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The increasing burden of cancer attributable to high body mass index in Brazil

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ABSTRACT

Background: Body mass index (BMI) has been constantly increasing over the last decades in most parts of the world, most notably in transitioning nations such as Brazil. High BMI (> 22 kg/m^2) is associated with an increased risk of 14 types of cancer. We estimated the extent to which reducing high BMI could lower cancer incidence in Brazil, nationally as well as at regional and state levels.

Methods: We calculated fractions of cancer incidence in 2012 attributable to high BMI as well as projections for attributable cases in 2025 using BMI data from representative national surveys and relative risks published in meta-analyses. Estimates of cancer incidence were retrieved from GLOBOCAN and the Brazilian National Cancer Institute.

Results: We found that 15,465 (3.8%) of all new cancer cases diagnosed in Brazil in 2012 were attributable to high BMI, with a higher burden in women (5.2%) than in men (2.6%). The cancer sites contributing most to the number of attributable cases were breast (n = 4777), corpus uteri (n = 1729), and colon (n = 681) in women, and colon (n = 1062), prostate (n = 926), and liver (n = 651) in men. The highest population attributable fractions (PAFs) for all cancers were found in the richer states of the country, located in the south (1.5% men/3.4% women) and the southeast (1.5% men/3.3% women).

Conclusions: Cancer cases attributable to high BMI will reach 29,490, which will be 4.6% of all cancers in Brazil in 2025; the extent will be greater in women (6.2% or 18,837) than in men (3.2% or 10,653). This information is a tool to support policy makers for future cancer prevention strategies in Brazil.

1. Introduction

Fourteen million new cancer cases (excluding non-melanoma skin cancers) were diagnosed worldwide in 2012. By 2025, the number of new cancer cases is projected to increase by 37% worldwide, and even higher increases are expected in countries with low (46%) to medium human development (41%) [1]. Brazil is an illustrative example of the cancer prevention challenges in transitioning nations. Being the fifth largest country in the world in both area and population (e.g. 8,515,767 km^2 and around 200 million inhabitants), this country is facing rapid population growth as well as socioeconomic and environmental transformations [2]. At the same time it confronts health challenges from countries in transition (e.g. infections and malnutrition) and from the highly developed world (e.g. overconsumption of ultra-processed foods, obesity, and diabetes), leading to persistent and massive health inequalities [2]. Furthermore, describing the burden of cancer in these 'two worlds' (i.e. within-country) is important to inform cancer prevention strategies in transitioning countries.

In Brazil, more than 400,000 new cancer cases occurred in 2012, and around 640,000 cases are expected by 2025 based only on expected changes in population structure [1]. The increase in the prevalence of risk factors associated with westernization may also lead to further

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increases in the burden of cancer. In fact, obesity prevalence – defined as body mass index (BMI) ≥30 kg/m^2 – has constantly increased over the last decades [3], reaching 17.4% in men and 25.2% in women aged ≥20 years in 2013. There is convincing evidence that overweight and obesity are associated with an increased risk of at least 14 types of cancer, namely breast (postmenopausal), colon, corpus uteri, gallbladder, kidney, liver, multiple myeloma, esophagus (adenocarcinoma), ovary, pancreas, prostate (advanced stage), rectum, stomach/cardia, and thyroid [4–14]. The incidence of these cancers represented almost half of all cancer cases diagnosed in Brazil in 2012 [1]. Therefore, reducing overweight and obesity may have a substantial impact on cancer prevention in Brazil.

In this study, we estimated the extent to which reducing high BMI could lower cancer incidence in Brazil, nationally as well as at regional and state levels. We also present projections of the potentially preventable cancers due to high BMI for the year 2025.

2. Materials and methods

In order to quantify the extent to which high BMI contributes to cancer incidence in Brazil, we estimated fractions of cancers in 2012 and 2025 attributable to high BMI (> 22 kg/m^2) in Brazil. Population attributable fractions (PAFs) were calculated according to sex, age, cancer site, and geographic area. Regarding the geographic areas, three levels of analysis were considered: (1) country level: Brazil; (2) regional level: five sets of states (north, northeast, midwest, southeast, and south); (3) state level: 26 states (e.g. Sao Paulo, Rio de Janeiro) and one federal district (Distrito Federal). All data input and scripts used in our study are available at https://osf.io/sve7y/.

2.1. Data input

2.1.1. BMI distribution

We obtained BMI data from the National Household Budget Survey [15] and the National Health Survey [16] conducted in 2002 and 2013, respectively. Both surveys were nationally representative and collected height and weight data from the adult population aged ≥20 years. Both body weight (in kg) and height (in cm) were objectively measured by trained researchers using portable electronic scales and stadiometers [15–17].

