

Suspected Cancer

in Primary Care

Guidelines for investigation, referral
and reducing ethnic disparities

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© Ministry of Health 2009

Published by: New Zealand Guidelines Group (NZGG)
PO Box 10 665, The Terrace, Wellington, New Zealand

ISBN (Print): 978-1-877509-12-4

ISBN (Electronic): 978-1-877509-13-1

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Statement of intent

New Zealand Guidelines Group (NZGG) produces evidence-based best practice guidelines to help health care practitioners, policy makers, and consumers make decisions about health care in specific clinical circumstances. The evidence is developed from systematic reviews of international literature and placed within the New Zealand context.

While NZGG guidelines represent a statement of best practice based on the latest available evidence (at the time of publishing), they are not intended to replace the health practitioner's judgment in each individual case.

Citation: New Zealand Guidelines Group. Suspected cancer in primary care: guidelines for investigation, referral and reducing ethnic disparities. Wellington: New Zealand Guidelines Group; 2009.

Currency review date: 2014

Cover concept: The process of discovery or identification is conceptualised through bringing one (or more) flowers into focus.

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Me mahi tahi tātou mo te oranga o te katoa

We must work together for the wellbeing of all

Endorsements

The following organisations have endorsed the content of this guideline:



The Royal New Zealand
College of General Practitioners



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Introduction

Purpose

The aim of this guideline is to help primary care practitioners make a timely and appropriate referral by alerting practitioners to the features that should raise their suspicion of cancer.

The guideline summarises current New Zealand and overseas evidence to inform the management of people presenting to primary care with signs and/or symptoms suggestive of cancer. *Clinical Guideline 27: Referral Guidelines for Suspected Cancer*, published by The National Institute for Health and Clinical Excellence (2005), provided key direction in the development of this guideline. The guideline also summarises the evidence for disparity in the incidence, stage and mortality rate of cancer in New Zealand, and discusses possible reasons for the differences observed.

The need for the guideline

Cancer is now a leading cause of death in New Zealand, accounting for 29% of deaths from all causes.¹ The incidence of cancer is increasing, mainly due to population growth and ageing. A key government report from 2003 estimated that the number of people developing cancer in New Zealand would increase from 16,000 to 22,000 by 2011.¹ Deaths from the disease were forecast to increase from 7500 to approximately 9000 by 2012.¹ In addition, cancer mortality is making an increasing contribution to the gap in life expectancy between Māori and Pacific peoples and the non-Māori, non-Pacific population.¹

The aim of the national Cancer Control Strategy is to reduce the impact and incidence of the disease and to reduce inequalities.¹ This guideline was commissioned by the Ministry of Health to help meet this need.

A recent Australian paper quoted data indicating that the average general practitioner will encounter approximately four new patients diagnosed with a potentially fatal cancer each year.² The need for this guideline in practice is imperative for four main reasons:

1. to improve access to care and clinical outcomes
2. to reduce late or missed cancer diagnoses
3. to reduce variation in clinical care
4. to facilitate more appropriate utilisation of finite health care resources.

Evidence-based guidelines, such as these, help focus thinking around the diagnostic process. Much research on clinical signs and symptoms, and the diagnostic accuracy of investigations for specific cancers reinforces current clinical practice. The guideline is of significant value in highlighting where this is the case, and the areas where evidence and clinical practice currently may differ.

This guideline includes a chapter entitled *Disparities and Access to Care*, which reviews factors that can lead to a delay in diagnosis and referral. In particular, factors leading to disparities in cancer diagnosis and outcomes amongst ethnic minorities are presented. This chapter also outlines issues to be considered by those responsible for providing primary care services (including managers and funders, as well as practitioners). Practitioners will be able to use the recommendations in this chapter to help improve service delivery for their patients, either directly by application, or through lobbying for quality improvement.

There is the potential for these guidelines to increase clinician readiness to consider a cancer diagnosis, with the possibility of an increase in the number of unnecessary referrals and less access to appropriate diagnosis for those of greatest need. However, by basing this guideline's recommendations on research evidence, it is hoped to achieve greater consistency in clinical practice and more efficient utilisation of cancer diagnostic services, along with improved cancer detection.

Scope of the guideline

This guideline aims to help practitioners in primary care:

1. recognise the signs and symptoms that are suggestive of a cancer diagnosis in primary care
2. refer people in a timely manner where cancer is suspected
3. be aware of the investigations that may be appropriate to undertake in the primary care setting.

The guideline covers the period from a person's first contact with a primary care practitioner with a sign or symptom suggestive of cancer up to their first specialist appointment. Recommendations for children and young people have also been developed and are presented in a separate chapter of this guideline. The guideline also offers guidance on helping to reduce disparities that currently exist within New Zealand.

Cancer screening, health promotion and prevention, case-finding in asymptomatic people, recurrence of a previous cancer and metastatic cancer were beyond the guideline scope and therefore are *not* included. Furthermore, the guideline does *not* cover all clinical scenarios or medical emergencies. Referral between secondary and tertiary care, and within each of these settings, is also *not* covered.

Target audience

The majority of the recommendations in this guideline relate to referral to a specialist or referral for investigation from primary care, as the guideline has been developed primarily for use by general practitioners. The guideline also provides a valuable resource for all other primary care practitioners when deciding to involve a general practitioner in patient care. Recommendations addressing disparity, general principles of care, and psychosocial support and information needs are directly relevant to all primary care practitioners. This guideline will also have significant implications for health service provider organisations and funders.

The guideline will also be of value to patients and their families as it will increase their awareness of the clinical process: from presentation to primary care with symptoms that might possibly be due to cancer, through to being seen by a specialist or diagnostic service where required. It will also increase their awareness of the symptoms and signs that should lead to seeking a medical opinion. As the research evidence presented covers only certain aspects of the clinical process used in primary care, it is essential to use this information within a clinical diagnostic process and not in isolation. Therefore, a clinical assessment by a trained practitioner is still essential.

Treaty of Waitangi

The New Zealand Guidelines Group acknowledges the importance of the Treaty of Waitangi to New Zealand, and considers the Treaty principles of partnership, participation and protection as central to improving Māori health. As part of its commitment to the Treaty, NZGG explicitly involves Māori consumers and health care practitioners in all its work. This guideline seeks to promote clinical practice that will improve Māori health.

Guideline development process

New Zealand Guidelines Group follows specific structured processes for guideline development. A general description of these processes in relation to this guideline is provided in this section, with further details outlined in Appendix A and the NZGG *Handbook for the Preparation of Explicit Evidence-based Guidelines* (www.nzgg.org.nz).

In brief, the guideline development process firstly involves convening a multidisciplinary group (known as the Guideline Development Team [GDT]) and developing a set of clinical questions to guide the systematic literature review (a full list of the questions developed for this guideline is presented in Appendix A). These clinical questions are developed in the context of the scope provided by the funder, the identification of gaps in current practice and those outcomes of primary importance to consumers. In the case of this particular New Zealand guideline, the *Referral Guidelines for Suspected Cancer* published by the National Institute for Health and Clinical Excellence (NICE)³ in 2005, is acknowledged as the 'seeding document'.

A systematic review of the literature is then conducted by experts in the appraisal of research evidence, the results of which are presented to the GDT in summary form. The GDT discusses this evidence and uses it to develop evidenced-based recommendations. These recommendations are graded based upon the level of evidence from which they are derived. A good practice point is made where evidence is lacking, but where the GDT believes it is important to make a recommendation about best practice.

The guidance

Key messages

- Māori and Pacific peoples often present with cancer at a later disease stage. A higher degree of suspicion is therefore indicated when Māori or Pacific people present with symptoms suggestive of cancer
- As Māori and Pacific peoples often cite communication with health care providers as a barrier to care, practitioners should provide information to Māori and Pacific peoples, preferably face-to-face and supported with appropriate written information
- A high index of suspicion of a new primary or metastatic disease (especially bone, brain, liver or lung) is needed in a person with a history of cancer
- A person returning to a primary care practitioner with the same symptom three or more times should be considered an indication for referral
- The greater the number of signs and/or symptoms present the more important it is for a practitioner to act
- Listening carefully to what caregivers say about a child's symptoms is essential as the interpretation of children's symptoms in a clinical situation can be difficult
- Practitioners and others providing cancer care should receive training and support in culturally competent, patient-centred care so that barriers to access and referral can be lessened

Presentation of the guidance

The first three chapters of this Guideline present information, recommendations and good practice points on overarching issues related to suspected cancer in primary care. The issues are: disparity and access to care, general principles of care, and psychosocial support and information needs. Each of these chapters is structured differently, the details of which are outlined at the beginning of each chapter to help orientate the reader.

The remaining guidance chapters present information, recommendations and good practice points related to specific cancers, and cancer in children and young people. These chapters first present the recommendations and good practice points, followed by contextual information on the epidemiology of that cancer in New Zealand. An overview of the bodies of literature from which the recommendations were developed (eg, risk factors, signs and symptoms, and investigations) is then provided. These specific cancer chapters conclude with a description of how the evidence was translated by the GDT into specific recommendations.

Definition of key terms

When using the guideline readers should keep the following definitions in mind.

Referral times

Immediate referral: The patient is seen within a few hours, or more quickly if required

Urgent referral: The patient is seen within two weeks

Referral: All other referrals

Symptom terms

Persistent: Signs or symptoms that continue to occur beyond a period of time that would normally be indicative of a self-limiting condition

Unexplained: Signs or symptoms where no diagnosis has been made to identify the cause after the patient has been assessed by a practitioner

Grades of recommendations

Each recommendation has been graded based on the quality of the evidence. Below are the definitions for each of the grades used in this guideline.

Recommendations	
Description	Grade
The recommendation is supported by good evidence (based on a number of studies that are valid, consistent, applicable and clinically relevant)	A
The recommendation is supported by fair evidence (based on studies that are valid, but there are some concerns about the volume, consistency, applicability and clinical relevance of the evidence that may cause some uncertainty but are not likely to be overturned by other evidence)	B
The recommendation is supported by international expert opinion	C
Grades indicate the strength of the supporting evidence rather than the importance of the evidence	

Good practice points

Description	
Where no evidence is available, best practice recommendations are made based on the experience of the Guideline Development Team, or feedback from consultation within New Zealand	✓

For further information about how recommendations are graded, see Appendix A, *Methods*.

1 Disparity and access to care

This chapter presents the recommendations on disparity and access to care, followed by contextual information on the quality of data on ethnicity, the epidemiology of cancer among ethnic groups in New Zealand and the barriers that specific groups may experience in accessing optimal care. The chapter concludes with a description of how the good practice points were developed.

Good practice points

Disparity and access to care	
All service providers should collect accurate ethnicity data to ensure that the effectiveness of health services in reducing disparities can be monitored	✓
For Māori, specific cancer services or service components should be provided where a need is identified	✓
For Pacific peoples, specific cancer services or service components should be provided where a need is identified	✓
Service providers should apply multidimensional strategies to address disparities in access to care Multidimensional strategies include: <ul style="list-style-type: none"> • training for practitioners in communication and cultural competency • auditing practice • utilising feedback processes • addressing costs of care • addressing communication barriers and other barriers to care (eg, appointment flexibility) 	✓
Service providers should support improvements in culturally competent, patient-centred care by monitoring practice, including review of patient experiences	✓
Service providers should consider disparity in developing policies on access to care, continuity of care and cultural competency	✓
Practitioners and others providing cancer care should enquire about a person's ethnicity to ensure that the person's health care preferences can be met	✓
Practitioners and others providing cancer care should receive training and support in culturally competent, patient-centred care	✓
Practitioners and others providing cancer care should ascertain a person's specific needs related to communication of information and ensure that these are met	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Context

One of the key roles of a general practitioner is to help facilitate the progress of patients through the health care system. This section of the guideline therefore draws attention to both the disparities that exist in health care and the potential barriers to accessing care. In addition, it aims to raise awareness at PHO and general practice level of initiatives that may be of use in reducing disparity and improving access to care for all New Zealanders.

The purpose of cultural competency training is to provide services that are acceptable to individual patients, and to address barriers to access and treatment for priority populations. Current data presented both within this chapter and throughout the guideline suggest that service provision has better met the needs of non-Māori non-Pacific populations. To achieve equity, a commitment to equity and allocation of appropriate resources is required.

Ethnicity data quality

The inclusion of ethnicity data in primary care activities is important to ensure that health service planners can monitor health trends by ethnicity and use ethnicity data to monitor progress in addressing disparities and improvement in health outcomes.

Evidence questions the reliability of some ethnicity records in primary care.^{4,5} Using the 'ever Māori' method for classifying ethnicity, Cormack et al.⁶ identified that Māori cancer registrations and deaths were undercounted by about 17% and 6%, respectively for the time period 1996–2001. Using the 'ever Māori' method, individuals are classified as Māori if this ethnic group is recorded in any ethnicity field of the death event record, the National Health Index (NHI), any other cancer registration or any hospitalisation.⁶

The GDT considered that there should be consistency in the collection of ethnicity data, quality improvement initiatives around ethnicity recording, and a consistent, systematic way of analysing data. These are important issues for accurately identifying disparity and for service planning and evaluation. Ethnicity data collection should follow the current Ministry of Health protocols.⁷

Disparity

The site-specific chapters of this guideline will provide the incidence and mortality rates of individual cancers for different ethnic groups (where available) as contextual background information. More general data, organised by ethnic group, are presented below to highlight the disparities that are known to exist.

Addressing the issue of cancer screening is outside the broad scope of this guideline. However, because of the impact that screening uptake can potentially have on disease outcomes, it is briefly included as part of this disparity chapter. It is of note that in this area there is a time lag of approximately five years before comparative epidemiological data are published in national reports.

Cancer in Māori

The incidence of all cancers combined and many individual cancers are higher in Māori than non-Māori. Furthermore, significant disparities in distribution of stage and survival for specific cancers and overall cancer survival exist between these groups.^{8,9} *Tatau Kahukura: Māori Health Chart Book* presents data on cancer in the Māori population compared with non-Māori similar to that cited below. This chart book is to be published every three years to document progress.¹⁰

Incidence

An analysis of cancer and death registration data for the period 2000–2004 identified the age-sex-standardised incidence rate for all cancers combined to be 9% higher for Māori than non-Māori (219.0 vs 200.5 per 100,000). In addition, incidence rates in Māori were higher for cancers of the lung, stomach, oesophagus, pancreas, liver, uterus, cervix, testis, thyroid, female breast and larynx, and multiple myeloma. In contrast, incidence rates were higher in non-Māori for a smaller number of malignancies (melanoma, Hodgkin's disease, brain, bladder, colorectal and prostate cancers). No significant difference in incidence rate was identified for oral, gallbladder, bone and mesothelial/soft tissue cancers, and non-Hodgkin's lymphoma and leukaemia.⁹

Mortality

The age-sex-standardised mortality rate for all cancers combined for the period 2000–2004 has been identified as 77% higher for Māori than non-Māori (117.5 vs 66.3 per 100,000). For individual cancers, mortality rates were significantly higher in Māori for cancers of the larynx, lung, stomach, oesophagus, pancreas, liver, cervix, uterus, thyroid, breast, testis, prostate, and for multiple myeloma, non-Hodgkin's lymphoma and oral cancers. In contrast, mortality rates in Māori were significantly lower for melanoma (rate ratio 0.26) and colon cancer (rate ratio 0.72) only.⁹

Stage at diagnosis

Cormack et al.⁹ presented data on disease stage at diagnosis using the New Zealand Cancer registry classification. Māori were significantly less likely to be diagnosed at an early (localised) stage of disease spread for oral cancer, melanoma and for cancers of the lung, rectum, testis, prostate, kidney, cervix and female breast. They were also significantly more likely to be diagnosed at a distant stage (spread to distant organs, tissues or distant lymph nodes) for oral and colorectal cancer, melanoma, and for cancers of the lung, prostate, kidney, cervix and female breast.

Age-sex adjusted disparities were significant for some cancers that have good treatment options and are potentially curable if treated early (eg, breast and colorectal cancer). Furthermore, after adjustment for age, sex and stage at diagnosis the risk of dying from oral and colorectal cancer, melanoma and cancers of the brain, female breast, lung, oesophagus, liver, prostate, bladder, ovary and uterus was still significantly higher in Māori than non-Māori.⁹

Screening uptake

Cormack et al. noted that national screening programme data have identified that equitable screening for breast and cervical cancer has not been achieved for Māori women.⁹ However, BreastScreen South Limited's results (70% of eligible Māori women screened in 2005) suggest that the inclusion of focused efforts and leadership are the key to achieving equity in screening.¹¹

Cancer in Pacific peoples in New Zealand

The term 'Pacific peoples' describes a diverse group of New Zealand-born individuals and migrants from South Pacific nations who identify with one or more of the Pacific Islands because of ancestry or heritage.

There is limited data available on cancer in Pacific peoples in New Zealand. The *Tupu Ola Moui: Pacific Health Chart Book 2004*¹² has provided useful baseline information and will be of value for analysing trends in data in the future.

Incidence

Pacific women had similar age-standardised registration rates in the period 1996–2000 for breast and lung cancer compared to the total New Zealand population.¹² Rates were higher in Pacific women for cervical cancer in the age group 45–64 years and lower for colorectal cancer in the age groups 45 years and over. Pacific men had higher registration rates for lung cancer in all age groups and for prostate cancer in the age group 65 years and over. However, rates for colorectal cancer were lower in the age groups 45 years and over.

Mortality

Pacific women had higher age-standardised mortality rates for breast cancer in the period 1996–2000 compared to the total New Zealand population. Mortality rates were also higher for cervical cancer in the 45–64 years age group and lung cancer in the age group 65 years and over. Lower rates were identified for colorectal cancer in the age groups 45 years and over. Pacific men had higher mortality rates for lung cancer in all age groups. In men aged 65 years and over, mortality rates were higher for prostate cancer and lower for colorectal cancer.¹²

An analysis of cancer registry data for the period 1994–2002 identified age-standardised 5-year relative survival rates by ethnicity (Māori, Pacific, non-Māori non-Pacific) and cancer site. Survival rates were lower in Pacific peoples compared with non-Māori non-Pacific for colorectal cancer and leukaemia, and for cancers of the bladder, breast, cervix, kidney, ureter and urethra. In addition, survival rates were lower in Pacific peoples compared with Māori for melanoma and cancers of the breast, cervix and ovary.¹³

Screening uptake

Compared to the general population, Pacific women had lower uptake rates for both breast screening (42% vs 63%) and cervical screening (49% vs 73%) in 2002.¹²

Cancer in Asian peoples in New Zealand

In the New Zealand context, 'Asian' is defined as people who identify with an Asian ethnicity (for example, Chinese, Indian, Korean) with or without other ethnicities with origins in the Asian continent using restricted geographical criteria. This definition includes people originating from Afghanistan to Japan (west to east) and China to Indonesia (north to south). This is consistent with Statistics New Zealand¹⁴ as cited in the *Asian Health Chart Book* published by the Ministry of Health in 2006.¹⁵

There is limited data available on cancer in Asian peoples in New Zealand. The *Asian Health Chart Book*¹⁵ has provided useful baseline information and will be of value for analysing trends in data in the future. In an attempt to reflect that Asian New Zealanders are not a homogenous group (differences exist in, for example, culture), the report identified three broad ethnic sub-groups (Chinese, Indian and 'Other Asian'). However, there are likely to be differences within each group. Data were presented for all cancers, lung cancer (as a proxy for smoking-related cancers), non-lung cancer (as a proxy for non-smoking-related cancers), breast cancer and stomach cancer.

Incidence

All Asian peoples in every age group (except 'Other Asian' females aged 65 years and over) had significantly lower age-standardised registration rates for all cancers combined in the period 1997–2001 compared to the total New Zealand population. Within Asian peoples, all 'Other Asians' had significantly higher rates than Chinese or Indian from the age of 45 years. In addition, registration rates for lung cancer (patients aged 65 years and over) and non-lung cancer (patients aged 25–64 years) were significantly lower for Chinese and Indian males and significantly lower for all Asian peoples respectively when compared to the total population. Rates for breast cancer were also significantly lower for all Asian women (aged 45 years and over). In contrast, registration rates for stomach cancer (patients aged 45 years and over) were significantly higher for Chinese women and 'Other Asian' men.¹⁵

Mortality

All Asian peoples in every age group had non-significant, lower age-standardised mortality rates in the period 1998–2002 for all cancers combined compared to the total New Zealand population. Within Asian peoples, all 'Other Asians' had non-significant, higher rates than Chinese or Indian. In addition, mortality rates for non-lung cancer (patients aged 25–64 years) and breast cancer (women aged 45 years and over) were lower for all Asian peoples and significantly lower for Chinese women respectively when compared to the total population. In contrast, mortality rates for lung cancer (patients aged 65 years and over) and stomach cancer (patients aged 45 years and over) were higher for 'Other Asian' men and for Chinese women, respectively.¹⁵

In Asian peoples (with the exception of Indian males), a tendency was identified for all cancer mortality and non-lung cancer mortality to increase as duration of residence in New Zealand increased, from less than 5 years to between 5 and 9 years.¹⁵

Screening uptake

All Asian women had lower uptake rates (not statistically significant) for both mammography (50–64 years of age, 2001–2002) and cervical screening (20–69 years of age, 2001–2003) compared to New Zealand European women.¹⁵

Trends in disparity

The information presented in this section summarises data from the monitoring report *Tracking Disparity: Trends in Ethnic and Socioeconomic Inequalities in Mortality, 1981–2004*.¹⁶ This section of the guideline focuses on data relating to ethnic inequalities.

In *Tracking Disparity* cancer mortality data was linked with census data and inequality trends in mortality rates were examined for four ethnic groups; Māori, Pacific peoples, Asian peoples and European/Other. The earliest collected data available to link was the 1981–1984 period and the most recently linked data was that collected in the 2001–2004 period.

The *Tracking Disparity* report uses the term ‘European/Other’ interchangeably with non-Māori non-Pacific non-Asian. ‘Non-Māori non-Pacific non-Asian’ is a constructed group used for analytical reference purposes. It largely comprises people of European ethnicities (including New Zealand European), but also includes people with African, Middle Eastern and Latin American ethnicities, and other ethnicities – most notably the growing ‘New Zealander’ group. For consistency, this guideline uses the term European/Other.

This section summarises inequalities data related to all-cause cancer. Unless otherwise stated, all data reported is age standardised. For data on specific cancers see the relevant site-specific chapter of this guideline.

Measuring and reporting inequalities in cancer mortality

In the *Tracking Disparity* report, inequality is measured on absolute and relative scales. The absolute scales indicate the absolute difference in mortality rates (termed absolute inequality), while the relative scale indicates the ratio of the rates (termed relative inequality). It is important to look at both the absolute and relative rates as absolute inequalities (rate differences) in New Zealand have tended to remain stable or decline since measurement began in the early 1980s, while relative inequalities (the rate ratios) have increased in the same period. Together, these data provide a full picture of the trends in cancer mortality inequalities.¹⁶

Ethnic inequalities in all cause cancer mortality

The mid 1990s saw a decline in all cancer mortality for European/Other men and women. From 1981–1984 to 2001–2004 there was a 17% reduction for men and a 13% reduction for women. While all-cancer mortality for this period was stable, among Māori and Pacific men there was a possible downward trend noted, and among both Māori and Pacific women, a possible upward trend.

In terms of inequality during this period, there were noted increases in absolute inequality between both Māori and Pacific women and the European/Other reference group (p for trend=0.07 and 0.08, respectively). While there was a trend for an increase in absolute inequalities for Māori men compared to European/Other men, this was not statistically significant ($p=0.14$). For Pacific men, absolute inequalities remained stable and for Asian peoples of both sexes inequality was negative ie, favouring Asian peoples.

However, relative inequality data indicated a different pattern in cancer mortality trends between ethnic groups. Notably, there were significant increases for Māori of both sexes (by about a third), with rate ratios increasing from 1.53 to 1.84 (p for trend=0.04) for men and 1.67 to 2.02 ($p=0.03$) for women. While Pacific women started with similar cancer mortality rates to European/Other women in the first period with a rate ratio of 0.95, this increased to 1.38 by 2001–2004 ($p=0.05$). Pacific men had about 10% to 50% higher cancer mortality than their European/Other counterparts at all points in time. Relative inequalities were stable for Asian peoples compared to European/Others.

In summation, whether measuring on an absolute or relative scale, the data reported in *Tracking Disparity* indicates that inequalities increased in all-cancer mortality for Māori and for Pacific women compared to the European/Other reference group from 1981–2004. The exception was for Pacific men, where no significant trend was observed. Inequality measures were also stable (and negative) for Asian peoples compared to the European/Other reference group.¹⁶

Explanations of disparity

Some disparity can be explained by the relative socioeconomic disadvantage amongst minority ethnic groups¹⁶ and relative differences in contact with factors that promote ill health, such as smoking. Studies have shown increasing mortality and morbidity with increased deprivation¹⁷ and that smoking and obesity are more prevalent among Māori than non-Māori.^{17,18}

Increasing lung cancer trends probably reflect increased tobacco use among Māori and Pacific peoples.¹⁹ Although small, the apparent contribution of smoking and socioeconomic position to ethnic inequalities in mortality increased in the time periods 1981–1984 and 1996–1999.²⁰

Action to address differences in socioeconomic status is likely to be important in reducing ethnic inequalities in health.²⁰ However, differences in socioeconomic status alone do not explain the observed differences in health status, cancer incidence or cancer mortality. Geographical variations also exist in terms of accessibility to general practitioners²¹ and mortality rates.²²

The disparity data (presented in the previous section) suggest that inequities may exist between Māori and non-Māori in access to cancer detection, diagnosis and investigation. Furthermore, it has been reported that Māori are less likely to have timely or equitable access to high-quality cancer treatments and services.⁹

Access to care

The results from a descriptive report by Crengle et al. identified Māori use of general practitioner services to be lower than expected, and lower average consultation duration for Māori compared to non-Māori.²³ Although Crampton et al.²⁴ did not identify a significant difference between ethnicity and average duration of general practitioner visits, annual exposure to primary medical care was greater for those of European ethnicity (94 minutes), compared to Asian, Pacific peoples and Māori (68, 75 and 86 minutes, respectively).

A further study also found that, after adjustment for age, gender and socioeconomic deprivation, Māori, Pacific and Asian peoples had similar or lower general practitioner consultation rates than European New Zealanders.²⁵ Māori and Pacific people's consultation rates would be expected to be higher than European rates given their poorer health status.²⁵

Any barrier that prevents optimal access to care at any point of the patient's pathway has the potential to have an adverse impact on patient outcomes. The GDT acknowledged that this is not solely restricted to the management of cancer. It is equally applicable to medical services for other medical conditions. Although there is a lack of data cited specifically in the New Zealand cancer context, there is a large body of international literature on access to medical care in differing health care settings. A systematic review of this literature was beyond the scope of the guideline. For further details of the approach taken to the literature review, see Appendix A, *Methods*. The GDT considered the full investigation of this issue as a high priority for future health services research.

Barriers for Māori

Traditionally, Māori tend to have a more holistic view of health than the Western-influenced view of the majority of the general New Zealand population. Māori belief systems, such as views about reliance on the whānau (family), individual mana, death and dying, and practices associated with tapu/noa, continue to influence health behaviour. These views may influence, for example, preferences for care, individual help-seeking behaviour and responses to health care providers.²⁶

Two key Government publications have provided a framework for the Ministry of Health, District Health Boards and key stakeholders to take a leadership role in improving Māori health outcomes.^{27,28} *He Korowai Oranga: Māori Health Strategy* provided a framework for the health and disability sectors to take responsibility for the part it plays in supporting the health status of the whānau,²⁷ while objectives for Māori health are set out in *Whakatātaka Tuarua: Māori Health Action Plan 2006–2011*.²⁸

Qualitative research has identified barriers to care from the Māori perspective from interview data. Based on this research, a conceptual framework was developed to address the issue. The framework comprises four key areas: costs of care, communication, structural barriers and cultural fit. Cultural fit refers to the 'fit' of the health care provider with the patient with respect to language, attitudes, and beliefs. An individual's level of comfort when seeking health care will depend upon health care practitioner attitudes and the delivery of culturally appropriate health care. Specific barriers within each key area identified by this research are shown in Box 1.1.²⁹ Additional references that support Jansen's findings at either the general concept or specific example level are also cited.

Barriers to care will undoubtedly vary according to the specific context. In addition, there is likely to be overlap between the key areas (eg, structural barriers can increase costs; communication barriers will be compounded when cultural differences between Māori patient and health care provider exist). Each of these barriers is greater for nga hunga hauā (Māori with disabilities). For Māori with significant disabilities the impact of multiple barriers can be overwhelming, even though they comprise one of the most vulnerable populations.²⁹

Box 1.1 Specific examples of barriers to care from a Māori perspective

Barrier	Specific examples
Costs of care^{i,ii}	<p>Direct:</p> <ul style="list-style-type: none"> • consultation cost^{ii,iii} • prescription chargesⁱⁱⁱ • cost of general practitioner house call <p>Indirect:</p> <ul style="list-style-type: none"> • loss of wages (time off work)ⁱⁱⁱ • perception of 'value for money' • financial cost of travel to receive care • ability to travel (childcare issues)ⁱⁱⁱ
Communication^{iv}	<p>Health literacy</p> <p>Lack of knowledge of available services</p> <p>Experience of unfavourable attitudes to Māori</p>
Structural barriersⁱⁱ	<p>Distance to travel for care^v</p> <p>Appointment availability at a suitable time</p> <p>Waiting times</p> <p>System inflexibility</p> <p>Physical barriers</p> <p>Lack of choice of provider (eg, Māori health care practitioner)</p>
Cultural fitⁱⁱ	<p>Perceptions of being patronised, treated with a lack of respect and/or racism^{vi,vii}</p> <p>Previous bad experiences^{i,iv,vi}</p> <p>Perceptions of illness and death</p> <p>Unfulfilled preference for a Māori health care practitioner</p> <p>Disempowerment (culturally appropriate 'shyness')ⁱ</p> <p>Feeling uncomfortable in unfamiliar (non-Māori) settings</p> <p>Lack of acknowledgment of whānau/Māori processes (eg, desire for whānau to take prime responsibility and a preference to suffer rather than be a burden)</p>

Sources:

- ⁱ Ellison-Loschmann L, et al. Am J Public Health 2006;96:612–7.¹⁷
- ⁱⁱ Baxter J. Barriers to health care for Māori with known diabetes. Te Rōpū Rangahau Hauora a Ngāi Tahu; 2002.³⁰
- ⁱⁱⁱ Bolitho S, et al. Nurs Prax N Z 2006;22:23–33.³¹
- ^{iv} Walker T, et al. NZ Med J 2008;121(1279).³²
- ^v Brabyn L, et al. NZ Med J 2004;117(1199):U996.²¹
- ^{vi} CBG Health Research Limited. Improving access to primary health care. 2005.³³
- ^{vii} Harris R, et al. Lancet 2006;367:2005–09.³⁴

Adapted with permission from: Jansen P. Māori consumer use and experience of health and disability and ACC services. Mauri Ora Symposium, Wellington; April 2006.

