# Problem Set 3

#### Introduction

The research aimed to investigate survival outcomes in individuals diagnosed with stage 3 and stage 4 Diffuse Histiocytic Lymphoma (DHL) using three analytical approaches: log-linear Poisson regression models, Kaplan-Meier survival curves, and Cox proportional hazards models. We hypothesized that stage 4 of DHL at diagnosis is associated with worse survival outcomes compared to stage 3 DHL at diagnosis.

### Methods

## Log-linear Poisson Models

Survival times of patients were binned into intervals to facilitate comparison between stage 3 and stage 4 DHL groups.

The total time of exposure was divided into roughly ten bins. The number of deaths and person-days experienced for each of the two groups in each bin was determined. Log-linear Poisson regression models were applied to analyze the relationship between binned survival times and disease stage, with models including spline at 60 days survival and interaction between stage and survival time explored. These models were compared using AIC and the model with continuous time was selected.

## Kaplan-Meier survival curves

Kaplan-Meier survival analysis was conducted to estimate and visualize survival probabilities over time for stage 3 and stage 4 DHL patients. The survival curves provided insights into differences in survival outcomes between the two stages, highlighting potential disparities in survival probabilities.

# Cox Proportional Hazard Models

Cox proportional hazard models were employed to assess the association between disease stage and time to death using the Breslow method to manage ties. The models estimated hazard ratios (HRs) and 95% confidence intervals (CIs) to quantify the magnitude and direction of the association between disease stage and survival outcomes.

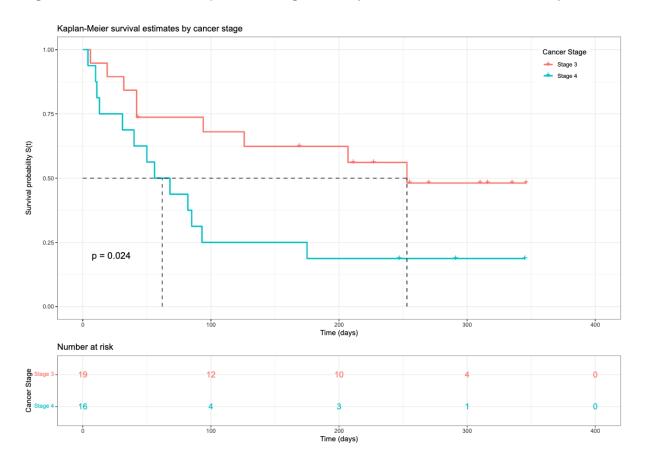
#### Results

The log-linear Poisson regression models revealed significant differences in survival times between stage 3 and stage 4 DHL patients. Notably, the analysis suggested that individuals with stage 4 DHL experienced shorter survival times compared to those with stage 3 DHL. The mortality rate of individuals with stage 4 DHL is 2.57 (95% C.I 1.10 – 6.23) times that of individuals with stage 3 DHL at any point in time during the follow-up of the study.

Consistent with the Poisson regression findings, the Kaplan-Meier curves demonstrated a clear distinction in survival outcomes between the two stages, with stage 4 patients exhibiting lower survival probabilities throughout the follow-up period (log-rank p-value

0.024). The median survival time for stage 3 participants was 253 days compared to 62 days for stage 4 participants.

Furthermore, the Cox proportional hazards models of time to death on stage confirmed the previous findings, indicating that stage 4 DHL was associated with a significantly higher hazard of death compared to stage 3 DHL (HR: 2.61, 95% C.I 1.10 – 6.17).



# Conclusion

In summary, the findings from the log-linear Poisson regression models, Kaplan-Meier survival curves, and Cox proportional hazards models collectively suggest that stage 4 DHL is associated with poorer survival outcomes compared to stage 3 DHL. These results underscore the importance of early detection, timely intervention, and targeted treatment strategies for individuals diagnosed with advanced-stage DHL, emphasizing the need for comprehensive and multidisciplinary approaches to improve patient outcomes and quality of life.