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Incidence of rare cancers in the city of São Paulo, Brazil

Maria Teresa Bustamante-Teixeira[1], Maria do Rosário D.O. Latorre[2], Maximiliano R. Guerra[1], Luana F. Tanaka[2,3], Laura Botta[4], Annalisa Trama[4] and Gemma Gatta[4]

Abstract

Introduction: Rare cancers are a challenge for clinical practice as well as for epidemiology and public health. Studies on this subject are few and limited to the study of cases with scarce epidemiologic information. This study aimed to evaluate the incidence of rare cancers and to compare the demographic, anatomic, and histologic characteristics of rare and nonrare (common) cancers.

Methods: Incidence data were obtained from the Population-based Cancer Registry of São Paulo, Brazil. Rare neoplasms were those defined in the RARECARE list, which takes into account an incidence lower than 6/100,000/year.

Results: In São Paulo, 20.4% of tumors had an incidence lower than 6/100,000/year from 1997 to 2012, being therefore considered as rare tumors. We identified 11 entities with an incidence greater than 6/100,000/year (common neoplasms) and 186 entities with an incidence lower than 6/100,000/year (rare neoplasms). The mean annual incidence of all cancers was 365 per 100,000 in São Paulo between 1997 and 2012, and the incidence of all rare tumors was 74.5 per 100,000.

Conclusions: This study presents the burden of rare cancers in Brazil. It is expected to be an incentive for further studies of these entities in order to know the epidemiologic profile of rare tumors in Brazil and to provide a more effective diagnostic and therapeutic approach.

Keywords

Rare tumors, incidence, population-based cancer registry, Brazil

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Introduction

Cancer is the second leading cause of death due to disease in Brazil, surpassed only by cardiovascular diseases. The majority of studies and publications address the most frequent neoplasms, such as breast, lung, or prostatic cancers, and few include rare tumors, especially in Brazil. Nevertheless, rare neoplasms are a challenge for clinical practice, public health, as well as epidemiology. The scarcity of epidemiologic information on this subject[1,2] reinforces the importance of developing studies that describe the occurrence of rare cancers and identify their causes and the best approach for their prevention, detection, and treatment, since they also represent a public health problem. For Brazil, it is even more relevant to address this issue, since this information, although available, has not yet been analyzed.

There is no internationally agreed-upon definition of rare cancers and many reference organizations have put forward different proposals.[1,3] At first, such tumors should

[1]Graduate Program in Collective Health of the Federal University of Juiz de Fora, Brazil
[2]Population-Based Cancer Registry of São Paulo, Public Health Faculty, São Paulo University, Brazil
[3]Chair of Epidemiology, Department of Sport and Health Sciences, Technical University of Munich, Germany
[4]Evaluative Epidemiology Unit, Fondazione IRCCS, Istituto Nazionale dei Tumori di Milano, Milan, Italy

Corresponding author:
Maria Teresa Bustamante-Teixeira, Graduate Program in Collective Health of the Federal University of Juiz de Fora, Rua José Lourenço Kelmer, s/n, Campus Universitário, Bairro São Pedro, CEP: 36036-900, Juiz de Fora, MG, Brazil.
Email: teitabt@hotmail.com

follow the same classification used for the group of rare diseases, including those with a prevalence lower than 5/10,000 inhabitants according to the European Union, or lower than 200,000 people according to the Orphan Drug Act in the United States, which represents a prevalence lower than 7/10,000 inhabitants. The Surveillance of Rare Cancers in Europe, the RARECARE project, proposed a definition and a list for rare cancers.[4] According to this project, neoplasms with a crude incidence rate lower than 6/100,000/year are considered as rare tumors, since it was a consensus among the RARECARE group that the incidence is the most appropriate indicator to measure the frequency of these tumors, due to the particularities of the natural history of this disease. There are neoplasms that have a higher prevalence and are rare and vice versa. As the prevalence is influenced by survival, rare tumors with high survival result in a high prevalence (e.g. testicular cancer), while others with worse prognosis have a low prevalence (e.g. squamous cell carcinoma of the lung).[5] Currently, studies that have analyzed the burden of rare cancer in Japan and in the United States have used the RARECARE list, reinforcing its adequacy.

Cancer incidence data are obtained from population-based cancer registries (PBCR), which aim to collect and record all cancer cases in a given city or area. They produce information that allows to describe and to monitor the cancer incidence, prevalence, and survival in a geographically defined population. In Brazil, there are about 20 PBCRs, located mainly in the capitals, covering approximately 20% of the Brazilian population.[6] Of these, 16 have produced data regularly and have been included in at least one of the last two publications of the International Agency for Research on Cancer of the World Health Organization,[7,8] and the registry of São Paulo is one of them.