Barriers for Pacific peoples

Traditionally, Pacific cultures are orientated towards the social group and concepts of health are holistic. Many Pacific peoples living in New Zealand use traditional methods of healing as well as Western medicine.³⁵ Although there are commonalities, each Pacific nation has its own particular cultural beliefs, customs, values and traditions.³⁶

The *Pacific Health and Disability Action Plan* sets out the strategic direction and actions for improving health outcomes for Pacific peoples. Six priority areas are identified (child and youth health, promoting healthy lifestyles and well-being, primary health care and preventative services, provider development and workforce development, promoting participation of the disabled, health and disability information and research).³⁷

Limited information is available on Pacific peoples' access to care to inform the debate. However, Pacific peoples have been reported to experience similar access issues to Māori. Practical barriers to care (eg, cost, lack of time and difficulty in obtaining an appointment)^{12,33} and cultural constraints (eg, discomfort with their health care provider and a dislike of drugs)^{12,33} have been identified. Specific barriers to access that have been reported for Pacific peoples in New Zealand include English being a second language for many patients over 40 years old, heavy family commitments taking priority over the need for health care and a lack of understanding of the nature and/or need for the appointment.³³

Barriers for other ethnic groups

Although beyond the scope of the literature review for this guideline, it is likely that some of the issues previously raised will also apply to other New Zealanders, especially those in lower socioeconomic groups.

Possible solutions to barriers

No studies were identified that evaluated the effectiveness of cultural competence training on health outcomes in the US Agency for Healthcare Research and Quality's sponsored review of strategies to improve the quality of health care and/or reduce disparities for ethnic minorities. However, there was strong evidence to suggest that such training can improve the knowledge of health care providers and good evidence that it can improve the attitudes and skills of health care providers and improve patient satisfaction. The review also identified strong evidence that provider tracking and reminder systems are effective in improving the quality of care for minority patients.³⁸

While there is a lack of robust evidence that specifically addresses the issue of Māori and Pacific peoples' access to cancer services, some emerging models of care offer considerable potential. BreastScreen South Limited is one example of a successful multidimensional approach to reducing barriers to care for Māori. This service has achieved equitable screening coverage for Māori women as a result of a multi-year programme that included community consultation, personal invitations and reminders to Māori women, as well as marae-based mobile screening.¹¹

The literature reviewed and GDT opinion indicate that the initiatives shown in Box 1.2 have the *potential* to improve access to care. In the absence of a full systematic review of all the national and international evidence, the GDT produced a list of some of the possible ways that they considered health care providers could help reduce barriers to access. Where references are cited, these solutions have been suggested by others or attempted in practice. In some cases, this was at a 'general concept' level.

While many solutions are targeted at individual practitioners, the GDT acknowledged that some have significant implications for PHOs and DHBs. For example, policies on cultural competency will need to be developed, and training and support will be required for practitioners. The Royal New Zealand College of General Practitioners published guidance in 2007³⁹ that provides a framework to assist general practitioners in creating and/or maintaining culturally competent practices. This includes sections on cultural competence with respect to Māori, Pacific peoples and Asian peoples. At a provider level, inequalities can be addressed through quality improvement programmes that focus on Māori and other priority populations.

As each of the four key areas – costs of care, communication, structural barriers and cultural fit – are linked, interventions will need to address multiple issues. Barwick⁴⁰ reported that an English review of interventions designed to reduce health disparities showed that the more successful programmes tended to demonstrate systematic, intensive, multifaceted and/or multidisciplinary approaches. There is also evidence to suggest that a focus on the priority population will result in improved care for all patients, while interventions aimed at the general population maintain disparity.⁴¹

Box 1.2	Potential solutions to barriers to care
Barrier	Potential solutions
Costs of careⁱ	<p>Direct:</p> <ul style="list-style-type: none"> targeted funding for priority populations^{ii,iii,iv} improved practice awareness of transport subsidies <p>Indirect:</p> <ul style="list-style-type: none"> targeted marketing of services for priority populations appointment flexibility (eg, extended hours, after hours, 'drop-in' facility)^{ii,iv}
Communication	<p>Training in communication (with feedback) for health care providersⁱⁱⁱ</p> <p>Easier access to health care providers (eg, by phone, text, computer, 'drop-in')</p> <p>Use of community health workers^{iv,v,vi}</p> <p>Interpreters for migrant populations^v</p> <p>Trilingual interpreters for people with disabilities (eg, deaf Māori)</p> <p>Provision of appropriate (language and cultural) patient information in multiple ways (eg, verbal, written, web-based)^{ii,iv,v,vi,ix}</p> <p>Ensuring patients are aware of the referral pathway and expected time-frames</p> <p>Health care provider acting as an advocate for patients where the medical need is important and a delay has occurred</p> <p>Targeted appointment reminders to the patient from secondary care that includes a contact name and details (eg, by letter, phone, text as appropriate)</p>
Structural barriers	<p>Delivery of services away from traditional settings^{ii,iv,v,vi,ix} (eg, outreach clinics, marae, church, rural settings)</p> <p>Workforce development^x</p> <p>Formal practice tracking of referrals for suspected cancer</p> <p>Ensuring practitioners have easily accessible up-to-date information on their local referral pathway to secondary care and other supportive care services</p>
Cultural fit^{ii,xi}	<p>Training in cultural competency (with feedback) to increase awareness of culturally determined nature of behaviour relating to health care^{iii,v,vi,xii}</p> <p>Recognising and removing power imbalances that can impact on attitudes to health providers, health promotion, and health care, and potentially responsiveness to advice and services^{vi,xiii}</p> <p>Access to health care providers from ethnic minority backgrounds^{iii,v,viii,xi,xiii}</p>

continued over...

Box 1.2

continued...

Note: if no reference is cited the solution was based on the opinion of the GDT

Sources:

- i Crampton P, et al. *Int J Health Serv* 2005;35(3):465–78.⁴²
- ii Baxter J. Barriers to health care for Māori with known diabetes. Dunedin, New Zealand: Te Rōpū Rangahau Hauora a Ngāi Tahu; 2002.³⁰
- iii Walker T, et al. *NZ Med J* 2008;121(1279).³²
- iv CBG Health Research Limited. Improving access to primary health care. 2005.³³
- v Barwick H. Improving access to primary care for Māori and Pacific peoples. Wellington: Ministry of Health; 2000.⁴⁰
- vi Boyd M et al. The Whānau Ora Cancer Care Coordination Research Project – final report. n.d.⁴³
- vii Cormack D, et al. Access to cancer services for Māori. Wellington: Ministry of Health; 2005.⁶
- viii Ministry of Health. Towards a cancer control strategy for New Zealand Marihi Tauporo discussion document: submission analysis. 2004.³⁵
- ix Bax K, et al. *NZ Med J* 2006;119 (1236):U2025.⁴⁴
- x Ratima MM, et al. *Med J Aust* 2007;186:541–3.⁴⁵
- xi Crengle S. *Pac Health Dialog* 2000;7:48–53.⁴⁶
- xii Durie M. *BMJ* 2003;327:408–9.⁴⁷
- xiii Ellison-Loschmann L, et al. *Am J Public Health* 2006;96:612–7.¹⁷

Recommendation development

The GDT wished to draw attention, using good practice points, to a number of areas that they considered important in helping to reduce disparity and to improve access to care. Some are directed at service providers, while others focus on practitioner strategies.

Good practice points aimed at service providers included the importance of collecting accurate ethnicity data, and providing services that are specific for Māori and Pacific peoples. In addition, one good practice point aimed to explicitly raise the awareness of the importance of multidimensional approaches by service providers to addressing disparity. Two other good practice points are focused on specific approaches – review of practice and considering disparity when instituting policies on access to care, continuity of care and cultural competency.

Good practice points were also incorporated to highlight the GDT view that practitioner training in cultural competency, awareness of a person's ethnicity and the need to actively identify a person's specific communication needs are vital to addressing disparity in care.

2 General principles of care

This chapter begins by presenting good practice points on general principles of care in relation to suspected cancer in the primary care setting. These are followed by contextual information on principles of care and on delay to care.

While the recommendations contained in this guideline focus on the referral of people with signs and symptoms suggestive of cancer, many of these signs and symptoms may be indicative of other conditions. Therefore, a finding negative for cancer does not necessarily preclude further investigation or action by the practitioner.

Good practice points

General principles of care	
A person presenting with symptoms and/or signs suggestive of cancer requires urgent investigation, which may include referral to a specialist team	✓
For a person presenting with the same symptoms, or symptom complex, three or more times, a practitioner needs to exclude cancer, and referral to a specialist must be considered	✓
A practitioner should be aware that the need to consider action increases as the number of presenting signs and/or symptoms increases Combinations of signs and/or symptoms have a higher predictive value than a single sign or symptom in isolation	✓
A practitioner should pay careful attention to caregiver reports of a child's symptoms	✓
A person presenting with symptoms and/or signs suggestive of cancer should be assessed through a detailed history and examination, irrespective of the presence of risk factors	✓
A practitioner should have a high index of suspicion of a new primary or metastatic disease (especially bone, brain, liver or lung) in a person with a history of cancer	✓
A practitioner should have a raised index of suspicion in a person with a strong family history of cancer	✓
A practitioner should consider pre-existing comorbidity and the preference of the person/whānau in making the decision to refer to a specialist	✓
Good practice points are the opinion of the Guideline Development Team, or developed from feedback from consultation within New Zealand where no evidence is available.	

Good practice points**Delay**

For a person with advanced disease, referral directly to the palliative care service at first presentation may be appropriate	✓
A practitioner should consider immediate telephone contact with an appropriate specialty service when they have a high index of suspicion of cancer	✓
A practitioner should ensure a referral: <ul style="list-style-type: none"> • is made in a timely manner • provides relevant and sufficiently detailed information to the specialist, including the most appropriate way to contact the patient 	✓
A practitioner should ensure that patients are aware of the time-frames (where available) for: <ul style="list-style-type: none"> • receiving an acknowledgment of the referral • being seen by a specialist or an investigation service 	✓
A practitioner should follow-up all referrals that are made to a specialist to ensure that the referral is processed, especially if they have a high index of suspicion of cancer	✓
A practitioner should be aware of both patient factors and practitioner factors that may result in a delayed referral	✓
Good practice points are the opinion of the Guideline Development Team, or developed from feedback from consultation within New Zealand where no evidence is available.	

Principles of care

Context

During the course of the GDT meetings, a number of issues related to general principles of care were discussed. The GDT wished to draw attention to these areas by producing a series of good practice points.

Recommendation development

Repeated consultations and presentations, for the same symptom or symptom complex, by a person to a primary care practitioner(s) were noted as being more important than a single presentation⁴⁸ as the signs and symptoms for many cancers are non-specific. The GDT also noted that as combinations of signs and symptoms were likely to be more important than a single sign or symptom in isolation,⁴⁹ the greater the number of signs and/or symptoms present the more important it is for the practitioner to act.

The GDT also wished to highlight the importance of personal and family history of cancer in raising levels of suspicion and, in the paediatric setting, listening carefully to what caregivers had to say about children's symptoms. Although the GDT viewed that risk factors

should be considered in conjunction with signs and symptoms, they chose to specifically highlight with a good practice point the importance of assessing the person through a detailed history and examination, irrespective of the presence of risk factors.

Although referral decisions should always take into account the wishes of the person/whānau, this was considered to be of particular importance where comorbidities existed. In some cases (eg, a very elderly person with significant pre-existing comorbidities), the person/whānau and practitioner may jointly decide that the more appropriate course of action is not to refer for further investigations, but to refer directly to palliative care. Other areas highlighted in the good practice points included:

- considering contacting a specialist service by telephone in specific circumstances
- ensuring timeliness and appropriate information provision in the referral to the specialist
- providing information to people on expected timeframes for the acknowledgment of a referral
- being seen by a specialist or investigation service.

Although metastatic disease and palliative care were beyond the guideline scope, the GDT considered it appropriate to add a further two good practice points to highlight specific aspects of these important areas of cancer care.

With the current systems in place in New Zealand primary care, the GDT considered that the tracking of all referrals was not realistic. However, they wished to specifically note, through a good practice point, the importance of follow-up of any referral where there was a high index of suspicion of cancer.

During GDT discussions, a number of other 'system-related' issues were identified. Although it was not considered appropriate to cover these within the good practice points, the GDT wished to explicitly acknowledge them in the guideline text. Due to geographical distances to secondary/tertiary care services in some parts of New Zealand, the personal expertise of the primary care practitioner will determine who is the most appropriate 'specialist'. In addition, not all practitioners will have access to all the investigations referred to in the guideline recommendations. Access to investigations is currently in a state of flux and is likely to change over time due to the availability of funding and more widespread access to medical technology. In some areas local protocols are in place to streamline specific investigations before the first specialist appointment.

Delay

Context

The issue of delay to care has a number of different aspects. Two issues of particular relevance to this guideline are 'patient delay' (the time from the development of a symptom to the person's first presentation to their primary practitioner) and 'practitioner delay' (the time from the person's first presentation to primary care to the first specialist appointment). When developing the recommendations for this guideline, the GDT were conscious of the potential impact of practitioner delay, particularly with respect to undertaking investigations in the primary care setting.

Included studies

The literature was systematically searched for studies that investigated the factors associated with delay (patient and practitioner) and the consequences of delayed referral of a person presenting to the primary practitioner with suspected cancer.

Summary of findings

The literature around these issues was inconsistent, often limited and based mainly on retrospective studies. Patient and practitioner delays often accounted for a larger proportion of delay when compared to delays occurring in the secondary care setting.^{50–52} A systematic review concluded that patient delays were greater than practitioner delay for upper gastrointestinal cancer.⁵³ However, in childhood cancer, practitioner delays were generally longer than patient delays.⁵⁴

Although the clinical significance is unclear, those who saw their general practitioner first had longer delays to specialist referral than if they had presented to the emergency department, or if the cancer was discovered as part of a screening program or during investigation for another problem.^{50,55} Possible explanations include that those presenting to secondary care have advanced or more rapidly progressing disease, or that more 'system' delays occur in primary care.⁵⁰

Factors associated with delay

A number of factors were identified as associated with patient and practitioner delay.

Factors associated with patient delay:

- the person does not recognise the significance or seriousness of their symptom^{49,53,56–59}
- the symptom the person experiences is non-specific and common in the primary care setting (eg, cough, nausea, pain).^{49,56,60–63}

Factors associated with practitioner delay:

- the practitioner does not recognise, or appropriately investigate, symptoms suggestive of cancer^{49,53,56,64,65}
- an investigation shows a normal result when cancer is actually present^{49,56,61}
- the practitioner prescribes an empirical treatment (Bramble et al. cited by NICE⁴⁹)
- the person has multiple medical problems^{53,61,66}
- miscellaneous factors (eg, a lack of explicit follow-up appointment,^{49,56,61} multiple consecutive investigations in primary care).⁶⁷

Systemic problems (eg, waiting times for investigation⁶¹) may also result in delay.

Impact of delay

Overall, the evidence is both limited and inconsistent on the impact of delays on survival and stage at diagnosis. Longer delays may be associated with poorer survival^{68,69} and short delays may be associated with poor prognosis^{54,68,70} Furthermore, the duration of symptoms may not be associated with survival.^{55,71–75} The aggressiveness of the disease and the severity of the presenting symptoms may also play a role in the relationship between delayed diagnosis and cancer stage.^{54,68,70}

Recommendation development

The GDT noted during their discussions the importance of practitioners being aware of both the patient-related and practitioner-related factors that may result in a delayed referral. A good practice point was therefore included to reflect this view.

3 Psychosocial support and information needs

This chapter presents the recommendations for psychosocial support and information needs, followed by contextual information on the body of literature that they were developed from. The chapter concludes with a description of how the evidence was translated by the GDT into specific recommendations.

Recommendations

Psychosocial support and information needs	Grade
A practitioner should provide a person with information on the possible diagnosis (both benign and malignant) according to the person's wish for information*	C
For a person presenting with signs or symptoms suggestive of cancer a practitioner should provide information that encompasses where the person is being referred to, who they will be seen by and what to expect from the specialty service (including the type of tests that may be undertaken)*	C
A practitioner should meet the particular support and information needs as far as possible of people with special needs (for instance, people with learning disabilities or sensory impairment)*	C
A practitioner should address a person's need for continuing support while they are waiting for their referral appointment. This should include inviting the person to contact them again if they have concerns or further questions before their specialist appointment*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice points

Psychosocial support and information needs	
For a person presenting with signs or symptoms suggestive of cancer a practitioner should discuss with that person the type of information that would be helpful for their needs	✓
For a child or young person presenting with signs or symptoms suggestive of cancer a practitioner needs to communicate information in a way that meets the needs of that child or young person	✓
Where there is a reasonable suspicion of cancer in a child or young person, a practitioner should convey that possibility to the child or young person and their parent/guardian	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Background to recommendation development

Context

This section of the guideline is focused on the provision of psychological and social support to people who present to primary care with signs and symptoms suggestive of cancer. The phrase ‘psychological and social support’ refers, in this context, to the provision of any information relevant to a possible diagnosis of cancer and psychological and/or psychosocial support given to people by a primary health care practitioner whilst awaiting their first specialist appointment or investigation.

The period from first contact with a primary health care practitioner to the time of a definitive diagnosis can be marked by great uncertainty, anxiety and stress for a person who has signs and symptoms suggestive of cancer. It is a time when information and support is very important to the individuals and their families/whānau.⁴⁹

In New Zealand, there are key policies, strategies and consumer codes of rights that are directly relevant to both 1) the provision of information and 2) the psychological and/or psychosocial support given to people in the pre-diagnosis period. For example, the Health and Disability Code of Rights⁷⁶ sets out that at all times it is a consumer’s right to be treated with respect, dignity and independence, receive effective communication, be fully informed, make an informed choice and give informed consent, and receive support, that needs to be maintained at all times.

Both the Code and the Health Practitioner Competence Assurance Act 2003 require practitioners to take a culturally competent approach. The New Zealand Cancer Control Strategy¹ highlights the importance of quality care throughout the continuum of cancer. One of the goals in the strategy specifically aims to improve the quality of life for those with cancer, their family and whānau through support, rehabilitation and palliative care. The New Zealand Cancer Control Council has a number of specific objectives to help meet this goal. These include:

1. establishing integrated programmes of supportive care and rehabilitation with defined leadership
2. ensuring that all people with cancer and their families and whānau are able to access the appropriate resources for support and rehabilitation that they need
3. ensuring that those with cancer and their family and whānau have access to high quality information on treatment and care, including complementary and alternative medicine, which includes rongoā Māori.

Some key broad areas for action at a national level within each objective are also identified.¹

This section aims to provide brief guidance related to information provision, and the psychological and social support offered to people with signs and symptoms suggestive of cancer presenting to primary care. For more comprehensive guidance the reader is directed to the Ministry of Health’s *Guidance for Improving Supportive and Rehabilitative Care for Adults with Cancer in New Zealand*.⁷⁷ The principles and specific recommendations contained in that guidance are intended to apply equally to people in the pre-diagnosis stage of their disease. Further information and advice on psychological and social support for people with signs and symptoms indicative of cancer can be accessed from the local branches of the Cancer Society of New Zealand.

Included studies

Due to the lack of literature in this area, the information contained in this section was derived from a non-systematic review. This review focused specifically on identifying research that would indicate the relative effectiveness of information giving and psychological and social interventions in reducing psychological morbidity (ie, anxiety, depression, stress) during the pre-diagnosis stage of cancer. The literature was primarily observational or narrative in nature.

Summary of findings

In addition to the NICE guideline,³ one guideline⁷⁸ and one primary study⁷⁹ were identified.

The NICE guideline contained a comprehensive section on the care of individuals in the pre-diagnosis stage, and presented a number of recommendations on the support and information needs of people with suspected cancer, based on expert opinion.³ It stated that the pre-diagnosis stage involves an individual moving from being 'a person without cancer' to 'a person with cancer'. Careful thought should be given to what information and support should be offered at this stage, and what should be offered once the individual has a definitive diagnosis.

Good communication between health care practitioners and patients was emphasised as essential. Furthermore, the NICE guideline stated that good communication should be supported by the provision of evidence-based information offered in a form that is tailored to the needs of the individual.

A second UK guideline, *Cancer in Primary Care: A Guide to Good Practice*⁷⁸ emphasised the critical role general practitioners have in the management and assessment of people who present with symptoms that are potentially due to cancer. This guideline identified the potential information needs for patients in primary care according to the cancer diagnosis pathway (see Box 3.1).

Box 3.1	Patient information needs throughout the cancer diagnosis pathway
Patient pathway to cancer diagnosis	Potential information needs
Symptoms discovered	<ul style="list-style-type: none"> • Reassurance and advice to go and seek help • Information concerning symptoms and/or signs of cancer
Present to general practitioner or other member of the primary health care team	<ul style="list-style-type: none"> • Information concerning symptoms and/or signs of cancer • Information about tests required
Referred to specialist	<ul style="list-style-type: none"> • How to get to the hospital and what to expect during investigations • When and how the results will be given • Psychological support for the patient and carers including information on access to local primary care and support services • Sign-posting to the relevant information and support network
Adapted from: NHS Modernisation Agency, Macmillan Cancer Relief, National Cancer Action Team. <i>Cancer in primary care: a guide to good practice</i> . London: Department of Health; 2004.	

A primary study conducted by Reubsaet et al.⁷⁹ evaluated user satisfaction with the Dutch national cancer information helpline. Respondents (patients n=258, 39%; relatives/friends n=232, 35%; general public n=171, 26%) returned a survey questionnaire reporting on their overall satisfaction, anxiety and expectations.

The helpline educator's communication skills proved to be the best predictor of the impact of the helpline on levels of anxiety for both the general public and patient groups using the helpline. For relatives and friends surveyed, the information received was the only predictor of anxiety; this was also a significant predictor of anxiety for patients. All groups evaluated the impact of the information helpline in positive terms for overall satisfaction, anxiety and meeting expectations.

The authors concluded that it is important that educators assess the different needs, problems and expectations of those requesting information about cancer. This should then be followed up with information tailored to that individual. For example, if the practitioner has a thorough insight into the type of medical information an individual wants, this allows them to better meet an individual's expectations (ie, either to give more specific information or to be clear on what kind of information individuals do and do not expect).

Recommendation development

No formal evidence-based recommendations were made related to the psychosocial support and information needs of people in the pre-diagnosis stage. Rather, the GDT focused on developing a set of guiding principles for the primary care practitioner when providing supportive care to people with signs and symptoms suggestive of cancer.

A number of the concepts contained in the NICE guideline recommendations (based on expert opinion) were accepted with only minor wording modification. These related to the provision of information on potential diagnoses, information about the first specialist appointment, information for people with special needs and the need for continued support in the time between an individual consulting the primary care practitioner and the first specialist appointment.

In addition, the GDT chose to provide more explicit guidance than the NICE recommendations on the particular information needs of children and young people by including two good practice points specifically on this area. A further good practice point was included to highlight the importance of opening a dialogue with an individual about their personal information needs.

Good practice points specifically related to the delivery of culturally appropriate care are presented in Chapter 1, *Disparity and access to care*.

4 Lung cancer

This chapter presents the recommendations for lung cancer, followed by contextual information on the epidemiology of this cancer in New Zealand. An overview of the three bodies of literature from which the recommendations were developed (risk factors, signs and symptoms, and investigations) is then provided. The chapter concludes with a description of how the evidence was translated by the GDT into specific recommendations.

Recommendations	
Lung cancer: urgent referral (within two weeks)	Grade
<p>A person should be referred urgently to a specialist if they have:</p> <ul style="list-style-type: none"> • persistent haemoptysis and are smokers or ex-smokers aged 40 years or older • a chest x-ray suggestive of lung cancer (including pleural effusion and slowly resolving consolidation)* 	C
<p>A person should be referred urgently for a chest x-ray if they have:</p> <ul style="list-style-type: none"> • unexplained haemoptysis <p>OR</p> <ul style="list-style-type: none"> • any of the following unexplained, persistent (lasting more than 3 weeks or less than 3 weeks in people with known risk factors[†]) symptoms and signs: <ul style="list-style-type: none"> – chest and/or shoulder pain – shortness of breath – weight loss/loss of appetite – abnormal chest signs – hoarseness – finger clubbing – cervical and/or supraclavicular lymphadenopathy – cough – features suggestive of metastasis from a lung cancer (eg, in brain, bone, liver or skin)* <p>[†] Current or ex-smokers, smoking-related chronic obstructive pulmonary disease, previous exposure to asbestos, history of cancer (especially head and neck cancer)</p>	C
A person should be referred urgently to a specialist if they have a normal chest x-ray, but there is a high suspicion of lung cancer*	C
<p>Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.</p> <p>* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.</p>	

Good practice points**Lung cancer: referral/investigation**

The smoking status of all patients should be recorded and regularly updated in the practice notes	✓
After urgent referral for chest x-ray, the chest x-ray should be completed and reported within one week	✓
A person with risk factors* for lung cancer who has consolidation on an initial chest x-ray should have a repeat chest x-ray within 6 weeks to confirm resolution * Current or ex-smokers, smoking-related chronic obstructive pulmonary disease, previous exposure to asbestos, history of cancer (especially head and neck cancer)	✓
Sputum cytology is not recommended for the investigation of lung cancer	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Epidemiological background

New Zealand population

Lung cancer (including cancer of the bronchus or trachea^{8,80,81}) is the leading cause of cancer death in New Zealand men and the second highest cause of cancer death in women. In 2004, men were both diagnosed and died of lung cancer more frequently than women (Table 4.1).⁸¹

Table 4.1 Incidence and mortality rates of lung cancer for the New Zealand population in 2004 by gender

	Male	Female
Registration rate (per 100,000)	36.0	23.2
Mortality rate (per 100,000)	30.8	19.2

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Data on lung cancer survival give a cumulative relative survival after two years of 17%. In the first year, the chance of survival is 30%, and after four years of survival, there is a 92% chance of surviving to the end of the fifth year.⁸⁰

European/Other New Zealanders

Lung cancer mortality fell steadily by 43% during the period 1981–2004 among European/Other men and mortality rates stabilised among European/Other women since the early 1990s.¹⁶

Māori

Lung cancer was the leading cause of cancer death among Māori during the period 1996–2001. The incidence of lung cancer in Māori was more than three times higher than non-Māori in this time period (Table 4.2).⁸

Table 4.2 Incidence of lung cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	42.8	12.9

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Furthermore, the mortality:incidence ratio was 95% for Māori and 85% for non-Māori. Māori when compared to non-Māori, were more likely to be diagnosed with lung cancer and, after diagnosis, were more likely to die as a result of it. Māori were also more likely to be diagnosed at a later disease stage.⁸

Mortality rates among Māori men showed a 28% decline from 1996–1999 to 2001–2004, while rates among Māori women have increased slightly (40 vs 48 per 100,000 in 1981–1984 and 2001–2004, respectively).¹⁶

Pacific peoples

Lung cancer was the leading cause of cancer death among Pacific men and among Pacific women aged 65 years and over during the period 1996–2000. In this time period, for this age group, Pacific men had higher lung cancer registration rates compared to the total New Zealand population (751 vs 361 cases), whereas for Pacific women registration rates were similar to registration rates for the total New Zealand population (181 and 158 cases, respectively).¹²

Mortality rates among Pacific women have increased steadily since 1991–1994 (rate ratio: 0.77 in 1991–1994; 1.66 in 2001–2004). Comparable data on mortality trends for Pacific men since 1991–1994 were subject to difficulties in interpretation and hence have not been reported.¹⁶

Asian peoples

In the time period 1998–2002 in people aged 65 years and over, lung cancer mortality rates were 1.5 times higher for 'Other Asian' men compared to the total New Zealand population. Among Asian peoples, lung cancer registration rates were higher for 'Other Asian' than for Chinese and Indian ethnic groups (1997–2001).¹⁵

Background to recommendation development

Risk factors

The non-systematic review below summarises the key risk factors for lung cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that the incidence of lung cancer is low below the age of 50 years, and that the incidence peaks at about 80 years of age. Approximately 90% of lung cancer cases are attributed to smoking.⁴⁹ Asbestos exposure can cause mesothelioma.⁴⁹

In the NICE guideline recommendations, patients in the categories shown in Box 4.1 were defined as having a higher risk of developing lung cancer. Other risk factors identified by articles cited in the NICE guideline literature review are listed in Box 4.2.

Box 4.1	People at higher risk for lung cancer
	<p>The NICE recommendations define these people as at higher risk of developing lung cancer:</p> <ul style="list-style-type: none"> • current or ex-tobacco smokers • people with smoking-related chronic obstructive pulmonary disease (COPD) • previous exposure to asbestos • previous history of cancer (especially head and neck cancer) <hr/> <p>Source: National Institute for Health and Clinical Excellence. Referral guidelines for suspected cancer. NICE clinical guideline 27. London: 2005.</p>

Box 4.2	Additional risk factors for lung cancer
	<p>The NICE guideline literature review reported the following additional risk factors:</p> <ul style="list-style-type: none"> • occupational exposure to dust or microscopic particles eg, wood dust, silica* • past medical history of COPD, silicosis, tuberculosis* • family history of cancer* • exposure to known carcinogens eg, radon, chromium, nickel† <hr/> <p>* Ruano-Ravina et al. 2003 as cited in source † Macbeth et al. 1996 as cited in source</p> <hr/> <p>Source: National Collaborating Centre for Primary Care. Referral guidelines for suspected cancer in adults and children. Part 1. London: National Collaborating Centre for Primary Care; 2005.</p>

Recent evidence on the risk of lung cancer associated with cannabis smoking⁸² was not assessed for this guideline.

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for lung cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

Two primary studies, published since the NICE guideline, were identified by the literature review. These were a population-based, case-control study⁴⁸ and a case-series study.⁸³

The NICE recommendations for referral of suspected lung cancer were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies, and expert opinion. The literature review identified the symptoms shown in Box 4.3 as possible presenting features of lung cancer. Furthermore, patients with lung cancer may present with metastases.⁴⁹

Box 4.3 Initial signs and symptoms of lung cancer

Common signs and symptoms

- Cough (persistent or unexplained)
- Chest and/or shoulder pain
- Dyspnoea
- Haemoptysis
- Weight loss (unexplained)

Other signs and symptoms

- Finger clubbing
- Dysphagia
- Fever
- Hoarseness
- Pneumonia
- Superior vena cava obstruction
- Weakness
- Wheezing and stridor
- Enlarged lymph nodes

Source: National Collaborating Centre for Primary Care. Referral guidelines for suspected cancer in adults and children. Part 1. London: National Collaborating Centre for Primary Care; 2005.

In a methodologically robust, UK case-control study⁴⁸ of patients aged 40 years or more with primary lung cancer (n=247), signs and/or symptoms independently associated with the disease in the two years before diagnosis included loss of appetite, haemoptysis, dyspnoea, loss of weight, fatigue, chest pain, second attendance with cough and finger clubbing. Haemoptysis and dyspnoea remained associated with cancer at least 180 days before diagnosis. The positive predictive value (PPV) for haemoptysis as a single symptom was 2.4% (95% CI 1.4–4.1%). For a second presentation, the PPV increased to 17%. The PPV for cough also appeared to increase slightly as the number of presentations increased (first presentation 0.4%, 95% CI 0.3–0.5%; second presentation 0.58%, 95% CI 0.4–0.8%; third presentation 0.77%, 95% CI 0.54–1.1%).

