# Research Proposal:

## HPV Infection among Cambodian Patients with Head & Neck Squamous Cell Carcinoma

**Jacob E. Gardner**

MD/MPH Candidate, Case Western Reserve University, Class of 2025

jeg153@case.edu

jacobegardner.github.io

Jacob Gardner

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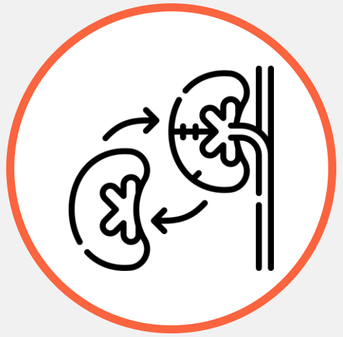
# Background: OSCC Risk Factors

Tobacco products
- Smoking & smokeless
- Relative risk: 1.2 – 9.7
- Dose-response relationship

Alcohol
- Relative risk: 1.5 – 12.3
- Dose-response relationship
- **Risk is multiplicative – not additive – with concurrent tobacco use**

Betel nut chewing
- Relative risk: 1.6 – 11.0
- Dose-response relationship
- Increased risk with tobacco added to quid



Immunocompromise
- Solid organ transplants
- HIV/AIDS
- Relative risk: 2.3 – 3.0

Human Papillomavirus (HPV)
- HPV-16 & 18 most common
- Relative risk: 3.0 – 6.0

# Background: HPV Vaccination in Cambodia

- HPV vaccines initially developed to prevent anogenital infection, now shown to prevent oral infections
    - FDA approved to prevent HNSCC in 2020
- October 5, 2023 – Cambodian MoH introduced one-dose HPV vaccination for 9-year-old girls into national immunization schedule.
- Effect of vaccination depends on
    - Choice of vaccine
    - Vaccine strategy
    - Vaccine uptake
    - Local prevalence of HPV types
    - Local attributable fractions