Rare tumors are not so rare, according to authors such as Gatta and collaborators[3] and Schaefer,[9] who highlight their importance as a public health problem. They represented 22% of all new cases diagnosed between 2000 and 2007 in the European Union, with approximately 2 million patients.[10] Studies have attempted to define the burden of rare cancers in United States[11] and Japan[12] and confirmed rare cancers as a priority. Evidence suggests that survival for rare tumors is worse than for common tumors,[3,11,13] and that there is no equity access to treatment among patients with rare tumors from different countries.[13–15] This situation has motivated organized actions, especially in Europe and the United States, to improve the methodology of clinical research on rare tumors, as well as the organization of health services, and the access of patients with these tumors to new therapies.[9] Studies on rare cancers usually compare rare and common cancers by age and sex according to specific clinical entities, within large anatomical sites, as proposed by RARECARE.[5,10–12] Following the same approach of these studies, we aimed to estimate the incidence of rare cancers and to compare the demographic, anatomic, and histologic characteristics of rare and non-rare (common) cancers based on data from the PBCR of São Paulo, Brazil, from 1997 to 2012.

Methods

This study was carried out in São Paulo, Brazil, the most populous city in the South American continent, with 11,376,685 inhabitants in 2012, about 6% of the national population. Incidence data were obtained from the PBCR of São Paulo and demographic data from the Brazilian Institute of Geography and Statistics–IBGE Foundation[16] for the period 1997 to 2012. The Brazilian PBCR data, including those of São Paulo, had their consistency and quality evaluated for the detection of errors or inconsistencies between the tumors' topography and morphology and also by sex and age at diagnosis.[17]

We adopted the definition and list of rare cancers proposed by the RARECARE project,[4] updated in November 2015, which defines as rare those with crude incidence lower than 6/100,000/year. The RARECARENet list is based on the combination of topographic and morphologic codes of the International Classification of Diseases for Oncology, third edition (ICD-O-3), and it is organized hierarchically in 3 tiers. The bottom tier on the list (tier 3) is the name of individual cancer entities and its corresponding ICD-O-3 morphology and topography codes. Tier 2 groups tumors perceived by clinicians as single diseases that are relevant for clinical management and research (218 entities). These categories are then further grouped, according to a consensus-based clinical perspective, into more general categories of tumors (tier 1: 65 entities), considered to involve the same clinical expertise and patient referral structure. Tier 2 entities, by definition, include only specific morphologies; thus, 198 rare cancers are identified in this tier. There are tumors that could not be classified as rare or common due to nonspecific morphologic coding in the database. These tumors were classified as "other."[3]

We used an algorithm created for Stata version 11[18] for the classification of these tumors. We calculated the absolute number, proportions, and rates for the neoplasms, considering age and sex. Incidence rates were estimated taking into account the number of cases that occurred in the period from 1997 to 2012 divided by the total number of person-years in the population of São Paulo during the same period.

Results

From 1997 to 2012, 627,436 cancer cases were identified in the PBCR of São Paulo. Of these, 489,077 were classified in tier 2 of the RARECARE list and are presented in Table 1. We identified 11 entities with an incidence greater than 6/100,000/year (common neoplasms) and 186 entities

Table 1. Number of cases (N) and incidence rates (IR) in São Paulo, Brazil, 1997–2012, by the RARECARE cancer list.[a]

