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Chinese and South Asian ethnicity, immigration status, and clinical cancer outcomes in the Ontario Cancer System

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Chinese and South Asian ethnicity, immigration status and clinical cancer outcomes in the Ontario Cancer System

Running head: Ethnicity and cancer outcomes

Precis: Chinese and South Asian ethnic groups have lower cancer mortality than the general (non-Chinese/non-South Asian and non-immigrant) Ontario population. After removing the well-documented protective effect of immigration, Chinese and South Asian ethnicity is associated with a cancer survival advantage in Ontario, Canada.

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Keywords: Ethnicity, cancer survival, immigration, Chinese, South Asian
Conflicts of Interest: None

Abstract

Background

In the United States, certain minority groups have been shown to have inferior cancer outcomes as compared to the Caucasian majority population; however, most research has not separated ethnicity from immigration status. The aim of this study was to determine the impact of ethnicity, independent of immigration status, on cancer outcomes in Chinese and South Asian populations in Ontario, Canada.

Methods

We conducted a population-based retrospective cohort study using administrative databases in Ontario, Canada. Incident cancer cases were captured in Canadian-born Chinese and South Asians, Chinese and South Asian immigrants, and the general Ontario reference population (non-Chinese/South Asian and non-immigrant) between 2000 and 2012. Subjects were followed until death (all-cause and cancer-specific), and Cox proportional hazard models were used to estimate the impact of Chinese and South Asian ethnicity on cancer outcomes, after adjusting for explanatory variables.

Results

423,678 cancer cases were identified: 6,631 in Canadian-born Chinese and 2,752 in Canadian-born South Asians. Following adjustment, the rate of all-cause mortality was lower for Canadian-born Chinese (HR 0.829; 95% CI 0.795-0.865), Canadian-born South Asian (HR 0.856; 95% CI 0.797-0.919), and Chinese immigrant (recent: HR 0.661; 95% CI 0.610-0.716; non-recent: HR 0.853; 95% CI 0.803-0.906) populations, compared to the general Ontario population. A similar effect was found for cancer-specific mortality.

Conclusions

Chinese and South Asian ethnic groups have lower cancer mortalities than the general Ontario population. After removing the well-documented protective effect of immigration, Chinese and South Asian ethnicities are associated with a cancer survival advantage in Ontario, Canada.

Introduction

Cancer represents a significant burden of disease in Canada, where 40% of Canadians will be diagnosed with a malignancy in their lifetime,[1] and 25% of people living in Ontario, Canada are expected to die of cancer in their lifetime.[2] Canada is a very heterogeneous and multicultural nation with a diverse ethnic and immigrant population, and nearly one in five Canadians identify as a visible minority group[3] defined as "persons, other than Aboriginal peoples, who are non-Caucasian in race or non-white in colour".[4] Chinese and South Asians (Indian, Pakistani, Bangladeshi and Sri Lankan) represent the two largest visible minority groups in Canada, comprising 21% and 25% of Canada's visible minority population respectively.[3] Canada's healthcare system is a publicly funded system that aims to provide universal healthcare insurance for all medically necessary services to all Canadian residents, including citizens, permanent residents and landed immigrants.[5] The publicly funded cancer system clearly needs to meet the unique needs and requirements of the diverse, multicultural population including vulnerable populations. This poses a significant challenge to the Canadian healthcare system as traditionally newcomer and visible minority populations end up in a lower socioeconomic status in their adoptive country, have lower health literacy and less access to healthcare, all of which have been shown to adversely affect cancer outcomes in the U.S.[6-8] Considering the cancer burden in the Ontario population, cancer outcomes in these minority populations are an important aspect in examining the province's single payer cancer system and ensuring equity in the cancer system, a stated goal of Ontario's cancer system.[9]

Significant differences exist between the demographic composition of immigrants and visible minorities between Canada and the United States. In contrast to Canada, the largest minority population in the U.S. is African American.[10] Furthermore, the immigrant experience differs between the two countries as immigrants to the U.S. are less likely to achieve higher levels of education or earn higher

wages than are Canadian immigrants.[11] Moreover, in contrast to the U.S. where illegal immigration is not infrequent,[12] Canadian immigration is overwhelmingly legal**.** There are also considerable variations in the modes of cancer care delivery between the U.S. and the single-payer publically-funded system in Canada. In the U.S. African Americans have been shown to bear a disproportionate burden of cancer death.[13-16] Disparities in cancer follow-up,[17] treatment regimens,[14,18,19] socioeconomic status, health insurance and racial bias[7,8,14,20,21] are thought to underlie these inequitable cancer outcomes. However racial disparities in the U.S. are not limited to African Americans, as Asian Americans (Chinese, Japanese, Korean, Filipino and Vietnamese) have been shown to have lower cancer screening rates,[22-24] and higher cancer mortality than the general population in certain malignancies such as stomach, liver and cervical cancer.[25,26] In Canada, universal healthcare and the differing immigrant experience may address some of these disparities in access to care for immigrant and visible minority population compared to the U.S. However understanding the Canadian experience with ethnicity, immigration status and cancer survival is an important first step before being able to understand the differing effect of the two healthcare systems, and this may be relevant to other countries with universal healthcare systems.

Although immigration might intuitively be thought of as a negative predictor of health, the 'healthy immigrant effect' – in which recent immigrants to a foreign country carry improved health outcomes compared to their adoptive population – has been previously documented.[27-31] Possible explanations for this effect include a positive selection bias whereby healthier individuals of a population are more likely to immigrate than their less healthy counterparts,[32,33] health screening of immigrants prior to acceptance into a country,[27] and relatively healthier habits of immigrants such as lower smoking, alcohol and obesity rates.[34] Although the healthy immigrant effect is generally thought to affect disease incidence, its impact on disease outcomes once a definitive diagnosis is established is less clearly understood. We have previously shown that recent immigrants to Canada have improved

cancer outcomes as compared to the general population, but that this survival advantage diminishes over time and mortality increases with each year spent in Canada.[35] These results suggest a prominent healthy immigrant effect; however, they do not explore the association between ethnicity (i.e., individuals born in Canada that identify as a visible minority ethnicity) and cancer outcomes, which is less well characterized in the literature. Cultural beliefs, health practices, treatment philosophy, social and community supports, and biology can differ amongst a Canadian-born minority population and an immigrant population, and these factors may have important implications for cancer outcomes. It is unknown if ethnicity and immigration status are independently associated with altered cancer outcomes, and the aim of this study is to examine the relationship between ethnicity and immigration and cancer outcomes in the Ontario Cancer System. To this end we investigated cancer outcomes in Chinese and South Asian immigrant and their counterpart Canadian-born populations using a population-based administrative healthcare database.

Methods

Population and data sources

We conducted a population-based retrospective cohort study using anonymized linkable administrative databases housed at the Institute for Clinical Evaluative Sciences (ICES) in Toronto, Ontario. These datasets were linked using unique encoded identifiers and analyzed at ICES. The study population was comprised of all incident cases of lung, colorectal, prostate, breast, head and neck and hematologic malignancies in Ontario diagnosed between January 1st, 2000 and December 31st, 2012 in patients ≥ 18 years of age and with a valid Ontario Health Insurance Plan number during the study time frame from the Ontario Cancer Registry. The end of the study follow-up period was March 31st, 2013. Patients with in-situ or previous malignancies were excluded from the study. Patient cases were ascertained from the Ontario Cancer Registry, which is known to capture 95% of the incident cases in the province.[36,37]

The study cohort was subdivided by ethnicity into Chinese and South Asian (Indian, Pakistani, Bangladeshi and Sri Lankan) populations, and within these ethnicity categories, further classified by immigration status (recent immigrant, non-recent immigrant, Canadian born). Chinese and South Asian ethnicities were identified using a previously-validated algorithm.[38] The algorithm employed surnames to identify patients with Chinese or South Asian ethnicity. Immigration status was defined by time from immigration to Canada to cancer diagnosis, where recent immigrant was between 0–10 years, non-recent immigrant between 11-25 years, and Canadian-born who were non-immigrants (or who had immigrated more than 25 years prior to their cancer diagnosis). Immigration status was identified using the Ontario portion of the Immigration, Refugees, and Citizenship Canada (IRCC)'s Permanent Resident Database, which identifies all legal immigrants who have arrived in Ontario from 1985 onwards. Demographic and disease specific characteristics were collected and described for each group.

