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A Collaborative Approach for the Development of a Standardized Set of Patient-Centered Outcomes in Head and Neck Cancers

Uma Abordagem Colaborativa para o Desenvolvimento de um Conjunto Padronizado de Resultados Centrados no Doente com Cancro de Cabeça e Pescoço

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ABSTRACT

Introduction: Head and neck cancers remain a significant health burden worldwide. Standardizing the care provided to these patients through the systematic measurement of established indicators is key to improve their outcomes. The aim of this study was to establish a relevant set of outcome indicators in this condition and identify measurement tools and requirements to do so.

Methods: One scientific committee and two regional working groups worked in a stepwise manner to narrow down an initial list of potential outcome indicators retrieved from an exhaustive literature review to a smaller set of outcome indicators according to their clinical practice. This was assessed by one representative of a head and neck cancer patient association until a final set of indicators was reached.

Results: A total of 164 outcome indicators comprising case-mix, outcomes, and adverse events dimensions were retrieved from the literature. These were reduced to a working set of 79 outcome indicators by the Scientific Committee and divided into seven categories including demographics, clinical status, tumor-related parameters, nutritional status, treatment, health and quality of life parameters and survival. Subsequently, these indicators were further reduced to a set of 50 indicators by the regional working groups and to a set of 49 indicators by the final Scientific Committee assessment. Finally, the discussed indicators were appraised by a head and neck cancer patient association, which added the 'rehabilitation' category, a key parameter to these patients.

Conclusion: An initial set of outcome indicators for head and neck cancer was systematically developed aiming to standardize the care provided to these patients across institutions at national level and identify measurement tools and requirements to measure those indicators. This standard set should be continuously improved and consistently adopted in the different clinical and national settings.

Keywords: Head and Neck Neoplasms; Patient-Centered Care; Patient Outcome Assessment; Quality Indicators, Health Care

RESUMO

Introdução: O cancro de cabeça e pescoço continua a ter um impacto considerável quer para o doente quer para os sistemas de saúde a nível mundial. Uniformizar os cuidados de saúde prestados a estes doentes, através da medição sistemática de indicadores estabelecidos, é fundamental para a melhoria contínua dos resultados em saúde. O objetivo deste estudo foi estabelecer um conjunto relevante de indicadores de resultados para o cancro de cabeça e pescoço e identificar ferramentas de medição e respetivos requisitos para a sua realização.

Métodos: Através de uma revisão exaustiva na literatura, obteve-se uma lista inicial de potenciais indicadores de resultados para o cancro de cabeça e pescoço. Um comité científico e dois grupos de trabalho regionais trabalharam em colaboração para reduzi-la por forma a obter um conjunto de indicadores ajustado à sua prática clínica. Esta lista foi depois avaliada por um representante de uma associação de doentes de cancro de cabeça e pescoço alcançando-se um conjunto final de indicadores.

Resultados: Da revisão literária, um total de 164 indicadores foram identificados abrangendo as dimensões de *case-mix*, resultados e eventos adversos. Estes foram, posteriormente, reduzidos a um conjunto de 79 indicadores pelo comité científico e divididos em sete categorias, incluindo demografia, estado clínico, parâmetros relacionados com o tumor, estado nutricional, tratamento, parâmetros de saúde e qualidade de vida, e sobrevida. Subsequentemente, essa lista foi ainda encurtada para 50 indicadores, pelos grupos de trabalho regionais, e reduzida para 49 indicadores pela avaliação final do comité científico. Por fim, os indicadores discutidos foram avaliados por um representante da associação de doentes, que acrescentou a categoria, 'reabilitação', parâmetro fundamental para estes doentes.

Conclusão: Um conjunto inicial de indicadores de resultados para cancro de cabeça e pescoço foi definido com o objetivo de padronizar a prática clínica a nível nacional e identificar as ferramentas de medição e os requisitos necessários para os medir. Este conjunto de indicadores deve ser continuamente melhorado e adotado de forma consistente nos diferentes contextos clínicos a nível nacional.