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected lung cancer underwent one or more of the investigations listed below:

- complete blood count
- chest x-ray
- spirometry
- sputum cytology.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One secondary study and two primary studies, published since the NICE guideline, were identified by the literature review. These included a structured literature review,⁸⁴ a population-based case-control study,⁴⁸ and a retrospective case-series study.⁸⁵

The studies reviewed for the NICE guideline⁴⁹ identified that a chest x-ray is the principal diagnostic investigation for lung cancer in primary care, that false negative chest x-ray results do occur, and that sputum cytology is not a discriminatory investigation in symptomatic patients.

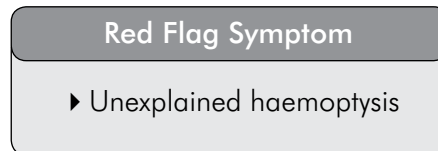
Hamilton and Sharp⁸⁴ systematically reviewed the literature for the features of lung cancer that present in primary care. They concluded, from studies of mainly descriptive or observational design, that although it was reasonable to recommend chest x-ray for unexplained dyspnoea, hoarseness or cervical lymphadenopathy, it was far less reasonable to refer people with these symptoms for chest x-ray to *exclude lung cancer* as other important diagnoses were more likely.

A UK case-series study⁸⁵ provided further evidence that false negative chest x-ray results are sometimes reported for people later diagnosed with lung cancer. In total, 23% of patients (38/164, 95% CI 16–32%), who had at least one chest x-ray requested from primary care in the year before diagnosis, had a negative result. False negative chest x-rays were reported for people with common symptoms of lung cancer, with the exception of hoarseness.

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT agreed with the NICE recommendations on the symptoms that should prompt referral to a specialist, symptoms that should prompt referral for a chest x-ray, risk factors that should prompt earlier referral in a symptomatic patient, and that a person with a normal chest x-ray should be referred urgently to a specialist where there is a high suspicion of lung cancer. Many of the NICE guideline recommendations were therefore accepted with only minor wording modification.

The GDT agreed with NICE recommendations on the importance of further investigation of patients presenting with haemoptysis. In their opinion, unexplained haemoptysis was the only symptom where a health care practitioner would need to consider a referral for chest x-ray on a single presentation. In the view of the GDT, the only instance where haemoptysis should not be acted upon at first presentation was in an otherwise asymptomatic, young person. The GDT therefore chose to add prominence to haemoptysis by classifying it as a 'red flag' symptom.



The GDT also chose to address a number of areas that were not covered in the NICE recommendations. Four additional good practice points were therefore developed. These relate to the follow-up of patients with lung cancer risk factors and consolidation on chest x-ray, the importance of accurate recording of smoking status in patient notes, reinforcing that sputum cytology is not an appropriate investigation in patients with suspected lung cancer, and specifying the timeframe within which an urgent chest x-ray should be completed and reported.

5 Gastrointestinal cancer

In this chapter, gastric and oesophageal, pancreatic and colorectal cancers are considered in turn. The recommendations for each of these cancers are presented first, followed by contextual information on the epidemiology of that cancer in New Zealand. An overview of the three bodies of literature from which the recommendations were developed (risk factors, signs and symptoms, and investigations) is then provided. Each section concludes with a description of how the evidence was translated by the GDT into specific recommendations. Liver cancer is considered separately at the end of the chapter.

Gastric and oesophageal cancer

For the purpose of this guideline, dyspepsia refers to all the sub-classifications (reflux-like, ulcer-like, dysmotility-like, non-specific) identified by the New Zealand guideline *Management of Dyspepsia and Heartburn*.⁸⁶ Thus, patients with epigastric pain or discomfort, heartburn or acid regurgitation, with or without bloating, nausea or vomiting are included within this definition.

Recommendations

Gastric and oesophageal cancer: urgent referral (within two weeks)	Grade
A person of any age with dyspepsia should be referred urgently for endoscopy or to a specialist if they have any of the following: <ul style="list-style-type: none"> gastrointestinal bleeding dysphagia progressive unexplained weight loss persistent vomiting iron deficiency anaemia epigastric mass* 	C
A person aged 55 years or older with unexplained and persistent recent-onset dyspepsia solely, should be referred urgently for endoscopy*	C
A person with dysphagia (specifically, interference with the swallowing mechanism that occurs within 5 seconds of having commenced the swallowing process) should be referred urgently*	C
For a person with unexplained weight loss or iron deficiency anaemia, without dyspepsia, the possibility of upper gastrointestinal cancer and need for urgent referral for investigation should be considered*	C
For a person with persistent vomiting and weight loss, without dyspepsia, the possibility of upper gastrointestinal cancer and need for urgent referral for investigation should be considered*	C

continued over...

Recommendations continued...**Gastric and oesophageal cancer: urgent referral (within two weeks)** **Grade**

For a person with unexplained worsening of their dyspepsia, the need for urgent referral to a specialist should be considered if they have any of the following known risk factors:

- Barrett's oesophagus
- known dysplasia, atrophic gastritis or intestinal metaplasia
- peptic ulcer surgery more than 20 years ago*

C

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.

* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.

Good practice point**Gastric and oesophageal cancer: urgent referral (within two weeks)**

A person of any age with dyspepsia and a family history of gastric cancer (onset <50 years) should be referred urgently for endoscopy or to a specialist

✓

Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.

Recommendations**Gastric and oesophageal cancer: referral/investigation** **Grade**

A practitioner should make the decision to refer a person with suspected upper gastrointestinal cancer to a specialist, irrespective of the person's *Helicobacter pylori* status*

C

For a person where the decision to refer to a specialist has been made, a complete blood count may be undertaken to assist specialist assessment*

C

For a person with new onset dyspepsia the need for a complete blood count to detect iron deficiency anaemia should be considered*

C

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.

* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.

Good practice point**Gastric and oesophageal cancer: referral/investigation**

For a person of Māori, Pacific Island or Asian origin, the practitioner should consider the possibility of gastric cancer at a younger age (approximately 10 years earlier) than the general population

✓

Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.

Epidemiological background

Oesophageal cancer

New Zealand population

Oesophageal cancer is rare, accounting for just over 1% (n=253) of all cancer registrations in New Zealand in 2004. In 2004, men were both diagnosed with oesophageal cancer and died more than twice as frequently from it as women (Table 5.1).⁸¹

Table 5.1 Incidence and mortality rates of oesophageal cancer in 2004 by gender

	Men	Women
Registration rate (per 100,000)	6.0	1.8
Mortality rate (per 100,000)	4.5	1.7

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Data on oesophageal cancer survival give a cumulative relative survival of approximately 12% after five years. In the first year, the chance of survival is 30% and after four years of survival, there is a 97% chance of surviving to the end of the fifth year.⁸⁰

Māori

The incidence of oesophageal cancer in Māori during 1996–2001 was approximately two-thirds higher than in non-Māori (Table 5.2). Furthermore, the mortality:incidence ratio was 93% for Māori and 88% for non-Māori. Māori when compared to non-Māori, were more likely to be diagnosed with oesophageal cancer and after diagnosis, were more likely to die as a result of it.⁸

Table 5.2 Incidence of oesophageal cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	2.8	1.7

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Gastric cancer

New Zealand population

Gastric cancer is the fourth leading cause of cancer death in New Zealand men. In 2004, men were both diagnosed with gastric cancer and died about twice as frequently from it as women (Table 5.3).⁸¹

Table 5.3 Incidence and mortality rates of gastric cancer in 2004 by gender

	Men	Women
Registration rate (per 100,000)	7.5	4.3
Mortality rate (per 100,000)	6.4	3.1

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Data on gastric cancer survival give a cumulative relative survival of approximately 20% after five years. In the first year, the chance of survival is 39%, and after four years of survival, there is a 92% chance of surviving to the end of the fifth year.⁸⁰

Māori

The incidence of gastric cancer in Māori during 1996–2001 was more than three times higher than for non-Māori (Table 5.4). Furthermore, the mortality:incidence ratio was 85% for Māori and 72% for non-Māori. Māori when compared to non-Māori, were more likely to be diagnosed with gastric cancer and after diagnosis, were 50% more likely to die as a result of it. In contrast to some cancers, Māori were more likely to be diagnosed at an early disease stage.⁸

Table 5.4 Incidence of gastric cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	9.8	3.2

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Asian peoples

In the time period 1998–2002 in patients aged 45 years and over, gastric cancer mortality rates were higher for Chinese women compared to the total New Zealand population. Gastric cancer registration rates were significantly higher for Chinese women and 'Other Asian' (not of Chinese or Indian ethnicity) men than in the total population (1997–2001).¹⁵ See Chapter 1, *Disparity and access to care* for specific definitions related to Asian ethnic groupings.

Background to recommendation development

Risk factors

As risk factor consideration is an integral part of practitioner assessment of a symptomatic patient, the non-systematic review below summarises the key risk factors for gastric and oesophageal cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that the incidence of oesophageal and gastric cancers increases from approximately 50 years of age. Other risk factors for oesophageal cancer included Barrett's oesophagus (40–125 fold risk) and for gastric cancer, smoking (1.5–2.5 fold risk).⁴⁹

Two further guidelines, one from Scotland,⁸⁷ the other from New Zealand,⁸⁶ provided data on the evidence-base for gastric and oesophageal cancer risk factors.

Risk factor evidence for gastric and oesophageal cancers identified by the SIGN *Management of Oesophageal and Gastric Cancer* guideline⁸⁷ is shown in Box 5.1.

Box 5.1	Major risk factors for gastric and oesophageal cancer identified by SIGN
Risk factor Cancer type	Level of evidence
Alcohol Squamous oesophageal and gastric cancers Longstanding symptomatic gastrooesophageal reflux disease and Barrett's oesophagus Oesophageal adenocarcinoma	Meta-analyses/systematic reviews of randomised controlled trials/randomised controlled trials (Good evidence that the relationship is causal)
Age over 55 years Oesophageal and gastric cancers Male gender Squamous oesophageal and oesophagogastric junction cancer Smoking Squamous oesophageal, oesophagogastric junction and gastric cancers Increasing body mass index Oesophageal adenocarcinoma and oesophagogastric junction cancers Diet (high intake of animal-based food) Gastric and oesophageal cancer Deprivation Squamous oesophageal and gastric cancer	Systematic reviews of cohort or case-control studies/ high quality primary cohort/ case-control studies (High probability that the relationship is causal)
<i>Helicobacter pylori</i> infection Gastric cancer – 2- to 3-fold increase	High quality primary cohort/ case-control studies (Moderate probability that the relationship is causal)
Source: Scottish Intercollegiate Guidelines Network. Management of oesophageal and gastric cancer. National clinical guideline No. 87. Edinburgh: SIGN; 2006.	

A New Zealand guideline⁸⁶ identified that although not all gastric cancers are associated with *Helicobacter pylori* infection, this bacterium is now recognised as a class I carcinogen by the World Health Organization. Progression from infection to gastric adenocarcinoma appears to be dependent on environmental and genetic factors. However, the precise mechanism has yet to be established.⁸⁶

Ethnicity also appears to be an important factor. Gastric cancer is more prevalent among some Māori, Pacific and East Asian peoples. Furthermore, a Māori family cohort with a genetic predisposition has been identified. These individuals can present with gastric cancer from adolescence onwards. Gastric cancer tends to occur a decade earlier in people of Māori, Pacific or Asian ethnicity compared to other New Zealanders.⁸⁶

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for gastric and oesophageal cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One secondary study and five primary studies, published since the NICE guideline, were identified by the literature review. These were a systematic review with meta-analysis,⁸⁸ four case-series studies^{64,83,89,90} and a population-based audit.⁹¹

The NICE recommendations for referral for suspected upper gastrointestinal cancer (cancer of the oesophagus, stomach and pancreas) were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified that although dyspepsia is a very common symptom complex in the general population, it is a poor predictor of these cancers. However, in a patient with dyspepsia, weight loss (2 kg or over) and dysphagia are associated features. Although potentially less discriminating than dysphagia and weight loss, other symptoms linked with gastric cancer included haematemesis, persistent vomiting, and anaemia. No evidence statements were made on other symptoms linked specifically with oesophageal cancer.⁴⁹

A meta-analysis⁸⁸ of 15 prospective cohort studies (57,363 patients) showed that 'alarm features' (dyspepsia, weight loss, dysphagia) and clinical diagnosis were relatively inaccurate predictors of an upper gastrointestinal cancer (alarm features, pooled sensitivity 67% [95% CI 54–83%], pooled specificity 66% [95% CI 55–79%], pooled positive LR 2.74 [95% CI 1.47–5.24]; clinical diagnosis, pooled sensitivity 29% [95% CI 10–88%], pooled specificity 97% [95% CI 96–99%]).

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected gastric and oesophageal cancer underwent one or more of the investigations listed below:

- complete blood count (CBC)
- ferritin

- ultrasound
- barium swallow.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One relevant New Zealand guideline, *Management of Dyspepsia and Heartburn*,⁸⁶ was identified. No secondary or primary studies, published since the NICE guideline, were discovered.

The NICE guideline recommendations were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified that endoscopy and biopsy detected more gastric and oesophageal cancers than radiography. However, the risk of a false-negative result on endoscopy or biopsy is higher if patients are taking medicines from the histamine type 2 receptor antagonist or proton pump inhibitor classes prior to these tests.⁴⁹

The New Zealand guideline on the management of dyspepsia and heartburn⁸⁶ provided no additional evidence.

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT agreed with the NICE recommendations on: referral of a person with dysphagia; referral of a person aged 55 years or older with unexplained and persistent recent-onset dyspepsia; referral of a person with unexplained weight loss or iron deficiency anaemia, without dyspepsia; and referral of a person with persistent vomiting and weight loss, without dyspepsia.

The GDT also agreed with the NICE recommendations on the risk factors that should prompt a practitioner to consider referral in a person with unexplained worsening dyspepsia, the importance of not allowing a person's *Helicobacter pylori* status to influence a decision to refer and the place of a CBC investigation. Once the decision to refer has been made, the GDT considered that requesting a CBC to ensure that the results are available for the first specialist appointment may aid the assessment process. Many of the NICE guideline recommendations were therefore accepted with only minor wording modification.

The GDT agreed, in principle, with the NICE recommendation on the specific signs and symptoms which, when combined with dyspepsia, should prompt further action. However, in the opinion of the GDT, urgent referral was considered necessary in a patient with dyspepsia presenting with any type of gastrointestinal bleeding, rather than chronic bleeding as specified by NICE. In addition, due to the limited use of the barium meal investigation in New Zealand, the finding of a suspicious barium meal test result was eliminated as a reason for referral.

The GDT also chose to address two areas not covered in the NICE recommendations. Good practice points were therefore developed that highlighted the need for a practitioner to be aware of the additional risk associated with a person having a family history of gastric cancer or being of Māori, Pacific Island or Asian ethnicity.

Pancreatic cancer

Recommendations

Pancreatic cancer	Grade
A person presenting with unexplained upper abdominal pain and weight loss should be referred urgently to a specialist*	C
A person should be referred urgently to a specialist if they have obstructive jaundice. An urgent ultrasound investigation may be considered if available to assist specialist assessment*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice point

Pancreatic cancer	
A person with an upper abdominal mass should be referred urgently to a specialist*	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	
* Good practice point consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Epidemiological background

New Zealand population

Pancreatic cancer is the fifth leading cause of cancer death in both men and women in New Zealand. In 2004, men were both diagnosed with pancreatic cancer and died slightly more frequently from it than women (Table 5.5).⁸¹

Table 5.5 Incidence and mortality rates of pancreatic cancer in 2004 by gender

	Men	Women
Registration rate (per 100,000)	6.3	4.7
Mortality rate (per 100,000)	5.8	4.4

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Data on pancreatic cancer survival give a cumulative relative survival of approximately 5% after five years. In the first year, the chance of survival is 16% and after four years of survival, there is a 95% chance of surviving to the end of the fifth year.⁸⁰

Māori

Pancreatic cancer was the sixth leading cause of cancer death among Māori during 1996–2001. The incidence of pancreatic cancer in Māori was about twice that of non-Māori in this time period (Table 5.6). The mortality:incidence ratio was 96% for Māori and 89% for non-Māori. Māori when compared to non-Māori, were more likely to be diagnosed with this disease but after diagnosis, were overall, no more likely to die as a result of it.⁸

Table 5.6 Incidence of pancreatic cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	5.2	2.7

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Background to recommendation development

Risk factors

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that the incidence of pancreatic cancer increased from approximately 50 years of age and that smoking is a risk factor (risk ratio 1.6–3.1).⁴⁹

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for pancreatic cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One primary study, published since the NICE guideline, was identified by the literature review. This study was of a case-series design.⁹²

The NICE recommendations for referral for suspected pancreatic cancer were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The two most commonly occurring symptoms on presentation were identified as abdominal pain and jaundice, featuring in about 70% and 50% of cases, respectively. Other non-specific signs and symptoms (eg, a change in bowel habit, nausea and vomiting, weight loss, and onset of diabetes) frequently occurred.⁴⁹

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected pancreatic cancer underwent one or more of the investigations listed below:

- ultrasound
- CBC
- ferritin
- liver function tests.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified.

The NICE recommendations were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified that jaundice associated with pancreatic cancer is usually obstructive and extrahepatic. Abdominal ultrasound was cited as an investigation which may be organised through primary care.⁴⁹

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT agreed with the NICE recommendations on referral of a person presenting with unexplained upper abdominal pain and weight loss, and referral of a person with obstructive jaundice. Providing referral was not delayed, the GDT also agreed with the NICE recommendation that arranging an ultrasound scan in primary care may be a useful aid to the specialist assessment process for obstructive jaundice. Some of the NICE guideline recommendations were therefore accepted with only minor wording modification.

In contrast to the NICE guideline, the GDT considered it appropriate to urgently refer any person with an upper abdominal mass, irrespective of the presence of dyspepsia. This guidance was incorporated as a good practice point.

Colorectal cancer

Recommendations

Colorectal cancer: urgent referral (within two weeks)		Grade
A person aged 40 years and older reporting rectal bleeding with a change of bowel habit towards looser stools and/or increased stool frequency persisting for 6 weeks or more should be referred urgently to a specialist*		C
A person aged 60 years and older with rectal bleeding persisting for 6 weeks or more without a change in bowel habit and without anal symptoms should be referred urgently to a specialist*		C
A person aged 60 years and older with a change in bowel habit to looser stools and/or more frequent stools persisting for 6 weeks or more without rectal bleeding should be referred urgently to a specialist*		C
A person presenting with a palpable rectal mass (intraluminal and not pelvic), should be referred urgently to a specialist, irrespective of age. Note that a pelvic mass outside the bowel should be referred urgently to a urologist or gynaecologist*		C
A man of any age with unexplained iron deficiency anaemia and a haemoglobin of 110 g/L or below, should be referred urgently to a specialist* Unexplained iron deficiency anaemia means unrelated to other sources of blood loss, for example, non-steroidal anti-inflammatory drug treatment or blood dyscrasia		C
A non-menstruating woman with unexplained iron deficiency anaemia and a haemoglobin of 100 g/L or below, should be referred urgently to a specialist* Unexplained iron deficiency anaemia means unrelated to other sources of blood loss, for example, non-steroidal anti-inflammatory drug treatment or blood dyscrasia		C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.		
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.		

Good practice points

Colorectal cancer: urgent referral (within two weeks)	
A person presenting with a right-sided abdominal mass, should be referred urgently for a surgical opinion	✓
A menstruating woman with unexplained iron deficiency anaemia* and a haemoglobin of 100 g/L or below, should be referred urgently to a specialist * Unexplained iron deficiency anaemia means unrelated to other sources of blood loss, for example, heavy menstrual bleeding, non-steroidal anti-inflammatory drug treatment or blood dyscrasia	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Recommendations

Colorectal cancer: referral/investigation		Grade
For a person with equivocal symptoms, a complete blood count may help in identifying the possibility of colorectal cancer by demonstrating iron deficiency anaemia. This should determine if a referral is needed and whether the person should be urgently referred to a specialist*		C
For a person where the decision to refer to a specialist has been made, a complete blood count may be considered to assist specialist assessment in the outpatient clinic*		C
For a person where the decision to refer to a specialist has been made, no examinations or investigations other than an abdominal and rectal examination, and a complete blood count should be undertaken as this may delay referral*		C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.		
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.		

Good practice points

Colorectal cancer: referral/investigation	
A person at low risk of colorectal cancer with a significant symptom (rectal bleeding or a change in bowel habit) and a normal rectal examination, no anaemia and no abdominal mass, should be managed by a strategy of treat, watch and review in three months	✓
In a person presenting with a left-sided abdominal mass, faecal loading should first be excluded as the cause. A referral should then be made for a surgical opinion	✓
Faecal occult blood and carcinogenic embryonic antigen testing are of little value in a person with symptoms suggestive of colorectal cancer and should not be used	✓
A person with any unexplained gastrointestinal symptoms and known high risk factors, for example, familial adenomatous polyposis, hereditary non-polyposis colorectal cancer, other familial colorectal syndromes or a past history of lower gastrointestinal cancer should be referred to a specialist	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Epidemiological background

New Zealand population

Colorectal cancer (cancers of the colorectum and anus^{8,80,81}) is the second leading cause of cancer death in New Zealand. In 2004, men were both diagnosed with colorectal cancer and died more frequently from it than women (Table 5.7).⁸¹

Table 5.7 Incidence and mortality rates of colorectal cancer in 2004 by gender

	Men	Women
Registration rate (per 100,000)	46.1	38.9
Mortality rate (per 100,000)	18.3	15.4

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Data on colorectal cancer survival give a cumulative relative survival of approximately 60% after five years. In the first year, the chance of survival is 78% and after four years of survival, there is a 97% chance of surviving to the end of the fifth year.⁸⁰

European/Other New Zealanders

The colorectal cancer mortality rate has steadily declined among European/Other women since the late 1980s and European/Other men since the early 1990s (Table 5.8).¹⁶

Table 5.8 Mortality rates of colorectal cancer by gender over time

	Rate (time period)	Rate (time period)
Male mortality rate (per 100,000)	22.3 (1991–94)	17.4 (2001–2004)
Female mortality rate (per 100,000)	17.5 (1986–89)	12.6 (2001–2004)

Source: Blakely T, et al. Tracking Disparity: Trends in ethnic and socioeconomic inequalities in mortality, 1981–2004. Wellington: Ministry of Health; 2007.¹⁶

Māori

The incidence of colorectal cancer in Māori during 1996–2001 was lower than non-Māori (Table 5.9). However, the mortality:incidence ratio was 57% for Māori and 41% for non-Māori. Māori when compared to non-Māori were less likely to be diagnosed with colorectal cancer but after diagnosis, were more likely to die as a result of it. Māori were more likely to be diagnosed at a later disease stage.⁸

Table 5.9 Incidence of colorectal cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	15.5	24.1

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Mortality rates among Māori increased from values below that of European/Other New Zealanders in the early 1980s to equivalent levels in the 1990s and beyond.¹⁶

Pacific peoples

During 1996–2000, both Pacific men and women in the age groups 45 years and over had lower colorectal cancer registration rates compared to the total New Zealand population. Although mortality rates were lower for Pacific men and women in these age groups, there is evidence to suggest that mortality rates had been rising in Pacific peoples over time.¹²

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises the key risk factors for colorectal cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that, although colorectal cancer was rare below the age of 40 years, the incidence increased with age. Ulcerative colitis was a risk factor, but the significance of family history in symptomatic patients was unclear.⁴⁹

Key risk factors identified by a New Zealand evidence-based guideline on the surveillance and management of groups at increased risk of colorectal cancer⁹³ and an Australian colorectal cancer guideline⁹⁴ are shown in Box 5.2.

Box 5.2	Key risk factors for colorectal cancer
	<ul style="list-style-type: none"> • Personal history of colorectal cancer, colorectal adenomas or longstanding extensive ulcerative colitisⁱ • Family history of familial adenomatous polyposis (FAP), hereditary non-polyposis colorectal cancer (HNPCC) or other familial colorectal cancer syndromesⁱ • Inactive lifestyleⁱⁱ • Obesityⁱⁱ • Alcoholⁱⁱ • Smokingⁱⁱ
	<p>Sources:</p> <ul style="list-style-type: none"> i New Zealand Guidelines Group. Surveillance and management of groups at increased risk of colorectal cancer. Wellington: NZGG; 2004. ii Australian Cancer Network Colorectal Cancer Guidelines Revision Committee. Guidelines for the prevention, early detection and management of colorectal cancer. Sydney: The Cancer Council Australia and Australian Cancer Network; 2005.

The New Zealand guideline identified that only very rarely have cancers been found in individuals with ulcerative colitis who do *not* have colitis extending proximal to the recto-sigmoid region and disease of greater than 10 years' duration.⁹³ Although the Australian guideline noted that dietary evidence was more equivocal, high-energy intake and dietary-fat intake were presented as risk factors.⁹⁴

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for colorectal cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One relevant guideline was identified by the literature review.⁹⁵ In addition, eight primary studies, published since the NICE guideline, were discovered. These included a population-based case-control study,⁹⁶ a cross-sectional survey,⁹⁷ four population-based case-series studies^{83,98–100} and two case-series studies.^{64,101}

The NICE recommendations for referral for suspected lower gastrointestinal cancer were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified that the symptoms associated with colorectal cancer (rectal bleeding, change in bowel habit, abdominal pain, mucus, tenesmus) are relatively common symptoms in the general population. However, a combination of signs and/or symptoms was a more sensitive and specific predictor of colorectal cancer than a single sign or symptom.

The most consistent single predictors were found to be blood mixed with or on the stool and change in bowel habit. A finding on rectal examination suggestive of cancer was a strong predictor. The most helpful combination was found to be age, bleeding mixed with or on the stool, change in bowel habit and raised erythrocyte sedimentation rate (ESR). Iron deficiency anaemia could also be the presenting sign. The authors also noted that although some patients with right-sided cancers present with a mass, the primary care studies reviewed did not consider the significance of abdominal examination to detect abdominal masses.⁴⁹

The evidence summary from a UK referral guideline for bowel cancer⁹⁵ provided additional information. This identified that a change in bowel habit to looser stools and/or increased frequency of defecation increased the risk of cancer and that the characteristics of rectal bleeding were of less value in identifying patients at either a high or low risk of bowel cancer. The diagnostic value of rectal bleeding was increased when it occurred in combination with a change in bowel habit and without anal symptoms. Conversely, rectal bleeding with no change in bowel habit and with anal symptoms and no anorectal mass had a very high negative predictive value. Furthermore, abdominal pain could decrease the diagnostic value of other symptom combinations, for example, rectal bleeding and a change in bowel habit.

In a methodologically robust UK case-control study⁹⁶ of patients aged 40 years or more with colorectal cancer ($n=349$), signs and symptoms independently associated with the disease in the two years before diagnosis included: rectal bleeding, weight loss, abdominal pain, diarrhoea, constipation, abnormal rectal examination, abdominal tenderness and haemoglobin below 10 g/100 ml (100 g/L). The highest positive predictive values (PPV) for these individual signs and symptoms were for rectal bleeding (2.4%, 95% CI 1.9–3.2%) and a haemoglobin below 10 g/100 ml (2.3%, 95% CI 1.6–3.1%). For a second presentation of rectal bleeding, the PPV increased to 6.8%. The highest PPVs for two signs

and/or symptoms were for abnormal rectal examination combined with either weight loss or rectal bleeding or diarrhoea (range, 7.4–11%) and for haemoglobin below 10 g/100 ml combined with either abdominal pain or abdominal tenderness (6.9% and >10%, respectively).

Although two studies identified the appearance of rectal blood as potentially important,^{97,100} the value of this clinically may be questionable. In a Danish cross-sectional survey of patients aged 40 years or older diagnosed with colorectal cancer (n=122),⁹⁷ PPVs for rectal bleeding and dark rectal blood were 7.1% (95% CI 6.0–8.2%) and 20.6% (95% CI 18.9–22.3%), respectively. A questionnaire survey of patients attending a UK sigmoidoscopy clinic with rectal bleeding (n=604), identified that dark blood per rectum and a combination of dark blood and blood mixed with stool had higher likelihood ratios (LR: 2.1 and 3.0, respectively) than blood mixed with stool (LR:1.5).¹⁰⁰ However, these values were too small to be of diagnostic value.

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected colorectal cancer underwent one or more of the investigations listed below:

- sigmoidoscopy
- proctoscopy
- CBC
- ferritin
- faecal occult blood
- carcinogenic embryonic antigen.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One guideline, a referral guideline from the Association of Coloproctology of Great Britain and Northern Ireland,⁹⁵ was identified by the literature review. No secondary or primary studies, published since the NICE guideline, were discovered.

The NICE guideline recommendations were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified the evidence cited below.⁴⁹ However, it was noted that some of the reviewed studies related to investigations in referred patients and that extrapolation to a primary care setting required caution. In addition, the primary care studies were limited by insufficient patient numbers with and without cancer, range of presenting symptoms or an adequate gold standard.

The principal investigations for colorectal cancer were identified as double contrast barium enema, colonoscopy and flexible sigmoidoscopy. The biochemical marker CEA was not found to be sufficiently sensitive or specific to be used as a diagnostic aid (sensitivity 30–40%, specificity 87%; Duffy et al. 2003 as cited in the NICE literature review⁵⁶).

Haemoglobin, ESR and white blood cell count had low sensitivity in detecting colorectal cancer. In patients experiencing symptoms, the sensitivity, specificity, and PPV of faecal occult blood tests (sensitivity 57–93%; specificity 72–89%, PPV 13–33%; Tate et al. 1990 as cited in the NICE literature review⁵⁶) was found to be too low to make these tests helpful. It was also specifically noted that rectal examinations undertaken in general practice failed to detect all cases of rectal cancer.⁵⁶

The referral guidelines from the Association of Coloproctology of Great Britain and Northern Ireland⁹⁵ provided no additional evidence.

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT agreed with the NICE recommendations on the need for urgent referral of a person in the following circumstances: aged 40 years and older with rectal bleeding, a change in bowel habit towards looser stools and/or increased stool frequency persisting for more than six weeks; aged 60 years and older with rectal bleeding persisting for more than six weeks without a change in bowel habit and without anal symptoms; aged 60 years and older with a change in bowel habit towards looser stools and/or increased stool frequency persisting for more than six weeks; the presence of a palpable rectal mass; a man, or non-menstruating woman, with unexplained iron deficiency anaemia and a reduced haemoglobin level.

The GDT also agreed with the NICE recommendations on the place of the CBC investigation and the importance of nothing other than a CBC, abdominal examination and rectal examination being undertaken in the primary care setting to avoid a delay in referral. Many of the NICE guideline recommendations were therefore accepted with only minor wording modification.

However, the GDT considered it important to provide more explicit advice than the NICE guideline on dealing with a right-sided abdominal mass and the place of 'treat, watch and review' as a management strategy. The GDT also discussed and placed a different emphasis to the NICE guideline with respect to risk factor advice.

