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JOINT RCGP / NCIN PRIMARY CARE WORKSHOP
'CANCER INTELLIGENCE FOR PRIMARY CARE'

THE USE OF ROUTINELY COLLECTED DATA FROM PRIMARY CARE IN RESEARCH ON CANCER

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Sources of routinely collected data

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- GPRD / CPRD
- QRESEARCH
- Individual analysis of records (e.g. CAPER)

Types of studies

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- Diagnostic
- Epidemiological
- Survivorship

British Journal of Cancer (2009) 101, S80 – S86

www.bjcancer.com

Full Paper

The CAPER studies: five case-control studies aimed at identifying and quantifying the risk of cancer in symptomatic primary care patients

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BACKGROUND: This paper reviews the background to five primary care case-control studies, collectively known as the CAPER studies (Cancer Prediction in Exeter). These studies, on colorectal, lung, prostate and brain tumours, sought to identify the particular features of cancer as reported to primary care. They also sought to quantify the risk of cancer for symptoms and primary care investigations, both individually and paired together.

METHODS: Two studies were on colorectal cancer: the former with 349 cases used hand searching and coding of entries, while the latter obtained 6442 cases from a national electronic database. The lung and prostate studies had 247 and 217 cases, respectively, and used manual methods. The brain study also used a national electronic database, which provided 3505 cases.

RESULTS: Generally, the symptoms matched previous series from secondary care, though the risks of cancer, expressed as positive predictive values, were lower. Rectal bleeding in colorectal cancer, and haemoptysis in lung cancer both had positive predictive values of 2.4%. The risk of a brain tumour with headache was one in a thousand.

INTERPRETATION: The results identify areas where current guidance on urgent referral for investigation of suspected cancer could be improved.

British Journal of Cancer (2009) **101,** S80 – S86. doi:10.1038/sj.bjc.6605396 www.bjcancer.com

Keywords: diagnosis; primary health care; predictive values

FULL PAPER

BJC

British Journal of Cancer (2013) 108, 25–31 | doi: 10.1038/bjc.2012.551

Keywords: oesophago-gastric cancer; primary care; symptoms; diagnosis; positive predictive values

The risk of oesophago-gastric cancer in symptomatic patients in primary care: a large case–control study using electronic records

