

## **Informed Consent Form**

**Dear Sir/Madam:**

We are about to conduct a clinical study titled "**Machine Learning-Based Risk Prediction for Head and Neck Cancerous Lesions: A Multidimensional Study Based on Demographic, Clinical, and Symptomatological Features.**" You may meet the inclusion criteria for this trial; therefore, we invite you to participate. The sponsor of this trial is Nanjing Drum Tower Hospital, and the Principal Investigator is Dr. Chuanyao Lin.

This Informed Consent Form will explain the study's purpose, procedures, potential benefits to you, the risks, inconveniences, or discomforts you may assume, and the key considerations of the trial. It will also outline alternative treatment options available to you and affirm your right to withdraw from the study at any time. Please read this document carefully and consider it thoroughly before making your decision. This form may contain words or information you do not understand; please be sure to ask your study doctor, who will answer your questions until you are satisfied. Before making a decision, you may take this unsigned form home to think it over or discuss it with your family, friends, or anyone you choose. If you decide to participate, please sign and date this form. Your signature will not result in the loss of any of your legal rights. The original signed form will be kept by the investigator, and you will retain a copy for your records.

## **1. Study Background**

Head and neck malignancies (primarily oral, pharyngeal, and laryngeal cancerous lesions) are the sixth most common cancer globally. In recent years, their incidence has continued to rise, posing a severe public health challenge. Because head and neck malignancies are anatomically deep-seated, early clinical symptoms (such as persistent hoarseness, foreign body sensation in the throat, and non-healing oral ulcers) are insidious and lack specificity. Clinically, these are highly similar to symptoms of benign conditions like chronic inflammation, which easily leads to missed diagnoses, misdiagnoses, and delayed treatment. Epidemiological studies show that over 60% of patients have already progressed to a locally advanced stage or present with cervical lymph node metastasis at the time of initial diagnosis. Patients with advanced cancer not only face complex treatment strategies, significant surgical trauma, and heavy financial burdens, but also suffer severe sequelae such as permanent impairment of speech and swallowing functions, leading to a precipitous drop in quality of life and a significantly reduced five-year survival rate.

Currently, the clinical diagnostic pathway for head and neck cancers relies heavily on a series of invasive and resource-intensive examinations. While electronic laryngoscopy can visually assess mucosal lesions, the procedure easily triggers the gag reflex and other discomforts, resulting in poor patient tolerance, and it is highly dependent on the specialist's experience. Imaging technologies like Computed

Tomography (CT) and Magnetic Resonance Imaging (MRI), though valuable adjunctive diagnostic tools providing vital anatomical information, are expensive and have limited accessibility in primary healthcare settings. Furthermore, histopathological biopsy—the gold standard for diagnosis—is an invasive procedure that not only causes physical and psychological distress but also carries the risk of potential complications. These combined factors restrict the feasibility of implementing large-scale, accessible early screening in communities and among high-risk populations, resulting in inefficient allocation of medical resources and a significant proportion of missed and delayed diagnoses in early-stage cases.

Therefore, this study, in collaboration with Shanghai Ninth People's Hospital, aims to explore the high-risk factors for head and neck cancerous lesions across different centers. The goal is to construct a primary screening risk stratification tool for early disease screening and facilitate multidisciplinary joint diagnosis and treatment, thereby effectively improving patients' quality of life and preventing complications.

## **2. Study Objective**

This study aims to utilize machine learning algorithms based on multi-center clinical data to develop a low-cost, non-invasive primary screening risk stratification tool. This tool will be used to identify individuals at high risk for head and neck malignancies and optimize early diagnostic and therapeutic pathways.

## **3. Conditions for Participation**

**Inclusion Criteria:** Patients seeking care at the Department of Otorhinolaryngology-Head and Neck Surgery, Nanjing Drum Tower Hospital, who sign the informed consent form, undergo a laryngoscopy, and have complete clinical data.

