EUROPEAN JOURNAL OF CANCER 45 (2009) 1248–1256

available at www.sciencedirect.com

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# The impact of socioeconomic factors on 30-day mortality following elective colorectal cancer surgery: A nationwide study

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ARTICLE INFO

*Article history:*
Received 10 October 2008
Received in revised form 18 November 2008
Accepted 25 November 2008
Available online 10 January 2009

*Keywords:*
Colorectal cancer
Denmark
Nationwide
Postoperative mortality
Socioeconomic status
Comorbidity
Lifestyle

ABSTRACT

We investigated postoperative mortality in relation to socioeconomic status (SES) in electively operated colorectal cancer patients, and evaluated whether social inequalities were explained by factors related to patient, disease or treatment. Data from the nationwide database of Danish Colorectal Cancer Group were linked to individual socioeconomic information in Statistics Denmark. Patients born before 1921 and those having local surgical or palliative procedures were excluded. A total of 7160 patients, operated on in the period 2001–2004, were included, of whom 342 (4.8%) died within 30 days of surgery. Postoperative mortality was significantly lower in patients with high income (odds ratio (OR) = 0.82 (0.70–0.95) for each increase in annual income of EUR 13,500), higher education versus short education (OR) = 0.60 (0.41–0.87), and owner-occupied versus rental housing (OR) = 0.73 (0.58–0.93). Differences in comorbidity and to a lesser extent lifestyle characteristics accounted for the excess risk of postoperative death among low-SES patients.

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## 1. Introduction

As surgical techniques and adjuvant therapy improve, it becomes more and more relevant to focus on areas such as socioeconomic status and lifestyle in the search for improving the outcome of colorectal cancer. In a society like the Danish one, with equal access for all to the health care system, colorectal cancer patients undergoing elective surgery should have the same chances of surviving the first 30 days after surgery, independent of socioeconomic status (SES). However, there is increasing evidence that a social gradient exists in several colorectal cancer outcomes such as screening participation,[1–3] stage at diagnosis,[4–6] and long-term survival.[7–11] Disparities between social groups in relation to the stage of disease at diagnosis, to the treatment received in hospital and also to pre-hospital factors such as lifestyle and comorbidity may result in different risks of postoperative death for the different social groups. Recently, a British study found that social deprivation was associated with higher postoperative mortality.[12]

The unique Danish person identification system when linked to the nationwide clinical database of the Danish Colorectal Cancer Group (DCCG) and the social registers in Statistics

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doi:10.1016/j.ejca.2008.11.035

Denmark made it possible to get individual socioeconomic information on colorectal cancer patients. The aim of the study was to investigate the impact of the SES indicators such as income, education, and housing status on postoperative mortality in electively operated colorectal cancer patients, and to assess whether social inequalities were explained by factors related to patient, disease or treatment.

## 2. Materials and methods

The study population was derived from the national colorectal cancer database, which includes about 93% of patients diagnosed in Denmark with a first-time adenocarcinoma of the rectum or colon.[13] The primary study sample included 12,236 patients diagnosed between 1st May 2001 and 31st Dec 2004. Due to various reporting errors, 52 of these patients were excluded, as were 670 patients not having surgery, 1090 patients having a palliative intended operation (i.e. ostomy only and explorative laparotomy only), or a local procedure, 328 patients with unreported type of surgery and 52 patients with malignant polyps. In addition, 1488 patients born before 1921 were excluded because the central registries do not have information on education from that period. A further 242 patients with missing information in one or more of the SES variables were excluded. This left 8314 patients of whom 7160 were operated electively and were included in the study population.