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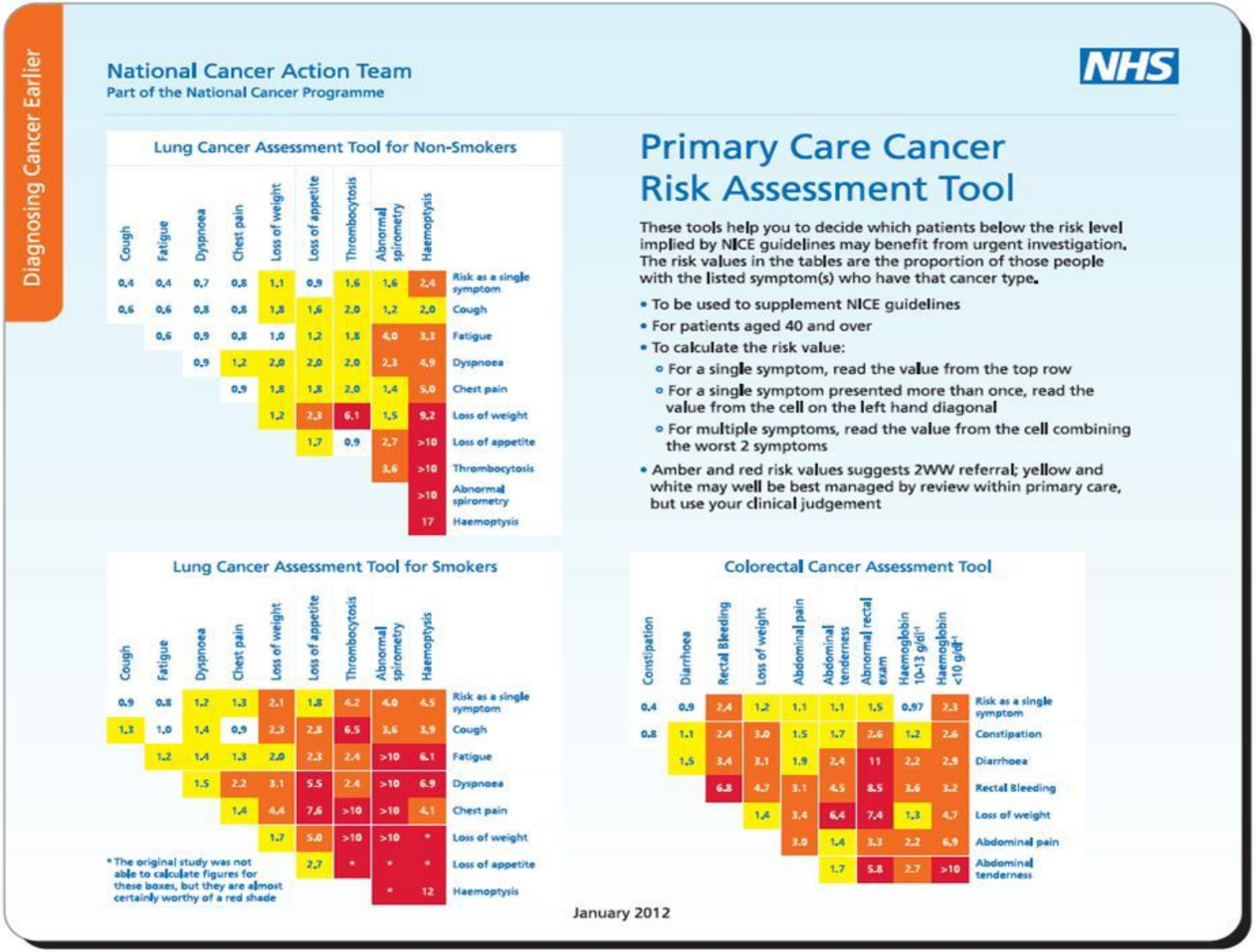
Background: Over 15000 new oesophago-gastric cancers are diagnosed annually in the United Kingdom, with most being advanced disease. We identified and quantified features of this cancer in primary care.

Methods: Case–control study using electronic primary-care records of the UK patients aged ⩾40 years was performed. Cases with primary oesophago-gastric cancer were matched to controls on age, sex and practice. Putative features of cancer were identified in the year before diagnosis. Odds ratios (ORs) were calculated for these features using conditional logistic regression, and positive predictive values (PPVs) were calculated.

Results: A total of 7471 cases and 32 877 controls were studied. Sixteen features were independently associated with oesophago-gastric cancer (all $P<0.001$): dysphagia, OR 139 (95% confidence interval 112–173); reflux, 5.7 (4.8–6.8); abdominal pain, 2.6 (2.3–3.0); epigastric pain, 8.8 (7.0–11.0); dyspepsia, 6 (5.1–7.1); nausea and/or vomiting, 4.9 (4.0–6.0); constipation, 1.5 (1.2–1.7); chest pain, 1.6 (1.4–1.9); weight loss, 8.9 (7.1–11.2); thrombocytosis, 2.4 (2.0–2.9); low haemoglobin, 2.4 (2.1–2.7); low MCV, 5.2 (4.2–6.4); high inflammatory markers, 1.7 (1.4–2.0); raised hepatic enzymes, 1.3 (1.2–1.5); high white cell count, 1.4 (1.2–1.7); and high cholesterol, 0.8 (0.7–0.8). The only PPV >5% in patients ⩾55 years was for dysphagia. In patients <55 years, all PPVs were <1%.

Conclusion: Symptoms of oesophago-gastric cancer reported in secondary care were also important in primary care. The results should inform guidance and commissioning policy for upper GI endoscopy.

