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## Occupation and cancer in Brazil: a perennial challenge

### *Ocupação e câncer no Brasil: um desafio perene*

#### Abstract

**Introduction:** cancer incidence is increasing worldwide, especially in low- and middle-income countries. **Objective:** to identify and synthesize knowledge about occupational exposure and cancer, with emphasis on Brazilian scientific publications. **Method:** essay based on reviews carried out in the SciELO and PubMed databases. **Results:** a recent study identified 47 occupational agents among the 120 classified as definitively carcinogenic to humans by the International Agency for Research on Cancer. Studies carried out in the last two decades suggested fractions of cancer attributable to occupation, ranging from 1.3% in Brazil to 8% in Finland, although the criteria for measuring exposure in these studies can be questioned. In Brazil, scientific production on occupation and cancer is limited. The Revista Brasileira de Saúde Ocupacional (RBSO) published, between January 2003 to July 2022, six articles on the subject. In the PubMed database, from 2012 to 2022, 14 studies carried out in Brazil were identified. **Conclusion:** expanding research in this subject in Brazil is imperative to obtain more accurate estimates of workers exposed to carcinogens and related malignant tumors, essential to support public health actions and to establish norms on exposure limits or agents banning, reducing the burden of cancer in the Brazilian society.

**Keywords:** cancer; work; occupational exposure; occupational health; Brazil.

#### Resumo

**Introdução:** a incidência do câncer tem aumentado continuamente no mundo, especialmente em países de baixa e média renda. **Objetivo:** identificar e sintetizar o conhecimento sobre exposição ocupacional e câncer, com ênfase na produção científica brasileira. **Métodos:** ensaio elaborado com base em revisões realizadas nas bases SciELO e PubMed. **Resultados:** um estudo recente identificou 47 agentes ocupacionais entre os 120 agentes classificados como definitivamente cancerígenos para humanos pela Agência Internacional de Pesquisa em Câncer. Estudos realizados nas duas últimas décadas indicaram frações de câncer atribuíveis à ocupação, variando de 1,3% no Brasil a 8% na Finlândia, embora os critérios para aferir a exposição nesses estudos possam ser questionados. No Brasil, a produção científica sobre ocupação e câncer é limitada. A Revista Brasileira de Saúde Ocupacional publicou, entre janeiro de 2003 e julho de 2022, seis artigos sobre o tema. Na base PubMed, de 2012 a 2022, foram identificados 14 estudos realizados no Brasil. **Conclusão:** ampliar pesquisas nesta área realizadas no país é imperativo para obtenção de estimativas mais precisas de trabalhadores expostos a cancerígenos e tumores malignos relacionados, essencial para subsidiar ações de saúde pública e normas sobre limites de exposição ou banimento de agentes, reduzindo o fardo do câncer na sociedade brasileira.

**Palavras-chave:** câncer; trabalho; exposição ocupacional; saúde do trabalhador; Brasil.



## Introduction

Cancer is a global disease, whose incidence, mortality, and survival vary across regions, countries or even between different geographical areas in a given country. Despite this variation, its incidence is increasing worldwide, especially in low-and-middle-income countries<sup>1</sup>. In South America, until 2040, projections indicate an increase above 65% in this rate in relation to 2020<sup>2</sup>. In Brazil, estimates for 2040 project increases of more than 60% in new cases and in more than 70% in deaths<sup>3</sup>.

The term cancer includes hundreds of diseases, which have numerous risk factors that require relevant preventive actions. Its multifactorial characteristic complicates the task of investigating the role of specific causal factors as multiple agents are simultaneously involved in interacting in the carcinogenesis process. Therefore, linking exposure to carcinogens in the workplace to the occurrence of cancer in workers requires perspectives from a wide range of disciplines in a gradual and cumulative process of knowledge. This is what we learned when reviewing the classic examples of the association between soot and scrotal skin cancer and that between asbestos and mesothelioma or malignant lung neoplasms<sup>4</sup>.

