Changes in the Incidence of Cancer in Bulawayo, Zimbabwe over a 50-Year Period

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ABSTRACT

Background: The cancer registry of Bulawayo (Zimbabwe) operated for 15 years in the preindependence period (1963–77), and was restarted in 2011. This allows comparison of incidence of cancers over a period of almost 50 years.

Methods: Age-standardized rates, with SEs, were calculated for 1963–1972 and 2011–2015. Detailed results are presented for those cancers for which there was a significant ($P < 0.05$) change in the rates between the two periods.

Results: There were declines in the rates of those cancers previously known to be common in East and Southern Africa (esophagus, liver, bladder), and the emergence of cancers associated with "westernization" of lifestyles (breast, prostate, large bowel). Cancers related to infection with HIV–AIDS (Kaposi sarcoma, non-Hodgkin lymphoma, eye cancers) have come to comprise a much larger proportion of the total burden, and cancer of the cervix (also AIDS-related) has shown a large increase in incidence—as elsewhere in sub-Saharan Africa (SSA). More surprising is the decline in cancer of the lung—formerly very high, but by 2011–2015, despite little change in the prevalence of smoking, rates were low—close to the average for SSA. This may relate, in part, to a decline in the numbers of miners, and ex-miners, residing in the city.

Conclusions: The changes in incidence are largely explained by differences in past exposure to environmental risk factors.

Impact: Few datasets from SSA can document temporal changes in the cancer epidemic on the continent. There are some anticipated observations, as well as unexpected findings meriting further investigation.

Introduction

Bulawayo is the second largest city of Zimbabwe, with an estimated population (2020) of 776,953 (1). A population-based registry covering the municipality was founded in 1963 and functioned for 15 years. It was located in an office in the Radiotherapy Centre at the Mpilo Central Hospital (Bulawayo, Zimbabwe) which, in addition to providing the only hospital service to the Black African population of the city of Bulawayo, also acted as the referral centre for cancer cases from the south-western part of Zimbabwe (until 1980, Rhodesia), including the provinces of Matabeleland (North and South), Masvingo, and Midlands. New cases of cancer were notified from all hospital wards and departments; case notes with a diagnosis of cancer or suspected cancer were sent to the registry on discharge or death. Results from the registry for 1963–1967 were published in Cancer Incidence in Five Continents (CI5) volumes II (2) and for 1968–1973 in volume III (3). The complete results for the 15-year period were published as a monograph (4), and in summary form by Parkin and colleagues (5).

The activity of the registry was restarted by the Ministry of Health and Child Care in 2011 to strengthen the Zimbabwe National Cancer Registry. The registry results have been published for 2011–2013 in the monograph Cancer in sub-Saharan Africa II (6) and for 2013–2015 in Cancer in sub-Saharan Africa III (7).

Here we compare the incidence rates in the Black (African) population of Bulawayo for the period 1963–1972 (during which registration was considered to be relatively complete) with those in the same population for the 5-year period 2011–2015. The changes observed illustrate the evolution of the cancer epidemic over a 50-year period, reflecting the general pattern of change in sub-Saharan Africa, as well as the results of factors specific to this population, including changes in occupational exposures, and the occurrence of the epidemic of human immunodeficiency virus (HIV)-AIDS.

Materials and Methods

The regional branch of the Zimbabwe National Cancer Registry is located in Mpilo Central Hospital (Bulawayo, Zimbabwe). Preindependence (the period 1963–1977), the hospital served the Black African population only, and registration was carried out by a single cancer registrar, supervised by the Head of the Radiotherapy Centre. She collected data on all cancer cases entering the hospital (usually conducting personal interviews) as well as from the pathology department and the death register for the province. A detailed description of the methodology is in Skinner and colleagues (4), and a summary in Parkin and colleagues (5).