For country-level analyses, we estimated BMI distribution (mean and standard deviation, SD) and the prevalence of overweight (25.0–29.9 kg/m^2) and obesity (≥30 kg/m^2) by sex and age group (20–34, 35–44, 45–54, 65–74, and ≥75 years) for the years 2002 and 2013 [15,16]. For regional- and state-level analyses, data on BMI distribution and prevalence of overweight and obesity in 2002 and 2013 were estimated by sex only (i.e. PAFs for these geographical areas were not estimated by age group due to absence of cancer incidence data – see Section 2.1.3. *Estimated cancer incidence*) [15,16].

2.1.2. Relative risk estimates

We included in our study only cancer sites with probable, convincing and sufficient evidence that they are associated with high BMI as reported by the World Cancer Research Fund (WCRF) Continuous Update Project [4–14] and the International Agency for Research on Cancer (IARC) [18]. We used meta-analyses from these sources to retrieve RR estimates per 1 kg/m^2 BMI increment and their 95% confidence intervals (95%CIs) for the association between high BMI and cancers of the breast (postmenopausal), colon, corpus uteri, gallbladder, kidney, liver, multiple myeloma, esophagus (adenocarcinoma), ovary, pancreas, prostate (advanced stage), rectum, stomach (cardia), and thyroid (Table S1).

2.1.3. Estimated cancer incidence

For country-level analyses, we retrieved estimates of new cancer cases in Brazil in 2012 by sex, age group (20–34, 35–44, 45–54, 65–74, and ≥75 years), and cancer site from the GLOBOCAN project [1]. These estimates were generated by modelling age-, sex-, and site-specific incidence/mortality ratios from 11 population-based cancer registries (PBCRs) across Brazil, which covered 13% of the population between 2003 and 2007 (i.e. classified as high-quality regional data according to GLOBOCAN 2012 [1]). We also obtained from GLOBLOCAN the number of cancer cases predicted for 2025 due to expected changes in population structure [1].

For the regional- and state-level analyses, we retrieved the estimated number of cancer cases in 2012 by sex and cancer site from the Brazilian National Cancer Institute (NCI) [19]. These estimates were modelled using data from 19 PBCRs across Brazil (fulfilled using data derived from 260 hospital-based cancer registries, HBCRs) and mortality statistics systems [19]. These estimates have been officially used to inform policy makers and cancer-prevention strategies in Brazil [19].

To obtain separate estimates for cancers of the colon, rectum, and stomach/cardia and esophageal adenocarcinoma we applied sex-specific adjustment factors for these subtypes in Brazil as reported in Cancer in Five Continents Volume X (CI5 X) [20–22]. For prostate cancer, we obtained the proportion of cases in advanced stage (stage 3 or 4) from the HBCR from Sao Paulo (i.e. 27% of 7000 cases diagnosed in 2012) [23]. Breast cancer (postmenopausal) was defined as cases aged ≥45 years (Table S2).

2.2. Data analysis

2.2.1. Calculation of PAF

PAFs by sex and age group were calculated on the country level, and PAFs by sex were calculated at the regional and state levels using the following equation [24]:

$$\mathrm{PAF} = \frac{\int \mathrm{RR}(x)\mathrm{P}(x)\mathrm{d}x - \int \mathrm{RR}(x)\mathrm{P}^*(x)\mathrm{d}x}{\int \mathrm{RR}(x)\mathrm{P}(x)\mathrm{d}x}$$

where P(x) is the population distribution of BMI (mean and SD), P*(x) is the counterfactual distribution of BMI, RR(x) is the relative risk of cancer associated with BMI (per 1 kg/m^2 increment), and dx indicates that the integration was done with respect to the BMI level. We used a log-logit function to represent each RR value across BMI units [25]. The counterfactual distribution of BMI was defined as mean 22 kg/m^2 and SD 1 kg/m^2 (i.e. the mid-point of normal-weight category). We thereby defined high BMI as any BMI level > 22 kg/m^2. No increased cancer risk was assumed below this value. The same reference group and approach were used in a recent study that estimated the global burden of cancer attributable to high BMI [25].

2.2.2. Number of cancer cases attributable to BMI

To obtain the number of cancer cases attributable to high BMI, we applied PAF estimates from 2002 to cancer cases in 2012, assuming a 10-year lag period. This 10-year lag period has been consistently used in the PAF literature [25–27] to account for the latent period for the development of cancer. The precise latent period between high BMI and cancer is not well established, but previous prospective studies have found beneficial effects of weight loss on cancer incidence after 10 years of follow up [28,29].

For country-level analyses, we applied PAF estimates by sex and age group from 2002 to cancer cases in 2012 (e.g. PAF calculated for 35–44-year-olds in 2002 were applied to cancer cases among 45–54-year-olds 2012). Then we summed up the age-specific number of cases attributable to high BMI (numerator) and divided by the total number of cases ≥35 years old (denominator, except in the case of breast cancer where the denominator was considered cases ≥45 years old) to obtain age-weighted PAFs. For regional- and state-level analyses, we calculated the number of cancer cases attributable to high BMI, applying PAF estimates by sex from 2002 to cancer cases ≥35 years old in 2012. This version of PAF (not age-weighted) was also estimated at country level

Table 1
Estimated population attributable fractions (PAFs) in 2002 and numbers of cancer cases due to high body mass index (BMI) in Brazil in 2012.