In 1975, Doll carried out a relevant review of occupational risk factors for cancer, dividing results into two periods: before and after 1915. In the first period, much of the knowledge derived from clinicians and pathologists' case reports and from epidemiological observations. In the second period, advances in laboratory experiments influenced the detection of occupational carcinogens<sup>5</sup>. Still in the 1970s, the International Agency for Research on Cancer of the World Health Organization (IARC/WHO) started its Monographs program, which systematically evaluated the carcinogenic potential of agents, complex mixtures, and occupations. The first volume of the Monographs was published in 1971<sup>6</sup>. Currently, we find a vast amount of information about risks factors in different work environments and occupations that expose workers to excessive risks of cancer.

This study neither includes in-depth analyses of particular situations nor attempts to list occupational carcinogens and relate them to different types of cancer, as other authors have already competently done so<sup>7,8</sup>. We aimed to review and summarize in general terms the knowledge about the impact of exposure to occupational carcinogens, particularly in the Brazilian scientific production.

## Occupational carcinogens: characterization and magnitude

Exposures to carcinogens frequently occur in work environments. However, several such agents are also in the overall environment. The IARC Monographs program has evaluated the carcinogenic potential of chemical and physical agents considering epidemiological research results, animal models experiments, and studies with structure-activity analyses. From 1971 to 2022, it examined more than 1000 agents<sup>9</sup>, classifying them into one of the following categories: carcinogenic to humans (Group 1), probably carcinogenic to humans (Group 2A), possibly carcinogenic to humans (Group 2B), and not classifiable as to its carcinogenicity to humans (Group 3). However, the IARC provides no indications on the relevance of occupational exposure to agents<sup>10</sup>.

In 2004, Siemiatycki et al.<sup>7</sup> carried out an investigation to recognize which agent the IARC had evaluated up to 2003 (about 880) were mainly present in occupational settings. To assess occupational exposure, the authors used a substantial number of workers exposed at relevant levels to an agent. Their results showed 28 occupational agents in Group 1, 27 in Group 2, 113 in Group 3, and 18 occupations or industries that involved excessive cancer risks.

Loomis et al.<sup>8</sup> updated the data but examined only IARC Group 1 agents. Of the 120 agents classified in Group 1 up to 2017, the authors recognized as occupational carcinogens those with sufficient evidence of carcinogenicity obtained in whole or in part by epidemiological studies in exposed workers and found that the occurrence of exposure in workers had been documented in the monograph of an agent. Based on these criteria, they classified 47 agents as occupational. A much more expressive number than that recorded by Siemiatycki et al.<sup>7</sup> in Group 1.

Many countries produce their own lists of occupational carcinogens. The United States of America (USA) has two main lists: the NIOSH (National Institute for Occupational Safety and Health) list, which lists 131 potential occupational carcinogens and undergoes continuous revision<sup>11</sup>; and the NTP (National Toxicology Program), which, in its 15th report on occupational carcinogens published in December 2021, lists 256 substances known or able to cause cancer in humans<sup>12</sup>. However, the criteria and methods used to classify occupational carcinogens into these two lists remains unclear.

In Brazil, following Ordinance MS/GM 1339 from 1999<sup>13</sup>, the Ministry of Health released a list of work-related diseases with their respective risk factors. It listed malignant neoplasms and related them to etiological agents or occupational risk factors. The Ordinance proposal proposed an annual list review but that is yet to take place. In 2012, the National Cancer Institute (Instituto Nacional do Câncer - INCA) published its “Guidelines for work-related cancer surveillance,” which also followed the logic of relating malignant neoplasms with occupational risk factors<sup>14</sup>. To classify agents, the Guidelines followed IARC criteria. The most recent INCA publication “Environment, work and cancer: epidemiological, toxicological and regulatory aspects”<sup>15</sup>, also based on IARC criteria, points out the link between certain agents, going beyond only occupational carcinogens and malignant neoplasms.

## Cancer attributable to occupational exposures

The demarcation of surveillance priorities requires the establishment of the attributable fraction of cancer as a result of occupational exposures. The reference study for it was published in 1981 – ‘The causes of cancer’<sup>16</sup>. The proportion of overall cancer deaths due to occupation in the US population totaled 4%, varying for anatomic locations. For example, 12.5% of lung cancer deaths were attributed to occupations.