# Background: HPV Vaccination in Cambodia

Choice of vaccine

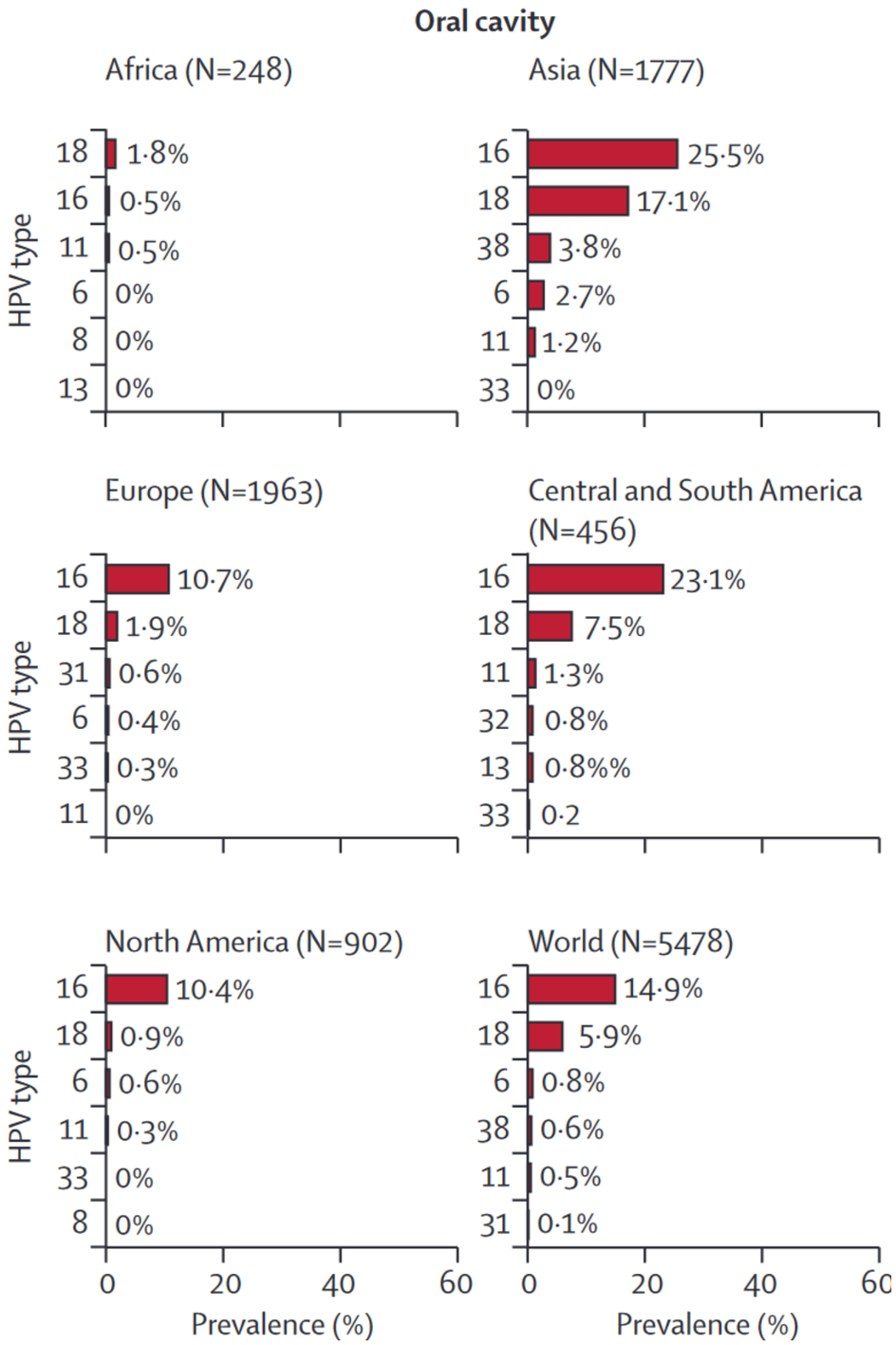
- Cervarix (bivalent): HPV-16, 18
- Gardasil (quadrivalent): HPV-6, 11, 16, 18
- Gardasil9 (nonavalent): HPV-6, 11, 16, 18, 33, 45, 52, 58

