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REVIEW ARTICLE

Is early diagnosis of oral cancer a feasible objective? Who is to blame for diagnostic delay?

I Gómez[1], S Warnakulasuriya[2], PI Varela-Centelles[1], P López-Jornet[3], M Suárez-Cunqueiro[1], P Diz-Dios[1], J Seoane[1]

[1]*Department of Stomatology, School of Medicine and Dentistry, University of Santiago de Compostela, Santiago de Compostela, Spain;* [2]*King's College London Dental Institute at Guy's, King's and St Thomas' Hospitals, London and WHO Collaborating Centre for Oral Cancer and Precancer, London, UK;* [3]*Department of Oral Medicine, School of Dentistry, University of Murcia. Spain*

Worldwide, oral cancer has one of the lowest survival rates and poor prognosis remains unaffected despite recent therapeutic advances. Reducing diagnostic delay to achieve earlier detection is a cornerstone to improve survival. Thus, intervention strategies to minimize diagnostic delays resulting from patient factors and to identify groups at risk in different geographical areas seem to be necessary. The identification of a 'scheduling delay' in oral cancer justifies the introduction of additional educational interventions aimed at the whole health care team at dental and medical practices. The access to and the kind of healthcare system in a particular country are also relevant in this context, particularly the referral system. The design of a simple, clear, fail-safe, fast-track referral scheme for those suspected with cancer may diminish greatly the length of the delay. Moreover, there is a need for future investigations, which are methodologically adequate, that consider cultural and geographical aspects and use patient survival as the final outcome, that are able to recognize the agents/factors responsible for diagnostic delay by patients as well as healthcare providers and those attributable to the healthcare systems.
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Oral cancer is a global health problem with increasing incidence and mortality rates (Parkin *et al*, 2005; Gillison, 2007). The highest age standardized rates of oral cancer are reported in parts of Europe (France, Hungary, Spain and Croatia), South East Asia (Sri Lanka, Pakistan, Bangladesh and India) and Brazil (IARC, 2004). Geographical variations in oral cancer incidence seem to reflect disparity in the rates of tobacco, areca nut and alcohol consumption (Warnakulasuriya, 2009).

Moreover, rising trends of oral cancer in young and middle-aged men, particularly of tongue cancer, have been reported in Brazil, India, several European countries and the USA (Llewellyn *et al*, 2001). Worldwide, oral cancer has one of the lowest survival rates and remains unaffected despite recent therapeutic advances (CRUK, 2005).

Variables such as age, gender, immunological or nutritional status, size and location of the tumour, disease stage, nodal status, oncogene expression, proliferation markers and DNA content have been assessed as independent prognostic markers for oral cancer (Montoro *et al*, 2008; Rapidis *et al*, 2009). However, tumour stage at diagnosis is recognized as the most important prognostic marker for oral squamous cell carcinoma (Massano *et al*, 2006). Unfortunately, almost half of the oral cancers are diagnosed at advanced stages (III or IV), with 5-year survival rates ranging from 20% to 50%, depending on tumour sites (Neville and Day, 2002; Warnakulasuriya, 2009) and an upward trend in oral cancer mortality was recorded in most European countries up to the late 1980s (LaVecchia *et al*, 2004). Early detection is a cornerstone to improve survival and to reduce diagnostic delay. High mortality is frequently associated with advanced stages and positive neck metastasis (Rogers *et al*, 2009).

What is diagnostic delay in oral cancer?

Several research groups have studied the concept of delay in diagnosis of oral cancer, but using heterogeneous criteria (Allison *et al*, 1998a), which could in part explain the intercountry differences observed in diagnostic delay of oral cancer (Table 1). During the 1970s,

Correspondence: Prof. Saman Warnakulasuriya, King's College London Dental Institute at Guy's, King's and St Thomas' Hospitals, London and WHO Collaborating Centre for Oral Cancer and Precancer, Denmark Hill campus, Bessemer Rd, London SE 5 9RS, UK.Tel: +44 20 3 299 2430, Fax: 020 3299 3624, E-mail: s.warne@kcl.ac.uk
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Table 1 Reports on diagnostic delay of oral cancer. An international perspective

Report	*Country*	*Location*	*Patients*	*Median of the delay*	*Delay > 3 months (%)*	*Delay range*
Elwood and Gallagher (1985)	Canada	Mouth	134	3 months	64 (> 2 months)	NA
Jovanovic *et al* (1992)	Holland	Mouth	50	46 days	NA	14–724 days
Kowalski (1994)	Brazil	Mouth and oropharynx	336	NA	57.4	NA
Gorsky and Dayan (1995)	Israel	Mouth and oropharynx	543	4 months	NA	NA
Wildt *et al* (1995)	Denmark	Mouth	167	4 months	NA	19–783 days
Allison *et al* (1998c)	Canada	Upper aerodigestive tract	199	NA	58.5	NA
Kerdpon and Sriplung (2001a,b)	Thailand	Mouth and lip	161	141.8 days (mean)	NA	0–1085 days
Pitiphat *et al* (2002)	Greece	Mouth and pharynx	105	30 days	20 (> 3.5 weeks)	0–170 days
Carvalho *et al* (2002)	Brazil	Lip, mouth, oropharynx	417	NA	27.57 (> 2 months)	NA
Onizawa *et al* (2003)	Japan	Mouth	152	2.7 months		0.4–63 months
McGurk *et al* (2005)	UK	H & N	613	3 months	51.22	NA
Tromp *et al* (2005)	Holland	H & N	306	NA	78.4	NA
Scott *et al* (2005)	UK	Mouth	245	3 months	44	0–36 months
Brouha *et al* (2007)[a]	Holland	H&N	306	14 days	NA	0–570 days

NA, not available; H&N, head and neck.
[a]Specialist's delay: median delay of 14 days for diagnosis, additional delay of 21 days for the work-up.

the prognostic relevance of the time lapse in diagnosis of oral cancer was emphasized and two time factors were considered: (i) the time that elapses from the first symptoms until the patient consults a physician or a dentist and (ii) the period during which the patient is under professional care up until a final diagnosis is made (Shafer, 1975; Bruun, 1976). Since then, different models of diagnostic delay in oral cancer have been proposed (Andersen *et al*, 1995). Nowadays, diagnostic delay is most often categorized as (i) *patient delay* – the period between the patient first noticing a sign or symptom and their first consultation with a health care professional concerning that sign or symptom (Yu *et al*, 2008; Teppo and Alho, 2009); and (ii) *provider/professional delay* – the period from the patient's first consultation with a health care professional and the definitive pathological diagnosis (Teppo and Alho, 2008; Yu *et al*, 2008). The overall diagnostic delay would include the period elapsed since the first symptom or sign until the definitive diagnosis.

