

SECTION 1:

Background

1 INTRODUCTION

Cancer is a significant cause of illness and death in Aotearoa/New Zealand. Ethnic disparities in cancer risk, incidence and outcome are documented and long-standing. Comprehensive and detailed data on Māori and non-Māori cancer patterns and disparities are essential for current and future cancer control policy and programmes. Māori communities have the right to a high-quality, comprehensive evidence base to inform cancer control strategies, service development and community interventions, as well as to enable monitoring for equity of access and outcomes.

This chartbook of Māori and non-Māori cancer statistics provides analyses of ethnic variations in cancer incidence, mortality, stage at diagnosis and survival in Aotearoa/New Zealand, using national cancer registrations and mortality data from 1996 to 2001 (inclusive). The results provide insights into the nature and extent of cancer disparities between Māori and non-Māori, and potential points of action for improving Māori cancer outcomes. The report aims to inform cancer control policy, purchasing, service development and evaluation, and to act as a catalyst for actions to reduce the unequal impact of cancer within Māori whānau and broader communities.

THE UNEQUAL IMPACT OF CANCER

Cancer has a significant and disproportionate impact on Māori. Incidence and mortality rates for Māori and non-Māori differ for all cancers combined and for specific cancer sites (Pomare, Keefe-Ormsby et al 1995; Minister of Health 2003; NZHIS 2005). Inequalities in cancer death rates between Māori and non-Māori increased during the 1980s and 1990s, as did the contribution of cancer to inequalities in life expectancy between Māori and non-Māori (Ajwani, Blakely et al 2003a; Blakely, Ajwani et al 2004). There is also evidence of lower survival for Māori (Gill and Martin 2002; Cormack, Robson et al 2005; Jeffreys, Stevanovic et al 2005). In addition, there are differences in the distribution of risk and protective factors for cancer (Ministry of Health 2004a), as well as disparities in access to cancer services, including breast and cervical screening (Ministry of Health 2004b).

These patterns are consistent with substantial international evidence of ethnic disparities in cancer incidence and outcomes (Haynes and Smedley 1999; Shavers and Brown 2002; Smedley, Stith et al 2002). They also exist within the context of other health and social inequalities in Aotearoa/New Zealand that reflect entrenched disparities in access to the goods, services and opportunities of society.

WHAT IS CANCER?

Cancer is the name given to a range of diseases characterised by abnormal cell growth and spread. It can affect any site in the body. There are a number of factors that are known to increase or decrease the risk of cancer. Some of these are common across different cancer sites, while others are unique to a certain type of cancer. However, the causes of many cancers remain unknown (Australian Institute of Health and Welfare (AIHW) and Australasian Association of Cancer Registries (ACC) 2004). Because cancers develop and progress in different ways, there is a range of options for detection, management and treatment. The cancer care pathway is therefore often complex and involves a range of individuals, services and organisations.

CANCER CONTROL IN AOTEAROA/NEW ZEALAND

In recent years a number of countries, including Australia, the United States of America, Canada and Aotearoa/New Zealand, have developed cancer control strategies designed to approach cancer control and cancer care provision in a more integrated and systematic way. Following several years of work and development, the *New Zealand Cancer Control Strategy* (Minister of Health 2003) was released in August 2003. This was followed in March 2005 by the release of the *Cancer Control Action Plan* outlining how the goals and objectives of the strategy will be implemented over the next five years. An independent Cancer Control Council was also established in 2005.¹

CANCER SURVEILLANCE IN NEW ZEALAND

New Zealand has a national cancer registry, the New Zealand Cancer Registry (NZCR), which collects information on all new primary malignant cancer cases. The New Zealand Health Information Service (NZHIS) administer the NZCR.² The population-based register has existed since 1948. The statutory requirement for cancer laboratories to report to the NZCR was introduced by the Cancer Registry Act 1993 and came into force under the Cancer Registry Regulations 1994. This has contributed to improvements in the quality and completeness of information on the NZCR (Ministry of Health 2002).

The NZCR includes information on each cancer case (such as site, stage and pathology), as well as demographic information such as age, gender and ethnicity. This information is gathered from laboratory reports, discharge reports from public and private hospitals, death certificates and autopsy reports (Ministry of Health 2002).

An annual report entitled *Cancer: New registrations and deaths* is produced by the NZHIS.

SCOPE OF THE CHARTBOOK

This chartbook focuses on cancer patterns for Māori and non-Māori, including cancer incidence, mortality, stage at diagnosis and survival. In order to meet the varying needs of users, the chartbook includes summary tables and figures designed to provide an overview of Māori and non-Māori cancer, as well as more detailed site-specific data.

There is a range of additional information outside the scope of this chartbook that would contribute to a more comprehensive understanding of cancer for Māori and non-Māori, including information on histology, access to cancer services (including screening, investigative, diagnostic and treatment services), and receipt and timeliness of cancer care. These are areas for further analyses and reporting.

