# Learning Objectives

## HNSCC & Study Design

* Define HNSCC, its causes, burden, demographics

Head and neck squamous cell carcinoma is a group of cancers that arise in the mucosal surfaces of the head and neck — oral cavity, pharynx, and larynx. The major risk factors are tobacco and alcohol, and more recently HPV infection. Globally, it’s an important public health problem, with higher incidence in men, and particularly high rates in South Asia due to betel quid chewing.

* Provide a definition of cause

The definition of cause we will use is: a factor is a cause of an event if its event operation increases the frequency of the event.

* Define incidence and prevalence & relationship

Incidence is new cases per unit time, prevalence is existing cases at a given time. They are related by the duration of disease: prevalence roughly equals incidence times duration.

The simplest measure of frequency is prevalence: the frequency of a characteristic, or the proportion of a group which has the characteristic, at one point.

An incidence rate is the frequency of incidents, events such as deaths or new diagnoses of disease, over a defined time period; it has units of time.

prevalence rate (P) equals average incidence rate (I) multiplied by average duration (D)

* Surveillance example (heterogeneity in HNSCC)

In many high income countries, the group of HNSCC caused by tobacco and alcohol has decreased, while the incidence of HPV-related HNSCC has increased. This indicates that these opposite trends coexist, showing that HNSCC is a heterogeneous disease.

* Describe cohort, case-control, clinical trials

Cohort studies we are comparing groups of individuals who are classified by their exposure to the putative causal factor.

Cohort studies are observational studies testing for causality. The study chooses a group of people who have thee- same characteristic (usually a disease-free person), classifies them into two different groups (exposed and unexposed) and observes them to measure the outcome(ed,ed-,e-d,e-d-).

case-control studies compare a group of individuals who have experienced the

outcome under study with a group who have not.;

groups of individuals are defined in terms of whether they have or have not already experienced the outcome under consideration, and the exposure is then measured

clinical trials are experimental, randomizing people to interventions and following outcomes.

Participants are chosen by basic criteria and assigned to different groups randomly(treatment group and control group), and followed to evaluate the effect of health outcomes.

* Basic measures of association

Risk difference is just subtraction of risks, relative risk is ratio of risks, odds ratio comes from odds in case-control studies. Each design tends to pair with one measure more naturally.

* Systematically describe study results

You always want to summarize: What was the exposure or intervention? What was the outcome? What was the study design? What was the study population? And what was the main result — for example, risk of progression at 6 months was 25% vs 50%.

## Cancer Biology Basics

* Explain what cancer is

Cancer is fundamentally uncontrolled cell growth. Cells divide when they shouldn’t, resist signals to stop, avoid dying, invade nearby tissues, and sometimes spread to distant sites.

* Describe the Hallmarks of Cancer

The hallmarks of cancer include self-sufficiency in growth signals, insensitivity to anti-growth signals, evading apoptosis, limitless replicative potential, sustained angiogenesis, and the ability to invade and metastasize.

* Describe several drivers of cancer

Drivers of cancer include mutations in DNA, chronic exposure to carcinogens like tobacco or UV light, viral infections such as HPV, and failures of DNA repair. These alter oncogenes and tumor suppressor genes, pushing the cell toward malignancy.

## Validity

* Define validity; internal vs external

When we say a study result is valid, we mean it reflects the truth. Internal validity means the result is true for the study participants. External validity means whether we can generalize it to the source or target population.

The internal validity of a study is a measure of how confident we can be that a difference in outcome between these two groups can be attributed to the effects of the exposure or intervention.

The external validity of a study refers to the ability to apply the results of the study to a wider population.

* Major threats to validity

The major threats to validity are selection bias, observation bias, and confounding. Interaction is often discussed alongside these because it changes how we interpret associations.

* **Evaluate validity from subject selection**

Think about the funnel: target population, source population, eligible population, study entrants, and study completers. At each step, if selection is not representative or is biased, validity can be compromised.

* Misclassification & observation bias

Misclassification means you measured exposure or outcome incorrectly. If misclassification happens equally across groups, it’s nondifferential; if it differs between groups, it produces differential observation bias.

* Confounding and interaction

Confounding occurs when a third factor is associated with both exposure and outcome, distorting the relationship—for example, smoking confounds the relationship between coffee drinking and lung cancer. Interaction means the effect of exposure depends on another variable—for example, the effect of asbestos exposure on lung cancer risk is much stronger among smokers.

Confounding is defined as a distortion of an exposure–outcome association brought about by the association of another factor with both outcome and exposure.

This large variation in the association between cervical cancer and smoking demonstrates effect modification (also called interaction).

## Evolution & Treatment (HNSCC specifics)

* Evolution and cancer connection

Cancer evolves because cells accumulate mutations and those with growth advantages are selected. Within a tumor, you often see clonal selection—subclones that are resistant to treatment become dominant after therapy.

* General cancer treatment

The main treatment modalities are surgery, radiation, chemotherapy, and increasingly immunotherapy. Often, these are combined—multimodal therapy is common.

* HNSCC treatment specifics

For HNSCC, treatment depends on stage and HPV status. HPV-positive oropharyngeal cancers tend to respond better to radiation and chemotherapy, and there are trials investigating treatment de-escalation in that group. HPV-negative tumors are more aggressive and require standard intensive therapy.

## Cell Cycle & Molecular Drivers

* Cell-cycle dysfunction in cancer

Every cancer has cell cycle dysregulation. The checkpoints that normally control progression from G1 to S, or from G2 to M, fail. As a result, cells keep dividing when they shouldn’t, and damaged DNA is passed on.

* Tumor suppressor vs proto-oncogene

Tumor suppressors are like brakes—for example, p53 or RB. When they are lost or inactivated, cells divide unchecked. Proto-oncogenes are like accelerators—when mutated or overexpressed, they become oncogenes, pushing the cell cycle forward. The difference is between brakes versus accelerators of cell division.