

Rural–Urban Disparities in Time to Diagnosis and Treatment for Colorectal and Breast Cancer

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Abstract

Background: Longer cancer pathways may contribute to rural–urban survival disparities, but research in this area is lacking. We investigated time to diagnosis and treatment for rural and urban patients with colorectal or breast cancer in Victoria, Australia.

Methods: Population-based surveys (2013–2014) of patients (aged ≥ 40 , approached within 6 months of diagnosis), primary care physicians (PCPs), and specialists were collected as part of the International Cancer Benchmarking Partnership, Module 4. Six intervals were examined: patient (symptom to presentation), primary care (presentation to referral), diagnostic (presentation/screening to diagnosis), treatment (diagnosis to treatment), health system (presentation to treatment), and total interval (symptom/screening to treatment). Rural and urban intervals were compared using quantile regression including age, sex, insurance, and socioeconomic status.

Results: 433 colorectal (48% rural) and 489 breast (42% rural) patients, 621 PCPs, and 370 specialists participated. Compared with urban patients, patients with symptomatic colorectal cancer from rural areas had significantly longer total intervals at the 50th [18 days longer, 95% confidence interval (CI): 9–27], 75th (53, 95% CI: 47–59), and 90th percentiles (44, 95% CI: 40–48). These patients also had longer diagnostic and health system intervals (6–85 days longer). Breast cancer intervals were similar by area of residence, except the patient interval, which was shorter for rural patients with either cancer in the higher percentiles.

Conclusions: Rural residence was associated with longer total intervals for colorectal but not breast cancer; with most disparities postpresentation.

Impact: Interventions targeting time from presentation to diagnosis may help reduce colorectal cancer rural–urban disparities. *Cancer Epidemiol Biomarkers Prev*; 27(9); 1036–46. ©2018 AACR.

Introduction

In many countries, rural populations have poorer cancer outcomes than urban counterparts (1–4). In Australia, survival inequities have been found between rural and urban patients with colorectal cancer, but not breast cancer (5). Similar outcomes are seen in the Australian state of Victoria, where 5-year relative survival is 3% lower for patients with colorectal cancer living outside the capital city but no variation for women with breast cancer (6).

Several factors may drive inequities for rural patients with cancer. While improving access to high-quality specialist treatment has been the focus of most policy efforts in this area in Australia (7), delayed diagnosis and treatment for symptomatic and screen-detected patients may also be important (8–10), and partly explain differences by cancer type.

Mechanisms for prolonged cancer pathways for rural patients include attitudinal, awareness, and access differences. Attitudes such as stoicism, fatalism, and machismo, and a more self-reliant culture have been linked with delayed help-seeking in rural populations (11, 12). Differences in awareness of symptoms may also prolong the time to seek medical help, but studies examining geographic variation in symptom awareness are lacking. Differential access to primary care, diagnostic, and specialist services may also be important. In the United States, rural counties have a lower density of gastroenterologists, surgeons, and radiation oncologists than urban counties (13), while Victorian data shows rural general practitioners, primary care physicians (PCPs), have less direct access to colorectal cancer diagnostic tests (colonoscopy) but not breast cancer tests (X-ray and ultrasound; ref. 14). Reduced workforce and test availability could lead rural PCPs to exert a higher threshold before referral for cancer investigations (15).

Few studies have examined whether time to cancer diagnosis and treatment differs for rural and urban patients. A systematic review collating studies to 2003 found rural residence was associated with longer time from first symptom to presentation and PCP referral for colorectal cancer (16). However, more recent research from Scotland and Canada is equivocal (17–20). In Australia, only two studies report diagnostic intervals for rural

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patients with colorectal and breast cancer (11, 21, 22). While intervals were shorter for rural patients with breast than colorectal cancer, neither study included an urban comparison group, nor examined time to commencing treatment. Indeed, no Australian or international study has compared intervals for rural and urban patients across the full pathway from first symptom or screening test to treatment. Determining these intervals is important to understand whether, and when, rural-urban variation occurs. To address this research gap, we compared rural and urban patient intervals across the whole pathway to treatment for colorectal or breast cancer in Victoria, Australia.

Materials and Methods

Research setting

Victoria is the second most populous Australian state, with 6.3 million inhabitants, a quarter of whom live in regional or remote areas (23). It is the smallest state on the mainland, accounting for 3% of Australia's land mass at 227 010 km², approximately the size of England, Wales, and Scotland combined (<http://www.ga.gov.au/scientific-topics/national-location-information/dimensions/area-of-australia-states-and-territories>). Australians have universal access to primary care, with 85.7% of attendances involving no fee to the consumer (24). Public hospital care is free, while treatment in private hospitals is available via user-pays or private health insurance (PHI). Around half the adult population purchase PHI, although uptake is lower in regional (47%) and remote (43%) areas than major cities (56%) (25). Regardless of insurance status, access to specialist or hospital services is via referral from a qualified health practitioner, usually a PCP. Australia has national screening programs for colorectal and breast cancer. At the time of the study (2013–2014), people aged 50, 55, and 65, and aged 60 after July 2013, were eligible for colorectal cancer screening (fecal immunochemical test), and women aged 50–74 for mammographic screening every two years (26).

Ethics approval

Cancer Council Victoria's Human Research Ethics Committee approved the project (HREC1125). Written informed consent was obtained from all participants.

Study design and sample size

Data were collected as part of the International Cancer Benchmarking Partnership (ICBP), Module 4 (27). ICBP is an international research collaborative investigating factors driving cancer survival differences between countries (28). Module 4 examined time to cancer diagnosis and treatment in 10 jurisdictions using a cross-sectional, pen-and-paper survey of patients, their PCP and treating specialist, supplemented with registry data.

