Survival disparities in colorectal cancer: investigating the role of stage at diagnosis through mediation analysis

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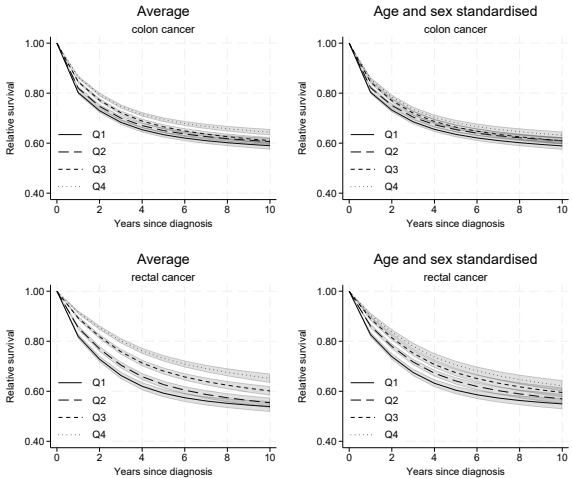
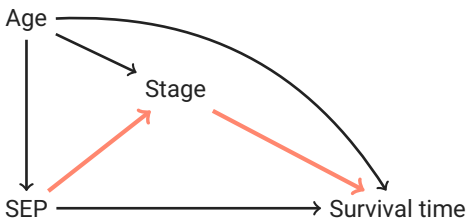
Survival disparities in CRC survival in Sweden



Syriopoulou E, Osterman E, Miething A, Nordenvall C, Andersson TM-L. Income disparities in loss in life expectancy after colon and rectal cancers: a Swedish register-based study. *J Epidemiol Community Health* 2024;78(6): 402–408.

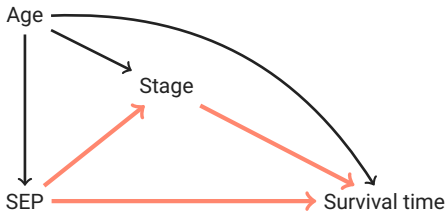
Why are there differences by socioeconomic position?

Could stage at diagnosis partly explain the survival differences between the income groups?



This is a mediation analysis question!

Partitioning the total survival difference



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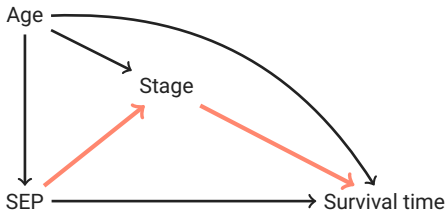
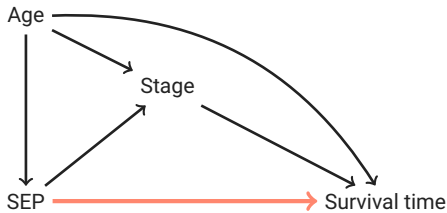


Natural indirect effect: quantifies how much of the observed difference is due to stage differences in the two groups

Partitioning the total survival difference



Natural indirect effect: quantifies how much of the observed difference is due to stage differences in the two groups

Natural direct effect: quantifies the differences in relative survival that are *not* due to stage differences

Mediation analysis

Mediation analysis is a useful tool for our setting.

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However, we still need to deal with the complex mechanisms that contribute towards cancer disparities:

- Cancer-related mortality differences
- Other cause mortality differences

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- Cancer-related mortality differences
- Other cause mortality differences

In our analysis, we used mediation analysis methods into the relative survival framework[1].

- Main idea: using the relative survival framework allows to isolate cancer-related factors.

[1] Syriopoulou E, Rutherford MJ, Lambert PC. Understanding disparities in cancer prognosis: An extension of mediation analysis to the relative survival framework. *Biometrical Journal*. 2021; 63: 341–353.

Data

- Data from the Colorectal Cancer Database (CRCBaSe).
- All adults diagnosed with a first-time diagnosis of colon or rectal cancers in Sweden between 2008–2021 and follow-up time to the end of 2021.
- Socioeconomic position was defined using a household-based income indicator to account for the availability of material resources and health awareness among individuals with lower individual disposable income but access to more household resources.
  - Disposable income per consumption unit for a family is obtained by the sum of the disposable income of all members of the family divided with the consumption weight that applies to the household.
  - For each individual, it was obtained as the average of the 3 years prior to their diagnosis.

