Reversal of the Polypharmacy-Survival Relationship in Poor Prognosis Cancer Patients

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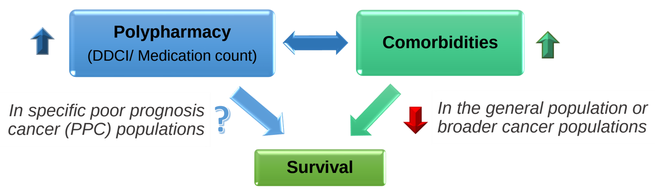
Background

- Estimation of prognosis is vital for informing decisions around care and its value, especially in patients with poor prognosis cancer (PPC) where there is a high risk of under- or over-treatment.
- An established risk stratification tool is the Charlson Comorbidity Index derived from admitted patient care episodes.[1]
- As prescribing data are becoming more available, concomitant medication counts offer the potential for more accurate prognostication.
- Polypharmacy serves as a risk measure and proxy for comorbidity, notably with the Drug Derived Complexity Index (DDCI).[2]
- In both the general population and broader cancer populations, more medications or an elevated DDCI is strongly linked to worse health outcomes and survival.[2]

Aims

- To quantitatively assess the relationship between DDCI, medication counts, and survival in specific PPC populations.



Methods

- **Study design:** Retrospective cohort study
- **Study population:** Lung cancer and upper gastrointestinal (GI) cancer patients diagnosed between 2015 and 2021, and having a metastatic disease or no active anti-cancer treatment in Lothian health board (Edinburgh Cancer Centre)
- **Data sources:** Electronic health records including the Scottish Cancer Registry, and Prescribing Information System (PIS)
- **Variables:**
  - Drug Derived Complexity Index (DDCI)
  - Medication count ≥ 5 (Polypharmacy)

    calculated using data from 5 years preceding the cancer diagnosis.
  - Primary outcome: Overall survival from the diagnosis of poor prognosis cancer
- **Data analysis:**
  - Kaplan-Meier analysis estimated survival probabilities based on DDCI quartiles and medication count categories (< 5 or ≥ 5)
  - Multivariate Cox proportional hazard regression analysed the relationship of DDCI, and medication count with overall survival, adjusted for age, gender, metastatic status at diagnosis, treatment status, and other relevant factors.

Results

- There were 3755 and 2654 patients in the lung and the upper GI cohort, respectively.
- Median survival was better with:
  - Higher DDCI quartiles in both PPC groups
  - Higher medication counts in the lung cohort

Table 1 - Median survival in DDCI quartiles in the lung and upper GI cancer cohorts

DDCI quartile	Median survival in the lung cohort with 95% CI (in months)	DDCI quartile	Median survival in the upper GI cohort with 95% CI (in months)
Q1 (<9)	2.08 (1.83 – 2.43)	**Q1 (<9)**	3.10 (2.56 – 3.76)
Q2 (9 - 13)	4.63 (4.33 – 5.26)	**Q2 (9 - 12)**	4.65 (4.13 – 5.56)
Q3 (14 - 17)	6.06 (5.53 – 6.93)	**Q3 (13 - 16)**	6.43 (5.70 – 7.20)
Q4 (≥ 18)	6.73 (5.90 – 7.63)	**Q4 (≥ 17)**	6.40 (5.76 – 7.36)

Lung cancer cohort (n = 3755) **Upper GI cancer cohorts (n = 2654)**

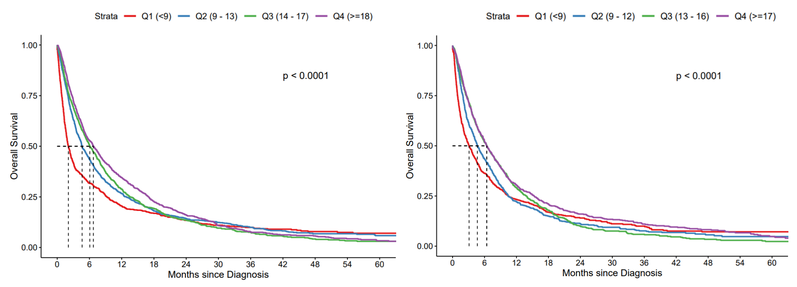


Figure 1 - Survival curves with DDCI quartiles in lung and upper GI cancer cohorts

