The economics of squamous cell carcinoma of the head and neck

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Purpose of review

The current review presents a brief overview of the recent literature on the costs of squamous cell carcinoma of the head and neck (SCCHN), one of the most common forms of cancer. SCCHN is a relatively deadly disease. Approximately 50% of patients survive to 5 years, and surgery and chemoradiotherapy can leave survivors with pain, disfigurement, and disability that further add to the burden of the disease.

Recent findings

Earlier diagnosis of SCCHN increases the likelihood of treating with a single modality, lowers the risk of mortality, decreases medical expenditures, and improves patients' quality of life. Unfortunately, more than one-half of new cases of oral cancer are diagnosed at an advanced stage. Patients with SCCHN have been shown to use significantly more healthcare resources than similar patients without SCCHN, with resource use varying by cancer stage.

Summary

Although there have been a number of treatment innovations for SCCHN in the past 5 years, the lack of economic data complicates the task of evaluating these new interventions. In this time of mounting concerns over healthcare costs, more emphasis on economic data is clearly warranted.

Keywords

costs, economics, head and neck cancer, healthcare policy, treatments

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Abbreviations

EBRT	external beam radiation therapy
HNC	head and neck cancer
SSCHN	squamous cell carcinoma of the head and neck

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Introduction

Head and neck cancer (HNC) describes a diverse group of cancers, including carcinoma of the lip, salivary glands, sinuses, oral cavity, pharynx, and larynx. In 2002 there were approximately 874 000 new cases of cancer of the oral cavity, pharynx, and larynx worldwide – the fifth-highest incidence of all cancers [1]. Approximately 90% of these cancers are squamous cell carcinomas of the head and neck (SCCHNs) [2,3]. Using electronic databases, we identified economic analyses of SCCHN and its treatments and retrieved relevant articles published between 2004 and 2006. To facilitate comparisons between studies, we adjusted all amounts to October 2006 US dollars using published foreign exchange rates [4] and the US Medical Care Consumer Price Index [5]. The purpose of this paper is to provide a brief overview of the epidemiology and treatment of HNC and to describe the current literature on the economics of this disease.

Epidemiology and treatment

Men are more than twice as likely as women to be diagnosed with HNC [6]. There are also racial disparities in the incidence and mortality rates of HNC. Black men have a higher incidence of the disease than men in any other racial/ethnic group or than women from all racial/ethnic groups; the same holds true for mortality rates [7].

A number of genetic and environmental/behavioral factors put individuals at risk for developing HNC. A 2004 report by the US Surgeon General [8] stated that smoking and/or tobacco use causes oral cavity and pharynx cancers, and that a combination of smoking and alcohol use causes a majority of laryngeal cancers. Additional environmental risk factors include poor dental hygiene, poor nutrition, prolonged exposure to ultraviolet light, and human papillomavirus [9]. A number of studies now show that having a family history or genetic predisposition to cancer are significant risk factors for developing primary or secondary HNC [10–12]. These genetic vulnerabilities in combination with environmental factors can put individuals at even greater risk for HNC [12]. The overall 5-year survival rate is around 60% in the United States, but the rate is much lower for black patients than white patients, and specifically for black men (35.6% versus 60.6% for white men) [7].

Most SCCHN cases are treated with surgery, radiotherapy, chemotherapy, or a combination of all three [13]. The pain, disfigurement, and physical disabilities that

frequently arise from the disease and its treatment have serious effects on survivors' quality of life. A multispecialty team of providers is often needed to assist patients through their treatments for SCCHN, and recovery can take months and often years.

A number of advances in therapies for SCCHN have been developed in the past several years, most notably the regulatory approval of cetuximab (Erbitux; ImClone Systems, New York, USA/Bristol-Myers Squibb, New York, USA) in the United States. Other innovations include induction chemotherapy, new microsurgical and minimally invasive surgical techniques, increased use of imaging technologies, accelerated radiotherapy, and advances in radiotherapy planning and delivery.

Economics: definitions

In health economics, total costs encompass direct costs (for which payments are made), indirect costs (by which resources are lost), and intangible costs. Direct costs are associated with emergency department and hospital services, physician services, medications, therapies, diagnostic procedures, laboratory tests, ancillary therapies, and other healthcare services. Indirect costs result from lost productivity, disability, and premature death due to a disease or condition. Intangible costs are primarily psychosocial in nature.

