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# Time from diagnosis to treatment of colorectal cancer in an Australian cohort: how it varies and relates to survival



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| Complete List of Authors: | Roder, David; University of South Australia, Cancer Research Institute<br>Karapetis, Christos; Flinders University, Medical Oncology<br>Olver, Ian; University of South Australia, Cancer Research Institute<br>Keefe, Dorothy; South Australia Department of Health, South Australian Cancer Service; The University of Adelaide, Adelaide Medical School<br>Padbury, Robert; Flinders University, Medical Oncology<br>Moore, James; Royal Adelaide Hospital, Colorectal Surgery; The University of Adelaide, Adelaide Medical School<br>Joshi, Rohit; The University of Adelaide, Adelaide Medical School; Adelaide Oncology and Haematology, Cancer Research and Clinical Trials<br>Wattchow, David; Southern Adelaide Local Health Network, Surgery and Perioperative Medicine; Flinders University, Medical Oncology<br>Worthley, Dan; South Australian Health and Medical Research Institute, Gastrointestinal Cancer Biology<br>Miller, Caroline; South Australian Health and Medical Research Institute, Population Health; The University of Adelaide, School of Public Health<br>Holden, Carol; South Australian Health and Medical Research Institute, Population Health<br>Buckley, Elizabeth; University of South Australia, Cancer Research Institute<br>Powell, Kate; South Australian Health and Medical Research Institute, Population Health<br>Buranyi-Trevarton, Dianne; South Australia Department of Health, South Australian Cancer Service<br>Fusco, Kellie; University of South Australia, Cancer Research Institute<br>Price, Timothy ; The Queen Elizabeth Hospital, Clinical Cancer Research; The University of Adelaide, Adelaide Medical School |
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# Time from diagnosis to treatment of colorectal cancer in an Australian cohort: how it varies and relates to survival

Roder D*[1], Karapetis C[2], Olver I[1], Keefe D[3, 5], Padbury R[2], Moore J[5, 6], Joshi R[5,7], Wattchow D[2, 4], Worthley DL[8], Miller C[9,10], Holden C[9], Buckley E[1], Powell K[9], Buranyi-Trevarton D[3], Fusco K[1], Price T[5, 11]

[1] Cancer Research Institute, University of South Australia, Adelaide, SA, Australia

[2] Medical Oncology, Flinders University, Bedford Park, SA, Australia

[3] South Australian Cancer Service, South Australia Department of Health, Adelaide, SA, Australia

[4] Surgery and Perioperative Medicine, Southern Adelaide Local Health Network, Bedford Park, SA, Australia

[5] Adelaide Medical School, University of Adelaide, Adelaide, SA, Australia

[6] Colorectal Surgery, Royal Adelaide Hospital, Adelaide, SA, Australia

[7] Adelaide Oncology and Haematology, Cancer Research and Clinical Trials, North Adelaide, SA, Australia

[8] Gastrointestinal Cancer Biology, South Australian Health and Medical Research Institute, Adelaide, SA, Australia

[9] Population Health, South Australian Health and Medical Research Institute, Adelaide, SA, Australia

[10] School of Public Health, The University of Adelaide, Adelaide, SA, Australia

[11] Clinical Cancer Research, Queen Elizabeth Hospital, Woodville, SA, Australia

* Corresponding author

Email: david.roder@unisa.edu.au

Phone: +61 8 8302 2640

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**Abstract**

*Objectives*

Determine time to treatment of colorectal cancer and survival

*Background*

Contrary evidence exists of associations of time to treatment following diagnosis with survival. Some early studies indicated lower survival with longer time, but others showed the reverse, potentially reflecting early scheduling of high-risk cases. We investigated time to treatment at four major public hospitals for benchmarking and to explore associations with survival.

*Methodology*

Clinical registry data were used where diagnosis was recorded as preceding treatment. Times to treatment were analysed employing rank-order tests and multiple logistic regression. Disease-specific survival was analysed by time to treatment using unadjusted Kaplan-Meier estimates and adjusted Cox proportional hazards regression.

*Participants*

South Australian registry data, 1980-2010.

*Results*

Treatment (any type) commenced for 87% of surgical cases ≤60 days of diagnosis, with 80% had surgery within this period. Of those receiving radiotherapy, 59% began this treatment ≤60 days, and of those receiving systemic therapy, the corresponding proportion was 56%. Adjusted analyses showed treatment delay >60 days was more likely for rectal cancers, 2006-2010 diagnoses, residents of northern than other metropolitan regions, and for surgery, younger ages <50 years, and unexpectedly, those residing closer to metropolitan services. Adjusting for clinical and sociodemographic factors, and diagnostic year, better survival occurred in ≤ 2 years from diagnosis for time to treatment >30 days. Survival in the 3-10 years post-diagnosis generally did not differ by time to treatment, except for lower survival for any treatment >90 days for surgical cases.

*Conclusions*

- Lower survival ≤2 years from diagnosis for cancers treated ≤30 days from diagnosis is consistent with other study results attributed to preferencing more complicated cases for earlier care.
- Lower 3-10-year survival for treatment of surgical cases for cancers first treated > 90 days from diagnosis is consistent with the U-shaped relationship reported in some other studies.

**Key words**

Oncology epidemiology, protocols & guidelines, quality in health care, public health, colorectal surgery

## Strengths and limitations of this study

Strengths

- Broad clinical registry data available on diagnosis, treatment, and sociodemographic covariables
- strong engagement of lead clinicians and health administrators responsible for colorectal cancer management in South Australia
- translation of results into policy and practice in South Australia will be facilitated by members of the research team who are also participants in a formal population-wide program administered by research, government and provider representatives to improve colorectal cancer management and decrease colorectal cancer deaths

Limitations

- Sufficiently precise diagnostic and treatment dates limited to 65% of registry cases
- Data limited to four major public hospitals

## Introduction

Australia has a high age-standardised incidence of colorectal cancer about 87% above the world average.[1] The corresponding colorectal cancer mortality rate is lower although still about 22% above the world average.[1] Colorectal cancer is second only to prostate cancer in numbers reported annually by Australian cancer registries and second only to lung cancer in numbers of cancer deaths.[2] Age-standardised incidence has been stable, with the 2012-2014 rate falling within 1-2% of the rate for 1982-1984, but with the colorectal cancer mortality rate approximately halved between these periods.[2] This difference reflects increases in 5-year relative survival from 52% in 1982-1986 to 70% in 2011-2015.[3, 4]

South Australian clinical registry data for colorectal cancer covering four major public hospitals showed equivalent survival and survival increases to national figures during 1980-2010, with five-year disease-specific survival increasing from 48% to 63% for all stages combined.[5] Stage distributions were largely unchanged, with survival increases attributed to gains in stage-specific survival.[5] Increases were particularly pronounced for regional stage.[5] Survival increases followed increased use of adjuvant systemic therapies, particularly for regional disease.[5] For rectal cancers, a significant increase in use of adjuvant radiotherapy was reported. The increases in adjuvant therapy were consistent with clinical practice guidelines.[5] Systemic therapies evolved from a common use of single-agent 5FU to 5FU and leucovorin. FOLFOX (± bevacizumab) and capecitabine (± oxaliplatin) also became more common protracted infusion of 5FU for colonic cancer and with radiotherapy for rectal cancers.[5]

While survival increases were attributed to changes in use of systemic therapy and radiotherapy, and increased surgical specialization,[5] other influences were possible. One was changes in time from diagnosis to surgical treatment.[6] In the United Kingdom, treatment delays were regarded as negatively related to survival and concerns were expressed that delays may be increasing due to increased demands for colonoscopy from population screening.[7, 8] While there is limited evidence of effects of treatment delays on survival, early evidence points to a possible negative effect.[6, 7, 8] Delays were also viewed negatively as a likely source of psychosocial stress.[6, 8] Cancer UK has indicated that ideally treatment would commence within one month of diagnosis but has recommended commencement within two months as a realistic target.[9]

Evidence of effects of time to treatment on survival have been mixed.[10-18] Early studies generally pointed to lower survival with longer delay, but later studies varied with some showing better survival for longer delay, and some showing a U-shaped relationship with lower survival at both ends of the follow-up period.[6-8, 10-18] This has raised questions of whether the relationship varies with the clinical environment, with lower survival for short delays potentially reflected triaging of more aggressive cancers for early treatment in some settings.[12, 13, 15, 17]

In this study we explore times from diagnosis to treatment, trends in these times, variations across the patient population, and associations with survival. To establish a historic baseline, we analysed colorectal cancer data (2000-2010 diagnoses) from the South Australian registry data. Analyses indicated times to treatment and outcomes across the patient population at these hospitals by cancer stage, patient age, sex, socioeconomic status, service access, local health network of residence (as applying in the study period) and diagnostic epoch. We investigated whether a U-shaped relationship existed between time to treatment and survival, as reported elsewhere.[6, 17]

The study was restricted to cancers where the registry had enough diagnostic detail from biopsies and other clinical sources to record a diagnosis date in advance of treatment, thereby providing an intervening period for analysis (65% of cases). This is analogous to common registry practice of restricting survival analyses to cancers where diagnosis dates preceded dates of death.[19]

**Methods**

Our data source was the South Australian clinical cancer registry, which is authorised under Section 64, Part 7 of the South Australian Health Care Act (2008) to support service monitoring and quality assurance.[5] Research ethics approval was obtained from the South Australian Human Research Ethics Committee. Data were extracted for the 2000-2010 diagnostic period and dates of diagnosis and treatment checked from available pathology and clinical reporting to optimize accuracy. Times to treatment start were calculated in days from diagnosis to treatment of 2,746 colorectal cancers.[20] Cases were excluded where presenting acutely with bowel obstruction or perforation and treated surgically on day one.

*Public and Patient Involvement*

Registry development and workplans had substantial patient and consumer involvement through a formalized cancer planning and monitoring processes. Funders reviewing workplans included the Cancer Council South Australia through the Beat Cancer Project. Specialist clinics identify topics for review, of which some are based on/prompted by the questions raised by patients.

The use of the registry was approved by the Department of Health Research Ethics Committee and University of South Australia Research Ethics Committee, both with active consumer involvement, thereby providing another level of public and consumer input.

This study involved the use of routinely collected registry data specifically authorized under state law and planned by clinical experts and consumers.

Participants all attended specialized oncology clinics with whom we work. We work with these clinics in developing consumer messages for distribution to patients and other relevant stakeholder groups.

Analyses were undertaken for surgical, radiotherapy and systemic therapies respectively, and for any of these treatments among surgical cases. Cases were classified by: Australian Clinico-Pathological Stage and grade,[21] age at diagnosis, sex, area socioeconomic status,[22] geographic access to specialist radiotherapy and other specialist metropolitan services based on postcode address (coded as high, medium or low), local health network of residence, as applying during the study period (i.e., northern metropolitan, central metropolitan, southern metropolitan, country south and country north), and diagnostic period (2000-2005 and 2006-2010) (see Tables 1-3). Operational definitions are available in previous publications.[5, 21, 22]

Time from diagnosis to treatments start was categorised in days for cross-tabulations with clinical and sociodemographic variables. The Spearman rank test was used to analyse ordinal clinical and sociodemographic predictors; Kruskal-Wallis ANOVA for multinomial predictors, and Whitney U test for predictors measured on a binary scale.[23, 24] For multiple logistic regression analyses of time as the outcome variable, time was reduced to a binary outcome of "$>30$ or $\leq 30$ days" and "$>60$ or $\leq 60$ days" respectively.[23, 24]

Disease-specific survival was analysed by time to treatment using Kaplan-Meier product-limit estimates (unadjusted) and Cox proportional hazards regression (adjusted for co-variables shown in Tables 2 and 3).[23, 24] The decision to use disease-specific survival rather than relative survival was supported by similar results applying to the two methods in South Australia at a population level.[5] Also, there were not lifetables (as required for relative survival) for patients referred to specialist clinics at these hospitals who often had extensive comorbidity and other complications.[5] Results are

presented using conventional non-hierarchical analyses as they were similar by hospital setting without evidence of clustering.

**Results**

**A. Time from diagnosis to treatment start (colorectal)**

Unadjusted analyses – Time from diagnosis to treatment start (Table 1)

*Surgery:* The proportion of surgical cases receiving surgery ≤60 days of diagnosis was 80% (59% ≤30 days). Time to first surgical treatment was associated with: (a) age at diagnosis (p<0.001) - shorter time for older patients; (b) sex (p=0.003) – shorter time for females; (c) local health network of residence (p=0.026) – longer time for northern metropolitan; (d) tumour sub-site (p<0.001) – longer time for rectum; and (e) diagnostic period (p<0.001) – longer time for 2006-2010. Significant associations were not found for other characteristics (p≥0.118).

*Radiotherapy:* The proportion receiving radiotherapy whose treatment started ≤60 days was 59% (21% ≤30 days). Time to radiotherapy was associated with: (a) age at diagnosis (p=0.042) – longer time for older patients; and (b) tumour sub-site (p<0.001) – shorter time for rectum (note: radiotherapy was uncommon for colonic cancers). Significant associations were not found for other characteristics (p≥0.114).

*Systemic therapy:* The proportion receiving systemic therapy whose treatment started ≤ 60 days was 56% (15% ≤30 days). Time to systemic therapy was associated with: (a) age at diagnosis (p<0.001) – longer time for older patients; (b) local health network of residence (p=0.004) – shorter time for northern metropolitan; (c) tumour sub-site (p=0.018) – shorter time for rectum; (d) stage (p=0.003) – shorter time for stages A and D (note: systemic therapy was uncommon for stage A); and (e) diagnostic period (p<0.001) – longer time for 2006-2010. Significant associations were not found by other characteristics (p≥0.120).

*Any treatment (surgical cases):* The proportion receiving any treatment who did so starting ≤60 days of diagnosis was 87% (62% ≤30 days). Time to any treatment was associated with: (a) age at diagnosis (p=0.048) – although a clear age gradient was not evident; (b) sex (p=0.017) – shorter time for females; (c) local health network of residence (p<0.001) – longer time for the northern metropolitan area; (d) tumour sub-site (p<0.001) – longer time for rectum; and (e) diagnostic period (p<0.001) – longer time for 2006-2010. Significant associations were not found for other characteristics (p≥0.104).

Table 1: Percentage of colorectal patients by treatment type and days from diagnosis to treatment start: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | | | | | Radiotherapy | | | | | | Systemic therapy | | | | | | Any Treatment | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | ≤30 | 31 - 60 | 61 - 90 | ≥90 | P value | n | ≤30 | 31 - 60 | 61-90 | ≥90 | P value | n | ≤30 | 31 - 60 | 61 - 90 | ≥90 | P value | n | ≤30 | 31-60 | 61-90 | ≥90 | P value |
| **All cases** | 1675 | 59.0 | 21.2 | 6.0 | 13.9 | - | 616 | 20.9 | 37.8 | 17.4 | 23.9 | - | 1556 | 15.3 | 40.7 | 24.6 | 19.5 | - | 1675 | 61.7 | 25.6 | 7.1 | 5.6 | - |
| **Age at diagnosis (years):** | | | | | | | | | | | | | | | | | | | | | | | | |
| <50 | 91 | 59.3 | 11.0 | 4.4 | 25.3 | <0.001 | 79 | 24.1 | 45.6 | 7.6 | 22.8 | 0.042 | 189 | 19.6 | 47.1 | 19.0 | 14.3 | <0.001 | 91 | 65.9 | 22.0 | 3.3 | 8.8 | 0.048 |
| 50 - 59 | 210 | 52.9 | 20.0 | 5.7 | 21.4 | | 118 | 22.0 | 40.7 | 17.8 | 19.5 | | 322 | 16.5 | 44.1 | 20.5 | 18.9 | | 210 | 58.7 | 28.4 | 7.7 | 5.3 | |
| 60 - 69 | 388 | 52.3 | 22.9 | 5.9 | 18.8 | | 188 | 20.7 | 35.6 | 12.3 | 22.3 | | 498 | 16.1 | 38.0 | 26.7 | 19.3 | | 388 | 57.1 | 29.1 | 6.8 | 7.0 | |
| 70 - 79 | 570 | 61.1 | 23.0 | 5.6 | 10.4 | | 175 | 20.1 | 36.0 | 16.0 | 28.0 | | 469 | 12.6 | 39.0 | 26.7 | 21.7 | | 570 | 61.9 | 26.2 | 7.2 | 4.8 | |
| 80+ | 416 | 65.4 | 20.0 | 7.0 | 7.7 | | 56 | 17.9 | 33.9 | 21.4 | 26.8 | | 78 | 11.5 | 38.5 | 28.2 | 21.8 | | 416 | 66.1 | 21.2 | 7.7 | 5.1 | |
| **Sex:** | | | | | | | | | | | | | | | | | | | | | | | | |
| Males | 893 | 56.0 | 21.9 | 5.9 | 16.1 | 0.003 | 400 | 19.8 | 38.5 | 18.0 | 23.8 | 0.567 | 910 | 16.3 | 39.0 | 23.8 | 20.9 | 0.649 | 893 | 59.2 | 27.3 | 7.1 | 6.4 | 0.017 |
| Females | 782 | 62.4 | 20.3 | 6.0 | 11.3 | | 216 | 23.1 | 36.6 | 16.2 | 24.1 | | 646 | 13.9 | 43.0 | 25.5 | 17.5 | | 782 | 64.4 | 23.8 | 7.0 | 4.7 | |
| **Socioeconomic:** | | | | | | | | | | | | | | | | | | | | | | | | |
| Low | 544 | 56.3 | 22.8 | 5.9 | 15.1 | 0.118 | 206 | 16.0 | 43.2 | 18.9 | 21.8 | 0.826 | 507 | 13.4 | 39.4 | 26.4 | 20.7 | 0.664 | 544 | 58.8 | 28.0 | 6.6 | 6.6 | 0.104 |
| Low-Med | 388 | 60.3 | 19.8 | 6.7 | 13.1 | | 137 | 24.8 | 36.5 | 16.8 | 21.9 | | 374 | 16.6 | 44.9 | 21.9 | 16.6 | | 388 | 62.7 | 24.9 | 7.0 | 5.4 | |
| Med-High | 345 | 58.6 | 21.4 | 5.5 | 14.5 | | 128 | 24.2 | 35.2 | 18.8 | 21.9 | | 320 | 16.3 | 40.0 | 27.5 | 16.3 | | 345 | 61.9 | 24.1 | 8.1 | 5.8 | |
| High | 398 | 61.8 | 20.1 | 5.8 | 12.3 | | 145 | 21.4 | 33.8 | 14.5 | 30.3 | | 355 | 15.8 | 38.6 | 22.0 | 23.7 | | 398 | 64.4 | 24.5 | 6.8 | 4.3 | |
| **Accessibility:** | | | | | | | | | | | | | | | | | | | | | | | | |
| High | 1353 | 58.9 | 20.4 | 6.4 | 14.3 | 0.584 | 475 | 22.1 | 36.4 | 16.8 | 24.6 | 0.764 | 1223 | 16.4 | 40.3 | 24.0 | 19.3 | 0.12 | 1353 | 61.8 | 25.1 | 7.3 | 5.9 | 0.992 |
| Med-High | 228 | 61.0 | 23.2 | 3.9 | 11.8 | | 94 | 17.0 | 44.7 | 21.3 | 17.0 | | 228 | 10.1 | 41.2 | 28.1 | 20.6 | | 228 | 62.1 | 27.3 | 6.6 | 4.0 | |
| Poor | 94 | 55.3 | 27.7 | 4.3 | 12.8 | | 47 | 17.0 | 38.3 | 14.9 | 29.8 | | 105 | 13.3 | 43.8 | 23.8 | 19.0 | | 94 | 58.5 | 29.8 | 5.3 | 6.4 | |
| **Local Health Network:** | | | | | | | | | | | | | | | | | | | | | | | | |
| Northern metro | 242 | 45.9 | 24.4 | 12.0 | 17.8 | 0.026 | 106 | 18.9 | 34.9 | 19.8 | 26.4 | 0.12 | 248 | 16.1 | 41.5 | 24.2 | 7.3 | 0.004 | 242 | 49.6 | 30.4 | 12.1 | 7.9 | <0.001 |
| Central metro | 618 | 61.7 | 20.2 | 6.8 | 11.3 | | 202 | 21.8 | 32.7 | 17.8 | 27.7 | | 495 | 17.8 | 36.6 | 26.5 | 19.2 | | 618 | 64.1 | 24.0 | 7.3 | 4.7 | |
| Southern metro | 417 | 64.3 | 17.7 | 3.4 | 14.6 | | 134 | 25.4 | 40.3 | 14.2 | 20.1 | | 426 | 16.7 | 42.7 | 20.7 | 20.0 | | 417 | 66.8 | 23.0 | 4.8 | 5.3 | |
| Country South | 155 | 52.9 | 27.7 | 1.9 | 17.4 | | 74 | 25.7 | 40.5 | 14.9 | 18.9 | | 159 | 8.8 | 41.5 | 28.3 | 21.4 | | 155 | 56.5 | 31.2 | 3.9 | 8.4 | |
| Country North | 241 | 60.2 | 22.0 | 5.0 | 12.9 | | 100 | 11.2 | 46.9 | 19.4 | 22.4 | | 228 | 11.0 | 44.5 | 25.1 | 19.4 | | 241 | 61.9 | 26.2 | 7.4 | 4.5 | |
| **Sub-site:** | | | | | | | | | | | | | | | | | | | | | | | | |
| Colon | 1098 | 65.0 | 22.1 | 4.9 | 7.9 | <0.001 | 86 | 11.6 | 12.8 | 14.0 | 61.6 | <0.001 | 898 | 13.1 | 40.2 | 27.4 | 19.3 | 0.018 | 1098 | 66.2 | 23.4 | 6.0 | 4.5 | <0.001 |
| Rectum | 577 | 47.5 | 19.4 | 8.0 | 25.1 | | 530 | 22.5 | 41.9 | 17.9 | 17.7 | | 658 | 18.2 | 41.3 | 20.7 | 19.8 | | 577 | 53.1 | 29.9 | 9.2 | 7.8 | |
| **ACPS stage:** | | | | | | | | | | | | | | | | | | | | | | | | |
| A | 280 | 53.9 | 30.4 | 7.9 | 7.9 | 0.460 | 50 | 24.0 | 44.0 | 14.0 | 18.0 | 0.114 | 47 | 25.5 | 36.2 | 21.3 | 17.0 | 0.003 | 280 | 55.4 | 32.5 | 7.9 | 4.3 | 0.114 |
| B | 654 | 61.5 | 23.9 | 4.7 | 9.9 | (A-D) | 147 | 21.1 | 38.8 | 21.8 | 18.4 | | 249 | 13.3 | 40.2 | 27.7 | 18.9 | | 654 | 63.3 | 26.7 | 5.7 | 4.3 | |
| C | 412 | 55.6 | 17.2 | 6.8 | 20.4 | | 231 | 16.0 | 40.7 | 21.2 | 22.1 | | 696 | 6.6 | 47.3 | 27.6 | 18.5 | | 412 | 58.9 | 25.6 | 8.8 | 6.8 | |

| | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| B | 279 | 63.8 | 12.5 | 5.0 | 18.6 | | 162 | 25.9 | 29.0 | 10.5 | 34.6 | | 516 | 26.6 | 33.1 | 19.6 | 20.7 | | 279 | 68.6 | 17.3 | 6.5 | 7.6 | |
| (UK) | (50) | (51.5) | (18.2) | (12.1) | (18.2) | | (26) | (27.3) | (59.1) | (4.5) | (9.1) | | (48) | (26.9) | (34.6) | (15.4) | (23.1) | | (50) | (59.2) | (20.4) | (10.2) | (10.2) | |
| **Diagnosis years:** | | | | | | | | | | | | | | | | | | | | | | | | |
| 2000 - 2005 | 869 | 65.0 | 17.5 | 5.4 | 12.1 | <0.001 | 335 | 23.9 | 34.0 | 15.8 | 26.3 | 0.898 | 782 | 17.4 | 44.2 | 21.2 | 17.1 | <0.001 | 869 | 68.0 | 21.4 | 6.2 | 4.4 | <0.001 |
| 2006 - 2010 | 806 | 52.5 | 25.2 | 6.6 | 17.8 | | 281 | 17.4 | 42.3 | 19.2 | 21.0 | | 774 | 13.2 | 37.1 | 27.9 | 21.8 | | 806 | 54.8 | 30.3 | 8.0 | 7.0 | |

*Excludes cases where insufficient data on date of diagnosis (see "Methods")

ACPS- Australian Clinico-Pathological Staging; UK – unknown

Adjusted analyses – Predictors of treatment start >30 days from diagnosis (Table 2).

*Surgery:* Significant predictors of time to surgical treatment >30 days included: (a) local health network of residence – relative odds (RO) of 0.55 (0.39, 0.76) for metropolitan central and 0.44 (0.31, 0.63) for metropolitan southern compared with metropolitan northern; (b) tumour site – RO for rectum of 2.07 (1.66, 2.57); (c) tumour stage – RO of 0.65 (0.45, 0.93) for stage D (distant metastasis) compared with stage A; (d) grade – RO for high grade (poorly differentiated) at 0.47 (0.25, 0.87) compared with low grade; and (e) diagnostic period – RO of 1.82 (1.48, 2.24) for 2006-2010.

*Radiotherapy:* Only tumour site was predictive of time to radiotherapy start >30 days – RO of 0.40 (0.19, 0.83) for rectum (note: radiotherapy was much less common for colonic than rectal cancers[5]).

*Systemic therapy:* Significant predictors of time to systemic treatment start >30 days included: (a) tumour site – RO for rectum of 0.65 (0.48, 0.89); (b) tumour stage – RO for stage C of 3.93 (1.85, 8.36); and (c) diagnostic period – RO of 0.65 (0.48, 0.89) for 2006-2010.

*Any treatment (surgical cases):* Significant predictors of time to start of any treatment >30 days included: (a) local health network of residence – RO of 0.56 (0.40, 0.78) for metropolitan central and 0.44 (0.30, 0.63) for metropolitan southern compared with metropolitan northern; (b) tumour site – RO of 1.76 (1.41, 2.19) for rectum; (c) tumour stage – RO of 0.56 (0.38, 0.80) for stage D compared with stage A; (d) grade – RO of 0.52 (0.28, 0.95) for high compared with low grade; and (e) diagnostic period – RO of 1.86 (1.51, 2.29) for 2006-2010.

*Supplementary analyses with tumour stage classified as stage D vs A-C:* RO odds for surgery start >30 days was lower for stage D for surgery at 0.69 (0.51, 0.92), radiotherapy at 0.56 (0.35, 0.88), systemic therapy at 0.30 (0.22, 0.41), and any treatment (surgical cases) at 0.64 (0.47, 0.86). The RO for systemic treatment start >30 days for stage D vs A-C was 0.45 (0.30, 0.67) for 2000-2005 compared with 0.16 (0.10, 0.27) for 2006-2010.

Table 2: Relative odds (95% CLs) of treatment for colorectal cancer starting >30 days of diagnosis by treatment type, stage, and socioeconomic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Systemic therapy | | Any treatment | |
|---|---|---|---|---|---|---|---|---|
| | **N** | **RO (95% CLs)** | **n** | **RO (95% CLs)** | **n** | **RO (95% CLs)** | **n** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 91 | 1.00 | 79 | 1.00 | 189 | 1.00 | 91 | 1.00 |
| 50 - 59 | 210 | 1.15 (0.68, 1.95) | 118 | 1.06 (0.52, 2.15) | 322 | 1.18 (0.71, 1.94) | 210 | 1.20 (0.70, 2.05) |
| 60 - 69 | 388 | 1.16 (0.71, 1.90) | 188 | 1.16 (0.60, 2.25) | 498 | 1.25 (0.79, 2.00) | 388 | 1.26 (0.76, 2.08) |
| 70 - 79 | 570 | 0.95 (0.59, 1.53) | 175 | 1.13 (0.58, 2.22) | 469 | 1.51 (0.93, 2.45) | 570 | 1.20 (0.73, 1.95) |
| 80+ | 416 | 0.82 (0.50, 1.34) | 56 | 1.09 (0.44, 2.73) | 78 | 2.20 (0.95, 5.10) | 416 | 1.04 (0.63, 1.72) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 893 | 1.00 | 400 | 1.00 | 910 | 1.00 | 893 | 1.00 |
| Female | 782 | 0.85 (0.69, 1.05) | 216 | 0.72 (0.47, 1.11) | 646 | 1.08 (0.80, 1.47) | 782 | 0.88 (0.72, 1.09) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 544 | 1.00 | 206 | 1.00 | 507 | 1.00 | 544 | 1.00 |
| Low-med | 388 | 1.17 (0.87, 1.59) | 137 | 0.73 (0.40, 1.33) | 374 | 0.92 (0.61, 1.39) | 388 | 1.14 (0.84, 1.54) |
| Med-high | 345 | 1.06 (0.78, 1.42) | 128 | 0.55 (0.30, 1.01) | 320 | 0.89 (0.58, 1.38) | 345 | 0.98 (0.73, 1.32) |
| High | 398 | 1.05 (0.77, 1.42) | 145 | 0.78 (0.42, 1.46) | 355 | 0.94 (0.61, 1.45) | 398 | 1.05 (0.77, 1.42) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 1353 | 1.00 | 475 | 1.00 | 1223 | 1.00 | 1353 | 1.00 |
| Med-high | 228 | 0.62 (0.36, 1.08) | 94 | 1.28 (0.45, 3.65) | 228 | 0.78 (0.30, 2.00) | 228 | 0.75 (0.43, 1.31) |
| Poor | 94 | 0.83 (0.45, 1.52) | 47 | 1.14 (0.36, 3.58) | 105 | 0.60 (0.23, 1.57) | 94 | 0.89 (0.49, 1.63) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 242 | 1.00 | 106 | 1.00 | 248 | 1.00 | 242 | 1.00 |
| Central metro | 618 | 0.55 (0.39, 0.76) | 202 | 0.90 (0.47, 1.72) | 495 | 0.99 (0.62, 1.57) | 618 | 0.56 (0.40, 0.78) |
| Southern metro | 417 | 0.44 (0.31, 0.63) | 134 | 0.68 (0.35, 1.33) | 426 | 0.84 (0.52, 1.35) | 417 | 0.44 (0.30, 0.63) |
| Country South | 155 | 0.86 (0.51, 1.43) | 74 | 0.52 (0.20, 1.38) | 159 | 2.40 (0.90, 6.39) | 155 | 0.78 (0.47, 1.30) |
| Country North | 241 | 0.78 (0.43, 1.43) | 100 | 1.60 (0.49, 5.18) | 228 | 2.03 (0.76, 5.39) | 241 | 0.73 (0.40, 1.34) |
| **Tumour site:** | | | | | | | | |
| Colon (ref.) | 1098 | 1.00 | 86 | 1.00 | 898 | 1.00 | 1098 | 1.00 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Rectum (incl. Rectosig.) | 577 | 2.07 (1.66, 2.57) | 530 | 0.40 (0.19, 0.83) | 658 | 0.65 (0.48, 0.89) | 577 | 1.76 (1.41, 2.19) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 280 | 1.00 | 50 | 1.00 | 47 | 1.00 | 280 | 1.00 |
| B | 654 | 0.87 (0.64, 1.17) | 147 | 1.03 (0.46, 2.28) | 249 | 1.78 (0.81, 3.90) | 654 | 0.80 (0.59, 1.08) |
| C | 412 | 0.99 (0.72, 1.37) | 231 | 1.56 (0.72, 3.38) | 696 | 3.93 (1.85, 8.36) | 412 | 0.89 (0.65, 1.23) |
| D | 279 | 0.65 (0.45, 0.93) | 162 | 0.71 (0.33, 1.55) | 516 | 0.83 (0.40, 1.71) | 279 | 0.56 (0.38, 0.80) |
| (UK) | (50) | (0.67, (0.31, 1.48)) | (26) | (0.93 (0.28, 3.06)) | (48) | (0.84 (0.27, 2.62)) | (50) | (0.65 (0.33, 1.25)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 58 | 1.00 | 25 | 1.00 | 37 | 1.00 | 58 | 1.00 |
| Mod diff. | 1212 | 0.68 (0.39, 1.20) | 429 | 1.34 (0.50, 3.58) | 1054 | 1.18 (0.43, 3.22) | 1212 | 0.72 (0.42, 1.25) |
| Poorly undiff. | 285 | 0.47 (0.25, 0.87) | 99 | 0.87 (0.62, 5.67) | 309 | 1.28 (0.45, 3.68) | 285 | 0.52 (0.28, 0.95) |
| (UK) | (120) | (1.48 (0.75, 2.95)) | (63) | (1.02 (0.33, 3.12)) | (156) | (0.41, (0.14, 1.17)) | (120) | (1.44 (0.74, 2.81)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 869 | 1.00 | 335 | 1.00 | 782 | 1.00 | 869 | 1.00 |
| 2006 - 2010 | 806 | 1.82 (1.48, 2.24) | 281 | 1.48 (0.97, 2.26) | 774 | 0.65 (0.48, 0.89) | 806 | 1.86 (1.51, 2.29) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff. – differentiated; undiff. - undifferentiated.

