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Does socioeconomic status influence the prospect of cure from colon cancer – A population-based study in Sweden 1965–2000

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ABSTRACT

Aim of study: Differences in the survival of colon cancer patients by socioeconomic status have been demonstrated in several populations, but the underlying reasons for the differences are not well understood. By simultaneously estimating the proportion of patients cured from colon cancer and the survival times of the 'uncured' we hope to increase understanding of how socioeconomic status affects survival following a diagnosis of colon cancer.

Methods: We conducted a population-based cohort study of 58,873 patients diagnosed with colon cancer in Sweden 1965–2000. Socioeconomic status was classified based on occupation. We fitted mixture cure models and Poisson regression models adjusted for age, sex and calendar period.

Results: We observed higher excess mortality, lower proportion cured and shorter survival times among the uncured in patients from lower socioeconomic groups compared to the highest socioeconomic group. There was no evidence that the gap between the socioeconomic groups reduced over time. Farmers had the lowest odds of cure (odds ratio (OR) 0.85, 95% confidence interval (CI) 0.75–0.95) compared to higher non-manual workers followed by self-employed (0.91, 0.81–1.03), manual workers (0.93, 0.85–1.03) and lower non-manual workers (0.98, 0.89–1.08).

Conclusion: Patients from lower socioeconomic groups in Sweden experience worse survival following a diagnosis of colon cancer. Differences exist in both the cure proportion and the survival time of the uncured, suggesting that socioeconomic differences cannot be attributed solely to lead time bias. Although this study has furthered our understanding of socioeconomic differences in survival, more detailed studies are required in order to identify, and subsequently remove, the underlying reasons for the differences.

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1. Introduction

Social class is associated with mortality for many malignancies including colon cancer.[1] The underlying reasons for social class differences in cancer patient survival are not fully understood, but are believed to depend on a combination of factors related to the biological properties of the tumour, the presence of co-morbidities, the health care system and social or psychological factors.[2] We have studied patient survival with respect to socioeconomic status (SES) within the framework of statistical cure models in a cohort of individuals diagnosed with colon cancer in Sweden over a 35-year period. Cure models for relative survival are a relatively recent development[3,4] and provide greater possibilities, compared to standard models, for gaining insight into possible explanations for observed differences in patient survival. In particular, these models simultaneously estimate two dimensions of patient survival, the cure proportion and the survival of the uncured. The cure proportion is not affected by lead time implying that we can use these models to assess the extent to which any differences may be explained by lead time bias. Such bias might arise in studies of survival if some groups of patients are systematically diagnosed earlier in the natural disease history, thereby prolonging the survival time even if the date of death remains unchanged.[5]

2. Materials and methods

2.1. Data

The nationwide population-based Swedish Cancer Register (SCR) was established in 1958. Notification of newly diagnosed tumours is mandatory by law for health care providers and laboratories and registration is close to complete.[6]

For the current study, we considered primary tumours of the colon (ICD-7: 153x) reported from 1965 to 2000 with follow-up to the end of 2004. We restricted the analysis to adenocarcinomas (C24 code 096[7]) and carcinoma not otherwise specified (C24 code 996[7]) which accounted for 85.0% and 5.2% of all colon cancers, respectively.

We classified SES using the Swedish socioeconomic index constructed by Statistics Sweden based on data from population and housing censuses conducted every 5 years from 1960 to 1990. The original classification consists of 18 categories of the economically active population, primarily based on self-reported occupation. In the most recent census information about occupation is retrieved from the statement of earnings reported to the Swedish Tax Office. The original classification of the socioeconomic index was then aggregated to form the five categories used in the current study; manual workers, lower non-manual workers, higher non-manual workers, farmers and self-employed.[8]

We classified patients according to the most recent non-missing SES prior to diagnosis and assigned retired patients to the last reported SES group. Patients for whom no information regarding previous occupation could be confirmed were classified as unknown.

