An analysis of competing mortality risks among colorectal cancer survivors in Queensland, 1996-2009

Paramita Dasgupta,[1] Danny R Youlden, [1] Peter D Baade[1,2,3]

[1] Cancer Council Queensland, Brisbane, Australia

[2] School of Public Health, Queensland University of Technology, Brisbane, Australia

[3] Griffith Health Institute, Griffith University, Gold Coast, Australia

Corresponding Author: A/Prof Peter D Baade,
Senior Research Fellow (Biostatistics)
Viertel Centre for Research in Cancer Control

Cancer Council Queensland, PO Box 201, Spring Hill QLD 4001 Australia

Email: peterbaade@cancerqld.org.au

Fax: +61 7 3259 8527; Phone: +61 7 3634 5317

Key words:

Colorectal cancer, competing risks, survival inequalities, Fine and Gray modeling

Word length:

Manuscript word count (excluding title page, abstract, references, and tables): 4025
Abstract word count: 249
References: 47
Tables: 3
Supplementary Material: 1 Table
Figures: 3

Abstract

Purpose: Colorectal cancer survivors are at risk of dying from other causes including comorbidities and second malignancies. This study was undertaken to identify demographic and clinical predictors of cancer-specific and competing causes of mortality.

Methods: The crude probabilities of mortality attributed to colorectal cancer, other cancers and non-cancer causes were estimated for 19,415 residents of Queensland, Australia, who were diagnosed with a first primary colorectal cancer between 1996 and 2007 when aged 20-79 years and survived at least two months, with follow-up to the end of 2009. Multivariate competing risk analysis was used to analyse covariate effects on the cumulative probability of the different mortality types.

Results: Five year cumulative probabilities of colorectal cancer, other cancers and non-cancer mortality were 29.4% (95% CI 29.3, 30.7), 2.0% (95% CI 1.8, 2.2) and 5.7% (95% CI 5.3, 6.0), respectively. Factors associated with an increased risk of non-cancer mortality included older age, male gender, unmarried status, localized disease, first primary colon cancers, no surgery and the presence of comorbidities. Apart from diagnosis of a metachronous secondary cancer, being older, unmarried or in blue collar occupations were independent predictors of increased mortality due to other cancers.

Conclusions: A better understanding of the role of competing events and the ability to predict risk of such events have the potential to translate into more effective individualized strategies for colorectal cancer management. The control of comorbidities and reducing cancer risk through clinical management and lifestyle changes should be an important and attainable goal for CRC survivors.

Introduction

Colorectal cancer (CRC) remains an important public health problem(1) and a leading cause of cancer-related mortality worldwide.(2) Earlier diagnosis and improved treatments(3) mean that more patients are likely to survive longer after a CRC diagnosis.(4) These survivors are also at increased risk of mortality from other cancers and non-cancer causes.(5)

Despite the significantly increased risks of subsequent malignancies in CRC patients being extensively documented,(6, 7) the survival impact of secondary cancers has not been well established. Using a clinical trial database in the United States, Zamboni and colleagues reported poorer conditional survival for nearly 7,000 CRC patients subsequently diagnosed with second cancers,(8) whereas a hospital-based review of about 1,000 Korean patients(9) found no significant differences in mortality risk. However the smaller sample size and inherent selection bias of such studies can limit their applicability to the general population.

The standard Kaplan-Meier estimator of CRC survival, which censors non-CRC mortality rather than specifically acknowledging that patients dying from other causes are no longer at risk of CRC mortality, may be biased in competing-risk situations.(10) The recommended approach(10, 11) for estimating the probability of mortality occurring in a competing risk setting is to use cumulative probability functions (CPFs). The CPF is a function of the hazards for all competing events, so only persons who remain alive are considered at risk of CRC mortality. In contrast, the Kaplan-Meier estimator which only considers the hazard for CRC mortality treats people who die from competing events as censored.(10, 12)

Similarly, covariate effects in cause-specific Cox proportional hazards models pertain solely to CRC mortality without considering how the covariates act on competing events. Their interpretation in terms of survival probabilities can therefore be misleading in competing risk situations.(10, 11) An alternative approach that directly models covariate effects on the cumulative probabilities for different types of mortality was proposed by Fine and Gray.(13) These Fine and Grey models are being increasingly used to explore predictors of site-specific and competing mortality for various cancers and thus develop prognostic models for stratifying patients according to their competing mortality risks.(14-16)

The choice between the widely accepted Cox proportional hazards model and the Fine and Gray competing risk methodology depends on the research question(s) of interest. Since the first approach focuses on the covariates associated with risk of CRC mortality, it is well suited to assess whether potential prognostic factors are indeed associated with an increased hazard of CRC mortality. However, simply modeling the covariate effects on CRC mortality gives an incomplete picture of the mortality faced by people diagnosed with CRC, because it ignores deaths caused by other conditions. If the interest is in identifying predictors of competing mortality, then modeling covariate effects on the cumulative probabilities of all mortality events is essential. These differences are important since a covariate may appear to increase the probability of CRC mortality simply by lowering the rate of occurrence of non-CRC mortality even if it does not affect the rate of CRC mortality.(10, 11, 15, 17)

In this study we used competing risk methodology to examine the impact of various demographic and clinical factors on the probability of mortality from CRC, other cancers or non-cancer causes for a large population-based cohort of CRC patients from Queensland, Australia. To our knowledge there have been no large-scale population-based epidemiological studies with long-term follow up examining the predictors of mortality risks among CRC survivors from cancer and then separately from non-cancer causes. This information is crucial to inform the development of a criterion framework for individually tailored therapies by identifying patient subgroups at higher risk for competing events or CRC-specific mortality.

Methods

Ethical approval to conduct this study was obtained from the University of Queensland Social and Behavioural Sciences Ethical Review Committee. Queensland Health gave legislative consent to access routinely collected population-based cancer incidence data in Queensland and to link this with the Queensland Hospital Admitted Patient Data Collection.(18)

Study cohort

All incident cases of invasive CRC (ICD-O-3 codes C18- C20, C21.8) diagnosed between January 1, 1996 and December 31, 2007 (inclusive) were extracted from the state-wide population-based Queensland Cancer Registry, to which all confirmed invasive cancers diagnosed among Queensland residents must be legally reported.(19) We then restricted our cohort to those aged 20-79 at diagnosis since CRC is very rare among younger individuals and inaccuracies in death certification are more likely in the older age group.(20) Variables extracted included age, year, sex, marital status, occupation, CRC site (colon C18; rectum C19-C20, C218), country of birth and incidence of subsequent primary cancers (to 31 December 2009). Our choice of covariates was restricted to those collected by the registry or accessible from administrative data bases. Second primary cancers were defined according to IARC rules (21) as histologically distinct invasive tumours that developed after a prior cancer diagnosis. Individuals were classified as having either a synchronous (diagnosed within 2 months) or metachronous (diagnosed after 2 months) second cancer while those diagnosed with both these types (0.2% of the final cohort) were included in the 'metachronous' group.(6) Patients with no further primary cancers were categorized as 'solitary' CRC cases.

Treatment and comorbidities

A deterministic linkage between the Queensland Cancer Registry and the Queensland Hospital Admitted Patient Data Collection provided information on CRC-related surgery and hospital comorbidities. The latter are defined as a condition that either co-exists with the principal diagnosis (CRC) or arose during a hospital stay and which influence a patient's clinical management.(18) The ICD-10-AM diagnostic codes (22)from hospital records were used to identify the most frequently occurring comorbidities for our cohort, namely diabetes (E10-E14), cerebrovascular (I60-I64), heart (I20-I50) and kidney disease (N00-N05, N10-N19).

Colorectal cancer staging

The procedure used to extract CRC stage at diagnosis using information recorded on pathology forms has been described previously.(23, 24) Localized cases (stages I-II) were collectively classified as "early stage" while

regional and metastatic disease (stages III-IV) were categorized as “advanced stage”(7) to allow sufficient numbers for modelling.

Travel distances

Actual road travel distances from a patient’s residence to the closest radiation facility were calculated using geographical information system software and a street network database on a year-specific basis to account for the increasing coverage of such facilities over time.(24) Where full address details were not available (13.1% of records in the final cohort), location was geocoded to the centroid of the patient’s postcode at diagnosis. Radiation centres in Queensland are generally affiliated to major centres for cancer care; hence these distances are a proxy measure of access to optimum cancer treatment.