On the basis of Module 4 sample size calculations (27), additional patients were recruited for this study to conduct comparisons by residential location (200 rural; 200 urban). Details regarding the design and methodology of the international study are reported elsewhere (27); a summary is provided here.

Survey

Patient, PCP, and specialist surveys developed by the Module 4 team assessed key events and dates preceding a cancer diagnosis and treatment, routes to diagnosis, symptoms, and patient sociodemographics (27).

Recruitment, eligibility, and data collection

Recruitment was conducted from July 2013 to November 2014 through the Victorian Cancer Registry. Eligible patients were Victorian residents aged 40 years or more with a confirmed colorectal (International Classification of Diseases codes: C18.0–C18.9, C20.0–C20.9) or breast cancer (C50.0–C50.9). Exclusion criteria were: male breast cancer patients; patients with synchronous invasive primary cancers, or previous colorectal or breast cancer; metastatic cancer from elsewhere to the index organ; or non-Victorian residence. Patients were approached within 3 to 6 months of diagnosis to optimize response rates and limit recall bias.

After confirming eligibility with the patient's specialist, the registry mailed the study invitation, survey, and reply-paid envelope to the patient. Reminder letters were sent one month after the initial approach. Patients who returned surveys provided contact details for their PCP and first treating specialist. Surveys and the patient's consent were sent to the nominated doctor by the research team.

Data preparation

Survey data were supplemented with registry data on date of diagnosis and disease stage. Triangulation of data from various sources provided detailed information regarding pathways that might otherwise vary or be missing from a single source. To prioritize data sources and define diagnostic routes, intervals, and other variables, hierarchical data rules developed for Module 4 were followed (27).

Routes to diagnosis. Diagnostic route was determined using PCP and patient data. Data rules addressed disagreement between PCP and patient responses, multiple responses, and missing or "other" presentation (see Supplementary Data). For Victorian data, free-text comments were reviewed for all cases reporting a screen-detected cancer with symptoms, as well as cases reporting "investigation for another problem." Diagnostic route was dichotomized to symptomatic or screen-detected presentation. Symptomatic patients included those diagnosed via a healthcare professional, emergency presentation, incidental finding or other presentation (e.g., anemia).

Dates. Key dates, data source, and source hierarchy used to calculate intervals were:

- date first noticed a symptom or completed a screening test (patient data)
- date of first presentation to a healthcare provider (PCP then patient data)
- date of referral, transferring responsibility to another practitioner, that is, referral to specialist (PCP data)
- date of diagnosis (registry, specialist, PCP then patient data)
- date of first treatment (specialist then patient data)

Registry-based date of diagnosis was defined using an international standard for incidence date (<http://www.encl.eu/images/docs/recommendations/incideng.pdf>). Missing day in a date was imputed to "16" unless this resulted in an out-of-range (i.e., negative or very large) interval. Negative intervals were recoded to 0 days and intervals longer than a year to 365 days.

Variables

Outcome variables. The primary outcomes comprised six intervals: the patient, primary care, diagnostic, treatment, health system,

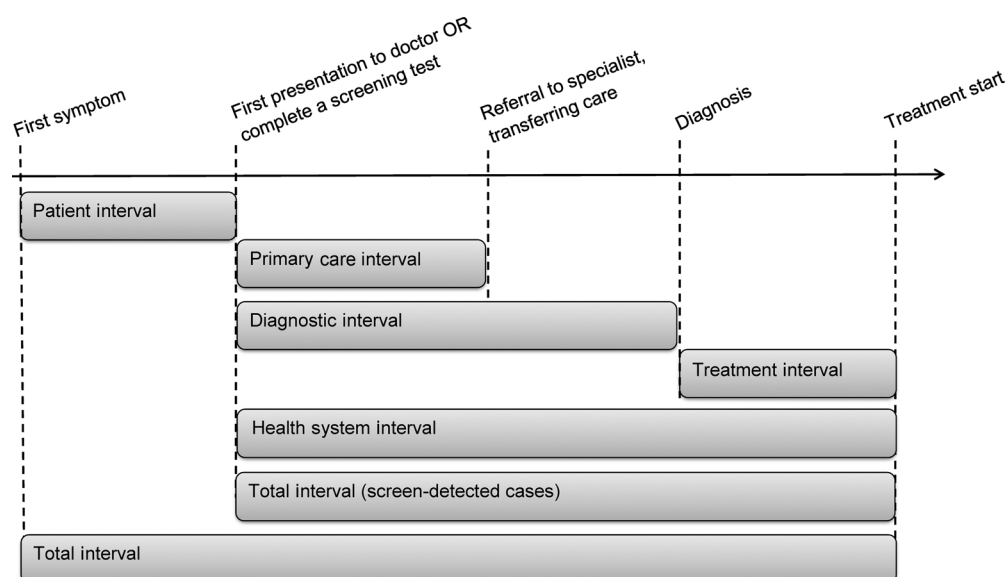


Figure 1.

Intervals in the pathway to cancer treatment. All intervals were calculated for symptomatic patients. For screen-detected patients, the diagnostic, treatment, and total (screen-detected cases) intervals were calculated.

and total intervals (Fig. 1). Time points and intervals were defined using Aarhus statement recommendations (29, 30).