¹ The *New Zealand Cancer Control Strategy* and related documents are available on the Ministry of Health website (www.moh.govt.nz).

² Further information on the New Zealand Cancer Registry is available on the NZHIS website (www.nzhis.govt.nz).

2 METHODS

DATA SOURCES

Deaths and cancer registrations registered between 1 January 1996 and 31 December 2001 were obtained from the NZHIS. Cancer site was classified according to the Tenth Revision of the International Classifications of Diseases, Australian Modification (ICD-10-AM) for the whole six-year period.³ For the years 1996–1999, cause of death was coded according to the International Classifications of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) classification. Beginning with deaths in 2000, ICD-10-AM was used. We recoded all deaths into the ICD-10-AM classification groupings. ICD codes used are listed in Appendix One.

Analysis was restricted to invasive neoplasms (*in situ* tumours are not included).

Cancer registrations flagged as ‘multiple’ were excluded. Multiple registrations are defined as a second cancer record for the same person where the site and morphological type are the same. For the survival analysis (hazard ratios), where there was more than one registration for a person within a site or site group, the first was included and subsequent registrations were excluded.

Age-sex-ethnicity-specific population estimates for each year from 1996 to 2001 inclusive served as denominators for computing cancer incidence and mortality rates. They were obtained from Statistics New Zealand’s revised estimates of the mid-year resident Māori ethnic group population and total New Zealand population for 1991–2001. These estimates include adjustments for: missing responses to the ethnicity question; the estimated net undercount at the 2001 Census as measured by the 2001 Post-enumeration Survey; the estimated number of Māori residents temporarily overseas on census night; and estimated external migration, births and deaths. New ethnicity questions on birth registrations and death registrations were introduced in September 1995, resulting in significant increases in the number of births and deaths registered as Māori (around double those registered as Māori in 1994). The population estimates for the December quarter 1995 onwards are based on births and deaths compiled using the new questions (Statistics New Zealand technical notes on population estimates). Denominators for the non-Māori rates were constructed by subtracting the Māori population estimates from the total New Zealand population estimates for each year.

ETHNICITY CLASSIFICATION – EVER MĀORI METHOD

Deaths and cancer registrations were classified as Māori if Māori was coded as one of the ethnic groups in any ethnicity field of the death event, the National Health Index (NHI), any other cancer registration, or any hospitalisation since 1996. Otherwise they were classified as non-Māori. This method of classifying ethnicity (the ‘ever Māori’ method) was used to minimise the known undercount of Māori cancer registrations and deaths. It increased the number of cancer registrations classified as Māori by 16.6% and deaths by 6%. This method appears to give reasonable estimates for both registrations and deaths during our period of analysis (see Appendix Two for further detail).

³ The ICD-10-AM and the ICD-9-CMA-II are international schemes for classifying morbidity and mortality in a standardised way.

Appendix Three compares hazard ratios using the ‘ever Māori’ method, ‘ever Māori up to registration’ and ‘Māori on registrations’ only. On average, the ‘ever Māori’ method produces the lowest hazard ratios, and thus the most conservative estimates of survival disparities between Māori and non-Māori.

INCIDENCE RATE

The cancer incidence rate is the number of newly diagnosed cancers of a specific site/type registered in a specified population during a year, usually expressed as the number of cancers (registrations) per 100,000 per year. That is,

$$\text{incidence rate} = (\text{new cancers/population}) \times 100,000.$$

The *numerator* of the incidence rate is the number of new cancers; the *denominator* of the incidence rate is the size of the population. The population used depends on the rate to be calculated. For example, for cancer sites that occur in only one sex (e.g. cervical cancer), the sex-specific population is used (i.e. females). The number of new cancers may include multiple primary cancers occurring in one patient.

MORTALITY RATE

The cancer mortality rate is the number of deaths for which cancer is given as the underlying cause of death occurring in a specified population during a year, usually expressed as the number of deaths due to cancer per 100,000 per year. That is,

$$\text{mortality rate} = (\text{cancer deaths/population}) \times 100,000.$$

The *numerator* of the mortality rate is the number of deaths; the *denominator* of the mortality rate is the size of the population.

AGE-STANDARDISED RATES

Differences in the age structure of the Māori population (relatively young) and the non-Māori population (relatively old) make it necessary to adjust for age when comparing health outcomes. Direct standardisation applies age-specific rates to a standard population structure. The age-standardised rate is the rate that would be expected for the group if it had the same age distribution as the standard population. It is a weighted average of the age-specific incidence or mortality rates, where the weights are the proportions of persons in the corresponding age groups of a standard population. The results are affected by the age distribution of events (e.g. deaths) in each population and the relative differences across age groups (the age-specific rate ratios). If these vary between the populations being compared, the selection of standard population can affect the magnitude of rates and ratios, relative ranking of causes, and trends in rates and ratios.

