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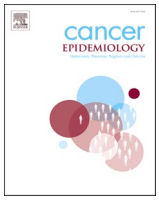

Cancer mortality in Germany-born Americans and Germans

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ABSTRACT

Introduction: Comparing cancer mortality and associated risk factors among immigrant populations in a host country to those in their country of origin reveals disparities in cancer risk, access to care, diagnosis, and disease management. This study compares cancer mortality between the German resident population and Germany-born individuals who migrated to the US.

Methods: Cancer mortality data from 2008–2018 were derived for Germans from the World Health Organization database and for Germany-born Americans resident in four states (California, Florida, Massachusetts, and New York) from respective Departments of Vital Statistics. We calculated age-standardized mortality rates (ASMRs) using the European standard population and standardized mortality ratios (SMR) compared to the German resident population along with 95% confidence intervals (CIs).

Results: Germany-born American males had lower ASMRs (253.8 per 100,000) than German resident population (325.6 per 100,000). The difference in females was modest, with ASMRs of 200.7 and 203.7 per 100,000, respectively. For all cancers, Germany-born American males had an SMR of 0.72 (95% CI: 0.70–0.74) and females 0.98 (95% CI: 0.95–1.00). Male SMRs among Germany-born Americans were significantly below one for oral cavity, stomach, colorectal, liver, lung, prostate, and kidney cancer. Among females, SMRs were below one for oral cavity, stomach, colorectal, gallbladder, breast, cervix uteri, and kidney cancer. For both sexes, SMRs were over one for bladder cancer (1.14 for males, 1.21 for females). Mortality was higher for lung cancer (SMR: 1.68), non-Hodgkin's lymphoma (1.18) and uterine cancer (1.22) among Germany-born American females compared to the German resident population.

Conclusion: Germany-born American males but not females showed lower cancer mortality than German resident population. Disparities may stem from variations in risk factors (e.g., smoking and alcohol use) as well as differences in screening practices and participation, cancer treatment, besides some residual potential "healthy immigrant effect".

1. Introduction

Comparisons of population-based cancer indicators between the United States (US) and Western Europe are relatively rare. This is primarily due to the greater diversity within the American population, including significant proportions of Hispanics (19%) and Black individuals (14%) [1]. These demographic differences can easily account for variations in cancer indicators, as they are intertwined with factors such as socio-economic status, access to healthcare, and a level of mistrust in the healthcare system within certain populations [2]. These factors are inherent aspects of the racial structure and disparities present in the US, which is a multi-racial society characterized by a higher degree of economic inequality compared to many parts of Europe [3]. Conducting such comparisons can be valuable in uncovering the specific factors that contribute to differences in healthcare systems and lifestyle choices that may influence cancer outcomes. Population-based analyses, which encompass entire populations, are crucial for providing unbiased insights and a comprehensive understanding of the issues at hand. The US has been a destination for immigrants from all parts of the world for centuries, receiving millions of immigrants from Europe, especially until

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the mid-twentieth century. Despite this, there have been relatively few analyses in this context. In one study, Italian immigrants in the US exhibited lower mortality rates for most cancers compared to those residing in Italy [4].

Immigrant populations often experience mortality rates that deviate from those in their native countries due to altered exposure to risk factors or lifestyle changes. High-quality care and improved screening campaigns can also influence cancer mortality trends [5,6]. The 'healthy immigrant effect' may also play a role; the observed health advantage among immigrants can be due to factors such as migratory selection, sociocultural resources, and genetic influences [7].

This study aims to analyze cancer mortality disparities between Germany-born Americans (living in California, Florida, Massachusetts, and New York) and the German resident population, taking into consideration that the Germany-born American demographic skews older, reflecting historical migration patterns to the US.

