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Review Article

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Digital health in head and neck cancer: a systematic review

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Abstract

Objective. Digital health tools are increasingly being recognised as effective interventions in monitoring chronic health conditions. This systematic review addressed how digital health is currently utilised in patients with head and neck cancer as an adjunct to care.

Method. Studies of the development or evaluation of an eHealth, telemedicine or telemonitoring tool were eligible. A narrative synthesis was performed as per Preferred Reporting Items for Systematic Review and Meta-Analyses reporting guidelines.

Results. Twenty-nine studies of digital health tools in head and neck cancer were identified. Nine were randomised, controlled trials but most had concern of bias. Fourteen (48 per cent) of the interventions used multiple modes of delivery. The primary digital tool functions are symptom tracking and self-care, prehabilitation and rehabilitation, psychological support, and education, including decision aids. Most tools aimed to support patients during active cancer treatment.

Conclusion. There are a small number of digital health tools for head and neck cancer patients; however, there is a lack of well-designed randomised, controlled trials to demonstrate effectiveness.

Introduction

Digital health is an umbrella term encompassing eHealth, telemedicine and telemonitoring. The World Health Organization highlights its role in the future of healthcare 'in strengthening health systems and public health, increasing equity in access to health services, and working towards universal health coverage'. The adoption of digital communication within healthcare has accelerated since the start of the coronavirus disease 2019 pandemic,¹ helping to facilitate remote consultations and maintain clinical services throughout lockdowns. There is growing recognition of the role digital health can play in monitoring of chronic conditions and providing equitable access to patients in remote and rural communities.² Digital health solutions can allow the expansion of clinical care in a resource efficient manner. This is reflected in a key ambition of the UK government's NHS Long Term Plan to make better use of data and digital technologies.³

The use of mobile devices has become ubiquitous in everyday life. Recent statistics show that approximately 83 per cent of the global population own a smart phone,⁴ with younger age, higher levels of education and higher income associated with greater digital connectivity.⁵ Ownership is higher in developed economies such as the UK where 92 per cent of people own a smart phone, including 83 per cent of those over 55,⁶ and 97 per cent of households have internet access.⁷

Head and neck cancer accounts for approximately 5.3 per cent of malignancies worldwide, with incidence of human papilloma virus (HPV) related oropharyngeal cancer increasing, especially in developed countries.⁸ Head and neck cancer and its treatment have significant negative physical and psychological effects that persist beyond treatment and often continue lifelong. Head and neck cancer patients undergoing curative management have surgical resection, including total laryngectomy and neck dissection, radiotherapy, chemotherapy or combined modality treatment, all of which are physically and psychologically demanding. Once patients complete treatment, they suffer from wide-ranging morbidity, which may include dysphagia, dependence on tube feeding, loss of voice, trismus, neck pain and stiffness, and severe xerostomia. They can also experience significant levels of anxiety about cancer recurrence,⁹ body image disturbance,¹⁰ isolation and depression.¹¹ Digital health tools could be used to address symptoms alongside standard treatment and may lead to quality-of-life benefits.

This systematic review aimed to address how digital health is currently being used in patients with a diagnosis of head and neck cancer as an adjunct to usual care in order to improve outcomes relating to the disease or its treatment.

Materials and methods

The remit and search strategy of the review were established and registered with Prospero a priori (CRD42021264791).¹² Findings were reported in concordance with the Preferred

© The Author(s), 2023. Published by Cambridge University Press on behalf of J.L.O. (1984) LIMITED Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') reporting guideline.¹³ We also conducted an exploratory search of the Apple App Store for 'head and neck' and 'laryngectomy' to identify mobile applications available to the general public.

Eligibility criteria

Studies were deemed eligible for inclusion if they described development, evaluation or trial of an eHealth, telemedicine or telemonitoring tool as defined by Aapro *et al.*¹⁴ These all involve provision of healthcare 'supported by telecommunications or digital technology' to support or optimise services. Studies using both quantitative and qualitative methods were included if they presented original data. Full inclusion and exclusion criteria are listed below.

Inclusion criteria were: any publication type that included original research regarding the development, evaluation or a clinical trial of an eHealth, telemedicine or telemonitoring tool; any publication assessing a tool intended for use by patients with a diagnosis of head and neck cancer or their carers and not used for diagnosis or screening; adult patients with head and neck cancer (including sinonasal, oral, oropharyngeal, laryngeal, salivary gland and thyroid) who were either the intended user or a defined group within the usership of the digital health tool; and publication where the full-text was available in the English language.

Exclusion criteria were: telemedicine or telephone consultation used to provide routine care as an alternative to face-to-face appointments (the use of telemedicine platforms for clinical consultation throughout the pandemic has been extensively reported in the literature and is not the intended subject of this review); patient questionnaires performed on digital or web-based platforms without an intervention; and malignancy of the head and neck other than those listed, such as upper oesophageal or cutaneous cancer.

Search and information sources

Searches were conducted on Embase (1974 to 15 April 2022), Ovid Medline (1996 to 15 April 2022) and Cinahl (1999 to 15 April 2022) for relevant studies performed in the last 10 years. Given the rapidly evolving nature of digital platforms and mHealth, this time limit was applied to ensure an accurate description of the current digital environment. The full search terms are listed in Appendix 1. Where a tool was the subject of multiple published papers, such as during piloting, sub-group analysis or cost-analysis, only the main publication describing the tool was included in the review. Bibliographies of the included records were screened to identify further relevant records. EndNote20 reference management tool (Clarivate, London, UK) was used to collate records and remove duplicates.

Selection process

Title and abstract screening were performed by the first author (KH), and two authors (KH and LL) independently screened the full text of the records. A third reviewer (CD) resolved any disagreements regarding inclusion.

Data items and charting

For each record, the country of origin, year of publication, study type, sample size, population of interest, intervention,

outcome/s being assessed and key results were obtained. Where head and neck cancer patients made up a subset of the study population but were not presented separately in the results, an attempt was made to contact the corresponding author to obtain this data. If the author could not be contacted or the subset data was not available, the record was included as a narrative description of the tool without assessment of head and neck cancer specific outcomes.

Critical appraisal of evidence

Randomised, controlled trials (RCTs) were analysed for risk of bias based on the Cochrane Risk of Bias 2 tool by one author (KH) and allocated a score of low risk, some concerns or high risk.¹⁵ All records were included in the review regardless of bias status. Non-RCTs were not subject to a formal risk of bias assessment.

Synthesis of results

The data items described above were obtained from each record and summarised in tabular form. A narrative synthesis of the key functions and outputs of the digital health tools was performed. Given the heterogeneous nature of the RCTs, it was not possible to perform statistical comparison of outcomes or a meta-analysis.