The GDT chose not to include the NICE guideline recommendations related to family history of colorectal cancer and personal history of ulcerative colitis. In keeping with the New Zealand guideline on management of those at increased risk of colorectal cancer,⁹³ the GDT wished to note the importance of referral of a person with unexplained gastrointestinal symptoms and known high risk factors for colorectal cancer using a good practice point.

Furthermore, to increase the comprehensiveness of this guideline, the GDT chose to address additional areas. Good practice points were therefore developed on management of a menstruating woman with iron deficiency anaemia and management of a person with a left-sided abdominal mass. The GDT also chose to highlight the point that CEA and faecal occult blood testing are inappropriate investigations in patients with suspected colorectal cancer.

Although there are gastrointestinal signs and/or symptoms other than rectal bleeding associated with colorectal cancer (eg, abdominal pain, rectal mucus), the GDT considered that these were not specific enough to warrant inclusion in the guideline recommendations. However, it was noted that such symptoms have a higher predictive value when they occur in high risk populations. Furthermore, they may be indicative of other conditions and may therefore still require treatment.

Liver cancer

Primary liver cancer was not included as part of the NICE guideline on referral for suspected cancer.³ A systematic review of the clinical questions for liver cancer was outside the scope of this guideline. However, due to the high prevalence in Māori, the GDT considered it an additional and important area on which to provide some brief information and guidance. The good practice point reinforces accepted practice for surveillance of people with chronic liver disease recommended by the Hepatitis Foundation of New Zealand (Hornell, J on behalf of Hepatitis Foundation of New Zealand 2008, pers. comm. 18 November). This is followed by brief epidemiological background on liver cancer in New Zealand.

Good practice point

Liver cancer

A person with chronic hepatitis B or C should have a blood test for alpha fetoprotein undertaken every six months as a screening test for hepatocellular carcinoma



Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.

Epidemiological background

New Zealand population

Primary cancer of the liver and intrahepatic bile ducts is rare, accounting for just under 1% (n=164) of all cancer registrations in 2004.⁸¹ Data on survival give a cumulative relative survival of approximately 12% after five years. In the first year, the chance of survival is 24% and after four years of survival, there is a 96% chance of surviving to the end of the fifth year.⁸⁰

Māori

Although cancer of the liver and intrahepatic bile ducts was rare in non-Māori, it was the seventh leading cause of cancer death in Māori during 1996–2001. The incidence of this cancer in Māori men in this time period was more than four times higher than in non-Māori men, and rates among Māori women were twice as high as in non-Māori women (Table 5.10). Overall, the mortality:incidence ratio was 84% for Māori and 79% for non-Māori. Māori when compared to non-Māori, were more likely to be diagnosed with this disease and, after diagnosis, Māori men were 40% more likely to die as a result of it than non-Māori men.⁸

Table 5.10 Incidence of cancer of the liver and intrahepatic bile ducts in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Male registration rate (per 100,000)	9.2	2.0
Female registration rate (per 100,000)	1.9	0.9

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Major risk factors

Although cirrhosis has been identified as the major risk factor for liver cancer development, other important risk factors include chronic hepatitis B and hepatitis C infection.¹⁰² While hepatitis B infection was considered the strongest epidemiological risk factor associated with hepatocellular cancer in many countries, hepatitis C infection was considered most important in Western countries and Japan.¹⁰²

6 Breast cancer

Breast cancer occurring in both women and men is covered as part of this guideline. A separate New Zealand Guidelines Group guideline on the management of early breast cancer is due for publication in 2009.

This chapter presents the recommendations for breast cancer, followed by contextual information on the epidemiology of this cancer in New Zealand. An overview of the three bodies of literature from which the recommendations were developed (risk factors, signs and symptoms, and investigations) is then provided. The chapter concludes with a description of how the evidence was translated by the GDT into specific recommendations.

Recommendations

Breast cancer: urgent referral (within two weeks)		Grade
A woman with a palpable hard, fixed or tethered breast lump should be referred urgently to a specialist*		C
A person presenting with unilateral eczematous skin or nipple change that does not respond to topical treatment, or with nipple distortion of recent onset, should be referred urgently to a specialist*		C
A person presenting with spontaneous unilateral bloody nipple discharge should be referred urgently to a specialist*		C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details. * Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.		

Recommendations

Breast cancer: referral/investigation		Grade
A palpable breast lump in a woman should be investigated*		C
A woman with an abscess or mastitis which does not settle after one course of antibiotics should be referred to a specialist†		C
A woman over 40 years of age with a breast abscess that has settled should be referred for mammography†		C
Persistent, unilateral, unexplained breast pain in a postmenopausal woman should be investigated‡		C
For a person presenting solely with breast pain, with no palpable abnormality, referral to a specialist may be considered in the event of failure of initial treatment and/or unexplained persistent symptoms. Initial mammography is not recommended‡		C
<p>Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.</p> <p>* Recommendation consistent with: National Breast Cancer Centre. The investigation of a new breast symptom: a guide for general practitioners. Australia: National Breast Cancer Centre; 2006.</p> <p>† Recommendation consistent with: Scottish Intercollegiate Guidelines Network. Management of breast cancer in women. National clinical guideline No. 84. Edinburgh: SIGN; 2005.</p> <p>‡ Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.</p>		

Good practice points

Breast cancer: referral/investigation	
An adult man with a unilateral, firm subareolar mass should be referred to a specialist*	✓
For a person presenting with symptoms and/or signs suggestive of breast cancer, investigation may be instigated by the practitioner, but should not delay referral to a specialist	✓
A woman under 30 years of age presenting with generalised lumpiness in the breast tissue, where a focal area of concern, unchanged following a menstrual period, is identified, should be referred to a specialist. If a woman has a family history of premature breast cancer an earlier referral for investigation should be considered	✓
<p>Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.</p> <p>* Good practice point consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.</p>	

Epidemiological background

New Zealand population

Breast cancer is the leading cause of cancer death in New Zealand women.⁸¹ Incidence data on breast cancer in New Zealand is presented in Table 6.1. Data on breast cancer survival give a cumulative relative survival of approximately 82% after five years. In the first year, the chance of survival is 95%, and after four years of survival, there is a 97% chance of surviving to the end of the fifth year.⁸⁰

Table 6.1 Incidence of breast cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	65.1	53.9

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

European/Other New Zealanders

The breast cancer mortality rate fell by 20% from 1981–1984 to 2001–2004 among European/Other women. This decline has predominantly occurred since the late 1980s.¹⁶

Māori

Breast cancer was the leading cause of cancer death among Māori women during 1996–2001. The incidence of this cancer in Māori women was over 20% higher than non-Māori for this time period (Table 6.1).

Furthermore, the mortality:incidence ratio was 33% for Māori and 24% for non-Māori.⁸ Māori women when compared to non-Māori, were more likely to be diagnosed with breast cancer and, after diagnosis, were two-thirds more likely to die as a result of it. Māori women were also more likely to be diagnosed at a later disease stage.⁸

Pacific peoples

Breast cancer was the leading cause of cancer death during 1996–2000 among Pacific women under 65 years of age. In this time period, breast cancer registration rates were similar to the total New Zealand population for all ages (see Table 6.1), but mortality rates were higher.¹²

Asian peoples

Breast cancer registration rates were lower in all Asian ethnic groups (Chinese, Indian, 'Other Asian') than in the total population during 1997–2001. Among Asian peoples, registration rates were significantly higher for Indian and 'Other Asian' women than for Chinese women. In the time period 1998–2002, in women aged 45 years and older, breast cancer mortality rates were significantly lower for Chinese women compared to the total New Zealand population.¹⁵

Background to recommendation development

Risk factors

As risk factor consideration is an integral part of practitioner assessment of a symptomatic patient, the non-systematic review below summarises the key risk factors for breast cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

Women

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that, although rare below the age of 30 years, the breast cancer incidence in English and Welsh women increased sharply with age. Family history of breast cancer, older age at birth of first child and hormone replacement therapy treatment have all been associated with an increased likelihood of developing the disease. It was also identified that no evidence existed to suggest that risk factor information was useful for determining which symptomatic women should be referred.⁴⁹

An Australian guideline¹⁰³ on the investigation of a new breast symptom identified the importance in considering risk factors (eg, previous personal history of breast cancer or a strong family history of breast or ovarian cancer). Indeed, family history is a strong risk factor for the development of breast cancer; the chance that a woman in more developed countries will develop the disease increased as the number of affected first-degree relatives increased.¹⁰⁵ Furthermore, a combination of familial ovarian and breast cancer, or several cases of familial ovarian cancer, may pre-dispose to an increased risk of breast cancer due to BRCA1 mutation.¹⁰⁵

A past history of breast cancer, specific precursor lesions (atypical ductal carcinoma, lobular carcinoma, ductal carcinoma *in situ*) and increased breast density were identified as factors with a higher level of risk ($RR > 2.0$) in a recent New Zealand Health Technology Assessment systematic review.¹⁰⁶

The key risk factors for the development of breast cancer in women are summarised in Box 6.1.

Men

The NICE guidelines literature review identified that breast cancer was more common in men over the age of 50 years. Risk factors cited from a single secondary study by Giordano published in 2002 included testicular abnormalities (undescended testis, congenital inguinal hernia, orchidectomy, orchitis, testicular injury), infertility, Klinefelter syndrome, positive family history, benign breast conditions (nipple discharge, breast cysts, breast trauma), radiation exposure and Jewish ancestry. However, the evidence for the significance of any risk factor in the estimation of disease risk in symptomatic men is unknown.⁴⁹

Box 6.1	Key risk factors for the development of breast cancer in women
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- Personal history of breast cancerⁱ
- Presence of specific precursor lesions (atypical ductal carcinoma, lobular carcinoma, ductal carcinoma *in situ*)ⁱⁱ
- Increased breast densityⁱⁱ
- Increased age at birth of first childⁱⁱⁱ
- Treatment with hormone replacement therapyⁱⁱⁱ
- Family history of breast cancer^{i,iii}
- Family history of ovarian cancerⁱ

Sources:

- i National Breast Cancer Centre. The investigation of a new breast symptom: a guide for general practitioners. Australia: National Breast Cancer Centre; 2006.
- ii Weir R, Day P, Ali W. Risk factors for breast cancer in women. A systematic review of the literature. NZHTA Report 2007;10 (2).
- iii National Collaborating Centre for Primary Care. Referral guidelines for suspected cancer in adults and children. Part 1. London: National Collaborating Centre for Primary Care; 2005.

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for breast cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

Two guidelines were identified by the literature review.^{103,104} No secondary or primary studies, published since the NICE guideline, were discovered.

The NICE recommendations for referral for suspected breast cancer in women were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified that general practitioners are often consulted by women with breast symptoms that included lumps and/or pain. The presence of a palpable mass or skin or nipple change was associated with an increased likelihood of a breast cancer diagnosis. However, the absence of a palpable mass did not eliminate the possibility of this diagnosis. Although research evidence on the characteristics of malignant breast lumps was sparse, expert opinion supported the view that benign lumps were more likely to be smooth and well demarcated. In contrast, malignant lumps were more likely to have poorly defined margins and be less mobile.⁴⁹

The NICE recommendations for breast cancer in *men* were based on a single secondary study by Giordano in 2002. The sign that most commonly occurred at presentation was a subareolar mass. Nipple signs (retraction, ulceration, discharge, bleeding) and local pain occurred less frequently.⁴⁹

A guideline was published by SIGN on the *Management of Breast Cancer in Women* in 2005.¹⁰⁴ As little published evidence was identified on the signs and symptoms most likely to be associated with the diagnosis of breast cancer, they recommended that practitioners followed the 2007 Scottish Cancer Group Referral Guideline for referral from primary to specialist care.

This latter guideline incorporated work from the UK National Health Service Breast Screening Programme and the Cancer Research Campaign and gave specific referral criteria related to four key areas: lumps, pain, nipple symptoms and skin changes. Referral criteria for breast lumps included women with 1) an abscess that had settled in those aged over 40 years and 2) an abscess or mastitis that had failed to settle after a single antibiotic course. Persistent, unilateral breast pain post-menopause was also cited as one of the pain-related referral criteria. Nipple-related symptoms that were considered a prompt for referral included persistent or bloodstained nipple discharge, new nipple retraction and nipple eczema unresponsive to topical treatment with steroids. Referral criteria for skin changes included skin tethering, fixation or ulceration.¹⁰⁴

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected breast cancer underwent one or more of the investigations listed below:

- mammography (not as a screening test)
- ultrasound
- cytology of nipple discharge
- fine needle aspirate (FNA)
- cancer antigen 15-3.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE recommendations were based on evidence from cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified no evidence for a role in primary care for laboratory tests in the initial investigation of women with breast lumps. Expert opinion considered there to be no role for the use of FNA in UK primary care and, furthermore, that investigative mammography and/or FNA may delay specialist referral of patients with breast cancer.⁴⁹

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT accepted some of the international recommendations. They agreed with the Australian recommendation that a palpable breast lump should be investigated, and with NICE regarding the features of a breast lump that should precipitate an urgent referral. Whereas NICE specified a 'discrete, hard lump with fixation, with or without skin tethering', in their recommendation, the GDT chose to specify a 'hard, fixed or tethered palpable breast lump'. The GDT also agreed with the NICE recommendations related to the action required in the event of a person presenting with unilateral eczematous skin, nipple symptoms or with breast pain alone.

In principle, the GDT agreed with the SIGN recommendations related to the presence of an abscess or mastitis. However, while SIGN explicitly referred to a 'non-lactational' abscess or mastitis that had not settled, the GDT chose to remove this qualification. The SIGN recommendation on the investigation of a postmenopausal woman presenting with persistent, unilateral pain was accepted for inclusion in this guideline with the addition of the word 'unexplained' as a qualifier to this symptom.

The GDT made a decision to change the NICE recommendation on referral for men with specific breast symptoms. They altered the urgency from 'urgent' to standard referral and also removed the age criterion. The GDT also chose to exclude the NICE recommendation on breast lumps in women aged less than 30 years, preferring instead to formulate referral advice for women in this age group with 'generalised lumpy breast tissue and a focal area of concern'. In addition, the GDT considered that investigation of a symptomatic patient could be instigated in primary care provided this did not delay referral. Good practice points in this guideline reflect these decisions.

7

Gynaecological cancer

This chapter considers cervical, ovarian, uterine and vulval cancers in turn. The recommendations for each of these cancers are presented first, followed by contextual information on the epidemiology of that cancer in New Zealand. An overview of the three bodies of literature from which the recommendations were developed (risk factors, signs and symptoms, and investigations) is then provided. Each section concludes with a description of how the evidence was translated by the GDT into specific recommendations.

Cervical cancer

Recommendations

Cervical cancer	Grade
For a woman presenting with intermenstrual bleeding, postcoital bleeding, postmenopausal bleeding or vaginal discharge, a full pelvic examination including speculum examination of the cervix is indicated and should be recommended*	C
A woman with clinical features suggestive of cervical cancer on examination of the cervix should be referred urgently to a specialist A cytology test is not required before referral, and a previous negative cytology result is not a reason to delay referral*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details. * Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice points

Cervical cancer	
A woman presenting with persistent abnormal vaginal bleeding should be referred to a specialist	✓
A woman presenting with symptoms suggestive of cervical cancer who has not fully participated in a cervical screening programme should be referred immediately for investigation	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Epidemiological background

New Zealand population

Overall, the incidence of cervical cancer is relatively low, accounting for 0.8% ($n=154$) of all cancer registrations in 2004.⁸¹ Data on cervical cancer survival give a cumulative relative survival of approximately 72% after five years. In the first year, the chance of survival is 88% and after four years of survival, there is a 97% chance of surviving to the end of the fifth year.⁸⁰

Māori

Although cervical cancer was not a major cause of cancer death in non-Māori women, it was the fourth leading cause in Māori during 1996–2001. The incidence of cervical cancer in Māori women was more than twice that of non-Māori in this time period (Table 7.1). Furthermore, the mortality:incidence ratio was 46% for Māori and 22% for non-Māori. Māori women when compared to non-Māori, were more likely to be diagnosed with cervical cancer, were more likely to be diagnosed at a later disease stage, and after diagnosis, were more than twice as likely to die as a result of cervical cancer.⁸

Table 7.1 Incidence of cervical cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	14.2	6.3

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Data on cervical cancer survival for Māori give a cumulative relative survival after five years of 63%, compared to 83% for non-Māori women. Survival rates are worse for Māori than for non-Māori women in the first two years following diagnosis (first year chance of survival 81% vs 89%; second year 88% vs 92%). After this, survival rates year to year are similar (approximately 96% surviving from the fourth to the fifth year).⁸⁰

Pacific peoples

During 1996–2000, Pacific women in the 45–64 years age group had both higher cervical cancer registration rates and higher mortality rates compared to the total New Zealand population.¹²

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises the key risk factors for cervical cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that cervical cancer is rare in women younger than 20 years, rapidly increases in incidence between the ages of 25 and 35 years, and reaches a peak incidence in the 35–39 year age group.⁵⁶

Their literature review also cited a review article by Paley in 2001, which reported early sexual activity, smoking, multiple sexual partners and an immunocompromised state as the factors with the most impact on the risk of developing cervical cancer.⁵⁶

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for cervical cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE guideline recommendations for referral for suspected cervical cancer were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. Expert opinion suggested that abnormal bleeding (postcoital, postmenopausal and intermenstrual) can be presenting features of gynaecological cancer.⁵⁶

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected cervical cancer underwent any of the investigations listed below:

- cervical smear
- pelvic ultrasound.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE guideline literature review identified that cervical cancer occurred in some women who had had regular cervical smears, including women who had been screened on two or more occasions in the last five years.⁵⁶ Due to a lack of evidence on the value of any primary care investigation for women with suspected cervical cancer NICE made no recommendations on investigations.

Recommendation development

Based on the NICE guideline literature review, the GDT agreed with the NICE recommendations on the appropriate examination of women with intermenstrual bleeding, postcoital bleeding, postmenopausal bleeding or vaginal discharge. They also agreed that a woman should be referred urgently if the results of an examination of the cervix are suspicious, irrespective of previous cytology. These NICE recommendations were therefore accepted with only minor wording modification.

NICE viewed consideration of an urgent referral as necessary in a woman with persistent intermenstrual bleeding and a negative pelvic examination. However, the GDT rejected this recommendation preferring to include a good practice point advising that any woman presenting with persistent abnormal bleeding should be referred. The GDT also chose to include an additional good practice point recommending immediate referral for investigation for symptomatic women who had not fully participated in a cervical screening programme.

Ovarian cancer

Recommendation	
Ovarian cancer	Grade
In a woman with any unexplained, non-specific abdominal symptoms alone (bloating, constipation, abdominal or back pain, urinary symptoms), ovarian cancer should be considered, abdominal palpation undertaken and a pelvic examination considered*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details. * Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Epidemiological background

New Zealand population

Ovarian cancer is the fourth leading cause of cancer death in New Zealand women.⁸¹ Incidence data on ovarian cancer in New Zealand is presented in Table 7.2. Data on ovarian cancer survival give a cumulative relative survival of approximately 46% after five years. In the first year the chance of survival is 70% and, after four years of survival, there is a 95% chance of surviving to the end of the fifth year.⁸⁰

Māori

The incidence of ovarian cancer in Māori women during 1996–2001 was approximately 28% higher than non-Māori (Table 7.2). However, the mortality:incidence ratio was 42% for Māori and 45% for non-Māori. Māori women when compared to non-Māori, were more likely to be diagnosed with this disease but, after diagnosis, were no more likely, overall, to die as a result of it. Māori women were more likely to be diagnosed at an earlier disease stage.⁸

Table 7.2 Incidence of ovarian cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	9.3	7.3

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises the key risk factors for ovarian cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that ovarian cancer incidence increased with age, with the incidence being about six times higher in women aged 70 years or over, compared to women aged 40 years or younger.⁵⁶

Their literature review also cited a review article by Bell et al. in 1998 that reported genetic predisposition as the most significant risk factor for ovarian cancer. The highest risk was associated with having a first-degree or second-degree relative with ovarian cancer (RR 2.2–4.4).⁵⁶

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for ovarian cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

Three primary studies of case-control design, published since the NICE guideline, were identified by the literature review.^{107–109}

The NICE recommendations for referral for suspected ovarian cancer were based on expert opinion. The NICE literature review identified that this cancer may present with non-specific symptoms. These included tiredness, abdominal discomfort, gastrointestinal and urinary symptoms and back pain. Associated signs included a palpable mass and an enlarged abdomen.⁵⁶

The only methodologically robust primary study¹⁰⁹ evaluated the symptoms preceding an ovarian cancer diagnosis (n=1985, non-cancer controls n=6024) in US women aged 68 years or older. The frequency and adjusted odds ratio (OR) for four symptom groups occurring from one to three months before diagnosis were: abdominal pain 30.6% (OR 6.2; 95% CI 5.2–7.4), abdominal swelling 16.5% (OR 39.2; 95% CI 22.5–68.1), gastrointestinal symptoms 8.4% (OR 2.0; 95% CI 1.5–2.7) and pelvic pain 5.4% (OR 4.2; 95% CI 2.5–7.1).

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected ovarian cancer underwent one or more of the investigations listed below:

- pelvic ultrasound
- Ca 125.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

As there was no evidence identified in the NICE literature review on the value of any primary care investigation for women with suspected ovarian cancer, NICE made no recommendations on investigations.⁵⁶

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT agreed with the single NICE recommendation on ovarian cancer. This recommendation, regarding the abdominal symptoms that should prompt a practitioner to consider the possibility of ovarian cancer, and the appropriate physical examinations to undertake, was therefore accepted with only minor wording modification. Due to a lack of evidence, the GDT decided to make no recommendations or good practice points on investigations for ovarian cancer.

Uterine cancer

Recommendations

Uterine cancer	Grade
A woman who is <i>not</i> on hormone replacement therapy presenting with unexplained postmenopausal bleeding should be referred urgently to a specialist*	C
A woman on hormone replacement therapy presenting with persistent or unexplained postmenopausal bleeding after cessation of hormone replacement therapy for 6 weeks should be referred urgently to a specialist*	C
A woman presenting with postmenopausal bleeding and taking tamoxifen, should be referred urgently to a team specialising in the management of gynaecological cancer as tamoxifen can increase the risk of endometrial cancer*	C
A woman presenting with a palpable abdominal or pelvic mass on examination that is not obviously uterine fibroids, gastrointestinal or urological in origin should be referred urgently for ultrasound scan or to a specialist*	C
A woman presenting with heavy or irregular menstrual bleeding should have a transvaginal ultrasound of the endometrium if any of the following apply: <ul style="list-style-type: none"> • weight over 90 kg • age over 45 years • risk factors for endometrial hyperplasia or carcinoma, such as nulliparity, family history of colon or endometrial cancer, exposure to unopposed oestrogens† 	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details. * Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005. † New Zealand Guidelines Group. Guidelines for the management of heavy menstrual bleeding. Wellington: NZGG; 1998.	

Good practice points

Uterine cancer	
A premenopausal woman presenting with an alteration in bleeding pattern and taking tamoxifen should have a transvaginal ultrasound of the endometrium and/or be referred to a specialist	✓
A woman with an abnormal ultrasound finding should be referred to a specialist	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Epidemiological background

New Zealand population

Uterine cancer accounted for 1.7% (n=330) of all cancer registrations in 2004.⁸¹ Data on uterine cancer survival give a cumulative relative survival of approximately 75% after five years. In the first year, the chance of survival is 87% and after four years of survival, there is a 98% chance of surviving to the end of the fifth year.⁸⁰

Māori

Uterine cancer was the fifth most commonly diagnosed cancer in Māori women during 1996–2001. The incidence of uterine cancer in Māori women was 60% higher than in non-Māori in this time period (Table 7.3). Furthermore, the mortality:incidence ratio was 27% for Māori and 20% for non-Māori. Māori women when compared to non-Māori, were more likely to be diagnosed with uterine cancer and after diagnosis, were two-thirds more likely to die as a result of it.⁸

Table 7.3 Incidence of uterine cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	9.9	6.1

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Further data on uterine cancer survival for Māori women give a cumulative relative survival of 61% after five years, compared to 77% for non-Māori women.⁸⁰

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises the key risk factors for uterine cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that although rare in women younger than 35 years, uterine cancer is more common in women aged 50 years or older (approximately 50 cases per 100,000).⁵⁶

The NICE guideline literature review also cited a review article by Paley in 2001, which included obesity, chronic anovulation, oestrogen secreting tumours, tamoxifen use and unopposed exogenous oestrogen administration in a summary of risk factors for uterine cancer.⁵⁶

To ensure alignment with other New Zealand national recommendations, risk factor evidence from *Guidelines for the Management of Heavy Menstrual Bleeding* was included. In addition to the previously cited risk factors, nulliparity and family history of colon or endometrial cancer were also reported as risk factors for uterine cancer.¹¹⁰

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for uterine cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE recommendations for referral for suspected uterine cancer were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies. The NICE guideline literature review identified a single guideline on postmenopausal bleeding and a risk factor review as evidence. In the evidence summary, post-menopausal bleeding was considered (expert opinion) as a reason to investigate uterine cancer.⁵⁶

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected uterine cancer underwent any of the investigations listed below:

- pelvic ultrasound
- pipelle biopsy.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One relevant New Zealand national guideline was identified. No secondary or primary studies published since the NICE guideline⁵⁶ were identified.

As there was no evidence on the value of any primary care investigation for women with suspected uterine cancer, NICE made no recommendations on investigations.

The New Zealand *Guidelines for the Management of Heavy Menstrual Bleeding* included a recommendation on the place of ultrasound in symptomatic women with risk factors for uterine cancer (see recommendations).¹¹⁰

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT agreed with the NICE recommendations on referral of a woman with an unexplained palpable abdominal or pelvic mass, referral of women with unexplained postmenopausal bleeding, and urgent referral for a woman on tamoxifen presenting with postmenopausal bleeding. However, the GDT wished to also explicitly note that women taking tamoxifen who have postmenopausal bleeding should be referred to a team specialising in the management of gynaecological cancer. Many of the NICE guideline recommendations were therefore accepted with minor wording modification.

To ensure consistency, the GDT also wished to include the recommendation from the 1998 New Zealand *Guidelines for the Management of Heavy Menstrual Bleeding* on the place of transvaginal ultrasound investigation in symptomatic women.

To increase the comprehensiveness of guidance, the GDT wished to note two additional areas. Good practice points were therefore developed with regard to the appropriate course of action where there is an alteration in bleeding pattern for a premenopausal woman taking tamoxifen, and also when an abnormal ultrasound finding occurs.

Vulval cancer

Recommendations	
Vulval cancer	Grade
A woman presenting with vulval symptoms should be recommended to have a vulval examination. If an unexplained vulval lump is found, she should be referred urgently to a specialist*	C
A woman presenting with vulval bleeding due to ulceration (excluding infection eg, herpes, cyst infections) should be referred urgently to a specialist*	C
A woman presenting with vulval symptoms of pruritus or pain may be managed using a period of 'treat, watch and wait', with active follow-up until symptoms are resolved or a diagnosis is confirmed by referral or biopsy*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details. * Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Epidemiological background

Vulval cancer is very uncommon, accounting for about 0.3% (n=52) of all cancer registrations in New Zealand in 2004. Three cases occurred in the age group 30–39 years, 15 in the age group 40–59 years, and 34 in those aged 60 years and over.⁸¹ This small number of cases does not allow any meaningful statistical analysis.

Background to recommendation development

Risk factors

As risk factor consideration is an integral part of practitioner assessment of a symptomatic patient, the non-systematic review below summarises the key risk factors for vulval cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review made no comment in its evidence summary on the risk factors for vulval cancer. However, it cited a review article by Ghurani and Penalver in 2001 which reported granulomatous infection, herpes simplex virus, human papillomavirus, chronic immunosuppression, hypertension, diabetes and obesity as factors associated with vulval cancer.⁵⁶

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for vulval cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE recommendations for referral for suspected vulval cancer were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified that the presenting signs and/or symptoms of this cancer included vulval bleeding, pruritis, pain and a lump or other lesion.⁵⁶

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected vulval cancer underwent the investigation listed below:

- vulval biopsy.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

As the NICE literature review found no evidence on the value of any primary care investigation for women with suspected vulval cancer, NICE made no recommendations on investigations.⁵⁶

Recommendation development

Based on the NICE guideline literature review, the GDT agreed with the NICE recommendations on the need for an urgent referral for a woman presenting with an unexplained vulval lump or vulval bleeding due to ulceration. However, the GDT wished to explicitly exclude ulceration resulting from infection (such as herpes and cysts) in the recommendation wording.

The GDT also agreed with the NICE recommendation on the place of 'treat, watch and wait' and active follow-up in a woman presenting with vulval pruritus or pain. However, they wished to explicitly state that the diagnosis of vulval cancer may be confirmed either by referral to a specialist, or histologically by biopsy. For some patients in New Zealand, specialist referral has major time and financial implications due to the geographical location of their home in relation to the major referral centres.

All of the NICE guideline recommendations were therefore accepted with only minor wording modification. Due to a lack of evidence, the GDT decided to make no further recommendations or good practice points on investigations for vulval cancer.

8 Urological cancer

In this chapter, bladder and renal, prostate, testicular and penile cancers are considered in turn. The recommendations for each of these cancers are presented first, followed by contextual information on the epidemiology of the disease in New Zealand. An overview of the three bodies of literature from which the recommendations were developed (risk factors, signs and symptoms, and investigations) is then provided. Each section concludes with a description of how the evidence was translated by the GDT into specific recommendations.

Bladder and renal cancer

Recommendations	
Bladder and renal cancer	Grade
A person of any age presenting with painless macroscopic haematuria should be referred urgently to a specialist* In a younger person, cancer is unlikely to be the cause of the bleeding	C
A person aged 40 years and older presenting with recurrent or persistent urinary tract infection associated with haematuria should be referred urgently to a specialist*	C
A person with an abdominal mass identified clinically or on imaging that is thought to arise from the urinary tract should be referred urgently to a specialist*	C
A person presenting with symptoms suggestive of a urinary infection who also presents with macroscopic haematuria should be referred urgently to a specialist if investigation does not confirm infection*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice point	
Bladder and renal cancer	
A person with persistent microscopic haematuria, with no obvious cause (eg, menstruation) may have non-cancerous renal pathology and should be assessed for renal disease, including tests for proteinuria, estimated glomerular filtration rate (eGFR) and serum creatinine. Further action should be based upon clinical assessment	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Epidemiological background

Bladder cancer

New Zealand population

Bladder cancer accounted for just over 3% (n=626) of all cancer registrations in 2004. In 2004, men were both diagnosed and died of bladder cancer over three times more frequently than women (Table 8.1).⁸¹

Table 8.1 Incidence and mortality rates of bladder cancer in 2004 by gender

	Men	Women
Registration rate (per 100,000)	15.0	4.1
Mortality rate (per 100,000)	3.8	1.1

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Data on bladder cancer survival give a cumulative relative survival of approximately 73% after five years. In the first year, the chance of survival is 85% and after four years of survival, there is a 97% chance of surviving to the end of the fifth year.⁸⁰

Māori

Bladder cancer was rare in Māori during 1996–2001, although it was the fifth most commonly diagnosed cancer in non-Māori men and the tenth most commonly diagnosed in non-Māori women during this time period. The incidence of bladder cancer in Māori was half that of non-Māori in this time (Table 8.2). However, the mortality:incidence ratio was 42% for Māori and 23% for non-Māori. Māori when compared to non-Māori, were less likely to be diagnosed with this disease but after diagnosis, were twice as likely to die as a result of it.⁸

Table 8.2 Incidence of bladder cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	2.6	5.2

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Renal cancer

New Zealand population

Cancer of the kidney (excluding the renal pelvis) accounted for about 2% (n=401) of all cancer registrations in 2004. In 2004, men were both diagnosed and died more frequently of this cancer than women (Table 8.3).⁸¹

Table 8.3 Incidence and mortality rates of renal cancer in 2004 by gender

	Men	Women
Registration rate (per 100,000)	9.5	5.1
Mortality rate (per 100,000)	3.7	1.6

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Data on cancer of the kidney give a cumulative relative survival rate of approximately 57% after five years. In the first year, the chance of survival is 70% and after four years of survival, there is a 97% chance of surviving to the end of the fifth year.⁸⁰

Māori

The incidence of cancer of the kidney in Māori during 1996–2001 was similar to that of non-Māori (Table 8.4). However, the mortality:incidence ratio was 54% for Māori and 33% for non-Māori. Māori when compared to non-Māori, were no more likely to be diagnosed with this disease but after diagnosis, were 50% more likely to die as a result of it. Māori were less likely to be diagnosed with localised disease.⁸

Table 8.4 Incidence of renal cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	4.1	3.9

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises key risk factors for bladder and renal cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that bladder and renal cancers more commonly occurred in men, and that renal cancer was rare below the age of 35 years and bladder cancer rare below 50 years. Beyond these ages the incidence rises.⁵⁶

Risk factors identified in a review article cited by the NICE guideline literature review are shown in Box 8.1.