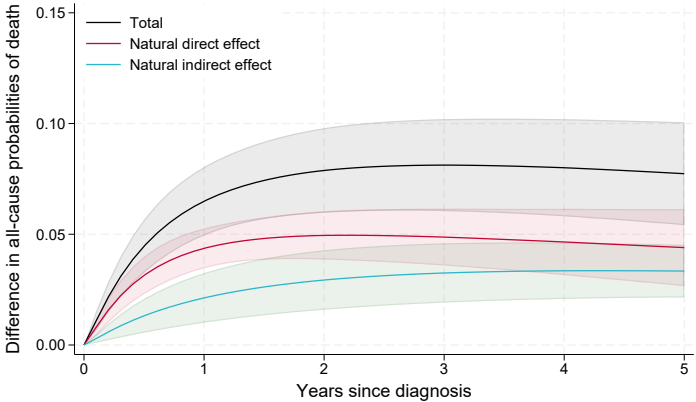
Analysis

- We apply mediation analysis as described in the paper[1].
- Separately analysis for colon and rectal cancers.
- For the survival outcome, we fitted flexible parametric relative survival models.
  - Included sex, age (continuous, non-linear effect), stage and individualised income (4 groups).
  - Allowed for time-dependent effects for all variables.
  - Interactions were also included between sex and income, and income and age at diagnosis, and income and stage.
  - We had to further construct lifetables by SEP and for this we used matched controls that were available in CRCBaSe.
- Multinomial regression model was fitted for stage including age, sex and income - allowing for interactions with income.

Descriptives

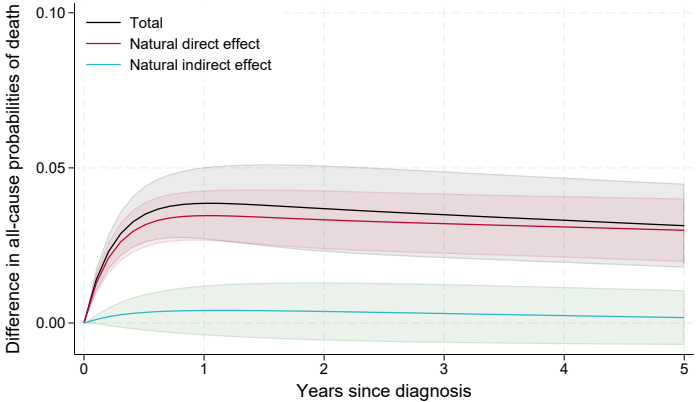
		Lowest income	Highest income
Colon cancer			
Age at diagnosis		76(54–87)	70(59–82)
Sex	Males	4,764(40%)	8,800(58%)
	Females	7,072(60%)	6,473(42%)
Stage at diagnosis	I	1,788(15%)	2,655 (18%)
	II	3,907(33%)	4,884(29%)
	III	3,618(31%)	4,788(31%)
	IV	2,523(21%)	3,346(22%)
Rectal cancer			
Age at diagnosis		74(51–86)	68(57–70)
Sex	Males	2,839(52%)	4,604(67%)
	Females	2,637(48%)	2,310(33%)
Stage at diagnosis	I	1,004(18%)	1,576(23%)
	II	1,129(21%)	1,278(18%)
	III	2,001(37%)	2,746(40%)
	IV	1,342(24%)	1,314(19%)

Mediation analysis - rectal cancer



- At 5 years there is a total difference of 7.8 percentage points in standardised all-cause survival between the highest and lowest income groups.
- 3.4 percentage points is due to stage differences
- i.e. 43% of the total difference is mediated through stage

Mediation analysis - colon cancer



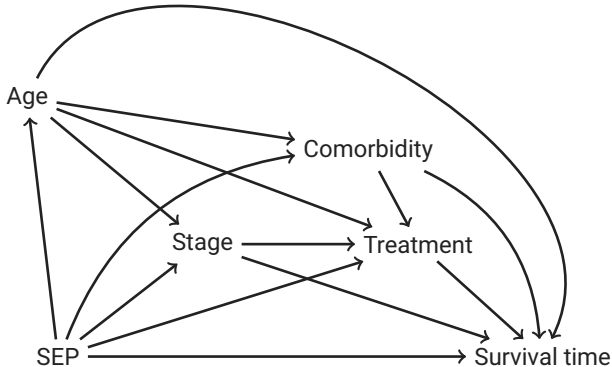
- At 5 years there is a total difference of 3.1 percentage points n standardised all-cause survival between the highest and lowest income groups.
- Almost entirely driven by factors other than stage
- i.e. 5.5% of the total difference is mediated through stage

Conclusions

- It is important but challenging to understand the reasons that drive the survival differences.
- Mediation analysis into the relative survival framework can be a useful tool for exploring such settings in a systematic way.
- There is a code example available on GitHub:
  `https://github.com/syriop-elisa/mediation-example-stpm3`

Next step

Exploring multiple mediators (stage, treatment*, comorbidity) at once.



* Osterman E, Syriopoulou E, Martling A, Andersson TM-L, Nordenvall C. Despite multi-disciplinary team discussions the socioeconomic disparities persist in the oncological treatment of non-metastasized colorectal cancer. *Eur J Cancer* 2024;199