Adjusted analyses – Predictors of treatment start exceeding >60 days (Table 3)

*Surgery:* Predictors of time to surgery >60 days for surgical cases included: (a) age at diagnosis – RO of 0.50 (0.29, 0.85) for 70-79 and 0.48 (0.27, 0.85) for 80+ compared with <50years ; (b) service accessibility – RO of 0.37 (0.18, 0.74) for medium and 0.40 (0.18, 0.89) for poor compared with high metropolitan service accessibility; (c) local health network of residence – RO of 0.58 (0.39, 0.86) for metropolitan central and 0.51 (0.33, 0.78) for metropolitan south compared with metropolitan north; (d) tumour site – RO for rectum of 3.39 (2.59, 4.42); (e) tumour stage – RO of 2.32 (1.54, 3.50) for stage C and 1.76 (1.11, 2.78) for stage D compared with stage A; (f) grade – RO of 0.51 (0.27, 0.98) for intermediate and 0.38 (0.18, 0.79) for high compared with low grade; and (g) diagnostic period – RO of 1.56 (1.20, 2.03) for 2006-2010.

*Radiotherapy:* Predictors of time to radiotherapy start >60 days for cases treated by radiotherapy included (a) older age at diagnosis – compared with age<50 years, RO of 2.22 (1.20, 4.09) for 60-69 years, 2.00 (1.08, 3.71) for 70-79 years, and 2.30 (1.04, 5.08) for 80+ years; and (b) tumour site – RO lower at 0.18 (0.11, 0.32) for rectum (note: radiotherapy was uncommon for colonic cases).

*Systemic therapy:* Predictors of time to systemic treatment start >60 days for cases treated by systemic therapy included: (a) older age at diagnosis – compared with under 50 years, RO of 1.72 (1.20, 2.47) for 60-69 years, 1.83 (1.27, 2.64) for 70-79 years and 2.08 (1.19, 3.63) for 80+ years; and (b) tumour sub-site – RO for rectum of 0.78 (0.63, 0.97); and (c) diagnostic period – RO higher at 1.65 (1.33, 2.03) for 2006-2010.

*Any treatment (surgical cases):* Predictors of time to start of any treatment >60 days included: (a) local health network of residence – RO at 0.56 (0.36, 0.86) for metropolitan central and 0.42 (0.26, 0.69) for metropolitan south compared with metropolitan north; (d) tumour site – RO for rectum at 1.82 (1.34, 2.46); (d) grade – RO of 0.43 (0.20, 0.93) for high compared with low grade; and (e) diagnostic period – RO of 1.59 (1.18, 2.15) for 2006-2010.

*Supplementary analyses with tumour stage classified as stage D vs A-C:* The RO for surgery start >60 days did not vary, with RO for stage D of 1.18 (0.84, 1.66) for surgery, 0.92 (0.61, 1.38) for radiotherapy, 0.83 (0.66, 1.31) for systemic therapy, and 1.10 (0.74, 1.64) for any treatment (surgical cases).

Table 3: Relative odds (95% CLs) of treatment for colorectal cancer starting >60 days of diagnosis by treatment type, stage, and socio-demographic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Systemic therapy | | Any treatment (surgical cases) | |
|---|---|---|---|---|---|---|---|---|
| | **n** | **RO (95% CLs)** | **n** | **RO (95% CLs)** | **n** | **RO (95% CLs)** | **n** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 91 | 1.00 | 79 | 1.00 | 189 | 1.00 | 91 | 1.00 |
| 50 – 59 | 210 | 0.79 (0.94, 1.42) | 118 | 1.54 (0.80, 2.99) | 322 | 1.31 (0.89, 1.94) | 210 | 1.00 (0.54, 2.27) |
| 60 – 69 | 388 | 0.73 (0.42, 1.27) | 188 | 2.22 (1.20, 4.09) | 498 | 1.72 (1.20, 2.47) | 388 | 1.11 (0.54, 2.27) |
| 70 – 79 | 570 | 0.50 (0.29, 0.85) | 175 | 2.00 (1.08, 3.71) | 469 | 1.83 (1.27, 2.64) | 570 | 1.10 (0.55, 2.22) |
| 80+ | 416 | 0.48 (0.27, 0.85) | 56 | 2.30 (1.04, 5.08) | 78 | 2.08 (1.18, 3.63) | 416 | 1.25 (0.61, 2.56) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 893 | 1.00 | 400 | 1.00 | 910 | 1.00 | 893 | 1.00 |
| Female | 782 | 0.79 (0.61, 1.04) | 216 | 0.93 (0.64, 1.35) | 646 | 0.93 (0.75, 1.15) | 782 | 0.89 (0.66, 1.20) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 544 | 1.00 | 206 | 1.00 | 507 | 1.00 | 544 | 1.00 |
| Low-med | 388 | 1.37 (0.94, 2.01) | 137 | 1.01 (0.61, 1.68) | 374 | 0.74 (0.55, 1.00) | 388 | 1.30 (0.84, 2.01) |
| Med-high | 345 | 1.06 (0.73, 1.55) | 128 | 0.95 (0.57, 1.57) | 320 | 0.90 (0.67, 1.22) | 345 | 1.17 (0.77, 1.78) |
| High | 398 | 1.05 (0.71, 1.55) | 145 | 1.21 (0.72, 2.01) | 355 | 0.94 (0.69, 1.27) | 398 | 1.07 (0.68, 1.68) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 1353 | 1.00 | 475 | 1.00 | 1223 | 1.00 | 1353 | 1.00 |
| Med-High | 228 | 0.37 (0.18, 0.74) | 94 | 1.36 (0.54, 3.39) | 228 | 1.23 (0.71, 2.12) | 228 | 0.47 (0.21, 1.06) |
| Poor | 94 | 0.40 (0.18, 0.89) | 47 | 1.50 (0.57, 3.95) | 105 | 0.92 (0.50, 1.69) | 94 | 0.55 (0.23, 1.35) |
| **Local Health Network:** | | | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Northern metro (ref.) | 242 | 1.00 | 106 | 1.00 | 248 | 1.00 | 242 | 1.00 |
| Central metro | 618 | 0.58 (0.39, 0.86) | 202 | 0.84 (0.49, 1.44) | 495 | 1.24 (0.89, 1.74) | 618 | 0.56 (0.36, 0.86) |
| Southern metro | 417 | 0.51 (0.33, 0.78) | 134 | 0.56 (0.31, 1.00) | 426 | 0.95 (0.67, 1.34) | 417 | 0.42 (0.26, 0.69) |
| Country South | 155 | 0.80 (0.44, 1.48) | 74 | 0.43 (0.18, 1.02) | 159 | 1.16 (0.66, 2.04) | 155 | 0.80 (0.40, 1.59) |
| Country North | 241 | 1.24 (0.59, 2.59) | 100 | 0.56 (0.21, 1.50) | 228 | 1.02 (0.56, 1.86) | 241 | 0.97 (0.42, 2.25) |
| **Tumour site:** | | | | | | | | |
| Colon (ref.) | 1098 | 1.00 | 86 | 1.00 | 898 | 1.00 | 1098 | 1.00 |
| Rectum (incl. Rectosig.) | 577 | 3.39 (2.59, 4.42) | 530 | 0.18 (0.11, 0.32) | 658 | 0.78 (0.63, 0.97) | 577 | 1.82 (1.34, 2.46) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 280 | 1.00 | 50 | 1.00 | 47 | 1.00 | 280 | 1.00 |
| B | 654 | 1.21 (0.80, 1.82) | 147 | 1.28 (0.62, 2.64) | 249 | 1.24 (0.64, 2.40) | 654 | 0.88 (0.56, 1.39) |
| C | 412 | 2.32 (1.54, 3.50) | 231 | 1.73 (0.87, 3.43) | 696 | 1.21 (0.65, 2.26) | 412 | 1.39 (0.88, 2.19) |
| D | 279 | 1.76 (1.11, 2.78) | 162 | 1.37 (0.67, 2.82) | 516 | 1.01 (0.53, 1.90) | 279 | 1.19 (0.71, 1.99) |
| (UK) | (50) | (1.43 (0.59, 3.51)) | (26) | (0.38 (0.10, 1.54)) | (48) | (0.97 (0.35, 2.68)) | (50) | (1.46 (0.63, 3.37)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 58 | 1.00 | 25 | 1.00 | 37 | 1.00 | 58 | 1.00 |
| Mod diff. | 1212 | 0.51 (0.27, 0.98) | 429 | 0.98 (0.40, 2.42) | 1054 | 1.08 (0.54, 2.19) | 1212 | 0.52 (0.23, 1.03) |
| Poorly/undiff. | 285 | 0.38 (0.18, 0.79) | 99 | 1.18 (0.44, 3.14) | 309 | 1.10 (0.53, 2.29) | 285 | 0.43 (0.20, 0.93) |
| (UK) | (120) | (1.09 (0.51, 2.37) | (63) | (0.66 (0.23, 1.87)) | (156) | (0.58 (0.27, 1.27)) | (120) | (0.99 (0.44, 2.25)) |
| **Diagnostic year:** | | | | | | | | |
| 2000 - 2005 | 869 | 1.00 | 335 | 1.00 | 782 | 1.00 | 869 | 1.00 |
| 2006 - 2010 | 806 | 1.56 (1.20, 2.03) | 281 | 0.91 (0.64, 1.30) | 774 | 1.65 (1.33, 2.03) | 806 | 1.59 (1.18, 2.15) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

**B. <u>Time from diagnosis to treatment start by sub-site (colon and rectum)</u>**

Colon (Supplementary Tables s1 & s2)

- Predictors of time to treatment start >30 days in adjusted analysis included: (a) *For surgery:* age 60-69 years compared with <50 years; northern metropolitan compared with central metropolitan and southern metropolitan; stage A compared with stages B and D; and diagnosis in 2006-2010; (b) *For radiotherapy:* no significant predictors (small numbers); (c) *For systemic therapy*: diagnosis in 2006-2010; (d) *For any treatment (surgical cases)*: northern metropolitan compared with central metropolitan and southern metropolitan areas; stage A compared with stages B and C; and diagnosis in 2006-2010.
- Predictors of time to treatment start of >60 days in adjusted analysis included: (a) *For surgery:* northern metropolitan compared with central and southern metropolitan areas; and more advanced stages C and D compared with stage A; (b) *For radiotherapy:* no significant predictors (small

numbers); (c) *For systemic therapy*: diagnosis in 2006-2010; and (d) *For any treatment (surgical cases)*: northern metropolitan compared with central and southern metropolitan areas.

Rectum (Supplementary Tables s3 & s4)

- Predictors of time to treatment start of >30 days in adjusted analysis included: (a) *For surgery:* age 70+ compared with <50 years; northern metropolitan compared with central and southern metropolitan areas; and diagnosis in 2006-2010; (b) *For radiotherapy:* low compared with medium-high socioeconomic status; and diagnosis in 2006-2010; (c) *For systemic therapy*: stage C; and (d) *For any treatment (surgical cases)*: diagnosis in 2006-2010.
- Predictors of time to treatment start of >60 days in adjusted analysis included: (a) *For surgery:* younger age <50 compared with 70+ years; high service accessibility; northern metropolitan compared with central and southern metropolitan areas; and stage C compared with stage A; better differentiation; and 2006-2010; (b) *For radiotherapy:* aged over 50 years; (c) *For systemic therapy*: aged over 50 years; central metropolitan compared with northern metropolitan area; and stage C; and (d) *For any treatment (surgical cases)*: low grade lesions; and diagnosis in 2006-2010.

**C. Survival by time from diagnosis to treatment start**

*Unadjusted analysis* (Table 4)

*Surgical treatment:* Compared with time to initial surgery >30 days, survival was lowest in the first two years from diagnosis when time to initial surgery was ≤30 days, but changed with further follow-up, such that by 10 years from diagnosis, survival was lower when time to initial surgery was >90 days compared with ≤ 30 days (p=0.017).

*Radiotherapy:* Survival was lowest in the first year when time to radiotherapy start was ≤30 days and reached statistical significance compared with a time of 61-90 days (p=0.009), but not with 31-60 days (p=0.295) or >90 days (p=0.280). After the first year of follow-up, survival was lowest for >90 days.

*Systemic therapy:* The survival pattern varied, with time to treatment ≤30 days having the lowest survival at each follow-up time.

*Any treatment (surgical cases):* Compared with time to initial treatment >30 days, survival was lowest in the first two years from diagnosis when time to initial surgery was ≤30 days, but changed with further follow-up, such that by 10 years from diagnosis, survival was lower when time to initial surgery was >90 days compared with ≤ 30 days (p=0.021).

Table 4: Percentage survival (± standard error) from colorectal cancer by time from diagnosis (days) to commitment of specified treatment: South Australian major public hospitals, diagnoses 2000-2010*

| | | | Follow-up time from diagnosis (years) | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Specified treatment** | **Time (days)** | **Numbers of cases** | **1** | **2** | **3** | **4** | **5** | **10** |
| Surgical treatment | ≤30 | 988 | 85.4 ± 1.2 | 78.2 ± 1.5 | 72.9 ± 1.5 | 69.8 ± 1.6 | 67.5 ± 1.7 | 63.3 ± 2.0 |
| | 31 – 60 | 355 | 93.1 ± 1.6 | 89.9 ± 1.9 | 84.7 ± 2.2 | 81.9 ± 2.4 | 79.7 ± 2.5 | 75.9 ± 2.9 |
| | 61 – 90 | 100 | 92.9 ± 3.7 | 84.1 ± 4.6 | 77.5 ± 5.3 | 74.6 ± 5.5 | 72.6 ± 5.8 | 57.7 ± 9.0 |
| | >90 | 232 | 92.6 ± 2.2 | 82.4 ± 2.9 | 73.9 ± 3.2 | 67.4 ± 3.5 | 67.8 ± 3.7 | 50.4 ± 5.0 |
| Radiotherapy | ≤30 | 129 | 82.0 ± 4.0 | 70.0 ± 4.5 | 62.4 ± 4.7 | 58.0 ± 4.7 | 53.1 ± 4.8 | 44.4 ± 5.5 |
| | 31-60 | 233 | 87.0 ± 2.6 | 77.8 ± 3.0 | 68.2 ± 3.4 | 64.4 ± 3.5 | 61.3 ± 3.6 | 55.2 ± 4.4 |
| | 61 – 90 | 107 | 95.3 ± 3.2 | 87.5 ± 4.1 | 79.4 ± 4.7 | 73.8 ± 5.1 | 64.8 ± 5.5 | 49.0 ± 6.9 |
| | >90 | 147 | 87.6 ± 3.3 | 62.6 ± 4.3 | 53.1 ± 4.4 | 42.8 ± 4.3 | 39.2 ± 4.3 | 27.3 ± 4.3 |
| Systemic therapy | ≤30 | 238 | 68.0 ± 3.3 | 52.8 ± 3.4 | 43.4 ± 3.3 | 40.7 ± 3.3 | 38.4 ± 3.3 | 33.1 ± 3.4 |
| | 31 – 60 | 633 | 87.2 ± 3.4 | 73.8 ± 1.8 | 67.9 ± 2.0 | 62.8 ± 2.0 | 59.4 ± 2.1 | 49.5 ± 2.5 |
| | 61 – 90 | 382 | 92.3 ± 1.6 | 78.8 ± 2.3 | 68.9 ± 2.6 | 64.5 ± 2.7 | 59.8 ± 2.8 | 56.1 ± 3.0 |
| | >90 | 303 | 94.4 ± 1.7 | 78.1 ± 2.6 | 68.6 ± 2.9 | 63.2 ± 3.0 | 56.8 ± 3.1 | 45.1 ± 3.9 |
| Any treatment (surgical cases only) | ≤30 | 1030 | 85.5 ±1.1 | 78.1 ± 1.3 | 72.6 ± 1.4 | 69.4 ± 1.5 | 67.2 ± 1.6 | 63.1 ± 1.8 |
| | 31 – 60 | 428 | 93.4 ± 1.2 | 88.8 ± 1.5 | 83.8 ± 1.8 | 80.5 ± 2.0 | 78.0 ± 2.2 | 71.5 ± 2.9 |
| | 61 – 90 | 118 | 94.0 ± 2.2 | 85.9 ± 3.3 | 79.6 ± 3.9 | 74.8 ± 4.4 | 71.7 ± 4.7 | 56.6 ± 7.8 |
| | >90 | 99 | 91.7 ± 2.8 | 82.2 ± 3.9 | 71.9 ± 4.7 | 63.9 ± 5.2 | 57.1 ± 5.6 | 43.8 ± 8.2 |

* Kaplan-Meier product-limit estimate; date of censoring of live cases: Dec 31, 2012

*Adjusted analysis* (Table 5)

Because visual examination and interaction terms indicated a lack of proportionality of survival with time to treatment, results are split in Table 5 for follow-up of ≤2 and 3-10 years as mutually exclusive periods. Irrespective of treatment type, lower hazard ratios applied for periods ≤ 2 years with times to treatment of >30 days, after adjusting for age, sex, socioeconomic status, service accessibility, local health network of residence, tumour sub-site, stage, grade and diagnostic period. Hazard ratios similarly adjusted generally did not decrease across the 3-10 follow-up, suggesting no significant differences in conditional survival after two years for cases treated ≤30 days of diagnosis and >30 days. While there were higher hazard ratios for times of 61-90 and >90 days for 3-10-year follow-up from surgical treatment and radiotherapy respectively, statistical significance was only achieved for any treatment (surgical cases) when comparing time to treatment >90 compared with ≤30 days (p=0.022).

Table 5: Hazard ratios (95% confidence limits) of deaths from colorectal cancer by time from diagnosis (days) to commencement of specified treatment: South Australians major public hospitals, diagnoses 2000-2010*

| | | **Follow-up time from diagnoses** | | | |
|---|---|---|---|---|---|
| | | **≤ 2 years** | | **3-10 years** | |
| **Treatment** | **Time** | **Number of cases** | **Hazard ratios** | **Number of cases** | **Hazard ratios** |
| Surgical treatment | ≤30 | 988 | 1.00 | 714 | 1.00 |
| | 31 – 60 | 355 | 0.57 (0.40, 0.82) | 302 | 0.92 (0.62, 1.36) |
| | 61 – 90 | 100 | 0.59 (0.35, 1.02) | 76 | 1.13 (0.60, 2.10) |
| | >90 | 232 | 0.59 (0.41, 0.84) | 186 | 1.24 (0.85, 1.83) |
| Radiotherapy | ≤30 | 129 | 1.00 | 87 | 1.00 |
| | 31 – 60 | 233 | 0.85 (0.54, 1.32) | 173 | 1.00 (0.59, 1.72) |
| | 61 - 90 | 107 | 0.44 (0.23, 0.84) | 89 | 1.26 (0.70, 2.27) |
| | >90 | 147 | 0.62 (0.40, 0.98) | 89 | 1.60 (0.90, 2.85) |
| Systemic therapy | ≤30 | 238 | 1.00 | 120 | 1.00 |
| | 31 – 60 | 633 | 0.71 (0.55, 0.92) | 459 | 0.98 (0.66, 1.47) |
| | 61 – 90 | 382 | 0.51 (0.38, 0.70) | 289 | 1.01 (0.65, 1.55) |
| | >90 | 303 | 0.40 (0.30, 0.55) | 233 | 1.04 (0.68, 1.59) |
| Any treatment (surgical cases only) | ≤30 | 1030 | 1.00 | 744 | 1.00 |
| | 31 – 60 | 428 | 0.59 (0.43, 0.81) | 361 | 0.94 (0.66, 1.33) |
| | 61 – 90 | 118 | 0.48 (0.43, 0.81) | 95 | 1.11 (0.66, 1.89) |
| | >90 | 99 | 0.62 (0.37, 1.02) | 78 | 1.83 (1.12, 2.98) |

*4 Cox proportional hazards regression analyses (1 per treatment category), adjusting for age, sex, socioeconomic status, service accessibility, local health network, sub-site,

stage, grade and diagnostic period (see tables 2 and 3); date of censoring of live cases: Dec 31, 2012.

## Discussion

The proportion of surgical patients receiving any treatment for their cancer ≤60 days of diagnosis was 87%, with 80% receiving surgical treatment within 60 days of diagnosis. This broadly accords with targets set by Cancer UK.[9] The proportion receiving radiotherapy who started this therapy ≤60 days of diagnosis was 59%, whereas the corresponding percentage having systemic therapies who started this therapy ≤60 days of diagnosis was 56%. The longer delay for radiotherapy and systemic therapy is consistent with their common use as adjuvant therapies following surgery.[5]

Longer time to surgery applied for cancers of the rectum than colon potentially reflecting the increased use of MRI for rectal cancers, [25] and multimodal therapies,[5] which may have led to surgery delays through more multidisciplinary consultation and in some instances, neoadjuvant care.[26]

The longer time to surgery in 2006-2010 may also have been influenced by increasing use of multimodal therapies and more advanced diagnostics (e.g., MRI), increasing the need for multidisciplinary consultation.[5, 26] While the introduction of population-based screening may have contributed, the screening program was still at an early phase of development, being phased in from 2006 to 2020. Following more complete implementation of bowel screening, there may be increased pressure on services which may increase times to surgery.[7, 8] The higher proportion with a time to surgery >60 days for stages C and D compared with stage A may reflect time taken for symptom control, multidisciplinary team consultation, and provision of neoadjuvant therapies.[27, 28] The proportion with a time to surgery >60 days was lower for higher grade tumours, potentially due to a greater perceived urgency of surgical intervention for more aggressive tumours.

The proportion receiving surgery, who did so >60 days from diagnosis, tended to be lower among those aged 70+ years, central and southern compared with northern metropolitan areas, those diagnosed in 2000-2005 compared with 2006-2010, and unexpectedly, those residing closer to metropolitan services. The reasons are unclear but may reflect differences in service busyness and patterns of patient and service demand.

Of those receiving radiotherapy, the proportion starting this therapy >60 days from diagnosis tended to be higher for ages ≥60 years than the <50 years. A similar pattern applied for systemic therapy. The reasons are not known. Perhaps a longer recovery time post-surgery has been allowed for older cases post-surgery before commencing adjuvant therapies, or longer delays occurring due to higher levels of frailty and comorbidity, and more common complications of surgery.

Radiotherapy was relatively uncommon for colon cancers, as recommended in clinical guidelines and optimal care pathways, [27, 28] but when it was provided, it tended to start later than for rectal cases. Similarly, systemic therapies tended to commence later for colon than rectal cancers. Further research is needed to determine the reasons for these patterns. Systemic therapies were less likely to commence >30 days from diagnosis for 2006-2010 diagnoses. Conversely systemic therapies were more inclined to occur >60 days from diagnosis in 2006-2010. Again, further research is needed to explain these patterns.

Where the time from diagnosis to treatment was >30 days, the risk of death occurring ≤2 years of diagnosis was lower. This was evident by therapy type after adjusting for stage and grade, and sociodemographic factors. It may reflect the triaging for priority treatment ≤30 days for cases with elevated comorbidity or other risk factors not recorded by the registry. While a statistically significant U-shaped relationship of survival with time to treatment start was usually not apparent for specific therapies, as indicated in some other studies, [6, 17] the hazard ratio for 3-10 years was elevated when the time to first treatment was >90 days for surgical cases (p=0.022).

The present study has limitations. An opportunistic approach was taken in selecting cases where evidence was available on size of the gap between recorded diagnosis date and start of treatment. This raises questions about the representativeness of results. Nonetheless, results are similar to those of other recent studies in showing poorer short-term survival for cases receiving surgical treatment soon after diagnosis, and with a similar pattern applying for early treatment by radiotherapy and systemic therapies.[12, 14, 15, 17]

Results should not be construed as indicating a lack of benefit from early treatment, given likely confounding effects of patient selection in treatment scheduling. A positive feature was the approximate 87% of surgical cases receiving their first treatment (any treatment) ≤60 days and 80% treated surgically within this period (note: 83% for 2000-2005 and 78% for 2006-2010).[9] The indication of a temporal decline in this percentage warrants continued monitoring and investigation, particularly for patient groups where a higher proportion was not receiving surgical care ≤60 days of diagnosis (e.g., patients aged under 50 years, those with advanced disease, those with rectal cancer, and residents of the northern metropolitan rather than central or southern metropolitan areas).

The study highlights the benefit of linking diagnostic data to treatment data. Population-wide data linkage of population-based cancer registry, hospital, radiotherapy-centre, Medicare insurance and screening data, and potentially in the future, electronic medical record data and selected research databases will further strengthen the data infrastructure available for describing clinical management pathways and associations with survival across the population. Clinical registries will still be important for more detailed investigations for the sub-groups they cover, and for validating results of population-wide registry and administrative sources.

**Conclusions**

- Australia has a high incidence but a greatly reducing mortality from colorectal cancer due to survival gains. Equivalent survival gains have been found for major public hospitals in South Australia.
- Scientific evidence of effects of treatment delays on survival is mixed. Some recent studies show lower survival with shorter delays, attributing this to triaging of more aggressive and complicated cases for early treatment.
- Baseline data for major public hospitals in South Australia 2000-2010 indicate that for cases where the clinical registry recorded a diagnosis in advance of the surgery date, approximately 87% of surgical cases receiving any treatment and 80% of cases received their surgical treatment ≤60 days of diagnosis. This is broadly consistent with timeline targets of Cancer UK.
- Radiotherapy and systemic therapies generally started later, potentially reflecting their use as adjuvant therapies.
- Adjusted analyses indicated lower survival up to two years from diagnosis when treatment commenced ≤30 days of diagnosis, potentially reflecting triaging for early care of cases with aggressive cancers and higher clinical complexity. By comparison, adjusted analyses did not show differences in survival for follow-up periods from diagnosis of 3-10 years where longer times to treatment applied, except for time to any treatment (surgical cases) of >90 days when survival was lower.
- These results should not be interpreted as evidence of the importance or unimportance of delays, given selection factors in scheduling patient care. Further research is needed to assess effects of treatment delays on patients' anxiety.
- Treatment commencement was generally later in 2006-2010 than 2000-2005, possibly reflecting increased use of adjuvant therapies, MDTs, and more advanced diagnostics (e.g., MRIs). Increased demand may be placed on timeliness of clinical services with extensions in population screening.
- Further research is needed to optimize patient scheduling for care to reduce anxiety and mortality.

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**Ethics**

Research ethics approval from the South Australian Human Research Ethics Committee HREC/14/SAH/145.

**Informed consent**

Waiver of consent for use of de-identified data collected under authorisation of Part 7 of the South Australian Health Care Act. Note: large numbers of patients are deceased and many are in the terminal stages of their cancer. Consent processes would be intrusive and would invalidate the database as an unbiased data source.

**Author contributions**

Study concept: DR, TP; Study design: DR TP, CK, RP, JM; Data acquisition: DB, KP; Quality control of data: DB, KP, KF; Data analysis: DR, KF ; Data interpretation: DR, CK, IO, DK, RP, JM, RJ, DW, DLW, TP; Report writing: DR, KF; Review of report: DR, CK, IO, DK, RP, JM, RJ, DW, DLW, TP, CM, CH, EB. All authors read and approved the final manuscript.

**Data sharing**

The data for this study are available through the South Australian Cancer Service and SA Cancer Registry. Restrictions to data use apply as conditions of legal authorization and data custodian and ethics approval.

**Competing interests**

D Roder reports grants from Cancer Council SA, during the conduct of the study.

