

# Colorectal Cancer Incidence and Mortality Trends by Sex and Population Group in South Africa: 2002-2014.

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## Research article

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# Abstract

## Background

South Africa (SA) has experienced a rapid transition in the Human Development Index (HDI) over the past decade, which had an effect on the incidence and mortality rates of colorectal cancer (CRC). This study aims to provide CRC incidence and mortality trends by population group and sex in SA from 2002 to 2014.

## Methods

Incidence data were extracted from the South African National Cancer Registry and mortality data obtained from Statistics South Africa (STATS SA), for the period 2002 to 2014. Age-standardised incidence rates (ASIR) and age-standardised mortality rates (ASMR) were calculated using the STATS SA mid-year population as the denominator and the Segi world standard population data for standardisation. A Joinpoint regression analysis was computed for the CRC ASIR and ASMR by population group and sex.

## Results

A total of 33,232 incident CRC cases and 26,836 CRC deaths were reported during the study period. Of the CRC cases reported, 54% were males and 46% were females, and among deaths reported, 47% were males and 53% were females. Overall, there was a 2.5% annual average percentage change (AAPC) increase in ASIR from 2002 to 2014 (95% CI: 0.6- 4.5, p-value <0.001). For ASMR overall, there was 1.3% increase from 2002 to 2014 (95% CI: 0.1- 2.6, p-value <0.001). The ASIR and ASMR among population groups were stable, with the exception of the Black population group. The ASIR increased consistently at 4.3% for black males (95% CI: 1.9- 6.7, p-value <0.001) and 3.4% for black females (95% CI: 1.5- 5.3, p-value <0.001) from 2002 to 2014, respectively. Similarly, ASMR for black males and females increased by 4.2% (95% CI: 2.0- 6.5, p-value <0.001) and 3.4% (95% CI: 2.0- 4.8, p-value <0.01) from 2002 to 2014, respectively.

## Conclusions

The disparities in the CRC incidence and mortality trends may reflect socioeconomic inequalities across different population groups in SA. The rapid increase in CRC trends among the Black population group is concerning and requires further investigation and increased efforts for cancer prevention, early screening and diagnosis, as well as better access to cancer treatment.

## Introduction

Colorectal cancer (CRC) is regarded as a leading cause of cancer morbidity and mortality worldwide.[1] It is ranked third in cancer incidence and second in cancer mortality globally.[1] In 2019, there were 1.8 million new CRC cases and 880,792 CRC deaths worldwide.[1–3] In 2018, the age-standardised incidence rate (ASIR) and age-standardised mortality rate (ASMR) in the African region were estimated at 8.2 and 5.6 per 100000 population, respectively.[4] According to the Globocan report, the estimated ASIR and ASMR for South Africa (SA) in 2018 were 14.4 and 7.6 per 100000, respectively. [5]The latest South African National Cancer Registry (NCR) 2016 report observed 3884 cases of CRC with an estimated 6.81 and 11.01 ASIR per 100000 population for female and males, respectively. [6]

Disparities in CRC between countries exist based on the Human Development Index (HDI). HDI is a composite score of life expectancy, education and per capita income of countries. [7]Countries with a high HDI reported the highest CRC incidence rates, while low HDI countries reported the highest CRC mortality rates.[1] The CRC incidence of a country increases with increasing HDI status, as such, may be used to signal changes in socioeconomic status.[1] The rise in incidence rates in countries undergoing rapid developmental transition may be attributed to changes in diet, obesity, and other lifestyle factors such as higher alcohol and red meat consumption.[1,8,9] On the other hand, the increase in CRC mortality rates, observed in low HDI countries, may be attributed to minimal or lack of appropriate screening and early detection programmes, and poor access to cancer treatment.[8]

The HDI of SA has been increasing steadily since 1990.[7] Despite an increasing HDI, the Gini coefficient in SA is only 0.6, indicating considerable societal inequality.[10] Massive inequity in socioeconomic status and health access, among other factors, influence the health outcomes of the SA population. [11–13]As a result of the unique political history of SA, many of these inequalities are apparent when examining health trends by population groups (Black, White, Asian, and Coloured). To appropriately plan for

interventions, prevention, and control of CRC in the era of epidemiologic and economic transition, the evaluation of CRC patterns across population groups, and sex are necessary. This study aims to provide insights into the CRC incidence and mortality trends by population group and sex for SA.

## Methods

### Study design and data sources

A cross-sectional study was conducted using secondary data analysis of two datasets, to determine incidence trends and mortality trends for CRC between 2002 and 2014 in SA by sex and population groups.

To determine incident CRC trends, the NCR database was used. The NCR methodology is outlined in detail by Singh et al.[14] Briefly, the NCR collects data on all pathologically confirmed cancer cases from both public and private laboratories across SA. The NCR then collates, analyses, interprets and reports annual cancer incidences by age groups, population groups, and sex. All cancers are coded according to the International Classification of Diseases for Oncology, 3<sup>rd</sup> edition (ICD-O-3).[15] CRC cases, defined as ICD-O-3 codes C18, C19, and C20, from 2002 to 2014, were extracted from the NCR. The variables extracted included the year of diagnosis, sex, population group, age at diagnosis, and morphology and topography of cancer.

CRC deaths from 2002 to 2014 were extracted from the Statistic South Africa (STATS SA) mortality and causes of death database. STATS SA collates national mortality statistics for the registered causes of deaths from death certificates. We extracted the date of death, sex, population group, smoking status, marital status, education level, and age of the deceased for individuals whose first or underlying causes of death were recorded as CRC (ICD-O-3 codes C18, C19, and C20).