Rare (R) or common (C)[b] (tier 2 only)	Tier	Tumors	São Paulo (1997–2012)	
			N	IR[c]
	1	EPITHELIAL TUMORS OF NASAL CAVITY AND SINUSES	682	0.40
R	2	Squamous cell carcinoma with variants of nasal cavity and sinuses	291	0.17
R	2	Undifferentiated carcinoma of nasal cavity and sinuses	18	0.01
	1	EPITHELIAL TUMORS OF NASOPHARYNX	116	0.07
R	2	Squamous cell carcinoma with variants of nasopharynx	81	0.05
	1	EPITHELIAL TUMORS OF MAJOR SALIVARY GLANDS AND SALIVARY GLAND TYPE TUMORS	2,352	1.37
R	2	Epithelial tumors of major salivary glands	1,708	0.99
R	2	Salivary gland type tumors of head and neck	656	0.38
	1	EPITHELIAL TUMORS OF HYPOPHARYNX AND LARYNX	9,440	5.50
R	2	Squamous cell carcinoma with variants of hypopharynx	1,012	0.59
R	2	Squamous cell carcinoma with variants of larynx	6,278	3.65
	1	EPITHELIAL TUMORS OF OROPHARYNX	5,563	3.24
R	2	Squamous cell carcinoma with variants of oropharynx	4,076	2.37
	1	EPITHELIAL TUMORS OF ORAL CAVITY AND LIP	8,900	5.18
R	2	Squamous cell carcinoma with variants of oral cavity	6,294	3.66
R	2	Squamous cell carcinoma with variants of lip	916	0.53
	1	EPITHELIAL TUMORS OF ESOPHAGUS	9,290	5.41
R	2	Squamous cell carcinoma with variants of esophagus	5,348	3.11
R	2	Adenocarcinoma with variants of esophagus	1,632	0.95
R	2	Undifferentiated carcinoma of esophagus	47	0.03
	1	EPITHELIAL TUMORS OF STOMACH	25,650	14.93
C	2	Adenocarcinoma with variants of stomach	19,951	11.61
R	2	Squamous cell carcinoma with variants of stomach	207	0.12
R	2	Undifferentiated carcinoma of stomach	125	0.07
	1	EPITHELIAL TUMORS OF SMALL INTESTINE	1,616	0.94
R	2	Adenocarcinoma with variants of small intestine	1,129	0.66
R	2	Squamous cell carcinoma with variants of small intestine	39	0.02
	1	EPITHELIAL TUMORS OF COLON	33,486	19.49
C	2	Adenocarcinoma with variants of colon	27,617	16.08
R	2	Squamous cell carcinoma with variants of colon	87	0.05
R	2	Fibromyxoma and low grade mucinous adenocarcinoma (pseudomyxoma peritonei) of the appendix	52	0.03
	1	EPITHELIAL TUMORS OF RECTUM	13,835	8.05
C	2	Adenocarcinoma with variants of rectum	11,398	6.64
R	2	Squamous cell carcinoma with variants of rectum	278	0.16
	1	EPITHELIAL TUMORS OF ANAL CANAL	1,750	1.02
R	2	Squamous cell carcinoma with variants of anal canal	903	0.53
R	2	Adenocarcinoma with variants of anal canal	393	0.23
	1	EPITHELIAL TUMORS OF PANCREAS	7,512	4.37
R	2	Adenocarcinoma with variants of pancreas	3,894	2.27
	1	EPITHELIAL TUMORS OF LIVER AND INTRAEPATIC BILE TRACT (IBT)	3,260	1.90
R	2	Hepatocellular carcinoma of liver and IBT	2,555	1.49
R	2	Cholangiocarcinoma of IBT	345	0.20
R	2	Adenocarcinoma with variants of liver and IBT	75	0.04
	1	EPITHELIAL TUMORS OF GALLBLADDER AND EXTRAHEPATIC BILIARY TRACT (EBT)	3,409	1.98
R	2	Adenocarcinoma with variants of gallbladder	1,159	0.67
R	2	Adenocarcinoma with variants of EBT	780	0.45
R	2	Squamous cell carcinoma of gallbladder and EBT	47	0.03
	1	EPITHELIAL TUMOR OF TRACHEA	170	0.10
R	2	Squamous cell carcinoma with variants of trachea	90	0.05
	1	EPITHELIAL TUMOR OF LUNG	26,893	15.66
R	2	Squamous cell carcinoma with variants of lung	4,660	2.71
R	2	Adenocarcinoma with variants of lung	7,652	4.45
R	2	Adenosquamous carcinoma of lung	76	0.04
R	2	Large cell carcinoma of lung	310	0.18
R	2	Poorly differentiated endocrine carcinoma of lung	2,048	1.19
R	2	Salivary gland type tumors of lung	49	0.03
R	2	Sarcomatoid carcinoma of lung	73	0.04
	1	EPITHELIAL TUMORS OF THYMUS	142	0.08
R	2	Malignant thymoma	94	0.05
	1	EPITHELIAL TUMORS OF BREAST	77,311	45.01
C	2	Invasive ductal carcinoma of breast	51,587	30.03
R	2	Invasive lobular carcinoma of breast	5,425	3.16
R	2	Mammary Paget disease of breast	118	0.07
R	2	Special types of adenocarcinoma of breast	1,833	1.07
R	2	Metaplastic carcinoma of breast	108	0.06
R	2	Salivary gland type tumors of breast	88	0.05
R	2	Epithelial tumor of male breast	1,008	0.59
	1	EPITHELIAL TUMORS OF CORPUS UTERI	6,892	4.01
R	2	Adenocarcinoma with variants of corpus uteri	5,234	3.05
R	2	Squamous cell carcinoma with variants of corpus uteri	103	0.06
R	2	Clear cell adenocarcinoma, NOS	53	0.03
R	2	Mullerian mixed tumor	160	0.09
	1	EPITHELIAL TUMORS OF CERVIX UTERI	24,006	13.98
C	2	Squamous cell carcinoma with variants of cervix uteri	16,271	9.47
R	2	Adenocarcinoma with variants of cervix uteri	2,417	1.41
R	2	Undifferentiated carcinoma of cervix uteri	56	0.03
R	2	Mullerian mixed tumor of cervix uteri	28	0.02
	1	EPITHELIAL TUMORS OF OVARY AND FALLOPIAN TUBE	8,110	4.72

(continued)

Table 1. (continued)

