TITLE PAGE

Title: Rural–urban disparities in time to diagnosis and treatment for colorectal and breast cancer.[1,2,3]

Authors:

Rebecca J Bergin[1,2] ; Jon Emery[2]; Ruth C Bollard[3]; Alina Zalounina Falborg[4] ; Henry Jensen[4] ; David Weller[5]; Usha Menon[6] ; Peter Vedsted[4] ; Robert J Thomas[2,7,8]; Kathryn Whitfield[7]; Victoria White[1,9]

Affiliations:

[1] Centre for Behavioural Research in Cancer, Cancer Council Victoria, 615 St Kilda Rd, Melbourne, Australia 3000.

[2] Department of General Practice and Centre for Cancer Research, University of Melbourne, 10th floor, Victorian Comprehensive Cancer Centre, 305 Grattan St, Melbourne, Australia 3010.

[3] Division of Surgery, Ballarat Health Services, 1 Drummond St, Ballarat, Australia 3350.

[4] Research Unit for General Practice, Department of Public Health, Aarhus University, Bartholins Allé 2, 8000 Aarhus C, Denmark

[5] Centre for Population Health Sciences, University of Edinburgh, Doorway 1, Medical Quad Teviot Place, Edinburgh, EH8 9DX, United Kingdom

[6] Gynaecological Cancer Research Centre, Suite 1B, 149 Tottenham Court Road, London W1T 7DN, United Kingdom.

[7] Department of Health and Human Services Victoria, Victorian Government, 9th floor, 50 Lonsdale St, Melbourne, Australia, 3000.

[8] Faculty of Medicine, Dentistry and Health Sciences, Bdlg 181, University of Melbourne, Grattan St, Melbourne, Australia 3010.

[9] School of Psychology, Deakin University. 221 Burwood Hwy, Burwood, Australia, 3125.

Running title: Rural–urban disparities in time to colorectal cancer care.

---

[1] **Corresponding author**: Rebecca J Bergin, Centre for Behavioural Research in Cancer, Cancer Council Victoria, 615 St Kilda Rd, Melbourne, Australia 3000. Email: Rebecca.bergin@cancervic.org.au; Tel: +61 9514 6467.
[2] **Conflict of interest:** The authors declare no potential conflicts of interest.
[3] **Word count**: Abstract – 250; Main text – 4,125. **Figures and tables**: 6. **Supplementary files**: 2

Key words: rural health, colorectal cancer, breast cancer, early diagnosis, time to treatment.

Abbreviations: CCC: Lin's concordance correlation coefficient; ICBP: International Cancer Benchmarking Partnership; IRSD: Index of relative socio-economic disadvantage; PCP: primary care practitioner; PHI: Private health insurance; SES: Socio-economic status; UK: United Kingdom; US: United States.

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 six months of diagnosis), primary care physicians (PCP), 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 socio-economic status.

Results: 433 colorectal (48% rural) and 489 breast (42% rural) patients, 621 PCPs and 370 specialists participated. Compared to urban patients, symptomatic colorectal cancer patients 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 post-presentation.

Impact: Interventions targeting time from presentation to diagnosis may help reduce colorectal cancer rural–urban disparities.

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 five-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 cancer patients. 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 US, 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) (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 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 km^2, 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, though 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 (2013–14), people aged 50, 55 and 65, and aged 60 after July 2013, were eligible for colorectal cancer screening (faecal 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.

Based on Module 4 sample size calculations (27), additional patients were recruited for the present study in order 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 socio-demographics (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 (ICD 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 three to six months of diagnosis to optimise 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 was 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. In order to prioritise 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 dichotomised to symptomatic or screen-detected presentation. Symptomatic patients included those diagnosed via a healthcare professional, emergency presentation, incidental finding or other presentation (e.g. anaemia).

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, i.e. 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.encr.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 zero-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, and total intervals (Figure 1). Time-points and intervals were defined using Aarhus statement recommendations (29,30).

FIGURE 1

Interval data were analysed 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 (Figure 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 centres. As Victoria has few remote areas, a two-level variable was created: urban (major city) and rural (regional and remote categories).

Covariates: As socio-economic 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) (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 categorised 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 analysed separately given differences in pathways and intervals for each cancer type (33,34). Descriptive statistics summarised and compared rural and urban participant demographic, clinical and health service characteristics. Chi-square 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. Since the length of the interval in days is a continuous measure which has been rounded, we used the 'qcount' command (36,37). To estimate model parameters, 1000 jittered samples were produced and marginal effects with 95% confidence intervals 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) (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 non-participation. 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 five months (interquartile range: 4–6) post-diagnosis, and 90% within seven 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 non-respondents 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

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 to urban participants, rural participants were more likely to live in areas of low SES (p<.001) and were less likely to have PHI (p<.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).

TABLE 1

Intervals: The median patient interval for symptomatic patients with colorectal cancer was six days longer for rural compared to urban patients (Table 2). While 90% of urban patients with colorectal cancer were diagnosed within five months of their first presentation, one in 10 rural patients waited longer than six 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 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 six 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<.001) except the primary care (p=.812) and treatment intervals (p=.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=.047).

TABLE 2

Quantile regression

<u>Colorectal cancer</u>

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 to urban patients, ranging from 18 to 53 days longer (Table 3). While the patient interval was shorter for rural compared to 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.

<u>Breast cancer</u>

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

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 (four 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 to 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).