### 2.1. *Socioeconomic variables*

The socioeconomic data were derived by data linkage to the population-based Integrated Database for Labour Marked Research (IDA) administered by Statistics Denmark since 1980. The variables in the database are based on linkage between all inhabitants of Denmark (5.4 million in January 2004), all companies with more than one employee, the taxation authorities, the Registry Relating to Unemployment, the Integrated Student Registry, and the Central Population Registry.[14]

Gross income in Danish kroner (DKK), comprising all income subject to taxation (wages and salaries, all types of benefits and pensions), was obtained for each patient and any cohabiting partner. A thousand DKK equals approximately 135 Euros. Income was corrected for inflation using Statistics Denmark's price index. Yearly variation in income was accounted for by calculating the average income in the 5 years before the diagnosis. For patients living with a partner, the average income of both was calculated. Education was categorised into three groups, as short education (i.e. mandatory education of up to 7 and 9 years for patients born before and after 1st Jan 1958, respectively), medium education (between 8/10 and 12 years – latest grades of primary school, secondary school, and vocational education) and higher education (over 12 years). Housing status was categorised as 'owner-occupied' and 'rental'. Cohabitation status was categorised as 'single' and 'living with partner'.

### 2.2. *End-point*

The study end-point was postoperative mortality, defined as death from all causes within 30 days of surgery, whether in hospital or after discharge. Date of death was obtained from the Central Population Registry of Statistics Denmark, as were age and sex.

**Table 1 – American Society of Anesthesiologists (ASA) grade.**

| | |
|---|---|
| ASA I | A normal healthy patient |
| ASA II | A patient with mild systemic disease |
| ASA III | A patient with severe systemic disease |
| ASA IV | A patient with severe systemic disease that is a constant threat to life |
| ASA V | A moribund patient who is not expected to survive with or without the operation |

### 2.3. *Clinical variables*

The clinical data were provided through the DCCG database, which is based on questionnaires to surgeons. These included data on date of surgery, tumour stage (from the International Union Against Cancer (UICC)), localisation of the tumour, surgical procedure, level of specialisation of the surgeon in gastrointestinal surgery, and assessment of American Society of Anesthesiologists (ASA) grade (Table 1).

### 2.4. *Other covariates*

The DCCG database also includes data from questionnaires answered by the patients prior to their operation. The questionnaires gave self reported information on alcohol consumption (average number of drinks per week during the previous year – beer (bottles), wine (glasses) and spirits (units)), use of tobacco (current smoker, ex-smoker, never smoker), height (in cm) and weight (in kilograms). The body mass index (BMI) was calculated from the last two (as weight divided by the square of height in metres). The lifestyle data were missing for up to 32% of individuals, either because of missing information in the specific variables or because the whole questionnaire was not completed. Missing lifestyle values were substituted by multiple imputation procedures as described below.

### 2.5. *Comorbidity*

A number of comorbidity variables were created by linking the personal identification number to files of Danish National Patient Registry, which contains information on all patient contact with clinical hospital departments in Denmark, to files of Danish Psychiatric Central Research Register, which contains data on all psychiatric admissions and outpatient treatment, and to files of Register of Medicinal Product Statistics, which contains information on the total sales of medicinal products in Denmark. Information regarding somatic and psychiatric treatment was taken from the five years preceding the year of operation, and information on medicine was taken from the two years preceding the year of operation. The dichotomous comorbidity variables described whether or not the patients (i) received medical treatment for cardiovascular diseases, (ii) had been hospitalised for cardiovascular diseases, (iii) were medically treated or hospitalised for chronic obstructive pulmonary disease, (iv) were medically treated or hospitalised for diabetes, (v) were medically treated or hospitalised for depression or schizophrenia, and (vi) were medically treated or hospitalised for liver, kidney or connective tissue diseases (other). A complete list of ICD-10 and ICD-8 codes as well as ATC-codes used for this purpose appears in the Appendix. In the analyses, these variables were used together with the clinical variable of ASA as markers of comorbidity.