Survival data

The cohort was followed up to 31 December 2009, a minimum of 2 years from the time of initial diagnosis for each patient who was still alive at the end date. Survival was measured in days from date of CRC diagnosis to date of death or study end point. Causes of death were classified as CRC, other cancer causes or non-cancer causes. The Queensland Cancer Registry obtains details for all cancer patients who died in Queensland from the Registrar of Births, Deaths and Marriages.(19) Data matching with the National Death Index(25) and the Australian Bureau of Statistics(19) allows identification of interstate deaths. Case-specific reviews by specialised cancer coders using additional clinical information from various sources including pathology records, hospital data and autopsy reports to that in the death certificate are used to finalise cause of death. This allows a high degree of accuracy. However as with all registry-based studies the potential misclassification of cause of death remains a possibility.

Statistical analysis

The ‘stcompet’ command in Stata(26) was used to calculate the crude cumulative probability of cause of death while accounting for the dependence of the CPF on the hazards of all competing events. The resulting curves were compared across patient sub-groups by the Pepe and Mori test,(27) which is based on cumulative weighted differences of the cause-specific probabilities between two groups. The impact of censoring and death among the cohort is to progressively reduce the effective sample size over time. To reflect this, the weight used in the Pepe and Mori test decreases with increasing time after diagnosis so that differences at earlier time points when the sample size is large are given more importance than differences at later time points.(17) Since we were comparing two categories with the baseline category, we used a more conservative significance cut-off of $p<0.025$ for this analysis.

We then used the competing risk regression method of Fine and Gray(13) to estimate covariate effects on the probability of mortality due to CRC, other cancers and non-cancer causes. This approach allows direct modelling of the CPF for competing risks data by using a quantity that corresponds to the hazard of the sub-distribution for the failure event of interest, known as the sub-distribution hazard.(13) The sub-distribution hazard can be thought of as the probability of failure due to cause *k* at a given time, conditional on no cause *k*

failures having occurred so far.(11) This method distinguishes between patients who are still alive and those who have already died from competing causes through weighted estimators.(13) Only those people who are still alive at the end of the follow up period are considered censored. This approach also allows direct interpretation of the covariate effects on the CPF since the interpretation of the sub-hazard ratios is similar to that of hazard ratios. This means that an exponentiated positive regression coefficient for a covariate category implies a higher predicted probability of mortality compared to the reference category.(28) These competing mortality risks are not independent since a higher risk of death from one cause implies a lower risk of another cause. Estimated CPF using competing risks approach were compared visually to those generated using the standard Kaplan-Meier method.(29)

Potential violations of the proportional hazards assumption were tested by treating each covariate as a time varying coefficient, and including these in the final model only if the time-varying components were statistically significant.(30) Parameter estimates from the Fine and Gray models are presented as sub-hazard ratios (SHRs which can be thought of as the hazard ratio for the probability of failure due to a specific cause at a given time (that is the sub-distribution hazard) with 95% confidence intervals (95% CIs).

Estimates were initially adjusted for age at first cancer diagnosis, sex, country of birth, marital status, occupation, stage, site, surgical treatment, diabetes, other comorbidities, travel distance and secondary cancers. All available covariates (Table 2) that were significant at $p \leq 0.20$ in the initial multivariate analysis were retained in the final models.

All analyses were performed with Stata version 12.1 (StataCorp, TX).

Results

Study cohort

Between 1996 and 2007 there were 27,756 invasive CRC cases in Queensland of which 22,488 who were aged 20-79 years at diagnosis initially comprised the study cohort. The exclusion of patients who survived less than two months (n=1,101, 4.0%) and those who had a prior diagnosis of another invasive cancer (n=1,972, 7.1%) left a final cohort of 19, 415 patients with a first primary CRC.

More than half (57.6%) of this cohort were male, 63.8% were initially diagnosed with colon cancer and the median age at first diagnosis was 66 years. (interquartile range: 57-72 years) Around a third (36.3%) had advanced disease, 7.6% had diabetes, 3.4% had another of the specified comorbidities and the majority (87.4%) underwent CRC-related surgery. There were 535 (2.8%) synchronous and 2,026 (10.4%) metachronous secondary primaries recorded over the study period.

Mortality from colorectal cancer and competing causes

During the follow-up period (median 4.5 years, interquartile range 2.2-13.7 years), 8,106 patients (41.8%) died, with 5,937 (73.2%) of these deaths resulting from CRC, 560 (6.9%) from other cancers and 1,609 (19.9%) from non-cancer causes. Table 1 summarizes available characteristics by mortality status.

The overall five year cumulative probabilities of mortality due to CRC, other cancers and non-cancer causes were 29.4% (95% CI 29.3, 30.7), 2.0% (95% CI 1.8, 2.2) and 5.7% (95% CI 5.3, 6.0), respectively. (Fig. 1)

A comparison of the overall five year cumulative probability of mortality (with 95% CI) estimated by Kaplan-Meier and competing risks approaches suggests that the former consistently overestimates the probability of competing deaths due to other cancers or non-cancer causes. (Online Resource 1) Estimated curves by CRC stage (Fig. 2) and diagnosis age (Fig. 3) are also shown. The mortality curves for these particular covariates have been illustrated because they were generally representative of the magnitude of the differences between the cumulative probability curves estimated by the two methods, particularly for other-cancer and non-cancer mortality.

CRC mortality: The unadjusted probability of CRC mortality was lower for females, those born in non-English-speaking countries, surgically treated cases and those with metachronous secondary cancers. (Table 2) Higher probability of CRC mortality was evident for patients who were unmarried, in blue collar occupations, diagnosed with advanced disease, had comorbidities other than diabetes or lived further away from major cancer treatment centres.

Other cancer causes of mortality: Significant predictors of lower mortality risk from other cancers were younger age, being female, birth in non-English-speaking countries and advanced stage. (Table 2) In contrast, a surgical treatment and (as expected) a second cancer diagnosis (either synchronous or metachronous) were associated with greater likelihood of mortality from other cancers.

Non-cancer causes of mortality: Patients who were younger, female, had advanced CRC or developed metachronous second primaries were less likely to die from non-cancer causes, whereas increased non cancer mortality was associated with being unmarried, in blue collar occupation and having diabetes, or other comorbidities (Table 2).

Competing risk analysis

CRC mortality: Following multivariate competing risks regression, significant independent predictors for increased CRC mortality were being female, unmarried, in blue-collar occupations, advanced stage, comorbidities except diabetes and increasing travel distance (Table 3). Younger age at diagnosis, birth in non-English-speaking countries, surgery and second primary cancers (particularly metachronous) were independently associated with decreased mortality from CRC.

Other cancer mortality: The probability of competing mortality due to other cancers was lower for CRC patients aged below 60 years than those aged 60-79 years. In addition to the diagnosis of metachronous second cancers, other predictors of increased other cancer mortality were being unmarried or in blue collar occupations.

Non-cancer mortality: Increased non-cancer mortality was associated with being younger, unmarried, an initial colon cancer diagnosis, diabetes and other comorbidities, whereas being female, advanced stage, surgery and metachronous second cancers were statistically significant predictors of lower non-cancer mortality.

While females had significantly lower probability of CRC mortality in the bivariate competing risk analysis (Table 2), the direction of this association was reversed in the final multivariate model (Table 3). Further analysis (not shown) found evidence of a significant interaction effect ($p<0.001$) between sex and occupation, with females in the unemployed/not known category having increased risks of CRC mortality compared to males. In contrast there was no significant ($p>0.05$) evidence for a gender difference among the other occupation categories for CRC mortality, nor for the other types of mortality.

Discussion

Using a large population-based cohort of CRC patients, we identified various prognostic factors for CRC mortality and competing mortality from other cancers or non-cancer causes. Little is currently known about risk factors for competing mortality in CRC patients, particularly those based on competing risks methodology. We found that the standard Kaplan-Meier approach tends to overestimate mortality risks due to non-cancer or other-cancer causes. To our knowledge, this is the first Australian study to explore predictors of competing mortality for CRC survivors in Australia. Internationally, one population-based study from the United States reported increasing age, male sex, localized disease and comorbidities to be significant predictors of non-CRC mortality.(31) However that study combined all non-CRC deaths into a single category and the analysis was restricted to patients aged over 65 years.

Although the significantly increased probability of other cancer mortality for CRC patients having second primary cancers in our cohort was intuitively obvious, we provide quantitative evidence for synchronous versus metachronous cancers. Moreover, being diagnosed with a second cancer was protective in terms of CRC mortality and also non-cancer mortality in the case of metachronous cancers.

Gender differences in unmeasured biological, environmental and lifestyle factors,(32, 33) probably contributed to the observed variations in mortality probabilities between males and females in our cohort. For example, less aggressive treatments(32) and higher treatment-related toxicities have been reported for women(33) although men have higher risks of chronic diseases and adverse health behaviors.(34)

The survival advantage for married patients in our cohort may reflect increased social support to buffer the negative impact of stress-related biological processes and greater practical assistance while undergoing treatment.(35) Occupation can be seen as a measure of individual socioeconomic disadvantage; again,

underlying variations in currently unmeasured factors associated with socioeconomic status(36, 37) may have impacted the results.