### Statistical analysis

Stata® statistical software version 14.2 (StataCorp LLC, Texas, USA) was used to generate frequencies and calculate ASIR and ASMR by sex and population group. The estimated mid-year population from STATS SA was used as the denominator. The Segi world standard population was used for age standardisation.[16,17]

The age-standardised rates by year, sex, and population group were imported into Joinpoint regression statistical software for trend analysis for the study period. The model used by Joinpoint statistical software to create the trend patterns was described by Kim et al.[18] The average annual percentage change (AAPC) was considered significant at the p-value threshold of less than 0.05 using a two-sided test.

## Results

### Study population characteristics

A total of 33,232 incident CRC cases were reported during the study period, 56% from private healthcare sector laboratories, and 44% from public healthcare sector laboratories. Of CRC incident cases, 54% were males. Throughout the study period, the annual median incidence was 2,292 cases per year (interquartile range (IQR): 2132 - 3081). The mean age at diagnosis was 61 years ( $\pm 14.9$  standard deviation (SD) years). The White population group had the highest percentage of CRC cases (49%) compared to other population groups. (Table 1).

There were 26,836 CRC deaths with an annual median of 2,138 (IQR: 1982 -2321) between 2002 and 2014. Females accounted for 53% of all CRC deaths. The mean age at death was 65 years ( $\pm 14.9$  SD years), and 63% of the deaths were among adults over 60 years of age. The White population group reported the highest proportion of deaths for CRC at 41%, while the Asian population group reported the lowest deaths at 4%. The mortality incidence ratio by age group was highest among Black population group and lowest among White population group (data not shown). Almost 4% of individuals who died from CRC had no education, while 24% reached a high school level. A third of CRC deaths (33%) were reported amongst non-smokers, although 56% of this data was missing from the death registry. The smoking frequencies observed may reflect smoking cessation post-cancer diagnosis.

Table 1  
 Characteristics of Colorectal cancer cases and deaths (2002-2014)

	Colorectal cancer cases, (N=33,232) N(%)	Colorectal cancer death, (N=26,836) N(%)
<b>Age</b>		
Mean (SD)	61.70(±14.38)	65.19 (±14.91)
<b>Age group (years)</b>		
<15	24 (0.1%)	20 (0.1%)
15-30	894 (2.7%)	551 (2.1%)
31-45	3,578 (10.8%)	2,272 (8.5%)
46-60	9,817 (29.5%)	6,447 (24.0%)
>60	17,760 (53.4%)	16,915 (63.0%)
Missing	1,159 (3.5%)	631 (2.4%)
<b>Sex</b>		
Female	15,208 (45.8%)	14,109 (52.6%)
Male	17,995 (54.1%)	12,702 (47.3%)
Missing	29(0.1%)	25 (0.1%)
<b>Population group</b>		
Black	8,942 (26.9%)	7,163 (26.7%)
Coloured	4,613 (13.9%)	2,645 (9.9%)
Asian	1,878 (5.7%)	1,169 (4.4%)
White	1,6207 (48.8%)	10,919 (40.7%)
Missing	1,592 (4.8%)	4,940 (18.4%)
<b>Laboratory type</b>		
Private	18,666 (56.2%)	-
Public	14,566 (43.8%)	-
<b>Smoking Status</b>		
No	-	8,960 (33.4%)
Yes	-	2,726 (10.2%)
Missing	-	15,150 (56.5%)
<b>Marital status</b>		
Divorced	-	4,412 (16.4%)
Married	-	10,630 (39.6%)
Never_Married	-	4,887 (18.2%)
Widowed	-	2,648 (9.9%)
Missing	-	4,259 (15.9%)
<b>Education level</b>		

No_Education	-	1,074 (4.0%)
Primary_School	-	1,974 (7.4%)
High_School	-	6,391 (23.8%)
Tertiary	-	1,551 (5.8%)
Missing	-	15,846 (59.0%)

## Age-specific incidence and mortality rates

Figures 1 and 2 illustrate age-specific incidence and mortality rates for males and females in SA between 2002 and 2014. Rates in males and females increased proportionally until the age of 50 years, after which the rate for males was higher than the rate for females for both incidence and mortality. Rates peaked in the age group of 75 years and older.

## Age-standardised incidence rates trends

On average, for males and females combined, there was 2.5% annual average increase in ASIR from 2002 to 2014 (annual average percentage change (AAPC)=2.5, 95% CI: 0.6- 4.5, p-value < 0.001) (Table 2). ASIR ranged from 11.6 to 13.5 and 8.5 to 10.6 / 100,000 population for the study period among males and females, respectively. Overall the ASIR were higher among males compared with females (Figures 3 & 4).

Among males, the highest ASIR was observed among the White population group at 28.12 per 100,000 population in 2014. This rate was 1.3, 1.4, and 8.6 times higher than Coloured (19.83/100,000), Asian (21.31/100,000), and Black (3.26/100,000) population groups, respectively (Figure 4). While the CRC ASIR remained stable among males of the Coloured and Asian population groups, the ASIR among males of the Black population group increased consistently at 3.4% from 2002 to 2014 (AAPC=3.4, 95% CI: 1.5- 5.3, p-value < 0.001) (Table 2). Among males of the White population group, a significant decrease of 8.8% was observed from 2002 to 2007 (AAPC= -8.8, 95% CI: -14.0- -3.2, p-value < 0.001) followed by a 10.4% increase from 2007 to 2014 (AAPC= 10.4, 95%CI: 6.6- 14.4, p-value < 0.001) (Table 2).