Interval data were analyzed for two samples based on diagnostic route: (i) symptomatic patients (all six intervals), (ii) combined symptomatic and screen-detected patients (diagnostic, treatment, and total intervals). For screen-detected patients, the diagnostic interval was defined from date of performing a screening test to diagnosis, and the total interval from date of screening test to first treatment (Fig. 1).

Primary predictor variable. The primary predictor was residential location. Patient postcode was used to define area of residence using the Australian Statistical Geography Standard-Remoteness Areas index (31). The index defines areas based on road distance to service centers. As Victoria has few remote areas, a two-level variable was created: urban (major city) and rural (regional and remote categories).

Covariates. As socioeconomic status (SES) and health insurance uptake varies by residential location (25), these variables were included as covariates. SES was measured from patient's address using the area-based Index of Relative Socio-economic Disadvantage (IRSD; ref. 32). IRSD areas are classified using census data regarding income, employment, disability, family status, and education level. Three IRSD categories were defined with adequate cases for analysis representing the most disadvantaged (bottom 40% of the distribution); mid-level disadvantaged (41%–80%); and least disadvantaged areas (top 80%–100%).

Health insurance status was obtained from patient surveys and categorized as with PHI (private hospital cover) or without PHI (i.e., public patients). Age and sex were included in all models.

Analysis

Data for colorectal and breast samples were analyzed separately given differences in pathways and intervals for each cancer type

(33, 34). Descriptive statistics summarized and compared rural and urban participant demographic, clinical and health service characteristics. χ^2 tests compared categorical data and the Wilcoxon rank-sum test was used for continuous data.

Quantile regression. The relationship between residential location and intervals was determined using quantile regression. Quantile regression examines percentiles of an outcome variable distribution (35). In this study, we compared the median (50th), 75th, and 90th interval percentiles by residential location. As the length of the interval in days is a continuous measure that has been rounded, we used the "qcount" command (36, 37). To estimate model parameters, 1,000 jittered samples were produced and marginal effects with 95% confidence intervals (CIs) calculated at the mean for continuous and mode for categorical covariates. Complete cases (i.e., cases with interval and covariate data) were included in regression models.

An analysis stratified by insurance status was also conducted to explore the potential differential effect of PHI on rural and urban patient pathways. A second stratified analysis by sex in the colorectal cancer group examined the consistency of findings for men and women.

Data validity. After applying data rules, percentage positive agreement between patient and PCP-reported diagnostic route (symptomatic or screen-detected) and kappa (agreement adjusted for chance) were assessed for breast and colorectal data separately. Lin's concordance correlation coefficient (CCC; ref. 38) assessed the strength of agreement between dates from different sources. Source dates greater than a year apart were excluded as these were considered possible reporting errors or outliers.

Analyses were conducted in SPSS Statistics Version 20.0 and STATA Version 14.0. Statistical significance was set to 0.05 (two-tailed).

Results

Recruitment

Figure 2 shows the participant recruitment flow with reasons for nonparticipation. Response rates were higher in the breast (51%) than colorectal sample (41%). Analyses were performed on 433 colorectal and 489 breast respondents. Patient surveys were completed a median 5 months (interquartile range: 4–6) post-diagnosis, and 90% within 7 months of diagnosis.

PCPs completed surveys for 289 colorectal (74% response) and 332 breast (76% response) cancer patients. Specialists provided data for 144 colorectal (36% response) and 226 breast (51% response) cancer patients.

A comparison of disease and demographic characteristics between respondents and eligible patients showed few differences, with the exception that nonrespondents were more likely to be born in a non-English-speaking country and there were fewer colorectal cancer respondents aged over 70 than were eligible. When compared with all Victorian colorectal and breast cancer patients, respondents were younger, were less likely to have stage IV disease, and fewer colorectal respondents had rectal cancer. Patterns of response were consistent by residential location, except for rural colorectal cancer patients where there was no significant difference in the proportion born in English-speaking countries between those eligible and who responded.