In the main body of this report, age-adjusted rates were standardised to the average Māori population for 1996–2000, because these rates are a close approximation of the crude overall rates for Māori and thus better reflect the experience of the Māori population. Rates standardised to Segi’s world population or the World Health Organization (WHO) population are generally higher (because these standard populations are older and place greater weight on events at older ages). In some instances the rate ratios also differ. (See Appendix Four for a comparison of the three standards.) Cancer incidence and mortality rates and ratios standardised to Segi’s and the WHO world standards are presented in Appendices Five and Six.

STAGE OF DISEASE AT DIAGNOSIS

Cancer stage describes the extent of cancer spread from the site of origin at the time of initial diagnosis (Ries, Eisner et al 2003). The extent of disease information determines the stage at diagnosis.

The Summary Staging Classification

The localised-regional-distant summary staging scheme is used in descriptive and statistical analyses of cancer registry data, and is defined as follows.

- ***In situ* cancer** is early cancer that is present only in the layer of cells in which it began.
- **Localised cancer** is cancer that is limited to the organ in which it began, without evidence of spread.
- **Regional cancer** is cancer that has spread beyond the original (primary) site to nearby lymph nodes or organs and tissues.
- **Distant cancer** is cancer that has spread from the primary site to distant organs or distant lymph nodes.
- **Unstaged cancer** is cancer for which there is not enough information to indicate a stage (SEER 2005).

Prior to 1999, the NZCR classified stage of cancer disease as:

- *in situ*
- localised
- regional or node involvement
- remote or diffuse metastases
- not stated
- not applicable (lymphomas/leukaemias).

For cancers registered from 1999 on, the ‘regional or node involvement’ stage was divided into two categories, and the classification changed to:

- *in situ*
- localised to organ of origin
- invasion of adjacent tissue or organ
- regional lymph nodes
- distant
- not known
- not applicable.

In this report, regional-stage disease includes any cancers classified with ‘regional or node involvement’, ‘invasion of adjacent tissue or organ’, or ‘regional lymph nodes’. Distant-stage disease includes cancers classified as ‘remote or diffuse metastases’ or ‘distant’. Data are presented on invasive neoplasms only. *In situ* tumours are not included. The staging classification is not applicable to lymphomas (Hodgkin’s disease and non-Hodgkin’s disease), myeloma or leukaemias.

The stage distribution of new cases (percentage of cases diagnosed at localised, regional, distant and stage unknown) was calculated for Māori and non-Māori. Logistic regression analysis was used to compare the odds of being registered with unknown stage at diagnosis for Māori compared with non-Māori, adjusted for age at diagnosis. The odds of being diagnosed at localised or distant stage among Māori and non-Māori staged cancers were compared, adjusted for age at diagnosis. Odds ratios were calculated using the logistic procedure of SAS version 9.1 (SAS Institute Inc, Cary, NC).

CONFIDENCE INTERVALS AND P VALUES

A 95% confidence interval around an estimate, such as an incidence rate, is a range of values surrounding the rate that have a 95% probability of including the true population value (Beaglehole, Bonita et al 1993). Normally, if the 95% confidence intervals around two (or more) measures (e.g. rates) do not overlap, the difference between them is considered statistically significant. The difference may also be statistically significant when there is some overlap.

The p value is ‘the probability that chance alone would produce a difference between compared groups at least as big as the one observed’ (Ahlbom and Norell 1984). In most epidemiological research the difference is considered statistically significant if the p value is less than 0.05.

In this report, 95% confidence intervals for crude and age-standardised rates and rate ratios were calculated using the log-transformation method (Clayton and Hills 1993).

SURVIVAL ANALYSES

There are several techniques for conducting survival analyses. Each can produce different results, and each has its own strengths and limitations (Platel and Semmens 2004). In this chartbook we include two types of survival analysis: first, survival curves were generated to show a graphical representation of the Māori and non-Māori patterns of cancer-specific survival over five years; secondly, hazard ratios were calculated to estimate the relative risk of cancer-specific death after diagnosis, for Māori compared with non-Māori, adjusted for age. To estimate the contribution of differential stage at diagnosis to differences in survival, hazard ratios were also calculated and adjusted for age and stage at diagnosis. The percentage change after adjusting for stage indicates potential reductions in disparities if both populations had the same distribution of disease spread at diagnosis.

Relative survival rates are an alternative method of survival analysis. They are a ratio of the observed survival among the group registered with cancer divided by the expected survival of the general population with the same age-sex-ethnic distribution. The expected survival rates are obtained from life tables. Māori and non-Māori-non-Pacific five-year relative survival rates have been reported elsewhere (Jeffreys, Stevanovic et al 2005) and are not presented in this chartbook, although the results were generally similar to those reported here. However, the estimated contribution of stage at diagnosis to the survival disparities differed substantially between the two methods (cause-specific hazard ratios and relative survival rate ratios).