### 2.6. Statistical methods

Logistic regression models were used to examine the influence of the socioeconomic factors on the postoperative mortality using the LOGISTIC procedure of SAS 9.1.3. Stepwise analyses were performed as follows: The first model included each SES variable alone, while adjusting for confounding by age, sex and year of operation. In analyses of income or housing status, adjustment for confounding by cohabiting status was also performed, while analyses of education omitted this variable, since current cohabiting status cannot influence the educational status of the patient, and thus cannot be a confounder of the association between education and postoperative mortality. In the second model, which represents the total effect of the different SES variables on postoperative mortality, income was adjusted for confounding by education, and housing status was adjusted for confounding by education and income. Education was not adjusted further in step two, because income and housing status were considered to be mediators of the investigated association. In the additional models, patient, disease, and treatment factors were included and were used to examine support for a mediating effect of these factors.

A test for linear trend was performed where relevant. Linearity of continuous variables (age and income) was tested by introduction of the square of the variables, which was insignificant in both cases, and thus removed from the model. As income decreases significantly at 65 years of age, the typical age of retirement, a dichotomous variable, age below or above 65 years, was included in the model to test if the impact of income was different in the two age groups. Since the variable was insignificant in the models and no interaction was observed between this variable and income on mortality, the variable was withdrawn from the analyses and income was kept as a continuous variable. Interactions of age, sex and anatomical localisation of the tumour with education, income and housing status were investigated and found insignificant and consequently not reported. Further, all combinations of interactions between income, education, housing status and cohabiting status on postoperative mortality were investigated and not found.

Information on lifestyle was incomplete. Alcohol, smoking and BMI were missing in 32%, 29% and 31% of individuals, respectively. Substitution of the missing lifestyle data made it possible to use the available data in the regression analysis. Multiple imputation[15] was performed by using the ice procedure of StataMP10. Thereby 10 datasets with imputed lifestyle values were generated. The imputation was performed with a model somewhat richer than analysis including the following variables: age, sex, 30-day mortality, income, education, housing status, cohabiting status, occupation, specialist status of surgeon, tumour stage, ASA grade, localisation of tumour, type of surgery, comorbidity status from the National Patient Registry, curative versus palliative outcome of surgery, besides the lifestyle variables from the complete cases. After performing standard regression analyses on the 10 datasets, the MIANALYZE procedure of SAS 9.1.3 was used to combine the results and generate valid statistical inference. A *p*-value of $<0.05$ was used as level of significance in all analyses.

## 3. Results

Of the 7160 patients included in the study population, 342 died during the first postoperative 30 days, resulting in a surgical mortality of 4.8%. Baseline characteristics are summarised in Table 2. Patients who died within 30 days had a higher mean age than patients who survived, 74 versus 68 years, and were more likely to be men, to live in rental housing, to have more advanced tumour stage and ASA stage, and were less likely never to have smoked. Likewise, the average household income was lower in patients who died as compared to patients who survived the postoperative period.

The multivariate logistic regression analyses of each SES factor adjusted for potential confounders (Table 3, model 2) showed that with each rise in annual income of DKK 100,000 (approximating EUR 13,500), the odds of death within 30 days of surgery decreased by 18% (Table 3). In addition, the odds of postoperative death were 40% lower in patients having a higher level of education as compared to short education. Also, the odds were 27% lower in patients living in owner-occupied housing than in rental housing. As can be seen from the attenuation of the estimates from step 1 to step 2, the effect of income was somewhat confounded by education, and housing status by income and education. When adjusting education for income the effect of education became insignificant, indicating that the effect of education was mediated through income (data not shown).

The subsequent analyses explored whether the social gradients in income, education and housing status could be accounted for by factors related to the patients' lifestyle (tobacco, alcohol and BMI) and comorbidity, the treatment (surgical procedure, specialisation of the surgeon), and/or disease (UICC stage). Adjusting for lifestyle attenuated the association in all three SES parameters, and additionally, including comorbidity raised the odds ratios, so that all confidence intervals included 1, though estimates were still skewed. Further adjustment for factors relating to disease and treatment did not influence the estimates. Thus, differences in comorbidity and to a lesser extent lifestyle 'explained' the social gradient in the risk of dying within 30 days of the operation.