TABLE 4

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) (39). Concordance for date of first presentation between patient and PCP was poor for colorectal cancer (CCC=.87), but substantial for breast cancer (CCC=.96) (40). For each cancer type, concordance was substantial for date of diagnosis (patient and cancer registry: CCC≥.99) and almost perfect for first treatment (patient and specialist: CCC>.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 to urban patients, ranging from 2.5-weeks to two-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 focussed 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 to 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 US 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 methodological 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). Minimising 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.

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 UK, 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 UK (54,55), and Denmark's 'three-legged strategy' where diagnostic centres, fast-track pathways and low-risk clinics, public reporting of waiting times and punitive measures for non-compliant 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, standardised 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, though lower for 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 histopathological 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, non-responders 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 under-estimate differences between rural and urban patients.

While we attempted to reduce recall bias by recruiting patients within six 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=.87, 95% CI: 0.82–0.92; urban CCC=.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 sub-group 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.

ACKNOWLEDGEMENTS

REFERENCES

1. Haynes R, Pearce J, Barnett R. Cancer survival in New Zealand: ethnic, social and geographical inequalities. Soc Sci Med **2008**;67(6):928-37 doi 10.1016/j.socscimed.2008.05.005.
2. Coory MD, Ho T, Jordan SJ. Australia is continuing to make progress against cancer, but the regional and remote disadvantage remains. Med J Aust **2013**;199(9):605-8 doi 10.5694/mja13.10055.
3. Dejardin O, Remontet L, Bouvier AM, Danzon A, Tretarre B, Delafosse P*, et al.* Socioeconomic and geographic determinants of survival of patients with digestive cancer in France. Br J Cancer **2006**;95(7):944-9 doi 10.1038/sj.bjc.6603335.
4. Blake KD, Moss JL, Gaysynsky A, Srinivasan S, Croyle RT. Making the Case for Investment in Rural Cancer Control: An Analysis of Rural Cancer Incidence, Mortality, and Funding Trends. Cancer Epidemiol Biomarkers Prev **2017**;26(7):992-7 doi 10.1158/1055-9965.epi-17-0092.
5. AIHW. Cancer survival and prevalence in Australia: period estimates from 1982 to 2010. Canberra: Australian Institute of Health and Welfare; 2012.
6. Thursfield V, Farrugia H. Cancer in Victoria: Statistics & Trends 2015. Melbourne: Cancer Council Victoria; 2016.
7. Murphy C, Sabesan S, Steer C, Yates P, Booms A, Jones V*, et al.* Oncology service initiatives and research in regional Australia. Aust J Rural Health **2015**;23(1):40-8 doi 10.1111/ajr.12173.
8. Tørring ML, Murchie P, Hamilton W, Vedsted P, Esteva M, Lautrup M*, et al.* Evidence of advanced stage colorectal cancer with longer diagnostic intervals: a pooled analysis of seven primary care cohorts comprising 11 720 patients in five countries. Br J Cancer **2017**;117(6):888-97 doi 10.1038/bjc.2017.236.
9. Neal RD, Tharmanathan P, France B, Din NU, Cotton S, Fallon-Ferguson J*, et al.* Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review. Br J Cancer **2015**;112(S1):S92-S107 doi 10.1038/bjc.2015.48.
10. Rutter CM, Kim JJ, Meester RGS, Sprague BL, Burger EA, Zauber AG*, et al.* Effect of Time to Diagnostic Testing for Breast, Cervical, and Colorectal Cancer Screening Abnormalities on Screening Efficacy: A Modeling Study. Cancer Epidemiology Biomarkers &amp; Prevention **2018**;27(2):158.
11. Emery J, Walter F, Gray V, Sinclair C, Howting D, Bulsara M*, et al.* Diagnosing cancer in the bush: a mixed-methods study of symptom appraisal and help-seeking behaviour in people with cancer from rural Western Australia. Fam Pract **2013**;30(3):294-301 doi 10.1093/fampra/cms087.
12. Brundisini F, Giacomini M, DeJean D, Vanstone M, Winsor S, Smith A. Chronic disease patients' experiences with accessing health care in rural and remote areas: a systematic review and qualitative meta-synthesis. Ontario health technology assessment series **2013**;13(15):1-33.
13. Aboagye JK, Kaiser HE, Hayanga AJ. Rural–urban differences in access to specialist providers of colorectal cancer care in the united states: A physician workforce issue. JAMA Surgery **2014**;149(6):537-43 doi 10.1001/jamasurg.2013.5062.

14. Pirotta M, Forsdike K, Young J, Emery J. ICBP Module 3: Final report for the Department of Health and Cancer Council Victoria. Melbourne: University of Melbourne; 2014.

15. Lyratzopoulos G, Vedsted P, Singh H. Understanding missed opportunities for more timely diagnosis of cancer in symptomatic patients after presentation. Br J Cancer **2015**;112(S1):S84-S91 doi 10.1038/bjc.2015.47.

16. Mitchell ED, Macdonald S, Campbell NC, Weller D, Macleod U. Influences on pre-hospital delay in the diagnosis of colorectal cancer: a systematic review. Br J Cancer **2008**;98(1):60-70 doi 10.1038/sj.bjc.6604096.

17. Robertson R, Campbell NC, Smith S, Donnan PT, Sullivan F, Duffy R*, et al.* Factors influencing time from presentation to treatment of colorectal and breast cancer in urban and rural areas. Br J Cancer **2004**;90(8):1479-85 doi 10.1038/sj.bjc.6601753.

