

Full Paper

Risk factors for delayed presentation and referral of symptomatic cancer: evidence for common cancers

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BACKGROUND: It has been suggested that the known poorer survival from cancer in the United Kingdom, compared with other European countries, can be attributed to more advanced cancer stage at presentation. There is, therefore, a need to understand the diagnostic process, and to ascertain the risk factors for increased time to presentation.

METHODS: We report the results from two worldwide systematic reviews of the literature on patient-mediated and practitioner-mediated delays, identifying the factors that may influence these.

RESULTS: Across cancer sites, non-recognition of symptom seriousness is the main patient-mediated factor resulting in increased time to presentation. There is strong evidence of an association between older age and patient delay for breast cancer, between lower socio-economic status and delay for upper gastrointestinal and urological cancers and between lower education level and delay for breast and colorectal cancers. Fear of cancer is a contributor to delayed presentation, while sanctioning of help seeking by others can be a powerful mediator of reduced time to presentation. For practitioner delay, 'misdiagnosis' occurring either through treating patients symptomatically or relating symptoms to a health problem other than cancer, was an important theme across cancer sites. For some cancers, this could also be linked to inadequate patient examination, use of inappropriate tests or failing to follow-up negative or inconclusive test results.

CONCLUSION: Having sought help for potential cancer symptoms, it is therefore important that practitioners recognise these symptoms, and examine, investigate and refer appropriately.

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The possible influence of delays in diagnosis on survival and the risk factors for delay in patients with cancer have been the subject of considerable interest and controversy for many years. Survival from cancer in the United Kingdom is poorer than that of other European countries, and it has been suggested that this can be attributed to more advanced disease stage at presentation (Cancer Research UK, 2009). Consequently, there is a need to understand the diagnostic process, and to ascertain risk factors related to increased time to presentation and treatment. This is particularly relevant in the context of primary care, where many patients present with symptoms that may be indicative of cancer, but where the outcome of the diagnostic process is the exclusion of cancer in most cases. Furthermore, in countries with strong primary healthcare systems, such as the United Kingdom, this is typically the first point of contact for the majority of patients, making early recognition of cancer symptoms even more pertinent.

Minimising time to diagnosis of cancer is dependent on patients presenting with potential cancer symptoms and on primary care practitioners responding appropriately to those symptoms, either by arranging further investigation and/or referring for specialist input. Delay can occur at three phases during the diagnostic process: first, in the interval between the patient first noticing a symptom and first consulting a doctor (often referred to as patient

delay), second, between first consultation and referral by a practitioner (doctor or practitioner delay) and finally, between referral and diagnosis (hospital or system delay) (Nichols *et al*, 1981).

In addition to outlining the various points during which extraneous factors might adversely influence time to presentation and referral, considering delay in these phases enables identification of areas where interventions designed to reduce delay might be targeted. However, before such interventions can be developed, we need to better understand the factors that might lengthen or shorten the time taken by patients to seek help for symptoms and gain greater insights into how practitioners (usually in primary care) respond to these symptoms. This topic is not easily amenable to study by randomised trial, and as such, interpreting data available from observational studies is essential to increasing our understanding of the risk factors associated with delay and to facilitating development of effective new strategies to reduce the time involved. If longer delays do impact on survival, as has been shown for breast cancer (Richards *et al*, 1999), such strategies could save a significant number of lives.

MATERIALS AND METHODS

We report results from two systematic reviews of the world literature. The first relates specifically to breast cancer (Ramirez *et al*, 1999; Westcombe *et al*, 1999). The second covers other

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common cancers, namely colorectal, gynaecological, lung, upper gastrointestinal and urological (Macdonald *et al*, 2004, 2006; Mitchell *et al*, 2008). Both of these reviews described the extent of patient-mediated and practitioner-mediated delays and identified the factors that may cause such delays. The breast cancer literature was reviewed from 1966 to 1997, and 23 studies met the inclusion criteria; all were assessed as being of sufficient quality for inclusion (Ramirez *et al*, 1999). Literature relating to the other cancers was reviewed from 1970 to 2003, and 54 studies met the inclusion criteria for colorectal cancer (45 sufficient quality), 16 for gynaecological cancers (12 sufficient quality), 8 for lung cancer (4 sufficient quality), 25 for upper gastrointestinal cancers (18 sufficient quality) and 16 for urological cancers (11 sufficient quality). Taken together, therefore, 142 papers were reviewed, of which 113 were deemed of sufficient quality for inclusion in the analyses. Detailed methods of each review are described elsewhere, including the process of determining quality (Westcombe *et al*, 1999; Macdonald *et al*, 2004). This paper reports on and discusses risk factors for patient and primary care practitioner delay. It combines and summarises earlier reported results for breast, colorectal and upper gastrointestinal cancers, with previously unreported results for gynaecological, lung and urological cancers. Only risk factors derived from studies of sufficient quality are presented; these are reported as either increasing or reducing delay or as inconclusive, that is the evidence was neither in support of the factor predominately increasing nor reducing delay, and as such, the direction of influence cannot be determined definitively.

Terminology

The term 'delay' in the cancer literature is used both to refer to time delays and to denote advanced stage at presentation. More recently, authors have tended to avoid use of the word delay, not only because of this confusion, but also because the term implies an active decision for inaction. However, the term is used extensively in the literature and as such is impossible to avoid in a report of this nature. Any reference to delay in this paper refers to time delay.

RESULTS

Risk factors for patient delay

Demographic factors Several demographic factors have been studied in relation to their association with presentation for cancer symptoms.