New studies were conducted in this century to reexamine the fraction of cancer mortality attributable to occupations in different populations, with divergent results (**Table 1**). They show important methodological differences regarding exposure data, consensus criteria for carcinogenic agents, and incidence and mortality by types of neoplasia. The Brazilian study<sup>17</sup> was the most restrictive research as it considered only a selection of agents and occupations classified in IARC Group 1 (definitely carcinogenic). The other studies also included agents classified in Group 2A (probably carcinogenic to humans). Naturally, different approaches reflected the varying results<sup>17</sup>. The attributable fractions estimated in studies from the USA and the United Kingdom<sup>18,19</sup> resemble each other those obtained by Doll and Peto<sup>16</sup>. The Finnish study observed an attributable fraction of 8%, the highest among estimates<sup>21</sup>. On the other hand, the Brazilian study showed the smallest fraction — 1.3% (2.1% in men and 0.3% in women)<sup>17</sup>. All surveys showed higher proportions in men. Studies from Finland, the USA, and the United Kingdom highlighted the prominence of lung cancer and exposure to asbestos.

The Institute of Health Metrics and Evaluation has published a series of analyses on disease occurrences in the world under the generic title of Global Burden of Diseases (GBD). This sequence of analyses estimated the burden of cancer due to occupational exposures in different world regions<sup>22</sup>. Based on IARC reviews of agents up to 2014, the authors selected 14 major occupational carcinogens linked to eight malignant tumours. Exposure were based on CAREX (Carcinogen Exposure), a database created in the 1990s in Western Europe to estimate, by carcinogen, the number of exposed workers and the type of activity they performed by country<sup>23</sup>. The GBD authors<sup>22</sup> admitted that the prevalence of exposures among workers failed to change over time, extrapolating their data to all regions of the world and adjusting them for high-, medium-, and low-income countries. Tropical Latin America (a classification that includes Brazil) showed eight deaths from cancer per 100,000 inhabitants attributable to occupations. Half of this burden, i.e., four deaths per 100,000 inhabitants, would stem from exposure to asbestos. The limitations of this analysis are evident. The authors considered the CAREX estimates of the number of workers exposed to carcinogens in the 1990s in Western Europe to be stable and applicable to the rest of the world, examining a limited number of occupational carcinogens and malignant neoplasms.

**Table 1** 21st-century estimates of the fraction of cancer attributable to occupations. Finland, USA, United Kingdom, Brazil.

Studies	Nurminen and Karjalainen, 2001 <sup>21</sup> (Finland)	Steenland et al., 2003 <sup>19</sup> (USA)	Rushton et al., 2010 <sup>20</sup> (United Kingdom)	Azevedo and Silva et al., 2016 <sup>17</sup> (Brazil)
Exposure	1960-1984	1980-1983	1956-1995/1986-2005	2000 Census PNAD 2003
Incidence	No	No	Yes	Yes
Mortality	Yes	Yes	Yes	Yes
Carcinogens	IARC Groups 1 (22 agents) and 2A (22 agents)	IARC Group 1 and 2A	IARC Group 1 and 2A	IARC Group 1
Evaluated cancer types	26 tumors related to occupational exposure	Nine tumors related to occupational exposures	All types of cancer	All types of cancer
Fraction of cancer attributable to occupations	8% (Men: 14%; Women 2%)	From 2.4 to 4.8% (Men: 3.3-7.3%; Women: 0.8-1.0%)	5.3% (Men: 8.2%; Women: 2.3%)	1.3% (Men: 2.3%; Women: 0.3%)
Notes:	<ul style="list-style-type: none"> <li>Nearly half of work-related deaths were due to malignant tumors</li> <li>54% of occupation-related deaths were due to lung cancer.</li> <li>Of all lung cancer deaths, 24% were attributed to exposure to occupational carcinogens; half of which to asbestos</li> </ul>	<ul style="list-style-type: none"> <li>Lung cancer contributed to about 75% of all work-related cancer deaths</li> <li>Half of occupation-related lung tumor deaths were attributed to asbestos exposure</li> </ul>	<ul style="list-style-type: none"> <li>More than 8% of cancer deaths in men were due to occupational exposures and above 20% for lung cancer</li> <li>Nearly 70% of occupation-related deaths were due to lung cancer. More than half were due to exposure to asbestos, half of which was due to construction work</li> </ul>	<ul style="list-style-type: none"> <li>Unlike the other studies in the table, this one was not designed specifically for occupational exposure. The fraction attributable to multiple cancer risk factors was examined, which included occupation. Same approach as the classic study by Doll and Peto<sup>15</sup>.</li> </ul>

