



HN-CLEAR: Head and Neck Consensus Language for Ease and Reproducibility, a Multidisciplinary Consensus Mechanism for Head and Neck Pathology

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Background

The head and neck region harbors a diverse range of tissue types and pathologies in close anatomical proximity. It also includes some of the most common human malignancies such as squamous cell carcinoma of the skin and aerodigestive tract while also including infections, inflammatory disorders, and many rare entities such as salivary gland and

odontogenic neoplasms. The head and neck brings together pathologists with diverse training and sub-specialty backgrounds including head and neck, maxillofacial, endocrine pathology, dermatopathology, cytopathology, and other subspecialists as well as general surgical pathologists. The broad range of diagnostic terminologies and prognostic issues that influence patient management in head and neck pathology are further confounded by overlapping and confusing terminology and lack of robust evidence in many areas. Uniform

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and evidence-based diagnostic and prognostic terminologies are needed to inform the treatment of patients and support the design of clinical trials, epidemiological and fundamental research, cancer registries for education and preventive strategies, and assist policy makers in the allocation of health care resources.

The World Health Organization (WHO) Classification of Tumours [1], the American Joint Commission on Cancer (AJCC) [2], the Union of International Cancer Control (UICC) [3], and the International Collaboration on Cancer Reporting (ICCR) [4, 5], through their periodic iterations, provide diagnostic, prognostic, and pathology reporting guidelines for all organ systems including the head and neck and attempt to inform equitable patient care across geopolitical boundaries. These bodies require level III National Health and Medical Research Council (NHMRC) [6] evidence for including and updating diagnostic entities and prognostic parameters. Such evidence may not be available within the time frame of an edition, thus, hampering progressive inclusions. Also, the developments in pathology, largely fuelled by the advances in molecular diagnostic techniques, are fast outpacing the WHO, AJCC, UICC, and ICCR updates. These problems are certainly not unique to head and neck pathology. Indeed, co-operative groups such as the International Society of Urologic Pathology (ISUP) [7], International Association for the Study of Lung Cancer (IASLC) [8], and the Consortium to Inform Molecular and Practical Approaches to CNS Tumor Taxonomy (cIMPACT) [9], have been working to develop consensus recommendations for practicing pathologists that also intend to inform upcoming WHO diagnostic and AJCC staging iterations.

A co-operative group within head and neck pathology community is needed to refine the quality of diagnostic and prognostic information with the ultimate goal of improving patient outcomes and quality of life. To address this need, Head and Neck Consensus Language for Ease And Reproducibility (HN-CLEAR) is a global initiative to unify and strengthen the diagnostic and prognostic parameters in head and neck pathology through collection and analyses of high-quality data when available and the generation of new data when required. HN-CLEAR is sponsored by the North American Society of Head and Neck Pathology (NASHNP) and will have broad representation of pathologists across the globe supported by an international clinical advisory group to ensure relevance and facilitate implementation. The primary goal of HN-CLEAR is to provide consensus guidelines for currently ambiguous diagnostic or prognostic concepts through stringent collation and analyses of high level data. HN-CLEAR will evaluate the rapidly evolving immunohistochemistry and molecular information in the diagnosis, prognosis, and prediction for head and neck neoplasms. Similar to cIMPACT, IASLC, and ISUP, HN-CLEAR will complement (not supersede) the workings of WHO, AJCC,

and ICCR by providing robust evidence and terminology in a timely manner and drafting recommendations that can be included in upcoming iterations.

Structure

HN-CLEAR will conduct its work through three types of committees, a Steering Committee, a Clinical Advisory Panel, and the Working Groups. All three committees will have global representation to ensure that head and neck pathology issues across the world are addressed.

The Steering Committee will include head and neck pathologists with extensive experience in diagnostic head and neck pathology who are currently active in the field. Members are selected based on their expertise and experience in participating in international publications and consensus bodies such as the WHO, ICCR, UICC, or AJCC, and taking into account global representation and diversity through a process of nomination and selection by an independent group of three former NASHNP officers. A Chair of the Steering Committee is selected through internal voting by the members of the Steering Committee. The Chair and the members serve three year terms with additional terms possible after rotating off the Committee. All rotations will be in a staggered manner to ensure continuity of the work underway.

