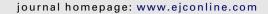Position Paper

The importance of early symptom recognition in the context of early detection and cancer survival

J.J. Ott [a,*], A. Ullrich [a], A.B. Miller [b]

[a] *Noncommunicable Diseases and Mental Health Cluster, World Health Organisation, 20 Avenue Appia, 1211 Geneva 27, Switzerland*
[b] *University of Toronto, Dalla Lana School of Public Health, Toronto, Canada*

ABSTRACT

Since there is evidence that stage is an important prognostic factor in cancer, interventions aimed at 'down-staging' are part of a comprehensive cancer control approach. Besides organised screening programmes, raising awareness of detectable signs and symptoms is recommended.

A precise definition of early cancer signs and symptoms, however, is lacking and there has also been no systematic review regarding the impact of awareness raising interventions on cancer outcomes.

We reviewed the scientific medical literature to assess the consistency and availability of a definition for early cancer symptoms as well as to assess the impact of early cancer diagnosis on survival. Although early diagnosis is an important factor for cancer survival, other considerations such as the cancer profile of a country, the characteristics of cancer types and the availability of devices for diagnosis should be taken into account in promoting early cancer detection. There is a clear need for research to categorise cancer types according to early symptoms in order to increase comparability of studies in this field and to provide guidance for health personnel in primary care settings in low income regions.

© 2009 Elsevier Ltd. All rights reserved.

1. Introduction

Cancers comprise a major part of the global chronic disease burden and increasingly contribute to the mortality in low and middle income countries (LMICs).[1] Projections indicate that demographic changes and population growth will result in an increase in cancer deaths from 7.1 million in 2002 to 11.5 million in 2030.[2] Worldwide, about one third of all cancers are estimated to be amenable to early detection and potential cure with treatment. Raising awareness in the general population about early symptoms is part of a comprehensive approach to control cancer.[3]

A large number of cancer patients could be saved from premature death and suffering if they had timely access to early detection programmes and to adequate treatment. In addition to socio-demographic variables such as age and socio-economic status (SES), cancer survival is determined by the availability of health education about cancer symptoms to the public and health care professionals, especially those working in primary care, and the access to appropriate diagnostic tests and effective treatment. Early diagnosis can arise from recognition of symptomatic cancers at an earlier stage, when the cancer is localised to the organ of origin and before it invades the surrounding tissue and thus has a higher

potential for cure. Early diagnosis is made in symptomatic patients who can detect the symptoms on their own or by health professionals, e.g. in primary care settings. Organised screening programmes, on the other hand, are aimed at detecting tumours through screening asymptomatic individuals and are defined as a site-specific search for malignancies at a stage prior to that detectable by the patient.[4] Currently, screening programmes are recommended for cancers of the breast and cervix.[3] Since screening is applied to a presumably asymptomatic population, it is not considered further here.

The main challenge for early diagnosis programmes is the sensitivity and specificity of signs and symptoms. The wide variation of first alarm symptoms has been shown in a study on malignancies of the upper gastrointestinal tract.[5] Many types of cancers show no specific symptoms at an early stage and are thus diagnosed at a more advanced disease stage. Colorectal cancer symptoms, for example, can be vague and confused with normal fluctuations in bowel habits experienced by the general population.[6–8] Also, head and neck squamous cell carcinomas present with nonspecific symptoms such as sore throat and neck nodes which are shared with common conditions, namely viral pharyngitis or tonsillitis.[9]

2. Early cancer diagnosis and survival

A delay in diagnosis with cancer being detected at a more advanced stage is a negative factor in cancer prognosis. For most cancer types, stage at diagnosis is identified to be one of the most important determinants for patient survival.[10–12] Earlier stage has been linked to better survival of selected cancers such as cancers of the breast,[13–17] cervix,[18] lung,[14,15] stomach,[15,19] prostate,[20,21] liver,[22] and urinary bladder.[14,23] Differences in melanoma skin cancer survival were also attributed to differences in early-stage diagnosis in two populations in the US.[24]

Oral cancer is another site that is very sensitive to early diagnosis. Treatment and stage of tumour at the time of diagnosis has been shown to be closely related to overall survival[25] and detection of small, early-stage oral cancers significantly reduced mortality and morbidity from this disease.[26] The fact that early oral cancer detection can be performed in primary care by medical practitioners, nurses or health care workers[26] underlines the general need and feasability of early cancer detection in countries with good access to primary care facilities.

