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REVIEW ARTICLE

Conceiving a national head and neck cancer screening programme

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Abstract

Background: This study was undertaken to determine the optimum approach to screening for head and neck cancer based on international experiences.

Objective: To determine whether or not head and neck cancer is suitable for screening, and, if so, what the ideal approach should be.

Methods: An electronic search of online databases up to and including May 2014 was conducted. Key search terms included 'head and neck', 'cancer', 'screening', 'larynx', 'oropharynx' and 'oral'.

Results: Subset analysis of high-risk cohorts showed statistically significant improvements in early detection of head and neck cancer via screening.

Conclusion: Current levels of public awareness regarding head and neck cancers are suboptimal, despite increased incidence and mortality. Scheduled and opportunistic screening, coupled with efforts to enhance education and health behaviour modification, are highly recommended for pre-defined, high-risk, targeted populations. This can enable early detection and therefore improve morbidity and mortality.

Key words: Head And Neck Cancer; Oral Cancer; Cancer; Screening; Human Papillomavirus

Introduction

Head and neck cancer is the sixth most common form of cancer worldwide. Head and neck cancer incorporates diseases of the upper aerodigestive tract, nasal and paranasal sinuses, and the salivary glands. Globally, over 600 000 new cases are diagnosed each year, with 66 per cent being diagnosed at stage III or IV disease, and 300 000 deaths per annum.[1,2] The incidence is on the rise worldwide, with an estimated mortality rate of 595 000 deaths per annum by 2030.[2,3]

A fundamental goal of screening programmes is improvement in overall survival. There is significant morbidity and mortality associated with head and neck cancer. Screening for these malignancies may allow for early diagnosis and translate into improved survival. This could also correspond with an economic and social benefit in the short and long term; however, the lower incidence of head and neck cancer and the significant cost implications of national screening may negate any perceived benefit. Screening programmes for 'target populations' with established high-risk factors may offer more realistic benefits, with justifiable cost ratios.

Prognostic factors play a key role in patient outcome. The principle head and neck cancer prognostic factors are disease stage, disease site and co-morbidities.[4] Stage of disease at presentation is the dominant prognostic factor in head and neck cancer.[5] Unfortunately, most head and neck cancers are diagnosed at an advanced stage, with an average five-year survival rate reduction from 80 per cent when the tumour is restricted to the primary site, to 30 per cent with regional or distant metastases.[5]

Otolaryngologists, oral surgeons, head and neck cancer specialists, and dentists are best equipped to conduct screening for head and neck cancers because of their unique knowledge of upper aerodigestive tract anatomy and pathology. This review article aimed to examine existing data and determine whether head and neck cancer may be amenable to

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screening on a national level, and, if so, aid in the design and implementation of such future programmes.

Screening principles

A fundamental objective of screening is an improvement in overall survival. The basic principles of modern screening were described in 1968 by Wilson and Jungner (Appendix I).[6] They listed 10 criteria which should ideally be met when considering screening a population for a medical condition. More recently, screening programmes being run in the UK have been adhering to a 22-point guide of the National Screening Committee. These criteria are an ongoing work in progress and were first published in 2011.[7]

Screening patients for pre-clinical disease is an established part of day-to-day medical practice.[8] The benefits of screening include: early detection and increased chance of curative intervention; reduction in mortality with routine screening; and excision of pre-cancerous lesions, reducing the risk of developing cancer. The cons of screening include: cost; false-negative findings; failure to prevent cancer; patient concern and anxiety; risks associated with screening; and cancer development between screening sessions. Screening can take a number of forms, ranging from cross-sectional public health efforts, to primary care based programmes, to periodic clinics organised by specialised physicians and surgeons in the field.

Public awareness of medical conditions is increased as a result of screening programmes.[9,10] Head and neck cancer is an enigma to much of the general public, and paradoxically more so to those at a high risk of developing a malignancy as a result of specific health behaviours.[10] Education of targeted high-risk populations regarding head and neck cancer via screening programmes may be warranted.

