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Full Length Research Paper

Cancer incidence in Malawi: Time trends in Blantyre 1996-2005 and predictions up to 2015

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As in many sub-Saharan countries, communicable diseases have been given greater public health priority in Malawi, although the magnitude of the cancer burden is increasing as a result of demographic changes, as well as the impact of the HIV pandemic. To be able to describe the patterns of cancer between 1996 and 2005 and to predict the incidence and total burden of cancer for 2015, we analysed data from the Malawi National Cancer Registry for the period from 1996 to 2005. We obtained age standardized incidence rates for the most common cancers in Malawi. Linear trend models were used to predict incidence rates and the burden of cancer for Blantyre for 2015. The most common cancers, in terms of age-standardized (world) incidence rates were Kaposi sarcoma (50.5 per 100,000 for males, 26.4 for females), cervical cancer (49.3 per 100,000), oesophageal cancer (22.3 for males, 14.6 for females), non-Hodgkin lymphoma (6.6 for males, 5.3 for females), eye cancer (4.4 for males, 5.4 for females), and breast cancer (11.9). Predictions based on the rather rapidly increasing trends would yield an upper limit of 2512 cases of cancer in Malawi by 2015; an absolute percentage increase of 193.4 % and 242.7 % among males and females, respectively. Based on our analysis we conclude that incidence rates of cancer in Blantyre have been increasing between 1996 and 2005. Apart from the AIDS pandemic in Malawi, population growth and ageing will also contribute to the projected threefold increase in the number of cancer cases.

Keywords: Cancer, incidence, predictions, time trends

INTRODUCTION

An estimated 12.7 million new cases of cancer worldwide occurred in 2008, and 7.6 million cancer deaths (Ferlay 2008). The cancer burden in high-income areas has surpassed that of low- and medium-income areas, in which 80% of the global population currently reside. The profile of the most common cancers differ markedly by

level of income within a given country or region; cancers of the prostate, lung and colorectum – frequent in westernized countries – do not, for instance, figure among the five most common cancers in Sub-Saharan Africa, where infection-related Kaposi sarcoma, and cancers of the cervix and liver often dominate, alongside female breast cancers (Parkin, Sitas et al. 2008).

As in many sub-Saharan countries, communicable diseases have been afforded a greater public health priority in Malawi, given the magnitude of the disease burden relative to cancer (World Health Organisation 2004). Malawi has been particularly affected by the HIV

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pandemic, with the prevalence of infection in adults aged between 15 and 49 years in Blantyre city estimated to be 22.3% in 2004 (National Statistical Office of Malawi 2005), the highest prevalence in the country; the national prevalence of HIV in Malawi was estimated at approximately 12% circa 2007 (National Aids Commission of Malawi 2008).

However, it is clear that non-communicable diseases, including cancer, will become an increasing burden on health services in Malawi, as in other low and middle income countries (Samb 2010). Knowledge of the cancer profile in Malawi can be derived from the Malawi Cancer Registry, which, although recording data from various parts of the country, has aimed at complete population coverage of the Blantyre District (urban and rural divisions). The first report covered the first five years of registration (1994-8) (Banda, Parkin et al. 2001), while more recent results (2000-2001) have been published in Parkin et al (2003) (Parkin 2003). The profile of childhood cancer was reported by Mukiibi et al (1995) (Mukiibi 1995) and Banda & Liomba (1999) (Banda 1999). There was a relatively high incidence of Kaposi sarcoma, as well as cancers of the oesophagus and cervix uteri, with more modest rates of prostate, breast and bladder cancer, as well as non-Hodgkin lymphomas.

The current report provides an update of the incidence to 2005, with the aim of describing and interpreting the incidence trends in the urban population of Blantyre within the last decade (1996-2005). We focus on the major types of cancer observed in the Blantyre population: Kaposi sarcoma, non-Hodgkin lymphoma, eye and oesophageal cancer, as well as cancers of the breast and cervix in women. Based on these trends, we predict the future cancer burden up to 2015; such information is valuable in planning cancer services and deciding on the allocation of finite resources to prevention, treatment and palliative care, as well as providing a baseline against which the success of interventions can be measured.

MATERIALS AND METHODS

The Malawi National Cancer registry was established in 1989, and became population-based for the Blantyre District (Urban and Rural), in 1993. Registration is carried out by a programme of regular visits by cancer registrars to all hospitals (government and private) in the District, with data recorded on cases of cancer from hospital records departments and clinical services, where cases might have been diagnosed or treated. There is no comprehensive system of death registrations in Malawi, and thus death certificates are not used as a source of information. Cancer diagnoses are coded according to the International Classification of Disease for Oncology (ICD-O). The CANREG system provided by IARC is used for the recording of cases; this includes checks at data entry for potential duplicates as well as for impossible or unlikely codes or combinations of codes,

and provides automatic code conversions to ICD-10.