Colorectal cancer has been extensively studied with regard to time at diagnosis. Although a relationship between colorectal cancer stage and survival was identified,[14,15,27,28] most of the studies did not find an association between delay in colorectal diagnosis (duration of symptoms) and disease stage or mortality, independent of sample characteristics.[29–32] When colon and rectal cancer were looked at separately, a delay in diagnoses affected survival differently and a shorter delay was only beneficial for rectal cancer, which was, however, not significant.[31,33] Colon cancer survival, on the other hand, was not influenced by early diagnosis, which is related to characteristics of the disease.[7] Colon cancer usually begins without specific symptoms and early diagnosis may have achieved little survival benefit since the presence of symptoms implies a substantial probability of an incurable tumour.

The case of colorectal cancers emphasises the relative importance of early diagnosis for different cancer types and indicates that the existence of a symptomatic phase of sufficient duration that offers a possible earlier diagnosis cannot generally be assumed.

3. Review of clinical definitions for earlier and later signs and symptoms

Although there is an official staging system classifying early and advanced cancer stage,[34] the terminology of early and advanced with regard to cancer signs and symptoms is not precise and is used differently by health care providers and in different countries. The manifestation of symptoms listed as suitable for early diagnosis greatly depends on location and nature of the tumour and some are only manifested at an advanced stage of the disease.[3]

There are few definitions from medical textbooks or national guidelines published providing a precise cancer-specific definition of an early symptom. The NICE guidelines for suspected cancer[35] are a comprehensive referral guide for primary care physicians. They categorise cancer symptoms according to level of urgency of referral. Summerton[36] published a textbook on diagnosis of cancer in primary care that describes symptoms presenting in primary care settings that could be considered to be early symptoms.

Analysis of population-based data from the UK has shown evidence for a very significant increased risk for particular cancer types (urinary tract, respiratory tract, oesophagus, colorectal) being detected after presentation with first symptoms such as haematuria, haemoptysis, dysphagia, and rectal bleeding frequently encountered in primary care.[37]

On the basis of current medical evidence, reference guides and the medical literature, Table 1 summarises cancers for which early diagnosis is applicable together with clinical symptoms that are usually ascribed to earlier presentation in cancer patients.

Early diagnosis is less applicable for cancers which present and develop symptoms generally at an advanced stage of the disease and thus have a low relative survival. Among them are lung cancers, which show unexplained or persistent symptoms such as chest pain, dyspnoea, hoarseness, finger clubbing, cough, haemoptysis.[35,38,41] In absence of clear symptoms, cancers of the liver also have a low survival and if symptoms such as hypoglycaemia, intraperitoneal haemorrhage, raised serum alpha-fetoprotein, ascites or hepatomegalia[38] appear, the disease is often in an advanced stage. This is similar for cancers of the upper gastrointestinal tract such as stomach cancer. The most common symptoms being reported for these cancers are unexplained weight loss, upper abdominal pain, upper abdominal mass, obstructive jaundice, persistent vomiting, iron deficiency anaemia and dysphagia.[35,37,38,41]

4. Impact of awareness intervention on cancer outcome

Education of the public and health care providers on early cancer signs is part of the early detection approach but there have

Table 1 – Possible early symptoms for specific cancers in adults.

