Original Article

Remote Triage Incorporating Symptom-Based Risk Stratification for Suspected Head and Neck Cancer Referrals: A Prospective Population-Based Study

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BACKGROUND: Remote triage for suspected head and neck cancer (HNC) referrals was adopted by many institutions during the initial peak of the coronavirus disease 2019 pandemic. Its safety in this population has not been established. **METHODS:** A 16-week, prospective, multicenter national service evaluation was started on March 23, 2020. Suspected HNC referrals undergoing remote triage in UK secondary care centers were identified and followed up for a minimum of 6 months to record the cancer status. Triage was supported by risk stratification using a validated calculator. **RESULTS:** Data for 4568 cases were submitted by 41 centers serving a population of approximately 26 million. These represented 14.1% of the predicted maximum referrals for this population outside of pandemic times, and this gave the study a margin of error of 1.34% at 95% confidence. Completed 6-month follow-up data were available for 99.8% with an overall cancer rate of 5.6% (254 of 4557). The rates of triage were as follows: urgent imaging investigation, 25.4% (n = 1156); urgent face-to-face review, 27.8%; (n = 1268); assessment deferral, 30.3% (n = 1382); and discharge, 16.4% (n = 749). The corresponding missed cancers rates were 0.5% (5 of 1048), 0.3% (3 of 1149), 0.9% (12 of 1382), and 0.9% (7 of 747; $P = .15$). The negative predictive value for a nonurgent triage outcome and no cancer diagnosis was 99.1%. Overall harm was reported in 0.24% (11 of 4557) and was highest for deferred assessments (0.58%; 8 of 1382). **CONCLUSIONS:** Remote triage, incorporating risk stratification, may facilitate targeted investigations for higher risk patients and prevent unnecessary hospital attendance for lower risk patients. The risk of harm is low and may be reduced further with appropriate safety netting of deferred appointments. *Cancer* 2021;127:4177-4189. © 2021 The Authors. *Cancer* published by Wiley Periodicals LLC on behalf of American Cancer Society. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

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Lay Summary:
• This large national study observed the widespread adoption of telephone assessment (supported by a risk calculator) of patients referred to hospital specialists with suspected head and neck cancer during the initial peak of the coronavirus disease 2019 pandemic.
• The authors identified 4568 patients from 41 UK centers (serving a population of more than 26 million people) who were followed up for a minimum of 6 months.
• Late cancers were identified, whether reviewed or investigated urgently (0.4%) or nonurgently (0.9%), but the overall rate of harm was low (0.2%), with the highest rate being seen with deferred appointments (0.6%).

KEYWORDS: harm, multicenter, national, observational, telemedicine.

INTRODUCTION

The emergence of coronavirus disease 2019 (COVID-19) in early 2020 led to significant changes in the normal practices for the diagnosis and management of cancer. This was especially pronounced in specialties such as ear, nose, and throat (ENT), head and neck surgery, and oral health, where aerosol-generating procedures were commonly performed.[1,2] Patients and health care services alike had an interest in avoiding hospital attendance to reduce the potential for spreading infection and to preserve resources for the pandemic response.[3] Part of the shift in practice included a sharp uplift in the use of telemedicine in place of face-to-face outpatient appointments.[4,5]

Patients referred from primary care to secondary care with suspected head and neck cancer (HNC) are at particular risk of harm from changes to the standard-of-care diagnostic pathway. In normal times, physical examination, combined with flexible transnasal endoscopy of the upper aerodigestive tract where indicated, is considered an essential facet of the new patient evaluation. Remote assessment necessarily forgoes this and relies on the patient history and the referral information provided by the primary care physician alone. However, it may also facilitate earlier patient contact, may use fewer outpatient resources, and may allow a more efficient route to targeted investigations in select patients.[6,7] Patients with cancer may be diagnosed faster, and those without cancer may be reassured more efficiently; this provides potential benefits to patients and health care services alike. However, remote triage was novel to most clinicians at the time it was widely adopted, and the safety of this practice in these patients had not been established. It is likely that an increase in telemedicine will remain to some degree in post-pandemic times, and so it is necessary to review its safety in this population.[8]

We had previously developed and validated a risk calculator (Head and Neck Cancer Risk Calculator version 2 [HaNC-RC-v2]) based on the symptom and demographic data of approximately 10,000 new patient referrals with suspected HNC.[9] This was disseminated just before the worst of the disruption brought about by the initial peak of COVID-19 in the United Kingdom and is freely available online. Communicating and understanding risk is an important element of shared decision-making between patients and clinicians in health care.[10] The use of a standardized triage system can further help in the understanding of the decision-making process and the role of clinical judgment for each patient. Effective risk stratification may have a prominent role in addressing a backlog of referrals to cancer services as resources strained by the pandemic recover and we refocus on the importance of valuing all lives equally.[11]

In the United Kingdom, since 2005, guidance from the National Institute for Health and Care Excellence has recommended that patients presenting to their primary care physicians with symptoms in the head and neck region suggestive of cancer be referred to secondary care via a rapid access pathway to be assessed within 2 weeks.[12] This pathway covers all cancers affecting the head and neck region, including the following: pharyngeal cancer, laryngeal cancer, oral cavity/lip cancer, thyroid cancer, cutaneous cancer, salivary gland cancer, nasal cavity/sinus cancer, and cancers affecting the ear. A number of other non-HNC malignancies may also inevitably be identified on this pathway if they present with symptoms in the head and neck (eg, thoracic lesions causing swallowing obstruction or hoarseness from injury to the recurrent laryngeal nerve and non-HNC metastasizing to cervical lymph nodes or lymphomas presenting as neck lumps).