Lung cancer cohort (n = 3755) **Upper GI cancer cohorts (n = 2654)**

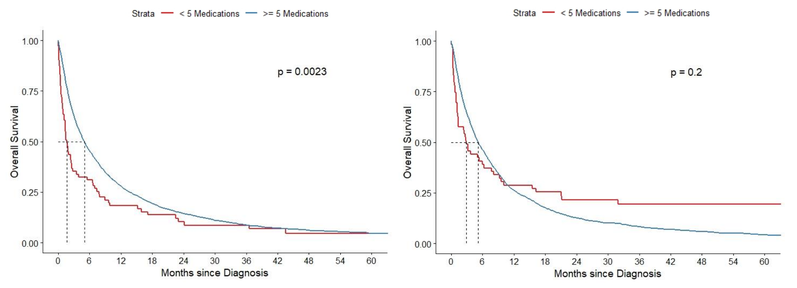


Figure 2 - Survival curves with medication count in lung and upper GI cancer cohorts

- Hazard ratios were lower in higher DDCI quartiles in lung and upper GI cohorts.

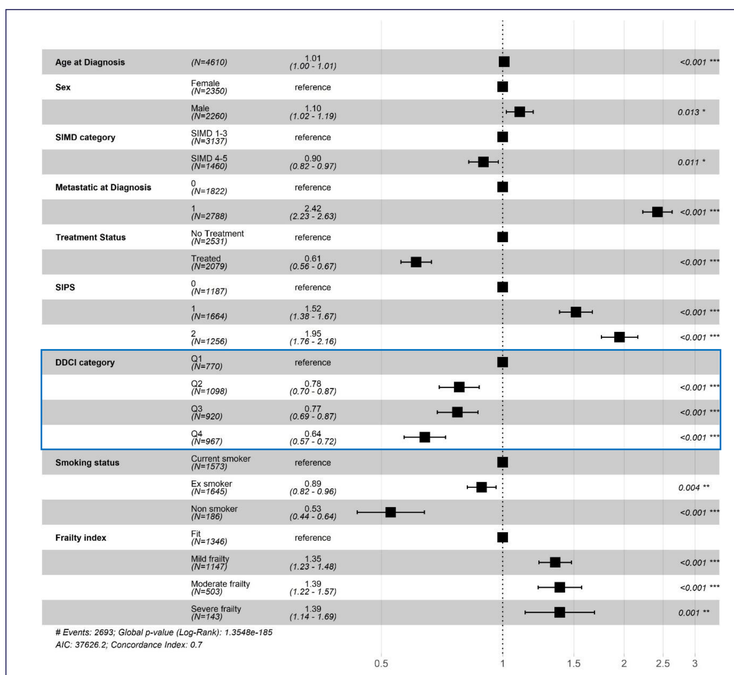


Figure 3- Hazard ratios with DDCI quartiles in the lung cancer cohort

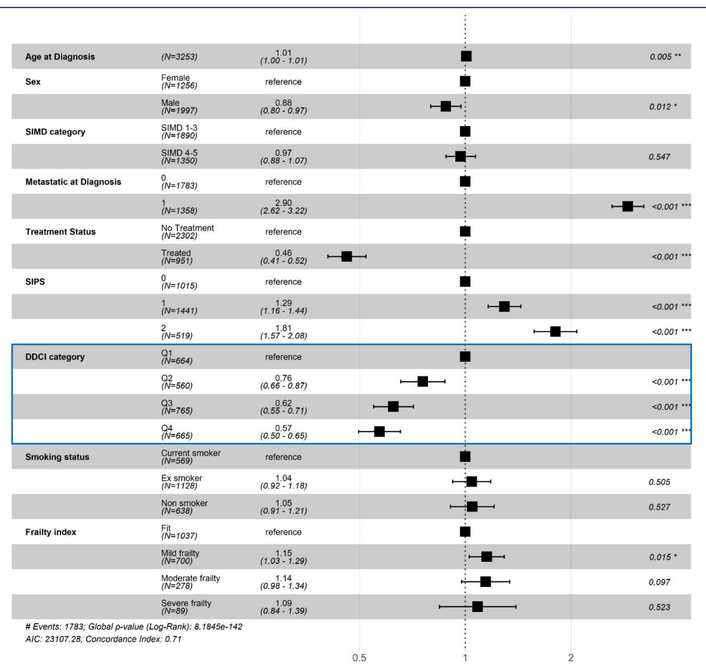


Figure 4 - Hazard ratios with DDCI quartiles in the upper GI cancer cohort

- Similarly, hazard ratios were lower with a higher medication count in both the lung and upper GI cohorts.