Outcomes and data analysis

The primary outcome of the study was time-to-death, which was measured from the time of cancer diagnosis (combined for all cancer types) and up to March 31st, 2013. Cancer-specific mortality was available for all patients diagnosed with cancer prior to January 1st, 2011, with a follow-up period to December 31st, 2011. Cox proportional hazards models were constructed to evaluate the effect of ethnicity and immigration status on the hazard rate for all-cause death, while cause-specific hazard models were used to model the hazard rate for cancer-specific mortality, treating non-cancer mortality as a competing risk.[39] We examined the effect of immigration separately among Chinese and South Asian populations. For example, Canadian-born Chinese, Chinese recent immigrants, and Chinese non-recent immigrants were compared to the general reference population. Similarly, Canadian-born South Asians, South Asian recent immigrants, and South Asian non-recent immigrants were compared to the general reference population. The general reference population consisted of non-Chinese/non-South Asian and non-immigrant patients with a new cancer diagnosis, with the exception of those who had immigrated to Canada prior to 1985 and did not have a corresponding record in the IRCC file and were therefore included in the reference population. We chose to exclude non-Chinese/non-South Asian immigrants from the reference population to isolate ethnicity and immigration status for our comparisons. To control for potential confounding effects, subsequent multivariable analysis was performed to adjust for age, sex, type of cancer, stage at diagnosis, metastatic status, year of cancer diagnosis, rural/urban status, quintile of neighborhood income, and comorbidities. Stage data were available for patients with colorectal, lung, breast and prostate cancer from 2007 onwards and for head and neck partial stage data were available from 2008. When stage data were not available we categorized solid tumors as metastatic or non-metastatic based on ICD10 codes and hematologic cancers as curative or non-curative.[35] Pre-existing comorbidities were categorized using the John

Hopkins weighted Aggregated Diagnosis Groups (ADGs) comorbidity score.[40] Quintile of neighborhood income was identified by linkage of the patient postal code from the Registered Persons Database to Statistics Canada 2006 Census data on average household income by postal code.

Secondary analysis was performed to investigate mortality stratified by cancer type. We matched Canadian-born Chinese and South Asian patients to the general population for the secondary analysis to isolate the impact of ethnicity on cancer outcomes given the heterogeneous nature of the study population. Matching occurred in a 1:1 ratio for age (+/-1 year), diagnosis (cancer type), year of cancer diagnosis, urban or rural status, stage at diagnosis, and sex where appropriate. We adjusted for comorbidity and socioeconomic status in subsequent regression analyses but did not match for these variables due to less consistently available data. Matching was done without replacement.

All analyses were performed with SAS 9.1.3 (SAS Institute, Cary, NC), and statistical significance was determined using 95% confidence intervals in order to estimate the effect sizes. No adjustments to the confidence intervals for multiple comparisons were made. The proportional hazards assumption was assessed for all Cox models using a log(-log(survival)) plot and a model with time-dependent covariate (time and log(time)) and no violation of the assumption was found. The study was approved by the Sunnybrook Health Sciences Centre Institutional review board, Toronto, Canada.

Results

Demographics

A total of 423,678 cancer cases were identified and included in the study cohort: 6,631 cancer cases were diagnosed in Canadian-born Chinese and 2,752 cancer cases were diagnosed in Canadian-born South Asians. 2,022 and 3,190 cancer cases were diagnosed in Chinese immigrants (recent and non-recent), and 1,009 and 1,339 cancer cases were diagnosed in South Asian immigrants (recent and non-recent). Canadian-born Chinese were more likely to be female (49.8% vs. 46.8% vs. 45.5%), be diagnosed with colorectal cancer (22.4% vs. 14.5% vs. 18.8%) and have less comorbid disease (ADG comorbidity score 13 vs. 15 vs. 16) compared to the Canadian-born South Asian and general populations, respectively. Recent Chinese immigrants were more likely to be female (55.9% vs. 50.5% vs. 45.5%), be diagnosed with colorectal cancer (20.3% vs. 7.3% vs. 18.8%) and have less comorbid disease (ADG comorbidity score 10 vs. 12 vs. 16) compared to recent South Asian immigrant and general populations, respectively. Demographic data are shown in Table 1.

Main analyses

Univariate analysis showed that the rate of all-cause and cancer-specific mortality was lower in Canadian-born Chinese and Canadian-born South Asian populations, as compared to the general population (Table 2). On multivariable analysis ethnicity retained its protective effect; the hazard rate for all-cause mortality was lower in Canadian-born Chinese (HR 0.829; 95% CI 0.795-0.865) and Canadian-born South Asian (HR 0.856; 95% CI 0.797-0.919) populations compared to the general population. A similar effect was found for cancer-specific mortality for Canadian-born Chinese (HR 0.853; 95% CI 0.812-0.897) and Canadian-born South Asians (HR 0.871; 95% CI 0.796-0.952). Multivariable analysis also showed that the rate of all-cause and cancer-specific mortality was lower in

Chinese immigrants (recent and non-recent) compared to the general population, and a similar trend was found for South Asian immigrants (Table 2).

To isolate the impact of ethnicity on outcomes, secondary univariate analyses based on Canadian-born Chinese and Canadian-born South Asian populations matched to the general population showed that Canadian-born Chinese had lower rates of all-cause and cancer-specific mortality for all the cancer subtypes with the exception of cancer-specific mortality for hematologic malignancies (Table 3). After adjusting for between-group differences, multivariable analyses showed that the lower rate of mortality for Canadian-born Chinese remained significant for lung (all-cause: HR 0.605; 95% CI 0.512-0.715; cancer-specific HR 0.593; 95% CI 0.491-0.717) and prostate (all-cause HR 0.704; 95% CI 0.503-0.985) cancer (Table 3).

Discussion

In this population-based retrospective cohort study we found that after removing the well-documented protective effect of immigration,[27-31] Chinese and South Asian ethnicities are associated with improved cancer outcomes. In particular, Canadian-born Chinese and South Asians have lower all-cause and cancer-specific mortality than the general Ontario population. A survival advantage was also found in Chinese immigrants (recent and non-recent), with a trend towards survival in South Asian immigrants (recent and non-recent). While improved cancer outcomes have been shown in Asian (Chinese, Japanese, Filipino, Korean, Vietnamese) populations in North America,[8,41-46] these studies have not separated the impact of immigration status from ethnicity. Thus, the results of this study are important in that they begin to disentangle the relative effects of immigration and ethnicity on cancer outcomes, highlighting a survival advantage associated with Chinese and South Asian ethnicities in Ontario, Canada that was independent of immigration.

The literature on the effect of Asian ethnicity on cancer outcomes remains controversial. Some studies have shown a protective effect of Asian ethnicity,[8,41-46] whereas some have not supported this,[47-49] and other research suggests variable outcomes with Korean Americans demonstrating worse and Japanese Americans demonstrating improved cancer survival compared to Caucasians.[50] Other studies have shown overall better cancer outcomes in Asian Americans but with worse outcomes in individual cancers such as breast and lung.[44,51] A Canadian study has shown that female Chinese Canadians have lower breast and cervical cancer mortality while South Asian Canadians have lower colorectal cancer mortality than the general British Columbia population, however immigrant and Canadian-born Chinese and South Asians were grouped together making it difficult to determine whether this is predominantly an effect of immigration or ethnicity.[43] Our study found a persistent survival advantage among Chinese cancer patients in Canada, whether immigrant or Canadian-born, arguing for a potential biologic

advantage, cultural advantage (for example increased family/caregiver support) or even perhaps an altered treatment philosophy due to cultural differences (for example increased aggressive treatment with anti-neoplastic agents). Interestingly Chinese, Japanese and Filipino American women have been previously shown to be more likely than non-Asian American women to pursue more aggressive cancer treatment for early stage breast cancer.[52-54] Thus, cultural beliefs and approaches to treatment of the Chinese ethnic population may have an important role in improved cancer survival in Canadian-born and immigrant Chinese. However, further work needs to be done to better understand the complex relationship between ethnicity, immigration status and cancer outcomes.