In consultation with the British Association of Otorhinolaryngology–Head and Neck Surgery (ENT UK) and the British Association of Head and Neck Oncologists (BAHNO) and through collaboration with the UK ENT Trainee Research Network (INTEGRATE), a national service evaluation was rapidly developed and implemented to monitor the unique shift in practice toward remote consultations.[13] This study aims to report the findings of this 16-week, prospective service evaluation of remote triage of suspected HNC referrals conducted during the initial peak of the COVID-19 pandemic in the United Kingdom.

MATERIALS AND METHODS

The protocol for this study was published in advance at https://entintegrate.co.uk. This article was prepared with reference to the Strengthening the Reporting of Observational Studies in Epidemiology checklist for cohort studies.[14]

Ethical Considerations

The Health Research Authority decision tool determined that the study design fell under the remit of a service evaluation, and so no ethical approval was required (available at http://hra-decisiontools.org.uk/research/).

Study Design and Setting

A national prospective service evaluation was conducted; it was supported by ENT UK and BAHNO and delivered via the INTEGRATE network. All UK ENT departments were invited to participate via social media and mailouts from the supporting organizations. Sites could open at any point during the prospective data collection period. Registration as per local governance guidelines was required to participate.

Participants

Patients who were referred on the suspected HNC pathway to secondary care and who were prospectively identified and completed remote triage over a telephone consultation were eligible for inclusion. These patients were referred by primary care physicians to secondary care HNC specialists for further assessment without any upfront requirement for imaging, procedures, or biopsies before this assessment.

Data Collection

Cases were identified over a 16-week period between March 23 and July 13, 2020. The final submission of data was accepted after a minimum 6-month follow-up. To be eligible for inclusion, cases were required to have complete demographic and symptom data with no null data points in these fields. To facilitate this, a standardized electronic case report form was created with Excel software (Microsoft Corporation, Redmond, Washington; see the supporting information); this incentivized the completion of data by displaying a risk stratification result from the HaNC-RC-v2 only if all relevant triage fields were accurately filled out.[9] Data were held offline at each center until the follow-up period had passed for all patients, whereupon the patient record was checked by the local team for a diagnosis of cancer at any time since the initial triage; it was classed as either on the urgent assessment pathway or "late" if at any time thereafter.

The following data were collected: patient demographics, smoking and alcohol history, symptoms as per the HaNC-RC-v2,[9] triage outcome, clinician and patient preferences for review/investigation, cancer diagnosis timing, and the primary site of the cancer (if identified). Data were not collected on the specific type of investigation requested, the grade of the clinicians completing the triage consultation, or the stage of cancer at the time of diagnosis.

The project management team handled only anonymized data, with all identifiable information removed before submission by the local teams. Where missing or ambiguous data were identified by the project management team, a query was raised with the local site to clarify each data point. Where missing data could not be resolved, that record was excluded from the relevant analysis.

Using the data tool with in-built risk stratification

Risk stratification was performed with the HaNC-RC-v2, which is open license and is freely available online at http://orlhealth.com/risk-calculator-2.html. This tool was validated in a population undergoing face-to-face assessment with suspected HNC. It was incorporated into the Excel Data Tool as a decision aid to assist experienced health care professionals in assessing patients after a rapid shift in practice toward remote triage as part of the COVID-19 pandemic response. The algorithm for the calculator had been developed to deliver a negative predictive value (NPV) of 98.6% for those classed as low risk. Clinicians were instructed to consider both the clinical history and the outcome of the risk stratification in proposing their management plan.

Data Analysis

The primary outcome was the diagnosis of cancer after a minimum of 6 months of follow-up. Cancers identified incidentally from investigations arising from the index referral but not related to the referral symptoms and cancers identified in the follow-up period that were not linked to the index referral were not included in the analysis. This was intended to ensure that the referral symptoms themselves could be relied upon as prognosticators of any subsequent cancer diagnosis and, as such, was indiscriminate as to the ultimate site/type of cancer diagnosed.

No a priori sample size calculation was performed. Categorical variables were compared via the χ^2 test with the Yates correction, with a 2-tailed P value of .05 taken as significant. The analysis was performed with R statistical software (R Foundation, Vienna, Austria).

Interim Reports

After 8 weeks, interim data were requested from participating centers, and a report was produced to allow rapid feedback of preliminary findings to the UK ENT community. The report was disseminated electronically via an ENT UK mailout on June 3, 2020, and was hosted online at https://entuk.org and https://entintegrate.co.uk (see the supporting information).

RESULTS

Centers and Submissions

Final data were submitted by 41 of 47 UK centers that registered interest in taking part (32 in England, 6 in Scotland, 2 in Wales, and 1 in Northern Ireland), with 4568 cases eligible for analysis with complete demographic and symptom data (median cases per center, 99; range, 10-337; interquartile range [IQR], 40-157). The median age for referrals was 58 years (range, 1-98 years; IQR, 46-69 years), and 57.1% were female (n = 2608).

The 41 centers serve a population of approximately 26 million people (Supporting Table 1). Our data, therefore, represent 14.1% of the predicted maximum referrals for this population and time period based on activity outside of pandemic conditions (referral rate, 404.5 per 100,000; 2019-2020)[15]; this allowed for a margin of error of 1.34% at a 95% confidence level for the study.