We obtained information on date of death and emigration from the Causes of Death Register and the Historic Population Register maintained by the Swedish National Board of Health and Welfare and Statistics Sweden, respectively. Record linkage was facilitated by the unique civic registration number assigned to all Swedish citizens.[9]

2.2. Study base

We identified 89,958 individuals with a diagnosis of colon cancer in the SCR from 1965 to 2000. For patients with multiple primary colon cancers (2428 individuals), we included the first primary cancer in the analyses. We excluded patients for whom the cancer was detected incidentally at autopsy ($n = 3932$) as well as patients with inconsistent follow-up information ($n = 4$). Moreover, we restricted the cohort to patients younger than 80 years at diagnosis (thereby excluding 20,740 patients) because cure models can be less reliable for older age groups. Lastly, 5702 retired patients with no previously reported occupational information and 707 patients with otherwise missing SES information were excluded leaving 58,873 patients for the final cohort. The median age at diagnosis was 68 years (range 12–79) and the average follow-up time was 6.3 years.

The research was approved by the Karolinska Institutet Ethical Review Board.

2.3. Statistical analyses

In population-based studies, patient survival is typically measured using relative survival, defined as the ratio of observed survival to expected survival in a comparable group from the general population, matched with respect to age, sex and calendar period. Relative survival is advantageous because it provides a measure of excess mortality associated with the diagnosis of cancer that does not require information on cause of death and captures excess mortality both directly due to the cancer and indirectly, e.g. due to treatment-related mortality.[5] We obtained Swedish population mortality rates from the Human Mortality Database[10] that contains death rates and life tables stratified on age, sex and calendar year. In order to account for the fact that the lower socioeconomic groups are more likely to experience co-morbid conditions and hence competing risks, these background mortality rates were subsequently expanded by us to incorporate socioeconomic-specific death rates.[11] We first modelled excess mortality using Poisson regression, providing estimates of excess mortality rate ratios, and will refer to these models as traditional models for cancer patient survival.[12] We then analysed the cohort using cure models.

2.4. Cure models

Statistical cure originates from the theory of relative survival and is defined at a group level as the proportion of patients who, at some time following diagnosis, no longer experience excess mortality compared to the general population. The proportion who are not cured are referred to as 'the uncured'. We used mixture cure models for estimating the proportion cured along with the distribution of survival times for the uncured.[3,13] Although cure models allow us to simultaneously estimate the cure proportion and the survival of

the uncured group the fact that cure is defined at a group level implies that we cannot make individual predictions about which of the two groups a specific patient belongs to. To compare cure proportions between, for example, SES categories, we estimated odds ratios of cure where interpretation is similar to that of logistic regression models. For the uncured group we report median survival times assuming a Weibull distribution for the underlying survival function. We also estimated the difference in median survival times comparing each SES group to the group of higher non-manuals. Confidence intervals for the difference in median survival times were calculated using the delta method. A more detailed description of cure models and their interpretation as well as the mathematical details are provided by Lambert and colleagues.[3,13]

2.5. Modelling approach

All patients were followed from the date of diagnosis until death, first emigration or 31st December 2004, whichever came first. All models included sex, age at diagnosis (categorised as <50 years, 50–59 years, 60–69 years and 70–79 years) and calendar period as a restricted cubic spline with five knots, including boundary knots. Modelling continuous variables as splines is a flexible way to account for non-linear trends.[14] Possible interaction effects between SES and all potential confounders considered were investigated and assessed formally using likelihood ratio (LR) tests.

Non-proportional excess hazards are common in studies of cancer survival with the excess mortality rate ratio typically being highest the first year following diagnosis.[15] Deviations from proportionality were accounted for by introducing interaction terms with follow-up time in the Poisson regression models and by modelling both the shape and scale parameters of the Weibull distribution when fitting cure models. Stata 11 (College Station, TX: StataCorp) was used for all analyses together with publically available commands for estimating and modelling relative survival.[16,17]

3. Results

A description of the patient characteristics is provided in Table 1. Lower and higher non-manual workers appear to be diagnosed at a relatively younger age than the remaining socioeconomic groups. In all socioeconomic groups, apart from lower non-manuals, males constitute the majority of the cases.