As shown in figure 5, the highest ASIR among females were observed in the year 2014 at 18.5 per 100,000 population for the White population group. The ASIR in 2014 were similar for Asian and Coloured population groups at (10.6/100,000) and (10.6/100,000) respectively. In the same year, Black females reported the lowest ASIR at 2.3 per 100,000 population. The ASIR among females of the Coloured and Asian population group remained stable, while the ASIR among females of the Black population group increased consistently at 4.3% from 2002 to 2014 (AAPC=4.3, 95% CI: 1.9- 6.7, p-value < 0.001). Among females of the White population group the ASIR trend remained stable until 2009, when ASIR increased by 14.9% from 2009 to 2014 (AAPC=14.9, 95% CI: 6.4- 24.2, p-value <0.01) (Table 2).

Table 2

Annual Average Percentage Change (AAPC) in CRC incidence and mortality rates by sex and population groups, 2002-2014.

Population group	Sex	Age-standardised Incidence		Age-standardised Mortality	
		Period	AAPC (95%CI)	Period	AAPC (95%CI)
Asian	Males	2002-2014	0.6 (-2.0,3.2)	2002-2014	2.4(-0.4, 5.4)
	Females	2002-2014	3.7 (-0.2, 7.7)	2002-2014	-0.3(-2.8, 2.3)
Coloured	Males	2002-2014	1.2 (-0.8,3.3)	2002-2014	3.0*(0.4,5.7)
	Females	2002-2014	2.5 (-0.0,5.2)	2002-2014	1.3(-0.5, 3.1)
White	Males	2002-2007	-8.8*(-14.0,-3.2)	2002-2014	0.5(-0.6,1.6)
	Males	2007-2014	10.4*(6.6,14.4)	-	-
	Females	2002-2009	-3.7 (-8.0, 0.9)	2002-2014	-0.2(-1.3,1.0)
	Females	2009-2014	14.9*(6.4,24.2)	-	-
Black	Males	2002-2014	3.4*(1.5,5.3)	2002-2014	4.2*(2.0,6.5)
	Female	2002-2014	4.3*(1.9,6.7)	2002-2014	3.4*(2.0,4.8)
All	All	2002-2014	2.5*(0.6,4.5)	2002-2014	1.3*(0.1,2.6)

\*The average annual percentage change (AAPC) is statistically significant: p-value <0.05

## Age-standardised mortality rates trends

On average, for males and females combined, the ASMR increased by 1.3% from 2002 to 2014 (AAPC=1.3, 95% CI: 0.1- 2.6, p-value <0.01) (Table 2). The overall ASMR ranged from 7.1 to 8.9 and 5.5 to 5.9 /100,000 population for the study period among males and females, respectively. Similar to ASIR, the overall ASMR was higher in males than females (Figures 5 & 6).

The highest ASMR in males was observed in the White population group in 2004 at 15.1 per 100,000 population, and this rate was 1.2, 1.7 and 6.0 times higher than the Asian (12.2/100,000), Coloured (8.6/100,000), and Black (2.5/100,000) population groups in 2004, respectively (Figure 5). For males, over the study period, the ASMR remained stable among the White and Asian population groups and increased consistently among the Coloured and Black population groups by 3.0% (AAPC=3.0, 95% CI: 0.4- 5.7, p-value <0.01) and 4.2% (AAPC=4.2, 95% CI: 2.0- 6.5, p-value <0.01) from 2002 to 2014, respectively (Table 2).

Among females the highest ASMR was reported among the White population group at 10.3 per 100,000 population in 2004, this rate was 1.4, 1.5 and 6.3 times higher than the Asian (7.3/100,000), Coloured (6.8/100,000) and the Black (1.6/100,000) population groups, respectively (Figure 6). Among females, a significant change in ASMR was only observed among the Black population group, where the ASMR increased by 3.4% from 2002 to 2014 (AAPC=3.4, 95% CI: 2.0- 4.8, p-value <0.01) (table 2). The ASMR of females among other population groups remained stable (Table 2).

## Discussion

This is the first study in SA to assess national CRC incidence and mortality trends by population group and sex. We reported overall ASIR from 11.6 to 13.5 and 8.5 to 10.6 per 100,000 population for the study period among males and females, respectively. The overall ASMR ranged from 7.1 to 8.9 and 5.5 to 5.9 per100,000 population for the study period among males and females respectively. The ASIR and ASMR were highest amongst the White population group and lowest amongst the Black population group. However, the Black population group demonstrated a consistent increase in both ASIR and ASMR for the study period. The

age at diagnosis was much closer to the age at death with the average age at diagnosis being 61 years and the average age at death being 65 years. These findings suggest that most cases are diagnosed at a late stage and hence mortality occurs soon after diagnosis. Screening and early detection of colorectal cancer are recommended as the survival is highly dependent on the stage at diagnosis. The age at diagnosis is comparable with other sub-Saharan African countries and the United State of America where most of the cases are diagnosed between the ages of 65 and 68 years. [19]

The incidence and mortality were higher in males compared to females. Our study found that there was no significant difference in the pattern of CRC age-specific incidence and mortality rates between males and females. The association between sex and CRC is not fully understood. The disparities found in other studies are partly attributed to differences in exposures and risk factors across sex, such as smoking behaviour and hormones.[20–22] Further studies are needed to understand the relationship between CRC and sex to implement possible interventions to reduce CRC incidence in South Africa.

