

# Sinonasal Cancer Cases in a Nationwide Hospital Cancer Registry in Brazil, 2007-2021

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## ABSTRACT

**Background:** Sinonasal cancers (SNC) are rare cancers with a high proportion attributable to occupational carcinogens. This study aims to describe the sociodemographic, clinical, and occupational characteristics of subjects with SNC in Brazil. **Methods:** Observational study conducted with secondary data from a network of Hospital Cancer Registries. We selected epithelial/unspecified SNC records with a year of diagnosis from 2007 to 2021. We performed descriptive statistics of SNC cases and calculated crude and age-standardized rates (ASR, standard: world population) by gender and Region of residence. **Results:** We identified 2,384 cases, 1,553 (65.1%) in men and 831 (34.9%) in women. The mean age at diagnosis was 59 years for both. Most SNC (50.7% in men and 53.2% in women) originated from the maxillary sinus. Most (65.5% in men and 54.5% in women) were squamous cell carcinomas. Information on occupation was missing in the years 2019-2021. Most male SNC patients (44.8%) were employed in group 6 (Agricultural, forestry, and fishing workers), while women had been mainly (34.6%) working in groups 8 (Workers in the production of industrial goods and services, machine operators) and in group 6 (27.6%). Crude SNC incidence rates were 1.0 per million person-years in men and 0.5 in women, while ASR were 1.0 and 0.4, respectively. In both genders, the highest ASR was in Minas Gerais (men: 1.9; women: 0.7). **Conclusions:** Establishing the profile of Brazilians with sinonasal cancer can stimulate epidemiologic research for monitoring this group of cancers with a high association with occupational exposures.

## 1. INTRODUCTION

Sinonasal cancers (SNC) are a group of cancers originating from the nasal cavity and paranasal sinuses [1]. They are rare cancers, accounting for less than 1% of malignant neoplasms and 4% of cancers in the head and neck [2]. In studies based on population-based registries in the US and

Europe, the SNC incidence rate is <1-2 per 100,000 person-years [3-5].

The International Agency for Research on Cancer (IARC) evaluated as 'sufficient' the association between SNC and exposure to several carcinogens, including wood and leather dust, nickel compounds, and tobacco smoking, and as 'limited' the association with carpentry and joinery activities,

hexavalent chromium, formaldehyde, and work in textiles manufacturing industry [6]. The association between adenocarcinoma and wood and leather dust is robust, with very high relative risks for heavily exposed workers [7]. A meta-analysis of 28 studies (11 cohort, 17 case-control) found the strongest associations for leather and wood dust and with adenocarcinomas [8]. Associations with formaldehyde, work in the textile and construction industries, and nickel and chromium compounds were also found.

In Brazil, the South and South-East regions account for 36.1% and 25.4% of the value of wood production, with the states of Paraná, Minas Gerais, and Santa Catarina as leaders. Of the total planted areas, 41.9% of eucalyptus is in the Southeast region, and 87.7% of pine are in the South region. Wood products account for 90% of the country's forest production value and have increased by 3.6% in 2017 [9]. In Brazil, the production of pine plywood reached the mark of 2,830,000 m<sup>3</sup> in 2018 (+103.3% compared to 2009, mainly in the State of Paraná with the most significant number of industries that produce plywood (49 sectors) followed by Santa Catarina (25), Pará (7), Mato Grosso (2), Acre (1), Maranhão (1), Mato Grosso do Sul (1) and Rondônia (1) [10].

Regarding leather, according to data from the Brazilian Institute of Geography and Statistics, in 1999, tanning of 5.8 million units was performed, and the South region (Rio Grande do Sul and Paraná) had greater prominence, with 2.5 million units (43.8% of national production). In 2012, tanning increased to 9.1 million units [11].

Data on SNC incidence in Brazil are scarce [12]. Even scarcer are studies on occupational exposure. A study on the association between SNC and occupational exposure to wood dust was performed at the Institute of Oncology Ophir Loyola Hospital in Belém, State of Pará, North-East Brazil, using a proportionate cancer incidence and mortality approach. However, the sample size (138 male wood workers) was so small that only a single SNC case was found [13].

