

## Main Article

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# Two-week-wait referrals in otolaryngology in a tertiary centre: cross-sectional study of benign outcomes, with a systematic review

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## Abstract

**Objective.** The two-week-wait referral is designed to improve early detection in cancer patients. This retrospective study analysed those ENT two-week-wait referrals to out-patient clinics in a tertiary head and neck oncology centre, from January to June 2018, which were not compliant with National Institute for Health and Care Excellence guidelines (2015 update).

**Methods.** Referral symptoms were statistically analysed against National Institute for Health and Care Excellence guidelines, with detailed analysis of reasons for non-compliance. In addition, a systematic review of similar previously published articles was conducted.

**Results.** There were 1107 patients referred through the two-week-wait pathway. Of these referrals, 52 per cent were compliant with National Institute for Health and Care Excellence 2015 guidelines. Six errors were identified for non-compliant referrals, most commonly inconsistencies in referral (e.g. globus sensation) and intermittent disease course (e.g. intermittent hoarseness). Of all patients referred, 93 per cent were diagnosed with benign conditions, with laryngopharyngeal reflux being the commonest. Twenty-two per cent of referred patients were discharged after the first visit.

**Conclusion.** Two-week-wait referral is inappropriately overused. There are many non-compliant referrals, and most of the outcomes are benign.

## Introduction

In 2000, the Department of Health developed the UK National Guidelines for referring suspected head and neck cancer cases through a fast-track, two-week-wait pathway. In England, this means that suspected cancer patients should be seen by a specialist within 14 days of the primary care referral, to facilitate early detection. The target in England is 93 per cent of 2-week-wait referrals seen within 14 days. In Northern Ireland, the two-week-wait pathway only applies to suspected breast cancer. This scheme does not exist in Scotland or Wales.<sup>1,2</sup> The National Institute for Health and Care Excellence (NICE) generated guidelines for two-week-wait head and neck cancer referrals in 2005.<sup>2</sup> This was refined in 2015, with the latest revision in 2021.<sup>1</sup> Despite this, the cancer detection rate is not significantly different from non-urgent referrals.<sup>3,4</sup> A recent retrospective study of head and neck cancer showed that 11.8 per cent of two-week-wait referral patients were diagnosed with cancer and 88.2 per cent with benign disease.<sup>5</sup>

There are currently insufficient data in the literature regarding the patients' journey after referral. This includes the pathway for diagnosed benign conditions before discharge back to primary healthcare.<sup>5</sup> This study explored the outcomes and pathways of all two-week-wait head and neck cancer referral patients for whom no pathology was identified or who were diagnosed with benign pathology.

## Materials and methods

A retrospective review audit was conducted in the first six months of 2018, from January to June, in a tertiary head and neck surgical centre. All patients referred to the ENT out-patient clinic through the two-week-wait pathway were included. All patients with suspected cancer are managed on a two-week-wait pathway, which allows data collection for comparison with national guidelines, as well as expedition of investigations and treatment in order to meet these targets. The outcome from the first specialist appointment was either a decision to continue on the two-week-wait pathway (for suspicious referrals) or to be taken off the pathway (for those with benign conditions). The durations between referral and the time of the first appointment and the time of secondary care completion were calculated. The analysis also included demographic details, social history as documented in the specialist clinic letter, and the presenting history. Compliance with 2005 NICE referral criteria and the 2015 update was analysed.

Clinical findings and outcomes were recorded anonymously. The data were collected from: clinic electronic letters stored on a shared-access network drive, the Integrated

Clinical Environment platform, and Infoflex healthcare data management software (to determine multidisciplinary team meeting outcomes). This study was an audit of clinical practice and therefore formal ethical approval was not required.

The data were analysed in comparison to similar publications and UK cancer research statistics. A systematic review of all published two-week-wait head and neck centres was conducted. Criteria for study inclusion were: a single centre where the national two-week-wait head and neck cancer clinic target was met; a minimum of six months' duration of data collection; use of the Department of Health (DoH) and NICE guidelines as standard; and reporting of results that include compliance of referral symptoms with NICE guidelines and cancer detection rates from these referrals.

## Results

There were 1107 referral patients who proceeded through the two-week-wait pathway during the study period. The average number of referrals per month was 184 (standard deviation = 14). Of the patients, 98.8 per cent were reviewed by a specialist within 2 weeks, with an average waiting time of 6 days. Social history details of smoking and alcohol use were documented in 74 per cent of specialist clinic letters. Performance status was rarely documented. Sixty per cent of the referrals were female. There were no urgent referrals for children and adolescents younger than 15 years old, with only 0.8 per cent from those aged 15–20 years. Most referrals fell in the age groups 40–60 years and 60–80 years, with 37.4 per cent for each group.