2. Materials and methods

We analyzed the number of deaths by sex and five-year age groups for all cancers combined and for 20 of the most common cancer sites among Germany-born Americans along with corresponding population denominators from 2008 to 2018. These data were retrieved from the California, Florida, Massachusetts, and New York Departments of Vital Statistics. These mortality datasets have a percentage of completeness of nearly 99% in terms of country of birth for all deceased individuals [8]. To determine the population denominators, we obtained combined population totals for each age group and sex from the American Community Survey data from 2008 to 2018. We focused on the "non-Hispanic White" population with the designated country of birth listed as Germany. These population estimates were pooled for the four states mentioned above [9].

For the same calendar period, we retrieved the corresponding official death certificate data and resident population estimates for German resident population (hereafter referred to as Germans), using the World Health Organization database [10].

We computed sex-specific death rates for each five-year age group (from 0–4 to 85 + years) during the period 2008–2018. Age-standardized mortality rates (ASMRs) were calculated for all ages, using the 2013 European Standard Population [11] and the World Standard Population [12]. We computed the standardized mortality ratios (SMRs) among the German US population compared to the Germans, and the corresponding 95% confidence intervals (CIs) using the Vandenbroucke Method [13], for all ages combined and stratified by age group (i.e. below 75 years old and 75 years or older). We used the Benjamini-Hochberg correction [14] for multiple comparisons. For data corresponding to Germans, ethics committee approval was not required given the use of anonymous public data only; for Germany-born Americans from the four US states, respective institutional review board authorizations were obtained as required. Statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, North Carolina).

3. Results

Table 1 shows the ASMRs using the European standard population for Germany-born Americans and the Germans according to sex. Mortality rates adjusted using the world standard population are presented in Supplementary Table 1.

Supplementary Table 2 gives the SMR for Germany-born Americans as compared to the general population of Germany according to sex during the period 2008–2018. Corresponding figures for selected major cancer sites, ordered from the highest to the lowest male rate, are displayed in Fig. 1. The mortality rate for all cancers combined was 235.75 and 200.72 per 100,000 for Germany-born American men and women, and 325.55 and 203.66 per 100,000 German men and women. The SMR for Germany-born Americans for all cancer deaths was 0.72 (95% CI: 0.70–0.74) in men and 0.98 (95% CI: 0.95–1.00) in women. The ranking for top causes of cancer death in men were lung (47.34/100,000 in Germany-born Americans and 75.94/100,000 in Germans), prostate (25.60/100,000 in Germany-born Americans and 39.81/100,000 in Germans), and colorectum (22.10/100,000 in Germany-born Americans and 38.06/100,000 in Germans). Corresponding SMRs for Germany-born American males as compared to the general male population of Germany were 0.63 (95% CI: 0.59–0.67) for lung, 0.64 (95% CI: 0.58–0.70) for prostate and 0.56 (95% CI: 0.51–0.62) for colorectal

Table 1
Mortality deaths and age-standardized mortality rates per 100,000 for various cancers in males and females in Germany-born Americans and Germans, 2008–2018.

Cancer site	Males				Females			
	Germany-born Americans		Germans		Germany-born Americans		Germans	
	Deaths	ASMR	Deaths	ASMR	Deaths	ASMR	Deaths	ASMR
Oral cavity	76	4.13	43,827	9.90	47	1.49	14,519	2.73
Oesophagus	180	10.10	44,904	10.40	83	2.58	13,300	2.45
Stomach	121	6.95	61,338	15.08	111	3.13	45,209	7.99
Colorectal	405	22.10	152,951	38.06	646	18.69	135,651	23.58
Liver	161	9.09	55,647	13.21	185	5.87	28,199	5.05
Gallbladder	7	-[a]	4302	1.07	36	1.11	10,801	1.90
Pancreas	361	19.55	90,168	21.59	540	15.18	92,135	16.44
Lung	867	47.34	322,436	75.94	1552	47.53	164,535	31.09
Skin melanoma	108	5.90	18,140	4.37	80	2.56	13,397	2.45
Breast	-	-	-	-	932	30.12	196,520	36.08
Cervix	-	-	-	-	59	2.48	17,302	3.33
Corpus	-	-	-	-	205	6.74	27,761	5.00
Ovary	-	-	-	-	365	12.37	62,274	11.47
Prostate	510	25.60	148,018	39.81	-	-	-	-
Bladder	257	13.03	42,179	11.26	161	4.25	20,414	3.47
Kidney	128	6.80	61,039	15.17	138	3.87	34,773	6.10
Brain and CNS	149	8.77	35,695	8.12	142	5.35	28,953	5.56
Non-Hodgkin's lymphomas	177	9.44	36,699	9.10	234	6.34	31,887	5.58
Multiple myeloma	98	5.15	16,539	3.99	103	2.77	14,608	2.62
Leukemias	222	11.68	46,389	11.59	243	6.83	38,752	6.85
All malignant cancers	4383	235.75	1330,429	325.55	6580	200.72	1126,093	203.66

