Essential data variables for a minimum dataset for head and neck cancer trials and clinical research

Baliga, Sujith; Abou-Foul, Ahmad K.; Parente, Pablo; Szturz, Petr; Thariat, Juliette; Shreenivas, Aditya; Nankivell, Paul; Bertolini, Federica; Blau, Julian; Blakaj, Dukagjin; Brennan, Sinead; Brunet, Aina; Bueno De Oliveira, Thiago; Burtness, Barbara; Carral Maseda, Alberto; Chow, Velda Ling-Yu; Chua, Melvin LK; de Ridder, Mischa; Garikipati, Satya; Hanai, Nobuhiro

DOI:
10.1016/j.ejca.2024.114038

Document Version
Publisher's PDF, also known as Version of record

Citation for published version (Harvard):
Baliga, S, Abou-Foul, AK, Parente, P, Szturz, P, Thariat, J, Shreenivas, A, Nankivell, P, Bertolini, F, Blau, J, Blakaj, D, Brennan, S, Brunet, A, Bueno De Oliveira, T, Burtness, B, Carral Maseda, A, Chow, VL-Y, Chua, MLK, de Ridder, M, Garikipati, S, Hanai, N, Ho, FCH, Huang, SH, Kiyota, N, Klinghammer, K, Kowalski, LP, Kwong, DL, McDowell, LJ, Merlano, MC, Nair, S, Economopoulou, P, Overgaard, J, Psyrri, A, Tribius, S, Waldron, J, Yom, SS & Mehanna, H 2024, 'Essential data variables for a minimum dataset for head and neck cancer trials and clinical research: HNCIG consensus recommendations and database', *European Journal of Cancer*, vol. 203, 114038. https://doi.org/10.1016/j.ejca.2024.114038

European Journal of Cancer 203 (2024) 114038

Contents lists available at ScienceDirect

European Journal of Cancer

journal homepage: www.ejcancer.com

Essential data variables for a minimum dataset for head and neck cancer trials and clinical research: HNCIG consensus recommendations and database

Sujith Baliga [a,1], Ahmad K. Abou-Foul [b,1], Pablo Parente [c], Petr Szturz [d,e], Juliette Thariat [f], Aditya Shreenivas [g], Paul Nankivell [h], Federica Bertolini [i], Julian Biau [j,k], Dukagjin Blakaj [l], Sinead Brennan [m], Aina Brunet [n], Thiago Bueno De Oliveira [o], Barbara Burtness [p], Alberto Carral Maseda [q], Velda Ling-Yu Chow [r], Melvin LK Chua [s,t], Mischa de Ridder [u], Satya Garikipati [v], Nobuhiro Hanai [w], Francis Cho Hao Ho [x], Shao Hui Huang [y], Naomi Kiyota [z], Konrad Klinghammer [aa], Luiz P. Kowalski [ab,ac], Dora L Kwong [ad], Lachlan J McDowell [ae,af], Marco Carlo Merlano [ag], Sudhir Nair [ah], Panagiota Economopoulou [ai], Jens Overgaard [aj], Amanda Psyrri [ai], Silke Tribius [ak], John Waldron [al], Sue S. Yom [am], Hisham Mehanna [an,*]

[a] Department of Radiation Oncology, The Ohio State University Wexner Medical Center, Columbus, OH, USA
[b] Institute for Head and neck studies and education, University of Birmingham, UK
[c] Department of Otolaryngology and Head and Neck Surgery, Hospital Universitario Lucus Augusti, Lugo, Spain
[d] Medical Oncology, Department of Oncology, Lausanne University Hospital (CHUV), 1011 Lausanne, Switzerland
[e] Faculty of Biology and Medicine, University of Lausanne (UNIL), 1011 Lausanne, Switzerland
[f] Department of Radiation Oncology, Comprehensive Cancer Centre François Baclesse, Caen, France
[g] Department of Hematology and Oncology, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, USA
[h] Institute for Head and Neck Studies and Education, University of Birmingham, UK
[i] Department of oncology, Modena University Hospital, Modena, Italy
[j] INSERM U1240 IMoST, University of Clermont Auvergne, Clermont-Ferrand, France
[k] Department of radiation therapy, Centre Jean Perrin, Clermont-Ferrand, France, University of Clermont Auvergne, Clermont-Ferrand, France
[l] Ohio State University, OH, USA
[m] St Luke's Radiation Oncology Network, Dublin, Ireland
[n] Department of Otorhinolaryngology and Head and Neck Surgery, Hospital Universitari Bellvitge, Institut d'Investigacio Biomedica (IDIBELL), Barcelona, Spain
[o] AC Camargo Cancer Center, Sao Paulo, Brazil
[p] Department of Internal Medicine and Yale Cancer Center, Yale School of Medicine, CT, USA
[q] Lucus Augusti University Hospital, Lugo, Spain
[r] Department of Surgery, The University of Hong Kong, Hong Kong, SAR China
[s] Oncology Academic Programme, Duke-NUS Medical School, Singapore
[t] Division of Radiation Oncology, National Cancer Centre Singapore, Duke-NUS Medical School, Singapore
[u] Department of radiotherapy, University Medical Center Utrecht, the Netherlands
[v] Sheffield Teaching Hospitals NHS Trust, Sheffield, UK
[w] Department of Head and Neck Surgery, Aichi Cancer Center Hospital, Aichi, Japan
[x] National University Cancer Institute, Singapore
[y] Department of Radiation Oncology, Princess Margaret Cancer Centre / University of Toronto, Tornoto, Canada
[z] Cancer Center, Kobe Univesity Hospital, Kobe, Japan

* Corresponding author.
E-mail addresses: Sujith.baliga@osumc.edu (S. Baliga), a.abou-foul@bham.ac.uk (A.K. Abou-Foul), plparente@gmail.com (P. Parente), szturz@gmail.com (P. Szturz), jthariat@gmail.com (J. Thariat), ashreenivas@mcw.edu (A. Shreenivas), p.c.nankivell@bham.ac.uk (P. Nankivell), bertolini.federica@aou.mo.it, federica.bertolini@tiscali.it (F. Bertolini), julian.biau@clermont.unicancer.fr (J. Biau), Blakaj.1@osu.edu (D. Blakaj), Sinead.brennan@slh.ie (S. Brennan), brunetain@gmail.com (A. Brunet), thiagobueno32@yahoo.com.br (T.B. De Oliveira), barbara.burtness@yale.edu (B. Burtness), alberto_carral@hotmail.com (A.C. Maseda), vlychow@gmail.com (V.L.-Y. Chow), gmsclkm@nus.edu.sg (M.L. Chua), M.deridder-5@umcutrecht.nl (M. de Ridder), s.garikipati@nhs.net (S. Garikipati), hanai@aichi-cc.jp (N. Hanai), Francisho@nus.edu.sg (F.C.H. Ho), shaohui.huang@rmp.uhn.ca (S.H. Huang), nkiyota@med.kobe-u.ac.jp (N. Kiyota), Konrad.klinghammer@charite.de (K. Klinghammer), lp_kowalski@uol.com.br (L.P. Kowalski), dlwkwong@hku.hk (D.L. Kwong), lachlan.mcdowell@health.qld.gov.au (L.J. McDowell), mcmerlano@gmail.com (M.C. Merlano), Sudhirvr@gmail.com (S. Nair), panagiota_oiko@hotmail.com (P. Economopoulou), jens@oncology.au.dk (J. Overgaard), dpsyrri@med.uoa.gr (A. Psyrri), s.tribius@asklepios.com (S. Tribius), john.waldron@rmp.uhn.ca (J. Waldron), sue.yom@ucsf.edu (S.S. Yom), h.mehanna@bham.ac.uk (H. Mehanna).

https://doi.org/10.1016/j.ejca.2024.114038
Received 27 February 2024; Accepted 17 March 2024
Available online 30 March 2024