Vaccine strategy

- 1 vs. 2 doses
- Offering catch-up vaccination
- Vaccination of males

Vaccine uptake

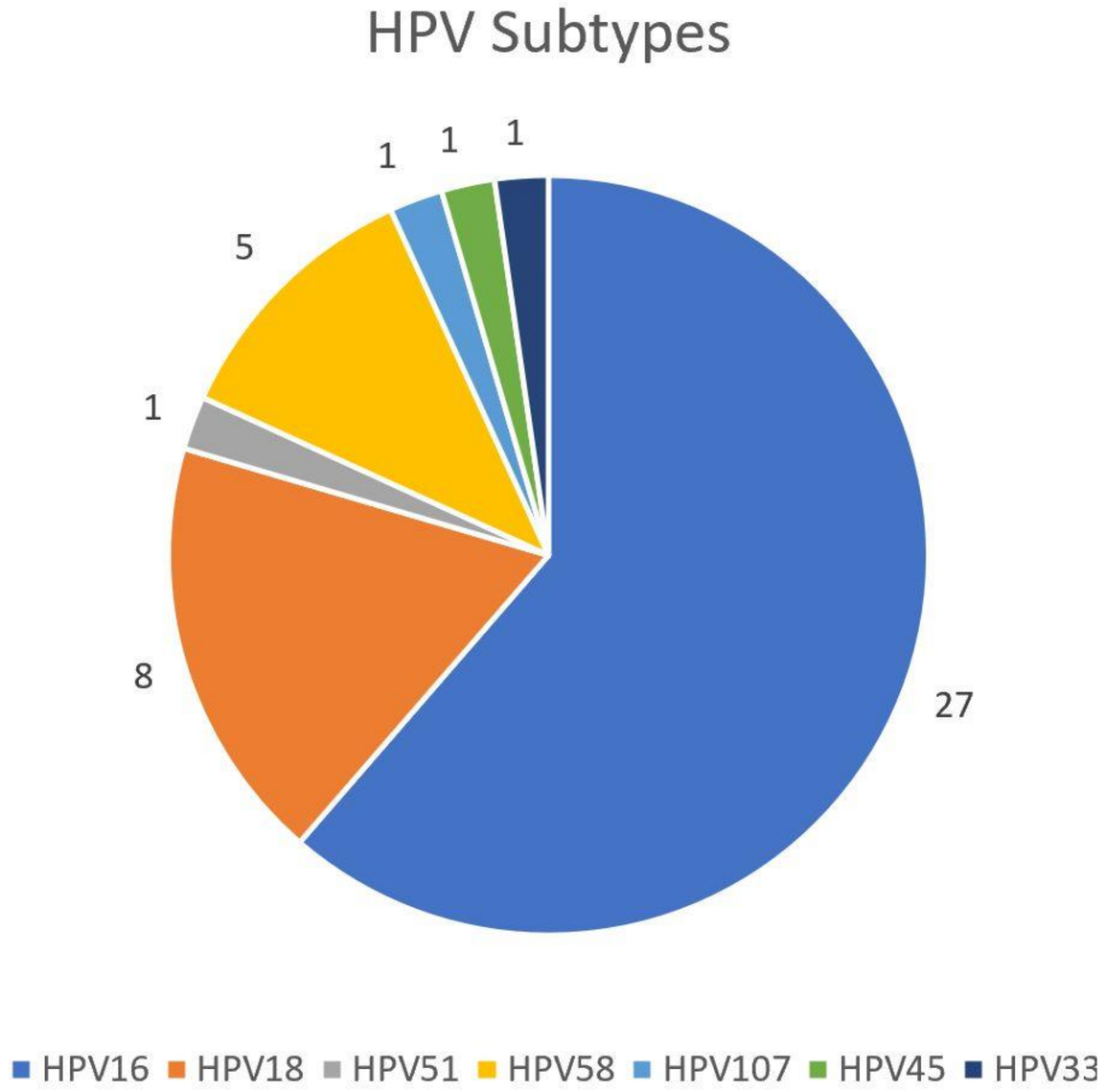
- 2017 HPV vaccine demonstration program
- 316 girls enrolled
- 84% completed the 2-dose regimen




Adapted from Ndiaye et al. 2014

Prevalence of HPV types & attributable fractions

- HPV DNA detected in ~24% of OSCC
  - **33%** of OSCC in Asia
- Attributable fraction: **6.8 – 16.3%**
  - Presence of HPV DNA within a tumor is insufficient to establish causality
  - HPV may be a “passenger infection”
- HPV-16 & 18 most commonly detected
  - Account for nearly 100% of HPV-positive OSCC
  - Type prevalence can vary across geographic regions and populations
  - **Problem:** Little known about prevalence of HPV types in Cambodia




Our group since 2018 – First study of HPV types among Cambodian cervical cancer patients

- Sequencing HPV DNA from 50 cervical tumor biopsies from Calmette Hospital
- HPV-16 & 18 detected in 81.4%
- HPV-58 detected in 11.6%
- 2.3% infected with type not protected against by nonavalent vaccine
- 18.6% infected with types not protected against by bivalent/quadrivalent vaccines

# HPV Infection among Cambodian Patients with Head & Neck Squamous Cell Carcinoma

Type

- Observational
- Cross-sectional
- Prospective cohort

Population

- Newly diagnosed, histologically confirmed HNSCC
- Age 18+

Sites

- Preah Ang Duong Hospital, Phnom Penh, Cambodia
- Khmer-Soviet Friendship Hospital, Phnom Penh, Cambodia
- Cleveland Clinic Lerner Research Institute, Cleveland, Ohio, USA

Specimens

- 50+ FFPE incisional biopsies
- 50+, 10ml blood samples
- 10+ surgical specimens of tumor with negative margins, (+) & (-) lymph nodes