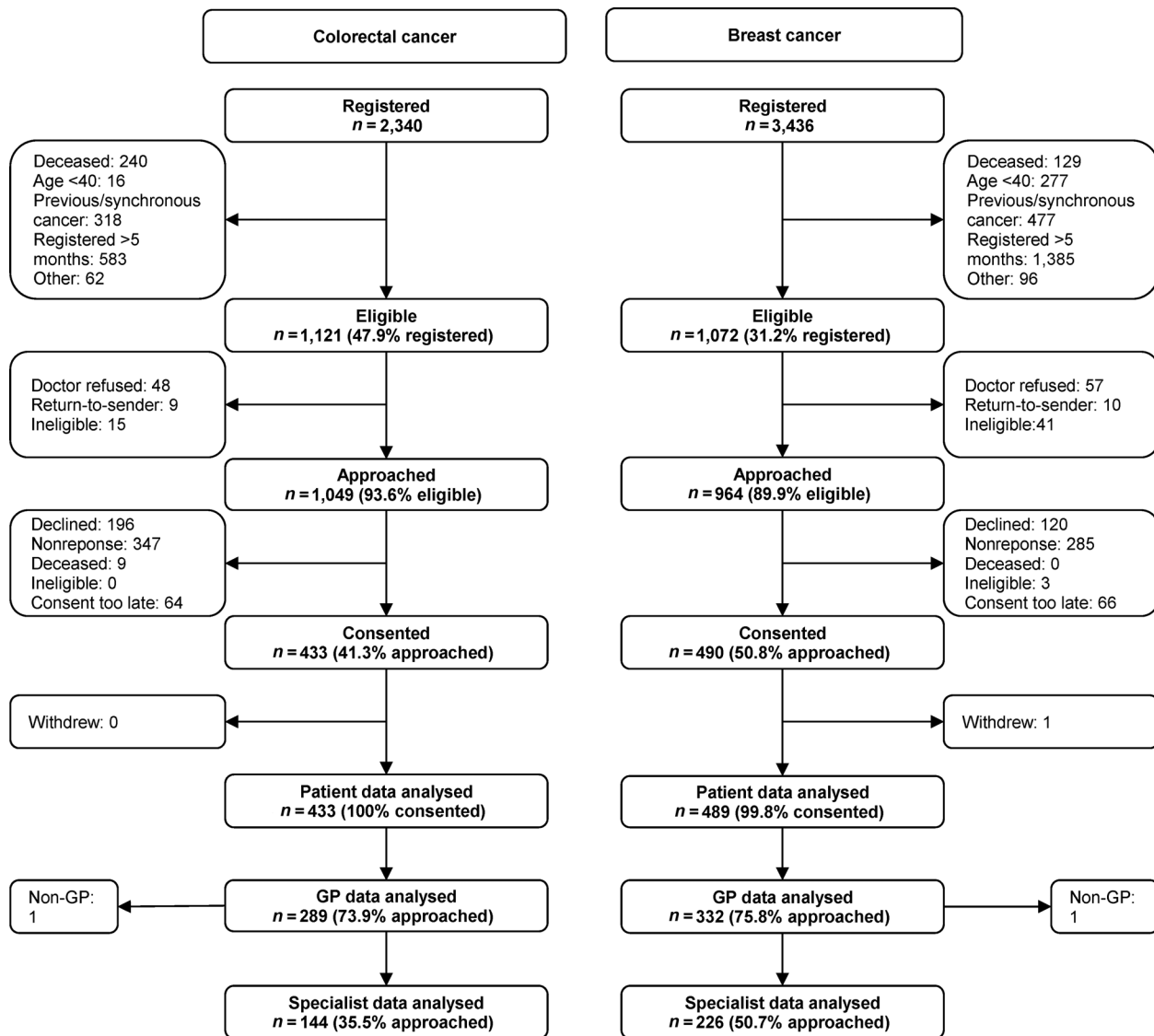


Figure 2.

Recruitment flowchart: colorectal and breast cancer patients. This flowchart differs from the ICBP Module 4 study due to recruitment of additional rural patients and inclusion of all cases regardless of time since diagnosis, resulting in higher numbers in the current study. The number of registered patients excludes cases registered when recruitment was paused then restarted due to new rural recruitment targets ($n = 155$ colorectal and $n = 2111$ breast cancer patients excluded), and a small number of cases approached by the registry for another study ($n = 1$ colorectal and $n = 80$ breast cancer patients).

Participant characteristics

Reflecting the over-sampled rural population, rural participants comprised 48% of colorectal and 42% of breast cancer participants (Table 1). For both cancer types, compared with urban participants, rural participants were more likely to live in areas of low SES ($P < 0.001$) and were less likely to have PHI ($P < 0.01$). Rural patients with breast cancer were also more likely to be married or have a partner than urban patients. Other clinical and demographic characteristics were similar across geographic areas for both cancers (Table 1).

Intervals

The median patient interval for symptomatic patients with colorectal cancer was 6 days longer for rural compared with urban patients (Table 2). While 90% of urban patients with colorectal cancer were diagnosed within 5 months of their first presentation, one in 10 rural patients waited longer than 6 months for a diagnosis. The median treatment interval was similar for rural and urban symptomatic patients with colorectal cancer. However, the median healthcare system and total intervals for these patients were longer for those living in rural than urban areas. For breast

Table 1. Characteristics for rural and urban study participants with colorectal and breast cancer