Age Older patient age was found to be a risk factor for delayed presentation with symptoms of breast cancer (Ramirez *et al*, 1999), but was unrelated to delay for colorectal cancer (Mitchell *et al*, 2008), urological cancers (Thornhill *et al*, 1987; Samet *et al*, 1988; Mansson *et al*, 1993; Risberg *et al*, 1996) and lung cancer (Worden and Weisman, 1975; Mor *et al*, 1990; Risberg *et al*, 1996). There was no conclusive evidence in relation to the influence of age on presentation with symptoms of upper gastrointestinal (Macdonald *et al*, 2006) or gynaecological cancers (Fruchter *et al*, 1980; Franceschi *et al*, 1983; Fowler *et al*, 1984; Smith and Anderson, 1985; Dhamija *et al*, 1993; Andersen *et al*, 1995; Coates *et al*, 1996; Risberg *et al*, 1996; Jones and Joura, 1999; Goff *et al*, 2000) (Tables 1 and 3–5).

Gender Overall, men were found to delay longer than women in presenting with bladder cancer (Mommensen *et al*, 1983; Mansson *et al*, 1993; Risberg *et al*, 1996) and with other urological cancers (Risberg *et al*, 1996). There was little evidence of any association between sex and time to presentation for either upper or lower gastrointestinal cancers (Macdonald *et al*, 2006; Mitchell *et al*, 2008) or for lung cancer (Worden and Weisman, 1975; Mor *et al*, 1990; Risberg *et al*, 1996; Bowen and Rayner, 2002).

Socio-economic status and education Lower socio-economic status was associated with increased delay by patients presenting with symptoms of upper gastrointestinal cancers (Macdonald *et al*, 2006) and by men with prostate cancer (Hackett *et al*, 1973; Samet *et al*, 1988; Fitzpatrick *et al*, 1998). However, there was no overall relationship between socio-economic status and delay for colorectal cancer (Mitchell *et al*, 2008), gynaecological cancers (Fruchter *et al*, 1980; Fowler *et al*, 1984; Andersen *et al*, 1995; Coates *et al*, 1996; Goff *et al*, 2000) or lung cancer (Hackett *et al*, 1973; Worden and Weisman, 1975; Mor *et al*, 1990). Similarly, although lower educational attainment was associated with greater delay for patients with breast (Ramirez *et al*, 1999) and colorectal cancers (Mitchell *et al*, 2008), it was not related to presentation for any of the urological (Mansson *et al*, 1993; Risberg *et al*, 1996) or gynaecological cancers (Fruchter *et al*, 1980; Franceschi *et al*, 1983; Dhamija *et al*, 1993; Andersen *et al*, 1995; Risberg *et al*, 1996) or for lung cancer (Mor *et al*, 1990; Risberg *et al*, 1996).

Ethnicity Non-white ethnic origin was a risk factor for longer delay in presenting with breast (Ramirez *et al*, 1999) and urological cancers (bladder and prostate) (Samet *et al*, 1988; Prout *et al*, 2000), but non-white patients were found to have a shorter time to presentation for stomach cancer (Macdonald *et al*, 2006). No association was found between ethnicity and time to presentation for gynaecological cancers (cervical and uterine) (Fruchter *et al*, 1980; Fowler *et al*, 1984; Coates *et al*, 1996).

Marital status Marital status or living with a partner was found to be unrelated to presentation patterns for breast, gynaecological, lung, upper gastrointestinal and urological cancers (Worden and Weisman, 1975; Franceschi *et al*, 1983; Thornhill *et al*, 1987; Mor *et al*, 1990; Mansson *et al*, 1993; Andersen *et al*, 1995; Fitzpatrick *et al*, 1998; Ramirez *et al*, 1999; Macdonald *et al*, 2006). It was not possible to draw a definitive conclusion in relation to its influence on colorectal cancer (Mitchell *et al*, 2008).

Clinical factors

Symptom type The type of symptoms with which patients present has a marked impact on presenting behaviour (Tables 1 and 3–5). Women diagnosed with breast cancer were more likely to delay if they had an atypical symptom, that is one that did not include a breast lump (Ramirez *et al*, 1999). Across the cancer groups, patients were typically less likely to delay if they experienced a more serious symptom, such as pain, or an alarming symptom, such as bleeding. This was found to be the case for upper gastrointestinal cancers (Macdonald *et al*, 2006) and gynaecological cancers (Smith and Anderson, 1985, 1987; Menon *et al*, 1991; Coates *et al*, 1996; Goff *et al*, 2000) for pain associated with colorectal cancer (Mitchell *et al*, 2008) and for bleeding associated with urological cancers (bladder and prostate) (Mansson *et al*, 1993; Fitzpatrick *et al*, 1998; Ho *et al*, 1998). Conversely, pain was a risk factor for increased delay in patients with urological cancers (Hackett *et al*, 1973; Attard, 1985; Mansson *et al*, 1993; Fitzpatrick *et al*, 1998), whereas the evidence for lung cancer was inconclusive (Hackett *et al*, 1973; Worden and Weisman, 1975). Perhaps, unsurprisingly, the onset of vague, non-specific, more common or multiple symptoms was likely to increase delay (Andersen *et al*, 1995; Goff *et al*, 2000; Fitch *et al*, 2002; Mitchell *et al*, 2008). For the majority of cancer groups studied, patients were more likely to present when symptoms were, or became, more incapacitating and impacted on daily life and activities (Hackett *et al*, 1973; Menon *et al*, 1991; Andersen *et al*, 1995; Sanden *et al*, 2000; Macdonald *et al*, 2006; Mitchell *et al*, 2008).