This study aims to describe the sociodemographic, clinical, and occupational characteristics of individuals affected with SNC in Brazil (8,514,877 km<sup>2</sup>, 215 million people), using data from a nationwide database collecting cancer records from hospital cancer registries.

## 2. METHODS

This study is part of the thematic project entitled: "Cancer of the nose and paranasal sinuses related to occupational health", approved by the Institutional Research Ethics Committee of Health Sciences Sector of the Federal University of Paraná (protocol code 3.948.059 and 2020/04/01). We performed a descriptive study of SNC occurrence and characteristics using data stored in the Hospital Cancer Registry Integrator (Portuguese acronym: IRHC, Integrator do Registro Hospitalar de Câncer) of the Brazilian Ministry of Health (Supplementary Table 1).

### 2.1. IRHC

The IRHC is a web system developed by the National Cancer Institute (Brazilian acronym: INCA, Instituto Nacional do Câncer) for consolidating cancer case records fed by hospitals providing care to cancer patients. It is used to monitor disease incidence, characterize the profile of patients throughout the national territory, highlight demographic aspects, monitor the resources used in diagnosis and treatment, and check the evolution of the disease and the general condition of patients over time. This record system is subsidized by the National Policy for Oncological Care, with data filled in by health professionals according to information recorded during care [14].

The dataset contained the following information: cancer site, coded according to the International Classification of Diseases, 10th revision (ICD-10); tumor morphology, coded according to the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) [15]; most prolonged held occupation, coded according to the Brazilian Classification of Occupations (Portuguese acronym: CBO, Classificação Brasileira de Ocupações) [16], a five-digit coding system used to list and identify all occupations in the Brazilian labor market recognized by the Ministry of Labor and Employment. Codes with one digit identify the main groups ("grande grupos"). Two-digit codes indicate subgroups ("subgrupos") closer to economically similar occupations within the main groups. Three-digit codes define base groups ("grupos de base"), used

to classify similar tasks. Individual occupations are identified with all five digits [16].

## 2.2 Data Selection

From the original file covering years of diagnosis 1996 to 2022, we selected records with a year of diagnosis 2007 to 2021 (because other years were incomplete) with ICD-10 codes: C30.0 (malignant neoplasm of nasal cavity), C31.0 (malignant neoplasm of maxillary sinus), C31.1 (malignant neoplasm of ethmoidal sinus), C31.2 (malignant neoplasm of frontal sinus), C31.3 (malignant neoplasm of sphenoid sinus), C31.8 (malignant neoplasm: overlapping sites of accessory sinuses), and C31.9 (malignant neoplasm of accessory sinus, unspecified) [15].

To select malignant epithelial SNC, we used the ICD-O-3 codes following the WHO 2017 Classification of Head and Neck Tumours [1]. In particular, we excluded records with non-epithelial morphology and non-malignant morphology (fifth digit of ICD-O-3 codes different from 3). In analogy with SNC registries, we kept into analysis SNC cases with unspecified or missing morphology.

## 2.3 Statistical Analysis

Separately for the two genders, we performed descriptive analyses of age at diagnosis, level of education, SNC site and morphology, and occupation. We classified morphology according to the WHO 2017 classification into the following categories: squamous cell carcinomas and variants, adenocarcinomas, neuroendocrine carcinomas, and other epithelial cancers. For occupation, we used the large CBO groups.

We used chi-squared and Student's t-tests to compare categorical and quantitative variables between genders, respectively. We calculated gender-specific crude SNC incidence rates using Brazilian population estimates by year (2007 to 2021, region, state, and age categories). Datasets were downloaded from the website of the Brazilian Institute of Statistics (Portuguese acronym: IBGE) [17]. We also calculated age-standardized rates (ASR) using the Segi's standard world population [18]. Statistical analyses were performed with Stata 17 [19]. For

age-standardized rates (ASR) calculation, we used the Stata command *distrate* [20]. The data are available upon request to the authors.