	Colorectal cancer			Breast cancer		
	Rural (n = 207)	Urban (n = 226)	Total (n = 433)	Rural (n = 205)	Urban (n = 284)	Total (n = 489)
Age						
Mean (SD)	66.9 (10.0)	66.4 (12.0)	66.6 (11.1)	60.3 (10.7)	60.0 (11.8)	60.0 (11.4)
Median (IQR)	67 (59, 74)	67 (58, 76)	67 (58, 75)	60 (51, 58)	58 (50, 68)	59 (50, 68)
Range	42–88	42–89	42–89	41–89	40–93	40–93
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gender						
Male	122 (59)	125 (55)	247 (57)	0 (0)	0 (0)	0 (0)
Female	85 (41)	101 (45)	186 (43)	205 (100)	284 (100)	489 (100)
Marital status						
Married/partner	150 (72)	174 (77)	324 (75)	160 ^a (78)	200 (70)	360 (74)
No partner	54 (26)	49 (22)	103 (24)	44 (21)	84 (30)	128 (26)
Missing	3 (1)	3 (1)	6 (1)	1 (0)	0 (0)	1 (0)
Education						
Basic (to secondary school)	124 ^a (60)	113 (50)	237 (55)	102 ^a (50)	113 (40)	215 (44)
Medium (vocational training)	49 (24)	53 (23)	102 (24)	57 (28)	78 (27)	135 (28)
High (university)	32 (15)	56 (25)	88 (20)	44 (21)	90 (32)	134 (27)
Missing	2 (1)	4 (2)	6 (1)	2 (1)	3 (1)	5 (1)
SES						
Most disadvantaged	110 ^c (53)	57 (25)	167 (39)	97 ^c (47)	52 (18)	149 (30)
Mid-disadvantaged	73 (35)	73 (32)	146 (34)	70 (34)	92 (32)	162 (33)
Least disadvantaged	24 (12)	96 (42)	120 (28)	36 (18)	139 (49)	175 (36)
Missing	0 (0)	0 (0)	0 (0)	2 (1)	1 (0)	3 (1)
Insurance						
No private health insurance	109 ^c (53)	76 (34)	185 (43)	86 ^b (42)	83 (29)	169 (35)
Private health insurance	98 (47)	150 (66)	248 (57)	119 (58)	201 (71)	320 (65)
Perceived health						
Very good/good	159 (77)	186 (82)	345 (80)	182 (89)	249 (88)	431 (88)
Fair, poor or very poor	45 (22)	36 (16)	81 (19)	21 (10)	35 (12)	56 (11)
Missing	3 (1)	4 (2)	7 (2)	2 (1)	0 (0)	2 (0)
Comorbidity						
No comorbidity	116 (56)	144 (64)	260 (60)	151 (74)	218 (77)	369 (75)
Medium (1–2)	84 (41)	76 (34)	160 (37)	53 (26)	65 (23)	118 (24)
High (3–4)	7 (3)	3 (1)	10 (2)	1 (0)	0 (0)	1 (0)
Missing	0 (0)	3 (1)	3 (1)	0 (0)	1 (0)	1 (0)
Presentation route						
Screen-detected	41 (20)	55 (24)	96 (22)	96 (47)	128 (45)	224 (46)
Symptoms	166 (80)	171 (76)	337 (78)	109 (53)	156 (55)	265 (54)
Primary cancer site						
Colon	168 (81)	189 (84)	357 (82)	n/a (n/a)	n/a (n/a)	n/a (n/a)
Rectum	39 (19)	37 (16)	76 (18)	n/a (n/a)	n/a (n/a)	n/a (n/a)
Stage						
Local (I & II)	120 (58)	143 (63)	263 (61)	172 (84)	249 (88)	421 (86)
Regional (III)	65 (31)	61 (27)	126 (29)	29 (14)	32 (11)	61 (12)
Advanced (IV)	21 (10)	19 (8)	40 (9)	3 (1)	2 (1)	5 (1)
Unknown	1 (0)	3 (1)	4 (1)	1 (0)	1 (0)	2 (0)
Treatment						
Surgery alone	106 (51)	135 (60)	241 (56)	24 (12)	40 (14)	64 (13)
Surgery & chemo	87 (42)	81 (36)	168 (39)	55 (27)	66 (23)	121 (25)
Surgery & RT	1 (0)	2 (1)	3 (1)	83 (40)	104 (37)	187 (38)
Surgery, chemo, RT	10 (5)	8 (4)	18 (4)	42 (20)	72 (25)	114 (23)
Chemo alone	1 (0)	0 (0)	1 (0)	0 (0)	0 (0)	0 (0)
Missing	2 (1)	0 (0)	2 (0)	1 (0)	2 (1)	3 (1)

NOTE: Significant difference by area of residence: ^a $P < 0.05$; ^b $P < 0.01$; ^c $P < 0.001$.

Abbreviations: IQR, interquartile range; n/a, not applicable; RT, radiotherapy.

Table 2. Interval percentiles (number of days) for colorectal and breast cancer patients by area of residence

Sample	Cancer	Interval	Rural residence			Urban residence		
			n (missing)	Median (IQR)	90th percentile	n (missing)	Median (IQR)	90th percentile
Symptomatic	CRC (n = 337)	Patient	151 (9%)	28 (2-86)	262	151 (12%)	22 (2-78)	276
		Primary care	85 (51%)	7 (0-47)	117	100 (42%)	9 (0-28)	74
		Diagnostic	149 (11%)	37 (10-104)	186	158 (8%)	27 (10-64)	160
		Treatment	160 (4%)	14 (0-30)	55	164 (4%)	14 (4-26)	44
		Health system	144 (15%)	60 (22-126)	201	153 (11%)	42 (27-88)	157
	Total	132 (20%)	99 (44-212)	365	130 (24%)	79 (35-165)	325	
	BC (n = 265)	Patient	107 (2%)	6 (1-31)	121	148 (5%)	10 (1-57)	171
		Primary care	66 (39%)	11 (7-22)	37	108 (31%)	7 (3-14)	35
		Diagnostic	107 (2%)	10 (5-21)	46	150 (4%)	12 (7-21)	45
		Treatment	107 (2%)	18 (11-28)	36	154 (1%)	13 (7-24)	37
Health system		105 (4%)	31 (21-44)	71	148 (5%)	28 (19-45)	67	
Total	101 (7%)	40 (29-93)	208	140 (10%)	45 (30-99)	192		
Symptomatic and screen-detected	CRC (n = 433)	Diagnostic	179 (14%)	37 (10-89)	156	190 (16%)	27 (9-63)	139
		Treatment	199 (4%)	16 (1-31)	51	216 (4%)	14 (2-26)	43
		Total	160 (23%)	92 (43-184)	360	161 (29%)	70 (28-133)	264
	BC (n = 489)	Diagnostic	190 (7%)	14 (6-27)	52	263 (7%)	15 (7-27)	41
		Treatment	201 (2%)	19 (11-28)	37	280 (1%)	15 (9-27)	37
		Total	182 (11%)	42 (29-70)	148	251 (12%)	43 (28-65)	127

NOTE: Median, 50th percentile; IQR, interquartile range - 25th, 75th percentiles; 90th percentile - 90% of patients have an interval length within this time. Abbreviations: BC, breast cancer; CRC, colorectal cancer.

cancer patients with symptoms, the median length of the patient, primary care and diagnostic interval was less than two weeks for both urban and rural patients, and the total interval was around 6 weeks across geographic areas.