Since 2013, the registry has had two full-time staff, supervised by the Head of the Radiotherapy Centre. The methods are described fully in Parkin and colleagues (7). Briefly, the main sources of information are from all hospitals and laboratories within the registration area, either publicly or privately owned, two private oncology clinics, the government pathology laboratory at Mpilo Central Hospital (Bulawayo,

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Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

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Cancer Epidemiol Biomarkers Prev 2021;30:867–73

doi: 10.1158/1055-9965.EPI-20-0669

Zimbabwe) plus one private laboratory, the Island Hospice Service and the Death Registry Unit of Registrar General (Ministry of Home Affairs and Cultural Heritage). Data collection is mainly active, from hospital records departments and key hospital services (gynecology, medical, pediatric, and surgical wards, and the Radiotherapy Centre). Almost all deaths are registered and are medically certified [although the information for home deaths may be based on information provided by relatives ("verbal autopsy")]. Deaths for which cancer is mentioned on the certificate are used to update the registry database, either by trace-back via the hospitals, or registered as death certificate only (DCO) cases.

In 2011–2015, the registry used the CanReg-4 computer system from IARC (8) for data entry and management. Data on registrations in 1963–72 were entered onto punch cards, which were later transferred to computer (4). These data were imported into the same CanReg-4 system as the more recent dataset.

Population at risk

For the period 1963–1972, the size and age structure of the Black population was derived from an estimate for 1965, based on the censuses of 1962 and 1969 (4). The 1962 census presented results in three broad age groups: 0–14, 14–44, 45+ years. The age distribution (5-year categories) within these broad groups was assumed to be the same as it was in 1969. Annual intercensal and post-censal estimates assumed a growth at the rate observed in 1965–1969 within age-sex groups. The average annual (Black) population in Bulawayo for the 10-year period was 179,698 (**Fig. 1**).

The results of the 2012 census (9) put the total population of Bulawayo at 653,339, with the Black population estimated at 640,946. For the period considered here (2011–2015), the population at risk was calculated from the official projections of the total population (1), and annual estimates of the non-Black population (12,393 at the census of 2012; **Fig. 1**).

Cases

For this study, all primary cases of cancer (ICD-10 C00–C96) occurring among Black individuals, resident in Bulawayo, were abstracted from the database for the two periods.

Statistical methods

The numbers of cases registered by 5-year age group, and the annual crude and age-specific incidence rates were calculated according to sex and ICD-10 category for the periods 1963–72 and 2011–2015. Age adjustment was carried out by calculation of age-standardized incidence rates (ASR), and their SEs using the direct method and world standard population (2), and the statistical significance of the deviation of the ratio between the ASRs from unity in the two periods was calculated according to Smith (10).

Results

A total of 1,282 cases (992 males and 290 females) were registered in 1963–1972 and 4,105 (1,576 males and 2,529 females) in 2011–2015. The pattern of cancers in men had changed markedly between the two periods: in 1963–72, the principal cancers were liver (26.3%), esophagus (16.5%), and lung (12.2%), while in 2011–15 they were prostate (22.8%), Kaposi sarcoma (13.6%), and esophagus (8.1%). In women, cancer of the cervix remained the most common in both periods (20.7% in 1963–72 and 36.1% in 2011–15), while breast cancer had become number 2 (13.7% of cases in 2011–15), overtaking esophageal cancer in frequency (which fell from 11.4% of cases in 1963–72 to 3.8% in 2011–15).

Detailed results for the major cancer sites in the two sexes are shown in the Supplementary Table S1.

In **Fig. 2**, we show the changes in incidence in males and females for those cancers where there was a statistically significant difference ($P < 0.05$) between the age-standardized rates in the two periods.

The most dramatic changes are the marked decreases in incidence of cancers of the liver [age-standardized rate ratio (ASRR) 0.18 in males, 0.30 in females ($P < 0.01$)], bladder [ASRR 0.1 in males ($P < 0.01$) and 0.17 in females ($P < 0.05$)], and, in males, of esophageal cancer [ASRR 0.29 ($P < 0.01$)] and respiratory system cancers—larynx [ASRR 0.25 ($P < 0.05$)] and lung [ASRR 0.1 ($P < 0.01$)]—in males.