[aa] Department of Hematology, Oncology and Cancer Immunology, Campus Benjamin Franklin Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin Hindenburgdamm, Berlin, Germany
[ab] Department of Head and Neck Surgery, University of São Paulo Medical School, São Paulo, Brazil
[ac] Department of Head and Neck Surgery and Otorhinolaryngology, A C Camargo Cancer Center, São Paulo, Brazil
[ad] Department of Clinical Oncology, Centre of Cancer Medicine, School of Clinical Medicine, LSK Faculty of Medicine, the University of Hong Kong, Hong Kong, SAR China
[ae] Faculty of Medicine, University of Queensland, Brisbane, Australia
[af] Department of Radiation Oncology, Princess Alexandra Hospital, Woollongabba, Australia, University of Queensland, Brisbane, Australia
[ag] Scientific Direction, Candiolo Cancer Center, FPO-IRCCS, Candiolo, Italy
[ah] Department of Surgical Oncology, Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, Mumbai, India
[ai] Medical Oncology Unit, 2nd Department of Internal Medicine, Attikon University Hospital, National and Kapodistrian University of Athens, Athens, Greece
[aj] Department of Experimental Clinical Oncology, Aarhus University Hospital, Denmark
[ak] Hermann, Holthusen Institute of Radiation Oncology Asklepios Klinik St. Georg Asklepios Tumorzentrum, Hamburg, Germany
[al] Princess Margaret Cancer Center University of Toronto, Canada
[am] University of California San Francisco, San Francisco, CA, USA
[an] Institute for Head and neck studies and education, University of Birmingham, Birmingham, UK

ARTICLE INFO

Keywords:
Head and Neck cancer
Head and neck squamous cell carcinoma
Cancer database
Data harmonisation
Collaborative research

ABSTRACT

The Head and Neck Cancer International Group (HNCIG) has undertaken an international modified Delphi process to reach consensus on the essential data variables to be included in a minimum database for HNC research. Endorsed by 19 research organisations representing 34 countries, these recommendations provide the framework to facilitate and harmonise data collection and sharing for HNC research. These variables have also been incorporated into a ready to use downloadable HNCIG minimum database, available from the HNCIG website.

1. Introduction

The global incidence and burden of head and neck cancer (HNC) is high, accounting for over 931,000 cases and 400,000 deaths worldwide in 2020, making it the sixth most common cancer worldwide. [1] Current treatment recommendations for the common HNC subtypes have set largely based on the results of large phase II/ III clinical trials undertaken by large national cancer research organisations, primarily in North America and Europe. [2–7] Although these trials are considered practice changing, the patient populations included are often restricted and homogenous, and do not encompass the variations seen in routine clinical implementation, or the geographic diversity seen in the global burden of HNC. Therefore, these clinical trials do not always reflect real world clinical practice. Conversely, for the rarer tumours in HNC, such as salivary gland or sino-nasal cancers, treatment recommendations are often based on retrospective collaborative data collection studies.

Therefore, leveraging pooled individual patient data and real-world studies, especially on an international level, can be of considerable benefit in setting and enhancing clinical practice recommendations, for example as demonstrated by the recent international HNCIG EPIC collaborative study. [8] However, there are significant ethical, regulatory, and logistical challenges to sharing this data. [9] One of the biggest challenges is the variability of the data collected, the endpoints used and the definitions of these variables between studies and between countries. Consequently, The Head and Neck Cancer International Group (HNCIG), a collaboration of 21 national clinical trial groups for head and neck cancer, has identified a pressing need to harmonise the data variables collected, and the definitions and end points used for HNC research in order to facilitate and expedite the conduct of large and multinational clinical trials studies, and the synthesis of clinical trials results.

To address this, we undertook a modified Delphi process with the primary objective of creating consensus recommendations for a minimum data set of variables that should be collected in a standardized manner and reported consistently in HNC clinical research, including real world registries and clinical trials.

[1] Baliga S and Abou-Foul AK contributed equally to this work (co-primary authors)

2. Methods

2.1. Participant selection

A study steering group was established by the Head and Neck Cancer International Group (HNCIG, www.hncig.com); a consortium of 21 prominent national head and neck oncology research groups. The multidisciplinary steering group led the overall study design and execution, and included academic head and neck surgeons and oncologists from five different healthcare systems (USA, France, UK, Spain and Switzerland), who had expertise in conducting Delphi consensus research (members provided in the appendix - Table A, p1).

To form a panel of experts for the consensus recommendations, all 21 member groups of the HNCIG were invited to nominate up to two experts to represent their group. Nominees had to be currently practicing head and neck oncologists or surgeons, considered national or international experts in their fields with track record in HNC research and willing to complete all three rounds of the online Delphi process. Nineteen of the invited organizations provided nominees, who participated in the process and were all included in the authorship of the manuscript. The participating organizations are shown in the appendix (Table B, p 1).

2.2. Consensus formation and data collection

In order to reach consensus on a minimum data set, we undertook an online process, conducted over three rounds using methods described previously [10], modified from the Delphi methodology developed originally by the Rand Corporation in the 1950 s [11] The nominated expert group members were invited to complete an online questionnaire, delivered by the Qualtrics online survey platform (Qualtrics, Provo, UT, USA). The surveys covered variables that were carefully selected by the steering committee relating to the following 12 domains: demographic, primary cancer, cancer staging, general treatment, surgical treatment, pathological assessment, systemic anticancer therapy, radiotherapy, response after primary treatment, diagnosis of progression/recurrence, treatment of progression/recurrence, and status at last follow up. Following literature searches and expert discussions, the steering group developed a set of survey questions, which were revised or modified as necessary over subsequent rounds to ensure clarity and

accommodate feedback received from the expert respondents. New questions were introduced in subsequent rounds to add granularity to particularly nuanced topics and to enable participants to reach consensus on the definitions to be used for the agreed variables. Prior to each round, a small group of expert head and neck clinicians piloted the questions for readability, and face and content validity. An overview of the modified Delphi process is illustrated in Figure 1. Each round was open for 14–21 days, and reminder emails were sent at regular intervals before the deadline. The respondents were informed that the intended core data set has to be applicable to all specialties within the HNC domain, and not limited to the specific subspecialty of the individual responder. After each round, the multi-disciplinary steering group collated and analysed the data, using predetermined criteria for agreement as per the Delphi methodology. Strong agreement was indicated by consensus of 80% or above for a statement, while agreement was indicated by 67–80%, and no agreement was indicated by 21–66%. Statements with 20% or less agreement were rejected (strong agreement against a statement). A statement was removed from the next round either when strong agreement or rejection was reached, or after completion of three rounds, whichever occurred first. Moreover, based on feedback from the expert group, three questions were deemed to be redundant and were withdrawn from subsequent rounds (Figure 1, appendix Table C, p 2–14). After the third round, statements that did not reach strong agreement but reached at least 67% or above were considered to have reached agreement. [12].

Results were iteratively shared with the expert participants after each round. As part of the Delphi process, respondents were reminded that they could change their response to a question in the next round, if they wished, depending on the results and emerging consensus of the previous rounds. In addition, a "free text" option was provided for individuals who wished to provide further details or explanations regarding specific points or choices.

