


## Research Article

# Persistent Unilateral Sore Throat: Should It Be Included in the 2-Week Wait Referral Criteria by NICE

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*Design and Setting.* A retrospective study was conducted on all 2WW referrals made to our tertiary head and neck centre in a 12-month period. *Methods.* Sensitivity, specificity, and PPV of presenting complaints in H&N cancer diagnosis using Excel® and the statistical package SPSS®. *Results.* The sensitivity and specificity of 2005 NICE guidelines in detecting H&N cancers were 91.2% and 59%, respectively; their PPV was 9%. The sensitivity and specificity of 2015 NICE guidelines were 75.4% and 71%, respectively; their PPV was 10.3%. Eight out of 85 patients who presented with unilateral sore throat for more than 4 weeks, with or without otalgia and normal otoscopy, had H&N cancer (PPV 9.5%). *Conclusions.* Although the 2015 NICE guidelines have a high rate in detecting H&N cancers, consideration of reincluding unilateral sore throat in the referral criteria might be necessary.

## 1. Introduction

Following the 1998 White Paper, a new approach was established by Cancer Services Collaborative to facilitate quick review for patients with a suspected cancer [1]. In 2000, the Department of Health (DoH) introduced the guidelines and established 2 week wait (2WW) urgent referral for patients with symptoms suspicious of cancer in order to have an early diagnosis, treatment, and subsequently better prognosis for cancer patients in UK.

Regarding head and neck (H&N) cancer, the DoH sets ten symptoms with high possibility of cancer for H&N referrals in 2000. These symptoms were refined to 8 symptoms by the National Institute for Health and Care Excellence (NICE) in 2005 [2]. In 2015, NICE published new guidance taking into consideration 3% positive predictive value (PPV), a threshold value to support the recommendations for pathway of suspected cancer. It refined symptoms to subsites with 5 symptoms suspecting head and neck cancer (HNC) for the urgent referral from general practice to secondary care [3] (Table 1).

Many studies have assessed the efficacy of 2WW pathway in the detection of cancer. Kumar et al. 2012 found that the cancer detection rate based on the 2000 NICE guidelines ranged from 6.3% to 14.6% [4]. Another study conducted on 4123 2WW referred patients found that 6% of them had H&N cancer diagnosis [5].

In our study, we focus on the efficacy of NICE guidelines in H&N cancer detection rate, compare the 2015 and 2005 NICE in detecting H&N cancer, and evaluate the positive predictive value (PPV) of persistent unilateral sore throat more than 4 weeks with or without otalgia, a symptom that was not included in the 2015 NICE guidelines.

## 2. Materials and Methods

We retrospectively studied all 2WW referrals seen in our H&N tertiary centre in a 12-month period (January 2016 to December 2016). Data was collected from hospital electronic database and patients' medical notes. We excluded patients with thyroid cancer, lymphoma, previous H&N cancers; those who did not attend their appointments or where data

TABLE 1: Symptoms suspecting cancer for urgent referral.

| DoH 2000 Guidelines   | NICE Guidelines 2005  | NICE Guidelines 2015  |
|---|---|---|
| Ulceration of oral mucosa persisting for > 3 weeks                                | Ulceration of oral mucosa persisting for > 3 weeks  | Ulceration of oral mucosa persisting for > 3 weeks  |
| All red or red and white patches of the oral mucosa                               | Unexplained red and white patches (including suspected lichen planus) of the oral mucosa                                      | A red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia |
| Hoarseness persisting for >6 weeks  | Hoarseness persists for more than 3 weeks   | Aged 45 or above persistent unexplained hoarseness  |
| Unresolving neck masses for > 3 weeks   | Unresolving neck lump for > 3 weeks   | Persistent unexplained lump in the neck   |
| Unexplained tooth mobility not associated with periodontal disease                | Unexplained tooth mobility not associated with periodontal disease  | Lump in the lip or oral cavity  |
| Unilateral nasal obstruction particularly when associated with purulent discharge | Unexplained persistent sore or painful throat   |   |
| Cranial neuropathies  | Persistent swelling in the parotid or submandibular gland   |   |
| Orbital masses  | Unilateral unexplained pain in the head and neck area for more than 4 weeks, associated with otalgia but with normal otoscopy |   |
| Dysphagia persisting for 3 weeks  |   |   |
| Oral swellings persisting for > 3 weeks   |   |   |