Palavras-chave: Avaliação de Resultados na Ótica do Doente; Cuidados Centrados no Doente; Cuidados de Saúde; Indicadores de Qualidade; Neoplasias da Cabeça e Pescoço

INTRODUCTION

According to the latest GLOBOCAN estimates, head and neck (H&N) cancer is the 8th most common cancer worldwide in terms of both incidence and mortality. With 450 000 deaths every year, the disease represents a significant global health burden.[1] Head and neck squamous cell carcinoma (HNSCC) is the most common histological

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subtype[2] and comprises a biologically and clinically heterogeneous group of tumors from the oral cavity, pharynx (oropharynx, hypopharynx and nasopharynx), larynx, sinonasal cavity and salivary glands, with disparate risk factors, molecular pathogenesis, treatment response, and prognosis.[3,4]

Well-established risk factors include tobacco and alcohol consumption, but oncogenic viruses as the human papillomavirus (HPV) are emerging as new etiological agents associated with oropharyngeal squamous cell carcinoma.[5] Additionally, also the microbiome and diet have been implicated as contributing factors in recent decades.[6]

The treatment strategy in H&N cancers aims to achieve the highest cure rate with the lowest morbidity risk. To achieve this, patients should undergo pre-treatment risk assessment incorporating both objective tumor parameters (such as tumor location, histology and TNM stage) and patient parameters (physiological age, comorbidities, nutritional status, previous history of cancer, occupation, expected functional outcome, personal preference). Disease management requires a multidisciplinary approach involving several medical specialties, as well as multimodal treatment involving surgery, radiation therapy, chemotherapy and, more recently, immunotherapy, each with trade-offs between treatment outcomes and quality of life (QoL).[7–11] Additionally, the multidisciplinary nature of the management approach of these patients can make it challenging to define the most relevant patient outcomes to consider and define a unified and robust treatment strategy.

In Europe, five-year survival rates of patients with head and neck tumors are poor and vary according to subsite: 61% for laryngeal, 49% for oral cavity, 41% for oropharyngeal, and 25% hypopharyngeal squamous cell carcinoma (SCC).[12] These suboptimal survival rates highlight the need for improved risk stratification to identify patients at higher risk of recurrence and tailor treatment for them.

The high prevalence of loco-regional recurrence and/or metastatic disease is responsible for the high mortality rates reported in HNSCC.[13] Indeed, patients with early disease stages carry a favorable prognosis, with five-year survival rates close to 80%, while for patients with locally advanced disease this rate is below 50%.[14]

Significant regional and between-hospital heterogeneity exists in the treatment patterns and quality of care delivered to these patients, with direct impact on their health outcomes. In addition to heterogeneous treatment practices, hospitals also use different quality indicators. Quality indicators are used by healthcare institutions to evaluate the quality of care provided and identify areas for improvement, but many indicators focus on treatment process and structure rather than on their relevance to patient outcomes. Besides not always having an impact on relevant patient outcomes, the registry of these indicators represents a significant burden for clinicians. Additionally, the lack of standardization in indicators collected across hospitals and of routine collection of such indicators limits the ability to retrieve useful insights into the quality of care provided nationally. Systematic outcome measurement is the cornerstone of value improvement and key in guiding improvement efforts and value-based reimbursement models in health care[15–17] and should be used as the basis to ensure high-value health care for all patients.

The conceptual framework of value-based health care is increasingly being used to improve the quality of care delivered to patients. This strategy is based on the premise that the value of health services, rather than the volume of services, is the most relevant indicator of the quality of care provided, with 'value' defined as the patient-relevant outcomes achieved relative to its costs over the full cycle of care.[18,19] The foundation of this strategy is a common definition of value, starting with outcomes, which should be patient-centered and include not only survival, but also the impact of the disease and its treatment on patients' quality of life and ability to live productive lives free of treatment or disease symptoms. In this sense, outcome indicators should integrate both established disease control measures and patient-reported outcome measures (PROMs).

Implementing a strategy of value-based health care for a specific medical condition requires the definition of a relevant set of outcome indicators relevant to both patients and stakeholders and respective collection and measurement using well-defined and standardized metrics. However, defining and measuring health outcomes is challenging, as they should encompass not only survival and overall disease control, but also treatment complications and health-related quality of life (HRQoL) during and after treatment. Efforts to measure and report health outcomes have been developed for some malignancies, such as lung, breast, colorectal, and prostate cancers, but no recommended set of outcomes exists for head and neck cancers.[20–25]

The primary aim of this initiative was to establish a Portuguese consensus on a relevant set of outcome indicators for head and neck cancers that could enable the standardization of the care provided to these patients across institutions at a national level and identify measurement tools and requirements to measure those indicators. Ultimately, the project aims to build evidence on head and neck cancers and thus improve the quality of care delivered to these patients.