3.1. Results from the Poisson model

Results from the Poisson regression model show that all SES groups experienced higher excess mortality compared to the group of higher non-manuals (Table 2). The excess mortality rates were 18% (95% confidence interval (CI): 11–26%) higher when comparing farmers to higher non-manuals. The corresponding estimates for manuals, self-employed and lower non-manuals were 11% (95% CI: 5–17%), 13% (95% CI: 6–21%) and 6% (95% CI: 0–12%). In general, women had a more favourable prognosis than men and excess mortality increased with age. There was no evidence that the effect of SES differed by period of diagnosis, indicating that the gap between the SES groups with respect to mortality has remained unchanged with calendar time ($p = 0.241$). When allowing non-proportional excess hazards for the effects of SES, we found strong evidence ($p < 0.001$) that the effect of SES was considerably more pronounced during the first six months following diagnosis (Fig. 1). We also found evidence of non-proportional effects of age and sex on excess mortality across follow-up time ($p < 0.001$). However, accounting for non-proportionality in those variables did not confound the effect of SES on mortality. Moreover, age at diagnosis did not seem to modify the effect of SES on mortality ($p = 0.371$).

3.2. Results from the cure model

The results from the cure model were consistent with the results from the Poisson model (Table 2). We found statistically significant effects of SES in both the odds of cure ($p = 0.003$)

Table 1 – Cohort characteristics of 58,873 patients diagnosed with colon cancer in Sweden 1965–2000.

	Higher non-manual workers, *n* (%)	Lower non-manual workers, *n* (%)	Farmers, *n* (%)	Self-employed, *n* (%)	Manual workers, *n* (%)	Total, *n*
Age at diagnosis						
<50 years	307 (8.8)	1597 (8.0)	208 (3.5)	234 (4.6)	1538 (6.2)	3884
50–59 years	675 (19.4)	3194 (16.1)	575 (9.8)	706 (14.0)	3558 (14.5)	8708
60–69 years	1167 (33.5)	6407 (32.2)	1784 (30.2)	1653 (32.8)	8343 (34.0)	19,354
70–79 years	1330 (38.3)	8680 (43.7)	3335 (56.5)	2451 (48.6)	11,131 (45.3)	26,927
Period of diagnosis						
1965–1974	493 (14.2)	3690 (18.6)	1782 (30.2)	1203 (23.8)	4440 (18.1)	11,608
1975–1984	747 (21.5)	5719 (28.8)	1962 (33.2)	1474 (29.2)	6797 (27.6)	16,699
1985–1994	1236 (35.5)	6609 (33.2)	1555 (26.4)	1521 (30.2)	8204 (33.4)	19,125
1995–2000	1003 (28.8)	3860 (19.4)	603 (10.2)	846 (16.8)	5129 (20.9)	11,441
Sex						
Males	2362 (67.9)	8547 (43.0)	3164 (53.6)	2930 (58.1)	13,313 (54.2)	30,316
Females	1117 (32.1)	11,331 (57.0)	2738 (46.4)	2114 (41.9)	11,257 (45.8)	28,557
Total, *n*	3479	19,878	5902	5044	24,570	58,873

Table 2 – The effect of socioeconomic status on excess mortality and the odds of statistical cure in 58,873 patients diagnosed with colon cancer in Sweden 1965–2000.