18. Turner M, Fielding S, Ong Y, Dibben C, Feng Z, Brewster DH*, et al.* A cancer geography paradox? Poorer cancer outcomes with longer travelling times to healthcare facilities despite prompter diagnosis and treatment: a data-linkage study. Br J Cancer **2017**;117(3):439–49 doi 10.1038/bjc.2017.180.

19. Gillis A, Dixon M, Smith A, Law C, Coburn NG. A patient-centred approach toward surgical wait times for colon cancer: a population-based analysis. Can J Surg **2014**;57(2):94-100 doi 10.1503/cjs.026512.

20. Johnston GM, MacGarvie VL, Elliott D, Dewar RA, MacIntyre MM, Nolan MC. Radiotherapy wait times for patients with a diagnosis of invasive cancer, 1992-2000. Clinical and Investigative Medicine **2004**;27(3):142-56.

21. Emery J, Gray V, Walter F, Cheetham S, Croager EJ, Slevin T*, et al.* The Improving Rural Cancer Outcomes Trial: a cluster-randomised controlled trial of a complex intervention to reduce time to diagnosis in rural cancer patients in Western Australia. Br J Cancer **2017**;117:1459–69 doi 10.1038/bjc.2017.310.

22. Emery J, Walter F, Gray V, Sinclair C, Howting D, Bulsara M*, et al.* Diagnosing cancer in the bush: a mixed methods study of GP and specialist diagnostic intervals in rural Western Australia. Fam Pract **2013**;30(5):541-50 doi 10.1093/fampra/cmt016.

23. ABS. Regional Population Growth, Australia, 2015–16. Regional Population Growth, Australia. Canberra: Australian Bureau of Statistics; 2017.

24. Australian Government Department of Health. Statistics under Medicare. Canberra: Commonwealth of Australia; 2017.

25. ABS. Patient Experiences in Australia: Summary of Findings, 2015–16. Canberra: Australian Bureau of Statistics; 2016.

26. AIHW. Cancer in Australia: an overview 2014. Canberra: Australian Institute of Health and Welfare; 2014.

27. Weller D, Vedsted P, Anandan C, Zalounina A, Fourkala EO, Desai R*, et al.* An investigation of routes to cancer diagnosis in 10 international jurisdictions, as part of the International Cancer Benchmarking Partnership: survey development and implementation. BMJ Open **2016**;6(7):e009641 doi 10.1136/bmjopen-2015-009641.

28. Butler J, Foot C, Bomb M, Hiom S, Coleman M, Bryant H*, et al.* The International Cancer Benchmarking Partnership: An international collaboration to inform cancer policy in Australia, Canada, Denmark, Norway, Sweden and the United Kingdom. Health Policy **2013**;112(1–2):148-55 doi 10.1016/j.healthpol.2013.03.021.

29. Weller D, Vedsted P, Rubin G, Walter FM, Emery J, Scott S*, et al.* The Aarhus statement: improving design and reporting of studies on early cancer diagnosis. Br J Cancer **2012**;106(7):1262-7 doi 10.1038/bjc.2012.68.
30. Olesen F, Hansen RP, Vedsted P. Delay in diagnosis: the experience in Denmark. Br J Cancer **2009**;101(S2):S5-S8 doi 10.1038/sj.bjc.6605383.
31. ABS. Australian Statistical Geography Standard (ASGS): Volume 5 – Remoteness Structure. Canberra: Australian Bureau of Statistics; 2013.
32. ABS. Census of Population and Housing: Socio-Economic Indexes for Areas (SEIFA), Australia, 2011 Canberra: Australian Bureau of Statistics; 2011.
33. Lyratzopoulos G, Saunders CL, Abel GA, McPhail S, Neal RD, Wardle J*, et al.* The relative length of the patient and the primary care interval in patients with 28 common and rarer cancers. Br J Cancer **2015**;112(S1):S35-S40 doi 10.1038/bjc.2015.40.
34. Helsper CCW, van Erp NNF, Peeters P, de Wit NNJ. Time to diagnosis and treatment for cancer patients in the Netherlands: Room for improvement? Eur J Cancer **2017**;87:113-21 doi 10.1016/j.ejca.2017.10.003.
35. Koenker R, Bassett G. Regression Quantiles. Econometrica **1978**;46(1):33-50 doi 10.2307/1913643.
36. Miranda A. QCOUNT: Stata program to fit quantile regression models for count data. Boston: Boston College Department of Economics; 2007.
37. Machado JAF, Santos Silva JMC. Quantiles for Counts. J Amer Statistical Assoc **2005**;100(472):1226-37 doi 10.1198/016214505000000330.
38. Lin LI. A concordance correlation coefficient to evaluate reproducibility. Biometrics **1989**;45(1):255-68.
39. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics **1977**;33(1):159-74 doi 10.2307/2529310.
40. McBride G. A proposal for strength-of-agreement criteria for Lin's concordance correlation coefficient. Hamilton, New Zealand: National Institute of Water & Atmospheric Research Ltd; 2005.
41. Meilleur A, Subramanian SV, Plascak JJ, Fisher JL, Paskett ED, Lamont EB. Rural residence and cancer outcomes in the United States: Issues and challenges. Cancer Epidemiol Biomarkers Prev **2013**;22(10):1657-67 doi 10.1158/1055-9965.epi-13-0404.
42. Dejardin O, Herbert C, Velten M, Buemi A, Menegoz F, Maarouf N*, et al.* Social and geographical factors influencing the delay in treatment for colorectal cancer. Br J Cancer **2004**;91(9):1751 doi 10.1038/sj.bjc.6602170.
43. Porter G, Urquhart R, Kendell C, Bu J, McConnell Y, Grunfeld E. Timely access and quality of care in colorectal cancer: a population-based cohort study using administrative data. BMC Research Notes **2013**;6:355- doi 10.1186/1756-0500-6-355.
44. Youl PH, Aitken JF, Turrell G, Chambers SK, Dunn J, Pyke C*, et al.* The impact of rurality and disadvantage on the diagnostic interval for breast cancer in a large population-based study of 3202 women in Queensland, Australia. Int J Env Res Public Health **2016**;13(11):e1156 doi 10.3390/ijerph13111156.
45. Richardson LC, Royalty J, Howe W, Helsel W, Kammerer W, Benard VB. Timeliness of breast cancer diagnosis and initiation of treatment in the National Breast and Cervical Cancer Early Detection Program, 1996-2005. Am J Public Health **2010**;100(9):1769-76 doi 10.2105/ajph.2009.160184.