## 4. Discussion

This nationwide Danish study showed a pronounced and inverse relation between SES and 30-day mortality after elective surgery for colorectal cancer. The social gradient was expressed by several SES parameters, i.e. income, education and housing status. Furthermore, the study found that the inequality was accounted for by patient factors (comorbidity and lifestyle), but not by treatment and disease factors.

Only one previous study had to our knowledge investigated the association between SES and 30-day mortality in

**Table 2 – Baseline characteristics of 7160 electively operated colorectal cancer patients born after 1920, Denmark, 2001–2004.**

| | Alive over 30 days after the operation N = 6818 | Dead within 30 days of the operation N = 342 | p-Value[a] |
|---|---|---|---|
| Age | | | <0.0001 |
| (median, interquartile range) | 68 (60–75) | 74 (69–79) | |
| Sex | | | <0.0001 |
| Male | 54 (3662) | 66 (224) | |
| Female | 46 (3156) | 34 (118) | |
| Income per year in Danish kroner | | | <0.0001 |
| (Median, interquartile range) | 175 622 (121 459–265 256) | 129 882 (105 643–197 572) | |
| Education | | | <0.0001 |
| Short | 38 (2557) | 51 (174) | |
| Medium | 45 (3085) | 39 (132) | |
| Higher | 17 (1176) | 11 (37) | |
| Housing status | | | <0.0001 |
| Rental | 35 (2402) | 49 (168) | |
| Owner-occupied | 65 (4416) | 51 (174) | |
| Cohabiting status | | | 0.02 |
| Single or widowed | 32 (2192) | 38 (131) | |
| Living with partner | 68 (4626) | 62 (211) | |
| Year of operation | | | 0.07 |
| 2001 | 17 (1178) | 18 (60) | |
| 2002 | 27(1843) | 21 (71) | |
| 2003 | 26 (1766) | 30 (101) | |
| 2004 | 30 (2031) | 32 (110) | |
| *Disease factors* | | | |
| Tumour stage, UICC | | | <0.0001 |
| I | 16 (1101) | 12 (42) | |
| II | 37 (2494) | 34 (117) | |
| III | 32 (2175) | 25 (84) | |
| IV | 15 (993) | 28 (94) | |
| Unknown | 1 (55) | 1 (5) | |
| Tumour localisation | | | 0.02 |
| Right colon | 29 (1953) | 35 (119) | |
| Left colon | 33 (2253) | 33 (112) | |
| Rectum | 38 (2612) | 32 (111) | |
| *Treatment factors* | | | |
| Specialisation of surgeon | | | 0.08 |
| Gastrointestinal surgery specialist | 61 (4185) | 57 (194) | |
| Not a specialist | 39 (2633) | 43 (148) | |
| Type of operation | | | <0.0001 |
| Right-sided hemicolectomia | 25 (1693) | 28 (95) | |
| Colectomia | 2 (130) | 3 (9) | |
| Transverse colonic resection | 2 (113) | 3 (9) | |
| Left-sided hemicolectomia | 6 (383) | 9(30) | |
| Hartmanńs operation | 9 (586) | 15 (51) | |
| Sigmoid resection | 23 (1534) | 16 (53) | |
| Anterior resection | 24 (1654) | 17 (59) | |
| Abdominoperineal resection (APR) | 10 (663) | 6 (19) | |
| Others | 1 (62) | 5 (17) | |
| *Comorbidity* | | | |
| ASA classification | | | <0.0001 |
| ASA I | 30 (2076) | 6 (22) | |
| ASA II | 48 (3380) | 39 (133) | |
| ASA III | 15 (1177) | 39 (133) | |
| ASA IV–V | 1 (113) | 8 (27) | |
| ASA unknown | 6 (414) | 8 (27) | |
| Cardiovascular disease (H) | | | |
| Yes | 27 (1845) | 48 (164) | <0.0001 |
| No | 73 (4973) | 52 (178) | |
| Cardiovascular disease (M) | | | |
| Yes | 44 (2993) | 61 (207) | <0.0001 |
| No | 56 (3825) | 39 (135) | |
| COPD (H + M) | | | |
| Yes | 10 (699) | 21 (71) | <0.0001 |
| No | 90 (6119) | 79 (271) | |