The protective effect of surgery on non-cancer mortality suggests that surgery may be a proxy for factors such as better overall health and higher level functional status. Increased medical surveillance following surgery may also result in the earlier detection and more timely treatment of comorbidities.(38)

Age and comorbidities (except diabetes) were associated with increased probabilities of both CRC and competing mortality for patients in our cohort. Advancing age has been related to inadequate surgery, non-receipt of multimodal therapies, reduced therapeutic efficacy and multiple comorbidities.(33, 39) Comorbidities themselves can significantly influence the clinical management of CRC patients (40) while diabetes in particular is associated with an increased likelihood of other chronic conditions as well as risk factors (notably obesity) for poorer prognosis. Residual confounding by unmeasured lifestyle and patient factors is also likely.(40, 41) We lacked the necessary data to explore these issues further.

The time lag for chronic comorbid conditions to manifest any adverse effects means that their prognostic impact is reduced if an advanced tumor or second cancer intervenes to cause an early death. Hence, for CRC patients with advanced disease or metachronous second primaries it is cancer rather than other conditions that primarily determines the outcome.

The risks of competing mortality events have not traditionally being considered when developing evidence-based clinical guidelines. Our study reinforces the identified need for greater surveillance of CRC survivors(38) via routine screening and follow-up, along with multicomponent lifestyle interventions for preventing second cancers and reducing the risk of chronic diseases,(5, 42) particularly among older patients.(5) Improved understanding of the relationship between prognostic factors and competing mortality risks may also serve to identify opportunities for promoting primary preventive health behaviors especially among high-risk patient populations.(43, 44) This is especially important with the number of CRC survivors expected to increase over coming decades.(5)

At a minimum, a healthy and physically active lifestyle(44) that can reduce both the risk of developing second cancers and chronic diseases as well as aid in the clinical management of already existing diseases should be a priority for CRC survivors. Improved prevention and/or management of comorbidities can be beneficial not only in reducing competing mortality risks but also allow the completion of more aggressive treatment regimes that enhance the overall prognosis for CRC patients.(45)

This study adds to the growing body of international evidence that competing mortality events are important among cancer survivors and become increasing likely with advanced age, other cancers and comorbidities.(16, 46) While we were limited in our capacity to control for all possible confounders and there is potential for misattribution of cause of death to have biased observed estimates to some extent, (47) we believe that the current results provide novel and important insights into the prognostic impact of various risk factors. They may

also provide the foundation for more detailed studies incorporating various lifestyle factors and detailed treatment modalities to further elucidate the underlying mechanisms behind observed variations in competing mortality risks among CRC survivors. Such studies are currently lacking and would be informative in the development of more effective clinical strategies to optimize favorable outcomes and reduce mortality.

Study strengths include a large population-based cohort for whom data were collected independently of the study hypotheses. The high degree of histological verification within the Queensland Cancer Registry(19) allowed differentiation of new primaries from metastatic CRC. Linkage to an administrative database of hospital records within Queensland provided information on surgical status and selected comorbidities. However, this data would be missing for a small proportion of patients who received subsequent treatment interstate. Missing medical information may also be related to errors in notification or data matching processes.(7)

As the Queensland Cancer Registry does not collect data on receipt and completion of non-surgical procedures notably radiation and systemic therapies, treatment toxicities, and lifestyle factors we were unable to control for these potential confounders.(5, 33, 37, 42) Information on individual comorbidities was limited to conditions recorded during a hospital stay and may not be comprehensive. Study results could also have been influenced by the lack of sensitivity and specificity of our occupation measure since it was not possible to disaggregate the 'unemployed/not known' category into more homogenous groupings such as 'home duties', 'retired' or unemployed' based on available data. The Queensland cancer registry also does not collect information on individual income and education.

CONCLUSIONS

This study has identified several important sub-groups of CRC patients (such as being older, unmarried, with localized disease, comorbidities or secondary cancers) who are at increased risk of dying from causes other than CRC. A better awareness among CRC patients and their doctors of the risk of competing causes of death, and the ability to quantify the extent of this risk, has the potential to translate into more effective individualized strategies for the clinical management of CRC cases. In particular strategies that reduce the incidence or impact of comorbidities, including second cancers, through clinical management, education and lifestyle changes should be a priority.

Funding

This study was supported by a grant from the (Australian) National Health and Medical Research Council (NHMRC) (ID561700). Associate Professor Peter Baade is supported by an NHMRC Career Development Fellowship (ID1005334).

Acknowledgments

The authors wish to thank staff working in the Queensland Cancer registry and Queensland Health for providing us with the data extracts used in this analysis.

References:

1. Gellad ZF, Provenzale D. (2010) Colorectal cancer: national and international perspective on the burden of disease and public health impact. Gastroenterology. 138: 2177-90.
2. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM (2010) GLOBOCAN 2008: Cancer incidence and mortality worldwide. Lyon, France: IARC accesed 20 May 2011. Available from: http://globcan.iarc.fr/.
3. Cunningham D, Atkin W, Lenz H-J, et al. (2010) Colorectal cancer. Lancet. 375: 1030-47.
4. Mariotto AB, Rowland JH, Ries LA, Scoppa S, Feuer EJ. (2007) Multiple cancer prevalence: a growing challenge in long-term survivorship. Cancer Epidemiol Biomarkers Prev. 16: 566-71.
5. Campo RA, Rowland JH, Irwin ML, Nathan PC, Gritz ER, Kinney AY. (2011) Cancer Prevention after Cancer: Changing the Paradigm—a Report from the American Society of Preventive Oncology. Cancer Epidemiology Biomarkers & Prevention.
6. Curtis RE, Freedman DM, Ron E, et al. (2006) *New Malignancies among cancer survivors: SEER cancer registries,1973-2000*:National Cancer Institute, Bethesda, MD.NIH Publ. No. 05-5302 accesed 10 Nov 2011. Available from: http://seer.cancer.gov/publications/mpmono/.
7. Dasgupta P, Youlden DY, Baade PD. (2012) Multiple primary cancers among colorectal cancer survivors in Queensland, Australia, 1996-2007. Cancer Causes Control. 23: 1387-98.
8. Zamboni BA, Yothers G, Choi M, et al. (2010) Conditional survival and the choice of conditioning set for patients with colon cancer: an analysis of NSABP trials C-03 through C-07. J Clin Oncol. 28: 2544-8.
9. Lee WS, Lee JN, Choi S, Jung M, Baek JH, Lee WK. (2010) Multiple primary malignancies involving colorectal cancer-clinical characteristics and prognosis with reference to surveillance. Langenbecks Archives of Surgery. 395: 359-64.
10. Andersen PK, Geskus RB, de Witte T, Putter H. (2012) Competing risks in epidemiology: possibilities and pitfalls. Int J Epidemiol. 41: 861-70.
11. Dignam JJ, Zhang Q, Kocherginsky M. (2012) The Use and Interpretation of Competing Risks Regression Models. Clin Cancer Res. 18: 2301-8.
12. Gooley TA, Leisenring W, Crowley J, Storer BE. (1999) Estimation of failure probabilities in the presence of competing risks: new representations of old estimators. Stat Med. 18: 695-706.
13. Fine JP, Gray RJ. (1999) A Proportional Hazards Model for the Subdistribution of a Competing Risk. Journal of the American Statistical Association. 94: 496-509.
14. Hanrahan EO, Gonzalez-Angulo AM, Giordano SH, et al. (2007) Overall Survival and Cause-Specific Mortality of Patients With Stage T1a,bN0M0 Breast Carcinoma. J Clin Oncol. 25: 4952-60.
15. Mell LK, Dignam JJ, Salama JK, et al. (2010) Predictors of competing mortality in advanced head and neck cancer. J Clin Oncol. 28: 15-20.
16. Rose BS, Jeong JH, Nath SK, Lu SM, Mell LK. (2011) Population-based study of competing mortality in head and neck cancer. J Clin Oncol. 29: 3503-9.
17. Pintile M. (2006) Competing Risks: A Practical Perspective: Wiley
18. Data Services Unit QH (2006) Queensland Hospital Admitted Patient Data Collection (QHAPDC) Manual 2006-2007. accesed 03 January 2012. Available from: http://www.health.qld.gov.au/hic/qhapdc2006/QHAPDC_Manual_0607.pdf.
19. Queensland Cancer Registry, Cancer Council Queensland. (2011) Cancer in Queensland: Incidence, Mortality, Survival and Prevalence, 1982 to 2008.
20. Grulich AE, Swerdlow AJ, Silva IDS, Beral V. (1995) Is the apparent rise in cancer mortality in the elderly real? analysis of changes in certification and coding of cause of death in England and Wales, 1970–1990. Int J Cancer. 63: 164-8.
21. International Agency for Research on Cancer, International Association of Cancer Registries, European Network of Cancer Regstries. (2005) International rules for multiple primary cancers. Asian Pac J Cancer Prev. 6: 104-6.
22. National Centre for Classification in Health (NCCH). (2006) International Statistical Classification of Diseases and Related Health Problems,10th revision, Australian Modification (ICD-10-AM). 5th ed. Sydney: Faculty of Health Sciences, University of Sydney.
23. Krnjacki LJ, Baade PD, Lynch BM, Aitken JF. (2008) Reliability of collecting colorectal cancer stage information from pathology reports and general practitioners in Queensland. Aust N Z J Public Health. 32: 378-82.
24. Baade PD, Dasgupta P, Aitken JF, Turrell G. (2011) Distance to the closest radiotherapy facility and survival after a diagnosis of rectal cancer in Queensland. Med J Aust. 195: 350-4.
25. Cramb SM, Garvey G, Valery PC, Williamson JD, Baade PD. (2012) The first year counts: cancer survival among Indigenous and non-Indigenous Queenslanders, 1997-2006. Med J Aust. 196: 270-4.

