

Introduction

Research questions:

- Does BMI influence survival in a real-world setting?
- Do changes in BMI levels during course of treatment affect chances of survival?

Aims:

- Investigate the impact of baseline BMI on overall survival (OS)
- Explore how changes in BMI during the course of treatment could be used to develop a survival model



Advanced melanoma (Luke, J.J., et al 2017; Garbe, C., et al. 2016):

- Least common but deadliest form of skin cancer
- Represents 90% of skin cancer related deaths



Body-Mass Index (BMI):

- BMI at baseline has been shown to impact survival outcomes
- Calculated with height (m) and weight (kg) at each prescription time (kg/m^2)
- Categorisation according to World Health Organization standards
- Recent studies suggest that obesity in patients with advanced melanoma is associated with improved survival outcomes (McQuade J.L., et al 2018; Smith L.K., et al 2020)

Methodology

Data:

- Real-world patients from the West of Scotland
- Treatments include chemotherapy, immunotherapy and targeted therapy
- 2784 appointments between 14th March 2008 and 30th March 2018

Survival analysis:

- Main outcome of interest was **overall survival**
- Kaplan-Meier curve** explores the association between BMI at baseline and overall survival
- Survival model is a **Cox Proportional-hazards model** with BMI as time-varying variable to investigate possible effects of changes over time on survival

Inclusion criteria:

- Patients diagnosed with advanced melanoma
- Over 18 years old at time of first appointment

Exclusion criteria:

- Underweight ($< 18.5 \text{ kg}/\text{m}^2$)
- Incomplete BMI values at any point of prescription

Cohort:
259 patients

Table 1 – Descriptive statistics for type of therapy, BMI and follow-up time at baseline

	Categories	N (%)
Type of therapy	Chemotherapy	58 (22.4)
	Immunotherapy	155 (59.8)
	Targeted therapy	46 (17.8)
BMI	Normal	68 (26.3)
	Overweight	101 (39)
	Obese	90 (34.7)
Follow-up time (months)	Median (IQR) [Range]	8 (3-15) [1-104]

Table 2 – Survival estimates by BMI category with number of patients and events (death)

BMI group	N	Events	Median OS months (CI)
Normal	68	54	6 (5-10)
Overweight	101	68	14 (10-17)
Obese	90	52	12 (9-23)