Survival curves

Cancer-specific (or corrected) survival curves were generated using Kaplan-Meier estimates. Also described as product limit estimates, the survival function is calculated each time a death from a given cancer occurs. The graphs are a series of horizontal lines with connecting vertical steps each time an event occurs. Points on the curve estimate the proportion of patients who survive at least a given period of time (Lee 1980). Mortality data from 1996–2001 were searched for matching encrypted Health Care User Identifiers of patients registered with cancer during the same period, and treated as a cancer-specific death if the death was coded to the same ICD grouping as the cancer registration.

Survival times were measured in days, and were censored (removed from the analysis at that point) at the date of death from causes other than the underlying cancer, or on 31 December 2001 (whichever occurred first). Patients dying of a different cancer or of ill-defined cancers were treated as dying of other causes under the assumption that deaths from the underlying cancer were independent of deaths from other causes.

Cause-specific analysis relies on accurate recording of the underlying cause of death, to differentiate cancer deaths from non-cancer deaths. This data analysis relied on the ‘underlying cause of death’ recorded on death registrations and was unable to be verified from other sources. Therefore, these survival curves should be interpreted with some caution. Active follow-up was not conducted and so we cannot account for any cancer patients who may have died outside of Aotearoa/New Zealand. However, we expect any impact of differential migration to be minor.

Survival curves were calculated using the LIFETEST procedure of SAS version 9.1 (SAS Institute Inc, Cary, NC). These curves display the cause-specific survival experience of Māori and non-Māori for all ages at diagnosis. No adjustment was made for age at diagnosis in these survival curves. Hazard ratios were calculated to provide age-adjusted measures of differences in survival (see below).

Hazard ratios

The hazards function estimates the risk of death per unit time, following cancer diagnosis (Lee 1980). Proportional hazards regression was used to estimate hazard ratios – the *relative* risk of dying from the cancer once diagnosed, for Māori compared with non-Māori, adjusted for sex and age at diagnosis.

Cancers where the date of diagnosis was the date of death did not contribute to the hazard ratio. Those who died of causes other than the diagnosed cancer were considered censored as of the date of death. This was under the assumption that there was no differential misclassification of non-cancer-specific causes of death between Māori and non-Māori. Those with no death record were assumed alive and were censored at 31 December 2001. This allowed us to compare Māori and non-Māori survival without regard to competing causes of death.

Cancer-specific hazard ratios and confidence intervals were calculated using the proportional hazards procedure (PHREG) of SAS version 9.1. The proportional hazards model assumes the relative risk of death between Māori and non-Māori remains constant over time. The assumption of proportionality and linear relationship with age were checked using the graphical and numerical methods of Lin, Wei et al (1993).

Māori to non-Māori hazard ratios were calculated for selected sites, adjusted for sex and age at diagnosis (as a categorical variable). Because the assumption of linearity did not hold when age was treated as a continuous variable, age categories were used. They were constructed separately for each cancer by dividing the total number of registrations for that cancer site into quintiles with equal numbers of registrations. However, the method of age adjustment made very little difference to the resulting hazard ratios.

To estimate the contribution of stage at diagnosis to the disparities in survival outcomes between Māori and non-Māori, we calculated hazard ratios adjusted for stage at diagnosis. These were calculated in two ways: first, including registrations with unknown stage at diagnosis as a stage category, and secondly, restricted to staged cancers only. Finally, we calculated hazard ratios for Māori compared with non-Māori at each stage of cancer spread at diagnosis, including unknown stage. The estimates for each gender and each stage were estimated from models with interaction terms.

Hazard ratios reported in the main body of this report were calculated using the ‘ever Māori’ method of ethnicity classification. In Appendix Three we also present hazard ratios calculated using other methods: the ‘ever Māori up to registration’ (includes as Māori anyone classified as Māori on any hospital admission or cancer registration prior to and including the current cancer registration); and ‘Māori on registration’ (includes as Māori only those who were identified as Māori on their cancer registration). Hazard ratios calculated using the ‘ever Māori up to registration’ classification resulted in hazard ratios 4% higher on average than the ‘ever Māori’ method, and the ‘Māori on registration’ method produced hazard ratios 5% higher on average. Thus, the ‘ever Māori’ method generally produced the most conservative estimates of survival disparities between Māori and non-Māori.

MODEL REPORTING

For some models there were few events for the number of variables in the model. This can result in poor estimates (Peduzzi, Concato et al 1995; Peduzzi, Concato et al 1996). Where there were fewer than 10 events per term in the model the estimates have been identified in the report, but we recommend that they be interpreted with caution. The results are not presented where there were fewer than five events per term in the model. Similar criteria were used for the number of observations for each value of categorical variables in the models; i.e. caution on less than 10 observations for each value, and where there were fewer than five observations for each value the estimates are not presented.

Separate estimates for hazard ratios by gender and stage groups are reported, although most of the interactions were not significant. This is likely to be in part due to relatively small numbers meaning that there was not enough power to detect differences. The estimates are included for completeness and to establish a baseline.

3 HOW TO READ THIS CHARTBOOK

STRUCTURE OF THE CHARTBOOK

This chartbook is divided into two main components plus appendices.