ASMR, Age-standardized mortality rates (at the European standard population); CNS, central nervous system.
[a] Number of deaths < 10, no age-adjusted rate computed.

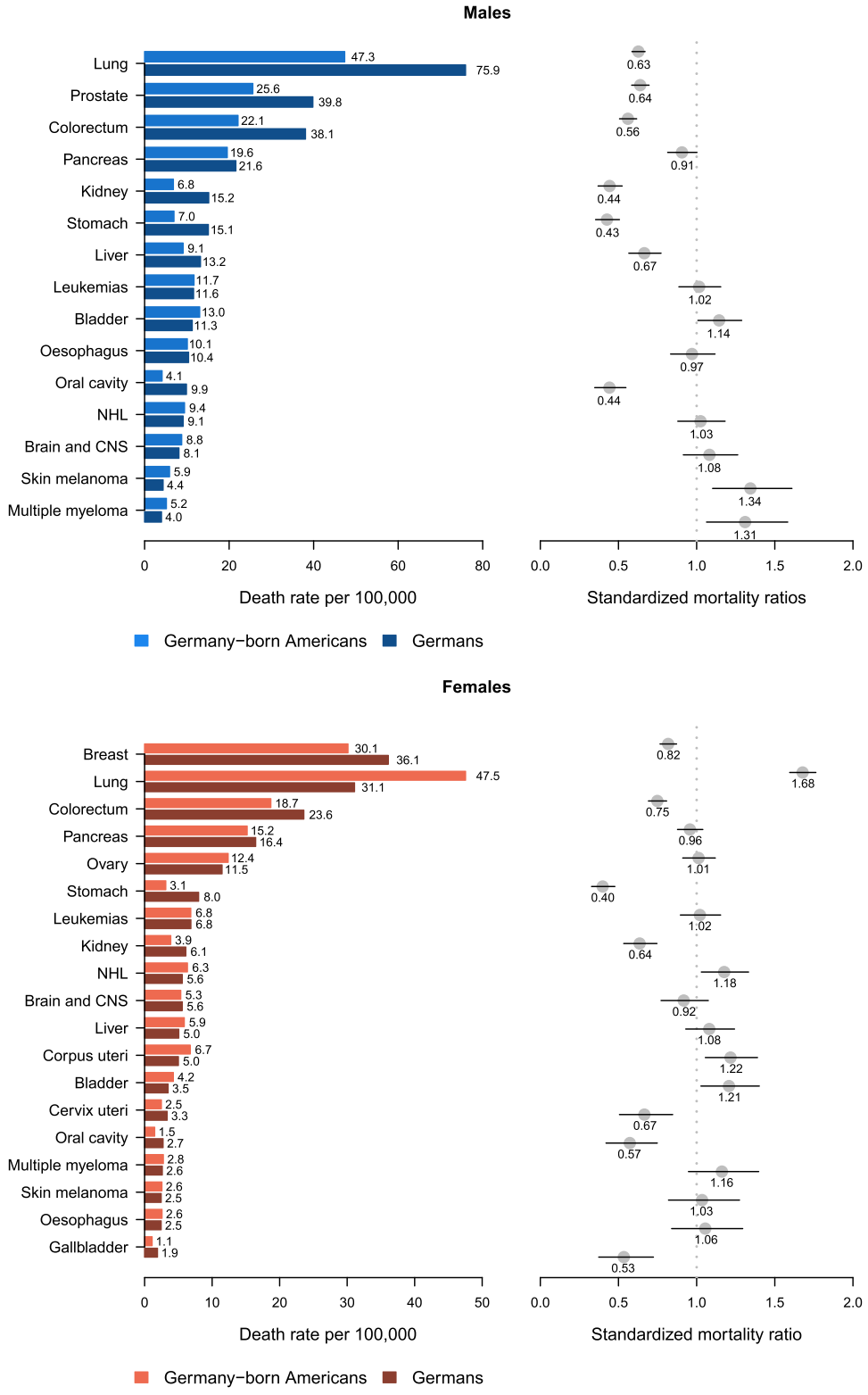

Fig. 1. Age-standardized mortality rates for Germans and Germany-born Americans and standardized mortality ratio for selected cancer sites and sex, 2008–2018.

cancer. For all cancer sites analyzed, higher mortality was observed among German males as compared to Germany-born Americans, except for bladder (with a SMR of 1.14, 95% CI: 1.01–1.29), skin melanoma (SMR: 1.34, 95% CI: 1.10–1.61), and multiple myeloma (SMR: 1.31, 95% CI: 1.06–1.58).

The leading causes of cancer death among women were lung (47.53/100,000 in Germany-born Americans and 31.09/100,000 in Germans), breast (ASMR: 30.12/100,000 in Germany-born Americans and 36.08/100,000 in Germans), and colorectum (18.69/100,000 in Germany-born Americans and 23.58/100,000 in Germans). The corresponding SMRs for Germany-born American females as compared to the general female population of Germany were 0.82 (95% CI: 0.77–0.87) for breast, 1.68 (95% CI: 1.60–1.76) for lung, and 0.75 (95% CI: 0.69–0.81) for colorectal cancer. For the other neoplasms, the SMRs were below one, except

for bladder (1.68, 95% CI: 1.60–1.76), corpus uteri cancer (1.22, 95% CI: 1.06–1.39), and non-Hodgkin lymphoma (NHL) (1.18, 95% CI: 1.03–1.33).

Table 2 reports the SMRs for select cancers in Germany-born Americans as compared to the general population of Germany, according to sex and stratified by age group (<75 and ≥75 years). The SMR for all cancer sites combined was 0.76 (95% CI: 0.72–0.79) for men younger than 75 and 0.69 (95% CI: 0.67–0.72) for men 75 and older. There were no substantial differences in the SMRs between the two age