Results

Selection and synthesis of evidence

The results of the search and selection process is illustrated in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') flow diagram (Figure 1). After duplicates were removed, 85 studies met the inclusion criteria and were sought for full-text review. After independent review by 2 authors, a total of 26 records were included in the analysis, which are summarised in Table 1. A further three studies were identified from cited papers of the included studies.

Characteristics of sources of evidence

Eighteen (62 per cent) studies of digital health interventions in head and neck cancer were by research groups based in the USA and Canada. Nineteen (66 per cent) studies were published in the second half of our review period. Seventeen (59 per cent) records were 'development studies' which aimed to assess the usability, feasibility and/or acceptability of the digital health intervention as the primary outcome. There were 10 RCTs. A statistical synthesis of the RCTs was not possible because of the heterogeneity in population, interventions and outcome measures. The remaining two studies were quasi-experimental: one single-arm and one non-RCT. Five studies, including 2 RCTs, described an intervention aimed at a mixed cancer population of which a proportion had head and neck cancer (5–30 per cent).

Results of synthesis

This systematic review aimed to address how digital health is currently being used in patients with a diagnosis of head and neck cancer as an adjunct to usual care to improve outcomes relating to the disease or its treatment. We found 29 studies of digital health tools in head and neck cancer. The purpose of these tools can be considered within four

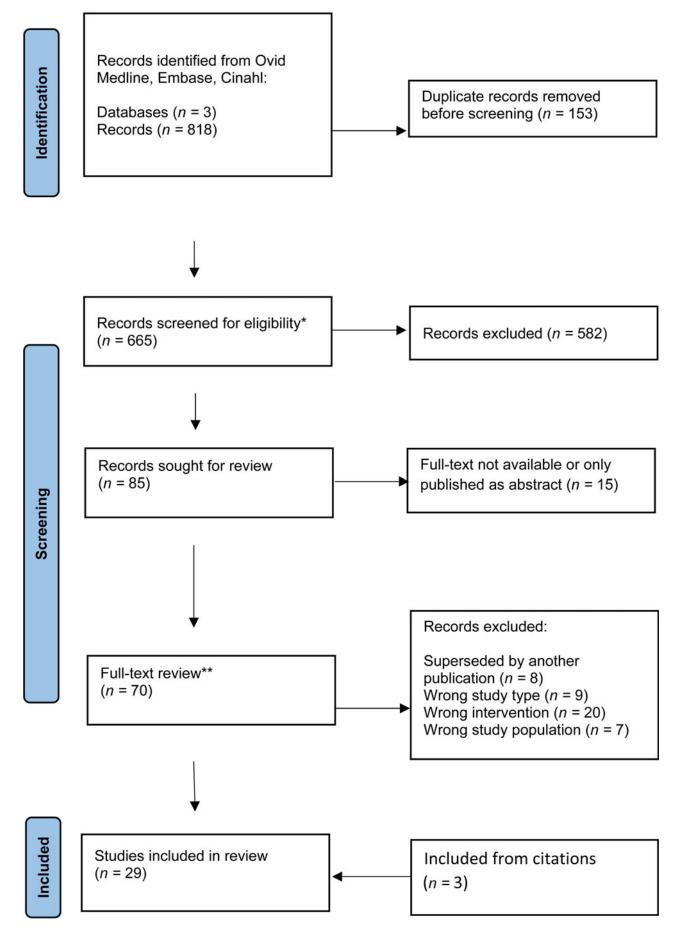


Figure 1. Study flow diagram. *Manual screening of title & abstract against inclusion and exclusion criteria. **Independent two-author review of full-text records with final decision by a third author if there was disagreement. Adapted from Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;**372**:n71.

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Author, country, year	Study type	Population	Intervention	Outcome/s	Result/s
Symptom tracking &	& self-care				
– Badr et al., ⁴³ USA, 2018	RCT; $n = 30$, 1:1 (equal division between intervention & control arms)	HNC patients undergoing radiotherapy & their spouses	Manual containing self-care, coping strategies, caregiving skills etc, plus educational DVD, plus 6 × 60-minute telephone sessions corresponding to manual sections for patient & spouse	Feasibility & acceptability. Secondary outcomes: physical symptoms (via MDASI-HN), psychological functioning (via PROMIS) & marital adjustment via Dyadic Adjustment Scale	Retention, 93%. Intervention arm had less severe HNC-specific symptoms ($p = 0.03$) & depressive symptoms & cancer-specific distress ($p < 0.05$). No difference in marital adjustment
– Berry <i>et al.</i> , ³² USA, 2014	RCT; <i>n</i> = 752 1:1 (equal division between intervention & control arms) of which 50 (6.6%) were HNC	Cancer patients starting a new therapeutic regimen	Self-reported cancer symptoms & Quality-of-Life tool. Based on result patients given self-care advice, coached to explore symptoms, make journal entries & view trends. Controls completed self-reported cancer symptoms & quality-of-life questionnaire without response	Data collected at baseline, 3–6 weeks into treatment & 2 weeks after. Change in Symptom Distress Scale-15 score	Symptom Distress Scale-15 score reduced by 1.2 in the intervention arm ($p = 0.02$). No sub-group analysis for HNC patients
– Di <i>et al.,⁴⁵</i> China, 2018	RCT; <i>n</i> = 132 (65 intervention & 67 control)	Patients completing (chemo)radiotherapy for nasopharyngeal carcinoma	Application functions include appointment reminder, rehabilitation exercises (nature not specified), patient-to-patient interaction & an 'online expert' element twice a week where a doctor answers patients' questions	Complications after radiotherapy & chemotherapy, rehabilitation exercise compliance, & quality of life at discharge & at 3 months & 6 months after discharge	At 6 months, incidence & severity of oral mucositis, trismus, xerostomia, & nasal obstruction in the intervention group was significantly lower than the control group ($p < 0.05$) & overall quality of life via EORTC QLQ-C30 was higher
- Hauth <i>et al.</i> , ¹⁶ Germany, 2019	Development study: n = 21 of which 4 (19%) participants had HNC	Cancer patients receiving treatment involving radiotherapy	Web-based application, 'PROMetheus', allowing patients to submit ePROMs (PRO-CTCAE) to the treating team. Scores indicating toxicity were highlighted to the clinical team	Usability by adherence to weekly web-based questionnaire. Acceptability is defined as meeting this requirement	17/21 (81%) patients submitted at least weekly data. Fatigue was the single most reported symptom
– Ma <i>et al.,³⁵</i> USA, 2021	Development study (n = 84)	Patients with HNC undergoing radiotherapy treatment	Chatbot (web-based interactive communication system) with artificial intelligence features used to help symptom reporting – weekly scheduled & on-demand chats. Results available to clinical teams & system produces individualised educational material & self-care advice	Presence & severity of patient-reported symptoms & adverse events & concordance with physician-reported outcomes. Engagement: defined as use of ChatBot at least once. Usability assessed via participant survey	Patients agreeing to participate were significantly younger ($p < 0.001$). Sixty of 84 (71%) engagement, with greatest use in the first 4 weeks of treatment. A total of 58% (35/60) reported at least 1 severe adverse event, & agreement with clinical reporting ranged from 31–65%
– Oldenmenger <i>et al.</i> , ⁴⁶ Netherlands, 2018	Development study: n = 84 of which 4 (5%) had HNC	Patients with cancer-related pain	Web application consisting of (1) pain diary to monitor patients' pain & analgesic intake, (2) pain education & (3) eConsult email-like function to communicate with nurse specialist	Trial period of 6 weeks. Diaries completed (%) as indicator of feasibility, number of pain assessments, frequency with which analgesics were changed & the number of eConsults participated in	A total of 40 (47.6%) patients stopped using the web application, 26 because of physical deterioration or death. Patients completed a median of 72% of the diaries (range, 18–100%) & analgesic change a median of twice
– Peltola <i>et al.</i> , ¹⁸ Finland, 2016	Development study (n = 5)	New HNC patients undergoing treatment with (chemo)radiotherapy	Self-assessment symptom questionnaires prompted weekly. Medical staff receive notification of reported side-effects to prompt action where indicated	Compliance with self-assessments	A total of 3/5 patients reported severe side-effects, and 4/5 patients had a trigger medical intervention (e.g. opioid analgesia & 1 admission for intravenous antibiotics)

