of lung cancer prevention should be considered to recognize the areas where action is required to prevent environment and occupation related lung cancer. The government and occupational health and safety organizations have taken many steps in the last few years that can help to protect workers from these exposures. But the dangers are still there, so there is a need to do more to limit these exposures around workplace. This whole situation guides us to advocate population-based intervention along with policy implementation.

Keywords: Environmental determinants; occupational determinants; lung cancer

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Background and rationale

Lung cancer is a leading cause of morbidity and mortality globally, accounting for 2,094 million cases and 1.8 million deaths per year (1). Lung cancer has become the most common cancer in the world for the last several decades and showing an increase in incidence in the developing countries (2). Lung cancer, unfortunately does not become clinically apparent until it reaches an advanced stage and more than 75% of lung cancers are diagnosed when disease is advanced or metastatic (3). In India, approximately 114,000 new lung cancer cases are reported each year (4).

According to GLOBOCAN 2018, lung cancer represented 11.6% of all types of cancers, out of which 80% were attributed to smoking (5-7). Outdoor air pollution caused 108,000 lung cancer deaths (8); solid fuels, used more in developing countries for cooking and heating, caused 36,000 lung cancer deaths (8,9); second-hand smoke was estimated to cause 21,000 lung cancer deaths (10).

The chances of getting lung cancer has increased with increase in household air pollution (11,12). Only 1 out of 10 patients diagnosed with lung cancer will survive the following 5 years (13). It has been noticed that smoking prevalence has declined in many developed countries (14) however; it is increasing in developing countries and also among women (15). In developing countries lung cancer is usually detected at an advanced stage (16,17) and this puts a greater economic impact on middle- or low-income families. Lung cancer has multiple risk factors, which are combination of the genetic and external factors (environmental & occupational) and the proportion of lung cancer cases attributable to preventable risk factors vary greatly across countries (18,19). The resulting evidence from various research studies, causally associate lung cancer with active and passive smoking, a variety of occupational agents, and indoor and outdoor air pollution (20).

Lung cancer can be preventable, because most risk factors of lung cancer can be prevented if people have sufficient knowledge about that and the government should make specific policy and guideline on these environmental and occupational risk factors which attribute to lung cancer such as tobacco (smoke and smokeless) consumption (21). Therefore, environmental and occupational interventions are a solution for diminishing the incidence and mortality of lung cancer, by abolishing these risk factors by means of primary prevention.

Environmental factors can be physical (ionizing and non-ionizing radiations such as exposure to radon or ultraviolet (UV) radiation, respectively), chemical (such as asbestos, dioxins, metals (such as arsenic chromium, nickel, cobalt, etc.) and other pollutants found in industrial emissions, house hold smoke and second-hand smoke. Parents who have occupational exposures may increase the risk of cancer in their progeny (22). Lung cancer is strongly linked to environmental & occupational exposure (23).

Exposure may be widespread, starting from outdoor and indoor air pollution, or could be restricted to an area close to a certain industrial site. These exposures have been associated with a variety of neoplasms, but most important among these is lung cancer. Occupational health risks are also directly related to physical, chemical and biological factors that present in the environment. Lung cancer has most commonly been linked with occupational exposures and for which evidence is strong (24). Exposure limit of various environmental and occupational risk factors are summarized in Table 1.

A WHO study found that at least 1.7 million cancer deaths annually could be prevented through healthy working and living environments (25). Changes in individual behavior are facilitated by wider contextual changes in the environments where individuals live and work. Respiratory diseases, for instance, are tied to lung cancer risk factors such as smoking and air pollution. Therefore, primary prevention can achieve a number of primary end points (21).

Environmental determinants of lung cancer

Chemical exposures

There is a strong evidence that exposure to industrial and manufacturing chemicals and harmful pesticides or aflatoxin can compose of cancer-trigger factors that present in our living and working environments. Agricultural and public health workers are mainly exposed to these hazardous pesticides during handling, dilution and application. Exposure is mainly by skin and by the respirable routes during application. Occupational pesticide usage is related to lung cancer in some cases but not all. In a study by Bonner et al., the occupational hazard ratio was elevated in the highest exposure category of lifetime to 3 chemicals used as pesticides, associating it with lung cancer incidence (26).