groups, except for cancers of the oral cavity, oesophagus, and brain and CNS, whose SMRs were lower among men < 75. Among women, the SMR was 1.01 (95% CI: 0.98–1.05) for those < 75 and 0.96 (95% CI: 0.93–0.99) for women ≥ 75. No significant differences in SMRs were observed between age groups for women, except for pancreatic and lung cancer, for which women aged < 75 showed lower SMRs as compared to ≥ 75.

4. Discussion

Total cancer mortality rates for all cancer types were lower in Germany-born Americans compared to the Germans, for men. For both sexes, a lower mortality was observed among Germany-born Americans for stomach, colorectal, and kidney cancers. A lower mortality was also reported for liver, lung, and prostate cancer among men, and breast and cervical cancer among women. However, Germany-born American women had higher mortality for lung and bladder cancers and NHL compared to German women.

Differences in cancer mortality may result from disparities both in factors related to cancer incidence, such as exposure to risk factors or implementation of screening to detect early-stage cancers, and disparities in factors related to cancer survival such as treatment and disease management [15]. Lower 5-year relative survival rates have been observed among Germans compared to those in the US for several common cancers, including colorectal, breast, prostate, liver, and lung [15,16]. The US provides access to innovative therapies also through the active participation of US residents in clinical trials. This leads to the availability of cutting-edge and potentially more effective treatments not yet accessible elsewhere. It also serves as an indicator of healthcare quality, linked to high funding for clinical research and a robust infrastructure supporting clinical trials [17].