Legend: PNAD: National Household Sample Survey (Pesquisa Nacional por Amostra de Domicílios); IARC: International Agency for Research on Cancer.

## Research on occupational exposure and cancer in Brazil

Brazil has scarce information on occupation and cancer. An investigation into theses and dissertations in occupational health carried out in graduate programs in Brazil and abroad from 1970 to 2004 showed that, of 1,018

theses and dissertations, no more than six (0.6 %) targeted cancer—the lowest proportion among all occupational health topics listed in the study<sup>24</sup>. This scenario has changed little in the last two decades.

From January 2003 to July 2022, SciELO only had six articles on occupational exposure and cancer in *Revista Brasileira de Saúde Ocupacional* (RBSO) pages. All were published from 2012 onward. Considering the RBSO position as a national reference for research dissemination in occupational health, the lack of research interest in this topic is unsettling. In 2012, RBSO published an editorial on the Guidelines on Surveillance of Work-Related Cancer, issued by INCA<sup>25</sup>. In 2013, an essay published on Occupational Health Surveillance<sup>26</sup>, pointed out the need for surveillance and the organization of an information system on exposure to carcinogenic agents. In 2017, the RBSO volume 42 supplement was dedicated to benzene, and although some articles focus on aspects of its genotoxicity, its carcinogenic property received a tangential mention. In 2019, three studies were published on exposure to potential carcinogens: crystalline silica in the rubber industry<sup>27</sup>, pesticides<sup>28</sup> and lead, cadmium, copper, and zinc<sup>29</sup>. However, these studies only poorly highlighted the links with cancer. Finally, in 2022 (up to July), an umbrella review evaluated occupational exposure and cancer<sup>30</sup>.

The first references on PubMed of studies on the subject of occupation and cancer in Brazil date from the late 1960s<sup>31,32</sup>. In the 1980s, the first case-control studies emerged, investigating risk factors for different malignant tumors but without reference to occupational conditions<sup>33,34</sup>. In the following decade, the theme emerged more clearly, with cross-sectional or ecological, three case-control<sup>35-37</sup>, and a cohort studies<sup>38</sup>. In the first decade of the 21st century, Brazilian studies in the country with several methodological approaches on occupation and cancer were published: case series, mutagenicity analyses, cross-sectional, ecological, case-control, and cohort studies<sup>39-54</sup> and an investigation of the prevalence of exposure to silica<sup>55</sup>.

At this point, we conducted a review on PubMed to follow the last decade evolution of research on occupation and cancer in Brazil. From January 31, 2012 to December 31, 2022, we screened studies using the following MeSH terms combination: ((Occupational Health) OR (occupation)) AND ((cancer) OR (neoplasms) OR (Hematologic Neoplasms) OR (mesotheliomas) OR (melanoma)) AND (Brazil)). To include additional research, we also manually searched the references of the chosen studies. We only included ecological, case-control, and cohort studies in this review, ignoring language restrictions. Our exclusion criteria included: (1) cell and animal studies; and (2) review, descriptive, cross-sectional studies, letters to editors, and case reports. If studies met our eligibility criteria after we screened their titles and abstracts, we retrieved their full text for full reading.

We collected 396 articles. After reading their titles, we excluded 362 studies. Reading the abstracts of the remaining 34 articles, we selected 14 for full reading. Of these, 12 were selected from the database and another two<sup>56,57</sup> were identified from bibliographical references. Thus, we included 14 studies in this review.