Sex, age (years)	Breast (postmenopause)			Colon			Corpus Uteri			Gallbladder			Kidney			Liver			Multiple Myeloma			Oesophagus (adenocarcinoma)		
	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n
Women																								
20–34	4.5	0	0	3.6	277	0	16.0	244	0	8.4	23	0	9.4	98	0	7.2	116	0	2.5	18	0	15.4	5	0
35–44	7.5	0	0	6.1	628	23	25.1	548	88	13.8	114	10	15.2	215	20	11.7	139	10	4.1	80	2	24.3	22	3
45–54	9.2	17,739	1325	7.4	1529	93	29.8	1039	261	16.7	371	51	18.4	406	62	14.3	488	57	5.1	172	7	28.9	86	21
55–64	10.0	15,986	1465	8.2	2000	149	32.2	1758	524	18.2	593	99	20.1	511	94	15.6	843	120	5.6	490	25	31.2	165	48
65–74	8.9	11,314	1135	7.2	2483	203	29.2	1492	481	16.3	682	124	18.0	525	105	13.9	1054	164	4.9	449	25	28.2	195	61
75 +	7.5	9559	852	6.0	2957	214	25.3	1285	375	13.8	810	132	15.3	543	98	11.7	1230	171	4.1	433	21	24.4	235	66
PAF[a]	7.1	54,598	3896	5.8	9597	555	24.3	6122	1486	13.2	2570	339	14.6	2200	321	11.2	3754	422	3.9	1624	64	23.5	704	165
PAFaw[b]	8.7	54,598	4777	7.1	9597	681	28.2	6122	1729	16.2	2570	415	17.2	2200	379	13.9	3754	523	5.0	1624	81	28.3	704	199
Men																								
20–34				7.8	261	0				8.3	22	0	10.2	125	0	7.6	148	0	4.1	10	0	18.3	7	0
35–44				12.1	421	33				12.7	68	6	15.7	321	33	11.7	178	14	6.4	162	7	27.1	118	22
45–54				12.7	1462	177				13.4	194	25	16.4	744	116	12.3	965	113	6.8	376	24	28.2	404	109
55–64				12.5	2266	288				13.2	338	45	16.2	937	154	12.2	1584	195	6.7	538	36	27.9	564	159
65–74				11.1	2459	307				11.7	418	55	14.4	809	131	10.8	1565	190	5.9	445	30	25.2	454	127
75 +				7.5	2320	258				7.9	416	49	9.8	666	96	7.3	1286	139	3.9	336	20	17.7	334	84
PAF[a]				10.4	8928	927				11.0	1434	157	13.5	3477	470	10.1	5578	563	5.5	1857	102	23.7	1873	444
PAFaw[b]				11.9	8928	1062				12.5	1434	180	15.3	3477	530	11.7	5578	651	6.3	1857	117	26.8	1873	501
Both																								
20–34	4.5	0	0	5.7	538	0	16.0	244	0	8.7	45	0	10.3	223	0	10.3	264	0	3.3	28	0	15.8	12	0
35–44	7.5	0	0	9.1	1049	56	25.1	548	88	13.7	182	16	16.2	536	53	16.2	317	24	5.3	242	9	24.1	140	25
45–54	9.2	17,739	1325	10.4	2991	270	29.8	1039	261	15.6	565	76	18.3	1150	178	18.3	1453	170	6.1	548	31	27.1	490	130
55–64	10.0	15,986	1465	10.9	4266	437	32.2	1758	524	16.4	931	144	19.2	1448	248	19.2	2427	315	6.4	1028	61	28.4	729	207
65–74	8.9	11,314	1135	9.8	4942	510	29.2	1492	481	14.7	1100	179	17.3	1334	236	17.3	2619	354	5.7	894	55	25.7	649	188
75 +	7.5	9559	852	7.7	5277	472	25.3	1285	375	11.7	1226	181	13.9	1209	194	13.9	2516	310	4.5	769	41	21.1	569	150
PAF[a]	7.1	54,598	3896	8.0	18,525	1482	24.3	6122	1486	12.4	4004	496	13.9	5677	791	10.5	9332	985	4.8	3481	166	23.6	2577	609
PAFaw[b]	8.7	54,598	4777	9.4	18,525	1743	28.2	6122	1729	14.9	4004	595	16.0	5677	909	12.6	9332	1174	5.7	3481	198	27.2	2577	700