Incidence data were extracted from the registry database by cancer site (coded using ICD-10), sex and age group (ages 0-14, 15-24, 25-34, 35-44, 45-54, 55 and over) and year of registration (1996-2005). Censuses were carried out in 1998 and 2008. The population of Blantyre District (urban and rural) was 809,397 in 1998 and slightly more than 1 million in 2008 (National Statistical Office of Malawi). The data extracted and analysed in this paper are restricted to this population, with residential status defined as persons who have lived in Blantyre for at least six months (Banda, Parkin et al. 2001). About 10% of registrations are incomplete due to missing ages.

Data on the underlying population-at-risk came from two sources. Population estimates for Blantyre for 1996 to 1997 and 1999 to 2005 were estimated via linear interpolation (Gerald 1984) using census data for the years 1987 (National Statistical Office of Malawi), 1998 (National Statistical Office of Malawi) and 2008, whereas more recent population data for 2000 and 2015 were available by sex and age from the tables of national population projections for 2009-2030 produced by the National Statistical Office of Malawi (NSO) (National Statistical Office of Malawi).

Trend analysis was restricted to the most frequent cancer types observed in Blantyre over the 10-year period. Annual age-specific and age-standardised incidence (world) rates (ASR) for 1996-2005 were calculated, where applicable, by sex for Kaposi sarcoma (ICD-10 C46), cancer of the eye (ICD-10 C69), non-Hodgkin lymphomas (ICD-10 C82-C85, C96), oesophageal cancer (ICD-10 C15), female breast (C50) and cervix cancer (ICD-10 C53). Of the 372 eye cancers, 75% were squamous cell carcinomas of the conjunctiva and 20% retinoblastomas). We also ascertained a residual group comprising "all other cancers combined" (see footnote, Table 1) to enable the prediction of the total cancer burden in 2010 and 2015. The all-ages ASR has been corrected for cases of unknown age by multiplying by T/K, where T is the total number of cancer- and sex-specific cases and K is the corresponding number for which age is known.

The study used time-linear models (Hakulinen and Dyba 1994; Dyba 1997; Dyba and Hakulinen 2000; Dyba and Hakulinen 2008) to predict cancer incidence for 2015 by extrapolating linear trends seen in the recent past, with the base of prediction set at 1996-2005. In the models, the number of cases of cancer in each age-sex group were assumed to have a Poisson distribution (Dyba and Hakulinen 2000). Incorporated in the prediction methods are specific models suitable for increasing and decreasing trends. As *a priori* analyses indicated increasing trends for the major cancer types in Malawi, we chose the following candidate models that avoided the prospect of an exponential explosion in incidence (Model1) and positive estimate of age standardised rate (Model2):