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Table 1. (Continued.)

Author, country, year	Study type	Population	Intervention	Outcome/s	Result/s		
– Peterson <i>et al.</i> , ¹⁷ USA, 2013	Development study (n = 50)	Patients receiving radiotherapy to bilateral necks for curative HNC treatment	Home-based sensors for collecting & communicating sitting/standing blood pressure, pulse, weight, & a symptom questionnaire. Data sent to the radiation therapy clinicians & reviewed daily to determine dehydration risk	Study completion: defined by completing the second & final day 6 assessment. Secondary outcomes were acceptability, perceived usefulness of the intervention & adherence to the monitoring protocol	A total of 50/85 (59%) eligible participants began the study & 48/50 (96%) of those completed the study. High levels of perceived usefulness, ease of use & acceptability & low concerns about data privacy. The tool identified dehydration events in 29 (60%) patients		
– Pfeifer et al., ¹⁹ USA, 2015	RCT; n = 86, 48:38, randomisation grid stratified by treatment modality	HNC patients undergoing any modality treatment	Telehealth symptom questionnaire completed daily. Algorithm presents self-management depending on symptoms, including recommendation on when to contact clinicians	Functional Assessment of Cancer Therapy-Head & Neck Scale & the Memorial Symptom Assessment Scale were used to assess primary outcomes of quality of life & symptom burden	Physical symptoms demonstrated the greatest improvement with the intervention. No change was observed in patients' social & emotional well-being. Quality of life & symptom burden were improved in the weeks after treatment but not during treatment		
– Salz et al., ²¹ USA, 2018	Development study (n = 10)	HNC survivors plus human- computer interaction experts, nurse practitioners	Head & Neck Survivorship Tool: Assessment & Recommendations ('HN-STAR') combines the patient treatment summary & symptom self-assessment to generate a clinical decision support tool which informs clinic appointments & ensures symptoms are addressed	Usability assessment via think-aloud study & usability checklist Qualitative feedback on ease of use & usefulness	Changes made as a result of feedback including reducing text, addition of function to omit unrelated symptoms from care plan & free-text space in self-assessment tool for additional symptoms. RCT protocol published 2021		
– Shah <i>et al.,²⁰</i> USA, 2021	Single-arm study (n = 91)	HNC patients discharged following major surgery	Telephone call within 72 hours of discharge with option to send photographs & video conference with physicians or nurse practitioners	Unscheduled hospital visits & re-admissions. Comparison with historical patient cohort from the preceding year	A total of 83/91 (91%) successfully contacted. Eighteen (21.7%) patients with wound concerns would have attended the emergency department without the intervention. Significant reduction in emergency room attendances compared with historical cohort		
– Van der Hout <i>et al.,²²</i> Netherlands, 2020	RCT; n = 625, 1:1 block random allocation of which 187 (29.9%) had HNC	Cancer survivors, 3 months to 5 years following completion of curative treatment	Web-based application Oncokompas monitors cancer-generic & site-specific symptoms & health-related quality of life, providing feedback & information based on the scores	Data collected at 1 week & 3 & 6 months. Primary outcome was patient activation (knowledge, skills & confidence for self-management). Secondary outcomes included health-related quality of life, mental adjustment to cancer, supportive care needs & self-efficacy measures	No difference in patient activation measure. HNC patients in intervention group had significantly less pain, social eating concerns, swallowing difficulty & trismus compared with controls, which was sustained over the trial period		
Prehabilitation & rel	Prehabilitation & rehabilitation						
 Cnossen et al.,²⁶ Netherlands, 2014 	Development study, n = 33	HNC patients undergoing radiotherapy as single or multi-modality treatment	Self-help swallowing & exercise programme ('Head Matters'): 15-minutes per day with 4 categories of prophylactic exercises. Patients given instruction leaflet, booklet with DVD, or website log-in plus weekly coaching session via telephone or email	Uptake among eligible patients, adherence (defined as at least one exercise a day) & exercise performance level via patient diaries. Barriers to exercise	Uptake: 83% of eligible participants. A total of 58% of patients performing exercises in all categories at least once a day. Performance level was not significantly different between intervention formats		

Table 1. (Continued.)

