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ORIGINAL ARTICLE – CLINICAL ONCOLOGY

Socioeconomic disparities in colorectal cancer survival: contributions of prognostic factors in a large Australian cohort

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Abstract

Purpose We quantified the contributions of prognostic factors to socioeconomic disparities in colorectal cancer survival in a large Australian cohort.

Methods The sample comprised 45 and Up Study participants (recruited 2006–2009) who were subsequently diagnosed with colorectal cancer. Both individual (education attained) and neighbourhood socioeconomic measures were used. Questionnaire responses were linked with cancer registrations (to December 2013), records for hospital inpatient stays, emergency department presentations, death information (to December 2015), and Medicare and Pharmaceutical Benefits claims for subsidised procedures and medicines. Proportions of socioeconomic survival differences explained by prognostic factors were quantified using multiple Cox proportional hazards regression.

Results 1720 eligible participants were diagnosed with colorectal cancer after recruitment: 1174 colon and 546 rectal cancers. Significant colon cancer survival differences were only observed for neighbourhood socioeconomic measure ($p = 0.033$): HR = 1.55; 95% CI 1.09–2.19 for lowest versus highest quartile, and disease-related factors explained 95% of this difference. For rectal cancer, patient- and disease-related factors were the main drivers of neighbourhood survival differences (28–36%), while these factors and treatment-related factors explained 24–41% of individual socioeconomic differences. However, differences remained significant for rectal cancer after adjusting for all these factors.

Conclusion In this large contemporary Australian cohort, we identified several drivers of socioeconomic disparities in colorectal cancer survival. Understanding of the role these contributors play remains incomplete, but these findings suggest that improving access to optimal care may significantly reduce these survival disparities.

Keywords Colorectal cancer · Socioeconomic status · Survival disparity · Cancer epidemiology

Introduction

Colorectal cancer (CRC) is the third-most common cancer and second-leading cause of cancer death worldwide (Bray et al. 2018). In many developed countries, including Australia, there have been substantial improvements in CRC survival in recent decades, due to advances in patients' care (Butler et al. 2013; Chawla et al. 2013). However, not all patients appear to have benefitted equally from these advances, with socioeconomic disparities in CRC survival being reported over the past decades (Beckmann et al. 2016; Stanbury et al. 2016a; Woods et al. 2006; Yu et al. 2008). The reasons for these survival differences are not well understood, although differences in disease stage at diagnosis, access and quality of treatment, and patients' characteristics are likely to be the potential causes (Woods et al. 2006).

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Identifying factors influencing CRC survival are crucial first steps towards addressing and reducing disparities in survival outcomes (Woods et al. 2006). In Australia, studies have attempted to disentangle the impact of several prognostic factors on socioeconomic disparities in CRC survival, and found that patients residing in higher socioeconomic neighbourhoods had longer survival after adjusting for stage at diagnosis, treatment received, and several other prognostic factors (Beckmann et al. 2016; Kelsall et al. 2009). However, these previous studies were limited by a relatively small sample size and lack of information on comorbidities (Kelsall et al. 2009), or not having individual socioeconomic measures or information on lifestyle factors (Beckmann et al. 2016), all of which may be associated with CRC patients' survival (Boyle et al. 2013; Woods et al. 2006). In this study, we investigated potential prognostic factors underlying survival disparities in CRC in a large Australian cohort (Banks et al. 2008), and quantified their contributions to the disparities.

Methods

The Sax Institute's 45 and Up Study is an ongoing Australian prospective cohort study of 267,153 people aged ≥ 45 years residing in New South Wales (NSW), Australia during 2006–2009 (Banks et al. 2008). Prospective participants were randomly sampled from Services Australia (formerly the Australian Government Department of Human Services) enrolment database, which provides near complete coverage of the population. People aged ≥ 80 years and residents of rural and remote areas were oversampled. Of those invited, 18% participated and participants included about 11% of the NSW population aged ≥ 45 years. A detailed description of the analytical approaches used in this study has previously been published (Yu et al. 2019). Briefly, the study sample comprised participants of the 45 and Up Study who were diagnosed with colon (C18), or rectal cancer (C19–C20) during follow-up, identified by linkage to the population-based NSW Cancer Registry up to December 2013.

To provide data on the patients' care pathway, and vital status, the survey data were linked with the NSW Admitted Patient Data Collection (APDC), NSW Emergency Department Data Collection (EDDC), Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) claims databases, and Cause of Death Unit Record File (COD-URF) (dates of availability of these health-related datasets are shown in the Supplementary Figure). Linkage to MBS and PBS records is facilitated by the Sax Institute using a unique identifier provided by Services Australia. All other datasets were probabilistically linked by the Centre for Health Record Linkage using a privacy-preserving approach to linkage (Centre for Health Record Linkage 2018).

Exclusions

Participants with any record of cancer before recruitment (either self-reported at baseline or those with a cancer diagnosis recorded in the NSW Cancer Registry between 1994 and baseline) were excluded, along with people first diagnosed at death or whose survival time was 0 days. Participants whose healthcare was subsidised by the Australian Government's Department of Veterans' Affairs were excluded as their prescription medicines have a separate billing arrangement and these data were not available. Those aged ≥ 85 years at diagnosis were also excluded since misclassification of cause of death has been shown to be more common for older cancer patients (Dekker et al. 2014; Makkar et al. 2018).