An important consideration is the possibility of altered or significant differences in tumor biology in Chinese vs. non-Chinese cancer patients. Our secondary analysis showed the trend of survival advantage for Chinese ethnicity across all cancers, but was statistically significant for lung and prostate cancers. This secondary analysis is hypothesis generating in that a closer examination of lung and prostate cancer in Chinese patients may reveal significant differences in tumor biology from Western patients. This is in keeping with previous research showing Asian ethnicity to be a favorable prognostic factor for survival in non-small cell lung cancer that is independent of smoking status, and differences in tumor biology and EGFR status were postulated to underlie this effect.[45] Although our results may suggest an underlying difference in tumor biology between Chinese and non-Chinese in certain malignancies, more research in this area is clearly needed.

While one may intuitively infer that immigrants and minority ethnic groups might have worse cancer outcomes due to associated hardships of immigration, assimilation barriers or lower socioeconomic status often seen in minority populations, the results of our study indicate that Chinese immigrants have better cancer outcomes than the general Ontario population. The 'healthy immigrant

effect' has been well documented where despite the difficulties of immigration the general health of new immigrants is improved over that of their adoptive population.[27-31] Our group has recently shown the healthy immigrant effect on cancer outcomes in a general immigrant population in Ontario, where with each year after immigration their cancer outcome regresses to that of the Canadian population.[35] The results of this study argue against the usually temporary 'healthy immigrant' effect, as non-recent immigrants with up to 25 years between immigration and diagnosis still retain a survival advantage. This is in contrast to the literature where with time immigrants usually undergo a process of acculturation, develop poorer health habits, and face pressures associated with lower socioeconomic status, all of which contribute to the decline in health with increasing years since immigration.[27,29,30] Although there was an increase in the hazard rate in non-recent compared to recent Chinese immigrants suggesting a degree of acculturation that negatively impacted cancer survival, non-recent Chinese immigrants still retained a significantly lower hazard rate compared to the general reference population. This finding is suggestive of a more permanent etiology for improved cancer outcomes in Chinese ethnic groups whether biological, cultural or behavioral in nature, and future research in this area is needed.

Similar to Canadian-born Chinese, Canadian-born South Asians also demonstrated a lower rate of cancer mortality than the general population indicating that South Asian ethnicity is associated with improved cancer outcomes. Although there was a trend towards improved survival in the South Asian immigrant population, this did not reach statistical significance. Moreover, the survival pattern differed between South Asian and Chinese immigrants, such that the hazard ratio was lower for non-recent South Asian immigrants compared to recent South Asian immigrants suggesting their cancer survival improved with time since immigration. However it is difficult to interpret this pattern as the South Asian population had a much smaller sample size than the Chinese population and this differing pattern of mortality may be a result of the smaller sample size. It is interesting to note that the multivariable

adjustment had a larger impact on cancer survival in the South Asian compared to Chinese populations. However, as the multivariable models were the same between the Chinese and South Asian populations this is also likely related to the smaller South Asian sample size. More research is warranted to further explore the effect of immigration on cancer survival in a South Asian population to determine if a persistent cancer survival advantage exists as seen in Chinese immigrants.

In contrast to the current results, ethnic differences in cancer survival in the U.S. exist whereby non-white minority populations demonstrate higher rates of cancer mortality than the majority Caucasian population.[13-16,25,48,49] Much of the literature in the U.S. has focused on the ethnic disparity in cancer outcomes between African American and white populations,[13-16] and this ethnic disparity in cancer survival is increasing over time.[16] However, poorer cancer outcomes in the U.S. are not only found in African Americans, as Asian ethnicity and immigrant status in the U.S. have been associated with worse cancer outcomes in certain cancer types. Asian and Pacific Islanders in the U.S. have higher stomach, liver and cervical cancer mortality than Caucasians,[25,26,49] and South Asians have a lower overall cancer survival compared to the U.S. Caucasian population.[48] Moreover, Chinese, Japanese and Filipino immigrants have a lower life expectancy and higher cancer mortality compared to a U.S. non-immigrant population.[25] Healthcare utilization has been shown to be lower in Asian Americans as lower breast and cervical cancer screening rates have been demonstrated in this population compared to Caucasians.[22-24] Interestingly, a lack of healthcare insurance in the U.S. disproportionately impacts Asian Americans, as 48% of uninsured Asian Americans did not have cervical cancer screening compared to 7% of uninsured Caucasians.[22] Access to private healthcare insurance [55,56] and regular healthcare[24,57] have consistently been shown to be among the strongest predictors of decreased cancer screening in Asian American populations. The disparity between the U.S. results and the current findings may suggest that easier access to care in a Canadian single-payer system contribute to improved cancer outcomes in Canadian-

born and immigrant Chinese and South Asians. However as the purpose of this study was to describe the Canadian experience with Chinese/South Asian ethnicity, immigration status and cancer outcomes it is difficult to draw any conclusions regarding the impact of differing healthcare systems on the current results. The relationship between modes of cancer care delivery between a private and public health care system and outcomes on vulnerable and minority populations needs to be further explored.

Limitations of this study include a lack of immigration status information prior to 1985. As a result, the general reference population may include immigrants (non-Asian) who came to Canada prior to 1985 who were not classified as immigrant. However as data were collected on incident cancer cases from 2000 onwards and immigration status was limited up to 25 years prior to diagnosis there is a relatively small window of immigration between 1975 and 1984 in which a patient could be non-classified. Therefore the non-classified immigrant patients are likely to be a very small percentage of the 406,735 patients in the reference population. Moreover this effect would likely bias the results towards the null hypothesis as Canadian immigrants have been shown to have improved cancer survival over the non-immigrant Canadian population.[35] A second limitation is the use of a name algorithm to detect Chinese and South Asian ethnicities, which excludes patients with names shared by two ethnicities and as a result its sensitivity is lower than its specificity. This may result in certain subgroups with common last names being excluded from our study. Thirdly, despite our best attempts to control for confounding factors we realize that there are many factors that may differ between ethnic and immigrant populations that are not identifiable in large administrative databases, such as differing levels of community/social supports and degree of acculturation. Fourth, we did not include cancer treatment as a covariate in the multivariable analysis as our initial research aim was to determine the effect of ethnicity and immigration on cancer outcomes as a predictor of cancer outcomes present at the index date (at the baseline time of cancer diagnosis). However exploring the impact of treatment on the

improved survival associated with Chinese and South Asian ethnicity, and how ethnicity might impact cancer treatment and the quality of cancer care, is the subject of future work. Fifth, although including urban/rural status as a covariate in the multivariable analysis is important due to the large geographical size of Ontario, the small proportion of rural patients in the Chinese and South Asian immigrant groups may lead to model instabilities. Lastly, the retrospective nature and use of an administrative database in this study prevents the ability to identify more specific family and cultural issues (such as attitude to treatments or decision-making processes) that may underpin the results of this study.

In conclusion, our study shows that Chinese and South Asian ethnic groups have lower cancer mortalities than the general non-immigrant Ontario population. These findings indicate that after removing the well-documented protective effect of immigration, Chinese and South Asian ethnicities are associated with a cancer survival advantage in Ontario.

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Author contributions

James Stevenson: Formal analysis, investigation, methodology, project administration, validation, visualization, writing – original draft, writing – review and editing. **Matthew Cheung**: Data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, writing- original draft, writing – review and editing. **Craig Earle**: Data curation, formal analysis, funding acquisition, investigation, methodology, project administration,

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Table 1. Demographics.