The selected articles include eight ecological, five case-control, and one cohort studies (**Table 2**). Pesticides, agricultural activities, and asbestos were the main investigated exposures. The studies examined distinct types of cancer. Most evaluated deaths from the disease as their main outcome.

Among the ecological studies on asbestos exposure, Algranti et al.<sup>56</sup> showed a growing trend in deaths from mesothelioma in Brazil, especially in São Paulo, a state that showed an increase in standardized mortality rates for this neoplasm. Based on the data, the authors extrapolated the projected peak mortality for mesothelioma in Brazil between 2021 and 2026, exhibiting a 15 to 20-year lag compared to developed countries. The authors related this fact to the history of the consumption of that fiber in Brazil. Another study found an excess of deaths due to malignant lung neoplasms in men aged 60 years and older in Osasco (a municipality that housed a large asbestos-cement industry in the previous century) in relation to the male population of São Paulo State and in the municipality of Sorocaba<sup>57</sup>. Saito et al.<sup>58</sup> observed that, in municipalities with a history of asbestos mining and asbestos-cement production, mortality rates due to mesothelioma, asbestosis, pleural plaques, and lung and ovarian cancer exceeded rates in all of Brazil.



**Table 2** Ecological, case-control, cohort studies on PubMed on occupation and cancer that were published in Brazil, from January 2012 to December 2022.

Author/ Year/Study location	Design/ Period of study	Exposure	Outcome	Main results
Miranda Filho et al., 2014 <sup>59</sup> Rio de Janeiro	Ecological Study 1996 and 2010.	Agriculture	Deaths from malignant neoplasm of the brain (ICD-10, C-71)	<b>Serrana Region</b> AAPC: 3.8%; 95%CI:0.8;5.6 RR (75-79 years): 33.63; 95%CI:15.24;74.22 <b>Metropolitan area</b> AAPC: -0.2%; 95%CI:-1.2;0.7 RR (75-79 years): 23.78; 95%CI:22.55;25.07
Koifman et al., 2014 <sup>61</sup> Brazil	Ecological Study 1996 and 2004.	Dentist (occupation code 063)	Deaths from malignant neoplasms (ICD-10, C00-C97)	<b>MOR (general population)</b> <b>Male dentists</b> <b>20-49 years old:</b> C00-C97: 4.29; 95%CI:3.42;5.47 C18-21: 3.24; 95%CI:1.30;6.67 C71: 1.70; 95%CI:0.55;3.96 C82-C85: 3.71;95%CI: 1.36;8.09 <b>50-79 years old:</b> C00-C97: 1.67;95%CI:1.54;1.81 C18-21: 2.40; 95%CI:1.81;3.15 C71: 2.08; 95%CI:1.33;3.10 C82-C85: 2.54;95%CI:1.55;3.91 <b>Female dentists:</b> <b>20-49 years old:</b> C00-C97: 2.26; 95%CI:1.91;2.67 C18-21: 2.47; 95%CI:1.13;4.69 C71: 5.56; 95%CI:3.35;8.67 C82-C85: 3.18; 95%CI:1.03;7.41 C50: 3.67; 95%CI:2.69;4.89 <b>50-79 years old:</b> C00-C97: 4.22; 95%CI:3.58;4.97 C18-21: 3.12; 95%CI:1.66;5.34 C71: 2.73; 95%CI:0.88;6.36 C82-C85: 6.17; 95%CI:2.47;12.7 C50: 5.19; 95%CI:3.69;7.09
Algranti et al., 2015 <sup>565</sup> Municipalities of São Paulo and other places in Brazil	Ecological Study	Asbestos	Deaths from mesothelioma (ICD-10, C45) and pleural cancer (ICD-10, C38.4)	<b>Crude average crude mortality rate ratio</b> <b>C45</b> Leme: 11.0 São Caetano do Sul: 8.4 Osasco: 5.2 Brazil: 1 <b>C38,4</b> Leme: 0.0 São Caetano do Sul: 4.2 Osasco: 1.7 Brazil: 1 <b>C45+C38,4</b> Leme: 4.4 São Caetano do Sul: 5.9 Osasco: 3.1 Brazil: 1 <b>C45</b> Trends in numbers of cases Brazil: R <sup>2</sup> = 0.63, p = 0.0012 São Paulo R <sup>2</sup> = 0.69, p = 0.0004 Standardized crude mortality rate São Paulo: R <sup>2</sup> = 0.35, p=0.0344

(Continues)

Table 2 Continuation...