Outcome and exposure measures

A patient's vital status was determined by linkage with COD-URF. Survival time was calculated from the date of diagnosis to the date of death from CRC or censored at the date of death from another cause or at the end of follow-up (December 2015).

Relative survival could not be estimated because relevant population life tables were not available, so we used the Surveillance, Epidemiology, and End Results cause-specific death classification (Howlader et al. 2010) to optimise the accuracy of the survival estimates as causes of death recorded in population-based registries can be inaccurate (Yin et al. 2011).

To take advantage of the data available and adhere to previous recommendations (Chang et al. 2012; Wallner and Griggs 2018), two measures of socioeconomic status (SES) were used in this study. Individual-level SES was determined using the patient's highest level of education attainment self-reported at baseline and classified as 'low' (school certificate or below), 'medium' (higher school certificate, or trade/apprenticeship), or 'high' (certificate/diploma, or university degree). Neighbourhood SES (nSES) was based on where the participant lived at baseline and grouped into four categories using quartiles of the state-wide distribution of an index of relative socioeconomic disadvantage from the 2011 Australian Census (Australian Bureau of Statistics 2013). This index represents the average SES of people living within a given neighbourhood, including education, employment and occupation variables (Australian Bureau of Statistics 2013).

A joint SES variable was derived to examine any possible interaction of the two SES measures on patients'

survival (Chang et al. 2012). nSES was split into low nSES (quartiles 1–2) and high nSES (quartiles 3–4), resulting in six categories: "high nSES/high education", "high nSES/medium education", "high nSES/low education", "low nSES/high education", "low nSES/medium education", and "low nSES/low education".

Prognostic factors

The prognostic factors were grouped into four broad categories: patient-, lifestyle-, disease-, or treatment-related. Patient-related factors were obtained from the baseline questionnaire, apart from comorbidities, including marital status (married/de facto or other), private health insurance status (yes/no) (Banks et al. 2009), and place of residence at recruitment (major cities or non-major cities) using the Australian Standard Geographic Classification Remoteness Structure (Australian Bureau of Statistics 2003). Comorbidities were measured using the Charlson Comorbidity Index (Charlson et al. 1987) using hospitalisation records for five years before diagnosis $(0, \geq 1)$ (Yap et al. 2018).

Data on lifestyle factors were derived from the baseline questionnaire, including tobacco smoking (ever smoker, never smoker including those former smokers who quit > 15 years ago because their risk of many comorbid conditions is close to that of never smokers (Moyer and Force 2014)), alcohol consumption (0, 1–14, > 14 standard drinks per week), and physical activity classified as sedentary (0 min per week), insufficient (1–149 min), sufficient (150–299 min) or high (300 + minutes) (Yu et al. 2019). Body mass index (BMI) was calculated using self-reported height and weight (< 25, 25–29.9, ≥ 30 kg/m^2) (National Health and Medical Research Council 2013).

Disease-related factors were derived from multiple data sources. Cancer stage at diagnosis from the Cancer Registry was grouped as localised, regional, distant, or unknown (Stanbury et al. 2016a). A recent assessment of this stage variable showed it to be an adequate surrogate staging system comparable to AJCC-TNM stage (Lawrance et al. 2019). Whether the patient's diagnosis followed an emergency presentation (yes/no) was determined by the date of diagnosis and dates of emergency department arrival and departure. As there is no uniform definition of emergency presentation before cancer diagnosis (Zhou et al. 2017), we used up to 14 days prior as the cut-point.

Anticancer treatments received were obtained from multiple sources and coded as yes/no based on any indication of treatment being provided according to the APDC, and MBS or PBS claims. Any such treatment (surgery, radiation therapy or systemic treatment) relating to CRC received up to six months after diagnosis was considered as a first course of treatment.

Statistical analyses

Patients with colon and rectal cancers were analysed separately after initial exploratory analysis suggested different survival patterns by education level ($P_{\text{interaction}} = 0.022$). Differences in prognostic factors between socioeconomic groups were tested using the ANOVA F test for continuous variables and the χ^2 test for categorical variables.

To better understand drivers of disparities in cancer outcomes like previous studies (Ellis et al. 2018; Hill et al. 2010; Ren et al. 2019; Seneviratne et al. 2015), we examined the proportions of the socioeconomic disparity in CRC survival explained separately by each group of prognostic factors using multiple Cox proportional hazards regression (Cox 1972). The hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated, with the highest SES category as the reference. Model one adjusted for sex, age, and year of diagnosis. Where significant differences in survival for SES were found in Model one, each group of prognostic factors (patient-, lifestyle-, disease-, and treatment-related factors) was then added to Model one individually. We first calculated overall disparity by subtracting one from the highest HR derived from Model one (e.g. the HR for nSES quartile 1 relative to nSES quartile 4) (Ren et al. 2019). The change in the highest HR for the same comparison after the addition of each group of factors was used to estimate the individual contribution of each group to the overall disparity. We added each group of prognostic factors individually, rather than adding them into Model one sequentially, because the order in which the factors are added could affect the estimate of the individual contribution of each (Seneviratne et al. 2015).