	Ethnic group: Chinese			Ethnic group: South Asian			Ethnic group: General Population
	Canadian-born	Recent immigrant	Non-recent immigrant	Canadian-born	Recent immigrant	Non-recent immigrant	Non-Chinese/Non-South Asian
N	6,631	2,022	3,190	2,752	1,009	1,339	406,735
Age at cancer diagnosis date							
Median (IQR)	64 (54-74)	61 (45-71)	65 (51-77)	63 (54-71)	61 (50-68)	65 (52-74)	67 (58-76)
Sex							
Female	3,303 (49.8%)	1,130 (55.9%)	1,621 (50.8%)	1,287 (46.8%)	510 (50.5%)	630 (47.1%)	184,955 (45.5%)
Male	3,328 (50.2%)	892 (44.1%)	1,569 (49.2%)	1,465 (53.2%)	499 (49.5%)	709 (52.9%)	221,780 (54.5%)
Urban residence							
Yes	-	-	-	-	-	-	340,613 (83.7%)
Income quintile							
Q1 (lowest)	1,156 (17.4%)	451 (22.3%)	673 (21.1%)	471 (17.1%)	299 (29.6%)	341 (25.5%)	75,331 (18.5%)
Q5 (highest)	1,352 (20.4%)	258 (12.8%)	469 (14.7%)	549 (19.9%)	68 (6.7%)	122 (9.1%)	86,456 (21.3%)
Cancer type							
Breast	1,681 (25.4%)	629 (31.1%)	824 (25.8%)	827 (30.1%)	338 (33.5%)	411 (30.7%)	84,161 (20.7%)
Colorectal	1,485 (22.4%)	410 (20.3%)	734 (23.0%)	399 (14.5%)	74 (7.3%)	146 (10.9%)	76,493 (18.8%)
Head & neck	389 (5.9%)	165 (8.2%)	166 (5.2%)	131 (4.8%)	78 (7.7%)	88 (6.6%)	14,518 (3.6%)
Lung	1,165 (17.6%)	359 (17.8%)	640 (20.1%)	247 (9.0%)	61 (6.0%)	130 (9.7%)	81,952 (20.1%)
Hematologic	692 (10.4%)	234 (11.6%)	299 (9.4%)	440 (16.0%)	192 (19.0%)	222 (16.6%)	52,185 (12.8%)
Prostate	1,219 (18.4%)	225 (11.1%)	527 (16.5%)	708 (25.7%)	266 (26.4%)	342 (25.5%)	97,426 (24.0%)
Stage							
No stage data	2,811 (47.3%)	1,025 (57.3%)	1,215 (42.0%)	1,087 (47.0%)	451 (55.2%)	482 (43.2%)	174,796 (49.3%)
Stage I	770 (13.0%)	196 (11.0%)	454 (15.7%)	272 (11.8%)	53 (6.5%)	134 (12.0%)	36,168 (10.2%)
Stage II	1,184 (19.9%)	264 (14.8%)	566 (19.6%)	565 (24.4%)	187 (22.9%)	270 (24.2%)	70,713 (19.9%)
Stage III	577 (9.7%)	180 (10.1%)	358 (12.4%)	231 (10.0%)	61 (7.5%)	119 (10.7%)	35,364 (10.0%)
Stage IV	597 (10.1%)	123 (6.9%)	298 (10.3%)	157 (6.8%)	65 (8.0%)	112 (10.0%)	37,509 (10.6%)
No stage data available	N=2,811	N=1,025	N=1,215	N=1,087	N=451	N=482	N=174,796
Metastasis	546 (19.4%)	199 (19.4%)	225 (18.5%)	132 (12.1%)	50 (11.1%)	55 (11.4%)	33,995 (19.4%)
No hospital data	406 (14.4%)	153 (14.9%)	198 (16.3%)	183 (16.8%)	89 (19.7%)	71 (14.7%)	23,920 (13.7%)
No metastasis	1,859 (66.1%)	673 (65.7%)	792 (65.2%)	772 (71.0%)	312 (69.2%)	356 (73.9%)	116,881 (66.9%)
Peri-diagnostic chemotherapy							
Yes	2,360 (35.6%)	873 (43.2%)	1,153 (36.1%)	970 (35.2%)	394 (39.0%)	501 (37.4%)	120,904 (29.7%)
Peri-diagnostic							

radiation therapy							
Yes	2,249 (33.9%)	633 (31.3%)	1,086 (34.0%)	995 (36.2%)	353 (35.0%)	511 (38.2%)	127,417 (31.3%)
Weighted ADG comorbidity score							
Median (IQR)	13 (5-21)	10 (4-19)	13 (5-21)	15 (6-22)	12 (5-20)	14 (6-23)	16 (6-25)

*Urban status data not shown for select groups due to a small cell in order to protect privacy.

Table 2A: All-cause mortality (all cancer combined)

	Ethnic group: Chinese			Ethnic group: South Asian		
	Canadian-born	Recent immigrant	Non-recent immigrant	Canadian-born	Recent immigrant	Non-recent immigrant
Number of events	2,269	608	1,069	762	279	381
Unadjusted Hazard ratio (95% C.I.)	0.753 (0.723-0.785)	0.583 (0.538-0.631)	0.828 (0.780-0.880)	0.582 (0.542-0.625)	0.561 (0.499-0.631)	0.670 (0.606-0.741)
Adjusted Hazard ratio (95% C.I.)	0.829 (0.795-0.865)	0.661 (0.610-0.716)	0.853 (0.803-0.906)	0.856 (0.797-0.919)	0.923 (0.821-1.039)	0.914 (0.826-1.011)
*Reference group: Non-Chinese/non-South Asian and non-immigrant general population						

Table 2B: Cancer specific mortality (all cancer combined)

	Ethnic group: Chinese			Ethnic group: South Asian		
	Canadian-born	Recent immigrant	Non-recent immigrant	Canadian-born	Recent immigrant	Non-recent immigrant
Number of events	1623	465	731	486	188	220
Unadjusted Hazard ratio (95% C.I.)	0.828 (0.788-0.870)	0.678 (0.619-0.743)	0.887 (0.825-0.954)	0.579 (0.529-0.633)	0.572 (0.496-0.660)	0.614 (0.538-0.700)
Adjusted Hazard ratio (95% C.I.)	0.853 (0.812-0.897)	0.689 (0.629-0.755)	0.876 (0.814-0.943)	0.871 (0.796-0.952)	0.921 (0.798-1.063)	0.876 (0.767-1.000)
*Reference group: Non-Chinese/non-South Asian and non-immigrant general population						

Table 3A. All-cause mortality by cancer type for Canadian-born Chinese and South Asians.

	Canadian-born Chinese				Canadian-born South Asian			
	Number of matched patients	**Number of events**	**Unadjusted Hazard Ratio (95% C.I.)**	**Adjusted Hazard Ratio (95% C.I.)**	**Number of matched patients**	**Number of events**	**Unadjusted Hazard Ratio (95% C.I.)**	**Adjusted Hazard Ratio (95% C.I.)**
Breast cancer	1674	219	0.687 (0.561-0.841)	0.848 (0.647-1.112)	823	117	0.878 (0.672-1.147)	0.941 (0.668-1.327)
Colorectal cancer	1467	566	0.837 (0.730-0.961)	0.924 (0.764-1.117)	392	129	0.804 (0.605-1.068)	1.046 (0.700-1.565)
Head and neck cancer	360	91	0.619 (0.454-0.843)	0.723 (0.450-1.162)	121	39	1.269 (0.759-2.122)	2.564 (0.752-8.738)
Lung cancer	1141	864	0.606 (0.534-0.687)	0.605 (0.512-0.715)	245	183	0.810 (0.621-1.057)	0.906 (0.627-1.310)
Hematologic cancer	660	308	0.963 (0.797-1.165)	1.03 (0.803-1.321)	421	175	0.984 (0.770-1.259)	1.020 (0.727-1.432)
Prostate cancer	1218	171	0.678 (0.537-0.857)	0.704 (0.503-0.985)	705	102	0.854 (0.636-1.147)	0.773 (0.510-1.170)

*Reference group: Non-Chinese/non-South Asian and non-immigrant general population

Table 3B. Cancer-specific mortality by cancer type for Canadian-born Chinese and South Asians.

	Canadian-born Chinese				Canadian-born South Asian			
	Number of matched patients	Number of events	Unadjusted Hazard Ratio (95% C.I.)	Adjusted Hazard Ratio (95% C.I.)	Number of matched patients	Number of events	Unadjusted Hazard Ratio (95% C.I.)	Adjusted Hazard Ratio (95% C.I.)
Breast cancer	1674	132	0.680 (0.529-0.874)	0.803 (0.565-1.142)	823	76	0.759 (0.551-1.045)	0.794 (0.518-1.217)
Colorectal cancer	1467	407	0.861 (0.730-1.016)	0.900 (0.719-1.128)	392	97	0.956 (0.680-1.343)	1.319 (0.822-2.115)
Head and neck cancer	360	70	0.667 (0.469-0.947)	0.568 (0.315-1.026)	121	29	2.273 (1.118-4.619)	-
Lung cancer	1141	704	0.615 (0.534-0.708)	0.593 (0.491-0.717)	245	129	0.756 (0.551-1.035)	0.734 (0.465-1.159)
Hematologic cancer	660	198	1.099 (0.859-1.406)	1.281 (0.922-1.780)	421	105	1.055 (0.766-1.453)	1.169 (0.720-1.896)
Prostate cancer	1218	80	0.822 (0.584-1.157)	0.953 (0.540-1.683)	705	38	0.727 (0.461-1.147)	0.543 (0.243-1.213)

*Reference group: Non-Chinese/non-South Asian and non-immigrant general population

Chinese and South Asian ethnicity, immigration status and clinical cancer outcomes in the Ontario Cancer System

Running head: Ethnicity and cancer outcomes

Precis: Chinese and South Asian ethnic groups have lower cancer mortality than the general (non-Chinese/non-South Asian and non-immigrant) Ontario population. After removing the well-documented protective effect of immigration, Chinese and South Asian ethnicity is associated with a cancer survival advantage in Ontario, Canada.