Our results align with findings from other studies indicating lower cancer mortality rates among immigrants compared to host country residents [18,19]. A possible 'healthy immigrant effect' could contribute to reduced mortality among immigrant Germans who, as per the definition of this effect, might have a health advantage over both the German population in their country of origin and US-born Americans [7].

Comparing death rates among Germany-born Americans with those for the US resident population in 2016 [20], mortality from all cancers combined in the immigrant population was lower for men (94.6 vs 107.2/100,000) and approximately close for women (83.8 vs 82.6/100,000), suggesting a possible healthy immigrant advantage. Moreover, Germany-born Americans had lower mortality rates for lung and colorectal cancer in men and similar rates in women when compared to the US resident population. Germany-born American men had also lower mortality rates for bladder cancer and similar rates for pancreatic cancer. Conversely, they had higher rates for stomach cancer in men and for breast cancer in women.

Smoking is responsible for almost one-fourth of all cancer deaths in Western countries [21]. The peak of smoking-attributable mortality among men was reached around 1980 in North America and in the late 1980′s in Western Europe, while for women it was around 2005 in North America and is now being reached in Western Europe [22,23]. In the US and Germany, the percentage of male smokers peaked around the 1960 s/1970 s and then declined, and over the years the prevalence of smokers seemed to decline earlier and much faster in the US than in Germany [24–27]. American women started smoking earlier than their European counterparts. In a Global Burden of Disease study, Germany ranked among the European countries with the highest prevalence of tobacco use during 1990–2015 [28]. This trend was stable or slightly decreasing, possibly due to the delayed implementation of smoking prevention measures compared to other European and North American countries [29].

For women, lung cancer mortality was higher among Germany-born Americans. This was the opposite in men, reflecting differences in smoking trends between Germany and the US. In Germany, female lung cancer incidence showed an unfavourable trend over the last two

Table 2
Standardized mortality ratios stratified for age group for selected cancers in Germany-born Americans as compared to the general population of Germany according to sex, 2008–2018.

Cancer site	Germany-born Americans											
	Males						Females					
	< 75 years			≥ 75 years			< 75 years			≥ 75 years		
	Deaths	SMR	95% CI	Deaths	SMR	95% CI	Deaths	SMR	95% CI	Deaths	SMR	95% CI
Oral cavity	42	0.34	0.25-0.45	34	0.69	0.48-0.94	20	0.47	0.28-0.69	27	0.69	0.45-0.97
Oesophagus	102	0.92	0.75-1.10	78	1.05	0.83-1.30	38	1.06	0.75-1.43	45	1.05	0.76-1.38
Stomach	56	0.49	0.37-0.63	65	0.38	0.29-0.48	36	0.41	0.29-0.56	75	0.39	0.31-0.49
Colorectal	192	0.72	0.62-0.82	213	0.47	0.41-0.53	224	0.96	0.84-1.09	422	0.67	0.61-0.74
Liver	92	0.79	0.64-0.96	69	0.55	0.43-0.68	93	1.48	1.19-1.80	92	0.85	0.68-1.03
Pancreas	167	0.90	0.77-1.04	194	0.91	0.79-1.04	169	0.84	0.71-0.97	371	1.02	0.92-1.13
Lung	446	0.62	0.57-0.68	421	0.63	0.57-0.69	656	1.28	1.18-1.37	896	2.18	2.04-2.33
Skin melanoma	50	1.39	1.03-1.80	58	1.31	0.99-1.67	32	1.01	0.69-1.39	48	1.05	0.78-1.37
Breast	-	-	-	-	-	-	430	0.87	0.79-0.95	502	0.78	0.71-0.85
Cervix	-	-	-	-	-	-	42	0.81	0.58-1.07	17	0.46	0.27-0.71
Corpus	-	-	-	-	-	-	113	1.75	1.44-2.09	92	0.88	0.71-1.07
Ovary	-	-	-	-	-	-	186	1.12	0.97-1.29	179	0.92	0.79-1.06
Prostate	121	0.75	0.62-0.89	389	0.61	0.55-0.67	-	-	-	-	-	-
Bladder	64	1.25	0.96-1.58	193	1.11	0.96-1.27	38	1.37	0.97-1.84	123	1.16	0.97-1.38
Kidney	51	0.49	0.36-0.63	77	0.42	0.33-0.52	39	0.60	0.43-0.81	99	0.65	0.53-0.78
Brain and CNS	95	1.07	0.86-1.29	54	1.11	0.83-1.42	79	0.91	0.72-1.12	63	0.92	0.71-1.17
Non-Hodgkin's lymphomas	75	1.25	0.98-1.55	102	0.90	0.74-1.09	63	1.11	0.85-1.40	171	1.20	1.03-1.39
Multiple myeloma	38	1.25	0.88-1.68	60	1.35	1.03-1.72	30	0.91	0.61-1.26	73	1.31	1.03-1.63
Leukemias	75	1.03	0.81-1.28	147	1.01	0.85-1.18	75	1.06	0.83-1.31	168	1.00	0.86-1.16
All malignant cancers	1912	0.76	0.72-0.79	2471	0.69	0.67-0.72	2645	1.01	0.98-1.05	3935	0.96	0.93-0.99