46.   Bergin R. Reducing outcome disparities for rural Victorians with colorectal cancer: understanding pathways to treatment and informing policy [Unpublished doctoral dissertation]. Melbourne, Australia: University of Melbourne; 2018.

47.   Webber C, Jiang L, Grunfeld E, Groome PA. Identifying predictors of delayed diagnoses in symptomatic breast cancer: a scoping review. Eur J Cancer Care (Engl) **2016**;26(2):Epub ahead of print 7 March 2016; doi:10.1111/ecc.12483.

48.   Brocken P, Prins JB, Dekhuijzen PNR, van der Heijden HFM. The faster the better?—A systematic review on distress in the diagnostic phase of suspected cancer, and the influence of rapid diagnostic pathways. Psychooncology **2012**;21(1):1-10 doi 10.1002/pon.1929.

49.   Banerjea A, Voll J, Chowdhury A, Siddika A, Thomson S, Briggs R*, et al.* Straight-to-test colonoscopy for 2-week-wait referrals improves time to diagnosis of colorectal cancer and is feasible in a high-volume unit. Colorectal Disease **2017**;19(9):819-26 doi 10.1111/codi.13667.

50.   ACE Programme. Improving diagnostic pathways for patients with suspected colorectal cancer: final report. Macmillan Cancer Support, June 2017.

51.   Day LW, Siao D, Inadomi JM, Somsouk M. Non-physician performance of lower and upper endoscopy: a systematic review and meta-analysis. Endoscopy **2014**;46(5):401-10 doi 10.1055/s-0034-1365310.

52.   Kolber MR, Wong CKW, Fedorak RN, Rowe BH, APC-Endo Study Physicians. Prospective study of the quality of colonoscopies performed by primary care physicians: the Alberta Primary Care Endoscopy (APC-Endo) study. PLOS one **2013**;8(6):e67017 doi 10.1371/journal.pone.0067017.

53.   Evans DV, Cole AM, Norris TE. Colonoscopy in rural communities: a systematic review of the frequency and quality. Rural & Remote Health **2015**;15(2):3057-69.

54.   Hiom SC. Diagnosing cancer earlier: reviewing the evidence for improving cancer survival. Br J Cancer **2015**;112:S1-S5 doi 10.1038/bjc.2015.23.

55.   Møller H, Gildea C, Meechan D, Rubin G, Round T, Vedsted P. Use of the English urgent referral pathway for suspected cancer and mortality in patients with cancer: cohort study. BMJ **2015**;351:h5102 doi 10.1136/bmj.h5102.

56.   Jensen H, Torring ML, Olesen F, Overgaard J, Fenger-Gron M, Vedsted P. Diagnostic intervals before and after implementation of cancer patient pathways - a GP survey and registry based comparison of three cohorts of cancer patients. BMC Cancer **2015**;15(308):1-10 doi 10.1186/s12885-015-1317-7.

57.   Vedsted P, Olesen F. A differentiated approach to referrals from general practice to support early cancer diagnosis - the Danish three-legged strategy. Br J Cancer **2015**;112(S1):S65-S9 doi 10.1038/bjc.2015.44.

58.   Durham DD, Robinson WR, Lee SS, Wheeler SB, Reeder-Hayes KE, Bowling JM*, et al.* Insurance-Based Differences in Time to Diagnostic Follow-up after Positive Screening Mammography. Cancer Epidemiology Biomarkers &amp; Prevention **2016**;25(11):1474.

59.   Lynch BM, Baade P, Fritschi L, Leggett B, Owen N, Pakenham K*, et al.* Modes of presentation and pathways to diagnosis of colorectal cancer in Queensland. Med J Aust **2007**;186(6):288-91.

60.   Hood K, Robling M, Ingledew D, Gillespie D, Greene G, Ivins R*, et al.* Mode of data elicitation, acquisition and response to surveys: a systematic review. Health Technol Assess **2012**;16(27):1-162 doi 10.3310/hta16270.

61.   Lynch BM, Youlden D, Fritschi L, Newman B, Pakenham KI, Leggett B*, et al.* Self-reported information on the diagnosis of colorectal cancer was reliable but not necessarily valid. J Clin Epidemiol **2008**;61(5):498-504 doi 10.1016/j.jclinepi.2007.05.018.