Author, country, year	Study type	Population	Intervention	Outcome/s	Result/s
– Constantinescu <i>et al.,²⁹</i> Canada, 2019	Development study, n = 5	Patients with a history of HNC	Three surface electromyography sensors to measure the activity of submental muscles during swallow & swallow-like exercises. Data transmitted via Bluetooth® to a smartphone application & presented as visual biofeedback to the user	Usability (including number of times patients needed help), system efficiency (including time-on-task) & user satisfaction were assessed over five tasks	Patients struggled to pair their device to their phone & with some tasks, indicating a lack of clarity in design
– Jansen <i>et al.</i> , ³¹ Netherlands, 2020	RCT; <i>n</i> = 92, 1:1	Patients treated with total laryngectomy in the last 5 years	Exercise programme targeting speech, swallowing & shoulder problems; intervention arms asked to perform exercises 3 times daily for 12 weeks. Available as booklet & DVD or online application plus weekly coaching via email or telephone. Self-care educational resource for both arms	Primary outcome: swallow problems measured by Swallowing Quality of Life questionnaire. Secondary outcomes: speech handicap index, shoulder disability questionnaire, quality of life (via EORTC QLQ-C30) & patient activation	Significant improvement in eating duration ($p = 0.022$), fear of eating ($p = 0.008$), mental health ($p = 0.030$) & social function ($p = 0.049$) with intervention at 6 months. No significant difference in speech & shoulder problems or patient activation
– MacDonald <i>et al.,⁵²</i> Canada, 2020	Development study: n = 35 of which 2 (6%) participants had HNC	Patients during & after acute cancer treatment at a tertiary cancer centre	Care@Home – 8-week programme comprised: (1) individualised exercise prescription supported with a mobile application (Physitrack®) & wearable (Fitbit TM) to track activity; (2) weekly e-modules to promote self-management skills; & (3) weekly telephone coaching from health professionals trained in motivational interviewing	Recruitment & retention determined by health coaching call attendance, Fitbit™ & Physitrack® usage & e-module completion. Physical measures including disability (WHO-DAS 2.0), physical activity (GSLTPAQ) & aerobic capacity & endurance (6-minute walk test) collected at end of intervention & at 3 months	A total of 30/35 (86%) wore the FitBit™ device for a mean 87% of intervention days, and 31/35 (89%) logged into the Physitrack® application at least once. Mean of 4 e-modules completed, but 7 (20%) did not log on. Significant reduction in disability & increase in moderate-strenuous activity at 3 months
– Shinn <i>et al.</i> , ²⁷ USA, 2019	Development study; n = 160	HNC patients about to start radiotherapy treatment for stage II–IV disease	Web-based intervention to increase patient adherence to prophylactic swallowing exercises during radiotherapy. Platform includes swallowing exercise videos & self-management advice with 10 weeks of content aimed at treatment stage	Adherence to swallowing exercises at 3 weeks, end of treatment & 4 weeks after treatment. Secondary outcomes: MD Anderson Dysphagia Inventory, pain & fatigue scores	A total of 84/160 (52%) did not complete adherence data & were excluded from adherence analysis. Average of 5.5 visits to website over 10 weeks. Of the included patients, 51% & 53% adhered to trismus & swallowing exercises, respectively
– Wall <i>et al.</i> , ²⁸ Australia, 2020	RCT, three-arm; <i>n</i> = 79, 1:1:1, random allocation	Patients with oropharyngeal squamous cell carcinoma receiving (chemo)radiotherapy	 Swallowing therapy interventions: (1) clinician-directed face-to-face therapy, (2) telepractice-assisted therapy using interactive application 'SwallowIT' & (3) patient self-directed therapy 	Data at baseline, 6 weeks & 3 months post-treatment. Primary outcome = functional oral intake. Secondary endpoints including nutrition, swallow physiology assessed by videofluroscopic swallow study, patient-reported functional measures & patient perceptions of the 3 interventions	No significant effects of service model observed with respect to any outcome. Swallow therapy adherence was low regardless of group with no significant difference between the groups
– Wang <i>et al.,⁴⁷</i> Taiwan, 2019	RCT, <i>n</i> = 68, 1:1, random allocation	Post-operative oral cancer patients following discharge	Intervention & active control instructed on a package of warm compress, masticatory muscle massage, jaw exercises & active & passive stretching plus the intervention group received remote support provided via telephone call	Adherence to the intervention protocol, maximal interincisal opening & mandibular function via the Mandibular Function Impairment Questionnaire	Significantly greater adherence to package, change in maximal interincisal opening & Mandibular Function Impairment in intervention group compared with active control (<i>p</i> < 0.001)

(Continued)

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Table 1. (Continued.)

Author, country, year	Study type	Population	Intervention	Outcome/s	Result/s
Psychological					
– Fang <i>et al.</i> , ³⁴ USA, 2020	Development study (<i>n</i> = 55)	HNC patients treated with radiotherapy	Web-based programme 'My Journey Ahead' provides information & strategies for managing symptoms including speech, swallow, oral care & psychological coping strategies	Coping with cancer-related stressors was assessed using the Cancer Behaviour Inventory-Brief version and psychological distress was assessed via the Brief Symptom Inventory-18. Programme evaluation was performed via a questionnaire	A total of 11/55 (20%) did not log into the website, and non-users had more recent diagnosis & cancer-related distress. No significant changes from baseline to post-programme in Cancer Behaviour Inventory-Brief version or Brief Symptom Inventory-18, but users found the website easy to use (4.7/5) & the information presented of value (4.2/5)
– Graboyes et al., ³³ USA, 2020	Development study (n = 68)	HNC survivors with body image disturbance	One-to-one telecognitive behavioural therapy delivered by clinical psychologist via tablet. BRIGHT (Building a Renewed ImaGe after Head & neck cancer Treatment) consists of 5 60-minute sessions plus extra tasks to be performed	Feasibility including study dropout, session completion & technical issues. Acceptability including content, number of sessions & likelihood of recommending intervention. The primary outcome was change in Body Image Scale score at 1 month	A total of 7/10 participants were female & 8/10 had free flap reconstruction. There was 1 drop-out. The remaining 8/9 patients would recommend the intervention. Nine of 9 had reduction in body image disturbance at 3 months (mean decrease in Body Image Scale score = 3.56 (confidence interval: 1.15– 5.96)
– Kilbourn <i>et al.,³⁶</i> USA, 2013	Development study (n = 16)	Recent diagnosis of HNC & receiving treatment involving radiotherapy	Easing & Alleviating Symptoms during Treatment ('EASE') programme delivered via 8 telephone counselling sessions: (1) ongoing assessment of physical, psychosocial & functional needs; (2) a psychoeducational component around management of treatment side effects, & (3) coping skills training	Acceptability measured via project records & post-intervention interviews & feasibility evidenced by retention rate – completing intervention defined as participating in at least 2 sessions. Quantitative measures collected: cancer-specific distress, quality of life, pain & social support	A total of 14/16 (87.5%) satisfied with phone counselling. Patients more engaged with counselling at beginning of treatment. A total of 63% were satisfied with the Easing & Alleviating Symptoms during Treatment ('EASE') programme & 16/21 (76.2%) completed at least 2 sessions. No significant improvement of quantitative measures from baseline
Education & decision	n aid				
– Bigelow <i>et al.,³⁸</i> USA, 2021	Development study (n = 26)	16 physicians (HNC surgeons & oncologists), 4 patient education experts & 6 oropharyngeal squamous cell carcinoma survivors	Decision-aid for patients with oropharyngeal squamous cell carcinoma undergoing curative treatment. Prototype including videos of HNC survivors, treatment timeline, treatment comparison & questionnaires to inform further clinic discussion	Alpha testing to determine comprehensibility, usability, acceptability & design by questionnaire & written feedback from users	Changes to the tool based on feedback & second cycle of tool assessment. Cycle 2: 100% felt the design was acceptable, & 77% indicated that they would be likely to use or share the decision aid
– D'Souza et al., ⁴⁰ Canada, 2013	Non-RCT, <i>n</i> = 103, patients recruited from 2 sites, treatment allocation by site	Newly diagnosed patients with stage III or IV primary or recurrent HNC	Multimode Comprehensive Tailored Information Package ('MCTIP'), a multimedia tool comprised of 5 parts: (1) booklet, (2) interactive computer booth with tailored information about site/stage/treatment, (3) animation, (4) take-home DVD & (5) database of clinical & social information	Hospital Anxiety & Depression Scale, difference of 2 points considered clinically significant. Face-to-face interviews at baseline & 3 & 6 months	Depression was significantly associated with younger age ($p = 0.04$) & unemployment ($p = 0.02$). Fewer patients in the test group had clinical levels of anxiety at 6 months ($p = 0.005$)