# HPV Infection among Cambodian Patients with Head & Neck Squamous Cell Carcinoma

## A 4-part study

**1**

HPV Epidemiology and Implications for Vaccination and HNSCC Treatment

**2**

Insights into the Biology and Clinical Behavior of HPV-Associated HNSCC using Spatial Transcriptomics

**3**

Constructing a Human-Immunized Single-Chain Variable Fragment Antibody Library

**4**

Geodemographic Comparisons

# 1.

# HPV Epidemiology and Implications for Vaccination and HNSCC Treatment

***Rationale*** – Predicting impact of HPV vaccination on HNSCC incidence in Cambodia.

***Rationale*** – Interpreting the applicability of HPV-based guideline changes & deintensification trials

- HPV testing not part of any Cambodian hospital's standard diagnostic procedures for HNSCC.
- Testing with p16 immunohistochemistry is most accurate only in "geographic regions where HPV is etiologically responsible for a high proportion of cancers." – NCCN Guidelines 2024

# 1.

# HPV Epidemiology and Implications for Vaccination and HNSCC Treatment

*Objectives*

1. Determine the fraction of HNSCC attributable to HPV infection in the Cambodian population.
2. Determine which subtypes of HPV are most prevalent in those cancers associated with HPV.

*Implications* – Results may help inform:

- If/how HPV testing is integrated into standard diagnostic protocols for HNSCC in Cambodia
- If results of ongoing treatment deintensification trials are applicable in Cambodia
- Future HPV vaccination strategy.

# 2.

# Insights into the Biology and Clinical Behavior of HPV-Associated HNSCC using Spatial Transcriptomics

*Rationale* – The biology underlying the clinical differences between HPV-associated and HPV-independent HNSCC are incompletely understood

- ST is a novel histological technique applied to tissue slides
- Produces visualizations of *what* genes are being expressed *where* within tissue.
- Observing and comparing gene expression profiles give unique viewpoint into underlying biology of tumor behavior.