Other ways of assessing 'time intervals' in the diagnostic pathway have been recently brought to the attention of the scientific community: *1st stage*: since the first symptom until the first contact with a healthcare professional; *2nd stage*: since the first visit to a healthcare professional until a referral letter is written; *3rd stage*: since issuing the referral letter until the first consultation at a specialized service and *4th stage*: since the first visit to the specialized service until a definitive diagnosis is reached (Onizawa *et al*, 2003). Furthermore, the delay encountered after definitive diagnosis, i.e. time to treatment, could also be considered (Peacock *et al*, 2008). This approach to stage the diagnostic pathway introduces some degree of complexity to data collection and allows the attribution of data to each of the above stages during retrospective analyses. Such estimates are needed if we are to formulate measures to improve referral guidelines to tackle diagnostic delays.

How do we measure diagnostic delay?

Diagnostic delay is measured by the number of days elapsed since the patient notices the first sign and/or symptom until a definitive diagnosis is reached. Many authors have used the mean or the median of the time distribution to categorize the diagnostic delay (Pitiphat *et al*, 2002; Onizawa *et al*, 2003; McGurk *et al*, 2005). The latter is more frequently used because it is not affected by extreme values and the distributions usually have very wide ranges. Other authors choose an arbitrary time point (more than 30 days) to discriminate between delayed and non-delayed cases (Brouha *et al*, 2005a; Tromp *et al*, 2005). Other arbitrary time points have also been considered (Pitiphat *et al*, 2002) under the assumption that the proposed time point was the minimum amount of time necessary to perform a definitive diagnosis of a suspicious lesion. Some authors have divided diagnostic delay into three intervals (< 1, 1–3 and > 3 months) (Carvalho *et al*, 2002; Tromp *et al*, 2005) and/or define it as a continuous variable without a specific time point (Hollows *et al*, 2000; Kerdpon and Sriplung, 2001a,b). Several studies suggest that 30% of patients delay seeking help for more than 3 months following the discovery of symptoms of oral cancer (Scott *et al*, 2006a).

Who is to blame?

Since Shafer's US study in 1975 that identified a 14.8% of mismanaged or delayed patients in a sample of 779

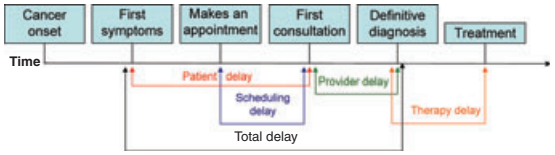

Figure 1 Types of diagnostic delay in oral cancer

carcinomas that made dentists, physicians and patients equally responsible for it (Shafer, 1975), others have also concluded that both patients and professionals were responsible for diagnostic delay (Morelatto *et al*, 2007). On the contrary, a recent investigation in Canada found that the longest delay was the time from first symptom to the initial visit to a health centre (mean 104.9 days; range 0–730 days), identifying the need for improving public awareness to reduce delay (Peacock *et al*, 2008). While patient delays in reporting oral cancer are well documented, reasons for such delays are poorly understood (Richards, 2007). Apart from patients' or professionals' delay, a new agent responsible for diagnostic delay has been incorporated to the initial scheme – accessibility, defined as the ability to obtain services based on patients' health needs (Guay, 2004) (Fig 1). Delays in scheduling of appointments at primary health centres may contribute to an increase in the so-called 'delay by patients', but lack of accessibility to the healthcare system should really not be quantified as patients' responsibility (Diz-Dios *et al*, 2005; Lopez-Jornet and Camacho-Alonso, 2006).

Is diagnostic delay related to the extension of the disease?

Tumour size and nodal status seem to be closely related to the chronology of tumour growth in oral cancer (Spiro *et al*, 1986; Brown *et al*, 1989; Parker *et al*, 1996). Using these two estimates, several research groups have tried to prove that diagnostic delay contributes to spread of the disease at the time of diagnosis. Although this relationship has been clearly demonstrated for certain tumours (Erwenne and Franco, 1989; Porta *et al*, 1991; Facione, 1993), the data for oral cancer are equivocal (Goy *et al*, 2009). A marked discrepancy could be observed among the reports that analyse the association between patient delay and tumour stage at diagnosis. Although several research groups could not prove this association (Allison *et al*, 1998b; Kantola *et al*, 2001; Kerdpon and Sriplung, 2001a,b), some recent studies have described a significant correlation between patients with advanced tumours at diagnosis and patient delay (O'Sullivan, 2001; Brouha *et al*, 2005b; Gomez *et al*, 2009).

One of the first attempts to ascertain this relationship was the one by Guggenheimer *et al* (1989), who studied a mixed sample of 149 oral and pharyngeal cancers and failed to find an association, even after considering patient delay and professional delay separately. Subsequent reports made this finding a commonplace (Jovanovic *et al*, 1992; Amir *et al*, 1999; Hollows *et al*, 2000; Kerdpon and Sriplung, 2001a,b), until Kowalski *et al* (1994) found a significant association between professional delay and tumour stage, but not between overall delay and spread of the disease, which may suggest the relevance of the memory bias in this kind of research. The introduction of patient survival as the outcome of the investigation and the use of multivariate analysis to adjust for confounding factors (Wildt *et al*, 1995) meant an improvement to the design of these studies; again, no associations could be identified for oral cancer (Wildt *et al*, 1995) or for head and neck cancer (Gorsky and Dayan, 1995). Another advance in the study design was the combination of data collection methods to include prospective and retrospective information to diminish the memory bias. This was the approach by McGurk *et al* (2005) who gathered a sample of 613 cases over 40 years and failed to identify any relationship between diagnostic delay and tumour stage. This particular study was performed on a mixed series of head and neck cancers and used an arbitrary time point (3 months) to distinguish between delayed and non-delayed cases.

The composition of the series analysed may be of interest, as Scott *et al* (2005) found no significant relationship between diagnostic delay and tumour stage, but they managed to identify a trend in this relationship for certain oral sites. In agreement with this, Carvalho *et al* (2002) observed in a series of 676 squamous cell carcinomas of the head and neck that patients with laryngeal and hypopharyngeal cancers were more likely to be diagnosed as having advanced disease than those with lip, oral and oropharyngeal tumours. Moreover, patients with upper aerodigestive tract carcinomas with professional delays longer than 1 month were found to have an increased risk of being diagnosed with late stage disease (Allison *et al*, 1998c). The starting point of the study of the diagnostic delay is the recognition of the signs and symptoms by the patient, and this recognition may be affected by their psychosocial characteristics. The first study to consider these variables was the one by Kumar *et al* (2001) on a sample of 79 patients. This report identifies a significant relationship between overall diagnostic delay and tumour stage. The same finding was described by Pitiphat *et al* (2002) from a case–control study which proved that the length of diagnostic delay was significantly greater in patients with advanced tumour stages (TNM stage IV). However, as stated earlier, other authors have not found any association between diagnostic delay and stage of the disease (McGurk *et al*, 2005).