	Results from Poisson model		Results from cure models[a]			
	All patients		Cured		Uncured	
	Excess mortality rate ratios	95% CI	Relative odds of cure	95% CI	Difference in median survival time (months)[b]	95% CI
Socioeconomic status group						
Higher non-manual worker	1.00	(Reference)	1.00	(Reference)	0	(Reference)
Manual worker	1.11	(1.05–1.17)	0.93	(0.85–1.03)	−2.42	(−3.95, −0.88)
Farmer	1.18	(1.11–1.26)	0.85	(0.75–0.95)	−2.62	(−4.36, −0.88)
Self-employed	1.13	(1.06–1.21)	0.91	(0.81–1.03)	−2.64	(−4.43, −0.85)
Lower non-manual worker	1.06	(1.00–1.12)	0.98	(0.89–1.08)	−1.80	(−3.36, −0.24)
Sex						
Man	1.00	(Reference)	1.00	(Reference)	0	(Reference)
Woman	0.92	(0.90–0.94)	1.12	(1.07–1.18)	0.35	(−0.36, 1.05)
Age at diagnosis						
<50 years	1	(Reference)	1.00	(Reference)	0	(Reference)
50–59 years	1.05	(1.00–1.10)	0.94	(0.86–1.02)	−0.21	(−1.48, 1.07)
60–69 years	1.09	(1.04–1.15)	0.94	(0.87–1.01)	−1.92	(−3.11, 0.73)
70–79 years	1.16	(1.11–1.22)	0.96	(0.89–1.04)	−4.48	(−5.95, −3.42)

All models are also adjusted for calendar period of diagnosis (continuously).

[a] Estimated from a mixture cure model with a logit link function assuming constant main effects.

[b] All differences are estimated at the reference level of the remaining covariates. The reference level for calendar year of diagnosis was set to 1990.

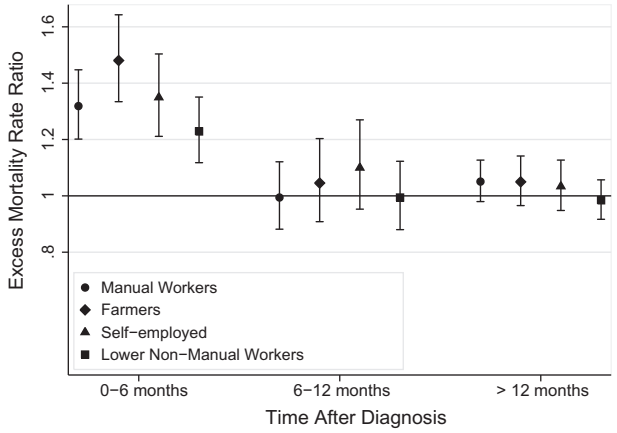

Fig. 1 – Effect of socioeconomic status on excess mortality compared to higher non-manual workers at various time points following a diagnosis of colon cancer.

and in the median survival times of the uncured ($p = 0.01$). Farmers had the lowest odds of cure with an estimated relative odds of 0.85 (0.75–0.95) compared to higher non-manuals. Note that the odds of cure is the cure proportion divided by one minus the cure proportion and the relative odds of cure is the ratio of two odds. Table 3 shows changes in cure proportions over time for the different age and SES groups in males based on a model that also included interactions between age at diagnosis and calendar period ($p < 0.001$) and SES and calendar period ($p = 0.298$). The latter interaction term was kept in the model, despite being non-significant, since one primary objective was to study the temporal trends of the association between SES and colon cancer mortality. There was no evidence of an additional interaction effect between SES and age at diagnosis ($p = 0.548$) in the cure model. The increase in cure proportions from 1980 to 2000 was in the order of 10–15% in all SES groups with only small differences observed between age groups. The estimated median survival times of the uncured males are shown in Table 4. For patients diagnosed in 1980 the median survival was in the range of 12.6 months (for manuals) to 15.1 months (for higher non-manuals) in the youngest age group. In the same year and for all SES groups the survival times decreased by age at diagnosis and ranged from 8.0 months (for manuals) to 10.3 months (for higher non-manuals) in the oldest age group. The differential survival pattern observed between age groups in the early years did, however, diminish as time progressed. The differences in median survival time comparing manuals, farmers, self-employed and lower non-manuals to the group of higher non-manuals did seem to decrease somewhat with calendar time (Table 4 and Fig. 2) but this trend could not be confirmed statistically (p for interaction = 0.135). The observed pattern was seen in all age groups, although it was more pronounced in the younger age groups and in particular when comparing the group of self-employed to the group of higher non-manuals (Fig. 2). The median survival times among the uncured females were slightly longer than those observed in the group of male patients ($p < 0.001$). The differences ranged from 0.5 to 1.5 months in all groups of Table 4 (data not shown).