Conversely, the incidence of cancers related to infection with HIV-AIDS have shown large increases in both sexes [ASRR for Kaposi sarcoma is 7.6 in males, 23.9 in females ($P < 0.01$), for non-Hodgkin lymphoma (NHL) 6.2 in males and 17.8 in females ($P < 0.01$), and for

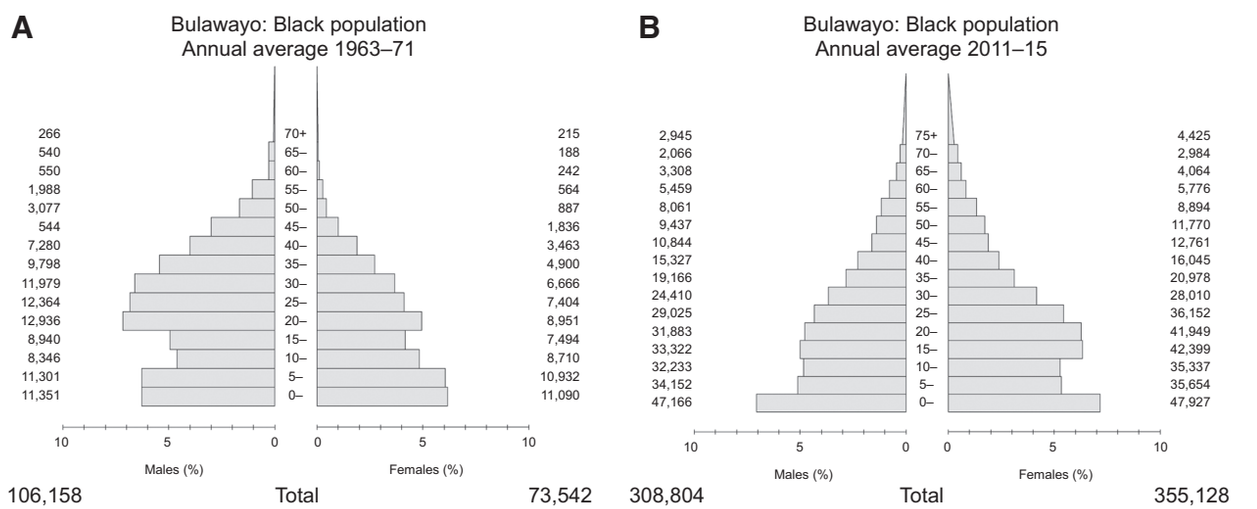

Figure 1.
Bulawayo: Black population. Annual average 1963–72 (**A**) and 2011–15 (**B**).