(*continued on next page*)

**Table 2 - *continued***

| | Alive over 30 days after the operation N = 6818 | Dead within 30 days of the operation N = 342 | *p*-Value[a] |
|---|---|---|---|
| Diabetes (H + M) | | | |
| Yes | 92 (6259) | 89 (304) | 0.06 |
| No | 8 (559) | 11 (38) | |
| Psychiatric disorder (H + M) | | | |
| Yes | 11 (720) | 18 (60) | <0.0001 |
| No | 89 (6098) | 82 (282) | |
| Other[b] (H + M) | | | |
| Yes | 6 (433) | 15 (52) | <0.0001 |
| No | 94 (6385) | 85 (290) | |
| *Lifestyle*[c] | | | |
| Alcohol | | | |
| Never | 21 | 30 | |
| ⩽ upper limit of recommendations[d] | 67 | 60 | |
| ⩽35 units/week | 9 | 6 | |
| >35 units/week | 3 | 5 | |
| Smoking | | | |
| Never-smoker | 29 | 15 | |
| Ex-smoker | 44 | 52 | |
| Current smoker | 27 | 33 | |
| Body mass index | | | |
| <30 kg/m$^2$ | 87 | 88 | |
| ⩾30 kg/m$^2$ | 13 | 12 | |

Values are percentages (numbers of patients in parentheses) – unless otherwise stated in brackets.
UICC: International union against cancer, ASA: American Society of Anaesthesiologists, H: hospitalisation, M: medical treatment.
a $X^2$ test (2-sided) or Wilcoxons test.
b Liver, kidney or connective tissue disease.
c Imputed values.
d Alcohol. Recommendations according to the National Board of Health. Below 14 units/week for women, below 21 units/week for men.

colorectal cancer patients.[12] That study included both elective and emergency patients and used an area-based SES-measure, the Townsend score, relating to the patients' postcode. The social gradient found was completely attenuated by disease factors and patient factors (ASA). Lifestyle information was not included in the study.

### 4.1. *Strengths and limitations*

The present study includes data on a well-defined Danish population of elective colorectal cancer patients from a clinical database with high completeness and validity of the clinical data reported by the surgeons.[13,16] We employ individual data on SES parameters, whereby misclassification, as often seen when using area-based indicators of SES, is reduced.[17] Furthermore, all information on socioeconomic status is collected prospectively and only for administrative purpose, thus, eliminating recall-bias. Using several different measures of SES is also an advantage, because the different measures cannot be used interchangeably as SES indicators, as they are not always correlated.[18] We chose to analyse patients having elective surgery only, since this patient group is much more homogeneous than are emergency patients. Further, the prognosis of emergency patients depends much on their clinical condition and consequently the impact of SES is minor. Moreover, the pre-operative treatment of elective patients is determined to a greater extent by guidelines rendering patients more comparable.