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Keywords: Ethnicity, cancer survival, immigration, Chinese, South Asian
Conflicts of Interest: None

Abstract

Background

In the United States, certain minority groups have been shown to have inferior cancer outcomes as compared to the Caucasian majority population; however, most research has not separated ethnicity from immigration status. The aim of this study was to determine the impact of ethnicity, independent of immigration status, on cancer outcomes in Chinese and South Asian populations in Ontario, Canada.

Methods

We conducted a population-based retrospective cohort study using administrative databases in Ontario, Canada. Incident cancer cases were captured in Canadian-born Chinese and South Asians, Chinese and South Asian immigrants, and the general Ontario reference population (non-Chinese/South Asian and non-immigrant) between 2000 and 2012. Subjects were followed until death (all-cause and cancer-specific), and Cox proportional hazard models were used to estimate the impact of Chinese and South Asian ethnicity on cancer outcomes, after adjusting for explanatory variables.

Results

423,678 cancer cases were identified: 6,631 in Canadian-born Chinese and 2,752 in Canadian-born South Asians. Following adjustment, the rate of all-cause mortality was lower for Canadian-born Chinese (HR 0.829; 95% CI 0.795-0.865), Canadian-born South Asian (HR 0.856; 95% CI 0.797-0.919), and Chinese immigrant (recent: HR 0.661; 95% CI 0.610-0.716; non-recent: HR 0.853; 95% CI 0.803-0.906) populations, compared to the general Ontario population. A similar effect was found for cancer-specific mortality.

Conclusions

Chinese and South Asian ethnic groups have lower cancer mortalities than the general Ontario population. After removing the well-documented protective effect of immigration, Chinese and South Asian ethnicities are associated with a cancer survival advantage in Ontario, Canada.

Introduction

Cancer represents a significant burden of disease in Canada, where 40% of Canadians will be diagnosed with a malignancy in their lifetime,[1] and 25% of people living in Ontario, Canada are expected to die of cancer in their lifetime.[2] Canada is a very heterogeneous and multicultural nation with a diverse ethnic and immigrant population, and nearly one in five Canadians identify as a visible minority group[3] defined as "persons, other than Aboriginal peoples, who are non-Caucasian in race or non-white in colour".[4] Chinese and South Asians (Indian, Pakistani, Bangladeshi and Sri Lankan) represent the two largest visible minority groups in Canada, comprising 21% and 25% of Canada's visible minority population respectively.[3] Canada's healthcare system is a publicly funded system that aims to provide universal healthcare insurance for all medically necessary services to all Canadian residents, including citizens, permanent residents and landed immigrants.[5] The publicly funded cancer system clearly needs to meet the unique needs and requirements of the diverse, multicultural population including vulnerable populations. This poses a significant challenge to the Canadian healthcare system as traditionally newcomer and visible minority populations end up in a lower socioeconomic status in their adoptive country, have lower health literacy and less access to healthcare, all of which have been shown to adversely affect cancer outcomes in the U.S.[6-8] Considering the cancer burden in the Ontario population, cancer outcomes in these minority populations are an important aspect in examining the province's single payer cancer system and ensuring equity in the cancer system, a stated goal of Ontario's cancer system.[9]

Significant differences exist between the demographic composition of immigrants and visible minorities between Canada and the United States. In contrast to Canada, the largest minority population in the U.S. is African American.[10] Furthermore, the immigrant experience differs between the two countries as immigrants to the U.S. are less likely to achieve higher levels of education or earn higher

wages than are Canadian immigrants.[11] Moreover, in contrast to the U.S. where illegal immigration is not infrequent,[12] Canadian immigration is overwhelmingly legal**.** There are also considerable variations in the modes of cancer care delivery between the U.S. and the single-payer publically-funded system in Canada. In the U.S. African Americans have been shown to bear a disproportionate burden of cancer death.[13-16] Disparities in cancer follow-up,[17] treatment regimens,[14,18,19] socioeconomic status, health insurance and racial bias[7,8,14,20,21] are thought to underlie these inequitable cancer outcomes. However racial disparities in the U.S. are not limited to African Americans, as Asian Americans (Chinese, Japanese, Korean, Filipino and Vietnamese) have been shown to have lower cancer screening rates,[22-24] and higher cancer mortality than the general population in certain malignancies such as stomach, liver and cervical cancer.[25,26] In Canada, universal healthcare and the differing immigrant experience may address some of these disparities in access to care for immigrant and visible minority population compared to the U.S. However understanding the Canadian experience with ethnicity, immigration status and cancer survival is an important first step before being able to understand the differing effect of the two healthcare systems, and this may be relevant to other countries with universal healthcare systems.

Although immigration might intuitively be thought of as a negative predictor of health, the 'healthy immigrant effect' – in which recent immigrants to a foreign country carry improved health outcomes compared to their adoptive population – has been previously documented.[27-31] Possible explanations for this effect include a positive selection bias whereby healthier individuals of a population are more likely to immigrate than their less healthy counterparts,[32,33] health screening of immigrants prior to acceptance into a country,[27] and relatively healthier habits of immigrants such as lower smoking, alcohol and obesity rates.[34] Although the healthy immigrant effect is generally thought to affect disease incidence, its impact on disease outcomes once a definitive diagnosis is established is less clearly understood. We have previously shown that recent immigrants to Canada have improved

cancer outcomes as compared to the general population, but that this survival advantage diminishes over time and mortality increases with each year spent in Canada.[35] These results suggest a prominent healthy immigrant effect; however, they do not explore the association between ethnicity (i.e., individuals born in Canada that identify as a visible minority ethnicity) and cancer outcomes, which is less well characterized in the literature. Cultural beliefs, health practices, treatment philosophy, social and community supports, and biology can differ amongst a Canadian-born minority population and an immigrant population, and these factors may have important implications for cancer outcomes. It is unknown if ethnicity and immigration status are independently associated with altered cancer outcomes, and the aim of this study is to examine the relationship between ethnicity and immigration and cancer outcomes in the Ontario Cancer System. To this end we investigated cancer outcomes in Chinese and South Asian immigrant and their counterpart Canadian-born populations using a population-based administrative healthcare database.

Methods

Population and data sources

We conducted a population-based retrospective cohort study using anonymized linkable administrative databases housed at the Institute for Clinical Evaluative Sciences (ICES) in Toronto, Ontario. These datasets were linked using unique encoded identifiers and analyzed at ICES. The study population was comprised of all incident cases of lung, colorectal, prostate, breast, head and neck and hematologic malignancies in Ontario diagnosed between January 1st, 2000 and December 31st, 2012 in patients ≥ 18 years of age and with a valid Ontario Health Insurance Plan number during the study time frame from the Ontario Cancer Registry. The end of the study follow-up period was March 31st, 2013. Patients with in-situ or previous malignancies were excluded from the study. Patient cases were ascertained from the Ontario Cancer Registry, which is known to capture 95% of the incident cases in the province.[36,37]

The study cohort was subdivided by ethnicity into Chinese and South Asian (Indian, Pakistani, Bangladeshi and Sri Lankan) populations, and within these ethnicity categories, further classified by immigration status (recent immigrant, non-recent immigrant, Canadian born). Chinese and South Asian ethnicities were identified using a previously-validated algorithm.[38] The algorithm employed surnames to identify patients with Chinese or South Asian ethnicity. Immigration status was defined by time from immigration to Canada to cancer diagnosis, where recent immigrant was between 0–10 years, non-recent immigrant between 11-25 years, and Canadian-born who were non-immigrants (or who had immigrated more than 25 years prior to their cancer diagnosis). Immigration status was identified using the Ontario portion of the Immigration, Refugees, and Citizenship Canada (IRCC)'s Permanent Resident Database, which identifies all legal immigrants who have arrived in Ontario from 1985 onwards. Demographic and disease specific characteristics were collected and described for each group.