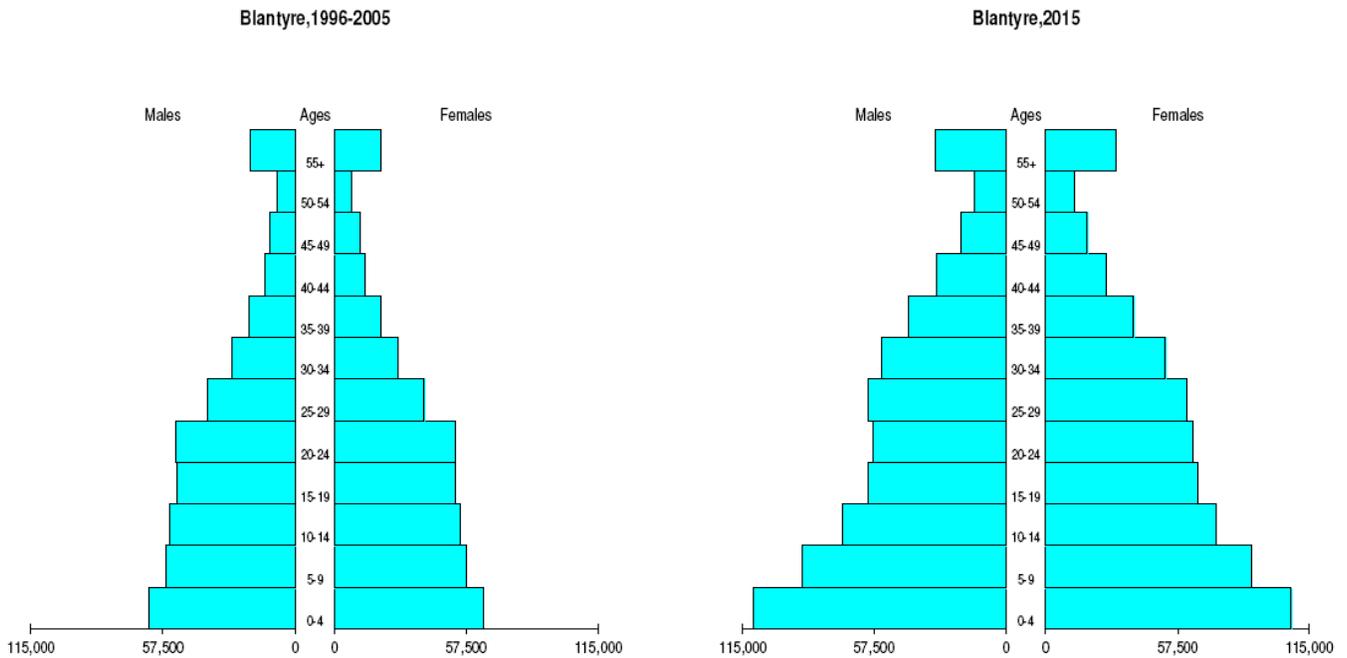


Figure 1. The Population Pyramids of Blantyre District
 Left Panel: Mean annual population for 1996-2005

Right Panel: Projected population for 2015

$$E \left[\frac{c_{it}}{n_{it}} \right] = \alpha_i + \beta_i t \dots\dots\dots (1) \quad \text{and}$$

$$E \left[\frac{c_{it}}{n_{it}} \right] = \alpha_i + \beta t \dots\dots\dots (2)$$

where

c_{it} is the number of cases of cancer in age group i and year t

n_{it} is the number of people (pyr) in age group i and year t

$E \left[\frac{c_{it}}{n_{it}} \right]$ is the expected value of incidence in age group i and year t

α_i is the intercept parameter - baseline incidence for age group i .

β_i is the slope parameter for age group i

β is a common parameter for all age groups

For most combinations of age, sex and cancer site, Model 1 was chosen, because the larger number of parameters gave a better fit. In some cases, however, Model 1 could not be localized due to data limitations, and then Model 2 was fitted instead. Model 2 was fitted for Kaposi sarcoma in women.

The fitted models were used to estimate predicted incidence rates for 2015. These incidence rates were then multiplied by the population forecasts for Blantyre to yield the corresponding number of predicted cancer cases.

To quantify the changes in the annual number of new cases of cancer in 2015 from the mean annual number

observed 1996-2005, the approach by Møller et al (2002) (Moller, Fekjaer et al. 2002) was adopted, with the net differences partitioned into changing risk of cancer and changing age structure and population size.

RESULTS

Population projections

The average and projected age-specific population pyramids for 1996-2005 and 2015 are displayed in Figure 1 in the left and right panel respectively.

The average population in 1996-2005 and population projection for 2000 estimated at 858,049 and 848442 respectively are projected to increase to 1,283,333. The population forecast for 2015 indicates that there will be 51% more inhabitants in Malawi than during the period 1996-2005 and 2000. Furthermore, the mean projected number of people aged 50 years or over in 2015 is forecasted to be 51% greater than the estimated population 1996-2005.

Age standardised incidence estimates (1996-2005)

A mean annual number of 791 cases of cancer were diagnosed 1996-2005 in Blantyre (Table 1), with a slight majority of these occurring in men (51.8%). Almost half of the male cancers were Kaposi sarcoma (ASR 54.1, comprising 47.9% of all male cancer cases), with oesophageal cancer (ASR 21.5, 10.5%), non-Hodgkin lymphoma (ASR 7.0, 7.3%) and eye cancer (ASR 4.7, 4.4%) the next three most frequent cancers among

Table 1. Mean annual number of cases and age standardised rates (ASR) by sex group for selected sites for Blantyre (1996-2005)

Site	ICD10	Mean annual number of cases 1996-2005	%	ASR(World)	Morphological verification (%)
Males					
Oesophagus	C15	43	11.0	21.5	18.5
Kaposi sarcoma	C46	196	48.0	54.1	10.6
Eye	C69	18	4.4	4.6	79.0
Non-Hodgkin lymphoma	C82-85,C96	30	7.3	7.0	66.6
Other cancers#		123	30.0	56.7	55.7
All cancers		410	100.0	143.0	32.0
Females					
Oesophagus	C15	24	6.3	13.4	12.4
Kaposi sarcoma	C46	98	26.0	27.8	12.6
Breast	C50	23	6.0	11.4	67.4
Cervix uteri	C53	103	27.0	47.6	51.6
Eye	C69	20	5.2	5.7	82.1
Non-Hodgkin lymphoma	C82-85,C96	21	5.5	5.4	68.8
Other cancers#		93	24.0	42.7	66.5
All cancers		382	100.0	152.8	46.2