Author/ Year/Study location	Design/ Period of study	Exposure	Outcome	Main results
Segatto et al., 2015 <sup>63</sup> Porto Alegre, state of Rio Grande do Sul, Brazil	Hospital-based case-control April 2012 to September 2013	Pesticides	Cases of cutaneous melanoma	<b>Use of pesticides for &gt; 10 years:</b> OR: 1.9; 95%CI: 1.2; 8.2 <b>Occupational exposure to pesticides:</b> OR: 3.2; 95%CI: 1.2; 6.8 <b>General use of pesticides</b> OR: 2.03; 95%CI: 1.03; 6.89 <b>Indoor use of pesticides four or more times a week</b> OR: 1.44; 95%CI: 1.11; 3.49
Boccolini et al., 2016 <sup>65</sup> Paraná, Santa Catarina, and Rio Grande do Sul	Case-control based on death certificates January 1996 to December 2005	Agricultural workers	Deaths from non- Hodgkin's lymphoma (ICD-10, C82-C85)	<b>20 – 39 years old:</b> Crude OR: 1.31; 95%CI: 1.05; 1.87 OR adjusted for gender, state of residence, education, and race: 2.06; 95%CI: 1.20; 3.14 <b>40 – 69 years old:</b> Crude OR: 0.80; 95%CI: 0.67; 0.95 OR adjusted for gender, state of residence, education, and race: 0.96; 95%CI: 0.75; 1.23
Fortes et al., 2016 <sup>64</sup> Brazil and Italy	Hospital-based case-control (2001 and 2003 for the Italian study and 2007 to 2013 for the Brazilian study)	Exposure to the sun and pesticides	Cases of cutaneous melanoma	<b>Pesticides</b> OR: 2.58; 95%CI: 1.18; 5.65 <b>Use of pesticides for 10 years or more</b> OR: 7.40; 95%CI: 1.91; 28.7 <b>Exposure to at least two types of pesticides</b> OR: 4.04; 95%CI: 1.20; 13.6 <b>Herbicides</b> OR: 3.08; 95%CI: 1.06; 8.97 <b>Fungicides</b> OR: 3.88; 95%CI: 1.17; 12.9 <b>Pesticides and occupational sun exposure</b> OR: 4.68; 95%CI: 1.29; 17.0
Azevedo e Silva et al., 2016 <sup>21</sup> Brazil	Ecological Study	Formaldehyde, paint, rubber industry, benzene, leather powder, silica, wood powder, nickel, asbestos, benzopyrene, diesel, iron/steel, radon, gamma radiation	Cancer of the esophagus (squamous), nasopharynx, sinonasal, larynx, lung, bladder, breast, ovary, mesothelioma, non-Hodgkin's lymphoma and leukemia	<b>Fraction of cancer attributable to occupation:</b> 1.3% <b>Men</b> 2.3% <b>Women</b> 0.3%

(Continues)



Table 2 Continuation...