62.   Larsen M, Hansen RP, Sokolowski I, Vedsted P. Agreement between patient-reported and doctor-reported patient intervals and date of first symptom presentation in cancer diagnosis – A population-based questionnaire study. Cancer Epidemiol **2014**;38(1):100-5 doi 10.1016/j.canep.2013.10.006.

63.   Beckmann KR, Bennett A, Young GP, Roder D. Treatment patterns among colorectal cancer patients in South Australia: a demonstration of the utility of population-based data linkage. J Eval Clin Pract **2014**;20(4):467-77 doi 10.1111/jep.12183.

64.   Licqurish S, Phillipson L, Chiang P, Walker J, Walter F, Emery J. Cancer beliefs in ethnic minority populations: a review and meta-synthesis of qualitative studies. Eur J Cancer Care (Engl) **2017**;26(1):e12556 doi 10.1111/ecc.12556.

65.   Baade PD, Dasgupta P, Aitken JF, Turrell G. Geographic remoteness and risk of advanced colorectal cancer at diagnosis in Queensland: a multilevel study. Br J Cancer **2011**;105(7):1039-41 doi 10.1038/bjc.2011.356.

66.   Massarweh NN, Chiang YJ, Xing Y, Chang GJ, Haynes AB, You YN*, et al.* Association between travel distance and metastatic disease at diagnosis among patients with colon cancer. J Clin Oncol **2014**;32(9):942-8 doi 10.1200/jco.2013.52.3845.

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
Socio-economic status												
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] $p<.05$; [b] $p<.01$; [c] $p<.001$. IQR – interquartile range; n/a – not applicable; RT – radiotherapy; SD – standard deviation.

			Rural residence				Urban residence			
Sample	**Cancer**	**Interval**	**n (missing)**	**Median**	**(IQR)**	**90th percentile**	**n (missing)**	**Median**	**(IQR)**	**90th percentile**
Symptomatic	CRC	Patient	151 (9%)	28	(2, 86)	262	151 (12%)	22	(2, 78)	276
	(n=337)	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	Patient	107 (2%)	6	(1, 31)	121	148 (5%)	10	(1, 57)	171
	(n=265)	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	Diagnostic	179 (14%)	37	(10, 89)	156	190 (16%)	27	(9, 63)	139
	(n=433)	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	Diagnostic	190 (7%)	14	(6, 27)	52	263 (7%)	15	(7, 27)	41
	(n=489)	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

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

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

Table 3: Difference in days for rural patients (urban reference group) at the 50th, 75th and 90th interval percentiles.								
		Colorectal cancer				Breast cancer		
		50th	75th	90th		50th	75th	90th
	n	Days diff. (95% CI)	Days diff. (95% CI)	Days diff. (95% CI)	n	Days diff. (95% CI)	Days diff. (95% CI)	Days diff. (95% CI)
Symptomatic								
Patient interval	302	7 (-31, 46)	4 (-11, 20)	**-58 (-87, -29)**	254	-2 (-5, 2)	**-37 (-48, -25)**	**-50 (-54, -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), socio-economic and insurance status. Bold indicates p<.05. CI – confidence interval; Diff. – difference.								

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**			
		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	No PHI	n=138	**24 (3, 44)**	16 (-16, 49)	-1 (-11, 9)	n=90	0 (-2, 3)	3 (-20, 25)	**-197 (-200, -194)**
	PHI	n=164	1 (-10, 12)	**-6 (-11, -1)**	**-13 (-18, -8)**	n=164	-3 (-17, 11)	**-23 (-42, -4)**	**-48 (-52, -45)**
Primary care interval	No PHI	n=78	**8 (3, 12)**	**42 (37, 48)**	**58 (50, 65)**	n=55	**6 (4, 8)**	**11 (9, 14)**	**39 (6, 72)**
	PHI	n=107	-2 (-7, 4)	-1 (-5, 2)	4 (0, 9)	n=119	2 (-2, 6)	1 (-2, 5)	-3 (-14, 9)
Diagnostic interval	No PHI	n=135	10 (-40, 59)	**30 (23, 37)**	**54 (21, 87)**	n=89	3 (0, 7)	-4 (-18, 9)	**29 (24, 34)**
	PHI	n=172	-3 (-5, 0)	-5 (-11, 2)	**18 (14, 22)**	n=167	-2 (-5, 0)	0 (-7, 8)	-5 (-10, 1)
Treatment interval	No PHI	n=150	-2 (-15, 12)	1 (-15, 17)	5 (0, 10)	n=85	**-4 (-7, -1)**	**-5 (-8, -1)**	-4 (-7, 0)
	PHI	n=174	0 (-6, 5)	**6 (2, 11)**	**16 (10, 23)**	n=167	6 (-4, 15)	**7 (3, 11)**	7 (-1, 15)
Health system interval	No PHI	n=131	**7 (2, 12)**	**43 (36, 51)**	**113 (92, 135)**	n=85	0 (-4, 4)	3 (-7, 12)	5 (0, 9)
	PHI	n=166	7 (-4, 18)	3 (-6, 11)	**25 (16, 34)**	n=167	3 (-3, 9)	2 (-15, 19)	**4 (0, 8)**
Total interval	No PHI	n=119	**10 (6, 14)**	**42 (35, 49)**	**68 (60, 76)**	n=82	11 (-1, 22)	**-62 (-84, -41)**	**-76 (-87, -65)**
	PHI	n=143	**25 (9, 41)**	**42 (30, 54)**	4 (-2, 11)	n=157	-3 (-16, 10)	-13 (-26, 0)	**68 (52, 84)**
Symptomatic and screen-detected								
Diagnostic interval	No PHI	n=156	3 (-7, 12)	22 (-3, 47)	**31 (4, 58)**	n=158	1 (-4, 6)	3 (-1, 7)	**32 (23, 42)**
	PHI	n=213	5 (-12, 21)	-4 (-43, 35)	**32 (26, 38)**	n=293	-1 (-4, 1)	-4 (-27, 19)	**-7 (-11, -3)**
Treatment interval	No PHI	n=177	-4 (-18, 11)	-1 (-6, 3)	10 (-7, 27)	n=160	-4 (-8, 1)	-4 (-10, 2)	-1 (-8, 5)
	PHI	n=238	2 (0, 5)	**8 (5, 11)**	**14 (3, 24)**	n=318	**6 (3, 9)**	**6 (2, 10)**	4 (-78, 86)
Total interval	No PHI	n=138	1 (-10, 11)	**20 (12, 28)**	**106 (103, 110)**	n=149	3 (-8, 14)	1 (-10, 13)	**-146 (-154, -137)**
	PHI	n=183	**14 (1, 27)**	**54 (38, 71)**	21 (-1, 42)	n=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 socio-economic status. Bold indicates p<.05. CI – confidence interval; Diff. – difference; PHI – private health insurance.								