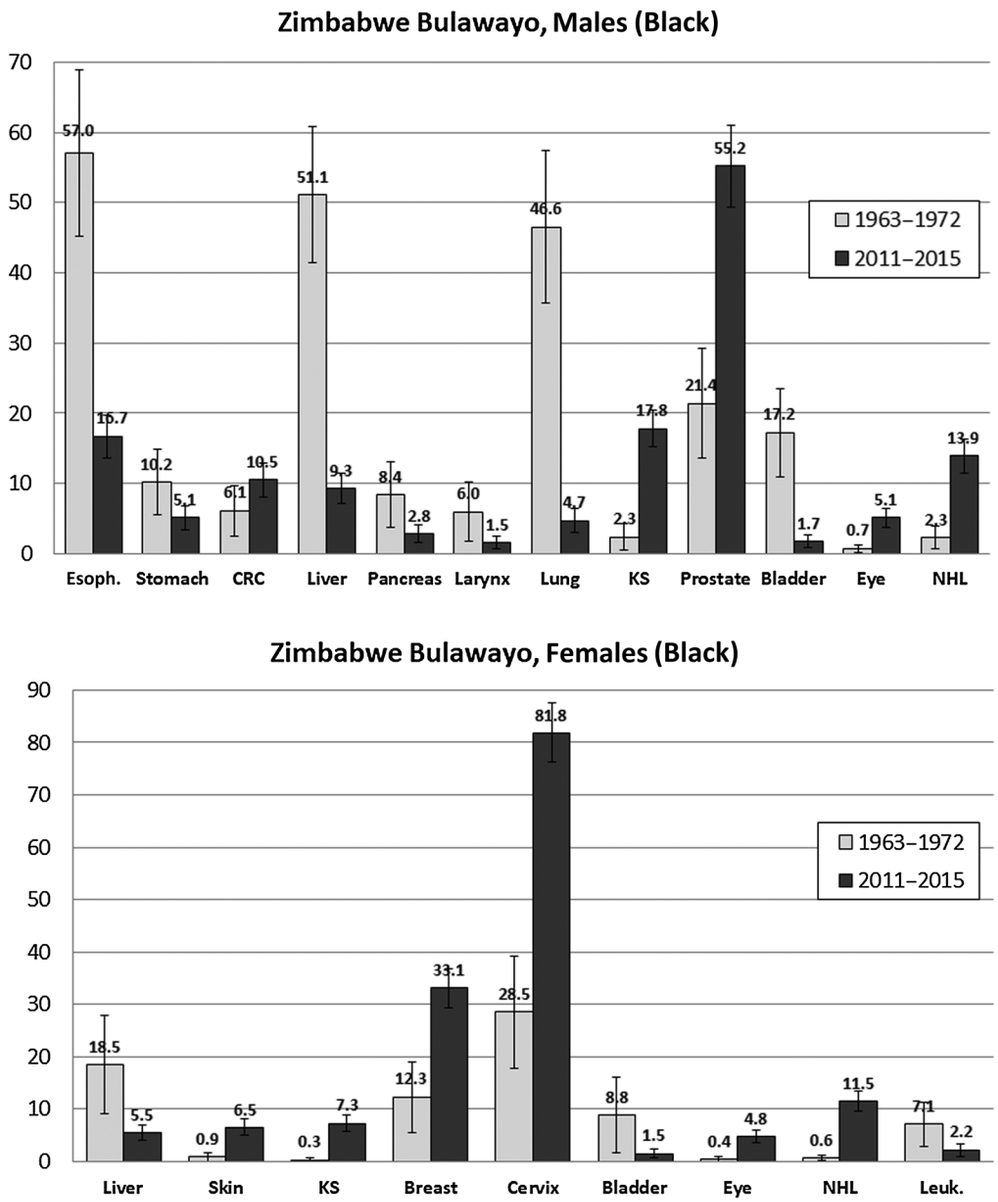

Figure 2.
Cancers showing statistically significant ($P < 0.05$) changes in age-standardized incidence rates between 1963–72 and 2011–15, in males and in females.

eye cancers 7.3 and 10.7, respectively ($P < 0.01$)].In women, the rates of cancers of the breast and cervix have about tripled [ASRR 2.7 and 2.9, respectively ($P < 0.01$)], while in men, the incidence of cancer of the prostate increased 2.6-fold ($P < 0.01$) and there was a significant increase ($P < 0.05$) in the incidence of colorectal cancers (ASRR = 1.71).

Figure 3 shows age-specific incidence rates in the two periods for the most common cancers in men: esophagus (**Fig. 3A**) and liver (**Fig. 3B**), and in women—cancer of the breast (**Fig. 3C**) and cervix uteri (**Fig. 3D**). The rate of change for these cancers appears to be more or less the same for all age groups—although for cancer of the esophagus, the differential is rather more in the older age groups [ASRR 0.39 at ages 0–49, 0.28 at age 50+ ($P < 0.1$)].