Data completeness

The cancer status at a minimum follow-up of 6 months was provided in 99.8% of the cases (n = 4557), with 11 records having incorrect patient identifiers recorded at the initial triage, which precluded local follow-up. The triage outcome was provided for 99.7% of the cases (n = 4555), and the clinician advice for management was provided for 98.5% of the cases (n = 4501).

Symptoms

Table 1 summarizes the incidence of presenting symptoms, smoking history, and alcohol history alongside their positive predictive values (PPVs) for cancer at any time and their triage outcomes. The nonnegative responses to these factors are presented with clinically interesting pairings in Figures 1 and 2. Figure 1 contrasts the incidence (inner ring) with the PPV (outer ring) for each factor. Figure 2 contrasts the discharge rate (inner ring) with the rate of triage directly to an investigation (outer ring) for each factor.

Diagnosis of Cancer

Table 2 summarizes the cancer status by triage outcome, clinician advice for assessment, and risk stratification with the HaNC-RC-v2. The overall rate of a cancer related to the referral symptoms in this population was 5.6% (254 of 4557), with a 5.0% rate on the urgent pathway (227 of 4568) and a 0.6% rate in the follow-up period (27 of 4330).

Triage outcome

The triage outcome indicates the decision made by the clinician using the information from the remote assessment and the risk stratification from HaNC-RC-v2. This was classed as either urgent assessment (a face-to-face clinical assessment and/or investigation; 53.2%) or nonurgent (deferred reviews or investigations and discharges; 46.8%). Triage outcome (urgent vs nonurgent) and cancer at any time were significantly associated (9.7% vs 0.9%; $P < .0001$). The sensitivity, specificity, PPV, and NPV for being triaged to an urgent assessment and having a related cancer diagnosed at any time were 92.5%, 49.1%, 9.7%, and 99.1%, respectively.

Late cancers were reported in 0.9% of those triaged as nonurgent and in 0.4% of those assessed urgently (19 of 2129 and 8 of 2197, respectively; $P = .0439$).

A more detailed breakdown by triage outcomes is given in Table 2. The rates of triage were as follows: urgent imaging investigation, 25.4% (n = 1156); urgent face-to-face review, 27.8% (n = 1268); assessment deferral, 30.3% (n = 1382); and discharge, 16.4% (n = 749). The corresponding late cancer rates were 0.5%, 0.3%, 0.9%, and 0.9% (5 of 1048, 3 of 1149, 12 of 1382, and 7 of 747, respectively). These rates were not significantly different ($P = .15$).

It should be noted that patients classed as nonurgent (deferred reviews or investigations and discharges) could not, by this definition, have cancers recorded as being found on the urgent pathway in this analysis.

Clinician advice for assessment

Clinician advice for assessment with a review/investigation was recorded as either yes (69.7%) or no (30.3%). Clinician advice for assessment and cancer at any time were significantly associated (7.3% vs 1.5%; $P < .0001$). The sensitivity, specificity, PPV, and NPV for a preference for review/investigation and having a related cancer diagnosed at any time were 91.6%, 31.5%, 7.3%, and 98.5%, respectively.

Late cancers were reported in 0.5% of those who were advised by their clinician for a review or investigation and in 0.7% of those not advised for further assessment (16 of 2925 and 10 of 1349, respectively; $P = .5840$).

It should be noted that 72.2% of those patients whose clinicians advised an assessment were seen urgently,

TABLE 1. Responses to Standardized Triage Questions (Based on HaNC-RC-v2) With PPVs for Cancer Found at Any Time and Response Rates by Triage Outcome

	All Responses		Cancer: PPVs and True Positives		Urgent						Nonurgent			
					Investigation				Review					
					Investigation First		Investigation at Any Time		Review First		Review at Any Time		Deferred		Discharged	
	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Overall		4568	5.6	254	25.3	1156	37.4	1707	27.8	1268	37.3	1703	30.3	1382	16.4	749
General																
Do you smoke?																
No	55.0	2513	4.7	117	25.9	652	36.0	905	23.1	580	32.3	811	32.2	809	18.4	462
Current smoker	16.6	757	7.9	60	29.9	226	48.1	364	35.1	266	47.3	358	24.0	182	10.8	82
Ex-smoker	28.4	1298	5.9	77	21.4	278	33.7	438	32.5	422	41.1	534	30.1	391	15.8	205
Do you drink alcohol?																
≤14 units/wk	88.9	4063	5.0	204	25.6	1041	37.0	1505	26.5	1078	35.8	1456	30.8	1250	16.8	682
>14 units/wk	9.9	451	10.0	45	21.1	95	38.8	175	38.8	175	49.9	225	26.2	118	13.7	62
Ex-excess	1.2	54	9.3	5	37.0	20	50.0	27	27.8	15	40.7	22	25.9	14	9.3	5
Have you lost any weight without trying?																
No	89.8	4102	5.0	207	24.2	991	35.1	1440	26.1	1071	35.0	1435	31.8	1304	17.6	723
Yes	10.2	466	10.1	47	35.4	165	57.3	267	42.3	197	57.5	268	16.7	78	5.6	26
Voice and airway																
Do you have a hoarse voice?																
No	61.0	2785	6.6	183	31.9	889	43.8	1221	24.2	674	35.9	1001	27.9	776	15.7	436
Yes	39.0	1783	4.0	71	15.0	267	27.3	486	33.3	594	39.4	702	34.0	606	17.6	313
Persistent	11.8	541	7.2	39	14.8	80	37.7	204	57.3	310	63.0	341	24.8	134	3.1	17
Intermittent	25.0	1142	2.8	32	15.0	171	22.9	261	23.1	264	29.1	332	38.3	437	23.4	267
Persistent but explained	2.2	100	0.0	0	16.0	16	21.0	21	20.0	20	29.0	29	35.0	35	29.0	29
Do you have noisy breathing?																
No	97.7	4465	5.6	248	25.4	1134	37.2	1660	26.8	1198	36.3	1620	30.8	1373	16.8	748
Yes	2.3	103	5.8	6	21.4	22	45.6	47	68.0	70	80.6	83	8.7	9	1.0	1
Swallowing																
Do you have a feeling of something stuck in your throat?																
No	66.5	3036	6.5	197	27.4	833	39.7	1206	27.1	822	37.2	1128	28.6	868	16.6	505
Yes	33.5	1532	3.7	57	21.1	323	32.7	501	29.1	446	37.5	575	33.6	514	15.9	244
Do you have a pain in your throat?																
No	66.0	3013	6.2	186	27.4	826	38.5	1161	23.9	719	34.3	1032	29.8	898	18.6	559
Yes	34.0	1555	4.4	68	21.2	330	35.1	546	35.3	549	43.2	671	31.1	484	12.2	190
Persistent bilateral/midline	9.8	448	4.9	22	22.8	102	38.8	174	41.5	186	49.3	221	25.2	113	10.5	47