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***Supplementary tables***

Table S1: Relative odds (95% CLs) of treatment for colon cancer starting >30 days of diagnosis by treatment type, stage, and socioeconomic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Systemic therapy | | Any treatment (surgical cases) | |
|---|---|---|---|---|---|---|---|---|
| | **n=1098** | **RO (95% CLs)** | **n=86** | **RO (95% CLs)** | **n=898** | **RO (95% CLs)** | **n=1098** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 53 | 1.00 | 13 | 1.00 | 109 | 1.00 | 53 | 1.00 |
| 50 - 59 | 116 | 1.61 (0.75, 3.46) | 14 | 1.03 (0.05, 21.46) | 176 | 0.84 (0.40, 1.76) | 116 | 1.28 (0.59, 2.78) |
| 60 - 69 | 226 | 2.10 (1.03, 4.28) | 20 | 2.82 (0.20, 40.71) | 273 | 0.91 (0.45, 1.83) | 226 | 1.86 (0.92, 3.80) |
| 70 - 79 | 396 | 1.65 (0.83, 3.28) | 28 | 3.49 (0.27, 45.20) | 292 | 1.37 (0.68, 2.79) | 396 | 1.55 (0.78, 3.09) |
| 80+ | 307 | 1.50 (0.74, 3.03) | 11 | NA | 48 | 2.52 (0.78, 8.17) | 307 | 1.43 (0.71, 2.88) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 562 | 1.00 | 56 | 1.00 | 491 | 1.00 | 562 | 1.00 |
| Female | 536 | 0.87 (0.67, 1.13) | 30 | 2.65 (0.27, 1.64) | 407 | 1.23 (0.79, 1.91) | 536 | 0.89 (0.68, 1.16) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 336 | 1.00 | 25 | 1.00 | 287 | 1.00 | 336 | 1.00 |
| Low-Med | 273 | 1.69 (0.99, 2.12) | 19 | 1.69 (0.09, 30.68) | 229 | 0.71 (0.39, 1.27) | 273 | 1.46 (1.00, 2.14) |
| Med-High | 224 | 1.31 (0.90, 1.90) | 20 | 7.01 (0.22, 223.56) | 185 | 0.93 (0.49, 1.78) | 224 | 1.28 (0.88, 1.88) |
| High | 265 | 1.12 (0.76, 1.67) | 22 | 1.37 (0.07, 27.36) | 197 | 0.85 (0.45, 1.62) | 265 | 1.09 (0.73, 1.62) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 899 | 1.00 | 66 | 1.00 | 716 | 1.00 | 899 | 1.00 |
| Med-High | 141 | 0.57 (0.28, 1.15) | 9 | NA | 127 | 0.41 (0.09, 1.97) | 141 | 0.57 (0.28, 1.16) |
| Poor | 58 | 0.71 (0.33, 1.57) | 11 | NA | 55 | 0.25 (0.05, 1.21) | 58 | 0.63 (0.28, 1.38) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 149 | 1.00 | 12 | 1.00 | 141 | 1.00 | 149 | 1.00 |
| Central metro | 421 | 0.49 (0.32, 0.75) | 33 | 0.31 (0.01, 6.39) | 291 | 0.85 (0.41, 1.76) | 421 | 0.48 (0.31, 0.73) |
| Southern metro | 281 | 0.39 (0.25, 0.63) | 16 | 0.58 (0.03, 11.80) | 252 | 0.83 (0.39, 1.78) | 281 | 0.37 (0.24, 0.60) |
| Country South | 88 | 0.69 (0.36, 1.33) | 10 | NA | 83 | 3.94 (0.70, 22.22) | 88 | 0.69 (0.36, 1.34) |
| Country North | 159 | 0.78 (0.37, 1.66) | 15 | NA | 131 | 2.42 (0.47, 12.36) | 159 | 0.76 (0.35, 1.63) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 169 | 1.00 | 3 | 1.00 | 12 | 1.00 | 169 | 1.00 |
| B | 471 | 0.67 (0.46, 0.98) | 20 | 43.60 (0.38, 49.56) | 130 | 1.60 (0.16, 16.54) | 471 | 0.65 (0.45, 0.95) |
| C | 252 | 0.69 (0.46, 1.06) | 21 | 24.12 (0.22, 26.91) | 409 | 1.76 (0.19, 16.48) | 252 | 0.66 (0.43, 1.00) |
| D | 180 | 0.54 (0.33, 0.86) | 39 | 4.39 (0.07, 27.89) | 320 | 0.24 (0.03, 2.17) | 180 | 0.44 (0.27, 0.72) |
| (UK) | (26) | (0.64 (0.26, 1.57)) | (3) | NA | (27) | (0.41 (0.04, 4.48)) | (26) | (0.58 (0.23, 1.43)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 38 | 1.00 | 5 | 1.00 | 18 | 1.00 | 38 | 1.00 |
| Mod diff. | 770 | 0.85 (0.43, 1.68) | 53 | 1.49 (0.11, 19.97) | 581 | 0.58 (0.07, 4.81) | 770 | 0.82 (0.41, 1.62) |
| Poorly/undiff. | 209 | 0.57 (0.27, 1.21) | 19 | 1.11 (0.06, 21.24) | 213 | 0.46 (0.05, 3.89) | 209 | 0.54 (0.26, 1.15) |
| (UK) | (81) | (1.87 (0.82, 4.26)) | (9) | NA | (86) | (0.13 (0.02, 1.11)) | (81) | (1.62 (0.71, 3.69)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 541 | 1.00 | 52 | 1.00 | 451 | 1.00 | 541 | 1.00 |
| 2006 - 2010 | 557 | 1.41 (1.09, 1.83) | 34 | 0.21 (0.03, 1.64) | 447 | 1.59 (1.02, 2.48) | 557 | 1.39 (1.07, 2.88) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; NA – not applicable; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

Table S2: Relative odds (95% CLs) of treatment for colon cancer starting >60 days of diagnosis by treatment type, stage, and socio-demographic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Systemic therapy | | Any treatment (surgical cases only) | |
|---|---|---|---|---|---|---|---|---|
| | **n=1098** | **RO (95% CLs)** | **n=86** | **RO (95% CLs)** | **n=898** | **RO (95% CLs)** | **n=1098** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 53 | 1.00 | 13 | 1.00 | 109 | 1.00 | 53 | 1.00 |
| 50 - 59 | 116 | 1.34 (0.51, 3.51) | 14 | 0.06 (0.00, 1.37) | 176 | 0.94 (0.57, 1.55) | 116 | 0.75 (0.25, 2.21) |
| 60 - 69 | 226 | 1.28 (0.51, 3.20) | 20 | 0.17 (0.01, 3.57) | 273 | 1.16 (0.73, 1.84) | 226 | 1.10 (0.41, 2.93) |
| 70 - 79 | 396 | 1.10 (0.45, 2.66) | 28 | 0.35 (0.02, 7.07) | 292 | 1.26 (0.80, 2.01) | 396 | 0.99 (0.38, 2.53) |
| 80+ | 307 | 1.00 (0.40, 2.47) | 11 | 0.30 (0.01, 7.36) | 48 | 1.60 (0.78, 3.29) | 307 | 1.01 (0.38, 2.65) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 562 | 1.00 | 56 | 1.00 | 491 | 1.00 | 562 | 1.00 |
| Female | 536 | 0.83 (0.57, 1.20) | 30 | 1.01 (0.23, 4.35) | 407 | 0.84 (0.64, 1.14) | 536 | 0.94 (0.62, 1.41) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 336 | 1.00 | 25 | 1.00 | 287 | 1.00 | 336 | 1.00 |
| Low-med | 273 | 1.58 (0.93, 2.71) | 19 | 0.40 (0.06, 2.51) | 229 | 0.75 (0.51, 1.10) | 273 | 1.65 (0.92, 2.98) |
| Med-high | 224 | 1.14 (0.68, 1.94) | 20 | 1.78 (0.26, 12.39) | 185 | 0.86 (0.58, 1.28) | 224 | 1.14 (0.64, 2.04) |
| High | 265 | 1.19 (0.67, 2.10) | 22 | 1.04 (0.15, 7.27) | 197 | 1.18 (0.78, 1.77) | 265 | 1.41 (0.75, 2.63) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 899 | 1.00 | 66 | 1.00 | 716 | 1.00 | 899 | 1.00 |
| Med-high | 141 | 0.54 (0.20, 1.42) | 9 | 8.99 (0.24, 331.28) | 127 | 1.57 (0.75, 3.30) | 141 | 0.45 (0.16, 1.25) |
| Poor | 58 | 0.65 (0.21, 1.97) | 11 | 3.90 (0.11, 141.05) | 55 | 0.83 (0.36, 1. 93) | 58 | 0.41 (0.12, 1.44) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 149 | 1.00 | 12 | 1.00 | 141 | 1.00 | 149 | 1.00 |
| Central metro | 421 | 0.56 (0.32, 0.98) | 33 | 0.16 (0.01, 1.98) | 291 | 0.91 (0.58, 1. 43) | 421 | 0.44 (0.24, 0.79) |
| Southern metro | 281 | 0.46 (0.25, 0.87) | 16 | 0.17 (0.01, 2.26) | 252 | 0.96 (0.61, 1.52) | 281 | 0.29 (0.14, 0.58) |
| Country South | 88 | 0.87 (0.36, 2.14) | 10 | 0.08 (0.00, 2.02) | 83 | 0.93 (0.43, 2.01) | 88 | 0.87 (0.34, 2.21) |
| Country North | 157 | 1.04 (0.38, 2.90) | 15 | 0.03 (0.00, 1.61) | 131 | 0.74 (0.33, 1. 76) | 157 | 1.23 (0.43, 3.57) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 169 | 1.00 | 3 | 1.00 | 12 | 1.00 | 169 | 1.00 |
| B | 471 | 1.02 (0.54, 1.91) | 20 | 0.79 (0.03, 23.99) | 130 | 0.43 (0.10, 1.74) | 471 | 0.80 (0.42, 1.53) |
| C | 252 | 2.34 (1.25, 4.40) | 21 | 0.57 (0.02, 18.97) | 409 | 0.29 (0.07, 1.15) | 252 | 1.54 (0.80, 2.96) |
| D | 180 | 2.25 (1.16, 4.35) | 39 | 0.94 (0.03, 26.42) | 320 | 0.26 (0.07, 1.03) | 180 | 1.49 (0.74, 2.98) |
| (UK) | (26) | (1.65 (0.51, 5.33)) | (3) | NA | (27) | (0.67 (0.14, 3.26)) | (26) | 1.35 (0.38, 4.76)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 38 | 1.00 | 5 | 1.00 | 18 | 1.00 | 38 | 1.00 |
| Mod diff. | 770 | 0.85 (0.31, 2.29) | 53 | 2.29 (0.31, 16.79) | 581 | 0.97 (0.35, 2.67) | 770 | 0.71 (0.26, 1.92) |
| Poorly/undiff. | 209 | 0.60 (0.20, 1.78) | 19 | 1.11 (0.12, 10.68) | 213 | 0.94 (0.33, 2.65) | 209 | 0.52 (0.17, 1.58) |
| (UK) | (81) | (1.84 (0.60, 5.62)) | (9) | NA | (86) | (0.40 (0.13, 1.20)) | (81) | (1.24 (0.39, 3.93)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 541 | 1.00 | 52 | 1.00 | 451 | 1.00 | 541 | 1.00 |
| 2006 - 2010 | 557 | 1.26 (0.87, 1.82) | 34 | 0.31 (0.08, 1.25) | 447 | 1.96 (1.48, 2.59) | 557 | 1.29 (0.86, 1.94) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; NA – not applicable; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

Table S3: Relative odds (95% CLs) of treatment for **rectal cancer** starting >30 days of diagnosis by treatment type, stage, and socioeconomic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Systemic therapy | | All treatment (surgical cases only) | |
|---|---|---|---|---|---|---|---|---|
| | **n=577** | **RO (95% CLs)** | **n=530** | **RO (95% CLs)** | **n=658** | **RO (95% CLs)** | **n=577** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 38 | 1.00 | 66 | 1.00 | 80 | 1.00 | 38 | 1.00 |
| 50 - 59 | 94 | 0.71 (0.31,1.62) | 104 | 1.30 (0.62,2.71) | 146 | 1.73 (0.86,3.48) | 94 | 1.03 (0.46, 2.29) |
| 60 - 69 | 162 | 0.57 (0.26,1.24) | 168 | 1.41 (0.71,2.79) | 225 | 1.57 (0.83,2.99) | 162 | 0.78 (0.37, 1.66) |
| 70 - 79 | 174 | 0.44 (0.20,0.95) | 147 | 1.35 (0.67,2.71) | 177 | 1.79 (0.90,3.54) | 174 | 0.83 (0.40, 1.76) |
| 80+ | 109 | 0.38 (0.17,0.85) | 45 | 1.40 (0.52,3.77) | 30 | 2.01 (0.58,6.97) | 109 | 0.70 (0.32, 1.55) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 331 | 1.00 | 344 | 1.00 | 419 | 1.00 | 331 | 1.00 |
| Female | 246 | 0.74 (0.52,1.07) | 186 | 0.68 (0.43,1.07) | 239 | 0.94 (0.61,1.45) | 246 | 0.79 (0.55, 1.14) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 208 | 1.00 | 181 | 1.00 | 220 | 1.00 | 208 | 1.00 |
| Low-med | 115 | 0.86 (0.50,1.45) | 118 | 0.80 (0.42,1.51) | 145 | 1.13 (0.62,2.07) | 115 | 0.81 (0.48, 1.37) |
| Med-high | 121 | 0.72 (0.44,1.19) | 108 | 0.50 (0.26,0.94) | 135 | 0.78 (0.43,1.42) | 121 | 0.63 (0.38, 1.03) |
| High | 133 | 1.06 (0.64,1.77) | 123 | 0.88 (0.45,1.70) | 158 | 1.00 (0.55,1.83) | 133 | 1.03 (0.62, 1.72) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 454 | 1.00 | 409 | 1.00 | 507 | 1.00 | 454 | 1.00 |
| Med-high | 87 | 0.74 (0.29,1.88) | 85 | 1.49 (0.50,4.44) | 101 | 1.00 (0.30,3.36) | 87 | 1.27 (0.49, 3.26) |
| Poor | 36 | 1.00 (0.36,2.76) | 36 | 1.25 (0.37,4.20) | 50 | 0.88 (0.25,3.05) | 36 | 1.58 (0.58, 4.33) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 93 | 1.00 | 94 | 1.00 | 107 | 1.00 | 93 | 1.00 |
| Central metro | 197 | 0.55 (0.31,0.97) | 169 | 0.86 (0.44,1.70) | 204 | 1.19 (0.64,2.23) | 197 | 0.61 (0.35, 1.06) |
| Southern metro | 136 | 0.40 (0.22,0.73) | 118 | 0.61 (0.30,1.23) | 174 | 0.89 (0.47,1.69) | 136 | 0.44 (0.24, 0.80) |
| Country South | 67 | 0.89 (0.37,2.10) | 64 | 0.45 (0.17,1.25) | 76 | 1.99 (0.62,6.41) | 67 | 0.70 (0.30, 1.63) |
| Country North | 84 | 0.67 (0.24,1.89) | 85 | 1.48 (0.44,5.02) | 97 | 2.61 (0.73,9.25) | 84 | 0.57 (0.20, 1.62) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 111 | 1.00 | 47 | 1.00 | 35 | 1.00 | 111 | 1.00 |
| B | 183 | 1.31 (0.79,2.18) | 127 | 0.90 (0.39,2.06) | 119 | 1.35 (0.57,3.21) | 183 | 1.18 (0.71, 1.95) |
| C | 160 | 1.65 (0.98,2.79) | 210 | 1.39 (0.63,3.10) | 287 | 3.81 (1.64,8.86) | 160 | 1.43 (0.85, 2.40) |
| D | 99 | 0.83 (0.46,1.51) | 123 | 0.67 (0.30,1.51) | 196 | 1.30 (0.58,2.95) | 99 | 0.79 (0.43, 1.44) |
| (UK) | 24 | (0.76 (0.28,2.06)) | 23 | (0.74 (0.23,2.39)) | 21 | (1.72 (0.44,6.71)) | 24 | (0.83 (0.30,2.28)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 20 | 1.00 | 20 | 1.00 | 19 | 1.00 | 20 | 1.00 |
| Mod diff. | 442 | 0.60 (0.21,1.68) | 376 | 1.59 (0.57,4.44) | 473 | 1.43 (0.43,4.70) | 442 | 0.78 (0.29, 2.08) |
| Poorly/undiff. | 76 | 0.52 (0.17,1.61) | 80 | 2.63 (0.81,8.52) | 96 | 2.14 (0.57,8.10) | 76 | 0.71 (0.24, 2.08) |
| (UK) | 39 | (1.38 (0.39,4.91)) | 54 | (1.31 (0.40,4.29)) | 70 | (0.72 (0.20,2.63)) | 39 | (1.57 (0.47,5.27)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 328 | 1.00 | 283 | 1.00 | 331 | 1.00 | 328 | 1.00 |
| 2006 - 2010 | 249 | 2.86 (1.98,4.12) | 247 | 1.76 (1.12,2.76) | 327 | 1.34 (0.88,2.04) | 249 | 3.09 (2.15, 4.43) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

Table S4: Relative odds (95% CLs) of treatment for **rectal cancer** starting >60 days of diagnosis by treatment type, stage, and socio-demographic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Systemic therapy | | All treatment (surgical cases only) | |
|---|---|---|---|---|---|---|---|---|
| | **n=577** | **RO (95% CLs)** | **n=530** | **RO (95% CLs)** | **n=658** | **RO (95% CLs)** | **n=577** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 38 | 1.00 | 66 | 1.00 | 80 | 1.00 | 38 | 1.00 |
| 50 - 59 | 94 | 0.53 (0.23, 1.19) | 104 | 2.41 (1.12, 5.17) | 146 | 2.45 (1.26, 4.74) | 94 | 1.28 (0.42, 3.93) |
| 60 - 69 | 162 | 0.49 (0.23, 1.05) | 168 | 3.28 (1.60, 6.71) | 225 | 3.46 (1.85, 6.49) | 162 | 1.17 (0.40, 3.38) |
| 70 - 79 | 174 | 0.25 (0.12, 0.55) | 147 | 2.69 (1.30, 5.56) | 177 | 3.47 (1.82, 6.60) | 174 | 1.21 (0.42, 3.48) |
| 80+ | 109 | 0.26 (0.11, 0.59) | 45 | 3.05 (1.24, 7.51) | 30 | 3.95 (1.54, 10.17) | 109 | 1.62 (0.55, 4.80) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 331 | 1.00 | 344 | 1.00 | 419 | 1.00 | 331 | 1.00 |
| Female | 246 | 0.77 (0.52, 1.13) | 186 | 0.91 (0.61, 1.36) | 239 | 1.04 (0.73, 1.46) | 246 | 0.89 (0.56, 1.42) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 208 | 1.00 | 181 | 1.00 | 220 | 1.00 | 208 | 1.00 |
| Low-med | 115 | 1.29 (0.73, 2.27) | 118 | 1.11 (0.65, 1.92) | 145 | 0.61 (0.38, 0.98) | 115 | 1.05 (0.53, 2.02) |
| Med-high | 121 | 1.04 (0.61, 1.78) | 108 | 0.95 (0.55, 1.62) | 135 | 0.94 (0.59, 1.50) | 121 | 1.25 (0.67, 2.33) |
| High | 133 | 1.03 (0.60, 1.77) | 123 | 1.28 (0.74, 2.22) | 158 | 0.71 (0.44, 1.14) | 133 | 0.81 (0.41, 1.58) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 454 | 1.00 | 409 | 1.00 | 507 | 1.00 | 454 | 1.00 |
| Med-high | 87 | 0.26 (0.09, 0.73) | 85 | 1.12 (0.41, 3.01) | 101 | 0.98 (0.42, 2.25) | 87 | 0.49 (0.13, 1.86) |
| Poor | 36 | 0.30 (0.10, 0.89) | 36 | 1.53 (0.55, 4.31) | 50 | 1.08 (0.45, 2.62) | 36 | 0.83 (0.22, 2.67) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 93 | 1.00 | 94 | 1.00 | 107 | 1.00 | 93 | 1.00 |
| Central metro | 197 | 0.53 (0.30, 0.95) | 169 | 0.88 (0.50, 1.55) | 204 | 1.70 (1.00, 2.89) | 197 | 0.71 (0.36, 1.38) |
| Southern metro | 136 | 0.49 (0.26, 0.91) | 118 | 0.55 (0.30, 1.03) | 174 | 0.84 (0.48, 1.44) | 136 | 0.63 (0.30, 1.30) |
| Country South | 67 | 0.69 (0.29, 1.61) | 64 | 0.45 (0.18, 1.14) | 76 | 1.36 (0.59, 3.17) | 67 | 0.71 (0.25, 2.05) |
| Country North | 84 | 1.25 (0.42, 3.74) | 85 | 0.70 (0.24, 2.01) | 97 | 1.10 (0.44, 2.72) | 84 | 0.67 (0.17, 2.71) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 111 | 1.00 | 47 | 1.00 | 35 | 1.00 | 111 | 1.00 |
| B | 183 | 1.46 (0.82, 2.58) | 127 | 1.26 (0.59, 2.67) | 119 | 1.64 (0.69, 3.91) | 183 | 1.04 (0.53, 2.02) |
| C | 160 | 2.30 (1.30, 4.05) | 210 | 1.76 (0.86, 3.58) | 287 | 2.70 (1.19, 6.12) | 160 | 1.15 (0.60, 2.24) |
| D | 99 | 1.34 (0.69, 1.61) | 123 | 1.25 (0.59, 2.67) | 196 | 1.95 (0.85, 4.51) | 99 | 0.83 (0.37, 1.86) |
| (UK) | 24 | (1.65 (0.58, 4.67)) | 23 | (0.35 (0.09, 1.43)) | 21 | (1.33 (0.38, 4.68)) | 24 | (1.45 (0.46,4.58)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 20 | 1.00 | 20 | 1.00 | 19 | 1.00 | 20 | 1.00 |
| Mod diff. | 442 | 0.30 (0.11, 0.82) | 376 | 1.25 (0.45,3.44) | 473 | 1.39 (0.50, 3.88) | 442 | 0.35 (0.13, 0.95) |
| Poorly/un-diff. | 76 | 0.26 (0.09, 0.79) | 80 | 1.70 (0.57,5.09) | 96 | 1.51 (0.50, 4.52) | 76 | 0.35 (0.11, 1.12) |
| (UK) | 39 | (0.64 (0.19, 2.18)) | 54 | (0.88 (0.28,2.84)) | 70 | (0.83 (0.27, 2.59)) | 39 | (0.76 (0.23,2.59)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 328 | 1.00 | 283 | 1.00 | 331 | 1.00 | 328 | 1.00 |
| 2006 - 2010 | 249 | 1.98 (1.35, 2.91) | 247 | 1.02 (0.70,1.50) | 327 | 1.21 (0.87, 1.69) | 249 | 2.01 (1.26, 3.18) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

# Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

| | | Reporting Item | Page Number |
|---|---|---|---|
| Title | #1a | Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| Abstract | #1b | Provide in the abstract an informative and balanced summary of what was done and what was found | 2 |
| Background / rationale | #2 | Explain the scientific background and rationale for the investigation being reported | 3 |
| Objectives | #3 | State specific objectives, including any prespecified hypotheses | 4 |
| Study design | #4 | Present key elements of study design early in the paper | 4 |
| Setting | #5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 4 |

| | | | |
|---|---|---|---|
| Eligibility criteria | #6a | Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. | 4 |
| | #6b | For matched studies, give matching criteria and number of exposed and unexposed | n/a |
| Variables | #7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 4,5 |
| Data sources / measurement | #8 | For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable. | 4 |
| Bias | #9 | Describe any efforts to address potential sources of bias | 10, 12 |
| Study size | #10 | Explain how the study size was arrived at | 4 |
| Quantitative variables | #11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | 4,5 |
| Statistical methods | #12a | Describe all statistical methods, including those used to control for confounding | 4,5 |
| | #12b | Describe any methods used to examine subgroups and interactions | 4,5 |
| | #12c | Explain how missing data were addressed | 4 |
| | #12d | If applicable, explain how loss to follow-up was addressed | n/a |
| | #12e | Describe any sensitivity analyses | 4,5 |
| Participants | #13a | Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable. | tables 1-5 |
| | #13b | Give reasons for non-participation at each stage | n/a |
| | #13c | Consider use of a flow diagram | n/a |

| | | | |
|---|---|---|---|
| Descriptive data | #14a | Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable. | 5-14 |
| | #14b | Indicate number of participants with missing data for each variable of interest | n/a |
| | #14c | Summarise follow-up time (eg, average and total amount) | n/a |
| Outcome data | #15 | Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable. | 5-14 |
| Main results | #16a | Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 5-14 |
| | #16b | Report category boundaries when continuous variables were categorized | 5-14 |
| | #16c | If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | n/a |
| Other analyses | #17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses | n/a |
| Key results | #18 | Summarise key results with reference to study objectives | 14-15 |
| Limitations | #19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. | 15 |
| Interpretation | #20 | Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. | 14-16 |
| Generalisability | #21 | Discuss the generalisability (external validity) of the study results | 16 |
| Funding | #22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 17 |

BMJ Open

# Time from diagnosis to treatment of colorectal cancer in a South Australian clinical registry cohort: how it varies and relates to survival



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| | |

# Time from diagnosis to treatment of colorectal cancer in a South Australian clinical registry cohort: how it varies and relates to survival

Roder D*[1], Karapetis C[2], Olver I[1], Keefe D[3, 5], Padbury R[2], Moore J[5, 6], Joshi R[5,7], Wattchow D[2, 4], Worthley DL[8], Miller C[9,10], Holden C[9], Buckley E[1], Powell K[9], Buranyi-Trevarton D[3], Fusco K[1], Price T[5, 11]

[1] Cancer Research Institute, University of South Australia, Adelaide, SA, Australia

[2] Medical Oncology, Flinders University, Bedford Park, SA, Australia

[3] South Australian Cancer Service, South Australia Department of Health, Adelaide, SA, Australia

[4] Surgery and Perioperative Medicine, Southern Adelaide Local Health Network, Bedford Park, SA, Australia

[5] Adelaide Medical School, University of Adelaide, Adelaide, SA, Australia

[6] Colorectal Surgery, Royal Adelaide Hospital, Adelaide, SA, Australia

[7] Adelaide Oncology and Haematology, Cancer Research and Clinical Trials, North Adelaide, SA, Australia

[8] Gastrointestinal Cancer Biology, South Australian Health and Medical Research Institute, Adelaide, SA, Australia

[9] Population Health, South Australian Health and Medical Research Institute, Adelaide, SA, Australia

[10] School of Public Health, The University of Adelaide, Adelaide, SA, Australia

[11] Clinical Cancer Research, Queen Elizabeth Hospital, Woodville, SA, Australia

* Corresponding author

Email: david.roder@unisa.edu.au

Phone: +61 8 8302 2640

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**Abstract**

*Objectives*

Some early studies indicated lower survival with longer time from diagnosis to cancer treatment, but others showed the reverse. Time to treatment of colorectal cancer and associations with survival were investigated.

*Setting*

Four major public hospitals in South Australia.

*Participants*

Clinical registry data for a cohort of colorectal cancer cases diagnosed in 2000-2010 and treated by surgery (n=1675), radiotherapy (n=616) and/or systemic therapy (n=1556).

*Outcome measures*

Time to treatment and survival from colorectal cancer were analysed by rank-order tests and adjusted Cox proportional hazards regression, respectively.

*Results*

Treatment (any type) commenced for 87% of surgical cases ≤60 days of diagnosis, with 80% having surgery within this period. Of those receiving radiotherapy, 59% began this treatment ≤60 days, and of those receiving systemic therapy, the corresponding proportion was 56%. Adjusted analyses showed treatment delay >60 days was more likely for rectal cancers, 2006-2010 diagnoses, residents of northern than other metropolitan regions, and for surgery, younger ages <50 years, and unexpectedly, those residing closer to metropolitan services**.** Adjusting for clinical and sociodemographic factors, and diagnostic year, better survival occurred in ≤ 2 years from diagnosis for time to treatment >30 days. Survival in the 3-10 years post-diagnosis generally did not differ by time to treatment, except for lower survival for any treatment >90 days for surgical cases.

*Conclusions*

1. Lower survival ≤2 years from diagnosis for cancers treated ≤30 days from diagnosis (i.e., a negative association of survival with shorter duration to treatment) is consistent with other study results attributed to preferencing more complicated cases for earlier care.
2. Lower 3-10-year survival for treatment of surgical cases for cancers first treated > 90 days from diagnosis is consistent with the U-shaped relationship reported in some other studies.

**Key words**

Oncology epidemiology, protocols & guidelines, quality in health care, public health, colorectal surgery

**Strengths and limitations of this study**

Strengths:

Where data were available, they were high-quality clinical registry data on diagnosis, treatment, and sociodemographic covariables.

Access to clinical service providers to assist with data interpretation.

Limitations:

Precise diagnostic and treatment data were limited to 65% of cases.

The study was observational and vulnerable to bias from practitioner choice and self-selection by patients into comparison groups. The ability to adjust for potential confounding was limited by the range of data available.

## Introduction

Australia has a high age-standardised incidence of colorectal cancer about 87% above the world average.[1] The corresponding colorectal cancer mortality rate is lower although still about 22% above the world average.[1] Colorectal cancer is second only to prostate cancer in numbers reported annually by Australian cancer registries and second only to lung cancer in numbers of cancer deaths.[2] Age-standardised incidence has been stable, with the 2012-2014 rate being within 1-2% of the rate for 1982-1984. By comparison, the age-standardized colorectal cancer mortality rate approximately halved between these periods.[2] This difference was accompanied by increases in 5-year relative survival from 52% in 1982-1986 to 70% in 2011-2015.[3, 4]

South Australian clinical registry data for colorectal cancer covering four major public hospitals showed equivalent survival and survival increases to national figures during 1980-2010, with five-year disease-specific survival increasing from 48% to 63% for all stages combined.[5] Stage distributions were largely unchanged, with survival increases mostly attributed to gains in stage-specific survival.[5] Increases were particularly pronounced for regional stage.[5] Survival increases followed increased use of adjuvant chemotherapies, particularly for regional disease.[5] For rectal cancers, a significant increase in use of adjuvant radiotherapy was reported. The increases in adjuvant therapy were consistent with clinical practice guidelines.[5] Chemotherapies evolved from common use of single-agent 5-FU (5-Fluorouracil) to 5-FU and leucovorin. FOLFOX (leucovorin calcium, 5-FU and oxaliplatin) ± bevacizumab and capecitabine (± oxaliplatin) also became more common, along with protracted infusion of 5-FU for colon cancer, and with radiotherapy for rectal cancers.[5]

While survival increases were attributed to changes in use of chemotherapy and radiotherapy, and increased surgical specialization,[5] other influences were possible. One was a change in time from diagnosis to surgical treatment.[6] In the United Kingdom, treatment delays were regarded as negatively related to survival and concerns were expressed that delays may be increasing due to increased demands for colonoscopy from population screening.[7, 8] While there is limited evidence of effects of treatment delays on survival, early evidence points to a possible negative effect.[6, 7, 8] Delays were also

viewed negatively as a likely source of psychosocial stress.[6, 8] Cancer UK has indicated that ideally treatment would commence within one month of diagnosis but has recommended commencement within two months as a realistic target.[9]

Evidence of effects of time to treatment on survival has been mixed.[10-18] Early studies generally pointed to lower survival with longer delay, but later studies varied with some showing better survival for longer delay, and some showing a U-shaped relationship with lower survival at both ends of the follow-up period.[6-8, 10-18] This has raised questions of whether the relationship varies with the clinical environment, with lower survival for short delays potentially reflected triaging of more aggressive cancers for early treatment in some settings.[12, 13, 15, 17]

In this study we explore times from diagnosis to treatment, trends in these times, variations across the patient population, and associations with survival. To establish a historic baseline, we analysed colorectal cancer data (2000-2010 diagnoses) from South Australian clinical registry data. Analyses indicated times to treatment and outcomes across the patient population at these hospitals by cancer stage, patient age, sex, socioeconomic status, service access, local health network of residence (as applying in the study period) and diagnostic epoch. We investigated whether a U-shaped relationship existed between time to treatment and survival, as reported elsewhere.[6, 17]

The study was restricted to cancers where the registry had enough diagnostic detail from biopsies and other clinical sources to record a diagnosis date in advance of treatment, thereby providing an intervening period for analysis (65% of cases). This is analogous to the common registry practice of restricting survival analyses to cancers where diagnosis dates preceded dates of death.[19]

**Methods**

Study design: A historic cohort design was used, including colorectal cancer patients diagnosed in 2000-2010 at four major public hospitals in South Australia. Ethics approval was obtained from the South Australian Human Research Ethics Committee (HREC/14/SAH/145) and University of South Australia Research Ethics Committee. Data sources and linkage: Our data source was the South Australian clinical cancer registry, which is authorised under Section 64, Part 7 of the South Australian Health Care Act (2008) to support service monitoring and quality assurance.[5] Dates and causes of death were obtained by linkage with official death records using full names, dates of birth, and sex, and for additional guidance, postcode of residence, for linkage purposes. Outcome measures: These were time in days from diagnosis to treatment start, and survival from diagnosis to death from colorectal cancer.

Dates of diagnosis and treatment were checked from available pathology and clinical reporting to optimize accuracy. Times to treatment start were calculated to treatment of 2,746 colorectal cancers.[20] Cases were excluded if presenting acutely with bowel obstruction or perforation and treated surgically on day one.

Analyses were undertaken for surgical, radiotherapy and chemotherapies respectively, and any of these treatments among surgical cases. Chemotherapies were most commonly 5-FU (Adrucil, 5-FU) given intravenously, capecitabine (Xeloda) given as a pill, oxaliplatin (Eloxatin) given intravenously, irinotecan (Camptosar) given intravenously, and raltitrexed (Tomudex) given intravenously (https://www.cancer. ca/en/cancer-information/cancer-type/colorectal/treatment/ chemotherapy/?region=on).

Cases were classified by: sub-site (colon or rectum), Australian Clinico-Pathological Staging (ACPS) as A, B, C, D or unknown (UK), and grade,[21] age at diagnosis, sex, residential area socioeconomic status,[22] geographic access to specialist radiotherapy and other specialist metropolitan services based on postcode address (coded as high, medium-high or poor), local health network of residence, as applying during the study period (i.e., northern metropolitan, central metropolitan, southern metropolitan, and for non-metropolitan areas to the south, country south, and for non-metropolitan areas to the north, country north), and diagnostic period (2000-2005 and 2006-2010) (see Tables 1-3). Operational definitions are available in previous publications.[5, 21, 22]

Time from diagnosis to treatments start was categorised in days for cross-tabulations with clinical and sociodemographic variables. Statistical analysis: The Spearman rank test was used to analyse ordinal clinical and sociodemographic predictors; Kruskal-Wallis ANOVA for multinomial predictors, and Mann-Whitney U test for predictors measured on a binary scale.[23, 24] For multiple logistic regression analyses of time as the outcome variable, time was reduced to a binary outcome of ">30 or ≤30 days" and ">60 or ≤60 days" respectively.[23, 24] The results were expressed as relative odds (i.e., odds ratios) with 95% confidence ranges. Disease-specific survival was analysed by time to treatment using Kaplan-Meier product-limit estimates (unadjusted) and Cox proportional hazards regression (adjusted for co-variables shown in Tables 2 and 3).[23, 24]

The decision to use disease-specific survival rather than relative survival was supported by evidence of similar results from these methods in South Australia at a population level.[5] Also, there were not lifetables (as required for relative survival) for patients referred to specialist clinics at these hospitals who often had extensive comorbidity and other complications.[5] Results are presented using conventional non-hierarchical analyses as they were similar by hospital setting without evidence of clustering.

*Public and Patient Involvement*

Registry development and workplans had substantial patient and consumer involvement through a formalized cancer planning and monitoring processes. Funders reviewing workplans included the Cancer Council South Australia through the Beat Cancer Project.

Specialist clinics identify topics for review, of which some are based on/prompted by the questions raised by patients.