The final model included the variables in Model one plus all factors with p value < 0.15 (Bursac et al. 2008), and stratified by stage to improve the model fit. All analyses were performed using SAS version 9.4. Tests for statistical significance were two-sided, $\alpha = 0.05$.

Results

Of the 267,153 participants in the 45 and Up Study, 1720 eligible participants were diagnosed with CRC at age < 85 years during follow-up (Fig. 1): 1174 colon and 546 rectal cancers.

The frequency distributions for selected variables by SES groups are presented in Tables 1 and 2 (colon and rectal cancer, respectively). Overall, patients with low SES for both measures tended to be older and have more comorbidities than their counterparts in the highest SES categories. As expected, fewer patients with lower SES

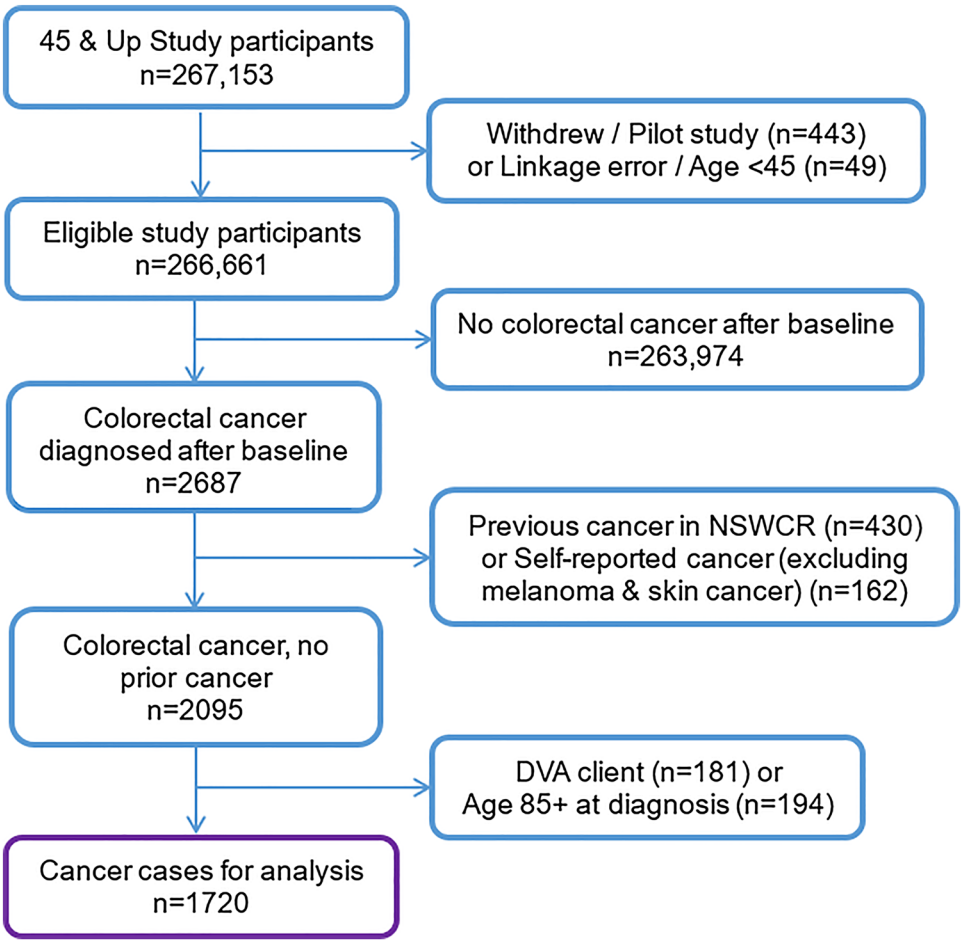

Fig. 1 Study sample selection flow chart. NSWCR: NSW Cancer Registry; DVA: Department of Veterans' Affairs

(both measures) had private health insurance coverage, compared to the highest SES categories for both colon and rectal cancers. Of note, there was no significant variation in the treatment received for colon and rectal cancers across nSES groups, whereas patients with low individual SES were less likely to receive surgery within six months for both colon and rectal cancers compared to those with high-level individual SES.

Colon cancer survival

Significant variation in colon cancer survival occurred only for nSES, with HR = 1.55, 95% CI 1.09–2.19 ($p = 0.033$) for patients living in neighbourhoods in the lowest versus the highest quartile, and disease-related factors explained almost all the variation (Table 3). A similar pattern was observed for the joint SES measure where patients living in low nSES areas had a greater risk of colon cancer death regardless of their individual-level SES. In the final model, all factors (with $p < 0.15$) together explained about 37% of the survival disparities, and variation in survival became non-significant ($p = 0.12$).