Sex, age (years)	Ovary			Pancreas			Prostate, advanced stage			Rectum			Stomach (cardia)			Thyroid			All BMI-related cancers[†]			All cancers[*]		
	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n
Women																								
20–34	2.1	380	0	3.5	79	0				1.8	207	0	7.8	44	0	1.8	2649	0		4140	0		15,780	0
35–44	3.6	713	15	5.8	124	4				3.0	500	9	12.7	102	8	3.0	2765	49		5950	241		21,154	241
45–54	4.4	1310	47	7.2	641	37				3.7	1193	36	15.5	199	25	3.7	2402	71		27,575	2093		41,623	2093
55–64	4.8	1374	60	7.9	1090	78				4.1	1560	58	16.9	265	41	4.0	1503	55		28,138	2816		45,514	2816
65–74	4.3	1043	50	7.0	1412	111				3.6	1938	80	15.1	338	57	3.6	931	38		23,856	2634		41,650	2634
75 +	3.5	862	37	5.8	1876	131				3.0	2307	84	12.8	425	64	3.0	811	29		23,333	2274		44,910	2274
PAF[a]	3.4	5302	179	5.6	5143	286				2.9	7498	216	12.2	1329	162	2.8	8412	238	7.7	108,853	8329	4.3	194,851	8329
PAFaw[b]	3.9	5302	209	7.0	5143	361				3.6	7498	267	14.7	1329	196	2.9	8412	242	9.2	108,853	10,059	5.2	194,851	10,059
Men																								
20–34				4.8	111	0	3.0	0	0	3.9	160	0	8.3	54	0	6.2	543	0		1441	0		7285	0
35–44				7.5	133	6	4.8	118	4	6.1	372	15	12.7	144	12	9.7	790	49		2825	201		9766	201
45–54				7.9	768	58	5.0	1224	58	6.4	1141	70	13.4	592	75	10.2	632	61		8502	886		29,154	886
55–64				7.8	1221	97	4.9	4760	238	6.3	1769	114	13.2	1067	143	10.0	333	34		15,377	1503		54,248	1503
65–74				6.9	1245	97	4.3	6871	338	5.6	1918	121	11.7	1157	153	8.9	144	14		17,485	1563		61,143	1563
75 +				4.6	1162	80	2.9	6612	287	3.7	1810	101	7.9	1092	128	6.0	102	9		16,136	1251		57,429	1251
PAF[a]				6.4	4529	292	4.0	19,585	793	5.2	7010	366	11.0	4051	444	8.3	2001	166	7.8	60,323	4724	2.2	211,740	4724
PAFaw[b]				7.5	4529	339	4.7	19,585	926	6.0	7010	421	12.6	4051	511	8.4	2001	168	9.0	60,323	5406	2.6	211,740	5406
Both																								
20–34	2.1	380	0	3.6	190	0	3.0	0	0	1.9	367	0	8.1	98	0	2.2	3192	0		5581	0		23,065	0

(*continued on next page*)

Table 1 (*continued*)

Sex, age (years)	Ovary			Pancreas			Prostate, advanced stage			Rectum			Stomach (cardia)			Thyroid			All BMI-related cancers[†]			All cancers[*]		
	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n	PAF	total	n
35–44	3.6	713	15	5.9	257	10	4.8	118	4	3.1	872	24	12.7	246	20	3.6	3555	98		8775	442		30,920	442
45–54	4.4	1310	47	6.7	1409	95	5.0	1224	58	3.5	2334	106	14.5	791	100	4.1	3034	132		36,077	2979		70,777	2979
55–64	4.8	1374	60	7.1	2311	175	4.9	4760	238	3.7	3329	172	15.2	1332	184	4.3	1836	89		43,515	4319		99,762	4319
65–74	4.3	1043	50	6.3	2657	208	4.3	6871	338	3.3	3856	201	13.7	1495	210	3.8	1075	52		41,341	4197		102,793	4197
75 +	3.5	862	37	4.9	3038	211	2.9	6612	287	2.6	4117	185	10.9	1517	192	3.0	913	38		39,469	3525		102,339	3525
PAF[a]	3.4	5302	179	6.0	9672	578	4.0	19,585	793	4.0	14,508	582	11.3	5380	606	3.9	10,413	404	7.7	169,176	13,053	3.2	406,591	13,053
PAFaw[b]	3.9	5302	209	7.2	9672	700	4.7	19,585	926	4.7	14,508	688	13.1	5380	707	3.9	10,413	410	9.1	169,176	15,465	3.8	406,591	15,465

PAFs expressed as percentages; PAFaw, age-weighted PAF (expressed as a percentage); total, total number of cases diagnosed; n, number of cases attributable to high BMI; All BMI-related cancers, all cancer sites included in our estimates, by sex; All cancers, all new cancer cases diagnosed in Brazil.

[*] All cancers excluding non-melanoma skin.

[†] Breast (postmenopause), Colon, Corpus uteri, Gallbladder, Kidney, Multiple myeloma, Esophagus (adenocarcinoma), Ovary, Pancreas, Prostate (advanced stage), Rectum, Stomach (cardia), Thyroid.

[a] This estimate is not age-weighted, but a 10-year lag period is assumed (e.g. PAFs calculated for women in 2002 were applied to a number of cases in women in 2012).