4. Discussion

Statistical cure models estimate two dimensions of patient survival, thereby providing greater possibilities for making inference about the underlying mechanisms for differences in patient survival. In the present study, we have shown that

Table 3 – Predicted cure proportions by socioeconomic status, year of colon cancer diagnosis and age at diagnosis in males.

Age at diagnosis	Year of diagnosis	Cure fraction in percent (95% CI)					
		Manual workers[a]	Farmers[a]	Self-employed[a]	Lower non-manual workers[a]	Higher non-manual workers[a]	All groups combined[b]
<50 years	1980	41.3 (39.2–43.3)	39.0 (36.4–41.6)	40.8 (38.0–43.5)	42.6 (40.5–44.7)	44.1 (40.9–47.3)	41.7 (39.8–43.7)
	1990	46.4 (43.9–48.8)	43.4 (39.7–47.0)	46.9 (40.7–53.2)	47.9 (45.4–50.5)	47.9 (44.7–51.2)	47.0 (44.6–49.3)
	2000	55.0 (50.6–59.3)	51.2 (45.0–57.3)	53.8 (48.1–59.5)	56.7 (52.3–61.0)	55.2 (49.6–60.8)	55.6 (51.5–59.7)
50–59 years	1980	40.2 (38.5–41.9)	37.9 (35.6–40.2)	39.7 (37.2–42.1)	41.5 (39.7–43.3)	43.0 (40.0–45.9)	40.5 (39.0–42.1)
	1990	42.9 (41.0–44.9)	39.9 (36.6–43.2)	42.1 (39.1–45.1)	44.4 (42.4–46.5)	44.4 (41.5–47.3)	43.4 (41.6–45.2)
	2000	49.1 (45.6–52.6)	45.3 (39.7–50.9)	47.9 (42.8–53.0)	50.8 (47.2–54.3)	49.3 (44.3–54.3)	49.7 (46.4–52.9)
60–69 years	1980	39.9 (38.4–41.4)	37.6 (35.5–39.7)	39.4 (37.1–41.6)	41.2 (39.6–42.8)	42.7 (39.8–45.5)	40.1 (38.8–41.5)
	1990	43.8 (42.1–45.5)	40.7 (37.7–43.8)	43.0 (40.1–45.8)	45.3 (43.5–47.1)	45.3 (42.5–48.1)	44.1 (42.6–45.6)
	2000	51.1 (48.0–54.3)	47.3 (42.0–52.6)	50.0 (45.1–54.8)	52.8 (49.6–56.1)	51.3 (46.5–56.2)	51.5 (48.6–54.4)
70–79 years	1980	40.2 (38.5–41.8)	37.8 (35.7–39.9)	39.6 (37.3–41.9)	41.4 (39.7–43.1)	42.9 (39.9–45.9)	40.3 (38.8–41.7)
	1990	44.7 (42.9–46.4)	41.6 (38.5–44.6)	43.8 (40.9–46.7)	46.2 (44.3–48.0)	46.1 (43.3–49.0)	44.8 (43.2–46.4)
	2000	52.6 (49.3–55.8)	48.8 (43.5–54.0)	51.4 (46.5–56.3)	54.3 (51.0–57.6)	52.8 (47.9–57.7)	52.7 (49.7–55.7)

[a] Estimated from a mixture cure model including adjustment for sex, age at diagnosis, SES, calendar period and interaction terms for calendar time * age at diagnosis and SES * calendar time.
[b] Estimated from a mixture cure model adjusted for sex, age at diagnosis and calendar period.