26. Coviello V, Boggess M. (2004) Cumulative incidence estimation in the presence of competing risks. Stata Journal. 4: 103-12.
27. Pepe MS, Mori M. (1993) Kaplan—meier, marginal or conditional probability curves in summarizing competing risks failure time data? Stat Med. 12: 737-51.
28. Wolbers M, Koller MT, Witteman JC, Steyerberg EW. (2009) Prognostic models with competing risks: methods and application to coronary risk prediction. Epidemiology. 20: 555-61.
29. Kim HT. (2007) Cumulative incidence in competing risks data and competing risks regression analysis. Clin Cancer Res. 13: 559-65.
30. Cleves MA, Gutierrez RG, Gould MW, Marchenko YV. (2010) An Introduction to Survival Analysis using Stata, Third Edition. Revised ed: Stata Press.
31. Lee M, Cronin KA, Gail MH, Feuer EJ. (2012) Predicting the absolute risk of dying from colorectal cancer and from other causes using population-based cancer registry data. Stat Med. 31: 489-500.
32. Koo JH, Leong RW. (2010) Sex differences in epidemiological, clinical and pathological characteristics of colorectal cancer. J Gastroenterol Hepatol. 25: 33-42.
33. Pal SK, Hurria A. (2010) Impact of Age, Sex, and Comorbidity on Cancer Therapy and Disease Progression. J Clin Oncol. 28: 4086-93.
34. Australian Institute of Health and Welfare (2012) *Australia's health 2012* Canberra:AIHW.Australia's Health series no.13. Cat.no; AUS 156. accesed 23 July 2012. Available from: http://www.aihw.gov.au/publication-detail/?id=10737422172&tab=3.
35. Pinquart M, Duberstein PR. (2010) Associations of social networks with cancer mortality: A meta-analysis. Crit Rev Oncol Hematol. 75: 122-37.
36. Aarts MJ, Lemmens VE, Louwman MW, Kunst AE, Coebergh JW. (2010) Socioeconomic status and changing inequalities in colorectal cancer? A review of the associations with risk, treatment and outcome. Eur J Cancer. 46: 2681-95.
37. Frederiksen BL, Osler M, Harling H, Ladelund S, Jorgensen T. (2009) Do patient characteristics, disease, or treatment explain social inequality in survival from colorectal cancer? Soc Sci Med. 69: 1107-15.
38. Cancer Council Australia Colonoscopy Surveillance Working Party (2011) *Clinical Practice Guidelines for Surveillance Colonoscopy- in adenoma follow up; following curative resection of colorectal cancer; and for cancer surveillance in inflammatory bowel disease.* Sydney:Cancer Council Australia, accesed 29 December 2011. Available from: http://wiki.cancer.org.au/australia/Guidelines:Colorectal_cancer/Colonoscopy_surveillance.
39. Young JM, Leong DC, Armstrong K, et al. (2007) Concordance with national guidelines for colorectal cancer care in New South Wales: a population-based patterns of care study. Med J Aust. 186: 292-5.
40. Lee L, Cheung WY, Atkinson E, Krzyzanowska MK. (2011) Impact of comorbidity on chemotherapy use and outcomes in solid tumors: a systematic review. J Clin Oncol. 29: 106-17.
41. Koroukian SM, Bakaki PM, Schluchter MD, Owusu C. (2011) Treatment and survival patterns in relation to multimorbidity in patients with locoregional breast and colorectal cancer. Journal of Geriatric Oncology. 2: 200-8.
42. Carmack CL, Basen-Engquist K, Gritz ER. (2011) Survivors at Higher Risk for Adverse Late Outcomes Due to Psychosocial and Behavioral Risk Factors. Cancer Epidemiology Biomarkers & Prevention. 20: 2068-77.
43. Hawkes AL, Lynch BM, Youlden DR, Owen N, Aitken JF. (2008) Health behaviors of Australian colorectal cancer survivors, compared with noncancer population controls. Support Care Cancer. 16: 1097-104.
44. Rock CL, Doyle C, Demark-Wahnefried W, et al. (2012) Nutrition and physical activity guidelines for cancer survivors. CA Cancer J Clin. 62: 242-74.
45. Kosinski L, Habr-Gama A, Ludwig K, Perez R. (2012) Shifting concepts in rectal cancer management. CA Cancer J Clin. 62: 173-202.
46. Mell LK, Jeong J-H, Nichols MA, Polite BN, Weichselbaum RR, Chmura SJ. (2010) Predictors of competing mortality in early breast cancer. Cancer. 116: 5365-73.
47. German RR, Fink AK, Heron M, et al. (2011) The accuracy of cancer mortality statistics based on death certificates in the United States. Cancer Epidemiol. 35: 126-31.

Figure Captions:

Fig.1 Cumulative probability of mortality due to colorectal cancer, other cancers and non-cancer causes for colorectal cancer patients in Queensland, 1996-2009.

Fig. 2 Cumulative probability of mortality by colorectal stage (early: n=9,439; advanced: n=7,052) estimated using Kaplan-Meier (KM) and Competing Risks (CR) methods for colorectal cancer patients in Queensland, 1996-2009: a) colorectal cancer mortality b) other cancer mortality c) non-cancer mortality. Note that a different scale is used for the various causes of mortality.

Fig. 3 Cumulative probability of mortality by age at initial diagnosis (20-59: n=6,030; 60-79: n=13,385) estimated using Kaplan-Meier (KM) and competing risks (CR) methods for colorectal cancer patients in Queensland, 1996-2009: a) colorectal cancer mortality b) other cancer mortality c) non-cancer mortality. Note that a different scale is used for the various causes of mortality.

Supplementary Material:

Online Resource 1 Five-year cumulative probability of mortality from colorectal cancer, other cancer causes and non-cancer causes stage estimated using Kaplan-Meier (KM) and Competing Risks (CR) methods for colorectal cancer patients, Queensland, 1996-2009

Table 1: Population characteristics by mortality status for colorectal cancer patients in Queensland, 1996-2009