METHODS

Working group

A multidisciplinary working group of 26 experts convened to develop a standardized set of outcome indicators for head and neck cancers. This group was organized in

three multidisciplinary teams: one scientific committee (corresponding to the study authors) and two regional workgroups (see the Acknowledgements section).

The Scientific Committee was composed of seven representatives of Medical Oncology, Surgical Oncology, Radiation Oncology, Otolaryngology, Nutrition, and Hospital Pharmacy and was responsible for project leadership and for providing guidance along its several phases.

Regional Workgroups consisted of two groups of eleven experts from the North and eight experts from the South of Portugal, responsible for advising and providing input on the relative importance of outcomes and respective ease of implementation in clinical practice. Regional workgroups comprised representatives from the same clinical areas represented in the Scientific Committee plus Nursing, Maxillofacial Surgery, and Rehabilitation Medicine.

Outcome indicator selection procedure

The definition of a standard set of indicators was a multidisciplinary process implemented through a stepwise approach composed of five phases (Fig. 1).

Phase 1 consisted of a literature review and initial selection of a comprehensive set of outcome indicators. In Phase 2, the Scientific Committee evaluated and discussed the comprehensive set of indicators retrieved from the literature and narrowed it down to a working set of indicators. In Phase 3, the indicators selected by the Scientific Committee were analyzed, discussed, and adjusted by the Regional Workgroups. Phase 4 consisted of a final expert round, in which the Scientific Committee evaluated and discussed the proposals of the Regional Workgroups. Finally, in Phase 5 a head and neck cancer patient association reviewed, commented, and suggested new outcome indicators to the Committees' list, which led to a final standard set of outcome indicators in head and neck cancers.

Phase 1 | Literature review and initial selection of a comprehensive set of potential outcome indicators

A structured literature review was conducted to retrieve an initial comprehensive set of potential outcome indicators. The literature search was based on (i) outcome standard sets previously defined for other malignancies by various entities, including the International Consortium for Health Outcomes Measurement (ICHOM), (ii) head and neck cancer-related clinical trials and studies, (iii) and identification of clinical outcomes, patient-reported outcomes (PROs), and measures of HRQoL in patients with head and neck cancer and respective measurement tools and frequency. The search included all types and stages of head and neck cancer.

Based on data retrieved from this literature review, indicators and measurement tools identified were categorized and compared with those referred in studies to corroborate their relevance for inclusion.

The retrieved results were systematized, and a preliminary comprehensive set of potential outcome indicators was obtained and conveyed to the Scientific Committee.

Phase 2 | Initial Scientific Committee meeting – Evaluation and initial filtering of the comprehensive set of outcome indicators

Phase 2 comprised two steps. In the first step, the members of the Scientific Committee independently analyzed the comprehensive set of potential outcome indicators, rating them on a 10-point Likert-type scale according to their importance in clinical practice and disease management (1 being the least important and 10 the most important) while simultaneously assessing their relevance for the different head and neck cancer sites. In this step, Scientific Committee experts had the opportunity to add new outcome indicators to the predefined list and suggest outcome clustering, changes, or exclusions. The level of consensus of the

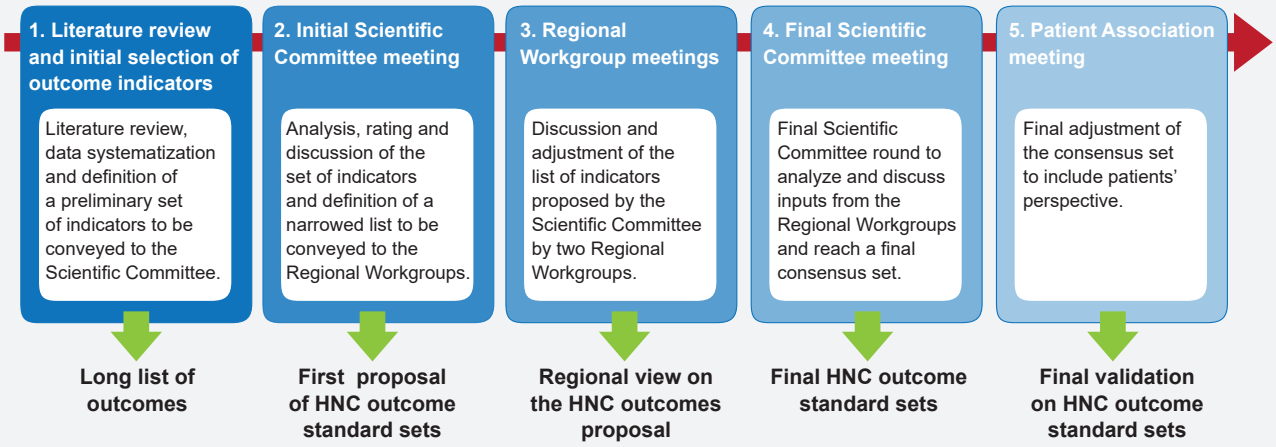

Figure 1 – Stepwise approach to the selection of a standard set of outcome indicators in head and neck cancers