# 3.
# Human-Immunized Single-Chain Variable Fragment Library

*Rationale*

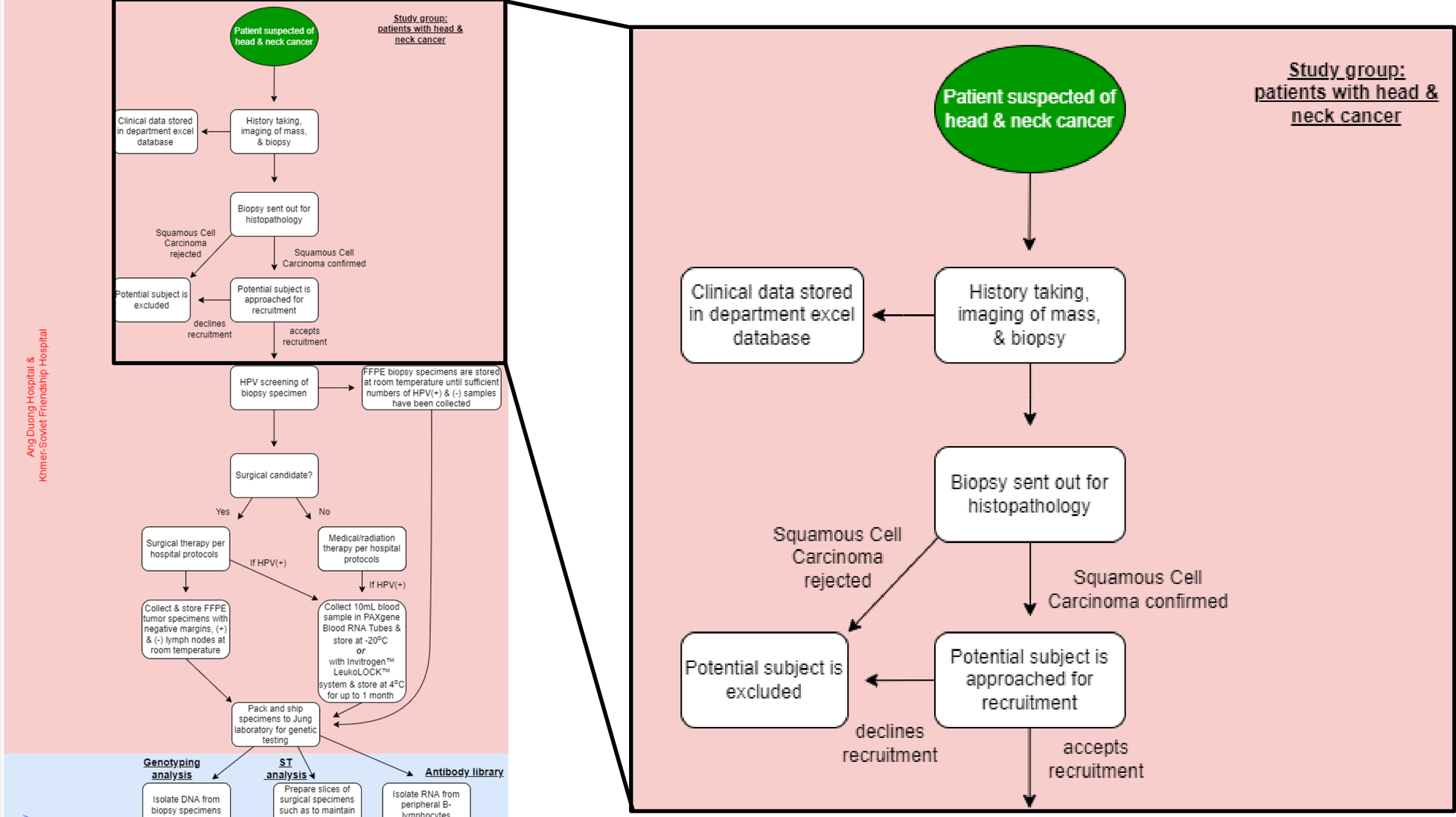
- Antibody and immunotherapy are a new front of cancer therapeutics
- HPV E7 protein validated as a clinically useful target for T-cell receptors and monoclonal antibodies.
- Single-chain variable fragment (scFv) have several advantages over T-cells and whole antibodies