The lack of sound scientific evidence supporting an association between diagnostic delay in oral cancer and the extent or advancement of disease at diagnosis (TNM III–IV) is evident. However, this fact is probably related to serious limitations and methodological flaws identified in the reports published to date (Goy *et al*, 2009). Many reports have employed different concepts to catalogue diagnostic delay, are subject to misclassification of stages of delay, have used retrospective designs

without strategies to diminish patient's memory bias and frequently classify the length of delay into categories with insufficient sample sizes. Moreover, the study of samples with heterogeneous intra oral locations introduces confounding factors in the analysis, as the patient's self-perception and self-exploration abilities depend on the site of the tumour (Wildt *et al*, 1995; Allison *et al*, 1998a; O'Sullivan, 2001; Tromp *et al*, 2005). For example, gingival locations are associated with advanced stages at diagnosis because of the early invasion of the adjacent bone tissue (T4 primary tumour) (Seoane *et al*, 2006), yet could present without time delay.

This lack of agreement may also be as a result of the different types of data collected, e.g.: continuous variables (Wildt *et al*, 1995; Hollows *et al*, 2000; Kantola *et al*, 2001; Kumar *et al*, 2001) *vs* categorical variables (Allison *et al*, 1998b; Kerdpon and Sriplung, 2001a,b), and to the different recording sources of patient delay data (standard questionnaires, interviews, hospital records, etc.). Different velocities of tumour growth could also reflect why some tumours remain small in size, despite delay. It could well happen that certain cancers remain silent during the initial stages and only induce detectable symptoms when they reach an advanced phase. This phenomenon could veil an idiosyncratic relationship between stage and delay (Scott *et al*, 2005). In this sense, the tumour growth rate constitutes a confounding factor in the study of the relationship between diagnostic delay and tumour stage. It has also been suggested that patients with very biologically aggressive tumours have a bad prognosis not necessarily due to any diagnostic delay, and tumours with low proliferative activity elicit good prognosis despite a long diagnostic delay (Kaufman *et al*, 1980; Evans *et al*, 1982; Allison *et al*, 1998a). In any case, a recent meta-analysis aimed at studying the strength of the association between diagnostic delay and tumour stage showed that diagnostic delay is a risk factor for tumour growth. The association is stronger when the study is restricted to oral cancer, particularly when the delay is longer than 1 month. The probability for delayed patients to present an advanced-stage oral cancer at diagnosis is 30% higher than that of a non-delayed patient (Gomez *et al*, 2009). We consider that new studies with sound epidemiological design and analysis may shed more light on the association between diagnostic delay and tumour stage in oral cancer. These studies must use standardized criteria to measure diagnosis and strategies to minimize recall bias. In addition, tumour proliferating activity should be measured (Gomez *et al*, 2009).

Is diagnostic delay related to survival from oral cancer?

Clinical stage at the time of diagnosis is recognized as the most important factor in survival following head and neck cancer (Allison *et al*, 1998a; McGurk *et al*, 2005). To the best of our knowledge, the studies that have specifically assessed the relationship of patient delay in oral cancer and how it affects prognosis or survival are scarce (Wildt *et al*, 1995; Kantola *et al*, 2001; Kowalski and Carvalho, 2001). The association between shorter diagnostic delay and higher survival rates is also controversial, as different reports could not demonstrate an impact of diagnostic delay on survival from head and neck carcinomas (Wildt *et al*, 1995; McGurk *et al*, 2005), particularly when dealing with tongue cancer where the impact of delays on survival was insignificant and often paradoxical: shorter delays showed a trend towards impaired survival (Teppo and Alho, 2008, 2009).

However, recent evidence shows that early diagnosis can significantly decrease the morbidity associated with treatment and may improve overall long-term survival (Peacock *et al*, 2008). Diagnostic delays have been shown to have prognostic significance in certain head and neck cancers: longer diagnostic delays worsened survival markedly in laryngeal cancer. Cut-off points at which the delays showed significant adverse impact on prognosis were ≥3 months in patient delay and ≥6 months in professional delay (Teppo and Alho, 2008). Furthermore, longer professional delay is an independent determinant of poor prognosis in laryngeal cancer (Teppo *et al*, 2003; Teppo and Alho, 2009). In this respect, methodologically sound reports have been able to demonstrate that diagnostic delay was associated with an increased risk of recurrence and oral cancer mortality, even for tongue sites (Kantola *et al*, 2001; Sandoval *et al*, 2009).

Can patients at risk of diagnostic delay be identified?

To identify patient factors for delay in oral cancer, a small number of well-designed investigations have been performed. These were reviewed by Scott *et al* (2006a). These studies have evaluated the association of sociodemographic and clinical variables, health-related behaviours and psychosocial factors with patient delay (Wildt *et al*, 1995; Allison *et al*, 1998b; Hollows *et al*, 2000; Kantola *et al*, 2001; Kerdpon and Sriplung, 2001a,b; Kumar *et al*, 2001; Onizawa *et al*, 2003; Brouha *et al*, 2005a; Rogers *et al*, 2007). Only a Thai report, using multivariate analyses, identifies the use of traditional herbal medication before visiting a healthcare professional as a significant independent predictor of patient delay (Kerdpon and Sriplung, 2001a,b). Neither sociodemographic variables (age, gender, marital status, area of residence, religion or education) (Wildt *et al*, 1995; Kantola *et al*, 2001; Kerdpon and Sriplung, 2001a,b; Onizawa *et al*, 2003; Brouha *et al*, 2005a) nor health-related behaviours (smoking, alcohol or betel quid use) could be related to patient delay (Hollows *et al*, 2000; Kerdpon and Sriplung, 2001a,b; Onizawa *et al*, 2003; Brouha *et al*, 2005a), except in one Dutch study that identified heavy drinking and heavy smoking to be associated with patient delay (Brouha *et al*, 2005a). This group also reported that patients' care-seeking behaviour contributes to an increased or lowered risk of delay (Tromp *et al*, 2005). For tongue cancer, longer patient delays and increased co-morbidity

were associated (Teppo and Alho, 2009). Socioeconomic status was associated (univariate analysis) with patient delay in India (Kumar *et al*, 2001). Younger patients (under the age of 45 years) could be delayed in the referral process as cancer is not suspected in that age group (Llewellyn *et al*, 2004). Psychosocial factors may play a role, but research in this area is meagre, theoretical and of poor quality (Scott *et al*, 2006b). More recent investigations into psychological factors involved in delay by patients indicate the importance of competing priorities, symptom misattribution perceived inability to access care and attempts to self-medicate prior to consulting a health care professional (Scott *et al*, 2008, 2009). Thus, application of psychosocial theoretical models to the investigations in the field of diagnostic delay should be attempted, as the perception of the signs of cancer by the individual may be misunderstood and lead the patient to erroneous behavioural responses that may adversely affect his/her demands or access to care (Scott *et al*, 2005). It seems necessary to support investigations aimed at understanding the role of patient delay in oral cancer in different geographical locations to harvest information that facilitates the design of public health interventions for early diagnosis of oral cancer amongst the identified risk groups. Following this trend, self-examination has the potential to enable patients to detect asymptomatic cancers at early stages (Peacock *et al*, 2008). Patients without symptoms might visit a health care professional every 6 or 12 months. Any self-examination conducted between these intervals might result in the detection of lesions before symptoms develop (Peacock *et al*, 2008). In addition, information campaigns about oral cancer based on media advertising, such as newspaper articles, TV/radio broadcasts, advertisements on billboards, etc., can be useful to raise cancer awareness, but its effects are generally transitory and the message is sometimes misunderstood (Stahl *et al*, 2004). However, information leaflets have a significant effect in raising the long-term oral cancer knowledge and secondary effect on disease awareness among the public (Petti and Scully, 2007).