Discussion

The incidence rates of all of the most common cancers of males in 1963–72 significantly declined during the 50-year period (esophagus, liver, lung, bladder). At the same time, cancers associated with "westernization" of lifestyles (breast, prostate, large bowel) increased in incidence, as did cancers related to infection with HIV-AIDS (Kaposi sarcoma, NHL, eye cancers), which have come to comprise a much larger proportion of the total burden, as did the incidence of the cancer of the cervix (also AIDS-related), which almost tripled during the period.

Data for the period 1963–1972 were evaluated to be of sufficient quality to be included in early volumes of CI5. In those years, the

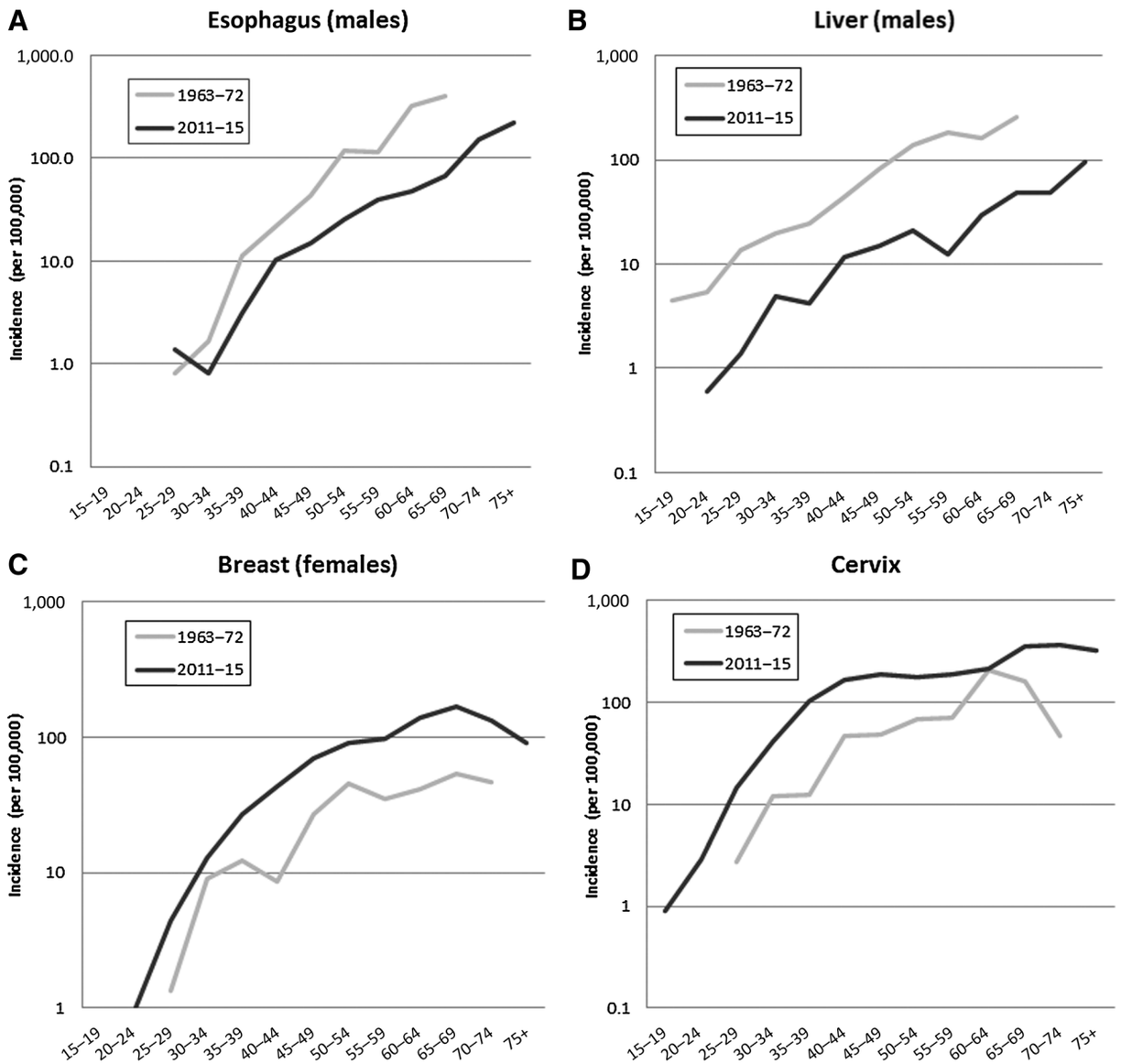

Figure 3.
Age-standardized incidence rates (per 100,000) for cancers of esophagus in males (**A**), liver in males (**B**), breast in females (**C**), and cervix (**D**), in 1963–72 and 2011–15.

data were collected from Mpilo hospital, which was the only facility providing diagnostic and hospital treatment for the Black (African) population, so that it is likely that the great majority of Black African cases resident in Bulawayo and reaching medical attention in those years were included. There was a rather high proportions of morphologically verified cases (92% overall; Supplementary Table S1); the registry did not record whether cases had been registered on the basis only of information on a DCO. For those years, there was some uncertainty about the accuracy of the estimated population at risk in the oldest age groups, although we tried to minimize this by collapsing them to relatively broad groups (70+ for females, 65+ for males) when calculating age-standardized rates. In the recent period, there are many more diagnostic and treatment services serving the population—some six public and private hospitals, two pathology laboratories, and a hospice as well as outpatient and hematology clinics, all of which are used as data sources by the registry (7). It remains to be seen whether the recent data will be deemed suitable for the next volume of CI5. Indicators of quality are reasonable (74% morphologically verified and 4.5% DCO) and the recorded rates are comparable with those in Harare (ref. 7; with the possible exception of cancers of the mouth and pharynx and leukemias, which appear to be relatively low).