#Other cancers comprise Oral cavity (ICD-10 C00-08), Nasopharynx (ICD-10 C11), Other pharynx (ICD-10 C09-10, C12-C13), Stomach (ICD-10 C16), Colon and rectum (ICD-10 C18-21), Liver (ICD-10 C22), Bronchus and lung (ICD-10 C33-34), Skin melanoma (ICD-10 C43), Other skin cancers (ICD-10 C44), Ovary (ICD-10 C56), Male breast cancer (ICD-10 C50), Other female genital cancers (ICD-10 C51-52, C57), Penis (ICD-10 C60), Prostate (ICD-10 C61), Bladder (ICD-10 C67), Thyroid (ICD-10 C73), Hodgkin's disease (ICD-10 C81), Leukaemia (ICD-10 C91-95) and a residual of other neoplasms whose ICD10 code follows: ICD10-C14, ICD10-C90, ICD10-C22-C26, C30-34, C40-44, C17-C45, ICD10-C47-C49, ICD10-C62-C66, ICD10-C71-C72, C74-C77, ICD10-C80

Malawian men.

All other cancer forms in combination constituted the remaining 30.1% of the male cancer burden over the 10-year period. The male: female ratio of the five cancer types diagnosed in both men and women indicated the preponderance of cancers in men, including Kaposi sarcoma (M:F ratio of 2.0), oesophageal cancer (1.8), non-Hodgkin lymphoma (1.4) and other cancer forms (1.3); eye cancer was the exception, with a M:F ratio of 0.9.

In women, over half of all diagnosed cancer cases in Malawi were either cervical cancer (ASR 47.6, constituting 27.0% of female cancer cases) or Kaposi sarcoma (ASR 27.8 per 100,000, 25.7%). Eye cancer (ASR 5.7, 5.2%), non-Hodgkin lymphoma (ASR 5.4, 5.5%), oesophageal cancer (ASR 13.3, 6.3%), and breast cancer (ASR 11.3, 6.0%) were the next four most frequent types of female cancers observed, and the six neoplasms explained over two-thirds of the total female cancer burden.

The basis of diagnosis of 36% and 42% of cancers in men and women respectively was morphological verification (MV). Most of cancers of the eye, breast and NHL were diagnosed using cytological or histological examination of tissue. Just a small proportion of Kaposi sarcoma and oesophageal cancer in both genders were diagnosed by cytology or histology.

Incidence trends

Age-specific incidence rates for Kaposi sarcoma, breast, oesophageal, cervical and eye cancer, as well as other cancers combined are shown in Figure 2.

For Kaposi sarcoma and cancer of the eye, incidence rates are greatest in the age group 35-44 in both sexes. For oesophageal cancer (men and women), breast (women) and cervical cancer (women) and other cancers (men and women), the incidence rates continue to rise with increasing age.

The age-standardised rates of Kaposi sarcoma, non-Hodgkin lymphoma, oesophageal and eye cancers, as well as other cancers combined, and the fitted trend between 1996 and 2005, together with the predicted rates for 2015 are shown below for men and women in Figures 3 and 4 respectively. Also shown is the average rate for the period 1996-2005, projected forward to 2015 (assuming no further change).

The cancer-specific trends are generally increasing in both sexes between 1996 and 2005, although there is considerable year-on-year random variation evident in the trends. In men, incidence rates of Kaposi sarcoma, non-Hodgkin lymphoma, oesophageal and eye cancer are predicted to increase (Figure 3).