Does the accessibility to the healthcare system condition the diagnostic delay?

The issue of the influence of the accessibility of the healthcare system on cancer diagnosis has been subjected to very little research (Diz-Dios *et al*, 2005). The accessibility, defined as the ability to obtain services based on oral health needs, can be limited by financial, structural and personal barriers (cultural, spiritual or language differences) and how health care systems operate.

Serious disparities in access to health care (Penchansky and Thomas, 1981) and, in particular, to oral health services exist across Europe, especially for low-income populations (uninsured, migrant, homeless, nursing home residents of institutions, elderly people, etc.). Ethnoregional differences have also been identified in the United States in terms of incidence and mortality rates of oral and pharyngeal cancers, affecting particularly Hispanic and African-American males (Cruz *et al*, 2006; McLean *et al*, 2006). Moreover, disparities in oral and pharyngeal cancer incidence, mortality and survival have been disclosed among black and white Americans (Morse and Kerr, 2006). This may result not only from the variation in the access to oral health care, but also from the different exposition to risk factors or from the limited resources in detection and prevention methods available for these individuals and population groups.

A recent meta-analysis has confirmed that oral cancer incidence is moderately associated with social and economic deprivation, with the highest rates occurring in the most disadvantaged sections of the population (Conway *et al*, 2008). In many developing countries, the imbalance in the distribution of resources for oral healthcare and lack of primary care providers is an issue of social and political concern. To minimize these structural barriers, some countries have developed strategies focussed on improving access problems, such as providing incentives to dentists to serve people enrolled in primary oral care services, and utilizing the primary health care approach for case-detection (Warnakulasuriya *et al*, 1984).

The geographical accessibility measures the extent to which services available and accessible to population will vary according to local means of transportation, as well as the local topography. In Europe, a 30-min travelling time from home or workplace may be considered a reasonable access. However, levels of acceptability can differ from country to country and, hence, should be defined by the local conditions. The use of these indicators of geographical accessibility may be a useful tool for oral healthcare planners to identify geographical areas at risk.

The improvements in the population's health education as well as its awareness of the need for equity, equality and accessibility to healthcare services have highlighted the imperfections in the organization of health services (Allison *et al*, 1998b). The identification of a 'scheduling delay' in oral cancer justifies the introduction of 'technical filters', able to discriminate patients with signs and symptoms that could be related to oral cancer, in the reception of healthcare centres.

Despite the fact that dental hygienists have been identified as vital to strategic interventions aimed at reducing missed opportunities for identification of high-risk groups for oral cancer, their potential contribution in the dental team for oral cancer detection schemes has not been harnessed. Their unique role in the early detection of oral cancer and the delivery of health educational messages reducing risk for this disease has been examined in questionnaire studies (Syme *et al*, 2001; Alonge and Naredran, 2003; Lopez-Jornet *et al*, 2007), but not demonstrated. Additional educational interventions for oral hygienists aimed at reducing the scheduling delay seem to be necessary (Diz-Dios *et al*, 2005; Lopez-Jornet and Camacho-Alonso, 2006). Such educational activities should also be programmed for the receptionists at dental offices and clinical nurse specialists (Trocino *et al*, 1997).

What can be done to increase accessibility?

Strategies to diminish overall diagnostic delay must include political measures that assure a reduction in the time needed to see a healthcare professional and the optimization of the oral primary care services, which need to be accessible to all, particularly to underserved populations. Moreover, specific educational measures aimed at giving selective access and priority to patients at high risk or with signs or symptoms of oral cancer seem to be particularly required. It was heartening to note that Spanish dentists do accurately prioritize patients seeking consultations for an oral cancer symptom compared with routine complaints (Lopez-Jornet and Camacho-Alonso, 2006).

In this sense, the 'waiting lists' are a relevant problem for all national health systems that grant citizens a free access to the healthcare system. Despite the existence of waiting lists, it is needed to ease activity planning and to favour an optimization of the existing resources, as the waiting lists substantially increase the scheduling delay in oral cancer. In this environment, access for the patients to a healthcare centre is very variable depending on his/her disorder; however, it is mandatory to warrant a rapid appointment to patients suspicious of having symptoms of oral cancer. To this end, '*Two weeks wait*' system was rolled out in December 2000 for Head and Neck cancer referrals in the United Kingdom (Department of Health, 2000; NIHCE, 2005). An audit of this initiative in the UK indicates that a high proportion of non-malignancies could come via the fast-track system to the hospitals because of low sensitivity of visual detector guidelines (Singh and Warnakulasuriya, 2006).

There are some countries where access to the healthcare system has some limitations that are adversely influencing marginal and lower-income (older than 65 included), uninsured groups (Gornick *et al*, 1996). In certain situations, the insurance covers expensive and complicated surgical procedures for the treatment of oral cancer but does not include routine, inexpensive dental procedures, including oral examinations for screening of oral cancer. Dental services are not affordable for low-income patients in many countries and thus, it is more likely that at-risk population visits a physician rather than a dentist. In these situations, an opportunistic oral examination should be performed for these patients during routine medical examinations (Penchansky and Thomas, 1981; Allison *et al*, 1998b; Horowitz *et al*, 2000; Yellowitz *et al*, 2000). Clinical presentation of oral cancer first seen by a dentist or physician could also be somewhat different (De Faria *et al*, 2003) and dentists may diagnose lower stage cancers (Holmes and Homer, 2003). Understanding practices of dental health professionals is vital to assess their contribution to reduce any delays in cancer prevention (Kujan *et al*, 2006).

Another factor to be taken into account is the time elapsed since the patient makes an appointment and is actually seen by a health professional. A scheme of priorities should be established, based upon the national load of cancer, availability of resources and capability of the healthcare system to develop programmes, with measurable objectives and aimed at obtaining results in the short, medium and long term. Accurate defining of a set of signs and symptoms of early oral cancer that should prompt an urgent referral should be achieved in consultation with expert working groups. These should be made available as referral guidelines to primary care physicians and dentists.

What makes a healthcare professional delay oral cancer diagnosis?