Head and neck cancer

In the UK, between 1990 and 2006, the incidence of some head and neck cancers more than doubled. The distribution of cancers by site varies by geographical location and may reflect populations of various ethnic groups.[11,12] Oral cancer incidence in the UK rose by 22 per cent from 1996 to 2005.[11]

A rising trend in oral cancer incidence has also been reported in Northern Ireland.[13,14] Mortality rates vary between head and neck cancer subsites, the highest being 1.07 per 100 000 population for oral cavity cancer.[15] The incidence of head and neck cancer in the Irish population has shown striking changes in a relatively short time period. Head and neck cancer rates increased by 119 per cent in females and 76.3 per cent in males in the period from 2001 to 2010.[16] In 2010, there were 598 cases of head and neck cancers in Ireland, with laryngeal cancer being the most prevalent.[17] Unfortunately, early diagnosis of head and neck cancer (stage I and II) was less than 20 per cent for some anatomical subsites. Data collected regarding stage at diagnoses for mouth, salivary glands, pharynx, nasal/middle ear/sinuses, and larynx in Ireland showed that only laryngeal cancer was diagnosed early, with less than 20 per cent of pharyngeal and nasal/middle ear/sinus malignancy cases being diagnosed early. For all head and neck cancer cases, early stage diagnosis occurred in approximately 30 per cent of cases.[17]

Head and neck cancer appears ideally suited to screening because of: the significant morbidity and mortality associated with the disease, the survival advantage of early diagnosis, the association of identifiable risk factors and identifiers, and the ability to diagnose early stage tumours with a clinical examination.[10]

The commonest risk factors for head and neck cancer are tobacco and alcohol abuse, which have a well-established synergistic effect.[2,18] Approximately 75 per cent of head and neck cancers worldwide are considered directly related to their use and abuse. The rising incidence of human papillomavirus (HPV)-associated head and neck cancers is changing the epidemiology and demographics of the disease, particularly in the oropharynx, in many parts of the world. Epstein–Barr virus (EBV) has been strongly associated with undifferentiated nasopharyngeal carcinoma (NPC) and Burkitt's lymphoma.[19] Nasopharyngeal carcinoma, while relatively rare worldwide, is commonly seen in Asia and parts of Africa. Other risk factors and identifiers which have specific implications include bidi smoking and paan chewing, advanced age, male sex,[20] sunlight,[9] low body mass index, poor diet, and poor dental hygiene.[2] Socioeconomic status may also be considered as a risk factor for head and neck squamous cell carcinoma (SCC). Lower socioeconomic status may be associated with oral pre-malignant lesions secondary to poor access to healthcare services, health-related behaviours and lifestyle risk factors.[21,22]

In developed countries, the incidence of HPV-positive head and neck SCCs is showing a rising trend, while HPV-negative head and neck SCC are gradually decreasing. Human papillomavirus positive oropharyngeal SCCs frequently present in younger people with no history of alcohol or tobacco use, and with higher socioeconomic status, often with low T (tumour) stage and early cervical nodal dissemination.[23] There is a survival benefit and a lower risk of recurrence than with HPV-negative tumours. The Radiation Therapy Oncology Group 0129 trial highlighted the existence of a new 'HPV' disease from a genetic, molecular and epidemiological perspective.[24] While the oral cavity is amenable to conventional oral examination, no published data on screening for oropharyngeal SCC exist. Screening for this may involve visual inspection for tonsillar asymmetry, mucosal abnormality and cervical node palpation. The role of cervical smear tests in the early detection and prevention of HPV-associated uterine cervical neoplasms is intriguing, but as of yet does not translate into clinically applicable screening modalities in the head and neck.

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Complete inspection of the oropharynx requires laryngoscopy, which increases the complexity of screening for this malignancy. It must also be noted that the risk factors and risk groups for oropharyngeal SCC are different to those for oral cancer.