Similarly, in women incidence rates of non-Hodgkin

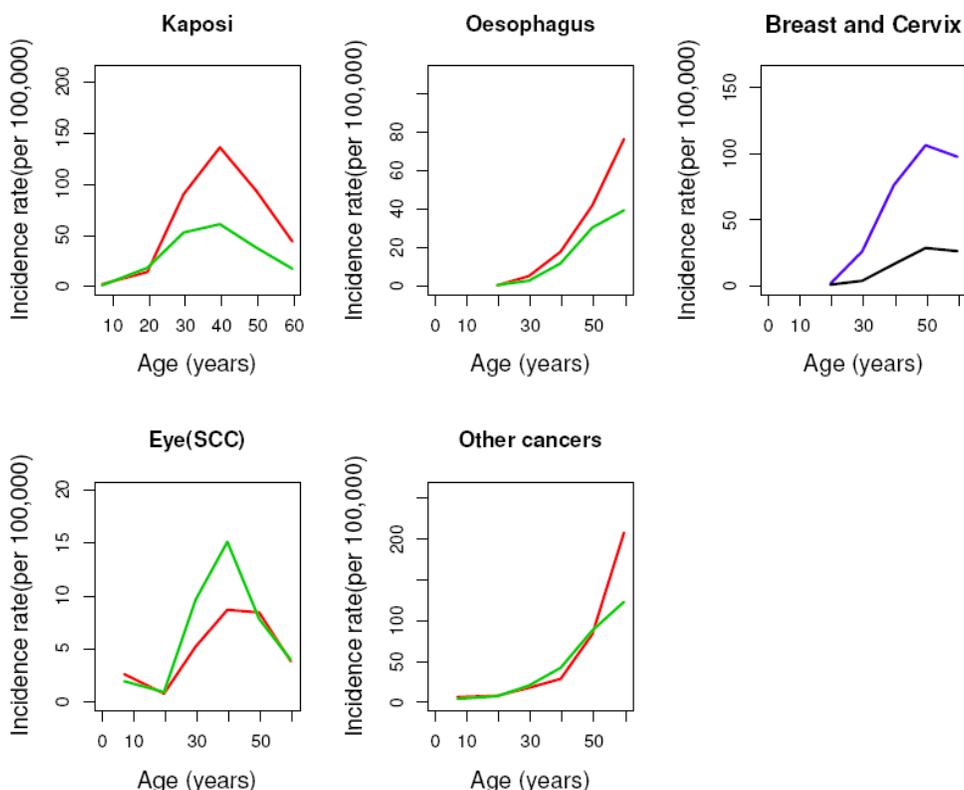


Figure 2. Age-specific incidence trends among males and females of Blantyre district, Malawi 1996-2005. Red line – Males; Green line- Females; Blue line - Cervical cancer; Black line - Breast cancer

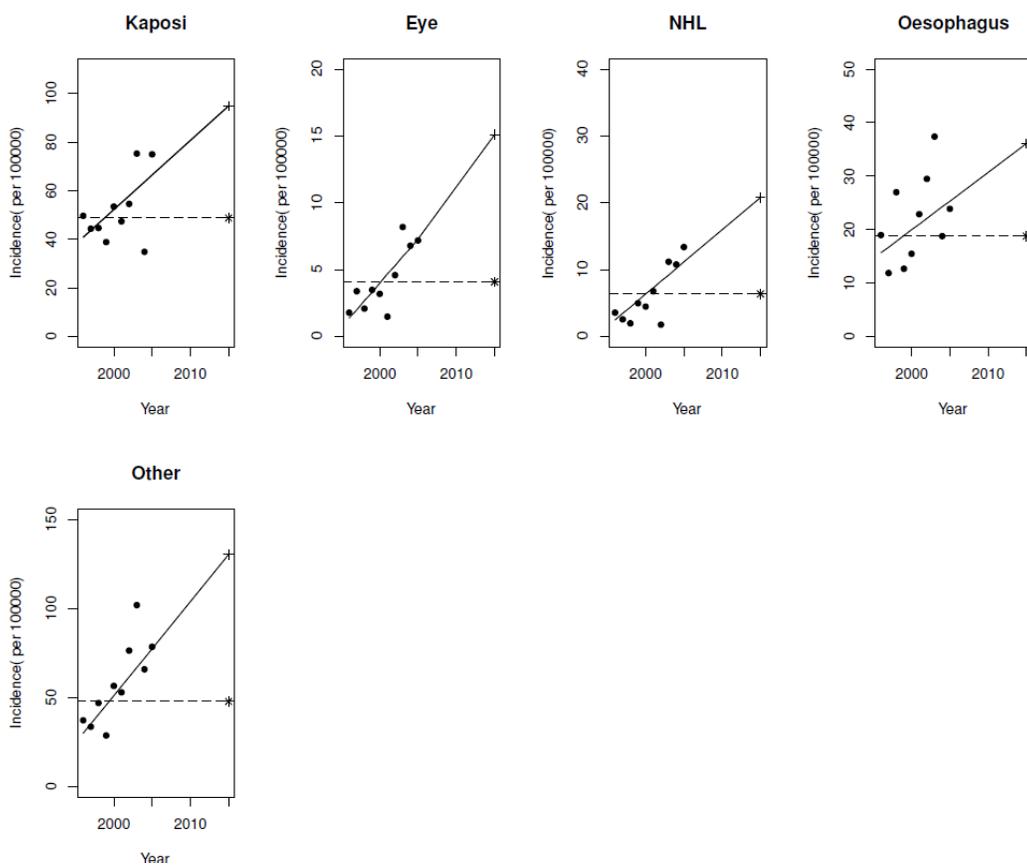


Figure 3. Age-standardised incidence trends for Kaposi sarcoma, and cancers of the oesophagus, eye and all other cancers combined among males in Blantyre, Malawi for 1996-2005 and projections for 2015. + 2015 Projected standardized incidence rate; * 1996-2005 Mean standardized incidence rate