For symptomatic patients, there were significant differences between colorectal and breast cancer interval distributions indicating faster time for breast patients in all (Wilcoxon rank-sum, $P < 0.001$) except the primary care ($P = 0.812$) and treatment intervals ($P = 0.347$). Results were similar for screen-detected and symptomatic cases combined, except the treatment interval was significantly shorter for colorectal than breast cancer cases ($P = 0.047$).

Quantile regression

Colorectal cancer. Setting age to its mean value and gender, SES, and insurance status to their modes, symptomatic rural patients had significantly longer total intervals at all percentiles compared with urban patients, ranging from 18 to 53 days longer (Table 3). While the patient interval was shorter for rural compared with

urban patients at the 90th percentile, the diagnostic and health system intervals were longer for rural patients at all percentiles, with statistically significant differences at the 90th percentile (i.e., the time by which 90% of patients were diagnosed or treated after presentation). The primary care interval was also longer in the higher percentiles (by 7 and 20 days for 75th and 90th percentiles, respectively), and rural patients had a 12-day longer treatment interval at the 90th percentile. A similar pattern of rural-urban variation was observed in the diagnostic, treatment and total intervals when symptomatic and screen-detected cases were combined.

Breast cancer. In adjusted analyses, rural residence was associated with a 37 and 50-day shorter patient interval at the 75th and 90th percentiles, respectively (Table 3). There was minimal variation in the other intervals for symptomatic women, and no statistically significant variation by area of residence when data for symptomatic and screen-detected patients were combined.

Table 3. Difference in days for rural patients (urban reference group) at the 50th, 75th, and 90th interval percentiles

	n	Colorectal cancer			Breast cancer			
		50th Days diff. (95% CI)	75th Days diff. (95% CI)	90th Days diff. (95% CI)	50th Days diff. (95% CI)	75th Days diff. (95% CI)	90th Days diff. (95% CI)	
Symptomatic								
Patient interval	302	7 (-31-46)	4 (-11-20)	-58 (-87 to -29)	254	-2 (-5-2)	-37 (-48 to -25)	-50 (-54 to -46)
Primary care interval	185	-4 (-37-29)	7 (4-10)	20 (-24-65)	174	3 (-1-7)	1 (-1-3)	-4 (-116-109)
Diagnostic interval	307	6 (-14-27)	15 (-15-45)	54 (48-61)	256	-3 (-5-0)	-1 (-9-7)	3 (-3-8)
Treatment interval	324	-1 (-6-3)	1 (-2-4)	12 (7-18)	259	4 (-4-12)	4 (-11-18)	3 (-12-17)
Health system interval	297	7 (3-11)	23 (-72-118)	85 (60-111)	252	2 (-1-6)	1 (-1-4)	3 (-19-25)
Total interval	262	18 (9-27)	53 (47-59)	44 (40-48)	239	-2 (-24-20)	-13 (-25-0)	0 (-4-5)
Symptomatic and screen-detected								
Diagnostic interval	369	8 (0-16)	6 (-29-40)	56 (-93-205)	451	-1 (-3-2)	-1 (-12-10)	12 (-3, 26)
Treatment interval	415	-1 (-5-3)	1 (-2-5)	10 (3-17)	478	1 (-1-4)	3 (-4-9)	3 (-1-8)
Total interval	321	7 (-8-21)	32 (14-51)	64 (40-87)	430	-2 (-11-7)	-5 (-10-0)	-17 (-36-3)

NOTE: Quantile regression marginal effects are calculated at the mean of age and mode for sex (colorectal), socioeconomic and insurance status. Bold indicates $P < 0.05$.

Abbreviation: Diff., difference.

Stratified analysis

Quantile regression analyses stratified by insurance status showed a similar pattern of results for patients with colorectal cancer (Table 4). While rural–urban differences were reduced with PHI, regardless of insurance status, symptomatic patients from rural areas had longer diagnostic and health system intervals in the 90th percentile. The total interval was also longer for rural than urban patients with colorectal cancer, regardless of PHI. In symptomatic patients without PHI, rural patients had a longer primary care interval than urban patients. In symptomatic patients with PHI, rural patients had longer treatment intervals in the higher percentiles than urban patients.

Consistent with the main analysis, for symptomatic women with breast cancer regardless of insurance status, women from rural areas had shorter patient intervals in the higher percentiles than urban women. Other intervals for symptomatic women with PHI were similar by residential location, although rural women had significantly longer diagnostic interval at the 75th percentile (seven days), health system, and total intervals at the 90th percentiles (4 and 68 days, respectively). Symptomatic women with breast cancer from rural areas without PHI had longer primary care interval, ranging 6–39 days longer, compared with urban women without PHI. Nonetheless, the total interval was shorter for rural than urban women without PHI in the higher percentiles.

In analyses stratified by sex in the colorectal cancer group, rural–urban differences were generally consistent for men and women, supporting the main findings of longer intervals for rural patients, particularly in the diagnostic, health system and total intervals (Supplementary Table S1).

Data validity

Agreement for diagnostic route between patient and PCP was almost perfect as defined by Landis and Koch (positive agreement, >95%; kappa > 0.85; ref. 39). Concordance for date of first presentation between patient and PCP was poor for colorectal cancer (CCC = 0.87), but substantial for breast cancer (CCC = 0.96; ref. 40). For each cancer type, concordance was substantial for date of diagnosis (patient and cancer registry: CCC ≥ 0.99) and almost perfect for first treatment (patient and specialist: CCC > 0.99).