In a follow-up to this study, Alavanja et al. evaluated the use of 43 pesticides and 654 lung cancer cases after 10 years of additional follow-up in the Agricultural Health Study (AHS), a prospective cohort study comprising...
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<td>Asbestos</td>
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<td>High</td>
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<td>Construction workers, electrician, mining, railroad, fire fighters</td>
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<td>Arsenic</td>
<td>NIOSH (REL): 0.002 mg/m³; OSHA (PEL): 0.010 mg/m³</td>
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<td>Beryllium</td>
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<td>Low</td>
<td>Intermediate</td>
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<td>Chromium</td>
<td>–</td>
<td>High</td>
<td>Intermediate</td>
<td>Low</td>
<td>Low</td>
<td>Stainless steel production &amp; welding, tanning industries</td>
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<tr>
<td>Nickel</td>
<td>OSHA (PEL): 1 mg/m³; TWA: 8 h</td>
<td>Intermediate</td>
<td>Low</td>
<td>Low</td>
<td>Intermediate</td>
<td>Battery makers, ceramic makers, electroplaters, glass workers, jewelers, metal workers, paint related workers &amp; welders</td>
</tr>
<tr>
<td></td>
<td>NIOSH (REL): 0.015 mg/m³; TWA: 10 h</td>
<td>Intermediate</td>
<td>Low</td>
<td>Low</td>
<td>Intermediate</td>
<td></td>
</tr>
</tbody>
</table>

NIOSH, National Institute for Occupational Safety and Health; OSHA, Occupational Safety and Health Administration; REL, recommended exposure limit; PEL, permissible exposure limit; TWA, time weighted average; EPA, Environmental Protection Agency.
57,310 pesticide applicators from Iowa and North Carolina. The authors found possible new associations for chlorimuron ethyl and parathion with lung cancer that have not been previously observed in the AHS, and are of the view that it needs to be further studied. Above cited study and several other studies along with this, support the theory that pesticides are indeed a major determinant of lung cancer (27).

Chlorophenols (CPs), dioxin compounds and related phenoxyacetic acids (PAs) are pesticide groups that have carcinogenetic effect on lung (28-30). Various studies reported a wide range of lung cancer in workplace site (31).

Meta-analysis with five cohort studies (32-36) with six reports, investigated the causes of lung cancer among workers of CPs related compounds (CPsR) plants. Collins et al. (37) evaluated two individual investigations with different types of CPs exposure. Among the studies, one multicenter analysis from IARC publications included 36 studies from previous reports (32). Overall, a total of 27,865 workers in CPsR production were involved in the meta-analysis. Five papers with six reports were included in the final analysis. The standardized mortality rate (SMR) for lung cancer from the random model was 1.18 [95% confidence interval (CI): 1.03–1.35, \( P=0.014 \)] (38).

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Indoor air pollution from household combustion

Burning coal inside home for the purpose of heating or cooking produces PM and gas emissions that may contain a number of cancer trigger factors, such as benzene, carbon monoxide, formaldehyde, and polycyclic aromatic hydrocarbons (PAHs). Indoor air pollution from household combustion of coal is carcinogenic to humans (group 1) (44). There is rich evidence that proved carcinogenicity in humans from household combustion of coal (12,45). Increasing level of smoke inside the home associated with an increasing risk of lung cancer (\( P<0.05 \)) (OR 1.62; 95% CI: 1.14–2.32) (46). Another research study findings showed that Individuals who carried the T-genotype of HIF-1\( \alpha \) rs2057482 were more susceptible to small cell carcinoma (OR 1.725; 95% CI: 1.047–2.842) (47).

Second-hand smoke

Tobacco and second-hand smoke are known to be a human carcinogen (48). Tobacco smoking is attributed to lung cancer in humans. The risk of death from lung cancer increases with increasing duration of smoking and with increasing numbers of cigarettes smoked. Studies support an association of environmental (passive or secondhand) tobacco smoke with cancer of the lung (49,50).

Many epidemiological studies, including case-control studies, have demonstrated increased risk for developing lung cancer following prolonged exposure to environmental tobacco smoke either second-hand aerosol from tobacco or electronic cigarettes (51). Exposure to environmental tobacco smoke during childhood is strongly associated with lung cancer (OR 3.9; 95% CI: 1.9–8.2) according to one research study (52). According to another study, those who had never smoked, both among men (\( P=0.02 \)) and women (\( P=0.001 \)), presented more frequently with adenocarcinoma histology (53).

Asbestos

Asbestos are naturally occurring fibrous silicates with important commercial use in acoustical and thermal insulation. They can be divided into two groups: chrysotile and the group of amphiboles, including amosite, crocidolite, anthophyllite, actinolite and tremolite fibres. All types of asbestos are carcinogenic and can cause lung cancer and mesothelioma. Biological effects of amphiboles
on the pleura and peritoneum seem to be stronger than those of chrysotile. There are many epidemiological studies available on asbestos-exposed workers, but only few on the health effects of household and residential exposure to asbestos. The main household exposure concerns are to the immediate family members of asbestos workers and arise from dust brought from workplace on clothes, while household sources of asbestos exposure are represented by the degradation, installation, removal and repair of asbestos-containing products. Residential exposure mainly results from asbestos mining related outdoor pollution or manufacturing in the nearby places in addition to natural exposure from the erosion of asbestos or asbestiform rocks. Assessing the non-occupational exposure to asbestos is difficult, since levels are generally low, and the duration and frequency of exposure and the type of exposure is seldom well defined. According to IARC, all forms of asbestos (chrysotile, crocidolite, amosite, tremolite, actinolite and anthophyllite) are carcinogenic to humans (group 1). Environmental Protection Agency (EPA) also classified asbestos as Group A carcinogen to human (54).