Box 8.1	Risk factors for bladder and renal cancer identified by the NICE guideline literature review
Cancer	Risk factors
Bladder	<ul style="list-style-type: none"> • Cigarette smoking • Occupational exposure eg, dyes, rubber, textiles, leather
Renal	<ul style="list-style-type: none"> • Chromosome mutations • Cigarette smoking • Excess body weight • Hypertension and/or antihypertensives • Increased parity • Occupational exposure eg, asbestos, petroleum products, dry cleaning solvents
<p>Source: Morganstern et al. 1998 as cited in National Collaborating Centre for Primary Care. Referral guidelines for suspected cancer in adults and children. Part 2. London: National Collaborating Centre for Primary Care; 2005.</p>	

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for bladder and renal cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

Two primary studies, published since the NICE guideline, were identified by the literature review. These were both of a case-series design.^{83,111}

The NICE recommendations for referral for suspected bladder and renal cancer were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified that macroscopic haematuria was the commonly occurring symptom of bladder cancer on presentation.⁵⁶

In a study of US women with irritative voiding symptoms (n=735);¹¹¹ microscopic haematuria, urgency, frequency, dysuria and nocturia were *not* significantly associated with bladder cancer at cystoscopy.

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected bladder or renal cancer underwent one or more of the investigations listed below:

- urine microscopy
- ultrasound

- intravenous pyelogram (urogram)
- urine cytology
- CT.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One primary study, published since the NICE guideline, was identified by the literature review.¹¹²

The NICE guideline literature review identified from a single secondary study by Lokeshwar and Soloway in 2001 that apart from tests of microscopic haematuria, other tumour marker urine tests were not sufficiently sensitive for primary care use.⁵⁶

Turney et al.¹¹² conducted a methodologically robust, prospective diagnostic study in 200 consecutive patients aged over 40 years with macroscopic haematuria, who attended a 'fast-track' clinic. This clinic included assessment by a clinical nurse specialist, same-day CT urography (CTU) and flexible cystoscopy, and urine cytology. The prevalence of bladder tumours in this patient group was 24%. When CTU and histopathological findings were compared, one false-positive and three false-negative diagnoses were found (sensitivity 0.93, specificity 0.99). The positive and negative predictive values for detecting bladder cancer using CTU were 0.98 and 0.97 respectively.

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT agreed with the NICE recommendations on the need for urgent referral of a person in the following circumstances: when painless macroscopic haematuria is present; when recurrent or persistent urinary tract infection associated with haematuria is present in a person aged 40 years and older; when there are symptoms suggestive of urinary infection combined with macroscopic haematuria, if infection is not subsequently confirmed; when an abdominal mass thought to arise in the urinary tract has been identified. These NICE recommendations were therefore accepted with only minor wording modification.

The GDT considered the two NICE recommendations on microscopic haematuria to be too prescriptive in the light of a known review by Malstrom,¹¹³ suggesting that microscopic haematuria is a poor predictor of cancers of the urinary tract. Therefore, the GDT chose not to include these recommendations in this guideline. However, the GDT wished to note through a good practice point, the importance of using laboratory tests to assess the renal function of a person with persistent microscopic haematuria, as they may have non-cancerous renal pathology.

Prostate cancer

As this guideline is focused on referral of people presenting to primary care with signs or symptoms suggestive of cancer, screening in asymptomatic people is beyond the guideline scope. Therefore, no recommendations have been made on management in relation to findings from routine prostate serum antigen (PSA) screening.

For further information on PSA screening, readers are referred to *Testing for Prostate Cancer: Information for Men and their Families*¹¹⁴ and *Testing for Prostate Cancer: A Consultation Resource*,¹¹⁵ published by the New Zealand Guidelines Group in 2008. These documents are available on the New Zealand Guidelines Group website www.nzgg.org.nz.

Recommendations

Prostate cancer	Grade				
A man presenting with lower urinary tract symptoms and found to have a hard, irregular prostate on digital rectal examination should be referred urgently to a specialist*	C				
A man presenting with lower urinary tract symptoms and a high PSA (10 ng/ml or more) should be referred urgently to a specialist*	C				
<p>A man with lower urinary tract symptoms in whom the prostate is normal on digital rectal examination but the age-specific PSA[†] is raised or rising, should be urgently referred to a specialist. For a man whose clinical state is compromised by other comorbidities, a discussion about management options with the man and/or a specialist in urological cancer may be more appropriate*</p> <p>[†] Age-based PSA values (upper limit of normal):</p> <table> <tr> <td>40–50 years: 2.5 ng/ml</td><td>50–60 years: 3.5 ng/ml</td></tr> <tr> <td>60–70 years: 4.5 ng/ml</td><td>70 years and over: 6.5 ng/ml</td></tr> </table> <p>Note: This is an example of an age-based range cited in the NZGG resource: <i>Testing for prostate cancer: a consultation resource</i>, 2008. Differences in PSA assay can lead to differences in age-based ranges reported by laboratories</p>	40–50 years: 2.5 ng/ml	50–60 years: 3.5 ng/ml	60–70 years: 4.5 ng/ml	70 years and over: 6.5 ng/ml	C
40–50 years: 2.5 ng/ml	50–60 years: 3.5 ng/ml				
60–70 years: 4.5 ng/ml	70 years and over: 6.5 ng/ml				
<p>A man should be recommended to have a digital rectal examination and a PSA test if he has any unexplained symptom suggestive of metastatic prostate cancer:</p> <ul style="list-style-type: none"> • lower back pain • bone pain • weight loss, especially in the elderly* 	C				
Prior to PSA testing, a practitioner should exclude urinary infection, especially in a man presenting with lower urinary tract symptoms. The PSA test should be postponed for at least 1 month after treatment of a proven urinary infection*	C				
<p>Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.</p> <p>* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.</p>					

Good practice points**Prostate cancer**

A man presenting with macroscopic haematuria should be referred urgently to a specialist	✓
A man found to have an enlarged, smooth prostate on digital rectal examination and a normal PSA should <i>only</i> be referred to a specialist if they have macroscopic haematuria	✓
An older man presenting with lower urinary tract symptoms (frequency, hesitancy, nocturia) should be recommended to have a digital rectal examination and a PSA test	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Epidemiological background

New Zealand population

Prostate cancer is the third most common cause of male cancer deaths in New Zealand (after lung and colorectal cancer). In 2004, 85% (n=496) of prostate cancer deaths occurred in men aged over 70 years.⁸¹ Data on prostate cancer survival give a cumulative relative survival of approximately 86% after five years. In the first year, the chance of survival is 94% and after four years of survival, there is a 98% chance of surviving to the end of the fifth year.⁸⁰

European/Other New Zealanders

Prostate cancer mortality rates increased among European/Other men through the 1980s and early to mid 1990s, but have stabilised since then. Overall, from 1981–1984 to 2001–2004 rates have increased by 10%.¹⁶

Māori

The incidence of prostate cancer in Māori men was lower than in non-Māori during 1996–2001 (Table 8.5). However, the mortality:incidence ratio was 29% for Māori and 15% for non-Māori.⁸

Table 8.5 Incidence of prostate cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	41.2	49.3

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

In the first year the chance of survival is 87% for Māori men and 94% for non-Māori.⁸⁰ Māori men when compared to non-Māori, were less likely to be diagnosed with this disease but, after diagnosis, were more than twice as likely to die as a result of it. Māori men were more likely to be diagnosed at a later disease stage.⁸

Pacific peoples

During 1996–2000, Pacific men aged 65 years or older had higher prostate cancer registration rates and higher mortality rates compared to the total New Zealand population.¹²

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises the key risk factors for prostate cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that although prostate cancer was rare in men aged under 45 years beyond this age the incidence rose sharply.⁵⁶

Their literature review also cited a systematic review by Zeegers et al. in 2003, which reported (from a meta-analysis using a random effects meta-regression model) that the relative risk of prostate cancer among first-degree family members (father, brother) was 2.53 (95% CI 2.24–2.85).⁵⁶

Additional risk information relating to age and family history is provided in the NZGG resource *Testing for Prostate Cancer: A Consultation Resource*.¹¹⁵

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for prostate cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One UK primary study of case-control design,¹¹⁶ published since the NICE guideline, was identified by the literature review.

The NICE recommendations for referral for suspected prostate cancer were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified that although prostate cancer often presented with symptoms that indicated urinary outflow obstruction, other symptoms included urinary tract infection and signs of metastatic spread (eg, bone pain). It was noted that although the majority of prostate cancers can be palpated on digital rectal examination, an abnormal examination result may result from other benign conditions.⁵⁶

In a methodologically robust case-control study¹¹⁶ of patients aged 40 years or more with prostate cancer (n=217), signs and/or symptoms independently associated with the cancer in the two years before diagnosis included urinary retention, impotence, frequency, hesitancy, nocturia, haematuria, weight loss, abnormal rectal examination deemed benign and abnormal rectal examination deemed malignant. The highest positive predictive values (PPV) of these individual signs and/or symptoms were for abnormal rectal examination deemed malignant (12.0%, 95% CI 5.0–37.0%) and urinary retention (3.1%, 95% CI 1.5–6.0%). The highest PPVs for two signs and/or symptoms were for abnormal rectal examination deemed malignant combined with either hesitancy or frequency/urgency or nocturia (range, 10.0–15.0%), for nocturia combined with weight loss (12.0%) and for abnormal rectal examination deemed benign combined with weight loss (9.4%).

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected prostate cancer underwent one or more of the investigations listed below:

- PSA
- urine microscopy
- ultrasound
- CT scan
- urine cytology.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE guideline recommendations were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The NICE literature review identified evidence that the PSA test has moderate sensitivity and specificity for prostate cancer.⁵⁶ An NZGG resource on PSA testing reports the estimated sensitivity ('true positives') as 74–84%, and the estimated specificity ('true negatives') as 90–94%.¹¹⁵

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT agreed with the NICE recommendations that a man with a hard, irregular prostate required urgent referral and that a man with unexplained lower back pain, bone pain or weight loss should be recommended to have a digital rectal examination and a PSA test. In contrast to NICE, the GDT did not consider it necessary for a man with erectile dysfunction to undergo these tests. This symptom was therefore excluded from the guideline recommendations.

The GDT also agreed with some of the NICE recommendations surrounding PSA testing. These included recommendations related to the need to urgently refer men with lower urinary tract symptoms and 1) a normal prostate on examination and a raised, or rising, age-specific PSA result 2) a high PSA level. However, the GDT chose to define a high PSA as 10 ng/ml or more, and quoted an example of an age-based PSA level from a recently published NZGG resource on PSA testing.¹¹⁵

The GDT also agreed with NICE on the importance of excluding urinary infection prior to PSA testing and the need to postpone the test for a minimum of a month following treatment of a proven infection. The GDT chose to exclude a NICE recommendation on the course of action necessary when an *asymptomatic* man had a borderline PSA as this was beyond the scope of the guideline.

Although NICE noted that a man with lower urinary tract symptoms should be recommended to have a digital rectal examination and a PSA test, the GDT considered this inappropriate. They chose instead to include a good practice point to highlight their view of the importance of conducting these tests in older men. During discussions, the GDT acknowledged that a man with lower urinary tract symptoms with features of renal failure secondary to significant outflow obstruction required investigation. However, because this guideline relates to cancer referral, no specific recommendation was considered appropriate for inclusion.

The GDT also chose to address two additional areas. Good practice points were therefore incorporated on how to manage patients found to have both a large, smooth prostate on digital rectal examination and macroscopic haematuria.

Testicular cancer

Recommendations	
Testicular cancer	Grade
A man with an unexplained swelling or mass in the body of the testis should be referred urgently to a specialist*	C
A man with a scrotal mass that does not transilluminate and/or the body of the testis cannot be distinguished, may be referred for an urgent ultrasound, but this should not delay referral to a specialist*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details. * Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Epidemiological background

New Zealand population

Testicular cancer is rare in New Zealand men, accounting for 0.7% (n=138) of all cancer registrations in 2004.⁸¹ Data on testicular cancer survival give a cumulative relative survival of approximately 95% after five years. In the first year, the chance of survival is 98% and, after four years of survival, there is a 99.9% chance of surviving to the end of the fifth year.⁸⁰

Māori

Although this cancer is rare in non-Māori, it was the fifth most commonly diagnosed cancer in Māori men during 1996–2001. The incidence of testicular cancer in Māori men was almost twice that of non-Māori in this time period (Table 8.6). Furthermore, the mortality:incidence ratio was 8% for Māori and 3% for non-Māori. Māori when compared to non-Māori, were more likely to be diagnosed with testicular cancer and after diagnosis, were three times as likely to die as a result of it. Māori men were more likely to be diagnosed at a later disease stage.⁸

Table 8.6 Incidence of testicular cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	10.9	5.9

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Background to recommendation development

Risk factors

As risk factor consideration is an integral part of practitioner assessment of a symptomatic patient, the non-systematic review below summarises the key risk factors for testicular cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that although testicular cancer can occur at any age, it most commonly occurred in men under 40 years.⁵⁶

The literature review also cited a review article by Gospodarowicz et al. in 1999 which reported that this cancer has been associated with a history of cryptorchidism and XY gonadal dysgenesis. In addition, prior testicular cancer is a risk factor for contra-lateral disease.⁵⁶

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for testicular cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One primary study, published since the NICE guideline, was identified by the literature review. This study was of a case-series design.¹¹⁷

In the absence of studies that addressed the diagnosis of testicular cancer in primary care, the NICE recommendations for referral for suspected testicular cancer were based on a general review article, a risk factor review and expert opinion. The literature review identified that testicular cancer often presented with testis enlargement (with or without pain) and sometimes with signs of metastatic spread (eg, back pain, breathlessness).⁵⁶

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected testicular cancer underwent the investigation listed below:

- ultrasound.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

As there was no evidence provided on the value of any primary care investigation for men with suspected testicular cancer, the NICE recommendation on investigation was based on expert opinion.⁵⁶

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT agreed, in principle, with the NICE recommendations on referral of a man with a swelling or mass in the body of the testis and also on the place of an ultrasound investigation. However, the GDT considered that only an 'unexplained' swelling or mass should warrant an urgent referral. This wording was therefore added as a qualifier. It was also important in the GDT's opinion that any ultrasound investigation undertaken in the primary care setting did not delay referral to a specialist. This was therefore explicitly stated in the recommendation. Both of the NICE recommendations were therefore accepted with only minor wording modification.

Penile cancer

Recommendations

Penile cancer	Grade
<p>A man should be referred urgently to a specialist if he has symptoms or signs of penile cancer including progressive ulceration or a mass in the glans or prepuce, sometimes also involving the skin of the penile shaft*</p> <p>Note: Lumps within the corpora cavernosa not involving penile skin are usually not cancer but indicate Peyronie's disease*</p>	C
<p>Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.</p> <p>* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.</p>	

Epidemiological background

Penile cancer is very rare, accounting for less than 0.1% (n=10) of all cancer registrations in 2004. All cases occurred in men aged 50 years or older.⁸¹ This small number of cases does not allow any meaningful statistical analysis.

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises the key risk factors for penile cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified no risk factor evidence for penile cancer.⁵⁶

Micali et al.¹¹⁸ in their 2006 narrative review on penile cancer described lack of circumcision, human papillomavirus infections and penile lichen sclerosus as predisposing risk factors.

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for penile cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

In the absence of studies that addressed penile cancer presentation in primary care, the NICE recommendations for referral for suspected penile cancer were based on expert opinion. Two review articles identified by the NICE review reported penile cancer as rare, with symptoms on presentation including a warty growth, erythema and induration.⁵⁶

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected penile cancer underwent the investigation listed below:

- physical examination.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

As there was no evidence on the value of any primary care investigation for men with suspected penile cancer, the NICE guideline made no recommendations on investigations.⁵⁶

Recommendation development

Based on the NICE guideline literature review, the GDT agreed with the NICE recommendation on the penile signs and/or symptoms that should warrant referral. The NICE recommendation was therefore accepted with only minor wording modification. Due to a lack of evidence, the GDT decided to make no recommendations or good practice points on investigations for penile cancer.

9

Skin cancer

This chapter presents some general recommendations for skin cancer, followed by sections containing information specifically related to melanoma, and squamous and basal cell carcinomas.

Recommendation

Skin cancer	Grade
All skin specimens should have histology obtained for that lesion*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice points

Skin cancer	
A person presenting with skin lesions suggestive of skin cancer should have histology obtained for that lesion or be referred to a specialist	✓
A person with a persistent or slowly evolving, unresponsive skin condition where the diagnosis is uncertain and cancer a possibility, should have histology obtained for that lesion	✓
A referral to a specialist should be considered if histology shows an indeterminate finding or incomplete excision*	
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	
* Good practice point consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Recommendation development

The GDT reviewed the general recommendations for skin cancer that were presented in the NICE guideline. As the prevalence of these cancers is much higher in New Zealand than the UK, there are substantial differences between the countries in the role primary care plays in the management of these conditions. Therefore, the GDT wished to include only one of the NICE recommendations. This related to the importance of obtaining histology for specimens from skin lesions. To ensure that curettings were also included, the word 'excised' that prefaced 'skin specimens' in the NICE recommendation was removed from the New Zealand recommendation. The GDT also wished to note, using good practice points, the importance of obtaining histology and/or specialist referral where the possibility of skin cancer exists.

Melanoma

The content in this section is derived from *Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand*,¹¹⁹ published in New Zealand by the New Zealand Guidelines Group, November 2008. A practitioner resource for primary care entitled *Melanoma: An Aid to Diagnosis*¹²⁰ was published concurrently. These documents are available on the New Zealand Guidelines Group website www.nzgg.org.nz. Further information on topics included and all references are available in the guideline.

The good practice point below was developed as a general recommendation by the GDT after review of relevant content extracted from *Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand*¹¹⁹ for this section of the guideline.

Good practice point

Melanoma

A person with a lesion suggestive of melanoma should have an excisional biopsy or be referred urgently to a specialist



Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.

Epidemiological background

New Zealand incidence and death rates from melanoma are among the highest in the world. Melanoma is the fourth most common type of cancer registration for both males and females, with a total of 1896 new registrations and 249 deaths reported by the New Zealand cancer registry in 2004. Māori have a very low registration rate compared to the New Zealand population as a whole but have a greater than expected number of cases with thicker lesions and more extensive disease at diagnosis. This is also true for Pacific peoples living in New Zealand. Thicker lesions are generally associated with a poorer prognosis.

The distribution of melanoma by body site is similar in Māori to the pattern seen in the New Zealand population overall, with the trunk and leg the most common sites. Pacific peoples have a higher proportion of acral lentiginous melanomas than other New Zealanders. Acral lentiginous melanomas tend to occur on the soles of the feet, palms of the hand and under the nails in darker skinned people.

See *Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand* 'Introduction' and 'Foreword' and Chapter 30, *Melanoma in Māori and melanoma in Pacific peoples in New Zealand* for further details.

Risk factors

Risk factor consideration is an integral part of practitioner assessment.

Exposure to ultraviolet radiation in sunlight

This is the primary cause of most melanoma but history of exposure is of limited clinical utility in New Zealand where the prevalence of sunburn is so high.

Age

The risk increases with increasing age.

Skin and hair colour, skin phototype and freckling

In populations of European origin there is a two-fold increase in risk for light versus medium/dark skin colour, red-blond versus black hair and blue versus dark brown eyes; Fitzpatrick phototype I (burn easily, never tan) compared with phototype IV (always tan, never burn); and heavily freckled versus no freckles. These phenotypes are not independent of one another. Combinations may further increase risk but do not multiply it.

Melanocytic naevi

There is an increased risk with increased naevi (7-fold increase in risk with greater than 100 naevi). Clinically atypical (dysplastic) naevi are associated with a higher melanoma risk independent of the count of common melanocytic naevi.

Previous melanoma or other skin cancer

Previous melanoma confers an up to 10-fold increase in risk. Non-melanoma skin cancer or premalignant lesions, such as actinic keratoses, confer an approximately four-fold increase in risk.

Family history of melanoma

International data indicates an approximately two-fold increase in risk with one first-degree relative with melanoma. Robust Australasian data are not yet available.

See *Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand*, Chapter 3, *Identification and management of high-risk individuals* for further details.

Signs and symptoms

About half of all melanomas are detected by the person who presents with a history of a new and/or changing lesion. It is important to pay close attention to any history of change (size, shape, or colour) even if the lesion shows no typical clinical features of melanoma. Except for appearance changes, most melanomas are asymptomatic, but there may be sensory changes, most commonly itch.

Practitioners should be aware of the appearance and clinical types of melanoma. Most melanomas (superficial spreading melanoma, lentigo maligna melanoma, and acral lentiginous melanoma) present with an initial flat phase and the features of these melanomas have been summarised by the ABCDE rule. Both the ABCDE (see Box 9.1) and the seven point checklist (see Box 9.2) are suitable for use in clinical assessment.

Box 9.1	ABCDE of melanoma
A	Asymmetry
B	Border irregularity
C	Colour variation (Note: black is not essential and may not be present in some melanomas, ie, nodular or amelanotic melanoma)
D	Diameter greater than 6mm. However, melanoma can be diagnosed when less than this in diameter
E	Evolution and/or elevation eg, lesions may enlarge and a flat lesion may become raised in a matter of a few weeks

Source: Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Sydney: The Cancer Council Australia and Australian Cancer Network; Wellington: New Zealand Guidelines Group; 2008.

Box 9.2	Seven point checklist
Major features	
Change in size of a previous lesion or obvious growth of a new lesion	
Irregular shape	
Irregular colour with a variety of shades of brown and black	
Minor features	
Diameter >7 mm (Note: greater than 6 mm recommended in the guideline)	
Inflammation	
Oozing, crusting or bleeding	
Change in sensation	

Source: Higgins et al. Clin Exp Dermatol 1992;17:313–315; cited in Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Sydney: The Cancer Council Australia and Australian Cancer Network; Wellington: New Zealand Guidelines Group; 2008.

Nodular melanomas account for only 15% of melanomas, but for the majority of thick melanomas. Nodular melanoma presents as a symmetrical, raised, firm, often uniformly coloured and non-pigmented nodule that is enlarging and becoming more raised. Bleeding and crusting are common. These melanomas are most often seen on the head and neck of older people, particularly men.

Clinical diagnosis of melanoma may be enhanced where clinicians are trained in and use dermoscopy in clinical assessment. Where there is a low index of suspicion for early, non-invasive melanoma, a short period of observation aided by measurement, a clinical photo, or dermoscopic imaging may be appropriate.

See *Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand*, Chapter 5, *Clinical diagnosis* for further details.

Investigations

Referral to a specialist or excisional biopsy is indicated where there is a high level of suspicion for melanoma or where the diagnosis is uncertain. Histology should be obtained for all biopsy or excised material. Locally advanced melanoma should be referred to a specialist without biopsy.

Melanoma guideline recommendations: biopsy

The optimal biopsy approach is complete excision with a 2 mm margin and upper subcutis – **Grade C***

Incisional, punch or shave biopsies may be appropriate in carefully selected clinical circumstances, for example, for large facial or acral lesions or where the suspicion of melanoma is low – **Grade C***

Partial biopsies may not be fully representative of the lesion and need to be interpreted in light of the clinical findings – **Grade C***

* Reproduced from: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Sydney: The Cancer Council Australia and Australian Cancer Network; Wellington: New Zealand Guidelines Group; 2008.

These recommendations are based on the following grading system, outlined in the guideline cited above.

A – Body of evidence can be trusted to guide practice

B – Body of evidence can be trusted to guide practice in most situations

C – Body of evidence provides some support for recommendation but care should be taken in its application

D – Body of evidence is weak and recommendation must be applied with caution

Good practice point: melanoma guideline

It is advisable to review unexpected pathology results with the reporting pathologist*

* Reproduced from: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Sydney: The Cancer Council Australia and Australian Cancer Network; Wellington: New Zealand Guidelines Group; 2008.

In the guideline cited above, good practice points are used when the conventional grading of evidence is not possible, and represent the views of the Guideline Development Group.

See *Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand* Chapter 6, *Biopsy* and Chapter 7, *Histopathological reporting of cutaneous melanoma* for further details.

Squamous cell carcinoma and basal cell carcinoma

Good practice points

Squamous cell carcinoma

A person with a skin lesion suggestive of squamous cell carcinoma should have histology obtained for that lesion or the person should be referred to a specialist	✓
Skin lesions suggestive of squamous cell carcinoma are non-healing, keratinizing or crusted lesions larger than 1 cm, with significant induration on palpation, a documented expansion over 8 weeks and are typically on the face, scalp or back of the hand*	
A person who has had an organ transplant and/or is immunosuppressed should have histology obtained for a new or growing skin lesion and should be referred to a specialist as indicated	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	
* Good practice point consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice points

Basal cell carcinoma

A person with a skin lesion suggestive of basal cell carcinoma should have histology obtained for that lesion	✓
Basal cell carcinomas are slow growing, usually without significant expansion over 8 weeks*	
A practitioner may treat a superficial basal cell carcinoma topically without obtaining a histological diagnosis, but in that case follow-up is mandatory	✓
A practitioner should refer a person with a clinically suspected or histologically confirmed basal cell carcinoma to a specialist where the practitioner deems management of the lesion to be beyond their skill set	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	
* Good practice point consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Epidemiological background

Squamous cell carcinoma of the skin and basal cell carcinoma are very common in New Zealand. However, the Cancer Registry Act 1993 does not require mandatory reporting of basal cell carcinoma and squamous cell carcinoma arising in the skin. Therefore, accurate registration figures for these skin cancers are not available from the New Zealand Health Information Service Cancer Registry data.⁸¹

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises the key risk factors for squamous and basal cell carcinomas. For further methodological details see Appendix A, *Methods*.

Summary of findings

The evidence summary from the NICE *Referral Guidelines for Suspected Cancer* identified immunosuppression as associated with basal cell carcinoma. Immunosuppression also increased the risk of squamous cell carcinoma of the skin (Box 9.3). Other risk factors for these skin cancers identified by review articles cited in the NICE guideline literature review are also shown in Box 9.3. The NICE literature review noted that risk factors identified for squamous cell carcinoma of the skin were not able to accurately distinguish patients with a positive diagnosis.⁵⁶

Box 9.3	Risk factors for squamous cell carcinoma and basal cell carcinoma identified by the NICE guideline literature review	
Carcinoma type		Risk factor
Squamous cell carcinoma Basal cell carcinoma		<ul style="list-style-type: none"> • Immunosuppression
Carcinoma type		Additional risk factors identified
Squamous cell carcinoma*		<ul style="list-style-type: none"> • Treatment with psoralens and ultraviolet A light (PUVA) • Very light skin colour, hazel or blue eyes and blonde or red hair • Being in an exclusively outdoor occupation • Severe versus no solar elastosis, freckling and facial telangiectasias • People with chronically injured or inflamed skin with longstanding ulcers, sinus tracts, osteomyelitis, radiation dermatitis or burn scars
Basal cell carcinoma†		<ul style="list-style-type: none"> • Factors relating to sun exposure, skin type and burning • Family history of skin cancer • Genetic risk factors (eg, albinism, xeroderma pigmentosa)
<p>* Hawrot et al., 2003 as cited in the source</p> <p>† Wong et al., 1989 as cited in the source</p>		
<p>Source: National Collaborating Centre for Primary Care. Referral guidelines for suspected cancer in adults and children. Part 2. London: National Collaborating Centre for Primary Care; 2005.</p>		

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for squamous and basal cell carcinomas in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One primary study of case-series design,¹²¹ published since the NICE guideline, was identified by the literature review.

Squamous cell carcinoma

The NICE recommendations for referral for squamous cell carcinoma of the skin were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies. The literature review identified that squamous cell carcinomas presented as keratinizing or crusted skin lesions that may ulcerate.⁵⁶

A prospective population-based case-series study, conducted in the US by Askari et al.¹²¹ described the presenting signs and symptoms of patients who had either been referred by a non-dermatological health care provider or had been seen in the general dermatology clinic. Of the 912 skin lesions histologically confirmed, 238 were squamous cell carcinoma. The most commonly reported symptoms were tenderness (40.8%) and change in size (33.2%).

Basal cell carcinoma

The NICE recommendations for referral for basal cell carcinoma were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies. The literature review identified that these carcinomas could be nodular, cystic or ulcerated skin lesions.⁵⁶

In the study by Askari et al., 411 basal cell carcinomas were histologically confirmed. The most commonly reported presenting symptom was bleeding (37.2%).¹²¹

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected squamous and basal cell carcinoma underwent one or more of the investigations listed below:

- biopsy (punch, shave, excision)
- dermoscopy (not as a screening test).

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One secondary study,¹²² published since the NICE guideline, was identified by the literature review.

The NICE guideline recommendations were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The NICE guideline literature review only considered excision biopsy, and identified the standard investigation for those presenting with suspected skin cancer to be biopsy with histological examination.⁵⁶

Although a methodologically robust systematic review of the diagnostic accuracy of a range of tests¹²² provided no direct report on the diagnostic accuracy of biopsy and dermoscopy within primary care, it was noted that dermoscopy of non-melanoma skin cancer is currently in its infancy and that agreement on diagnostic criteria has still to be established.

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT produced a series of good practice points. These were based on the wording of the NICE recommendations and reframed as good practice points to reflect the higher prevalence of basal cell carcinoma and squamous cell carcinoma in New Zealand, and the appropriate management in the New Zealand primary care setting.