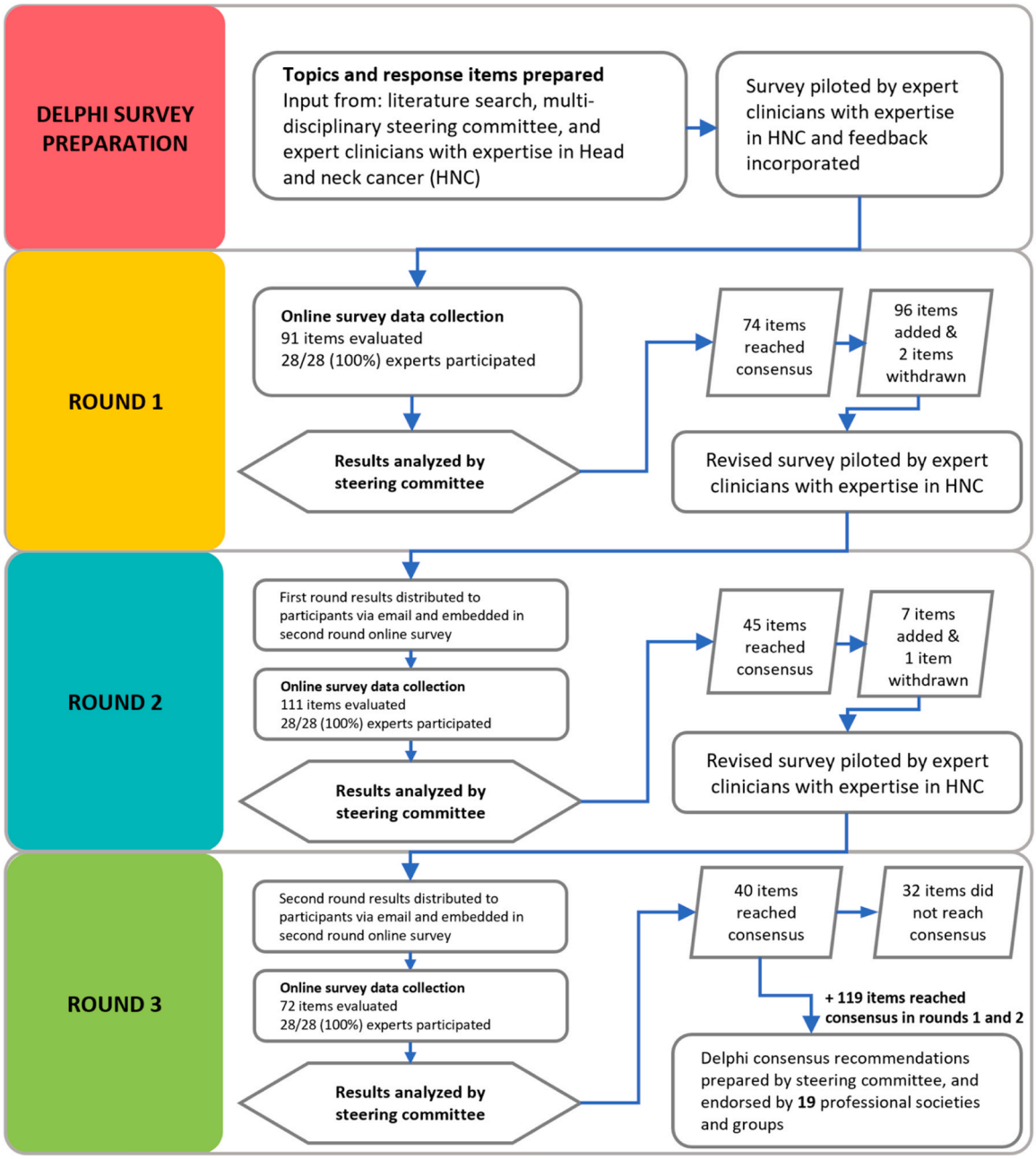

Fig. 1. The Head and Neck Cancer International Group modified Delphi process for the minimum head and neck cancer database.

Once the results were analysed, a database was constructed incorporating all the 'essential' variables and their component responses reaching strong agreement, agreement for or rejection against by the process. Variables that did not reach agreement were also incorporated, but marked as optional, indicating that these variables did not reach consensus.

This study was granted a research ethics waiver from the Research Ethics Department at the University of Birmingham (Birmingham, UK), application number ERN_2022–0401.

3. Findings

3.1. Process

Twenty-eight expert nominees representing 19 research groups participated in this study, as nine groups nominated two representatives each. There were five surgeons, thirteen radiation and ten medical oncologists. The full list of experts is provided in the appendix (Table B, p 1). All participants completed all three rounds of the Delphi process. The final recommendations were endorsed by **19** organisations and clinical research groups (Panel 1).

In total, 91 questions were asked in the first round; 111 questions in the second round; and 72 questions in the third round. 74/91 and 45/111 questions were removed after the first and second rounds respectively, after reaching strong agreement for (≥80%) or against (≤20%). Thirty-two questions asked in the third round failed to achieve any form of agreement (21–66%), appendix (Table C, p 2–14).

The reported rates of agreement reflect when the item first reached one of the agreement thresholds, and might have been after one, two, or all three rounds of questioning. Full results and agreement levels of the

The Canadian Cancer Trials Group (CCTG)

Cancer Research Ireland (CRI)

The Danish Head and Neck Cancer Group (DAHANCA)

The Dutch Head and Neck Society (NWHHT)

The Eastern Cooperative Oncology Group and American College of Radiology Imaging Network (ECOG-ACRIN)

The European Organization for Research and Treatment of Cancer (EORTC)

The French Head and Neck Cancer Group (GORTEC)

Fudan University Shanghai Cancer (FUSCC)

The German Interdisciplinary Working Group for Head and Neck Tumours (IAG-KHT)

The Head and Neck Cancer Study Group of the Japan Clinical Oncology Group (JCOG-HNCSG)

The Hellenic Cooperative Oncology Group (HeCOG)

Hong Kong Nasopharyngeal Cancer Study Group (HKNPCSG)

The Latin American Cooperative Oncology Group (LACOG)

The National Cancer Centre Singapore (NCCS)

The National Cancer Research Institute-UK (NCRI-UK)

Northwest Italian Oncology Group (GONO)

The Spanish Foundation for the Treatment of Head and Neck Tumours Group (FETTCC)

Tata Medical Centre (TMC), India

Trans-Tasman Radiation Oncology Group (TROG), Australia and New Zealand

Panel 1. National research groups endorsing the recommendations, in alphabetical order.

questions asked in all three rounds are provided in the appendix (Table C, pp 2–14). A summary of the consensus statements is available in Table 1.

3.2. Demographic variables

There was unanimous agreement (28/28,100%) that *biological sex* assigned at birth based on anatomy, *race/ethnicity*, and *performance status* should be included in any minimum HNC data set. Moreover, experts strongly agreed that *age at diagnosis* (27/28, 96.4%), and *co-morbidity index* (25/28, 89.3%), and also agreed that *baseline body mass index* (21/28, 75%) should be included in the minimum HNC database. There was also strong agreement that performance status and comorbidity index variables should be defined in the minimum database by *Eastern Cooperative Oncology Group (ECOG)/World Health Organization (WHO)/Zubrod scale* (89.3% (25/28), and *Charlson Comorbidity Index (CCI)* (28/28, 100%), respectively.

The panel also strongly agreed *against* the inclusion of *total annual household income* (4/28, 14.3%), but they could not reach agreement on the inclusion of *gender* (self-described of self-perceived gender) (10/28, 35.7%), *geriatric screening/assessment* (7/28, 25%), or socio-economic variables like *education level* (17/28, 60.7%), *employment status* (7/28, 25%), and *marital status* (16/28, 57.1%).

There was unanimous agreement (28/28, 100%) that *tobacco smoking status* should be included in the minimum HNC database. The experts also strongly agreed that for former or current smokers, *smoking pack-year index* (25/28, 89.3%) and *time from last smoked* (26/28, 92.86%) should be included, as well as *history of chewing tobacco or betel for* patients with oral cavity squamous cell carcinoma (OCSCC). Similarly, the panel unanimously agreed (28/28, 100%) that *alcohol consumption status* should be included in the minimum data set, with strong agreement to include *the number of standard alcohol units consumed per week* for former or current alcohol drinkers (26/28, 92.86%).

3.3. Primary cancer variables

The expert panel strongly agreed that the following primary tumour variables should be included: *date of diagnosis* (27/28, 96.4%), *primary tumour site* (28/28, 100%), *primary tumour sub-site* (23/28, 82.1%); recorded according to the 3rd Edition of the WHO International Classification of Diseases for Oncology (ICD-O-3) system [13], and *histological diagnosis* (28/28), and also *histological subtypes* as defined by WHO ICD-O-3 (keratinizing SCC, non-keratinizing SCC, etc.) for nasopharyngeal SCC (NPSCC). But the panel could not reach agreement on histological sub-types for non-NPSCC cases (16/28, 57.1%). The consensus panel also strongly agreed that HPV status recorded as *p16 status* (28/28, 100%) and *HPV RNA/DNA status* (24/28, 85.7%) should be recorded for primary oropharyngeal SCC (OPSCC), and that *Epstein–Barr virus (EBV) status* should be included for NPSCC, by recording *EBV encoded small RNAs (EBER)* results + /- *EBV DNA copy number* (24/28, 85.7%). The experts also rejected recording EBV status for NPSCC using *EBV DNA copy number* only (4/28, 14.3%). The expert panel strongly agreed that *programmed cell death ligand-1 (PD-L1) status* should be recorded for the recurrent/metastatic disease (26/28, 92.86%), but not for early-stage (stage I-II) disease in the non-recurrent/non-metastatic setting (2/28, 7.1%). However, there was no agreement on including *PD-L1 status* in the non-recurrent/non-metastatic advanced-stage (stage III-IV) disease (10/28, 35.7%).