# 4. Geodemographic Comparisons

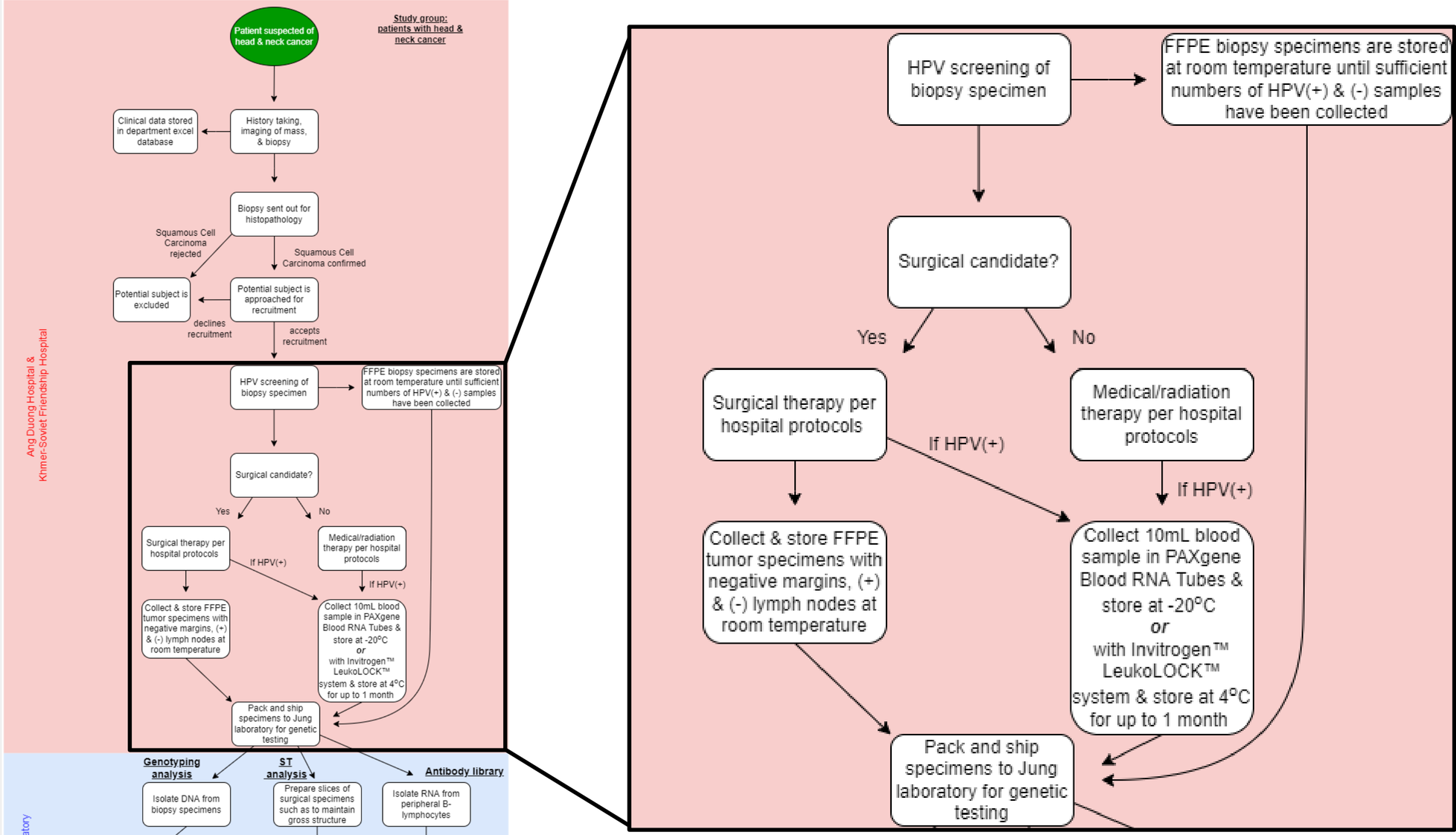
*Rationale*

- HPV type prevalences & HPV/HNSCC attributable fractions vary across geographic regions and populations
- Lifestyle, environmental, and cultural differences contribute to geodemographic trends and may impact the natural history of HPV infection and HNSCC.

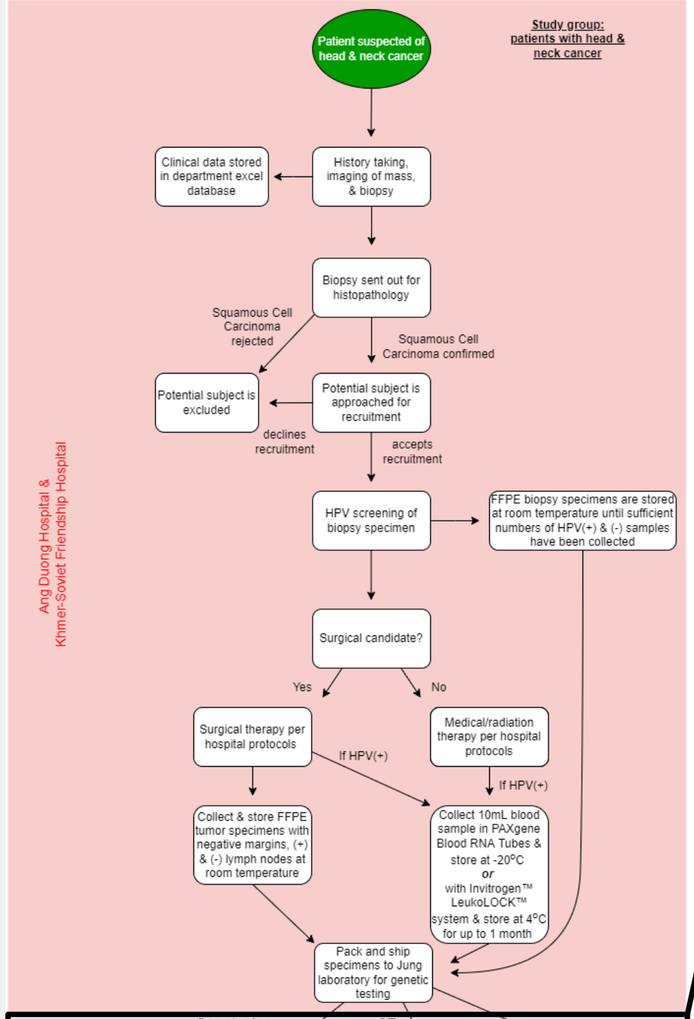
# Workflow (Part 1)