We found that between 2002 and 2014, the overall ASIR and ASMR increased by 2.5% and 1.3% respectively. As expected for countries undergoing rapid developmental transition and are considered to be medium-to-high HDI, the overall incidence and mortality rates of CRC in SA are increasing with increasing HDI.[7,23–25] The increase in ASIR is linked to changes in individual behaviour, in particular, lifestyle changes influenced by westernisation.[26] These lifestyle factors include excessive tobacco smoking, excessive alcohol consumption, lack of physical activity leading to obesity and poor diet, consumption of fast food and red meat, among other factors.[26–30] The increase in ASMR might be associated with quality of care within the country's health system, for example, inefficient resource allocation (human resources, equipment and medical supplies), lack of access to cancer treatment and or management, and poor health infrastructures may affect mortality rates.[26,31–37] Other factors include low or lack of awareness, and screening and early detection to detect and remove precancerous polyps as early as possible before they progress into cancerous lesions, as well as late diagnosis, translating into poor prognosis and ultimately increased mortality rates. [38–41]

Stable ASIR and ASMR were observed among the Asian population group and females of the Coloured population group over the study period. Stable ASIR but increasing ASMR was observed among Coloured males. The Asian and Coloured population groups account for 11% of the total population; thus, the numbers are likely too low to show a significant change in relation to other population groups.[42,47,48] However, the level of access to healthcare services among individuals of the Asian and Coloured population groups remained fairly similar four and ten years post-democracy (1994), a possible explanation for the rate of CRC diagnosis remaining stable. [49,50]

Among the White population group, the ASIR decreased from 2002 to 2007 for males and remained stable for females from 2002-2009, and then later increased from 2007 to 2014 for males, and from 2000 to 2014 for females. The ASMR remained stable throughout the study period for both males and females. The stabilisation or reduction observed between 2002 to 2009 may be partly attributed to the effects of withholding cancer reporting by private sector laboratories between 2005 and 2010 before the promulgation of Regulation 380 of the National Health Act no 61 of 2003.[51,52] An estimated 16% of the SA population seeks care in the private health sector, of which 92% are Whites, and hence the ASIR trends mimic the reporting levels during and few years after the data withholding period.[52] The stable ASMR was expected among the White population group, as 88% of the White population group have access to adequate healthcare services provided by the private healthcare sector. [53] The screening rates are higher than other population groups, which translates into early detection and treatment, and ultimately better prognosis and lower death rates, hence the stable mortality pattern observed.[54,55]

A consistent increase in ASIR and ASMR was observed among the Black population group throughout the study period. This may be explained by the rapid transition of the Black population group's socioeconomic status and change in lifestyle.[56,57] The increased adoption of western lifestyles and consequently, dietary changes as well as other risk factors for CRC may have led to an increase in CRC incidence among Black South Africans. This phenomenon is also observed by other African countries experiencing rapid westernisation.[58,59] Secondly, the incidence pattern may be attributed to an increase in cancer reporting for the Black population group, which constitutes >80% of the total SA population that was excluded from accessing quality healthcare services pre-democracy.[42,49,60] The ASMR trends observed may be explained by inequities in socioeconomic status differences. There is a general lack of access to quality healthcare services, late diagnosis of cancer, and limited treatment options available for poorer South Africans, as only 8% the Black population group can afford private medical insurance in SA.[53,61]

## Limitations

This study had several limitations. The incidence data used in this study was derived from the NCR. The NCR is a passive pathology-based cancer registry that collects histological, haematologically, and cytologically diagnosed cancer cases; therefore, CRC cases not diagnosed through laboratory means are excluded.[14] Between 2005 and 2007, cancer case reporting and data collection from private health facilities were limited due to concerns around confidentiality and the lack of legislature support on cancer reporting/surveillance in SA.[62] This may cause an underreporting of CRC incidence disproportionately amongst certain population groups that predominately utilised private healthcare facilities such as the non-Black population groups.[63] The lack of cancer staging in both the NCR and STATS SA data makes it more challenging to explore disparities in cancer incidence and mortality across population groups.

The data for cancer mortality was derived from STATS SA. Underreporting of death was likely across all population groups. In 2007, the completeness of mid-year estimates and vital statistics was below 90% as found by an evaluation [64]. This underreporting occurs because of delayed reporting, ill-defined causes of death, and misreporting or misclassification of cause of death.[65]

Despite these limitations, this is the first national study to report CRC ASIR and ASMR trends in SA. Improvements in the accuracy of reporting will occur with more triangulation of data sources. Secondly, the data sources used are the primary source of cancer statistics in SA. This study has reported the CRC ASIR and ASMR, which were comparable with other rates reported by previous regional and international studies. [66,67]

## Conclusions

The increase in CRC ASIR and ASMR is an indication of the epidemiological transition of disease burden in SA with increasing HDI. The disparities across population groups, in particular, the consistent and rapid increase in ASIR among the Black population group, requires further in-depth studies to delineate the factors driving the increasing rates. Programs for promoting healthier behaviours such as reducing alcohol intake, reducing tobacco smoking, and increasing physical activities are recommended to reduce the risk of CRC in SA. The inequalities can be bridged through universal health coverage, targeted screening, early detection, and high-quality cancer care provision, especially for previously disadvantaged population groups. Enhancement of cancer surveillance, in particular, population-based cancer registration is required to produce better quality cancer data for in-depth exploratory research to better inform policies and interventions for cancer prevention and control in SA.

## Abbreviations

AAPC: Average annual percentage change; APC: Annual percentage change, ASIR: Age-standardised incidence rate; ASMR: Age-standardised mortality rate; CRC: Colorectal Cancer; HDI: human development index; NCR: South African National Cancer Registry; SA: South Africa; STATS SA: Statistics South Africa.

## Declarations

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## AUTHORS' CONTRIBUTIONS

The conception of the study: ES KMC; Literature review: MN TM LM MCM; Data cleaning: PK WC LM MCM; Statistical analysis: WC LM; Data interpretation: WC LM MN, Paper writing: LM ES, Review/Edit paper: WC ES MSM KMC TM MN.