Co-morbidity The presence of co-existing morbidity was associated with reduced delay in patients with upper gastrointestinal cancers (Macdonald *et al*, 2006) and colorectal cancer (Mitchell *et al*, 2008). However, this was found to be unrelated to presenting

behaviour for lung cancer (Mor *et al*, 1990). There was evidence that regular visits to medical practitioners, including attendance for routine screening, was associated with shorter delay in patients with gynaecological cancers (uterine and cervical) (Menon *et al*, 1991; Coates *et al*, 1996) and prostate cancer (Samet *et al*, 1988; Fitzpatrick *et al*, 1998). The impact of a personal or family history of cancer on help-seeking behaviour was investigated across several sites, and in the main, there was no conclusive evidence as to its impact. However, for patients with prostate cancer, having had a previous cancer diagnosis (Samet *et al*, 1988) or having a relative with cancer (Hackett *et al*, 1973; Fitzpatrick *et al*, 1998) was typically associated with reduced time to presentation. Furthermore, there was evidence of a positive relationship between increased delay and having previously had a normal test result or the condition diagnosed as benign (Fruchter *et al*, 1980; Smith and Anderson, 1985).

Psychosocial factors

Awareness and interpretation of symptoms Symptom awareness, and more particularly patients' interpretation of symptoms, was a commonly reported theme. Non-recognition of the seriousness of symptoms, sometimes related to lack of knowledge about the disease, was the predominant risk factor for delay reported across all cancer sites (Worden and Weisman, 1975; Fruchter *et al*, 1980; Bosl *et al*, 1981; Attard, 1985; Smith and Anderson, 1985, 1987; Cochran *et al*, 1986; Mor *et al*, 1990; Menon *et al*, 1991; Mansson *et al*, 1993; Andersen *et al*, 1995; Coates *et al*, 1996; Ajayi and Adewole, 1998; Gascoigne *et al*, 1999; Ramirez *et al*, 1999; de Nooijer *et al*, 2001; Bowen and Rayner, 2002; Fitch *et al*, 2002; Khadra and Oakeshott, 2002; Kidanto *et al*, 2002; Macdonald *et al*, 2006; Mitchell *et al*, 2008) (Tables 1 and 3–5). Delay was often related to patients adopting a 'wait and see' approach, denying or redefining their symptoms in relation to benign disease or self-diagnosing and self-medicating before presentation to a practitioner (Macdonald *et al*, 2006; Mitchell *et al*, 2008).

Emotional response Concern related to recognition of a potential cancer symptom was also important in the decision to present. Fear that a symptom was indicative of cancer, or fear of

investigation, of treatment, or of powerlessness were also found to be factors in increasing time to presentation for upper and lower gastrointestinal cancers (Macdonald *et al*, 2006; Mitchell *et al*, 2008), urological cancers (Hackett *et al*, 1973; Fitzpatrick *et al*, 1998; Ho *et al*, 1998; de Nooijer *et al*, 2001; Sanden *et al*, 2000), gynaecological cancers (Fruchter *et al*, 1980; Smith and Anderson, 1985, 1987) and lung cancer (Hackett *et al*, 1973; Worden and Weisman, 1975; Mor *et al*, 1990). Similarly, embarrassment about symptoms resulted in longer delay for patients with colorectal (Mitchell *et al*, 2008) and urological cancers (testicular and prostate) (Fitzpatrick *et al*, 1998; Gascoigne *et al*, 1999).

Support Social support and the availability of advice were influential factors in patients' decisions to present with cancer symptoms. Patients with breast cancer, who did not disclose their symptoms within a week to someone close to them, were more likely to delay help seeking (Ramirez *et al*, 1999). For patients with colorectal cancer, social networks were identified as a potentially important factor in reducing delay, when patients either sought advice from or made decisions based on the experience of others (Mitchell *et al*, 2008). In keeping with this, lower levels of social support were found to be associated with increased delay in women with endometrial cancer (Cochran *et al*, 1986) (Table 1). However, the availability of social support was unrelated to delay for lung, upper gastrointestinal and urological cancers (Samet *et al*, 1988; Mor *et al*, 1990; Bowen and Rayner, 2002; Sanden *et al*, 2000; Macdonald *et al*, 2006).

Risk factors for practitioner delay

Patient demographic factors There was some evidence relating to the impact of certain patient characteristics on practitioners' referral behaviour (Tables 2–5).

Age and gender Older patients were referred more quickly for symptoms of breast, upper gastrointestinal and colorectal cancers (Ramirez *et al*, 1999; Macdonald *et al*, 2006; Mitchell *et al*, 2008). However, younger patients experienced less delay in referral when presenting with symptoms related to one of the urological cancers

Table 1 Risk factors for patient-mediated delay

Risk factor	Breast	Upper GI ^a	Colorectal	Uro ^b	Gyn ^c	Lung
<i>Demographic</i>						
Age (older)	↑	⊖	=	=	⊖	=
Sex (male)	N/A	=	=	↑	N/A	=
Socio-economic status (lower)	⊖	↑	=	↑	=	=
Education level (lower)	↑	⊖	↑	=	=	=
Ethnicity (non-white origin)	↑	↓	⊖	↑	=	⊖
Marital status (married/co-habiting)	=	=	⊖	=	=	=
<i>Clinical</i>						
Symptom type	↑	↑	↑	↑	↑	⊖
Symptom – pain	◇	↓	↓	↑	↓	⊖
Symptom – bleeding	◇	↓	⊖	↓	↓	⊖
Symptom impacts on daily life	⊖	↓	↓	↓	↓	↓
Co-morbidity	⊖	↓	↓	⊖	⊖	=
Infrequent care seeking	⊖	⊖	⊖	↑	↑	⊖
Personal/family history of cancer	⊖	⊖	⊖	↓	⊖	⊖
<i>Psychosocial</i>						
Non-recognition of symptom seriousness	↑	↑	↑	↑	↑	↑
Fear	⊖	↑	↑	↑	↑	↑
Embarrassment	⊖	⊖	↑	↑	⊖	⊖
Social support/advice	↓	=	↓	=	↓	=

Abbreviation: GI = gastrointestinal. Key: ↑ increases delay; ↓ reduces delay; = no impact on delay; ⊖ inconclusive evidence; ⊖ lacking evidence; ◇ any non-lump symptom. Risk factor included only if supported by studies providing strong or moderate levels of evidence (Sources: Ramirez *et al*, 1999; Macdonald *et al*, 2004, 2006; Mitchell *et al*, 2008).