[b] PAF age-weighted: BMI data by age groups are 10 years younger than cancer incidence age groups, assuming a 10-year time period (e.g. PAF calculated for 35–44-year-olds in 2002 were applied to a number of cases among 45–54-year-olds in 2012) and summed up the final number of cases attributable to high BMI.

for the sake of comparison.

Finally, projections of cancer cases attributable to high BMI in 2025 were estimated at the country level only by applying the PAF from 2013 to cancer cases predicted for 2025 [1].

3. Results

3.1. Burden of cancer attributable to high BMI in 2012

We estimated that 15,465 or 3.8% of all cancer cases in Brazil in 2012 were attributable to high BMI, with a higher burden in women (10,059 or 5.2%) than in men (5406 or 2.6%). These attributable cases represented 9.1% of all BMI-related cancers that occurred in 2012 (Table 1).

The cancer sites contributing most to the attributable cases were breast (n = 4777), corpus uteri (n = 1729), and colon (n = 681) in women, and colon (n = 1062), prostate (n = 926), and liver (n = 651) in men. The cancer sites with the highest PAF were esophageal adenocarcinoma (28.3%), corpus uteri (28.2%), and kidney cancer (17.2%) in women, and esophageal adenocarcinoma (26.7%), kidney (15.3%), and stomach (cardia) (12.6%) in men (Table 1).

The highest PAFs for all cancers were found in the richer states of the country, located in the southern (1.5% men/3.4% women) and southeastern (1.5% men/3.3% women) regions. In men, the highest PAFs for all cancers were in the states of Mato Grosso do Sul (1.7%) and São Paulo (1.7%). In women, we found the highest PAFs in the states of Rio Grande do Sul (3.8%), Rio de Janeiro and São Paulo (both 3.4%) (Fig. 1 and Tables S5 and S6).

3.2. Projections of cancer cases attributable to high BMI in 2025

Cancer cases attributable to high BMI will reach 29,490 or 4.6% of all cancers in Brazil in 2025, with a higher extent in women (6.2% or 18,837) than in men (3.2% or 10,653) (Figs. 2 and 3).

4. Discussion

4.1. Principal findings and comparison with previous studies

In Brazil, around 10,000 and 5000 cancer cases (5.2% and 2.6% of all cancers) in women and men, respectively, were attributable to high BMI in 2012. The cancer sites contributing most to these cases were postmenopausal breast (n = 4777) in women and colon (n = 1062) in men. The highest PAFs were found in the richer states of the country, located in the southern (1.5% men/3.4% women) and southeastern regions (1.5% men/3.3% women). In 2025, the absolute number of cancer cases attributable to high BMI in Brazil is expected to double (29,000 or 4.6%) relative to 2012 due to ageing of the population and increasing BMI.

The cancer sites included in our analyses accounted for almost half of all cancer cases in Brazil in 2012 [1]. Our estimates show that 9.1% of these cancers (9.0% men/9.2% women) were attributable to high BMI. These results are higher than previous findings for developing countries (i.e. with medium human development index; 5.3% men/8.2% women), but lower than estimates for the world (11.9% men/13.9% women), Latin America and the Caribbean countries (14.4% men/15.8% women), as well as for Brazil (13% men and women) [25]. The PAF difference between countries is due mainly to different BMI levels [25]. Our estimate is lower than previous estimates for Brazil because of different BMI data sources (a previous study used modelled BMI data [25]) and a different set of cancer sites included in the estimates. In addition, we estimated that 4.6% of all cancers in 2025 will be due to high BMI. A recent study using a different methodological approach – i.e. BMI estimated in adults > 30 years and a 12–20-year lag time period, projections of cancer incidence for 2020 – estimated that overweight and obesity are expected to account for 2.1% and 3.3% of