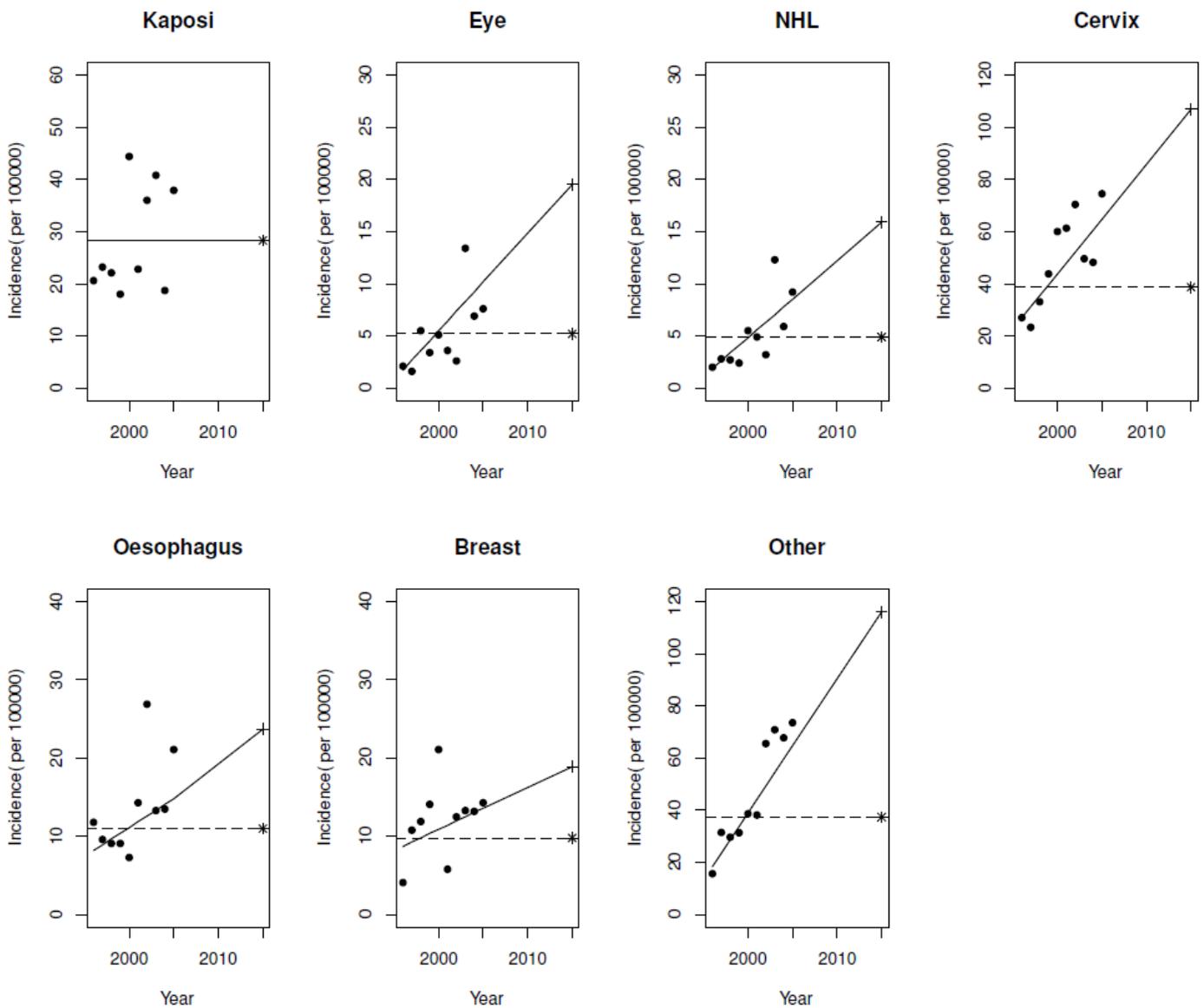


Figure 4. Age-adjusted incidence trends of cervical cancer, breast cancer, Kaposi sarcoma, oesophageal, eye and other cancers among females in Blantyre, Malawi for 1996-2005 and projection for 2015.
 + 2015 Projected standardized incidence rate; * 1996-2005 Mean standardized incidence rate
 The bold line is the projected trend and the dotted line is mean of ASR's of all the years from 1996 to 2005

lymphoma, oesophageal and eye cancer are predicted to increase (Figure 4). However, the age standardised incidence of Kaposi sarcoma in women is predicted to be constant up to 2015. In both sexes, the incidence rates of all other cancers are also predicted to increase. There are large year-to-year variations in the trends of the incidence rate of Kaposi sarcoma in men and other cancers. These, however, are unlikely to cause similar changes in incidence.