Part 1: Summary tables and figures

Part 1 provides an overview of patterns of cancer and disparities between Māori and non-Māori. It contains summary tables and figures of Māori and non-Māori incidence, mortality, stage at diagnosis, and hazard ratios for 1996–2001. Results are presented for all cancers combined (all sites) and by individual sites, for the total populations and by sex and age group.

Part 2: Site-specific tables and figures

Part 2 includes a series of site-specific tables and figures. Information for each site includes: a summary of key points; age-standardised incidence and mortality numbers, rates and rate ratios; age-specific incidence and mortality numbers, rates and rate ratios; distribution of stage at diagnosis (unadjusted and adjusted for age at diagnosis and sex) and odds ratios for being diagnosed at each stage; unadjusted cancer-specific survival curves for Māori and non-Māori; and cancer-specific mortality hazard ratios (adjusted for sex and age at diagnosis, and for stage) for each cancer site.

Part 3: Appendices

The appendices include information on the ICD codes used in the report (Appendix One), the ever-Māori method of ethnicity classification (Appendix Two), a comparison of hazard ratios using different methods of ethnicity classification (Appendix Three), standard populations (Appendix Four), and incidence and mortality tables age standardised to Segi's world population (Appendix Five) and to the WHO population (Appendix Six).

HOW TO READ THE TABLES, FIGURES AND GRAPHS

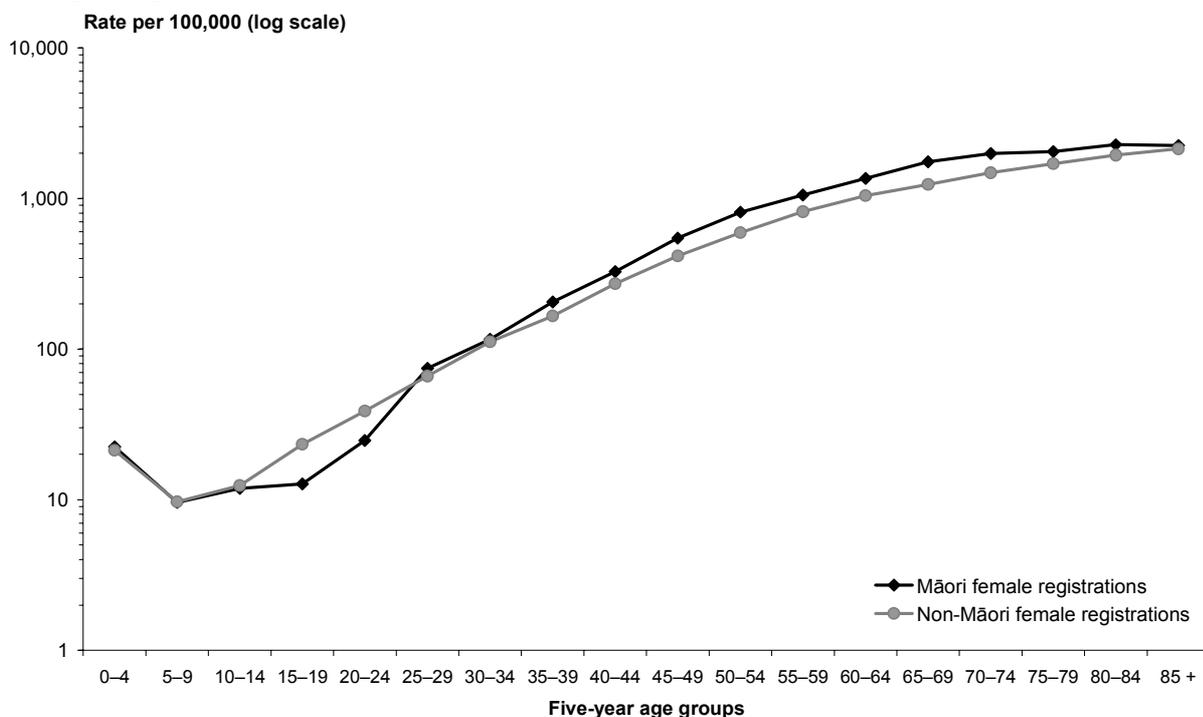
The methods of classification of ethnicity, calculation of rates, hazard ratios and survival curves, and classification of stage of disease at diagnosis are outlined in the methods section. The cancer sites are defined in the tables, figures and graphs according to the International Classification of Diseases (10th revision). For reasons of readability, category names are abbreviated in some tables, figures and graphs. The abbreviations and the ICD categories they correspond to are outlined in Appendix One.

Several different types of tables, figures and graphs are used in this report, some of which are discussed below. In addition, users of the chartbook should be aware that different axis scales (including log scales) are used.