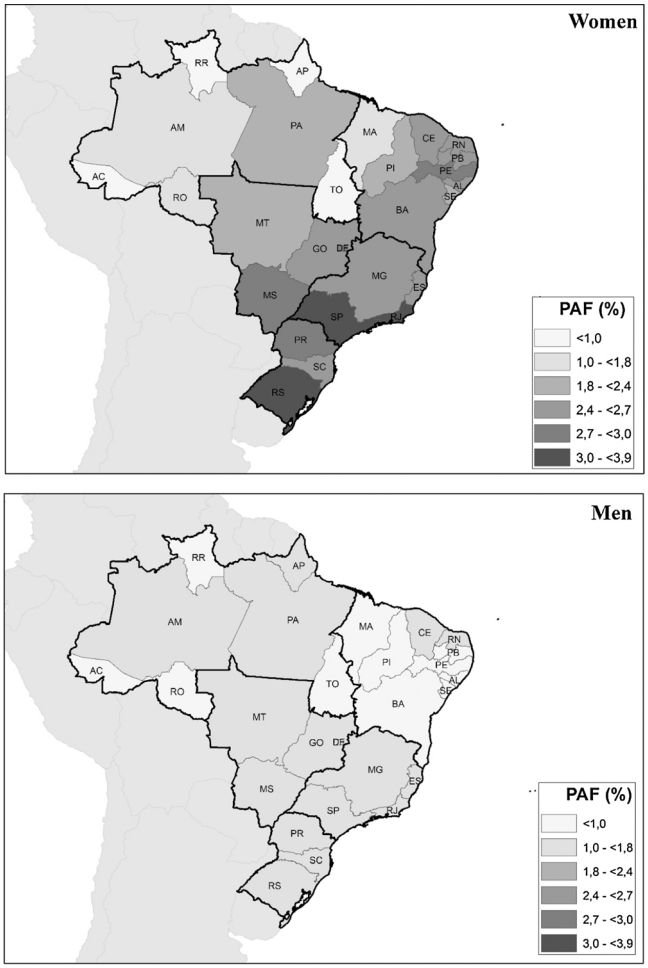

Fig. 1. Population attributable fractions (PAFs) (expressed as a percentage) of new cancer cases in 2012 attributable to high body mass index (BMI) in men and women, by state (27 Federative Units: AC, Acre; AL, Alagoas; AP, Amapá; AM, Amazonas; BA, Bahia; CE, Ceará; DF, Distrito Federal; ES, Espírito Santo; GO, Goiás; MA, Maranhão; MT, Mato Grosso; MS, Mato Grosso do Sul; MG; Minas Gerais; PA; Pará; PB, Paraíba; PR, Paraná; PE, Pernambuco; PI, Piauí; RJ, Rio de Janeiro; RN, Rio Grande do Norte; RS, Rio Grande do Sul; RO, Rondônia; RR, Roraima; SC, Santa Catarina; SP, São Paulo; SE, Sergipe; TO, Tocantins). Bold lines represent five regions: north (AC, RO, AM, RR, AP, PA, TO), northeast (MA, PI, CE, RN, PB, PE, AL, SE, BA), midwest (MT, MS, GO, DF), southeast (MG, SP, ES, RJ), and south (PR, SC, RS).

all cancers in men and women, respectively, in Brazil in 2020 [30].

This is the first study to estimate cancer cases attributable to high BMI across different geographic areas in Brazil. In all Brazilian states (except Amapá) the PAF for all cancers was higher in women than in men. In addition, our estimates indicate that cancer cases due to high BMI are greater in the southern and southeastern regions. These results suggest that cancer prevention interventions aiming at reducing weight would be more effective in states located in these geographic areas. However, the northern and northeastern regions presented greater relative increases in BMI between 2002 and 2013, reflecting the ongoing nutritional transition in poorer areas of the country.

4.2. Implications for cancer prevention and control

Preventive interventions aiming to reduce the burden of cancer in Brazil should focus on the major causes of cancer [31–33]. The most important factors that offer acceptable or practical preventive strategies are tobacco, alcohol, infections, and overweight and obesity [32].

Overweight and obesity increase the risk and progression of cancer via several molecular and metabolic mechanisms [34,35]. The insulin/insulin growth factor (IGF) axis is a key pathway linking obesity and cancer. Briefly, obesity causes insulin resistance, hyperinsulinemia, and elevated IGF, which activates several molecular pathways – e.g. phosphatidylinositol-3-kinase (PI3K) and Akt – associated with increased cellular proliferation [34,35]. Obesity is also related to chronic inflammation, which increases molecular signaling – e.g. nuclear factor kappa light chain enhancer of activated B cells (NF-κB) and cyclooxygenase-2 (COX-2) – related to sustained angiogenesis [34,35]. Finally, obesity is positively associated with sex hormones (e.g. estrone, estradiol) that induce several molecular pathways related to cellular growth, proliferation, and differentiation [34,35].

Overweight and obesity are common responses in individuals exposed to an obesogenic environment. Industrialization of food systems has profoundly changed traditional dietary cultures which were generally made up from fresh and minimally processed foods. Currently, the manufacture and sales of ultra-processed products have become dominant in the global food system [36]. In Latin American countries, sales of ultra-processed products increased 103% between 2000 and 2013 [37]. In the same period, there was a sharp increase in BMI among adults in these countries [37]. Public health interventions and policies (e.g. fiscal policies and regulations of labelling, marketing and selling of ultra-processed products) are necessary to reduce overweight and obesity at the population level. Concomitantly, policies, dietary guidelines and market innovations that value and promote fresh and minimally processed food can promote the development of food systems that are healthy, culturally appropriate and economically viable in Brazil [38].

Physical activity is associated with modest weight loss and maintenance in adults [39]. The promotion of active modes of life requires an integrated multisector approach to increase the number of opportunities to encourage physical activity [40,41]. Therefore, policies and environmental interventions (e.g. bicycle pathways, walkable sidewalks, and parks) are essential for supporting sustainable changes in physical activity for large portions of the population [42,43].