Cancer type(s)	Earlier symptoms	Symptoms associated with later stage
Breast	– Discrete, hard lump in breast[35] – Thickening in breast or armpit[38]	– Nipple/skin retraction, nipple discharge, axillary lump[38]
Gynaecological	– Vaginal bleeding (postcoital, intermenstrual, postmenopausal)[35,38] – Discharge[35,38,41]	– Palpable abdominal or pelvic mass[35] – Low back/abdominal pain, rectal and bladder symptoms (mostly ovarian cancer)[35,38,41]
Lower gastrointestinal tract (colorectal, anal)	Bleeding symptoms: – Rectal bleeding[6,9,32,35–38,40] – Iron-deficiency anaemia[32,35,36] Abdominal symptoms: – Change in bowel habits (persisting > 6 weeks)[6,35,36,40] – Abdominal pain[6,36,40] Systemic symptoms: – Unexplained weight loss[6,36,38] – Obstruction[38,39,41]	– Severe abdominal pain (from intestinal obstruction or perforation), ascites[38]
Prostate	– Urinary frequency, irregular urine flow, hesitancy, strong urine sensation combined with difficulty starting urination[38]	– Dull pain in lower pelvic area, pathologic fracture or bone pain from metastatic disease, swelling in legs due to disease spread[38]
Urinary bladder	– Haematuria[35,37,38,41] – Recurrent or persistent urinary tract infection associated with haematuria[35] – Less common: pain, frequent and difficult urination[38]	– Pallor from renal impairment or cachexia,[38] flank pain[41]
Testicular	– One sided testicular swelling[35,38] – Heavy or dragging feeling in scrotum[38] – Haematuria[41] – Mass in the body of the testis[35]	
Skin	– Change in size, colour and shape of existing mole[35,38] – Irregular shape and colour, itching or bleeding mole, inflammation[35,38]	– Enlarged nodes (lumps) in skin drainage area – e.g. axilla for arm, groin for leg
Head and neck	– Neck lump, painful throat, difficulty swallowing, unilateral otalgia[9,35,38,41]	– Masses (enlarged nodes) in neck
Larynx	– Hoarse voice[35,38,41]	– Dysphagia (pharyngeal involvement), otalgia[38,41]
Mouth, oral cavity	– Ulceration of oral mucosa (>3 weeks)[35,38,41] – Red and white patches of oral mucosa that are swollen, painful or bleeding[35,38,41]	– Masses (enlarged nodes) in neck
Thyroid	Swelling associated with either: – Increasing solitary nodule[35] – History of neck irradiation[35] – Hoarseness[35] – Cervical lymphadenopathy[35]	– Tracheal compression including stridor associated with thyroid swelling[35]
Haematological	Combinations of – Fatigue, night sweats, fever, weight loss, breathlessness, generalised itching, bruising, bleeding, recurrent infections, pain (bone, alcohol-induced, abdominal), lymphadenopathy[35]	– Spinal cord compression, renal failure[35]
Retinoblastoma	– Leukocoria[41]	– Invasion of optic nerve[41]

been few investigations on the impact of awareness campaigns on cancer outcomes. The assessment of a newspaper campaign to raise awareness of faecal blood as a possible sign of colorectal cancer indicated that the campaign would lead to more detection of early colorectal cancer cases since there were a number of neglected faecal bleeders in the population.[42] A prostate cancer awareness programme in the US resulted in a more favourable stage distribution among prostate cancer patients compared to the US national average[43] and a commu-

nity-based education programme raised women's awareness about cervical cancer in general and screening.[44]

One large study involving a control group assessed the efficacy of home letters for promoting early detection of gastro-oesophageal cancers. A marked improvement in resection rate and curability of gastro-oesophageal cancer was shown; however, survival was not affected.[45]

The lack of awareness of significance of symptoms is considered to be one of the most important causes for a delay of

diagnosis.[46,47] Other studies have also reported that non-recognition of symptom seriousness, unpleasant investigations, and the hope for spontaneous resolutions of symptoms are common reasons for delays in diagnosis.[39,48] The awareness and perception of cancer symptoms is related to socio-economic variables. Those individuals of lower social class and with fewer educational qualifications have been shown to have poorer knowledge of colorectal cancer[49] and breast cancer symptoms.[50]