Nasopharyngeal carcinoma is the commonest malignancy of the nasopharynx.[25] Risk factors include EBV exposure, male sex, family history, global location, Chinese or Asian ancestry,[26] and excessive alcohol consumption.[27] From 1990 to 2010, there was a 44 per cent increase in deaths attributable to NPC globally, from 45 000 to 65 000.[28] Incidence is less than 1 in 100 000 in most parts of the world. This increases to 21.4 per 100 000 in Chinese Hong Kong males.[29]

Prognostic factors play a key role in patient outcome. The principle head and neck cancer prognostic factors are disease stage, disease site and co-morbidities.[4] Stage of disease at presentation is the dominant prognostic factor in head and neck cancer.[5] The Royal College of Pathologists include further features related to clinical outcome such as tumour grade, pattern of invasion, proximity of malignancy to resection margins, and the presence of extranodal spread.[30] Screening aims to improve early detection and therefore improve patient outcomes.

Methods

Literature search

An electronic search of Medline, PubMed, Cochrane Library, Embase, Cumulative Index to Nursing and Allied Health Literature, Allied and Complementary Medicine Database, and Science Direct databases, up to and including May 2014, was conducted. Key terms used in the search algorithm included 'head and neck', 'cancer', 'screening', 'larynx', 'oropharynx' and 'oral'. No chronological restraints or language restrictions were applied.

Inclusion criteria

This systemic review was limited to papers that focused on head and neck cancer, screening, and screening programmes for head and neck cancers.

Results

Only one prospective, cluster-randomised trial conducted on head and neck cancer screening was reported in the literature (Table I). Other data reporting on head and neck screening programmes that are included in this body of work are listed in Table II.

There have been numerous studies conducted to determine the value of head and neck cancer screening programmes. Indeed, the Head and Neck Cancer Alliance website has information on 356 independent screening sites in the USA. There are, however, no national screening programmes established in the USA for head and neck cancer, and the US Preventive Services Task Force does not recommend routine screening.[31] Identification of at-risk populations is especially important when screening for head and neck cancer, and this has been the greatest challenge to the cost-effectiveness and potential oncological gains in individual studies. The American Head and Neck Society believes that early detection via screening for SCC of the oral cavity and upper aerodigestive tract may provide significant potential benefit for the high-risk patient.[32]

Global experience of screening

Screening for head and neck cancer by visual inspection is safe, non-invasive, simple and presumably cost-effective. Screening techniques in studies discussed here range from conventional oral examination alone to the inclusion of additional methods such as neck palpation, flexible pharyngoscopy and laryngoscopy. More expensive, newer techniques and diagnostic aids have been developed, but none have improved substantially on the sensitivity and/or specificity of the conventional oral examination. These include toluidine blue stain, brush cytology, tissue reflectance and autofluorescence.[33]

Kerala, India

A high rate of oral cancer has been recorded in the Indian subcontinent, where it is the most common form of cancer and cancer-related death in men in India.[34,35] The largest trial of head and neck cancer screening conducted to date was carried out in Kerala, India, a region with a high rate of oral cancer.[34] This is the only prospective cluster-randomised trial conducted on head and neck cancer screening. The study screened 87 655 participants by community-based visual screening undertaken by non-medical health workers. The results suggested that screening a high-risk cohort has the potential to prevent at least 37 000 deaths from oral cancer globally per annum in a targeted population.

The trial investigated whether visual examination of the oral cavity, a simple, acceptable and accurate screening tool,[36–41] would lead to a decrease in oral cancer mortality. Thirteen clusters were identified for the purpose of the study. Seven received three rounds of oral visual examination at three-year intervals. The remaining six formed the control group and received standard care. The study subjects were interviewed for details concerning occupation and habits, such as paan chewing, tobacco smoking and alcohol use. Screening was repeated every three years for up to three 'rounds'.

Patients considered screen-positive by the presence of one or more notable lesions were subsequently referred to specialised clinics. Those participants with a negative screen were advised to receive repeat screening after three years. Confirmed oral cancer cases were referred for treatment options, which included surgery, radiotherapy and/or chemotherapy.