Outcomes and data analysis

The primary outcome of the study was time-to-death, which was measured from the time of cancer diagnosis (combined for all cancer types) and up to March 31st, 2013. Cancer-specific mortality was available for all patients diagnosed with cancer prior to January 1st, 2011, with a follow-up period to December 31st, 2011. Cox proportional hazards models were constructed to evaluate the effect of ethnicity and immigration status on the hazard rate for all-cause death, while cause-specific hazard models were used to model the hazard rate for cancer-specific mortality, treating non-cancer mortality as a competing risk.[39] We examined the effect of immigration separately among Chinese and South Asian populations. For example, Canadian-born Chinese, Chinese recent immigrants, and Chinese non-recent immigrants were compared to the general reference population. Similarly, Canadian-born South Asians, South Asian recent immigrants, and South Asian non-recent immigrants were compared to the general reference population. The general reference population consisted of non-Chinese/non-South Asian and non-immigrant patients with a new cancer diagnosis, with the exception of those who had immigrated to Canada prior to 1985 and did not have a corresponding record in the IRCC file and were therefore included in the reference population. We chose to exclude non-Chinese/non-South Asian immigrants from the reference population to isolate ethnicity and immigration status for our comparisons. To control for potential confounding effects, subsequent multivariable analysis was performed to adjust for age, sex, type of cancer, stage at diagnosis, metastatic status, year of cancer diagnosis, rural/urban status, quintile of neighborhood income, and comorbidities. Stage data were available for patients with colorectal, lung, breast and prostate cancer from 2007 onwards and for head and neck partial stage data were available from 2008. When stage data were not available we categorized solid tumors as metastatic or non-metastatic based on ICD10 codes and hematologic cancers as curative or non-curative.[35] Pre-existing comorbidities were categorized using the John

Hopkins weighted Aggregated Diagnosis Groups (ADGs) comorbidity score.[40] Quintile of neighborhood income was identified by linkage of the patient postal code from the Registered Persons Database to Statistics Canada 2006 Census data on average household income by postal code.

Secondary analysis was performed to investigate mortality stratified by cancer type. We matched Canadian-born Chinese and South Asian patients to the general population for the secondary analysis to isolate the impact of ethnicity on cancer outcomes given the heterogeneous nature of the study population. Matching occurred in a 1:1 ratio for age (+/-1 year), diagnosis (cancer type), year of cancer diagnosis, urban or rural status, stage at diagnosis, and sex where appropriate. We adjusted for comorbidity and socioeconomic status in subsequent regression analyses but did not match for these variables due to less consistently available data. Matching was done without replacement.

All analyses were performed with SAS 9.1.3 (SAS Institute, Cary, NC), and statistical significance was determined using 95% confidence intervals in order to estimate the effect sizes. No adjustments to the confidence intervals for multiple comparisons were made. The proportional hazards assumption was assessed for all Cox models using a log(-log(survival)) plot and a model with time-dependent covariate (time and log(time)) and no violation of the assumption was found. The study was approved by the Sunnybrook Health Sciences Centre Institutional review board, Toronto, Canada.

Results

Demographics

A total of 423,678 cancer cases were identified and included in the study cohort: 6,631 cancer cases were diagnosed in Canadian-born Chinese and 2,752 cancer cases were diagnosed in Canadian-born South Asians. 2,022 and 3,190 cancer cases were diagnosed in Chinese immigrants (recent and non-recent), and 1,009 and 1,339 cancer cases were diagnosed in South Asian immigrants (recent and non-recent). Canadian-born Chinese were more likely to be female (49.8% vs. 46.8% vs. 45.5%), be diagnosed with colorectal cancer (22.4% vs. 14.5% vs. 18.8%) and have less comorbid disease (ADG comorbidity score 13 vs. 15 vs. 16) compared to the Canadian-born South Asian and general populations, respectively. Recent Chinese immigrants were more likely to be female (55.9% vs. 50.5% vs. 45.5%), be diagnosed with colorectal cancer (20.3% vs. 7.3% vs. 18.8%) and have less comorbid disease (ADG comorbidity score 10 vs. 12 vs. 16) compared to recent South Asian immigrant and general populations, respectively. Demographic data are shown in Table 1.

Main analyses

Univariate analysis showed that the rate of all-cause and cancer-specific mortality was lower in Canadian-born Chinese and Canadian-born South Asian populations, as compared to the general population (Table 2). On multivariable analysis ethnicity retained its protective effect; the hazard rate for all-cause mortality was lower in Canadian-born Chinese (HR 0.829; 95% CI 0.795-0.865) and Canadian-born South Asian (HR 0.856; 95% CI 0.797-0.919) populations compared to the general population. A similar effect was found for cancer-specific mortality for Canadian-born Chinese (HR 0.853; 95% CI 0.812-0.897) and Canadian-born South Asians (HR 0.871; 95% CI 0.796-0.952). Multivariable analysis also showed that the rate of all-cause and cancer-specific mortality was lower in

Chinese immigrants (recent and non-recent) compared to the general population, and a similar trend was found for South Asian immigrants (Table 2).

To isolate the impact of ethnicity on outcomes, secondary univariate analyses based on Canadian-born Chinese and Canadian-born South Asian populations matched to the general population showed that Canadian-born Chinese had lower rates of all-cause and cancer-specific mortality for all the cancer subtypes with the exception of cancer-specific mortality for hematologic malignancies (Table 3). After adjusting for between-group differences, multivariable analyses showed that the lower rate of mortality for Canadian-born Chinese remained significant for lung (all-cause: HR 0.605; 95% CI 0.512-0.715; cancer-specific HR 0.593; 95% CI 0.491-0.717) and prostate (all-cause HR 0.704; 95% CI 0.503-0.985) cancer (Table 3).

Discussion

In this population-based retrospective cohort study we found that after removing the well-documented protective effect of immigration,[27-31] Chinese and South Asian ethnicities are associated with improved cancer outcomes. In particular, Canadian-born Chinese and South Asians have lower all-cause and cancer-specific mortality than the general Ontario population. A survival advantage was also found in Chinese immigrants (recent and non-recent), with a trend towards survival in South Asian immigrants (recent and non-recent). While improved cancer outcomes have been shown in Asian (Chinese, Japanese, Filipino, Korean, Vietnamese) populations in North America,[8,41-46] these studies have not separated the impact of immigration status from ethnicity. Thus, the results of this study are important in that they begin to disentangle the relative effects of immigration and ethnicity on cancer outcomes, highlighting a survival advantage associated with Chinese and South Asian ethnicities in Ontario, Canada that was independent of immigration.

The literature on the effect of Asian ethnicity on cancer outcomes remains controversial. Some studies have shown a protective effect of Asian ethnicity,[8,41-46] whereas some have not supported this,[47-49] and other research suggests variable outcomes with Korean Americans demonstrating worse and Japanese Americans demonstrating improved cancer survival compared to Caucasians.[50] Other studies have shown overall better cancer outcomes in Asian Americans but with worse outcomes in individual cancers such as breast and lung.[44,51] A Canadian study has shown that female Chinese Canadians have lower breast and cervical cancer mortality while South Asian Canadians have lower colorectal cancer mortality than the general British Columbia population, however immigrant and Canadian-born Chinese and South Asians were grouped together making it difficult to determine whether this is predominantly an effect of immigration or ethnicity.[43] Our study found a persistent survival advantage among Chinese cancer patients in Canada, whether immigrant or Canadian-born, arguing for a potential biologic

advantage, cultural advantage (for example increased family/caregiver support) or even perhaps an altered treatment philosophy due to cultural differences (for example increased aggressive treatment with anti-neoplastic agents). Interestingly Chinese, Japanese and Filipino American women have been previously shown to be more likely than non-Asian American women to pursue more aggressive cancer treatment for early stage breast cancer.[52-54] Thus, cultural beliefs and approaches to treatment of the Chinese ethnic population may have an important role in improved cancer survival in Canadian-born and immigrant Chinese. However, further work needs to be done to better understand the complex relationship between ethnicity, immigration status and cancer outcomes.