Cancer survival has been reported to be dependent on social status for many cancer types with stage at diagnoses being an important factor.[48] In Denmark, cancer patients of higher SES were found to have higher relative survival partly due to earlier diagnosis compared to those of lower SES.[51,52] Several SES indicators were significantly associated with delay in colorectal cancer treatment in a study in Germany.[39] Population-based data from the UK also indicate longer delay of diagnosis and treatment among those of lower SES compared to higher SES groups[53] and women of lower SES showed a higher likelihood of having an advanced stage breast or cervical cancer diagnosis than higher social class women.[54,55]

Raising awareness may be the most feasible and cost-effective strategy for LMICs to reduce the proportion of people with a late stage cancer diagnosis provided the availability of treatment services. However, there is no evidence published on the impact of such programmes on cancer outcomes, which would support advocacy in this field.

5. Discussion

Early cancer detection is a key part of national comprehensive cancer control and can be promoted in every country.[56] However, several considerations have to be taken into account in promoting early cancer diagnosis and there are some limitations to this approach.

First, the effect of early diagnosis is mediated by the stage of disease when definite diagnosis is made and treatment is provided. Early detection may thus be effective due to its association with a limited spread of the tumour at diagnosis, but it could also be influenced by a short interval between clinical onset of disease and diagnosis.

Secondly, the importance of early diagnosis greatly depends on the cancer type and the incidence of a particular cancer. Less aggressive and slower growing tumours may exist for longer periods without creating symptoms than rapidly growing aggressive tumours. In case of a high proportion of aggressive tumours, a benefit for survival may not be seen for early stages.[4] For some cancers, such as of the liver and pancreas and for mesothelioma, survival is rather low, independent of an early diagnosis with a localised tumour.[12] Diagnosis at an advanced stage of disease, on the other hand, did not lead to a lower survival in the case of Hodgkin's disease and testicular cancer.[12]

A third factor to be taken into consideration when promoting early diagnosis is the context of the health care system, which determines the availability of devices and capacity for assessing cancer stage (e.g. endoscopies, imaging techniques, tumour markers), and human resources. Most of the studies on early-stage diagnosis and cancer survival were conducted in high income countries of Europe and in the US where recent developments and utilisation of diagnostic techniques may have led to differential time trends in cancer survival. In adopting the high technology of these countries to LMICs, cost-effectiveness and coverage of the population are important criteria.

One difficulty is that if early diagnosis programmes are successful, survival may simply increase because of a lead time effect. This may well have occurred when breast cancer mortality results remained stable in the US and Canada in spite of clear indications that size at detection was being reduced, together with increasing utilisation of breast conserving therapy. It was not until adjuvant chemotherapy and tamoxifen was introduced that breast cancer mortality started to decline.[57]

Given these possible limitations of early diagnosis, there is a clear need for research to show how useful a symptom is at predicting cancer and which symptoms will rule out cancer.[11] The cancers and symptoms presented for early diagnosis in this paper are selected on the basis of the medical literature. None of the published information provided a categorisation of cancers eligible and useful for early diagnosis with respective early symptoms, which would be highly valuable for the comparability of studies in this field.

6. Conclusion

A reduction in cancer deaths is a health care priority and efforts in down-staging cancer can significantly increase cancer survival for many cancer sites such as of the breast, cervix, skin, oral, prostate, and possibly of the lung, stomach, liver and bladder. However, generally low attention is paid to early diagnosis or the need for cultural-sensitive approaches to early cancer detection which take country-specific priorities, socio-economic differences and the health system context into account.

Cancer control requires substantial public health interventions. In the long term, primary prevention will lead to a reduction in cancer incidence. However, in the short term, a reduction in cancer mortality will require improvements in early detection and treatment. This creates the need for new resources in many countries, or the reallocation of currently used resources on expensive forms of tertiary care, to early detection at the primary care level and improved diagnosis and treatment at the secondary care level.

Planning and provision of medical services for cancer and other non-communicable diseases has so far not been seen as central in primary care. However, despite the barriers for delivering cancer care at the primary care level, early recognition is particularly relevant in the context of primary care, where many patients present with symptoms suggestive of cancer. The detection of many cancer types can be integrated into primary care services in low resource countries since they are cost-effective and some do not require diagnostic facilities of high technology, such as in the case of inspection of the mouth and breast palpation.