Characteristic	Alive	Died		
		Colorectal Cancer	Other Cancers	Non-Cancer
All patients in cohort	11,309 (58.2)	5,937 (30.6)	560 (2.9)	1,609 (8.3)
Age at first cancer diagnosis				
20 to 59	3,977 (66.0)	1,830 (30.3)	74 (1.2)	149 (2.5)
60 to 79	7,332 (54.8)	4,107 (30.7)	486 (3.6)	1,460 (10.9)
Sex				
Male	6,258 (55.9)	3,547 (31.7)	377 (3.3)	1,018 (9.1)
Female	5,051 (61.5)	2,390 (29.1)	183 (2.2)	591 (7.2)
Country of birth[1]				
Australia	8,422 (57.3)	4,588 (31.2)	447 (3.1)	1,237 (8.4)
Other English-speaking	1,430 (58.2)	767 (31.3)	66 (2.7)	192 (7.8)
Non-English-speaking	1,457 (64.3)	582 (25.6)	47 (2.1)	180 (8.0)
Marital status				
Married	7,793 (60.2)	3,912 (30.2)	348 (2.7)	895 (6.9)
Not married[2]	3,169 (52.6)	1,974 (32.7)	208 (3.4)	679 (11.3)
Unknown	347 (79.4)	51 (11.7)	-[3]	35 (8.0)
Occupation				
Professional/White collar	3,213 (49.1)	2,604 (39.8)	237 (3.6)	490 (7.5)
Blue collar	1,264 (39.3)	1,520 (47.2)	138 (4.2)	298 (9.3)
Unemployed/Not known[4]	6,832 (70.8)	1,813 (18.8)	185 (1.9)	821 (8.5)
Initial cancer stage[5]				
Early (Stage I-II)	6,837 (72.4)	1,310 (13.9)	343 (3.6)	949 (10.1)
Advanced (Stage III-IV)	2,835 (40.2)	3,684 (52.3)	135 (1.9)	398 (5.6)
Unknown	1,637 (56)	938 (32.1)	87 (2.9)	262 (9)
Initial cancer site[6]				
Colon	7,175 (57.9)	3,739 (30.2)	382 (3.1)	1,088 (8.8)
Rectum	4,134 (58.8)	2,198 (31.3)	178 (2.5)	521 (7.4)
Surgical treatment				
Had surgery	10,160 (59.9)	4,935 (29.1)	502 (3.0)	1,362 (8.0)
No surgery	1,149 (46.8)	1,002 (40.8)	58 (2.3)	247 (10.1)
Diabetes *(E10-E14)*				
No	9,413 (60.8)	4,502 (29.1)	446 (2.8)	1,132 (7.3)
Yes	747 (51)	433 (29.5)	56 (3.8)	230 (15.7)
Unknown	1,149 (46.8)	1,002 (40.8)	58 (2.3)	247 (10.1)
Other *comorbidities*[7]				
No	9,899 (60.8)	4,701 (28.9)	476 (2.8)	1,215 (7.5)
Yes	261 (39.1)	234 (35)	26 (3.9)	147 (22.0)
Unknown	1,149 (46.8)	1,002 (40.8)	58 (2.3)	247 (10.1)
Travel distance				
0-99 km	8,181 (60.2)	3,905 (28.8)	371 (2.7)	1,123 (8.3)
100-249 km	1,287 (55.5)	747 (32.2)	73 (3.2)	210 (9.1)
250 km or more	1,841 (52.4)	1,285 (36.6)	116 (3.2)	276 (7.8)
Secondary primary cancers[8]				
None	9,963 (59.1)	5,524 (32.8)	0	1,367 (8.1)
Synchronous	265 (49.5)	165 (30.8)	57 (10.7)	48 (9.0)
Metachronous	1,081 (53.4)	248 (12.2)	503 (4.8)	194 (9.6)

1. Other English-speaking: those born in New Zealand, United Kingdom, Ireland, or North America; non-English-speaking: those not born in Australia, New Zealand, United Kingdom, Ireland or North America.
2. Includes single, divorced, separated or widowed.
3. Not shown due to less than 5 observed counts.
4. Includes not in labour force or unspecified employment status.
5. Early stage includes local and regional cases while advanced stage includes distant and metastatic cases.
6. Colorectal sites defined as: Colon (ICDO3: C18) and Rectal (ICDO3: C19-C20, C218).
7. Heart disease (I20-I50), cerebrovascular disease (I60-I64) or kidney disease (N00-N05, N10-N19).
8. Synchronous: diagnosed within first 2 months; Metachronous: diagnosed more than 2 months after initial cancer diagnosis.

Table 2: Five-year cumulative probability of mortality from colorectal cancer, other cancer causes and non-cancer causes for colorectal cancer patients, Queensland, 1996-2009

		Colorectal Cancer Causes		Other Cancer Causes		Non-Cancer Causes	
	number	CPr (95% CI) [1]	p[2]	CPr (95% CI) [1]	p[2]	CPr (95% CI) [1]	p[2]
All patients in cohort	19,415	29.4 (29.3, 30.7)		2.0 (1.8, 2.2)		5.7 (5.3, 6.0)	
Age at first cancer diagnosis							
20 to 59	6,030	29.2 (28.6, 30.1)	p=0.163	0.9 (0.6, 1.1)	p<0.001	1.9 (1.6, 2.3)	p<0.001
60 to 79	13,385	30.3 (29.3, 31.9)	ref	2.5 (2.2, 2.8)	ref	7.3 (6.9, 7.8)	ref
Sex							
Male	11,200	31.2 (30.3, 32.1)	ref	2.3 (2.0, 2.6)	ref	6.5 (6.0, 7.0)	ref
Female	8,215	28.4 (27.4, 29.4)	p<0.001	1.6 (1.3, 1.9)	p=0.003	4.5 (4.1, 5.0)	p<0.001
Country of birth[3]							
Australia	14,694	31.2 (29.9, 31.8)	ref	2.1 (1.8, 2.3)	ref	5.7 (5.3, 6.2)	ref
Other English-speaking	2,455	30.7 (28.8, 32.6)	p=0.995	2.2 (1.7, 2.9)	p=0.879	5.6 (4.7, 6.6)	p=0.515
Non-English-speaking	2,266	25.3 (23.5, 27.2)	p<0.001	1.2 (0.8, 1.8)	p=0.002	5.2 (4.3, 6.3)	p=0.113
Marital status							
Married	12,948	29.8 (28.9, 30.6)	ref	2.0 (1.7, 2.2)	ref	4.9 (4.5, 5.3)	ref
Not married[4]	6,030	32.0 (30.8, 33.2)	p<0.001	2.3 (1.8, 2.6)	p=0.934	7.4 (6.7, 8.1)	p<0.001
Unknown	437	11.2 (8.5, 14.4)	p<0.001	1.4 (0.4, 3.6)	p=0.557	4.8 (3.0, 7.2)	p=0.691
Occupation							
Professional/White collar	6,544	38.9 (37.7, 40.2)	ref	2.6 (2.3, 3.1)	ref	5.6 (5.0, 6.2)	ref
Blue collar	3,220	46.5 (44.7, 48.3)	p<0.001	3.1 (2.5, 3.8)	p=0.287	7.4 (6.5, 8.4)	p<0.001
Unemployed/Not known[5]	9,651	18.4 (17.6, 19.2)	p<0.001	1.1 (0.9, 1.4)	p<0.001	5.1 (4.6, 5.6)	p=0.038
Initial cancer stage[6]							
Early (Stage I-II)	9,439	12.9 (12.2, 13.6)	ref	2.4 (2.1, 2.8)	ref	6.4 (5.9, 7.0)	ref
Advanced (Stage III-IV)	7,052	52.7 (51.5, 53.9)	p<0.001	1.4 (1.1, 1.8)	p<0.001	4.3 (3.8, 4.8)	p<0.001
Unknown	2,924	31.8 (30.0, 33.5)	p<0.001	1.9 (1.5, 2.5)	p=0.272	6.3 (5.5, 7.4)	p=0.491
Initial cancer site[7]							
Colon	12,384	29.7 (28.8, 30.5)	p=0.745	2.1 (1.9, 2.4)	p=0.038	5.9 (5.5, 6.3)	p=0.086
Rectum	7,031	30.6 (29.5, 31.8)	ref	1.7 (1.4, 2.0)	ref	5.3 (4.7, 5.8)	ref
Surgical treatment							
Had surgery	16,959	28.7 (28.0, 29.4)	p<0.001	2.0 (1.8, 2.3)	p=0.006	5.6 (5.3, 6.0)	p=0.530
No surgery	2,456	39.4 (37.4, 41.3)	ref	1.5 (1.0, 2.0)	ref	5.9 (5.0, 7.0)	ref
Diabetes (E10-E14)[8]							
No	15,493	28.6 (27.9, 29.3)	ref	2.0 (1.8, 2.2)	ref	5.0 (4.6, 5.4)	ref
Yes	1,466	29.7 (27.3, 32.2)	p=0.125	2.8 (2.0, 3.9)	p=0.493	12.4 (10.6, 14.3)	p<0.001
Other comorbidities[8,9]							
No	16,291	28.5 (27.8, 29.2)	ref	2.0 (1.8, 2.3)	ref	5.2 (4.8, 5.6)	ref
Yes	668	33.3 (29.7, 37.0)	p=0.002	2.5 (1.5, 4.0)	p=0.213	15.8 (13.1, 18.8)	p<0.001
Travel distance							
0-99 km	13,580	28.3 (27.6, 29.1)	ref	2.0 (1.7, 2.2)	ref	5.7 (5.3, 6.2)	ref
100-249 km	2,317	31.4 (29.5, 33.4)	p=0.002	2.1 (1.6, 2.8)	p=0.635	6.2 (5.2, 7.3)	p=0.447
250 km or more	3,518	35.6 (33.9, 37.2)	p<0.001	1.9 (1.5, 2.5)	p=0.682	5.1 (4.3, 5.9)	p=0.239
Secondary primary cancers[10]							
None	16,854	32.5 (31.8, 33.3)	ref	-[11]		5.8 (5.4, 6.2)	ref
Synchronous	535	30.9 (26.9, 35.0)	p=0.204	10.6 (8.1, 13.5)	ref	6.9 (4.8, 9.3)	p=0.052
Metachronous	2,026	9.5 (8.3, 10.9)	p<0.001	14.8 (13.2, 16.4)	p<0.001	4.2 (3.4, 5.2)	p<0.001