A large number of epidemiological and occupational studies have reported that exposure to asbestos via inhalation causes lung cancer and mesothelioma (55-59). Study on workers with heavy exposure to asbestos showed an increased risk of lung cancer [relative risk (RR) 1.74; 95% CI: 1.25–2.41] and a similar increase in risk to those with low exposure up to 20 years (RR 0.94; 95% CI: 0.77–1.15) (60). Carcinogenicity of asbestos depends upon its length of fiber. Long and intermediate length-range asbestos fibers (>5 µm) are proven to be more carcinogenic to humans than short fibers. An autopsy study of Italian shipyard workers showed that chrysotile was the most common type of asbestos fiber in asbestos-related lung plaques. Most of those fibers were found to be of 8 mm in length (61). Use of asbestos has continued in much of Asia, Africa and India has been a major consumer of asbestos after China (62).

**Metals**

Arsenic is both an environmental and occupational lung carcinogen which most commonly exists in the form of arsenite and arsenate. Occupational exposures occur primarily among workers who work and inhale dust from coal, copper ore mines and smelters. The IARC concluded that arsenic exposure via inhalation increases lung cancer risk (63). Many case-control studies were performed in Argentina, Bangladesh, Chile, and Taiwan, that examined the associations between higher concentrations (e.g., >100 µg/L) of arsenic in drinking water and lung cancer. It is not known if the lack of evidence of an association below 100 µg/L is the result of a threshold effect or not (64).

According to EPA & IARC, it is probable human carcinogen and there is sufficient evidence that beryllium compound causes lung cancer (65-69). Many research studies found a significantly increased risk of lung cancer associated with hexavalent chromium (OR 1.94; 95% CI: 1.10–3.43; P=0.015) (70). Cumulative hexavalent chromium exposure was associated with an increased lung cancer risk (71). Environment protection agency has not evaluated nickel as a class of compounds for potential human carcinogenicity (72). Occupational exposure to nickel compounds could be attributed to lung cancer (73-75).

**Vinyl chloride**

In poly vinyl chloride packers and baggers, the risk for lung cancer increased significantly with exposure to poly vinyl chloride dust (OR 1.2003; 95% CI: 1.0772–1.3469; P=0.0010) (76), and vinyl chloride (OR 1.05; 95% CI: 0.68–1.62) (77). However, the exposure levels for the majority of the population are very low (78-80).

**Ionizing radiation**

Natural radiation comes from many sources including many naturally-occurring radioactive materials found in soil, water and air, like Radon, a naturally-occurring gas which comes from rock and soil, and is the main source of natural radiation. Ionizing radiation includes radon, X-rays and gamma rays, but radon represents a far smaller risk for lung cancer (81,82). Results of many research studies provided direct evidence of an association between residential radon and lung cancer risk, a finding predicted by extrapolation of results from occupational studies on radon-exposed underground miners. The excess OR (EOR) was 0.10 per Bq/m$^3$ with 95% confidence limits –0.01 to 0.26 (83) & RR was 0.08 (95% CI: 0.03–0.16; P=0.0007) (84).

Contamination by uranium is often cited as a risk factor in ionizing radiation epidemiology, but the dose-effect relationship is rarely studied and retrospective assessment of individual exposure is generally insufficient. Moreover, it is difficult to distinguish between uranium radiotoxicity, its
chemical toxicity and the radiotoxicity of its progeny (85).

**Occupational determinants of lung cancer**

**Bartenders**

In Canadian Labour Force Ten percent sample study, a total of 9,739 deaths from cancer between 1965 and 1979 were identified. Based on the criteria of strength of association, bartenders with lung cancer seem most likely to be caused by excess smoking and/or alcohol consumption (86). Secondhand smoke (SHS) exposure has been consistently identified as a public health hazard and cause of lung cancer. The U.S. EPA classified SHS as a group A carcinogen (87) and the IARC also classified SHS as carcinogenic to humans. Siegel et al. (88) demonstrated that the nicotine concentrations in the 5 B’s (bars, bowling alleys, billiard halls, betting establishments, and bingo parlours) were 2.4 to 18.5 times higher than in offices or residences, and found to be 1.5 to 11.7 times higher than in restaurants.