CI, confidence interval; CNS, central nervous system; SMR, standardized mortality ratio.

decades, reaching an age-standardized (world population) incidence rate of 22/100,000, while the male trend has been declining to a rate of 39/100,000 [20]. In the US, incidence rates have been appreciably declining in both sexes (with a faster decline for men) starting from the early 2000 s, reaching age-standardized incidence rates of 28 for women and 34/100,000 for men [20].

In comparison to the Germans, Germany-born American men had notably lower rates for other tobacco-related cancers, such as kidney and oral cancer. Oral cancer is also associated with alcohol consumption, which could partly explain differences in mortality across the two populations. Annual per capita alcohol consumption is higher in Germany (12 litres) than in the US (9 litres) [30]. For kidney cancer, well-known risk factors include obesity and hypertension. The prevalence of obesity is lower in Germany than in the US [31], while hypertension is more prevalent among Germans [32]. Better management of hypertension, earlier diagnosis and adoption of modern therapy may at least in part explain the lower rates among Germany-born Americans.

An excess of bladder cancer mortality was found among Germany-born Americans compared to Germans. An important risk factor for bladder cancer, in addition to smoking, is carcinogen exposure in the workplace, particularly aromatic amines [33]. Therefore, the difference in bladder cancer mortality rates could be influenced by the regulations governing the use of aromatic amines [34].

Breast cancer mortality was lower for Germany-born American women. There has been an increase in the incidence of breast cancer worldwide [35]; however, mortality trends have been favorable over the last 30 years with a decrease of about 40% in the US and 30% in Germany [36,37]. Screening has played an important role in these trends. For women aged 40–74 years who attend their routine screening every 1–2 years, breast cancer mortality could be reduced of 20% [38,39]. Breast cancer screening programs started in 1995 in the US and in 2005 in Germany, with respective participation rates of 81% and 54% [40].

Mortality rates for ovarian cancer did not differ appreciably between the two populations, whereas corpus rates were higher in Germany-born American women, in line with the current increasing incidence and mortality rates that affect women of all races in the US [41]. The excess mortality from corpus cancer in the US is due to a higher prevalence of overweight and obesity in the US [31,42]. For cervical cancer, Germany-born American women showed a lower mortality rate than Germans. This pattern reflects earlier and greater use of screening for cervical cancer in the US as well as higher prevalence of human papillomavirus in Germany than in the US [43].