Much of health economics research involves understanding the cost of an intervention in relation to the benefits derived from it. The most common analytical approaches are cost-minimization analysis and cost-effectiveness analysis. The latter often uses the cost per additional life-year (or quality-adjusted life-year) as the measure of treatment effectiveness. The sections that follow provide estimates of the direct and indirect costs of SCCHN.

Direct costs associated with head and neck cancer

An extensive 2006 report from the United Kingdom [14••] contained a section on resource use and costs associated with oral cancer and precancer, with data derived from 147 case reviews at two hospitals. Mean inpatient lengths of stay in the first year after diagnosis ranged from 1.86 days for patients with precancerous lesions to 29.90 days for patients with stage IV cancer. Patients with precancer had an average of 6.68 outpatient visits in the first year after diagnosis, compared with 18.37 outpatient visits for patients with stage IV cancer. The mean per-patient cost of managing oral cancer in the first year after diagnosis, including inpatient and outpatient expenditures, ranged from $3443 for precancer patients to $24 890 for stage IV cancer patients. Over 3 years, the overall cost of management for all oral cancer patients averaged $74 997 per patient.

Table 1 Resource use by patients with SCCHN over 5 years among Medicare patients

Variable	SCCHN cohort ($n = 4536$)	Comparison cohort ($n = 4536$)
Rate of hospitalization (%)	82	55
Mean number of hospitalizations	2.5	1.4
Mean number of inpatient days	24	12
Rate of skilled nursing care use (%)	22	13
Mean number of days of skilled nursing care	9	5
Rate of home healthcare use (%)	48	26
Rate of hospice care use (%)	14	3

All $P < 0.001$. Adapted from Lang *et al.* [13].

In a 2004 SEER-Medicare database study by Lang *et al.* [13], patients with SCCHN were shown to use significantly more healthcare resources than similar control individuals without SCCHN in terms of hospitalization, outpatient care, home healthcare, and hospice services (Table 1). Resource use varied widely according to disease severity; for example, patients with distant cancer had a mean inpatient hospital stay of 30 days, compared with 16 days for those with local cancer [13].

In a 2004 study, Lee *et al.* [15] reviewed the literature published between 1990 and 2002 that addressed the economics of SCCHN. The estimates of the total cost to society from head and neck cancer ranged from around $1.3 billion in Germany to just over $2 billion in the United States. The mean per-patient estimates of the total cost of care ranged from $9398 for Greek oral cancer patients to $25 936 for US SCCHN patients.

Variation in cost by treatment modality

Six studies published in English within the past 3 years have focused on various treatments for HNC [16••,17,18•, 19••,20•,21••]. Below, we briefly review the recent cost data related to these treatments.

Braaksma *et al.* [16••] assessed the costs of weekly paclitaxel treatment with or without antitoxicity treatment intensification using amifostine. Although no significant antitoxic benefit was observed for amifostine, the costs of treatment and toxicity were significantly greater for the amifostine group than the no-amifostine group ($21 445 versus $14 836).

Nijdam and colleagues [17,18•] conducted two studies comparing the costs of alternative forms of treatment for different types of HNC. In the first study [17], hospital and follow-up costs associated with various forms of treatment were compared for patients with tonsillar fossa and/or soft palate tumors. Patients who underwent neck surgery followed by external beam radiation therapy (EBRT) incurred higher overall costs compared with patients who underwent EBRT and brachytherapy with

or without neck dissection ($14 276 versus $10 496 and $6909, respectively).

In a second study, Nijdam *et al.* [18•] calculated the overall costs (e.g. costs of treatment preparation, surgical costs, other medical costs such as blood transfusion, and follow-up treatment costs) of EBRT alone or in conjunction with either brachytherapy or surgical resection for patients with oropharyngeal cancer. Overall, the surgical resection group had the highest mean costs ($30 476 for the surgical group versus $22 906 in the EBRT only group and $19 502 in the EBRT and brachytherapy group); no significant group differences were observed for 5-year locoregional control, disease-free survival, or overall survival.

Two recent studies [19••,20•] have compared the costs of different surgical techniques. Brookes *et al.* [19••] compared the difference in hospital costs accrued by patients whose tracheotomy sites were either sutured or not sutured at the time of decannulation; patients in the suture group had a faster time to swallowing, shorter hospital stays, and an average per-patient cost saving of $11 609. Smeele *et al.* [20•] reported no differences in the medical costs associated with free flap reconstruction versus pedicled flap construction among patients with squamous cell carcinoma of the oral cavity or oropharynx.