Figure legends

Figure 1: Intervals in the pathway to cancer treatment.

Figure 1 depicts intervals in the pathway to treatment examined in the current study. All intervals were calculated for symptomatic patients. For screen-detected patients, the diagnostic, treatment and total (screen-detected cases) intervals were calculated.

Figure 2: Recruitment flowchart: colorectal and breast cancer patients

Figure 2 shows the participant recruitment flowchart. 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).

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
Socio-economic status												
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<.05; [b] p<.01; [c] p<.001. IQR – interquartile range; n/a – not applicable; RT – radiotherapy; SD – standard deviation.

Sample	Cancer	Interval	Rural residence				Urban residence			
			n (missing)	Median	(IQR)	90th percentile	n (missing)	Median	(IQR)	90th percentile
Symptomatic	CRC	Patient	151 (9%)	28	(2, 86)	262	151 (12%)	22	(2, 78)	276
	(n=337)	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	Patient	107 (2%)	6	(1, 31)	121	148 (5%)	10	(1, 57)	171
	(n=265)	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	Diagnostic	179 (14%)	37	(10, 89)	156	190 (16%)	27	(9, 63)	139
	(n=433)	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	Diagnostic	190 (7%)	14	(6, 27)	52	263 (7%)	15	(7, 27)	41
	(n=489)	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

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

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

Table 3: Difference in days for rural patients (urban reference group) at the 50th, 75th and 90th interval percentiles.								
		Colorectal cancer				**Breast cancer**		
		50th	**75th**	**90th**		**50th**	**75th**	**90th**
	n	**Days diff. (95% CI)**	**Days diff. (95% CI)**	**Days diff. (95% CI)**	**n**	**Days diff. (95% CI)**	**Days diff. (95% CI)**	**Days diff. (95% CI)**
Symptomatic								
Patient interval	302	7 (-31, 46)	4 (-11, 20)	**-58 (-87, -29)**	254	-2 (-5, 2)	**-37 (-48, -25)**	**-50 (-54, -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), socio-economic and insurance status. Bold indicates p<.05. CI – confidence interval; Diff. – difference.