Risk Assessment Tools



Diagnosing Cancer Earlier

National Cancer Action Team
Part of the National Cancer Programme

NHS

Primary Care Cancer Risk Assessment Tool

These tools help you to decide which patients below the risk level implied by NICE guidelines may benefit from urgent investigation. The risk values in the tables are the proportion of those people with the listed symptom(s) who have that cancer type.

- To be used to supplement NICE guidelines
- For patients aged 40 and over
- To calculate the risk value:
  - For a single symptom, read the value from the top row
  - For a single symptom presented more than once, read the value from the cell on the left hand diagonal
  - For multiple symptoms, read the value from the cell combining the worst 2 symptoms
- Amber and red risk values suggests 2WW referral; yellow and white may well be best managed by review within primary care, but use your clinical judgement

Lung Cancer Assessment Tool for Non-Smokers

Cough	Fatigue	Dyspnoea	Chest pain	Loss of weight	Loss of appetite	Thrombocytosis	Abnormal spirometry	Haemoptysis	
0.4	0.4	0.7	0.8	1.1	0.9	1.6	1.6	2.4	Risk as a single symptom
0.6	0.6	0.8	0.8	1.8	1.6	2.0	1.2	2.0	Cough
	0.6	0.9	0.8	1.0	1.2	1.8	4.0	3.3	Fatigue
		0.9	1.2	2.0	2.0	2.0	2.3	4.9	Dyspnoea
			0.9	1.8	1.8	2.0	1.4	5.0	Chest pain
				1.2	2.3	6.1	1.5	9.2	Loss of weight
					1.7	0.9	2.7	>10	Loss of appetite
							3.6	>10	Thrombocytosis
								>10	Abnormal spirometry
								17	Haemoptysis

Lung Cancer Assessment Tool for Smokers

Cough	Fatigue	Dyspnoea	Chest pain	Loss of weight	Loss of appetite	Thrombocytosis	Abnormal spirometry	Haemoptysis	
0.9	0.8	1.2	1.3	2.1	1.8	4.2	4.0	4.5	Risk as a single symptom
1.3	1.0	1.4	0.9	2.3	2.8	6.5	3.6	3.9	Cough
	1.2	1.4	1.3	2.0	2.3	2.4	>10	6.1	Fatigue
		1.5	2.2	3.1	5.5	2.4	>10	6.9	Dyspnoea
			1.4	4.4	7.6	>10	>10	4.1	Chest pain
				1.7	5.0	>10	>10	*	Loss of weight
					2.7	*	*	*	Loss of appetite
							*	12	Haemoptysis

* The original study was not able to calculate figures for these boxes, but they are almost certainly worthy of a red shade

Colorectal Cancer Assessment Tool

Constipation	Diarrhoea	Rectal Bleeding	Loss of weight	Abdominal pain	Abdominal tenderness	Abnormal rectal exam	Haemoglobin 10-13 g/dl[1]	Haemoglobin <10 g/dl[1]	
0.4	0.9	2.4	1.2	1.1	1.1	1.5	0.97	2.3	Risk as a single symptom
0.8	1.1	2.4	3.0	1.5	1.7	2.6	1.2	2.6	Constipation
	1.5	3.4	3.1	1.9	2.4	11	2.2	2.9	Diarrhoea
		6.8	4.7	3.1	4.5	8.5	3.6	3.2	Rectal Bleeding
			1.4	3.4	6.4	7.4	1.3	4.7	Loss of weight
				3.0	1.4	3.3	2.2	6.9	Abdominal pain
					1.7	5.8	2.7	>10	Abdominal tenderness

January 2012

Research

Julia Hippisley-Cox and Carol Coupland

Symptoms and risk factors to identify men with suspected cancer in primary care:

derivation and validation of an algorithm

Abstract

Background
Early diagnosis of cancer could improve survival so better tools are needed.

Aim
To derive an algorithm to estimate absolute risks of different types of cancer in men incorporating multiple symptoms and risk factors.