^aDuodenum, oesophagus, pancreas, small intestine, stomach. ^bBladder, kidney, prostate, testes. ^cCervix, endometrium, ovary, uterus, vagina, vulva.

Table 2 Risk factors for practitioner-mediated delay

Risk factor	Breast	Upper GI ^a	Colorectal	Uro ^b	Gyn ^c	Lung
<i>Patient demographics</i>						
Age (older)	↓	↓	↓	↑	⊖	↑
Sex (male)	N/A	↓	⊖	↓	N/A	⊖
Socio-economic status (lower)	⊖	↓	↑	⊖	=	⊖
Education level (lower)	⊖	⊖	⊖	↑	↑	↑
Ethnicity (non-white origin)	↓	⊖	⊖	⊖	=	⊖
<i>Presenting symptom and history</i>						
Symptom – pain	◇	↓	⊖	⊖	↓	⊖
Symptom – bleeding	◇	↓	⊖	↓	⊖	⊖
Co-morbidity	⊖	⊖	↓	⊖	⊖	⊖
Frequent care seeking/multiple providers	⊖	=	↑	⊖	↑	⊖
<i>Practitioner response</i>						
Initial misdiagnosis	↑	↑	↑	↑	↑	⊖
Inadequate examination/inappropriate tests	⊖	↑	↑	↑	↑	⊖
Treatment for benign condition	⊖	↑	⊖	⊖	⊖	⊖
Use of referral guidelines	⊖	↓	↓	⊖	⊖	⊖

Abbreviation: GI = gastrointestinal. Key: ↑ increases delay; ↓ reduces delay; = no impact on delay; ⊖ inconclusive evidence; ⊖ lacking evidence; ◇ any non-lump symptom. Risk factor included only if supported by studies providing strong or moderate levels of evidence (Sources: Ramirez *et al*, 1999; Macdonald *et al*, 2004, 2006; Mitchell *et al*, 2008).

^aDuodenum, oesophagus, pancreas, small intestine, stomach. ^bBladder, kidney, prostate, testes. ^cCervix, endometrium, ovary, uterus, vagina, vulva.

(Mansson *et al*, 1993; Risberg *et al*, 1996) or to lung cancer (Risberg *et al*, 1996). There was no conclusive evidence on the direction of effect for patient age and practitioner delay for gynaecological cancers (Fruchter *et al*, 1980; Fowler *et al*, 1984; Risberg *et al*, 1996). Men with upper gastrointestinal cancers (Macdonald *et al*, 2006) and urological cancer (bladder) (Mommensen *et al*, 1983; Mansson *et al*, 1993) were less likely than women to have experienced delayed referral, although the evidence relating to colorectal cancer was inconclusive (Mitchell *et al*, 2008).

Socio-economic status, education and ethnicity Patients from lower socio-economic groups experienced a shorter wait to referral for upper gastrointestinal cancer (Macdonald *et al*, 2006), but greater delay than more affluent patients in referral for colorectal cancer (Mitchell *et al*, 2008). Although socio-economic status was unrelated to referral for symptoms of gynaecological cancers (Fowler *et al*, 1984; Goff *et al*, 2000), lower educational attainment was associated with delayed referral in this group, as it was for patients with symptoms of lung and urological cancers (Risberg *et al*, 1996). There was little evidence on the influence of ethnicity, although non-white women with breast cancer experienced less practitioner delay (Ramirez *et al*, 1999), whereas this was unrelated to referral for gynaecological cancer (cervical) (Fowler *et al*, 1984).

Presenting symptom and medical history As was the case in patient delay, presenting with a breast symptom other than a lump was associated with greater delay by practitioners (Ramirez *et al*, 1999). Typically, pain as a presenting symptom resulted in shorter time to referral for patients with upper gastrointestinal cancers (Macdonald *et al*, 2006) and gynaecological cancer (ovarian) (Goff *et al*, 2000; Fitch *et al*, 2002). This was also found to be the case for bleeding in upper gastrointestinal cancers (Macdonald *et al*, 2006) and urological cancer (bladder) (Mommensen *et al*, 1983; Mansson *et al*, 1993). Patients with co-existing disease were likely to be referred more quickly for symptoms of colorectal cancer (Mitchell *et al*, 2008), but the evidence relating to upper gastrointestinal cancers was inconclusive (Macdonald *et al*, 2006). However, time to referral for colorectal cancer was increased for patients who frequently consulted their general practitioner (Mitchell *et al*, 2008), and the involvement of multiple care providers resulted in delay for patients with gynaecological cancer (ovarian) (Fowler *et al*, 1984; Goff *et al*, 2000). Frequency of attendance was

unrelated to referral for upper gastrointestinal cancers (Macdonald *et al*, 2006).

