

# Graphical displays for subgroup analysis in clinical trials

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## Introduction

Subgroup analyses are a routine part of clinical trials to investigate the treatment effect in subsets of the population under study. The purpose of this assessment may be to ensure that there are no groups of patients for whom the treatment is harmful despite being effective in the majority of patients or to identify groups of patients that may benefit from a treatment when the overall effect is small or zero. Graphical approaches play a key role in subgroup analyses to visualize effect sizes of subgroups, aid identification of groups that respond differentially, and communicate the results to a wider audience. However, many existing approaches do not capture the core information and/or are prone to lead to misinterpretation of subgroup effects. In this work, we critically appraise existing visualization techniques, propose useful extensions to increase their utility and attempt to develop an effective visualization approach. The graphical techniques considered include level plots, contour plots, bar charts, Venn diagrams, tree plots, forest plots, Galbraith plots, L'Abbé plots, the subpopulation treatment effect pattern plot (STEPP), alluvial plots and UpSet plots.

We illustrate the methods using a dataset of a treatment for prostate cancer [1] with survival endpoint and six subgroup defining covariates: existence of bone metastasis (bm), disease stage (3 or 4), performance rating (pf: 0, normal; 1, limitation of activity), history of cardiovascular events (hx), age, and weight.

## Direct comparison of treatment effects

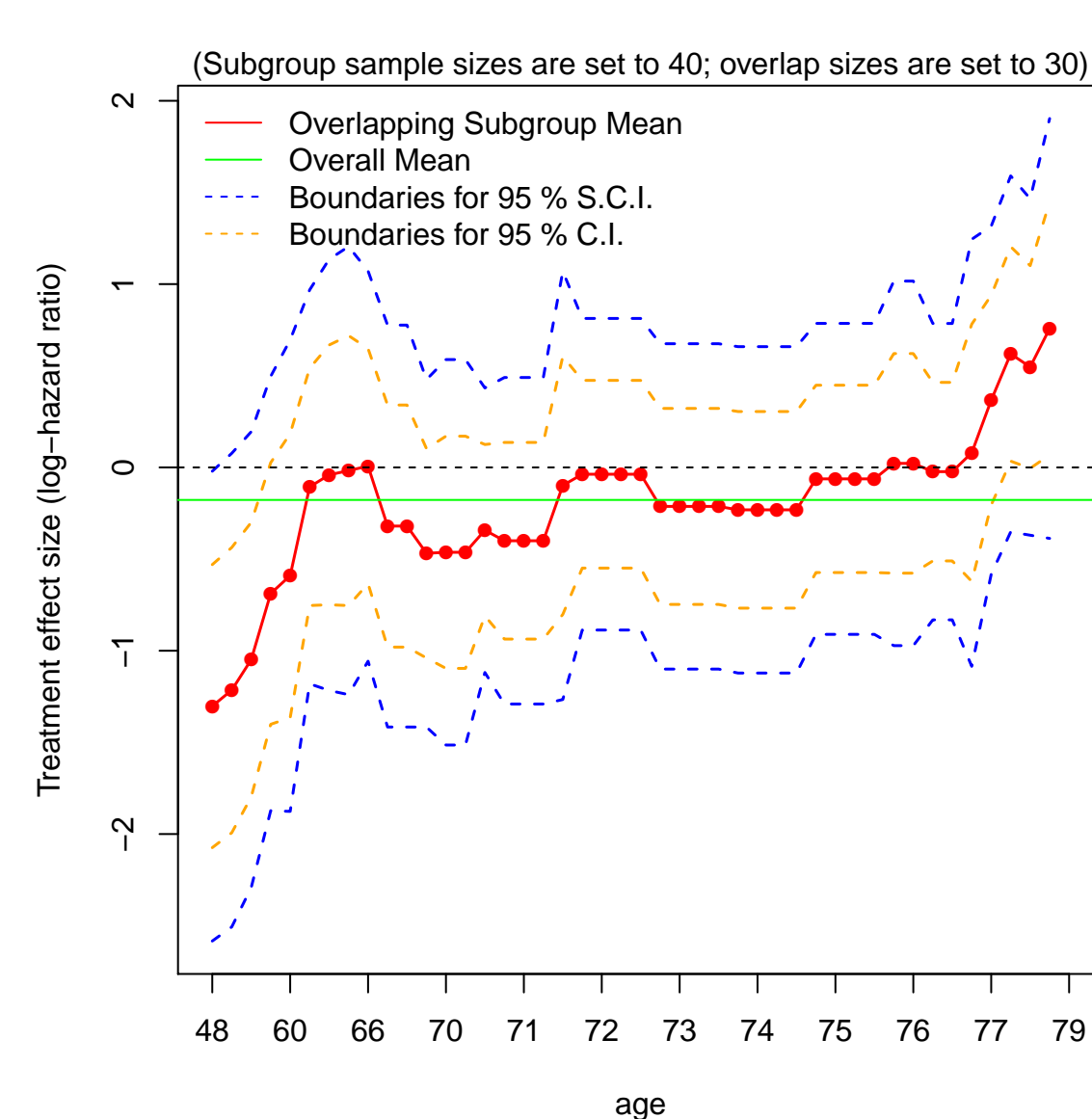