In order to evaluate means to improve early detection, further studies providing evidence for the percentage of cancers being diagnosed at an advanced stage are required as well as the evaluation of early detection programmes.

To reduce the overall cancer burden, steps need to be taken to improve the impact of early diagnosis, which will

require the work of health care practitioners at the primary care level to be supported by the leaders of health care in respective countries and by responsible politicians. In some countries, medical scientists can re-enforce these activities by facilitating research into ways necessary to raise the consciousness of cancer in the general population.

Addressing the reasons for late cancer diagnosis is a particular challenge for primary care, which is usually the patient's first contact with the health system and the area to which the delay is applicable. This also involves significant challenges for practitioners in assessing cancer symptoms to avoid misdiagnoses that contribute to delays.[48]

Conflict of interest statement

None declared.

REFERENCES

1. Strong K, Mathers C, Epping-Jordan J, Resnikoff S, Ullrich A. Preventing cancer through tobacco and infection control: how many lives can we save in the next 10 years? *Eur J Cancer Prev* 2008;**17**:153–61.
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* 2006;**3**:e442.
3. World Health Organization. Cancer control. Knowledge into action. WHO Guide for effective programmes: early detection. Geneva: World Health Organization; 2007.
4. Austin DF, Dunn JE. Cancer symptoms, clinical stage, and survival rates. *Am J Public Health* 1980;**70**:474–5.
5. Vakil N, Moayyedi P, Fennerty MB, Talley NJ. Limited value of alarm features in the diagnosis of upper gastrointestinal malignancy: systematic review and meta-analysis. *Gastroenterology* 2006;**131**:390–401.
6. Keddie N, Hargreaves A. Symptoms of carcinoma of the colon and rectum. *Lancet* 1968;**292**:749–50.
7. Korsgaard M, Pedersen L, Sorensen HT, Laurberg S. Delay of treatment is associated with advanced stage of rectal cancer but not of colon cancer. *Cancer Detect Prev* 2006;**30**:341–6.
8. Curless R, French J, Williams GV, James OF. Comparison of gastrointestinal symptoms in colorectal carcinoma patients and community controls with respect to age. *Gut* 1994;**35**:1267–70.
9. Pitchers M, Martin C. Delay in referral of oropharyngeal squamous cell carcinoma to secondary care correlates with a more advanced stage at presentation, and is associated with poorer survival. *Br J Cancer* 2006;**94**:955–8.
10. Pontén J, Adami HO, Bergström R, et al. Strategies for global control of cervical cancer. *Int J Cancer* 1995;**60**:1–26.
11. Summerton N. General practitioners and cancer: primary care oncology needs more research if it is to develop. *BMJ* 2000;**320**:1090–1.
12. Teppo L, Dickman PW, Hakulinen T, et al. Cancer patient survival – patterns, comparisons, trends – a population-based Cancer Registry study in Finland. *Acta Oncol* 1999;**38**:283–94.
13. Carter CL, Allen C. Henson. Relation of tumour size, lymph node status, and survival in 24, 740 breast cancer cases. *Cancer* 1989;**63**:181–7.
14. Maguire A, Porta M, Malats N, et al. Cancer survival and the duration of symptoms. An analysis of possible forms of the risk function. *Eur J Cancer* 1994;**30**:785–92.
15. Porta M, Gallén M, Malats N, Planas J. Influence of "diagnostic delay" upon cancer survival: an analysis of five tumour sites. *J Epidemiol Community Health* 1991;**45**:225–30.
16. Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. Influence of delay on survival in patients with breast cancer: a systematic review. *Lancet* 1999;**353**:1119–26.