TABLE 2: Cancer detection rate in patients referred through 2 ww pathway and compliant with NICE guidelines.

| Symptoms  | Frequency (%) | Cancer positive | Included in 2005 NICE guidelines | Included in 2015 NICE guidelines | PPV (%) |
|---|---------------|-----------------|----------------------------------|----------------------------------|---------|
| Neck lump: new or persisting for > 3 weeks            | 270 19.8%     | 32              | Yes                              | Yes                              | 12.2%   |
| Hoarseness Persisting for > 3 weeks                   | 147 11.1%     | 10              | Yes                              | Yes                              | 6.8%    |
| Persistent painful sore throat                        | 137 10%       | 9               | Yes                              | No                               | 6.5%    |
| Unilateral neck pain and otalgia with normal otoscopy | 23 1.3%       | 1               | Yes                              | No                               | 4.3%    |
| Total   | 577           | 52              |                                  |                                  | 9%      |

was missing and those cases managed by our oral and maxillofacial colleagues.

The collected data were analysed using Excel® (Microsoft, Redmond, WA, US) and the statistical package SPSS®. 2010 and 2015 NICE Guidance's sensitivity, specificity, and positive predictive value (PPV) were calculated.

### 3. Results

**3.1. 2-Week Wait Referrals.** A total number of 1553 patients were referred from primary care general practitioners (GP) through 2WW pathway to our H&N centre within a 12-month period. We excluded 186 patients who did not fulfill inclusion criteria. Out of the remaining 1367 patients, 627

were males (45.8%), and 740 were females (54.2%). Their mean age was 59 (age range 16-95). 82.3% were above 45 years of age.

**3.2. Cancer Detection Rates through the 2WW Pathway.** Only 57 out of the 1367 patients (4.2%) we included in this study were diagnosed with H&N cancers. The cancer detection rate of the 2005 guidelines was 9% (52/577) and the detection rate of the 2015 guidelines was 10% (42/417).

The commonest symptoms referred via the 2WW pathway and those with high PPV for detection of cancer are presented in Tables 2 and 3. For example, we have the following:

- (1) *Those patients presented with a new or persisting neck lump for > 3 weeks: 32 out of 270 patients, who were*

TABLE 3: Cancer detection rate in a patient referred through 2 ww pathway and NOT compliant with NICE guidelines.