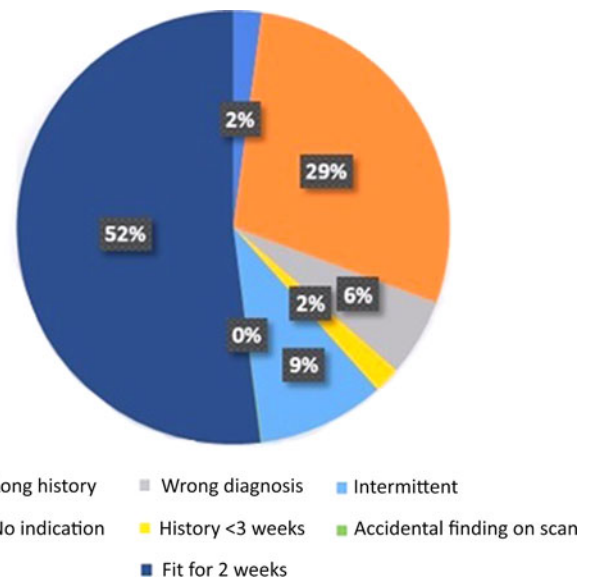
Fifty-two per cent of the referrals were compliant with the NICE 2015 guideline criteria. The commonest head and neck regions of concern in the primary care letters were the larynx (33 per cent), pharynx (27 per cent) and neck (18 per cent).

Six errors were identified in the 48 per cent of non-compliant referrals. The first (29 per cent of all referrals) was 'no consistent indication' from the guidelines. The 'intermittent course' was the second error. For example, 105 (9 per cent) of the referrals had intermittent hoarseness of voice. The third (6 per cent) was 'wrong' referrals, such as lump in the neck where there was nothing obvious or palpable to the specialist, or when there was a mismatch between the patient's complaint in the specialist appointment and the original indication in the urgent referral letter from primary care. The fourth and fifth errors were either very long history, of more than a year, or a very short history, of less than three weeks. The last error was the concern resulting from accidental findings on imaging where the patient was asymptomatic. **Figure 1** illustrates the percentages of all compliant and non-compliant referrals.

The commonest general symptoms resulting in referral were: voice change (27.2 per cent), neck lump (25.9 per cent) and globus sensation (18.7 per cent). All patients with intermittent hoarseness and recent neck lump, and 99.4 per cent of those with globus sensation, had a benign outcome, whereas 93 per cent and 81.8 per cent of all referred patients with persistent hoarseness and persistent neck lump, respectively, had a benign outcome.

In 489 patients, there were 'red flag' symptoms appropriate for referral, but the diagnosis was benign. In general, there was low sensitivity for cancer, with a high rate of a benign outcome for each symptom, of between 82.6 and 96.3 per cent (**Table 1**).

During the study period, 1035 patients (93 per cent of all referrals) were diagnosed with benign conditions, and 47 per



**Fig. 1.** Percentages of all referrals compliant and non-compliant with National Institute for Health and Care Excellence guidelines.

cent of them had been appropriately referred on the two-week-wait pathway. **Table 2** illustrates the most commonly diagnosed benign conditions. Laryngopharyngeal reflux was the commonest diagnosis (21 per cent). Eighteen per cent of patients were reassured as being 'ENT clear' after their first specialist visit. Although 18.7 per cent of patients had globus sensation on presentation, only 4 per cent were diagnosed with globus pharyngeus.

All patients with globus sensation and reflux-related findings were treated with a proton pump inhibitor and followed up before being discharged. Of all two-week-wait referrals, 243 patients (22 per cent) were discharged following their first visit. The average number of specialist visits was 1.7, after which 58 per cent of patients were discharged back to primary care. Referral to speech and language therapy was undertaken for 7 per cent of all two-week-wait referral patients.

Sixty-three patients (5.7 per cent of all referrals, 6.1 per cent of patients with benign outcomes) were referred for barium swallow study. No barium swallow study resulted in a diagnosis of cancer. Furthermore, 16.1 per cent of all patients on the two-week-wait pathway were referred for a neck ultrasound; for these patients, 96.1 per cent of the outcomes were benign.

A systematic review of relevant literature yielded nine studies.<sup>2–10</sup> Three studies were excluded because the authors did not report the compliance with NICE criteria in their results.<sup>7,9,10</sup> Another cohort study between two centres was excluded.<sup>4</sup> **Table 3** shows the five centres included and their results. The sample size in the pooled analysis was 4218 patients. The rate of benign outcomes in two-week-wait referral patients, across all five centres, was 89.8 per cent. Of all referrals, 68 per cent were compliant with DoH and NICE guidance.