Rectal cancer survival

Greater variation was observed for rectal cancer survival, with a clear pattern of increasing hazards of death with lower SES for both SES measures (Table 4). With minimal adjustment (age, year of diagnosis and sex), the risk of dying from rectal cancer was tripled (HR = 3.72, 95% CI 1.86–7.43) for patients living in neighbourhoods in the lowest, versus the highest quartile. After further adjustment, the disparities narrowed, with patient- and disease-related factors being the main contributors to the survival disparities. All the factors (with $p < 0.15$) together in the final model explained 33% of the overall survival disparities by nSES, however, the survival disparities remained significant ($p = 0.0044$).

With only minimal adjustment, the estimated risk of dying for patients with rectal cancer who had low individual-level SES was doubled (HR = 2.26, 95% CI 1.44–3.54) versus those who had high SES (Table 4). Further adjustment for patient-, disease- and treatment-related factors explained 33, 41, and 24% of the disparities, respectively. Survival disparities remained significant ($p = 0.011$), after adjusting for all the factors (with $p < 0.15$) in the final model, which together explained 67% of the survival disparities.

Table 1 Characteristics of colon cancer cases diagnosed during 2006–2013 among 45 and up study participants, NSW Australia

	By neighbourhood socioeconomic measure					
	Total	nSES 1 (Lowest)	nSES 2	nSES 3	nSES 4 (Highest)	*p* value*
No. of cases (%)	1174	320 (27%)	331 (28%)	274 (23%)	249 (21%)	
Patients' characteristics						
Age at diagnosis mean (SD), years	70.0 (8.9)	71.5 (8.6)	69.4 (8.8)	69.6 (9.4)	69.5 (8.7)	0.0065
Male, *n* (%)	585 (49.8%)	157 (49.1%)	154 (46.5%)	140 (51.1%)	134 (53.8%)	0.35
Marital status						0.0023
Married/de facto	837 (71.3%)	205 (64.1%)	240 (72.5%)	197 (71.9%)	195 (78.3%)	
Private health insurance						< 0.0001
Yes	699 (59.5%)	135 (42.2%)	186 (56.2%)	184 (67.2%)	194 (77.9%)	
Residence						< 0.0001
Major cities	590 (50.3%)	117 (36.6%)	124 (37.5%)	151 (55.1%)	198 (79.5%)	
Non-Major cities	584 (49.7%)	203 (63.4%)	207 (62.5%)	123 (44.9%)	51 (20.5%)	
Charlson comorbidity index						0.0005
0	898 (76.5%)	220 (68.8%)	253 (76.4%)	226 (82.5%)	199 (79.9%)	
≥ 1	276 (23.5%)	100 (31.2%)	78 (23.6%)	48 (17.5%)	50 (20.1%)	
Lifestyle factors						
Tobacco smoking						0.53
Ever smoker	268 (22.8%)	69 (21.6%)	85 (25.7%)	61 (22.3%)	53 (21.3%)	
Never smoker†	906 (77.2%)	251 (78.4%)	246 (74.3%)	213 (77.7%)	196 (78.7%)	
Alcoholic drinks (per week)						< 0.0001
0	398 (33.9%)	136 (42.5%)	109 (32.9%)	99 (36.1%)	54 (21.7%)	
1–14	555 (47.3%)	138 (43.1%)	156 (47.1%)	125 (45.6%)	136 (54.6%)	
> 14	209 (17.8%)	41 (12.8%)	60 (18.1%)	50 (18.3%)	58 (23.3%)	
Missing	12 (1.0%)					
Moderate/vigorous physical activity						0.041
Sedentary	68 (5.8%)	28 (8.8%)	18 (5.4%)	13 (4.7%)	9 (3.6%)	
Insufficient	231 (19.7%)	72 (22.5%)	65 (19.6%)	52 (19.0%)	42 (16.9%)	
Sufficient	152 (12.9%)	50 (15.6%)	35 (10.6%)	33 (12.0%)	34 (13.7%)	
High	695 (59.2%)	164 (51.3%)	202 (61.0%)	168 (61.3%)	161 (64.7%)	
Unspecified	28 (2.4%)		11 (3.3%)	8 (2.9%)		
Body mass index						0.17
Normal	394 (33.6%)	96 (30.0%)	119 (36.0%)	87 (31.8%)	92 (37.0%)	
Overweight	439 (37.4%)	114 (35.6%)	116 (35.1%)	115 (42.0%)	94 (37.8%)	
Obese	270 (23.0%)	92 (28.8%)	76 (23.0%)	54 (19.7%)	48 (19.3%)	
Missing	71 (6.0%)	18 (5.6%)	20 (6.0%)	18 (6.6%)	15 (6.0%)	
Disease-related factors						
Cancer stage						0.062
Localised	393 (33.5%)	99 (30.9%)	97 (29.3%)	103 (37.6%)	94 (37.8%)	
Regional	479 (40.8%)	119 (37.2%)	148 (44.7%)	108 (39.4%)	104 (41.8%)	
Distant	234 (19.9%)	78 (24.4%)	69 (20.9)	48 (17.5%)	39 (15.7%)	
Unknown	68 (5.8%)	24 (7.5%)	17 (5.1%)	15 (5.5%)	12 (4.8%)	
Emergency presentation (prior to diagnosis)						
2-weeks prior	115 (9.8%)	39 (12.2%)	33 (10.0%)	28 (10.2%)	15 (6.0%)	0.10
Treatment-related factors						
Surgery in 6 months	984 (83.8%)	262 (81.9%)	278 (84.0%)	236 (86.1%)	208 (83.5%)	0.57
Systemic therapy in 6 months	428 (36.5%)	121 (37.8%)	127 (38.4%)	94 (34.3%)	86 (34.5%)	0.63