A weakness of the study is the high proportion of missing information on the lifestyle characteristics. The ideal condition would naturally have been to have complete information on all patients. Under the circumstances, substituting the missing lifestyle data is the best alternative.[15,19,20] Using multiple imputations makes it possible to analyse the total population. As an alternative, we could have made complete-case analyses on the subpopulation with no missing values. This subpopulation, though, is characterised by a postoperative mortality of only 2.7%, as compared to 8.5% in the subpopulation with missing values. Furthermore, patients with complete data had a slightly lower mean age (66 versus 69 years), lower ASA grade and higher SES than those with missing data. As a consequence, making complete case analyses would potentially have induced some serious bias. However, we cannot exclude the possibility that some selection bias persists in the multiple imputation model. Bias may also arise from the design of the questionnaire, in which only smoking habits at a fixed point in time are reported rather than those from a lifetime viewpoint. Patients who decide to quit smoking due to a current, severe illness will identify themselves as ex-smokers even though they have just stopped and so have the same risk as a regular smoker.[21] Finally, it is well known that reporting of smoking, alcohol, weight and height may be inaccurate, usually understated.[22,23] Accuracy of self reporting may vary by social class, thus inducing differential bias, which may diminish the effect of lifestyle.

**Table 3 – Risk of dying within 30 days from an elective colorectal cancer operation among 7160 patients born after 1920, Denmark, 2001–2004.**

| | Each SES factor analysed separately, adjusted for baseline confounders[a] | | Adjusted for baseline confounders and SES confounders[b] | | Stepwise inclusion of mediators | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Model | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | |
| | | | | | Patient factors | | | | Disease factors | | Treatment factors | |
| | | | | | Model 2 + alcohol + tobacco + bmi | | Model 3 + comorbidity | | Model 4 + stage | | Model 5 + specialist surgeon + type of operation | |
| | OR | 95% CI | OR | 95% CI | OR | 95% CI | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Income (per 100 000 dkk increase) | 0.78 | (0.64–1.03) | 0.82 | (0.70–0.95) | 0.86 | (0.74–0.995) | 0.91 | (0.79–1.05) | 0.90 | (0.78–1.04) | 0.90 | (0.78–1.04) |
| Short education (ref.) | 1 | | 1 | | 1 | | 1 | | 1 | | 1 | |
| Medium education | 0.81 | (0.64–1.03) | 0.81 | (0.64–1.03) | 0.84 | (0.66–1.08) | 0.89 | (0.69–1.14) | 0.90 | (0.69–1.15) | 0.88 | (0.68–1.14) |
| Long education | 0.60 | (0.41–0.87) | 0.60 | (0.41–0.87) | 0.65 | (0.44–0.96) | 0.78 | (0.53–1.15) | 0.78 | (0.53–1.16) | 0.76 | (0.51–1.13) |
| *p*-value – Wald test | 0.02 | | 0.02 | | 0.07 | | 0.38 | | 0.41 | | 0.35 | |
| *p*-value – test for trend | 0.004 | | 0.004 | | 0.02 | | 0.17 | | 0.18 | | 0.15 | |
| Rental housing (ref.) | 1 | | 1 | | 1 | | 1 | | 1 | | 1 | |
| Owner-occupied housing | 0.67 | (0.53–0.85) | 0.73 | (0.58–0.93) | 0.76 | (0.60–0.97) | 0.86 | (0.67-1.09) | 0.87 | (0.68–1.11) | 0.86 | (0.67–1.10) |

Abbreviations: OR = Odds ratio, 95% CI = 95% confidence interval, ASA = American Society of Anaesthesiology, dkk = Danish kroner, Ref. = reference value, *p*-value = probability value.

a Baseline confounders: Income and housing status is adjusted for age, sex, year of operation, and cohabiting status. Education is adjusted for age, sex, and year of operation.

b Income is adjusted for education and baseline confounders. Education is only adjusted for baseline confounders (identical to model 1). Housing status is adjusted for income, education and baseline line confounders.

The inclusion of comorbidity in the models raised the odds ratios towards one and rendered the associations between the SES variables and 30-day mortality insignificant. Yet, the estimates were still somewhat below one. More comprehensive measures of comorbidity than those used here may have approached the estimates further to one, as may possibly more accurate measurement of lifestyle factors.