TABLE 1. *Continued*

	All Responses		Cancer: PPVs and True Positives		Urgent								Nonurgent			
					Investigation				Review							
					Investigation First		Investigation at Any Time		Review First		Review at Any Time		Deferred		Discharged	
	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Persistent unilateral	6.4	292	9.9	29	32.5	95	58.9	172	57.5	168	69.2	202	8.6	25	1.0	3
Intermittent bilateral/midline	12.4	567	1.4	8	13.9	79	20.6	117	19.2	109	25.0	142	47.4	269	19.2	109
Intermittent unilateral	5.4	248	3.6	9	21.8	54	33.5	83	34.7	86	42.7	106	31.0	77	12.5	31
Do you have pain when you swallow?																
No	89.3	4078	5.1	209	25.0	1021	35.4	1444	24.6	1004	33.9	1383	32.2	1313	17.8	727
Yes	10.7	490	9.2	45	27.6	135	53.7	263	53.9	264	65.3	320	14.1	69	4.5	22
Do you have any difficulty swallowing?																
No	82.3	3759	5.2	194	23.8	895	34.8	1307	25.9	973	34.9	1313	31.6	1189	18.3	689
Yes	17.7	809	7.4	60	32.3	261	49.4	400	36.5	295	48.2	390	30.7	248	29.0	235
Persistent	6.5	296	14.2	42	39.2	116	66.2	196	48.6	144	64.2	190	11.1	33	1.0	3
Intermittent	11.2	513	3.5	18	28.3	145	39.8	204	29.4	151	39.0	200	31.2	160	11.1	57
Do you have a new swelling in your mouth?																
No	93.9	4291	5.4	232	25.4	1092	36.5	1565	26.1	1122	35.6	1527	31.1	1335	17.0	729
Yes	6.1	277	7.9	22	23.1	64	51.3	142	52.7	146	63.5	176	17.0	47	7.2	20
Do you have a new ulcer in your mouth?																
No	96.7	4417	5.6	249	25.5	1127	37.3	1649	26.6	1174	36.2	1597	30.9	1365	16.7	738
Yes	3.3	151	3.3	5	19.2	29	38.4	58	62.3	94	70.2	106	11.3	17	7.3	11

Oral

TABLE 1. *Continued*

	All Responses		Cancer: PPVs and True Positives		Urgent								Nonurgent			
					Investigation				Review							
					Investigation First		Investigation at Any Time		Review First		Review at Any Time		Deferred		Discharged	
	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Miscellaneous		4568														
Do you have any new ear pain?																
No	88.8	4057	5.3	215	25.2	1024	36.0	1460	25.6	1038	35.0	1419	31.6	1280	17.4	704
Yes	11.2	511	7.6	39	25.8	132	48.3	247	45.0	230	55.6	284	20.0	102	8.8	45
Do you have any new lumps in your neck?																
No	73.2	3346	3.0	100	15.3	513	25.4	850	27.7	926	33.6	1125	36.0	1205	20.6	690
Yes	26.8	1222	12.6	154	52.6	643	70.1	857	28.0	342	47.3	578	14.5	177	4.8	59
Persistent	21.6	986	14.6	144	55.9	551	75.6	745	30.6	302	51.3	506	11.3	111	2.1	21
Fluctuating/reducing	5.2	236	4.2	10	39.0	92	47.5	112	16.9	40	30.5	72	28.0	66	16.1	38
Do you have a new growth on your skin on your head and neck?																
No	99.0	4522	5.5	247	25.3	1146	37.1	1679	27.4	1241	37.0	1674	30.4	1374	16.5	748
Yes	1.0	46	15.2	7	21.7	10	60.9	28	58.7	27	63.0	29	17.4	8	2.2	1

Abbreviations: HaNC-RC-v2, Head and Neck Cancer Risk Calculator version 2; PPV, positive predictive value.