Table 4 – Predicted median survival times of the uncured by socioeconomic status, year of colon cancer diagnosis and age at diagnosis in males.

Age at diagnosis	Year of diagnosis	Median survival time in months (95% CI)					
		Manual workers[a]	Farmers[a]	Self-employed[a]	Lower non-manual workers[a]	Higher non-manual workers[a]	All groups combined[b]
<50 years	1980	12.6 (11.7–13.6)	12.5 (11.3–13.7)	12.4 (11.2–13.7)	13.1 (12.1–14.2)	15.1 (13.4–17.0)	13.0 (12.1–14.0)
	1990	14.4 (13.0–15.9)	14.4 (12.4–16.6)	15.6 (13.4–18.2)	14.9 (13.5–16.5)	16.6 (14.7–18.8)	14.9 (13.6–16.4)
	2000	15.1 (12.6–18.1)	15.4 (11.7–20.1)	16.9 (13.4–21.4)	15.8 (13.2–18.8)	17.1 (13.6–21.5)	15.8 (13.3–18.7)
50–59 years	1980	12.4 (11.6–13.2)	12.3 (11.3–13.4)	12.2 (11.2–13.4)	12.9 (12.1–13.8)	14.9 (13.4–16.7)	12.8 (12.0–13.5)
	1990	14.5 (13.4–15.6)	14.5 (12.7–16.5)	15.1 (13.5–17.0)	15.0 (13.9–16.3)	16.8 (15.0–18.7)	15.0 (13.9–16.1)
	2000	15.5 (13.4–17.9)	15.8 (12.4–20.2)	17.4 (14.1–21.4)	16.2 (14.0–18.6)	17.5 (14.3–21.5)	16.1 (14.1–18.3)
60–69 years	1980	10.7 (10.1–11.4)	10.6 (9.7–11.5)	10.6 (9.7–11.6)	11.3 (10.6–12.0)	13.2 (11.7–14.8)	11.0 (10.4–11.6)
	1990	13.8 (12.9–14.8)	13.8 (12.2–15.6)	14.5 (13.0–16.2)	14.4 (13.4–15.5)	16.1 (14.5–18.0)	14.2 (13.4–15.1)
	2000	16.0 (14.1–18.3)	16.4 (13.0–20.6)	17.9 (14.7–22.0)	16.7 (14.6–19.1)	18.1 (14.7–22.1)	16.6 (14.7–18.7)
70–79 years	1980	8.0 (7.4–8.6)	7.9 (7.1–8.6)	7.9 (7.2–8.8)	8.4 (7.8–9.1)	10.1 (8.9–11.6)	8.2 (7.6–8.7)
	1990	11.6 (10.7–12.5)	11.4 (9.9–13.1)	12.3 (10.8–13.9)	12.2 (11.2–13.2)	13.9 (12.2–15.8)	12.0 (11.1–12.8)
	2000	14.8 (12.6–17.4)	15.0 (11.5–19.5)	16.9 (13.4–21.3)	15.6 (13.3–18.2)	17.1 (13.5–21.6)	15.4 (13.3–17.9)

[a] Estimated from a mixture cure model including adjustment for sex, age at diagnosis, SES, calendar period and interaction terms for SES * age at diagnosis and SES * calendar time.
[b] Estimated from a mixture cure model adjusted for sex, age at diagnosis and calendar period.

colon cancer patients from lower SES groups have a relatively worse prognosis than patients in the highest SES group. The SES differences in excess mortality cannot be fully explained by lead time bias since, when applying cure models, differences were observed in both the cure proportion and in the median survival times of the 'uncured'.