The Steering Committee will be supported by a Clinical Advisory Panel consisting of head and neck surgeons, oral and maxillofacial surgeons, endocrine surgeons, medical and radiation oncologists/therapists, and a biostatistician with the possibility of other types of clinical personnel and patient advocates. The Clinical Advisory Panel members are also initially nominated and selected in the same manner as the Steering Committee. They also serve 3 year terms.

New members are nominated by the Chair, based on the criteria and considerations listed above, and added after approval by the Committees. The 3-year term limit with the requirement to rotate off the committees should promote flexibility, diversity, and international representation.

The Steering Committee and the Clinical Advisory Panel will work closely to identify topics for development of consensus recommendations, by inviting and constituting a Working Group of pathologists and clinicians with relevant expertise to review data and draft consensus recommendations.

Working Groups will include up to 15 members with subject matter expertise. Clinicians, biologists, and statisticians with relevant expertise will also be included. At least two members of the Steering Committee and one member of the Clinical Advisory panel will serve on the Working Group.

Topics for consideration will be solicited from the head and neck medical community by the Steering Committee.

A standard topic solicitation form will be emailed using the email addresses within NASHNP, WHO, and ICCR list servers as well as the records of local governing bodies or colleges if available and/or permitted, for example, the Royal College of Pathologists of Australasia, Head and Neck Structured Pathology Reporting Committee, etc. to assure broad, global opportunity and participation.

In an ideal year, work will be performed on one common issue and one rarer topic simultaneously by two different Working Groups. However, the expectation is for at least one Working Group to be active annually.

The Working Groups will

1. Review the literature on the chosen topic.
2. Collate and analyze the available data. Stringent methodologies will be adopted to ensure that all data collection and analyses are methodical, unbiased, and robust. Any of the following methods, most suited to the topic and available data may be used:
 - (a) Meta- analyses of data collated using Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). The studies will be registered through Prospective Register of Systematic Reviews (PROSPERO).
 - (b) In case of rare entities, where data may be lacking, a survey of practicing pathologists with relevant expertise using Delphi study protocols. Circulation of slide examples of entities with development of terminology may be used.
 - (c) Generation of data with inter-observer variability analyses.
3. Formulate proposed consensus recommendations including possible alternatives.
4. Present the consensus recommendations to the Steering Committee and the Clinical Advisory panel.
5. Prepare a manuscript with consensus recommendations for publication and outline mechanisms for implementation.

The Steering Committee will liaise with the Chair of the Working Group to review the study methodologies, draft consensus recommendations, approve the consensus recommendations, and ensure timely completion and dissemination of the recommendations through scientific presentations and freely accessible publications. Activities will be supported by the NASHNP and global head and neck pathology community as needed.

Impact

The goal of HN-CLEAR is to develop consistent diagnostic terminology and prognostic parameters through considered scientific deliberations and supported by robust evidence. The global participation in HN-CLEAR will ensure that head and neck pathology-related diagnostic challenges faced by all pathologists will be prioritized, and the developed guidelines will be compatible with multiple health care systems. Input from the diverse clinical team is critical to ensure that clinically relevant issues impacting patient care are addressed. Involvement of the broad head and neck community is important for dissemination and efficient clinical implementation so that the recommendations also inform the future iterations of WHO, AJCC, UICC, and ICCR diagnostic and staging guidelines.

As Sir William Osler famously said: “As is our pathology, so is our practice.” Thus, we would like to invite all head and neck, maxillofacial, and endocrine pathologists across the world to consider joining the efforts of HN-CLEAR as the teams strive to improve the care provided to patients with head and neck diseases.

Author Contributions RG, MB, JAB, KDH, KM, RRS, LDRT, IW are members of the Steering Committee. PA, BB, RBB, JRC, RF, SH, DNH, RL, and JY are members of the Clinical Advisory Committee NAC, BLN, and PMS: Officers of NASHNP JSL: developed the concept of HN-CLEAR. RG Chairs the first HN-CLEAR steering committee.

Data Availability Not applicable.

Declarations

Competing interests The authors declare no competing interests.

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