3.4. Cancer staging variables

The expert panel unanimously agreed (28/28, 100%) that *clinical tumour category (cT)*, *clinical nodal category (cN)*, *clinical distant metastasis category (cM)*, and the *edition (version) of the UICC/AJCC TNM staging system* should be included as initial staging variables. There was also strong agreement that *overall UICC/AJCC TNM clinical staging group* (25/28, 89.3%), and *primary tumour laterality* (23/28, 82.1%); recorded as right, left, midline, bilateral (separate primaries), and unknown, should be included. Moreover, the panel agreed that *primary tumour size* on imaging (22/28, 78.6%) should be included in the minimum database, but there was no agreement for the inclusion of *primary tumour volume* on imaging, (7/28, 25%).

The panel strongly agreed to include *involved nodal levels* (23/28, 82.1%), *laterality of involved cervical lymph node* (23/28, 82.1%), the *presence of extranodal extension on imaging* (iENE) (23/28, 82.1%), and the *number of involved nodes (single or multiple)* (25/28, 89.3%) for TNM-8 cN1 HPV-associated OPSCC.

3.5. Surgical treatment variables

There was unanimous agreement (28/28, 100%) that if surgical resection was performed with curative intent in the primary disease setting, the *date of surgery* and *surgery site* should be recorded in the minimum HNC database. The panel also strongly agreed that the *radicality (extent) of primary tumour resection* (24/28, 85.7%) and the *surgical approach* (24/28, 85.7%) should be included, and they reached agreement for the inclusion of the *main surgical device used* in the non-open approach (*20/28, 71.4%)* and *the surgical reconstruction performed* (if any*)* (20/28, 71.4%). There was strong agreement that if ND was performed, then *laterality* (28/28, 100%), *dissected nodal levels* (26/28, 92.86%), and the *radicality of ND* (23/28, 82.1%) should also be included.

There was strong agreement (26/28, 92.86%) that if surgery was performed, information regarding *major intra- or post-operative adverse events (AE)* within 30 days of index surgery should be included as a surgical treatment variable. There was also agreement (22/28, 78.6%) that intra- or post-operative AEs could be recorded individually using a *predefined list* + /- using *Clavien-Dindo classification.* [14] However, the experts could not reach agreement whether using only a predefined list of AEs (16/28, 57.1%) or the *Clavien-Dindo classification* (6/28, 21.4%) or both together (6/28, 21.4%) is appropriate for the minimum data set. If a predefined list of AEs is to be used, there was strong agreement to include *death* (25/26, 96.2%), *flap failure* (if applicable) (27/28, 96.4%), *intra- or post-operative haemorrhage* (28/28, 100%), and *return to the operating room* (23/28, 82.1%). There was also agreement to include *anastomotic leak* (20/28, 71.4%), *cerebrovascular accidents* (21/28, 75%), *pulmonary embolism* (22/28, 78.6%), and *sepsis or septic shock* (22/28, 78.6%). The panel were not able to reach agreement level for the inclusion of other AEs like *acute kidney injury, cardiac arrest, coma, failure to wean off ventilator, multiple blood transfusions (two or more), myocardial infarction, re-intubation, and severe nerve Injury* (resulting in significant organ paresis or paralysis).

3.6. Pathological assessment variables

The expert panel unanimously agreed (28/28, 100%) that for patients who are surgically treated with curative intent in the primary disease setting, *pathological tumour category (pT) and pathological nodal category (pN)* should be recorded. There was also strong agreement that *pathological distant metastasis category (pM)* (27/28, 96.4%) and the *overall pathological staging group* (23/28, 82.1%) should be included. With regards to the pathological assessment variables of the resected primary tumour, there was strong agreement to include *primary tumour size* (25/28, 89.3%), *depth of invasion* in OCSCC (26/28, 92.9%), presence of *lympho-vascular invasion* (25/28, 89.3%), presence of *perineural invasion* (26/28, 92.9%), and the presence of *bone invasion* (26/28, 92.9%).

There was also strong agreement to include pathological status of both *peripheral (radial) and deep resection margins* separately (23/28, 82.1%). The expert panel strongly agreed that resection margin status should *not* be recorded in the minimum database as *two tiers (positive/*

Table 1
Consensus recommendations for variables to be included or recorded in a minimum head and neck cancer database/registry/clinical trials.