An important consideration is the possibility of altered or significant differences in tumor biology in Chinese vs. non-Chinese cancer patients. Our secondary analysis showed the trend of survival advantage for Chinese ethnicity across all cancers, but was statistically significant for lung and prostate cancers. This secondary analysis is hypothesis generating in that a closer examination of lung and prostate cancer in Chinese patients may reveal significant differences in tumor biology from Western patients. This is in keeping with previous research showing Asian ethnicity to be a favorable prognostic factor for survival in non-small cell lung cancer that is independent of smoking status, and differences in tumor biology and EGFR status were postulated to underlie this effect.[45] Although our results may suggest an underlying difference in tumor biology between Chinese and non-Chinese in certain malignancies, more research in this area is clearly needed.

While one may intuitively infer that immigrants and minority ethnic groups might have worse cancer outcomes due to associated hardships of immigration, assimilation barriers or lower socioeconomic status often seen in minority populations, the results of our study indicate that Chinese immigrants have better cancer outcomes than the general Ontario population. The 'healthy immigrant

effect' has been well documented where despite the difficulties of immigration the general health of new immigrants is improved over that of their adoptive population.[27-31] Our group has recently shown the healthy immigrant effect on cancer outcomes in a general immigrant population in Ontario, where with each year after immigration their cancer outcome regresses to that of the Canadian population.[35] The results of this study argue against the usually temporary 'healthy immigrant' effect, as non-recent immigrants with up to 25 years between immigration and diagnosis still retain a survival advantage. This is in contrast to the literature where with time immigrants usually undergo a process of acculturation, develop poorer health habits, and face pressures associated with lower socioeconomic status, all of which contribute to the decline in health with increasing years since immigration.[27,29,30] Although there was an increase in the hazard rate in non-recent compared to recent Chinese immigrants suggesting a degree of acculturation that negatively impacted cancer survival, non-recent Chinese immigrants still retained a significantly lower hazard rate compared to the general reference population. This finding is suggestive of a more permanent etiology for improved cancer outcomes in Chinese ethnic groups whether biological, cultural or behavioral in nature, and future research in this area is needed.

Similar to Canadian-born Chinese, Canadian-born South Asians also demonstrated a lower rate of cancer mortality than the general population indicating that South Asian ethnicity is associated with improved cancer outcomes. Although there was a trend towards improved survival in the South Asian immigrant population, this did not reach statistical significance. Moreover, the survival pattern differed between South Asian and Chinese immigrants, such that the hazard ratio was lower for non-recent South Asian immigrants compared to recent South Asian immigrants suggesting their cancer survival improved with time since immigration. However it is difficult to interpret this pattern as the South Asian population had a much smaller sample size than the Chinese population and this differing pattern of mortality may be a result of the smaller sample size. It is interesting to note that the multivariable

adjustment had a larger impact on cancer survival in the South Asian compared to Chinese populations. However, as the multivariable models were the same between the Chinese and South Asian populations this is also likely related to the smaller South Asian sample size. More research is warranted to further explore the effect of immigration on cancer survival in a South Asian population to determine if a persistent cancer survival advantage exists as seen in Chinese immigrants.

In contrast to the current results, ethnic differences in cancer survival in the U.S. exist whereby non-white minority populations demonstrate higher rates of cancer mortality than the majority Caucasian population.[13-16,25,48,49] Much of the literature in the U.S. has focused on the ethnic disparity in cancer outcomes between African American and white populations,[13-16] and this ethnic disparity in cancer survival is increasing over time.[16] However, poorer cancer outcomes in the U.S. are not only found in African Americans, as Asian ethnicity and immigrant status in the U.S. have been associated with worse cancer outcomes in certain cancer types. Asian and Pacific Islanders in the U.S. have higher stomach, liver and cervical cancer mortality than Caucasians,[25,26,49] and South Asians have a lower overall cancer survival compared to the U.S. Caucasian population.[48] Moreover, Chinese, Japanese and Filipino immigrants have a lower life expectancy and higher cancer mortality compared to a U.S. non-immigrant population.[25] Healthcare utilization has been shown to be lower in Asian Americans as lower breast and cervical cancer screening rates have been demonstrated in this population compared to Caucasians.[22-24] Interestingly, a lack of healthcare insurance in the U.S. disproportionately impacts Asian Americans, as 48% of uninsured Asian Americans did not have cervical cancer screening compared to 7% of uninsured Caucasians.[22] Access to private healthcare insurance [55,56] and regular healthcare[24,57] have consistently been shown to be among the strongest predictors of decreased cancer screening in Asian American populations. The disparity between the U.S. results and the current findings may suggest that easier access to care in a Canadian single-payer system contribute to improved cancer outcomes in Canadian-

born and immigrant Chinese and South Asians. However as the purpose of this study was to describe the Canadian experience with Chinese/South Asian ethnicity, immigration status and cancer outcomes it is difficult to draw any conclusions regarding the impact of differing healthcare systems on the current results. The relationship between modes of cancer care delivery between a private and public health care system and outcomes on vulnerable and minority populations needs to be further explored.

Limitations of this study include a lack of immigration status information prior to 1985. As a result, the general reference population may include immigrants (non-Asian) who came to Canada prior to 1985 who were not classified as immigrant. However as data were collected on incident cancer cases from 2000 onwards and immigration status was limited up to 25 years prior to diagnosis there is a relatively small window of immigration between 1975 and 1984 in which a patient could be non-classified. Therefore the non-classified immigrant patients are likely to be a very small percentage of the 406,735 patients in the reference population. Moreover this effect would likely bias the results towards the null hypothesis as Canadian immigrants have been shown to have improved cancer survival over the non-immigrant Canadian population.[35] A second limitation is the use of a name algorithm to detect Chinese and South Asian ethnicities, which excludes patients with names shared by two ethnicities and as a result its sensitivity is lower than its specificity. This may result in certain subgroups with common last names being excluded from our study. Thirdly, despite our best attempts to control for confounding factors we realize that there are many factors that may differ between ethnic and immigrant populations that are not identifiable in large administrative databases, such as differing levels of community/social supports and degree of acculturation. Fourth, we did not include cancer treatment as a covariate in the multivariable analysis as our initial research aim was to determine the effect of ethnicity and immigration on cancer outcomes as a predictor of cancer outcomes present at the index date (at the baseline time of cancer diagnosis). However exploring the impact of treatment on the

improved survival associated with Chinese and South Asian ethnicity, and how ethnicity might impact cancer treatment and the quality of cancer care, is the subject of future work. Fifth, although including urban/rural status as a covariate in the multivariable analysis is important due to the large geographical size of Ontario, the small proportion of rural patients in the Chinese and South Asian immigrant groups may lead to model instabilities. Lastly, the retrospective nature and use of an administrative database in this study prevents the ability to identify more specific family and cultural issues (such as attitude to treatments or decision-making processes) that may underpin the results of this study.

In conclusion, our study shows that Chinese and South Asian ethnic groups have lower cancer mortalities than the general non-immigrant Ontario population. These findings indicate that after removing the well-documented protective effect of immigration, Chinese and South Asian ethnicities are associated with a cancer survival advantage in Ontario.

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Table 1. Demographics.