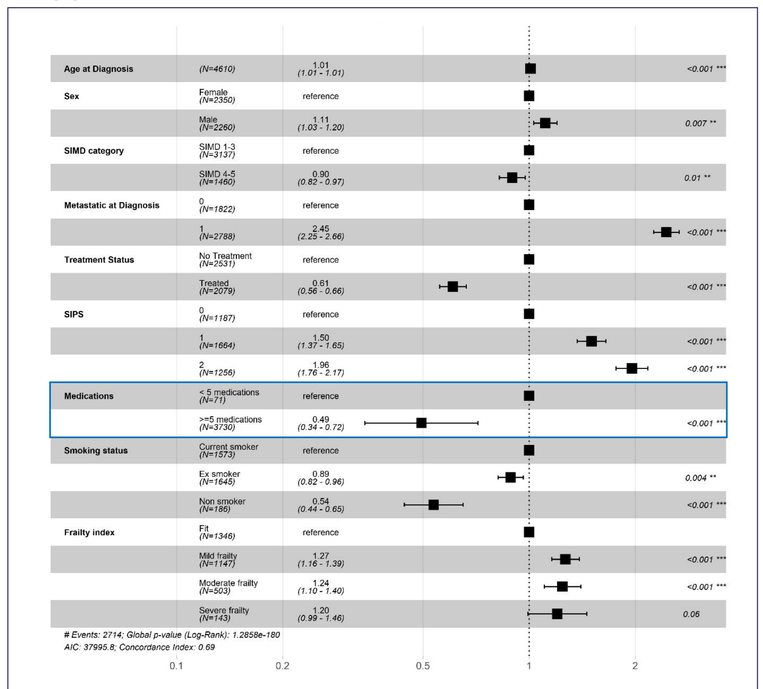


Figure 5 - Hazard ratio with medication count in the lung cancer cohort

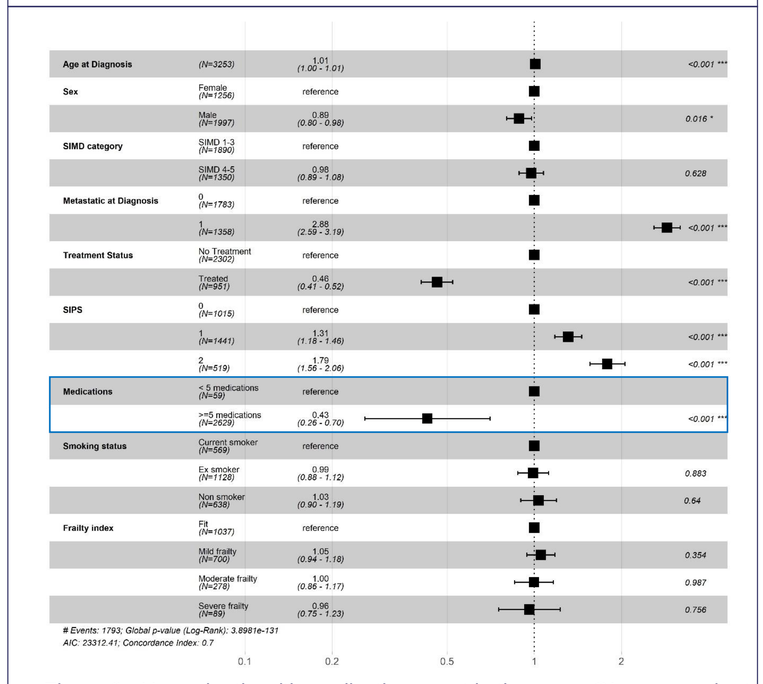


Figure 6 - Hazard ratio with medication count in the upper GI cancer cohort

Conclusions

- Polypharmacy and higher DDCI are predictive of better survival in specific PPC populations.
- **These results suggest that the use of standard prognosticators in these specific populations might yield unexpected or even erroneous predictions.**
- Further research is required to establish a potential causal link between higher medication counts and better survival in these populations.

References

1. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. Journal of Chronic Diseases. 1987 Jan;40(5):373–83.
2. Robusto F, Lepore V, D'Ettorre A, Lucisano G, De Berardis G, Bisceglia L, et al. The drug derived complexity index (Ddci) predicts mortality, unplanned hospitalization and hospital readmissions at the population level. Bai C, editor. PLoS ONE. 2016 Feb 19;11(2): e0149203.

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https://cancer-data.ecrc.ed.ac.uk/