Fig. 1: STEPP plot for age

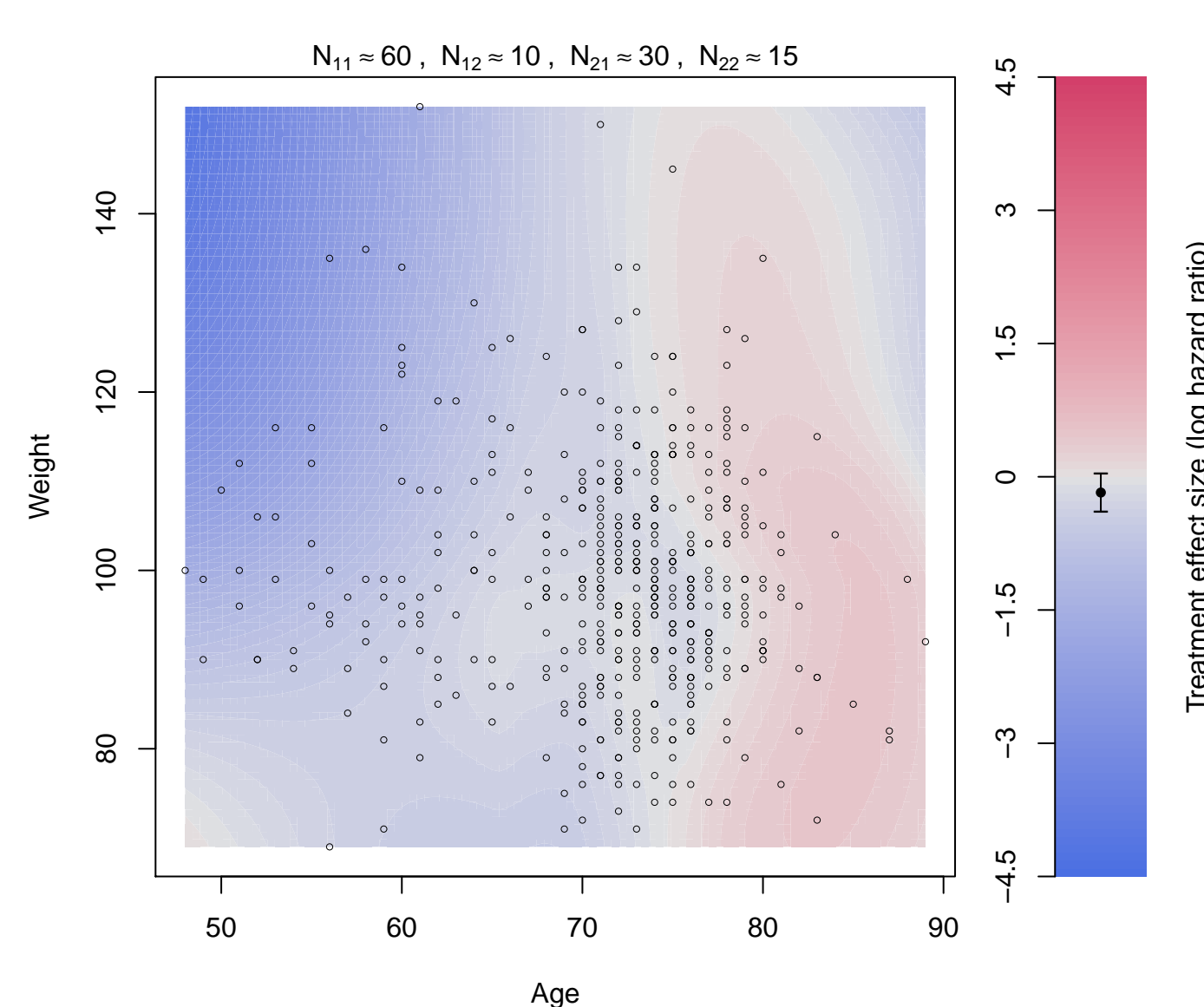


Fig. 2: Contour plot for age and weight

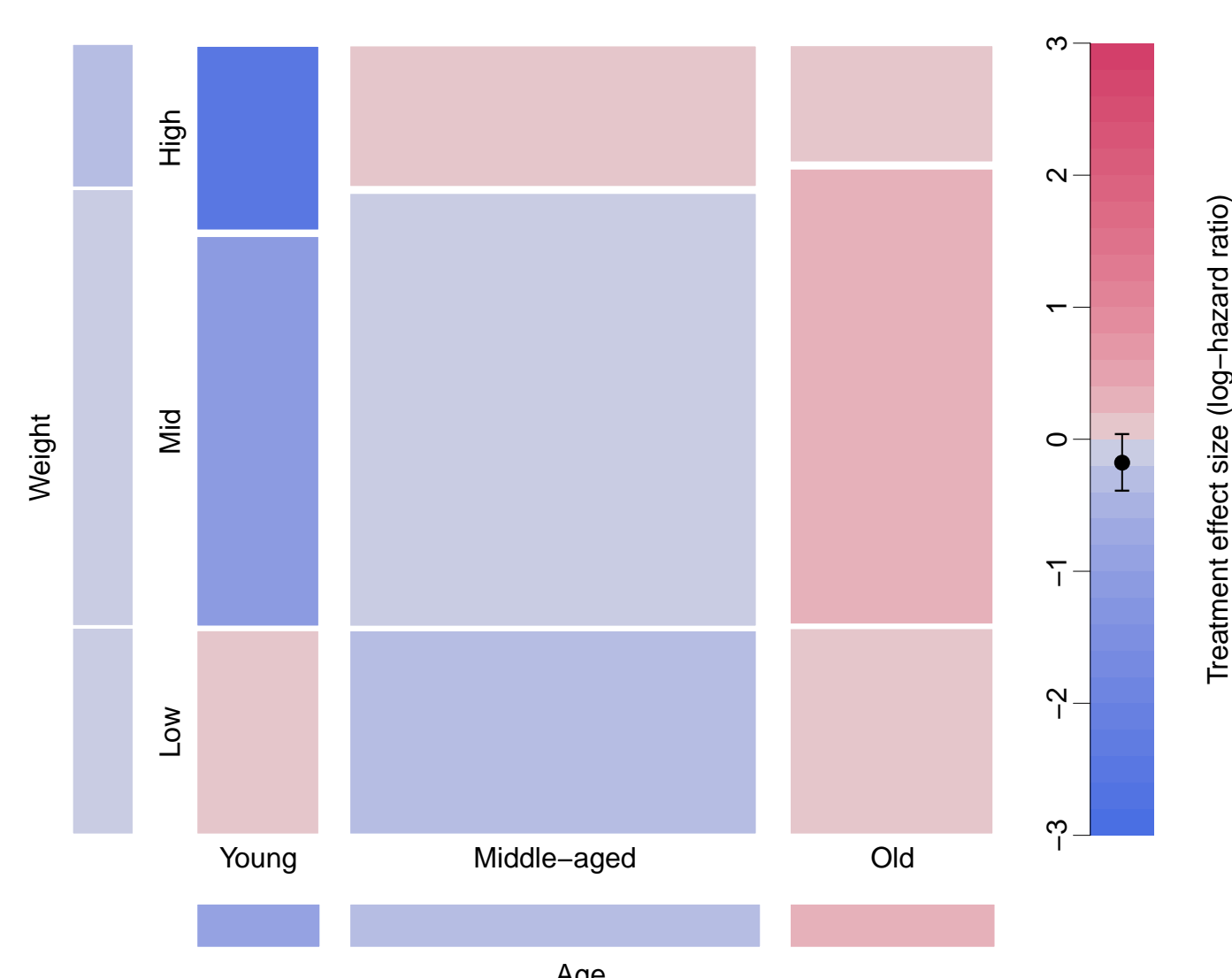


Fig. 3: Mosaic plot for age and weight

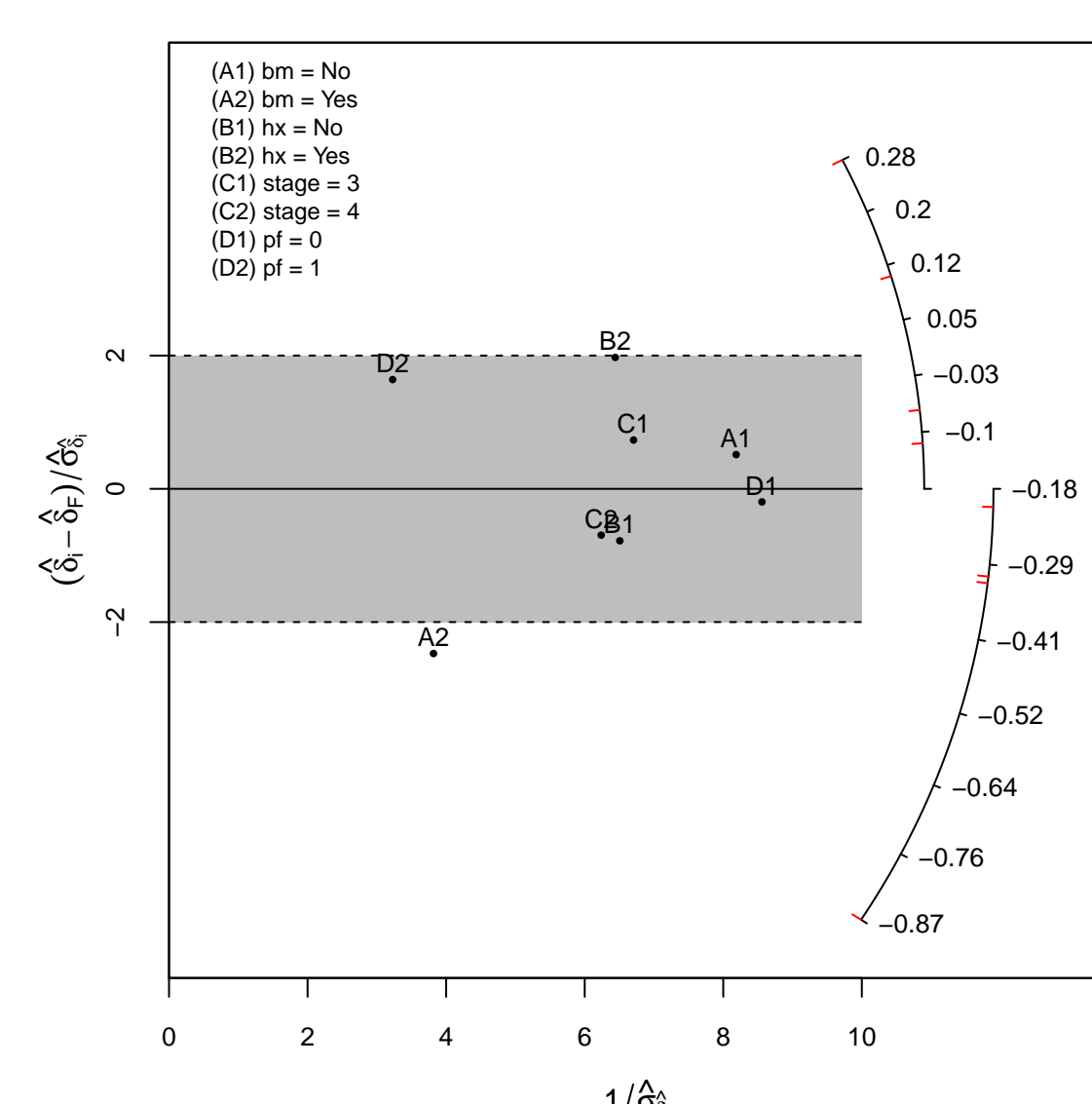


Fig. 4: Galbraith plot for subgroups

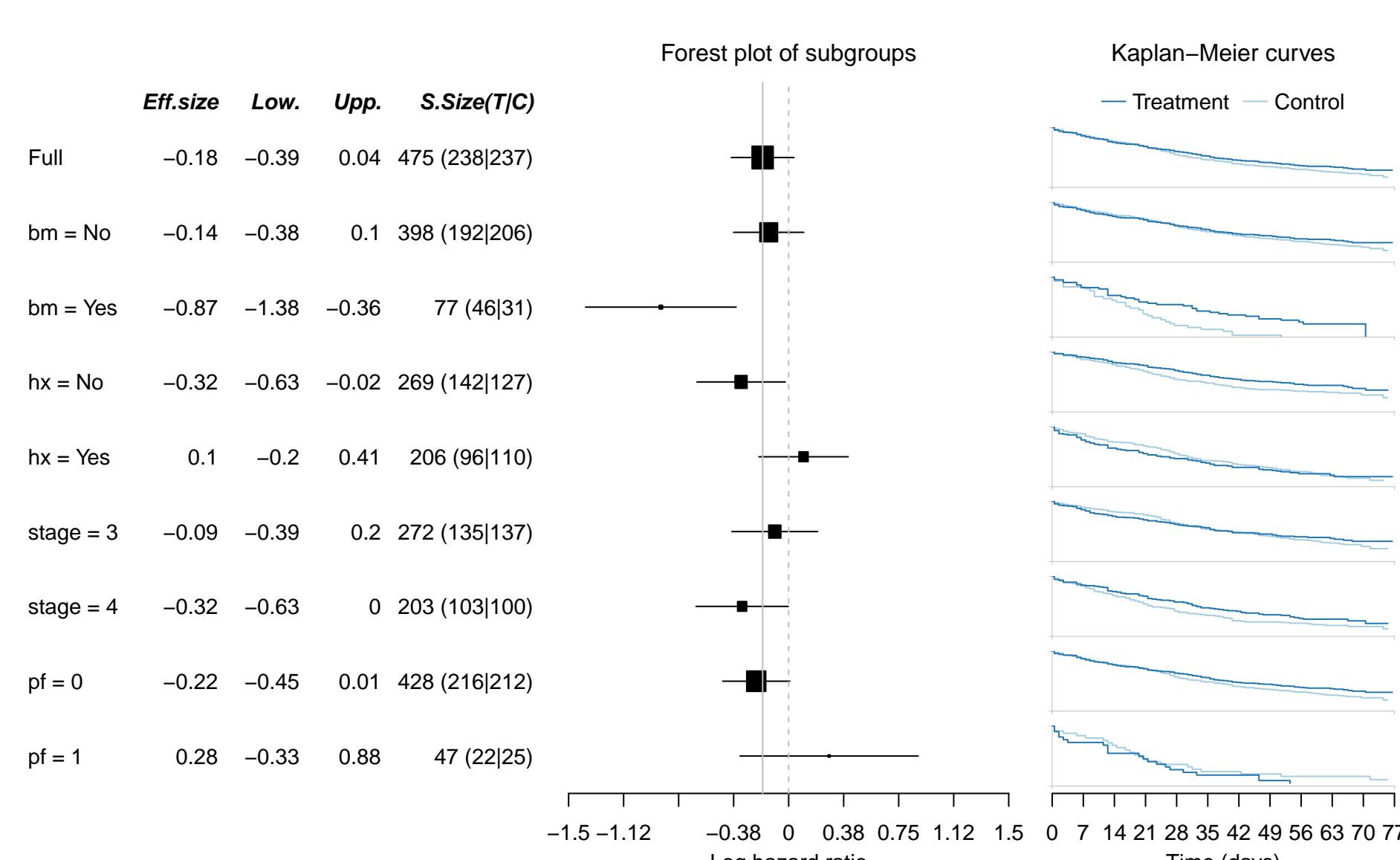


Fig. 5: Forest plot for subgroups with survival curves by treatment

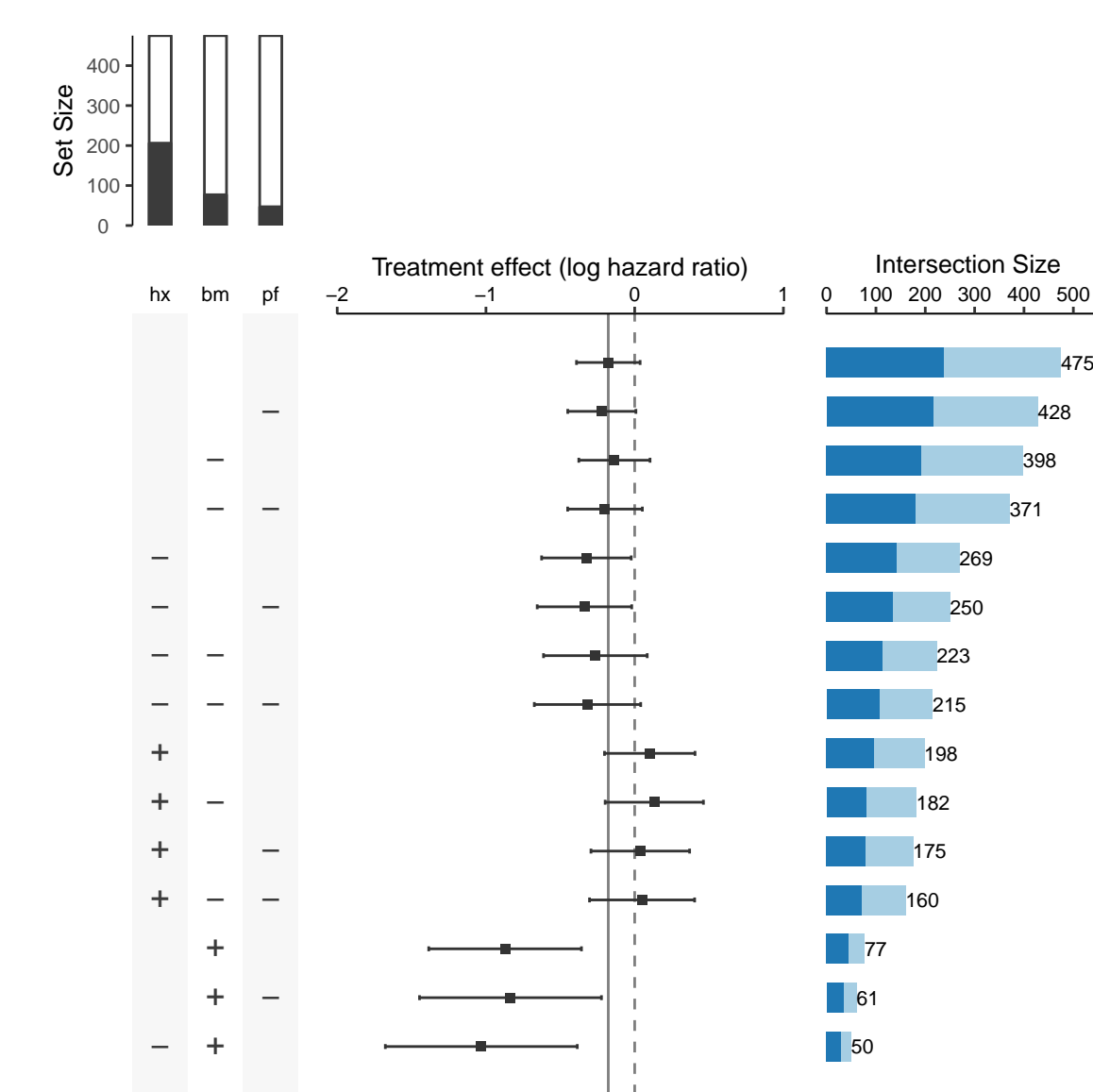


Fig. 6: Modified UpSet plot for subgroups

## Assessment Summary

	Criterion				
	Effect size	Sample size	Overlap	Heterogeneity	Many groups
STEPP	✓			✓	✓
Contour plot	✓		✓		✓
Mosaic plot	✓	✓	✓		✓
Level plot	✓	✓	✓		✓
Galbraith plot	✓	✓		✓	✓
Forest plot	✓	✓		✓	✓
UpSet plot	✓	✓	✓	✓	✓
Circle plot	✓	✓	✓		✓
Venn diagram	✓	✓	✓		✓
Bar chart	✓	✓	✓		✓
Tree plot	✓	✓	✓	✓	✓
L'Abbé plot	✓	✓		✓	✓
Alluvial diagram		✓	✓		✓