Finally, Davis *et al.* [21••] performed a decision analysis that compared the costs of surgical treatment plus radiotherapy versus larynx preservation using induction chemotherapy followed by radiotherapy for advanced laryngeal cancer. Results from this analysis indicated that the surgical option costs an average of $3394 less than organ preservation under most scenarios.

Cost-effectiveness of treatments

We identified three cost-effectiveness studies of HNC treatments published within the past 3 years [22,23,24••].

Kosuda *et al.* [22] reported that the use of sentinal lymph node radiolocalization as a navigation tool in surgical procedures for early-stage SCCHN is a cost-effective option, as compared with traditional ipsilateral neck dissection. This alternative technique would save an estimated $1356 per stage N0 patient in Japan, and would prevent seven surgical deaths from neck dissection for every 1000 patients undergoing the procedure.

Two articles reported the cost-effectiveness of alternative forms of radiotherapy. Hopper and colleagues [23] compared Foscan-mediated photodynamic therapy with palliative chemotherapy, extensive palliative surgery, or no treatment among patients with advanced-stage HNC. Foscan-mediated photodynamic therapy yielded significantly better health gains than the other three options. Foscan-mediated photodynamic therapy was cost-effective at $28 201/life-year saved versus no treatment, which was itself more cost-effective than palliative chemotherapy.

Finally, Lundkvist and colleagues [24••] conducted a cost-effectiveness analysis of proton therapy versus conventional radiotherapy among HNC patients aged 65 years or older. Their analysis revealed that, despite a higher total per-patient cost for proton therapy than for conventional therapy (difference of $5033), 1.02 quality-adjusted life-years were gained. This yielded a cost per quality-adjusted life-year of $4921.

Indirect costs of head and neck cancer

In the United States, the Centers for Disease Control and Prevention publish annual statistics on smoking-related mortality, years of potential life lost, and productivity losses (Table 2). The 2005 report [25], which assessed data from 1997–2001, found that cancers of the lip, oral cavity, pharynx, and larynx were responsible for 11 331 annual deaths and 131 479 years of potential life lost. In addition, these cancers were responsible for nearly $2.8 billion per year in productivity losses (costs associated with the decrease in production and income attributable to a disease or disability – does not include healthcare expenditures, disability, or absenteeism).

A 2006 study of the burden of major cancers due to smoking in Korea [26•], which has one of the highest rates of male smokers in the world, included data on cancers of the lip, oral cavity, and pharynx, as well as cancer of the larynx. The study used disability-adjusted life years lost (sum of the years of life lost due to premature mortality from a disease and the years of

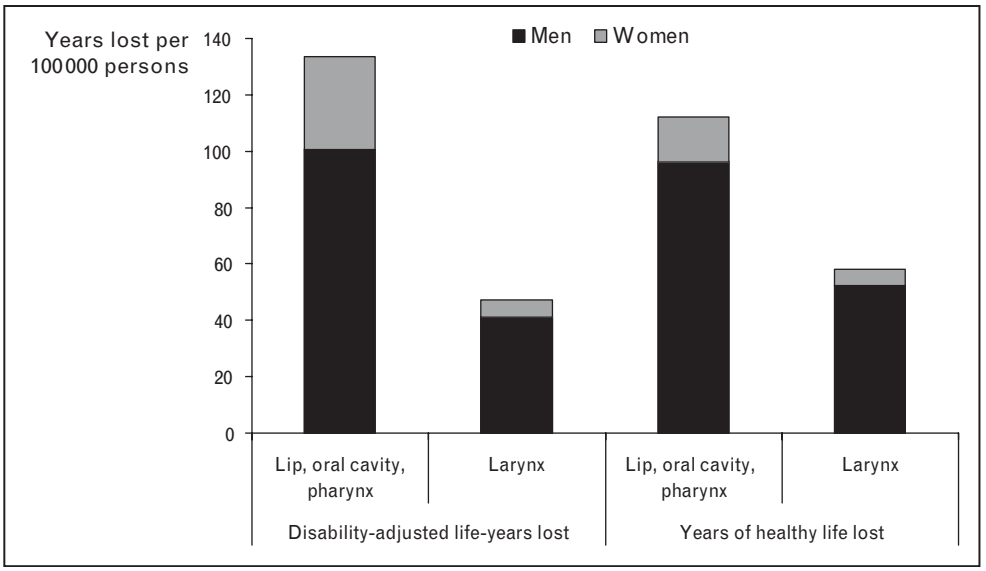
Table 2 Annual deaths, estimated years of potential life lost (YPLL), and estimated productivity losses by sex and cause of death*