## ETHICAL CONSIDERATION

This study is covered by the ethical waiver granted by the University of Witwatersrand for NCR to perform its legislative mandate of cancer surveillance in South Africa and any related research studies that do not involve human tissue.

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## AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

## COMPETING INTERESTS

No conflict of interests declared by the authors.

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## Figures

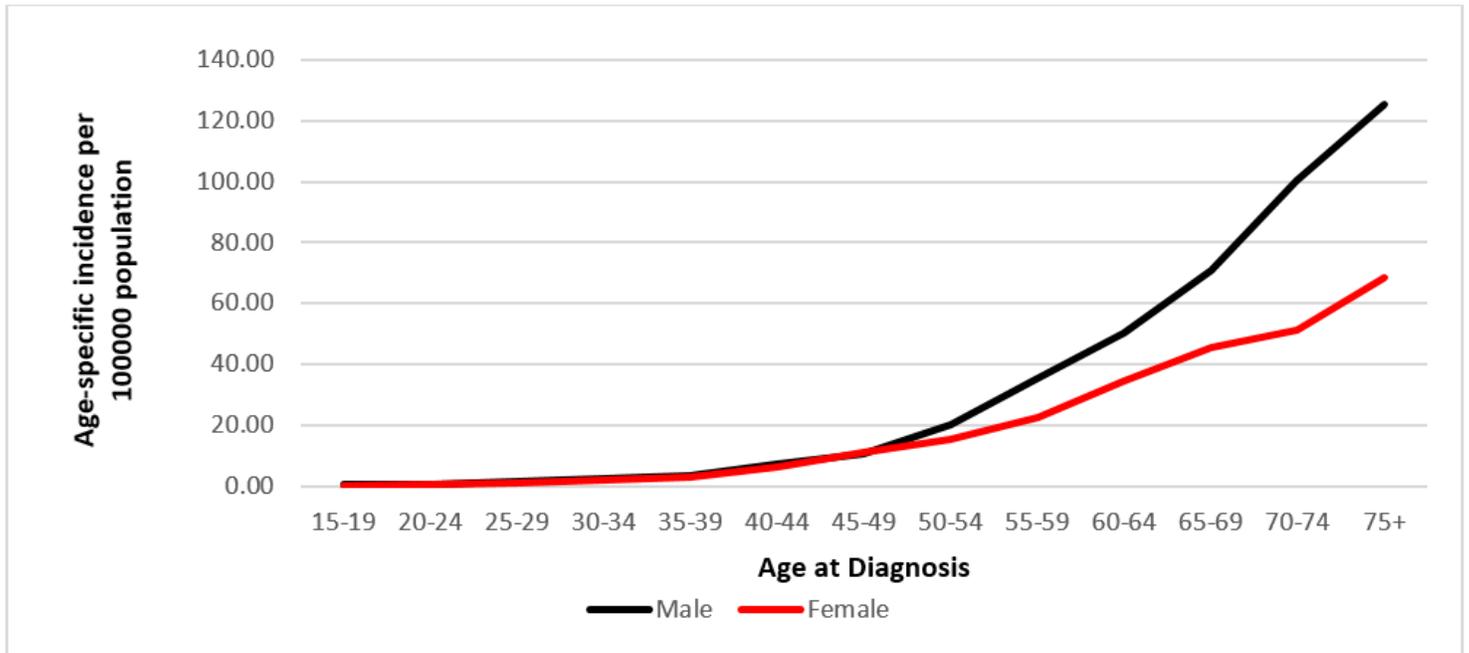


Figure 1