experts was then evaluated, and indicators were clustered according to their relative importance levels: (i) 'high importance' – indicators rating between 9 and 10, (ii) 'medium importance' – indicators rating between 7 and 8, and (iii) 'low importance' – indicators rating between 1 and 6.

In the second step, the Scientific Committee convened to analyze and discuss the results from the previous step. Indicators clustered as 'high importance' were swiftly validated and included in the standard set. The remaining were individually discussed and assessed for the need to be grouped, changed, or excluded. The Scientific Committee also had the opportunity to add new indicators if relevant for the disease treatment or management. A Delphi methodology was applied in this step.

At the end of Phase 2, a set of outcome indicators was obtained and conveyed to the Regional Workgroups for evaluation and discussion.

Phase 3 | Regional Working Group meetings – Evaluation and discussion of the set of outcome indicators

In Phase 3, the set of outcome indicators proposed by the Scientific Committee was discussed by two Regional Working Groups. Similarly to Phase 2, experts from each working group previously analyzed individually the list of indicators according to their relative importance on a 10-point Likert-type scale (from 1 – least important to 10 – most important) and according to their feasibility of implementation in clinical practice on a 5-point Likert-type scale (from 1 – very difficult to implement to 5 – very easy to implement). They then convened and a Delphi methodology was also applied, whereby outcome indicators were evaluated individually. Similarly to Phase 2, the level of expert consensus was also assessed. Indicators that scored between 9 and 10 in the importance rating and 5 in the feasibility of implementation rating were swiftly validated and included in the standard set. The remaining indicators were individually discussed and assessed for the need to be grouped, changed, or excluded.

At the end of Phase 3, a third set of outcome indicators was retrieved and conveyed to the Scientific Committee for final validation.

Phase 4 | Final Scientific Committee meeting – Definition of the final standard set of outcome indicators

Phase 4 consisted of a final expert round with the Scientific Committee to analyze and discuss inputs from the Regional Working Groups and reach a final consensus on a standard set of outcome indicators to be implemented in the management of patients with head and neck cancers in the future.

Additionally, several aspects related to the selected indicators were also discussed at this phase, including their category, preferred designation, definition, measure/response options, metrics, inclusion criteria (i.e., if the indicator is applicable to all patients or to specific head and neck cancer subtypes), time of collection, and reporting source.

Phase 5 | Patient Association meeting – Final validation of the standard set of outcome indicators

The fifth and final phase of the process sought to include the perspective of patients, besides that of the medical community, in an integrated approach to the definition of outcome measures in head and neck cancers. To do this, an interview was conducted with a member of a head and neck cancer Patient Association to retrieve his feedback on the predefined list of indicators, in which he had the opportunity to comment and/or add indicators valued by head and neck patients.

RESULTS

The progress along the five phases of this project regarding selection of indicators is depicted in Fig. 2.

Phase 1

The literature search identified six randomized clinical trials and 60 studies in head and neck cancer, as well as four reports on standard outcome sets previously defined for other malignancies. All literature sources were reviewed until a saturation of outcome indicators was achieved at 164 indicators, which comprised the initial comprehensive set of outcome indicators conveyed to the Scientific Committee. The retrieved indicators were divided in three dimensions with several categories each: (i) case-mix (ii) outcomes and (iii) adverse events (Table 1).