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		
		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	No PHI	n=138 **24 (3, 44)**	16 (-16, 49)	-1 (-11, 9)	n=90 0 (-2, 3)	3 (-20, 25)	**-197 (-200, -194)**
	PHI	n=164 1 (-10, 12)	**-6 (-11, -1)**	**-13 (-18, -8)**	n=164 -3 (-17, 11)	**-23 (-42, -4)**	**-48 (-52, -45)**
Primary care interval	No PHI	n=78 **8 (3, 12)**	**42 (37, 48)**	**58 (50, 65)**	n=55 **6 (4, 8)**	**11 (9, 14)**	**39 (6, 72)**
	PHI	n=107 -2 (-7, 4)	-1 (-5, 2)	4 (0, 9)	n=119 2 (-2, 6)	1 (-2, 5)	-3 (-14, 9)
Diagnostic interval	No PHI	n=135 10 (-40, 59)	**30 (23, 37)**	**54 (21, 87)**	n=89 3 (0, 7)	-4 (-18, 9)	**29 (24, 34)**
	PHI	n=172 -3 (-5, 0)	-5 (-11, 2)	**18 (14, 22)**	n=167 -2 (-5, 0)	0 (-7, 8)	-5 (-10, 1)
Treatment interval	No PHI	n=150 -2 (-15, 12)	1 (-15, 17)	5 (0, 10)	n=85 **-4 (-7, -1)**	**-5 (-8, -1)**	-4 (-7, 0)
	PHI	n=174 0 (-6, 5)	**6 (2, 11)**	**16 (10, 23)**	n=167 6 (-4, 15)	**7 (3, 11)**	7 (-1, 15)
Health system interval	No PHI	n=131 **7 (2, 12)**	**43 (36, 51)**	**113 (92, 135)**	n=85 0 (-4, 4)	3 (-7, 12)	5 (0, 9)
	PHI	n=166 7 (-4, 18)	3 (-6, 11)	**25 (16, 34)**	n=167 3 (-3, 9)	2 (-15, 19)	**4 (0, 8)**
Total interval	No PHI	n=119 **10 (6, 14)**	**42 (35, 49)**	**68 (60, 76)**	n=82 11 (-1, 22)	**-62 (-84, -41)**	**-76 (-87, -65)**
	PHI	n=143 **25 (9, 41)**	**42 (30, 54)**	4 (-2, 11)	n=157 -3 (-16, 10)	-13 (-26, 0)	**68 (52, 84)**
Symptomatic and screen-detected							
Diagnostic interval	No PHI	n=156 3 (-7, 12)	22 (-3, 47)	**31 (4, 58)**	n=158 1 (-4, 6)	3 (-1, 7)	**32 (23, 42)**
	PHI	n=213 5 (-12, 21)	-4 (-43, 35)	**32 (26, 38)**	n=293 -1 (-4, 1)	-4 (-27, 19)	**-7 (-11, -3)**
Treatment interval	No PHI	n=177 -4 (-18, 11)	-1 (-6, 3)	10 (-7, 27)	n=160 -4 (-8, 1)	-4 (-10, 2)	-1 (-8, 5)
	PHI	n=238 2 (0, 5)	**8 (5, 11)**	**14 (3, 24)**	n=318 **6 (3, 9)**	**6 (2, 10)**	4 (-78, 86)
Total interval	No PHI	n=138 1 (-10, 11)	**20 (12, 28)**	**106 (103, 110)**	n=149 3 (-8, 14)	1 (-10, 13)	**-146 (-154, -137)**
	PHI	n=183 **14 (1, 27)**	**54 (38, 71)**	21 (-1, 42)	n=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 socio-economic status. Bold indicates p<.05. CI – confidence interval; Diff. – difference; PHI – private health insurance.
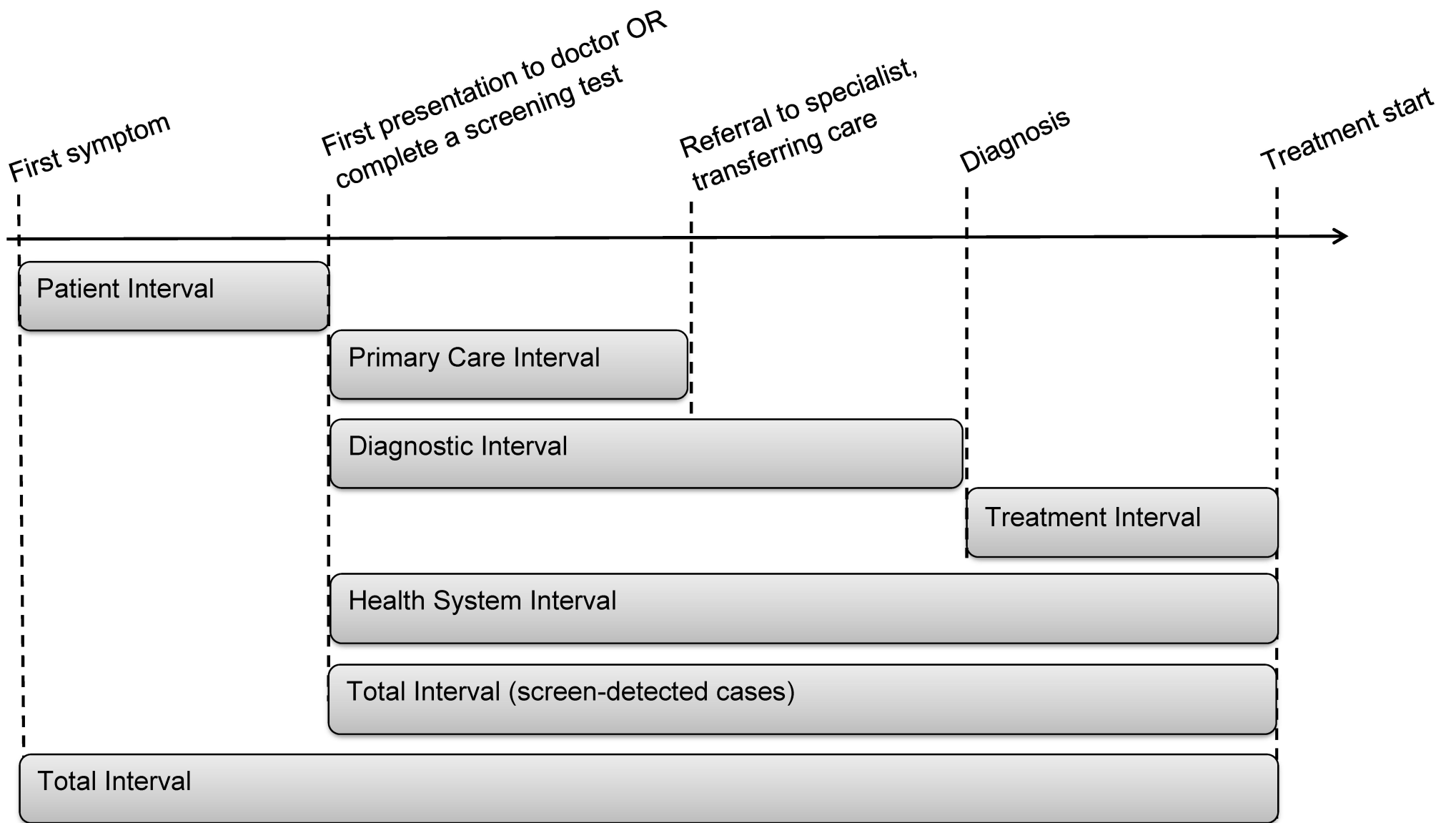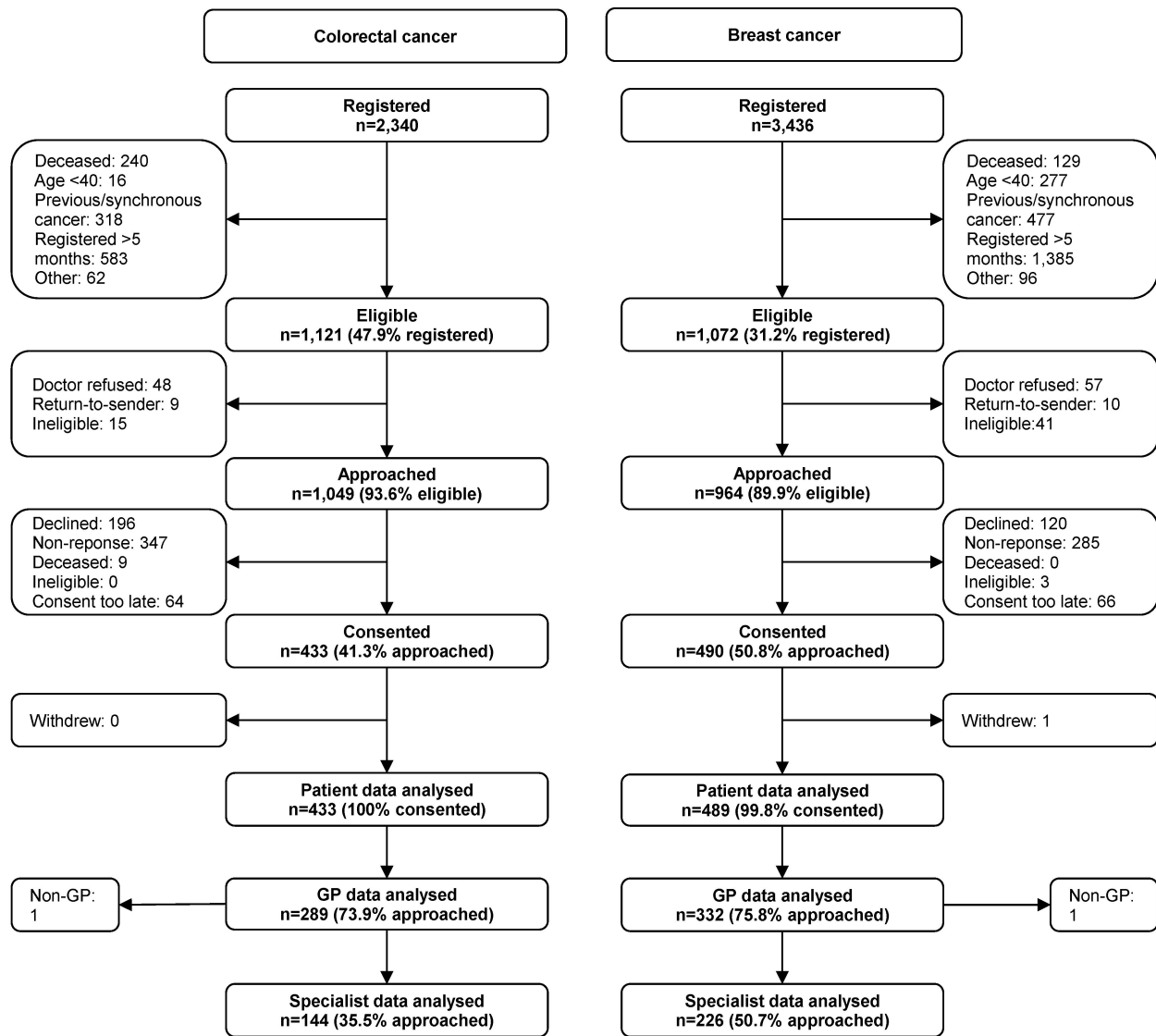
Figure 1