**Ceramic industry**

In a study of 30-year mortality and respiratory morbidity of refractory ceramic fiber workers, authors showed no increase in SMR for lung cancer (89). Similarly, Meijers and co-authors suggested that the disease process resulting in silicosis in the ceramic industry carries an increased risk of lung cancer, which is supportive of a nongenotoxic pathway. The authors found no increase in overall and cause-specific mortality in the total group of ceramic workers, and a statistically significant cumulative dose-response relation for silica exposure and lung cancer also did not emerge (90). Overall, inference can be made that lung cancer might be merely indirectly related with exposure to silica, although the dose may differ for silicotic and nonsilicotic individuals (91).

**Coal gasification and coke production**

A significant risk of lung cancer was observed among the coal/coke and related product industry with RR of 1.55 (95% CI: 1.01–2.37) (92). Excess of lung cancer in association with coal gasification was found (93,94). In addition to PAHs, workers in coal gasification may be exposed to many compounds, including asbestos, silica, arsenic, cadmium, lead, nickel, hydrocarbons, sulfur dioxide, sulfuric acid, aldehydes, etc. In UK, Helmet respirator, the Airstream helmet, was introduced with the aim of reducing exposure to PAH aerosols and consequent lung cancer risks for workers on the coke oven tops.

**Construction industry**

Approximately 70 different substances are listed in NIOSH to which U.S. construction workers are potentially exposed (95).

Many epidemiological studies conducted in different countries, found significantly raised mortality rate for lung cancer among construction workers (96-105) although some failed to find the association (106-109). Elevated mortality for lung cancer has also been reported for several specific construction trades such as bricklayers (97,100,103,105,109-115); craft workers (110,112); electricians (100,113); carpenters (97,99,100,103,111,115-117); painters (100,105,111,117); operating engineers (118); roofers, waterproofers, allied workers (97,103,117); and insulation workers (97,100,104,109,118).

In one of the studies, it was observed that construction workers were more at risk of developing lung cancer when they were exposed for longer duration. This risk has not been seen in supervisors, engineers and higher officials working in construction as their exposure was not as high as others working at construction sites.

**Glass factory**

Carcinogenic effects of exposure to man-made mineral fibers (glass filaments, ceramic fibers, and slag wool) have been demonstrated. In humans, slag wool and glass production workers have been shown to have elevated lung cancer risks (119,120). Population-based case-control studies in Sweden (121) and Canada (122) also found increased risks for lung cancer in glass-workers.

**Mason**

Bricklayers may be exposed to several lung carcinogens, including asbestos and crystalline silica. That is why bricklayers and allied craft workers are at risk from diseases associated with heavy exposure to inorganic dust, mainly lung cancer. SMRs and proportionate mortality ratios (PMRs) for lung cancer (SMR =158; 130–190 and PMR =144) were significantly elevated in these workers (110,112). In an Italian case-controlled study, authors found increased lung cancer risk for bricklayers (OR 1.57; 95% CI: 1.12–2.21; 147 cases, 81 controls). There were increased risk for squamous cell (OR
2.03; 95% CI: 1.32–3.13, 56 exposed cases) and small cell carcinomas (OR 2.29; 95% CI: 1.29–4.07, 21 exposed cases), while not for adenocarcinoma (OR 1.06; 95% CI: 0.68–1.65, 41 exposed cases).

**Painter**

A large number of workers are engaged in paint-related occupations and there is increasing concern regarding health effects from paint-related exposures. Several hazardous chemicals (including benzene, phthalates, chromium, and lead oxides) have been reduced or replaced in paint in some countries, although they are still used elsewhere. There have been indications that painters are at an excess risk for cancer, and in particular lung cancer (124,125). Raman Kumar et al, showed painters had an OR of lung cancer of 1.3 (95% CI: 0.9–2.2). Regarding exposures, ORs were: for wood varnishes and stains, 1.6 (95% CI: 1.0–2.3); for wood and gypsum paints, 1.3 (95% CI: 0.9–1.7); and for metal coatings, 1.1 (95% CI: 0.8–1.6) thereby suggesting that some exposures in paint-related occupations, particularly wood varnishes and stains, increase the risk of lung cancer (126).

**Rubber industry**

According to IARC, occupational exposures in the rubber manufacturing industry have been considered carcinogenic to humans (127,128). Two compounds which are largely involved in production of tyres and rubber goods are 1,3-butadiene and benzene, and both of them are established as carcinogens to humans (129,130). Several types of chemical compounds are used in production of tyres and rubber goods which can be carcinogenic to humans. In a recent meta-analysis performed on observational studies (published until April 2016) on occupational exposures in the rubber manufacturing industry and cancer risk, showed a borderline statistically significant increased risk (SRR =1.08; 95% CI: 0.99–1.17) (131).