The detection rate of oral pre-cancerous lesions and oral cancer in the first, second and third rounds of

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TABLE I
PROSPECTIVE, CLUSTER-RANDOMISED TRIAL

Authors	Year	Patients (*n*)	Age (mean (SD, range); years)	Sex ratio (M:F)	Abnormality detection rate
Sankaranarayanan *et al.*[34]	2005	87 655	49 (0.7, 48–50)	NR	0.03* 0.01† 0.01‡

*First round of screening; †second round of screening; ‡third round of screening. SD = standard deviation; M = male; F = female; NR = not reported

screening were 28.0, 11.6 and 11.3 per 1000 screened individuals, respectively. The positive predictive value of the screening test to detect oral pre-cancerous lesions and invasive cancer was 74 per cent. The programme sensitivity to detect oral cancer was 64 per cent (131 of 205). While the 21 per cent absolute reduction in oral cancer mortality in all individuals in the intervention group compared with the control group was not significant, a statistically significant reduction in mortality of 34 per cent was recorded in the subgroup of tobacco or alcohol users. The authors concluded that oral visual screening has the potential to prevent at least 37 000 deaths from oral cancer worldwide every year among smokers and drinkers.

Cuba

Only one country has an established national screening programme for head and neck malignancies. The Cuban programme has been in existence since 1984. It requires all citizens aged 15 years and above to undergo an annual oral visual inspection by dentists.[42] Any individual with a defined abnormality is referred to a specialist for further management.

Frenández Garrote *et al*. examined the data collected between 1984 and 1990.[41] In 1989, 3218 males and 2873 females were referred for maxillofacial opinion. Only 33 per cent of males and 36 per cent of females complied with their referral. The reasons for referral included: normal variations ($n = 4779$, 54.9 per cent), leukoplakia ($n = 2367$, 27.2 per cent), other pre-malignant lesions ($n = 852$, 9.8 per cent), oral cancer ($n = 705$, 8.1 per cent) and benign lesions. The programme identified 16 per cent of the 4412 incidences of oral cancer between 1984 and 1990. Stage I diagnosis increased from 22.8 per cent in 1983 to 48.2 per cent in 1990. There was a corresponding decrease in diagnoses of stage II–IV cases, from 77.2 to 51.8 per cent. No change in incidence was reported. The major problem identified by this work was the lack of compliance, with less than 30 per cent of individuals following up with their referral.[41]

UK Bangladeshi community

Between 2006 and 2008, oral cancer screening was conducted in the UK among a Bangladeshi community that exhibits a high prevalence of oral cancer risk factors.[11,43] The screening involved visual examination of the oral cavity and oropharynx, and neck palpation, by two registered dental practitioners. A total of 1320 participants were screened and 44.7 per cent were identified as having possibly malignant disorders. The mean age of the screened population was 42.3 ± 15.9 years. Seventy-five (3.79 per cent) of those screened were referred for oral medicine consultation. In all, 55 patients followed up on their referral. This work demonstrates the feasibility of conducting oral cancer screening using a mobile dental clinic with dental practitioners. A referral rate of 5.7 per cent is similar to that of the work carried out in the Kerala trial.

USA

A survey-based study with a non-experimental intervention component was conducted by otolaryngologists and maxillofacial surgeons of attendees at three separate National Association for Stock Car Auto Racing weekend events in Hampton, Georgia, USA.[44] The study aimed to investigate the implications of screening for head and neck cancers in a community-based environment. Forty-three per cent of the screened participants were daily alcohol users, and 54

TABLE II
REPORTS OF HEAD AND NECK CANCER SCREENING PROGRAMMES

Authors	Year	Patients (*n*)	Age (mean (range); years)	Sex ratio (M:F)	Abnormality detection rate (%)
Frenández Garrote *et al.*[41]	1995	12 990 677	NR	NR	0.23
Santana *et al.*[42]	1997	10 167 999	NR	NR	0.03
Hapner & Wise[44]	2011	568	44* (18–73)	59:41	45 (of those with smoking history)
Shuman *et al.*[45]	2013	1573	54 (18–100)	33:67	21
O'Sullivan[46]	2011	220	NR (18–73)	2.39:1	29
Gourin *et al.*[9]	2009	89	56 (23–83)	43:57	11
Shuman *et al.*[10]	2010	761	58 (17–100)	58:42	5