The good practice points for suspected squamous cell carcinoma of the skin included obtaining histology as a defined step and as a possible alternative to referral to a specialist, unless the person has had an organ transplant or is otherwise immunosuppressed. The GDT noted that a large number of factors influence referral decisions for squamous cell carcinomas, including location on the body, patient age and extent of the lesion.

The good practice points for basal cell carcinoma reflected the fact that this condition may be managed in a primary care setting. In the opinion of the GDT, the particular skill set needed for appropriate general practitioner management would be determined by where on the body the carcinoma was located.

10 Brain and central nervous system cancer

This chapter presents the recommendations for brain and central nervous system (CNS) cancer in adults, followed by contextual information on the epidemiology of this cancer in New Zealand. An overview of the three bodies of literature from which the recommendations were developed (risk factors, signs and symptoms, and investigations) is then provided. The chapter concludes with a description of how the evidence was translated by the GDT into specific recommendations.

Recommendations

Brain and CNS cancer: urgent referral (within two weeks)	Grade
A person presenting with symptoms related to the CNS (including progressive neurological deficit, new onset seizures, headaches, mental changes, cranial nerve palsy, unilateral sensorineural deafness) where a brain tumour is suspected, should be referred urgently to a specialist*	C
A person presenting with headaches of recent onset accompanied by either features suggestive of raised intracranial pressure (eg, vomiting, drowsiness, postural related headache, headache with pulse synchronous tinnitus) or other focal or non-focal neurological symptoms (eg, blackout, change in personality or memory) should be referred urgently to a specialist*	C
A person presenting with a new, qualitatively-different unexplained headache that becomes progressively severe, should be referred urgently to a specialist*	C
A person presenting with suspected recent onset seizures, as determined by the clinical history, should be referred urgently to a specialist. An imaging investigation with a CT or MRI scan may be considered where available, but this should not delay referral*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details. * Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Recommendations

Brain and CNS cancer: referral/investigation	Grade
A person developing new signs related to the CNS should be considered for referral to a specialist*	C
A practitioner with concerns about the interpretation of a person's symptoms and/or signs should consider discussion of these concerns with a specialist. Referral for MRI or CT scanning should also be considered*	C
A practitioner should consider discussion with a specialist when a person presents with unexplained headaches of recent onset, present for at least 1 month <i>without</i> features suggestive of raised intracranial pressure*	C
A practitioner should reassess and re-examine a person with signs and symptoms that may be related to the CNS where there is failure to improve as expected*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice point

Brain and CNS cancer: referral/investigation
A person presenting with a single, unexplained seizure, should undergo a physical examination (including cardiac, neurological, mental state), and be referred to a specialist
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.

Epidemiological background

New Zealand population

Brain cancer is the tenth leading cause of cancer death in both New Zealand men and women. In 2004, men were both diagnosed with brain cancer and died more frequently of it than women (Table 10.1).⁸¹

Table 10.1 Incidence and mortality rates of brain cancer in 2004 by gender

	Men	Women
Registration rate (per 100,000)	5.8	4.2
Mortality rate (per 100,000)	4.8	3.1

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Data on brain cancer survival give a cumulative relative survival of approximately 18% after five years. In the first year the chance of survival is 34%, and after four years of survival, there is a 93% chance of surviving to the end of the fifth year.⁸⁰ However, survival is based on tumour grade. The source of the survival figure data made no distinction between different grades of tumour.

Māori

The incidence of brain cancer in Māori men during 1996–2001 was one-third lower than non-Māori men, whereas the incidence of brain cancer among Māori and non-Māori women was the same during this time period (Table 10.2).⁸

Table 10.2 Incidence of brain cancer in Māori and non-Māori by gender, 1996–2001

	Māori	non-Māori
Male registration rate (per 100,000)	3.7	5.6
Female registration rate (per 100,000)	3.4	3.4

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Overall, the mortality:incidence ratio was 80% for Māori and 69% for non-Māori. There was no difference seen in incidence or survival for Māori women compared to non-Māori women. However, although Māori men were less likely to be diagnosed with this cancer, after diagnosis they were more likely to die as a result of it than non-Māori men.⁸

Background to recommendation development

Risk factors

As risk factor consideration is an integral part of practitioner assessment of a symptomatic patient, the non-systematic review below summarises the key risk factors for brain and CNS cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified no evidence for risk factors in its evidence summary. No reference was made to risk factors for brain and CNS cancer in any of the included studies.⁵⁶

No additional studies were identified by the risk factor literature review.

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for brain and CNS cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One primary study in adult patients, of case-control design,¹²³ published since the NICE guideline, was identified by the literature review.

The NICE recommendations for referral for suspected brain and CNS cancer were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. Their literature review identified that brain tumours may present with seizures, focal neurological disturbance or other non-specific symptoms (eg, behavioural disturbance, slowness). Dizziness was a poor predictor of brain cancer, and the majority of people who present with headache do not have brain cancer. The following factors increased the chance of a headache being cancer: presence of vomiting, 'non-tension' type pain, and headache present for less than ten weeks.⁵⁶

A methodologically robust UK case-control study¹²³ evaluated the clinical features associated with brain tumours in the six months preceding the diagnosis of a primary brain tumour ($n=3505$, non-cancer controls $n=17,173$). The authors concluded that although new-onset seizures should be investigated, isolated headache represented too small a risk to justify investigation. The odd ratios ($p<0.005$) for specific symptoms were: new-onset seizure 87.0 (95% CI 42.0–180.0), weakness 23.0 (95% CI 7.1–77.0), headache 6.7 (95% CI 5.6–8.0), confusion 11.0 (95% CI 7.6–16.0), memory loss 2.7 (95% CI 1.7–4.2), visual disorder 2.0 (95% CI 1.2–3.3).

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected brain and CNS cancer underwent one or more of the investigations listed below:

- skull x-ray
- CT brain scan.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE guideline recommendation was based on expert opinion. The literature review identified the most useful investigations to be CT or MRI scans of the brain. No other primary care investigation was found to be of diagnostic utility.⁵⁶

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT agreed with the NICE recommendations on the CNS-related symptoms, the symptoms when combined with headache, types of headache and type of seizure that should prompt urgent referral to a specialist. In addition, in the case of a suspected recent onset seizure, the GDT opinion was that an imaging investigation with a CT or MRI scan may be considered, providing that this did not delay the referral. This was therefore added to the recommendation wording.

The GDT also agreed with the NICE recommendation that considering referral to a specialist when a person developed new CNS signs is an appropriate course of action. The GDT also agreed that considering a discussion with a specialist was appropriate when a person presented with a recent onset of headaches of at least one month's duration without symptoms of raised intracranial pressure, or where the practitioner had concerns about the interpretation of a person's symptoms. In the latter case, the GDT also noted that if rapid access to scanning was available, referral for an MRI or CT scan could also be considered. The GDT also agreed with NICE about the importance of re-examination and reassessment of a person when they fail to improve as expected. Many of the NICE guideline recommendations were therefore accepted with only minor wording modification.

In contrast to the recommendation in the NICE guideline, the GDT considered that a single, unexplained seizure warranted both a physical examination *and* referral to a specialist. This was therefore included as a good practice point. The GDT felt it unnecessary to include a NICE guideline recommendation related to rapid progression of 'other neurological features' (subacute focal neurological deficit, cognitive impairment, personality and behavioural changes). The NICE guideline recommendation related to referral of patients with CNS symptoms and a previously diagnosed cancer was also not included as it was considered beyond the scope of this guideline.

11 Bone cancer and soft tissue sarcoma

This chapter first presents one general recommendation for both bone cancer and soft tissue sarcoma. *Primary* bone cancer and soft tissue sarcoma are then considered in turn. The recommendations for each of these cancers are presented, followed by contextual information on the epidemiology of the cancer in New Zealand. An overview of the three bodies of literature from which the recommendations were developed (risk factors, signs and symptoms, and investigations) is then provided. Each section concludes with a description of how the evidence was translated by the GDT into specific recommendations.

For information on multiple myeloma please refer to Chapter 12, *Haematological cancer*.

Recommendation

Bone cancer and soft tissue sarcoma		Grade
A person presenting with increasing, unexplained or persistent bone pain or tenderness, particularly pain at rest (and especially if not in the joint), or an unexplained limp, should undergo urgent investigation by the practitioner*		C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.		
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.		

Recommendation development

Two of the three general recommendations for bone cancer and sarcoma in the NICE guideline were considered by the GDT for inclusion, but deemed too general for this site-specific chapter. The content contained within those recommendations is addressed by the recommendations presented in Chapter 2, *General principles of care*. However, the GDT did view the NICE recommendation related to the importance of practitioner investigation of increasing, unexplained or persistent bone pain or tenderness, or an unexplained limp, as appropriate for inclusion in this chapter.

Bone cancer

Recommendations

Bone cancer	Grade
A practitioner should urgently refer a person to a specialist if their x-ray result indicates possible bone cancer*	C
A person with a normal x-ray but persistent symptoms should undergo follow-up and/or a repeat x-ray, or should be referred to a specialist Other investigations may be useful dependent upon the clinical findings*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice points

Bone cancer	
A person with symptoms or signs suggestive of primary or secondary bone cancer should have an x-ray completed and reported within 5 days	✓
A practitioner should consider primary or secondary bone cancer in a person where a fracture is suspected in the absence of a history of trauma	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Epidemiological background

New Zealand population

Primary bone cancer (including articular cartilage cancers) is very rare, accounting for about 0.2% (n=46) of all cancer registrations in 2004.⁸¹ Metastatic bone cancer, beyond the scope of this guideline, is far more common than primary bone cancer.

Māori

The incidence of primary bone cancer was the same for Māori and non-Māori during 1996–2001 (Table 11.1). The mortality:incidence ratio was 56% for Māori and 44% for non-Māori. Māori when compared to non-Māori, were no more likely to be diagnosed with bone cancer but after diagnosis, were estimated to be approximately one-third more likely to die as a result of it (not statistically significant).⁸

Table 11.1 Incidence of bone cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	0.9	0.9

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises the key risk factors for bone cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that although primary bone tumours were rare, they could occur at any age. Primary bone cancers most commonly occurred between the age of 10 and 25 years. A second peak incidence for primary bone tumours occurred in the elderly. This age group was more likely to have Paget's disease. No further reference was made to risk factors for bone cancer in any of the studies included in the literature review.⁵⁶

No additional studies were identified by the risk factor literature review.

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for bone cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE recommendations for referral for suspected primary bone cancer were based on controlled studies without randomisation, cohort studies, non-experimental descriptive studies, case-control or case-series studies. The literature review identified that regional pain was the most common symptom on presentation. Other common presenting symptoms included a palpable mass and tenderness.⁵⁶

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected bone cancer underwent one or more of the investigations listed below:

- x-ray
- CT scan
- fine needle aspirate.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE guideline recommendations were based on evidence from cohort studies, non-experimental descriptive studies, case-control or case-series studies. The literature review identified an x-ray to be the first investigation when a primary bone tumour was suspected.⁵⁶

Recommendation development

During discussions the GDT noted the difficulty of diagnosing bone cancer. Based on the NICE guideline literature review, the GDT agreed with the NICE guideline recommendations on both the need for urgent referral where there is a suspicious x-ray result and the necessity for further action where an x-ray is normal, but symptoms persist. Two of the NICE recommendations were therefore accepted with only minor wording modification.

The NICE guideline recommendations also included referral for an immediate x-ray in a person with a suspected spontaneous fracture. However, the GDT chose instead to add a good practice point to remind practitioners to consider bone cancer in a person with a suspected fracture in the absence of a history of trauma. The GDT also wished to note, using a good practice point, their view that when a suspicion of bone cancer exists, an x-ray should be completed and reported within five days.

Soft tissue sarcoma

For recommendations related to head and neck symptoms refer to Chapter 13, *Head and neck cancer*.

Recommendation

Soft tissue sarcoma	Grade
A person with HIV disease and suspected Kaposi's sarcoma should be referred to a specialist*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice points

Soft tissue sarcoma	
A person with an unexplained palpable soft tissue lump (ie, excluding a sebaceous cyst or lipoma) that is increasing in size, or hard, fixed or tethered should undergo an appropriate imaging investigation of the lump (ultrasound, MRI or CT scan) and should be referred to a specialist <i>before</i> any biopsy or fine needle aspirate	✓
For a person presenting with symptoms and/or signs suggestive of soft tissue sarcoma, referral for an ultrasound, MRI or CT scan may be made, but this should not delay referral to a specialist	✓
A practitioner may excise or biopsy lumps in subcutaneous tissue, but should refer a person with a lump beneath deep fascia to a specialist	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Epidemiological background

Due to the different ways in which soft tissue sarcomas could be recorded using the cancer sites registration codes,⁸¹ it is not possible to report the incidence of these cancers in this guideline.

In the seminal report by Robson and colleagues in 2006 on Māori and non-Māori cancer statistics, mesothelial and soft tissue cancers were combined. Although the incidence of these cancers was similar in both Māori and non-Māori, after diagnosis, Māori were more likely to die as a result of the cancer.⁸

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises the key risk factors for soft tissue sarcoma. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that although soft tissue sarcomas were rare, they could occur at any age. Soft tissue sarcomas most commonly occurred in people aged over 30 years. No further reference was made to risk factors for soft tissue sarcoma in any of the studies included in the literature review.⁵⁶

No additional studies were identified by the risk factor literature review.

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for soft tissue sarcoma in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE recommendations for referral for suspected soft tissue sarcoma were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies. The literature review identified that a palpable mass (with or without pain or discomfort) was the most common symptom on presentation. In decreasing order of frequency, sarcomas most commonly occurred on the lower limbs, upper limbs and trunk.⁵⁶

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected soft tissue sarcoma underwent one or more of the investigations listed below:

- ultrasound
- CT
- fine needle aspirate (FNA)
- x-ray.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

As there was no evidence on primary care investigations for soft tissue sarcoma, the NICE guideline made no recommendations on investigations.⁵⁶

Recommendation development

Based on the NICE guideline literature review, the GDT agreed with the NICE recommendation on the need to refer a person with HIV disease and suspected Kaposi's sarcoma. This NICE guideline recommendation was therefore accepted with only minor wording modification. In terms of the specific features that should prompt referral of a palpable lump, the GDT made substantial changes to the NICE recommendation. Pain was not considered a useful discriminatory feature and was therefore excluded. Furthermore, the GDT expressed concern about specifying a minimum size of lump for referral and therefore excluded this information.

In contrast to NICE, the GDT decided to indicate those lumps that were appropriate for practitioner excision or biopsy, and to clarify the place of investigations. Expert advice on sarcoma was that where sarcoma was suspected, primary care investigations should not delay referral and that only imaging investigations (ultrasound, MRI or CT scan) were appropriate in the primary care setting. Furthermore, it was advised that injudicious use of biopsy or FNA could prejudice future surgery. This expert advice was reflected in the good practice points developed.

12 Haematological cancer

This chapter presents the recommendations for haematological cancer (leukaemia, lymphoma and multiple myeloma) in adults, followed by contextual information on the epidemiology of these cancers in New Zealand. An overview of the three bodies of literature from which the recommendations were developed (risk factors, signs and symptoms, and investigations) is then provided. The chapter concludes with a description of how the evidence was translated by the GDT into specific recommendations.

Leukaemia and lymphoma in children are considered separately in Chapter 14, *Cancer in children and young people*.

Recommendation

Haematological cancer: general recommendation	Grade
<p>A person should have a full examination, investigation (including a complete blood count and blood film), and referral to a specialist should be considered if they have combinations of the following symptoms and signs unexplained convincingly by another illness or injury:</p> <ul style="list-style-type: none"> • sustained fatigue • drenching night sweats • fever • weight loss • generalised itching • breathlessness • gingival swelling and bleeding • bruising • bleeding • recurrent infections • bone pain • alcohol-induced pain • abdominal pain • lymphadenopathy • splenomegaly. <p>The urgency of referral depends on the severity of the symptoms and signs, and findings of investigations*</p>	C
<p>Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.</p> <p>* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.</p>	

Recommendation

Haematological cancer: immediate referral	Grade
<p>A person with spinal cord compression or renal failure where myeloma is suspected should be referred immediately to a specialist*</p>	C
<p>Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.</p> <p>* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.</p>	

Recommendation

Haematological cancer: urgent referral (within two weeks)	Grade
A person with persistent unexplained splenomegaly should be urgently referred to a specialist*	C
<p>Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.</p> <p>* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.</p>	

Recommendations

Haematological cancer: referral/investigation	Grade
<p>A person should undergo investigation and/or be referred to a specialist if they have lymphadenopathy with <i>one or more</i> of the following features:</p> <ul style="list-style-type: none"> • persistence for 6 weeks or more • lymph nodes increasing in size • lymph nodes greater than 2 cm in size • widespread nature • associated splenomegaly, night sweats or weight loss* 	C
A person presenting with persistent unexplained fatigue should have a complete blood count, blood film and C-reactive protein. The practitioner should repeat these tests at least once if the person's condition remains unexplained and does not improve*	C
A person with unexplained lymphadenopathy should have a complete blood count, blood film and C-reactive protein*	C
A person presenting with unexplained bruising, bleeding, and purpura or symptoms suggesting anaemia should have a complete blood count, blood film, clotting screen and C-reactive protein*	C
A person presenting with persistent, unexplained bone pain should have a complete blood count, x-ray, urea and electrolytes, liver and bone profile, PSA test (in males) and C-reactive protein*	C
<p>Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.</p> <p>* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.</p>	

Good practice point

Haematological cancer: referral/investigation
<p>For a person presenting with symptoms and/or signs suggestive of myeloma, a Bence-Jones protein and serum protein electrophoresis may be undertaken, but should not delay referral to a specialist</p>
<p>Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.</p>

Epidemiological background

Leukaemia

New Zealand population

Leukaemia is the seventh leading cause of cancer death in both New Zealand men and women. In 2004, men were both diagnosed and died more frequently than women from leukaemia (Table 12.1).⁸¹

Table 12.1 Incidence and mortality rates of leukaemia in 2004 by gender

	Men	Women
Registration rate (per 100,000)	13.2	10.6
Mortality rate (per 100,000)	4.9	4.2

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Data on leukaemia survival give a cumulative relative survival of approximately 49% after five years. In the first year, the chance of survival is 68% and, after four years of survival, there is a 93% chance of surviving to the end of the fifth year.⁸⁰

Māori

The overall incidence of leukaemia in Māori and non-Māori during 1996–2001 was similar (Table 12.2). However, the mortality:incidence ratio was 49% for Māori and 36% for non-Māori. Māori when compared to non-Māori, were no more likely to be diagnosed with this leukaemia but after diagnosis, were 40% more likely to die as a result of it.⁸

Differences in disparity between Māori and non-Māori were observed with respect to different types of leukaemia. Although incidence rates were similar for lymphoid leukaemia, myeloid leukaemia rates were over 30% higher in Māori.⁸

Table 12.2 Incidence of leukaemia in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	8.4	7.7

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Hodgkin's lymphoma

New Zealand population

Hodgkin's lymphoma is very rare, accounting for about 0.4% (n=80) of all cancer registrations in 2004. In 2004, men were diagnosed with Hodgkin's lymphoma more frequently than women (Table 12.3).⁸¹

Table 12.3 Incidence of Hodgkin's lymphoma in 2004 by gender

	Men	Women
Registration rate (per 100,000)	2.0	1.4

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Māori

The incidence of Hodgkin's lymphoma in Māori during 1996–2001 was lower than the incidence in non-Māori (Table 12.4). However, the mortality:incidence ratio was 27% for Māori and 12% for non-Māori. Māori when compared to non-Māori, were less likely to be diagnosed with Hodgkin's lymphoma but after diagnosis, were more likely to die as a result of it.⁸

Table 12.4 Incidence of Hodgkin's lymphoma in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	1.1	1.7

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Non-Hodgkin's lymphoma

New Zealand population

Non-Hodgkin's lymphoma is the eighth leading cause of cancer death in New Zealand men and the sixth leading cause in New Zealand women. In 2004, men were both diagnosed and died more frequently than women from non-Hodgkin's lymphoma (Table 12.5).⁸¹

Table 12.5 Incidence and mortality rates of Non-Hodgkin's lymphoma in 2004 by gender

	Men	Women
Registration rate (per 100,000)	12.7	9.5
Mortality rate (per 100,000)	4.6	4.0

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Data on non-Hodgkin's lymphoma survival give a cumulative relative survival of approximately 54% after five years. In the first year, the chance of survival is 71% and after four years of survival, there is a 96% chance of surviving to the end of the fifth year.⁸⁰

Māori

The incidence of non-Hodgkin's lymphoma was similar in Māori and non-Māori during 1996–2001 (Table 12.6). However, the mortality:incidence ratio was 48% for Māori and 41% for non-Māori. Māori when compared to non-Māori, were no more likely to be diagnosed with non-Hodgkin's lymphoma but after diagnosis, were over 40% more likely to die as a result of it.⁸

Table 12.6 Incidence of non-Hodgkin's lymphoma in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	6.9	6.8

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Multiple myeloma

New Zealand population

Multiple myeloma and malignant plasma cell neoplasms are rare, accounting for 1.2% (n=240) of all cancer registrations in 2004. In 2004, men were diagnosed and died more frequently of these cancers than women (Table 12.7).⁸¹

Table 12.7 Incidence and mortality rates of multiple myeloma in 2004 by gender

	Men	Women
Registration rate (per 100,000)	4.6	3.2
Mortality rate (per 100,000)	2.5	1.8

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Māori

The incidence of this disease in Māori during 1996–2001 was almost twice that of non-Māori (Table 12.8). Furthermore, the mortality:incidence ratio was 56% for Māori and 52% for non-Māori. Māori when compared to non-Māori, were more likely to be diagnosed with this disease and, after diagnosis, were 60% more likely to die as a result of it.⁸

Table 12.8 Incidence of multiple myeloma in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	3.9	2.1

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises the key risk factors for haematological cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified the evidence cited below for each of the specified haematological cancers. The key features in terms of age at diagnosis are summarised in Box 12.1. Exposure to chemicals used in the rubber industry, Epstein-Barr virus and socioeconomic factors were all reported to have been associated with an increased likelihood of developing haematological cancer. However, the authors identified that these factors were of no help in referral decisions in patients who are either symptomatic, or have laboratory test results indicative of these cancers.⁵⁶

Box 12.1 Age-related features of haematological cancer

Haematological cancer	Features
Acute leukaemia	Peaks in the 5–9 year age group and then rises after the age of 49 years
Chronic myeloid leukaemia	Rare in childhood
Chronic lymphocytic leukaemia	Does not occur in childhood, rare in young adults, occurs most frequently in later life
Hodgkin's lymphoma	Peaks at 20–25 and 75–79 years of age
Non-Hodgkin's lymphoma	Increases after about 45 years of age
Multiple myeloma	Extremely rare below 35 years, then increases after the age of 50

Source: National Collaborating Centre for Primary Care. Referral guidelines for suspected cancer in adults and children. Part 2. London: National Collaborating Centre for Primary Care; 2005.

No additional studies were identified by the risk factor literature review.

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for haematological cancer in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies published since the NICE guideline were identified by the literature review.

The NICE recommendations for referral for haematological cancers were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The authors of the literature review included a strong caveat that their findings should be interpreted with caution as only a small number of relevant studies were found.

Their literature review identified that although fatigue may be a symptom on presentation for haematological cancers, it is not possible to distinguish it as a specific cause of haematological malignancy. Similarly, insufficient evidence existed to identify the precise significance of fever, bruising, bleeding or anaemia in haematological cancer diagnosis.⁵⁶

Bone pain was a common symptom of multiple myeloma on presentation. Although lymphadenopathy was a common sign of lymphoma on presentation to primary care, it was more often caused by alternative diagnoses.⁵⁶

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected haematological cancer underwent one or more of the investigations listed below:

- complete blood count (CBC)
- lymph node biopsy
- Bence-Jones protein
- CT chest/abdomen
- chest x-ray
- serum protein electrophoresis
- lactate dehydrogenase.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE recommendations were based on evidence from level 2 studies or systematic reviews of level 2 studies of the accuracy of diagnostic tests. The level 2 studies included not more than one of the following design characteristics: narrow population, poor reference standard, the comparison between the reference and index test is not blind, or being a case-control study.

The literature review identified that haemoglobin and blood film test results often prompted patient referral where a suspicion of a haematological cancer existed. Furthermore, a blood film detected white cell dyscrasias in leukaemia. In addition, it identified that although not a routine primary care investigation, a biopsy was definitive for lymphadenopathy. In patients experiencing lymphadenopathy, an abnormal chest x-ray result may also be associated with a positive cancer diagnosis.⁵⁶

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT agreed with the NICE recommendations on the combination of unexplained signs and/or symptoms that should prompt an examination and investigation (including CBC and blood film) of a person and prompt a practitioner to consider referral to a specialist. However, the GDT did add an extra symptom (gingival swelling and bleeding) to the list produced by NICE. The GDT also agreed with the NICE recommendations on the need for immediate referral where spinal cord compression or renal failure resulting from myeloma is suspected, the need for urgent referral in the case of persistent, unexplained splenomegaly, and the features of lymphadenopathy that should prompt further action. The GDT also agreed with the investigations recommended by NICE for a person presenting with the following unexplained symptoms: persistent fatigue; lymphadenopathy; bruising, bleeding, and purpura or symptoms suggestive of anaemia; and bone pain. The majority of the investigation recommendations from NICE included conducting 'a full [complete] blood count, blood film and erythrocyte sedimentation rate, plasma viscosity or C-reactive protein (according to local policy)'. In the New Zealand context, C-reactive protein was considered by the GDT to be the appropriate test to use. Many of the NICE recommendations were therefore accepted with only minor wording modification.

The GDT also chose to address one further area. A good practice point was therefore developed on the use of Bence-Jones protein and serum protein electrophoresis as primary care investigations for myeloma. The GDT highlighted during their discussions that the results of initial investigations may indicate the need for further investigations.

13 Head and neck cancer

In this chapter, oral (lip, oral cavity and pharynx) and laryngeal cancer, and thyroid cancer are considered in turn. This subdivision of head and neck cancer reflects clinical practice in the primary care setting. The recommendations are presented first in each section, followed by contextual information on the epidemiology of these diseases in New Zealand. An overview of the three bodies of literature from which the recommendations were developed (risk factors, signs and symptoms, and investigations) is then provided. Each section concludes with a description of how the evidence was translated by the GDT into specific recommendations.

Oral cancer and cancer of the larynx

Recommendations	
Oral cancer and cancer of the larynx: urgent referral (within two weeks)	Grade
A person with persistent symptoms and signs related to the oral cavity where a definitive diagnosis of a benign lesion cannot be made should be referred to a dentist or specialist or followed-up until the symptoms and signs disappear An urgent referral to a specialist should be made if the symptoms and signs have not disappeared after 6 weeks*	C
A person presenting with unexplained ulceration of the oral mucosa or a mass persisting for more than 3 weeks should be referred urgently to a dentist or specialist*	C
A person presenting with unexplained tooth mobility persisting for more than 3 weeks should be referred urgently to a dentist*	C
A person should be referred urgently to a specialist if they have unexplained red and white patches of the oral mucosa (including suspected lichen planus) with <i>one or more</i> of the following features: <ul style="list-style-type: none"> • painful • swollen • bleeding. A non-urgent referral to a specialist should be made in the absence of these features. If oral lichen planus is confirmed, the person should be monitored for oral cancer as part of routine dental examination*	C

continued over...

Recommendations continued...

Oral cancer and cancer of the larynx: urgent referral (within two weeks)		Grade
A person presenting with an unexplained, painless new lump in the neck, or a pre-existing lump that has recently changed over a period of 3 to 6 weeks, should be referred urgently to a specialist*		C
A person with an unexplained persistent swelling in the parotid or submandibular gland should be referred urgently to a specialist*		C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.		
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.		

Good practice points

Oral cancer and cancer of the larynx: urgent referral (within two weeks)	
A person presenting with unexplained persistent sore or painful throat or mouth, (particularly unilateral pain) for more than 4 weeks, should be referred urgently to a specialist	✓
A person presenting with unilateral unexplained pain in the head and neck area for more than 4 weeks, or with paraesthesia or dysaesthesia in an area of nerve distribution should be referred urgently to a specialist*	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	
* Good practice point consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Recommendation

Oral cancer and cancer of the larynx: referral/investigation	Grade
For a person presenting with symptoms and/or signs suggestive of head and neck cancer (with the exception of persistent hoarseness where a chest x-ray is indicated), no investigations in primary care are recommended as they can delay referral*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice point

Oral cancer and cancer of the larynx: referral/investigation	
A person presenting with hoarseness persisting for more than 3 weeks (particularly if a smoker aged 50 years or older, or a heavy drinker) should be referred to an ear, nose and throat specialist, and for a chest x-ray	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Epidemiological background

New Zealand population

Oral cancer (cancer of the lip, oral cavity and pharynx) accounted for 1.5% (n=292) of all cancer registrations in 2004, while cancer of the larynx accounted for 0.4% of registrations (n=72).⁸¹

Data on survival for oral cancer and cancer of the larynx give a cumulative relative survival of approximately 57% after five years. In the first year, the chance of survival is 79% and, after four years of survival, there is a 95% chance of surviving to the end of the fifth year.⁸⁰

Māori

The incidence of oral cancer was similar in Māori and non-Māori during 1996–2001 (Table 13.1). However, the mortality:incidence ratio was 53% for Māori and 29% for non-Māori. Māori when compared to non-Māori, were no more likely to be diagnosed with oral cancer but after diagnosis, Māori men were more than twice as likely to die as a result of it than non-Māori men. Māori men were less likely to be diagnosed at an early disease stage.⁸

Table 13.1 Incidence of oral cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	3.6	3.4

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

The incidence of cancer of the larynx in Māori during 1996–2001 was 1.5 times higher than non-Māori (Table 13.2). The mortality:incidence ratio was 31% for Māori and 38% for non-Māori. Māori when compared to non-Māori, were more likely to be diagnosed with laryngeal cancer but after diagnosis, were no more likely to die as a result of it.⁸

Table 13.2 Incidence of cancer of the larynx in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	1.3	0.8

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Background to recommendation development

Risk factors

As risk factor consideration is an integral part of practitioner assessment of a symptomatic patient, the non-systematic review below summarises the key risk factors for oral cancer and cancer of the larynx. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review identified that the incidence of laryngeal cancer increased with age. In addition, tobacco smoking and excessive alcohol intake were found to be independently associated with squamous cell carcinoma (the most commonly occurring cancer in the head and neck).⁵⁶

The literature review also cited a systematic review by Llewellyn in 2001 that reported chewing of betel quid (betel leaf combined with areca nut and calcium hydroxide) as a major risk factor for oral cancer in older Asian populations.⁵⁶

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for head and neck cancer (including oral cancer and cancer of the larynx) in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One guideline, a Scottish guideline on the diagnosis and management of head and neck cancer, was identified by the literature review.¹²⁴

One primary study of cohort design,¹²⁵ published since the NICE guideline, was also found.