Practitioner response The most commonly identified themes associated with delayed referral across the cancer sites related to initial diagnosis and activity of the practitioner. Misdiagnosis, occurring either through treating patients symptomatically or by relating symptoms to a health problem other than cancer, resulted in increased time to referral for breast, colorectal, gynaecological, upper gastrointestinal and urological cancers (Bosl *et al*, 1981; Attard, 1985; Gascoigne *et al*, 1999; Jones and Joura, 1999; Ramirez *et al*, 1999; Goff *et al*, 2000; Fitch *et al*, 2002; Macdonald *et al*, 2006; Mitchell *et al*, 2008). Although there was support for the existence of a similar pattern in relation to diagnosis of lung cancer (Table 4), the evidence was of relatively poor quality (Pereira *et al*, 1991; Silva *et al*, 1992; Bowen and Rayner, 2002; Koyi *et al*, 2002). Failure to fully or adequately examine patients, use of inappropriate or inadequate tests and receiving or failing to follow-up inconclusive, negative or false negative test results contributed to the delay (Fruchter *et al*, 1980; Bosl *et al*, 1981; Hernes *et al*, 1996; Goff *et al*, 2000; Macdonald *et al*, 2006; Mitchell *et al*, 2008). Similarly, prescribing treatment for benign conditions, such as acid suppression in patients subsequently diagnosed with upper gastrointestinal cancers (Macdonald *et al*, 2006), or antibiotics in patients with testicular cancer (Bosl *et al*, 1981) also increased time to referral. There is some evidence to suggest that appropriate referral and use of referral guidelines is associated with reduced delay for upper gastrointestinal cancers (Macdonald *et al*, 2006) and colorectal cancer (Mitchell *et al*, 2008).

DISCUSSION

Reasons for delay in presentation by patients with symptoms of cancer and influences on time to referral by practitioners are complex and multi-factorial according to the combined findings of two systematic reviews of the literature on common cancers. The predominant risk factor for patient delay is a lack of interpretation by patients of the serious nature of their symptoms. Across the common cancers, symptom type is predictive of delay in presentation. If a symptom is atypical, or vague in nature, the risk of delayed presentation can be increased. Conversely, if the

Table 3 Risk factors associated with delay for gynaecological cancers

Author(s)	Location	Study type	Participants	Cancer site	Factors which increase delay	Factors which reduce delay	No impact on delay	Evidence
<i>Patient-associated factors</i>								
Fruchter et al (1980)	NY, USA	Prospective observational	97 patients	Cervix	Non-recognition of symptom seriousness; previous normal test result; fear		Age; ethnicity; education; income; place of birth	Moderate
Franceschi et al (1983)	Italy	Prospective observational	173 patients (aged 33–84; median 59)	Endometrium	Age – younger; pre-menopausal women	Increased patient awareness ^a	Marital status; education; parity; BMI; contraception	Strong
Fowler et al (1984)	NC, USA	Retrospective observational	271 patients	Cervix			Age; ethnicity; insurance cover	Moderate
Smith and Anderson (1985)	IA, USA	Prospective observational	82 patients (aged 20–54)	Ovary	Non-recognition of symptom seriousness; re-appearance of previous benign condition; fear	Symptom type – abdominal pain or swelling, irregular bleeding; age – older		Strong
Cochran et al (1986)	CA, USA	Prospective observational	37 patients (48–72; median 64)	Endometrium	Attributing symptoms to menopause; marital dissatisfaction; lower social support	Recognition of symptom seriousness (attributing to cancer); longer time since menopause		Moderate
Smith and Anderson (1987)	IA, USA	Prospective observational	98 patients (aged 20–54; median 49)	Endometrium	Non-recognition of symptom seriousness; fear	Symptom type – irregular bleeding, discharge, abdominal pain		Strong
Menon et al (1991)	India	Observational	117 patients	Cervix	Non-recognition of symptom seriousness; symptom type – irregular bleeding, vaginal discharge; lack of attendance for check-ups	Symptom type – pus discharge, continuous bleeding		Moderate
Dhamija et al (1993)	India	Cross-sectional	1411 ever-married women	Cervix	Lack of patient awareness ^a	Age – younger; education level – higher ^a		Insufficient
Andersen et al (1995)	OH, USA	Prospective observational	34 patients (aged 24–75; mean 50)	Endometrium, vulva, ovary, vagina	Age – older; innocuous or diffuse symptoms; attributing symptoms to normal life circumstances	Symptom becomes more prominent/serious	Marital status; education; employment; family circumstances; religion	Strong
Coates et al (1996)	GA, LA, CA, USA	Prospective observational	331 patients (aged 20–79)	Uterus	Infrequent care seeking; income – lower; marital status – divorced; occupation – blue collar/service; no health insurance; smoker	Recognition of symptom seriousness; age – older; symptom type – vaginal bleeding	Ethnicity	Moderate
Risberg et al (1996)	Norway	Cross-sectional	252 cancer patients (mean age 58; 52% men, 48% women), 5% with gynaecological cancer	All			Age; education level	Strong
Ajayi and Adewole (1998)	Nigeria	Cross-sectional	254 women (aged 20–65)	Cervix	Lack of patient awareness ^a			Insufficient
Jones and Joura (1999)	New Zealand	Retrospective observational	102 patients (aged 36–94)	Vulva	Lack of patient awareness ^a		Age	Insufficient
Goff et al (2000)	USA; Canada	Observational	1725 patients (aged 18–84; median 52)	Ovary	Ignoring symptoms; multiple symptoms	Age – older	Health insurance; symptom type	Insufficient
Fitch et al (2002)	Toronto, Canada	Qualitative interviews	18 women (aged 35–73; mean 53)	Ovary	Non-recognition of symptom seriousness; symptom type – vague			Strong
Kidanto et al (2002)	Tanzania	Case–control	267 patients, 89 with cancer (mean age 49); 178 controls (mean age 46)	Cervix	Non-recognition of symptom seriousness; lack of knowledge			Moderate