The ethics committees approving this study (Department of Health Research Ethics Committee and University of South Australia Ethics Committee) both had active consumer involvement, thereby providing another level of public and consumer input.

This study involved the use of routinely collected registry data specifically authorized under state law and planned by clinical experts and consumers. Participants all attended specialized gynaecological oncology clinics with whom we work. We work with these clinics in developing consumer messages for distribution to their patients and other relevant stakeholder groups.

**Results**

**A. Time from diagnosis to treatment start (colorectal)**

Unadjusted analyses – Time from diagnosis to treatment start

*Surgery:* The proportion of surgical cases receiving surgery ≤60 days of diagnosis was 80% (59% ≤30 days) (Table 1). Time to first surgical treatment was associated with: (a) age at diagnosis ($p<0.001$) - shorter time for older patients; (b) sex ($p=0.003$) – shorter time for females; (c) local health network of residence ($p=0.026$) – longer time for northern metropolitan; (d) tumour sub-site ($p<0.001$) – longer time for rectum; and (e) diagnostic period ($p<0.001$) – longer time for 2006-2010. Significant associations were not found for other characteristics ($p\geq0.118$).

*Radiotherapy:* The proportion receiving radiotherapy whose treatment started ≤60 days was 59% (21% ≤30 days). Time to radiotherapy was associated with: (a) age at diagnosis ($p=0.042$) – longer time for older patients; and (b) tumour sub-site ($p<0.001$) – shorter time for rectum (note: radiotherapy was uncommon for colon cancers). Significant associations were not found for other characteristics ($p\geq0.114$).

*Chemotherapy:* The proportion receiving chemotherapy whose treatment started ≤ 60 days was 56% (15% ≤30 days). Time to chemotherapy was associated with: (a) age at diagnosis ($p<0.001$) – longer time for older patients; (b) local health network of residence ($p=0.004$) – shorter time for northern metropolitan; (c) tumour sub-site ($p=0.018$) – shorter time for rectum; (d) stage ($p=0.003$) – shorter time for stages A and D (note: chemotherapy was uncommon for stage A); and (e) diagnostic period ($p<0.001$) – longer time for 2006-2010. Significant associations were not found by other characteristics ($p\geq0.120$).

*Any treatment (surgical cases):* The proportion receiving any treatment who did so starting ≤60 days of diagnosis was 87% (62% ≤30 days). Time to any treatment was associated with: (a) age at diagnosis ($p=0.048$) – although a clear age gradient was not evident; (b) sex ($p=0.017$) – shorter time for females; (c) local health network of residence ($p<0.001$) – longer time for the northern

metropolitan area; (d) tumour sub-site ($p<0.001$) – longer time for rectum; and (e) diagnostic period ($p<0.001$) – longer time for 2006-2010. Significant associations were not found for other characteristics ($p\geq0.104$).

Table 1: Unadjusted analysis of percentages of colorectal patients by treatment type and days from diagnosis to treatment start: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery (surgery cases) | | | | | | Radiotherapy (radiotherapy cases) | | | | | | Chemotherapy (chemotherapy cases) | | | | | | Any Treatment (surgery cases) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | ≤30 | 31 - 60 | 61 - 90 | ≥90 | P value | n | ≤30 | 31 - 60 | 61- 90 | ≥90 | P value | n | ≤30 | 31 - 60 | 61 - 90 | ≥90 | P value | n | ≤30 | 31-60 | 61-90 | ≥90 | P value |
| **All cases** | 1675 | 59.0 | 21.2 | 6.0 | 13.9 | - | 616 | 20.9 | 37.8 | 17.4 | 23.9 | - | 1556 | 15.3 | 40.7 | 24.6 | 19.5 | - | 1675 | 61.7 | 25.6 | 7.1 | 5.6 | - |
| **Age at diagnosis (years):** | | | | | | | | | | | | | | | | | | | | | | | | |
| <50 | 91 | 59.3 | 11.0 | 4.4 | 25.3 | <0.001 | 79 | 24.1 | 45.6 | 7.6 | 22.8 | 0.042 | 189 | 19.6 | 47.1 | 19.0 | 14.3 | <0.001 | 91 | 65.9 | 22.0 | 3.3 | 8.8 | 0.048 |
| 50 - 59 | 210 | 52.9 | 20.0 | 5.7 | 21.4 | | 118 | 22.0 | 40.7 | 17.8 | 19.5 | | 322 | 16.5 | 44.1 | 20.5 | 18.9 | | 210 | 58.7 | 28.4 | 7.7 | 5.3 | |
| 60 - 69 | 388 | 52.3 | 22.9 | 5.9 | 18.8 | | 188 | 20.7 | 35.6 | 12.3 | 22.3 | | 498 | 16.1 | 38.0 | 26.7 | 19.3 | | 388 | 57.1 | 29.1 | 6.8 | 7.0 | |
| 70 - 79 | 570 | 61.1 | 23.0 | 5.6 | 10.4 | | 175 | 20.1 | 36.0 | 16.0 | 28.0 | | 469 | 12.6 | 39.0 | 26.7 | 21.7 | | 570 | 61.9 | 26.2 | 7.2 | 4.8 | |
| 80+ | 416 | 65.4 | 20.0 | 7.0 | 7.7 | | 56 | 17.9 | 33.9 | 21.4 | 26.8 | | 78 | 11.5 | 38.5 | 28.2 | 21.8 | | 416 | 66.1 | 21.2 | 7.7 | 5.1 | |
| **Sex:** | | | | | | | | | | | | | | | | | | | | | | | | |
| Males | 893 | 56.0 | 21.9 | 5.9 | 16.1 | 0.003 | 400 | 19.8 | 38.5 | 18.0 | 23.8 | 0.567 | 910 | 16.3 | 39.0 | 23.8 | 20.9 | 0.649 | 893 | 59.2 | 27.3 | 7.1 | 6.4 | 0.017 |
| Females | 782 | 62.4 | 20.3 | 6.0 | 11.3 | | 216 | 23.1 | 36.6 | 16.2 | 24.1 | | 646 | 13.9 | 43.0 | 25.5 | 17.5 | | 782 | 64.4 | 23.8 | 7.0 | 4.7 | |
| **Socioeconomic:** | | | | | | | | | | | | | | | | | | | | | | | | |
| Low | 544 | 56.3 | 22.8 | 5.9 | 15.1 | 0.118 | 206 | 16.0 | 43.2 | 18.9 | 21.8 | 0.826 | 507 | 13.4 | 39.4 | 26.4 | 20.7 | 0.664 | 544 | 58.8 | 28.0 | 6.6 | 6.6 | 0.104 |
| Low-Med | 388 | 60.3 | 19.8 | 6.7 | 13.1 | | 137 | 24.8 | 36.5 | 16.8 | 21.9 | | 374 | 16.6 | 44.9 | 21.9 | 16.6 | | 388 | 62.7 | 24.9 | 7.0 | 5.4 | |
| Med-High | 345 | 58.6 | 21.4 | 5.5 | 14.5 | | 128 | 24.2 | 35.2 | 18.8 | 21.9 | | 320 | 16.3 | 40.0 | 27.5 | 16.3 | | 345 | 61.9 | 24.1 | 8.1 | 5.8 | |
| High | 398 | 61.8 | 20.1 | 5.8 | 12.3 | | 145 | 21.4 | 33.8 | 14.5 | 30.3 | | 355 | 15.8 | 38.6 | 22.0 | 23.7 | | 398 | 64.4 | 24.5 | 6.8 | 4.3 | |
| **Accessibility:** | | | | | | | | | | | | | | | | | | | | | | | | |
| High | 1353 | 58.9 | 20.4 | 6.4 | 14.3 | 0.584 | 475 | 22.1 | 36.4 | 16.8 | 24.6 | 0.764 | 1223 | 16.4 | 40.3 | 24.0 | 19.3 | 0.12 | 1353 | 61.8 | 25.1 | 7.3 | 5.9 | 0.992 |
| Med-High | 228 | 61.0 | 23.2 | 3.9 | 11.8 | | 94 | 17.0 | 44.7 | 21.3 | 17.0 | | 228 | 10.1 | 41.2 | 28.1 | 20.6 | | 228 | 62.1 | 27.3 | 6.6 | 4.0 | |
| Poor | 94 | 55.3 | 27.7 | 4.3 | 12.8 | | 47 | 17.0 | 38.3 | 14.9 | 29.8 | | 105 | 13.3 | 43.8 | 23.8 | 19.0 | | 94 | 58.5 | 29.8 | 5.3 | 6.4 | |
| **Local Health Network:** | | | | | | | | | | | | | | | | | | | | | | | | |
| Northern metro | 242 | 45.9 | 24.4 | 12.0 | 17.8 | 0.026 | 106 | 18.9 | 34.9 | 19.8 | 26.4 | 0.12 | 248 | 16.1 | 41.5 | 24.2 | 7.3 | 0.004 | 242 | 49.6 | 30.4 | 12.1 | 7.9 | <0.001 |
| Central metro | 618 | 61.7 | 20.2 | 6.8 | 11.3 | | 202 | 21.8 | 32.7 | 17.8 | 27.7 | | 495 | 17.8 | 36.6 | 26.5 | 19.2 | | 618 | 64.1 | 24.0 | 7.3 | 4.7 | |
| Southern metro | 417 | 64.3 | 17.7 | 3.4 | 14.6 | | 134 | 25.4 | 40.3 | 14.2 | 20.1 | | 426 | 16.7 | 42.7 | 20.7 | 20.0 | | 417 | 66.8 | 23.0 | 4.8 | 5.3 | |
| Country South | 155 | 52.9 | 27.7 | 1.9 | 17.4 | | 74 | 25.7 | 40.5 | 14.9 | 18.9 | | 159 | 8.8 | 41.5 | 28.3 | 21.4 | | 155 | 56.5 | 31.2 | 3.9 | 8.4 | |
| Country North | 241 | 60.2 | 22.0 | 5.0 | 12.9 | | 100 | 11.2 | 46.9 | 19.4 | 22.4 | | 228 | 11.0 | 44.5 | 25.1 | 19.4 | | 241 | 61.9 | 26.2 | 7.4 | 4.5 | |
| **Sub-site:** | | | | | | | | | | | | | | | | | | | | | | | | |
| Colon | 1098 | 65.0 | 22.1 | 4.9 | 7.9 | <0.001 | 86 | 11.6 | 12.8 | 14.0 | 61.6 | <0.001 | 898 | 13.1 | 40.2 | 27.4 | 19.3 | 0.018 | 1098 | 66.2 | 23.4 | 6.0 | 4.5 | <0.001 |
| Rectum | 577 | 47.5 | 19.4 | 8.0 | 25.1 | | 530 | 22.5 | 41.9 | 17.9 | 17.7 | | 658 | 18.2 | 41.3 | 20.7 | 19.8 | | 577 | 53.1 | 29.9 | 9.2 | 7.8 | |
| **ACPS stage:** | | | | | | | | | | | | | | | | | | | | | | | | |
| A | 280 | 53.9 | 30.4 | 7.9 | 7.9 | 0.460 | 50 | 24.0 | 44.0 | 14.0 | 18.0 | 0.114 | 47 | 25.5 | 36.2 | 21.3 | 17.0 | 0.003 | 280 | 55.4 | 32.5 | 7.9 | 4.3 | 0.114 |
| B | 654 | 61.5 | 23.9 | 4.7 | 9.9 | (A-D) | 147 | 21.1 | 38.8 | 21.8 | 18.4 | | 249 | 13.3 | 40.2 | 27.7 | 18.9 | | 654 | 63.3 | 26.7 | 5.7 | 4.3 | |
| C | 412 | 55.6 | 17.2 | 6.8 | 20.4 | | 231 | 16.0 | 40.7 | 21.2 | 22.1 | | 696 | 6.6 | 47.3 | 27.6 | 18.5 | | 412 | 58.9 | 25.6 | 8.8 | 6.8 | |
| D | 279 | 63.8 | 12.5 | 5.0 | 18.6 | | 162 | 25.9 | 29.0 | 10.5 | 34.6 | | 516 | 26.6 | 33.1 | 19.6 | 20.7 | | 279 | 68.6 | 17.3 | 6.5 | 7.6 | |
| (UK) | (50) | (51.5) | (18.2) | (12.1) | (18.2) | | (26) | (27.3) | (59.1) | (4.5) | (9.1) | | (48) | (26.9) | (34.6) | (15.4) | (23.1) | | (50) | (59.2) | (20.4) | (10.2) | (10.2) | |
| **Diagnosis years:** | | | | | | | | | | | | | | | | | | | | | | | | |
| 2000 - 2005 | 869 | 65.0 | 17.5 | 5.4 | 12.1 | <0.001 | 335 | 23.9 | 34.0 | 15.8 | 26.3 | 0.898 | 782 | 17.4 | 44.2 | 21.2 | 17.1 | <0.001 | 869 | 68.0 | 21.4 | 6.2 | 4.4 | <0.001 |
| 2006 - 2010 | 806 | 52.5 | 25.2 | 6.6 | 17.8 | | 281 | 17.4 | 42.3 | 19.2 | 21.0 | | 774 | 13.2 | 37.1 | 27.9 | 21.8 | | 806 | 54.8 | 30.3 | 8.0 | 7.0 | |

*Excludes cases where insufficient data on date of diagnosis (see "Methods")

ACPS- Australian Clinico-Pathological Staging; UK – unknown

Adjusted analyses – Predictors of treatment start >30 days from diagnosis.

*Surgery:* Significant predictors of time of surgical cases to surgical treatment >30 days included: (a) local health network of residence – relative odds (RO) of 0.55 (0.39, 0.76) for metropolitan central and 0.44 (0.31, 0.63) for metropolitan southern compared with metropolitan northern; (b) tumour site – RO for rectum of 2.07 (1.66, 2.57); (c) tumour stage – RO of 0.65 (0.45, 0.93) for stage D (distant metastasis) compared with stage A; (d) grade – RO for high grade (poorly differentiated) at 0.47 (0.25, 0.87) compared with low grade; and (e) diagnostic period – RO of 1.82 (1.48, 2.24) for 2006-2010 (Table 2).

*Radiotherapy:* Only tumour site was predictive of time of radiotherapy cases to radiotherapy start >30 days – RO of 0.40 (0.19, 0.83) for rectum (note: radiotherapy was much less common for colon than rectal cancers[5]).

*Chemotherapy:* Significant predictors of time of chemotherapy cases to chemotherapy treatment start >30 days included: (a) tumour site – RO for rectum of 0.65 (0.48, 0.89); (b) tumour stage – RO for stage C of 3.93 (1.85, 8.36); and (c) diagnostic period – RO of 0.65 (0.48, 0.89) for 2006-2010.

*Any treatment (surgical cases):* Significant predictors of time to start of any treatment >30 days included: (a) local health network of residence – RO of 0.56 (0.40, 0.78) for metropolitan central and 0.44 (0.30, 0.63) for metropolitan southern compared with metropolitan northern; (b) tumour site – RO of 1.76 (1.41, 2.19) for rectum; (c) tumour stage – RO of 0.56 (0.38, 0.80) for stage D compared with stage A; (d) grade – RO of 0.52 (0.28, 0.95) for high compared with low grade; and (e) diagnostic period – RO of 1.86 (1.51, 2.29) for 2006-2010.

*Supplementary analyses with tumour stage classified as stage D vs A-C:* RO among surgical cases for surgery start >30 days was lower for stage D for surgery at 0.69 (0.51, 0.92); with corresponding RO for radiotherapy start at 0.56 (0.35, 0.88), chemotherapy start at 0.30 (0.22, 0.41), and any treatment (surgical cases) at 0.64 (0.47, 0.86). The RO for chemotherapy treatment start >30 days for stage D vs A-C was 0.45 (0.30, 0.67) for 2000-2005 compared with 0.16 (0.10, 0.27) for 2006-2010.

Table 2: Adjusted analysis of relative odds (95% CLs) of treatment for colorectal cancer starting >30 days of diagnosis by treatment type, stage, and socioeconomic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery (surgery cases) | | Radiotherapy (radiotherapy cases) | | Chemotherapy (chemotherapy cases) | | Any treatment (surgery cases) | |
|---|---|---|---|---|---|---|---|---|
| | **N** | **RO (95% CLs)** | **n** | **RO (95% CLs)** | **n** | **RO (95% CLs)** | **n** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 91 | 1.00 | 79 | 1.00 | 189 | 1.00 | 91 | 1.00 |
| 50 – 59 | 210 | 1.15 (0.68, 1.95) | 118 | 1.06 (0.52, 2.15) | 322 | 1.18 (0.71, 1.94) | 210 | 1.20 (0.70, 2.05) |
| 60 – 69 | 388 | 1.16 (0.71, 1.90) | 188 | 1.16 (0.60, 2.25) | 498 | 1.25 (0.79, 2.00) | 388 | 1.26 (0.76, 2.08) |
| 70 - 79 | 570 | 0.95 (0.59, 1.53) | 175 | 1.13 (0.58, 2.22) | 469 | 1.51 (0.93, 2.45) | 570 | 1.20 (0.73, 1.95) |
| 80+ | 416 | 0.82 (0.50, 1.34) | 56 | 1.09 (0.44, 2.73) | 78 | 2.20 (0.95, 5.10) | 416 | 1.04 (0.63, 1.72) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 893 | 1.00 | 400 | 1.00 | 910 | 1.00 | 893 | 1.00 |
| Female | 782 | 0.85 (0.69, 1.05) | 216 | 0.72 (0.47, 1.11) | 646 | 1.08 (0.80, 1.47) | 782 | 0.88 (0.72, 1.09) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 544 | 1.00 | 206 | 1.00 | 507 | 1.00 | 544 | 1.00 |
| Low-med | 388 | 1.17 (0.87, 1.59) | 137 | 0.73 (0.40, 1.33) | 374 | 0.92 (0.61, 1.39) | 388 | 1.14 (0.84, 1.54) |
| Med-high | 345 | 1.06 (0.78, 1.42) | 128 | 0.55 (0.30, 1.01) | 320 | 0.89 (0.58, 1.38) | 345 | 0.98 (0.73, 1.32) |
| High | 398 | 1.05 (0.77, 1.42) | 145 | 0.78 (0.42, 1.46) | 355 | 0.94 (0.61, 1.45) | 398 | 1.05 (0.77, 1.42) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 1353 | 1.00 | 475 | 1.00 | 1223 | 1.00 | 1353 | 1.00 |
| Med-high | 228 | 0.62 (0.36, 1.08) | 94 | 1.28 (0.45, 3.65) | 228 | 0.78 (0.30, 2.00) | 228 | 0.75 (0.43, 1.31) |
| Poor | 94 | 0.83 (0.45, 1.52) | 47 | 1.14 (0.36, 3.58) | 105 | 0.60 (0.23, 1.57) | 94 | 0.89 (0.49, 1.63) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 242 | 1.00 | 106 | 1.00 | 248 | 1.00 | 242 | 1.00 |
| Central metro | 618 | 0.55 (0.39, 0.76) | 202 | 0.90 (0.47, 1.72) | 495 | 0.99 (0.62, 1.57) | 618 | 0.56 (0.40, 0.78) |
| Southern metro | 417 | 0.44 (0.31, 0.63) | 134 | 0.68 (0.35, 1.33) | 426 | 0.84 (0.52, 1.35) | 417 | 0.44 (0.30, 0.63) |
| Country South | 155 | 0.86 (0.51, 1.43) | 74 | 0.52 (0.20, 1.38) | 159 | 2.40 (0.90, 6.39) | 155 | 0.78 (0.47, 1.30) |
| Country North | 241 | 0.78 (0.43, 1.43) | 100 | 1.60 (0.49, 5.18) | 228 | 2.03 (0.76, 5.39) | 241 | 0.73 (0.40, 1.34) |
| **Tumour site:** | | | | | | | | |
| Colon (ref.) | 1098 | 1.00 | 86 | 1.00 | 898 | 1.00 | 1098 | 1.00 |
| Rectum (incl. Rectosig.) | 577 | 2.07 (1.66, 2.57) | 530 | 0.40 (0.19, 0.83) | 658 | 0.65 (0.48, 0.89) | 577 | 1.76 (1.41, 2.19) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 280 | 1.00 | 50 | 1.00 | 47 | 1.00 | 280 | 1.00 |
| B | 654 | 0.87 (0.64, 1.17) | 147 | 1.03 (0.46, 2.28) | 249 | 1.78 (0.81, 3.90) | 654 | 0.80 (0.59, 1.08) |
| C | 412 | 0.99 (0.72, 1.37) | 231 | 1.56 (0.72, 3.38) | 696 | 3.93 (1.85, 8.36) | 412 | 0.89 (0.65, 1.23) |
| D | 279 | 0.65 (0.45, 0.93) | 162 | 0.71 (0.33, 1.55) | 516 | 0.83 (0.40, 1.71) | 279 | 0.56 (0.38, 0.80) |
| (UK) | (50) | (0.67, (0.31, 1.48)) | (26) | (0.93 (0.28, 3.06)) | (48) | (0.84 (0.27, 2.62)) | (50) | (0.65 (0.33, 1.25)) |
| **Grade:** | | | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Well diff. (ref.) | 58 | 1.00 | 25 | 1.00 | 37 | 1.00 | 58 | 1.00 |
| Mod diff. | 1212 | 0.68 (0.39, 1.20) | 429 | 1.34 (0.50, 3.58) | 1054 | 1.18 (0.43, 3.22) | 1212 | 0.72 (0.42, 1.25) |
| Poorly undiff. | 285 | 0.47 (0.25, 0.87) | 99 | 0.87 (0.62, 5.67) | 309 | 1.28 (0.45, 3.68) | 285 | 0.52 (0.28, 0.95) |
| (UK) | (120) | (1.48 (0.75, 2.95)) | (63) | (1.02 (0.33, 3.12)) | (156) | (0.41, (0.14, 1.17)) | (120) | (1.44 (0.74, 2.81)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 869 | 1.00 | 335 | 1.00 | 782 | 1.00 | 869 | 1.00 |
| 2006 - 2010 | 806 | 1.82 (1.48, 2.24) | 281 | 1.48 (0.97, 2.26) | 774 | 0.65 (0.48, 0.89) | 806 | 1.86 (1.51, 2.29) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff. – differentiated; undiff. - undifferentiated.

Adjusted analyses – Predictors of treatment start exceeding >60 days

*Surgery:* Predictors of time to surgery >60 days for surgical cases included: (a) age at diagnosis – RO of 0.50 (0.29, 0.85) for 70-79 and 0.48 (0.27, 0.85) for 80+ compared with <50years ; (b) service accessibility – RO of 0.37 (0.18, 0.74) for medium-high and 0.40 (0.18, 0.89) for poor compared with high metropolitan service accessibility; (c) local health network of residence – RO of 0.58 (0.39, 0.86) for metropolitan central and 0.51 (0.33, 0.78) for metropolitan south compared with metropolitan north; (d) tumour site – RO for rectum of 3.39 (2.59, 4.42); (e) tumour stage – RO of 2.32 (1.54, 3.50) for stage C and 1.76 (1.11, 2.78) for stage D compared with stage A; (f) grade – RO of 0.51 (0.27, 0.98) for intermediate and 0.38 (0.18, 0.79) for high compared with low grade; and (g) diagnostic period – RO of 1.56 (1.20, 2.03) for 2006-2010 (Table 3).

*Radiotherapy:* Predictors of time to radiotherapy start >60 days for cases treated by radiotherapy included (a) older age at diagnosis – compared with age<50 years, RO of 2.22 (1.20, 4.09) for 60-69 years, 2.00 (1.08, 3.71) for 70-79 years, and 2.30 (1.04, 5.08) for 80+ years; and (b) tumour site – RO lower at 0.18 (0.11, 0.32) for rectum (note: radiotherapy was uncommon for colon cases).

*Chemotherapy:* Predictors of time to chemotherapy treatment start >60 days for cases treated by chemotherapy included: (a) older age at diagnosis – compared with under 50 years, RO of 1.72 (1.20, 2.47) for 60-69 years, 1.83 (1.27, 2.64) for 70-79 years and 2.08 (1.19, 3.63) for 80+ years; and (b) tumour sub-site – RO for rectum of 0.78 (0.63, 0.97); and (c) diagnostic period – RO higher at 1.65 (1.33, 2.03) for 2006-2010.

*Any treatment (surgical cases):* Predictors of time to start of any treatment >60 days included: (a) local health network of residence – RO at 0.56 (0.36, 0.86) for metropolitan central and 0.42 (0.26, 0.69) for metropolitan south compared with metropolitan north; (b) tumour site – RO for rectum at 1.82 (1.34, 2.46); (c) grade – RO of 0.43 (0.20, 0.93) for high compared with low grade; and (d) diagnostic period – RO of 1.59 (1.18, 2.15) for 2006-2010.

*Supplementary analyses with tumour stage classified as stage D vs A-C:* The RO for surgery start >60 days did not vary, with RO for stage D of 1.18 (0.84, 1.66) for surgery (surgery cases), 0.92 (0.61, 1.38) for radiotherapy (radiotherapy cases), 0.83 (0.66, 1.31) for chemotherapy (chemotherapy cases), and 1.10 (0.74, 1.64) for any treatment (surgical cases).

Table 3: Adjusted analysis of relative odds (95% CLs) of treatment for colorectal cancer starting >60 days of diagnosis by treatment type, stage, and socio-demographic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery (surgery cases) | | Radiotherapy (radiotherapy cases) | | Chemotherapy (chemotherapy cases) | | Any treatment (surgery cases) | |
|---|---|---|---|---|---|---|---|---|
| | n | RO (95% CLs) | n | RO (95% CLs) | n | RO (95% CLs) | n | RO (95% CLs) |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 91 | 1.00 | 79 | 1.00 | 189 | 1.00 | 91 | 1.00 |
| 50 – 59 | 210 | 0.79 (0.94, 1.42) | 118 | 1.54 (0.80, 2.99) | 322 | 1.31 (0.89, 1.94) | 210 | 1.00 (0.54, 2.27) |
| 60 – 69 | 388 | 0.73 (0.42, 1.27) | 188 | 2.22 (1.20, 4.09) | 498 | 1.72 (1.20, 2.47) | 388 | 1.11 (0.54, 2.27) |
| 70 – 79 | 570 | 0.50 (0.29, 0.85) | 175 | 2.00 (1.08, 3.71) | 469 | 1.83 (1.27, 2.64) | 570 | 1.10 (0.55, 2.22) |
| 80+ | 416 | 0.48 (0.27, 0.85) | 56 | 2.30 (1.04, 5.08) | 78 | 2.08 (1.18, 3.63) | 416 | 1.25 (0.61, 2.56) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 893 | 1.00 | 400 | 1.00 | 910 | 1.00 | 893 | 1.00 |
| Female | 782 | 0.79 (0.61, 1.04) | 216 | 0.93 (0.64, 1.35) | 646 | 0.93 (0.75, 1.15) | 782 | 0.89 (0.66, 1.20) |
| **Socioeconomi** | | | | | | | | |
| Low (ref.) | 544 | 1.00 | 206 | 1.00 | 507 | 1.00 | 544 | 1.00 |
| Low-med | 388 | 1.37 (0.94, 2.01) | 137 | 1.01 (0.61, 1.68) | 374 | 0.74 (0.55, 1.00) | 388 | 1.30 (0.84, 2.01) |
| Med-high | 345 | 1.06 (0.73, 1.55) | 128 | 0.95 (0.57, 1.57) | 320 | 0.90 (0.67, 1.22) | 345 | 1.17 (0.77, 1.78) |
| High | 398 | 1.05 (0.71, 1.55) | 145 | 1.21 (0.72, 2.01) | 355 | 0.94 (0.69, 1.27) | 398 | 1.07 (0.68, 1.68) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 1353 | 1.00 | 475 | 1.00 | 1223 | 1.00 | 1353 | 1.00 |
| Med-High | 228 | 0.37 (0.18, 0.74) | 94 | 1.36 (0.54, 3.39) | 228 | 1.23 (0.71, 2.12) | 228 | 0.47 (0.21, 1.06) |
| Poor | 94 | 0.40 (0.18, 0.89) | 47 | 1.50 (0.57, 3.95) | 105 | 0.92 (0.50, 1.69) | 94 | 0.55 (0.23, 1.35) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 242 | 1.00 | 106 | 1.00 | 248 | 1.00 | 242 | 1.00 |
| Central metro | 618 | 0.58 (0.39, 0.86) | 202 | 0.84 (0.49, 1.44) | 495 | 1.24 (0.89, 1.74) | 618 | 0.56 (0.36, 0.86) |
| Southern | 417 | 0.51 (0.33, 0.78) | 134 | 0.56 (0.31, 1.00) | 426 | 0.95 (0.67, 1.34) | 417 | 0.42 (0.26, 0.69) |
| Country South | 155 | 0.80 (0.44, 1.48) | 74 | 0.43 (0.18, 1.02) | 159 | 1.16 (0.66, 2.04) | 155 | 0.80 (0.40, 1.59) |
| Country North | 241 | 1.24 (0.59, 2.59) | 100 | 0.56 (0.21, 1.50) | 228 | 1.02 (0.56, 1.86) | 241 | 0.97 (0.42, 2.25) |
| **Tumour site:** | | | | | | | | |
| Colon (ref.) | 1098 | 1.00 | 86 | 1.00 | 898 | 1.00 | 1098 | 1.00 |
| Rectum (incl. Rectosig.) | 577 | 3.39 (2.59, 4.42) | 530 | 0.18 (0.11, 0.32) | 658 | 0.78 (0.63, 0.97) | 577 | 1.82 (1.34, 2.46) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 280 | 1.00 | 50 | 1.00 | 47 | 1.00 | 280 | 1.00 |
| B | 654 | 1.21 (0.80, 1.82) | 147 | 1.28 (0.62, 2.64) | 249 | 1.24 (0.64, 2.40) | 654 | 0.88 (0.56, 1.39) |
| C | 412 | 2.32 (1.54, 3.50) | 231 | 1.73 (0.87, 3.43) | 696 | 1.21 (0.65, 2.26) | 412 | 1.39 (0.88, 2.19) |
| D | 279 | 1.76 (1.11, 2.78) | 162 | 1.37 (0.67, 2.82) | 516 | 1.01 (0.53, 1.90) | 279 | 1.19 (0.71, 1.99) |
| (UK) | (50) | (1.43 (0.59, 3.51)) | (26) | (0.38 (0.10, 1.54)) | (48) | (0.97 (0.35, 2.68)) | (50) | (1.46 (0.63, 3.37)) |
| **Grade:** | | | | | | | | |
| Well diff. | 58 | 1.00 | 25 | 1.00 | 37 | 1.00 | 58 | 1.00 |
| Mod diff. | 1212 | 0.51 (0.27, 0.98) | 429 | 0.98 (0.40, 2.42) | 1054 | 1.08 (0.54, 2.19) | 1212 | 0.52 (0.23, 1.03) |
| Poorly/undiff. | 285 | 0.38 (0.18, 0.79) | 99 | 1.18 (0.44, 3.14) | 309 | 1.10 (0.53, 2.29) | 285 | 0.43 (0.20, 0.93) |
| (UK) | (120) | (1.09 (0.51, 2.37) | (63) | (0.66 (0.23, 1.87)) | (156) | (0.58 (0.27, 1.27)) | (120) | (0.99 (0.44, 2.25)) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Diagnostic year:** | | | | | | | | |
| 2000 - 2005 | 869 | 1.00 | 335 | 1.00 | 782 | 1.00 | 869 | 1.00 |
| 2006 - 2010 | 806 | 1.56 (1.20, 2.03) | 281 | 0.91 (0.64, 1.30) | 774 | 1.65 (1.33, 2.03) | 806 | 1.59 (1.18, 2.15) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

**B. Time from diagnosis to treatment start by sub-site (colon and rectum)**

Colon

- Predictors of time to treatment start >30 days in adjusted analysis included: (a) *For surgery (surgery cases):* age 60-69 years compared with <50 years; northern metropolitan compared with central metropolitan and southern metropolitan; stage A compared with stages B and D; and diagnosis in 2006-2010; (b) *For radiotherapy (radiotherapy cases):* no significant predictors (small numbers); (c) *For chemotherapy (chemotherapy cases)*: diagnosis in 2006-2010; (d) *For any treatment (in surgical cases)*: northern metropolitan compared with central metropolitan and southern metropolitan areas; stage A compared with stages B and D; and diagnosis in 2006-2010 (Supplementary Tables s1 & s2).
- Predictors of time to treatment start of >60 days in adjusted analysis included: (a) *For surgery:* northern metropolitan compared with central and southern metropolitan areas; and more advanced stages C and D compared with stage A; (b) *For radiotherapy:* no significant predictors (small numbers); (c) *For chemotherapy*: diagnosis in 2006-2010; and (d) *For any treatment (surgical cases)*: northern metropolitan compared with central and southern metropolitan areas (Supplementary Tables s1 & s2).