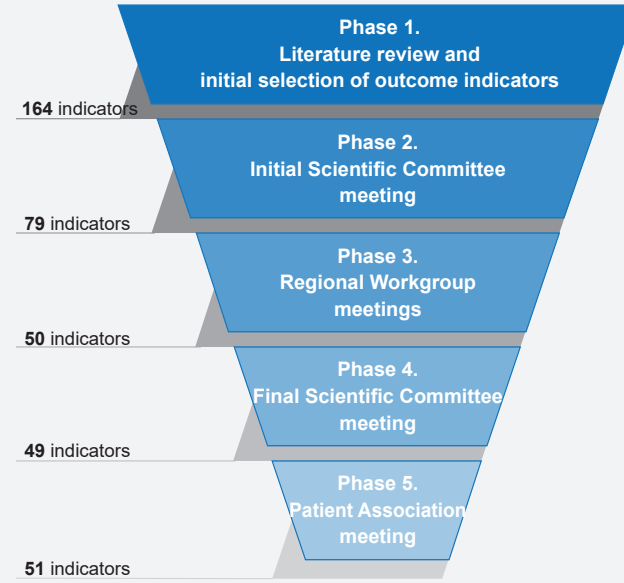

Figure 2 – Selection of head and neck cancers outcome indicators throughout the different phases of the project

Table 1 – Initial comprehensive set of outcome indicators retrieved from the literature search (section 1 of 4)

Dimension	Category	Indicator
Case-mix	Demographics	Age
		Gender
		Ethnicity
		Place of residence
		Smoking history
		Alcohol history
		Education level
		Employment situation
		Income
		Private health insurance
		Marital status
		Family history of cancer
	Tumor-related	Tumor site
		TNM status
		Stage of disease
		Recurrence/Metastases
		Histological type
	Baseline clinical status	Human papilloma virus
		p16 status
		Malignant lesions
		Performance status
		Tumor markers
		Anemia
		Mental illness at diagnosis
		Dysphagia
		Comorbidities
	Nutritional status	Weight loss
		Body mass index
		Nutritional status
		Muscle mass
		Diet type
Outcomes	Survival	Overall survival
		Progression-free survival
		Death related to cancer
		Death unrelated to cancer
	Treatment	Type of treatment
		Treatment intent
		Radiation dose
		Tumor response
		Adverse effects
		Treatment compliance

Table 1 – Initial comprehensive set of outcome indicators retrieved from the literature search (section 2 of 4)

Dimension	Category	Indicator
	Clinical status	Performance status
		Spinal accessory nerve function
		Perioperative complications
		Shoulder capacity
	Health and quality of life	Overall well-being
		Physical functioning
		Social functioning
		Emotional functioning
		Cognitive functioning
		Fatigue and vitality
		Pain
		Activity
		Shoulder capacity
		Mood
		Anxiety
		Recreation
		Shortness of breath
		Nausea and vomiting
		Loss of appetite
		Insomnia
		Constipation
		Diarrhea
		Economic difficulties
		Personal care
		Weight changes
		Swallowing problems
		Problems with taste/smell
		Oral cavity problems
		Trouble speaking
		Problems with social meals
		Sexual problems
		Cough
		Aphonia
		Appearance
		Eating problems
		Use of analgesics
		Use of oral nutritional supplements
		Need for tube feeding
		Smoking habits
		Alcohol consumption
		Emotional functioning

Table 1 – Initial comprehensive set of outcome indicators retrieved from the literature search (section 3 of 4)

Dimension	Category	Indicator
	Nutritional status	Nutritional status
		Weight
		Fat percentage
		Body composition
		Tube feeding complications
Adverse events	Hematology	Neutropenia
		Anemia
		Thrombocytopenia
		Leukopenia
		Myelosuppression
		Febrile neutropenia
		Thrombosis
	Parameter variation	Weight loss
		ALT increase
	Chemistry	Hypomagnesemia
		Hypokalemia
		Hyponatremia
	Cardiovascular disorders	Hemorrhage
		Epistaxis
		Atrial fibrillation
	Skin disorders	Skin reaction/dermatitis
		Pruritus
		Dry skin
		Skin reaction to injection
		Hyperpigmentation
	Metabolism and nutrition disorders	Dehydration
		Anorexia
		Loss of appetite
	Reproductive system disorders	Erectile dysfunction
	Gastrointestinal disorders	Sickness
		Mucositis
		Dysphagia
		Diarrhea
		Vomiting
		Constipation
		Sensitive tongue, saliva accumulation
		Defective salivary incontinence
		Dyspepsia

Phase 2

At this phase, the comprehensive list of outcome indicators retrieved from the literature review was initially reduced to 159 potential outcome indicators stemming from the individual analysis of Scientific Committee members. A total of 77 outcome indicators with high importance (rate of importance 9 − 10), 71 indicators with medium importance (rate of importance 7 − 8), and 11 indicators with low

Table 1 – Initial comprehensive set of outcome indicators retrieved from the literature search (section 4 of 4)