4.3. Limitations of the study

This study has several assumptions and limitations. First, calculating the PAF underlies the assumption that high BMI causes cancer. We assumed that the effects of high BMI on cancer risk would take on average 10 years to manifest [28,29]. However, the precise latent period between high BMI and cancer is not well established, and it may be different according to BMI level (e.g. shorter lag time for obese relative to overweight) and across cancer sites. Second, based on a previous study [25], we used a log-logit function to characterize the association between BMI and cancer. Third, we used RR estimates from large meta-analyses of observational studies conducted by WCRF [4–14] and IARC [18] that retrieved data mainly from US and European cohorts, as data from other world regions are scarce. However, the magnitude of the effect of BMI on cancer can vary between population subgroups and countries. The prevalence of effect modifiers (e.g. smoking) is one of the possible sources of RR heterogeneity between populations [44]. Therefore, whether the magnitude of RR is applicable to a transitioning nation such as Brazil is unknown and warrants further research. RR estimates were adjusted by multiple confounders, but there remains the possibility of residual confounding.

The use of BMI data and estimated cancer incidence should also be interpreted with caution. BMI served as a proxy for body fatness, but it is important to acknowledge its limitation in differentiating lean and adipose tissues [45]. Regarding the estimated cancer incidence, we used data from GLOBOCAN 2012 [1] and the Brazilian NCI reports [19]. Both sources modelled cancer incidence estimates using PBCR and national mortality data [1,19]. PAF for all cancers on the regional and state levels are slightly underestimated because the Brazilian NCI does not provide estimates for cancers with relatively low incidence (cancers

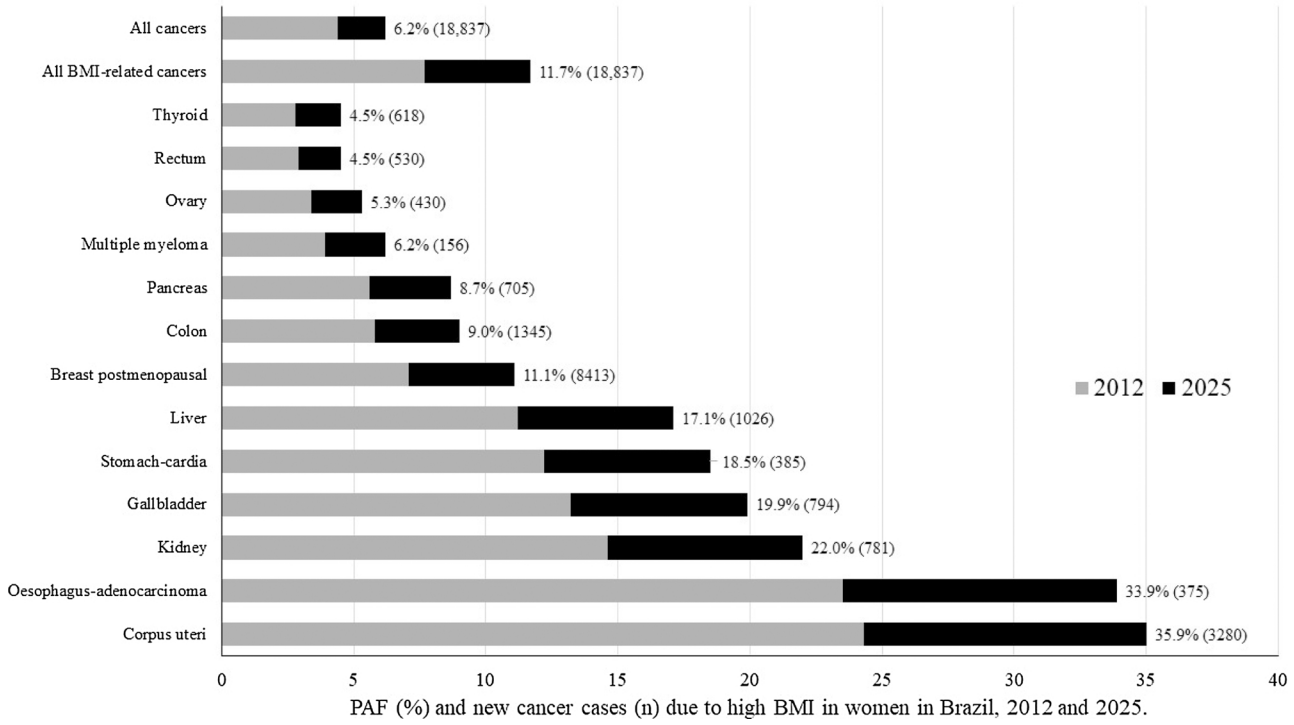

Fig. 2. Population attributable fractions (PAFs) (expressed as a percentage) of new cancer cases attributable to high body mass index (BMI) in women in Brazil, 2012 and 2025. n, number of cases attributable to high BMI; All BMI-related cancers, all cancer sites included in our estimates in 2012; All cancers, all new cancer cases diagnosed in Brazil in 2012.