Rare (R) or common (C)[b] (tier 2 only)	Tier	Tumors	São Paulo (1997–2012)	
			N	IR[c]
R	2	Adenocarcinoma with variants of ovary	4,612	2.68
R	2	Mucinous adenocarcinoma of ovary	601	0.35
R	2	Clear cell adenocarcinoma of ovary	109	0.06
R	2	Mullerian mixed tumor of ovary	35	0.02
R	2	Adenocarcinoma with variants of fallopian tube	37	0.02
	1	NONEPITHELIAL TUMORS OF OVARY	294	0.17
R	2	Sex cord tumors of ovary	52	0.03
R	2	Malignant/immature teratomas of ovary	99	0.06
R	2	Germ cell tumor of ovary	143	0.08
	1	EPITHELIAL TUMORS OF VULVA AND VAGINA	2,475	1.44
R	2	Squamous cell carcinoma with variants of vulva and vagina	1,301	0.76
R	2	Adenocarcinoma with variants of vulva and vagina	277	0.16
R	2	Paget disease of vulva and vagina	25	0.01
	1	TROPHOBLASTIC TUMOR OF PLACENTA	55	0.03
R	2	Choriocarcinoma of placenta	55	0.03
	1	EPITHELIAL TUMORS OF PROSTATE	55,751	32.46
C	2	Adenocarcinoma with variants of prostate	48,314	28.13
R	2	Squamous cell carcinoma with variants of prostate	71	0.04
	1	TESTICULAR AND PARATESTICULAR CANCERS	2,380	1.39
R	2	Non seminomatous testicular cancer	596	0.35
R	2	Seminomatous testicular cancer	950	0.55
R	2	Spermatocytic seminoma	27	0.02
	1	EPITHELIAL TUMORS OF PENIS	1,234	0.72
R	2	Squamous cell carcinoma with variants of penis	766	0.45
R	2	Adenocarcinoma with variants of penis	26	0.02
	1	EPITELIAL TUMORS OF KIDNEY	7,098	4.13
R	2	Renal cell carcinoma with variants	5,116	2.98
R	2	Squamous cell carcinoma with variants of kidney	53	0.03
	1	EPITHELIAL TUMORS OF PELVIS AND URETER	669	0.39
R	2	Transitional cell carcinoma of pelvis and ureter	542	0.32
R	2	Transitional cell carcinoma of urethra	47	0.03
	1	EPITHELIAL TUMORS OF URETHRA	155	0.09
	1	EPITHELIAL TUMORS OF BLADDER	14,616	8.51
C	2	Transitional cell carcinoma of bladder	10,825	6.30
R	2	Squamous cell carcinoma with variants of bladder	182	0.11
R	2	Adenocarcinoma with variants of bladder	461	0.27
	1	EPITHELIAL TUMORS OF EYE AND ADNEXA	437	0.25
R	2	Squamous cell carcinoma with variants of eye and adnexa	239	0.14
	1	EPITHELIAL TUMORS OF MIDDLE EAR	71	0.04
	1	MALIGNANT MESOTHELIOMA	234	0.14
R	2	Mesothelioma of pleura and pericardium	169	0.10
	1	MALIGNANT SKIN MELANOMA	11,410	6.64
C	2	Malignant skin melanoma	11,410	6.64
	1	MALIGNANT MELANOMA OF MUCOSA AND EXTRACUTANEOUS	28	0.02
R	2	Malignant melanoma of mucosa and extracutaneous	28	0.02
	1	MALIGNANT MELANOMA OF UVEA	359	0.21
R	2	Malignant melanoma of uvea	359	0.21
	1	EPITHELIAL TUMORS OF SKIN	138,570	80.67
C	2	Basal cell carcinoma of skin	108,285	63.04
C	2	Squamous cell carcinoma with variants of skin	30,285	17.63
	1	ADNEXAL CARCINOMA OF SKIN	629	0.37
R	2	Adnexal carcinoma of skin	619	0.36
	1	NEUROBLASTOMA AND GANGLIONEUROBLASTOMA	362	0.21
R	2	Neuroblastoma and ganglioneuroblastoma	362	0.21
	1	NEPHROBLASTOMA	357	0.21
R	2	Nephroblastoma	357	0.21
	1	RETINOBLASTOMA	247	0.14
R	2	Retinoblastoma	247	0.14
	1	HEPATOBLASTOMA	50	0.03
R	2	Hepatoblastoma	50	0.03
	1	OLFACTORY NEUROBLASTOMA	40	0.02
R	2	Olfactory neuroblastoma	40	0.02
	1	EXTRAGONADAL GERM CELL TUMORS	134	0.08
R	2	Nonseminomatous germ cell tumors	68	0.04
R	2	Germ cell tumors of central nervous system (CNS)	35	0.02
	1	SOFT TISSUE SARCOMA	5,778	3.36
R	2	Soft tissue sarcoma of head and neck	327	0.19
R	2	Soft tissue sarcoma of viscera[d]	246	0.14
R	2	Soft tissue sarcoma of retroperitoneum and peritoneum[d]	198	0.12
R	2	Soft tissue sarcoma of pelvis[d]	173	0.10
R	2	Soft tissue sarcoma of skin[d]	522	0.30
R	2	Soft tissue sarcoma of brain and other parts of the nervous system[d]	183	0.11
R	2	Embryonal rhabdomyosarcoma of soft tissue	110	0.06
R	2	Alveolar rhabdomyosarcoma of soft tissue	51	0.03
R	2	Ewing sarcoma of soft tissue	27	0.02
R	2	Soft tissue sarcoma of limbs[d]	1,044	0.61
R	2	Soft tissue sarcoma of superficial trunk[d]	502	0.29
R	2	Soft tissue sarcoma of mediastinum[d]	27	0.02
R	2	Soft tissue sarcoma of breast[d]	222	0.13