Statements	Agreement level^
1. Demographic variables	
-Age at diagnosis-Biological sex (assigned at birth based on anatomy) as Male/Female-Race/ethnicity-Comorbidity index score (Charlson Comorbidity Index)-Performance status score (ECOG/WHO/Zubrod scale)-Tobacco smoking status (defined as Never smoked, former/previous smoker, Current smoker, -Unknown smoking status)-Smoking Pack-year index (for former or current smokers)-Time from last smoking (time from quitting smoking) (for former or current smokers)-History of chewing tobacco or betel nuts (for OCSCC)-Alcohol consumption status (defined as Never, former/previous, Current, Unknown)-Number of standard alcohol units consumed per week (for former or current alcohol drinkers)	Strong agreement
Baseline (pre-treatment) body mass index	Agreement
-Comorbidity index score (Adult Comorbidity Evaluation, ACE-27)-Comorbidity index score (Washington University Head and Neck Comorbidity Index)-Comorbidity index score (The Osaka head and neck comorbidity index)-Comorbidity index score (Kaplan-Feinstein index)-Performance status score (Karnofsky performance scale)-Performance status score (American Society of Anaesthesiologists physical status)-Total annual household income	Statement/Variable rejected
-Gender (self-described of self-perceived gender)-Geriatric screening / assessment-Education level-Employment status-Marital status	No agreement
2. Primary Cancer variables	
-Date of diagnosis-Primary tumour site -Primary tumour sub-site -Histological diagnosis-Histological subtypes as defined by WHO ICD-O-3 (for NPSCC)-Epstein–Barr virus status using EBV encoded small RNAs + /- EBV DNA copy number (for NPSCC)-p16 status (for OPSCC)-Human papillomavirus status (HPV DNA/RNA status), (for OPSCC)-Expression of PD-L1 (for recurrent/metastatic disease)	Strong agreement
-Epstein–Barr virus status using EBV DNA copy number (for NPSCC)-Expression of PD-L1 (for early-stage disease (stage I-II) in the non-recurrent/non-metastatic setting)	Statement/Variable rejected
-Histological subtypes as defined by WHO ICD-O-3 (for non-NPSCC)-Epstein–Barr virus status using only EBV encoded small RNAs (for NPSCC)-Epstein–Barr virus status using EBV encoded small RNAs AND EBV DNA copy number (for NPSCC)-Expression of PD-L1 (for advanced-stage disease (stage III-IV) in the non-recurrent/non-metastatic setting	No agreement
3. Cancer staging variables	
-Clinical tumour category (cT) according to the UICC/AJCC TNM system-Clinical Nodal category (cN) according to the UICC/AJCC TNM system-Clinical distant metastasis category (cM) according to the UICC/AJCC TNM system-Overall UICC/AJCC TNM clinical staging group-The edition (version) of the UICC/AJCC TNM staging system used-Primary tumour laterality: right, left, midline tumour, bilateral (separate primaries), unknown-Primary tumour crossing the midline: yes, no, unknown (for lateralised tumours)-Involved nodal levels-laterality of involved cervical lymph node(s): ipsilateral, bilateral, contralateral -Number of involved nodes: single vs multiple (for TNM-8 cN1 HPV-associated OPSCC)-The presence of extranodal extension on imaging	Strong agreement
-Tumour size on imaging	Agreement
Tumour volume on imaging	No agreement
4. General treatment variables	
-Whether surgical resection was performed should be included as a general treatment variable-Whether systemic therapy was administered should be included as a general treatment variable-Whether radiotherapy was delivered should be included as a general treatment variable	Strong agreement
5. Surgical treatment variables *For patients who are surgically treated with curative intent in the primary disease setting, who may or may not have received adjuvant or neoadjuvant therapy*	
-Date of surgery-Surgery site: primary tumour, neck dissection, both-Radicality (extent) of primary tumour resection-Laterality of ND: unilateral, bilateral, contralateral, unknown-Dissected nodal levels: Level I, level II, level III, etc.-Radicality (extension) of ND: Selective ND, modified-radical ND, extended radical, etc.-Surgical approach: open (external), transoral, transnasal, etc.-Major intra or postoperative adverse events within 30 days of index surgery-Individual adverse events recorded from a predefined list: death, flap failure (If applicable), intra or post-operative haemorrhage, return to the operating room	Strong agreement
-Major intra or postoperative adverse events within 30 days of index surgery could be recorded individually from a predefined list + /- recorded by the Clavien-Dindo classification (Grade I-V)-Individual adverse events recorded from a predefined list: anastomotic leak (if applicable), cerebrovascular accident, pulmonary embolism, sepsis/septic shock (including sources like lungs, surgical wound, urinary tract, etc.)-Surgical reconstruction: no flap (primary closure), pedicled flap, free flap, unknown-The main surgical device used for the approach: robot, endoscope, microscope, etc. (for surgeries where the approach was not open)	Agreement
-Individual adverse events recorded from a predefined list: vertebral Osteomyelitis	Statement/Variable rejected
-Major intra or postoperative adverse events within 30 days of index surgery should only be recorded individually from a predefined list -Major intra or postoperative adverse events within 30 days of index surgery should only be recorded by the Clavien-Dindo classification (Grade I-V)-Major intra or postoperative adverse events within 30 days of index surgery should be recorded individually from a predefined list AND recorded by the Clavien-Dindo classification (Grade I-V)-Individual adverse events recorded from a predefined list: acute kidney injury, cardiac arrest, coma, failure to wean off ventilator, multiple blood transfusions (two or more), myocardial infarction, re-intubation, severe nerve injury (resulting in significant organ paresis or paralysis)	No agreement
6. Pathological assessment variables*For patients who are surgically treated with curative intent in the primary disease setting, who may or may not have received adjuvant or neoadjuvant therapy*	
-Pathological tumour category (pT)-Pathological Nodal category (pN)-Pathological distant metastasis category (pM)-Overall pathological staging group-Resected primary tumour size-Depth of invasion of the resected primary tumour (for OCSCC)-Lympho-vascular invasion in the resected primary tumour-Perineural invasion in the resected primary tumour-Bone invasion in the resected primary tumour-Pathological status of peripheral (radial) AND deep resection margins recorded separately-Total number of dissected neck lymph nodes-Number of positive (metastatic) dissected nodes -Laterality of positive (metastatic) dissected nodes -Nodal level(s) of positive (metastatic) dissected nodes-The size of largest positive (metastatic) dissected node-The presence of pathological extranodal extension	Strong agreement
-Resection margin status could be recorded as three tiers positive/close/negative + /- as the width of the closest margin in millimetres -For HPV-negative OPSCC: negative/clear margins should be defined for the minimum database as tumour present within $\geq$ 5 mm from resection margin	Agreement
-Resection margin status should only be recorded as two tiers (positive/negative) -Resection margin status should only be recorded as the width of the closest margin in millimetres -Resection margin status should be recorded as two tiers (positive/negative) AND as the width of the closest margin in millimetres	Statement/Variable rejected
-Resection margin status should only be recorded as three tiers positive/close/negative -Resection margin status could be recorded as three tiers positive/close/negative AND as the width of the closest margin in millimetres -Positive/involved margins should be defined for the minimum database as tumour present at resection margin (tumour at inked resection edge, or 0 mm margin)-Positive/involved margins should be defined for the minimum database as tumour present $<$ 1 mm from resection margin- For HPV-associated OPSCC: negative/clear margins should be defined for the minimum database as tumour present within $\geq$ 5 mm from resection margin- For HPV-associated OPSCC: negative/clear margins should be defined for the minimum database as tumour present within $\geq$ 3 mm from resection margin- For HPV-associated OPSCC: negative/clear margins should be defined for the minimum database as tumour present within $\geq$ 1 mm from resection margin	No agreement
7. Systemic anticancer therapy variables*For patients who are treated with systemic anticancer therapy with curative intent in the primary setting*	
-Sequence of systemic therapy administration: concurrent, adjuvant, induction, etc.-Start and end dates of systemic therapy-Number of chemotherapy cycles delivered-Name(s) of systemic anticancer medication(s) given-Doses of cisplatin given per cycle (to allow the calculation of cumulative dose)-Completion status of the prescribed cycles of systemic therapy-Name(s) of stopped (not completed) systemic anticancer medication(s): if applicable-	Strong agreement

(*continued on next page*)

Table 1 (*continued*)

Reason(s) for not completing systemic anticancer medication(s) (if applicable) should only be -recorded as 'treatment-related (toxicity)' and 'non-treatment related'-Significant adverse events (severe toxicity or severe side-effects) from chemotherapy should be recorded	
-Doses of other (non-cisplatin) systemic anticancer medication(s) given per cycle	No agreement
8. Radiotherapy treatment variables*For patients who are treated with radiotherapy with curative intent in the primary setting*	
-Radiotherapy setting: primary/definitive, adjuvant-Radiotherapy treatment technique: eg. IMRT, SBRT, etc.-Radiotherapy treatment sites-Radiotherapy start and end dates-Interval between surgery (if applicable) and the start of adjuvant radiotherapy-Radiotherapy total dose, dose per fraction, and number of fractions-Radiotherapy doses to low, intermediate, and high-risk target volumes-Radiotherapy fractionation pattern-Completion status of the prescribed course of radiotherapy-Reason(s) for not completing radiotherapy should only be recorded as 'treatment-related (toxicity)' and 'non-treatment related'-Interruption status of the prescribed course of radiotherapy-For interrupted radiotherapy course, the total duration of interruptions-Significant adverse events (severe toxicity or severe side-effects) from radiotherapy should be recorded using Common Terminology Criteria for Adverse Events (CTCAE)	Strong agreement
-Significant adverse events (severe toxicity or severe side-effects) from radiotherapy should be recorded using Radiation Therapy Oncology Group (RTOG) criteria	Statement/Variable rejected
9. Variables related to response after primary treatment	
-Response to curative-intent therapy should be recorded in the minimum database-After definitive (chemo)radiotherapy, post-treatment response should be recorded in the minimum database	Strong agreement
10. Variables related to the diagnosis of progression/recurrence	
-Diagnosis of disease progression or recurrence -Date of progression or recurrence diagnosis-Method(s) used to diagnose progression or recurrence: clinical only, clinical/imaging only, biopsy, etc.-The imaging modality used to diagnose progression or recurrence (if applicable)-Diagnosis of local failure: yes/no-Diagnosis of regional (nodal) failure: yes/no-Diagnosis of distant metastasis: yes/no-Site(s) of distant metastasis (if applicable)-Number of times a head and neck cancer has recurred	Strong agreement
11. Variables related to treatment of progression/recurrence	
-Treatment modality for head and neck cancer that has recurred or progressed: Surgery, systemic anticancer therapy, radiotherapy, etc-Outcome (response) to treatment-Intention of surgery (for surgically treated patients)-Date of surgery (for surgically treated patients)-Surgery site (for surgically treated patients): primary tumour, ND, both-Extent (radicality) of surgery at primary site (if applicable): for surgically treated patients-Laterality of ND (if applicable): for surgically treated patients-Dissected nodal levels (if applicable): for surgically treated patients-Radicality (extension) of ND (if applicable): for surgically treated patients-The presence of pathological extranodal extension (if applicable): for surgically treated patients- Major intra or postoperative adverse events within 30 days of index surgery for a disease that has recurred or progressed could be recorded individually from a predefined list + /- recorded by the Clavien-Dindo classification (Grade I-V)-Pathological status of peripheral (radial) and deep resection margins (if applicable)-Intention of treatment with systemic anticancer therapy (if applicable)-Start and end dates of systemic treatment (if applicable)-Name(s) of systemic anticancer medication(s) given (if applicable)-Number of cycles of immunotherapy or chemotherapy given (if applicable)-Intention of radiotherapy (if applicable)-Radiotherapy start and end dates (if applicable)-Total dose, dose per fraction, and number of fractions of radiotherapy (if applicable)-Radiotherapy treatment sites (if applicable)	Strong agreement
Surgical reconstruction (for surgically treated tumour that has recurred or progressed)	No agreement
12. Variables related to status at last follow up	
-Date of last clinical follow up-Patient status at last clinical follow up (disease and survival status)-New head and neck cancer diagnosis (second primary tumour): yes/no- Date of death (for deceased patients)- Cause of death (for deceased patients): recorded as 'Related to this cancer' vs 'Not-related to this cancer'	Strong agreement