Professional diagnostic delay in oral cancer has several definitions in the literature: the time elapsed since the first consultation to a healthcare professional until the first consultation to the treating professional (Allison *et al*, 1998b), or until the appointment for treatment (Kowalski *et al*, 1994). It has also been defined as the time since first consultation to the receipt of the referral letter at the specialized services (Scully *et al*, 1986; Schnelter, 1992; Hollows *et al*, 2000). However, the commonly accepted definitions consider the time elapsed since the first consultation by a healthcare professional until a definitive diagnosis is reached (Dimitroulis *et al*, 1992; Wildt *et al*, 1995; Hollows *et al*, 2000) or treatment is instituted. Both these definitions employed by research groups and the grouping or ungrouping of the different time periods make comparisons difficult. This accounts for the reduced number of reviews addressing this issue.

Some causes of professional delay due to patient factors have been suggested: sociodemographic (age, gender and race); previous health experiences (previous professional and family experiences with cancer, routine screening practices); lack of known aetiological factors (alcohol, tobacco, etc.); cognitive interpretation of the symptoms (ignorance/knowledge); conflict of responsibilities (patient co-morbidity) and distance to/existence of specialized referral services (Allison *et al*, 1998a).

There are no reports relating professional diagnostic delay either with sociodemographic features of the clinicians, or with their health experiences. However, there are a number of studies investigating a hypothetical relationship between the academic degrees of the clinicians and how this relates to the rapidity of diagnosis- particularly between dentists and general medical practitioners- with equivocal results (Adams *et al*, 1974; Amsel *et al*, 1983; Scully *et al*, 1986; Gorsky and Dayan, 1995; Allison *et al*, 1998b; Holmes and Homer, 2003; Llewellyn *et al*, 2004). Certain research groups find that general medical practitioners refer oral cancer patients quicker than do dentists, putting this down to a higher index of suspicion by the former (Scully *et al*, 1986; Schnelter, 1992), whereas other researchers attribute this phenomenon to the high prevalence of ulcerated lesions within the oral cavity caused by inflammatory processes and to the low incidence of oral cancer (Onizawa *et al*, 2003). Dental clinicians who are more familiar with these oral lesions offer some form of treatment instead of the option of an immediate referral, which would be chosen by the

general medical practitioners, who are less comfortable with the management of such lesions (Onizawa *et al*, 2003). This trend has been observed even after the introduction of new clinical practice guidelines that should have made clinicians feel more secure when dealing with such referral processes, rather than delaying patient referral (McLeod *et al*, 2005). Moreover, some knowledge gaps have been identified among general medical and dental practitioners and undergraduate students in their awareness of oral cancer risk factors and the application of preventive measures (Carter and Ogden, 2007; Gillison, 2007; Ni Riordain and McCreary, 2009) as well as a worrying ignorance on changes (signs) associated with early forms of oral cancer (Carter and Ogden, 2007). Early oral cancer often causes only subtle changes or is asymptomatic (McGurk *et al*, 2005; Yu *et al*, 2008), besides the individual's interpretation of potentially malignant oral symptoms is often misguided (Scott *et al*, 2007). In this situation, ignorance of early signs of oral cancer may be the most important delaying factor. Erythroplakia, as the most frequent clinical presentation of early oral carcinoma, followed by erythroleukoplakia and leukoplakia are particularly mistaken and their recognition needs to be emphasized in future teaching of both medical and dental students and health care professionals (Carter and Ogden, 2007). Diagnosis of small-sized carcinomas should also include carcinomas smaller than 2 cm of diameter and depths of invasion lower than 4 mm (Woolgar, 2006), as tumour thickness is a very exact predictor for subclinical node metastases, local recurrence and survival (Gonzalez-Moles *et al*, 2002).

However, several reports support the emerging opinion that asymptomatic cancers are more likely to be detected in a dental setting (Axell, 1993), and a dental care provider is more likely to detect a lesion during a routine appointment than a medical provider (Gellrich *et al*, 2003; Holmes and Homer, 2003; Lim *et al*, 2003), thus reducing the overall diagnostic delay. The findings reported in these studies are backed by a recent report that states that head and neck cancer patients who were not under the regular supervision and care of a dentist were more likely to have longer diagnostic delay (Yu *et al*, 2008).

Identified causes of professional diagnostic delay were not to practice a full clinical examination (Robbins *et al*, 1950), unspecific or inflammatory clinical signs (Bruun, 1976), low index of suspicion (Holland, 1982) and lack of familiarity and experience with the disease (Guggenheimer *et al*, 1989). Co-morbidity has also been suggested (Allison *et al*, 1998b), as in these situations the clinicians tend to prioritize the stabilization of the existing disease before paying attention to new symptoms.

The characteristics of the patient and the kind of relationship he/she maintains with the clinician (attendance pattern) may have a part in the professional delay, as well as the age of the patient and holding a university degree may reduce the professional delay (Allison *et al*, 1998b).

Specialist's delay in management of oral cancer or head and neck cancer in larger cancer centres needs to be audited. One such recent report suggests that whereas oral tumours may be diagnosed and treated quickly, others such as glottic carcinomas may take considerable time for diagnosis (Brouha *et al*, 2007). Unsurprisingly, large (T3–T4) tumours showed significantly less specialist delay than small tumours (T1–T2). In this Dutch study, specialist delay ranged from 0 to 570 days, with a median of 14 days. It took a further 21 days for the work-up and the waiting time for treatment was 47 days.

Conclusions and future researches

The detection of oral cancer at an early stage 'is the most effective means to improve survival and reduce morbidity, disfigurement, duration of treatment and hospital costs associated with this disease' (Scott *et al*, 2008). A review of published studies suggests delay in diagnosis of head and neck, including oral cancer is common (Goy *et al*, 2009). A number of reports have blamed mainly patients (Jovanovic *et al*, 1992; Wildt *et al*, 1995; Tromp *et al*, 2005), clinicians –providers/professional delay – (Kowalski *et al*, 1994; Gorsky and Dayan, 1995; Onizawa *et al*, 2003) or both (Allison *et al*, 1998a,b; Morelatto *et al*, 2007) for late diagnosis.

The efforts aimed at early diagnosis of oral cancer should be prioritized towards screening programmes designed to detect the disease during its asymptomatic phases. Patient delay could be reduced by auto-examination of the signs (early clinical manifestations) and by educational interventions aimed at the general population, particularly at those in the risk groups for oral cancer.

Professional diagnostic delay in oral cancer will depend on the interpretation that the clinician makes of the patient's signs and symptoms, consideration given to demographic and social records of the patient and patient's previous experiences. Training and clinical interests, the clinician's index of suspicion and a sound knowledge of the disease presentation also play a role. In this context, to reduce diagnostic delay, it seems mandatory to develop appropriate initiatives to increase knowledge and favour preventive attitudes both at undergraduate and professional (medical and dental) level by life-long learning education.

A distance learning programme to assist in the early detection of oral cancer will soon be available on the World Wide Web (http://www.ocedr.org), a resource by the WHO Collaborating Centre for Oral Cancer and Precancer in the UK. The access to and the kind of healthcare system, particularly the referral system, in a particular country are also relevant. The design of a simple, clear, fail-safe, fast-track referral scheme for those suspected of cancer may diminish greatly the length of the delay. A critical review of the literature suggests the need for future investigations, which are methodologically adequate, that consider cultural and geographical aspects and use patient survival as the final outcome; able to recognize the agents/factors

responsible for diagnostic delay (patient, healthcare provider and health system) and aimed at designing interventions that permit an early diagnosis of oral cancer.