Rectum

- Predictors of time to treatment start of >30 days in adjusted analysis included: (a) *For surgery (surgery cases):* age 70+ compared with <50 years; northern metropolitan compared with central and southern metropolitan areas; and diagnosis in 2006-2010; (b) *For radiotherapy (radiotherapy cases):* low compared with medium-high socioeconomic status; and diagnosis in 2006-2010; (c) *For chemotherapy (chemotherapy cases)*: stage C; and (d) *For any treatment (surgical cases)*: northern metropolitan compared with southern metropolitan; and diagnosis in 2006-2010 (Supplementary Tables s3 & s4).
- Predictors of time to treatment start of >60 days in adjusted analysis included: (a) *For surgery:* younger age <50 compared with 70+ years; high service accessibility; northern metropolitan compared with central and southern metropolitan areas; and stage C compared with stage A; better differentiation; and 2006-2010; (b) *For radiotherapy:* aged over 50 years; (c) *For chemotherapy*: aged over 50 years; central metropolitan compared with northern metropolitan area; and stage C; and (d) *For any treatment (surgical cases)***:** low compared with higher grade lesions **;** and diagnosis in 2006-2010 (Supplementary Tables s3 & s4).

**C. Survival by time from diagnosis to treatment start**

*Unadjusted analysis*

*Surgical treatment:* Compared with time to initial surgery >30 days, survival was lowest in the first two years from diagnosis when time to initial surgery was ≤30 days, but changed with further follow-up, such that by 10 years from

diagnosis, survival was lower when time to initial surgery was >90 days compared with ≤ 30 days (p=0.017) (Table 4).

*Radiotherapy:* Survival was lowest in the first year when time to radiotherapy start was ≤30 days and reached statistical significance compared with a time of 61-90 days (p=0.009), but not with 31-60 days (p=0.295) or >90 days (p=0.280). After the first year of follow-up, survival was lowest for >90 days.

*Chemotherapy:* The survival pattern varied, with time to treatment ≤30 days having the lowest survival at each follow-up time.

*Any treatment (surgical cases):* Compared with time to initial treatment >30 days, survival was lowest in the first two years from diagnosis when time to initial surgery was ≤30 days, but changed with further follow-up, such that by 10 years from diagnosis, survival was lower when time to initial surgery was >90 days compared with ≤ 30 days (p=0.021).

Table 4: Unadjusted analysis of percentage survival (± standard error) from colorectal cancer by time from diagnosis (days) to commitment of specified treatment: South Australian major public hospitals, diagnoses 2000-2010*

| | | | **Follow-up time from diagnosis (years)** | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Specified treatment** | **Time (days)** | **Numbers of cases** | **1** | **2** | **3** | **4** | **5** | **10** |
| Surgical treatment (surgery cases) | ≤30 | 988 | 85.4 ± 1.2 | 78.2 ± 1.5 | 72.9 ± 1.5 | 69.8 ± 1.6 | 67.5 ± 1.7 | 63.3 ± 2.0 |
| | 31 – 60 | 355 | 93.1 ± 1.6 | 89.9 ± 1.9 | 84.7 ± 2.2 | 81.9 ± 2.4 | 79.7 ± 2.5 | 75.9 ± 2.9 |
| | 61 – 90 | 100 | 92.9 ± 3.7 | 84.1 ± 4.6 | 77.5 ± 5.3 | 74.6 ± 5.5 | 72.6 ± 5.8 | 57.7 ± 9.0 |
| | >90 | 232 | 92.6 ± 2.2 | 82.4 ± 2.9 | 73.9 ± 3.2 | 67.4 ± 3.5 | 67.8 ± 3.7 | 50.4 ± 5.0 |
| Radiotherapy (radiotherapy cases) | ≤30 | 129 | 82.0 ± 4.0 | 70.0 ± 4.5 | 62.4 ± 4.7 | 58.0 ± 4.7 | 53.1 ± 4.8 | 44.4 ± 5.5 |
| | 31-60 | 233 | 87.0 ± 2.6 | 77.8 ± 3.0 | 68.2 ± 3.4 | 64.4 ± 3.5 | 61.3 ± 3.6 | 55.2 ± 4.4 |
| | 61 – 90 | 107 | 95.3 ± 3.2 | 87.5 ± 4.1 | 79.4 ± 4.7 | 73.8 ± 5.1 | 64.8 ± 5.5 | 49.0 ± 6.9 |
| | >90 | 147 | 87.6 ± 3.3 | 62.6 ± 4.3 | 53.1 ± 4.4 | 42.8 ± 4.3 | 39.2 ± 4.3 | 27.3 ± 4.3 |
| Chemotherapy (chemotherapy cases) | ≤30 | 238 | 68.0 ± 3.3 | 52.8 ± 3.4 | 43.4 ± 3.3 | 40.7 ± 3.3 | 38.4 ± 3.3 | 33.1 ± 3.4 |
| | 31 – 60 | 633 | 87.2 ± 3.4 | 73.8 ± 1.8 | 67.9 ± 2.0 | 62.8 ± 2.0 | 59.4 ± 2.1 | 49.5 ± 2.5 |
| | 61 – 90 | 382 | 92.3 ± 1.6 | 78.8 ± 2.3 | 68.9 ± 2.6 | 64.5 ± 2.7 | 59.8 ± 2.8 | 56.1 ± 3.0 |
| | >90 | 303 | 94.4 ± 1.7 | 78.1 ± 2.6 | 68.6 ± 2.9 | 63.2 ± 3.0 | 56.8 ± 3.1 | 45.1 ± 3.9 |
| Any treatment (surgery cases) | ≤30 | 1030 | 85.5 ±1.1 | 78.1 ± 1.3 | 72.6 ± 1.4 | 69.4 ± 1.5 | 67.2 ± 1.6 | 63.1 ± 1.8 |
| | 31 – 60 | 428 | 93.4 ± 1.2 | 88.8 ± 1.5 | 83.8 ± 1.8 | 80.5 ± 2.0 | 78.0 ± 2.2 | 71.5 ± 2.9 |
| | 61 – 90 | 118 | 94.0 ± 2.2 | 85.9 ± 3.3 | 79.6 ± 3.9 | 74.8 ± 4.4 | 71.7 ± 4.7 | 56.6 ± 7.8 |
| | >90 | 99 | 91.7 ± 2.8 | 82.2 ± 3.9 | 71.9 ± 4.7 | 63.9 ± 5.2 | 57.1 ± 5.6 | 43.8 ± 8.2 |

* Kaplan-Meier product-limit estimate; date of censoring of live cases: Dec 31, 2012

*Adjusted analysis*

Because visual examination and interaction terms indicated a lack of proportionality of survival with time to treatment, results are split in Table 5 for follow-up of ≤2 and 3-10 years as mutually exclusive periods. Irrespective of treatment type, lower hazard ratios applied for periods ≤ 2 years with times to treatment of >30 days, after adjusting for age, sex, socioeconomic status, service accessibility, local health network of residence, tumour sub-site, stage, grade and diagnostic period. Hazard ratios similarly adjusted generally did not decrease across the 3-10 follow-up, suggesting no significant differences in conditional survival after two years for cases treated ≤30 days of diagnosis and >30 days. While there were higher hazard ratios for times of 61-90 and >90 days for 3-10-year follow-up from surgical treatment and radiotherapy respectively, statistical significance was only achieved for any treatment (surgical cases) when comparing time to treatment >90 compared with ≤30 days (p=0.022).

Table 5: Adjusted analysis of hazard ratios (95% confidence limits) of deaths from colorectal cancer by time from diagnosis (days) to commencement of specified treatment: South Australians major public hospitals, diagnoses 2000-2010*

| | | **Follow-up time from diagnoses** | | | |
|---|---|---|---|---|---|
| | | **≤ 2 years** | | **3-10 years** | |
| **Treatment** | **Time** | **Number of cases** | **Hazard ratios** | **Number of cases** | **Hazard ratios** |
| Surgical treatment (surgical cases) | ≤30 | 988 | 1.00 | 714 | 1.00 |
| | 31 – 60 | 355 | 0.57 (0.40, 0.82) | 302 | 0.92 (0.62, 1.36) |
| | 61 – 90 | 100 | 0.59 (0.35, 1.02) | 76 | 1.13 (0.60, 2.10) |
| | >90 | 232 | 0.59 (0.41, 0.84) | 186 | 1.24 (0.85, 1.83) |
| Radiotherapy (radiotherapy cases) | ≤30 | 129 | 1.00 | 87 | 1.00 |
| | 31 – 60 | 233 | 0.85 (0.54, 1.32) | 173 | 1.00 (0.59, 1.72) |
| | 61 - 90 | 107 | 0.44 (0.23, 0.84) | 89 | 1.26 (0.70, 2.27) |
| | >90 | 147 | 0.62 (0.40, 0.98) | 89 | 1.60 (0.90, 2.85) |
| Chemotherapy (chemotherapy cases) | ≤30 | 238 | 1.00 | 120 | 1.00 |
| | 31 – 60 | 633 | 0.71 (0.55, 0.92) | 459 | 0.98 (0.66, 1.47) |
| | 61 – 90 | 382 | 0.51 (0.38, 0.70) | 289 | 1.01 (0.65, 1.55) |
| | >90 | 303 | 0.40 (0.30, 0.55) | 233 | 1.04 (0.68, 1.59) |
| Any treatment (surgery cases) | ≤30 | 1030 | 1.00 | 744 | 1.00 |
| | 31 – 60 | 428 | 0.59 (0.43, 0.81) | 361 | 0.94 (0.66, 1.33) |
| | 61 – 90 | 118 | 0.48 (0.43, 0.81) | 95 | 1.11 (0.66, 1.89) |
| | >90 | 99 | 0.62 (0.37, 1.02) | 78 | 1.83 (1.12, 2.98) |

*4 Cox proportional hazards regression analyses (1 per treatment category), adjusting for age, sex, socioeconomic status, service accessibility, local health network, sub-site, stage, grade and diagnostic period (see tables 2 and 3); date of censoring of live cases: Dec 31, 2012.

## Discussion

The proportion of surgical patients receiving any treatment for their cancer ≤60 days of diagnosis was 87%, with 80% receiving surgical treatment within 60 days of diagnosis. This broadly accords with targets set by Cancer UK.[9] The proportion receiving radiotherapy who started this therapy ≤60 days of diagnosis was 59%, whereas the corresponding percentage having chemotherapies who started this therapy ≤60 days of diagnosis was 56%. The longer delay for radiotherapy and chemotherapy is consistent with their common use as adjuvant therapies following surgery.[5]

Longer time to surgery applied for cancers of the rectum than colon potentially reflecting the increased use of magnetic resonance imaging for rectal cancers, [25] and multimodal therapies,[5] which may have led to surgery delays through more multidisciplinary consultation and in some instances, neoadjuvant care.[26]

The longer time to surgery in 2006-2010 may also have been influenced by increasing use of multimodal therapies and more advanced diagnostics (e.g., magnetic resonance imaging), increasing the need for multidisciplinary consultation.[5, 26] While the introduction of population-based screening may have contributed, the screening program was still at an early phase of development, being phased in from 2006 to 2020. Following more complete implementation of bowel screening, there may be increased pressure on services which may increase times to surgery.[7, 8] The higher proportion with a time to surgery >60 days for stages C and D compared with stage A may reflect time taken for symptom control, multidisciplinary team consultation, and provision of neoadjuvant therapies.[27, 28] The proportion with a time to surgery >60 days was lower for higher grade tumours, potentially due to a greater perceived urgency of surgical intervention for more aggressive tumours.

The proportion receiving surgery, who did so >60 days from diagnosis, tended to be lower among those aged 70+ years, central and southern compared with northern metropolitan residential areas, those diagnosed in 2000-2005 compared with 2006-2010, and unexpectedly, those residing closer to metropolitan services. The reasons are unclear but may reflect differences in service busyness and patterns of patient and service demand.

Of those receiving radiotherapy, the proportion starting this therapy >60 days from diagnosis tended to be higher for ages ≥60 years than the <50 years. A similar pattern applied for chemotherapy. The reasons are not known. Perhaps a longer recovery time post-surgery has been allowed for older cases post-surgery before commencing adjuvant therapies, or longer delays occurring due to higher levels of frailty and comorbidity, and more common complications of surgery.

Radiotherapy was relatively uncommon for colon cancers, as recommended in clinical guidelines and optimal care pathways.[27, 28] When it was provided, it tended to start later than for rectal cases. Similarly, chemotherapies tended to commence later for colon than rectal cancers. Further research is needed to determine the reasons for these patterns. Chemotherapies were less likely to commence >30 days from diagnosis for 2006-2010 diagnoses. Conversely chemotherapies were more inclined to occur >60 days from diagnosis in 2006-2010. Again, further research is needed to explain these patterns.

Where the time from diagnosis to treatment was >30 days, the risk of death occurring ≤2 years of diagnosis was lower. This was evident by therapy type after adjusting for stage and grade, and sociodemographic factors. It may reflect the triaging for priority treatment ≤30 days for cases with elevated comorbidity or other risk factors not recorded by the

registry. While a statistically significant U-shaped relationship of survival with time to treatment start was usually not apparent for specific therapies, as indicated in some other studies, [6, 17] the hazard ratio for 3-10 years was elevated when the time to first treatment was >90 days for surgical cases (p=0.022).

The present study has limitations. An opportunistic approach was taken in selecting cases where a gap presented between recorded diagnosis date and start of treatment. Also: (a) precise diagnostic and treatment data were limited to 65% of cases, which could have led to bias; (b) the study was observational and vulnerable to bias from practitioner choice and self-selection by patients into comparison groups; and (c) the ability to adjust for potential confounding influences was limited by the range of data available. Nonetheless, results are similar to those of other recent studies in showing poorer short-term survival for cases receiving surgical treatment soon after diagnosis, and with a similar pattern applying for early treatment by radiotherapy and chemotherapies.[12, 14, 15, 17]

Results should not be construed as indicating a lack of benefit from early treatment, given likely confounding effects of patient selection in treatment scheduling. A positive feature was the approximate 87% of surgical cases receiving their first treatment (any treatment) ≤60 days and 80% treated surgically within this period (note: 83% for 2000-2005 and 78% for 2006-2010).[9] The indication of a temporal decline in this percentage warrants continued monitoring and investigation, particularly for patient groups where a higher proportion was not receiving surgical care ≤60 days of diagnosis (e.g., patients aged under 50 years, those with advanced disease, those with rectal cancer, and residents of the northern metropolitan rather than central or southern metropolitan areas).

The study highlights the benefit of linking diagnostic data to treatment data. Population-wide data linkage of population-based cancer registry, hospital, radiotherapy-centre, Medicare insurance and screening data, and potentially in the future, electronic medical record data and selected research databases will further strengthen the data infrastructure available for describing clinical management pathways and associations with survival across the population. This is expected to enable finer sub-group analyses. Clinical registries will still be important for more detailed investigations for the sub-groups they cover, and for validating results of population-wide registry and administrative sources.

**Conclusions**

1. Baseline data for major public hospitals in South Australia 2000-2010 indicate that for cases where the clinical registry recorded a diagnosis in advance of the surgery date, approximately 87% of surgical cases receiving some treatment and 80% of cases received their surgical treatment ≤60 days of diagnosis. This is broadly consistent with timeline targets of Cancer UK.
2. Radiotherapy and chemotherapies generally started later, potentially reflecting their use as adjuvant therapies.
3. Adjusted analyses indicated lower survival up to two years from diagnosis when treatment commenced ≤30 days of diagnosis, potentially reflecting triaging for early care of cases with aggressive cancers and higher clinical complexity. By comparison, adjusted analyses did not show differences in survival for follow-up periods from diagnosis of 3-10 years where longer times to treatment applied, except for time to any treatment type (surgical cases) of >90 days when survival was lower.

4. These results should not be interpreted as evidence of the importance or unimportance of delays, given selection factors in scheduling patient care.
5. Treatment commencement was generally later in 2006-2010 than 2000-2005, possibly reflecting increased use of adjuvant therapies, increased use of multidisciplinary teams, and more advanced diagnostics (e.g., magnetic resonance imaging). Increased demand may be placed on timeliness of clinical services with extensions in population screening.
6. Further research is needed to optimize patient scheduling for better outcomes.

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**Informed consent**

Waiver of consent for use of de-identified data collected under authorisation of Part 7 of the South Australian Health Care Act. Note: large numbers of patients had deceased, and many are in the terminal stages of their cancer. Consent processes would be intrusive and would invalidate the database as an unbiased data source.

**Author contributions**

Study concept: DR, TP; Study design: DR TP, CK, RP, JM; Data acquisition: DB, KP; Quality control of data: DB, KP, KF; Data analysis: DR, KF ; Data interpretation: DR, CK, IO, DK, RP, JM, RJ, DW, DLW, TP; Report writing: DR, KF; Review of report: DR, CK, IO, DK, RP, JM, RJ, DW, DLW, TP, CM, CH, EB. All authors read and approved the final manuscript.

**Data sharing**

The data for this study are available through the South Australian Cancer Service and SA Cancer Registry. Restrictions to data use apply as conditions of legal authorization and data custodian and ethics approval.

**Competing interests**

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***Supplementary tables***

Table S1: Relative odds (95% CLs) of treatment for colon cancer starting >30 days of diagnosis by treatment type, stage, and socioeconomic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Chemotherapy | | Any treatment (surgical cases) | |
|---|---|---|---|---|---|---|---|---|
| | **n=1098** | **RO (95% CLs)** | **n=86** | **RO (95% CLs)** | **n=898** | **RO (95% CLs)** | **n=1098** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 53 | 1.00 | 13 | 1.00 | 109 | 1.00 | 53 | 1.00 |
| 50 - 59 | 116 | 1.61 (0.75, 3.46) | 14 | 1.03 (0.05, 21.46) | 176 | 0.84 (0.40, 1.76) | 116 | 1.28 (0.59, 2.78) |
| 60 - 69 | 226 | 2.10 (1.03, 4.28) | 20 | 2.82 (0.20, 40.71) | 273 | 0.91 (0.45, 1.83) | 226 | 1.86 (0.92, 3.80) |
| 70 - 79 | 396 | 1.65 (0.83, 3.28) | 28 | 3.49 (0.27, 45.20) | 292 | 1.37 (0.68, 2.79) | 396 | 1.55 (0.78, 3.09) |
| 80+ | 307 | 1.50 (0.74, 3.03) | 11 | NA | 48 | 2.52 (0.78, 8.17) | 307 | 1.43 (0.71, 2.88) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 562 | 1.00 | 56 | 1.00 | 491 | 1.00 | 562 | 1.00 |
| Female | 536 | 0.87 (0.67, 1.13) | 30 | 2.65 (0.27, 1.64) | 407 | 1.23 (0.79, 1.91) | 536 | 0.89 (0.68, 1.16) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 336 | 1.00 | 25 | 1.00 | 287 | 1.00 | 336 | 1.00 |
| Low-Med | 273 | 1.69 (0.99, 2.12) | 19 | 1.69 (0.09, 30.68) | 229 | 0.71 (0.39, 1.27) | 273 | 1.46 (1.00, 2.14) |
| Med-High | 224 | 1.31 (0.90, 1.90) | 20 | 7.01 (0.22, 223.56) | 185 | 0.93 (0.49, 1.78) | 224 | 1.28 (0.88, 1.88) |
| High | 265 | 1.12 (0.76, 1.67) | 22 | 1.37 (0.07, 27.36) | 197 | 0.85 (0.45, 1.62) | 265 | 1.09 (0.73, 1.62) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 899 | 1.00 | 66 | 1.00 | 716 | 1.00 | 899 | 1.00 |
| Med-High | 141 | 0.57 (0.28, 1.15) | 9 | NA | 127 | 0.41 (0.09, 1.97) | 141 | 0.57 (0.28, 1.16) |
| Poor | 58 | 0.71 (0.33, 1.57) | 11 | NA | 55 | 0.25 (0.05, 1.21) | 58 | 0.63 (0.28, 1.38) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 149 | 1.00 | 12 | 1.00 | 141 | 1.00 | 149 | 1.00 |
| Central metro | 421 | 0.49 (0.32, 0.75) | 33 | 0.31 (0.01, 6.39) | 291 | 0.85 (0.41, 1.76) | 421 | 0.48 (0.31, 0.73) |
| Southern metro | 281 | 0.39 (0.25, 0.63) | 16 | 0.58 (0.03, 11.80) | 252 | 0.83 (0.39, 1.78) | 281 | 0.37 (0.24, 0.60) |
| Country South | 88 | 0.69 (0.36, 1.33) | 10 | NA | 83 | 3.94 (0.70, 22.22) | 88 | 0.69 (0.36, 1.34) |
| Country North | 159 | 0.78 (0.37, 1.66) | 15 | NA | 131 | 2.42 (0.47, 12.36) | 159 | 0.76 (0.35, 1.63) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 169 | 1.00 | 3 | 1.00 | 12 | 1.00 | 169 | 1.00 |
| B | 471 | 0.67 (0.46, 0.98) | 20 | 43.60 (0.38, 49.56) | 130 | 1.60 (0.16, 16.54) | 471 | 0.65 (0.45, 0.95) |
| C | 252 | 0.69 (0.46, 1.06) | 21 | 24.12 (0.22, 26.91) | 409 | 1.76 (0.19, 16.48) | 252 | 0.66 (0.43, 1.00) |
| D | 180 | 0.54 (0.33, 0.86) | 39 | 4.39 (0.07, 27.89) | 320 | 0.24 (0.03, 2.17) | 180 | 0.44 (0.27, 0.72) |
| (UK) | (26) | (0.64 (0.26, 1.57)) | (3) | NA | (27) | (0.41 (0.04, 4.48)) | (26) | (0.58 (0.23, 1.43)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 38 | 1.00 | 5 | 1.00 | 18 | 1.00 | 38 | 1.00 |
| Mod diff. | 770 | 0.85 (0.43, 1.68) | 53 | 1.49 (0.11, 19.97) | 581 | 0.58 (0.07, 4.81) | 770 | 0.82 (0.41, 1.62) |
| Poorly/undiff. | 209 | 0.57 (0.27, 1.21) | 19 | 1.11 (0.06, 21.24) | 213 | 0.46 (0.05, 3.89) | 209 | 0.54 (0.26, 1.15) |
| (UK) | (81) | (1.87 (0.82, 4.26)) | (9) | NA | (86) | (0.13 (0.02, 1.11)) | (81) | (1.62 (0.71, 3.69)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 541 | 1.00 | 52 | 1.00 | 451 | 1.00 | 541 | 1.00 |
| 2006 - 2010 | 557 | 1.41 (1.09, 1.83) | 34 | 0.21 (0.03, 1.64) | 447 | 1.59 (1.02, 2.48) | 557 | 1.39 (1.07, 2.88) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; NA – not applicable; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

Table S2: Relative odds (95% CLs) of treatment for colon cancer starting >60 days of diagnosis by treatment type, stage, and socio-demographic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Chemotherapy | | Any treatment (surgical cases only) | |
|---|---|---|---|---|---|---|---|---|
| | **n=1098** | **RO (95% CLs)** | **n=86** | **RO (95% CLs)** | **n=898** | **RO (95% CLs)** | **n=1098** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 53 | 1.00 | 13 | 1.00 | 109 | 1.00 | 53 | 1.00 |
| 50 - 59 | 116 | 1.34 (0.51, 3.51) | 14 | 0.06 (0.00, 1.37) | 176 | 0.94 (0.57, 1.55) | 116 | 0.75 (0.25, 2.21) |
| 60 - 69 | 226 | 1.28 (0.51, 3.20) | 20 | 0.17 (0.01, 3.57) | 273 | 1.16 (0.73, 1.84) | 226 | 1.10 (0.41, 2.93) |
| 70 - 79 | 396 | 1.10 (0.45, 2.66) | 28 | 0.35 (0.02, 7.07) | 292 | 1.26 (0.80, 2.01) | 396 | 0.99 (0.38, 2.53) |
| 80+ | 307 | 1.00 (0.40, 2.47) | 11 | 0.30 (0.01, 7.36) | 48 | 1.60 (0.78, 3.29) | 307 | 1.01 (0.38, 2.65) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 562 | 1.00 | 56 | 1.00 | 491 | 1.00 | 562 | 1.00 |
| Female | 536 | 0.83 (0.57, 1.20) | 30 | 1.01 (0.23, 4.35) | 407 | 0.84 (0.64, 1.14) | 536 | 0.94 (0.62, 1.41) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 336 | 1.00 | 25 | 1.00 | 287 | 1.00 | 336 | 1.00 |
| Low-med | 273 | 1.58 (0.93, 2.71) | 19 | 0.40 (0.06, 2.51) | 229 | 0.75 (0.51, 1.10) | 273 | 1.65 (0.92, 2.98) |
| Med-high | 224 | 1.14 (0.68, 1.94) | 20 | 1.78 (0.26, 12.39) | 185 | 0.86 (0.58, 1.28) | 224 | 1.14 (0.64, 2.04) |
| High | 265 | 1.19 (0.67, 2.10) | 22 | 1.04 (0.15, 7.27) | 197 | 1.18 (0.78, 1.77) | 265 | 1.41 (0.75, 2.63) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 899 | 1.00 | 66 | 1.00 | 716 | 1.00 | 899 | 1.00 |
| Med-high | 141 | 0.54 (0.20, 1.42) | 9 | 8.99 (0.24, 331.28) | 127 | 1.57 (0.75, 3.30) | 141 | 0.45 (0.16, 1.25) |
| Poor | 58 | 0.65 (0.21, 1.97) | 11 | 3.90 (0.11, 141.05) | 55 | 0.83 (0.36, 1. 93) | 58 | 0.41 (0.12, 1.44) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 149 | 1.00 | 12 | 1.00 | 141 | 1.00 | 149 | 1.00 |
| Central metro | 421 | 0.56 (0.32, 0.98) | 33 | 0.16 (0.01, 1.98) | 291 | 0.91 (0.58, 1. 43) | 421 | 0.44 (0.24, 0.79) |
| Southern metro | 281 | 0.46 (0.25, 0.87) | 16 | 0.17 (0.01, 2.26) | 252 | 0.96 (0.61, 1.52) | 281 | 0.29 (0.14, 0.58) |
| Country South | 88 | 0.87 (0.36, 2.14) | 10 | 0.08 (0.00, 2.02) | 83 | 0.93 (0.43, 2.01) | 88 | 0.87 (0.34, 2.21) |
| Country North | 157 | 1.04 (0.38, 2.90) | 15 | 0.03 (0.00, 1.61) | 131 | 0.74 (0.33, 1. 76) | 157 | 1.23 (0.43, 3.57) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 169 | 1.00 | 3 | 1.00 | 12 | 1.00 | 169 | 1.00 |
| B | 471 | 1.02 (0.54, 1.91) | 20 | 0.79 (0.03, 23.99) | 130 | 0.43 (0.10, 1.74) | 471 | 0.80 (0.42, 1.53) |
| C | 252 | 2.34 (1.25, 4.40) | 21 | 0.57 (0.02, 18.97) | 409 | 0.29 (0.07, 1.15) | 252 | 1.54 (0.80, 2.96) |
| D | 180 | 2.25 (1.16, 4.35) | 39 | 0.94 (0.03, 26.42) | 320 | 0.26 (0.07, 1.03) | 180 | 1.49 (0.74, 2.98) |
| (UK) | (26) | (1.65 (0.51, 5.33)) | (3) | NA | (27) | (0.67 (0.14, 3.26)) | (26) | 1.35 (0.38, 4.76)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 38 | 1.00 | 5 | 1.00 | 18 | 1.00 | 38 | 1.00 |
| Mod diff. | 770 | 0.85 (0.31, 2.29) | 53 | 2.29 (0.31, 16.79) | 581 | 0.97 (0.35, 2.67) | 770 | 0.71 (0.26, 1.92) |
| Poorly/undiff. | 209 | 0.60 (0.20, 1.78) | 19 | 1.11 (0.12, 10.68) | 213 | 0.94 (0.33, 2.65) | 209 | 0.52 (0.17, 1.58) |
| (UK) | (81) | (1.84 (0.60, 5.62)) | (9) | NA | (86) | (0.40 (0.13, 1.20)) | (81) | (1.24 (0.39, 3.93)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 541 | 1.00 | 52 | 1.00 | 451 | 1.00 | 541 | 1.00 |
| 2006 - 2010 | 557 | 1.26 (0.87, 1.82) | 34 | 0.31 (0.08, 1.25) | 447 | 1.96 (1.48, 2.59) | 557 | 1.29 (0.86, 1.94) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; NA – not applicable; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

Table S3: Relative odds (95% CLs) of treatment for **rectal cancer** starting >30 days of diagnosis by treatment type, stage, and socioeconomic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Chemotherapy | | All treatment (surgical cases only) | |
|---|---|---|---|---|---|---|---|---|
| | **n=577** | **RO (95% CLs)** | **n=530** | **RO (95% CLs)** | **n=658** | **RO (95% CLs)** | **n=577** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 38 | 1.00 | 66 | 1.00 | 80 | 1.00 | 38 | 1.00 |
| 50 - 59 | 94 | 0.71 (0.31,1.62) | 104 | 1.30 (0.62,2.71) | 146 | 1.73 (0.86,3.48) | 94 | 1.03 (0.46, 2.29) |
| 60 - 69 | 162 | 0.57 (0.26,1.24) | 168 | 1.41 (0.71,2.79) | 225 | 1.57 (0.83,2.99) | 162 | 0.78 (0.37, 1.66) |
| 70 - 79 | 174 | 0.44 (0.20,0.95) | 147 | 1.35 (0.67,2.71) | 177 | 1.79 (0.90,3.54) | 174 | 0.83 (0.40, 1.76) |
| 80+ | 109 | 0.38 (0.17,0.85) | 45 | 1.40 (0.52,3.77) | 30 | 2.01 (0.58,6.97) | 109 | 0.70 (0.32, 1.55) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 331 | 1.00 | 344 | 1.00 | 419 | 1.00 | 331 | 1.00 |
| Female | 246 | 0.74 (0.52,1.07) | 186 | 0.68 (0.43,1.07) | 239 | 0.94 (0.61,1.45) | 246 | 0.79 (0.55, 1.14) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 208 | 1.00 | 181 | 1.00 | 220 | 1.00 | 208 | 1.00 |
| Low-med | 115 | 0.86 (0.50,1.45) | 118 | 0.80 (0.42,1.51) | 145 | 1.13 (0.62,2.07) | 115 | 0.81 (0.48, 1.37) |
| Med-high | 121 | 0.72 (0.44,1.19) | 108 | 0.50 (0.26,0.94) | 135 | 0.78 (0.43,1.42) | 121 | 0.63 (0.38, 1.03) |
| High | 133 | 1.06 (0.64,1.77) | 123 | 0.88 (0.45,1.70) | 158 | 1.00 (0.55,1.83) | 133 | 1.03 (0.62, 1.72) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 454 | 1.00 | 409 | 1.00 | 507 | 1.00 | 454 | 1.00 |
| Med-high | 87 | 0.74 (0.29,1.88) | 85 | 1.49 (0.50,4.44) | 101 | 1.00 (0.30,3.36) | 87 | 1.27 (0.49, 3.26) |
| Poor | 36 | 1.00 (0.36,2.76) | 36 | 1.25 (0.37,4.20) | 50 | 0.88 (0.25,3.05) | 36 | 1.58 (0.58, 4.33) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 93 | 1.00 | 94 | 1.00 | 107 | 1.00 | 93 | 1.00 |
| Central metro | 197 | 0.55 (0.31,0.97) | 169 | 0.86 (0.44,1.70) | 204 | 1.19 (0.64,2.23) | 197 | 0.61 (0.35, 1.06) |
| Southern metro | 136 | 0.40 (0.22,0.73) | 118 | 0.61 (0.30,1.23) | 174 | 0.89 (0.47,1.69) | 136 | 0.44 (0.24, 0.80) |
| Country South | 67 | 0.89 (0.37,2.10) | 64 | 0.45 (0.17,1.25) | 76 | 1.99 (0.62,6.41) | 67 | 0.70 (0.30, 1.63) |
| Country North | 84 | 0.67 (0.24,1.89) | 85 | 1.48 (0.44,5.02) | 97 | 2.61 (0.73,9.25) | 84 | 0.57 (0.20, 1.62) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 111 | 1.00 | 47 | 1.00 | 35 | 1.00 | 111 | 1.00 |
| B | 183 | 1.31 (0.79,2.18) | 127 | 0.90 (0.39,2.06) | 119 | 1.35 (0.57,3.21) | 183 | 1.18 (0.71, 1.95) |
| C | 160 | 1.65 (0.98,2.79) | 210 | 1.39 (0.63,3.10) | 287 | 3.81 (1.64,8.86) | 160 | 1.43 (0.85, 2.40) |
| D | 99 | 0.83 (0.46,1.51) | 123 | 0.67 (0.30,1.51) | 196 | 1.30 (0.58,2.95) | 99 | 0.79 (0.43, 1.44) |
| (UK) | 24 | (0.76 (0.28,2.06)) | 23 | (0.74 (0.23,2.39)) | 21 | (1.72 (0.44,6.71)) | 24 | (0.83 (0.30,2.28)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 20 | 1.00 | 20 | 1.00 | 19 | 1.00 | 20 | 1.00 |
| Mod diff. | 442 | 0.60 (0.21,1.68) | 376 | 1.59 (0.57,4.44) | 473 | 1.43 (0.43,4.70) | 442 | 0.78 (0.29, 2.08) |
| Poorly/undiff. | 76 | 0.52 (0.17,1.61) | 80 | 2.63 (0.81,8.52) | 96 | 2.14 (0.57,8.10) | 76 | 0.71 (0.24, 2.08) |
| (UK) | 39 | (1.38 (0.39,4.91)) | 54 | (1.31 (0.40,4.29)) | 70 | (0.72 (0.20,2.63)) | 39 | (1.57 (0.47,5.27)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 328 | 1.00 | 283 | 1.00 | 331 | 1.00 | 328 | 1.00 |
| 2006 - 2010 | 249 | 2.86 (1.98,4.12) | 247 | 1.76 (1.12,2.76) | 327 | 1.34 (0.88,2.04) | 249 | 3.09 (2.15, 4.43) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