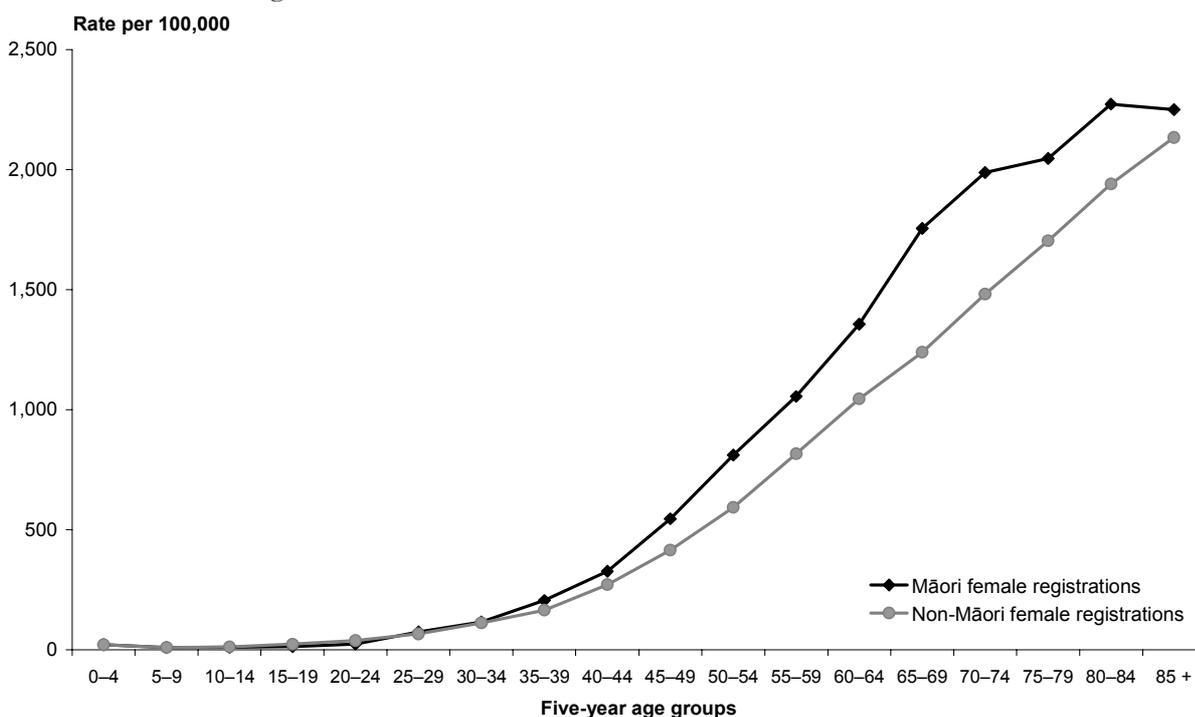
Logarithmic (log) scales

Log scales are used at times in this chartbook because they provide a more informative comparison of small and large values. The relationships between Māori and non-Māori rates (e.g. rate ratios) are also more clearly visible across the age groups in the log scale graphs, because the proportionality is maintained. A logarithmic scale increases multiplicatively, as in the vertical (y) axis below, so the intervals on the axis represent increasingly large intervals on a normal interval scale.