**Sandblasting**

Crystalline silica exposure occurs in the workers employed in foundries, stonework, sandblasting, and potteries. Besides its well-known relation to silicosis, silica exposure in recent years has been associated with lung cancer. The IARC determined that inhaled crystalline silica from occupational sources is a definite (group 1) human carcinogen (132). Steenland et al. found a 60 percent excess of lung cancer overall, in the silica exposed cohort when compared with the U.S. population (SMR =1.60, 95% CI: 1.31–1.93). The cohort experienced high mortality for all causes combined (SMR =1.23, 95% CI: 1.16–1.31), in part due to elevations in causes related to silica exposure (133). A case report by Güngen et al. demonstrated a case of lung adenocarcinoma in 35-year-old female with history of working in denim sandblasting for 18 months (134). On molecular level, critical role of the inflammatory mediator LTβR and its receptor BLT1 has been demonstrated in promoting the silica mediated lung tumor growth (135).

**Truck drivers**

Trucking industry workers who have been regularly exposed to diesel exhaust (DE) have an elevated risk of lung cancer with each increasing year of work. As per IARC, DE is considered as a probable human carcinogen. The epidemiologic evidence is based on various studies of lung cancer among truck drivers, bus drivers, shipyard workers, and railroad workers. Steenland et al. found a lifetime excess risk 10 times higher than the 1 per 1,000 excess risk allowed by Occupational Safety and Health Administration (OSHA) in setting regulations (136). Similar findings were also reported by Garshick et al., where they studied 31,135 male workers employed in the unionized U.S. trucking industry and found elevated risk of lung cancer in trucking industry workers (137). Several published critical reviews and epidemiologic meta-analyses (138-140) have reached to the conclusions supportive of DE exposure increasing lung cancer risk.

**Traffic police**

Traffic police often spend at least several hours per day driving or directing traffic in congested areas. These activities may result in exposure to carcinogenic airborne pollutants derived from motor vehicle exhaust, such as benzene, PAHs, and persistent organic pollutants, for example dioxin (141,142). Personal benzene exposures among police officers were three to five times higher than those observed among controls (143). PM is a major air pollution constituent that can induce inflammation, free radical formation, oxidative DNA damage, cytotoxicity, and mutagenesis within the respiratory tract (144). Although the frequency or extent of exposure to these agents amongst most law enforcement officers is not anticipated to be extensive, particularly with appropriate training and safety...
precautions. Potential exposure to these agents represents a growing concern within this occupation (145). Many studies have reached to conclusion supportive of exposure to traffic police, with an increased lung cancer risk.

**Uranium mining**

It is well established that high radon exposures increase the risk of lung cancer mortality in uranium miners. In a recently concluded joint cohort analysis of Czech, French, and Canadian uranium miners (employed in 1953 or later), they found that there is strong evidence for an increased risk of lung cancer mortality from low occupational radon exposures (146). Ramkissoon et al. described the risks of lung cancer by histological subtypes associated with exposure to radon decay products among the Ontario Uranium Miners cohort by using a retrospective cohort design. Authors found differences in the magnitude of the risks across four histological subtypes of lung carcinoma; the strongest association was noted for small cell lung carcinoma, followed by squamous cell, large cell, and lastly adenocarcinoma, which showed no significant association with exposure to radon decay products (147).

**Existing policies and interventions**

Although lung cancer is a global public health problem but many governments have not yet included lung cancer prevention in their health guidelines. Existing policies and guidelines related to environmental risk factors of lung cancer by different organizations and countries are summarized in Table 2.

**Asbestos (48)**

Consumer Product Safety Commission (CPSC) has banned consumer patching compounds, free form of asbestos that could be respirable. Special guidelines have been set for marketing and transportation of this material by Department of Transportation (DOT). Maximum contamination level as per Safe Drinking Water Act has been fixed to 7 million fibers per liter for fibers longer than 10 μm. Toxic Substances Control Act Rules have been established for identifying, analyzing, and disposing of asbestos if asbestos is found in schools and public area.

**Ionizing radiation (148)**

Public Health Service Act (PHSA) and the Atomic Energy Act (AEA) directs authorities to measure environmental radiation levels, develop protective action guides, and provide assistance to the states for the safe storage and/or disposal of radioactive wastes.

**Vinyl chloride (149)**

CPSC has banned self-pressurized products intended for household use that contains vinyl chloride. DOT finds vinyl chloride as a hazardous material, and special requirements have been set for marking, labeling, and transporting this material. As per Clean Water Act Effluent Guidelines, it is listed as a toxic pollutant. Aerosol drug products have been withdrawn from the market and may not be compounded, because contained vinyl chloride was found to be unsafe or not effective. It is also banned from use in cosmetic aerosol products.

**Indoor pollution**

EPA has regulated household particulate emissions by giving wood heater model lines referred to as EPA-certified wood heaters (150). According to this model some guidelines should be followed to reduce household pollutions generated from coal combustion (as well as sulfur dioxide and oxides of nitrogen) levels (151).