The large increases in incidence of cancers related to HIV-AIDS—Kaposi sarcoma, eye cancers, NHL, and cervix uteri are not surprising. The epidemic in Africa only began in the 1980s, and by the time of the second period presented, HIV prevalence in adults (15–49 years) in Bulawayo was between 19.1% (2010–11) and 14.3% (2015), and higher in females than in males (11, 12).

On the other hand, the declines in the incidence of cancers of the esophagus, larynx, and lung among males must be related to decreases in exposures to other risk factors.

The incidence of lung cancer in men in Bulawayo in 1963–72 is the highest recorded (in a nonselected population) in Africa, with an age-adjusted (world standard) rate of 46.6 per 10^5, comparable with those in California at the same period (3). The high risk in Black males from Southern Africa has been noted previously (13), with rates in Natal, South Africa, in the early 1960s much the same as in Bulawayo (2). On the basis of smoking histories obtained at interview by the cancer registrar, Parkin and colleagues (5) estimated that OR of lung cancer associated with tobacco smoking was 5.2, and with a prevalence of 41% cigarette smokers (among cases of cancer not associated with smoking), the proportion of lung cancer attributable to cigarette smoking was estimated as 49%, and to all forms of tobacco, 60%.

It is not immediately apparent why there appears to have been such a precipitate decline in incidence in men. Although lung cancer is probably underdiagnosed in Africa the age-standardized rate in 2011–2015, at 4.7 per 10^5, is similar to that in U.S. nonsmokers (14) and not far from the average for sub-Saharan Africa (15), but it is very unlikely that accuracy of diagnosis is so much lower in the 21st century than in the 1960s. Tobacco smoking remains relatively common in Zimbabwe (prevalence of tobacco smoking in men in 2012 was 31.5% (16)). Bulawayo lies in the centre of Matabeleland (split into three provinces), the seat of many mining enterprises, mainly gold, but also coal, nickel, chrome, copper, and asbestos (17). It is quite likely that many ex-miners reside in the city—indeed, during the early years of the registry, 40% of male cancer cases gave a history of ever having been a miner. Mining is associated with an appreciable increased risk of respiratory diseases, including cancer (18, 19), and this risk persists in retired workers (20). Some of the decline in incidence of lung cancer may relate to a decrease in the number of ex-miners in the population, and lower exposure levels in more recent cohorts of miners, although a history of mining was associated with only a small increase in risk of lung cancer in the early study (5).