Average age-specific incidence rates, 2002 - 2014

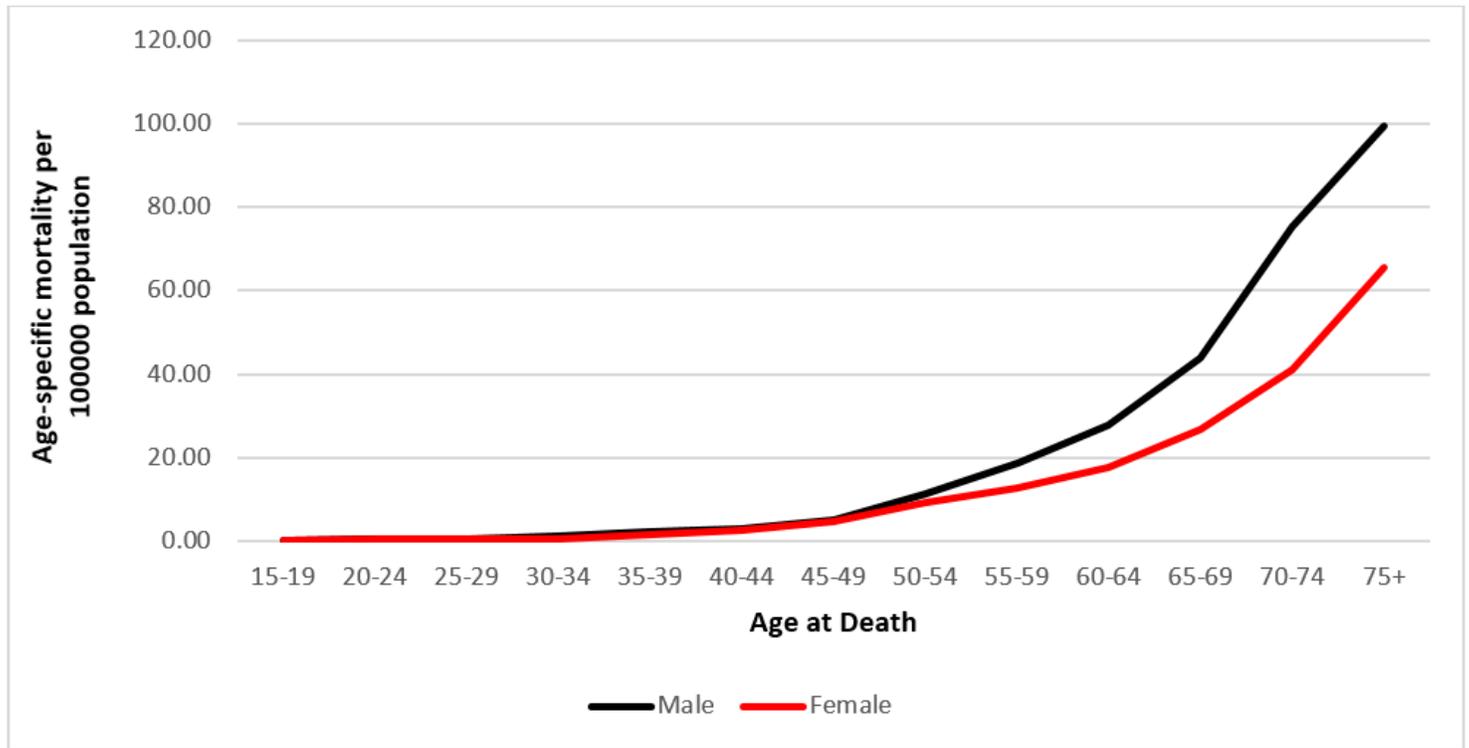


Figure 2

Average age-specific mortality rate, 2002-2014

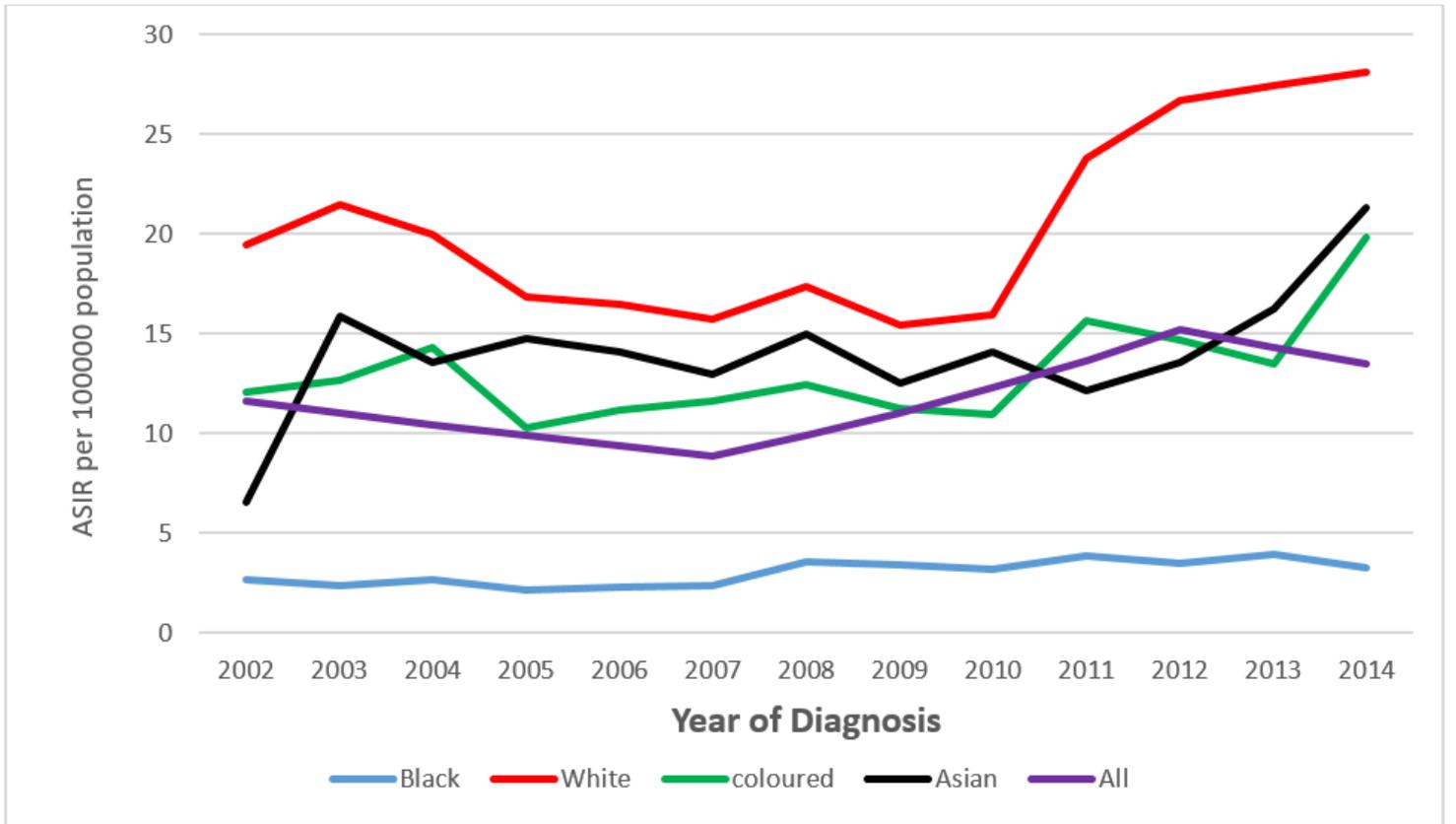


Figure 3

CRC age-standardised incidence rate among males, 2002-2014

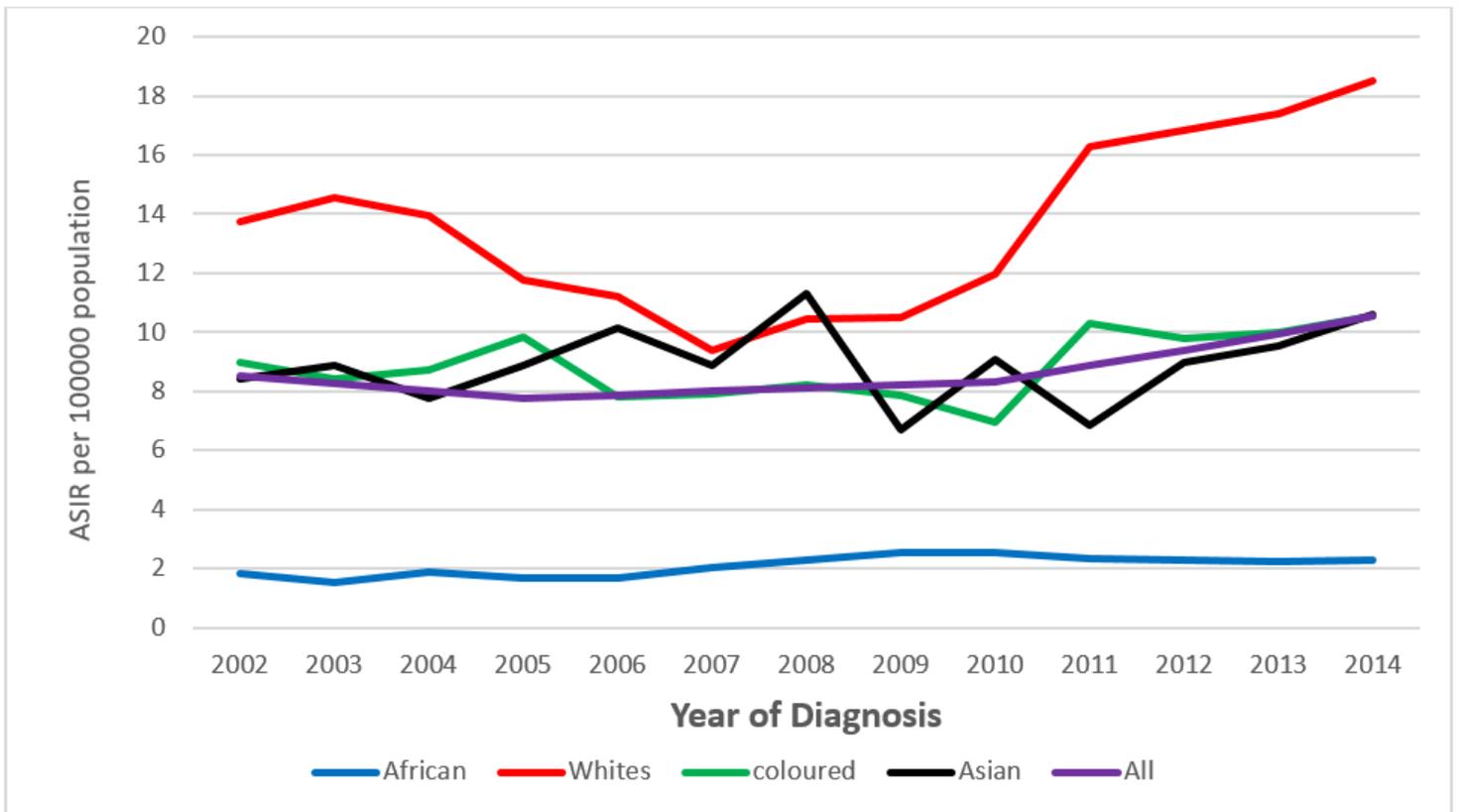