OCSCC = Oral cavity squamous cell carcinoma, NPSCC= Nasopharyngeal squamous cell carcinoma, OPSCC = Oropharyngeal squamous cell carcinoma, ICD-O-3 = The 3rd Edition of the WHO International Classification of Diseases for Oncology, HPV= Human papillomavirus, EBV= Epstein–Barr virus status, UICC/AJCC = Union for International Cancer Control/ American Joint Committee on Cancer, ND= Neck dissection, IMRT= Intensity modulated radiotherapy, SBRT= Stereotactic body radiotherapy

ˆStrong agreement indicates a threshold of 80% and above. Agreement indicates a threshold of 67% and above after the third round for statements not considered to have reached a strong agreement.

negative) (4/28, 14.3%), nor only as *width of the closest resection margin in millimetres* (2/28, 7.1%). Instead, there was agreement (21/28, 75%) that resection margin status could be recorded in three tiers (positive/close/negative) + /- the *width of the closest resection margin in millimetres*. Moreover, the experts were unable to reach agreement towards a definition for 'positive resection margins' for all head and neck SCC to be adopted for the minimum data set; and were divided between *tumour present at resection margin* (13/28, 46.4%) and tumour present < 1 mm from resection margin (15/28, 53.6%). A similar lack of agreement was also observed around the definition of 'negative resection margins' in HPV-associated OPSCC, as they were divided between tumour present within ≥ 5 mm from resection margin (13/28, 46.4%) vs ≥ 3 mm (9/28, 32.1%) vs ≥ 1 mm (6/28, 21.4%). However, for HPV-negative cancers, the experts reached agreement (19/28, 67.9%) that 'negative resection margins' should be defined as tumour present within ≥ 5 mm from resection margin.

If ND was performed, there was strong agreement that the *total number of resected neck nodes* (24/28, 85.7%), *number of positive nodes* (27/28, 96.4%), *laterality of positive nodes* (24/28, 85.7%), *nodal levels of positive nodes* (24/28, 85.7%), *size of the largest resected metastatic neck node* (23/28, 82.1%), and the presence of *pathological extranodal extension (pENE)* (28/28, 100%) should all be included as core pathological assessment variables.

3.7. Systemic anticancer therapy variables

There was unanimous agreement (28/28, 100%) that for patients who are treated with systemic anticancer therapy with curative intent in the primary setting, *administration sequence* (e.g. concurrent, adjuvant, induction, etc.), and *the name of systemic anticancer medication(s)* should be recorded. Moreover, the expert consensus group strongly agreed to include *start and end dates of systemic therapy* (25/28, 89.3%), *number of chemotherapy cycles delivered* (26/28, 92.9%), and the *doses of cisplatin given per cycle* to allow the calculation of cisplatin cumulative dose (27/28, 96.4%). However, there was no agreement around the inclusion of *doses of other (non-cisplatin) systemic anticancer medication(s) given per cycle* (17/28, 60.7%).

The experts panel also reached strong agreement to include *completion status of prescribed number of cycles of systemic therapy* (26/28, 92.9%), *names of stopped (not completed) systemic anticancer medication (s)* (26/28, 92.9%), and the *reason for not completing the systemic therapy course* (26/28, 92.9%).

3.8. Radiotherapy core variables

There was unanimous agreement (28/28, 100%) that for patients treated with radiotherapy with curative intent, *radiotherapy setting* (primary-definitive and adjuvant) should be included as a radiotherapy core variable. The expert respondents also strongly agreed to include *radiotherapy treatment technique* (27/28, 96.4%), *radiotherapy treatment*

sites (25/28, 89.3%), *radiotherapy start and end dates* (26/28, 92.9%), *interval between surgery and the start of adjuvant radiotherapy* (28/28, 100%), *radiotherapy total dose, dose per fraction, and number of fractions* (27/28, 96.4%), *radiotherapy dose to the low, intermediate, and high risk target volumes* (27/28, 96.4%), and the *fractionation pattern of radiotherapy* (25/28, 89.3%). There was also strong agreement that *completion status of prescribed radiotherapy course* (26/28, 92.9%), the *reason for not completing the prescribed radiotherapy course* (26/28, 92.9%), the *total duration of radiotherapy interruptions* (27/28, 96.4%) should be included in the minimum database. Moreover, there was unanimous agreement (28/28, 100%) that *significant AEs from chemotherapy and/or radiotherapy* should be recorded using *Common Terminology Criteria for Adverse Events* (CTCAE) criteria [15].

3.9. Variables related to the diagnosis of progression/recurrence

The consensus panel strongly agreed (27/28, 96.4%) that the following should be recorded: *HNC progression or recurrence after primary treatment, date of diagnosis of progression or recurrence* (28/28, 100%), *method of diagnosis of progression or recurrence* (23/28, 82.1%), the *imaging modality used for progression or recurrence diagnosis* (24/28, 85.7%), and the *number of times a HNC has recurred* (27/28, 96.4%), as well as the diagnosis of *local failure* (27/28, 96.4%), *regional failure* (26/28, 92.9%), *distant metastasis status* (28/28, 100%), and the *site(s) of distant metastasis* (25/28, 89.3%).

3.10. Variables related to treatment of progression/recurrence

There was strong agreement that the *treatment modality* for HNC that has recurred or progressed (including *surgery* (28/28, 100%), *systemic anticancer therapy* (28/28, 100%), *and radiotherapy* (26/28, 92.9%)), in addition to *treatment outcome (response)* (26/28, 92.9%), should be included in any minimum HNC data set. For HNC that has either recurred or progressed after primary treatment, and has subsequently been surgically treated, the experts strongly agreed to include *intention of surgery* (25/28, 89.3%), *date of surgery* (28/28, 100%), *surgery site* (27/28, 96.4%), *extent of salvage surgery at primary site* (28/28, 100%), *laterality of ND*(26/28, 92.9%), *ND levels* (26/28, 92.9%), *radicality of ND* (27/28, 96.4%), the *presence of pENE* (25/28, 89.3%), *pathological status of peripheral and deep resection margins* (26/28, 92.9%), and information regarding *major intra or postoperative AEs* within 30 days of index surgery (26/28, 92.9%).

For HNC that has either recurred or progressed after primary treatment, and has subsequently been treated with systemic anticancer therapy, there was strong agreement to include *intention of systemic anticancer treatment* (28/28, 100%), the *start and end dates of systemic anticancer therapy* (24/28, 85.7%), the *name(s) of systemic anticancer medication(s) given* (28/28, 100%), and the *number of cycles of immunotherapy or chemotherapy* given (26/28, 92.9%). Moreover, the experts strongly agreed that if radiotherapy was given for HNC that has recurred or progressed, *intention of treatment* (25/28, 89.3%), the *start and end dates of radiotherapy* (27/28, 96.4%), *total dose, dose per fraction, and number of fractions of radiotherapy delivered* (27/28, 96.4%), and the *treatment sites* (27/28, 96.4%) should be included in the minimum HNC dataset.