Table 1.	(Continued.)
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Author, country, year	Study type	Population	Intervention	Outcome/s	Result/s
– Manne <i>et al.</i> , ²³ USA, 2020	Development study (<i>n</i> = 66)	Survivors of oropharyngeal cancer diagnosed 1–3 years previously	Web-based, interactive information & support needs tool 'Empowered Survivor' ('ES'). Six modules including managing swallowing difficulty & oral self-exam	Three surveys at baseline, 2 months & 6 months. Feasibility measured as study enrolment & retention. Acceptability assessed by use & evaluation of 'Empowered Survivor' on post-intervention questionnaire. Primary outcomes: oral self-care, cancer survivorship preparedness & health-related quality of life	Acceptance rate 66/317 (20.8%) of eligible participants, and 81.8% of participants viewed at least 3 modules. Mean Likert score from 1–5 (5 being positive): ease-of-use, 4.21; use of information, 3.82; satisfaction with tool, 3.86. Significant improvement in all domains from baseline ($p < 0.05$)
– Peterson <i>et al.,</i> ³⁹ Netherlands, 2019	Development study (phase 1: $n = 9$, phase 2: $n = 14$, phase 3: n = 9) plus physicians	HNC patients treated with total laryngectomy or (chemo)radiotherapy	Interactive web-based decision aid for patients with primary T_3 to T_4 larynx cancer receiving curative treatment	Phase 1: needs assessment & barriers to counselling process via semi-structured interview. Phase 2: comprehensibility & usability via think-out-loud task & questionnaire. Phase 3: feasibility via same method as phase 2	As a result of alpha-testing, text changed to pictures & animations, with changes to layout. In beta-testing, median score for usability & comprehensibility was 5 out of 5. All patients would advise new patients to use the tool
– Sawka <i>et al.,⁴¹</i> Canada, 2012	RCT, <i>n</i> = 74 (37 intervention & control arms)	Patients with $pT_1/2N_0M_0$ papillary thyroid cancer	Decision aid for patients with early-stage papillary thyroid cancer where accepting or declining adjuvant radioactive iodine would be clinically appropriate	Self-administered medical knowledge questionnaire administered before & after exposure to decision aid versus control (usual care & counselling). Secondary outcome of decisional conflict via Decisional Conflict Scale	Mean difference in medical knowledge between groups was $1.9/10$ ($p < 0.001$) & decisional conflict was significantly lower in decision aid group ($p < 0.001$). Rates of adjuvant radioactive iodine treatment not significantly different between groups
– Sterba <i>et al.</i> , ⁴⁴ USA, 2019	Development study, n = 26	HNC survivors who received at least two treatment modalities	SNAP tablet-based assessment questionnaire including patient unmet needs, fear of recurrence, caregiver distress etc. Generates individualised care plan which is discussed with nurse in clinic	Feasibility & acceptability. Change in outcome variables from baseline to 6-week follow up. Primary outcomes were depression, unmet needs, survivorship knowledge, dyadic coping, caregiver burden	SNAP session protocol steps were completed for all patients. Care plans included an average of 19 messages, 13 educational materials & 4.5 referrals. SNAP sessions made survivors & their caregivers feel prepared for the post-treatment period (84% survivors, 80% caregivers), ensured they had the right amount of information (100%, 84%), provided practical information (92%, 88%) & was helpful emotionally (80%, 80%)
– Wang <i>et al.</i> , ⁴² Taiwan, 2020	RCT, <i>n</i> = 100, 1:1, random allocation	Patients with oral cancer undergoing surgery	Mobile application with information about oral cancer & treatment, instructions for self-recording symptoms & sign-posting to available support groups	Cancer Needs Questionnaire, EORTC QTQ-C30 & the Science & Technology Acceptance Model scale.	Multiple regression analysis demonstrated that the experimental group had significantly greater improvement in physiological needs compared with the control group ($p = 0.022$). Technology Acceptance Model score improved with application use

RCT = randomised, controlled trial; HNC = head and neck cancer; DVD = digital versatile disc; MDASI-HN = MD Anderson Symptom Inventory – Head and Neck; PROMIS = Patient-Reported Outcomes Measurement Information System; EORTC QTQ-C30 = European Organisation for Research & Treatment of Cancer quality of life questionnaire for cancer patients; ePROM = electronic patient-reported outcome measure; PRO-CTCAE = Patient Reported Outcomes-Common Terminology Criteria for Adverse Event; WHO-DAS 2.0 = World Health Organization's Disability Assessment Schedule 2.0; GSLTPAQ = Godin-Shephard Leisure-Time Physical Activity Questionnaire; SNAP = Survivorship Needs Assessment Planning

categories: symptom tracking and self-care, prehabilitation or rehabilitation, psychological support, and education, including decision aids.