## Discussion

### Comparison with existing literature

The numbers of two-week-wait referrals have increased dramatically across all specialties in the National Health Service. Over 2.5 years, from January 2004 to December 2006, 1079 patients were referred to a tertiary centre.<sup>2</sup> The same tertiary centre showed 4460 referrals in the following four years (January 2007 to December 2010).<sup>4</sup> Another busy tertiary

**Table 1.** Relations between 'red flag' symptoms and benign outcomes

Parameter	Persist hoarseness	Oral ulcer	Oral swelling	Dysphagia	Persist neck lump	Oral bleed	Otalgia	Sore throat
Frequency of each symptom in 2ww referrals ( <i>n</i> (%))	159 (17.8)	10 (1.1)	39 (4.4)	50 (5.6)	209 (23.4)	13 (1.5)	32 (3.5)	108 (12.1)
% of benign outcomes for each symptom	90.5	90.0	89.7	91.8	82.6	92.3	90.3	96.3
% of symptom presentation in cases with benign outcome	13.8	0.9	3.4	4.4	16.5	1.2	2.7	10.1

2ww = two-week-wait

**Table 2.** Common benign conditions in urgent referrals

Benign diagnoses	Cases ( <i>n</i> )	% out of all benign outcomes	% out of all referrals
Reactive LN	48	5	4
Globus pharyngeus	39	4	4
Reflux	214	21	19
Dysphonia	70	7	6
ENT clear	195	19	18
Laryngitis	24	2	2
Dysmotility	10	1	1

LN = lymph node

centre in Glasgow had 2116 annual referrals from June 2015 to May 2016.<sup>5</sup> A fourth tertiary centre recorded 622 over one year, from July 2009 to 2010.<sup>6</sup> In a district general hospital, the number dropped to 177 patients over a one-year study period.<sup>3,7</sup> The national two-week-wait targets should be met in 95–100 per cent of cases.<sup>3,7</sup> In our centre, two-week-wait clinics achieved the national target, despite the extremely high volume of referrals in this six-month period because of one or more of the six errors identified in the referrals.

### Reasons for non-compliant referral

The appropriateness of referrals to head and neck two-week-wait clinics remains low despite NICE guidelines. The cancer detection rate in ENT is lower than in other specialties; for instance, rates of 23 per cent and 12.8 per cent have been reported for urology and breast two-week-wait referrals.<sup>7</sup> Possible contributing factors include the poor predictive value of head and neck symptoms for cancer; the lack of ENT experience among general practitioners; the poor availability of diagnostic aids in primary care; and the high rate of general practitioner consultations for ENT problems (25–50 per cent).

Tikka *et al.* implemented an online calculator in 2016, which was refined recently for primary care, with a predictive value cut-off of 0.08 before referral to secondary care.<sup>4,11</sup> They showed that common red flag symptoms included in NICE guidelines have low sensitivity and low positive predictive values: 45.4 per cent and 17 per cent for neck lump, 17.38 per cent and 7.76 per cent for hoarseness, and 7.3 per cent and 13 per cent for dysphagia, respectively.<sup>4</sup> Our study showed a high percentage of benign outcomes associated with all red flag symptoms in NICE guidelines.

Globus sensation and intermittent hoarseness were the commonest symptoms resulting in non-compliant referrals in the cohort study by Tikka *et al.* and others.<sup>2,4,5</sup> These authors suggested that two-week-wait referrals were

unnecessary.<sup>4,11</sup> As in our study, 9.2 per cent of the referral patients in Douglas and colleagues' study had intermittent hoarseness.<sup>5</sup> The lack of experience in history-taking that can differentiate globus from odynophagia, explains the persistently high referral rate. Globus sensation documented in the referral letter is frequently found to be dysphagia in the patient's own words during consultation, and vice versa.<sup>5</sup> Furthermore, patients frequently confuse intermittent sore throat with persistent odynophagia. The latter has a five-times increased risk of cancer.<sup>4</sup> The three-week duration might not be sufficient for patients to establish an intermittent course. Our study showed positive predictive values of 1 per cent for globus sensation and 0 per cent for intermittent hoarseness. All patients referred with odynophagia and/or sore throat were pooled together in this study, showing a predictive value of 4 per cent. Regular e-learning modules for healthcare on head and neck cancer presentations, and communication between ENT consultants and general practitioners, would improve history-taking and reduce inappropriate referrals.<sup>6</sup>

The vast majority of patients are reassured after their visit to the specialist. Douglas *et al.* showed that 42.6 per cent of patients were discharged after one clinic appointment, while another 26.8 per cent were followed up for suspected benign pathology.<sup>5</sup> Only 21.8 per cent of patients were actively investigated for cancer. The commonest diagnoses in discharged patients were: reflux (7.1 per cent), globus pharyngeus (5.5 per cent), functional dysphonia (5.1 per cent) and reactive lymphadenopathy (2.6 per cent). The authors did not discuss patients investigated for benign pathology.<sup>5</sup> Our study showed the same types of benign conditions, but with a different order of frequency, whereby reflux and functional dysphonia were the commonest diagnoses. There was a higher rate of 'ENT clear' outcomes in our study than the 5.5 per cent of asymptomatic cases reported by Douglas *et al.*<sup>5</sup>