Author/ Year/Study location	Design/ Period of study	Exposure	Outcome	Main results
Krawczyk et al., 2016 <sup>60</sup> Região Serrana do Rio de Janeiro: Teresópolis, Nova Fribourg, Bom Jardim, Cantagalo, Duas Barras, and Sumidouro	Ecological Study 1999-2013	Agricultural workers	Cancer deaths	<b>Men 30-69 years</b> <b>Reference group: non-agricultural workers in the mountainous region of Rio de Janeiro</b> Stomach= MOR:1.55; 95%CI:1.13;2.12 Esophageal cancers= MOR:1.93; 95%CI:1.38;2.7 <b>Reference group: non-agricultural workers in Rio de Janeiro</b> Stomach= MOR: 2.30; 95%CI:1.72;3.08 Esophageal cancers= MOR: 3.12; 95%CI:2.30;4.24 <b>Reference group: non-agricultural workers in Porto Alegre</b> Stomach= MOR: 2.28 95%CI:1.69;3.08 Esophageal cancers= MOR:1.72; 95%CI:1.26;2.34
Fernandes et al., 2019 <sup>57</sup> Osasco, Sorocaba, and São Paulo State	Ecological Study 1980 to 2016	Asbestos	Deaths from lung cancer (ICD-9, C162) (ICD-10, C33-34)	Men Osasco = AAPC: 0.7%; 95%CI:0.1;1.3 Sorocaba = AAPC: -1.5%; 95%CI:-2.4;-0.6 São Paulo State = AAPC: -0.1; 95%CI:-0.3;0.1 <b>Period-age-cohort model from 1996 onward:</b> Osasco: increased risk of death Sorocaba: reduced risk of death São Paulo State: reduced risk of death
Santos et al., 2020 <sup>62</sup> Southern and Southeastern Brazil	Ecological Study 2006 to 2017	Male mechanics	Deaths from hypopharyngeal ICD-10, C10; nasopharynx ICD-10, C13; larynx ICD-10, C11; ICD-10 lung, C32; and bladder cancers ICD-10, C67; myeloid leukemia ICD-10, C92; and all ICD-10, C91-95 leukemias	Oropharyngeal:MOR:1.84; 95%CI:1.66;2.11 Hypopharynx: MOR:1.39; 95%CI:1.07;1.81 Larynx: MOR: 1.45; 95%CI:1.32;1.59 Lung: MOR: 1.07; 95%CI:1.01;1.12 Bladder: MOR:1.16; 95%CI:1.02;1.32 Leukemia: MOR:0.85; 95%CI:0.75;0.96
Fernandes et al., 2021 <sup>68</sup> State of São Paulo	Cohort 1995 to 2016	Asbestos	Cancer deaths	Men: Overall Mortality = SMR: 1.1; 95%CI:0.98;1.23 Mesothelioma = SMR: 69.4; 95%CI:22.55;162.1 Asbestosis = SMR: 975.7; 95%CI:396.4;2031 Peritoneal cancer = SMR: 5.0; 95%CI:0.13;27.78 Laryngeal cancer = SMR: 1.4; 95%CI:0.30;4.20 Lung cancer = SMR: 1.5; 95%CI:0.82;2.64

(Continues)

Table 2. Continuation...

Author/ Year/Study location	Design/ Period of study	Exposure	Outcome	Main results
Saito et al., 2022 <sup>58</sup> Five municipalities that mined asbestos and 24 that housed cement- asbestos industry plants in Brazil	Ecological Study 2000 to 2017	Asbestos	Deaths from mesothelioma (ICD-10, C45X), asbestosis (ICD-10, J61), pleural plaques (ICD-10, J92.0), lung cancer (ICD-10, C34), and ovarian cancer (ICD-10, C56)	<b>Men:</b> Mesothelioma = SRR: 1.70; 95%CI:1.45;1.99 Asbestosis= SRR: 6.35; 95%CI:4.86;8.28 Pleural Plaques = SRR: 5.06; 95%CI:3.69;6.89 Lung cancer= SRR: 1.33; 95%CI:1.31;1.34 <b>Women:</b> Mesothelioma = SRR: 1.17;95%CI:0.95;1.43 Asbestosis = SRR: 1.86; 95%CI:0.96;3.39 Pleural Plaques = SRR: 0.86; 95%CI:0.35;1.79 Lung cancer = SRR: 1.19; 95%CI:1.17;1.20 Ovary = SRR: 1.34; 95%CI:1.31;1.37
Áfio et al., 2022 <sup>66</sup> Reference Hospital in the State of Ceará	Hospital-based case-control study 2019 and 2021	Occupations	Lymphohematopoietic cancers, multiple myeloma, leukemias, or non-Hodgkin's lymphoma	<b>Rural workers</b> OR <sub>crude</sub> = 5.00; 95%CI:1.91;13.06 OR <sub>adjusted</sub> = 3.38; 95%CI:1.20;9.54 <b>Commercial workers</b> OR <sub>crude</sub> = 0.26; 95%CI:0.10;0.70 OR <sub>adjusted</sub> = 0.30; 95%CI:0.10;0.88
Brey et al., 2022 <sup>67</sup> Philanthropic Hospital in Curitiba-PR	Hospital-based case-control study February and October 2019	Known (list A) or suspected (list B) occupations associated with lung cancer	Cases of lung cancer (ICD-10, C34; including its subcategories)	<b>Painters (list A)</b> OR= 14.3; 95%CI:1.8;116.5