Colorectal cancer

Registered
n=2,340

Deceased: 240
Age <40: 16
Previous/synchronous
cancer: 318
Registered >5
months: 583
Other: 62

Eligible
n=1,121 (47.9% registered)

Doctor refused: 48
Return-to-sender: 9
Ineligible: 15

Approached
n=1,049 (93.6% eligible)

Declined: 196
Non-reponse: 347
Deceased: 9
Ineligible: 0
Consent too late: 64

Consented
n=433 (41.3% approached)

Withdrew: 0

Patient data analysed
n=433 (100% consented)

Non-GP:
1

GP data analysed
n=289 (73.9% approached)

Specialist data analysed
n=144 (35.5% approached)

Breast cancer

Registered
n=3,436

Deceased: 129
Age <40: 277
Previous/synchronous
cancer: 477
Registered >5
months: 1,385
Other: 96

Eligible
n=1,072 (31.2% registered)

Doctor refused: 57
Return-to-sender: 10
Ineligible:41

Approached
n=964 (89.9% eligible)

Declined: 120
Non-reponse: 285
Deceased: 0
Ineligible: 3
Consent too late: 66

Consented
n=490 (50.8% approached)

Withdrew: 1

Patient data analysed
n=489 (99.8% consented)

Non-GP:
1

GP data analysed
n=332 (75.8% approached)

Specialist data analysed
n=226 (50.7% approached)

Figure 2