**Second-hand tobacco smoke**

As per National Institute for Occupational Safety and Health (NIOSH), environmental tobacco smoke is considered a potential occupational carcinogen and exposure should be reduced to the lowest feasible concentration (152). In India, the Cigarettes and Other Tobacco Products Act 2003 prohibits smoking of tobacco in public places, except in special smoking zones in hotels, restaurants, airports and open spaces (153).

**Chemical exposure**

Pesticides maximum residue limits (MRLs) in food is guided by WHO guidelines on this issue. The Joint Food and Agriculture Organization of the United Nations
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<td>USA</td>
<td>National Institute of Environmental Health and Safety</td>
<td>Consumer Product Safety Commission (CPSC): banned respirable asbestos&lt;br&gt;Department of Transportation (DOT): gave guideline for transportation&lt;br&gt;Safe Drinking Water Act: MCL 7 million/L&lt;br&gt;Toxic Substances Control Act: identify asbestos in public area for public places&lt;br&gt;Mine Safety and Health Administration: permissible exposure limit (PEL) for miners are full-shift limit =0.1 fiber/cm$^3$ (8-h time-weighted average); excursion limit =1 fiber/cm$^3$ (30-min sample)&lt;br&gt;OSHA: ceiling concentration =1 fiber/cm$^3$ (excursion limit) as averaged over a sampling period of 30 min. Permissible exposure limit (PEL) =0.1 fiber/cm$^3$ for fibers longer than 5 μm having a length-to-diameter ratio of at least 3 to 1</td>
</tr>
<tr>
<td>Ionizing radiation</td>
<td>USA</td>
<td>–</td>
<td>Public Health Service Act (PHSA): measure environmental radiation level&lt;br&gt;Atomic Energy Act (AEA): Safe storage/disposal of radioactive waste</td>
</tr>
<tr>
<td>Vinyl chloride</td>
<td>USA</td>
<td>National Institute of Environmental Health and Safety</td>
<td>Consumer Product Safety Commission (CPSC): self-pressurized product that contain vinyl chloride are banned&lt;br&gt;Department of Transportation (DOT): gave vinyl chloride transportation&lt;br&gt;Food and Drug Administration (FDA): 0.22 μg/L&lt;br&gt;Clean Water Act: MCL 0.002 mg/L</td>
</tr>
<tr>
<td>Outdoor air pollution</td>
<td>India</td>
<td>Union cabinet, government of India</td>
<td>Special purpose: vehicle, Fasal Avshesh Upyog Nigam (FAUN), to serve as a standalone institutional mechanism to deal with crop residue&lt;br&gt;Municipal Corporation of Delhi (MCD) and Government of NCT of Delhi: implement a policy for tagging vehicles, through the creation of different colour tags representing different levels of emission standards in vehicles; set up a green police force for metropolitan cities</td>
</tr>
<tr>
<td>Household combustion of coal</td>
<td>USA</td>
<td>EPA</td>
<td>Wood heater model</td>
</tr>
<tr>
<td>Second hand smoke</td>
<td>USA</td>
<td>NIOSH</td>
<td>Exposure reduced to feasible level&lt;br&gt;COTPA; 2003: banned smoking at public places</td>
</tr>
<tr>
<td>Chemical exposure</td>
<td>India</td>
<td>Food Agriculture organization (FAO)</td>
<td>Minimum pesticide level on food products</td>
</tr>
<tr>
<td>Arsenic</td>
<td>USA</td>
<td>National Institute of Environmental Health and Safety</td>
<td>National Emission Standard Act: TQ 15,000 lb&lt;br&gt;National Institute for Occupational Safety and Health (NIOSH): immediately dangerous to life or health (IDLH) limit =5 life mg/m$^3$ for inorganic compounds (as As). Ceiling recommended exposure limit =0.002 mg/m$^3$ (15 min) for inorganic compounds (as As)</td>
</tr>
</tbody>
</table>
Table 2 (continued)