Dimension	Category	Indicator
	General disorders	Fatigue
		Fever/Pyrexia
		Pain
		Flu-like symptoms
		Mouth pain
		Apathy
		Trismus
		Hyposalivation (xerostomia)
	General disorders and administration site reactions	Infusion reactions
	Immunological disorders	Infection
		Paronychia
	Musculoskeletal disorders	Fibrosis
		Arthralgia
		Osteonecrosis
	Neurological disorders	Dizziness
		Dysgeusia
		Partial seizures
		Insomnia
	Eye disorders	Conjunctivitis
	Dental disorders	Stomatitis
		Radiation caries
	Renal and urinary disorders	Kidney failure
	Respiratory disorders	Dyspnea
		Cough
	Other/Not classified	Muscle mass loss
		Nephrotoxicity
		Neurotoxicity
		Laryngeal toxicity
		Ototoxicity
		Skin toxicity
		Hematologic toxicity
		Ulcers
		Suppuration
		Odor
		Swelling
		Gastrointestinal perforation
		Wound complications
		Cheilitis
		Muscle spasms
		Palmoplantar erythrocytosis
		Pneumonia
		Death caused by toxicity
		Hyperthyroidism
		Hypothyroidism

importance (rate of importance 1 − 6) were rated. These were subsequently discussed and readjusted according to the experts' opinion and clinical practice. The main changes to the initial set retrieved from Phase 1 were the grouping of 'clinical basal' and 'clinical status' categories in a single one named 'clinical status' within the 'baseline' dimension, and the exclusion of the 'adverse events' dimension and its incorporation in the 'treatment' category within the 'outcomes' dimension. This resulted in a working set of 79 outcome indicators at the end of Phase 2, organized in two main dimensions: (i) baseline, including demographics, clinical status, tumor-related parameters, and nutritional status, and (ii) outcomes, including survival, treatment, and health and quality of life parameters [Table 1 in Appendix 1 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/18180/15008)]. This working set of 79 indicators was conveyed to the Regional Workgroups.

Phase 3

From the working set of 79 outcome indicators selected by the Scientific Committee, 10 were excluded, 32 were grouped, and 13 were added by Regional Workgroups, resulting in a set of 50 indicators at the end of Phase 3 [Table 2 in Appendix 1 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/18180/15008)]. To reach this set of indicators, the main adjustments performed by the Regional Workgroups to the list of outcome indicators conveyed by the Scientific Committee were (i) grouping of socioeconomic indicators into a new indicator designated 'socioeconomic status'; (ii) grouping of the several nutritional status indicators in a single indicator designated 'nutritional status'; (iii) restructuring of 'health and quality of life' indicators in two new indicators designated 'overall functional status' and 'overall quality of life'; (iv) grouping of oral evaluation indicators in a single indicator designated 'oral pre-malignant lesions'; (v) grouping of disease stage and TNM status in a single indicator designated 'disease stage'; (vi) grouping of 'type of treatment' and 'therapeutic approach' indicators in a single one designated 'therapeutic approach'; and (vii) inclusion of 'airway complications', 'stomatological assessment', 'dysphonia', 'recurrence-free survival', 'treatment adherence', 'surgical approach', and 'ostomy complications' as new indicators.

Phase 4

The set of 50 outcome indicators selected by the Regional Working Groups were again discussed and adjusted by the Scientific Committee, resulting in a final set of 49 indicators. This set was conveyed to the Patient Association for final assessment and validation [Table 3 in Appendix 2 (Appendix 2: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/18180/15009)].

Phase 5

In the last phase of the project, the perspective of patients with head and neck cancer was incorporated in the previously defined set, resulting in a final set of 51 outcome indicators [Table 3 in Appendix 2 (Appendix 2: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/18180/15009)]. The main adjustment made was inclusion of the category 'rehabilitation', as many patients will require some type of rehabilitation along their patient journey (e.g., speech, feeding, social, psychological rehabilitation, among others). The 'rehabilitation' category included comprised two indicators: 'need for rehabilitation' and 'rehabilitation initiation date', which intends to account for the time between diagnosis and rehabilitation start, a key parameter in the rehabilitation progress of patients.

The need to include the caregiver's perspective on the 'overall quality of life' indicator was also mentioned, since patients can experience difficulties in objectively perceiving their status and the voice of caregivers is important for an external and more integrative view of the daily reality of patients.

Overall, patients considered this initiative extremely relevant to eradicate the disparities in the management of head and neck cancers.