Author contributions

All co-authors contributed equally to the planning, drafting and editing of this manuscript.

References

Adams RS, Pullon PA, Lee F (1974). Expanding the role of the dentist in the detection of oral and laryngeal cancer. *J Am Dent Assoc* **89:** 607–610.

Allison P, Locker D, Feine JS (1998a). The role of diagnostic delays in the prognosis of oral cancer: a review of the literature. *Oral Oncol* **34:** 161–170.

Allison P, Franco E, Feine J (1998b). Predictors of professional diagnostic delays for upper aerodigestive tract carcinoma. *Oral Oncol* **34:** 127–132.

Allison P, Franco E, Black M, Feine J (1998c). The role of professional diagnostic delays in the prognosis of upper aerodigestive tract carcinoma. *Oral Oncol* **34:** 147–153.

Alonge OK, Naredran S (2003). Opinions about oral cancer prevention and early detection among dentists practising along the Texas-Mexico border. *Oral Dis* **9:** 41–45.

Amir Z, Kwan SYL, Landes D, Feber T, Williams SA (1999). Diagnostic delays in head and neck cancers. *Eur J Cancer Care (Engl)* **8:** 198–203.

Amsel Z, Strawitz JG, Engstrom PF (1983). The dentist as a referral source of first episode head and neck cancer patients. *J Am Dent Assoc* **106:** 195–197.

Andersen BL, Cacioppo JT, Roberts DC (1995). Delay in seeking a cancer diagnosis: delay stages and psychophysiological comparison processes. *Br J Soc Psychol* **34:** 33–52.

Axell T (1993). The professional role of the dentist under the aspects of precancer and cancer diagnosis and management. *Int Dent J* **43:** 609–611.

Brouha XDR, Tromp DM, Hordijk GJ, Winnubst JAM, Leeuw JRJ (2005a). Role of alcohol and smoking in diagnostic delay in head and neck cancer patients. *Acta Otolaryngol* **125:** 552–556.

Brouha XDR, Tromp DM, Hordijk GJ, Winnubst JAM, Leeuw RJ (2005b). Oral and pharyngeal cancer: analysis of patient delay at different tumor stages. *Head Neck* **27:** 939–945.

Brouha XDR, Tromp DM, Koole R, Hordijk GJ, Winnubst JAM, de Leeuw JRJ (2007). Professional delay in head and neck cancer patients: Analysis of diagnostic pathway. *Oral Oncol* **43:** 551.

Brown B, Barnes L, Mazariegos J, Taylor F, Johnson J, Wagner RL (1989). Prognostic factors in mobile tongue and floor of the mouth carcinoma. *Cancer* **64:** 1195–1202.

Bruun JP (1976). Time lapse by diagnosis of oral cancer. *Oral Surg Oral Med Oral Pathol* **42:** 139–149.

Cancer Research UK (2005). Cancerstats. *Oral Cancer UK*. London: Cancer Research UK.

Carter LM, Ogden GR (2007). Oral cancer awareness of general medical and general dental practitioners. *Br Dent J* **203:** 248–249.

Carvalho AL, Pintos J, Schlecht NF *et al* (2002). Predictive factors for diagnosis of advanced-stage squamous cell carcinoma of the head and neck. *Arch Otolaryngol Head Neck Surg* **128:** 313–318.

Conway DI, Petticrew M, Marlborough H, Berthiller J, Hashibe M, Macpherson LMD (2008). Socioeconomic inequalities and oral cancer risk: a systematic review and meta-analysis of case–control studies. *Int J Cancer* **122:** 2811–2819.

Cruz GD, Salazar CR, Morse DE (2006). Oral and pharyngeal cancer incidence and mortality among hispanics, 1996–2002: the need for ethnoregional studies in cancer research. *Am J Public Health* **96:** 2194.

De Faria PR, Cardoso SV, De A, Nishioka S, Silva SJ, Loyola AM (2003). Clinical presentation of patients with oral squamous cell carcinoma when first seen by dentist or physician in a teaching hospital in Brazil. *Clin Oral Invest* **7:** 46–51.

Department of Health (2000). *Referral guidelines for suspected cancer*. London: Stationary office.

Dimitroulis G, Reade P, Wiesenfeld D (1992). Referral patterns of patients with oral squamous cell carcinoma, Australia. *Oral Oncol* **28:** 23–27.

Diz-Dios P, Padrón-Gonzalez N, Seoane-Lestón J, Tomas-Carmona I, Limeres-Posse J, Varela-Centelles P (2005). "Scheduling delay" in oral cancer diagnosis: a new protagonist. *Oral Oncol* **41:** 142–146.

Elwood JM, Gallagher RP (1985). Factors influencing early diagnosis of cancer of the oral cavity. *Can Med Assoc J* **133:** 651–656.

Erwenne CM, Franco ELF (1989). Age and lateness of referral as determinants of extra-ocular retinoblastoma. *Opthal Pediatr Genetics* **10:** 179–184.

Evans SJW, Langdon JD, Rapidis AD, Johnson NW (1982). Prognostic significance of STNMP and velocity of tumour growth in oral cancer. *Cancer* **49:** 7773–7776.

Facione NC (1993). Delay versus help seeking for breast cancer symptoms: a critical review of the literature on patient and provider delay. *Soc Sci Med* **36:** 1521–1534.

Gellrich NC, Suarez-Cunqueiro M, Bremerich A, Schramm A (2003). Characteristics of oral cancer in a central European population. Defining dentist's role. *J Am Dent Assoc* **134:** 307–314.

Gillison ML (2007). Current topics in the epidemiology of oral cavity and oropharyngeal cancers. *Head Neck* **29:** 779–792.

Gomez I, Seoane J, Varela-Centelles P, Diz P, Takkouche B (2009). Is diagnostic delay related to advanced stage oral cancer? *A meta-analysis Eur J Oral Sci* **117:** 541–546.

Gonzalez-Moles MA, Esteban F, Rodriguez-Archilla A, Ruiz-Avila I, Gonzalez-Moles S (2002). Importance of tumour thickness measurement in prognosis of tongue cancer. *Oral Oncol* **38:** 394–397.

Gornick ME, Eggers PW, Reilly TW *et al* (1996). Effects of race and income on mortality and use of services among Medicare beneficiaries. *N Engl J Med* **335:** 791–799.

Gorsky M, Dayan D (1995). Referral delay in diagnosis of oro/oropharyngeal cancer in Israel. *Oral Oncol* **31B:** 166–168.

Goy J, Hall SF, Feldman-Stewart D, Groome PA (2009). Diagnostic delay and disease stage in head and neck cancer: a systematic review. *Laryngoscope* **119:** 889–898.