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Country/continent</th>
<th>Organization</th>
<th>Law/policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beryllium</td>
<td>USA</td>
<td>National Institute of Environmental Health and Safety</td>
<td>Food and Drug Administration (FDA): max limit 0.004 mg/L OSHA: acceptable peak exposure =0.025 mg/m³ (30-min maximum duration per 8-h shift); ceiling concentration =0.005 mg/m³; permissible exposure limit (PEL) =0.002 mg/m³ NOISH: IDLH limit =4 mg/m³; ceiling recommended exposure limit =0.0005 mg/m³</td>
</tr>
<tr>
<td>Chromium</td>
<td>USA</td>
<td>National Institute of Environmental Health and Safety</td>
<td>Food and Drug Administration (FDA): 0.1 mg/L in drinking water OSHA: workers’ exposure on an average of 0.005 mg/m³ chromium (VI), 0.5 mg/m³ chromium (III), and 1.0 mg/m³ chromium (0) for an 8 working hour workday</td>
</tr>
<tr>
<td>Nickel</td>
<td>USA</td>
<td>EPA</td>
<td>National Emission Hazard Act: TQ 1,000 lb OSHA: PEL =1 mg/m³ for elemental nickel and compounds other than nickel carbonyl; =0.001 ppm (0.007 mg/m³) for nickel carbonyl</td>
</tr>
<tr>
<td>Construction industry</td>
<td>India</td>
<td>DGFASLI, Ministry of Labor &amp; Employment</td>
<td>Building and Other Construction Workers Act 1996: Rule 39; Health and Safety Policy Rules 210, 211, 230 gives the procedure for reporting investigation of Accidents (including Occupational Diseases) and Dangerous occurrences</td>
</tr>
<tr>
<td></td>
<td>UK</td>
<td>Health &amp; Safety Executives (HSE)</td>
<td>Provide essential health and safety toolkit for the construction workers</td>
</tr>
<tr>
<td>Glass industry</td>
<td>Czech Republic</td>
<td>Ministry of Labour &amp; Trade</td>
<td>Marking of individual sorts of crystal glass</td>
</tr>
<tr>
<td></td>
<td>USA</td>
<td>OSHA</td>
<td>Guide threshold limit value</td>
</tr>
<tr>
<td>Rubber industry</td>
<td>USA</td>
<td>EPA</td>
<td>Plastics and rubber products manufacturing</td>
</tr>
<tr>
<td>Coal mining</td>
<td>Australia</td>
<td>New South Wales</td>
<td>Coal Industry Act 2001</td>
</tr>
<tr>
<td>Ceramic industry</td>
<td>Europe</td>
<td>European commission</td>
<td>Directives on emissions trading Directives on industrial emissions and on ceramic articles intended to come into contact with foodstuffs on packaging and packaging waste (84/500/EEC)</td>
</tr>
</tbody>
</table>

MCL, maximum contaminant level; OSHA, Occupational Safety and Health Administration; EPA, Environmental Protection Agency; NIOSH, National Institute for Occupational Safety and Health; COTPA, Cigarettes and Other Tobacco Products Act; TQ, threshold quantity; PEL, permissible exposure limit; DGFASLI, Directorate General of Factory Advice Service & Labor Institutes; IDLH, Immediately Dangerous to Life or Health.
(FAO)/WHO Meeting on Pesticide Residues (JMPR) evaluates those pesticides where contamination of food is likely (154). In India, the Food Safety and Standards Authority of India (FSSAI) was established under the Food Safety and Standards Act (155) to ensure safety of food materials from chemical contamination. These recommendations are important, considering the local needs of the states and research about specific crops, their diseases and insects.

**Metals**

**Arsenic (156)**

Arsenic compounds are identified as one of the 33 hazardous air pollutants that present the greatest threat to public health in urban areas as a part of Urban Air Toxics Strategy. Inorganic arsenic compounds are listed in the category of potential occupational carcinogens. A comprehensive set of guidelines has been established to prevent exposure to hazardous drugs in health-care settings by OSHA.

**Beryllium (157)**

Department of Energy (DOE) has established the Chronic Beryllium Disease Prevention Program to protect workers from excessive beryllium exposure and beryllium disease. Beryllium compounds are listed as hazardous air pollutants in EPA and Clean Air Act National Emission Standards for Hazardous Air Pollutants.

**Chromium (158)**

The U.S. EPA have established a maximum contaminant level of 0.1 mg/L for total chromium in drinking water. The FDA examines that the chromium concentration in bottled drinking water should not exceed 0.1 mg/L.

**Nickel (159)**

As per U.S. EPA, nickel compounds are listed as mobile-source air toxics for which regulations has to be developed. According to National Emission Standards for Hazardous Air Pollutants, nickel and its compounds come under the list of hazardous air pollutants. Nickel compounds are identified as one of the 33 hazardous air pollutants that present the greatest threat to public health in urban areas as per Urban Air Toxics Strategy.

**Intervention for primary prevention**

Primary prevention encompasses the elimination or reduction of recognized risk factors in susceptible populations and gives specific protection to prevent a disease. It is evident from various research studies that tobacco smoking is related to high incidence of lung cancer. Behaviour modification can help us to attain a fall in tobacco smoking, thereby reducing cases of lung cancer. There is a need to look into nontobacco risk factors, as lung cancer in nonsmokers is becoming a serious concern. This may be attributed to environmental and occupational risk factors. There is an increase in number of young lung cancer patients who are presenting to the hospital where target mutations are high in number in comparison to smokers. Effective primary preventive methods need to be explored as it is an important & cost-effective tool. Primary prevention for lung cancer involves identifying those risk factors associated with the development of lung cancer, as demonstrated by various epidemiological studies. Tobacco still plays the most important role but non-tobacco determinants must also be considered in the present scenario.