## 3. RESULTS

### 3.1 SNC Cases

The database contained 3,046 SNC records. We excluded 58 records with year of diagnosis before 2007 or after 2021, 570 records with non-epithelial morphology, and 34 records with non-malignant morphology, leaving 2,384 records of SNC cases in analysis, 1,553 in men (65.1%) and 831 (34.9%) in women (Table 1). The mean age at diagnosis was about 59 years in both genders, but women were

**Table 1.** Sociodemographic characteristics of individuals with sinonasal cancer, Brazil 2007–2021.

Variable	Men		Women		P-value*
	N	%	N	%	
All	1553	100	831	100	
Age (years), mean (SD)	59.0	(14.1)	59.1	(15.7)	0.85
Age category (years)					
<50	411	26.5	230	27.7	0.003
50-59	390	25.1	203	24.4	
60-69	366	23.6	176	21.2	
70-79	274	17.6	125	15.0	
80+	112	7.2	97	11.7	
Education					
None	199	12.8	125	15.0	0.17
Incomplete primary	601	38.7	291	35.0	
Complete primary	220	14.2	121	14.6	
Secondary	217	14.0	105	12.6	
Incomplete higher	7	0.4	4	0.5	
Complete higher	71	4.6	55	6.6	
Missing	238	15.3	130	15.6	

\*Chi-squared tests were used for all variables, except age (Student's t test).

more represented in the highest age category. There were no differences in the educational level.

The majority of SNC originated from the maxillary sinus, followed by nasal cavity, with similar distributions of cancer site in men and women (Table 2). Most SNC were squamous cell carcinomas. There were more adenocarcinomas in women. Morphology was unspecified or missing in 183 (7.7%) patients.

Information on occupation was lacking for 333 men and 248 women exclusively due to missing data in the years 2019–2021. Focusing on years 2007–2018, occupation distribution differed between the two genders (Table 3). Most male SNC patients were employed in group 6 (Agricultural, forestry and fishing workers), while women had been working in groups 8 (Workers in the production of industrial goods and services, machine operators) and in group 6. Within the two

genders, we found no different distribution of SNC morphology across occupational groups (results not shown). We looked at the more detailed three-digit CBO categories, but we found only a few cases who had been employed in jobs entailing exposure to wood or leather dusts (results not reported).

### 3.1 SNC Incidence

Overall, crude SNC incidence rates were 1.0 per million person-years in men and 0.5 in women, while ASR were 1.0 and 0.4, respectively. The highest number of cases and rates were found in the North-East, South-East, and South. (Figure 1). In both genders the highest rates were in Minas Gerais (men: n=337, crude rate: 2.2, ASR: 1.9; women: n=145, crude rate: 0.9, ASR: 0.7).

**Table 2.** Clinical characteristics of sinonasal cancers, Brazil 2007–2021.

Variable	Men		Women		P-value*
	N	%	N	%	
Cancer site (ICD-10 code)					
Nasal cavity (C30.0)	483	31.1	256	30.8	0.78
Maxillary sinus (C31.0)	788	50.7	442	53.2	
Ethmoidal sinus (C31.1)	44	2.8	20	2.4	
Frontal sinus (C31.2)	16	1.0	10	1.2	
Sphenoid sinus (C31.3)	26	1.7	11	1.3	
Overlapping lesion of accessory sinuses (C31.8)	39	2.51	22	2.6	
Malignant neoplasm: accessory sinuses, unspecified (C31.9)	157	10.1	70	8.4	
Cancer morphology					
Squamous cell carcinomas	1,018	65.5	453	54.5	<0.001
Adenocarcinomas	192	12.4	180	21.7	
Neuroendocrine carcinomas	26	1.7	12	1.4	
Other epithelial cancers	196	12.6	124	14.9	
Cancer, unspecified	70	4.5	40	4.8	
Missing	51	3.3	22	2.6	

Abbreviations: ICD-10, International Classification of Diseases, 10th revision.

\*Chi-squared test.