17. Sant M, Allemani C, Capocaccia R, et al. Stage at diagnosis is a key explanation of differences in breast cancer survival across Europe. *Int J Cancer* 2003;**106**:416–22.
18. Horn LC, Fischer U, Raptis G, Bilek K, Hentschel B. Tumor size is of prognostic value in surgically treated FIGO stage II cervical cancer. *Gynecol Oncol* 2007;**107**:310–5.
19. Barchielli A, Amorosi A, Balzi D, Crocetti E, Nesi G. Long-term prognosis of gastric cancer in a European country: a population-based study in Florence (Italy). 10-year survival of cases diagnosed in 1985–1987. *Eur J Cancer* 2001;**37**:1674–80.
20. Gann PH. Interpreting recent trends in prostate cancer incidence and mortality. *Epidemiology* 1997;**8**:117–20.
21. Vis AN, Roemeling S, Reedijk AM, Otto SJ, Schröder FH. Overall survival in the intervention arm of a randomized controlled screening trial for prostate cancer compared with a clinically diagnosed cohort. *Eur Urol* 2008;**53**:91–8.
22. Wang JH, Changchien CS, Hu TH, et al. The efficacy of treatment schedules according to Barcelona Clinic Liver Cancer staging for hepatocellular carcinoma – survival analysis of 3892 patients. *Eur J Cancer* 2008;**44**:1000–6.
23. Hellsten S, Ljungerud G, Glifberg I. Bladder carcinoma. Long-term survival and late recurrence. *Scand J Urol Nephrol* 1983;**17**:57–61.
24. Kirsner RS, Wilkinson JD, Ma F, Pacheco H, Federman DG. The association of Medicare health care delivery systems with stage at diagnosis and survival for patients with melanoma. *Arch Dermatol* 2005;**141**:753.
25. Sargeran K, Murtomaa H, Safavi SM, Vehkalahti MM, Teronen O. Survival after diagnosis of cancer of the oral cavity. *Br J Oral Maxillofac Surg* 2008;**46**:187–91.
26. Subramanian S, Sankaranarayanan R, Bapat B, et al. Cost-effectiveness of oral cancer screening: results from a cluster randomized controlled trial in India. *Bull World Health Organ* 2009;**87**:200–6.
27. Cicollalo L, Capocaccia R, Coleman MP, et al. Survival differences between European and US patients with colorectal cancer: role of stage at diagnosis and surgery. *Gut* 2005;**54**:268–73.
28. Ponz de Leon M, Benatti P, Di Gregorio C, et al. Staging and survival of colorectal cancer: are we making progress? The 14-year experience of a specialized cancer registry. *Dig Liver Dis* 2000;**32**:312–7.
29. Gonzalez-Hermoso F, Perez-Palma J, Marchena-Gomez J, Lorenzo-Rocha N, Medina-Arana V. Can early diagnosis of symptomatic colorectal cancer improve the prognosis? *World J Surg* 2004;**28**:716–20.
30. Olsson L, Bergkvist L, Exbom A. Symptom duration versus survival in non-emergency colorectal cancer. *Scand J Gastroenterol* 2004;**39**:252–8.
31. Ramos M, Esteva M, Cabeza E, Llobera J, Ruiz A. Lack of association between diagnostic and therapeutic delay and stage of colorectal cancer. *Eur J Cancer* 2008;**44**:510–21.
32. Stapley S, Peters TJ, Sharp D, Hamilton W. The mortality of colorectal cancer in relation to the initial symptom at presentation to primary care and to the duration of symptoms: a cohort study using medical records. *Br J Cancer* 2006;**95**:1321–5.
33. Arbman G, Nilsson E, Störgren-Fordell V, Sjödahl R. A short diagnostic delay is more important for rectal cancer than for colonic cancer. *Eur J Surg* 1966;**162**:899–904.
34. Wittekind Ch, Sobin LH. TNM classification of malignant tumours. New York: Wiley-Liss; 2002.

35. NICE. National Institute for Health and Clinical Excellence. Referral guidelines for suspected Cancer. London: NICE; 2005.

36. Summerton N. Diagnosing cancer in primary care. Radcliffe Medical Press; 1999.

37. Jones R, Latinovic R, Charlton J, Gulliford M. Alarm symptoms in early diagnosis of cancer in primary care: cohort study using General Practice Research Database. *BMJ* 2007;**334**:1040.