Survival curves for overall survival by BMI group at baseline

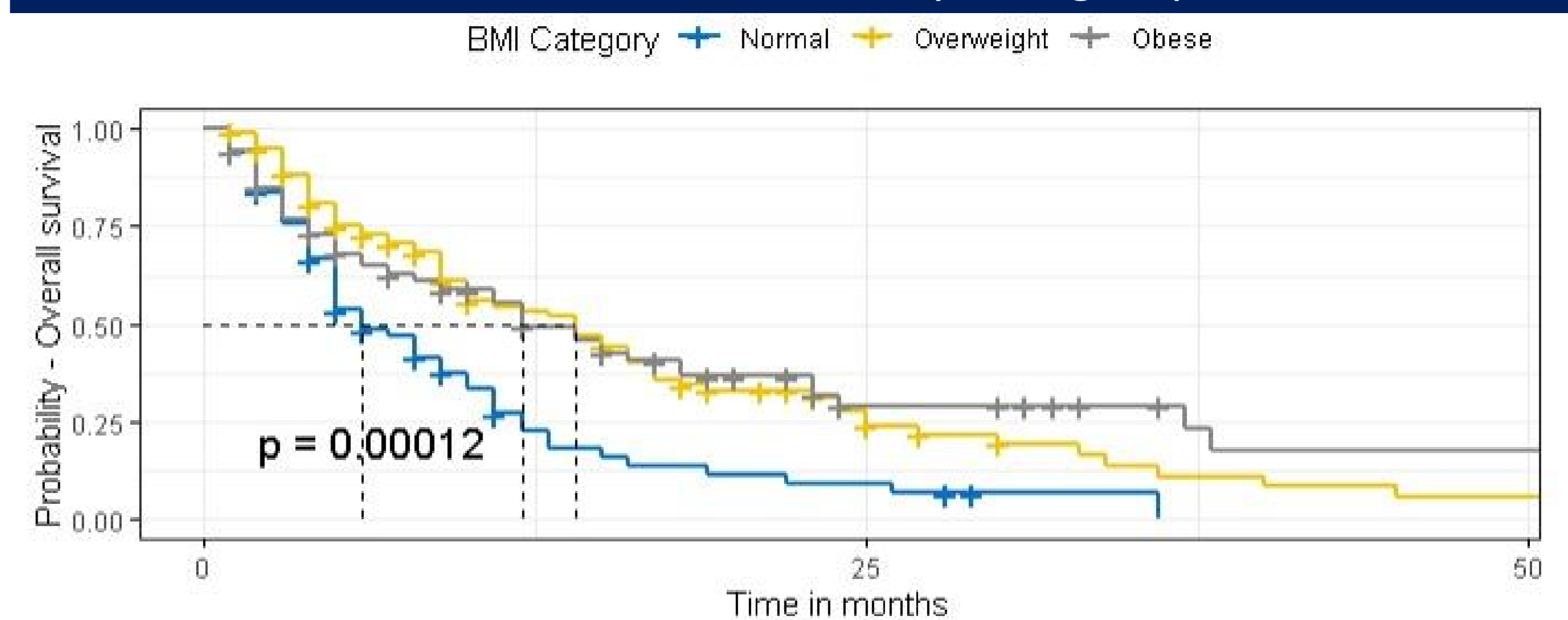


Figure 1 – Kaplan-Meier plot stratified by BMI category at baseline

Results - Survival model

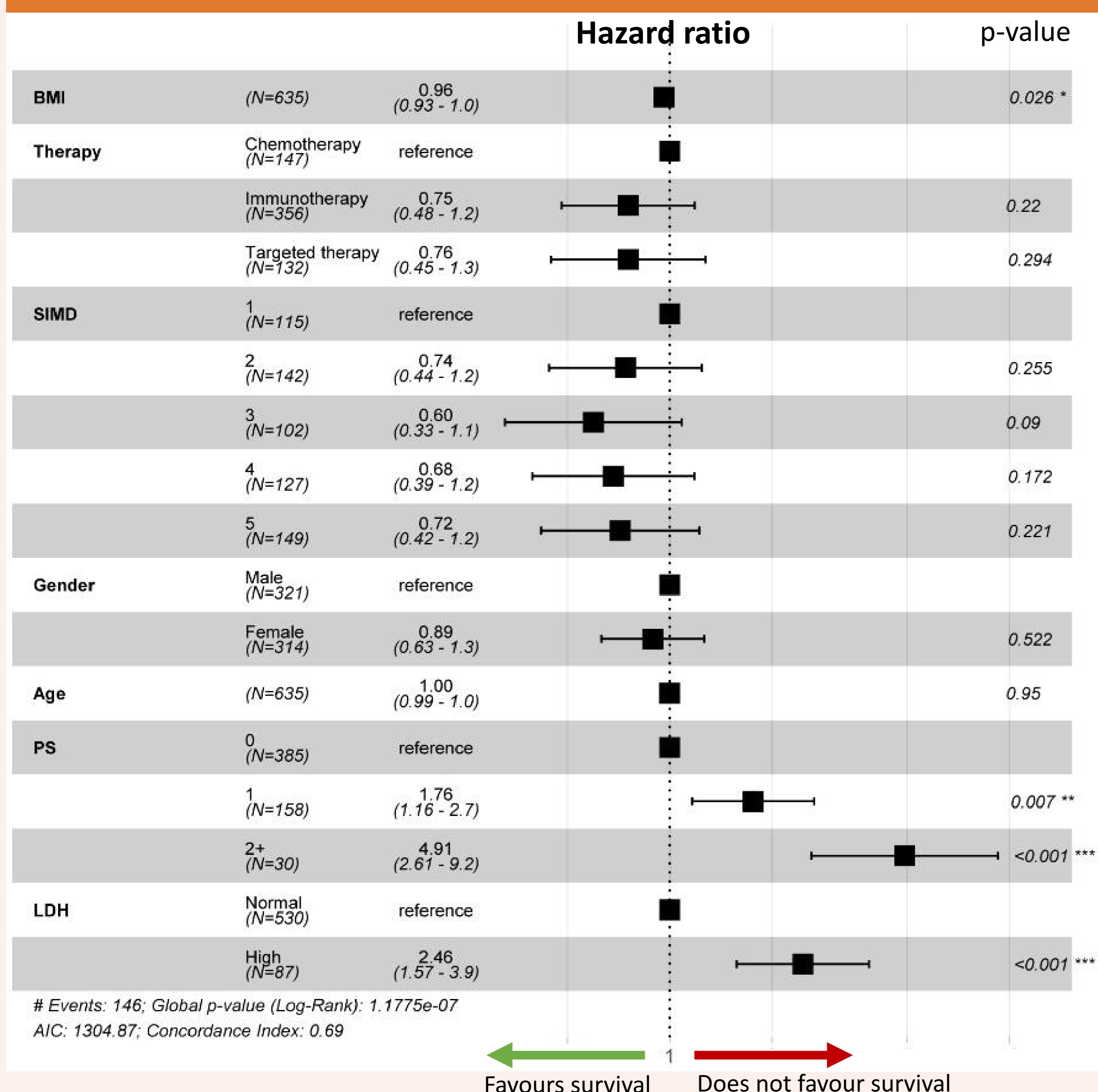


Figure 2 - Forest plot of survival model with BMI as a time-dependent covariate

Note: BMI is included as a time-dependent covariate in a multivariable Cox regression model; Other covariates are time-fixed (baseline); BMI – Body-Mass Index; SIMD – Scottish Index of Multiple Deprivation; PS – ECOG Performance Score; LDH – Lactate dehydrogenase. Chemotherapy includes dacarbazine, temozolomide and paclitaxel + carboplatin; Immunotherapy includes ipilimumab, nivolumab, pembrolizumab and ipilimumab + nivolumab; Targeted therapy includes dabrafenib, dabrafenib + trametinib and vemurafenib.

Conclusions

Survival curves :

- There was an association between patient BMI at baseline and survival with overweight or obese patients surviving longer than those with normal BMI.

Time-dependency Cox Proportional-hazards model:

- After adjusting the survival model for BMI time-dependency it is suggested that increasing BMI over the course of treatment was associated with increased survival

Limitations:

- Small sized cohort due to geographic limitations.
- Time-dependency models require careful interpretation as these associations may not be causal but could instead be influenced by other factors (unknown confounders).
- Further studies are needed.**

References

- Garbe, C., et al., *Diagnosis and treatment of melanoma. European consensus-based interdisciplinary guideline - Update 2016.* Eur J Cancer, 2016. 63: p. 201-17.
- Luke, J.J., et al., *Targeted agents and immunotherapies: optimizing outcomes in melanoma.* Nat Rev Clin Oncol, 2017. 14(8): p. 463-482.
- McQuade JL, Daniel CR, Hess KR, Mak C, Wang DY, Rai RR, et al. Association of body-mass index and outcomes in patients with metastatic melanoma treated with targeted therapy, immunotherapy, or chemotherapy: a retrospective, multicohort analysis. The Lancet Oncology. 2018;19(3):310-22.
- Smith LK, Arabi S, Lelliott EJ, McArthur GA, Sheppard KE. Obesity and the impact on cutaneous melanoma: Friend or foe? Cancers. 2020;12(6):1583.

Acknowledgements

Cancer Medicines Outcomes Programme (CMOP) is a collaborative project between NHS Greater Glasgow and Clyde and the University of Strathclyde



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