	By individual level SES				
	Total	Low	Medium	High	*p* value*
No. of cases^	1149	491 (43%)	228 (20%)	430 (37%)	

Table 1 (continued)

	By individual level SES				
	Total	Low	Medium	High	*p* value*
Patients' characteristics					
Age at diagnosis mean (SD), years	69.9 (8.9)	71.6 (8.1)	70.5 (9.2)	67.8 (9.2)	< 0.0001
Male, n (%)	574 (50.0%)	201 (40.9%)	155 (68.0%)	218 (50.7%)	< 0.0001
Marital status					0.11
Married/de facto	817 (71.1%)	333 (67.8%)	168 (73.7%)	316 (74.5%)	
Private health insurance					< 0.0001
Yes	687 (59.8%)	249 (50.7%)	123 (54.0%)	315 (73.3%)	
Residence					0.096
Major cities	578 (50.3%)	231 (47.0%)	114 (50.0%)	233 (54.2%)	
Non-Major cities	571 (49.7%)	260 (53.0%)	114 (50.0%)	197 (45.8%)	
Charlson comorbidity index					< 0.0001
0	878 (76.4%)	350 (71.3%)	170 (74.6%)	358 (83.3%)	
≥ 1	271 (23.6%)	141 (28.7%)	58 (25.4%)	72 (16.7%)	
Lifestyle factors					
Tobacco smoking					0.91
Ever smoker	262 (22.8%)	115 (23.4%)	51 (22.4%)	96 (22.3%)	
Never smoker†	887 (77.2%)	376 (76.6%)	177 (77.6%)	334 (77.7%)	
Alcoholic drinks (per week)					< 0.0001
0	388 (33.8%)	219 (44.6%)	54 (23.7%)	115 (26.7%)	
1–14	545 (47.4%)	192 (39.1%)	113 (49.6%)	240 (55.8%)	
> 14	207 (18.0%)	76 (15.5%)	57 (25.0%)	74 (17.2%)	
Missing	9 (0.8%)				
Moderate/vigorous physical activity					0.0002
Sedentary	67 (5.8%)	41 (8.4%)	14 (6.1%)	12 (2.8%)	
Insufficient	223 (19.4%)	99 (20.2%)	53 (23.3%)	71 (16.5%)	
Sufficient	150 (13.1%)	64 (13.0%)	28 (12.3%)	58 (13.5%)	
High	683 (59.4%)	273 (55.6%)	124 (54.4%)	286 (66.5%)	
Unspecified	26 (2.3%)				
Body mass index					0.075
Normal	388 (33.8%)	158 (32.2%)	75 (32.9%)	155 (36.1%)	
Overweight	432 (37.6%)	170 (34.6%)	97 (42.5%)	165 (38.4%)	
Obese	263 (22.9%)	134 (27.3%)	42 (18.4%)	87 (20.2%)	
Missing	66 (5.7%)	29 (5.9%)	14 (6.1%)	23 (5.4%)	
Disease-related factors					
Cancer stage					0.18
Localised	385 (33.5%)	159 (32.4%)	81 (35.5%)	145 (33.7%)	
Regional	471 (41.0%)	214 (43.6%)	76 (33.3%)	181 (42.1%)	
Distant	227 (19.8%)	91 (18.5)	53 (23.3%)	83 (19.3%)	
Unknown	66 (5.7%)	27 (5.5%)	18 (7.9%)	21 (4.9%)	
Emergency presentation (prior to diagnosis)					
2 weeks prior	110 (9.6%)	58 (11.8%)	17 (7.5%)	35 (8.1%)	0.08
Treatment-related factors					
Surgery in 6 months	962 (83.7%)	405 (82.5%)	180 (78.9%)	377 (87.7%)	0.0096
Systemic therapy in 6 months	421 (36.6%)	173 (35.2%)	80 (35.1%)	168 (39.1%)	0.42

*p value for F test for continuous variables and χ^2 test for categorical variables

†Never smoker includes those former smokers who quit > 15 years ago

^25 cases with missing value for education level

Table 2 Characteristics of rectal cancer cases diagnosed during 2006–2013 among 45 and Up Study participants, NSW Australia