| Symptoms                                   | Frequency (%) |       | Cancer positive | Included in 2005 NICE guidelines | Included in 2015 NICE guidelines | PPV (%) |
|--|---------------|-------|-----------------|----------------------------------|----------------------------------|---------|
| The sensation of a lump in the throat      | 181           | 14.3% | 0               | No                               | No                               | 0%      |
| Intermittent hoarseness                    | 115           | 9.1%  | 0               | No                               | No                               | 0%      |
| Intermittent sore throat                   | 78            | 5.7%  | 0               | No                               | No                               | 0%      |
| Discomfort in throat                       | 78            | 5.7%  | 0               | No                               | No                               | 0%      |
| Unilateral nasal obstruction and discharge | 53            | 3.9%  | 1               | No                               | No                               | 1.89%   |
| Unilateral OME                             | 42            | 3.1%  | 0               | No                               | No                               | 0%      |
| Dysphagia for > 3 weeks                    | 33            | 2.4%  | 2               | No                               | No                               | 6.06%   |
| Intermittent sore throat and hoarseness    | 33            | 2.4%  | 0               | No                               | No                               | 0%      |
| Unilateral nasal obstruction only          | 27            | 2.1%  | 0               | No                               | No                               | 0%      |
| Presence of blood in the mouth             | 24            | 1%    | 1               | No                               | No                               | 4.17%   |
| Unilateral nasal discharge only            | 22            | 1.6%  | 0               | No                               | No                               | 0%      |
| Unexplained septum ulcer                   | 18            | 1.3%  | 0               | No                               | No                               | 0%      |
| Persistent unexplained facial palsy        | 18            | 1.2%  | 1               | No                               | No                               | 5.56%   |
| Unilateral neck pain                       | 16            | 1.2%  | 0               | No                               | No                               | 0%      |
| Tightness throat                           | 12            | 0.9%  | 0               | No                               | No                               | 0%      |
| Smell disturbance                          | 11            | 0.8%  | 0               | No                               | No                               | 0%      |
| Unexplained septum Perforation             | 9             | 0.7%  | 0               | No                               | No                               | 0%      |
| Persistent unexplained sore nose           | 9             | 0.7%  | 0               | No                               | No                               | 0%      |
| Taste disturbance                          | 6             | 0.4%  | 0               | No                               | No                               | 0%      |
| Blood in the ear                           | 5             | 0.4%  | 0               | No                               | No                               | 0%      |
| Total                                      | 790           |       | 5               |                                  |                                  |         |

referred with this symptom, were diagnosed with cancer (PPV 12.2%).

- (2) *Hoarseness of voice persisting more than three weeks:* 10 out of 147 patients who were referred with this symptom were diagnosed with cancer (PPV 6.8%).
- (3) *Persistent sore throat:* 9 out of 137 patients who were referred with this symptom were diagnosed with cancer (PPV 6.5%).

**3.3. Efficacy of 2005 and 2015 NICE Guidelines.** The sensitivity and specificity of the 2005 NICE guidelines were found to be 91.2% and 59%, respectively, in detecting H&N cancers via the 2WW pathway. Their PPV was 9%. The sensitivity and specificity of the 2015 NICE guidelines were found to be 75.4% and 71%, respectively. Their PPV was 10.3%.

**3.4. Noncancer Diagnoses following a 2WW Referral.** The most common noncancer diagnosis in our 2WW referrals was laryngopharyngeal reflux (454 patients). No abnormality

was found in 241 patients. Other diagnoses can be seen in Table 4.

**3.5. Analysis of Persistent Sore Throat.** We received 137 referrals of patients with a persistent sore throat. 9 of them were found to have H&N cancer. In further analysis, we found the following (Table 5):

(i) 17 (12.4%) patients had persistent unilateral sore throat for less than four weeks: none of them was diagnosed with H&N cancer.

(ii) 57(41.6%) patients had persistent unilateral sore throat more than four weeks. Cancer was detected in 5 patients (PPV 8.8%).

(iii) 28 (20.4%) patients had persistent unilateral sore throat with otalgia with normal otoscopy. Cancer was detected in 3 patients (PPV 10.5%).

(iv) The remaining 35 patients had a nonspecific persistent sore throat. One patient was cancer positive (PPV 2%).

Overall, unilateral sore throat for more than 4 weeks with or without otalgia and normal otoscopy has a high PPV or 9.5%.

TABLE 4: Final diagnosis of patients referred through 2 ww pathway.