Clinicians were asked the outcome of the remote consultation. If the patient underwent imaging or a diagnostic procedure, then *investigation* was chosen. If the patient underwent a face-to-face review, then *review* was chosen. Where *first* is specified, this was the initial activity after remote triage. Where *at any time* is specified, the activity took place at some point in the patient's diagnostic workup. The depth of red indicates the rate for that response is higher than the mean, and the depth of green indicates the rate for that response is lower than the mean.
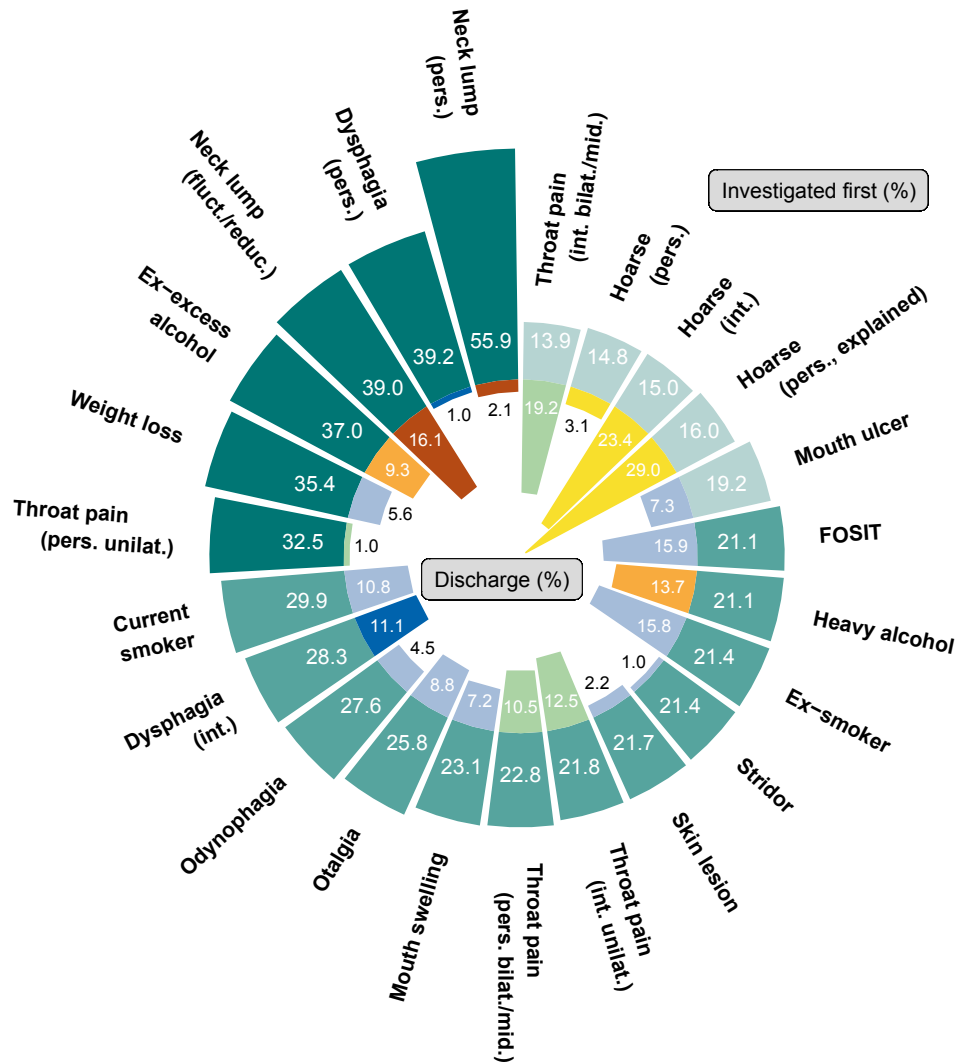
Figure 1. The outer ring displays the PPVs of the nonnegative responses to symptom, smoking, and alcohol triage questions, which are contrasted against the incidences of these responses on the inner ring. Colors besides blue in the inner-ring group together responses with more than 2 tiers that would compete with each other. bilat indicates bilateral; fluct./reduc., fluctuating/reducing; FOSIT, feeling of something in the throat; int., intermittent; mid., midline; pers., persistent; PPV, positive predictive value; unilat.; unilateral.

whereas only 10.0% of those not advised for further assessment were (2265 of 3139 vs 136 of 1362). This limited the potential for the reporting of urgent cancers in the latter group.

Risk stratification

Risk was stratified as either high (31.3%) or low (68.7%), as determined by the HaNC-RC-v2. Stratification to high risk and a cancer at any time were significantly associated (13.0% vs 2.2%; $P < .0001$) with the following diagnostic parameters: the sensitivity, specificity, PPV, and NPV were 73.2%, 71.1%, 13.0%, and 97.8%, respectively.

Late cancers were reported in 0.6% of the high-risk group versus 0.6% of the low-risk group (7 of 1249 vs 20 of 3081; $P = .9023$).

It should be noted that 91.5% of the high-risk group were seen and/or assessed urgently, whereas only 35.7% of the low-risk group were (1306 of 1427 vs 1118 of 3128). This limited the potential for the reporting of urgent cancers in the low-risk group.