Table 3 (Continued)

Author(s)	Location	Study type	Participants	Cancer site	Factors which increase delay	Factors which reduce delay	No impact on delay	Evidence
<i>Practitioner-associated factors</i>								
Fruchter <i>et al</i> (1980)	NY, USA	Prospective observational	97 women	Cervix	Inconclusive test results; inadequate examination; failure to follow-up negative result; patient age – younger			Moderate
Fowler <i>et al</i> (1984)	NC, USA	Retrospective observational	271 patients	Cervix	Involvement of several physicians		Age; ethnicity; insurance cover	Moderate
Risberg <i>et al</i> (1996)	Norway	Cross-sectional	252 cancer patients (mean age 58; 52% men, 48% women), 5% with gynaecological cancer	All		Patient age – younger; patient education level – higher		Strong
Jones and Joura (1999)	New Zealand	Retrospective observational	102 patients (aged 36–94)	Vulva	Initial misdiagnosis ^a			Insufficient
Goff <i>et al</i> (2000)	USA; Canada	Observational	1725 patients (aged 18–84; median 52)	Ovary	Multiple providers of care; incomplete/inappropriate examination; initial misdiagnosis; multiple symptoms		Type of physician initially seen; health insurance; symptom type	Insufficient
Fitch <i>et al</i> (2002)	Canada	Qualitative interviews	18 women (aged 35–73; mean 53)	Ovary	Symptom type – vague; misinterpretation of symptoms	Symptom type – pain		Strong

Abbreviation: BMI = body mass index. ^aStudy infers findings.

symptom is more serious or alarming and includes a lump, bleeding or pain, then the risk of delayed presentation is typically reduced. Patients may fail to recognise or appreciate atypical or vague symptoms, which may mediate delayed presentation. Where symptoms are understood and thought to be serious, there is a reduced time to presentation, and whatever the cancer site, the catalyst for presentation is often when a symptom becomes incapacitating or impacts on normal activities, rather than the presence of the symptom alone. However, the difficulty is that common cancer symptoms are often attributable to benign disease. The complexity of this process can be illustrated by considering breast cancer, where there is robust evidence that patients delay less with the well-known symptom of lump, compared with the less recognised non-lump symptoms, which result in greater delay. This contrasts with the evidence for urological cancers, where pain increases delay, perhaps as a result of symptoms being misinterpreted as being due to a benign cause such as cystitis. In other cancers too, such as those of the gastrointestinal tract, potential cancer symptoms can frequently have a benign interpretation.

Patient delays are also influenced by a range of demographic and psychosocial factors. Taken together, lower socio-economic status and education level are risk factors for delayed presentation of several common cancers, but not for others. Similarly, non-white ethnic origin impacts on delayed presentation for some, but not all common cancers. Neither age nor gender is associated with delayed presentation with the exception of breast cancer (older age) and bladder cancer (male sex). Across the common cancers, then demographic risk factors for patient delay seem inconsistent. This may be a consequence of the fact that the cancers have not been equally researched in terms of risk factors for delay. Although the review of the literature for breast cancer was based on 23 studies deemed to be of adequate quality, and the upper and lower gastrointestinal results were based on 18 and 45 studies, respectively, only 11 urological, 12 gynaecological and 4 lung cancer studies were of sufficient quality to be included in the

synthesis of evidence. Further, it is possible that some of the factors we have described are not independent of each other; the ways in which they may relate to each other are not clear.

General population surveys in the United Kingdom indicate a widespread lack of awareness of the symptoms of cancer (Grunfeld *et al*, 2002; McCaffery *et al*, 2003; Linsell *et al*, 2008; Robb *et al*, 2009). These low levels of symptom awareness may partly explain why the type of symptom and recognition of the seriousness of symptoms are consistent risk factors for delayed patient presentation. These surveys also suggest that cancer symptom awareness is poorer among those who are less well educated, those with lower socio-economic status and those from black and minority ethnic groups (Wardle *et al*, 2001; Grunfeld *et al*, 2002; Robb *et al*, 2009). Not only are levels of awareness of cancer symptoms low among the general population, but so too is knowledge of the risk factors for developing cancer. Equally, these surveys report that people hold negative beliefs and attitudes about the benefits of seeking medical help for cancer, which include fear, embarrassment, reluctance to bother the general practitioner and nihilism about cancer treatments (Grunfeld *et al*, 2002; Robb *et al*, 2009). These barriers may explain the finding from our review that fear and embarrassment are risk factors for patient delay.

Qualitative research with people diagnosed with cancer further enhances the findings of such surveys. Reported barriers to early help seeking are vague and mild symptoms, absence of pain or lump, belief that the symptom will go away, intermittent symptoms, lack of awareness of cancer risk and previous benign diagnosis (Smith *et al*, 2005). Competing demands and priorities, fears about cancer treatments and anxieties about 'bothering the doctor' have also been identified as issues related to delayed presentation in breast cancer (Burgess *et al*, 2001). Qualitative interviews have enabled the identification of eventual triggers to help seeking, such as worsening symptoms, new additional symptoms, the presence of a symptom that is recognised as serious or is affecting daily life and the influence of family and