Symptom tracking and self-care

Eleven of the digital health tools identified in the review facilitate symptom-tracking, mostly in patients actively undergoing (chemo)radiotherapy. The eHealth tools from Hauth *et al.*¹⁶ and Peterson *et al.*¹⁷ collect data during radiotherapy, and this is made available to clinical teams in real-time, facilitating early detection of treatment toxicity. The studies by Peltola *et al.*¹⁸ and Pfeifer *et al.*¹⁹ both used telehealth to provide patient symptom questionnaires during active treatment and provide tailored self-management advice. Shah *et al.*²⁰ demonstrated the use of eHealth as an adjunct to follow up in the immediate post-operative period after major surgery and the potential to reduce use of unscheduled care.²⁰

There has been increasing emphasis on the concept of longterm survivorship in head and neck cancer, especially with growing numbers of patients with HPV-related oropharyngeal cancer surviving curative treatment. The head and neck cancer survivorship tool created by Salz et al. helps clinicians address cancer-related symptoms at clinic appointments.²¹ The RCT by Van der Hout et al. compares a web-based selfmanagement programme for cancer survivors to usual care with specific head and neck cancer elements. They demonstrated an improvement in mouth pain, social eating, swallowing and trismus with the intervention compared with standard care.²² As well as modules to improve empowerment and selfmanagement in oral cancer survivors, the online intervention by Manne et al. taught patients how to conduct surveillance for lesions through self-examination.²³ This is the only tool that describes the use of eHealth to help patients monitor for recurrence.

Prehabilitation and rehabilitation

The efficacy of prophylactic swallowing exercises on swallowing outcome in head and neck cancer patients is the subject of ongoing international RCTs.^{24,25} If they demonstrate a benefit to swallowing outcome, there will be an expectation for speech and language services to provide exercises to patients. The digital tools created by Cnossen et al. provided a swallowing exercise programme that can be performed independently at home and may be adapted for this purpose.²⁶⁻²⁸ The smartphone-enabled swallowing trainer developed by Constantinescu et al.²⁹ gives feedback on the physiological mechanism of swallow to aid rehabilitation. Adherence to swallowing exercises in head and neck cancer is a problem, with identified barriers being time investment and patients not understanding the benefit.³⁰ In the RCT by Jansen *et al.*, 17 of 41 (41 per cent) participants for whom adherence data was available reported low adherence to the rehabilitation programme despite several measures to optimise this.³¹

Psychological support

Berry *et al.*³² presented a generic cancer tool that encourages self-management of psychological symptoms with an alert to contact clinicians in circumstances such as suicidal ideation. Graboyes *et al.* created an intervention to specifically address psychological distress around body image,³³ whereas Fang *et al.* addressed more general cancer-related psychosocial

challenges.³⁴ Importantly, they found that head and neck cancer patients who were more recently diagnosed and had higher baseline levels of cancer-specific distress were less likely to engage with the tool. Furthermore, both Ma *et al.*³⁵ and Kilbourn *et al.*³⁶ found that engagement declined during the second half of treatment, which the authors attributed to increasing treatment toxicity and fatigue.

Education and decision aids

Decisional conflict is experienced by patients where there is uncertainty about the best course of action when there is potential for significant risk or poor outcome. Decision aids help patients to process evidence-based information alongside personal values and have been shown to reduce decisional conflict in cancer patients.³⁷ Bigelow *et al.* and Peterson *et al.* both described the challenge of developing a decision aid that contains all the relevant clinical information without being too complex or overwhelming.^{38,39} A multi-modal approach to providing tailored information to patients was used in the nonrandomised trial by D'Souza et al. and demonstrated a significant reduction in anxiety in users.⁴⁰ Furthermore, Sawka et al. showed a significant reduction in decisional conflict related to adjuvant radioactive iodine treatment in patients with early papillary thyroid carcinoma when using a decision aid.41 A key function of the mobile application described by Wang et al. was to signpost patients to external resources with relevant information.⁴² Two interventions were designed for use by patients and a caregiver. For example, Badr et al. provided intensive telephone-based support to patients and their spouses in separate but complementary sessions.⁴³ Similarly, the Survivorship Needs Assessment Planning ('SNAP') tabletbased tool by Sterba et al. includes assessment of caregiver distress to inform a personalised care plan.⁴⁴ In summary, a range of digital tools related to information giving, education and decision-making is demonstrated with signs of possible utility in reducing anxiety and decisional conflict.

Methods of delivery

Table 2 shows the methods used to deliver the interventions. Sixteen (62 per cent) of the interventions used more than one method with off or online software being the most common, whereas only 5 (19 per cent) studies utilised a smartphone application. Only Constantinescu *et al.* addressed the potential for commercial wearable devices (FitBitTM activity tracker) in head and neck cancer patient monitoring.

Twelve studies reported interventions that involved additional interaction with the clinical team, either via telephone, video conference or face-to-face. For example, the intervention described by Badr *et al.* involved six hours of telephone sessions for the patient and their spouse provided by a mental health counsellor.³⁹ The telemedicine programme from Graboyes *et al.* is delivered on a one-to-one basis with a clinical psychologist, and therefore it must be considered whether the intervention is scalable in most health services.³⁰ The studies by Di and Li⁴⁵ and Oldenmenger *et al.*⁴⁶ included a human-to-human interaction element in a more limited capacity with clinical contact being available via email or web chat if required. In the study by Wang *et al.*, selective use of remote telephone support was shown to be useful for improving adherence to interventions.⁴⁷

An exploratory search of the Apple App Store for 'head and neck' and 'laryngectomy' found only two results. One

Table 2. Method of intervention delivery

Author	Face-to-face	Paper-based	DVD	Telephone/ video call	Programme/ website	Mobile application	Wearable
Badr <i>et al</i> . ⁴³		Yes	Yes	Yes			
Berry et al. ³²				Yes	Yes		
Bigelow et al. ³⁸					Yes		
Cnossen <i>et al</i> . ²⁶		Yes	Yes	Yes	Yes		
Constantinescu et al. ²⁹						Yes	Yes
Di et al. ⁴⁵					Yes	Yes	
D'Souza <i>et al.</i> ⁴⁰		Yes	Yes		Yes		
Fang et al. ³⁴					Yes		
Graboyes <i>et al</i> . ³³				Yes			
Hauth <i>et al.</i> ¹⁶					Yes		
Jansen et al. ³¹	Yes	Yes	Yes	Yes	Yes		
Kilbourn <i>et al.</i> ³⁶				Yes			
Ma et al. ³⁵					Yes		
MacDonald <i>et al</i> . ⁵²				Yes	Yes	Yes	Yes
Manne <i>et al.</i> ²³				Yes	Yes		
Oldenmenger et al.46					Yes		
Peltola <i>et al.</i> ¹⁸					Yes		
Petersen et al. ³⁹					Yes		
Peterson <i>et al.</i> ¹⁷				Yes		Yes	
Pfeifer <i>et al</i> . ¹⁹				Yes			
Salz et al. ²¹	Yes				Yes		
Sawka <i>et al.</i> ⁴¹					Yes		
Shah <i>et al</i> . ²⁰				Yes			
Shinn <i>et al.</i> ²⁷					Yes		
Sterba <i>et al</i> . ⁴⁴	Yes				Yes		
Van der Hout <i>et al</i> . ²²					Yes		
Wall et al. ²⁸					Yes		
Wang et al. ⁴²					Yes	Yes	
Wang et al. ⁴⁷	Yes	Yes		Yes			

application for head and neck cancer patients, called 'head and neck cancer manager' can help patients track symptoms, set appointment reminders and connect to care providers. The tool is compliant with US laws for protection of health information. There was one application for laryngectomy patients created by Atos medical, a developer and manufacturer of laryngectomy devices, which provided product information and education related to usage. There is no evaluation of the application content in the medical literature.