Table S4: Relative odds (95% CLs) of treatment for **rectal cancer** starting >60 days of diagnosis by treatment type, stage, and socio-demographic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Chemotherapy | | All treatment (surgical cases only) | |
|---|---|---|---|---|---|---|---|---|
| | **n=577** | **RO (95% CLs)** | **n=530** | **RO (95% CLs)** | **n=658** | **RO (95% CLs)** | **n=577** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 38 | 1.00 | 66 | 1.00 | 80 | 1.00 | 38 | 1.00 |
| 50 - 59 | 94 | 0.53 (0.23, 1.19) | 104 | 2.41 (1.12, 5.17) | 146 | 2.45 (1.26, 4.74) | 94 | 1.28 (0.42, 3.93) |
| 60 - 69 | 162 | 0.49 (0.23, 1.05) | 168 | 3.28 (1.60, 6.71) | 225 | 3.46 (1.85, 6.49) | 162 | 1.17 (0.40, 3.38) |
| 70 - 79 | 174 | 0.25 (0.12, 0.55) | 147 | 2.69 (1.30, 5.56) | 177 | 3.47 (1.82, 6.60) | 174 | 1.21 (0.42, 3.48) |
| 80+ | 109 | 0.26 (0.11, 0.59) | 45 | 3.05 (1.24, 7.51) | 30 | 3.95 (1.54, 10.17) | 109 | 1.62 (0.55, 4.80) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 331 | 1.00 | 344 | 1.00 | 419 | 1.00 | 331 | 1.00 |
| Female | 246 | 0.77 (0.52, 1.13) | 186 | 0.91 (0.61, 1.36) | 239 | 1.04 (0.73, 1.46) | 246 | 0.89 (0.56, 1.42) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 208 | 1.00 | 181 | 1.00 | 220 | 1.00 | 208 | 1.00 |
| Low-med | 115 | 1.29 (0.73, 2.27) | 118 | 1.11 (0.65, 1.92) | 145 | 0.61 (0.38, 0.98) | 115 | 1.05 (0.53, 2.02) |
| Med-high | 121 | 1.04 (0.61, 1.78) | 108 | 0.95 (0.55, 1.62) | 135 | 0.94 (0.59, 1.50) | 121 | 1.25 (0.67, 2.33) |
| High | 133 | 1.03 (0.60, 1.77) | 123 | 1.28 (0.74, 2.22) | 158 | 0.71 (0.44, 1.14) | 133 | 0.81 (0.41, 1.58) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 454 | 1.00 | 409 | 1.00 | 507 | 1.00 | 454 | 1.00 |
| Med-high | 87 | 0.26 (0.09, 0.73) | 85 | 1.12 (0.41, 3.01) | 101 | 0.98 (0.42, 2.25) | 87 | 0.49 (0.13, 1.86) |
| Poor | 36 | 0.30 (0.10, 0.89) | 36 | 1.53 (0.55, 4.31) | 50 | 1.08 (0.45, 2.62) | 36 | 0.83 (0.22, 2.67) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 93 | 1.00 | 94 | 1.00 | 107 | 1.00 | 93 | 1.00 |
| Central metro | 197 | 0.53 (0.30, 0.95) | 169 | 0.88 (0.50, 1.55) | 204 | 1.70 (1.00, 2.89) | 197 | 0.71 (0.36, 1.38) |
| Southern metro | 136 | 0.49 (0.26, 0.91) | 118 | 0.55 (0.30, 1.03) | 174 | 0.84 (0.48, 1.44) | 136 | 0.63 (0.30, 1.30) |
| Country South | 67 | 0.69 (0.29, 1.61) | 64 | 0.45 (0.18, 1.14) | 76 | 1.36 (0.59, 3.17) | 67 | 0.71 (0.25, 2.05) |
| Country North | 84 | 1.25 (0.42, 3.74) | 85 | 0.70 (0.24, 2.01) | 97 | 1.10 (0.44, 2.72) | 84 | 0.67 (0.17, 2.71) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 111 | 1.00 | 47 | 1.00 | 35 | 1.00 | 111 | 1.00 |
| B | 183 | 1.46 (0.82, 2.58) | 127 | 1.26 (0.59, 2.67) | 119 | 1.64 (0.69, 3.91) | 183 | 1.04 (0.53, 2.02) |
| C | 160 | 2.30 (1.30, 4.05) | 210 | 1.76 (0.86, 3.58) | 287 | 2.70 (1.19, 6.12) | 160 | 1.15 (0.60, 2.24) |
| D | 99 | 1.34 (0.69, 1.61) | 123 | 1.25 (0.59, 2.67) | 196 | 1.95 (0.85, 4.51) | 99 | 0.83 (0.37, 1.86) |
| (UK) | 24 | (1.65 (0.58, 4.67)) | 23 | (0.35 (0.09, 1.43)) | 21 | (1.33 (0.38, 4.68)) | 24 | (1.45 (0.46,4.58)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 20 | 1.00 | 20 | 1.00 | 19 | 1.00 | 20 | 1.00 |
| Mod diff. | 442 | 0.30 (0.11, 0.82) | 376 | 1.25 (0.45,3.44) | 473 | 1.39 (0.50, 3.88) | 442 | 0.35 (0.13, 0.95) |
| Poorly/un-diff. | 76 | 0.26 (0.09, 0.79) | 80 | 1.70 (0.57,5.09) | 96 | 1.51 (0.50, 4.52) | 76 | 0.35 (0.11, 1.12) |
| (UK) | 39 | (0.64 (0.19, 2.18)) | 54 | (0.88 (0.28,2.84)) | 70 | (0.83 (0.27, 2.59)) | 39 | (0.76 (0.23,2.59)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 328 | 1.00 | 283 | 1.00 | 331 | 1.00 | 328 | 1.00 |
| 2006 - 2010 | 249 | 1.98 (1.35, 2.91) | 247 | 1.02 (0.70,1.50) | 327 | 1.21 (0.87, 1.69) | 249 | 2.01 (1.26, 3.18) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

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In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

| | | Reporting Item | Page Number |
|---|---|---|---|
| Title | #1a | Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| Abstract | #1b | Provide in the abstract an informative and balanced summary of what was done and what was found | 2 |
| Background / rationale | #2 | Explain the scientific background and rationale for the investigation being reported | 3 |
| Objectives | #3 | State specific objectives, including any prespecified hypotheses | 4 |
| Study design | #4 | Present key elements of study design early in the paper | 4 |
| Setting | #5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 4 |

| | | | |
|---|---|---|---|
| Eligibility criteria | #6a | Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. | 4 |
| | #6b | For matched studies, give matching criteria and number of exposed and unexposed | n/a |
| Variables | #7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 4,5 |
| Data sources / measurement | #8 | For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable. | 4 |
| Bias | #9 | Describe any efforts to address potential sources of bias | 10, 12 |
| Study size | #10 | Explain how the study size was arrived at | 4 |
| Quantitative variables | #11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | 4,5 |
| Statistical methods | #12a | Describe all statistical methods, including those used to control for confounding | 4,5 |
| | #12b | Describe any methods used to examine subgroups and interactions | 4,5 |
| | #12c | Explain how missing data were addressed | 4 |
| | #12d | If applicable, explain how loss to follow-up was addressed | n/a |
| | #12e | Describe any sensitivity analyses | 4,5 |
| Participants | #13a | Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable. | tables 1-5 |
| | #13b | Give reasons for non-participation at each stage | n/a |
| | #13c | Consider use of a flow diagram | n/a |

| | | | |
|---|---|---|---|
| Descriptive data | #14a | Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable. | 5-14 |
| | #14b | Indicate number of participants with missing data for each variable of interest | n/a |
| | #14c | Summarise follow-up time (eg, average and total amount) | n/a |
| Outcome data | #15 | Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable. | 5-14 |
| Main results | #16a | Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 5-14 |
| | #16b | Report category boundaries when continuous variables were categorized | 5-14 |
| | #16c | If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | n/a |
| Other analyses | #17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses | n/a |
| Key results | #18 | Summarise key results with reference to study objectives | 14-15 |
| Limitations | #19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. | 15 |
| Interpretation | #20 | Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. | 14-16 |
| Generalisability | #21 | Discuss the generalisability (external validity) of the study results | 16 |
| Funding | #22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 17 |

BMJ Open

# Time from diagnosis to treatment of colorectal cancer in a South Australian clinical registry cohort: how it varies and relates to survival

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| | |

# Time from diagnosis to treatment of colorectal cancer in a South Australian clinical registry cohort: how it varies and relates to survival

Roder D*[1], Karapetis C[2], Olver I[1], Keefe D[3, 5], Padbury R[2], Moore J[5, 6], Joshi R[5,7], Wattchow D[2, 4], Worthley DL[8], Miller C[9,10], Holden C[9], Buckley E[1], Powell K[9], Buranyi-Trevarton D[3], Fusco K[1], Price T[5, 11]

[1] Cancer Research Institute, University of South Australia, Adelaide, SA, Australia

[2] Medical Oncology, Flinders University, Bedford Park, SA, Australia

[3] South Australian Cancer Service, South Australia Department of Health, Adelaide, SA, Australia

[4] Surgery and Perioperative Medicine, Southern Adelaide Local Health Network, Bedford Park, SA, Australia

[5] Adelaide Medical School, University of Adelaide, Adelaide, SA, Australia

[6] Colorectal Surgery, Royal Adelaide Hospital, Adelaide, SA, Australia

[7] Adelaide Oncology and Haematology, Cancer Research and Clinical Trials, North Adelaide, SA, Australia

[8] Gastrointestinal Cancer Biology, South Australian Health and Medical Research Institute, Adelaide, SA, Australia

[9] Population Health, South Australian Health and Medical Research Institute, Adelaide, SA, Australia

[10] School of Public Health, The University of Adelaide, Adelaide, SA, Australia

[11] Clinical Cancer Research, Queen Elizabeth Hospital, Woodville, SA, Australia

* Corresponding author

Email: david.roder@unisa.edu.au

Phone: +61 8 8302 2640

**Word count: 4,546**

**Abstract**

*Objectives*

Some early studies indicated lower survival with longer time from diagnosis to cancer treatment, but others showed the reverse. We investigated time to treatment of colorectal cancer and associations with survival.

*Setting and participants*

Clinical registry data for colorectal cancer cases diagnosed in 2000-2010 at four major public hospitals in South Australia and treated by surgery (n=1675), radiotherapy (n=616) and/or systemic therapy (n=1556).

*Design*

A historic cohort design, with rank-order tests for ordinal clinical and sociodemographic predictors and multiple logistic regression for comparing time from diagnosis to treatment. Unadjusted Kaplan-Meier estimates and adjusted Cox proportional hazards regression were used to investigate disease-specific survival by time to treatment.

*Outcome measures*

Time to treatment and survival from diagnosis to death from colorectal cancer.

*Results*

Treatment (any type) commenced for 87% of surgical cases ≤60 days of diagnosis, with 80% having surgery within this period. Of those receiving radiotherapy, 59% began this treatment ≤60 days, and of those receiving systemic therapy, the corresponding proportion was 56%. Adjusted analyses showed treatment delay >60 days was more likely for rectal cancers, 2006-2010 diagnoses, residents of northern than other metropolitan regions, and for surgery, younger ages <50 years, and unexpectedly, those residing closer to metropolitan services**.** Adjusting for clinical and sociodemographic factors, and diagnostic year, better survival occurred in ≤ 2 years from diagnosis for time to treatment >30 days. Survival in the 3-10 years post-diagnosis generally did not differ by time to treatment, except for lower survival for any treatment >90 days for surgical cases.

*Conclusions*

The lower survival ≤2 years from diagnosis for treatment ≤30 days of diagnosis is consistent with other studies attributed to preferencing more complicated cases for earlier care. Lower 3-10-year survival for surgical cases first treated >90 days from diagnosis is consistent with previously reported U-shaped relationships.

**Key words**

Oncology epidemiology, protocols & guidelines, quality in health care, public health, colorectal surgery

**Strengths and limitations of this study**

Strengths:

Where data were available, they were high-quality clinical registry data on diagnosis, treatment, and sociodemographic covariables.

Access to clinical service providers to assist with data interpretation.

Limitations:

Precise diagnostic and treatment data were limited to 65% of cases.

The study was observational and vulnerable to bias from practitioner choice and self-selection by patients into comparison groups. The ability to adjust for potential confounding was limited by the range of data available.

## Introduction

Australia has a high age-standardised incidence of colorectal cancer about 87% above the world average.[1] The corresponding colorectal cancer mortality rate is lower although still about 22% above the world average.[1] Colorectal cancer is second only to prostate cancer in numbers reported annually by Australian cancer registries and second only to lung cancer in numbers of cancer deaths.[2] Age-standardised incidence has been stable, with the 2012-2014 rate being within 1-2% of the rate for 1982-1984. By comparison, the age-standardised colorectal cancer mortality rate approximately halved between these periods.[2] This difference was accompanied by increases in 5-year relative survival from 52% in 1982-1986 to 70% in 2011-2015.[3, 4]

South Australian clinical registry data for colorectal cancer covering four major public hospitals showed equivalent survival and survival increases to national figures during 1980-2010, with five-year disease-specific survival increasing from 48% to 63% for all stages combined.[5] Stage distributions were largely unchanged, with survival increases mostly attributed to gains in stage-specific survival.[5] Increases were particularly pronounced for regional stage.[5] Survival increases followed increased use of adjuvant chemotherapies, particularly for regional disease.[5] For rectal cancers, a significant increase in use of adjuvant radiotherapy was reported. The increases in adjuvant therapy were consistent with clinical practice guidelines.[5] Chemotherapies evolved from common use of single-agent 5-FU (5-Fluorouracil) to 5-FU and leucovorin. FOLFOX (leucovorin calcium, 5-FU and oxaliplatin) ± bevacizumab and capecitabine (± oxaliplatin) also became more common, along with protracted infusion of 5-FU for colon cancer, and with radiotherapy for rectal cancers.[5]

While survival increases were attributed to changes in use of chemotherapy and radiotherapy, and increased surgical specialization,[5] other influences were possible. One was a change in time from diagnosis to surgical treatment.[6] In the United Kingdom, treatment delays were regarded as negatively related to survival and concerns were expressed that delays may be increasing due to increased demands for colonoscopy from population screening.[7, 8] While there is limited evidence of effects of

treatment delays on survival, early evidence points to a possible negative effect.[6, 7, 8] Delays were also viewed negatively as a likely source of psychosocial stress.[6, 8] Cancer UK has indicated that ideally treatment would commence within one month of diagnosis but has recommended commencement within two months as a realistic target.[9]

Evidence of effects of time to treatment on survival has been mixed.[10-18] Early studies generally pointed to lower survival with longer delay, but later studies varied with some showing better survival for longer delay, and some showing a U-shaped relationship with lower survival at both ends of the follow-up period.[6-8, 10-18] This has raised questions of whether the relationship varies with the clinical environment, with lower survival for short delays potentially reflected triaging of more aggressive cancers for early treatment in some settings.[12, 13, 15, 17]

In this study we explore times from diagnosis to treatment, trends in these times, variations across the patient population, and associations with survival. To establish a historic baseline, we analysed colorectal cancer data (2000-2010 diagnoses) from the South Australian registry data. Analyses indicated times to treatment and outcomes across the patient population at these hospitals by cancer stage, patient age, sex, socioeconomic status, service access, local health network of residence (as applying in the study period) and diagnostic epoch. We investigated whether a U-shaped relationship existed between time to treatment and survival, as reported elsewhere.[6, 17]

The study was restricted to cancers where the registry had enough diagnostic detail from biopsies and other clinical sources to record a diagnosis date in advance of treatment, thereby providing an intervening period for analysis (65% of cases). This is analogous to common registry practice of restricting survival analyses to cancers where diagnosis dates preceded dates of death.[19]

**Methods**

A historic cohort design was used, including colorectal cancer patients diagnosed in 2000-2010 at four major public hospitals in South Australia  Our data source was the South Australian clinical cancer registry, which is authorised under Section 64, Part 7 of the South Australian Health Care Act (2008) to support service monitoring and quality assurance.[5] Ethics approval: Research ethics approval was obtained from the South Australian Human Research Ethics Committee (HREC/14/SAH/145) and University of South Australia Research Ethics Committee. Data sources and linkage: Data were extracted from the clinical registry and dates and causes of death by linkage with official death records using full names, dates of birth, and sex, and for additional guidance, postcode of residence, for linkage purposes. Outcome measures: These were time in days from diagnosis to treatment start, and survival from diagnosis to death from colorectal cancer.

Dates of diagnosis and treatment were checked from available pathology and clinical reporting to optimize accuracy. Times to treatment start were calculated to treatment of 2,746 colorectal cancers.[20]

Cases were excluded if presenting acutely with bowel obstruction or perforation and treated surgically on day one.

Analyses were undertaken for surgical, radiotherapy and chemotherapies respectively, and any of these treatments among surgical cases. Chemotherapies were most commonly 5-FU (Adrucil, 5-FU) given intravenously, capecitabine (Xeloda) given as a pill, oxaliplatin (Eloxatin) given intravenously, irinotecan (Camptosar) given intravenously, and raltitrexed (Tomudex) given intravenously (https://www.cancer. ca/en/cancer-information/cancer-type/colorectal/treatment/ chemotherapy/?region=on).

Cases were classified by: sub-site (colon or rectum), Australian Clinico-Pathological Staging (ACPS) as A, B, C, D or unknown (UK), and grade,[21] age at diagnosis, sex, area socioeconomic status,[22] geographic access to specialist radiotherapy and other specialist metropolitan services based on postcode address (coded as high, medium-high or poor), local health network of residence, as applying during the study period (i.e., northern metropolitan, central metropolitan, southern metropolitan, and for non-metropolitan areas to the south, country south, and FOR non-metropolitan areas to the north, country north), and diagnostic period (2000-2005 and 2006-2010) (see Tables 1-3). Operational definitions are available in previous publications.[5, 21, 22]

Time from diagnosis to treatments start was categorised in days for cross-tabulations with clinical and sociodemographic variables. Statistical analysis: The Spearman rank test was used to analyse ordinal clinical and sociodemographic predictors; Kruskal-Wallis ANOVA for multinomial predictors, and Whitney U test for predictors measured on a binary scale.[23, 24] For multiple logistic regression analyses of time as the outcome variable, time was reduced to a binary outcome of ">30 or ≤30 days" and ">60 or ≤60 days" respectively.[23, 24] The results were expressed as relative odds (i.e., odds ratios) with 95% confidence ranges. Disease-specific survival was analysed by time to treatment using Kaplan-Meier product-limit estimates (unadjusted) and Cox proportional hazards regression (adjusted for co-variables shown in Tables 2 and 3).[23, 24]

The decision to use disease-specific survival rather than relative survival was supported by evidence of similar results from these methods in South Australia at a population level.[5] Also, there were not lifetables (as required for relative survival) for patients referred to specialist clinics at these hospitals who often had extensive comorbidity and other complications.[5] Results are presented using conventional non-hierarchical analyses as they were similar by hospital setting without evidence of clustering.

*Public and Patient Involvement*

Registry development and workplans had substantial patient and consumer involvement through a formalized cancer planning and monitoring processes. Funders reviewing workplans included the Cancer Council South Australia through the Beat Cancer Project. Specialist clinics identify topics for review, of which some are based on/prompted by the questions raised by patients.

The use of the registry was approved by the Department of Health Research Ethics Committee and University of South Australia, both with active consumer involvement, thereby providing another level of public and consumer input.

This study involved the use of routinely collected registry data specifically authorized under state law and planned by clinical experts and consumers.

Participants all attended specialized gynaecological oncology clinics with whom we work. We work with these clinics in developing consumer messages for distribution to their patients and other relevant stakeholder groups.

**Results**

**A. Time from diagnosis to treatment start (colorectal)**

Unadjusted analyses – Time from diagnosis to treatment start.

Results are presented in Table 1 by treatment type.

*Surgery:* The proportion of surgical cases receiving surgery ≤60 days of diagnosis was 80% (59% ≤30 days). Time to first surgical treatment was associated with: (a) age at diagnosis ($p<0.001$) - shorter time for older patients; (b) sex ($p=0.003$) – shorter time for females; (c) local health network of residence ($p=0.026$) – longer time for northern metropolitan; (d) tumour sub-site ($p<0.001$) – longer time for rectum; and (e) diagnostic period ($p<0.001$) – longer time for 2006-2010. Significant associations were not found for other characteristics ($p\geq0.118$).

*Radiotherapy:* The proportion receiving radiotherapy whose treatment started ≤60 days was 59% (21% ≤30 days). Time to radiotherapy was associated with: (a) age at diagnosis ($p=0.042$) – longer time for older patients; and (b) tumour sub-site ($p<0.001$) – shorter time for rectum (note: radiotherapy was uncommon for colonic cancers). Significant associations were not found for other characteristics ($p\geq0.114$).

*Chemotherapy:* The proportion receiving chemotherapy whose treatment started ≤ 60 days was 56% (15% ≤30 days). Time to chemotherapy was associated with: (a) age at diagnosis ($p<0.001$) – longer time for older patients; (b) local health network of residence ($p=0.004$) – shorter time for northern metropolitan; (c) tumour sub-site ($p=0.018$) – shorter time for rectum; (d) stage ($p=0.003$) – shorter time for stages A and D (note: chemotherapy was uncommon for stage A); and (e) diagnostic period ($p<0.001$) – longer time for 2006-2010. Significant associations were not found by other characteristics ($p\geq0.120$).

*Any treatment (surgical cases):* The proportion receiving any treatment who did so starting ≤60 days of diagnosis was 87% (62% ≤30 days). Time to any treatment was associated with: (a) age at diagnosis (p=0.048) – although a clear age gradient was not evident; (b) sex (p=0.017) – shorter time for females; (c) local health network of residence (p<0.001) – longer time for the northern metropolitan area; (d) tumour sub-site (p<0.001) – longer time for rectum; and (e) diagnostic period (p<0.001) – longer time for 2006-2010. Significant associations were not found for other characteristics (p≥0.104).

Table 1: Unadjusted analysis of percentages of colorectal patients by treatment type and days from diagnosis to treatment start: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | | | | | Radiotherapy | | | | | | Chemotherapy | | | | | | Any Treatment | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | ≤30 | 31 - 60 | 61 - 90 | ≥90 | P value | n | ≤30 | 31 - 60 | 61-90 | ≥90 | P value | n | ≤30 | 31 - 60 | 61 - 90 | ≥90 | P value | n | ≤30 | 31-60 | 61-90 | ≥90 | P value |
| **All cases** | 1675 | 59.0 | 21.2 | 6.0 | 13.9 | - | 616 | 20.9 | 37.8 | 17.4 | 23.9 | - | 1556 | 15.3 | 40.7 | 24.6 | 19.5 | - | 1675 | 61.7 | 25.6 | 7.1 | 5.6 | - |
| **Age at diagnosis (years):** | | | | | | | | | | | | | | | | | | | | | | | | |
| <50 | 91 | 59.3 | 11.0 | 4.4 | 25.3 | <0.001 | 79 | 24.1 | 45.6 | 7.6 | 22.8 | 0.042 | 189 | 19.6 | 47.1 | 19.0 | 14.3 | <0.001 | 91 | 65.9 | 22.0 | 3.3 | 8.8 | 0.048 |
| 50 - 59 | 210 | 52.9 | 20.0 | 5.7 | 21.4 | | 118 | 22.0 | 40.7 | 17.8 | 19.5 | | 322 | 16.5 | 44.1 | 20.5 | 18.9 | | 210 | 58.7 | 28.4 | 7.7 | 5.3 | |
| 60 - 69 | 388 | 52.3 | 22.9 | 5.9 | 18.8 | | 188 | 20.7 | 35.6 | 12.3 | 22.3 | | 498 | 16.1 | 38.0 | 26.7 | 19.3 | | 388 | 57.1 | 29.1 | 6.8 | 7.0 | |
| 70 - 79 | 570 | 61.1 | 23.0 | 5.6 | 10.4 | | 175 | 20.1 | 36.0 | 16.0 | 28.0 | | 469 | 12.6 | 39.0 | 26.7 | 21.7 | | 570 | 61.9 | 26.2 | 7.2 | 4.8 | |
| 80+ | 416 | 65.4 | 20.0 | 7.0 | 7.7 | | 56 | 17.9 | 33.9 | 21.4 | 26.8 | | 78 | 11.5 | 38.5 | 28.2 | 21.8 | | 416 | 66.1 | 21.2 | 7.7 | 5.1 | |
| **Sex:** | | | | | | | | | | | | | | | | | | | | | | | | |
| Males | 893 | 56.0 | 21.9 | 5.9 | 16.1 | 0.003 | 400 | 19.8 | 38.5 | 18.0 | 23.8 | 0.567 | 910 | 16.3 | 39.0 | 23.8 | 20.9 | 0.649 | 893 | 59.2 | 27.3 | 7.1 | 6.4 | 0.017 |
| Females | 782 | 62.4 | 20.3 | 6.0 | 11.3 | | 216 | 23.1 | 36.6 | 16.2 | 24.1 | | 646 | 13.9 | 43.0 | 25.5 | 17.5 | | 782 | 64.4 | 23.8 | 7.0 | 4.7 | |
| **Socioeconomic:** | | | | | | | | | | | | | | | | | | | | | | | | |
| Low | 544 | 56.3 | 22.8 | 5.9 | 15.1 | 0.118 | 206 | 16.0 | 43.2 | 18.9 | 21.8 | 0.826 | 507 | 13.4 | 39.4 | 26.4 | 20.7 | 0.664 | 544 | 58.8 | 28.0 | 6.6 | 6.6 | 0.104 |
| Low-Med | 388 | 60.3 | 19.8 | 6.7 | 13.1 | | 137 | 24.8 | 36.5 | 16.8 | 21.9 | | 374 | 16.6 | 44.9 | 21.9 | 16.6 | | 388 | 62.7 | 24.9 | 7.0 | 5.4 | |
| Med-High | 345 | 58.6 | 21.4 | 5.5 | 14.5 | | 128 | 24.2 | 35.2 | 18.8 | 21.9 | | 320 | 16.3 | 40.0 | 27.5 | 16.3 | | 345 | 61.9 | 24.1 | 8.1 | 5.8 | |
| High | 398 | 61.8 | 20.1 | 5.8 | 12.3 | | 145 | 21.4 | 33.8 | 14.5 | 30.3 | | 355 | 15.8 | 38.6 | 22.0 | 23.7 | | 398 | 64.4 | 24.5 | 6.8 | 4.3 | |
| **Accessibility:** | | | | | | | | | | | | | | | | | | | | | | | | |
| High | 1353 | 58.9 | 20.4 | 6.4 | 14.3 | 0.584 | 475 | 22.1 | 36.4 | 16.8 | 24.6 | 0.764 | 1223 | 16.4 | 40.3 | 24.0 | 19.3 | 0.12 | 1353 | 61.8 | 25.1 | 7.3 | 5.9 | 0.992 |
| Med-High | 228 | 61.0 | 23.2 | 3.9 | 11.8 | | 94 | 17.0 | 44.7 | 21.3 | 17.0 | | 228 | 10.1 | 41.2 | 28.1 | 20.6 | | 228 | 62.1 | 27.3 | 6.6 | 4.0 | |
| Poor | 94 | 55.3 | 27.7 | 4.3 | 12.8 | | 47 | 17.0 | 38.3 | 14.9 | 29.8 | | 105 | 13.3 | 43.8 | 23.8 | 19.0 | | 94 | 58.5 | 29.8 | 5.3 | 6.4 | |
| **Local Health Network:** | | | | | | | | | | | | | | | | | | | | | | | | |
| Northern metro | 242 | 45.9 | 24.4 | 12.0 | 17.8 | 0.026 | 106 | 18.9 | 34.9 | 19.8 | 26.4 | 0.12 | 248 | 16.1 | 41.5 | 24.2 | 7.3 | 0.004 | 242 | 49.6 | 30.4 | 12.1 | 7.9 | <0.001 |
| Central metro | 618 | 61.7 | 20.2 | 6.8 | 11.3 | | 202 | 21.8 | 32.7 | 17.8 | 27.7 | | 495 | 17.8 | 36.6 | 26.5 | 19.2 | | 618 | 64.1 | 24.0 | 7.3 | 4.7 | |
| Southern metro | 417 | 64.3 | 17.7 | 3.4 | 14.6 | | 134 | 25.4 | 40.3 | 14.2 | 20.1 | | 426 | 16.7 | 42.7 | 20.7 | 20.0 | | 417 | 66.8 | 23.0 | 4.8 | 5.3 | |
| Country South | 155 | 52.9 | 27.7 | 1.9 | 17.4 | | 74 | 25.7 | 40.5 | 14.9 | 18.9 | | 159 | 8.8 | 41.5 | 28.3 | 21.4 | | 155 | 56.5 | 31.2 | 3.9 | 8.4 | |
| Country North | 241 | 60.2 | 22.0 | 5.0 | 12.9 | | 100 | 11.2 | 46.9 | 19.4 | 22.4 | | 228 | 11.0 | 44.5 | 25.1 | 19.4 | | 241 | 61.9 | 26.2 | 7.4 | 4.5 | |
| **Sub-site:** | | | | | | | | | | | | | | | | | | | | | | | | |
| Colon | 1098 | 65.0 | 22.1 | 4.9 | 7.9 | <0.001 | 86 | 11.6 | 12.8 | 14.0 | 61.6 | <0.001 | 898 | 13.1 | 40.2 | 27.4 | 19.3 | 0.018 | 1098 | 66.2 | 23.4 | 6.0 | 4.5 | <0.001 |
| Rectum | 577 | 47.5 | 19.4 | 8.0 | 25.1 | | 530 | 22.5 | 41.9 | 17.9 | 17.7 | | 658 | 18.2 | 41.3 | 20.7 | 19.8 | | 577 | 53.1 | 29.9 | 9.2 | 7.8 | |
| **ACPS stage:** | | | | | | | | | | | | | | | | | | | | | | | | |
| A | 280 | 53.9 | 30.4 | 7.9 | 7.9 | 0.460 | 50 | 24.0 | 44.0 | 14.0 | 18.0 | 0.114 | 47 | 25.5 | 36.2 | 21.3 | 17.0 | 0.003 | 280 | 55.4 | 32.5 | 7.9 | 4.3 | 0.114 |
| B | 654 | 61.5 | 23.9 | 4.7 | 9.9 | (A-D) | 147 | 21.1 | 38.8 | 21.8 | 18.4 | | 249 | 13.3 | 40.2 | 27.7 | 18.9 | | 654 | 63.3 | 26.7 | 5.7 | 4.3 | |
| C | 412 | 55.6 | 17.2 | 6.8 | 20.4 | | 231 | 16.0 | 40.7 | 21.2 | 22.1 | | 696 | 6.6 | 47.3 | 27.6 | 18.5 | | 412 | 58.9 | 25.6 | 8.8 | 6.8 | |
| D | 279 | 63.8 | 12.5 | 5.0 | 18.6 | | 162 | 25.9 | 29.0 | 10.5 | 34.6 | | 516 | 26.6 | 33.1 | 19.6 | 20.7 | | 279 | 68.6 | 17.3 | 6.5 | 7.6 | |
| (UK) | (50) | (51.5) | (18.2) | (12.1) | (18.2) | | (26) | (27.3) | (59.1) | (4.5) | (9.1) | | (48) | (26.9) | (34.6) | (15.4) | (23.1) | | (50) | (59.2) | (20.4) | (10.2) | (10.2) | |
| **Diagnosis years:** | | | | | | | | | | | | | | | | | | | | | | | | |
| 2000 - 2005 | 869 | 65.0 | 17.5 | 5.4 | 12.1 | <0.001 | 335 | 23.9 | 34.0 | 15.8 | 26.3 | 0.898 | 782 | 17.4 | 44.2 | 21.2 | 17.1 | <0.001 | 869 | 68.0 | 21.4 | 6.2 | 4.4 | <0.001 |
| 2006 - 2010 | 806 | 52.5 | 25.2 | 6.6 | 17.8 | | 281 | 17.4 | 42.3 | 19.2 | 21.0 | | 774 | 13.2 | 37.1 | 27.9 | 21.8 | | 806 | 54.8 | 30.3 | 8.0 | 7.0 | |

*Excludes cases where insufficient data on date of diagnosis (see "Methods")

ACPS- Australian Clinico-Pathological Staging; UK – unknown

Adjusted analyses – Predictors of treatment start >30 days from diagnosis.