| Diagnosis                              | Frequency | Percent |
|--|-----------|---------|
| Head and neck malignancy               | 57        | 4.2%    |
| Laryngopharyngeal Reflux               | 454       | 33.2%   |
| No abnormality /reassured              | 240       | 17.6%   |
| Functional dysphonia                   | 96        | 7%      |
| Globus pharyngus                       | 76        | 5.6%    |
| Reactive /Normal lymph nodes           | 57        | 2.8%    |
| Benign salivary glands lesions         | 38        | 2.8%    |
| Idiopathic unilateral vocal cord Palsy | 36        | 2.6%    |
| Reinke's oedema                        | 25        | 1.8%    |
| Infections                             | 23        | 1.7%    |
| Vocal cord nodules                     | 19        | 1.4%    |
| Septal deviation                       | 17        | 1.3%    |
| Cervical lipoma                        | 16        | 1.2%    |
| Laryngeal polyps                       | 12        | 0.9%    |
| Sebaceous Cysts                        | 12        | 0.9%    |
| Retention tonsillar cysts              | 10        | 0.8%    |
| Cervical TB                            | 7         | 0.5%    |
| Hyperkeratosis vocal cord              | 7         | 0.5%    |
| Laryngeal papillomatosis               | 5         | 0.4%    |
| Mild cord dysplasia                    | 5         | 0.4%    |
| Moderate vocal cord dysplasia          | 3         | 0.2%    |
| Cervical toxoplasmosis                 | 2         | 0.1%    |
| Bronchogenic carcinoma                 | 2         | 0.1%    |
| Granuloma arytenoid                    | 2         | 0.1%    |
| Vallecular cysts                       | 2         | 0.1%    |
| Neurofibroma                           | 2         | 0.1%    |
| Carotid body tumour                    | 2         | 0.1%    |
| Thyroglossal cyst                      | 2         | 0.1%    |
| Other diagnosis                        | 138       | 10.1%   |
| Total                                  | 1367      | 100%    |

TABLE 5: Analysis of a persistent sore throat.

| Symptom  | Frequency (%) |       | Cancer positive |       |
|--|---------------|-------|-----------------|-------|
| Unilateral pain in throat < 4 weeks  | 17            | 12.4% | 0               | 0%    |
| Unilateral pain in throat >4 weeks   | 57            | 41.6% | 5               | 8.8%  |
| Unilateral pain in throat and otalgia with normal otoscopy                                   | 28            | 20.4% | 3               | 10.7% |
| Nonspecific Sore throat  | 35            | 25.5% | 1               | 2%    |
| Total  | 137           | 100%  | 9               | 6.5%  |
| Unilateral pain in the throat more than 4 weeks with or without otalgia with normal otoscopy | 85 /137       | 62%   | 8               | 9.5%  |

## 4. Discussion

### 4.1. Comparison with Existing Literature

4.1.1. *Cancer Detection Rates.* 2015 NICE Guidelines had lower sensitivity (75.4%) in comparison with 2005 guidelines (91%); however, 2015 guidance has higher PPV for diagnosing cancer and higher specificity.

4.1.2. *Persistent Unilateral Pain in Head and Neck.* Persistent unilateral sore throat with otalgia is an important presenting complaint for diagnosing H&N cancer, especially for oropharyngeal, laryngeal, and hypopharyngeal malignancy [6].

In our study analysis, unilateral sore throat for more than 4 weeks with or without otalgia had a 9.5% PPV in H&N cancer diagnosis. Tikka et al. [7] showed higher PPV (14.2%) for unilateral persistent neck pain more than 4 weeks with

or without otalgia and normal otoscopy, but this finding was based on a smaller number of patients (49). This symptom of unilateral sore throat was not included in 2015 NICE guidelines for 2WW referral criteria. Although there has been no official reason for that, we assume that general practice is overwhelmed with a wide variety of sore throat presentations. Therefore onward referral to a tertiary centre might not necessarily be the best option in all these cases. Our study suggests that unilateral sore throat for more than 4 weeks has a high PPV for diagnosing cancer and we would recommend that this symptom is added on the following NICE guidelines on 2WW for H&N cancers.

**4.2. Strengths and Limitations.** The major drawback of our study is that it is a retrospective study. Most published studies on 2WW referral pathways were retrospective; a prospective design would offer more robust outcomes. Data were recorded in the patient first appointment by different grades of ENT doctors. This could be considered bias in methodology. This study is unique as it has included the highest number of referred patients in a single centre, since the 2015 NICE guidelines were published.