DISCUSSION

The rise in healthcare costs and treatment advances have emphasized the importance of value-based health care. This framework is increasingly being acknowledged in the provision of health services, as it has the potential to substantially improve patient outcomes.[26]

The standardization of outcome measures that are meaningful to patients is intrinsic to this value-based approach but has been a major challenge that only recently started to be addressed in several medical conditions. In head and neck cancers, it represented an unmet need, emphasized by the fact that this is a complex disease that requires a multidisciplinary approach from several medical specialties that do not always communicate in an optimal way towards the best patient management. The present collaborative approach set out to tackle this unmet need.

The development of a standardized set of patient-centered outcomes in head and neck cancers was a national project that convened a multidisciplinary working group. The standard set of outcome indicators retrieved at the end of the project was based on a literature review and clinical and patient input and is believed to capture key outcomes relevant to patients with head and neck cancer over the full cycle of care, from diagnosis to treatment completion, survivorship, and rehabilitation. Its implementation will enable health institutions and practices to restructure health care delivery based on a value-centered approach.

The project sought to aggregate several medical specialties participating in head and neck cancer management and also include the perspective of patients on the outcomes that matter to them, in an effort to obtain an integrated vision of a standard set of outcomes to be systematically measured in all patients with this condition. The retrieved consensus comprised 51 indicators from eight different outcome hierarchy levels: demographics, clinical status, tumor-related characteristics, nutritional status, treatment, survival, rehabilitation, and health and quality of life, which should be routinely implemented in clinical practice.

The set of indicators devised from this project represents a proof-of-concept and intends to pave the way for broader adoption and for endorsement by national policies and regulatory entities. Although randomized controlled trials remain the gold standard for comparison of treatment outcomes, outcome measurement in routine clinical practice can better reflect outcomes in a real-life setting and have a more direct impact for patients.

Centers are now encouraged to implement the standard set-in healthcare institutions and systematically collect that information in the clinical practice, so that health care delivery to these patients can be improved in years to come. This can be done in a stepwise manner, beginning with retrieval of a small group of indicators and subsequently expanding it to include a larger number. This structured data collection has several challenges, as it will require investment in human resources and information technology, training clinical staff, and redesigning the clinical workflow. Most importantly, it will require a change in clinical attitudes. However, its implementation, not only at the point of care but also for retrospective and comparative analyses, is key for quality improvement within health institutions and to generate evidence.

The main strength of this study is the combination of the perspective of a relevant team of experts and a patient association related to head and neck cancers to obtain the most accurate set of indicators relevant for patients. This cross-disciplinary effort improves the consistency of data and their relevance to patients, besides health services. The main limitation is that this project is a proof-of-concept, and its output represents a starting point in the definition of a true global outcome standard set in head and neck cancers. Therefore, it should be subject to additional and regular discussion, review, and adjustments.

The experience of collecting these outcomes in clinical practice will be important to understand their applicability and make any necessary adjustments. In the future, they should be updated, ideally on an annual basis, based on feedback from implementing Centers and developments in the field of head and neck cancer.

CONCLUSION

The aim of this initiative was to develop a standardized set of patient-centered outcome indicators to be systematically used during disease management to evaluate the quality of care in head and neck cancers across disease management and patient journey. Through a literature review and clinical and patient inputs, a set of indicators was achieved, which represents a proof-of-concept to be further validated and widespread adopted in the different clinical settings. The routine and systematic collection of these indicators will allow monitoring and comparing head and neck cancer patient outcomes within and across institutions and improve them in the long term.

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AUTHOR CONTRIBUTIONS

All authors report substantial contributions to the conception of the work; Drafting the work and revising it critically for important intellectual content; Final approval of the version to be published; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