**Communication**

There is need for appropriate communication strategies to propagate the scientific and political messages to the society. The message that lung cancer has environmental and occupational causes is clear among the scientific community but not known to general population. Media has always played a key role in disseminating messages to a large population, to increase public perception about the disease, to educate people in general and to target groups for behavior modifications and to generate awareness about environmental and occupational determinants of lung cancer.

Supporting cancer campaigns and creating conditions to facilitate behavioral modification is essential, but it should be done with collective efforts.

Communication is the best means to raise awareness on the part of and to influence a large number of people. In addition, effective communication with national decision-makers requires new ideas and innovations to ensure wellbeing. Benefits should be measured not only in terms of productivity, but as health, social and environmental benefits.

**Multi-sectoral approach**

There is a need for establishing a multi-sectoral approach and partnerships to undertake primary prevention to deal with environmental and occupational determinants of lung
cancer. Population or community-based interventions on the part of health and non-health sectors, such as environment, occupational, housing, industry and trade, and by community organizations, private enterprises are needed. Other key stakeholders should be involved to reduce environmental and occupational exposures to ensure lung cancer prevention. The role of trade unions is also important to report the health issues of the employees to accomplish a transition to clean and safe industry. Additionally, media should be involved in the dissemination of information in a collaborative manner. Scientific research is supported by citizens through taxes and therefore there should be proper communication of purpose and results of research. The current difficulties in coordination of all stakeholders involved in implementation, such as different Ministries: Health, Environment, Labour, Agriculture, Industry, Finance, etc., underlines the importance of a multisectoral approach to primary prevention of lung cancer.

**Research**

Research in the area of lung cancer prevention is important to recognize the areas where action is required to prevent environment and occupation related lung cancer. There is a need of strengthening of cross-sectional research on environment- and occupation-related risk factors attributing to lung cancer in nonsmokers. Population at risk should be identified, and link with timing of exposures to be established. Research on bio-genetic level to see genetic and epigenetic interactions with environmental risk factors to support the development of evidence-based preventive strategies; analyzing the molecular and cellular mechanisms, involved in the origin, development and progression of, environmentally-related lung cancer; encouraging analytical research—it includes risk assessment of environmental and occupational exposures; ensuring the rapid transfer of research outcomes to control measures for the benefit of all populations.

**Challenges & opportunities**

We can prevent lung cancer by effectual, attainable and affordable environmental and occupational interventions. There are many evidences based on research and knowledge about a particular risk factor that is related to environment & occupation for lung cancer, but action is not taken yet in many of the developing countries. Asbestos is still being used and very commonly in many developing countries including China and India. Some countries have guidelines to use tanning beds (160–163). In many countries there is no guideline on occupational hazards by their respective occupational health institutions, and no prevention policy of occupational lung cancer by the government. It has not been given high priority (164). Research to measure the magnitude of air pollution and its seasonal variations on lung cancer is needed (165). Exposure to environmental pollution varies across countries and cities, but availability of data is limited (166). There is need for strong mechanisms and methods to reduce exposure to substances that are used under unaware conditions, especially at developing world. There are studies that tell the environmental risk factors for lung cancer and its genetic susceptibility (167,168) but more research is needed. There is an increased risk of lung cancer due to environmental pollution (169-171). Policies to reduce the pollution level should be in priority. There should be monitoring and evaluation of carcinogenic risk factor data and it should be available for chemical and commercial industries, and testing should be performed before products are introduced in the market. More research is needed on incidence of lung cancer in non-smoker who are exposed to environmental pollution (172).

**Conclusions**

Trying different ways to prevent lung cancer is an effective way to reduce deaths and it would be highly cost-effective in terms of reduction of health-care costs. Primary prevention efforts need to be intensified to eliminate or minimize physical, chemical and biological exposures to known carcinogens and for the implementation of environmental interventions, including in work settings, to reduce the incidence of lung cancer, and the clinical, personal, economic and social burdens related to it.

Sincere efforts are required to address many carcinogens found in the environment, over which the individual has little control, and which require broad, public health driven action by public authorities at the national, regional and even international levels, engaging all stakeholders in a multi-sectoral, collaborative approach. These interventions have become important in view of increasing incidence of lung cancer in nonsmokers. There is a need for identification of the gaps and barriers, which will help to define a road map to better address the environmental and occupational determinants of lung cancer, and to develop a range of proposals for primary prevention to introduce environmental and occupational exposures into the global cancer agenda.
Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

25. An estimated 12.6 million deaths each year are attributable to unhealthy environments [Online]. WHO 2019. Available online: https://www.who.int/news-room/detail/15-03-2016-an-estimated-12-6-million-deaths-each-year-are-attributable-to-unhealthy-environments


165. Parascandola M. Ambient air pollution and lung cancer in Poland: research findings and gaps. J Health Inequal 2018;4:3-8.