Design and setting
Cohort study using data from 452 UK QResearch® general practices for development and 224 for validation.

Method
Included patients were males aged 25–89 years. The primary outcome was incident diagnosis of cancer over the next 2 years (lung, colorectal, gastro-oesophageal, pancreatic, renal, blood, prostate, testicular, other cancer). Factors examined were: 'red flag' symptoms such as weight loss, abdominal distension, abdominal pain, indigestion, dysphagia, abnormal bleeding, lumps; general symptoms such as tiredness,

BACKGROUND

The UK has one of the poorest survival rates for cancer in Europe.[1] This is thought to be partly related to late presentation and delays in diagnosis and treatment. Earlier diagnosis could improve with more targeted investigation of symptomatic patients and increased public awareness of symptoms as encouraged by the National Awareness and Early Diagnosis Initiative (NAEDI).[2] It has been estimated that such an approach might save 5000 lives a year without any new medical advances.[3] In general terms, the earlier the cancer is diagnosed, the more treatment options are available and the better the prognosis. The challenge is to make the correct diagnosis as early as possible despite the non-specific nature of cancer symptoms and signs. This is particularly the case for primary care where GPs need to differentiate those patients for whom further investigation is warranted

team.[10] It's apparent that many of the general symptoms (for example, appetite, weight loss, anaemia, abdominal pain), and some of the more specific symptoms (for example, rectal bleeding), are predictive of multiple types of cancer. In addition, in clinical practice, patients generally consult with one or more symptoms rather than as a suspected case of a particular type of cancer. It is the clinician's job to decide whether a patient's symptoms might indicate serious disease such as cancer, which types of cancer are the most likely, what investigations and referrals might be needed, and the degree of urgency. With this in mind, the scientific approach used to develop the QCancer models was adapted from the individual 'cancer-based approach' towards a more 'symptoms-based approach' which incorporates multiple risk factors and symptoms in one model to predict risk of multiple types of cancer. A symptoms-

QRESEARCH

ClinRisk

Welcome to the QCancer®-2013 risk calculator for men: http://qcancer.org/male

Reset | For women | Information | Publications | About | Copyright | Contact Us | Algorithm | Software

Calculate risk

About you

Age (25-89): 48

UK postcode: leave blank if unknown

Postcode: CH1 2NH

Clinical information

Smoking status: non-smoker

Alcohol status: 3+ units per day

Do you have...

- a family history of gastrointestinal cancer? ☐
- a family history of prostate cancer? ☐
- type 2 diabetes? ☐
- chronic pancreatitis? ☐
- chronic obstructive airways disease (COPD)? ☐

Do you currently have...

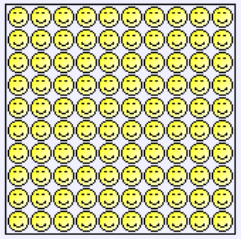
- loss of appetite? ☐
- unintentional weight loss? ☐
- abdominal pain? ☐
- abdominal swelling? ☐
- difficulty swallowing? ☐
- heartburn or indigestion: neither
- rectal bleeding? ☐
- blood when you vomit? ☐

Your risk of having one of the following cancers, as yet undiagnosed is:

Cancer	Type	Risk
No cancer		99.61%
Any cancer		0.39%
	other	0.13%
	colorectal	0.07%
	blood	0.06%
	prostate	0.03%
	renal tract	0.02%
	lung	0.02%
	gastro-oesophageal	0.02%
	testicular	0.02%
	pancreatic	0.01%

You have a 0.39% risk of having a cancer as yet undiagnosed, and correspondingly, a 99.61% chance that you are clear.