	By neighbourhood socioeconomic measure					
	Total	nSES 1 (Lowest)	nSES 2	nSES 3	nSES 4 (Highest)	*p* value*
No. of cases	546	134 (25%)	166 (30%)	145 (27%)	101 (18%)	
Patients' characteristics						
Age at diagnosis mean (SD), years	67.2 (9.2)	69.5 (8.5)	66.9 (8.9)	66.8 (9.4)	64.9 (9.7)	0.0012
Male, *n* (%)	356 (65.2%)	95 (70.9%)	99 (59.6%)	94 (64.8%)	68 (67.3%)	0.22
Marital status						0.0024
Married/de facto	383 (70.1%)	77 (57.5%)	120 (72.3%)	108 (74.5%)	78 (77.2%)	
Private health insurance						< 0.0001
Yes	316 (57.9%)	53 (39.6%)	96 (57.8%)	90 (62.1%)	77 (76.2%)	
Residence						< 0.0001
Major cities	249 (45.6%)	36 (26.9%)	53 (31.9%)	83 (57.2%)	77 (76.2%)	
Non-major cities	297 (54.4%)	98 (73.1%)	113 (68.1%)	62 (42.8%)	24 (23.8%)	
Charlson Comorbidity Index						0.015
0	448 (80.1%)	104 (77.6%)	130 (78.3%)	121 (83.5%)	93 (92.1%)	
≥ 1	98 (17.9%)	30 (22.4%)	36 (21.7%)	24 (16.6%)	8 (7.9%)	
Lifestyle factors						
Tobacco smoking						0.41
Ever smoker	136 (24.9%)	32 (32.9%)	48 (28.9%)	36 (24.8%)	20 (19.8%)	
Never smoker[†]	410 (75.1%)	102 (76.1%)	118 (71.1%)	109 (75.2%)	81 (80.2%)	
Alcoholic drinks (per week)						0.46
0	164 (30.0%)	44 (32.8%)	53 (31.9%)	44 (30.3%)	23 (22.8%)	
1–14	273 (50.0%)	57 (42.5%)	86 (51.8%)	76 (52.4%)	54 (53.5%)	
> 14	105 (18.9%)	31 (23.1%)	26 (15.7%)	23 (15.9%)	23 (22.8%)	
Missing	6 (1.1%)					
Moderate/vigorous physical activity						0.032
Sedentary	32 (5.9%)					
Insufficient	85 (15.6%)	22 (16.4%)	30 (18.1%)	25 (17.2%)	8 (7.9%)	
Sufficient	98 (17.9%)	22 (16.4%)	33 (19.9%)	25 (17.2%)	18 (17.8%)	
High	314 (57.5%)	81 (60.5%)	78 (47.0%)	86 (59.3%)	69 (68.2%)	
Unspecified	17 (3.1%)					
Body mass index						0.029
Normal	181 (33.2%)	37 (27.6%)	50 (30.1%)	47 (32.4%)	47 (46.5%)	
Overweight	203 (37.2%)	51 (38.1%)	59 (35.5%)	57 (39.3%)	36 (35.6%)	
Obese	131 (24.0%)	37 (27.6%)	47 (28.3%)	34 (23.5%)	13 (12.9%)	
Missing	31 (5.7%)	9 (6.7%)	10 (6.0%)	7 (4.8%)	5 (5.0%)	
Disease-related factors						
Cancer stage						0.069
Localised	191 (35.0%)	53 (39.6%)	53 (31.9%)	51 (35.2%)	34 (33.7%)	
Regional	227 (41.6%)	46 (34.3%)	73 (44.0%)	62 (42.8%)	46 (45.5%)	
Distant	80 (14.7%)	25 (18.7%)	27 (16.3)	22 (15.2%)	6 (5.9%)	
Unknown	48 (8.8%)	10 (7.5%)	13 (7.8%)	10 (6.9%)	15 (14.9%)	
Emergency presentation (prior to diagnosis)						
2-weeks prior	26 (4.8%)					0.06

Table 2 (continued)