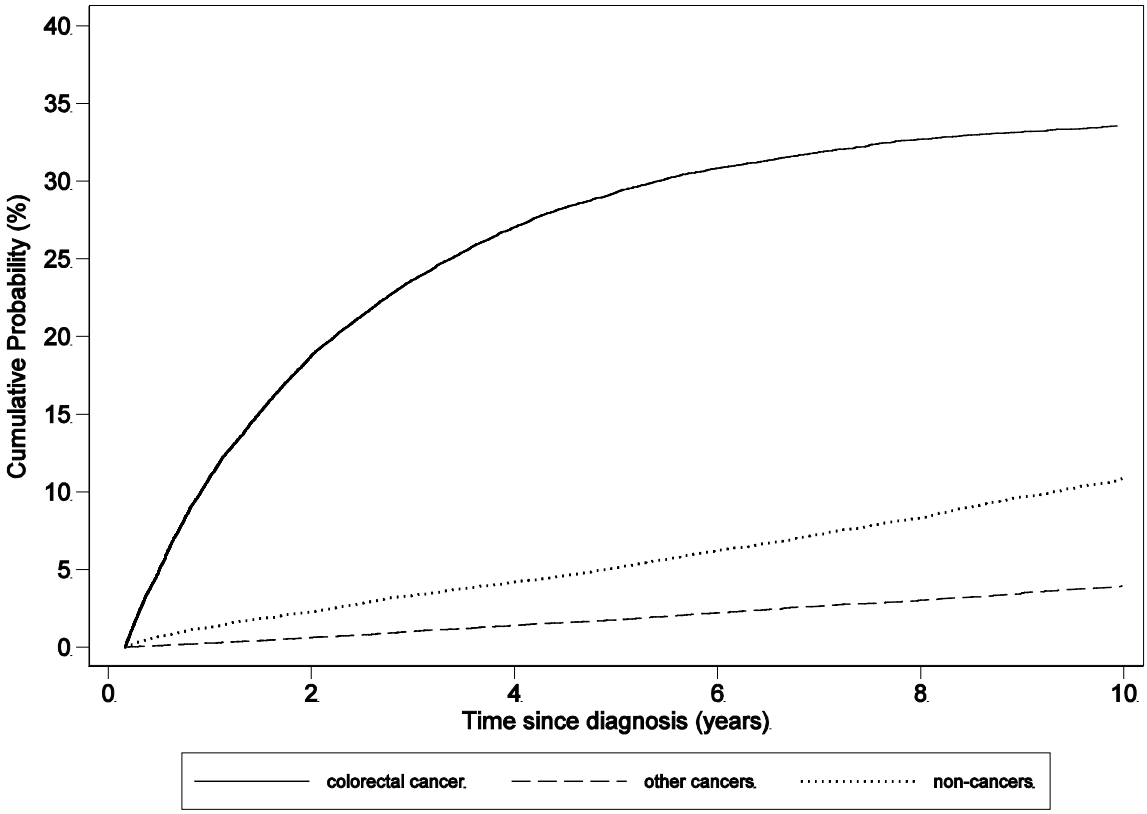
1. CPr: Five-year cumulative probability of mortality with 95% confidence intervals (CI)
2. p values were computed from Pepe and Mori test, restricting follow-up to five years. They represent the significance of the difference between the category-specific probability and the reference category ("ref").
3. Other English-speaking: those born in New Zealand, United Kingdom, Ireland, or North America; non-English-speaking: those not born in Australia, New Zealand, United Kingdom, Ireland or North America.
4. Includes single, divorced, separated or widowed.
5. Includes not in labour force or unspecified employment status.
6. Early stage includes local and regional cases while advanced stage includes distant and metastatic cases.
7. Colorectal sites defined as: Colon (ICDO3: C18) and Rectal (ICDO3: C19-C20, C218).
8. Patients with unknown diabetes or other comorbidities status have same values as those with no surgical treatment.
9. Heart disease (I50), cerebrovascular disease (I60-I64) or kidney disease (N00-N05, N10-N19).
10. Another primary cancer diagnosed within 2 months of the first cancer (synchronous) or more than 2 months afterwards (metachronous).
11. No deaths of this type were possible for people with colorectal cancer only.

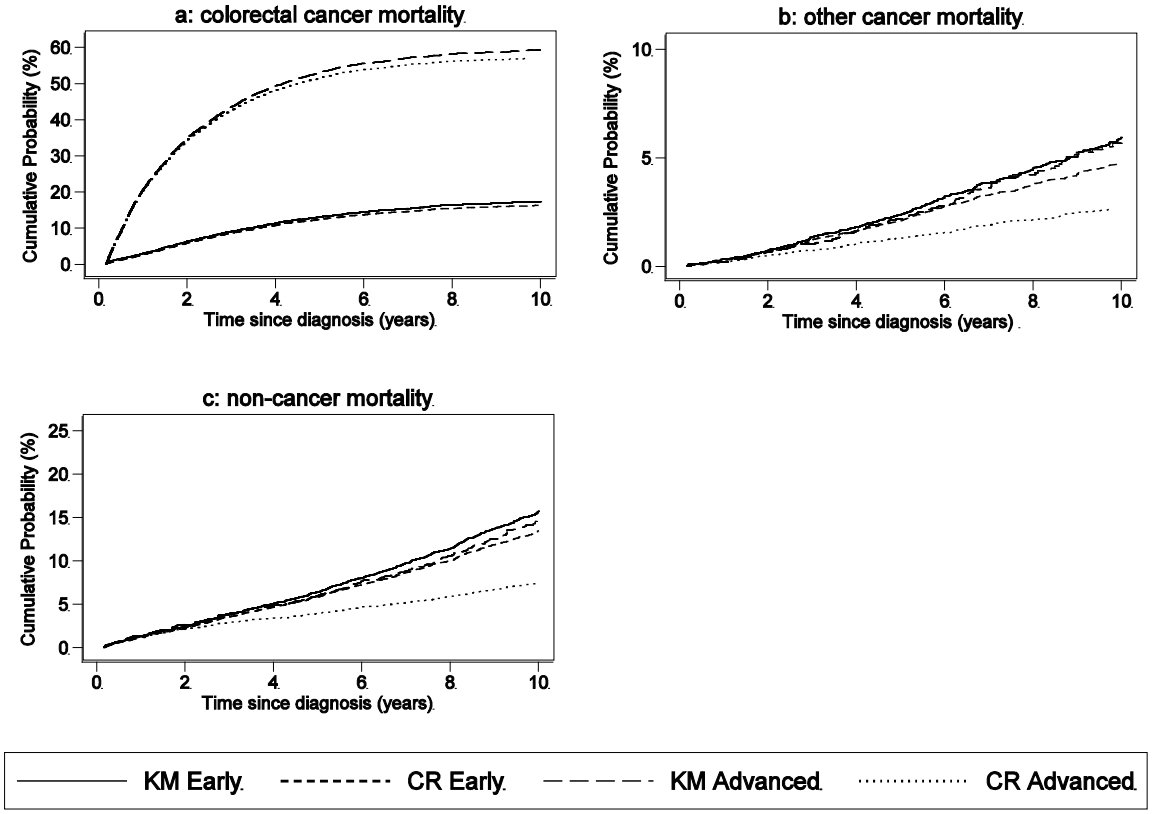
Table 3: Multivariate Fine and Grey analysis of factors associated with mortality due to colorectal cancer, other cancers or non-cancer causes for colorectal cancer patients in Queensland, 1996-2009