Total cancer burden prediction for 2015

The mean annual number of male cancer cases in Blantyre for 1996-2005 was 410. If the rates observed in this decade were maintained, the numbers would increase to 618 by 2015, a 51% increase due to the

projected increase (and ageing) of the population (Table 2). From the trends-based model, an increase to 1147 cases is predicted by 2015 (Table 2); a rise of 180%.

The numbers of non-Hodgkin lymphoma, eye and other cancer cases among men are projected to have the greatest increase of over 200% between 1996-2005 and 2015.

For Kaposi sarcoma, the number of cases is projected to increase by over 120%. The smallest increase in number of cases due to risk is predicted for oesophageal cancer. The total annual number of female cases of cancer in 2015 is predicted to increase by 841 cases which is an increase of over 200%. There are large projected increases in the number of female cases of oesophageal cancer, Kaposi sarcoma, non-Hodgkin lymphoma, eye cancer, cervical, breast cancer and other cancers.

Table 2. Percentage changes in the projected annual number of cases for 2015 relative to the mean annual number of cases for 1996-2005 in Blantyre, Malawi by sex and site.

Site	ICD10	OBSERVED 1996-2005		PREDICTED CASES 2015				
		Mean annual cases N(%)	No change in rates			Prediction		
			N(%)	%Change	N(%)	Lower	Upper	%Change
Males								
Oesophagus	C15	43(10.5)	65(10.5)	51.2	89(7.8)	44	135	107.0
Kaposi sarcoma	C46	196(47.8)	299(48.4)	52.6	454(39.6)	78	830	131.6
Eye	C69	18(4.4)	27(4.4)	50.0	76(6.6)	52	100	322.2
Non-Hodgkin lymphoma	C82-85;C96	30(7.3)	46(7.4)	53.3	145(12.6)	98	191	383.3
Other#		123(30.0)	181(29.3)	47.2	383(33.4)	300	465	211.4
Total		410(100.0)	618(100)	50.7	1147(100)	572	1721	179.8
Females								
Oesophagus	C15	24(6.3)	39(6.3)	62.5	62(5.1)	36	89	158.3
Kaposi sarcoma	C46	98(25.7)	159(25.6)	62.2	221(18.1)	98	344	125.5
Breast	C50	23(6.0)	38(6.1)	65.2	59(4.8)	25	93	156.5
Cervix	C53	103(27.0)	171(27.5)	66.0	328(26.8)	245	411	218.4
Eye	C69	20(5.2)	33(5.3)	65.0	94(7.7)	52	137	370.0
Non-Hodgkin lymphoma	C82-85;C96	21(5.5)	33(5.3)	57.1	93(7.6)	47	139	342.9
Other#		93(24.3)	149(24)	60.2	366(29.9)	307	426	293.5
Total		382(100.0)	622(100)	62.8	1223(100)	810	1639	220.2

#Other cancers comprise Oral cavity (ICD-10 C00-08), Nasopharynx (ICD-10 C11), Other pharynx (ICD-10 C09-10, C12-C13), Stomach (ICD-10 C16), Colon and rectum (ICD-10 C18-21), Liver (ICD-10 C22), Bronchus and lung (ICD-10 C33-34), Skin melanoma (ICD-10 C43), Other skin cancers (ICD-10 C44), Ovary (ICD-10 C56), Male breast cancer (ICD-10 C50), Other female genital cancers (ICD-10 C51-52, C57), Penis (ICD-10 C60), Prostate (ICD-10 C61), Bladder (ICD-10 C67), Thyroid (ICD-10 C73), Hodgkin's disease (ICD-10 C81), Leukaemia (ICD-10 C91-95) and a residual of other neoplasms whose ICD10 code follows: ICD10-C14, ICD10-C90, ICD10-C22-C26, C30-34, C40-44, C17-C45, ICD10-C47-C49, ICD10-C62-C66, ICD10-C71-C72, C74-C77, ICD10-C80

DISCUSSION

The growth and ageing of the world population will lead to an increase in the global burden from non-communicable diseases including cancer, and the increase is projected to be particularly marked in low and middle income countries (Mathers 2006). Our analysis confirms that similar changes can be anticipated in Malawi; the shifting demographics will inevitably increase the numbers of cancer cases diagnosed each year. However, our results suggest that, over and above this effect, the increasing incidence rates will result in an even larger contribution of cancer to the disease burden, with the number of cases of cancer in 2015 predicted to be up to three times those observed on average over the study period 1996-2005.