	By neighbourhood socioeconomic measure					
	Total	nSES 1 (Lowest)	nSES 2	nSES 3	nSES 4 (Highest)	*p* value*
Treatment-related factors						
Surgery in 6 months	431 (78.9%)	98 (73.1%)	130 (78.3%)	122 (84.1%)	81 (80.2%)	0.16
Systemic therapy in 6 months	255 (46.7%)	58 (43.3%)	83 (50.0%)	70 (48.3%)	44 (43.6%)	0.59
Radiation therapy in 6 months	158 (28.9%)	37 (27.6%)	56 (33.7%)	40 (27.6%)	25 (24.8%)	0.40
	By individual level SES					
	Total	Low	Medium	High		*p* value*
No. of cases ^	538	196 (36%)	128 (24%)	214 (40%)		
Patients' characteristics						
Age at diagnosis mean (SD), years	67.0 (9.2)	68.7 (8.8)	67.9 (9.1)	65.0 (9.2)		< 0.0001
Male, *n* (%)	351 (65.2%)	111 (56.6%)	96 (75.0%)	144 (67.3%)		0.0023
Marital status						0.12
Married/de facto	377 (70.1%)	127 (64.8%)	92 (71.9%)	158 (73.8%)		
Private health insurance						< 0.0001
Yes	312 (58.0%)	88 (44.9%)	72 (56.3%)	152 (71.0%)		
Residence						0.0062
Major cities	247 (45.9%)	73 (37.2%)	61 (47.7%)	113 (52.8%)		
Non-major cities	291 (54.1%)	123 (62.8%)	67 (52.3%)	101 (47.2%)		
Charlson comorbidity index						0.34
0	443 (82.3%)	160 (81.6%)	101 (78.9%)	182 (85.0%)		
≥ 1	95 (17.0%)	36 (18.4%)	27 (21.1%)	32 (15.0%)		
Lifestyle factors						
Tobacco smoking						0.94
Ever smoker	136 (25.3%)	51 (26.0%)	31 (24.2%)	54 (25.2%)		
Never smoker†	402 (74.7%)	145 (74.0%)	97 (75.8%)	160 (75.8%)		
Alcoholic drinks (per week)						0.23
0	162 (30.1%)	72 (36.7%)	30 (23.4%)	60 (28.0%)		
1–14	269 (50.0%)	86 (43.9%)	69 (52.6%)	114 (53.3%)		
> 14	101 (18.8%)	36 (18.4%)	27 (21.1%)	38 (17.8%)		
Missing	6 (1.1%)					
Moderate/vigorous physical activity						0.13
Sedentary	32 (5.9%)	14 (7.1%)	11 (8.8%)	7 (3.3%)		
Insufficient	84 (15.6%)	39 (19.9%)	16 (12.5%)	29 (13.6%)		
Sufficient	98 (18.2%)	37 (18.9%)	19 (14.8%)	42 (19.3%)		
High	309 (57.4%)	99 (50.5%)	79 (61.7%)	131 (61.2%)		
Unspecified	15 (2.8%)					
Body mass index						0.0019
Normal	176 (32.7%)	50 (25.5%)	41 (32.0%)	85 (39.7%)		
Overweight	201 (37.4%)	66 (33.7%)	53 (41.4%)	82 (38.37%)		
Obese	130 (24.2%)	63 (32.1%)	28 (22.9%)	39 (18.2%)		
Missing	31 (5.8%)	17 (8.7%)	6 (4.7%)	8 (3.7%)		
Disease-related factors						
Cancer stage						0.11
Localised	188 (34.6%)	65 (33.2%)	41 (32.0%)	82 (38.3%)		
Regional	224 (41.6%)	80 (40.8%)	55 (43.0%)	89 (41.6%)		
Distant	79 (14.7%)	39 (19.9%)	18 (14.1%)	22 (10.3%)		

Table 2 (continued)

	By individual level SES				
	Total	Low	Medium	High	*p* value*
Unknown	47 (8.7%)	12 (6.1%)	14 (10.9%)	21 (9.8%)	
Emergency presentation (prior to diagnosis)					
2-weeks prior	26 (4.8%)			10 (4.7%)	0.46
Treatment-related factors					
Surgery in 6 months	425 (79.0%)	144 (73.5%)	97 (75.8%)	184 (86.0%)	0.0048
Systemic therapy in 6 months	252 (46.8%)	83 (42.4%)	59 (46.1%)	110 (51.4%)	0.18
Radiation therapy in 6 months	156 (29.0%)	48 (24.5%)	40 (31.3%)	68 (31.8%)	0.22

*p value for F test for continuous variables and χ^2 test for categorical variables

^Eight cases with missing values for individual-level SES

†Never smoker includes those former smokers who quit > 15 years ago

Regressions for the joint SES measure revealed similar patterns: those with low individual-level SES and living in a low nSES area had the highest risk of dying (HR = 3.86, 95% CI 2.02–7.37), versus those with high individual-level SES who lived in a high nSES area. Patient-, disease-, and treatment-related factors explained 35, 38 and 21% of the overall variation, respectively. After including all the factors in the final model, 52% of the survival disparities were explained but the disparities remained significant ($p = 0.0028$).

Results for the final models for colon and rectal cancer can be found in Supplementary Tables 1–2.

Discussion

In this large Australian cohort study, we found that socioeconomic survival disparities continue to exist after a diagnosis of CRC, with the extent of this disparity varying by CRC sub-site and the SES measures used. By sub-site, the magnitude of the survival disparity was greater for rectal than for colon cancer. By SES measure, the magnitude of the survival disparity was greater for the neighbourhood measure than for an individual's SES. For the joint SES measure, we found that colon cancer patients living in a low SES neighbourhood had a higher risk of death, irrespective of their individual-level SES. Rectal cancer patients with high individual-level SES living in low nSES areas had over two times the risk of death compared to their counterparts living in high nSES areas. This is in the context of the Australian healthcare system that provides universal health care coverage to residents, with free access to essential care, and private health insurance covering some of the costs of specialist care and treatment in private facilities.

While disease-related factors are the main driver for the observed survival disparity for colon cancer, we found treatment-related factors are also independent significant contributors to the SES disparity for colon cancer (Supplementary Table 1). In addition, we found that lifestyle factors (smoking status, alcohol consumption and physical activity) also contribute significantly to the SES disparity for rectal cancer (Supplementary Table 2). These results highlight the importance of early detection and optimal treatment in reducing survival disparities for both colon and rectal cancer.