Results are presented in Table 2 by treatment type.

*Surgery:* Significant predictors of time to surgical treatment >30 days included: (a) local health network of residence – relative odds (RO) of 0.55 (0.39, 0.76) for metropolitan central and 0.44 (0.31, 0.63) for metropolitan southern compared with metropolitan northern; (b) tumour site – RO for rectum of 2.07 (1.66, 2.57); (c) tumour stage – RO of 0.65 (0.45, 0.93) for stage D (distant metastasis) compared with stage A; (d) grade – RO for high grade (poorly differentiated) at 0.47 (0.25, 0.87) compared with low grade; and (e) diagnostic period – RO of 1.82 (1.48, 2.24) for 2006-2010.

*Radiotherapy:* Only tumour site was predictive of time to radiotherapy start >30 days – RO of 0.40 (0.19, 0.83) for rectum (note: radiotherapy was much less common for colonic than rectal cancers[5]).

*Chemotherapy:* Significant predictors of time to chemotherapy treatment start >30 days included: (a) tumour site – RO for rectum of 0.65 (0.48, 0.89); (b) tumour stage – RO for stage C of 3.93 (1.85, 8.36); and (c) diagnostic period – RO of 0.65 (0.48, 0.89) for 2006-2010.

*Any treatment (surgical cases):* Significant predictors of time to start of any treatment >30 days included: (a) local health network of residence – RO of 0.56 (0.40, 0.78) for metropolitan central and 0.44 (0.30, 0.63) for metropolitan southern compared with metropolitan northern; (b) tumour site – RO of 1.76 (1.41, 2.19) for rectum; (c) tumour stage – RO of 0.56 (0.38, 0.80) for stage D compared with stage A; (d) grade – RO of 0.52 (0.28, 0.95) for high compared with low grade; and (e) diagnostic period – RO of 1.86 (1.51, 2.29) for 2006-2010.

*Supplementary analyses with tumour stage classified as stage D vs A-C:* RO odds for surgery start >30 days was lower for stage D for surgery at 0.69 (0.51, 0.92), radiotherapy at 0.56 (0.35, 0.88), chemotherapy at 0.30 (0.22, 0.41), and any treatment (surgical cases) at 0.64 (0.47, 0.86). The RO for chemotherapy treatment start >30 days for stage D vs A-C was 0.45 (0.30, 0.67) for 2000-2005 compared with 0.16 (0.10, 0.27) for 2006-2010.

Table 2: Adjusted analysis of relative odds (95% CLs) of treatment for colorectal cancer starting >30 days of diagnosis by treatment type, stage, and socioeconomic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Chemotherapy | | Any treatment | |
|---|---|---|---|---|---|---|---|---|
| | **N** | **RO (95% CLs)** | **n** | **RO (95% CLs)** | **n** | **RO (95% CLs)** | **n** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 91 | 1.00 | 79 | 1.00 | 189 | 1.00 | 91 | 1.00 |
| 50 - 59 | 210 | 1.15 (0.68, 1.95) | 118 | 1.06 (0.52, 2.15) | 322 | 1.18 (0.71, 1.94) | 210 | 1.20 (0.70, 2.05) |
| 60 - 69 | 388 | 1.16 (0.71, 1.90) | 188 | 1.16 (0.60, 2.25) | 498 | 1.25 (0.79, 2.00) | 388 | 1.26 (0.76, 2.08) |
| 70 - 79 | 570 | 0.95 (0.59, 1.53) | 175 | 1.13 (0.58, 2.22) | 469 | 1.51 (0.93, 2.45) | 570 | 1.20 (0.73, 1.95) |
| 80+ | 416 | 0.82 (0.50, 1.34) | 56 | 1.09 (0.44, 2.73) | 78 | 2.20 (0.95, 5.10) | 416 | 1.04 (0.63, 1.72) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 893 | 1.00 | 400 | 1.00 | 910 | 1.00 | 893 | 1.00 |
| Female | 782 | 0.85 (0.69, 1.05) | 216 | 0.72 (0.47, 1.11) | 646 | 1.08 (0.80, 1.47) | 782 | 0.88 (0.72, 1.09) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 544 | 1.00 | 206 | 1.00 | 507 | 1.00 | 544 | 1.00 |
| Low-med | 388 | 1.17 (0.87, 1.59) | 137 | 0.73 (0.40, 1.33) | 374 | 0.92 (0.61, 1.39) | 388 | 1.14 (0.84, 1.54) |
| Med-high | 345 | 1.06 (0.78, 1.42) | 128 | 0.55 (0.30, 1.01) | 320 | 0.89 (0.58, 1.38) | 345 | 0.98 (0.73, 1.32) |
| High | 398 | 1.05 (0.77, 1.42) | 145 | 0.78 (0.42, 1.46) | 355 | 0.94 (0.61, 1.45) | 398 | 1.05 (0.77, 1.42) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 1353 | 1.00 | 475 | 1.00 | 1223 | 1.00 | 1353 | 1.00 |
| Med-high | 228 | 0.62 (0.36, 1.08) | 94 | 1.28 (0.45, 3.65) | 228 | 0.78 (0.30, 2.00) | 228 | 0.75 (0.43, 1.31) |
| Poor | 94 | 0.83 (0.45, 1.52) | 47 | 1.14 (0.36, 3.58) | 105 | 0.60 (0.23, 1.57) | 94 | 0.89 (0.49, 1.63) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 242 | 1.00 | 106 | 1.00 | 248 | 1.00 | 242 | 1.00 |
| Central metro | 618 | 0.55 (0.39, 0.76) | 202 | 0.90 (0.47, 1.72) | 495 | 0.99 (0.62, 1.57) | 618 | 0.56 (0.40, 0.78) |
| Southern metro | 417 | 0.44 (0.31, 0.63) | 134 | 0.68 (0.35, 1.33) | 426 | 0.84 (0.52, 1.35) | 417 | 0.44 (0.30, 0.63) |
| Country South | 155 | 0.86 (0.51, 1.43) | 74 | 0.52 (0.20, 1.38) | 159 | 2.40 (0.90, 6.39) | 155 | 0.78 (0.47, 1.30) |
| Country North | 241 | 0.78 (0.43, 1.43) | 100 | 1.60 (0.49, 5.18) | 228 | 2.03 (0.76, 5.39) | 241 | 0.73 (0.40, 1.34) |
| **Tumour site:** | | | | | | | | |
| Colon (ref.) | 1098 | 1.00 | 86 | 1.00 | 898 | 1.00 | 1098 | 1.00 |
| Rectum (incl. Rectosig.) | 577 | 2.07 (1.66, 2.57) | 530 | 0.40 (0.19, 0.83) | 658 | 0.65 (0.48, 0.89) | 577 | 1.76 (1.41, 2.19) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 280 | 1.00 | 50 | 1.00 | 47 | 1.00 | 280 | 1.00 |
| B | 654 | 0.87 (0.64, 1.17) | 147 | 1.03 (0.46, 2.28) | 249 | 1.78 (0.81, 3.90) | 654 | 0.80 (0.59, 1.08) |
| C | 412 | 0.99 (0.72, 1.37) | 231 | 1.56 (0.72, 3.38) | 696 | 3.93 (1.85, 8.36) | 412 | 0.89 (0.65, 1.23) |
| D | 279 | 0.65 (0.45, 0.93) | 162 | 0.71 (0.33, 1.55) | 516 | 0.83 (0.40, 1.71) | 279 | 0.56 (0.38, 0.80) |
| (UK) | (50) | (0.67, (0.31, 1.48)) | (26) | (0.93 (0.28, 3.06)) | (48) | (0.84 (0.27, 2.62)) | (50) | (0.65 (0.33, 1.25)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 58 | 1.00 | 25 | 1.00 | 37 | 1.00 | 58 | 1.00 |
| Mod diff. | 1212 | 0.68 (0.39, 1.20) | 429 | 1.34 (0.50, 3.58) | 1054 | 1.18 (0.43, 3.22) | 1212 | 0.72 (0.42, 1.25) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Poorly undiff. | 285 | 0.47 (0.25, 0.87) | 99 | 0.87 (0.62, 5.67) | 309 | 1.28 (0.45, 3.68) | 285 | 0.52 (0.28, 0.95) |
| (UK) | (120) | (1.48 (0.75, 2.95)) | (63) | (1.02 (0.33, 3.12)) | (156) | (0.41, (0.14, 1.17)) | (120) | (1.44 (0.74, 2.81)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 869 | 1.00 | 335 | 1.00 | 782 | 1.00 | 869 | 1.00 |
| 2006 - 2010 | 806 | 1.82 (1.48, 2.24) | 281 | 1.48 (0.97, 2.26) | 774 | 0.65 (0.48, 0.89) | 806 | 1.86 (1.51, 2.29) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff. – differentiated; undiff. - undifferentiated.

Adjusted analyses – Predictors of treatment start exceeding >60 days.

Results are presented in Table 3 by treatment type.

*Surgery:* Predictors of time to surgery >60 days for surgical cases included: (a) age at diagnosis – RO of 0.50 (0.29, 0.85) for 70-79 and 0.48 (0.27, 0.85) for 80+ compared with <50years ; (b) service accessibility – RO of 0.37 (0.18, 0.74) for medium-high and 0.40 (0.18, 0.89) for poor compared with high metropolitan service accessibility; (c) local health network of residence – RO of 0.58 (0.39, 0.86) for metropolitan central and 0.51 (0.33, 0.78) for metropolitan south compared with metropolitan north; (d) tumour site – RO for rectum of 3.39 (2.59, 4.42); (e) tumour stage – RO of 2.32 (1.54, 3.50) for stage C and 1.76 (1.11, 2.78) for stage D compared with stage A; (f) grade – RO of 0.51 (0.27, 0.98) for intermediate and 0.38 (0.18, 0.79) for high compared with low grade; and (g) diagnostic period – RO of 1.56 (1.20, 2.03) for 2006-2010.

*Radiotherapy:* Predictors of time to radiotherapy start >60 days for cases treated by radiotherapy included (a) older age at diagnosis – compared with age<50 years, RO of 2.22 (1.20, 4.09) for 60-69 years, 2.00 (1.08, 3.71) for 70-79 years, and 2.30 (1.04, 5.08) for 80+ years; and (b) tumour site – RO lower at 0.18 (0.11, 0.32) for rectum (note: radiotherapy was uncommon for colonic cases).

*Chemotherapy:* Predictors of time to chemotherapy treatment start >60 days for cases treated by chemotherapy included: (a) older age at diagnosis – compared with under 50 years, RO of 1.72 (1.20, 2.47) for 60-69 years, 1.83 (1.27, 2.64) for 70-79 years and 2.08 (1.19, 3.63) for 80+ years; and (b) tumour sub-site – RO for rectum of 0.78 (0.63, 0.97); and (c) diagnostic period – RO higher at 1.65 (1.33, 2.03) for 2006-2010.

*Any treatment (surgical cases):* Predictors of time to start of any treatment >60 days included: (a) local health network of residence – RO at 0.56 (0.36, 0.86) for metropolitan central and 0.42 (0.26, 0.69) for metropolitan south compared with metropolitan north; (d) tumour site – RO for rectum at 1.82 (1.34, 2.46); (d) grade – RO of 0.43 (0.20, 0.93) for high compared with low grade; and (e) diagnostic period – RO of 1.59 (1.18, 2.15) for 2006-2010.

*Supplementary analyses with tumour stage classified as stage D vs A-C:* The RO for surgery start >60 days did not vary, with RO for stage D of 1.18 (0.84, 1.66) for surgery, 0.92 (0.61, 1.38) for radiotherapy, 0.83 (0.66, 1.31) for chemotherapy, and 1.10 (0.74, 1.64) for any treatment (surgical cases).

Table 3: Adjusted analysis of relative odds (95% CLs) of treatment for colorectal cancer starting >60 days of diagnosis by treatment type, stage, and socio-demographic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Chemotherapy | | Any treatment (surgical cases) | |
|---|---|---|---|---|---|---|---|---|
| | **n** | **RO (95% CLs)** | **n** | **RO (95% CLs)** | **n** | **RO (95% CLs)** | **n** | **RO (95%** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 91 | 1.00 | 79 | 1.00 | 189 | 1.00 | 91 | 1.00 |
| 50 – 59 | 210 | 0.79 (0.94, 1.42) | 118 | 1.54 (0.80, 2.99) | 322 | 1.31 (0.89, 1.94) | 210 | 1.00 (0.54, |
| 60 – 69 | 388 | 0.73 (0.42, 1.27) | 188 | 2.22 (1.20, 4.09) | 498 | 1.72 (1.20, 2.47) | 388 | 1.11 (0.54, |
| 70 – 79 | 570 | 0.50 (0.29, 0.85) | 175 | 2.00 (1.08, 3.71) | 469 | 1.83 (1.27, 2.64) | 570 | 1.10 (0.55, |
| 80+ | 416 | 0.48 (0.27, 0.85) | 56 | 2.30 (1.04, 5.08) | 78 | 2.08 (1.18, 3.63) | 416 | 1.25 (0.61, |
| **Sex:** | | | | | | | | |
| Male (ref.) | 893 | 1.00 | 400 | 1.00 | 910 | 1.00 | 893 | 1.00 |
| Female | 782 | 0.79 (0.61, 1.04) | 216 | 0.93 (0.64, 1.35) | 646 | 0.93 (0.75, 1.15) | 782 | 0.89 (0.66, |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 544 | 1.00 | 206 | 1.00 | 507 | 1.00 | 544 | 1.00 |
| Low-med | 388 | 1.37 (0.94, 2.01) | 137 | 1.01 (0.61, 1.68) | 374 | 0.74 (0.55, 1.00) | 388 | 1.30 (0.84, |
| Med-high | 345 | 1.06 (0.73, 1.55) | 128 | 0.95 (0.57, 1.57) | 320 | 0.90 (0.67, 1.22) | 345 | 1.17 (0.77, |
| High | 398 | 1.05 (0.71, 1.55) | 145 | 1.21 (0.72, 2.01) | 355 | 0.94 (0.69, 1.27) | 398 | 1.07 (0.68, |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 1353 | 1.00 | 475 | 1.00 | 1223 | 1.00 | 1353 | 1.00 |
| Med-High | 228 | 0.37 (0.18, 0.74) | 94 | 1.36 (0.54, 3.39) | 228 | 1.23 (0.71, 2.12) | 228 | 0.47 (0.21, |
| Poor | 94 | 0.40 (0.18, 0.89) | 47 | 1.50 (0.57, 3.95) | 105 | 0.92 (0.50, 1.69) | 94 | 0.55 (0.23, |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 242 | 1.00 | 106 | 1.00 | 248 | 1.00 | 242 | 1.00 |
| Central metro | 618 | 0.58 (0.39, 0.86) | 202 | 0.84 (0.49, 1.44) | 495 | 1.24 (0.89, 1.74) | 618 | 0.56 (0.36, |
| Southern metro | 417 | 0.51 (0.33, 0.78) | 134 | 0.56 (0.31, 1.00) | 426 | 0.95 (0.67, 1.34) | 417 | 0.42 (0.26, |
| Country South | 155 | 0.80 (0.44, 1.48) | 74 | 0.43 (0.18, 1.02) | 159 | 1.16 (0.66, 2.04) | 155 | 0.80 (0.40, |
| Country North | 241 | 1.24 (0.59, 2.59) | 100 | 0.56 (0.21, 1.50) | 228 | 1.02 (0.56, 1.86) | 241 | 0.97 (0.42, |
| **Tumour site:** | | | | | | | | |
| Colon (ref.) | 1098 | 1.00 | 86 | 1.00 | 898 | 1.00 | 1098 | 1.00 |
| Rectum (incl. Rectosig.) | 577 | 3.39 (2.59, 4.42) | 530 | 0.18 (0.11, 0.32) | 658 | 0.78 (0.63, 0.97) | 577 | 1.82 (1.34, 2.46) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 280 | 1.00 | 50 | 1.00 | 47 | 1.00 | 280 | 1.00 |
| B | 654 | 1.21 (0.80, 1.82) | 147 | 1.28 (0.62, 2.64) | 249 | 1.24 (0.64, 2.40) | 654 | 0.88 (0.56, |
| C | 412 | 2.32 (1.54, 3.50) | 231 | 1.73 (0.87, 3.43) | 696 | 1.21 (0.65, 2.26) | 412 | 1.39 (0.88, |
| D | 279 | 1.76 (1.11, 2.78) | 162 | 1.37 (0.67, 2.82) | 516 | 1.01 (0.53, 1.90) | 279 | 1.19 (0.71, |
| (UK) | (50) | (1.43 (0.59, | (26) | (0.38 (0.10, | (48) | (0.97 (0.35, | (50) | (1.46 (0.63, |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 58 | 1.00 | 25 | 1.00 | 37 | 1.00 | 58 | 1.00 |
| Mod diff. | 1212 | 0.51 (0.27, 0.98) | 429 | 0.98 (0.40, 2.42) | 1054 | 1.08 (0.54, 2.19) | 1212 | 0.52 (0.23, |
| Poorly/undiff. | 285 | 0.38 (0.18, 0.79) | 99 | 1.18 (0.44, 3.14) | 309 | 1.10 (0.53, 2.29) | 285 | 0.43 (0.20, |
| (UK) | (120) | (1.09 (0.51, 2.37) | (63) | (0.66 (0.23, | (156) | (0.58 (0.27, | (120) | (0.99 (0.44, |
| **Diagnostic year:** | | | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 2000 - 2005 | 869 | 1.00 | 335 | 1.00 | 782 | 1.00 | 869 | 1.00 |
| 2006 - 2010 | 806 | 1.56 (1.20, 2.03) | 281 | 0.91 (0.64, 1.30) | 774 | 1.65 (1.33, 2.03) | 806 | 1.59 (1.18, |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

**B. Time from diagnosis to treatment start by sub-site (colon and rectum)**

Colon

Results are presented in supplementary Tables s1 & s2.

- Predictors of time to treatment start >30 days in adjusted analysis included: (a) *For surgery:* age 60-69 years compared with <50 years; northern metropolitan compared with central metropolitan and southern metropolitan; stage A compared with stages B and D; and diagnosis in 2006-2010; (b) *For radiotherapy:* no significant predictors (small numbers); (c) *For chemotherapy*: diagnosis in 2006-2010; (d) *For any treatment (surgical cases)*: northern metropolitan compared with central metropolitan and southern metropolitan areas; stage A compared with stages B and D; and diagnosis in 2006-2010.
- Predictors of time to treatment start of >60 days in adjusted analysis included: (a) *For surgery:* northern metropolitan compared with central and southern metropolitan areas; and more advanced stages C and D compared with stage A; (b) *For radiotherapy:* no significant predictors (small numbers); (c) *For chemotherapy*: diagnosis in 2006-2010; and (d) *For any treatment (surgical cases)*: northern metropolitan compared with central and southern metropolitan areas.

Rectum

Results are presented in supplementary Tables s3 & s4.

- Predictors of time to treatment start of >30 days in adjusted analysis included: (a) *For surgery:* age 70+ compared with <50 years; northern metropolitan compared with central and southern metropolitan areas; and diagnosis in 2006-2010; (b) *For radiotherapy:* low compared with medium-high socioeconomic status; and diagnosis in 2006-2010; (c) *For chemotherapy*: stage C; and (d) *For any treatment (surgical cases)*: northern metropolitan compared with southern metropolitan; and diagnosis in 2006-2010.
- Predictors of time to treatment start of >60 days in adjusted analysis included: (a) *For surgery:* younger age <50 compared with 70+ years; high service accessibility; northern metropolitan compared with central and southern metropolitan areas; and stage C compared with stage A; better differentiation; and 2006-2010; (b) *For radiotherapy:* aged over 50 years; (c) *For chemotherapy*: aged over 50 years; central metropolitan compared with northern metropolitan area; and stage C; and (d) *For any treatment (surgical cases)***:** low compared with higher grade lesions **;** and diagnosis in 2006-2010.

**C. Survival by time from diagnosis to treatment start**

*Unadjusted analysis*

Results are present in Table 4.

*Surgical treatment:* Compared with time to initial surgery >30 days, survival was lowest in the first two years from diagnosis when time to initial surgery was ≤30 days, but changed with further follow-up, such that by 10 years from diagnosis, survival was lower when time to initial surgery was >90 days compared with ≤ 30 days (p=0.017).

*Radiotherapy:* Survival was lowest in the first year when time to radiotherapy start was ≤30 days and reached statistical significance compared with a time of 61-90 days (p=0.009), but not with 31-60 days (p=0.295) or >90 days (p=0.280). After the first year of follow-up, survival was lowest for >90 days.

*Chemotherapy:* The survival pattern varied, with time to treatment ≤30 days having the lowest survival at each follow-up time.

*Any treatment (surgical cases):* Compared with time to initial treatment >30 days, survival was lowest in the first two years from diagnosis when time to initial surgery was ≤30 days, but changed with further follow-up, such that by 10 years from diagnosis, survival was lower when time to initial surgery was >90 days compared with ≤ 30 days (p=0.021).

Table 4: Unadjusted analysis of percentage survival (± standard error) from colorectal cancer by time from diagnosis (days) to commitment of specified treatment: South Australian major public hospitals, diagnoses 2000-2010*

| | | | Follow-up time from diagnosis (years) | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Specified treatment** | **Time (days)** | **Numbers of cases** | **1** | **2** | **3** | **4** | **5** | **10** |
| Surgical treatment | ≤30 | 988 | 85.4 ± 1.2 | 78.2 ± 1.5 | 72.9 ± 1.5 | 69.8 ± 1.6 | 67.5 ± 1.7 | 63.3 ± 2.0 |
| | 31 – 60 | 355 | 93.1 ± 1.6 | 89.9 ± 1.9 | 84.7 ± 2.2 | 81.9 ± 2.4 | 79.7 ± 2.5 | 75.9 ± 2.9 |
| | 61 – 90 | 100 | 92.9 ± 3.7 | 84.1 ± 4.6 | 77.5 ± 5.3 | 74.6 ± 5.5 | 72.6 ± 5.8 | 57.7 ± 9.0 |
| | >90 | 232 | 92.6 ± 2.2 | 82.4 ± 2.9 | 73.9 ± 3.2 | 67.4 ± 3.5 | 67.8 ± 3.7 | 50.4 ± 5.0 |
| Radiotherapy | ≤30 | 129 | 82.0 ± 4.0 | 70.0 ± 4.5 | 62.4 ± 4.7 | 58.0 ± 4.7 | 53.1 ± 4.8 | 44.4 ± 5.5 |
| | 31-60 | 233 | 87.0 ± 2.6 | 77.8 ± 3.0 | 68.2 ± 3.4 | 64.4 ± 3.5 | 61.3 ± 3.6 | 55.2 ± 4.4 |
| | 61 – 90 | 107 | 95.3 ± 3.2 | 87.5 ± 4.1 | 79.4 ± 4.7 | 73.8 ± 5.1 | 64.8 ± 5.5 | 49.0 ± 6.9 |
| | >90 | 147 | 87.6 ± 3.3 | 62.6 ± 4.3 | 53.1 ± 4.4 | 42.8 ± 4.3 | 39.2 ± 4.3 | 27.3 ± 4.3 |
| Chemotherapy | ≤30 | 238 | 68.0 ± 3.3 | 52.8 ± 3.4 | 43.4 ± 3.3 | 40.7 ± 3.3 | 38.4 ± 3.3 | 33.1 ± 3.4 |
| | 31 – 60 | 633 | 87.2 ± 3.4 | 73.8 ± 1.8 | 67.9 ± 2.0 | 62.8 ± 2.0 | 59.4 ± 2.1 | 49.5 ± 2.5 |
| | 61 – 90 | 382 | 92.3 ± 1.6 | 78.8 ± 2.3 | 68.9 ± 2.6 | 64.5 ± 2.7 | 59.8 ± 2.8 | 56.1 ± 3.0 |
| | >90 | 303 | 94.4 ± 1.7 | 78.1 ± 2.6 | 68.6 ± 2.9 | 63.2 ± 3.0 | 56.8 ± 3.1 | 45.1 ± 3.9 |
| Any treatment (surgical cases only) | ≤30 | 1030 | 85.5 ±1.1 | 78.1 ± 1.3 | 72.6 ± 1.4 | 69.4 ± 1.5 | 67.2 ± 1.6 | 63.1 ± 1.8 |
| | 31 – 60 | 428 | 93.4 ± 1.2 | 88.8 ± 1.5 | 83.8 ± 1.8 | 80.5 ± 2.0 | 78.0 ± 2.2 | 71.5 ± 2.9 |
| | 61 – 90 | 118 | 94.0 ± 2.2 | 85.9 ± 3.3 | 79.6 ± 3.9 | 74.8 ± 4.4 | 71.7 ± 4.7 | 56.6 ± 7.8 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | >90 | 99 | 91.7 ± 2.8 | 82.2 ± 3.9 | 71.9 ± 4.7 | 63.9 ± 5.2 | 57.1 ± 5.6 | 43.8 ± 8.2 |

* Kaplan-Meier product-limit estimate; date of censoring of live cases: Dec 31, 2012

*Adjusted analysis*

Results are presented in Table 5.

Because visual examination and interaction terms indicated a lack of proportionality of survival with time to treatment, results are split in Table 5 for follow-up of ≤2 and 3-10 years as mutually exclusive periods. Irrespective of treatment type, lower hazard ratios applied for periods ≤ 2 years with times to treatment of >30 days, after adjusting for age, sex, socioeconomic status, service accessibility, local health network of residence, tumour sub-site, stage, grade and diagnostic period. Hazard ratios similarly adjusted generally did not decrease across the 3-10 follow-up, suggesting no significant differences in conditional survival after two years for cases treated ≤30 days of diagnosis and >30 days. While there were higher hazard ratios for times of 61-90 and >90 days for 3-10-year follow-up from surgical treatment and radiotherapy respectively, statistical significance was only achieved for any treatment (surgical cases) when comparing time to treatment >90 compared with ≤30 days (p=0.022).

Table 5: Adjusted analysis of hazard ratios (95% confidence limits) of deaths from colorectal cancer by time from diagnosis (days) to commencement of specified treatment: South Australians major public hospitals, diagnoses 2000-2010*

| | | **Follow-up time from diagnoses** | | | |
|---|---|---|---|---|---|
| | | **≤ 2 years** | | **3-10 years** | |
| **Treatment** | **Time** | **Number of cases** | **Hazard ratios** | **Number of cases** | **Hazard ratios** |
| Surgical treatment | ≤30 | 988 | 1.00 | 714 | 1.00 |
| | 31 – 60 | 355 | 0.57 (0.40, 0.82) | 302 | 0.92 (0.62, 1.36) |
| | 61 – 90 | 100 | 0.59 (0.35, 1.02) | 76 | 1.13 (0.60, 2.10) |
| | >90 | 232 | 0.59 (0.41, 0.84) | 186 | 1.24 (0.85, 1.83) |
| Radiotherapy | ≤30 | 129 | 1.00 | 87 | 1.00 |
| | 31 – 60 | 233 | 0.85 (0.54, 1.32) | 173 | 1.00 (0.59, 1.72) |
| | 61 - 90 | 107 | 0.44 (0.23, 0.84) | 89 | 1.26 (0.70, 2.27) |
| | >90 | 147 | 0.62 (0.40, 0.98) | 89 | 1.60 (0.90, 2.85) |
| Chemotherapy | ≤30 | 238 | 1.00 | 120 | 1.00 |
| | 31 – 60 | 633 | 0.71 (0.55, 0.92) | 459 | 0.98 (0.66, 1.47) |
| | 61 – 90 | 382 | 0.51 (0.38, 0.70) | 289 | 1.01 (0.65, 1.55) |
| | >90 | 303 | 0.40 (0.30, 0.55) | 233 | 1.04 (0.68, 1.59) |
| Any treatment (surgical cases only) | ≤30 | 1030 | 1.00 | 744 | 1.00 |
| | 31 – 60 | 428 | 0.59 (0.43, 0.81) | 361 | 0.94 (0.66, 1.33) |
| | 61 – 90 | 118 | 0.48 (0.43, 0.81) | 95 | 1.11 (0.66, 1.89) |
| | >90 | 99 | 0.62 (0.37, 1.02) | 78 | 1.83 (1.12, 2.98) |

*4 Cox proportional hazards regression analyses (1 per treatment category), adjusting for age, sex, socioeconomic status, service accessibility, local health network, sub-site, stage, grade and diagnostic period (see tables 2 and 3); date of censoring of live cases: Dec 31, 2012.

## Discussion

The proportion of surgical patients receiving any treatment for their cancer ≤60 days of diagnosis was 87%, with 80% receiving surgical treatment within 60 days of diagnosis. This broadly accords with targets set by Cancer UK.[9] The proportion receiving radiotherapy who started this therapy ≤60 days of diagnosis was 59%, whereas the corresponding percentage having chemotherapies who started this therapy ≤60 days of diagnosis was 56%. The longer delay for radiotherapy and chemotherapy is consistent with their common use as adjuvant therapies following surgery.[5]

Longer time to surgery applied for cancers of the rectum than colon potentially reflecting the increased use of magnetic resonance imaging for rectal cancers, [25] and multimodal therapies,[5] which may have led to surgery delays through more multidisciplinary consultation and in some instances, neoadjuvant care.[26]

The longer time to surgery in 2006-2010 may also have been influenced by increasing use of multimodal therapies and more advanced diagnostics (e.g., magnetic resonance imaging), increasing the need for multidisciplinary consultation.[5, 26] While the introduction of population-based screening may have contributed, the screening program was still at an early phase of development, being phased in from 2006 to 2020. Following more complete implementation of bowel screening, there may be increased pressure on services which may increase times to surgery.[7, 8] The higher proportion with a time to surgery >60 days for stages C and D compared with stage A may reflect time taken for symptom control, multidisciplinary team consultation, and provision of neoadjuvant therapies.[27, 28] The proportion with a time to surgery >60 days was lower for higher grade tumours, potentially due to a greater perceived urgency of surgical intervention for more aggressive tumours.