**Table 3.** Occupational characteristics of individuals with sinonasal cancer, Brazil 2007–2018<sup>1</sup>.

Occupational group (CBO)	Men		Women		P-value*
	N	%	N	%	
0 - Members of the armed forces, police and firefighters	47	3.8	3	0.5	<0.001
1 - Senior members of public authorities, directors of public interest organizations and companies, managers	35	2.9	6	1.0	
2 - Science and arts professionals	51	4.2	54	9.3	
3 - Mid-level technicians	33	2.7	18	3.1	
4 - Administrative service workers	98	8.0	37	6.3	
5 - Service workers, trade sellers in shops and markets	113	9.3	68	11.7	
6 - Agricultural, forestry and fishing workers	547	44.8	161	27.6	
7 - Workers in the production of industrial goods and services (craft works)	150	12.3	32	5.5	
8 - Workers in the production of industrial goods and services (machine operators)	66	5.4	202	34.6	
9 - Workers in repair and maintenance services	80	6.6	2	0.3	
Total	1,220	100	583	100	

Abbreviations: CBO, Brazilian Classification of Occupations.

<sup>1</sup>Years 2019–2021 excluded because of missing information on occupation (men: n=333, women: n=248).

\*Chi-squared test.

Gender	Region	SNC cases	Person-years (millions)	Crude rate	ASR
Men	Centro-Oeste	51	113.2	0.5	0.5
	Nordeste	474	404.8	1.2	1.2
	Norte	75	129.9	0.6	0.7
	Sudeste	640	620.2	1.0	0.9
	Sul	313	212.3	1.5	1.2
	Brazil	1553	1480.4	1.0	1.0
Women	Centro-Oeste	15	114.9	0.1	0.1
	Nordeste	285	426.8	0.7	0.6
	Norte	37	128	0.3	0.3
	Sudeste	338	653.3	0.5	0.4
	Sul	156	220.3	0.7	0.5
	Brazil	831	1543.3	0.5	0.4

**Figure 1.** Sinonasal cancer incidence by geographical Region, Brazil 2007–2021.

<sup>1</sup>Abbreviations: ASR, age-standardized rates per million person-years (standard: Segi's world population).



#### 4. DISCUSSION

In this study we found that SNC incidence was 1 or less cases per million person-years, that SNC were more prevalent in males (64%), that most SNC occurred in the maxillary sinus, and that squamous cell carcinoma was the prevailing morphology. About half of subjects had been employed in the agricultural, forestry, and fishing sector. Conversely, in women one fourth were employed in this sector, while about one third had been working in the production of industrial goods and services. SNC rates were highest in South and North-East Regions.

The incidence estimates in this hospital-based study are much lower than those found in other countries using population-based registries, while in general similar was the distribution of cases by cancer site and morphology [3-5]. A large US study based on the Surveillance, Epidemiology, and End result (SEER) database examined 6,379 SNC cases (including non-epithelial subtypes like melanoma and esthesioneuroblastoma) in the period 1973-2006 [3]. The most frequent cancer sites were the nasal cavity (43.9%) and maxillary sinus (35.9%), while the most frequent histological types were squamous cell carcinoma (51.6%) and adenocarcinoma (12.6%). The incidence rate was of 0.56 per 100,000, with a male:female ratio of 1.8:1. In the Dutch study on 3329 SNC cases (including olfactorius neuroblastomas and melanomas) recorded in the period 1973-2009 incidence was below 2 per 100,000 person-years in males and below 1 in females [5]. The most frequent cancer sites were the nasal cavity (60.5%) and the maxillary sinus (22.3%), while the most represented histological types were the squamous cell carcinoma (47.9%) followed by adenocarcinoma (15.2%). The Danish study covered the period 1980-2014 and found similar patterns [4]. The majority of 1,720 patients were male (62%), the primary location was the nasal cavity (71%), and most were squamous cell carcinomas (61%). Incidence was less than 1 per 100,000.