Bias of evidence

A summary of the risk-of-bias assessment for the 10 RCTs is demonstrated in Table 3. Overall, one study demonstrated a low risk-of-bias, eight studies had methodological flaws which raised some concerns about bias and one study had a high risk-of-bias. A common feature is the inability to blind the participants to treatment allocation as this is not possible when the intervention involves engagement with an eHealth tool.

Summary of the evidence

The aim of this systematic review was to address how digital health is currently being used as an adjunct to usual care to improve outcomes relating to head and neck cancer or its treatment. Three key themes emerged from this review: the apparent value of symptom-tracking and self-management, issues with engagement, and how digital tools can provide psychological support.

Firstly, the most common function of digital tools is symptom-tracking and self-care advice designed for patients undergoing active treatment. This reflects the recognised morbidity associated with head and neck cancer treatment and the need for greater support at this time. Four of the RCTs focusing on active treatment support were able to demonstrate improvement of physical symptoms in the intervention group. Remote symptom monitoring has also been shown to be effective in reducing symptom burden in several other cancer types. For example, the multi-centre 'eSMART' trial of Advanced Symptom Management System ('ASyMS') during chemotherapy treatment for breast cancer, colorectal cancer,

Table 3. Summary of the risk-of-bias assessment for the 10 randomised, controlled trials

Study	Randomisation process	Deviations from intended intervention/s	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Badr et al. ⁴³	No detail given on allocation process & group patient characteristics not described. Imbalance in spousal anxiety at baseline*	Unable to blind participants or those delivering intervention. Intention-to-treat analysis included couples deviating from protocol [†]	1/15 couples lost to follow up from both intervention & control groups ¹	Validated scoring tools for HNC-specific physical symptoms, depression & anxiety & marital adjustment. An objective scoring system was used to measure the assessed parameters [†]	Protocol published on ClinicalTrials.gov in advance of enrolment & outcomes reported as planned [†]	Some concerns*
Berry et al. ³²	Computer randomisation of 1:1 in blocks of 4. Participants significantly younger ($p =$ 0.04) in intervention group*	Unable to blind participant. Intention-to-treat analysis from point of randomisation in all eligible participants with outcome data [†]	A total of 30.5% missing data, likely comprising older ($p =$ 0.0002) & ethnic minority patients ($p = 0.06$). Older patients have greater effect size & therefore likely impact is to diminish effect size*	Symptom Distress Scale-15, although originally validated for lung cancer, is a widely used scoring system in multiple cancers including HNC. Symptom Distress Scale-15 is self-reported & therefore not subject to bias by assessors [†]	Single outcome domain specified prior to randomisation [†]	Some concerns*
Di et al. ⁴⁵	Random number table method, no difference in several key variables [†]	Unable to blind allocation. As intervention was self-guided & self-reported it was unclear what intervention each patient experienced*	Outcome of exercise compliance incomplete; 2 examples given*	Patients' use of application was self-reported & therefore compliance with intervention was subject to reporting bias*	Results presented on compliance appear to be selected from multiple outcome measures not detailed in the methodology [‡]	High [‡]
Jansen et al. ³¹	Randomised 1:1 & stratified for potentially influencing factors but method not stated. Significant baseline difference in health-related quality of life in favour of intervention*	Participants & researchers aware of assigned intervention & no changes from assigned intervention. Intention-to-treat analysis [†]	Greater number lost to follow up in intervention arm, but not likely to influence overall result [†]	Outcome measures self-reported by participants & could be influenced by knowledge of treatment allocation. Recruitment below required sample size for power*	Result reports were in accordance with pre-specified plan [†]	Some concerns*
Pfeifer et al. ¹⁹	Randomisation grid that 'considered treatment modalities' was consulted. No significant difference between groups [†]	No participants or any of research team blinded [†]	A total of 6/48 (12.5%) allocated to intervention did not receive the intervention. Further 3/48 did not complete. No intention-to-treat analysis*	Validated outcome measures appropriate to clinical question [†]	Outcome measures Functional Assessment of Cancer Therapy-Head & Neck scale & Memorial Symptom Assessment Scale broken down into component parts during statistical analysis, not stated in methods & no adjustment for multiple comparisons*	Some concerns*
Sawka et al. ⁴¹	Computer block (in 2 or 4) randomisation $1:1^{\dagger}$	Participant/study staff not blinded, but statistician blinded at point of data analysis [†]	No missing outcome data [†]	Method of measuring knowledge acquisition & decisional conflict was appropriate; both were performed in same visit & therefore effects may be short-lived [†]	Data analysed according to pre-specified plan published on ClinicalTrials.gov. [†]	Low [†]
Van der Hout <i>et al.</i> ²²	Block (size 68) randomisation of 1:1, stratified by tumour type & performed by independent person [†]	Unable to blind participants. A total of 48% in intervention arm did not engage with the intervention but were included in intention-to-treat analysis [†]	Total missing data: 17.7% control & 29.7% intervention, but in HNC subgroup missing data more closely matched (74.4% vs 68.7%)*	Patient-activation measure validated & widely used; however, self-reported score may be influenced by knowledge of group allocation*	Intention-to-treat. Multiple subgroup analysis with no correction for multiple testing or separate power calculation*	Some concerns*