(continued)

Table 1. (continued)

Rare (R) or common (C)[b] (tier 2 only)	Tier	Tumors	São Paulo (1997–2012)	
			N	IR[c]
R	2	Soft tissue sarcoma of uterus[d]	566	0.33
R	2	Soft tissue sarcomas of other genitourinary tract (vulva, vagina, ovary, penis, prostate, testis, kidney, renal pelvis, ureter, bladder, urethra)	131	0.08
	1	BONE SARCOMA	1,592	0.93
R	2	Osteogenic sarcoma	671	0.39
R	2	Chondrogenic sarcomas	324	0.19
R	2	Notochordal sarcomas, chordoma	77	0.04
R	2	Ewing sarcoma	274	0.16
R	2	Epithelial tumors, adamantinoma	46	0.03
	1	GASTROINTESTINAL STROMAL SARCOMA	99	0.06
R	2	Gastrointestinal stromal sarcoma	99	0.06
	1	KAPOSI SARCOMA	1,106	0.64
R	2	Kaposi sarcoma	1,106	0.64
	1	NEUROENDOCRINE TUMORS	2,307	1.34
R	2	Well-differentiated not functioning endocrine carcinoma of pancreas and digestive tract	384	0.22
R	2	Poorly differentiated endocrine carcinoma of pancreas and digestive tract	437	0.25
R	2	Endocrine carcinoma of thyroid gland	503	0.29
R	2	Neuroendocrine carcinoma of skin	109	0.06
R	2	Typical and atypical carcinoid of the lung	195	0.11
R	2	Neuroendocrine carcinoma of other sites	613	0.36
R	2	Pheochromocytoma, malignant	29	0.02
	1	CARCINOMAS OF PITUITARY GLAND	181	0.11
R	2	Carcinoma of pituitary gland	181	0.11
	1	CARCINOMAS OF THYROID GLAND	25,147	14.64
C	2	Carcinoma of thyroid gland	25,147	14.64
	1	CARCINOMAS OF PARATHYROID GLAND	78	0.05
R	2	Carcinomas of parathyroid gland	78	0.05
	1	CARCINOMA OF ADRENAL CORTEX	298	0.17
R	2	Carcinoma of adrenal cortex	298	0.17
	1	TUMORS OF CNS	8,257	4.81
R	2	Astrocytic tumors of CNS	4,013	2.34
R	2	Oligodendroglial tumors of CNS	250	0.15
R	2	Ependymal tumors of CNS	213	0.12
R	2	Malignant meningiomas	113	0.07
	1	EMBRYONAL TUMORS OF CNS	452	0.26
R	2	Embryonal tumors of CNS	453	0.26
	1	LYMPHOID DISEASES	26,896	15.66
R	2	Hodgkin lymphoma, classical	3,714	2.16
R	2	Other non-Hodgkin, mature B-cell lymphoma	2,021	1.18
R	2	Mantle cell lymphoma	108	0.06
R	2	Prolymphocytic leukemia, B cell	22	0.01
R	2	Hodgkin lymphoma, nodular lymphocyte predominance	28	0.02
R	2	Precursor B/T lymphoblastic leukemia/lymphoblastic lymphoma (and Burkitt leukemia/lymphoma)	2,229	1.30
R	2	T cutaneous lymphoma (Sezary syndrome, Mycosis fungoides)	347	0.20
R	2	Other T-cell lymphomas and natural killer cell neoplasms	918	0.53
R	2	Diffuse B lymphoma	2,536	1.48
R	2	Follicular B lymphoma	776	0.45
R	2	Hairy cell leukemia	90	0.05
R	2	Plasmacytoma/multiple myeloma (and heavy chain diseases)	4,330	2.52
	1	ACUTE MYELOID LEUKEMIA AND RELATED PRECURSOR NEOPLASMS	3,269	1.90
R	2	Acute promyelocytic leukemia (AML with t[15;17] with variants	67	0.04
R	2	AML	2,889	1.68
	1	MYELOPROLIFERATIVE NEOPLASMS	1,755	1.02
R	2	Chronic myeloid leukemia	1,501	0.87
R	2	Other myeloproliferative neoplasms	221	0.13
R	2	Mast cell tumor	33	0.02
	1	MYELODYSPLASTIC SYNDROME AND MYELODYSPLASTIC/MYELOPROLIFERATIVE DISEASES	99	0.06
R	2	Other myelodysplastic syndrome	72	0.04
R	2	Chronic myelomonocytic leukemia	25	0.01
	1	HISTIOCYTIC AND DENDRITIC CELL NEOPLASMS	93	0.05
R	2	Histiocytic malignancies	86	0.05
	1	OTHER	41,984	24.44
		All tier 1	585,504	340.86
		All tier 2	489,078	284.72
		TOTAL	627,436	365.27