For prostate cancer, Germany-born American men had lower mortality compared to Germans. Differences in incidence and stage distributions over time and across countries may at least partly explain these trends [44]. The observed patterns are partly influenced by the effects of early detection due to the more widespread utilization of prostate-specific antigen (PSA) testing in the US, although the impact is likely modest [45]. In Germany, about 1.5 million PSA tests were performed in 2002, representing about 12% of the German male population over the age of 50. In contrast, in 2001, 57% of US males aged 50 and over had undergone a PSA test in the previous year [46,47]. Earlier adoption of effective (antiandrogen) therapy in the US may also play a role [48,49].

For both sexes, there was a lower colorectal cancer mortality among Germany-born Americans than in Germany. Among men, this may partly be explained by the aforementioned smoking and alcohol consumption patterns, which are well-known modifiable risk factors for the development of colorectal cancer [50]. In addition, earlier diagnosis and screening may also play a role. Germany and the US both benefit from colonoscopy screening programmes. However, more Americans than Europeans have likely benefited from screening for CRC. In 2006, 60% of Americans reported having been screened for CRC [51], while approximately only 25% of the German population aged 50 years and older had undergone a colorectal endoscopy in the previous decade [52].

For infection-related digestive cancers, such as stomach and liver cancer, Germany-born Americans recorded lower mortality compared to Germans, although this was not significant for liver cancer among women. Liver cancer is mainly linked to chronic hepatitis, alcohol consumption, and metabolic conditions [53–57]. Some differences in dietary factors, which are loosely associated to gastric cancer [58,59], might explain the lower rates in Germany-born Americans. In particular, 67% of US adults consumed fruit on a given day [60] compared to 46% in Germany [61]. However, future investigations may be needed to investigate the most common dietary patterns in the two countries. The main risk factor for gastric cancer is Helicobacter pylori, for which the prevalence is lower in the US than in Germany [62,63].

For skin melanoma, there was a higher mortality risk for Germany-born American men than for German men. This is reflective of the lower latitude for the majority of the US than Germany, leading to greater UV exposure [64].

In comparison with Germans, excess mortality among German-born Americans was recorded for multiple myeloma among both older-aged men and women, and NHL among older-aged women. The NHL trend is consistent with a prior study comparing mortality between Italy-born Americans and Italians [4].

There are strengths and limitations to be noted in this study. Mortality certification in both the US and Germany is valid for most cancers and in the period considered there were no relevant changes in classification, coding, and registration. Additionally, the criteria for death certification remained consistent over time and there are similarities between the US and Germany. As a result, the observed variations in cancer mortality between Germany-born Americans and Germans are unlikely to be influenced by substantial bias. However, there was no available data on socioeconomic status and risk factors, particularly for the Germany-born American population. Furthermore, as we only considered data on cancer mortality and no information on incidence, it becomes difficult to distinguish between the influences of exposure to risk factors, the timing of diagnosis, or the impact of screening and treatment quality. Additionally, Germany-born Americans will include individuals born in military facilities in Germany and who migrated back to the US. However, the number of cancers developed in this population is likely small and this limitation is further reduced by limiting the Germany-born American population under study to those of non-Hispanic White race.

5. Conclusion

Cancer mortality was lower for Germany-born Americans than for Germans, particularly among men. These disparities are consistent with differences in risk factors as well as different patterns of healthcare use such as a higher screening prevalence in the US and earlier adoption of modern effective therapy. A notable finding was the opposite patterns for lung cancer by sex, where the high female smoking prevalence rates in the US may have adversely affected immigrant women compared to men for this deadly cancer.

CRediT authorship contribution statement

Mignozzi Silvia: Data curation, Formal analysis, Methodology, Writing – original draft. **Santucci Claudia:** Data curation, Formal analysis, Methodology, Writing – original draft. **La Vecchia Carlo:** Conceptualization, Writing – review & editing. **Pinheiro Paulo Santos:** Conceptualization, Writing – review & editing. **Medina Heidy Nataly:** Writing – review & editing. **Negri Eva:** Funding acquisition, Writing – review & editing.

Declaration of Competing Interest

All authors have declared no conflicts of interest.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.canep.2023.102519.

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