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REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68:394-424.
2. El-Naggar AK, Chan JK, Grandis JR, Takata T, Slootweg P. WHO Classification of Head and Neck Tumours. In: WHO Classification of Tumours, 4th ed. Lyon: IARC Press; 2017.
3. The Cancer Genome Atlas Network. Comprehensive genomic characterization of head and neck squamous cell carcinomas. Nature. 2015;517:576-82.
4. Leemans CR, Snijders PJ, Brakenhoff RH. The molecular landscape of head and neck cancer. Nat Rev Cancer. 2018;18:269-82.
5. Taberna M, Mena M, Pavón MA, Alemany L, Gillison ML, Mesía R. Human papillomavirus-related oropharyngeal cancer. Ann Oncol. 2017;28:2386-98.
6. Miranda-Galvis M, Loveless R, Kowalski LP, Teng Y. Impacts of environmental factors on head and neck cancer pathogenesis and progression. Cells. 2021;10:389.
7. Pfister DG, Spencer S, Adelstein D, Adkins D, Anzai Y, Brizel DM, et al. Head and neck cancers, version 3.2020, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Cancer Netw. 2020;18:873-98.
8. Seiwert TY, Burtness B, Mehra R, Weiss J, Berger R, Eder JP, et al. Safety and clinical activity of pembrolizumab for treatment of recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-012): an open-label, multicentre, phase 1b trial. Lancet Oncol. 2016;17:956-65.
9. Cohen EE, Soulières D, Le Tourneau C, Dinis J, Licitra L, Ahn MJ, et al. Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study. Lancet. 2019;393:156-67.
10. Ferris RL, Blumenschein G, Fayette J, Guigay J, Colevas AD, Licitra L, et al. Nivolumab for recurrent squamous-cell carcinoma of the head and neck. N Engl J Med. 2016;375:1856-67.
11. Burtness B, Harrington KJ, Greil R, Soulières D, Tahara M, Castro Jr G, et al. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. Lancet. 2019;394:1915-28.
12. Gatta G, Capocaccia R, Botta L, Mallone S, De Angelis R, Ardanaz E, et al. Burden and centralised treatment in Europe of rare tumours: results of RARECAREnet—a population-based study. Lancet Oncol. 2017;18:1022-39.
13. Braakhuis BJ, Brakenhoff RH, René Leemans C. Treatment choice for locally advanced head and neck cancers on the basis of risk factors: biological risk factors. Ann Oncol. 2012;23:x173-7.
14. Chow LQ. Head and neck cancer. N Engl J Med. 2020;382:60-72.
15. U.S. Department of Health and Human Services. Better, smarter, healthier: In historic announcement, HHS sets clear goals and timeline for shifting Medicare reimbursements from volume to value. 2015. [cited 2021 Mar 04]. Available from: https://www.hhs.gov/about/news/2015/01/26/better-smarter-healthier-in-historic-announcement-hhs-sets-clear-goals-and-timeline-for-shifting-medicare-reimbursements-from-volume-to-value.html.
16. Porter MT. Redefining health care: creating value-based competition on results. Cambridge: Harvard Bus Press; 2006.
17. Lee VS, Kawamoto K, Hess R, Park C, Young J, Hunter C, et al. Implementation of a value-driven outcomes program to identify high variability in clinical costs and outcomes and association with reduced cost and improved quality. JAMA. 2016;316:1061.
18. Porter ME. What is value in health care? N Engl J Med. 2010;363:2477-81.
19. Porter ME, Larsson S, Lee TH. Standardizing patient outcomes measurement. N Engl J Med. 2016;374:504-6.
20. Cramer-van der Welle CM, van Loenhout L, van den Borne BE, Schramel FM, Dijksman LM. 'Care for Outcomes': systematic development of a set of outcome indicators to improve patient-relevant outcomes for patients with lung cancer. BMJ Open. 2021;11:e043229.
21. Ong WL, Schouwenburg MG, van Bommel AC, Stowell C, Allison KH, Benn KE, et al. A standard set of value-based patient-centered outcomes for breast cancer. JAMA Oncol. 2017;3:677.
22. Zerillo JA, Schouwenburg MG, van Bommel AC, Stowell C, Lippa J, Bauer D, et al. An international collaborative standardizing a comprehensive patient-centered outcomes measurement set for colorectal cancer. JAMA Oncol. 2017;3:686.
23. Martin NE, Massey L, Stowell C, Bangma C, Briganti A, Bill-Axelson A, et al. Defining a standard set of patient-centered outcomes for men with localized prostate cancer. Eur Urol. 2015;67:460-7.
24. Morgans AK, van Bommel AC, Stowell C, Abrahm JL, Basch E, Bekelman JE, et al. Development of a standardized set of patient-

centered outcomes for advanced prostate cancer: an international effort for a unified approach. Eur Urol. 2015;68:891-8.
25. International Consortium for Health Outcomes Measurement (ICHOM). Patient-centered outcome measures. [cited 2021 Mar 05]. Available from: https://www.ichom.org/standard-sets/.
26. Berenson RA, Kaye DR. Grading a physician's value - the misapplication of performance measurement. N Engl J Med. 2013;369:2079-81.