## Indirect comparison

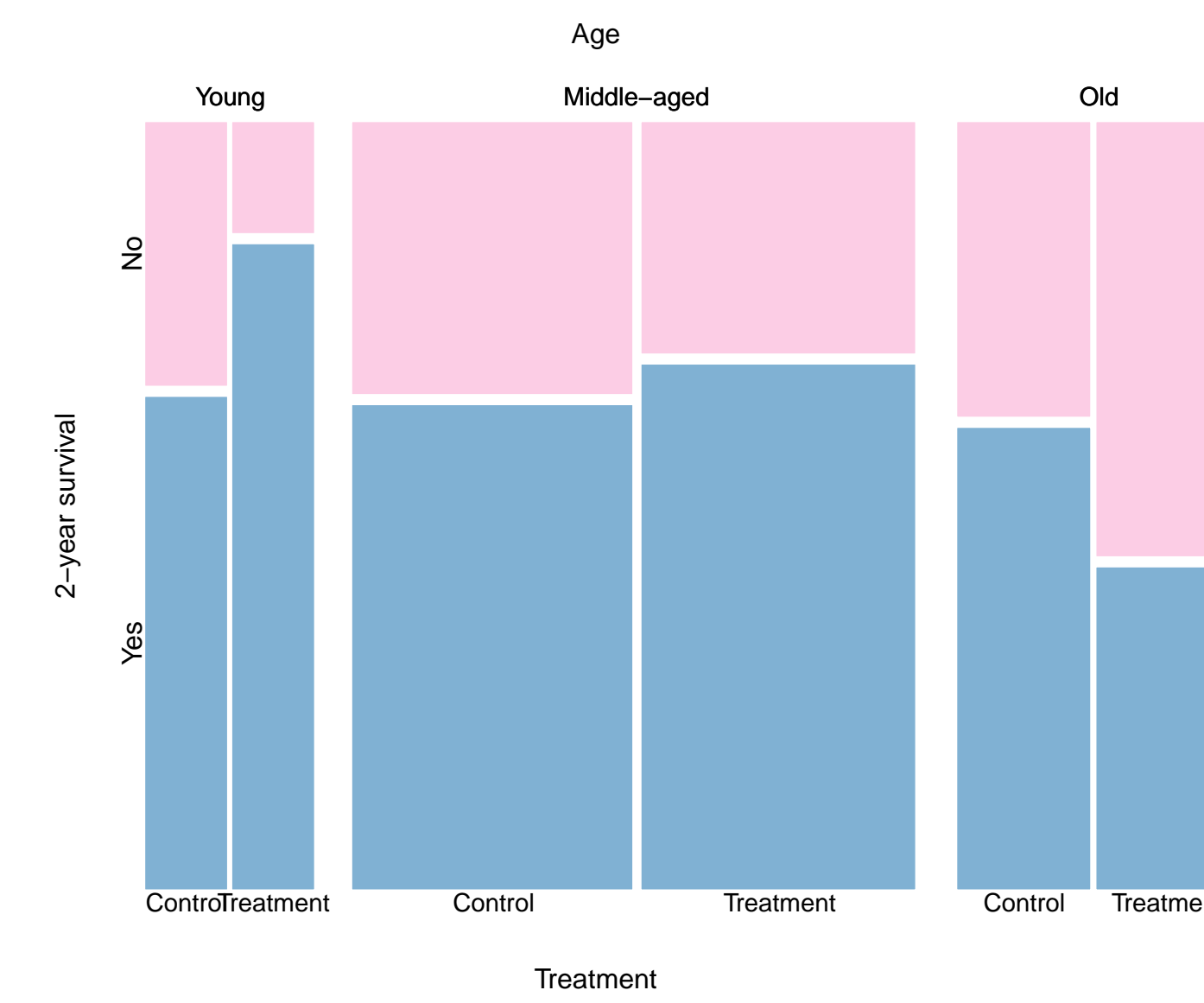


Fig. 7: Mosaic plot for survival rate by treatment and age

## Subgroup composition

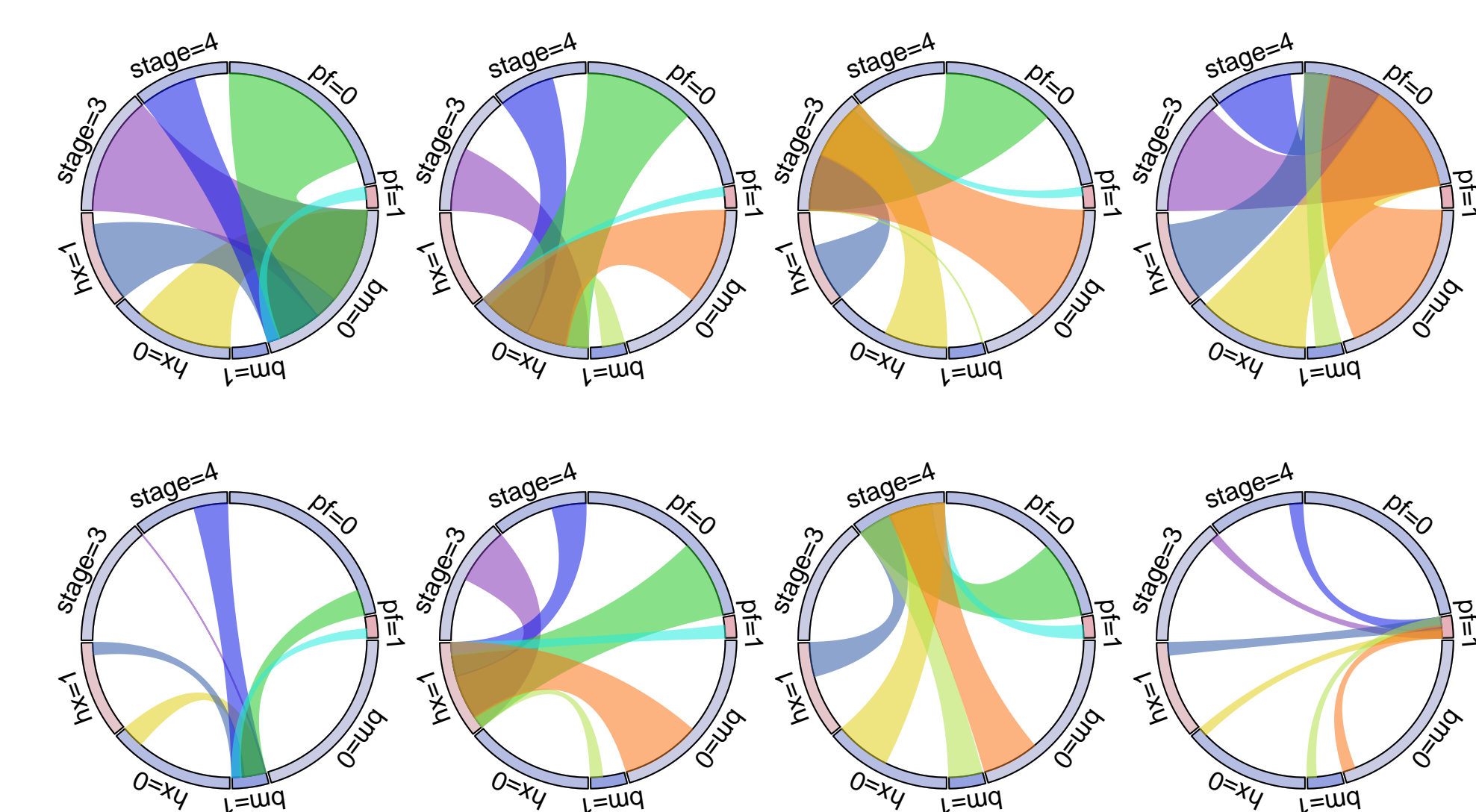


Fig. 8: Circle plot for overlap of subgroups

## References

- [1] David P. Byar and Sylvan B. Green. The choice of treatment for cancer patients based on covariate information: application to prostate cancer. *Bulletin du Cancer*. 67:477–490. 1980.

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