	Men			Women			Total		
	Deaths	YPLL	PLoss	Deaths	YPLL	PLoss	Deaths	YPLL	PLoss
Lip, oral cavity, and pharynx	4973	65 153	1 461 865	2525	19 710	342 104	7498	82 863	1 803 969
Larynx	3017	38 241	806 012	816	10 375	179 545	3833	48 616	985 557
Total	7990	101 394	2 267 877	3341	30 085	521 649	11 331	131 479	2 789 526

PLoss, productivity loss in thousands of dollars, adjusted for inflation to 2006 US dollars. Adopted from Centers for Disease Control and Prevention [25]. *Causes of death determined by the International Classification of Diseases 10th Revision codes.

Figure 1 The burden of head and neck cancers in Korea

Figure derived from Lee *et al.* [26•].



healthy life lost as a result of disability – reported per 100 000 persons) and years of healthy life lost (sum of the total years of life lost due to premature mortality and the total year-equivalents lost due to reduced functioning – reported per 100 000 persons) as indicators, with similar results for each indicator (Fig. 1). The total burden of cancers of the lip, oral cavity, and pharynx was more than twice that of laryngeal cancers, and the rates of life-years lost were far less for women than for men. The estimates for HNC were much lower than the burden attributed to cancer of the lung, trachea, and bronchus, but higher than the burden attributed to smoking-related kidney and urinary cancer.

Analysis and discussion

According to cancer registry data, more than one-half of all new cases of oral cancer in the United States were diagnosed at an advanced stage in 2004 [27•]. Earlier diagnosis of SCCHN increases the likelihood of treatment with a single modality, lowers the risk of mortality, decreases medical expenditures, and improves patients' quality of life [28]. Most early cases are detectable with a simple, noninvasive, 5-min clinical examination, and new techniques, such as using serum protein profiles, could potentially improve screening practices [3,29,30].

A 2006 report from the United Kingdom [14••] provided insights, using a decision-analytic model, on the cost-effectiveness of screening for oral cancer in medical and dental primary care practices. While not conducting any screening was the least expensive (and least effective) option, opportunistic screening for high-risk patients in general medical and dental practice was thought to be potentially cost-effective, with incremental costs of $29 084–47 818 per quality-adjusted life-year gained.

Continuity and frequency of care have recently been brought to light as potential factors in earlier diagnosis of SCCHN. In a 2006 database study of 10 662 cases of head and neck cancer diagnosed from 1991 to 2000, Reid and Rozier [27•] discovered that continuous care by an internist was significantly associated with an earlier stage of cancer at diagnosis, while continuous care by a family or general practitioner did not have similar effects. The same group has also shown that more frequent physician visits are associated with a reduced risk of diagnosis at an advanced stage [31].

The most cost-saving scenario is one that prevents SCCHN altogether. Since this form of cancer is closely associated with tobacco use and excessive alcohol consumption, efforts to prevent SCCHN must involve efforts to reduce the use of tobacco and problem drinking. A 2003 study using dynamic multistate modeling [32] found that a substantial number of life-years could be saved by programs that target young people, partly because such programs have been shown to be more successful in achieving their aims. Programs aimed at current users were shown to be most effective over the short term, but long-term results showed larger effects from programs aimed at nonusers. On the other hand, the incidence of lung cancer has fallen at the same time and in the same population as oral cancer rates have risen [33,34], suggesting that alcohol consumption may be a more important causal factor [35]; thus, smoking cessation

programs may be less effective in preventing oral cancer than hoped.

Implications

Cost-effectiveness analyses are meant to provide guidance for choosing among potential interventions. As health spending continues to grow rapidly, approaches to care that ignore costs fail to meet the needs of consumers, employers, health plans, and federal and state governments. In the current environment, most processes for making clinical decisions are based on evidence of efficacy, rather than evidence of value. So, how should we evaluate a treatment's value?

When clinicians and payers seek to make value-based decisions about a particular treatment, the cost of that treatment should be only one of many factors considered. Other factors may be at least as important, such as effectiveness, adverse effects, and patient preferences, which may translate into downstream economic consequences. When head-to-head studies demonstrate comparable results in efficacy between or among treatments, cost should be taken into account – but the cost of a treatment goes far beyond its acquisition cost. Other variables that may come into play include the length of hospital stay, cost of labor, and patients' quality of life.

Given the life-threatening nature of cancer, issues of cost have not been prominent in decision-making regarding the choice of treatment. Only recently have we begun to understand how economic factors enter into how oncologists perceive the value of new treatments [36••].