	Ethnic group: Chinese			Ethnic group: South Asian			Ethnic group: General Population
	Canadian-born	Recent immigrant	Non-recent immigrant	Canadian-born	Recent immigrant	Non-recent immigrant	Non-Chinese/Non-South Asian
N	6,631	2,022	3,190	2,752	1,009	1,339	406,735
Age at cancer diagnosis date							
Median (IQR)	64 (54-74)	61 (45-71)	65 (51-77)	63 (54-71)	61 (50-68)	65 (52-74)	67 (58-76)
Sex							
Female	3,303 (49.8%)	1,130 (55.9%)	1,621 (50.8%)	1,287 (46.8%)	510 (50.5%)	630 (47.1%)	184,955 (45.5%)
Male	3,328 (50.2%)	892 (44.1%)	1,569 (49.2%)	1,465 (53.2%)	499 (49.5%)	709 (52.9%)	221,780 (54.5%)
Urban residence							
Yes	-	-	-	-	-	-	340,613 (83.7%)
Income quintile							
Q1 (lowest)	1,156 (17.4%)	451 (22.3%)	673 (21.1%)	471 (17.1%)	299 (29.6%)	341 (25.5%)	75,331 (18.5%)
Q5 (highest)	1,352 (20.4%)	258 (12.8%)	469 (14.7%)	549 (19.9%)	68 (6.7%)	122 (9.1%)	86,456 (21.3%)
Cancer type							
Breast	1,681 (25.4%)	629 (31.1%)	824 (25.8%)	827 (30.1%)	338 (33.5%)	411 (30.7%)	84,161 (20.7%)
Colorectal	1,485 (22.4%)	410 (20.3%)	734 (23.0%)	399 (14.5%)	74 (7.3%)	146 (10.9%)	76,493 (18.8%)
Head & neck	389 (5.9%)	165 (8.2%)	166 (5.2%)	131 (4.8%)	78 (7.7%)	88 (6.6%)	14,518 (3.6%)
Lung	1,165 (17.6%)	359 (17.8%)	640 (20.1%)	247 (9.0%)	61 (6.0%)	130 (9.7%)	81,952 (20.1%)
Hematologic	692 (10.4%)	234 (11.6%)	299 (9.4%)	440 (16.0%)	192 (19.0%)	222 (16.6%)	52,185 (12.8%)
Prostate	1,219 (18.4%)	225 (11.1%)	527 (16.5%)	708 (25.7%)	266 (26.4%)	342 (25.5%)	97,426 (24.0%)
Stage							
No stage data	2,811 (47.3%)	1,025 (57.3%)	1,215 (42.0%)	1,087 (47.0%)	451 (55.2%)	482 (43.2%)	174,796 (49.3%)
Stage I	770 (13.0%)	196 (11.0%)	454 (15.7%)	272 (11.8%)	53 (6.5%)	134 (12.0%)	36,168 (10.2%)
Stage II	1,184 (19.9%)	264 (14.8%)	566 (19.6%)	565 (24.4%)	187 (22.9%)	270 (24.2%)	70,713 (19.9%)
Stage III	577 (9.7%)	180 (10.1%)	358 (12.4%)	231 (10.0%)	61 (7.5%)	119 (10.7%)	35,364 (10.0%)
Stage IV	597 (10.1%)	123 (6.9%)	298 (10.3%)	157 (6.8%)	65 (8.0%)	112 (10.0%)	37,509 (10.6%)
No stage data available	N=2,811	N=1,025	N=1,215	N=1,087	N=451	N=482	N=174,796
Metastasis	546 (19.4%)	199 (19.4%)	225 (18.5%)	132 (12.1%)	50 (11.1%)	55 (11.4%)	33,995 (19.4%)
No hospital data	406 (14.4%)	153 (14.9%)	198 (16.3%)	183 (16.8%)	89 (19.7%)	71 (14.7%)	23,920 (13.7%)
No metastasis	1,859 (66.1%)	673 (65.7%)	792 (65.2%)	772 (71.0%)	312 (69.2%)	356 (73.9%)	116,881 (66.9%)
Peri-diagnostic chemotherapy							
Yes	2,360 (35.6%)	873 (43.2%)	1,153 (36.1%)	970 (35.2%)	394 (39.0%)	501 (37.4%)	120,904 (29.7%)
Peri-diagnostic							

radiation therapy							
Yes	2,249 (33.9%)	633 (31.3%)	1,086 (34.0%)	995 (36.2%)	353 (35.0%)	511 (38.2%)	127,417 (31.3%)
Weighted ADG comorbidity score							
Median (IQR)	13 (5-21)	10 (4-19)	13 (5-21)	15 (6-22)	12 (5-20)	14 (6-23)	16 (6-25)

*Urban status data not shown for select groups due to a small cell in order to protect privacy.

Table 2A: All-cause mortality (all cancer combined)

	Ethnic group: Chinese			Ethnic group: South Asian		
	Canadian-born	Recent immigrant	Non-recent immigrant	Canadian-born	Recent immigrant	Non-recent immigrant
Number of events	2,269	608	1,069	762	279	381
Unadjusted Hazard ratio (95% C.I.)	0.753 (0.723-0.785)	0.583 (0.538-0.631)	0.828 (0.780-0.880)	0.582 (0.542-0.625)	0.561 (0.499-0.631)	0.670 (0.606-0.741)
Adjusted Hazard ratio (95% C.I.)	0.829 (0.795-0.865)	0.661 (0.610-0.716)	0.853 (0.803-0.906)	0.856 (0.797-0.919)	0.923 (0.821-1.039)	0.914 (0.826-1.011)
*Reference group: Non-Chinese/non-South Asian and non-immigrant general population						

Table 2B: Cancer specific mortality (all cancer combined)

	Ethnic group: Chinese			Ethnic group: South Asian		
	Canadian-born	Recent immigrant	Non-recent immigrant	Canadian-born	Recent immigrant	Non-recent immigrant
Number of events	1623	465	731	486	188	220
Unadjusted Hazard ratio (95% C.I.)	0.828 (0.788-0.870)	0.678 (0.619-0.743)	0.887 (0.825-0.954)	0.579 (0.529-0.633)	0.572 (0.496-0.660)	0.614 (0.538-0.700)
Adjusted Hazard ratio (95% C.I.)	0.853 (0.812-0.897)	0.689 (0.629-0.755)	0.876 (0.814-0.943)	0.871 (0.796-0.952)	0.921 (0.798-1.063)	0.876 (0.767-1.000)
*Reference group: Non-Chinese/non-South Asian and non-immigrant general population						

Table 3A. All-cause mortality by cancer type for Canadian-born Chinese and South Asians.

	Canadian-born Chinese				Canadian-born South Asian			
	Number of matched patients	Number of events	Unadjusted Hazard Ratio (95% C.I.)	Adjusted Hazard Ratio (95% C.I.)	Number of matched patients	Number of events	Unadjusted Hazard Ratio (95% C.I.)	Adjusted Hazard Ratio (95% C.I.)
Breast cancer	1674	219	0.687 (0.561-0.841)	0.848 (0.647-1.112)	823	117	0.878 (0.672-1.147)	0.941 (0.668-1.327)
Colorectal cancer	1467	566	0.837 (0.730-0.961)	0.924 (0.764-1.117)	392	129	0.804 (0.605-1.068)	1.046 (0.700-1.565)
Head and neck cancer	360	91	0.619 (0.454-0.843)	0.723 (0.450-1.162)	121	39	1.269 (0.759-2.122)	2.564 (0.752-8.738)
Lung cancer	1141	864	0.606 (0.534-0.687)	0.605 (0.512-0.715)	245	183	0.810 (0.621-1.057)	0.906 (0.627-1.310)
Hematologic cancer	660	308	0.963 (0.797-1.165)	1.03 (0.803-1.321)	421	175	0.984 (0.770-1.259)	1.020 (0.727-1.432)
Prostate cancer	1218	171	0.678 (0.537-0.857)	0.704 (0.503-0.985)	705	102	0.854 (0.636-1.147)	0.773 (0.510-1.170)

*Reference group: Non-Chinese/non-South Asian and non-immigrant general population

Table 3B. Cancer-specific mortality by cancer type for Canadian-born Chinese and South Asians.

	Canadian-born Chinese				Canadian-born South Asian			
	Number of matched patients	Number of events	Unadjusted Hazard Ratio (95% C.I.)	Adjusted Hazard Ratio (95% C.I.)	Number of matched patients	Number of events	Unadjusted Hazard Ratio (95% C.I.)	Adjusted Hazard Ratio (95% C.I.)
Breast cancer	1674	132	0.680 (0.529-0.874)	0.803 (0.565-1.142)	823	76	0.759 (0.551-1.045)	0.794 (0.518-1.217)
Colorectal cancer	1467	407	0.861 (0.730-1.016)	0.900 (0.719-1.128)	392	97	0.956 (0.680-1.343)	1.319 (0.822-2.115)
Head and neck cancer	360	70	0.667 (0.469-0.947)	0.568 (0.315-1.026)	121	29	2.273 (1.118-4.619)	-
Lung cancer	1141	704	0.615 (0.534-0.708)	0.593 (0.491-0.717)	245	129	0.756 (0.551-1.035)	0.734 (0.465-1.159)
Hematologic cancer	660	198	1.099 (0.859-1.406)	1.281 (0.922-1.780)	421	105	1.055 (0.766-1.453)	1.169 (0.720-1.896)
Prostate cancer	1218	80	0.822 (0.584-1.157)	0.953 (0.540-1.683)	705	38	0.727 (0.461-1.147)	0.543 (0.243-1.213)

*Reference group: Non-Chinese/non-South Asian and non-immigrant general population