[a]RARECARE cancer list (http://www.rarecare.eu); those with 20 cases or less in the analyzed period are excluded.
[b]In São Paulo.
[c]Crude incidence rate per 100,000.
[d]Includes all the entities listed for the soft tissue of the head and neck.
Rare cancer IR $<$6/100,000 and common cancer IR $\geqslant$6/100,000.
Source: Population-based cancer registry from São Paulo.

Table 2. Number of cases, incidence rate, and incidence distribution of rare and common cancers in São Paulo, Brazil, 1997–2012.

All sites	Number of cases	Incidence rate per 100,000	Incidence distribution, %
Common (11 entities)	361,090	210.21	57.6
Rare	127,988	74.51	20.4
IR <0.5/100,000	22,527	13.11	3.6
IR 0.5–<1.0/100,000	16,287	9.48	2.6
IR 1–<6.0/100,000	89,174	51.91	14.2
Other[a]	138,359	NA	22.0
All	**627,436**	**365.27**	**100.0**

[a]Refers to some types of cancer that cannot be classified as rare or common due to nonspecific morphologic coding.

Table 3. Common cancers, number of cases (N), and crude incidence rate (IR) per 100,000, São Paulo, Brazil, 1997–2012.

Tumor	N	IR
Adenocarcinoma with variants of stomach	19,951	11.61
Adenocarcinoma with variants of colon	27,617	16.08
Adenocarcinoma with variants of rectum	11,398	6.64
Invasive ductal carcinoma of breast (females)	51,587	30.03
Squamous cell carcinoma with variants of cervix uteri	16,271	9.47
Adenocarcinoma with variants of prostate	48,314	28.13
Transitional cell carcinoma of bladder	10,825	6.30
Malignant skin melanoma	11,410	6.64
Basal cell carcinoma of skin	108,285	63.04
Squamous cell carcinoma with variants of skin	30,285	17.63
Carcinoma of thyroid gland	25,147	14.64

with an incidence lower than 6/100,000/year (rare neoplasms). The mean annual incidence of all cancers was 365.3 per 100,000, and the incidence of all rare tumors was 74.5 per 100,000 (Table 2).

Rare tumors accounted for 20.4% of incident tumors in São Paulo between 1997 and 2012. Of these, 22,527 cases had an incidence lower than 0.5/100,000/year and are considered very rare tumors. They correspond to 3.6% of all new cases of tumors diagnosed in the period and are represented by 151 different entities. Another 16,287 (2.6%) cases classified in 14 different entities showed an incidence between 0.5 and <1/100,000/year, while 89,174 (14.2%) cases classified in 22 entities showed an incidence between 1 and <6/100,000/year in São Paulo (Table 2). The 11 types of common cancers that accounted for 57.6% of all incident cases are presented in Table 3.

Figure 1 shows the age-specific incidence rates for rare and common tumors. Rare tumors were more frequent in individuals up to 24 years old, and there was a predominance of common tumors after age 25. Rare tumors had a higher proportion in men than in women (22.5% vs 18.6%, $p < 0.001$).

Among all rare tumors, 82.8% were solid tumors and 17.2% were hematologic diseases. Table 4 presents the incidence rates and the proportional incidence of rare and common tumors, according to site. Other refers to tumors that could not be classified as rare or common due to nonspecific morphologic coding. In São Paulo, they accounted for 22% of all tumors registered in the period. Rare tumors accounted for only 4% of the tumors of the male genital system and 11% of the tumors of the breast, contrasting with 69% of the hematopoietic system, 62% of the respiratory tract, and 37% of the female genital system.