It is possible that colon cancer is diagnosed earlier in the natural history among the higher compared to the lower SES groups, either due to reduced 'patient delay' (time from onset of signs or symptoms to first contact with the health care system) or reduced 'doctor delay' (time from contact with the health care system to diagnosis and treatment). Diagnosis earlier in the natural history will, by definition, prolong survival time even if the time of death is unchanged and it is this difference that is referred to as lead time. Earlier diagnosis may also delay the time of death or increase the potential for cure. That is, early diagnosis can most certainly affect the cure proportion but the cure proportion is not affected by lead time. If more recently diagnosed tumours are, on average, diagnosed earlier in the natural history we might think that the increased lead time would manifest in longer survival times among the uncured. This is not, however, necessarily the case. Patients who are now curable due to earlier diagnosis may have had longer than average survival times so removing them from the 'uncured' group can result in a lower median survival time for the remaining uncured.

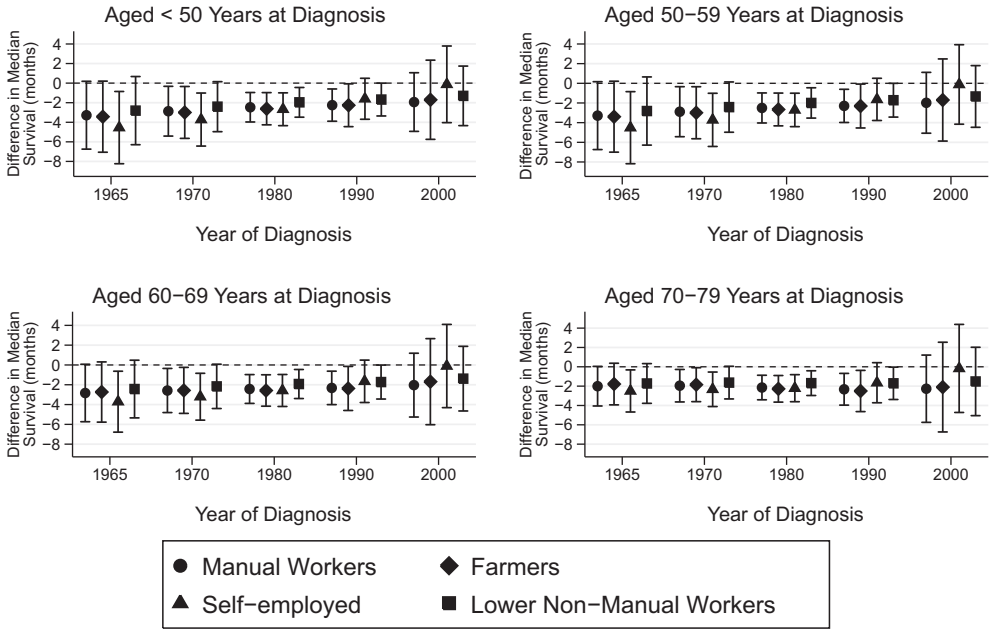

Fig. 2 – Differences in median survival times in the uncured in months compared to higher non-manual workers.

Age up to 80 years is most influential on the median survival of the 'uncured'; sex has a more pronounced effect on the cured proportion whereas SES influences both the cured proportion and the survival of the uncured. The odds of cure was lowest for farmers compared to higher non-manuals, closely followed by the self-employed and manuals.

Within each age group, the differences in cure proportion by SES remained almost unaffected by calendar time although a clear general improvement in the cure proportion with time was seen. We observed a tendency towards diminishing differences between SES groups with calendar time when comparing the median survival times of the uncured although this pattern did not reach statistical significance. Thus, these findings suggest that the underlying reasons for the differences between SES groups have remained through decades.