The NICE recommendations for referral for suspected oral cancers and cancer of the larynx were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified that just over 3% of patients who had attended a 'Hoarse Voice Clinic' with hoarseness of at least four weeks duration were subsequently diagnosed with laryngeal cancer.⁵⁶

The Scottish guideline on the diagnosis and management of head and neck cancer specified a number of criteria for which urgent referral was recommended. This included persistent throat discomfort (particularly unilateral) of at least four weeks' duration.¹²⁴

The methodologically robust Finnish population-based cohort study of Alho et al.¹²⁵ provided information on the frequency of symptoms associated with head and neck cancer obtained from a cross-sectional questionnaire. Of 221 patients with histologically confirmed squamous cell cancer of the tongue, pharynx or larynx the most common symptom at the initial primary care visit was hoarseness (28%), throat pain (20%), a change in the tongue (11%) and tongue pain (10%). The authors concluded that head and neck cancer symptoms were common primary care symptoms. However, almost 80% (94/122) of patients with a prolonged pain or change in the tongue or persistent hoarseness on presentation had cancer of the tongue or glottis. For patients with other head and neck cancers, presenting symptoms were more variable. Cancers of the tongue and glottis generally resulted in early symptom manifestation. Conversely, cancers of the pharynx and supraglottis generally presented when advanced.

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected head and neck cancer (including oral cancer and cancer of the larynx) underwent one or more of the investigations listed below:

- fine needle aspirate
- biopsy
- ultrasound
- chest x-ray
- CT.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

As there was no evidence on the value of any primary care investigation for diagnosing oral cancer and cancer of the larynx, the single NICE recommendation was based on expert opinion. It was not recommended that primary care investigations were undertaken, other than a chest x-ray for persistent hoarseness.⁵⁶

Recommendation development

Based on the NICE guideline literature review and the evidence identified by NZGG, the GDT agreed with the NICE recommendations that a person should be referred urgently in the following cases: when signs and/or symptoms related to the oral cavity have persisted for six weeks and a definitive diagnosis of a benign lesion cannot be made; when unexplained ulceration of the oral mucosa or a mass persisting for more than three weeks are present; when there is unexplained, persistent swelling in the parotid or submandibular gland. Although the GDT agreed with the NICE guideline recommendations on the features of a lump in the neck that should prompt an urgent referral, they also chose to include the term 'painless' as a qualifier for this symptom. In two instances (oral cavity symptoms and oral mucosal ulceration or mass), the GDT wished to explicitly include a dentist as an alternative referral option. This was therefore added to the recommendation wording. The GDT concurred with NICE that unexplained tooth mobility persisting for more than three weeks should prompt urgent referral to a dentist.

The GDT were in agreement with the NICE guideline recommendations about the features associated with unexplained red and white patches of the oral mucosa that should prompt an urgent referral, and about how people with confirmed oral lichen planus should be monitored. The GDT also agreed with the NICE recommendation that no primary care investigation for suspected oral and laryngeal cancer (other than a chest x-ray for persistent hoarseness) was appropriate.

As substantial changes were made by the GDT to two of the NICE recommendations, these were framed as good practice points. The GDT considered that an explicit symptom time-frame should be added to the NICE recommendation on a sore or painful throat and that it should be broadened to also include a sore or painful mouth. The recommendation on unilateral, unexplained pain in the head and neck was also broadened substantially to include the presence of paraesthesia or dysaesthesia in an area of nerve distribution. The GDT disagreed with the NICE recommendation on the action that should be taken when a person presents with hoarseness lasting for more than three weeks. In contrast to NICE, which recommended that a chest x-ray was undertaken first and the referral decision based on the x-ray result, the GDT considered that a person should be referred simultaneously to an ear, nose and throat specialist, and for chest x-ray.

Thyroid cancer

Recommendations

Thyroid cancer	Grade
A person presenting with symptoms of tracheal compression including stridor due to thyroid swelling should be referred immediately to secondary care for emergency care*	C
<p>A person should be referred urgently to a specialist if they have a thyroid swelling AND <i>one or more</i> of the following:</p> <ul style="list-style-type: none"> • a solitary nodule increasing in size • a history of neck irradiation • a family history of an endocrine tumour • unexplained hoarseness or voice changes • cervical lymphadenopathy • young age (pre-pubertal) • age 65 years and older* 	C
<p>A person should have thyroid function tests if they present with a thyroid swelling without stridor and do not have any of the following features:</p> <ul style="list-style-type: none"> • a solitary nodule increasing in size • a history of neck irradiation • a family history of an endocrine tumour • unexplained hoarseness or voice changes • cervical lymphadenopathy • young age (pre-pubertal) • age 65 years and older <p>A referral to an endocrinologist (or if unavailable a physician) should be made if the person has a goitre and normal thyroid function tests</p> <p>A referral to an endocrinologist (or if unavailable a physician) may be considered if the person has hyperthyroidism or hypothyroidism and an associated goitre*</p>	C
<p>Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.</p> <p>* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.</p>	

Good practice point

Thyroid cancer	
For a person presenting with symptoms and/or signs suggestive of thyroid cancer, a referral for an ultrasound investigation may be made, but this should not delay referral to a specialist	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Epidemiological background

New Zealand population

Thyroid cancer is rare, accounting for 1% (n=191) of all cancer registrations in 2004. Although men were diagnosed at just under half the rate of women in 2004, mortality rates were similar (Table 13.3).⁸¹

Table 13.3 Incidence and mortality rates of thyroid cancer in 2004 by gender

	Men	Women
Registration rate (per 100,000)	2.3	5.3
Mortality rate (per 100,000)	0.4	0.5

Source: NZHIS. Cancer: New registrations and deaths 2004. Wellington: Ministry of Health; 2007.⁸¹

Data on thyroid cancer survival give a cumulative relative survival of approximately 92% after five years. In the first year, the chance of survival is 94% and after four years of survival, there is a 99% chance of surviving to the end of the fifth year.⁸⁰

Māori

The incidence of thyroid cancer in Māori during 1996–2001 was about 40% higher than non-Māori (Table 13.4). The mortality:incidence ratio was 8% for Māori and 4% for non-Māori. Māori when compared to non-Māori, were more likely to be diagnosed with thyroid cancer, but after diagnosis, survival was similar.⁸

Table 13.4 Incidence of thyroid cancer in Māori and non-Māori, 1996–2001

	Māori	non-Māori
Registration rate (per 100,000)	3.7	2.6

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises the key risk factors for thyroid cancer. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review cited a 'meta-review' by Musholt et al. in 2000 that identified a hereditary predisposition to papillary thyroid carcinoma. No further reference was made to risk factors for thyroid cancer in any other study included in the NICE literature review.⁵⁶

No additional studies were identified by the risk factor literature review.

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for head and neck cancer (including thyroid cancer) in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE recommendations for referral for suspected thyroid cancer were based solely on expert opinion. The NICE *Referral Guidelines for Suspected Cancer* literature review identified a single guideline on thyroid cancer and made no statements in their evidence summary related to this cancer.⁵⁶

Investigations

A systematic review of the literature sought diagnostic studies in which primary care patients with suspected head and neck cancer (including thyroid cancer) underwent one or more of the investigations listed below:

- thyroid function tests
- thyroglobulin
- ultrasound
- fine needle aspirate
- CT scan
- biopsy.

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

As there was no evidence on the value of any primary care investigation for suspected thyroid cancer, NICE made only two recommendations based on expert opinion.⁵⁶

Recommendation development

Based on the NICE guideline literature review, the GDT agreed with the NICE recommendations on the need for immediate referral for a person presenting with symptoms of tracheal compression resulting from thyroid swelling, the specific instances (signs and/or symptoms, history, family history, age groups) which, when combined with thyroid swelling, should prompt an urgent referral, and the place of thyroid function tests in primary care. Three of the NICE guideline recommendations were therefore accepted with only minor wording modification.

A further NICE recommendation specifically recommended against the use of investigations other than thyroid function tests (eg, ultrasonography, isotope scanning). However, in contrast, the GDT considered that ultrasound has a place as a potential primary care investigation, provided that specialist referral was not delayed. A good practice point was therefore included to reflect this view.

14 Cancer in children and young people

This chapter presents the recommendations for cancer in children and young people. General recommendations are presented first followed by specific recommendations for the cancers included in the NICE guideline: leukaemia, lymphoma, brain and central nervous system (CNS) tumours, neuroblastoma, Wilms' tumour, soft tissue sarcoma, bone sarcomas and retinoblastoma. While not an exhaustive list of cancers occurring in children and young people (eg, hepatoblastoma and germ cell tumours are not included), symptoms associated with these additional cancers would be identified by recommendations included in this chapter.

Brief contextual information on the epidemiology of cancer in children and young people in New Zealand is then given. An overview of the three bodies of literature from which the recommendations were developed (risk factors, signs and symptoms, and investigations) is then provided. The chapter concludes with a description of how the evidence was translated by the GDT into specific recommendations.

General recommendations

Recommendations	
Cancer in children and young people	Grade
A child or young person presenting several times (eg, 3 or more times) with the same problem, who is apparently unwell, but with no clear diagnosis, should be referred urgently to a specialist*	C
A practitioner should take note of caregiver observation, insight and knowledge of the child when considering the need to refer urgently*	C
A practitioner should refer a child or young person to a specialist if there is persistent caregiver anxiety, even when the practitioner considers that the symptoms are most likely to have a benign cause*	C
A practitioner should be aware of the association between specific syndromes and some cancers (eg, Down's syndrome and leukaemia, neurofibromatosis and CNS tumours) and should be alert to the potential significance of unexplained symptoms in children or young people with such syndromes*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details. * Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice points**Cancer in children and young people**

A child presenting with persistent back pain should be examined and have a complete blood count and blood film.* An x-ray or referral to a specialist should also be considered



For a child or young person presenting with symptoms and/or signs suggestive of cancer, investigation may be instigated by the practitioner, but should not delay referral to a specialist



Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.

* Good practice point consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.

Specific recommendations**Recommendation****Leukaemia****Grade**

A child or young person should be referred immediately if they have:
unexplained petechiae
OR
hepatosplenomegaly*

C

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.

* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.

Good practice point**Leukaemia**

A child or young person should have a complete blood count and blood film if they have *one or more* of the following symptoms or signs unexplained convincingly by another illness:



- persistent or increasing pallor
- sustained fatigue
- continuing unexplained irritability
- fever
- any infection that does not resolve as expected
- generalised lymphadenopathy
- persistent or unexplained bone pain
- unexplained bruising

An immediate referral to a specialist should be made if the blood film or complete blood count indicates leukaemia

Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.

Recommendations

Lymphoma	Grade
A child or young person presenting with hepatosplenomegaly should be referred immediately to a specialist*	C
A child or young person with a mediastinal or hilar mass on chest x-ray should be referred immediately to a specialist*	C
<p>A child or young person should be referred urgently to a specialist if they have lymphadenopathy with <i>one or more</i> of the following, particularly if there is no evidence of local infection:</p> <ul style="list-style-type: none"> • non-tender, firm or hard lymph nodes • lymph nodes greater than 2 cm in size • progressively enlarging lymph nodes • other features of general ill-health, fever or weight loss • axillary node involvement (in the absence of local infection or dermatitis) • supraclavicular node involvement* 	C
<p>Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.</p> <p>* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.</p>	

Good practice point

Lymphoma	
<p>A child or young person should be referred immediately to a specialist if they have shortness of breath* in association with:</p> <ul style="list-style-type: none"> • non-tender, firm or hard lymph nodes • lymph nodes greater than 2 cm in size • progressively enlarging lymph nodes • other features of general ill-health, fever or weight loss • axillary node involvement (in the absence of local infection or dermatitis) • supraclavicular node involvement <p>* Particularly if the shortness of breath is not responding to bronchodilators</p>	✓
<p>Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.</p>	

Recommendations

Brain and CNS tumours (in children aged 2 years and older)		Grade
A child or young person presenting with a reduced level of consciousness should be an emergency admission to hospital*		C
A child or young person presenting with recurrent headache and vomiting that cause early morning waking or occur on waking (signs of raised intracranial pressure) should be referred immediately to a specialist*		C
A child or young person should be referred either immediately or urgently if they have <i>one or more</i> of the following neurological symptoms and signs: <ul style="list-style-type: none"> • new-onset seizures • cranial nerve abnormalities • visual disturbances • gait abnormalities • motor or sensory signs • unexplained deteriorating school performance or developmental milestones • unexplained behavioural and/or mood changes* 		C
A child or young person presenting with persistent headache should have a neurological examination*		C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details. * Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.		

Good practice point

Brain and CNS tumours (in children aged 2 years and older)	
A child presenting with precocious puberty (breast development in girls under 8 years; appearance of pubic hair or genital enlargement in boys under 9 years) should be referred urgently to a specialist	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Recommendation

Brain and CNS tumours (in children aged younger than 2 years)	Grade
<p>A child younger than 2 years should be referred immediately or urgently to a specialist if they have <i>one or more</i> symptoms suggestive of a CNS tumour</p> <p>Immediate referral:</p> <ul style="list-style-type: none"> • new-onset seizures • bulging fontanelle • extensor attacks • persistent vomiting <p>Urgent referral:</p> <ul style="list-style-type: none"> • abnormal increase in head size • arrest or regression of motor development • altered behaviour • abnormal eye movements • lack of visual following appropriate to age* 	C
<p>Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.</p> <p>* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.</p>	

Good practice point

Brain and CNS tumours (in children aged younger than 2 years)	
<p>A child younger than 2 years presenting with a squint which has recently become apparent should be referred urgently to a specialist</p>	✓
<p>Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.</p>	

Recommendations

Neuroblastoma	Grade
An infant younger than 1 year presenting with an abdominal or thoracic mass or skin nodules, should be referred immediately to a specialist*	C
A child or young person should be referred urgently to a specialist if they have <i>one or more</i> of the following: <ul style="list-style-type: none"> • unilateral proptosis • unexplained back pain • unexplained urinary retention* 	C
A child or young person with symptoms suggestive of neuroblastoma should have an abdominal examination (and/or urgent abdominal ultrasound) A chest x-ray and complete blood count should also be considered An urgent referral to a specialist should be made if a mass is identified*	C
A child or young person should have a complete blood count if they have: <ul style="list-style-type: none"> • persistent or unexplained bone pain (regardless of x-ray findings) • pallor • fatigue • unexplained irritability • unexplained fever • generalised lymphadenopathy • unexplained bruising • as neuroblastoma may present with metastatic disease* 	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice point

Neuroblastoma
A child or young person with any infection that does not resolve as expected should have a complete blood count
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.

Recommendation

Wilms' tumour	Grade
A child or young person with persistent or progressive abdominal distension should have an abdominal examination. An immediate referral to a specialist should be made if a mass is identified*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice point

Wilms' tumour	
A child or young person with haematuria should have a midstream specimen of urine, renal ultrasound and blood pressure measured	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Recommendations

Soft tissue sarcoma	Grade
<p>A child or young person should be referred urgently to a specialist if they have an unexplained mass (at almost any site), with <i>one or more</i> of the following features:</p> <ul style="list-style-type: none"> • deep to the fascia • non-tender • progressively enlarging • associated with a regional lymph node that is enlarging • greater than 2 cm in diameter* 	C
<p>A practitioner should consider head and neck or genitourinary sarcoma when a child or young person presents with <i>one or more</i> symptoms or signs suggestive of sarcoma.</p> <p>Head and neck sarcomas:</p> <ul style="list-style-type: none"> • proptosis • persistent unexplained unilateral nasal obstruction with or without discharge and/or bleeding • aural polyps/discharge <p>Genitourinary tract:</p> <ul style="list-style-type: none"> • urinary retention • scrotal swelling • bloodstained vaginal discharge* 	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Recommendations

Bone sarcomas (osteosarcoma and Ewing's sarcoma)	Grade
A child or young person with persistent localised bone pain and/or swelling should have an x-ray An urgent referral to a specialist should be made if a bone tumour is suspected*	C
A child or young person with rest pain, persistent back pain or unexplained limp should have further investigation. This should include x-ray, consultation with a paediatrician or referral to a specialist*	C
A practitioner should consider the possibility of a bone sarcoma irrespective of history of an injury*	C
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice point

Bone sarcomas (osteosarcoma and Ewing's sarcoma)	
A practitioner should consider the possibility of a tumour irrespective of a normal plain x-ray. If pain persists, a repeat x-ray should be undertaken after an interval or referral to a specialist should be made	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Recommendations

Retinoblastoma	Grade
A child with a white pupillary reflex (leukocoria) noted by the caregiver, identified in photographs or found on examination, should be referred urgently to a specialist	C
A practitioner should pay careful attention to a caregiver report of an odd appearance in their child’s eye*	
A practitioner should consider the possibility of retinoblastoma in a child presenting with visual problems and a family history of retinoblastoma	C
Offspring of a parent who has had retinoblastoma, or siblings of an affected child, should be referred to a specialist ophthalmologist*	
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix A for grading details.	
* Recommendation consistent with: Referral guidelines for suspected cancer. NICE clinical guideline 27. 2005.	

Good practice points**Retinoblastoma**

A child presenting with a new squint should be referred urgently to a specialist	✓
A pre-school child whose caregiver reports a significant reduction in the child's sight should be referred urgently to an ophthalmologist	✓
Opinion of the Guideline Development Team, or feedback from consultation within New Zealand where no evidence is available.	

Epidemiological background

New Zealand population

In 2004, cancer in children and young people (under 15 years of age) accounted for approximately 0.6% (n=124) of all cancer registrations. In 2004, the two most commonly occurring cancers in this age group were leukaemia (n=43, 35%) and brain cancer (n=14, 11%). A total of 20 cancer deaths occurred in 2004 in this age group, of which 7 (35%) resulted from leukaemia.⁸¹

Māori

The incidence of all cancers in Māori and non-Māori females under 15 years of age was similar during 1996–2001. However, the incidence in Māori males in this age group was lower than for non-Māori males during this time period (Table 14.1).⁸

Table 14.1 Incidence of all cancers in Māori and non-Māori children and young people (younger than 15 years) by gender, 1996–2001

	Māori	non-Māori
Male registration rate (per 100,000)	16.1	18.2
Female registration rate (per 100,000)	14.8	14.3

Source: Robson B, et al. Unequal impact: Māori and non-Māori cancer statistics 1996–2001. Wellington: Ministry of Health; 2006.⁸

Cancer mortality rates were higher for Māori than for non-Māori, irrespective of gender (Table 14.2).⁸

Table 14.2 Mortality rate for all cancers in Māori and non-Māori children and young people (younger than 15 years) by gender, 1996–2001

	Māori	non-Māori
Male mortality rate (per 100,000)	6.5	4.3
Female mortality rate (per 100,000)	4.6	3.6

Source: Robson B, et al. *Unequal impact: Māori and non-Māori cancer statistics 1996–2001*. Wellington: Ministry of Health; 2006.⁸

Leukaemia and brain cancers were the most commonly occurring cancers and also the most common cause of cancer death in Māori in this age group.⁸

Background to recommendation development

Risk factors

Risk factor consideration is an integral part of practitioner assessment of a symptomatic patient. The non-systematic review below summarises the key risk factors for cancer in children and young people. For further methodological details see Appendix A, *Methods*.

Summary of findings

The NICE *Referral Guidelines for Suspected Cancer* literature review cited a review article by Linet et al. in 2003 which reported the known risk factors for leukaemia, lymphoma, brain tumours, bone tumours and soft tissue sarcoma in childhood. The reported findings are summarised below.⁵⁶

Leukaemia

Female gender, being of white race[sic] (acute lymphoblastic leukaemia), exposure to ionising radiation, the presence of specific syndromes or disease states, including Fanconi and Bloom syndrome and neurofibromatosis, were reported as known risk factors for childhood leukaemia. Acute lymphoblastic leukaemia occurred more frequently in the 2–4 year age group, whilst acute myeloid leukaemia occurred more commonly in infancy.⁵⁶

The NICE guideline literature review also cited two other review articles that considered the association between Down's syndrome and leukaemia. The first review article (Stiller et al., 2002) identified the risk of acute lymphoblastic and non-lymphocytic leukaemias as about ten times higher in people with Down's syndrome in the 5–29 year age range than in people who do not have Down's syndrome.⁵⁶ The second review article (Hasle et al., 2001) stated that although leukaemia constituted a higher proportion of the total number of cancers in children with Down's syndrome, this syndrome was not a significant risk factor for leukaemia.⁵⁶

Lymphoma

Male gender and being of white race[sic] were reported as known risk factors for childhood lymphoma. This disease occurred more commonly in adolescence. Additional known risk factors reported for non-Hodgkin's lymphoma included immunosuppressive therapy and immunodeficiency syndromes.⁵⁶

Brain tumours

Male gender, being of white race[sic], exposure to ionising radiation and genetic disorders were reported as known risk factors for childhood brain tumours. Genetic disorders specifically reported in the NICE guideline literature review as increasing risk of brain tumour included neurofibromatosis (Stiller et al., 2002), and neurofibromatosis, tuberous sclerosis, nevoid basal cell syndrome, Turcot syndromes and Li-Fraumeni syndrome (Linnet et al., 2003). Brain tumours more commonly occurred in infancy.⁵⁶

Malignant bone tumours and soft tissue sarcoma

Male gender was reported as a known risk factor for both malignant bone tumours and soft tissue sarcoma. For bone tumours, being of white race[sic] was a known risk factor, as were certain genetic disorders (hereditary retinoblastoma, Rothmund-Thomson syndrome, Li-Fraumeni syndrome). For soft tissue sarcoma, being of black race[sic] and certain genetic disorders (neurofibromatosis, Li-Fraumeni syndrome) were reported risk factors. Bone tumours most commonly occurred around 13–18 years of age, whilst soft tissue sarcoma more commonly occurred around 15–19 years.⁵⁶

Signs and symptoms

A systematic review of the literature sought comparative studies of symptom recognition/identification for cancer in children and young people in primary care settings or in primary care populations. Screening studies and studies conducted in secondary care settings were excluded. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

One secondary study and six primary studies, published since the NICE guideline, were identified by the literature review. These included a systematic review of cohort and case-series studies,¹²⁶ and six case studies.^{127–132} The systematic review by Wilne et al.¹²⁶ did not consider presentation in primary care per se, and patients identified in the case studies were not necessarily drawn from a primary care population. These studies were considered by the GDT to add nothing further to the NICE literature review findings.

The NICE recommendations for referral for suspected cancer in children and young people were based on cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified that cancer is rare in childhood and that initial signs and symptoms may indicate a number of common conditions. Additional evidence cited for each of the specified cancers in children and young people is summarised below.⁵⁶

Leukaemia

Leukaemia generally presented with a short history of 'weeks'. Possible symptoms on presentation included fatigue, upper respiratory tract infection, fever, abdominal pain, lymphadenopathy, headache and anorexia.⁵⁶

Lymphomas

Hodgkin's lymphoma – usually presented with a history of 'months'. While lymphadenopathy (usually cervical/supraclavicular and non-tender) was a common sign on presentation, systemic symptoms (eg, itching and night sweats) only occurred in a small proportion of patients.

Non-Hodgkin's lymphoma – possible symptoms on presentation for non-Hodgkin's lymphoma included lymphadenopathy, breathlessness, superior vena cava obstruction and abdominal distension. Symptom progression generally occurred more quickly with this lymphoma type. Lymphadenopathy was more frequently benign in younger children.⁵⁶

Brain and CNS tumours

Headache, vomiting, visual problems, convulsions, behavioural problems and neurological symptoms may be potentially associated with brain tumours. In children under one year, signs also included bulging fontanelles and/or enlargement of the head. In children older than 18 months, papilloedema may be seen on presentation.⁵⁶

Neuroblastoma

Swelling was the most common sign of neuroblastoma on presentation. Some babies may present with skin nodules. Furthermore, as most children and young people with this diagnosis will have metastatic disease, other features on presentation could include malaise, pallor, bone pain and fever and may also resemble acute leukaemia.⁵⁶

Wilms' tumour

A painless abdominal mass was the most common sign of Wilms' tumour on presentation.⁵⁶

Bone and soft tissue sarcomas

Osteosarcoma and Ewing's sarcoma most commonly presented with local tenderness. Tenderness was frequently associated with a mass or pain when moving a joint. Fibrosarcomas most commonly presented with a soft-tissue mass that was increasing in size.⁵⁶

Retinoblastoma

Retinoblastoma most commonly presented with leukocoria and strabismus.⁵⁶

Investigations

A systematic review of the literature sought diagnostic studies in which children and young people presenting to primary care with suspected cancer underwent one or more of the investigations listed below:

- complete blood count (CBC)
- plain x-ray
- urine catecholamines
- alpha feto protein (AFP) – germ cell
- beta human chorionic gonadotropin
- biopsy
- fine needle aspirate (FNA).

The list of investigations for inclusion in the literature review was produced by the GDT members by informal consensus. However, the GDT emphasised that the use of urine catecholamines (for neuroblastoma), AFP and beta human chorionic gonadotrophin (germ cell tumours) would be dictated by clinical suspicion. If these diagnoses were being considered, urgent referral to a specialist would be justified. Furthermore, there was rarely a place for biopsy or FNA before referral to a specialist oncology service, and only then, after discussion with that service.

Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded from the systematic literature search. Due to a lack of relevant literature, all studies, irrespective of their methodological design, were presented to the GDT to consider in the development of recommendations.

Summary of findings

No secondary or primary studies, published since the NICE guideline, were identified by the literature review.

The NICE recommendations were based on evidence from cohort studies, non-experimental descriptive studies, case-control or case-series studies and expert opinion. The literature review identified only that a leukaemia diagnosis can be indicated by CBC and blood film results if this disease is suspected in a child or young person. No further evidence statements were included as part of this guideline.⁵⁶

Recommendation development

There was limited additional evidence since the publication of the NICE guideline about these relatively rare conditions. The GDT therefore considered it difficult to make practical use of the 'new' evidence.

The GDT reviewed the NICE guideline literature review, the general recommendations and the specific recommendations for each individual cancer. In the majority of cases, the GDT was in agreement with the NICE recommendations and accepted them for inclusion in this New Zealand guideline with only minor wording modification.

The GDT chose to include fewer general recommendations than the NICE guideline. The GDT specifically wished to highlight the importance of action when there was repeated presentation to a practitioner; the importance of caregiver observation, insights and anxiety; the need for awareness of the association between some tumours and specific syndromes; and that primary care investigations should not delay referral. In contrast to the NICE guideline, the GDT viewed that an x-ray could be considered in addition to a specialist referral in a child with persistent back pain.

Important changes that the GDT made to the condition-specific recommendations of NICE are identified below. Changes were made to some of the actions associated with specific symptoms or investigations. Where a blood count indicated leukaemia, and when a child or young person presented with shortness of breath in association with signs of lymphoma or features of general ill-health, the GDT considered that an immediate, rather than an urgent referral was warranted. In addition, when haematuria was evident on presentation (see Wilms' tumour recommendation), the GDT viewed it reasonable to investigate in primary care rather than urgently refer to a specialist.

With respect to recommendations for leukaemia and neuroblastoma, the NICE guideline considered that a child or young person with persistent or recurrent upper respiratory tract infections required a CBC. However, in the opinion of the GDT it was more appropriate to expand this to encompass any type of infection that does not resolve as expected. For neuroblastoma, changes were also made to the symptoms that should prompt referral. 'Unilateral' was added as a qualifier for proptosis and 'leg weakness' was removed as this was considered to be a very rare presentation for neuroblastoma.

Qualifiers were also added to specific symptoms on two further occasions to ensure that a single presentation of that symptom did not prompt a referral. 'Persistent' was added to 'back pain' for bone sarcoma and 'recurrent' added to 'headache and vomiting' for brain and CNS tumours in those aged two years and more. Qualifiers (shown in brackets here) were also added to the three symptoms considered by the GDT to be less discriminatory as a single symptom for leukaemia: pallor (persistent or increasing), fatigue (sustained), irritability (continuing).

The GDT also considered it important to provide much more explicit advice than the NICE guideline on management of squints (brain and CNS tumours in those aged younger than 2 years, and retinoblastoma recommendations), and reduction in visual acuity (retinoblastoma recommendations). The GDT also chose to address two additional areas. Good practice points were therefore incorporated advising how to proceed in the event of a normal x-ray result in possible sarcoma, and on identifying and managing precocious puberty as a potential symptom for brain and CNS tumours. To ensure that precocious puberty in boys could be easily assessed in primary care, the criteria chosen were based on visual appearance (Tanner stage 2 or above¹³³) rather than measurement of testicular size.

15 Implementation

At the time of writing this chapter, the Ministry of Health has advised it intends to contract out the development of an implementation plan for this guideline. This chapter therefore provides only a brief overview of implementation issues.

Overview

If guidelines are to achieve their intended objectives, they must be implemented in ways that support, encourage, and facilitate their use.¹³⁴ Factors at individual, regional and organisational levels have been identified as influencing guideline implementation.^{135–137} One of the difficulties encountered internationally is that guideline implementation occurs in the context of conflicting pressures for clinical autonomy, professional standardisation and quality improvement.¹³⁸ Adopting any new innovation or medical knowledge needs to be considered in context. Principled and structured approaches to the development of implementation solutions are necessary following guideline development, where key steps include:

- analysis of gaps between current and best practice
- prioritisation of these gaps in terms of impact on population health; in the context of this guideline, prioritisation needs to take into account issues of disparity in access and health outcomes between Māori, Pacific people and people who are non-Māori and non-Pacific
- identification of actions, barriers and enablers that either exacerbate or ameliorate gaps; in the context of this guideline, barriers which reinforce disparity are likely to include costs of care; communication; structural barriers; cultural fit (see Box 1.1)
- development of strategies to reduce barriers, and to close gaps; in the context of this guideline, specific action is likely to be required to improve the access and care of Māori and Pacific populations.

Organisational level barriers can include inappropriate skill levels to implement recommendations, a lack of facilities or equipment, or time and resource constraints. Structural change also impacts on implementation as changing roles and responsibilities make it difficult to know where to focus implementation activities and to provide the support needed for change. Regional issues may include a misalignment between local current practice and desired practice.

Both practitioner and patient variables can reinforce individual barriers to guideline implementation. Practitioners' attitudes and beliefs, their opinions about best practice, and their skill level and previous experience all influence how likely they are to implement guideline recommendations in their every day practice. Patients can also influence implementation with their own knowledge and attitudes about what they expect. For example, a person may not feel they have received an appropriate level of care unless they receive 'treatment' from a general practitioner, often in the form of medication or referral, even when this is not clinically indicated.

Multilevel approach

Guideline implementation initiatives are unlikely to achieve their objectives without explicit consideration of a multilevel approach to change.¹³⁵ To this end, the New Zealand Guidelines Group has identified four principles which should characterise implementation. These are:

1. strong visibility of the guideline
2. multifaceted approaches to support both health care professionals and patients to adopt guideline recommendations
3. recognition that all implementation activities should be considered across their national, regional and local contexts. Central agencies (such as the Ministry of Health or NZGG) should trust, facilitate and create opportunities for change, not attempt to 'direct' it
4. a commitment to supporting the sector to measure performance in implementing guideline recommendations.

Key priorities for implementation of this guideline

This guideline offers several key recommendations for practitioners relevant to all of the cancers addressed in this guideline. Four overarching priorities are common to these key recommendations:

- that all indications for referral are picked up
- that timely and appropriate investigations are ordered, and followed-up as appropriate
- in view of disparities in access and health outcomes between Māori and non-Māori, that Māori-specific cancer services or service components should be provided where a need is identified, and that service providers should improve culturally competent, patient-centred care by monitoring practice, including review of patient experiences
- that patients, families and carers can access appropriate support and information.