Projections of cancer incidence rates make the implicit assumption that the trends observed in the past that are used as a prediction base (1996-2005 in this paper) are accurately measured, and that they will continue into the future, either unchanged (as in our short term predictions), or with pre-defined modifications (Bray 2006). This assumption was validated by exploratory analyses.

The observed trends in 1995-2006 include rather dramatic increases in incidence for almost all cancers considered, and it seems likely that the temporal pattern

observed is partly based on artefact, due, for example, to changes in the completeness of case ascertainment by the cancer registry in the last few years. During the decade under study there were changes to the registration methodology that would have contributed. Several new hospitals serving the catchment population were opened, and added to the case finding sources, and active search for cases was extended to all hospitals, having been confined prior to 1999 to the major teaching hospital (Queen Elizabeth Central Hospital), with reliance on passive surveillance at smaller centres. Given these uncertainties concerning the reasons for the increasing trends in the period 1996-2005, as well as the implausibly high rate of change for some cancer sites, it would be prudent to interpret the rates and number of cases based on the predicted change in incidence with extreme caution as they surely represent the upper limit of the cancer burden in 2015. Conversely, those based on stability of rates (those observed in 1996-2005) represent the lower limit of future burden circa 2015. Nevertheless population growth and ageing alone will yield an increase in cancer cases of 448 - 57% by 2015, assuming rates remain fixed. Blantyre is the commercial capital of Malawi and migration into Blantyre City is always high as people look for financial or job opportunities. Besides, the total fertility rate of Blantyre -4.3% by 2004 - is high enough to

lead to the projected increase in the total population in 2015.

AIDS-related cancers (Kaposi sarcoma, non-Hodgkin lymphoma and eye cancers) comprised 60% of cancers in men in 1996-2005, and 36% of cancers in women; a further 26% of female cancers were cancers of the cervix, also considered to be "AIDS-defining". While it is possible that the increases in incidence of these cancers relates to the epidemic of HIV-AIDS, it should be noted that, although the prevalence of HIV increased in the years up to 1998 (when it peaked in adults aged 15-49 at around 15% (UNAIDS 2011)), prevalence has been declining since then, to around 11% in 2009. In addition, the availability and provision of antiretroviral therapy – which suppresses manifestations of HIV and AIDS such as cancer - has increased, from almost zero circa 2004, to more than 50% of AIDS patients in 2009 (UNAIDS 2011). Similar changes in Uganda have resulted in quite marked declines in the incidence of Kaposi Sarcoma (Parkin 2010). The incidence of Kaposi sarcoma, the cancer with the strongest association with HIV, has increased at slower rate than any other of the malignancies considered, and the increasing incidence of the "other cancer" category (12-13% per year in 1996-2005), which does not include any HIV-related malignancies, also implies that HIV infection is unlikely to be the principal cause of the increase in incidence. The big increase in the projected number of cases of Kaposi sarcoma is almost entirely due to population increase and ageing, since incidence rates are projected to remain fixed.

Mlombe et al (2009) had previously noted the increasing incidence of oesophageal cancer (Mlombe 2009). The increase in the observed incidence trend of breast cancer trends during 1996-2005 is similar to that observed in Kampala, Uganda in 1991-2006 (where it was ~5% per year (23)). Risk factors for breast cancer are increasing in prevalence in the population of Malawi, for example, contraceptive use among currently married women increased from 13.0% in 1992 to 30.6% in 2000 and 32.5% by 2004 and declining fertility, although it is unlikely that these could account for such large increases in incidence.

Our analysis illustrates that cancer is already a significant health problem in Blantyre. Projections based on demographic projections, or on incorporating recent trends reveal that cancer is very likely to become a major public health issue in the coming decades. While some of the trend-based predicted increase in incidence most likely results from a changing accrual of cases over time, part of the increase in the cancer burden in Malawi probably in part the result of rising trends in several cancers common in western countries, linked to social and economic transitions and consequent changes in lifestyle. Increases in the prevalence of tobacco consumption and HIV-induced immune-suppression will also have an important effect on the risk of cancer by 2015. The forecasted population growth (due to natural means and internal migration) and ageing in Malawi will certainly mean there are more cancer patients in Blantyre in Malawi in the next decades, irrespective of the true temporal patterns. This demands that urgent

consideration be given to the orientation of preventive and curative services for cancer (and other non-communicable diseases) in the years ahead (Samb 2010).

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