of the gallbladder, kidney, liver, and pancreas, and multiple myeloma). The incidence of these cancer sites represented 7% of all cancer cases diagnosed in Brazil in 2012 [1]. PAF by age group could not be performed on the regional and state levels given the absence of cancer incidence data. High BMI is associated with an increased risk of developing some subtypes of cancer (colon cancer, rectal cancer, cancer of the stoma cardia, esophageal adenocarcinoma, advanced-stage prostate cancer, and postmenopausal breast cancer). Therefore, to obtain conservative estimates of attributable cases for these cancer sites we calculated the proportion of these subtypes using data from CI5 X

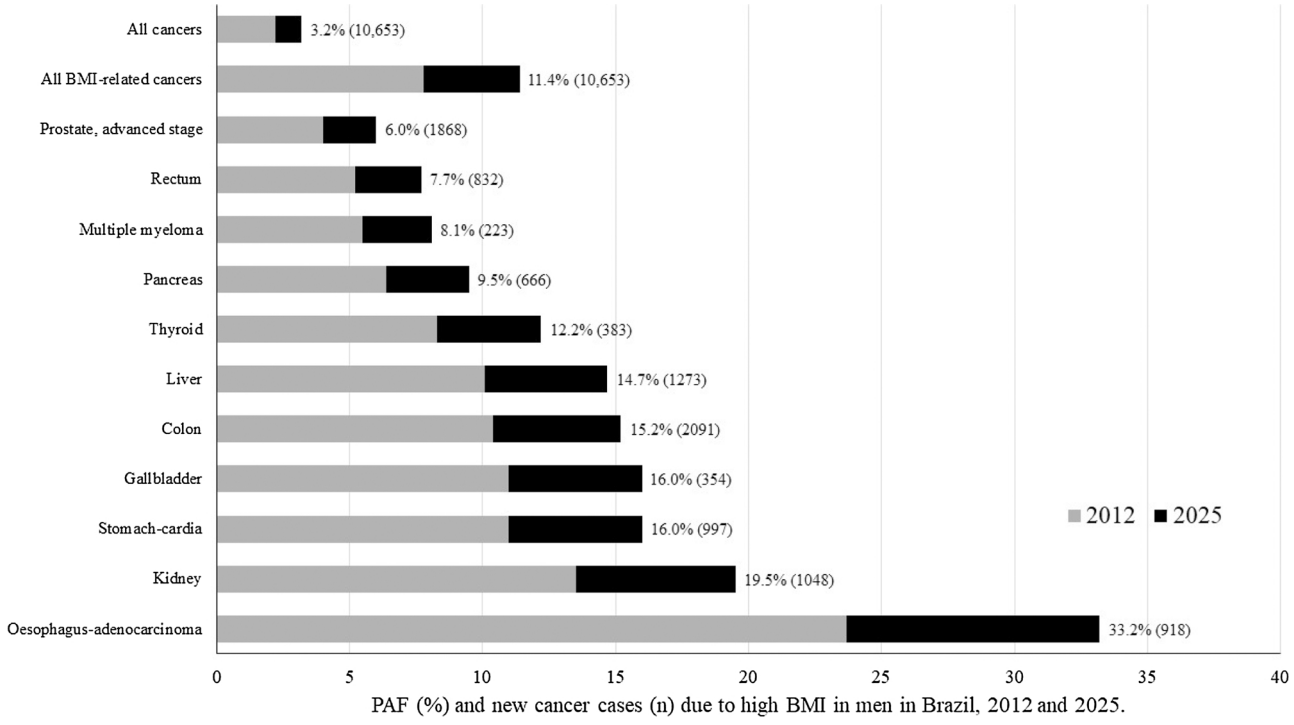

Fig. 3. Population attributable fractions (PAFs) (expressed as percentages) of new cancer cases attributable to high body mass index (BMI) in men in Brazil, 2012 and 2025. n, number of cases attributable to high BMI; All BMI-related cancers, all cancer sites included in our estimates in 2012; All cancers, all new cancer cases diagnosed in Brazil in 2012.

[20,21,22] and HBCR [23]; how applicable these adjustment factors might be to all geographic areas is unclear but relevant for future investigations.

5. Conclusions

In conclusion, high BMI is responsible for 15,000 or 4% of all cancers diagnosed in Brazil in 2012. There were substantial differences in PAF estimates according to cancer site, sex, and geographic area. In 2025, the number of cancer cases attributable to high BMI is expected to double relative to that in 2012, reaching 29,000 or 4.6% of all cancer cases, as a result of population aging and increasing BMI.

Authorship contribution statement

LFMR, MA, FMR, RBL, RC, EG, and JEN conceived and designed the study. LFMR, FMR, RC, and RBL acquired and collated the data. LFMR analyzed the data. All authors drafted and critically revised the manuscript for important intellectual content and gave final approval of the version to be published.

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Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi: https://doi.org/10.1016/j.canep.2018.03.006.

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