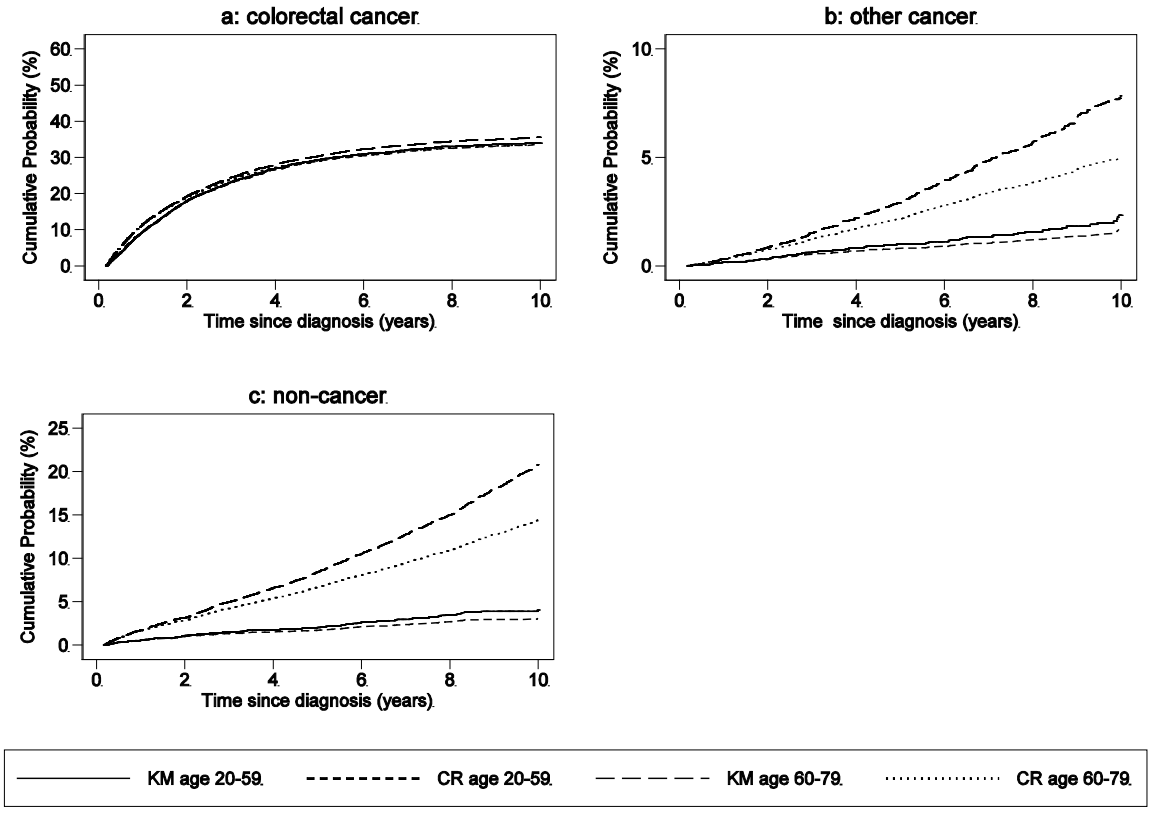
	number	Colorectal Cancer SHR (95% CI)	Other Cancer SHR (95% CI)	Non-Cancer SHR (95% CI)
Age at first cancer diagnosis		p < 0.001	p < 0.001	p < 0.001
20 to 59	6,030	0.68 (0.64, 0.73)	0.55 (0.43, 0.71)	0.23 (0.20, 0.28)
60 to 79	13,385	1.00	1.00	1.00
Sex		p < 0.001	-[1]	p < 0.001
Male	11,200	1.00		1.00
Female	8,215	1.18 (1.12, 1.25)		0.75 (0.67, 0.84)
Country of birth[2]		p=0.039	-[1]	-[1]
Australia	14,694	1.00		
Other English-speaking	2,455	1.01 (0.94, 1.09)		
Non-English-speaking	2,266	0.90 (0.82, 0.98)		
Marital status		p < 0.001	p=0.021	p=0.003
Married	12,948	1.00	1.00	1.00
Not married[3]	6,030	1.13 (1.07, 1.20)	1.39 (1.17, 1.65)	1.60 (1.44, 1.77)
Unknown	437	0.53 (0.39, 0.71)	1.12 (0.39, 3.22)	1.08 (0.76, 1.55)
Occupation		p < 0.001	p < 0.001	p=0.001
Professional/White collar	6,544	1.00	1.00	1.00
Blue collar	3,220	1.30 (1.22, 1.39)	1.23 (1.02, 1.52)	1.09 (0.94, 1.26)
Unemployed/Not known[4]	9,651	0.41 (0.39, 0.44)	0.44 (0.36, 0.54)	0.85 (0.75, 0.96)
Initial cancer stage[5]		p < 0.001	p=0.033	p < 0.001
Early (Stage I-II)	9,439	1.00	1.00	1.00
Advanced (Stage III-IV)	7,052	4.67 (4.39, 4.98)	0.88 (0.71, 1.06)	0.54 (0.48, 0.62)
Unknown	2,924	2.55 (2.34, 2.78)	1.26 (0.99, 1.60)	0.88 (0.77, 1.02)
Initial cancer site[6]		-[1]	-[1]	p < 0.001
Colon	12,384			1.15 (1.03, 1.27)
Rectum	7,031			1.00
Surgical treatment		p < 0.001	-[1]	p < 0.001
Had surgery	16,959	0.60 (0.56, 0.65)		0.74 (0.64, 0.86)
No surgery	2,456	1.00		1.00
Diabetes (E10-E14)[7]		-[1]	p=0.143	p < 0.001
No	15,493		1.00	1.00
Yes	1,466		1.24 (0.93, 1.65)	2.30 (1.99, 2.65)
Other comorbidities[7,8]		p = 0.001	-[1]	p < 0.001
No	16,291	1.00		1.00
Yes	668	1.25 (1.09, 1.44)		2.56 (2.14, 3.05)
Travel distance		p < 0.001	-[1]	p=0.150
0-99 km	13,580	1.00		1.00
100-249 km	2,317	1.07 (1.02, 1.16)		1.03 (0.89, 1.19)
250 km or more	3,518	1.13 (1.06, 1.21)		0.88 (0.77, 1.01)
Secondary primary cancers[9]		p < 0.001	p < 0.001	p < 0.001
None	16,854	1.00	-[10]	1.00
Synchronous	535	0.83 (0.70, 0.97)	1.00	0.96 (0.72, 1.28)
Metachronous	2,026	0.30 (0.27, 0.34)	2.66 (1.62, 2.99)	0.72 (0.62, 0.84)

SHR = Sub-distribution hazard ratios from Fine and Grey models; CI=confidence interval.

1. Not included in final model as were not significant at p≤ 0.20 in initial multivariate models that included all available covariates.
2. Other English-speaking: those born in New Zealand, United Kingdom, Ireland, or North America; non-English-speaking: those not born in Australia, New Zealand, United Kingdom, Ireland or North America.
3. Includes single, divorced, separated or widowed.
4. Includes not in labour force or unspecified employment status.
5. Early stage includes local and regional cases while advanced stage includes distant and metastatic cases.
6. Colorectal sites defined as: Colon (ICDO3: C18) and Rectal (ICDO3: C19-C20, C218).
7. Unknown diabetes and other comorbidities category were omitted due to co-linearity with no surgical treatment category.
8. Heart disease (I20-I50), cerebrovascular disease (I60-I64) or kidney disease (N00-N05, N10-N19).
9. Synchronous: diagnosed within first 2 months and Metachronous: diagnosed more than 2 months after initial cancer diagnosis.
10. No deaths of this type were possible for people with colorectal cancer only.


Cumulative Probability (%)
40
35
30
25
20
15
10
5
0
0
2
4
6
8
10
Time since diagnosis (years)
colorectal cancer
other cancers
non-cancers


a: colorectal cancer mortality
Cumulative Probability (%)
0
10
20
30
40
50
60
0
2
4
6
8
10
Time since diagnosis (years)
b: other cancer mortality
Cumulative Probability (%)
0
5
10
0
2
4
6
8
10
Time since diagnosis (years)
c: non-cancer mortality
Cumulative Probability (%)
0
5
10
15
20
25
0
2
4
6
8
10
Time since diagnosis (years)
KM Early
CR Early
KM Advanced
CR Advanced


a: colorectal cancer
Cumulative Probability (%)
0
10
20
30
40
50
60
0
2
4
6
8
10
Time since diagnosis (years)
b: other cancer
Cumulative Probability (%)
0
5
10
0
2
4
6
8
10
Time since diagnosis (years)
c: non-cancer
Cumulative Probability (%)
0
5
10
15
20
25
0
2
4
6
8
10
Time since diagnosis (years)
KM age 20-59
CR age 20-59
KM age 60-79
CR age 60-79

Online Resource 1: Five-year cumulative probability of mortality from colorectal cancer, other cancer causes and non-cancer causes stage estimated using Kaplan-Meier (KM) and Competing Risks (CR) methods for colorectal cancer patients, Queensland, 1996-2009