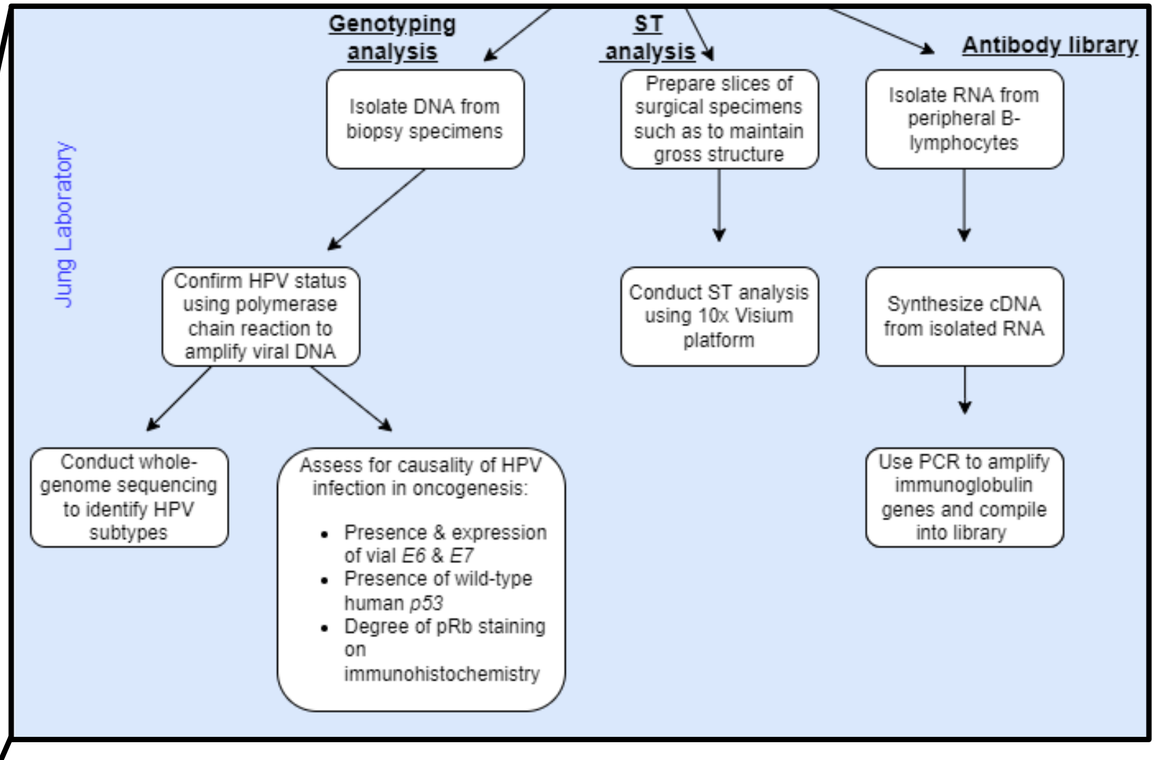


# Workflow (Part 2)



# Workflow (Part 3)



# Conclusions

Awareness of oral cancer and its causes among healthcare professionals and the general public is important for prevention

We propose an interdepartmental, multi-site study → requires cooperation between many professionals

Oral cancer in Cambodia can be prevented with HPV vaccination – this study intends to find out by how much

Novel laboratory techniques – proposed in this study – can reveal more about the nature of HPV-induced cancers

# Thank you!

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