**Exclusion Criteria:** Patients who refuse to sign the informed consent form or have incomplete clinical data.

#### **4. Number of Participants and Duration**

This trial is planned to span 4 to 5 years. A retrospective pilot study has already been conducted, collecting data from 8,000 patients for model construction. The current phase is a prospective validation study, aiming to recruit 3,000 subjects. This project involves four centers: Nanjing Drum Tower Hospital, Changzhou No. 4 People's Hospital, Cixi People's Hospital, and Shanghai Ninth People's Hospital. Enrollment will be competitive across the centers.

#### **5. Is Participation and Completion Mandatory?**

Your participation in this trial is entirely voluntary. If you decide to participate, you will be required to sign this informed consent form and will receive a copy of it. If you choose to participate, you may still request to withdraw at any time, and your withdrawal will not affect your standard treatment.

By participating in this clinical study, you will need to complete an initial visit and at least one follow-up visit at our hospital. Your clinical data, questionnaires, and demographic information will be used for research purposes. Six months after your initial visit, you may need to undergo a telephone follow-up or an outpatient follow-up visit to determine the progression of your condition and your treatment status.

You will need to undergo an initial visit, during which an electronic laryngoscopy will be performed at the ENT Department of Nanjing Drum Tower Hospital to determine the nature of your disease. At the 6-month follow-up, you will need to undergo another electronic laryngoscopy at the same department to evaluate your recovery.

## **6. Study Procedures**

Collect basic clinical information and relevant quality-of-life questionnaires from outpatients at the Department of Otorhinolaryngology-Head and Neck Surgery.

Based on laryngoscopy reports and subsequent surgical biopsy pathology reports, categorize enrolled patients into a diseased group and a non-diseased group for downstream data processing and analysis.

Screen high-risk factor data. On the retrospective training set, use feature selection methods such as LASSO regression to identify predictive variables most strongly associated with the outcome.

Apply machine learning to construct a clinical risk factor predictive model.

Collect external validation datasets to verify the reliability and validity of the model.

## **7. Study Content**

The data we need from you primarily includes the following:

Demographics: Age (years), Gender, Education level (middle school or below / high school / college or above), Occupation (manual labor / non-manual labor / retired).

Lifestyle: Smoking index (pack-years = packs per day  $\times$  years smoked), Alcohol consumption (yes/no; frequency/amount), History of betel nut chewing, Preference for spicy/hot food.

Medical History: HPV infection status (serum HPV16/18 antibodies or oropharyngeal swab PCR results), Reflux gastritis (clinical diagnosis via gastroscopy), Diabetes, Immunosuppressive status.

Symptom Characteristics: Type of chief complaint (hoarseness, odynophagia, foreign body sensation, neck mass, etc.), Duration ( $< 2$  weeks /  $\geq 2$  weeks), Presence of progressive worsening.

Laryngeal Questionnaires: Reflux Symptom Index (RSI), Voice Handicap Index-10 (VHI-10).

Electronic Laryngoscopy: Laryngoscopy result report (normal / inflammation / suspicious neoplasm / definite space-occupying lesion; unilateral/bilateral; vocal cord involvement).

## **8. Participant Responsibilities**

Provide accurate past medical history and current condition information.

Inform the principal investigator of any health issues that arise during the study period.

Follow the instructions of the research staff and study doctors.

Feel free to ask questions at any time if anything is unclear.

## **9. Alternative Treatment Options**

You may choose not to participate in this study. This will not have any adverse effects on your access to routine care.

## **10. Potential Side Effects, Risks, and Discomforts**

None.

**11. Potential Benefits and Risks**

Potential Benefits: This study collaborates with Changzhou No. 4 People's Hospital, Cixi People's Hospital, and Shanghai Ninth People's Hospital to explore high-risk demographic, symptomatological, and clinical factors associated with head and neck cancerous lesions across different centers. The goal is to identify specific high-risk diagnostic factors for these lesions, enabling early screening and lifestyle interventions for such patients. Your participation in this study may not bring significant direct clinical benefits to your own diagnosis or treatment. However, this project will provide new insights and paradigms for the diagnosis and treatment of head and neck cancerous lesions, as well as an understanding of the demographic and lifestyle factors related to their pathogenesis. This will greatly benefit the future diagnosis and lifestyle intervention of patients with head and neck cancers, improving their quality of life.