Example: log scale



Same data not on a log scale



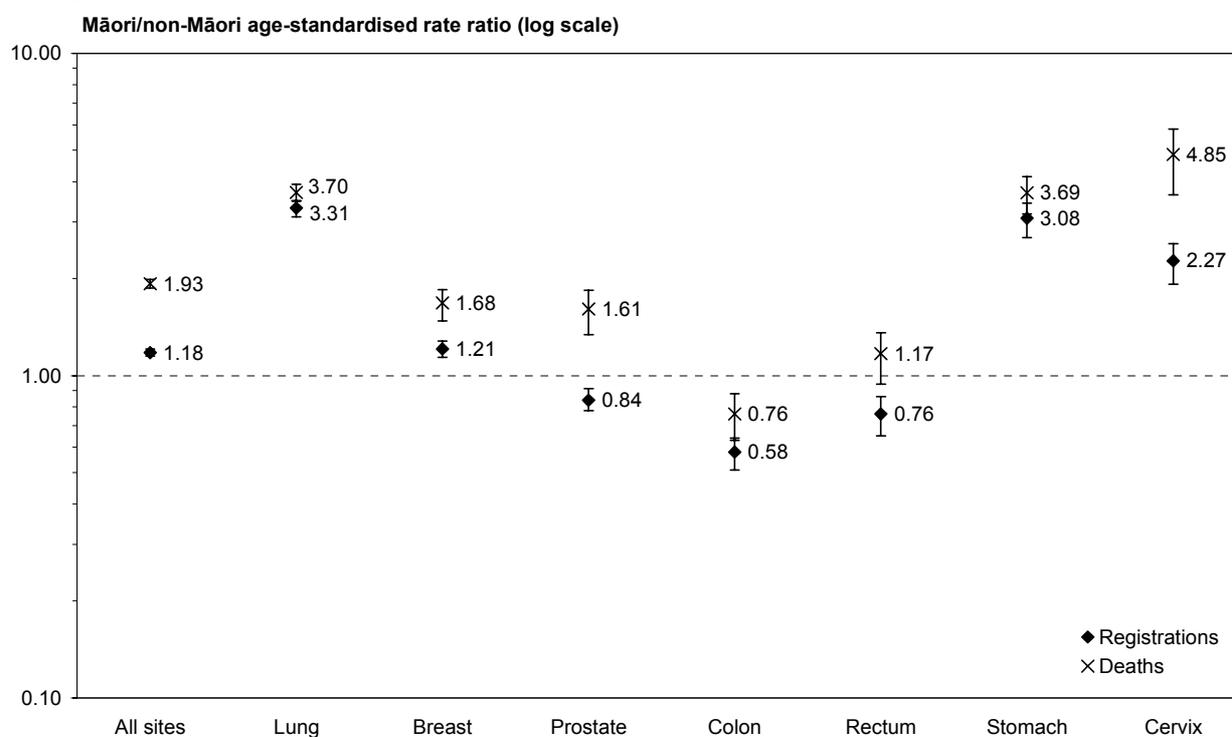
Rate ratios

Rate ratios in this chartbook illustrate Māori risk relative to non-Māori risk. The ratio is calculated by dividing the Māori rate by the non-Māori rate. Any point above 1 indicates a higher rate (of cancer registrations or deaths) among Māori compared with non-Māori, while any point below 1 indicates Māori have a lower rate than non-Māori. In the example below, the registration rate ratio for prostate cancer was below 1, indicating the incidence of prostate cancer was lower among Māori than non-Māori men, while the mortality rate ratio was above 1, indicating Māori had a higher death rate than non-Māori from prostate cancer.

The bars extending out from each point represent 95% confidence limits on the ratios. The confidence interval (CI) is narrow on the ratios for 'all sites', because the rates were calculated from relatively large numbers. However, for cancer of the cervix, where deaths are relatively rare, the confidence intervals on the mortality ratio are wider.

This graph uses a log scale to maintain the proportionality of ratios below 1 and over 1.

Example:

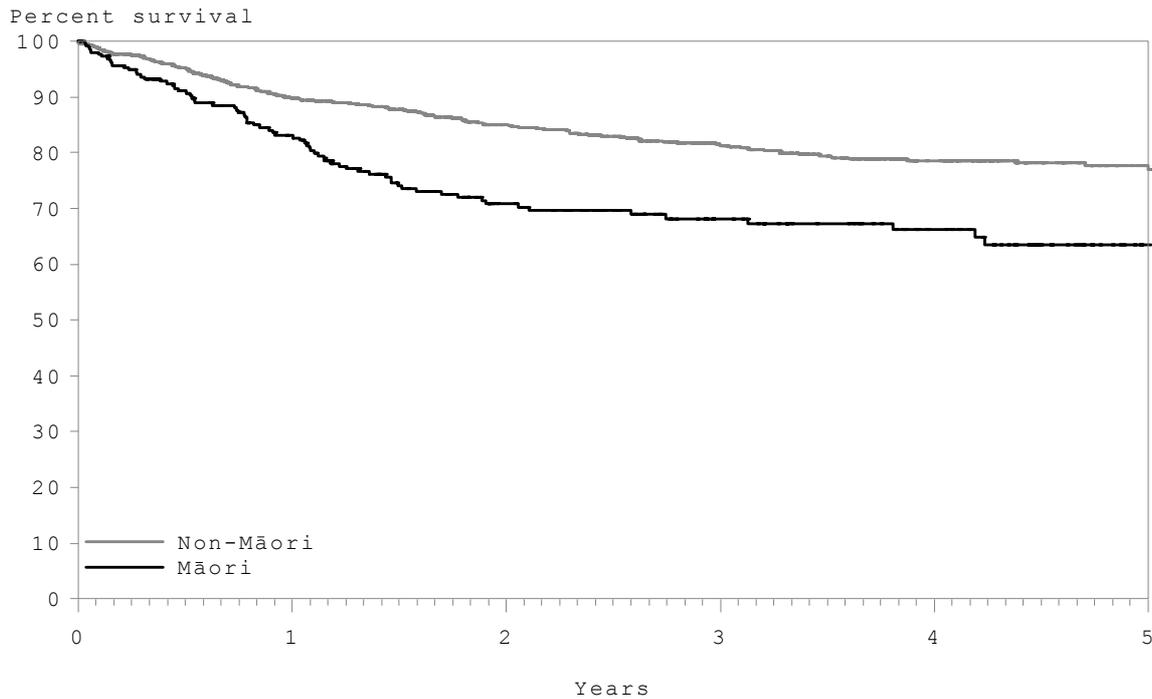


Survival curves

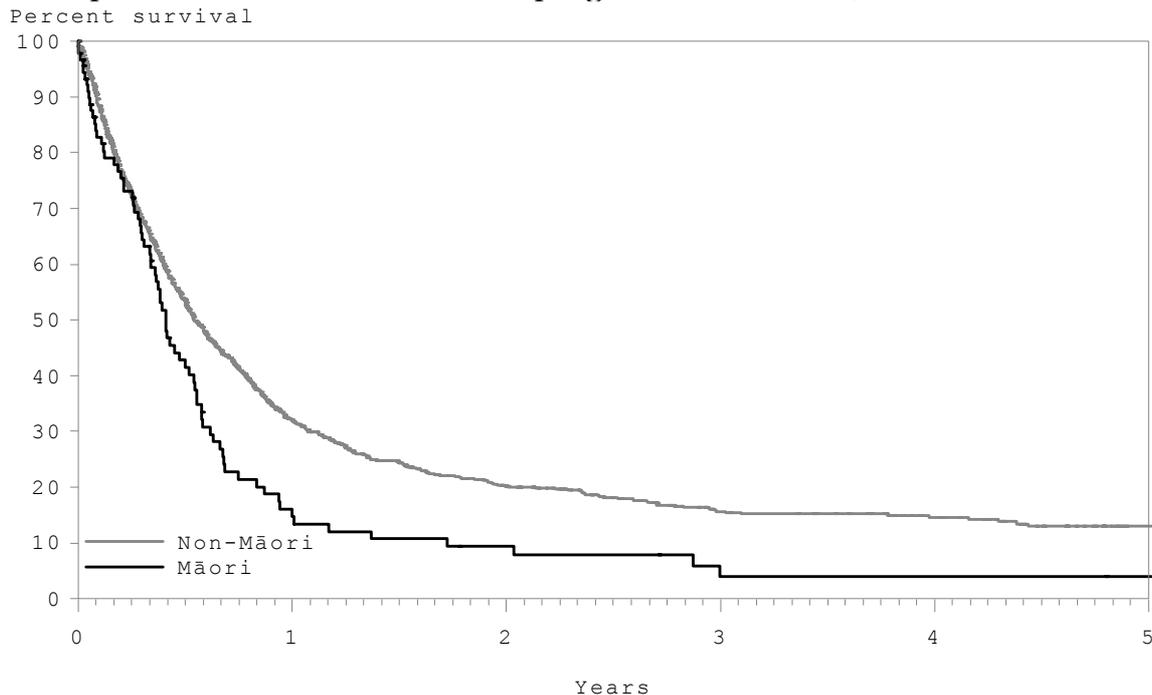
Survival curves depict an estimate of the proportion of people not dying from their cancer over time. The vertical axis ('percent survival') represents the proportion of people not dying from the cancer as a percentage, while the horizontal axis ('years') shows time from diagnosis. The flat sections of the curve represent periods with no cancer deaths (although there may be censored observations of people who died from other causes or who reached the end of the follow-up period). The survival curves in this chartbook are cancer-specific and cover a period of five years. They are not adjusted for age.

The first example below presents cancer-specific survival curves for non-Māori (the upper curve) and Māori (the lower curve) diagnosed with cervical cancer. The second example shows survival curves for oesophageal cancer. The curves for cervical cancer are relatively shallow, indicating a relatively high survival rate. The lower survival from oesophageal cancer is shown by the deeper curves. In the cervical cancer example the majority were still alive at the end of five years, but in the oesophageal example the median survival time (i.e. the point at which 50% are left surviving) for both Māori and non-Māori is less than one year. In both examples the curves for non-Māori are higher than those for Māori, indicating a higher proportion of non-Māori surviving at each point of time over the five years.

Example 1: Māori and non-Māori cervical cancer survival, 1996–2001



Example 2: Māori and non-Māori oesophageal cancer survival, 1996–2001



INTERPRETATION ISSUES

- Readers should be aware that use of the Māori population standard as well as the ‘ever Māori’ method of classifying ethnicity mean that results presented in this chartbook may not be directly comparable with those reported elsewhere.
- Readers should be mindful that the site-specific groupings (such as brain cancer, bone cancer or thyroid cancer) in fact reflect groupings of diseases that can affect different age groups, and may have very different aetiologies and/or prognoses. They should therefore not be treated as one disease.
- Caution should be taken when interpreting rates and ratios that are in grey text, because they have been calculated from small numbers (see notes on modelling in the methods section).
- The hazard ratios presented in this report do not take account of confounding by type of cancer within each cancer site (e.g. small-cell lung cancer versus non-small-cell lung cancer). There may also be residual confounding within stage categories.
- In relation to the staging information included in this chartbook, the NZHIS notes that staging information was not adequate prior to 1997 (NZHIS 2004). Caution should therefore be taken when interpreting the staging data included in this chartbook. For some cancers there was a significant decreasing trend over time in the proportion of cancers with unknown stage or extent of disease.
- Our use of the terms ‘significant’ or ‘not significant’ refer to the statistical sense (i.e. $p < 0.05$) rather than importance or clinical significance.