Ultrasound and ultrasound fine needle aspiration (FNA) during the clinic have shown advantages in terms of immediate reassurance and discharge from clinic, which benefit both the clinician and patient.<sup>5</sup> Investigation with ultrasound prior to clinic has been shown, within a Scottish setting, to be of limited value and a waste of resources, so it has been discouraged in primary care.<sup>5</sup> The one-stop clinic, with both a cytologist and a radiologist present in the clinic, proved to be an overuse of resources, as only 15 per cent required a cytologist for FNA cytology and only 12.8 per cent required a radiologist for interpretation of the ultrasound.<sup>6</sup> However, it can still be of good value in neck lump clinics.<sup>6</sup> The one-stop clinic is used in our centre, but is not fully integrated within all urgent clinics. It is run by a sonographer with a special interest in the head and neck, alternating with a consultant radiologist; however, the clinic lacks a cytologist, so another patient appointment is inevitable to discuss the FNA results.

**Table 3.** Systematic review of studies investigating compliance with guidelines

Study	Year of data collection	Location of centre studied	Study period start year	Study period end year	Sample size (n)	Cancer cases (n)	Benign cases (n)	Referrals compliant with guidelines (n)	Referrals not compliant with guidelines (n)
Douglas <i>et al.</i> <sup>5</sup>	2018	Glasgow	2015	2016	2116	235	1881	1395	721
Prichard <i>et al.</i> <sup>6</sup>	2013	Birmingham	2009	2010	622	35	587	510	112
Hobson <i>et al.</i> <sup>3</sup>	2008	Stockport	2004	2005	177	22	155	107	70
McKie <i>et al.</i> <sup>2</sup>	2008	Newcastle	2004	2006	1079	118	998	798	318
Duvvi <i>et al.</i> <sup>8</sup>	2003	Cheshire	2002	2003	187	19	168	67	120
Total		n = 5			4218	429 (10.2%)	3789 (89.8%)	2877 (68%)	1341 (32%)

Studies by Allam and Nijim,<sup>9</sup> Lyons *et al.*,<sup>10</sup> and Gardner and Wijesekara,<sup>7</sup> were excluded because of the lack of statistical data on compliance with National Institute for Health and Care Excellence guidelines. Study by Tikka *et al.*<sup>4</sup> was excluded because it was a cohort study of two centres.

The pooled analysis of the systemic review showed that 32 per cent of referrals were not compliant with NICE guidelines, with 89.8 per cent of referred patients having a benign outcome. The chi-square test showed no significant difference ( $\chi^2 = 0.67$ ,  $p = 0.4$ ) in benign outcome in our centre from the pooled analysis, whereas there was a significant difference in terms of guideline compliance ( $\chi^2 = 25.9$ ,  $p < 0.00001$ ).

### Implications for research and practice

The lack of knowledge shown through the six referral errors, in particular the 'inconsistent' and 'wrong' referrals, causes rapid and unnecessary saturation of the service. The large number of such errors and the abundance of non-red-flag symptoms contributed to the high rate of benign outcomes (Table 1).

- Two-week-wait referrals are still associated with a low rate in the early identification of cancer
- More than half of the referrals are not compliant with national guidelines
- The commonest reasons for non-compliant referrals were: inconsistencies in referral and intermittent disease course

Regular teaching sessions for primary healthcare on guidelines, e-learning modules on head and neck cancer presentations, and tertiary site placement of general practitioner trainees to build special interest, could improve the use of resources. The regular application of clinical governance in every general practice, together with feedback and communication from secondary or tertiary centres, might help spot an early surge in service use. Furthermore, patient education may have more effect than striving for a two-week-wait target.<sup>3,6</sup>

### Strengths and limitations

The use of national guidelines such as the NICE guidance would ensure unified assessment in many general practices and would prevent a confounding bias. This study was longitudinal, retrospective and observational. Selection bias, by limiting data collection to six months, might miss any anticipated fluctuation in referrals throughout the year. The data collection did not consider the analysis of the total head and neck cancer consultations in primary practice before referral to the tertiary centre.

### Conclusion

Most patients who undergo two-week-wait referral for head and neck symptoms are diagnosed with benign conditions. In this study, the reasons for referrals that did not comply with NICE guidelines were mostly related to misinterpretation of non-red-flag symptoms and the intermittent course of the disease. Errors in the referral scheme could be reduced by training primary care and improving awareness within the population regarding explanations for their presenting complaint.

**Data availability statement.** The data used to support the findings of this study are available from the corresponding author upon request.

**Competing interests.** None declared

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