3.11. Variables related to status at last follow up

There was strong agreement that the minimum HNC data set should include these follow-up variables: *date of last clinical follow-up* (27/28, 96.4%), *patient status at last clinical follow-up* (27/28, 96.4%), and the *diagnosis of new HNC* (27/28, 96.4%). For deceased patients, there was strong agreement to include *date of death* (28/28, 100%), and *cause of death* (27/28, 96.4%).

3.12. Minimum database

An HNCIG minimum database was constructed, containing 143 essential variables and 31 optional variables. It is available to download for free from HNCIG website, www.hncig.com.

4. Discussion

Using a modified Delphi process, experts from 19 clinical research organisations have for the first time reached consensus on a wide range of clinical variables constituting a minimum head and neck oncology data set. The final recommendations were endorsed by 19 international HNC organisations and cooperative groups, and provide a framework for standardisation of data collection, sharing, synthesis and meta-analysis of future head and neck cancer research. To further assist HNC researchers around the world, we have established a downloadable open access HNCIG minimum database incorporating these essential variables (downloadable from www.hncig.com). Not all these variables have to be collected in every research project, but each project will likely need to collect a large proportion of these variables, and hence these recommendations will considerably help standardise and expedite such research.

Due to the range of variables and the lack of standardisation hitherto, there were some challenges in achieving consensus on some variables. As an example, survey respondents could not agree on the inclusion of socio-economic variables such as education level, income, employment, and marital status, all of which have shown to impact cancer specific outcomes. [16,17].

Co-morbidity and performance status measures have been shown to correlate with survival outcomes in oncology. [18,19] Our Delphi survey showed strong consensus for the inclusion of the CCI and ECOG performance status. The former can be challenging to collect as it requires knowledge of a patient's comorbid conditions such as congestive heart failure, chronic obstructive pulmonary disease (COPD), dementia, liver disease, etc. Furthermore, it is important to note that performance status has limited value in the assessment of fitness for therapy in elderly patients. Nevertheless, there was no agreement for inclusion of geriatric assessment tools. Further work is needed in this area.

As expected, both smoking and alcohol consumption were considered to be essential variables to include in the database. While cigarette and betel nut use can be quantified, the best method to measure alcohol use varies among researchers and countries. The use of standard alcohol units gained consensus as a method to measure the burden of alcohol consumption and should be used going forward.

The use of molecular biomarkers such as HPV to prognosticate outcomes and de-escalate treatment is increasingly being utilized in HNC clinical trials. [20] There was unanimous agreement that p16 status should be included to determine HPV status and considered as an essential variable. Interestingly, while HPV DNA/RNA status did not achieve consensus for inclusion in the first round, by the third round over 85% of respondents agreed it should be used as an essential variable. This may be a reflection of the results of a recent study by Mehanna *et al.* [8], which demonstrated that patients with discordant p16 and HPV RNA/DNA status had worse prognosis than those with p16 + /HPV+ oropharyngeal cancer, suggesting that both p16 status and HPV status should be reported. [8] PD-L1 status did not achieve consensus for use in all cases, and was only recommended to be collected for patients with recurrent/ metastatic disease, where immunotherapy is likely to be used and has been shown to have a survival benefit. [21].

There was general strong agreement to record key pathological variables such as lymphovascular invasion, perineural invasion, surgical resection margins, and bone invasion. However, there was significant discordance regarding a preferred way for recording margin status in the database, and especially the definition of close margins, which reflects discordance in the literature. [22] In our survey, respondents eventually reached some agreement that both the "tiers" of margin status (positive

vs close vs negative) and the width of the closest resection margin should be recorded. However, even amongst this group of international experts, the definition of close and positive margins could not be agreed upon. That is likely because the definition of surgical margins might be dependent on the anatomical site (e.g. glottis, oropharynx or oral cavity), and especially for HPV positive disease. [23–25] It is difficult to achieve 5-mm clear margins in oropharyngeal cancer given the anatomy, especially for HPV positive disease. [26,27] In our study, there was no clear definition of how a negative margin should be assigned in HPV-mediated tumours, with only 46% of respondents requiring a margin $\geq$ 5 mm. Therefore, in our opinion, recording the width of the closest margin would be important as it would allow for future research to determine the importance of margin status for recurrence and survival, and enable more evidence-based recommendations.

Standardization of the reporting of radiation dose, technique, and treatment volume is not well defined in HNC research. In most studies, only the total dose is given, and other critical variables such as number of fractions, radiotherapy start and end dates, radiotherapy interruptions, and technique are rarely reported. Indeed, radiotherapy interruptions have been associated with a decrease in survival in HNC. [28,29] It is therefore important to note that while the majority of respondents in this survey were not radiation oncologists, they reached a consensus that more granular detail of radiotherapy data would be important for future studies and HNC research.

Progression of HNC, whether local or distant, is associated with a very poor prognosis, and survival is dismal. Future research in recurrent/metastatic HNC will require international collaboration given the sparsity of published evidence. The survey respondents agreed on several important variables, including the type of therapeutic intervention received (radiation, surgery, and chemotherapy), the treatment intent, as well as the number of cycles of chemotherapy and the radiation dose given at time of progression or recurrence.

Despite utilizing a rigorous modified Delphi methodology to establish these consensus recommendations, there are several limitations to note. The study was limited to experts nominated by their respective cooperative group organizations, and it is possible that feedback from other prominent members in the wider head and neck research community is unaccounted for. Moreover, despite our efforts to incorporate representatives from the developing world, the majority of our respondents were from Europe and North America, and so it is unclear how feasible this minimum database could be implemented in resource constrained settings.

The other important component to standardisation of data collection and analysis is the definitions of the variables collected, especially for outcome measures. In this study, by specifying methods and systems for calculating some patient characteristics, such as smoking status, and by specifying the types of treatment and pathology variables to be collected, we have helped to standardise definitions of these variables. Further essential work on standardising the definitions of outcome measures has been undertaken by HNCIG, andwill be published in the near future.

5. Conclusion

The HNCIG has undertaken an international process to achieve consensus on the collection and reporting of data variables for HNC research. Endorsed by 19 research organisations representing 34 countries, these recommendations provide the framework to facilitate and harmonise data collection and sharing for HNC research. These variables have also been incorporated into a ready to use downloadable HNCIG minimum database, available from the HNCIG website www.hncig.com. Definitions of outcome endpoints are detailed in two separate articles.

Funding Statement

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Authors' contributions

SB, PP, HM and AKA-F conceived the study concept and initiated the study design. AKA-F, SB, PP, PS, JT, AS, HM and PCN were involved in study development, data analysis, and data interpretation of this Policy Review. All authors participated in data collection, manuscript preparation, and approved the final manuscript. HM is a senior investigator for the National Institute for Health Research (NIHR). The views expressed in this Policy Review are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