Discussion

This study presents the incidence of rare tumors in São Paulo, a topic not yet investigated in Brazil. Rare tumors accounted for 20.4% of all incident tumors in São Paulo between 1997 and 2012, showing their importance as a public health problem. In Europe, they accounted for 22% of all cancers from 1995 to 2002,[3] and 24% from 2000 to 2007,[10] whereas in Italy they accounted for 25% from 2000 to 2010.[19] Considering other studies that also used the RARECARE list, this percentage was 15% in Japan (1993–2007)[12] and 20% in the United States (2009–2013).[11]

We identified 11 entities categorized as common cancers in São Paulo, while there were 14 entities in Europe,[10] 16 in Japan,[12] and 19 in the United States.[11] The adenocarcinomas with variants of prostate, colon, and rectum, invasive ductal carcinomas of breast, and transitional cell carcinomas of bladder were considered

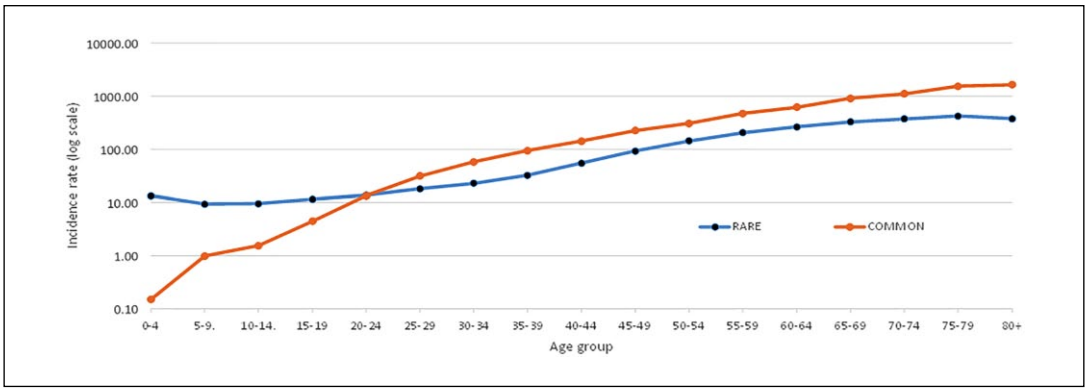

Figure 1. Age-specific incidence rate for rare and common cancers in São Paulo, Brazil, 1997–2012.

as common tumors (IR >6/100,000) in all these regions. São Paulo was the only country that showed rates higher than 6/100,000 for squamous cell carcinoma of cervix uteri (IR 9.47/100,000), whereas adenocarcinoma of corpus uteri was common in Europe and the United States. Carcinomas of thyroid gland, although rare in Europe, were common in São Paulo, Japan, and the United States, whereas adenocarcinomas of stomach were common in São Paulo, Europe, and Japan, but rare in the United States. We also emphasize that types of lung tumors (squamous cell carcinoma with variants of lung, poorly differentiated endocrine carcinoma of lung), as well as renal cell carcinoma, adenocarcinoma of pancreas, and other non-Hodgkin, mature B-cell lymphomas that were considered common in Europe, Japan, and the United States were rare in São Paulo. It should be noted that for the epithelial tumors of lung group (tier 1), São Paulo showed an incidence rate of 15.7/100,000, although all 7 subtypes of this entity were considered as rare. This rate was much lower than that observed for European registries (57.4/100,000), in which 3 subtypes were common and 4 were rare. This difference could be attributed to the quality of the PBCR data in São Paulo, since 44.7% of the epithelial tumors of lung were classified as other, even though 78% of cases have been diagnosed by microscopic verification.

The RARECARE list presents 186 rare cancers, identified from the European cancer registries taking part in the RARECARE project.[4] In São Paulo, 2 tumors considered rare in Europe[10] were common (squamous cell carcinoma with variants of cervix uteri, carcinoma of thyroid gland), whereas 7 entities classified as common in Europe were rare in São Paulo (adenocarcinoma with variants of pancreas, squamous cell carcinoma with variants of lung, poorly differentiated endocrine carcinoma of lung, invasive lobular carcinoma of breast, adenocarcinoma with variants of corpus uteri, renal cell carcinoma with variants, other non-Hodgkin, mature B-cell lymphoma) (Table 5). Such differences may reflect the diverse distribution of environmental, occupational, genetic, and lifestyle-related risk factors, as well as diagnostic capacity and the quality of cancer registries data.

Rare cancers occurred predominantly in young people under 24 years old in São Paulo, whereas in Europe, Italy, and Japan, they predominated in young people under 35 years old.[5,10,12] In the United States, rare tumors accounted for 71% of diagnosed cases in the population under 20 years old.[11] The highest proportion of rare tumors in men, observed in São Paulo, was also observed in the United States.[11]

The percentage of rare tumors in São Paulo was very similar to those found in the United States[11] and Europe,[3] represented mostly by solid tumors. However, when considering the distribution of rare and common tumors by site, we identified differences, for instance, in the respiratory tract, in which the percentage of rare tumors in São Paulo was 3 times higher than the proportion found in Europe (1988–2002)[3] (62% vs 21%), even though the percentage attributed to "other" in this location was similar (38% vs 30%).[3] This difference was also found in urinary system tumors (29% vs 8%), which could be explained by the difference in the incidence of some tumors of this group that were considered common in Europe and rare in São Paulo, such as renal cell carcinoma with variants, and also by the greater percentage difference in relation to tumors considered as "other" in this location (23% vs 14%).[3]

The data come from the PBCR of São Paulo, which has been operating since 1969 according to international standards and has its data evaluated periodically. The data quality indicators of the PBCR of São Paulo showed that the percentage of cases identified only by the death certificate was 7.1%, higher than that reported by the RARECARE project (3.0%) but within the acceptable range, while the percentage of cases diagnosed from microscopic examination was similar (88.5% vs 85.9%). Therefore, these indicators are satisfactory and show that these data can produce valid analyzes.