	Colorectal Cancer Causes		**Other Cancer Causes**		**Non-Cancer Causes**	
	CR (95% CI) [1]	KM (95%CI)[2]	CR (95% CI) [1]	KM (95%CI)	CR (95% CI) [1]	KM (95%CI)
All patients in cohort	29.4 (29.3, 30.7)	31.1 (30.4, 31.8)	2.0 (1.8, 2.2)	2.4 (2.3, 2.7)	5.7 (5.3, 6.0)	6.6 (6.2, 7.7)
Age at first cancer diagnosis						
20 to 59	29.2 (28.6, 30.1)	30.2 (29.0, 31.5)	0.9 (0.6, 1.1)	1.1 (0.8, 1.4)	1.9 (1.6, 2.3)	2.3 (1.9, 2.8)
60 to 79	30.3 (29.3, 31.9)	31.4 (30.6, 32.3)	2.5 (2.2, 2.8)	3.4 (3.0, 3.8)	7.3 (6.9, 7.8)	9.5 (8.9, 10.1)
Sex						
Male	31.2 (30.3, 32.1)	32.5 (31.6, 33.4)	2.3 (2.0, 2.6)	3.1 (2.7, 3.6)	6.5 (6.0, 7.0)	8.3 (7.7, 8.9)
Female	28.4 (27.4, 29.4)	29.1 (28.1, 30.2)	1.6 (1.3, 1.9)	2.1 (1.7, 2.5)	4.5 (4.1, 5.0)	5.7 (5.2, 6.4)
Country of Birth[3]						
Australia	31.2 (29.9, 31.8)	31.7 (30.9, 32.5)	2.1 (1.8, 2.3)	2.8 (2.5, 3.2)	5.7 (5.3, 6.2)	7.4 (6.9, 7.9)
Other English-speaking	30.7 (28.8, 32.6)	31.6 (29.7, 33.7)	2.2 (1.7, 2.9)	2.8 (2.1, 3.8)	5.6 (4.7, 6.6)	7.2 (6.1, 8.6)
Non-English-speaking	25.3 (23.5, 27.2)	26.2 (24.3, 28.2)	1.2 (0.8, 1.8)	1.6 (1.0, 2.4)	5.2 (4.3, 6.3)	6.2 (5.1, 7.4)
Marital status						
Married	29.8 (28.9, 30.6)	30.7 (29.9, 31.5)	2.0 (1.7, 2.2)	2.6 (2.3, 2.9)	4.9 (4.5, 5.3)	6.2 (5.7, 6.7)
Not married[4]	32.0 (30.8, 33.2)	33.3 (32.0, 34.6)	2.3 (1.8, 2.6)	3.1 (2.5, 3.6)	7.4 (6.7, 8.1)	9.6 (8.7, 10.6)
Unknown	11.2 (8.5, 14.4)	11.6 (8.9, 15.1)	1.4 (0.4, 3.6)	1.6 (0.2, 2.3)	4.8 (3.0, 7.2)	5.1 (3.3, 7.9)
Occupation						
Professional/White collar	38.9 (37.7, 40.2)	40.5 (39.3, 41.8)	2.6 (2.3, 3.1)	3.9 (3.3, 4.6)	5.6 (5.0, 6.2)	7.7 (6.9, 8.6)
Blue collar	46.5 (44.7, 48.3)	48.9 (47.1, 50.9)	3.1 (2.5, 3.8)	4.9 (3.9, 6.1)	7.4 (6.5, 8.4)	11.2 (9.8, 12.8)
Unemployed/Not known[5]	18.4 (17.6, 19.2)	18.8 (18.0, 19.7)	1.1 (0.9, 1.4)	1.4 (1.1, 1.7)	5.1 (4.6, 5.6)	5.9 (5.3, 6.5)
Initial cancer stage[6]						
Early (Stage I-II)	12.9 (12.2, 13.6)	13.4 (12.7, 14.2)	2.4 (2.1, 2.8)	2.7 (2.4, 3.1)	6.4 (5.9, 7.0)	7.1 (6.5, 7.7)
Advanced (Stage III-IV)	52.7 (51.5, 53.9)	54.4 (53.1, 55.6)	1.4 (1.1, 1.8)	2.5 (2.0, 3.1)	4.3 (3.8, 4.8)	6.7 (5.9, 7.6)
Unknown	31.8 (30.0, 33.5)	32.9 (31.1, 34.7)	1.9 (1.5, 2.5)	2.6 (2.0, 3.5)	6.3 (5.5, 7.4)	8.2 (7.0, 9.5)
Initial cancer site[7]						
Colon	29.7 (28.8, 30.5)	30.6 (29.7, 31.5)	2.1 (1.9, 2.4)	2.9 (2.6, 3.3)	5.9 (5.5, 6.3)	7.6 (7.0, 8.2)
Rectum	30.6 (29.5, 31.8)	31.8 (30.7, 33.0)	1.7 (1.4, 2.0)	2.2 (1.8, 2.7)	5.3 (4.7, 5.8)	6.6 (5.9, 7.3)

	Colorectal Cancer Causes		Other Cancer Causes		Non-Cancer Causes	
	CR (95% CI) [1]	KM (95%CI)[2]	CR (95% CI) [1]	KM (95%CI)	CR (95% CI) [1]	KM (95%CI)
Surgical treatment						
Had surgery	28.7 (28.0, 29.4)	29.7 (29.0, 30.5)	2.0 (1.8, 2.3)	2.7 (2.4, 3.0)	5.6 (5.3, 6.0)	7.0 (6.6, 7.5)
No surgery	39.4 (37.4, 41.3)	40.4 (38.5, 42.5)	1.5 (1.0, 2.0)	2.3 (1.6, 3.3)	5.9 (5.0, 7.0)	8.4 (7.1, 10.0)
Diabetes (E10-E14)[8]						
No	28.6 (27.9, 29.3)	29.5 (28.8, 30.3)	2.0 (1.8, 2.2)	2.6 (2.3, 2.9)	5.0 (4.6, 5.4)	6.3 (5.8, 6.7)
Yes	29.7 (27.3, 32.2)	31.6 (29.1, 34.3)	2.8 (2.0, 3.9)	3.9 (2.7, 5.5)	12.4 (10.6, 14.3)	16.0 (13.8, 18.5)
Other comorbidities[8,9]						
No	28.5 (27.8, 29.2)	29.4 (28.7, 30.2)	2.0 (1.8, 2.3)	2.7 (2.4, 3.0)	5.2 (4.8, 5.6)	6.5 (6.0, 7.0)
Yes	33.3 (29.7, 37.0)	36.4 (32.5, 40.5)	2.5 (1.5, 4.0)	3.2 (1.9, 5.4)	15.8 (13.1, 18.8)	20.8 (17.3, 24.9)
Travel distance						
0-99 km	28.3 (27.6, 29.1)	29.3 (28.5, 30.1)	2.0 (1.7, 2.2)	2.6 (2.2, 2.9)	5.7 (5.3, 6.2)	7.2 (6.7, 7.7)
100-249 km	31.4 (29.5, 33.4)	32.7 (30.7, 34.8)	2.1 (1.6, 2.8)	3.0 (2.2, 4.0)	6.2 (5.2, 7.3)	7.6 (6.4, 9.1)
250 km or more	35.6 (33.9, 37.2)	36.6 (34.9, 38.3)	1.9 (1.5, 2.5)	2.8 (2.2, 3.6)	5.1 (4.3, 5.9)	7.0 (6.0, 8.2)
Secondary primary cancers[10]						
None	32.5 (31.8, 33.3)	33.4 (32.7, 34.2)	-[11]	-[11]	5.8 (5.4, 6.2)	7.5 (7.0, 8.0)
Synchronous	30.9 (26.9, 35.0)	34.8 (30.5, 39.6)	10.6 (8.1, 13.5)	12.9 (9.9, 16.6)	6.9 (4.8, 9.3)	8.8 (6.3, 12.4)
Metachronous	9.5 (8.3, 10.9)	10.6 (9.3, 12.2)	14.8 (13.2, 16.4)	15.7 (14.1, 17.5)	4.2 (3.4, 5.2)	4.8 (3.9, 6.0)

1. CR: Five-year cumulative probability of mortality with 95% confidence intervals (CI) from competing risk analysis.
2. KM: Five-year cumulative probability of mortality with 95% confidence intervals (CI) from Kaplan-Meir analysis.
3. Other English-speaking: those born in New Zealand, United Kingdom, Ireland, or North America; Non-English-speaking: those not born in Australia, New Zealand, United Kingdom, Ireland or North America.
4. Includes single, divorced, separated or widowed.
5. Includes not in labour force or unspecified employment status.
6. Early stage includes local and regional cases while advanced stage includes distant and metastatic cases.
7. Colorectal sites defined as: Colon (ICD-O-3: C18) and Rectal (ICD-O-3: C19-C20, C218).
8. Patients with unknown diabetes or other comorbidities status have same values as those with no surgical treatment.
9. Heart disease (I50), cerebrovascular disease (I60-I64) or kidney disease (N00-N05, N10-N19).
10. Another primary cancer diagnosed within 2 months of the first cancer (synchronous) or more than 2 months afterwards (metachronous).
11. No deaths of this type were possible for people with colorectal cancer only.