38. Barr L, Cowan R, Nicolson M. Oncology. 2nd ed. Edinburgh: Elsevier; 2004.

39. Langenbach R, Schmidt J, Neumann J, Zirngibl H. Delay in treatment of colorectal cancer: multifactorial problem. *World J Surg* 2003;**27**:304–8.

40. Barret J, Jiwa M, Rose P, Hamilton W. Pathways to the diagnosis of colorectal cancer: an observational study in three UK cities. *Fam Pract* 2006;**23**:15–9.

41. Schmoll HJ, Höffken K, Possinger K, editors. Kompendium internistische onkologie. Standards in diagnostik und therapie. Teil 2. 4. Auflage. Heidelberg: Springer; 2006.

42. Hákkinen IP, Nylamo EI, Sóderstróm KO. The importance of self-observation of fecal blood in indicating a proper bowel examination. *Cancer Detect Prev* 1997;**21**:267–72.

43. DeAntoni E, Crawford ED, Stone NN, et al. Prostate Cancer Awareness Week, 1992: a summary of key findings. *Clin Invest Med* 1993;**16**:448–57.

44. Michielutte R, Dignan MB, Wells HB, Young LD, Jackson DS, Sharp PC. Development of a community cancer education program: the Forsyth County, NC cervical cancer prevention project. *Public Health Rep* 1989;**104**:542–51.

45. McCulloch P, Brown P, Martin B, Williams E. The effects of an awareness-raising program for patients and primary care physicians on the early detection of gastro-oesophageal cancer. *Surgery* 2003;**133**:154–61.

46. Arvanitakis C, Nikopoulos A, Giannoulis E, Theoharidis A, Georgilas V, Fotiou H. The impact of early or late diagnosis on patient survival in gastric cancer in Greece. *Hepato-Gastroenterology* 1992;**39**:355–7.

47. Rothwell JF, Feehan E, Reid I, Walsh TN, Hennessy TP. Delay in treatment for oesophageal cancer. *Br J Surg* 1997;**84**:690–3.

48. Macdonald S, Macleod U, Campbell NC, Weller D, Mitchell E. Systematic review of factors influencing patient and practitioner delay in diagnosis of upper gastrointestinal cancer. *Br J Cancer* 2006;**94**:1272–80.

49. Yardley C, Glover C, Allen-Mersh TG. Demographic factors associated with knowledge of colorectal cancer symptoms in a UK population-based survey. *Ann R Coll Surg Engl* 2000;**82**:205–9.

50. Linsell L, Burgess CC, Ramirez AJ. Breast cancer awareness among older women. *Br J Cancer* 2008;**99**:1221–5.

51. Dalton SO, Schüz J, Engholm G, et al. Social inequalities in incidence of survival from cancer in a population-based study in Denmark, 1994–2003: summary of findings. *Eur J Cancer* 2008;**44**:2074–86.

52. Hansen HP, Olesen F, Sorensen HT, Sokolowski I, Sondergaard J. Socioeconomic patient characteristics predict delay in cancer diagnosis: a Danish cohort study. *BMC Health Serv Res* 2008;**8**:49.

53. Neal RD, Allgar VL. Sociodemographic factors and delays in the diagnosis of six cancers: analysis of data from the National Survey of NHS Patients: Cancer. *Br J Cancer* 2005;**92**:1971–5.

54. Mandelblatt J, Andrews H, Kerner J, Zauber A, Burnett W. Determinants of late stage diagnosis of breast and cervical cancer: the impact of age, race, social class and hospital type. *Am J Public Health* 1991;**81**:646–9.

55. Richardson JL, Langholz B, Bernstein L, Burciaga C, Danley K, Ross RK. Stage and delay in breast cancer diagnosis by race, socioeconomic status, age and year. *Br J Cancer* 1992;**65**:922–6.

56. World Health Organization. *National cancer control programmes. Policies and managerial guidelines*. Geneva: World Health Organization; 1993.

57. Jatoi I, Miller AB. Why is breast cancer mortality declining? *Lancet Oncol* 2003;**4**:251–4.