*Average. M = male; F = female; NR = not reported

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per cent had a history of smoking tobacco, with 28 per cent being current smokers. A total of 568 high-risk attendees aged 18 to 73 years (average age of 44 years) were recruited for screening. Fifteen-minute consultations using visual examinations identified 43 per cent of the participants with a history of smoking who warranted specialist referral. The rate of positive findings was significantly higher in males than in females ($p < 0.05$). For the purpose of this work, a positive finding was deemed to be at least one of the following: a lump in the head and neck, or sore throat that had not healed; chronic sore throat; odynophagia; dysphagia; dysphonia; white or red patches on the gums, tongue or lining of the mouth; swelling of the jaw; bleeding in the mouth; bleeding through the nose; pain in the upper teeth or problems with dentures; swelling under the chin or around the jaw, or pain that did not go away in the face, chin or neck; and unexplained ear pain. These authors demonstrated that a community-based head and neck cancer screening programme can be effectively implemented at non-medical venues.[44]

A free screening session run as part of the 2008 Oral, Head and Neck Cancer Awareness Week, by John Hopkins Medicine, referred 11 per cent of participants for head and neck consultation.[9] They promoted their event via print newspaper, online newspaper, hospital newspaper, hospital displays, the Yul Brynner Foundation, hospital website and television interviews. One of their most significant findings was that the individuals presenting for the free cancer screening did not share the characteristics of the population at highest risk for the development of head and neck cancer based on risk factors and socioeconomic status.[9] This highlights the necessity of targeting the high-risk population rather than the 'well-walking'.

In 2010, the University of Michigan Medical School published data relating to the 14-year experience of a free annual head and neck cancer screening clinic.[10] A retrospective cohort study involving database analysis and chart review was conducted. Within this study, 1 per cent of participants were confirmed to have malignant or pre-malignant lesions, with 5 per cent of these going on to have findings considered suspicious for head and neck cancer on screening evaluation. It is notable that all participants were self-referred. The population studied for this work may fail to represent those at highest risk, as has been shown in previous studies. Lack of medical insurance was deemed a risk factor for having a lesion suspicious for head and neck cancer.[10]

A retrospective cohort study from the Memorial Sloan Kettering Cancer Center in New York, which reviewed attendance to a free annual screening clinic for head and neck malignancy between 2001 and 2012, revealed similar outcomes.[45] Files from 1573 patients were analysed. In total, 21 per cent ($n = 325$) had abnormal findings at screening, with 12 per cent ($n = 183$) having findings suspicious for cancer. While half of the patients denied tobacco use, 80 per cent admitted to alcohol consumption on at least a weekly basis. A follow-up compliance rate of 20 per cent was noted, resulting in three confirmed cancer diagnoses. As with other studies, the individuals presenting for the free cancer screening did not share the characteristics of the population at highest risk for the development of head and neck cancer based on risk factors and socioeconomic status. This study highlighted the importance of targeting patients at high risk and of ensuring appropriate follow up.[45]

Ireland

A pilot study was undertaken in 2006 to: investigate the feasibility, suitability and acceptability of oral cancer screening targeted at residents of four addiction treatment centres in Southern Ireland, and assess the potential benefits of a national targeted screening programme.[46] A total of 78 per cent of the residents (220 out of 283) took part in the study. Almost three-quarters of the study group were male (70.5 per cent, 148 out of 210). While the 210 participants ranged in age from 18 to 73 years, 60 per cent were under 40 years of age and only 8 per cent were over 60 years of age. Ten residents who denied a history of alcohol abuse during examination were excluded from the main study. Most participants were current (87.6 per cent) or ex-smokers (2.4 per cent), and, as expected, a high proportion had a history of alcohol abuse (94.8 per cent) with or without drug abuse.

Despite the youthful profile of the residents in the study, a high proportion (29 per cent) had 1 or more mucosal abnormalities: 42 (20 per cent) presented with a single lesion, 15 (7.1 per cent) had 2 mucosal abnormalities and 4 (1.9 per cent) had 3 such lesions. In fact, a total of 84 mucosal abnormalities or worrying symptoms were detected in the main study. Those with mucosal abnormalities were significantly older (mean age of 41.8 years; standard deviation (SD) = 14.3) than those without such lesions (mean age of 35.95 years; SD = 13.3) ($p < 0.05$). Thirteen of the 28 extra-oral lesions and ENT symptoms, and 19 of the 56 intra-oral lesions, were potentially significant. Despite a poor compliance rate for further investigation (33 per cent), two pre-malignant lesions were detected in the main study group, a detection rate of 0.9 per cent. Furthermore, a skin cancer was detected in the subgroup excluded from the main study. If these residents are included, the detection rate for malignant and pre-malignant lesions rises to 1.3 per cent (3 out of 220).[46]