wall et al. ²⁸	Computer randomisation of 1:1:1, stratified by baseline measure of dysphagia. Significant difference in type of radiation at baseline but this was adjusted for ¹	Unable to blind participants. Speech & language pathologists not blinded when performing videofluoscopic swallow study*	Despite relatively little missing data, the final sample size was below size required for power for some outcome measures*	Acceptable score of functional oral intake. Adherence & quality of life was self-reported. Independent rating of videofluoscopic swallow study by 2 speech & language pathologists to minimise bias [†]	Trial protocol not registered in advance. Intention-to-treat analysis & results as described in methodology*	Some concerns*
Wang et al. ⁴⁷	Computer randomisation of 1:1 performed by independent researcher & groups were balanced (no significant differences in demographic & clinical characteristics at baseline) [†]	Patients, care providers & outcome assessors blinded to group allocation [†]	A total of 4/34 patients excluded in both groups but unlikely to have affected results. Outcome data othenwise complete [†]	Mandibular Function Impairment Questionnaire has not been subject to Construct Validity-Hypothesis Testing. Jaw-opening measured by blinded researcher*	Analysis performed as stated in the method. Protocol published on ClinicalTrial.gov appears to be after study completion date*	Some concerns*
Wang et al. ⁴²	No detail given on process of random allocation. Cancer stage approaching significant difference ($p = 0.06$)*	Intervention was self-guided & no test of engagement & therefore unclear what patients experienced*	A total of 18% of intervention group & 15% of control group did not attend follow up but unlikely to have impacted result [†]	Outcomes were self-reported & not subject to assessor bias. Valid & reliable outcome measures used [†]	Study registered prior to participant enrolment & analysis performed as stated [†]	Some concerns*

Hodgkin's disease and non-Hodgkin's lymphoma demonstrated significant improvements in anxiety, health-related quality of life, self-efficacy and supportive care needs.⁴⁸ Recent evidence shows that new symptoms after cancer treatment, such as pain, are a strong indicator that the cancer has returned;⁴⁹ therefore, digital tools that track symptoms in the longer term may also lead to earlier detection of recurrence.

Self-assessment tools depend on patient engagement, and studies employed various ways to promote this among trial participants. For example, Peltola *et al.*¹⁷ used a weekly reminder email whereas Pfeifer *et al.*¹⁸ had a device connected to the landline that flashed when assessments were due. Despite these efforts, engagement with the digital health tools was often poor. Ma *et al.* and Kilbourn *et al.* suggested that engagement could decline as symptom burden increased,^{35,36} and this issue therefore requires consideration in the development of future interventions.

Patients with head and neck cancer have one of the highest incidence rates of suicide even compared with other cancer patients,⁵⁰ and body image disturbance is a significantly under-recognised issue, with prevalence as high as 89 per cent in the immediate post-treatment period.⁵¹ Psychological interventions are therefore an important component of post-operative care. The three studies identified in this review were development studies and were not powered or designed to prove clinical effectiveness. Nevertheless, the cognitive behavioural therapy intervention by Graboyes *et al.* resulted in improvement in body image disturbance at 1 month post-treatment compared with historical controls who showed no change in the first 12 months,^{9,32} thus indicating potential for this approach.

Strengths and limitations

Because of the heterogeneity of the tools, we could not perform a statistical synthesis of outcomes, and the interventions described in the included studies were sometimes complex and involved multiple elements. This review is therefore unable to extricate what benefits were a result of the digital tool as opposed to the other elements, such as enhanced clinical interaction.

A strength of this review is the broad definition of digital health used and the inclusive search criteria. It is possible that studies have been missed if they did not use any of the expected terminology, but the authors consider this to be unlikely. Two authors screened the records to ensure papers were eligible to be included in the review.

Conclusion

In conclusion, there are a small number of digital health interventions for head and neck cancer. Most of the digital tools aim to promote self-management of symptoms and focus on supporting head and neck cancer patients during active treatment. There is a noticeable gap in tools designed for long-term follow up and for delivery via smart-phone applications. Several studies have found improved outcomes associated with the use of digital health interventions, but currently there is a lack of well-designed RCTs to demonstrate their effectiveness. Cancer-related morbidity as a barrier to eHealth engagement should be carefully considered in the design and implementation of such tools.

Competing interests. None declared

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Appendix 1. Search terms

Ovid MEDLINE(R) <1996 to April 15, 2022>

1	exp Telemedicine/	37737
2	(digital adj1 health).mp.	2559
word, supple	tle, abstract, original title, name of substance word, subjec floating sub-heading word, keyword heading word, organi mentary concept word, protocol supplementary concept v e supplementary concept word, unique identifier, synonyr	sm vord, rare
3	(digital adj1 medicine).mp.	248
4	(web-based or (web adj1 based)).mp.	29769
5	1 or 2 or 3 or 4	67874
6	exp "Head and Neck Neoplasms"/	213765
7	exp Laryngeal Neoplasms/	13859

8	exp Mouth Neoplasms/	43599
9	exp Thyroid Neoplasms/	38857
10	exp Nasopharyngeal Neoplasms/	12067
11	exp Nose Neoplasms/	9925
12	exp Paranasal Sinus Neoplasms/	4957
13	exp oropharyngeal Neoplasms/	6972

14	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13	213765
15	5 and 14	266
16	limit 15 to (english language and humans and yr="2010 -Current")	232

Embase <1974 to 2022 April 15>

1	exp telemedicine/	55433
2	(digital adj1 health).mp.	4268
3	(digital adj1 medicine).mp.	496
4	web-based.mp.	51346
5	(web adj1 based).mp.	51724
6	1 or 2 or 3 or 4 or 5	109121
7	exp "head and neck cancer"/	193506
8	exp larynx cancer/	22608
9	exp oral cancer/	69790
10	exp thyroid cancer/	70813
11	exp paranasal sinus cancer/	3891
12	exp nasopharynx cancer/	23853
13	exp nose cancer/	5674
14	exp oropharyngeal cancer/	13541
15	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	271916
16	6 and 15	569
17	limit 16 to (human and english language)	542

Cinahl <1999 to Apr 15 2022>

S5 AND S14	Limiters - Human; Language: English Search modes - Boolean/Phrase (79)	
S14	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13	(54 353)
S13	(MH "Oropharyngeal Neoplasms+")	(1466)
S12	(MH "Nasopharyngeal Neoplasms+")	(2661)
S11	(MH "Paranasal Sinus Neoplasms")	(1077)
S10	(MH "Thyroid Neoplasms+")	(7605)
S9	(MH "Mouth Neoplasms+")	(13 427)
S8	(MH "Oral Neoplasms+")	(0)
S7	(MH "Laryngeal Neoplasms")	(3698)
S6	(MH "Head and Neck Neoplasms+") OR (MH "Squamous Cell Carcinoma of Head and Neck")	(54 353)
S5	S1 OR S2 OR S3 OR S4	(38 004)
S4	TX web-based OR TX web N1 based	(18 453)
S3	TX digital N1 medicine	(746)
S2	TX digital N1 health	(2615)
S1	(MH "Telemedicine+")	(17 340)