### 4.2. *Possible mechanisms and implications of the study*

The associations of income, education and housing status with 30-day mortality were attenuated when lifestyle and comorbidity were included in the models, rendering the estimates insignificant. This means that the effect was mediated through lifestyle and especially comorbidity. The mediating effect of comorbidity is to some extent expected since comorbidity is known to accumulate in people of low SES.[24–26] Further, population-based studies have documented that high comorbidity is associated with a higher postoperative mortality in colorectal cancer patients.[27,28] A more profound understanding of the interrelation between SES, comorbidity and postoperative mortality would require exact data on causes of death, which are difficult to obtain because of the low validity of death diagnosis and low autopsy rates. Also smoking, excessive alcohol consumption and obesity are reported more frequently among people of lower SES.[26,29] While smoking status is an established prognostic factor of postoperative mortality,[30–32] excess alcohol consumption has been reported to increase the incidence of complications in the postoperative course,[31,33,34] whereas abstainers have a higher surgical mortality.[32] In this study, current smokers and abstainers from alcohol had increased 30-day mortality (data not shown). Obesity has been reported to increase the incidence of wound infections, but has not consistently affected postoperative mortality.[35–37] Also in this study, we found no effect of obesity. Inclusion of lifestyle factors as potential mediators had only a minor impact on the association between SES and 30-day mortality, as discussed previously.

Disease and treatment factors did not account for the social gradient. Stage of disease, surgical procedure and specialisation of the surgeon were investigated as potential mediating factors, because they are reported to be independently associated with 30-day mortality,[38–40] and we hypothesised that they could be socially unequally distributed.

In conclusion, the study showed a marked increase in postoperative mortality after elective colorectal cancer surgery in low socioeconomic groups. The inequality was attributed to differences in comorbidity and, to a lesser extent, lifestyle. The study offers insight into the link between SES and postoperative mortality. Individually tailored approaches to peri- and post-operative care, paying special attention to comorbidity and lifestyle, might be effective in reducing the social inequality in postoperative mortality, as well as postoperative mortality in general, but this remains to be confirmed in specific intervention trials.

## Conflict of interest statement

None declared.

## Ethical approval

The project did not require approval by the Regional Committee on Biomedical Research Ethics.

## Acknowledgements

The authors are grateful to Lisbeth Nørgaard Møller for statistical assistance and helpful discussions.

*Grants:* This work was supported by The Danish Cancer Society [DP05043] and The Health Insurance Foundation [2008B084].

## Appendix

**ICD8, ICD10 and ATC codes used for generation of comorbidity variables.**

| | ICD8 | ICD10 | ATC |
|---|---|---|---|
| Cardiovascular diseases, hospitalisation | 344; 410;427.09; 427.10; 427.11; 427.19; 428.99; 430–438;440;442;444; 445; 782.49 | I10–I15; I20–I25; I46; I50.0–1–9; I60–I67 I69; I70; I71; I72; I74; G45.0–8–9; G46 | |
| Cardiovascular diseases, medical treatment | | | C01A;C01B; C01D; C02A; C02C; C02K C04; C07; C08; C09 |
| Chronic obstructive pulmonary disease | 490–493; 515–518 | J40–47; J96.1; J98.1–2 | R03 |
| Diabetes | 249–250 | E10; E11; E14; H360 | A10 |
| Depression/schizophrenia | 295; 296 | F30–33; F20 | N06A; N05A |
| Kidney diseases | 403; 404; 580–583; 584; 590.09; 593.19; 792 | I12; I13; N00–N05; N07; N11; N14; N17–N19 | |
| Liver diseases | 070.00; 070.02; 070.04; 070.06; 070.08; 573.00; 456.00–456.09; 571; 573.01; 573.04 | B150; B16-19; K70-73; K76.6; I85.0-9; | |
| Connective tissue diseases | 712; 7341; 4460; 4463 | M05; M06; M10; M30–M36; D86 | M09A; M04A; H05A; M01C |

Other: kidney, liver, and connective tissue diseases.

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