In our study maxillary sinus and squamous cell carcinoma prevailed in both genders and adenocarcinoma was most frequent in women than in males. This was different from an Italian study of 1,352 SNC cases in the National SNC Registry [2].

In that study the most frequent anatomical sites and morphologies were as following: in men, 50.0% nasal cavity, 23.5% ethmoidal sinus, and 16.7% maxillary sinus; in women, 51.7% nasal cavity, 25.1% maxillary sinus, and 13.9% ethmoidal sinus; adenocarcinomas were 45.7% in men and 18.2% in women, while squamous cell carcinomas were 32.9% in men and 45.9% in women. The higher prevalence of men in our study may reflect the predominantly male composition of the workforce in occupations exposed to wood dust [21, 22]. On the other hand, like other authors [3-5], we found a low proportion of adenocarcinomas (which are more strongly associated with wood and leather dusts), especially in men: since we do not have individual exposure information, we can only speculate that other agents played a role in SNC occurrence in men; or, conversely, we can hypothesize a greater role of wood and leather dusts in women (see also below).

Regarding the group of workers most affected by SNC in this study, those in Group 6 (agricultural, forestry and fishing workers) stood out, mainly located in the states of Minas Gerais and Bahia. Minas Gerais had over 9.55 million hectares of trees planted for the timber industry [23]. In Brazil, between 1990 and 2017, the production of forestry had an expansion of 52% in the area of forests (mostly eucalyptus and pine), that is, from 5 million hectares to 7.6 million hectares in 2017 [23].

The expansion in the number of planted areas is driving job creation in Brazil. There has been an increase of 10 million hectares, mainly in the production of eucalyptus for the pulp and paper industry, which occupies 7.6 million hectares in the Southeast (42.6%), while pine forests are in the South, with 51.6% of national production. The South and Southeast account for 63.8% of the value of forest production; Minas Gerais represents 28.3% of the national value of forest [24]. In the North-East region of Brazil, the state of Bahia alone has a total area of cultivated trees totaling 9 million hectares, which contributes to 1.2% of the gross domestic product. These issues increase the number of workers in this group and consequently there will be greater exposure to wood dust, both in the furniture and paper industries.

Regarding group 8 (workers in the production of industrial goods and services, machine operators), which was more frequent among women, we suggest the possibility that part of women with SNC had been working in the textile industry, which may involve exposures to various agents including chemicals and synthetic or natural fibers [12, 25]. Moreover, group 8 may include leather goods production, in which the majority of the workforce is female. An Italian study (1996-2019) found a high percentage (52.9%) of women with SNC who have been working in the textile industry [26]. In Brazil more than 9 million workers (mostly informal, 60% females) are employed in the textile sector [27].

In Brazil, the furniture segment consists of 22,482 companies, where 19,316 companies manufacture furniture with wood predominance, 1,789 companies manufacture furniture with metal predominance, 895 companies manufacture furniture with other materials, and 482 companies manufacture mattresses. In Brazil, the furniture industry is mainly concentrated in five states: São Paulo (18.5%); Paraná (13.9%); Minas Gerais (13.7%), Rio Grande do Sul (13.3%); and Santa Catarina (12.4%) [28].

The wood industry was the sector with the highest number of professional hires in the last 8 years, mainly in furniture production, with more than 50% of direct jobs and a positive growth rate, as evidenced by the study on the situation of wood processing companies in Minas Gerais, with jobs created in small and medium-sized companies and laminate manufacturing [29].

Regarding exposure to leather dust, the national tanning industry is represented by approximately 700 tanning units (65,000 workers), of which 72% are in the South and Southeast regions and 80% are small companies. It is important to emphasize that, even in the contemporary market, there are still artisanal tanneries, without any formalization, which produce rustic and handmade shoes for a small regional market [30].

#### 4.1 Strength and Limitations

This study has some strengths. First, we provided a nationwide picture of SNC cases in Brazil over a long time period (15 years). Second, clinical data in

the cancer hospital registries, including cancer site and morphology, is of high quality. Third, we calculated crude and age-standardized rates by exploiting official population databases.