The proportion receiving surgery, who did so >60 days from diagnosis, tended to be lower among those aged 70+ years, central and southern compared with northern metropolitan areas, those diagnosed in 2000-2005 compared with 2006-2010, and unexpectedly, those residing closer to metropolitan services. The reasons are unclear but may reflect differences in service busyness and patterns of patient and service demand.

Of those receiving radiotherapy, the proportion starting this therapy >60 days from diagnosis tended to be higher for ages ≥60 years than the <50 years. A similar pattern applied for chemotherapy. The reasons are not known. Perhaps a longer recovery time post-surgery has been allowed for older cases post-surgery before commencing adjuvant therapies, or longer delays occurring due to higher levels of frailty and comorbidity, and more common complications of surgery.

Radiotherapy was relatively uncommon for colon cancers, as recommended in clinical guidelines and optimal care pathways, [27, 28] but when it was provided, it tended to start later than for rectal cases. Similarly, chemotherapies tended to commence later for colon than rectal cancers. Further research is needed to determine the reasons for these patterns. Chemotherapies were less likely to commence >30 days from diagnosis for 2006-2010 diagnoses. Conversely chemotherapies were more inclined to occur >60 days from diagnosis in 2006-2010. Again, further research is needed to explain these patterns.

Where the time from diagnosis to treatment was >30 days, the risk of death occurring ≤2 years of diagnosis was lower. This was evident by therapy type after adjusting for stage and grade, and sociodemographic factors. It may reflect the triaging for priority treatment ≤30 days for cases with elevated comorbidity or other risk factors not recorded by the

registry. While a statistically significant U-shaped relationship of survival with time to treatment start was usually not apparent for specific therapies, as indicated in some other studies, [6, 17] the hazard ratio for 3-10 years was elevated when the time to first treatment was >90 days for surgical cases (p=0.022).

The present study has limitations. An opportunistic approach was taken in selecting cases where evidence was available on size of the gap between recorded diagnosis date and start of treatment. This raises questions about the representativeness of results. Nonetheless, results are similar to those of other recent studies in showing poorer short-term survival for cases receiving surgical treatment soon after diagnosis, and with a similar pattern applying for early treatment by radiotherapy and chemotherapies.[12, 14, 15, 17]

Results should not be construed as indicating a lack of benefit from early treatment, given likely confounding effects of patient selection in treatment scheduling. A positive feature was the approximate 87% of surgical cases receiving their first treatment (any treatment) ≤60 days and 80% treated surgically within this period (note: 83% for 2000-2005 and 78% for 2006-2010).[9] The indication of a temporal decline in this percentage warrants continued monitoring and investigation, particularly for patient groups where a higher proportion was not receiving surgical care ≤60 days of diagnosis (e.g., patients aged under 50 years, those with advanced disease, those with rectal cancer, and residents of the northern metropolitan rather than central or southern metropolitan areas).

The study highlights the benefit of linking diagnostic data to treatment data. Population-wide data linkage of population-based cancer registry, hospital, radiotherapy-centre, Medicare insurance and screening data, and potentially in the future, electronic medical record data and selected research databases will further strengthen the data infrastructure available for describing clinical management pathways and associations with survival across the population. Clinical registries will still be important for more detailed investigations for the sub-groups they cover, and for validating results of population-wide registry and administrative sources.

**Conclusions**

Baseline data for major public hospitals in South Australia in 2000-2010 indicate that for cases where the clinical registry recorded a diagnosis in advance of the surgery date, approximately 87% of surgical cases receiving any treatment and 80% of cases received their surgical treatment ≤60 days of diagnosis. This is broadly consistent with timeline targets of Cancer UK. Radiotherapy and chemotherapies generally started later, potentially reflecting their use as adjuvant therapies.

Adjusted analyses indicated lower survival up to two years from diagnosis when treatment commenced ≤30 days of diagnosis, potentially reflecting triaging for early care of cases with aggressive cancers and higher clinical complexity. By comparison, adjusted analyses did not show differences in survival for follow-up periods from diagnosis of 3-10 years where longer times to treatment applied, except for time to any treatment (surgical cases) of >90 days when survival was lower.

These results should not be interpreted as evidence of the importance or unimportance of delays, given selection factors in scheduling patient care. Treatment commencement was generally later in 2006-2010 than 2000-2005, possibly reflecting increased use of adjuvant therapies, increased use of multidisciplinary teams, and more advanced diagnostics (e.g., magnetic resonance imaging). Increased demand may be placed on timeliness of clinical services with extensions in population screening.

Further research is needed to optimize patient scheduling for better outcomes.

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**Informed consent**

Waiver of consent for use of de-identified data collected under authorisation of Part 7 of the South Australian Health Care Act. Note: large numbers of patients had deceased, and many are in the terminal stages of their cancer. Consent processes would be intrusive and would invalidate the database as an unbiased data source.

**Author contributions**

Study concept: DR, TP; Study design: DR TP, CK, RP, JM; Data acquisition: DB, KP; Quality control of data: DB, KP, KF; Data analysis: DR, KF ; Data interpretation: DR, CK, IO, DK, RP, JM, RJ, DW, DLW, TP; Report writing: DR, KF; Review of report: DR, CK, IO, DK, RP, JM, RJ, DW, DLW, TP, CM, CH, EB. All authors read and approved the final manuscript.

**Data sharing**

The data for this study are available through the South Australian Cancer Service and SA Cancer Registry. Restrictions to data use apply as conditions of legal authorization and data custodian and ethics approval.

**Competing interests**

D Roder reports grants from Cancer Council SA, during the conduct of the study.

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***Supplementary tables***

Table S1: Relative odds (95% CLs) of treatment for colon cancer starting >30 days of diagnosis by treatment type, stage, and socioeconomic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Chemotherapy | | Any treatment (surgical cases) | |
|---|---|---|---|---|---|---|---|---|
| | **n=1098** | **RO (95% CLs)** | **n=86** | **RO (95% CLs)** | **n=898** | **RO (95% CLs)** | **n=1098** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 53 | 1.00 | 13 | 1.00 | 109 | 1.00 | 53 | 1.00 |
| 50 - 59 | 116 | 1.61 (0.75, 3.46) | 14 | 1.03 (0.05, 21.46) | 176 | 0.84 (0.40, 1.76) | 116 | 1.28 (0.59, 2.78) |
| 60 - 69 | 226 | 2.10 (1.03, 4.28) | 20 | 2.82 (0.20, 40.71) | 273 | 0.91 (0.45, 1.83) | 226 | 1.86 (0.92, 3.80) |
| 70 - 79 | 396 | 1.65 (0.83, 3.28) | 28 | 3.49 (0.27, 45.20) | 292 | 1.37 (0.68, 2.79) | 396 | 1.55 (0.78, 3.09) |
| 80+ | 307 | 1.50 (0.74, 3.03) | 11 | NA | 48 | 2.52 (0.78, 8.17) | 307 | 1.43 (0.71, 2.88) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 562 | 1.00 | 56 | 1.00 | 491 | 1.00 | 562 | 1.00 |
| Female | 536 | 0.87 (0.67, 1.13) | 30 | 2.65 (0.27, 1.64) | 407 | 1.23 (0.79, 1.91) | 536 | 0.89 (0.68, 1.16) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 336 | 1.00 | 25 | 1.00 | 287 | 1.00 | 336 | 1.00 |
| Low-Med | 273 | 1.69 (0.99, 2.12) | 19 | 1.69 (0.09, 30.68) | 229 | 0.71 (0.39, 1.27) | 273 | 1.46 (1.00, 2.14) |
| Med-High | 224 | 1.31 (0.90, 1.90) | 20 | 7.01 (0.22, 223.56) | 185 | 0.93 (0.49, 1.78) | 224 | 1.28 (0.88, 1.88) |
| High | 265 | 1.12 (0.76, 1.67) | 22 | 1.37 (0.07, 27.36) | 197 | 0.85 (0.45, 1.62) | 265 | 1.09 (0.73, 1.62) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 899 | 1.00 | 66 | 1.00 | 716 | 1.00 | 899 | 1.00 |
| Med-High | 141 | 0.57 (0.28, 1.15) | 9 | NA | 127 | 0.41 (0.09, 1.97) | 141 | 0.57 (0.28, 1.16) |
| Poor | 58 | 0.71 (0.33, 1.57) | 11 | NA | 55 | 0.25 (0.05, 1.21) | 58 | 0.63 (0.28, 1.38) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 149 | 1.00 | 12 | 1.00 | 141 | 1.00 | 149 | 1.00 |
| Central metro | 421 | 0.49 (0.32, 0.75) | 33 | 0.31 (0.01, 6.39) | 291 | 0.85 (0.41, 1.76) | 421 | 0.48 (0.31, 0.73) |
| Southern metro | 281 | 0.39 (0.25, 0.63) | 16 | 0.58 (0.03, 11.80) | 252 | 0.83 (0.39, 1.78) | 281 | 0.37 (0.24, 0.60) |
| Country South | 88 | 0.69 (0.36, 1.33) | 10 | NA | 83 | 3.94 (0.70, 22.22) | 88 | 0.69 (0.36, 1.34) |
| Country North | 159 | 0.78 (0.37, 1.66) | 15 | NA | 131 | 2.42 (0.47, 12.36) | 159 | 0.76 (0.35, 1.63) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 169 | 1.00 | 3 | 1.00 | 12 | 1.00 | 169 | 1.00 |
| B | 471 | 0.67 (0.46, 0.98) | 20 | 43.60 (0.38, 49.56) | 130 | 1.60 (0.16, 16.54) | 471 | 0.65 (0.45, 0.95) |
| C | 252 | 0.69 (0.46, 1.06) | 21 | 24.12 (0.22, 26.91) | 409 | 1.76 (0.19, 16.48) | 252 | 0.66 (0.43, 1.00) |
| D | 180 | 0.54 (0.33, 0.86) | 39 | 4.39 (0.07, 27.89) | 320 | 0.24 (0.03, 2.17) | 180 | 0.44 (0.27, 0.72) |
| (UK) | (26) | (0.64 (0.26, 1.57)) | (3) | NA | (27) | (0.41 (0.04, 4.48)) | (26) | (0.58 (0.23, 1.43)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 38 | 1.00 | 5 | 1.00 | 18 | 1.00 | 38 | 1.00 |
| Mod diff. | 770 | 0.85 (0.43, 1.68) | 53 | 1.49 (0.11, 19.97) | 581 | 0.58 (0.07, 4.81) | 770 | 0.82 (0.41, 1.62) |
| Poorly/undiff. | 209 | 0.57 (0.27, 1.21) | 19 | 1.11 (0.06, 21.24) | 213 | 0.46 (0.05, 3.89) | 209 | 0.54 (0.26, 1.15) |
| (UK) | (81) | (1.87 (0.82, 4.26)) | (9) | NA | (86) | (0.13 (0.02, 1.11)) | (81) | (1.62 (0.71, 3.69)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 541 | 1.00 | 52 | 1.00 | 451 | 1.00 | 541 | 1.00 |
| 2006 - 2010 | 557 | 1.41 (1.09, 1.83) | 34 | 0.21 (0.03, 1.64) | 447 | 1.59 (1.02, 2.48) | 557 | 1.39 (1.07, 2.88) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; NA – not applicable; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

Table S2: Relative odds (95% CLs) of treatment for colon cancer starting >60 days of diagnosis by treatment type, stage, and socio-demographic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Chemotherapy | | Any treatment (surgical cases only) | |
|---|---|---|---|---|---|---|---|---|
| | **n=1098** | **RO (95% CLs)** | **n=86** | **RO (95% CLs)** | **n=898** | **RO (95% CLs)** | **n=1098** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 53 | 1.00 | 13 | 1.00 | 109 | 1.00 | 53 | 1.00 |
| 50 - 59 | 116 | 1.34 (0.51, 3.51) | 14 | 0.06 (0.00, 1.37) | 176 | 0.94 (0.57, 1.55) | 116 | 0.75 (0.25, 2.21) |
| 60 - 69 | 226 | 1.28 (0.51, 3.20) | 20 | 0.17 (0.01, 3.57) | 273 | 1.16 (0.73, 1.84) | 226 | 1.10 (0.41, 2.93) |
| 70 - 79 | 396 | 1.10 (0.45, 2.66) | 28 | 0.35 (0.02, 7.07) | 292 | 1.26 (0.80, 2.01) | 396 | 0.99 (0.38, 2.53) |
| 80+ | 307 | 1.00 (0.40, 2.47) | 11 | 0.30 (0.01, 7.36) | 48 | 1.60 (0.78, 3.29) | 307 | 1.01 (0.38, 2.65) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 562 | 1.00 | 56 | 1.00 | 491 | 1.00 | 562 | 1.00 |
| Female | 536 | 0.83 (0.57, 1.20) | 30 | 1.01 (0.23, 4.35) | 407 | 0.84 (0.64, 1.14) | 536 | 0.94 (0.62, 1.41) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 336 | 1.00 | 25 | 1.00 | 287 | 1.00 | 336 | 1.00 |
| Low-med | 273 | 1.58 (0.93, 2.71) | 19 | 0.40 (0.06, 2.51) | 229 | 0.75 (0.51, 1.10) | 273 | 1.65 (0.92, 2.98) |
| Med-high | 224 | 1.14 (0.68, 1.94) | 20 | 1.78 (0.26, 12.39) | 185 | 0.86 (0.58, 1.28) | 224 | 1.14 (0.64, 2.04) |
| High | 265 | 1.19 (0.67, 2.10) | 22 | 1.04 (0.15, 7.27) | 197 | 1.18 (0.78, 1.77) | 265 | 1.41 (0.75, 2.63) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 899 | 1.00 | 66 | 1.00 | 716 | 1.00 | 899 | 1.00 |
| Med-high | 141 | 0.54 (0.20, 1.42) | 9 | 8.99 (0.24, 331.28) | 127 | 1.57 (0.75, 3.30) | 141 | 0.45 (0.16, 1.25) |
| Poor | 58 | 0.65 (0.21, 1.97) | 11 | 3.90 (0.11, 141.05) | 55 | 0.83 (0.36, 1. 93) | 58 | 0.41 (0.12, 1.44) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 149 | 1.00 | 12 | 1.00 | 141 | 1.00 | 149 | 1.00 |
| Central metro | 421 | 0.56 (0.32, 0.98) | 33 | 0.16 (0.01, 1.98) | 291 | 0.91 (0.58, 1. 43) | 421 | 0.44 (0.24, 0.79) |
| Southern metro | 281 | 0.46 (0.25, 0.87) | 16 | 0.17 (0.01, 2.26) | 252 | 0.96 (0.61, 1.52) | 281 | 0.29 (0.14, 0.58) |
| Country South | 88 | 0.87 (0.36, 2.14) | 10 | 0.08 (0.00, 2.02) | 83 | 0.93 (0.43, 2.01) | 88 | 0.87 (0.34, 2.21) |
| Country North | 157 | 1.04 (0.38, 2.90) | 15 | 0.03 (0.00, 1.61) | 131 | 0.74 (0.33, 1. 76) | 157 | 1.23 (0.43, 3.57) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 169 | 1.00 | 3 | 1.00 | 12 | 1.00 | 169 | 1.00 |
| B | 471 | 1.02 (0.54, 1.91) | 20 | 0.79 (0.03, 23.99) | 130 | 0.43 (0.10, 1.74) | 471 | 0.80 (0.42, 1.53) |
| C | 252 | 2.34 (1.25, 4.40) | 21 | 0.57 (0.02, 18.97) | 409 | 0.29 (0.07, 1.15) | 252 | 1.54 (0.80, 2.96) |
| D | 180 | 2.25 (1.16, 4.35) | 39 | 0.94 (0.03, 26.42) | 320 | 0.26 (0.07, 1.03) | 180 | 1.49 (0.74, 2.98) |
| (UK) | (26) | (1.65 (0.51, 5.33)) | (3) | NA | (27) | (0.67 (0.14, 3.26)) | (26) | 1.35 (0.38, 4.76)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 38 | 1.00 | 5 | 1.00 | 18 | 1.00 | 38 | 1.00 |
| Mod diff. | 770 | 0.85 (0.31, 2.29) | 53 | 2.29 (0.31, 16.79) | 581 | 0.97 (0.35, 2.67) | 770 | 0.71 (0.26, 1.92) |
| Poorly/undiff. | 209 | 0.60 (0.20, 1.78) | 19 | 1.11 (0.12, 10.68) | 213 | 0.94 (0.33, 2.65) | 209 | 0.52 (0.17, 1.58) |
| (UK) | (81) | (1.84 (0.60, 5.62)) | (9) | NA | (86) | (0.40 (0.13, 1.20)) | (81) | (1.24 (0.39, 3.93)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 541 | 1.00 | 52 | 1.00 | 451 | 1.00 | 541 | 1.00 |
| 2006 - 2010 | 557 | 1.26 (0.87, 1.82) | 34 | 0.31 (0.08, 1.25) | 447 | 1.96 (1.48, 2.59) | 557 | 1.29 (0.86, 1.94) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; NA – not applicable; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

Table S3: Relative odds (95% CLs) of treatment for **rectal cancer** starting >30 days of diagnosis by treatment type, stage, and socioeconomic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Chemotherapy | | All treatment (surgical cases only) | |
|---|---|---|---|---|---|---|---|---|
| | **n=577** | **RO (95% CLs)** | **n=530** | **RO (95% CLs)** | **n=658** | **RO (95% CLs)** | **n=577** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 38 | 1.00 | 66 | 1.00 | 80 | 1.00 | 38 | 1.00 |
| 50 - 59 | 94 | 0.71 (0.31,1.62) | 104 | 1.30 (0.62,2.71) | 146 | 1.73 (0.86,3.48) | 94 | 1.03 (0.46, 2.29) |
| 60 - 69 | 162 | 0.57 (0.26,1.24) | 168 | 1.41 (0.71,2.79) | 225 | 1.57 (0.83,2.99) | 162 | 0.78 (0.37, 1.66) |
| 70 - 79 | 174 | 0.44 (0.20,0.95) | 147 | 1.35 (0.67,2.71) | 177 | 1.79 (0.90,3.54) | 174 | 0.83 (0.40, 1.76) |
| 80+ | 109 | 0.38 (0.17,0.85) | 45 | 1.40 (0.52,3.77) | 30 | 2.01 (0.58,6.97) | 109 | 0.70 (0.32, 1.55) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 331 | 1.00 | 344 | 1.00 | 419 | 1.00 | 331 | 1.00 |
| Female | 246 | 0.74 (0.52,1.07) | 186 | 0.68 (0.43,1.07) | 239 | 0.94 (0.61,1.45) | 246 | 0.79 (0.55, 1.14) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 208 | 1.00 | 181 | 1.00 | 220 | 1.00 | 208 | 1.00 |
| Low-med | 115 | 0.86 (0.50,1.45) | 118 | 0.80 (0.42,1.51) | 145 | 1.13 (0.62,2.07) | 115 | 0.81 (0.48, 1.37) |
| Med-high | 121 | 0.72 (0.44,1.19) | 108 | 0.50 (0.26,0.94) | 135 | 0.78 (0.43,1.42) | 121 | 0.63 (0.38, 1.03) |
| High | 133 | 1.06 (0.64,1.77) | 123 | 0.88 (0.45,1.70) | 158 | 1.00 (0.55,1.83) | 133 | 1.03 (0.62, 1.72) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 454 | 1.00 | 409 | 1.00 | 507 | 1.00 | 454 | 1.00 |
| Med-high | 87 | 0.74 (0.29,1.88) | 85 | 1.49 (0.50,4.44) | 101 | 1.00 (0.30,3.36) | 87 | 1.27 (0.49, 3.26) |
| Poor | 36 | 1.00 (0.36,2.76) | 36 | 1.25 (0.37,4.20) | 50 | 0.88 (0.25,3.05) | 36 | 1.58 (0.58, 4.33) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 93 | 1.00 | 94 | 1.00 | 107 | 1.00 | 93 | 1.00 |
| Central metro | 197 | 0.55 (0.31,0.97) | 169 | 0.86 (0.44,1.70) | 204 | 1.19 (0.64,2.23) | 197 | 0.61 (0.35, 1.06) |
| Southern metro | 136 | 0.40 (0.22,0.73) | 118 | 0.61 (0.30,1.23) | 174 | 0.89 (0.47,1.69) | 136 | 0.44 (0.24, 0.80) |
| Country South | 67 | 0.89 (0.37,2.10) | 64 | 0.45 (0.17,1.25) | 76 | 1.99 (0.62,6.41) | 67 | 0.70 (0.30, 1.63) |
| Country North | 84 | 0.67 (0.24,1.89) | 85 | 1.48 (0.44,5.02) | 97 | 2.61 (0.73,9.25) | 84 | 0.57 (0.20, 1.62) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 111 | 1.00 | 47 | 1.00 | 35 | 1.00 | 111 | 1.00 |
| B | 183 | 1.31 (0.79,2.18) | 127 | 0.90 (0.39,2.06) | 119 | 1.35 (0.57,3.21) | 183 | 1.18 (0.71, 1.95) |
| C | 160 | 1.65 (0.98,2.79) | 210 | 1.39 (0.63,3.10) | 287 | 3.81 (1.64,8.86) | 160 | 1.43 (0.85, 2.40) |
| D | 99 | 0.83 (0.46,1.51) | 123 | 0.67 (0.30,1.51) | 196 | 1.30 (0.58,2.95) | 99 | 0.79 (0.43, 1.44) |
| (UK) | 24 | (0.76 (0.28,2.06)) | 23 | (0.74 (0.23,2.39)) | 21 | (1.72 (0.44,6.71)) | 24 | (0.83 (0.30,2.28)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 20 | 1.00 | 20 | 1.00 | 19 | 1.00 | 20 | 1.00 |
| Mod diff. | 442 | 0.60 (0.21,1.68) | 376 | 1.59 (0.57,4.44) | 473 | 1.43 (0.43,4.70) | 442 | 0.78 (0.29, 2.08) |
| Poorly/undiff. | 76 | 0.52 (0.17,1.61) | 80 | 2.63 (0.81,8.52) | 96 | 2.14 (0.57,8.10) | 76 | 0.71 (0.24, 2.08) |
| (UK) | 39 | (1.38 (0.39,4.91)) | 54 | (1.31 (0.40,4.29)) | 70 | (0.72 (0.20,2.63)) | 39 | (1.57 (0.47,5.27)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 328 | 1.00 | 283 | 1.00 | 331 | 1.00 | 328 | 1.00 |
| 2006 - 2010 | 249 | 2.86 (1.98,4.12) | 247 | 1.76 (1.12,2.76) | 327 | 1.34 (0.88,2.04) | 249 | 3.09 (2.15, 4.43) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

Table S4: Relative odds (95% CLs) of treatment for **rectal cancer** starting >60 days of diagnosis by treatment type, stage, and socio-demographic factors: South Australian major public hospitals, 2000-2010 diagnoses*

| | Surgery | | Radiotherapy | | Chemotherapy | | All treatment (surgical cases only) | |
|---|---|---|---|---|---|---|---|---|
| | **n=577** | **RO (95% CLs)** | **n=530** | **RO (95% CLs)** | **n=658** | **RO (95% CLs)** | **n=577** | **RO (95% CLs)** |
| **Age at diagnosis (years):** | | | | | | | | |
| <50 (ref.) | 38 | 1.00 | 66 | 1.00 | 80 | 1.00 | 38 | 1.00 |
| 50 - 59 | 94 | 0.53 (0.23, 1.19) | 104 | 2.41 (1.12, 5.17) | 146 | 2.45 (1.26, 4.74) | 94 | 1.28 (0.42, 3.93) |
| 60 - 69 | 162 | 0.49 (0.23, 1.05) | 168 | 3.28 (1.60, 6.71) | 225 | 3.46 (1.85, 6.49) | 162 | 1.17 (0.40, 3.38) |
| 70 - 79 | 174 | 0.25 (0.12, 0.55) | 147 | 2.69 (1.30, 5.56) | 177 | 3.47 (1.82, 6.60) | 174 | 1.21 (0.42, 3.48) |
| 80+ | 109 | 0.26 (0.11, 0.59) | 45 | 3.05 (1.24, 7.51) | 30 | 3.95 (1.54, 10.17) | 109 | 1.62 (0.55, 4.80) |
| **Sex:** | | | | | | | | |
| Male (ref.) | 331 | 1.00 | 344 | 1.00 | 419 | 1.00 | 331 | 1.00 |
| Female | 246 | 0.77 (0.52, 1.13) | 186 | 0.91 (0.61, 1.36) | 239 | 1.04 (0.73, 1.46) | 246 | 0.89 (0.56, 1.42) |
| **Socioeconomic:** | | | | | | | | |
| Low (ref.) | 208 | 1.00 | 181 | 1.00 | 220 | 1.00 | 208 | 1.00 |
| Low-med | 115 | 1.29 (0.73, 2.27) | 118 | 1.11 (0.65, 1.92) | 145 | 0.61 (0.38, 0.98) | 115 | 1.05 (0.53, 2.02) |
| Med-high | 121 | 1.04 (0.61, 1.78) | 108 | 0.95 (0.55, 1.62) | 135 | 0.94 (0.59, 1.50) | 121 | 1.25 (0.67, 2.33) |
| High | 133 | 1.03 (0.60, 1.77) | 123 | 1.28 (0.74, 2.22) | 158 | 0.71 (0.44, 1.14) | 133 | 0.81 (0.41, 1.58) |
| **Accessibility:** | | | | | | | | |
| High (ref.) | 454 | 1.00 | 409 | 1.00 | 507 | 1.00 | 454 | 1.00 |
| Med-high | 87 | 0.26 (0.09, 0.73) | 85 | 1.12 (0.41, 3.01) | 101 | 0.98 (0.42, 2.25) | 87 | 0.49 (0.13, 1.86) |
| Poor | 36 | 0.30 (0.10, 0.89) | 36 | 1.53 (0.55, 4.31) | 50 | 1.08 (0.45, 2.62) | 36 | 0.83 (0.22, 2.67) |
| **Local Health Network:** | | | | | | | | |
| Northern metro (ref.) | 93 | 1.00 | 94 | 1.00 | 107 | 1.00 | 93 | 1.00 |
| Central metro | 197 | 0.53 (0.30, 0.95) | 169 | 0.88 (0.50, 1.55) | 204 | 1.70 (1.00, 2.89) | 197 | 0.71 (0.36, 1.38) |
| Southern metro | 136 | 0.49 (0.26, 0.91) | 118 | 0.55 (0.30, 1.03) | 174 | 0.84 (0.48, 1.44) | 136 | 0.63 (0.30, 1.30) |
| Country South | 67 | 0.69 (0.29, 1.61) | 64 | 0.45 (0.18, 1.14) | 76 | 1.36 (0.59, 3.17) | 67 | 0.71 (0.25, 2.05) |
| Country North | 84 | 1.25 (0.42, 3.74) | 85 | 0.70 (0.24, 2.01) | 97 | 1.10 (0.44, 2.72) | 84 | 0.67 (0.17, 2.71) |
| **ACPS stage:** | | | | | | | | |
| A (ref.) | 111 | 1.00 | 47 | 1.00 | 35 | 1.00 | 111 | 1.00 |
| B | 183 | 1.46 (0.82, 2.58) | 127 | 1.26 (0.59, 2.67) | 119 | 1.64 (0.69, 3.91) | 183 | 1.04 (0.53, 2.02) |
| C | 160 | 2.30 (1.30, 4.05) | 210 | 1.76 (0.86, 3.58) | 287 | 2.70 (1.19, 6.12) | 160 | 1.15 (0.60, 2.24) |
| D | 99 | 1.34 (0.69, 1.61) | 123 | 1.25 (0.59, 2.67) | 196 | 1.95 (0.85, 4.51) | 99 | 0.83 (0.37, 1.86) |
| (UK) | 24 | (1.65 (0.58, 4.67)) | 23 | (0.35 (0.09, 1.43)) | 21 | (1.33 (0.38, 4.68)) | 24 | (1.45 (0.46,4.58)) |
| **Grade:** | | | | | | | | |
| Well diff. (ref.) | 20 | 1.00 | 20 | 1.00 | 19 | 1.00 | 20 | 1.00 |
| Mod diff. | 442 | 0.30 (0.11, 0.82) | 376 | 1.25 (0.45,3.44) | 473 | 1.39 (0.50, 3.88) | 442 | 0.35 (0.13, 0.95) |
| Poorly/un-diff. | 76 | 0.26 (0.09, 0.79) | 80 | 1.70 (0.57,5.09) | 96 | 1.51 (0.50, 4.52) | 76 | 0.35 (0.11, 1.12) |
| (UK) | 39 | (0.64 (0.19, 2.18)) | 54 | (0.88 (0.28,2.84)) | 70 | (0.83 (0.27, 2.59)) | 39 | (0.76 (0.23,2.59)) |
| **Diagnosis year:** | | | | | | | | |
| 2000 - 2005 | 328 | 1.00 | 283 | 1.00 | 331 | 1.00 | 328 | 1.00 |
| 2006 - 2010 | 249 | 1.98 (1.35, 2.91) | 247 | 1.02 (0.70,1.50) | 327 | 1.21 (0.87, 1.69) | 249 | 2.01 (1.26, 3.18) |

*Derived from multivariate logistic regression (see "Methods")

RO – Relative odds; CLs – confidence limits; ref. – reference; ACPS- Australian Clinico-Pathological Staging; UK – unknown; diff – differentiated; undiff. - undifferentiated.

# Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

| | | Reporting Item | Page Number |
|---|---|---|---|
| Title | #1a | Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| Abstract | #1b | Provide in the abstract an informative and balanced summary of what was done and what was found | 2 |
| Background / rationale | #2 | Explain the scientific background and rationale for the investigation being reported | 3 |
| Objectives | #3 | State specific objectives, including any prespecified hypotheses | 4 |
| Study design | #4 | Present key elements of study design early in the paper | 4 |
| Setting | #5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 4 |

| | | | |
|---|---|---|---|
| Eligibility criteria | #6a | Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. | 4 |
| | #6b | For matched studies, give matching criteria and number of exposed and unexposed | n/a |
| Variables | #7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 4,5 |
| Data sources / measurement | #8 | For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable. | 4 |
| Bias | #9 | Describe any efforts to address potential sources of bias | 10, 12 |
| Study size | #10 | Explain how the study size was arrived at | 4 |
| Quantitative variables | #11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | 4,5 |
| Statistical methods | #12a | Describe all statistical methods, including those used to control for confounding | 4,5 |
| | #12b | Describe any methods used to examine subgroups and interactions | 4,5 |
| | #12c | Explain how missing data were addressed | 4 |
| | #12d | If applicable, explain how loss to follow-up was addressed | n/a |
| | #12e | Describe any sensitivity analyses | 4,5 |
| Participants | #13a | Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable. | tables 1-5 |
| | #13b | Give reasons for non-participation at each stage | n/a |
| | #13c | Consider use of a flow diagram | n/a |

| | | | |
|---|---|---|---|
| Descriptive data | #14a | Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable. | 5-14 |
| | #14b | Indicate number of participants with missing data for each variable of interest | n/a |
| | #14c | Summarise follow-up time (eg, average and total amount) | n/a |
| Outcome data | #15 | Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable. | 5-14 |
| Main results | #16a | Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 5-14 |
| | #16b | Report category boundaries when continuous variables were categorized | 5-14 |
| | #16c | If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | n/a |
| Other analyses | #17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses | n/a |
| Key results | #18 | Summarise key results with reference to study objectives | 14-15 |
| Limitations | #19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. | 15 |
| Interpretation | #20 | Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. | 14-16 |
| Generalisability | #21 | Discuss the generalisability (external validity) of the study results | 16 |
| Funding | #22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 17 |