CRediT authorship contribution statement

Sujith Baliga: Conceptualization, Formal analysis, Investigating, Methodology, Writing - original draft, Writing - review & editing, Visualization, Supervision. **Ahmad K. Abou-Foul:** Conceptualization, Formal analysis, Investigating, Methodology, Writing - original draft, Writing - review & editing, Visualization. **Paul Nankivell:** Writing- review & editing. **Melvin LK Chua:** Writing- review & editing. **Shao Hui Huang:** Writing- review and editing. **Luiz P. Kowalsi:** Writing - review & editing. **Dora L Kwong:** Writing - review & editing. **Marco Carlo Merlano:** writing -review & editing. **Hisham Mehanna:** Conceptualization, methodology, investigation, resources, writing-review and editing, supervision, project administration. **Dukagjin Blakaj:** Validation, Writing – review & editing. **Juliette Thariat:** Conceptualization, Formal analysis, Investigation, Methodology, Writing – review & editing. **Aditya Shreenivas:** Conceptualization, Formal analysis, Investigation, Writing – review & editing. **Panagiota Economopoulou:** Validation, Writing – review & editing. **Pablo Parente:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. **Petr Szturz:** Conceptualization, Data curation, Investigation, Methodology, Writing – review & editing. **Sudhir Nair:** Validation, Writing – review & editing. **Konrad Klinghammer:** Validation, Writing – review & editing. **Lachlan McDowell:** Validation, Writing – original draft. **Federica Bertolini:** Investigation, Validation, Writing – review & editing. **Julian Biau:** Methodology, Validation, Writing – review & editing. **Francis Ho:** Writing – review & editing. **Naomi Kiyota:** Validation, Writing – review & editing. **Mischa de Ridder:** Methodology, Writing – review & editing. **Satya Garikipati:** Methodology, Writing – review & editing. **Alberto Carral Maseda:** Methodology, Validation, Writing – review & editing. **Velda Ling-Yu Chow:** Validation, Writing – review & editing. **Thiago Bueno De Oliveira:** Writing – review & editing. **Barbara Burtness:** Methodology, Validation, Writing – review & editing. **Sinead Brennan:** Methodology, Validation, Writing – review & editing. **Aina Brunet:** Validation, Writing – review & editing. **Silke Tribius:** Validation, Writing – review & editing. **Yom S Sue:** Methodology, Validation, Writing – review & editing. **John Waldron:** Methodology, Validation, Writing – review & editing. **Jens Overgaard:** Validation, Writing – review & editing. **Nobuhiro Hanai:** Validation, Writing – review & editing. **Amanda Psyrri:** Validation, Writing – review & editing.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: HM is the director and a shareholder of Warwickshire Head and Neck Clinic; chair of the Head and Neck Cancer International Group (HNCIG); and past president of the British Association of Head and Neck Oncologists. HM also reports receiving honoraria from AstraZeneca; Speakers Bureau on MSD, Sanofi Pasteur, Merck; research Funding from GSK Biologicals, MSD, Sanofi Pasteur, GSK Plc, AstraZeneca; travel Accommodation Expenses from Sanofi, Pasteur, MSD, Merck. AP has the

following disclosures: Advisory board member with honoraria: Merck Serono, Roche, MSD, Astrazeneca, BMS, Bayer, Pfizer& Medical Education with honoraria: Medscape, Prime Oncology, Funding for research support: KURA, BMS, Merck Serono, Roche, BI, Genesis. All other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

The data that support the findings of this study are available from the corresponding author, [HM], upon reasonable request.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ejca.2024.114038.

References

[1] Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71(3):209–49.

[2] Yom SS, Torres-Saavedra P, Caudell JJ, et al. Reduced-dose radiation therapy for HPV-associated oropharyngeal carcinoma (NRG oncology HN002). J Clin Oncol 2021;39(9):956–65.

[3] Mehanna H, Robinson M, Hartley A, et al. Radiotherapy plus cisplatin or cetuximab in low-risk human papillomavirus-positive oropharyngeal cancer (De-ESCALaTE HPV): an open-label randomised controlled phase 3 trial. Lancet 2019;393(10166):51–60.

[4] Gillison ML, Trotti AM, Harris J, et al. Radiotherapy plus cetuximab or cisplatin in human papillomavirus-positive oropharyngeal cancer (NRG oncology RTOG 1016): a randomised, multicentre, non-inferiority trial. Lancet 2019;393(10166):40–50.

[5] Forastiere AA, Goepfert H, Maor M, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. N Engl J Med 2003;349(22):2091–8.

[6] Department of Veterans Affairs Laryngeal Cancer Study G, Wolf GT, Fisher SG, et al. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. N Engl J Med 1991;324(24):1685–90.

[7] Ang KK, Harris J, Wheeler R, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med 2010;363(1):24–35.

[8] Mehanna H, Taberna M, von Buchwald C, et al. Prognostic implications of p16 and HPV discordance in oropharyngeal cancer (HNCIG-EPIC-OPC): a multicentre, multinational, individual patient data analysis. Lancet Oncol 2023;24(3):239–51.

[9] Bentzen HB, Castro R, Fears R, Griffin G, Ter Meulen V, Ursin G. Remove obstacles to sharing health data with researchers outside of the European Union. Nat Med 2021;27(8):1329–33.

[10] Mehanna H, Hardman JC, Shenson JA, et al. Recommendations for head and neck surgical oncology practice in a setting of acute severe resource constraint during the COVID-19 pandemic: an international consensus. Lancet Oncol 2020;21(7):e350–9.

[11] D'alkey D. The delphi method: an experimental study of group opinion. Rand 1969.

[12] Guckenberger M, Belka C, Bezjak A, et al. Practice recommendations for lung cancer radiotherapy during the COVID-19 pandemic: an ESTRO-ASTRO consensus statement. Radio Oncol 2020;146:223–9.

[13] (⁋2019)⁋ WHO. International classification of diseases for oncology (⁋ICD-O)⁋, 3rd ed., 2nd revision. ⟨https://www.who.int/standards/classifications/other-classifications/international-classification-of-diseases-for-oncology⟩ (accessed 11/01/2024).

[14] Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250(2):187–96.

[15] National_Cancer_Institute. Common Terminology Criteria for Adverse Events. 2017. ⟨https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_8.5x11.pdf⟩ (accessed 11/01/2024).

[16] Clegg LX, Reichman ME, Miller BA, et al. Impact of socioeconomic status on cancer incidence and stage at diagnosis: selected findings from the surveillance, epidemiology, and end results: national longitudinal mortality study. Cancer Causes Control 2009;20(4):417–35.

[17] Bradley CJ, Given CW, Roberts C. Race, socioeconomic status, and breast cancer treatment and survival. J Natl Cancer Inst 2002;94(7):490–6.

[18] Buccheri G, Ferrigno D, Tamburini M. Karnofsky and ECOG performance status scoring in lung cancer: a prospective, longitudinal study of 536 patients from a single institution. Eur J Cancer 1996;32A(7):1135–41.

[19] West DW, Satariano WA, Ragland DR, Hiatt RA. Comorbidity and breast cancer survival: a comparison between black and white women. Ann Epidemiol 1996;6(5):413–9.

[20] Chung CH, Zhang Q, Kong CS, et al. p16 protein expression and human papillomavirus status as prognostic biomarkers of nonoropharyngeal head and neck squamous cell carcinoma. J Clin Oncol 2014;32(35):3930–8.

[21] Harrington KJ, Burtness B, Greil R, et al. Pembrolizumab with or without chemotherapy in recurrent or metastatic head and neck squamous cell carcinoma: updated results of the phase III KEYNOTE-048 study. J Clin Oncol 2023;41(4):790–802.

[22] Li MM, Puram SV, Silverman DA, Old MO, Rocco JW, Kang SY. Margin analysis in head and neck cancer: state of the art and future directions. Ann Surg Oncol 2019;26(12):4070–80.

[23] Zanoni DK, Migliacci JC, Xu B, et al. A proposal to redefine close surgical margins in squamous cell carcinoma of the oral tongue. JAMA Otolaryngol Head Neck Surg 2017;143(6):555–60.

[24] Ho CM, Ng WF, Lam KH, Wei WJ, Yuen AP. Submucosal tumor extension in hypopharyngeal cancer. Arch Otolaryngol Head Neck Surg 1997;123(9):959–65.

[25] Warner L, O'Hara JT, Lin DJ, et al. Transoral robotic surgery and neck dissection alone for head and neck squamous cell carcinoma: Influence of resection margins on oncological outcomes. Oral Oncol 2022;130:105909.

[26] Pool C, Weaver T, Zhu J, Goldenberg D, Goyal N. Surgical margin determination in the era of HPV-positive oropharyngeal cancer. Laryngoscope 2021;131(10):E2650–4.

[27] Hinni ML, Zarka MA, Hoxworth JM. Margin mapping in transoral surgery for head and neck cancer. Laryngoscope 2013;123(5):1190–8.

[28] Mazul AL, Stepan KO, Barrett TF, et al. Duration of radiation therapy is associated with worse survival in head and neck cancer. Oral Oncol 2020;108:104819.

[29] Fesinmeyer MD, Mehta V, Blough D, Tock L, Ramsey SD. Effect of radiotherapy interruptions on survival in medicare enrollees with local and regional head-and-neck cancer. Int J Radiat Oncol Biol Phys 2010;78(3):675–81.