Vågerö and Persson[2] suggested that differences in survival are likely to be explained by differential access to health care, social support and treatment, different biological tumour properties or earlier detection of the cancer with improvement in prognosis that favours patients in higher social groups. Stage at diagnosis is the strongest predictor for colon cancer survival and we would expect to see differences in both the cure proportion and the survival of the uncured if the distribution of stage depends on SES. However, stage of the disease may depend on a combination of patient, health care and tumour factors and disentangling the effect of each of these, and thereby the underlying reasons for differences in the initial staging, on survival differences is non-trivial. For example, Auvinen[18] demonstrated that adjusting for stage in the analyses of colon cancer survival in Finland explained half of the observed SES differences while the evidence from studies investigating the socioeconomic variation in colon cancer tumour factors[19,20] is inconclusive. We were unable to control for stage at diagnosis since such data are not available in the Swedish Cancer Register for the study period. However, when studying SES differences in patient survival as a measure of equity in the health care system, the primary analyses should not be adjusted for stage since stage is in the causal path, even if it is of interest in future studies to investigate the extent to which stage explains any observed differences.

Unequal use of adjuvant and palliative chemotherapy could be a reason for SES differences but because treatment with chemotherapy was rarely used in Sweden before 1990, in any patients, observed differences in both the cure proportion and the survival of the uncured are unlikely to be attributable to differential access to chemotherapy treatment or trials, at least until the most recent study period. Differential participation in screening is also an unlikely source to the observed differences since there was no official screening programme in Sweden during the study period and opportunistic screening is still uncommon.

The SES differences in excess mortality were however more pronounced during the first 6 months following diagnosis, which could reflect earlier detection and fewer deaths among the higher SES groups immediately postoperatively or due to irresectable metastases at diagnosis.

Both our traditional analysis of relative survival and the analysis using cure models reveal a temporal improvement in patient survival, irrespective of SES, particularly in the oldest age group, as was reported recently in a Finnish study.[13] Such comprehensive advances in survival are likely due to overall improved health, reduced post-surgical mortality and advances in treatment. For illustration, in the 1980s no patient group was treated with adjuvant chemotherapy in Sweden. This gradually changed during the 1990s when selected groups, mostly younger patients, received it. It was not until the year 2000 when patients up to 75 years with

high-risk stage II and stage III tumours regularly received adjuvant chemotherapy. Similarly, palliative chemotherapy was rarely used in the 1980s, selectively using 5-fluorouracil (modulated with calciumfolinate) alone during the early 1990s and more universally during the late 1990s. This possibly explains why the greatest improvements in median survival times are found in the oldest patients, and why it is not until the most recent years that they have reached the levels observed in the younger age groups.

Because statistical cure is defined at a group level it is conceptually different from medical cure that can be defined from the time an individual patient no longer experiences signs and symptoms or risk of recurrence of the cancer. Although cure models do not allow us to make individual predictions about patients' potential for cure, our clinical knowledge can provide clues as to the composition of the two groups. Patients with distant metastatic disease, occurring either synchronously with the primary cancer or metachronously, are most likely to belong to the uncured group. Locally inextirpable or locally recurrent disease contributes to deaths from the disease too, but as isolated phenomena they are rare in colon cancer as opposed to rectal cancer.[21] Patients diagnosed with stage IV cancer constitute approximately 20–25% of the patients with a newly diagnosed colon cancer whereas among the patients diagnosed in stages I–III, about one-third develop incurable metachronous metastases.[22] Thus, the two groups that are likely to dominate among the uncured (i.e. patients with distant metastatic disease at diagnosis or those who develop it following the diagnosis of the primary tumour) are approximately of the same size. This suggests that a substantial part of the median survival time of the uncured population (ranging from 15.4 to 16.6 months in 2000) should be ascribed to survival time free from severe disease. Because of this, comparisons of the median survival times in the present study with those obtained from chemotherapy trials,[23,24] where the survival time is measured from trial inclusion or usually the diagnosis of metastatic disease, must be carried out with caution.

In conclusion, we have shown that cure models are a useful tool that not only provide estimates of cancer patient survival that are easy to interpret but also give greater opportunity to quantify the magnitude of the SES differences in order to better understand the impact of the factors that are most likely to be the reasons for SES differences in patient survival.

Conflict of interest statement

The authors report no conflicts of interest. The funding association had no role in the design, the data collection, the analysis and interpretation of the results or in the writing of the manuscript.

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