Primary Cancer Site

Table 3 shows the primary sites of the 254 cancers reported in the study period that were related to the referral
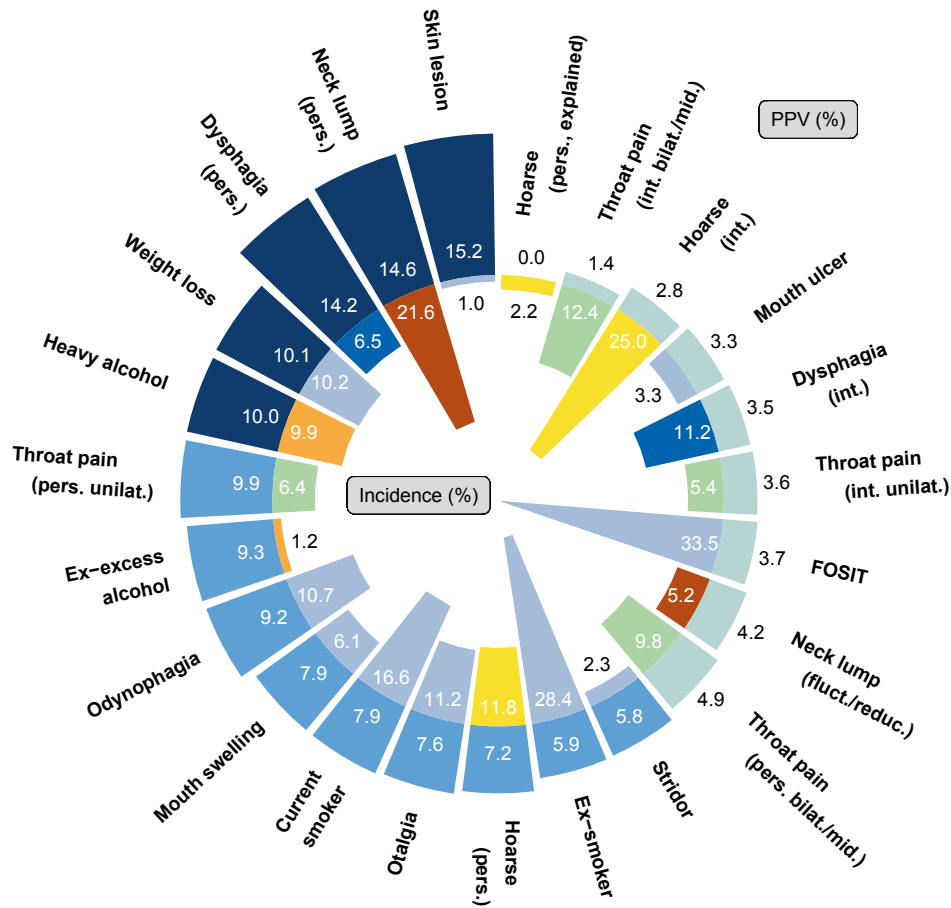
Figure 2. The outer ring displays the rates of triage directly to an urgent investigation for the nonnegative responses to symptom, smoking, and alcohol triage questions, which are contrasted against the rates of direct discharge for these responses on the inner ring. Colors besides blue in the inner-ring group together responses with more than 2 tiers that would compete with each other. bilat indicates bilateral; fluct./reduc., fluctuating/reducing; FOSIT, feeling of something in the throat; int., intermittent; mid., midline; pers., persistent; unilat.; unilateral.

symptoms. The median age for patients with cancer was 65.5 years (range, 21-94 years; IQR, 57-73 years), and 34.6% were female (88 of 254).

The most common cancers were oropharyngeal cancer (25.6%; n = 65), lymphoma (17.7%; n = 45), and laryngeal cancer (12.2%; n = 31). Figure 3 shows the distribution of cancers by age in comparison with the referral cohort as a whole.

Lymphoma, lung cancer, and esophageal cancer were the most common non-HNCs in the cohort. Non-HNCs represented 33.9% of cancers identified from these patients referred on the suspected HNC pathway (86 of 254).

Late Cancers and Harm

Eight of the 27 cases whose cancer was identified late had undergone an urgent assessment, and 4 of these

cases were classed as low risk; 19 cases were not urgently assessed, and 17 of these cases were classed as low risk (Supporting Table 2). The treating clinicians were contacted to obtain details of factors that may have contributed to the late diagnosis and any perceived harm from the delay (defined as either a worse prognosis or escalated treatment). It was felt that harm had resulted from the late diagnosis in 0.24% of the patients triaged (11 of 4557: 7 HNC cases and 4 non-HNC cases), with the highest relative rate among deferred appointments at 0.58% (8 of 1382) and with lower rates in those discharged (0.13%; 1 of 749), triaged to an urgent investigation (0.09%; 1 of 1156), or triaged to an urgent face-to-face review (0.08%; 1 of 1268). The sites of the primary cancer for those coming to harm are identified in Table 3.

TABLE 2. Cancers by Time of Diagnosis Alongside Triage Outcomes, Clinician Advice for Assessment, and Results of Risk Stratification