Conclusion

While SCCHN receives less attention than other, more prevalent forms of cancer, it remains an important health problem with substantial costs to society. There are relatively few studies of the cost of HNC in general, or of the costs and cost-effectiveness of various treatment modalities. In this time of mounting concerns over healthcare costs, more emphasis on economic data is clearly warranted.

Acknowledgement

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 136).

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

2 Vokes EE, Weichselbaum RR, Lippman SM, Hong WK. Head and neck cancer. N Engl J Med 1993; 328:184–194.

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

4 Board of Governors of the Federal Reserve System. G.5A foreign exhange rates (annual), Federal Reserve Statistical Release. Board of Governors of the Federal Reserve System; 3 January 2006. http://www.federalreserve.gov/Releases/g5a/. [Accessed 2 November 2006]

5 U.S. Bureau of Labor Statistics. U.S. Department of Labor, Bureau of Labor Statistics Data. U S Bureau of Labor Statistics. http://www.bls.gov/data/#tools. [Accessed 1 November 2006]

6 American Cancer Society. Cancer facts and figures 2005. Atlanta, GA: American Cancer Society; 2005.

7 National Cancer Institute, Surveillance Epidemiology and End Results (SEER), National Institutes of Health. Cancer of the oral cavity and pharynx. Bethesda, MD: National Cancer Institute; September 2006. http://seer.cancer.gov/statfacts/html/oralcav.html?statfacts_page=oralcav.html&x=13&y=15. [Accessed 20 October 2006]

8 U.S. Department of Health and Human Services, Centers for Disease Control and Prevention (CDC), National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. The health consequences of smoking 2004, Report of the Surgeon General: smoking among adults in the United States – respiratory health. Atlanta, GA: Centers for Disease Control and Prevention; 2004. http://www.cdc.gov/tobacco/sgr/sgr_2004/Factsheets/4.htm. [Accessed 5 May 2006]

9 American Cancer Society. Oral cavity and oropharyngeal cancer. Atlanta, GA: American Cancer Society; 20 October 2006. http://documents.cancer.org/5043.00/5043.00.pdf. [Accessed 1 November 2006]

10 Bongers V, Braakhuis BJ, Tobi H, *et al.* The relation between cancer incidence among relatives and the occurrence of multiple primary carcinomas following head and neck cancer. Cancer Epidemiol Biomarkers Prev 1996; 5:595–598.

11 Berwick M, Vineis P. Markers of DNA repair and susceptibility to cancer in humans: an epidemiologic review. J Natl Cancer Inst 2000; 92:874–897.

12 Garavello W, Negri E, Talamini R, *et al.* Family history of cancer, its combination with smoking and drinking, and risk of squamous cell carcinoma of the esophagus. Cancer Epidemiol Biomarkers Prev 2005; 14:1390–1393.

13 Lang K, Menzin J, Earle CC, *et al.* The economic cost of squamous cell cancer of the head and neck: findings from linked SEER–Medicare data. Arch Otolaryngol Head Neck Surg 2004; 130:1269–1275.

14 •• Speight PM, Palmer S, Moles DR, *et al.* The cost-effectiveness of screening for oral cancer in primary care. Health Technol Assess 2006; 10:1–144.
A thorough, detailed study that used primary data collection to inform a decision-analytic model of the incremental costs and outcomes of various screening programs for oral cancer.

15 Lee JM, Turini M, Botteman MF, *et al.* Economic burden of head and neck cancer. A literature review. Eur J Health Econ 2004; 5:70–80.

16 •• Braaksma M, van Agthoven AM, Nijdam W, *et al.* Costs of treatment intensification for head and neck cancer: concomitant chemoradiation randomised for radioprotection with amifostine. Eur J Cancer 2005; 41:2102–2111.
This paper reports the costs and clinical outcomes of a randomized trial of treatment intensification with amifostine.

17 Nijdam W, Levendag P, Noever I, *et al.* Cost analysis comparing brachytherapy versus surgery for primary carcinoma of the tonsillar fossa and/or soft palate. Int J Radiat Oncol Biol Phys 2004; 59:488–494.

18 • Nijdam W, Levendag P, Noever I, *et al.* Cancer in the oropharynx: cost calculation of different treatment modalities for controlled primaries, relapses and grade III/IV complications. Radiother Oncol 2005; 77:65–72.
A detailed assessment of the costs associated with various treatment modalities for oropharyngeal cancer.