Discussion

We compared multiple intervals to treatment for rural and urban patients with two cancers that differ in rural–urban survival inequities: colorectal and breast cancer. For colorectal cancer, where a survival difference exists, rural patients had a longer interval from first symptom or screening test to treatment compared with urban patients, ranging from 2.5 weeks to 2 months longer over multiple quantiles. The most important delays occurred after first presentation, with the diagnostic interval likely contributing most to prolonged pathways. While our findings also suggest that rural patients without PHI may be particularly vulnerable to prolonged diagnostic pathways, rural–urban differences were evident regardless of insurance status. In contrast, there were minimal differences in time to care for rural and urban women with or without insurance who had breast cancer, a cancer with no rural–urban survival inequities. Furthermore, rural–urban differences identified for colorectal cancer were broadly similar for women and men, demonstrating that sex does not explain rural disadvantage for these patients.

Consistent with other studies, we found that pathways were generally quicker for breast than colorectal cancer (33, 34). However, to our knowledge, few studies have specifically focused on associations between rurality and time to care, and none have compared intervals for rural and urban patients from first symptom or screening test to treatment. Comparison with previous research is complicated by the lack of studies examining the entire pathway, variable definitions of rurality, and inconsistencies in covariates included in analyses. Perhaps unsurprisingly, and as noted by others, findings from previous studies have been mixed (41). While in our study rural patients with colorectal cancer had a longer time from presentation to diagnosis and treatment (diagnostic and health system interval), Scottish and French studies found no such association (17, 42) and a Canadian study found the opposite—rural patients had greater odds of being diagnosed within four weeks compared with urban patients (43). Some studies report longer intervals for rural patients than we found, such as longer median patient and diagnostic intervals in Western Australia (11), and treatment interval for rural colon cancer patients in Ontario (19).

Results from previous research in breast cancer are similarly mixed. For example, another Australian study also found no rural–urban variation in the patient interval, but unlike our study, symptomatic and screen-detected rural women were more likely to have a diagnostic interval >30 days than urban women (44). A U.S. study found no geographic differences in time from mammography to treatment for women in the National Breast and Cervical Cancer Early Detection Program, however, rural women had a quicker diagnostic interval than metropolitan women (45). Differences between studies may relate to methodologic variation, but differences in geography, culture, and health system context may also be important. Within Australia, Victoria is a small state, with greater concentration of populations, few areas classified as remote and less medical workforce shortages than other states.

Our unexpected finding that rural patients sought help for symptoms more quickly than urban patients, particularly women with breast cancer, contrast findings from previous studies showing rural attitudes and self-reliance can delay help-seeking (11, 12). Our results suggest that stereotypical rural attitudes may be less prevalent in rural Victoria. This is consistent with qualitative research undertaken in Victoria that found no difference in attitudinal barriers to help-seeking for regional and urban patients with colorectal or breast cancer (46). Rural women with breast cancer in the current study were more likely to have a partner than urban women. Greater social support has been linked with quicker help-seeking, though evidence in breast cancer is limited (47). Further research is required to explore why the patient interval varies for rural populations in different national and international contexts.

The finding of longer pathways for rural patients with colorectal but not breast cancer is consistent with geographic variation in survival observed for these cancers in Australia. While further research should investigate the clinical significance of these results, there is increasing evidence that prolonged pathways are associated with colorectal and breast cancer mortality (8–10). Minimizing delay is also important to alleviate patient anxiety associated with prolonged waiting times (48). By using a pathways approach, we identified which period of the pathway should be the focus of policy interventions: the diagnostic interval.

Table 4. Difference in days for rural patients (urban reference group) stratified by private health insurance status at 50th, 75th, and 90th interval percentiles

	Colorectal cancer				Breast cancer			
	50 th Days diff. (95% CI)	75 th Days diff. (95% CI)	90 th Days diff. (95% CI)	n	50 th Days diff. (95% CI)	75 th Days diff. (95% CI)	90 th Days diff. (95% CI)	n
Symptomatic								
Patient interval	No PHI 138	24 (3-44)	16 (-16-49)	-1 (-11-9)	90	0 (-2-3)	3 (-20-25)	-197 (-200 to -194)
	PHI 164	1 (-10-12)	-6 (-11 to -1)	-13 (-18 to -8)	164	-3 (-17-11)	-23 (-42 to -4)	-48 (-52 to -45)
Primary care interval	No PHI 78	8 (3-12)	42 (37-48)	58 (50-65)	55	6 (4-8)	11 (9-14)	39 (6-72)
	PHI 107	-2 (-7-4)	-1 (-5-2)	4 (0-9)	119	2 (-2-6)	1 (-2-5)	-3 (-14-9)
Diagnostic interval	No PHI 135	10 (-40-59)	30 (23-37)	54 (21-87)	89	3 (0-7)	-4 (-18-9)	29 (24-34)
	PHI 172	-3 (-5-0)	-5 (-11-2)	18 (14-22)	167	-2 (-5-0)	0 (-7-8)	-5 (-10-1)
Treatment interval	No PHI 150	-2 (-15-12)	1 (-15-17)	5 (0-10)	85	-4 (-7 to -1)	-5 (-8 to -1)	-4 (-7-0)
	PHI 174	0 (-6-5)	6 (2-11)	16 (10-23)	167	6 (-4 to 15)	7 (3-11)	7 (-1-15)
Health system interval	No PHI 131	7 (2-12)	43 (36-51)	113 (92-135)	85	0 (-4-4)	3 (-7-12)	5 (0-9)
	PHI 166	7 (-4-18)	3 (-6-11)	25 (16-34)	167	3 (-3-9)	2 (-15-19)	4 (0-8)
Total interval	No PHI 119	10 (6-14)	42 (35-49)	68 (60-76)	82	11 (-1-22)	-62 (-84 to -41)	-76 (-87 to -65)
	PHI 143	25 (9-41)	42 (30-54)	4 (-2-11)	157	-3 (-16-10)	-13 (-26-0)	68 (52-84)
Symptomatic and screen-detected								
Diagnostic interval	No PHI 156	3 (-7-12)	22 (-3-47)	31 (4-58)	158	1 (-4-6)	3 (-1-7)	32 (23-42)
	PHI 213	5 (-12-21)	-4 (-43-35)	32 (26-38)	293	-1 (-4-1)	-4 (-27-19)	-7 (-11 to -3)
Treatment interval	No PHI 177	-4 (-18-11)	-1 (-6-3)	10 (-7-27)	160	-4 (-8-1)	-4 (-10-2)	-1 (-8-5)
	PHI 238	2 (0-5)	8 (5-11)	14 (3-24)	318	6 (3-9)	6 (2-10)	4 (-78-86)
Total interval	No PHI 138	1 (-10-11)	20 (12-28)	106 (103-110)	149	3 (-8-14)	1 (-10-13)	-146 (-154 to -137)
	PHI 183	14 (1-27)	54 (38-71)	21 (-1-42)	281	-1 (-8-6)	-6 (-15-2)	14 (-17-45)