In other words, in a crowd of 100 people with the same risk factors as you, 0 are likely to have a cancer as yet undiagnosed



Risk of a cancer as yet undiagnosed

Cite this article as: BMJ, doi:10.1136/bmj.39171.637106.AE (published 10 May 2007)

BMJ

RESEARCH

Alarm symptoms in early diagnosis of cancer in primary care: cohort study using General Practice Research Database

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doi: 10.1136/bmj.39171.637106.AE

ABSTRACT

Objective To evaluate the association between alarm symptoms and the subsequent diagnosis of cancer in a large population based study in primary care.

Design Cohort study.

Setting UK General Practice Research Database.

Patients 762 325 patients aged 15 years and older, registered with 128 general practices between 1994 and 2000. First occurrences of haematuria, haemoptysis, dysphagia, and rectal bleeding were identified in patients with no previous cancer diagnosis..

Main outcome measure Positive predictive value of first occurrence of haematuria, haemoptysis, dysphagia, or rectal bleeding for diagnoses of neoplasms of the urinary tract, respiratory tract, oesophagus, or colon and rectum during three years after symptom onset. Likelihood ratio

general practitioners refer less than 5% of their patients each year for specialist opinions and hospital investigations.[1,2] Referral from primary to secondary care is often triggered by a general practitioner's awareness of so called "alarm symptoms," features in the clinical presentation that are considered to predict serious, often malignant, disease. For example, guidelines on the identification of alarm symptoms form the core of the "two week rule" for urgent referral of patients suspected of having cancer,[3,4] and many clinical practice guidelines specify particular symptoms that mandate urgent investigation or referral.[5] However, the evidence base for the alarming nature of many alarm symptoms is weak, and general practitioners often use individual approaches to the collection and analysis of data in the course of consultations.[1]

FULL PAPER

BJC

British Journal of Cancer (2013), 1–6 | doi: 10.1038/bjc.2013.13

Keywords: herpes zoster; cancer; risk; database; epidemiology

The risk of a subsequent cancer diagnosis after herpes zoster infection: primary care database study

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Background: Herpes zoster and cancer are associated with immunosuppression. Zoster occurs more often in patients with an established cancer diagnosis. Current evidence suggests some risk of cancer after zoster but is inconclusive. We aimed to assess the risk of cancer following zoster and the impact of prior zoster on cancer survival.

Methods: A primary care database retrospective cohort study was undertaken. Subjects with zoster were matched to patients without zoster. Risk of cancer following zoster was assessed by generating hazard ratios using Cox regression. Time to cancer was generated from the index date of zoster diagnosis.

Results: In total, 2054 cancers were identified in 74029 patients (13428 zoster, 60601 matches). The hazard ratio for cancer diagnosis after zoster was 2.42 (95% confidence interval 2.21, 2.66) and the median time to cancer diagnosis was 815 days. Hazard ratios varied between cancers, and were highest in younger patients. There were more cancers in patients with zoster than those without for all age groups and both genders. Prior immunosuppression was not associated with change in risk, and diagnosis of zoster before cancer did not affect survival.

Conclusion: This study establishes an association between zoster and future diagnosis of cancer having implications for cancer case finding after zoster diagnosis.

BMJ

BMJ 2013;356:f114 doi: 10.1136/bmj.f114 (Published 16 January 2013)

RESEARCH

Exposure to bisphosphonates and risk of gastrointestinal cancers: series of nested case-control studies with QResearch and CPRD data

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Abstract

Objective To investigate the association between use of bisphosphonates estimated from prescription information and risk of gastrointestinal cancers.

Design Series of nested case-control studies.

Setting General practices in the United Kingdom contributing to the QResearch primary care database (660) and the Clinical Practice Research Datalink (CPRD) (643).

Participants Patients aged ≥50 with a diagnosis of a primary gastrointestinal cancer in 1997-2011, each matched with up to five controls by age, sex, practice, and calendar year.

Main outcome measures Odds ratios for incident gastrointestinal

Introduction

As an established drug for the treatment and prevention of osteoporosis,[1 2] bisphosphonates have been widely prescribed[3] and have a long term effect.[4] Although preclinical studies have shown that bisphosphonates have anti-tumour properties,[5 6] there is still a possibility that their adverse effects on the gastrointestinal tract, such as mucosal irritation, might cause ulceration[7] and could be linked to an increased risk of cancer.