The results of that pilot study suggest that an oral cancer screening programme targeted at individuals in addiction treatment centres may provide a feasible way to access persons with a history of tobacco and alcohol abuse. A high rate of untreated dental disease was seen in this study, suggesting a lack of engagement with general dental practitioner services. Opportunistic screening in primary care is therefore unlikely to capture this cohort. The inclusion of oral cancer

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screening in the routine medical examination given to residents of addiction treatment centres may provide an efficient and effective way to detect potentially malignant lesions in these high-risk individuals.[46]

In 2009, a group of head and neck cancer survivors, in collaboration with representatives from the Cork University Dental School and Hospital, Dublin Dental School and Hospital, Dental Health Foundation, and Irish Cancer Society, formed Mouth, Head and Neck Cancer Awareness Ireland in order to raise the profile of mouth, head and neck cancer among the general public and healthcare professionals. This collaboration resulted in the launch of a new mouth, head and neck cancer information leaflet and the establishment of an annual mouth cancer awareness day. The first awareness day, on 29 September 2010, was held at Cork University Dental School and Hospital, and Dublin Dental Hospital. The campaign was extended nationally in 2011 with the support of the Irish Dental Association and the general dental practitioners. Members of the public were invited, via a mixed media campaign, to attend at a participating dental surgery or dental hospital to receive free mouth cancer examinations and information on risk factor modification. To date, over 20 000 people have attended one of the annual mouth cancer awareness day events, and at least 22 oral cancers have been detected as a direct result of this campaign. However, the true number of people who might subsequently benefit from the information given to the 20 000 attendees is difficult to estimate.[47,48]

Conclusion

Screening for head and neck cancer to date is based on an initial simple, non-invasive, visual inspection, with additional methods employed when deemed necessary. Head and neck cancer screening needs to target those with recognisable risk factors and health behaviours associated with developing the disease. Therein lies the problem. Patients deemed at high risk are less likely to be aware of, and therefore attend, screening clinics. Within these populations, there are potential survival advantages and definite primary care benefits for adopting head and neck cancer screening programmes to enable early stage diagnosis and improve patient outlook. Various screening programmes have reported detection rates for confirmed malignancy or pre-malignant pathology from 0 to 3 per cent.[10] Cost-effectiveness is a core goal with respect to screening programmes. Conventional oral examination has been shown to be effective in detecting both malignant and pre-malignant pathologies. The usefulness of conventional oral examination as a screening tool has had varied results, with both support and doubt raised for it as a screening tool.[33]

Detection rates of malignancy in head and neck cancer screening are low. Populations deemed high risk for head and neck cancers are less likely to self-refer. Public awareness and education is paramount in improving prevention and early malignancy detection. Current levels of public awareness regarding head and neck cancer are suboptimal. Scheduled and opportunistic screening by appropriately trained individuals is highly recommended for targeted populations.

We recommend tailor-made screening programmes for specific populations known to be at risk of developing head and neck cancer. Methods for oral cavity examination are unsuitable in areas concerned with nasopharyngeal carcinoma. Identification of risk groups is essential for cost-effectiveness. Regional rather than national screening programmes may be suitable in some locations in light of population diversity. Opportunistic screening and population education is recommended for all.

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APPENDIX I
BASIC PRINCIPLES OF MODERN SCREENING*

The condition should be an important health issue
There should be an accepted treatment for patients with recognised disease
Facilities for diagnosis & treatment should be available
There should be a recognisable latent or early symptomatic stage
There should be a suitable test or examination
The test should be acceptable to the population
Natural history of the condition, including development from latent to declared disease, should be adequately understood
There should be an agreed policy on whom to treat as patients
Cost of case-finding (including diagnosis & treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole
Case-finding should be a continuing process & not a 'once & for all' project

*As described in 1968 by Wilson and Jungner.[6]

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