The striking geographic distribution of esophageal cancer in Africa, and the high rates in Eastern and Southern Africa, with a large excess of cases in males versus females is a long-standing observation, and has stimulated a lot of research into causative etiological factors (21, 22). As in high income countries, tobacco and alcohol are regularly identified as risk factors in case–control studies [e.g., Pacella-Norman and colleagues in 2002 (23)], and, based on interview data from the early period of registration, about half of the cases in men could be attributed to tobacco smoking (24). However, it is very unlikely that changes in smoking or alcohol exposure are responsible for the 3-fold decline in risk in men since that time, and misdiagnosis of gastric cancers in the early time period (without the availability of gastroscopy) is also unlikely. Gastric cancer incidence has also declined in males, and there has been almost no change in the type of carcinoma diagnosed. In 1963–72, more than 90% of cases had a histologic diagnosis and 98.5% of those with specified histology were squamous cell carcinomas. Although the proportion of cases with histology had fallen to 63% in the second period, the proportion of squamous cell carcinomas was still 95%. The rather larger differential in risk with increasing age (**Fig. 3**) is consistent with the risk factors being more prevalent in older generations (whatever they may be).

The incidence of liver cancer has declined significantly in both sexes. This is not due to misdiagnosis of metastatic cancers in the 1960s—in that period, over 90% of cases had a histological diagnosis, and 93% were hepatocellular carcinomas. In Africa, the major risk factors for liver cancer are chronic infection with hepatitis B and C (responsible for about half of liver cancer cases in Southern Africa (25)). Aflatoxin is also an important cause of liver cancer in sub-Saharan Africa, acting multiplicatively with hepatitis B (26).

It is impossible to know what changes in exposure to these important risk factors have occurred. Exposure to aflatoxins in foodstuffs appears to be an ongoing problem (27, 28). The prevalence of HBsAg positivity among adults in Zimbabwe was reported at 14.4% in 2010, although higher prevalence has been recorded historically (29). Prevalence of hepatitis C virus infection is much lower [about 1.6% (30)]. Zimbabwe introduced vaccination of infants against hepatitis B in the 1990s, and coverage was already well over 90% by 2011 (31) but this cannot have impinged on prevalence of infection in adults at risk of hepatocellular carcinoma.

Bladder cancer—especially squamous cell carcinoma (SCC)—is known to be linked to urinary schistosomiasis (32). In 1963–1972, 66% of the 70 bladder cancers registered with specified morphology were SCC. An association between bladder cancer risk and past history of bilharzia or hematuria (OR 3.9 for men, 5.7 for women) was noted in Bulawayo in the 1960s (33). Urinary schistosomiasis remains prevalent in Zimbabwe, although there is some evidence that prevalence is waning (34). The proportion of cases with a specified morphologic diagnosis in 2011–2015 was only 27%, so it is not possible to judge whether the decline in incidence is different according to cell type.

The incidence of breast cancer is increasing in almost all African cancer registries (35). Changing risk factor profiles—especially in relation to fertility, hormone use, body weight, diet, exercise, etc., in successive generations of women must account for these increasing trends, and for the greater rates of increase in older women seen in most series. In Bulawayo, the increase observed is equivalent to an average annual rate of increase of 2.2%, rather less than that observed in the capital, Harare, between 1990 and 2014 (3.8%), but similar to that in Kampala Uganda (2.1%) in the same period (35). In Bulawayo, the increase appears to be similar in premenopausal- and postmenopausal women (**Fig. 3**).