Table 4. Incidence and distribution for rare and common cancers by site in São Paulo, Brazil, 1997–2012.

Sites	N	Incidence rate/100,000	%
Digestive tract			
Rare	**28,735**	**16.7**	**25.9**
Common	58,966	34.3	53.1
Other	23,359	NA	21.0
All	111,060	64.7	100.0
Respiratory tract			
Rare	**26,741**	**15.6**	**62.4**
Common	0	0.0	0.0
Other	16,123	NA	37.6
All	42,864	25.0	100.0
Skin			
Rare	**619**	**0.4**	**0.4**
Common	149,980	87.3	99.6
Other	10	NA	0.0
All	150,609	87.7	100.0
Breast			
Rare	**8,580**	**5.0**	**11.1**
Common	51,587	30.0	66.7
Other	17,144	NA	22.2
All	77,311	45.0	100.0
Female genital tract			
Rare	**15,354**	**8.9**	**36.8**
Common	16,271	9.5	38.9
Other	10,152	NA	24.3
All	41,777	24.3	100.0
Male genital tract			
Rare	**2,444**	**1.4**	**4.1**
Common	48,314	28.1	81.4
Other	8,607	NA	14.5
All	59,365	34.6	100.0
Urinary system			
Rare	**6,456**	**3.8**	**28.6**
Common	10,825	6.3	48.0
Other	5,257	NA	23.3
All	22,538	13.1	100.0
Hematopoietic system			
Rare	**22,025**	**12.8**	**68.8**
Common	0	0.0	0.0
Other	9,994	NA	31.2
All	32,019	18.6	100.0
All sites			
Rare	**127,987**	**74.5**	**20.4**
Common	361,090	210.2	57.6
Other	138,359	NA	22.1
All	**627,436**	**365.3**	**100.0**

Particularly the analysis of rare tumors is subject to limitations due to the possibility of greater difficulty in the diagnosis and registration of rare tumors in relation to the common tumors, which may result in an underestimation of the rare tumors. In our study, of the 627,436 incident cases, 22% could not be classified as rare or common, and reflect the percentage of cases with unspecified morphology (ICD-O-3: M8000-8001) and poorly defined topography (ICD-O-3: C260, C268, C269, C390, C398, C399, C559, C579, C639, C689, C729, C759–C765, C767–C768), representing respectively 13.0% and 1.1% of total cases in São Paulo, and 8.2% and 0.7% in Europe.[3] We also considered an indicator of the proportion of poorly specified morphology codes, proposed by the RARECARE group,[20] which considers the percentage difference between tumors classified in tier 1 (for which information is more available) and tier 2 (more specific and therefore not available for unspecified morphology codes). This indicator was 16.5% in São Paulo, very close to the value recorded for the set of European cancer registries taking part in the RARECARE project, which was 15.5%.[20] We would like, with this first analysis, to improve the data quality on rare tumors, especially with regard to morphology, and conduct data quality studies as was done by RARECARE.[15]

We provide only crude incidence rate for cancer entities because it is the true indicator of the burden of cancer in the population and therefore useful in public health. For the same reason, we used the general population (male and female) as the denominator to calculate the incidence of sex-specific cancer. Thus, the overall incidence rates used in this article are suitable for classifying tumors as rare or common, as indicated by the RARECARE list,[4] but are not fully appropriated for comparing different populations. For this approach, age-standardized incidence rates have to be used; however, the only information on rare tumors we found in the literature was not age-adjusted.[10–12]

In conclusion, rare tumors represent a substantial percentage of cancer cases in São Paulo (20.4%), with an estimated incidence of 74.5 per 100,000/year, and about 8,000 new rare cases diagnosed per year. This research reinforces the importance of using cancer registries as data sources, and contributes to improving the quality of their information. The need for further research on the epidemiologic profile of rare tumors in Brazil was highlighted, as well as the importance of providing a more effective diagnostic and therapeutic approach for these tumors. Given that large databases provide a good estimate of rare cancers, networking is crucial. This article also emphasizes the need to create networks that include all Brazilian oncology associations and societies, and societies throughout Latin America, since the connection with clinical societies may increase the awareness of improving data quality in the cancer registry.

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The authors declare that there is no conflict of interest.

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