Guay AH (2004). Access to dental care: solving the problem for underserved populations. *J Am Dent Assoc* **135:** 1599–1605.

Guggenheimer J, Verbin RS, Johnson JT, Horkowitz CA, Myers EN (1989). Factors delaying the diagnosis of oral and oropharingeal carcinomas. *Cancer* **64:** 932–935.

Holland JC (1982). Psychologic aspects of cancer. In: Holland JF, Frei E, eds *Cancer Medicine*, 2nd edn. Philadelphia: Lea and Febiger, pp. 1175–1177.

Hollows P, McAndrew PG, Perini MG (2000). Delays in the referral and treatment of oral squamous cell carcinoma. *Br Dent J* **188:** 262–265.

Holmes JD, Homer LD (2003). Is detection of oral and oropharyngeal squamous cancer by a dental health care provider associated with a lower stage at diagnosis? *J Oral Maxillofac Surg* **61:** 285–291.

Horowitz AM, Drury TF, Canto MT (2000). Practices of Maryland dentists: oral cancer prevention and early detection-baseline from 1995. *Oral Dis* **6:** 282–288.

IARC (2004) *Globocan 2002. Cancer incidence, mortality and prevalence worldwide*. IARC: Lyon.

Jovanovic A, Kostense PJ, Schulten EAJM, Snow GB, van der Waal I (1992). Delay in diagnosis of oral squamous cell carcinoma; a report from the Netherlands. *Oral Oncol* **28B:** 37–38.

Kantola S, Jokinen K, Hyrykangas K, Mäntyselkä P, Alho OP (2001). Detection of tongue cancer in primary care. *Br J Gen Pract* **51:** 106–111.

Kaufman S, Grabau JC, Lore JH (1980). Symptomatology in head and neck cancer; a quantitative review of 385 cases. *Am J Public Health* **70:** 520–522.

Kerdpon D, Sriplung H (2001a). Factors related to delay in diagnosis of oral squamous cell carcinoma in southern Thailand. *Oral Oncol* **37:** 127–131.

Kerdpon D, Sriplung H (2001b). Factors related to advanced stage oral squamous cell carcinoma in Southern Thailand. *Oral Oncol* **37:** 216–221.

Kowalski LP, Carvalho AL (2001). Influence of time delay and clinical upstaging in the prognosis of head and neck cancer. *Oral Oncol* **37:** 94–98.

Kowalski LP, Franco EL, Torloni H *et al* (1994). Lateness of diagnosis of oral and oropharyngeal carcinoma: factors related to the tumour, the patient and health professionals. *Oral Oncol* **30B:** 167–173.

Kujan O, Duxbury AJ, Glenny AM, Thakker NS, Sloan P (2006). Opinions and attitudes of the UK's GDPs and specialists in oral surgery, oral medicine and surgical dentistry on oral cancer screening. *Oral Dis* **12:** 194–199.

Kumar S, Heller RF, Pandey U, Tewari V, Bala N, Oanh KTH (2001). Delay in presentation of oral cancer: a multifactor analytical study. *Natl Med J India* **14:** 13–17.

LaVecchia C, Lucchini F, Negri E, Levi F (2004). Trends in oral cancer mortality in Europe. *Oral Oncol* **40:** 433–439.

Lim K, Moles DR, Downer MC, Speight DM (2003). Opportunistic screening for oral cancer and precancer in general dental practice: results of a demonstration study. *Br Dent J* **194:** 497–502.

Llewellyn CD, Johnson NW, Warnakulasuriya KA (2001). Squamous cell carcinomas of the oral cavity in young people: a comprehensive literature review. *Oral Oncol* **37:** 401–408.

Llewellyn CD, Johnson NW, Warnakulasuriya S (2004). Factor associated with delay in presentation among younger patients with oral cancer. *Oral Surg, Oral Med, Oral pathol, Oral Radiol Endod* **97:** 707–713.

Lopez-Jornet P, Camacho-Alonso F (2006). New barriers in oral cancer: patient accessibility to dental examination-a pilot study. *Oral Oncol* **42:** 1022–1025.

Lopez-Jornet P, Camacho-Alonso F, Molina Miñano F (2007). Knowledge and attitude towards risk factors in oral cancer held by dental hygienists in the Autonomous Community of Murcia (Spain): a pilot study. *Oral Oncol* **43:** 602–606.

Massano J, Regateiro FS, Januario G, Ferreira A (2006). Oral squamous cell carcinoma: review of prognostic and predictive factors. *Oral Surg, Oral Med, Oral Pathol* **102:** 67–76.

McGurk M, Chan C, Jones J, O'Regan E, Sherriff M (2005). Delay in diagnosis and its effect on outcome in head and neck cancer. *Br J Oral Maxillofac Surg* **43:** 281–284.

McLean A, LeMay W, Vila P, Wegner M, Remington P (2006). Disparities in oral and pharyngeal cancer incidence and mortality among Wisconsin residents, 1999–2002. *Wiscoin Med J* **105:** 32–35.

McLeod NHM, Saeed NR, Ali EA (2005). Oral cancer: delays in referral and diagnosis persist. *Br Dent J* **198:** 681–684.

Montoro JR, Hicz HA, Livingstone D, Melo DH, Tiveron RC, Mamede RC (2008). Prognostic factors in squamous cell carcinoma of the oral cavity. *Braz J Otorhinolaryngol* **74:** 861–866.

Morelatto RA, Herrera MC, Fernandez EN, Corball AG, Lopez de Blanc SA (2007). Diagnostic delay in oral squamous cell carcinoma in two diagnostic centres in Cordoba, Argentina. *J Oral Pathol Med* **36:** 405–408.

Morse DE, Kerr AR (2006). Disparities in oral and pharryngeal cancer incidence, mortality and survival among black and white Americans. *J Am Dent Assoc* **137:** 203–212.

National Institute for Health and Clinical Excellence (2005). *Referral guidelines for suspected cancers*. Clinical Guideline 27; London: NIHCE.

Neville BW, Day TA (2002). Oral cancer and precancerous lesions. *CA Cancer J Clin* **52:** 195–215.

Ni Riordain R, McCreary C (2009). Oral cancer – current knowledge, practices and implications for training among an Irish general medical practitioner cohort. *Oral Oncol* **45:** 958–962.

O'Sullivan EM (2001). Some insights into the potential for the earlier detection of oral cancer: a population-based study. *In: 7th International Congress on Oral Cancer, April 2001*, The Hague, Netherlands, *Oral Oncol* **37:** 553.

Onizawa K, Nishihara K, Yamagata K, Yusa H, Yanagawa T, Yoshide H (2003). Factors associated with diagnostic delay of oral squamous cell carcinoma. *Oral Oncol* **39:** 781–788.

Parker SL, Tong T, Bolden S, Wingo PA (1996). Cancer statistics 1996. *CA Cancer J Clin* **46:** 5–28.