**AAPC:** Average annual percent change; **RR:** relative risk; **MOR:** Mortality odds ratio; **SRR:** Standardized rate ratio; **OR:** Odds ratio; **DRA:** diseases related to asbestos exposure; **SMR:** Standardized mortality rate ratio

An ecological study conducted in the mountainous agricultural region of Rio de Janeiro State showed a growing trend in brain cancer mortality rates, with a higher risk of death due to increasing age, compared to the population of the Metropolitan Region of Rio de Janeiro<sup>59</sup>. An additional investigation in the same region found a high probability of death from stomach and esophageal cancer in agricultural workers compared to non-agricultural workers in the region and in the municipalities of Rio de Janeiro and Porto Alegre<sup>60</sup>.

Moreover, two other ecological studies investigated the association between professional practice in certain occupations and the risk of death from cancer. Koifman et al.<sup>61</sup> found a higher probability of death from non-Hodgkin's lymphoma, breast cancer, colon rectum, lung, brain, and all malignant neoplasm, among dentists of all genders in the age range from 20 to 79 years compared to the general population. Santos et al.<sup>62</sup> found higher mortality from oropharyngeal, hypopharyngeal, laryngeal, lung, and bladder cancer but lower mortality from all leukemias in male mechanics. Azevedo and Silva et al.<sup>17</sup> estimated the fraction of cancer deaths attributable to occupational exposures, finding a low impact on the general population, although it is clear that the risks may be much more relevant for some categories of workers.

Additionally, two hospital-based case-control studies aimed to investigate the risk factors for melanoma. The first study examined exposure to pesticides<sup>63</sup>, whereas the second, including data from 95 Brazilian patients and 304 cases from Italy, investigated exposure to pesticides and solar radiation<sup>64</sup>. Both studies found an increased risk of melanoma among exposed workers. Another case-control study based on death certificates

was conducted in southern Brazil, indicating a higher risk of death from non-Hodgkin's lymphoma in young agricultural workers (20-39 years) compared to non-agricultural workers<sup>65</sup>. In 2022, two other hospital-based case-control studies were published. Áfio et al.<sup>66</sup> found that rural workers were more likely to have lymphohematopoietic tumors, multiple myeloma, leukemia, or non-Hodgkin's lymphoma. Brey et al.<sup>67</sup> found a higher risk of developing lung cancer among painters.

The only cohort study published in the period, in 2021, evaluated mortality in former workers of an asbestos-cement industry in the municipality of Osasco<sup>68</sup>, observing an excess of deaths in this population due to pleural and peritoneal malignant neoplasms, lung cancer, and asbestosis.

## Final considerations

Although the general population is subject to a discreet exposure to occupational carcinogens, some environments have a significant number of workers exposed to high levels of carcinogenic agents. Therefore, understanding and monitoring substances, complex mixtures, or radiations with carcinogenic potential in workplaces and labor processes and occupations with an excessive risk of cancer form the foundation for planning surveillance and control activities.

In Brazil professional experience remains underexplored in medical anamnesis and is often absent in disease databases. Such constraints lead to the loss of valuable sources of information for examining potential correlations between cancer and occupation.

It is likely (indeed almost certain) that the scope of the review for this study excluded some studies. We admit this limitation, but the eventually unmentioned authors would certainly agree that these omissions fail to change the overall described framework. Conducting research is essential for a better understanding of the extent of workers' exposure and the most frequent malignant tumors. Considering its increasing incidence, developing knowledge about occupational hazards is a priority for establishing regulations on exposure limits or banishing carcinogens, thereby reducing the burden of cancer in Brazil.

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