19 •• Brookes JT, Seikaly H, Diamond C, *et al.* Prospective randomized trial comparing the effect of early suturing of tracheostomy sites on postoperative patient swallowing and rehabilitation. J Otolaryngol 2006; 35:77–82.
A comprehensive cost-saving analysis conducted using data from a randomized, blinded, controlled clinical trial of tracheotomy site suturing in patients with HNC.

20 • Smeele LE, Goldstein D, Tsai V, *et al.* Morbidity and cost differences between free flap reconstruction and pedicled flap reconstruction in oral and oropharyngeal cancer: matched control study. J Otolaryngol 2006; 35:102–107.
This paper evaluates differences in cost between two reconstructive techniques for oral and oropharyngeal cancer.

21 •• Davis GE, Schwartz SR, Veenstra DL, Yueh B. Cost comparison of surgery vs organ preservation for laryngeal cancer. Arch Otolaryngol Head Neck Surg 2005; 131:21–26.
Report of cost comparison results from a decision-analysis model of undergoing surgery versus organ preservation in laryngeal cancer. The hypothetical model of patients with stage III or stage IV disease utilizes cost inputs derived from various sources, including data from a study conducted at Yale–New Haven Hospital.

22 Kosuda S, Kusano S, Kohno N, *et al.* Feasibility and cost-effectiveness of sentinel lymph node radiolocalization in stage N0 head and neck cancer. Arch Otolaryngol Head Neck Surg 2003; 129:1105–1109.

23 Hopper C, Niziol C, Sidhu M. The cost-effectiveness of Foscan mediated photodynamic therapy (Foscan-PDT) compared with extensive palliative surgery and palliative chemotherapy for patients with advanced head and neck cancer in the UK. Oral Oncol 2004; 40:372–382.

24 •• Lundkvist J, Ekman M, Ericsson SR, *et al.* Proton therapy of cancer: potential clinical advantages and cost-effectiveness. Acta Oncol 2005; 44:850–861.
The only cost-effectiveness analysis conducted within the past year. This important paper evaluated the cost–benefit ratio of proton therapy for left-sided breast cancer, prostate cancer, childhood medulloblastoma, and HNC.

25 Centers for Disease Control and Prevention. Annual smoking-attributable mortality, years of potential life lost, and productivity losses – United States, 1997–2001. MMWR Morb Mortal Wkly Rep 2005; 54:625–628.

26 • Lee H, Yoon SJ, Ahn HS. Measuring the burden of major cancers due to smoking in Korea. Cancer Sci 2006; 97:530–534.
An exploration of the total burden in life years lost of smoking-related cancers in Korea.

27 • Reid BC, Rozier RG. Continuity of care and early diagnosis of head and neck cancer. Oral Oncol 2006; 42:510–516.
An interesting investigation of the association between receiving continuous care and stage of diagnosis for head and neck cancers in a Medicare population.

28 Zavras A, Andreopoulos N, Katsikeris N, *et al.* Oral cancer treatment costs in Greece and the effect of advanced disease. BMC Public Health 2002; 2:12.

29 Gourin CG, Xia ZS, Han Y, *et al.* Serum protein profile analysis in patients with head and neck squamous cell carcinoma. Arch Otolaryngol Head Neck Surg 2006; 132:390–397.

30 Mignogna MD, Fedele S, Lo RL. The World Cancer Report and the burden of oral cancer. Eur J Cancer Prev 2004; 13:139–142.

31 Reid BC, Warren JL, Rozier G. Comorbidity and early diagnosis of head and neck cancer in a Medicare population. Am J Prev Med 2004; 27:373–378.

32 Van Genugten ML, Hoogenveen RT, Mulder I, *et al.* Future burden and costs of smoking-related disease in the Netherlands: a dynamic modeling approach. Value Health 2003; 6:494–499.

33 Conway DI, Stockton DL, Warnakulasuriya KA, *et al.* Incidence of oral and oropharyngeal cancer in United Kingdom (1990–1999) – recent trends and regional variation. Oral Oncol 2006; 42:586–592.

34 Jemal A, Siegel R, Ward E, *et al.* Cancer statistics, 2006. CA Cancer J Clin 2006; 56:106–130.

35 Boffetta P, Hashibe M. Alcohol and cancer. Lancet Oncol 2006; 7:149–156.

36 •• Nadler E, Eckert B, Neumann PJ. Do oncologists believe new cancer drugs offer good value? Oncologist 2006; 11:90–95.
A recent, revealing survey of oncologists' attitudes toward the relative value of oncology drugs.