Parkin DM, Bray F, Ferlay J, Pisani P (2005). Global cancer statistics, 2002. *CA Cancer J Clin* **55:** 74–108.

Peacock ZS, Pogrel MA, Schmidt DC (2008). Exploring the reasons for delay in treatment of oral cancer. *J Amer Dent Assoc* **139:** 1346–1352.

Penchansky R, Thomas JW (1981). The concept of access. Definition and relationship to consumer satisfaction. *Med Care* **19:** 127–140.

Petti S, Scully C (2007). Oral cancer knowledge and awareness: primary and secondary effects of an information leaflet. *Oral Oncol* **43:** 408–415.

Pitiphat W, Diehl SR, Laskaris G, Cartsos V, Douglass CW, Zavras AI (2002). Factors associated with delay in the diagnosis of oral cancer. *J Dent Res* **81:** 192–197.

Porta M, Gallen M, Malats N, Planas J (1991). Influence of diagnostic delay upon cancer survival: an analysis of tumour sites. *J Epidemiol Community Health* **45:** 225–230.

Rapidis AD, Gullane P, Langdon JD, Lefebvre JL, Scully C, Shah JP (2009). Major advances in the knowledge and understanding of the epidemiology, aetiopathogenesis, diagnosis, management and prognosis of oral cancer. *Oral Oncol* **45:** 299–300.

Richards D (2007). Patient delay in reporting oral cancer is poorly understood. *Evid Based Dent* **8:** 21.

Robbins GF, Conte AJ, Leach JE, McDonald M (1950). Delay in the diagnosis and treatment of cancer. *JAMA* **143:** 546–548.

Rogers SN, Pabla R, McSorley A, Lowe D, Brown JS, Vaughan ED (2007). An assessment of deprivation as a factor in the delays in presentation, diagnosis and treatment in patients with oral and oropharyngeal squamous cell carcinoma. *Oral Oncol* **43:** 648–655.

Rogers SN, Brown JS, Woolgar JA, *et al* (2009). Survival following primary surgery for oral cancer. *Oral Oncol* **45:** 201–211.

Sandoval M, Font R, Manos M *et al* (2009). The role of vegetable and fruit comsumption and other habits on survival following the diagnosis of oral cancer: a prospective study in Spain. *Int J Oral Maxillofac Surg* **38:** 31–39.

Schnelter JFC (1992). Oral cancer diagnosis and delays in referral. *Br J Oral Maxillofac Surg* **30:** 210–213.

Scott SE, Grunfeld EA, McGurk M (2005). The idiosyncratic relationship between diagnostic delay and stage of oral squamous cell carcinoma. *Oral Oncol* **41:** 396–403.

Scott SE, Grunfeld EA, McGurk M (2006a). Patient's delay in oral cancer: a systematic review. *Community Dent Oral Epidemiol* **34:** 337–343.

Scott SE, Grunfeld EA, Main J, McGurk M (2006b). Patient delay in oral cancer: a qualitative study of patients' experiences. *Psychooncology* **15:** 475–485.

Scott SE, McGurk M, Grunfeld EA (2007). The process of symptom appraisal: cognitive and emotional responses to detecting potentially malignant oral symptoms. *J Psychosom Res* **62:** 621–630.

Scott S, McGurk M, Grunfeld E (2008). Patient delay for potentially malignant oral symptoms. *Eur J Oral Sci* **116:** 141–147.

Scott SE, Grunfeld EA, Auyeung V, McGurk M (2009). Barriers and triggers to seeking help for potentially malignant oral symptoms: implications for interventions. *J Public Health Dent* **69:** 34–40.

Scully C, Malmos D, Levers BGH, Porter SR, Prime SS (1986). Sources and patterns of referrals of oral cancer: role of general practitioners. *Br Med J* **293:** 599–601.

Seoane J, Varela-Centelles PI, Walsh TF, Lopez-Cedrun JL, Vazquez I (2006). Gingival squamous cell carcinoma: diagnostic delay or rapid invasion? *J Periodontol* **77:** 1229–1233.

Shafer WG (1975). Initial mismanagement and delay in diagnosis of oral cancer. *J Am Dent Assoc* **90:** 1262–1264.

Singh P, Warnakulasuriya S (2006). The two-week wait cancer initiative on oral cancer, the predictive value of urgent referrals to an oral medicine unit. *Br Dent J* **201:** 717–720.

Spiro RH, Huvos AG, Wong GY, Spiro JD, Gnecco CA, Strong EW (1986). Predictive value of tumour thickness in squmaous carcinoma confined to the tongue and floor of the mouth. *Am J Surg* **152:** 345–350.

Stahl S, Meskin LH, Brown LJ (2004). The American Dental Association's oral cancer campaign: the impact on consumers and dentists. *J Am Dent Assoc* **135:** 1261–1267.

Syme SE, Drury TF, Horowitz AM (2001). Maryland dental hygienists' knowledge and opinions of oral cancer risk factors and diagnostic procedures. *Oral Dis* **7:** 177–184.

Teppo H, Alho OP (2008). Relative importance of diagnostic delays in different head and neck cancers. *Clin Otolaryngol* **33:** 325–330.

Teppo H, Alho OP (2009). Comorbidity and diagnostic delay in cancer of the larynx, tongue and pharynx. *Oral Oncol* **45:** 692–695.

Teppo H, Koivunen P, Hyrynkangas K, Alho OP (2003). Diagnostic delays in laryngeal carcinoma: professional delay is a strong independent predictor of survival. *Head Neck* **25:** 389–394.

Trocino L, Byers JF, Peach AG (1997). Nurses' attitudes towards patient and family education: implications for clinical nurse specialists. *Clin Nurse Spec* **11:** 77–84.

Tromp DM, Brouha DR, Hordijk GJ, Winnubst JAM, Leeuw RJ (2005a). Patient and tumour factors associated with advanced carcinomas of the head and neck. *Oral Oncol* **41:** 313–319.

Warnakulasuriya KA, Ekanayake AN, Sivayoham S *et al* (1984). Utilization of primary health care workers for early detection of oral cancer and precancer cases in Sri Lanka. *Bull World Health Organ* **62:** 243–250.

Warnakulasuriya S (2009). Global epidemiology of oral and oropharyngeal cancer. *Oral Oncol* **45:** 309–316.

Wildt J, Bundgaard T, Bentzen SM (1995). Delay in the diagnosis of oral squamous cell carcinoma. *Clin Otolaryngol* **20:** 21–25.

Woolgar JA (2006). Histopathological pronosticators in oral and oropharyngeal squamous cell carcinoma. *Oral Oncol* **2006:** 42.

Yellowitz JA, Horowitz AM, Drury TF, Goodman HS (2000). Survey of U.S. dentist's knowledge and opinions about oral pharyngeal cancer. *J Am Dent Assoc* **131:** 653–651.

Yu T, Wood RE, Tenenbaum HC (2008). Delays in diagnosis of head and neck. *J Can Dent Assoc* **74:** 61.