This was a retrospective cohort and the population of this study was limited to the patients who were only referred through 2WW pathway as a 2ww to our Head and Neck Unit at Sheffield Teaching Hospitals, Sheffield.

Unfortunately, we do not have data about the total numbers of all patients with sore throat admitted to our ENT not as a 2WW. This was out of the study objectives. I think it would be a great idea to perform a study looking at that but that would mean lots of challenges (we see more than 25,000 new referrals to ENT at Sheffield Teaching Hospitals per year)

We found that the majority of these patient were referred as a 2WW from primary care after exhausting all treatment medications (various lots of antibiotics and pain killers) and patients are still symptomatic; however, we could not analyse it as it was missed in some patients, a lot depending on how well the patients were interviewed regards to symptoms and previous treatments received.

Other factors which could have triggered the 2ww referral were smoking and alcohol history.

Head and neck cancer symptoms are unspecific; oropharyngeal cancers can be diagnosed in patients presenting only with sensation of lump with no other ENT symptoms.

However, from our study we would recommend our colleagues in primary care to have a very low threshold to refer a patient as a 2WW for being suspicious of head and neck cancer especially if they have unilateral sore throat for > 5 weeks and especially if that has become associated with otalgia with normal otoscopy.

Our colleagues in primary care face many challenging in screening head and neck cancer patients taking in consideration that many symptoms are unspecific and they have very limited time for patients which could make taking a comprehensive clinical history very challenging.

**4.3. Implications for Research and/or Practice.** 2WW referrals have a high detection rate of cancers if they are compliant

with 2015 NICE guidelines (10%). We recommend investing more resources in more education in H&N cancer symptoms for general practitioners. This can be achieved with the help of an 'e-Learning for Healthcare' module online, as well as continuous feedback from H&N colleagues (via written feedback, meetings, and telephone advice). The aim would be to be confident in making (or ruling-out) a cancer diagnosis have more appropriate 2WW referrals [8].

Open discussion between GPs and patients around cancer should be encouraged when referring them for symptoms suspicious of cancer in order to line up referrals with NICE guidelines and to decrease patients pressure on primary practice for urgent referrals [9].

## 5. Conclusion

The newest NICE guidelines for an urgent referral via the 2WW pathway in 2015 have higher specificity and positive predictive value for cancers in comparison to previous guidelines, possibly because it narrowed the referral items to only 5 symptoms. Our study confirmed the low cancer detection rate via the 2WW urgent referral pathway, similar to previous studies [7, 10, 11].

Persistent unilateral sore throat for more than 4 weeks with or without otalgia with normal otoscopy was included in the 2005 NICE guidelines for an urgent referral via the 2WW pathway but not in the 2015 NICE updates with no cited reasons [7]. This study raises our concern that this symptom has a high PPV (9.5%) of positive cancer and should be reconsidered when designing future guidelines.

## 6. Summary

- (i) The newest NICE guidelines for an urgent referral via the 2WW pathway in 2015 have higher specificity and positive predictive value for cancers in comparison to previous guidelines.
- (ii) Persistent unilateral sore throat for more than 4 weeks with or without otalgia with normal otoscopy has high cancer predictive value and was not included in NICE guidelines 2015.
- (iii) Persistent sore throat can be reconsidered to be included in the 2-week wait referral criteria updates by NICE.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request, and the patient's data used to support these findings are included in the article.

## Ethical Approval

The analysis was based on existing data that had been anonymised and therefore did not require the approval of the ethics committee.

## Conflicts of Interest

The authors have declared no conflicts of interest.

## Authors' Contributions

Ahmed Allam carried out conception and design, analysis and interpretation, writing the article, critical revision of the article, data collection, and literature search. Hazem Nijim carried out conception and design, analysis and interpretation, writing the article, critical revision of the article, data collection, literature search, and final approval of the article.

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The institution where work was preformed is the Department of Otolaryngology, Sheffield Teaching Hospitals, Sheffield, UK.

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