Potential Risks: This is a non-interventional study that will not affect or interfere with your routine medical diagnosis and treatment; therefore, it will not add any extra risks. If you have any questions during the study, you may consult the study doctor or the Ethics Committee.

**12. New Information During the Study**

If new information becomes available during the study, your study doctor will inform you promptly and discuss with you whether you wish to continue participating in the trial. If you decide to withdraw, your study doctor will arrange follow-up care for you. If you choose to continue, you may be asked to sign a new informed consent form. Alternatively, if your study doctor determines that withdrawing from the study is in your best interest, they will explain the reasons and arrange your subsequent treatment.

**13. Your Rights**

Participation in this study is entirely voluntary. You may withdraw your informed consent at any time without providing a reason. Your decision to participate or not will not result in any prejudice or affect your medical care. It is your right not to participate or to withdraw midway; you do not have to participate in this study to receive treatment for your illness. If you choose to withdraw, in the interest of your safety and the objective evaluation of the study, we ask that you cooperate with the study doctor to complete the relevant end-of-study evaluations and laboratory tests. You may consult your study doctor at any time if you have questions during the research.

#### **14. Costs and Compensation for Study-Related Injury**

As this study primarily involves the collection of patients' clinical data and related quality-of-life questionnaires, and solely informs patients that their clinical data will be used for this study (in addition to clinical examinations) upon signing the informed consent, this study poses absolutely no physical harm or risk to your health. Therefore, there is no compensation provided for transportation, lost wages, etc.

#### **15. Privacy and Confidentiality**

Any personal information and data obtained about you during the trial will be kept strictly confidential. Your clinical data and questionnaire reports will be identified by a study number/code rather than your name. Information that could identify you will not be disclosed to anyone outside the research team without your permission. All research members and the sponsor are required to keep your identity confidential. Your files will be stored in a locked filing cabinet accessible only to research personnel. To ensure the study is conducted according to regulations, government regulatory authorities, monitors authorized by the sponsor, or Ethics Committee members may access your study-related information at the research site when necessary; however, they are bound not to disclose your information to third parties. Although the study results may be published, your identity will not be revealed in

these publications. The study data will be kept at Nanjing Drum Tower Hospital, Affiliated Hospital of Nanjing University Medical School. The research report will be submitted to the National Medical Products Administration (formerly CFDA) and the sponsor.

By signing this written informed consent form, you agree that the study doctor may collect and process your personal information ("Study Data") for this study, including: personal data regarding your date of birth, gender, ethnicity, and physical/mental health status. Unless you withdraw your consent, this means your study data may be used indefinitely. If you withdraw your informed consent, the study doctor and sponsor will stop using your personal data; however, personal data already shared prior to the withdrawal may still be used.

The study doctor will use the study data to conduct clinical research. The sponsor may use the data to: conduct clinical research, support applications for marketing authorization of investigational drugs, and develop new pharmaceutical products, diagnostics, or medical devices.

You have the right to request access to the personal data held by the study doctor and the sponsor. You also have the right to request corrections to any inaccuracies in your personal data, and the right to withdraw your informed consent at any time. If you wish to exercise these rights, please contact the study doctor.

## **16. Post-Study Treatment**

None.

## **17. Contact Information**

If a study-related injury occurs, or if you have any questions regarding the study or the study procedures, please contact: Doctor's Name: Chuanyao Lin Address: Nanjing Drum Tower Hospital Phone: 13913854033

**Version: 3.0**

**Version Date: January 22, 2026**

If you have any questions related to your rights as a subject, please contact the Medical Ethics Committee of Nanjing Drum Tower Hospital, Affiliated Hospital of Nanjing University Medical School at: Phone: 025-68182923.