Figure 4

CRC age-standardised incidence rate among females, 2002-2014

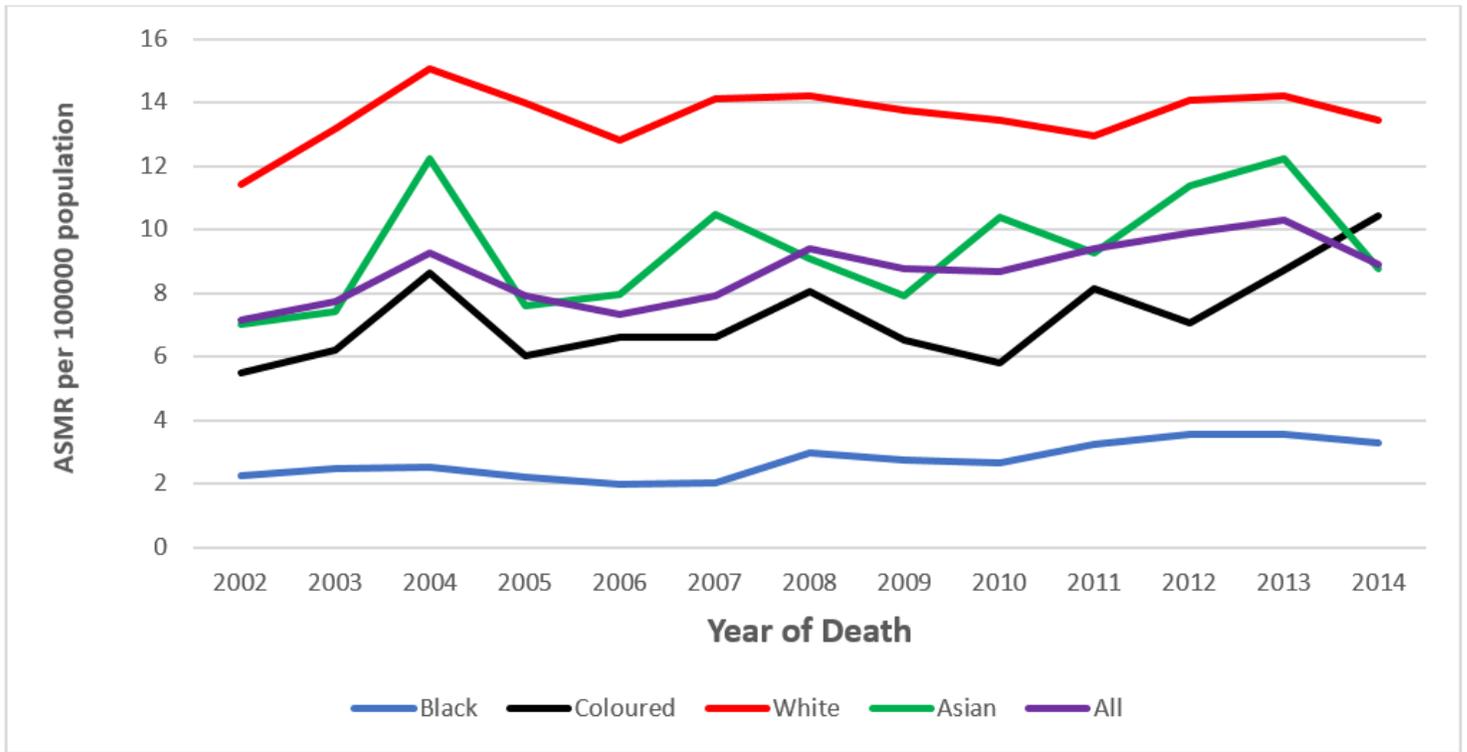


Figure 5

CRC age-standardised mortality rate among males, 2002-2014

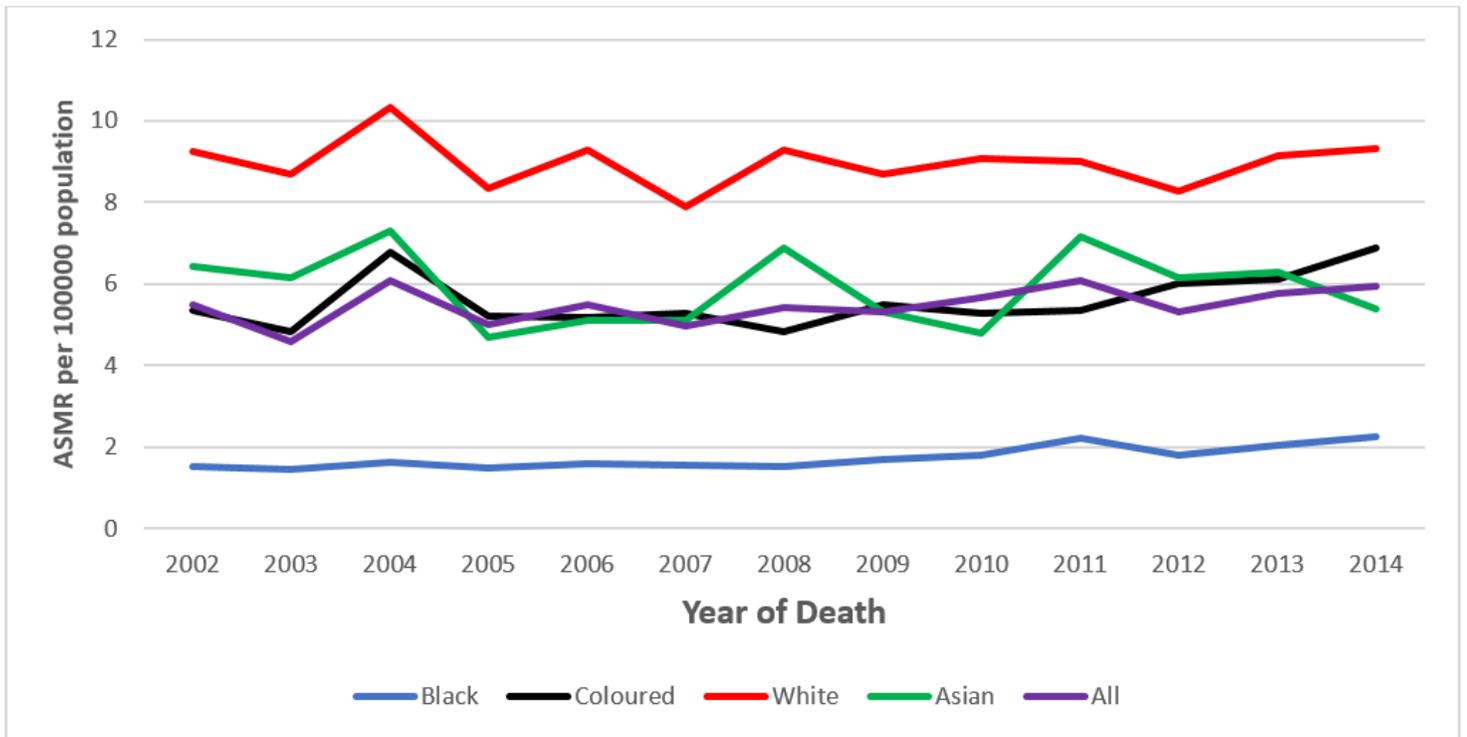


Figure 6

CRC age-standardised mortality rate among females, 2002-2014