NOTE: Quantile regression marginal effects are calculated at the mean of age and mode for sex (colorectal only) and socioeconomic status. Bold indicates $P < 0.05$. Abbreviations: Diff., difference; PHI, private health insurance.

As noted earlier, longer diagnostic intervals may be due to variation in access to diagnostic tests (13, 14). Interventions to improve colonoscopy access include novel referral systems and alternative provider models. In the United Kingdom, rapid diagnostic pathways using direct access or nurse-based triage reduced colonoscopy waiting time and were cost-effective (49, 50). Alternative colonoscopy provider models may also improve access, with both nurse and PCP-delivered endoscopy having evidence of quality and safety (51, 52), including in rural areas (53).

National policies have also been shown to reduce time to cancer diagnosis and improve patient outcomes. These include cancer pathway and waiting time policies in the United Kingdom (54, 55), and Denmark's "three-legged strategy" where diagnostic centers, fast-track pathways, and low-risk clinics, public reporting of waiting times and punitive measures for noncompliant hospitals, is improving the timeliness of cancer care (56, 57).

Determining which intervention strategies to introduce will require further consideration of the efficacy, feasibility, acceptability, health system, and economic implications of these options. While initiatives such as public reporting of colonoscopy waiting times may be helpful, interventions tailored to rural settings are likely to be more effective in reducing disparities. As in other studies (58, 59), we found that insurance status moderated interval length. Thus, interventions that target the timeliness of diagnostic services in the public system may offer most benefit to rural patients with colorectal cancer.

Strengths of our study include the use of a rigorously developed, standardized survey and robust data preparation procedures, which were designed by an international team of researchers using best-practice recommendations. This enhances the validity and consistency of study findings. Other strengths include population-based recruitment with reasonable response rate, reducing selection bias. The PCP response was particularly high. This may be due to the patient-specific request and pen-and-paper, rather than electronic, data collection method (60). Data validity was acceptable for key variables, although lower for the date of first presentation, which is consistent with previous research (61, 62).

Limitations include selection and response bias. As with similar studies, stage IV patients were underrepresented (59). Our cancer registry recruitment procedure required potential participants to have a confirmed histopathologic diagnosis, usually from surgery. While most Australians with stage I–III colorectal cancer receive surgery (63), this recruitment requirement likely reduced the number of stage IV patients approached. In addition, nonresponders were more likely to have been born in a non-English speaking country. It is difficult to determine the direction of these biases on our findings. Migrants often live in urban areas and may have longer cancer pathways, particularly in initial help-seeking (64). However, as others have noted, rural patients may be more likely to have late-stage disease, possibly due to delayed pathways (65, 66). Hence, we may over- or underestimate differences between rural and urban patients.

While we attempted to reduce recall bias by recruiting patients within 6 months of diagnosis, poor concordance between colorectal cancer patient and PCP date of presentation suggests some bias influencing patient recall or PCP reporting of relevant visits. However, as concordance did not vary by

residential location (rural CCC = 0.87, 95% CI: 0.82–0.92; urban CCC = 0.81, 95% CI: 0.75–0.88), recall bias is unlikely to explain our findings.

We also used a dichotomous measure of rurality due to sample size limitations, thus we were unable to examine the effect of increasing remoteness with time to care. The small number of screen-detected and rectal cancer patients also precluded subgroup analysis. Small sample size for some intervals could lead to extreme results, particularly in the 90th percentile, and findings away from the median should be interpreted with care. There was also a high proportion of missing data and wide confidence intervals for some intervals, limiting the study in identifying rural–urban variation (type II error). Future research should examine small-area variation with larger samples to provide more in-depth understanding of disparities.

In summary, rural patients with colorectal cancer experienced longer time from first symptom or screening test to treatment than urban counterparts. In contrast, there were minimal differences between rural and urban breast cancer patient pathways to treatment. While findings need to be confirmed with other studies, our data suggest that interventions targeting the diagnostic interval may reduce time to care and hence reduce rural–urban outcome inequities in colorectal cancer.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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