The increasing incidence of cancer of the cervix is also consistent with trends elsewhere in Africa, where there are few effective population screening programmes (36). The increase in Bulawayo is equivalent to an annual percentage change of 2.4%, rather higher than the rates of increase in Harare (1.2%) and Kampala (1.3%; ref. 36). Although cervix cancer has become a relatively rare cancer in high-income countries, this is the consequence of the implementation of successful prevention programmes—notably by screening for preinvasive cancers (37). In sub-Saharan Africa, where about 20% of the global burden of cervix cancer cases occur, a high prevalence of human papillomavirus (38), the epidemic of HIV-AIDS—which has been particularly severe in Western Zimbabwe (39) and the lack of population-wide screening programmes are the major contributors to the rising incidence.

Prostate cancer incidence has been increasing in many parts of the world, even in the years prior to the introduction of the PSA test for latent prostatic cancer (40). There have been marked increases in incidence since the early 1990s in Kampala (41) and Harare (42), as well as in the rural population of Eastern Cape province of South Africa (43), and mortality rates are increasing in South Africa (44). In Harare, the incidence in the Black population has risen more rapidly than in Whites (45). Prostate cancer is now the most common cancer of men in Bulawayo, as it is in all but six countries of sub-Saharan Africa (15). The reason for these marked increases in incidence in Africa is unknown. Few environmental risk factors have been

identified for prostate cancer, and changes in those that are known cannot explain the large changes in incidence. Probably, it reflects improvements in diagnosis among elderly men with urinary symptoms, following increasing availability of PSA testing, diagnostic ultrasound, and CT scans.

Conclusions

There are very few sets of data from sub-Saharan Africa which can give us insights into the evolution of the cancer epidemic over the past half century. Only the cancer registry of Ibadan (Nigeria) has been able to operate continuously since the 1960s (7). These data from Bulawayo in Western Zimbabwe are therefore very precious. Although there are questions about the quality of diagnosis, and completeness of registration over time, many of the changes observed are so huge that it is quite inconceivable that the direction of change, if not their precise magnitude, are due to artefact. Apart from the dramatic changes wrought by the epidemic of HIV-AIDS, many of the trends are compatible with the profile of cancer becoming more "westernized" (increases in large bowel, breast and prostate cancers) with decreases in some cancers formerly associated with this region of Africa (esophagus, liver, bladder). The continued high rate of cancer of the cervix is an exception—its decline in high-income countries has nothing to do with lifestyle change, rather the result of a planned preventive intervention, which at long last is envisaged for Africa (46).

Authors' Disclosures

No disclosures were reported.

Authors' Contributions

D.M. Parkin: Conceptualization, investigation, methodology, writing–original draft, writing–review and editing. **T. Chingonzoh:** Resources, data curation, writing–review and editing. **S. Vuma:** Resources, data curation, writing–review and editing. **B. Liu:** Project administration, writing–review and editing. **E. Chokunonga:** Data curation, validation, project administration, writing–review and editing. **N. Ndlovu:** Writing–review and editing. **M. Borok:** Resources, supervision, funding acquisition, writing–review and editing.

Acknowledgments

We would like to pay tribute to the pioneering work of Molly Skinner, radiotherapist in Mpilo Hospital, who founded and supervised the cancer registry between 1963 and 1977, and Agnes Ndlovu, the cancer registrar, who carefully compiled all of the data from those early years. We also acknowledge the work of the two cancer registrars responsible for data collection in 2011–2015 (Tongai Tapera and Sukoluhle Mguni), and Jacques Ferlay (IARC) for assistance with the analysis.

No financial support was available for the preparation of this article.

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Received July 17, 2020; revised November 14, 2020; accepted February 2, 2021; published first February 22, 2021.

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