However, this work has also several limitations. First, not all individuals with SNC are admitted to oncologic hospitals; therefore, the rates we calculated are underestimated and should be taken as a rough estimate of true incidence rates. In fact, in our study ASR ranged 0.5-1.2 per million person-years in males and 0.1-0.6 in females, while in 6 population-based cancer registries in Brazil ASR ranged 0.9-6.0 in males and 1.0-3.0 in females [18]. Second, only the main occupation is recorded in the IHRC, and no other information on possible occupational exposure is collected. Even when we looked at the more detailed three-digit categories the information was insufficient to infer occupational exposures. Third, IHRC has no information on exposure to non-occupational risk factors for SNC, including smoking habits.

It should be noted that lack of information on occupational exposure and lifestyle habits is not unique to this study. The aims of population and cancer registries include monitoring incidence rates, evaluate survival, and treatment, not the association with occupational agents [18]. For cancers like mesotheliomas and SNC with a high etiological fraction (i.e., in which most cases are caused by occupation) a dedicated registry would be necessary like that operating in Italy [2, 26] aimed at investigating lifetime occupational history with a standardized questionnaire administered to the patients by trained interviewers.

#### 5. CONCLUSIONS

In this study we found that the majority of subjects with SNC were males. Most subjects had ever employed in two sectors: agricultural, forestry and fishing (both genders) and production of industrial goods and services (women). These findings are possibly consistent with exposure to wood and leather dusts or chemicals in these occupational groups. The low proportion of men with adenocarcinoma points to a lower role of wood and leather dusts and may indicate that other agents may be involved in SNC etiology.

In conclusion, the present study, although with several limitations, was a first attempt to describe SNC cases and occurrence in Brazil. We suggest that detailed lifetime work history using a standardized questionnaire should be collected from SNC patients to assess their occupational exposures. This would benefit them because they would be eligible for compensation in case occupational exposure is documented. Moreover, this could lead to the identification of workplaces entailing exposure to carcinogens and ultimately to the implementation of preventive measures.

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**INSTITUTIONAL REVIEW BOARD STATEMENT:** The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Ethics Committee of Health Sciences Sector of the Federal University of Paraná (protocol code 3.948.059 and 2020/04/01).

**DECLARATION OF INTEREST:** The authors declare no conflict of interest.

**AUTHOR CONTRIBUTION STATEMENT:** F.J.K., C.M., L.P.K., L.A.N. and C.O.R. contributed to the design and implementation of the research. F.J.K., L.P.K., L.A.N., C.O.R. and P.R.B.G. drafted the first version of the manuscript. D.C. and F.J.K. contributed to the analysis of results; all authors contributed to the writing of the manuscript.

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## SUPPLEMENTARY MATERIAL

**Supplementary Table 1.** Hospital Cancer Registries in Brazil, by State.

State	Number of Hospital Cancer Registries*	Population**
Acre	1	830,026
Alagoas	5	3,127,511
Amazonas	3	3,941,175
Amapá	1	733,508
Bahia	16	14,136,417
Ceara	13	8,791,688
Distrito Federal	13	2,817,068
Espírito Santo	8	3,833,486
Goiás	5	7,055,228
Maranhão	4	6,775,152
Minas Gerais	42	20,538,718
Mato Grosso do Sul	8	2,756,700
Mato Grosso	6	3,658,813
Pará	4	8,116,132
Paraíba	5	3,974,495
Pernambuco	14	9,058,155
Piauí	3	3,269,200
Paraná	25	11,443,208
Rio de Janeiro	33	16,054,524
Rio Grande do Norte	8	3,302,406
Rondônia	3	1,581,016
Roraima	1	636,303
Rio Grande do Sul	32	10,880,506
Santa Catarina	22	7,609,601
Sergipe	3	2,209,558
São Paulo	89	44,420,459
Tocantins	2	1,511,459
<b>TOTAL</b>	<b>369</b>	

Source: \*Integrador do Registro Hospitalar de Câncer (2023)\*\*População Residente, Área territorial e Densidade demográfica – IBGE.