Broad guideline dissemination

In the experience of the New Zealand Guidelines Group, a guideline's key messages should be disseminated as widely as possible, as part of the initial awareness-raising of a new guideline and to support implementation activities. In this case, key audiences are primary health practitioners, patients and support services throughout New Zealand, via dissemination in multiple formats.

NZGG has been funded to develop summary statements of the most important recommendations for general practitioners. This should be followed up by the production of materials for use in primary care clinical training. Publicity of this guideline should also be sought in the academic, clinical professional and public media, and consideration should be given to production of materials for other audiences, including patients, their family/whānau and carers, professional associations, health care and social service agencies, and the voluntary sector.

Other potential implementation activities

While dissemination in some form is a prerequisite to practitioner awareness of a guideline, evidence strongly suggests that simple publication and/or merely passive dissemination of guidelines are usually ineffective in changing the way that physicians care for patients.^{134,139} Some key factors to implementation success include selection and adaptation of guidelines to local conditions, reminders, educational outreach and interactive educational workshops.¹⁴⁰

Methods for measuring and documenting baseline clinical practice, identifying any gap between this and evidence-based practices contained in the guideline, and developing clinical protocols or other measures to close that gap, are likely to be priorities for development.¹⁴¹

In the New Zealand primary care context, it is notable that in a 2007 Ministry of Health consultation exercise on health information capability in primary care, a key theme related to 'improving performance and evidence-based decisions' was identified in responses.¹⁴² Of responses on this theme, 53% related to the need to develop measures of performance in evidence-based care.

Levels of computerisation in primary care have increased rapidly in recent years, and New Zealand has been top-ranked in an international survey of the use of electronic tools to assist routine clinical processes and communication.¹⁴³ There is also evidence that the use in primary care in New Zealand of electronic clinical decision support systems may improve patients' care.^{144,145} However, the usefulness of electronic or other aids at the point of care appears to depend very much on the clinical context, and the particular kinds of decision involved. Importantly, there is evidence that computerised decision support may be more useful for management than for diagnosis.¹⁴⁶ This possibility has implications for this diagnosis-oriented guideline.

Implementation plan

The implementation plan which the Ministry is to commission is likely to consider the full range of potential activities, appraising their usefulness using the four steps outlined at the start of this chapter.

Guideline developers must understand the context and environment in which uptake is being encouraged to identify potential barriers, opportunities and solutions.¹⁴⁷ Implementation activities should therefore take into account existing strategies and plans, and seek to work with established networks. In this context, guideline implementation will need to align with the New Zealand Cancer Control Strategy Action Plan 2005–2010¹⁴⁸ and Cancer Control Programme Sector Plan.¹⁴⁹ The latter outlines specific responsibilities for the Ministry of Health, for the New Zealand Regional Cancer Networks, for DHBs and for other stakeholders. For this reason, the Ministry's planned implementation planning work for this guideline will need to fully involve these stakeholders.

As much as guidelines are themselves tools to alter clinical practice to better align with evidence, at least as much effort is required following guideline development to plan and implement change in a structured and effective way.

The Ministry of Health intends to contract out the development of an implementation plan for this guideline as the first step. This planning work will need to involve a structured and stepwise approach to identify and prioritise practice gaps, identify barriers and enablers, and to feasibility-test proposed solutions. This in turn requires effective engagement with sector stakeholders in national, regional and local contexts. In this way, effective change and improved care for consumers can be better assured.

Appendices

A: Methods

B: Guideline Development Team

C: Consultation

D: Abbreviations and glossary

Appendix A:

Methods

This appendix provides an overview of the research process. It describes in detail the literature review that was undertaken, the clinical questions and the process by which the recommendations and good practice points were developed.

In January 2007, New Zealand Guidelines Group convened a multidisciplinary Guideline Development Team (GDT). GDT members were nominated by a diverse range of stakeholder groups, including the Royal New Zealand College of General Practitioners, Royal Australian and New Zealand College of Radiologists, oncology specialists, Pasifika Medical Association, Te Ora and consumers (see Appendix B for a list of the GDT members).

Seven meetings of the full GDT were held. The aim of the first meeting was to train members of the GDT in the processes of guideline development, make decisions about the scope of the guideline and identify relevant clinical questions within the parameters initially set by the Ministry of Health. The *Referral Guidelines for Suspected Cancer* published by the National Institute for Health and Clinical Excellence (NICE)³ in 2005 and developed in relation to the National Health Service in England and Wales, is acknowledged as the 'seeding document' for this New Zealand guideline. Other relevant clinical guidelines were identified and some preliminary literature searching conducted to help in defining appropriate clinical questions.

Once clinical questions were defined (see next page for the full list), a literature review of the evidence for each clinical question was undertaken, relevant studies and guidelines were appraised for quality, and evidence tables were compiled. For study designs where no appraisal checklist was available (eg, case-series) a brief narrative overview was prepared. Guidelines were assessed using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument.¹⁵⁰ An overall summary of the body of evidence for each question (a 'Considered Judgment Form'¹⁵¹) was then prepared. Before each meeting of the GDT, evidence tables for a set of clinical questions were circulated to team members, together with the Considered Judgment Forms. The GDT reviewed and discussed the evidence in the light of their clinical experience, and recommendations and good practice points were drafted by consensus.

The development of this guideline proved to be particularly challenging for both the GDT and research team for several reasons. Developing appropriate search strategies to answer the clinical questions was problematic, and there were often limitations in the evidence located in terms of quality and scope. It was identified that for many cancers there has been a dearth of evidence published since the NICE guideline.³ Furthermore, the bulk of the research literature identified used research designs that precluded critical appraisal using formal assessment tools. In addition, little research was conducted in the primary care setting.

Clinical questions

Disparities and access to care

1. What are the disparities (if any) in cancer incidence and/or outcomes (mortality rate or survival) among Māori/Pacific/Asian peoples in New Zealand?
2. What contributes to these disparities?
3. What barriers to access to health services for Māori/Pacific/Asian peoples in New Zealand are reported in the literature?
4. What interventions have been reported in the literature to reduce disparities and/or barriers to access to health services for Māori/Pacific/Asian peoples in New Zealand and what was their efficacy?
5. What interventions are reported in the international literature to reduce disparities and/or barriers to access to health services for people who are suspected to have cancer?

Signs and symptoms, diagnostic accuracy and delay

A set of overarching clinical questions,⁴⁹ based on those developed for the NICE recommendations, were developed iteratively by the GDT and research team. The final version of the questions, applied to every cancer site included in the guideline, is shown below.

1. In patients presenting to primary care, what signs, symptoms and other clinical features are predictive of (specified) cancer?
2. In patients attending primary care services, with symptoms that may be caused by (specified) cancer, what is the diagnostic accuracy of signs, symptoms and/or investigations for (specified) cancer?
3. In patients attending primary care services with symptoms indicative of (specified) cancer, which factors are associated with delayed referral? Which factors influence delay by patient and which delay by provider?

Risk factors

1. What are the major, known risk factors for (specified) cancer?

Review of the literature

General comments

Two relevant, general guidelines were identified as part of the scoping process: *Referral Guidelines for Suspected Cancer* published by the Scottish Cancer Group¹⁵² in 2002 and by NICE³ in 2005. These guidelines were developed for use within the National Health Service in Scotland¹⁵² and within the National Health Service in England and Wales,³ respectively. The NICE guideline, being the more recent and extensive, was appraised for methodological quality using the AGREE instrument.¹⁵⁰ As it was deemed to be well-developed and suitable for updating, the decision was made following review and GDT discussion that it should be used as the 'seeding' or base guideline for this New Zealand guideline. However, the GDT noted

that disparity and access to care were not covered, and that the guideline would need further, in-depth review, taking account of the New Zealand context. The GDT decided that the New Zealand guideline should include all common cancers and exclude 'cancer of unknown origin' (ie, metastatic cancer). All cancers covered in the NICE guideline were therefore included. In addition, the GDT viewed it necessary to consider primary liver cancer due to its high prevalence in the Māori and Pacific populations and hence relevance in the New Zealand context.

It was not possible to identify all the links between the evidence cited, the evidence statements and the final recommendations for specific cancers in the literature review underpinning the NICE guidance^{49,56} It was explicitly stated in the review's methodology⁴⁹ that it had been necessary to make some pragmatic decisions around the literature:

The methodology team and the GDG (Guideline Development Group) [from the NICE guideline] agreed that a full literature search and critical appraisal process could not be undertaken for all [clinical questions] due to the time and resource limitations within the guideline development process. The methodology team, in liaison with the GDG, identified those [questions] where a full literature search and critical appraisal were essential.

The New Zealand GDT and research team found themselves in a similar position. Difficulty was experienced in developing search strategies for locating relevant and meaningful evidence. Little evidence was found from study designs located at higher points of the level of evidence hierarchy. Most of the literature was therefore of case-series design, rather than systematic review or meta-analysis, and therefore was not amenable to quality assessment using formal critical appraisal methods. Furthermore, it was inappropriate to extrapolate findings from secondary care, yet only a small volume of evidence was sited in the primary care setting. In light of these factors, reliance needed to be placed on the clinical and practical experience of the GDT, and their expert knowledge of the literature, to direct the research team to appropriate literature where gaps were perceived in the evidence presented by NICE.

The research team determined inclusion criteria for each clinical question and designed literature searches with the help of the Wellington School of Medicine Information Specialist. Only studies published in English were included.

Full details of the following are available on request: search strategies with the search date; inclusion criteria; excluded studies (including the reason for exclusion).

Disparities and access to care

The GDT and the research team acknowledged at the outset that much of the literature relevant to the disparities and access questions would be difficult to locate due to the breadth of the topic and potential inconsistencies in indexing. In addition, the majority was likely to be found in the 'grey literature' and therefore inaccessible through mainstream databases. Guidance from the GDT experts in this area was therefore key. They produced a brief document that included a summary of the topic area and some of the relevant literature to help inform the research team's search. By necessity, a pragmatic approach was taken to this literature review. A formal systematic search was only conducted for the literature relating to cancer. Searches related to interventions were restricted to systematic reviews of studies

conducted internationally. The GDT were aware and openly acknowledged that there would be difficulties with assessing the applicability of such studies in the New Zealand context.

Searches were conducted of the following databases from 1996:

- Medline
- Cinahl
- Australasian Medical Index
- Index New Zealand.

In addition, internet searches of relevant websites including the Ministry of Health, specific DHBs recommended by the GDT experts, and Te Ora were conducted. The reference lists of any retrieved literature were also reviewed for any additional relevant material. On the advice of the GDT experts, the evidence for disparities in cancer incidence, mortality and survival was taken from two publications: *Unequal Impact: Māori and Non-Māori Cancer statistics 1996–2001*⁸ and *Haurora: Māori Standards of Health IV*.⁹ The majority of the literature identified for the disparity questions was not amenable to formal critical appraisal.

Psychosocial support and information needs

The GDT considered that a full systematic review of the literature was beyond the scope of this guideline. A non-systematic review of literature published since the NICE guideline (2004) was undertaken. This review was restricted to identifying research indicating the relative effectiveness of information giving and psychological and social interventions in reducing psychological morbidity during the pre-diagnosis stage of cancer.

Epidemiology

The GDT considered that each site-specific chapter should be introduced with a brief epidemiology section to provide contextual information of specific relevance to New Zealand, and to indicate whether or not disparities in incidence, access to treatments or outcomes were known to exist. Similarly, if it was known that no disparity existed then that was also noted. Information from published cancer registration and mortality data, and Ministry of Health reports that provided data on cancer in Māori, Pacific and Asian peoples were noted wherever possible.

Signs and symptoms, diagnostic accuracy and delay

The GDT determined that these research questions (see 'Clinical questions', page 149) required a systematic review of the literature, including retrieval of any relevant guidelines, published since the NICE guidance.³

Signs and symptoms

Comparative studies of symptom recognition/identification for (specified) cancer in primary care settings or in primary care populations were sought. Screening studies (which usually exclude symptomatic people) and studies conducted in secondary care settings were excluded.

Diagnostic accuracy

Diagnostic studies in which primary care patients with suspected (specified) cancer underwent one or more of a specified list of investigations were sought. Screening studies and studies conducted in secondary care settings without a source population of primary care patients, or where primary care patients were not analysed separately from tertiary referrals, were excluded. The list of investigations for inclusion was produced by the GDT members by informal consensus. Any clinical examination viewed as an accepted standard of care was not included eg, digital rectal examination for prostate cancer.

Delay

Studies that investigated the factors associated with delay, and the consequences of delayed referral of a person presenting to the primary practitioner with suspected cancer were sought.

Searches were conducted of the following databases from 2004:

- Medline
- EMBASE
- Cinahl
- Cochrane Library.

Risk factors

The GDT considered that a full systematic review of the literature to identify the risk factors for each individual cancer site was beyond the scope of this guideline. However, as the evidence identified from the literature searches for 'signs and symptoms' clinical question 1 (see 'Clinical questions', page 149) identified few relevant publications, additional searches were considered necessary. Therefore, supplementary searches conducted for each of the cancer sites to identify guidelines that may have reported risk factors explicitly. Articles were only retrieved and appraised if they identified risk factors that were not already considered as part of the NICE evidence review^{49,56} or other previously appraised guidelines or systematic reviews, and if they presented risk factors that were quantified as being significant predictors of cancer (focusing on those with RR of >2.0).

Searches were conducted of the following databases from 2005:

- National Guidelines Clearinghouse (guidelines)
- Cochrane Library (guidelines and systematic reviews)
- Kings Fund Guidelines (guidelines)
- Turning Research Into Practice [TRIP] (guidelines and systematic reviews)
- International Network of Agencies for Health Technology Assessment [INAHTA] (HTA outputs)
- New Zealand Health Technology Assessment [HTA] (systematic reviews)
- Guidelines International Network [GIN] (guidelines)
- Medline (guidelines)
- EMBASE (guidelines).

Development of recommendations and good practice points

The GDT reviewed the available evidence and systematically discussed each of the NICE guideline recommendations³ and the recommendations from any other relevant national clinical guidelines in the context of their clinical practice. The recommendations for this New Zealand guideline were developed by informal consensus.

In formulating recommendations if, in the opinion and experience of the GDT, significant or material changes to the English or other national guidance was deemed appropriate for New Zealand, the recommendation was framed as a good practice point. In cases where other national recommendations were accepted, minor wording modification was often required to reflect the style of New Zealand Guidelines Group recommendations.

In line with the NICE guidance, recommendations were rarely made on *risk factors* in their own right. Due to the difficulties of establishing the degree of risk attributable to various factors for different cancers (in particular the complex interaction between risk factors such as age and environmental exposure) the GDT decided not to routinely document relative or absolute risk. With respect to developing recommendations, the GDT were cautious in their inclusion of risk factors. Risk factors were considered to be most useful when combined with specific signs or symptoms.

Further details on recommendation development for each specified cancer are outlined in the relevant chapter.

Summary

The aim of the GDT was to produce a relevant, evidence-based, clinically useful and user-friendly document for practitioners in primary care. By necessity, the expert knowledge and experience of the GDT was invaluable in bridging the gap between international expert opinion (the NICE guideline recommendations), limited robust evidence and practice in the New Zealand context. For this reason, no recommendation in this guideline received a rating higher than a C grading. See 'Evidence and recommendation grading system'.

Evidence and recommendation grading system

Details of the grading system

The evidence was assessed and graded, and recommendations were developed using the three-step process described in the *NZGG Handbook for the Preparation of Explicit Evidence-based Clinical Practice Guidelines*.¹⁵¹

Step 1: Study appraisal

Studies that met the inclusion criteria for each clinical question were appraised and graded for quality, using relevant checklists developed by the Scottish Intercollegiate Guidelines Network (SIGN).¹⁵³ These were modified to incorporate summary levels of evidence for the validity, magnitude/precision of effect and applicability of each study. An overall summary level of evidence was assigned to each study, as follows:

- + assigned when all or most of validity criteria met
- ~ assigned when some of criteria met and where unmet criteria are not likely to affect the validity, magnitude/precision or applicability of the results markedly
- x assigned when few or none of the criteria met.

Intermediate grades (+/~, ~/x) were assigned when overall study quality fell between these categories. Studies that met few or none of the quality criteria were excluded.

For every study included in our evidence review, the level of evidence assigned is listed alongside the citation in the reference list at the end of the guideline.

Step 2: Weighing the evidence

Evidence tables were prepared for each clinical question and were summarised on 'Considered Judgment Forms'.¹⁵¹ The Guideline Development Team (GDT) considered the body of evidence and made recommendations, based on the validity, quantity, consistency and clinical impact of the whole body of evidence.

Step 3: Developing recommendations

Grading of the recommendations was based on the quality of the evidence, which does not equate to the importance of the recommendation. When there was no evidence to answer a specific question, recommendations were based on the consensus of the GDT and were classified as 'good practice points'.

Grading of recommendations

Recommendations	
Description	Grade
The recommendation is supported by good evidence (based on a number of studies that are valid, consistent, applicable and clinically relevant)	A
The recommendation is supported by fair evidence (based on studies that are valid, but there are some concerns about the volume, consistency, applicability and clinical relevance of the evidence that may cause some uncertainty but are not likely to be overturned by other evidence)	B
The recommendation is supported by international expert opinion	C
Grades indicate the strength of the supporting evidence rather than the importance of the evidence	

Good practice points	
Description	
Where no evidence is available, best practice recommendations are made based on the experience of the Guideline Development Team, or feedback from consultation within New Zealand	✓

Appendix B:

Guideline Development Team

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Medical Web Editor, WONCA (World Organisation of National Colleges and Academies of General Practice/Family Practice)

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Invited by NZGG

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Consumer Perspective

Chairperson of Kenzie's Gift, Auckland

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Declarations of competing interests

Dr Peter Jansen is a Director of Mauri Ora Associates and is Medical Advisor to ACC Treatment Injury Unit.

Appendix C:

Consultation

A draft of this guideline was circulated to 337 individuals and organisations for comment in August 2008 as part of the peer review process. Comments were received from the following organisations and individuals:

Australasian Musculoskeletal
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Australia and New Zealand Association
of Paediatric Surgeons

Australian and New Zealand Head
and Neck Society

Julie Berquist, Cancer Nurse

Susan Bidwell, Information Specialist
and NZGG Board Member

Breast Cancer Network

Cancer Society of New Zealand

College of Nurses Aotearoa (NZ)

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Health Organisation

General Practice Nursing Alliance

Lorraine Hammersley, Clinical Nurse
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Hauora Taranaki Primary
Health Organisation

Healthwest Primary Health Organisation
He Oranga Pounamu

Internal Medicine Society Australia
and New Zealand

Andrew Kennedy-Smith, Urologist

Bridie Kent, Associate Professor of
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Michael Lamont

Ross Lawrenson, Professor of Primary
Care and NZGG Board Member

Manawatu Centre Cancer Society

MidCentral Health District Health Board

MidCentral Health
Psycho-Oncology Service

Midland Cancer Network

New Zealand Breast Cancer Foundation

New Zealand College of Midwives

New Zealand Dental Association

New Zealand Society for Oncology

New Zealand Society of
Otorhinolaryngology –
Head and Neck Surgery

Catherine Parata, Cancer Nurse

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Royal Australasian College of Surgeons

Royal New Zealand College
of General Practitioners

Ann Shaw, Health Promoter

Silver Ribbon Foundation
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Te Runanga O Kirikiriroa

Urological Society of Australia
and New Zealand

Waitemata District Health Board

Agadha Wickremesekera

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Hammond Williamson, Family Practitioner

Appendix D:

Abbreviations and glossary

Abbreviations

AFP	Alpha feto protein
CBC	Complete blood count
CEA	Carcinogenic embryonic antigen
CI	Confidence interval
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CT	Computerised tomography
DHB	District Health Board
ESR	Erythrocyte sedimentation rate
FNA	Fine needle aspirate
GDT	Guideline Development Team
LR	Likelihood ratio
MRI	Magnetic resonance imaging
NICE	National Institute for Clinical and Health Excellence
OR	Odds ratio
PHO	Primary Health Organisation
PPV	Positive predictive value
PSA	Prostate specific antigen
RR	Relative risk
SIGN	Scottish Intercollegiate Guideline Network

Glossary

Albinism	A congenital condition (present from birth) where there is little or no colour (pigment) in the skin, hair, and eyes
Alcohol-induced pain	Pain associated with alcohol ingestion
Anaemia	Condition where there is less than the normal number of red blood cells or less than the normal quantity of haemoglobin in the blood
Anorexia	Symptom of poor appetite, whatever the cause
Atrophic gastritis	Chronic inflammation of the stomach lining that causes the breakdown of the mucous membranes of the stomach
Barrett's oesophagus	An abnormal change in the cells of the lower end of the oesophagus thought to be caused by damage from chronic acid exposure. Considered to be a pre-malignant condition
Bence-Jones protein	Small proteins (light chains of immunoglobulin) found in the urine. Testing for these proteins is done to diagnose and monitor multiple myeloma and other similar diseases
Biopsy	Removal of a sample of tissue for examination under a microscope to check for cancer cells
Carcinogen	A cancer-causing substance or agent
Chromosome mutations	An inherited change in the DNA of a gene or chromosome. Hereditary mutations play a key role in genetic diseases and certain types of cancer
Clotting screen	A group of tests designed to detect possible problems with a person's blood coagulation or clotting mechanism. These tests can indicate if a person has a tendency to bleed
Clubbing	A thickening of the ends of the fingers and toes, as a sign of different diseases, mostly of the heart and lungs
Cognitive impairment	A dysfunction of any of the mental processes of perception, memory, judgment and reasoning
Computerised tomography	An imaging method that uses special x-ray equipment and computers to create cross-sectional pictures of the inside of the body
Confidence interval	Usually reported as a 95% confidence interval (CI) which is the range of values within which we can be 95% sure that the true value of the population lies (eg, for an NNT of 10 with a 95% CI of 5 to 15, we would have 95% confidence that the true NNT value lies between 5 and 15)
Consolidation (of the lung)	Clinical term for the characteristic signs of lobar pneumonia
C-reactive protein	A test which measures the concentration in blood serum of a special type of protein produced in the liver that is present during episodes of acute inflammation or infection
Cryptorchidism	Failure of one or both testes to descend into the scrotum

Cumulative relative survival	The proportion of patients alive after a specified number of years of follow-up where all excess mortality experience by the patient is attributed to the cancer
Cystic	Describes a fluid or semi-solid filled sac
Cytology	The microscopic study of body cells
Dermatitis	Inflammation of the skin
Dermatology	Branch of medicine dealing with the skin and its diseases
Dermoscopy	Examination of the skin using a skin surface microscope (dermascope)
Dyscrasia	Abnormality of the blood cells
Dyspepsia	For the purposes of this guideline, dyspepsia refers to all sub-classifications (reflux-like, ulcer-like, dysmotility-like, non-specific) identified by the New Zealand national guideline <i>Management of Dyspepsia and Heartburn</i> . ⁸⁶ Dyspepsia therefore includes epigastric pain or discomfort, heartburn or acid regurgitation, with or without bloating, nausea or vomiting
Dysphagia	Difficulty in swallowing
Dysplasia	Formation of abnormal tissue
Dyspnoea	Difficulty or pain in breathing
Dysuria	Difficulty or pain on passing urine
Endocrine	Relating to endocrine glands or their secretions (hormones)
Erythema	Reddening of the skin
Estimated Glomerular Filtration Rate (eGFR)	A screening test for chronic renal disease which describes the flow rate of filtered fluid through the kidney
Fine needle aspiration	A diagnostic procedure where a thin, hollow needle is inserted into a tumour to extract cells that will be examined under a microscope
Gastric	Referring to the stomach
Glottis	The middle part of the larynx, the area where the vocal cords are located
Gonadal dysgenesis	Abnormal development of a gonad (ovary or testicle)
Haematemesis	A condition in which someone vomits blood, usually because of internal bleeding
Haematuria	Presence of red blood cells in the urine Microscopic haematuria – red blood cells are only visible under a microscope Macroscopic haematuria – blood is visible in the urine
Haemoptysis	A condition in which someone coughs up blood from the lungs
Hepatosplenomegaly	Enlargement of both the liver and the spleen
Hypertension	Abnormally high blood pressure

Immediate referral	See Referral
Immunosuppression	Preventing normal activity of the body's immune system
Induration	Localised hardening of soft tissue. The area becomes firm but not as hard as bone
Intraluminal	Within the lumen. The lumen is the space inside a tubular structure eg, colon
Keratinising	Conversion into horny (keratinous) tissue
Lesion	Abnormal change in a body tissue
Leukaemia	Any of several malignant diseases where an unusual number of leucocytes (white blood cells) form in the blood
Likelihood ratio	The ratio of the probability that an individual with the target condition has a specified test result to the probability that an individual without the target condition has the same specified test result
Lipoma	Benign tumour formed of fatty tissue
Lymph node	Any of the small, oval or round bodies, located along the lymphatic vessels, that supply lymphocytes to the bloodstream and remove bacteria and foreign particles from the lymph
Lymphadenopathy	Disease or swelling of the lymph glands
Magnetic resonance imaging	An imaging technique that uses a powerful magnetic field, radio frequency pulses and a computer to produce detailed pictures of organs, soft tissues, bone and other internal body structures
Malignant	Refers to cells or tumours growing in an uncontrolled fashion. Such growths may spread to and disrupt nearby normal tissue, or reach distant sites via the bloodstream
Metastasis	Spreading of malignant disease from one part of the body to another through the bloodstream or the lymphatic vessels
Mortality:incidence (M/I) ratio	Provides a measure of disease severity. In general, the expected outcome is worse the closer the M/I value is to 1.0. An M/I value over 1.0 represents the poorest prognosis, which means that more people die from a particular type of cancer than were diagnosed in the same year
Myeloma	A cancer of plasma cells
Neoplasm	A tumour
Night sweats	Profuse sweating, usually during sleep
Noa	Ordinary, safe
Nocturia	A need to pass urine frequently at night
Obstructive jaundice	A yellowish discolouration of the skin, the conjunctival membranes over the sclerae (whites of the eyes), and other mucous membranes caused by hyperbilirubinaemia (increased levels of bilirubin in the blood) as a result of interruption to the drainage of bile in the biliary system

Odds ratio	The odds of an event happening in the experimental group expressed as a proportion of the odds of an event happening in the control group. The closer the OR is to one, the smaller the difference in effect between the experimental intervention and the control intervention. If the OR is greater (or less) than one, then the effects of the treatment are more (or less) than those of the control treatment
Osteomyelitis	Inflammation of the interior of a bone
Palpation	Examine manually ie, by touch
Papilloedema	A swelling of the optic nerve, at the point where the nerve joins the eye, that is caused by an increase in fluid pressure within the skull (intracranial pressure)
Parity	The number of times a woman has given birth
Persistent	Persistent (symptoms or signs). See Symptoms and signs
Petechiae	Pinhead sized bruises
Positive predictive value	The chance of having a disease given a positive test result
Primary care	Primary-level health, disability, social and community services care provided by a range of health workers including general practitioners and nurses
Primary study	A report of original findings in the form of a research article with sections on methods and results
Proptosis	Forward displacement or bulging of one or both eyes
Pruritis	An itch or sensation that makes a person want to scratch
Purpura	Bruising due to bleeding into the skin. Can vary in size from pinheads called petechiae to large bruises called echymoses
Rate ratio	The ratio of the rate in the exposed population to that of the unexposed. More commonly used in population-based studies
Referral	Immediate referral – in this guideline, immediate referral means the patient is seen within a few hours, or more quickly if required Urgent referral – in this guideline, urgent referral means the patient is seen within 2 weeks
Relative risk	The ratio of risk of disease or death among the exposed to the risk among the unexposed – usage is synonymous with risk ratio
Renal failure	Severe deterioration in kidney function
Risk factor	An aspect of personal behavior or lifestyle, or environmental exposure, or an inherited characteristic that is associated with an increased risk of a person developing a disease
Risk ratio	See Relative risk
Rongoā Māori	In its wider sense, refers to the traditional medical system of the indigenous people of New Zealand. Rongoā Māori includes herbal remedies, physical therapies such as massage and manipulation, and spiritual healing ¹⁵⁴

Sarcoma	A cancer of connective tissue such as bone, muscle or cartilage
Sebaceous cyst	A benign or harmless growth which forms when the release of sebum (a fluid produced by sebaceous glands in the skin), is blocked. It occurs under the skin and is most often found on the scalp, face, ears, and genitals
Secondary cancer/tumour	Cancer that comes back where it first started or cancer that has spread to another part of the body
Secondary care	Public hospitals, hospital-based services and specialist services
Secondary study	Summary of primary studies in the context of the particular information or idea under study
Seizure	Involuntary movement (sudden contraction of the muscles) or changes in consciousness brought on by a burst of electrical activity in the brain
Serum protein electrophoresis	A test which measures specific proteins (ie, albumin and globulin) in the blood to help identify some diseases, such as multiple myeloma, macroglobulinaemia, or amyloidosis
Soft tissue	Refers to tissues that connect, support, or surround other structures and organs of the body and includes muscle, fat, fibrous tissue, blood vessels, and other supporting tissue
Spinal cord compression	The act of exerting an abnormal amount of pressure on the spinal cord by a vertebral fracture, a tumour, abscess, ruptured intervertebral disc or other lesion
Splenomegaly	Enlargement of the spleen
Strabismus	Condition in which the eyes focus on different points
Stridor	A sharp high sound made when air passes an obstruction in the upper airway (larynx)
Subcutaneous	Beneath the skin
Supraglottis	The part of the larynx above the glottis (where the vocal cords are located)
Symptoms and signs	<p>What the patient reports or what is observed that may indicate a condition or disease</p> <p>Persistent signs or symptoms – in this guideline, ‘persistent’ is used to mean signs or symptoms that continue to occur beyond a period of time that would normally be indicative of a self-limiting condition</p> <p>Unexplained – in this guideline, ‘unexplained’ is used to mean signs or symptoms where no diagnosis has been made to identify the cause after the patient has been assessed by a practitioner</p>
Tapu	Sacred, forbidden, special
Telangiectasia	Condition in which the small blood vessels, especially in the face and thighs, are permanently dilated producing dark red blotches
Tenesmus	Painful, ineffectual straining to empty the bowel
Tertiary referral	Referral to a specialist health care service or centre

Tinnitus	A condition in which someone hears a ringing sound in the ears
Ultrasound	The therapeutic use of high frequency sound waves believed to enhance the healing of soft tissues following injury
Unexplained	Unexplained (symptoms or signs) See Symptoms and signs
Urea and electrolytes	A test which includes the measurement of the urea, sodium, potassium, CO ₂ and chloride concentrations in venous blood
Urgent referral	See Referral
Urinary frequency	Needing to urinate more often than usual
Urinary hesitation	Delay when starting to pass urine
Urinary retention	The inability to pass urine, usually because the urethra is blocked or because the prostate gland is enlarged
Xeroderma pigmentosa	A hereditary condition in which the skin and the tissue covering the eye is extremely sensitive to the ultraviolet part of sunlight

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