		Cancers								
		Urgent			Late			Any Time		
	% of All Cases	%	Cancers	Total	%	Cancers	Total	%	Cancers	Total
By triage outcome				4555			4326			4553
Urgent assessment	53.2	9.4	227	2424	0.4	8	2197	9.7	235	2424
Investigation first	25.4	9.3	108	1156	0.5	5	1048	9.8	113	1156
Investigation at any time	37.5	13.1	224	1707	0.5	8	1483	13.6	232	1707
Review first	27.8	9.4	119	1268	0.3	3	1149	9.6	122	1268
Review at any time	37.4	12.7	217	1703	0.3	5	1486	13.0	222	1703
Nonurgent	46.8	0.0	0	2131	0.9	19	2129	0.9	19	2129
Deferred	30.3	0.0	0	1382	0.9	12	1382	0.9	12	1382
Discharged	16.4	0.0	0	749	0.9	7	747	0.9	7	747
By clinician advice				4501			4274			4499
Clinician advised for assessment	69.7	6.8	214	3139	0.5	16	2925	7.3	230	3139
Clinician did not advise for assessment	30.3	0.8	11	1362	0.7	10	1349	1.5	21	1360
By risk stratification				4568			4330			4557
High risk	31.3	12.5	179	1429	0.6	7	1249	13.0	186	1428
Low risk	68.7	1.5	48	3139	0.6	20	3081	2.2	68	3129
Overall	100	5.0	227	4568	0.6	27	4330	5.6	254	4557

TABLE 3. Sites of Primary Cancer by Time of Diagnosis Alongside Proportions Found Late and Numbers Identified as Coming to Harm

	Cancers							
	Urgent		Late		Any Time			
Site of Primary Cancer	%	No.	%	No.	%	No.	Proportion Found Late, %	No. Coming to Harm
Oropharynx	27.3	62	11.1	3	25.6	65	4.6	1
Lymphoma	18.5	42	11.1	3	17.7	45	6.7	—
Larynx	10.6	24	25.9	7	12.2	31	22.6	5
Thyroid	9.3	21	11.1	3	9.4	24	12.5	—
Lung	4.8	11	18.5	5	6.3	16	31.3	1
Esophageal	4.4	10	11.1	3	5.1	13	23.1	2
Unknown primary	4.0	9	0.0	0	3.5	9	0.0	—
Hypopharynx	3.5	8	0.0	0	3.1	8	0.0	—
Oral cavity	3.5	8	0.0	0	3.1	8	0.0	—
Salivary	3.5	8	0.0	0	3.1	8	0.0	—
Skin	3.1	7	0.0	0	2.8	7	0.0	—
Breast	1.8	4	0.0	0	1.6	4	0.0	—
Nasal cavity	1.3	3	3.7	1	1.6	4	25.0	1
Nasopharynx	1.3	3	3.7	1	1.6	4	25.0	—
Leukemia	0.9	2	0.0	0	0.8	2	0.0	—
Ovarian	0.9	2	0.0	0	0.8	2	0.0	—
Colorectal	0.4	1	0.0	0	0.4	1	0.0	—
Liver	0.0	0	3.7	1	0.4	1	100.0	1
Prostate	0.4	1	0.0	0	0.4	1	0.0	—
Renal	0.4	1	0.0	0	0.4	1	0.0	—
Total	89.4	227	10.6	27	100.0	254	10.6	11

DISCUSSION

This is the first multicenter study to report the effectiveness of remote triage incorporating risk stratification in patients referred to secondary care with suspected HNC.[16] It is also the first study of patients with suspected HNC to report medium-term outcomes to identify cancers that may have been missed by current diagnostic practices. This prospective multicenter study is uniquely placed to learn lessons from the changes in practice brought about by the initial peak of the COVID-19 pandemic in the United Kingdom, and it offers significant insight into a real-world use of a remote triage system incorporating risk stratification in suspected HNC referrals. The robust, prospectively collected patient-level data allowed direct linkage of the referral symptoms to
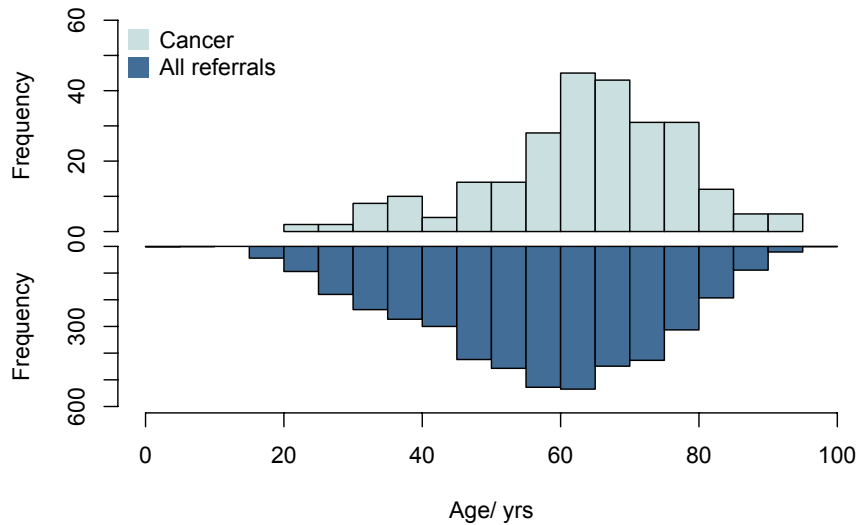
Figure 3. Age distribution of (*Top*) patients with cancer and (*Bottom*) all suspected head and neck cancer referrals. Note that the scales differ by a factor of 10.

the diagnosis of a related cancer and removed potentially distracting incidental cancers that may have contaminated similar studies relying on retrospective database queries.[17]

Despite the pressures on hospitals and clinicians during the initial peak of the COVID-19 pandemic, there was widespread and meaningful engagement, with 41 centers contributing data and nearly complete 6-month outcomes (99.8%). This has demonstrated stakeholder support for the use of a standardized symptom inventory to record the assessment of patients with suspected HNC.