Table 4 Risk factors associated with delay for lung cancer

Author(s)	Location	Study type	Participants	Cancer site	Factors which increase delay	Factors which reduce delay	No impact on delay	Evidence
<i>Patient-associated factors</i>								
Hackett et al (1973)	MA, USA	Prospective observational	563 patients (aged 17–91; mean 62; 46% men, 54% women), 6% with lung cancer	Lung	Symptom type – pain; social class – lower; procrastination; worry over health; family history	Worry; incapacitated by symptoms; acknowledgement of cancer		Strong
Worden and Weisman (1975)	MA, USA	Prospective observational	125 patients (aged 19–59, 38% men, 62% women), 18% with lung cancer	Lung	Non-recognition of symptom seriousness; denial; powerlessness; cancer site – lung compared with breast, Hodgkin	Cancer site – lung compared with melanoma	Age; sex; marital status; socio-economic status; family history; presenting symptoms	Strong
Mor et al (1990)	RI, USA	Prospective observational	625 patients (aged 45–90; 31% men, 69% women), 19% with lung cancer	Lung	Non-recognition of symptom seriousness; symptom type – nagging cough; belief that symptoms would 'go away'; fear of cancer		Age; sex; marital status; education; socio-economic status; social support; co-morbidity	Strong
Risberg et al (1996)	Norway	Cross-sectional	252 cancer patients (mean age 58; 52% men, 48% women), 16% with lung cancer	Lung		Cancer site – lung compared with GI, urological, Hodgkin; sex – female	Age; education	Strong
Bowen and Rayner (2002)	England	Prospective observational	37 patients, 51% men (aged 45–80; mean 65), 49% women (aged 44–90; mean 67)	Lung	Non-recognition of symptom seriousness; lack of awareness of symptoms	Sex – female; advice from social network		Insufficient
Koyi et al (2002)	Sweden	Prospective observational	134 patients, 63% men (aged 48–90, mean 72); 37% women (aged 35–90, mean 70)	Lung	Lack of awareness; difficulty in accessing primary care ^a			Insufficient
<i>Practitioner-associated factors</i>								
(Pereira et al (1991))	Brazil	Prospective observational	100 patients	Lung	Lack of awareness; inadequate tests ^a			Insufficient
(Silva et al (1992))	Brazil	Prospective observational	300 patients	Lung		Improved GP awareness ^a		Insufficient
Risberg et al (1996)	Norway	Cross-sectional	252 cancer patients (mean age 58; 52% men, 48% women), 16% with lung cancer	Lung		Patient age – younger; patient education level – higher		Strong
Bowen and Rayner (2002)	England	Prospective observational	37 patients, 19 men (mean age 65), 18 women (mean age 67)	Lung	Lack of symptom awareness			Insufficient
Koyi et al (2002)	Sweden	Prospective observational	134 patients, 63% men (aged 48–90, mean 72); 37% women (aged 35–90, mean 70)	Lung	Lack of suspicion ^a	Low threshold for referral ^a		Insufficient

^aStudy infers findings; (non-English language paper).

friends (Burgess et al, 2001; Smith et al, 2005), findings supported by the evidence presented in this paper.

Overall, research into the risk factors for patient delay indicates that presentation with cancer is not a straightforward or linear process. Knowledge of symptoms and risk may be necessary, but not sufficient to determine help seeking for cancer. People's attitudes, beliefs and social context clearly influence the process of medical help seeking. To develop strategies to reduce patient delays, the risk factors for delayed presentation need to be placed into an explanatory framework. This aids understanding of the complexities of the delay process and highlights where and how interventions could be targeted. A framework for understanding patient delay in breast cancer is described by Bish et al (2005). This model incorporates symptom appraisal, attitudes towards help-seeking and translating intentions to seek help into behaviour. It

draws on health psychology models, including self-regulation theory (Leventhal et al, 1984), theory of planned behaviour (Ajzen, 1991) and implementation intentions (Gollwitzer, 1999). A similar model (Andersen et al, 1995) has been suggested for other cancers. Basing an intervention to promote behaviour change in an explanatory framework informed by psychological theory and empirical evidence increases the likelihood that it will be effective (Bish et al, 2005; Serlachius and Sutton, 2009).

To impact on presentation with cancer symptoms, we need a greater understanding of the psychological and sociological factors influencing patients' help-seeking behaviour. In addition, we need to devise culturally sensitive strategies, not only to improve awareness of cancer, but also to aid interpretation of symptom seriousness by patients. Ideally, an intervention to reduce delayed presentation of cancer would promote early help-seeking