The first publication on the possible association was from the US Food and Drug Administration (FDA) Adverse Event Reporting System, which listed 23 cases of oesophageal cancer in users of oral alendronate between 1995 and 2008.[8] An

JAMA Psychiatry
Formerly Archives of General Psychiatry

Original Article | February 2007

Relative Risk of Cardiovascular and Cancer Mortality in People With Severe Mental Illness From the United Kingdom's General Practice Research Database FREE

David P. J. Osborn, PhD; Gus Levy, MSc; Irwin Nazareth, PhD; Irene Petersen, PhD; Amir Islam, MBA; Michael B. King, PhD

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Arch Gen Psychiatry. 2007;64(2):242-249. doi:10.1001/archpsyc.64.2.242.

This article was corrected | View correction

ABSTRACT

Context People with severe mental illness (SMI) appear to have an elevated risk of death from cardiovascular disease, but results regarding cancer mortality are conflicting.

Objective To estimate this excess mortality and the contribution of antipsychotic medication, smoking, and social deprivation.

Design Retrospective cohort study.

Setting United Kingdom's General Practice Research Database.

Patients Two cohorts were compared: people with SMI diagnoses and people without such diagnoses.

Main Outcome Measure Mortality rates for coronary heart disease (CHD), stroke, and the 7 most common cancers in the United Kingdom.

Results A total of 46 136 people with SMI and 300 426 without SMI were selected for the study. Hazard ratios (HRs) for CHD mortality in people with SMI compared with controls were 3.22 (95% confidence interval [CI], 1.99-5.21) for people 18 through 49 years old, 1.86 (95% CI, 1.63-2.12) for those 50 through 75 years old, and 1.05 (95% CI, 0.92-1.19) for those older than 75 years. For stroke deaths, the HRs were 2.53

BJC OPEN

British Journal of Cancer (2011) 105, S29 – S37

www.bjcancer.com

Full Paper

Long-term health outcomes in a British cohort of breast, colorectal and prostate cancer survivors: a database study

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BACKGROUND: The community-based incidence of cancer treatment-related long-term consequences is uncertain. We sought to establish the burden of health outcomes that have been associated with treatment among British long-term cancer survivors.

METHODS: We identified 26 213 adults from the General Practice Research Database who have survived 5 years or more following breast, colorectal or prostate cancer. Four age-, sex- and general practice-matched non-cancer controls were selected for each survivor. We considered the incidence of treatment-associated health outcomes using Cox proportional hazards models.

RESULTS: Breast cancer survivors had an elevated incidence of heart failure (hazards ratio (HR) 1.95, 95% confidence interval (CI) 1.27–3.01), coronary artery disease (HR 1.27, 95% CI 1.11–1.44), hypothyroidism (HR 1.26, 95% CI 1.02–1.56) and osteoporosis (HR 1.26, 95% CI 1.13–1.40). Among colorectal cancer survivors, there was increased incidence of dementia (HR 1.68, 95% CI 1.20–2.35), diabetes (HR 1.39, 95% CI 1.12–1.72) and osteoporosis (HR 1.41, 95% CI 1.15–1.73). Prostate cancer survivors had the highest risk of osteoporosis (HR 2.49, 95% CI 1.93–3.22).

CONCLUSIONS: The study confirms the occurrence of increased incidence of chronic illnesses in long-term cancer survivors attributable to underlying lifestyle and/or cancer treatments. Although the absolute risk of the majority of late effects in the cancer survivors cohort is low, identifying prior risk of osteoporosis by bone mineral density scanning for prostate survivors should be considered. There is an urgent need to improve primary care recording of cancer treatment.

British Journal of Cancer (2011) **105,** S29 – S37; doi:10.1038/bjc.2011.420 www.bjcancer.com

Research on primary care management and treatment of cancer

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