A small proportion of patients who were assessed urgently and were discharged from the urgent pathway were diagnosed with cancers at a later time (0.4%). Although this rate was lower than that for those triaged as nonurgent (0.9%), it has still highlighted the need for suspected cancer diagnostic services to be judged on medium-term outcomes to allow for delayed re-presentation and not to use the point of discharge as the definitive end point of pathway performance. Because of the natural history of HNC, it was felt that 6 months was an appropriate timescale for a patient to re-present or to have had his or her deferred assessment expedited and receive a cancer diagnosis linked to the referral symptoms. It is acknowledged that the standard urgent pathway for suspected HNC referrals would have had some disruption for those included in the current study due to the COVID-19 pandemic.

The sensitivity and specificity of the HaNC-RC-v2 in this population were lower than those recorded in the validation work that produced the algorithm, although the NPV of 97.8% remained high.[9,18,19] A number of

factors may have influenced this difference in algorithm performance: the symptom landscape of patients presenting to their primary care physicians may have been affected by the pandemic; the referral practices of primary care physicians may have been affected by fewer patients undergoing face-to-face assessments in primary care[4]; the population differed slightly because this service evaluation included only those referred from primary care on the suspected HNC referral pathway and not routine head and neck patients who also contributed to the HaNC-RC-v2; the primary outcome for the current study was cancer at a minimum of 6 months, and this thereby also took into account late diagnoses; the overall incidence of cancer in this study was lower; patients contributing to the HaNC-RC-v2 were also examined, and this may have influenced how symptoms were recorded by clinicians[20,21]; and this multicenter, national study involved a greater number of clinicians over a wider geographical area than that used to generate the HaNC-RC-v2. Further analysis of the data collected in this study will help to inform future risk stratification algorithms for suspected HNC referrals undergoing remote triage.

The overall cancer incidence of 5.6% identified in this study is consistent with rates reported in the literature and by national data sets, which vary between 3.6% and 11.8%, and it also corresponds with a national trend toward lower incidence rates in this population over time as the number of suspected cancer referrals to secondary care increases.[9,17,22-24] As the number of referrals increases, risk stratification may become even more important for

appropriate hospital resource allocation and the identification of cancers, which represent a diminishing proportion of the referrals coming in. However, burdening primary care physicians with collecting and recording symptom data for risk stratification is unlikely to be appropriate. First, the referral to secondary care, in part, helps to allay patient anxieties because they feel they are getting specialist input. Second, accurate and consistent recording of symptom data may rely on clinical experience from a specialist. Indeed, encouraging more referrals from primary care is desirable in order to identify cancers at an earlier stage in the hope of improving the prognosis and/or reducing the treatment intensity.[25] Appropriate risk stratification could be part of the strategy to handle higher volumes of referrals to deliver on these goals in the future.

The majority of patients who were felt to have come to harm were observed in the deferred group (8 of 11): they did not undergo any urgent assessment and were not discharged back to primary care. Clinicians may choose to monitor a patient's symptoms to provide an opportunity for resolution with conservative management or a "trial of time," but this should not be at the expense of appropriate examinations and/or investigations in higher risk patients. It should be noted that the practice of deferring appointments was likely exacerbated by the pandemic and reflected prevailing public health advice at that time to reduce hospital visits. Certain symptoms and practices were identified by this service evaluation as being at particular risk of a late diagnosis, and head and neck clinicians should be particularly mindful of thoracic pathology manifesting with head and neck symptoms (Tables 1 and 3). A history of intermittent hoarseness may be indicative of a weak vocal cord from a palsied recurrent laryngeal nerve brought on by a lung lesion or mediastinal mass, and so it should prompt direct visualization or appropriate cross-sectional imaging. Reports of dysphagia in the presence of a normal upper aerodigestive tract examination should prompt urgent esophageal endoscopy to rule out more distal lesions.[26] This study confirmed the finding of a third of cancers on the suspected HNC referral pathway being non-HNCs and corroborated previous reports.[23]

Limitations

The following limitations are acknowledged: the use of only local data may have missed patients who subsequently presented to other units; it is not possible to assert that consecutive patients were included from all centers or submitted by each clinician; local practices may have

included prescreening of suspected HNC appointments to ensure that they were suitable for remote triage; we received no data on patients for whom the remote triage and risk stratification process was incomplete; and the rate of oral cancer was lower than anticipated and reflected low engagement from oral surgery and maxillofacial specialties.

In conclusion, remote triage, augmented by risk stratification, was widely adopted in the care of suspected HNC referrals in response to the initial peak of the COVID-19 pandemic. Appropriately implemented, it may facilitate more targeted investigations for high-risk patients and prevent unnecessary hospital attendance for the lowest risk patients. Deferring appointments without appropriate escalation to urgent assessment or discharge with safety netting may be associated with a particular risk of harm.

CONFLICT OF INTEREST DISCLOSURES
The authors made no disclosures.

AUTHOR CONTRIBUTIONS
John C. Hardman: Conceptualization, data curation, formal analysis, investigation, methodology, project administration, validation, visualization, writing–original draft, and writing–review and editing. **Theofano Tikka:** Conceptualization, data curation, formal analysis, investigation, methodology, project administration, validation, visualization, and writing–review and editing. **Vinidh Paleri:** Conceptualization, data curation, formal analysis, investigation, methodology, project administration, supervision, validation, visualization, writing–review and editing, and final responsibility for the decision to submit the manuscript for publication. All authors had full access to all of the de-identified data.

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