Table 5 Risk factors associated with delay for urological cancers

Author(s)	Location	Study type	Participants	Cancer site	Factors which increase delay	Factors which reduce delay	No impact on delay	Evidence
<i>Patient-associated factors</i>								
Hackett <i>et al</i> (1973)	MA, USA	Prospective observational	563 patients (aged 17–91; mean 62, 46% men, 54% women), 9% with prostate cancer	Prostate	Symptom type – pain; social class – lower; procrastination; worry over health; family history	Worry; incapacitated by symptoms; acknowledgement of cancer		Strong
Bosl <i>et al</i> (1981)	MN, USA	Retrospective observational	335 patients (mean age 31)	Testicular	Non-recognition of symptom seriousness			Moderate
Mommsen <i>et al</i> (1983)	Denmark	Prospective observational	212 patients (mean age 66; 78% men, 22% women)	Bladder	Symptom type – cystitis	Sex – female		Moderate
Attard (1985)	England	Retrospective observational	23 patients	Testicular	Non-recognition of symptom seriousness; symptom type – painless			Insufficient
Thornhill <i>et al</i> (1987)	Ireland	Retrospective observational	217 patients	Testicular	Presence of atypical symptoms; symptom type – dragging sensation	Improved patient awareness ^a	Age; marital status; area of residence	Strong
Samet <i>et al</i> (1988)	NM, USA	Prospective observational	800 patients, (aged 65–100, mean 72), 32% with prostate cancer	Prostate	Site – prostate compared with breast and colorectal; ethnicity – white Hispanic	Previous cancer diagnosis; regular check-ups	Age; income; availability of vehicle; social support; participation in screening	Strong
Mansson <i>et al</i> (1993)	Sweden	Cross-sectional	343 patients (aged 27–94; 77% men, 23% women)	Bladder	Non-recognition of symptom seriousness; symptom type – urgency, pain	Symptom type – haematuria	Age; sex; education; marital status	Strong
Hernes <i>et al</i> (1996)	Norway	Retrospective observational	352 patients (aged 15–83, median 32)	Testicular	Lack of patient awareness ^a	Cancer type – non-seminoma		Insufficient
Risberg <i>et al</i> (1996)	Norway	Cross-sectional	252 cancer patients (mean age 58; 52% men, 48% women), 15% with urological cancer	Testicular, prostate, bladder, kidney	Cancer site – kidney, bladder, prostate	Cancer site – testicular; sex – female	Age; education level	Strong
Fitzpatrick <i>et al</i> (1998)	Ireland	Cross-sectional	280 randomly selected men, (aged 40–69, mean 53)	Prostate	Lack of patient awareness; social class – lower; embarrassment; fear of treatment	Living with female partner; history of urinary tract disease; symptom type – pain, bleeding; saw GP > 1 in past year; having a relative with cancer		Moderate
Ho <i>et al</i> (1998)	Northern Ireland	Prospective observational	100 haematuria clinic patients (aged 18–97, mean 57; 64% men, 36% women)	Bladder	Fear of cancer; previous haematuria	Improved patient awareness ^a		Insufficient
Gascoigne <i>et al</i> (1999)	Wales	Qualitative interviews	11 patients and carers	Testicular	Non-recognition of symptom seriousness; embarrassment			Strong
Prout <i>et al</i> (2000)	USA	Prospective observational	497 patients (aged 20–79)	Bladder	Ethnicity – black			Strong
Sanden <i>et al</i> (2000)	Sweden	Qualitative interviews	21 patients (aged 20–49)	Testicular	Symptom type – intermittent symptoms; adopting a 'wait and see' approach; fear of cancer diagnosis	Symptom impacting on everyday activity; advice from social network		Insufficient
de Nooijer <i>et al</i> (2001)	The Netherlands	Qualitative interviews	23 patients (mean age 52; 43% men, 57% women), 22% with testicular cancer, 10 GPs	Testicular	Non-recognition of symptom seriousness; fear of cancer	Fear of cancer; trust in GP		Strong
Khadra and Oakeshott (2002)	England	Cross-sectional	202 men; (aged 18–50, mean 32)	Testicular	Lack of patient awareness ^a			Insufficient
<i>Practitioner-associated factors</i>								
Bosl <i>et al</i> (1981)	MN, USA	Retrospective observational	335 patients (mean age 31)	Testicular	Lack of awareness; initial misdiagnosis; inadequate examination; inappropriate treatment			Moderate

Table 5 (Continued)

Author(s)	Location	Study type	Participants	Cancer site	Factors which increase delay	Factors which reduce delay	No impact on delay	Evidence
Mommsen et al (1983)	Denmark	Prospective observational	212 patients (mean age 66; 78% men, 22% women)	Bladder	Symptom type – cystitis (especially men); patient sex – female	Symptom type – haematuria (especially men)		Moderate
Attard (1985)	England	Retrospective observational	23 patients	Testicular	Initial misdiagnosis			Insufficient
Mansson et al (1993)	Sweden	Cross-sectional	343 patients (aged 27–94; 77% men, 23% women)	Bladder	Symptom type – urgency	Symptom type – haematuria plus pain; patient sex – male; patient age – younger		Strong
Hernes et al (1996)	Norway	Retrospective observational	352 patients (aged 15–83, median 32)	Testicular	Lack of awareness; inadequate use of tests ^a			Insufficient
Risberg et al (1996)	Norway	Cross-sectional	252 cancer patients (mean age 58; 52% men, 48% women), 15% with urological cancer	Testicular, prostate, bladder, kidney		Patient age – younger; patient education level – higher		Strong
Ho et al (1998)	Northern Ireland	Prospective observational	100 haematuria clinic patients (aged 18–97, mean 57; 64% men, 36% women)	Bladder	Inappropriate referral ^a			Insufficient
Gascoigne et al (1999)	Wales	Qualitative interviews	11 patients and carers	Testicular	Initial misdiagnosis			Strong

Abbreviation: GP = general practitioner. ^aStudy infers findings.

behaviour by people with a high cancer risk, but would not promote anxiety among those at low risk. It is important that patients are neither made unnecessarily anxious, nor should general practitioners be overburdened by consultations with 'the worried well'. The demographic risk factors for patient delay and low cancer awareness suggest the population groups that we should target with interventions to promote early presentation. The evidence suggests a general focus on populations that are socially deprived and less educated, as well as those from black and minority ethnic groups. Interventions related to breast cancer should be targeted at older women. However, further research is needed to clarify relevant risk factors for delayed time to presentation for some particularly under-researched cancers, such as lung and prostate.

When people do present to their doctor with potential cancer symptoms, timely investigation and onwards referral are clearly important. The reviews reported here suggest that patients with particular demographic profiles are likely to experience practitioner delay, including, for some cancer sites, women and those with lower educational attainment. There is also evidence that vague and atypical symptoms are not only associated with patient

delays, but also with practitioner delays. The challenge is that among the hundreds of patients with potential cancer symptoms that every general practitioner sees each year, only eight of these will actually have the disease. This review also suggests the need for effective use of referral guidelines for general practitioners, as well as better use of, and access to, diagnostic services.

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Conflict of interest

The authors declare no conflict of interest.

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