Our study showed that differences in stage at diagnosis and emergency department presentation explained most of the neighbourhood survival disparities for colon cancer. For rectal cancer, the effects of those prognostic factors had less impact on the neighbourhood survival differences than for individual-level SES, with approximately two-thirds and one-third of the survival disparities, respectively, remaining unexplained. Our results suggest that adjustment for lifestyle factors had minimal impact on the survival disparities. This could be due to the similar patterns of these lifestyle factors by socioeconomic groups in the study cohort.

The socioeconomic survival disparities were greater for rectal cancer than for colon cancer and may be partially explained by differences in treatment patterns. Currently, surgical resection with stage-appropriate neoadjuvant combined-modality therapy is the main treatment for rectal cancer. Both the quality of surgical treatment and timing of initiation of neoadjuvant/adjuvant therapies may vary between patients in different socioeconomic groups, thus affecting their survival. Generally, more technically challenging surgical procedures are often required when treating rectal cancer (Archampong et al. 2010). The unexplained residual disparities in rectal cancer survival could be because patients with lower SES are less likely to receive optimal treatment (Chawla et al. 2013; te Marvelde et al. 2019), as prior research showed that CRC patients had similar survival outcomes regardless of socio-demographic background when receiving guideline-driven treatment in clinical trials (Nur et al. 2008; Unger et al. 2018; Yoon et al. 2015). Additionally, rectal cancer patients with low SES may have

Table 3 Adjusted Hazard Ratios (HRs) for death from colon cancer by socioeconomic status and contributions of factors to overall survival disparities

Models*	Model 1		Model 2		Model 3		Model 4		**Model 5**		**Final model**	
By nSES	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)
nSES 4 (Highest)	1.00		1.00		1.00		1.00		1.00		1.00	
nSES 3	1.08	(0.74–1.57)	1.10	(0.75–1.61)	1.04	(0.71–1.52)	0.97	(0.66–1.42)	1.10	(0.75–1.61)	1.05	(0.73–1.50)
nSES 2	1.41	(1.00–2.00)	1.41	(0.98–2.04)	1.36	(0.96–1.94)	1.11	(0.78–1.57)	1.43	(1.01–2.02)	1.17	(0.82–1.67)
nSES 1 (Lowest)	1.55	(1.09–2.19)	1.50	(1.03–2.18)	1.44	(1.01–2.05)	1.03	(0.73–1.46)	1.43	(1.01–2.03)	1.03	(0.70–1.52)
p value	0.033		0.095		0.08		0.87		0.09		0.79	
Contribution to overall disparities			9%		20%		95%		22%		91%	
By individual SES†												
High	1.00											
Medium	1.43	(1.03–1.97)										
Low	1.19	(0.90–1.57)										
p value	0.10											
Contribution to overall disparities												
Joint nSES and individual SES												
High/high	1.00		1.00		1.00		1.00		1.00		1.00	
High/medium	1.14	(0.67–1.95)	1.08	(0.63–1.84)	1.16	(0.68–1.98)	1.21	(0.71–2.08)	1.27	(0.74–2.16)	1.18	(0.69–2.03)
High/low	1.34	(0.87–2.06)	1.29	(0.84–1.99)	1.30	(0.84–2.01)	1.68	(1.09–2.61)	1.23	(0.80–1.90)	1.48	(0.95–2.31)
Low/high	1.46	(0.96–2.22)	1.43	(0.93–2.20)	1.46	(0.96–2.22)	1.19	(0.79–1.80)	1.49	(0.98–2.26)	1.33	(0.87–2.05)
Low/medium	2.16	(1.42–3.29)	2.06	(1.33–3.20)	2.18	(1.43–3.33)	1.97	(1.28–3.03)	1.85	(1.21–2.81)	1.73	(1.12–2.68)
Low/low	1.46	(1.00–2.13)	1.34	(0.90–2.00)	1.34	(0.91–1.97)	1.19	(0.81–1.73)	1.35	(0.93–1.97)	1.11	(0.75–1.64)
p value	0.014		0.035		0.013		0.017		0.11		0.12	
Contribution to overall disparities			9%		-2%		16%		27%		37%	

*Model 1: included SES measure, age at and year of diagnosis, and sex; Model 2: model 1 plus patient-related factors (marital status, private health insurance, place of residence and comorbidity); Model 3: model 1 plus lifestyle factors (smoking status, alcohol consumption, physical activity and BMI); Model 4: model 1 plus disease-related factors (stage at diagnosis, emergency presentation); Model 5: model 1 plus treatment-related factors (surgery, systemic therapy); **Final model**: model 1 plus all factors with p value remain less than 0.15 in the full model stratified by stage at diagnosis after removal of non-significant variables

†No further analyses for a measure of SES were performed due to non-significant associations in Model 1

Table 4 Adjusted Hazard Ratios (HRs) for death from rectal cancer by socioeconomic status and contribution of factors to overall survival disparities

Models*	Model 1		Model 2		Model 3		Model 4		Model 5		Final model	
By nSES	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)
nSES 4 (Highest)	1.00		1.00		1.00		1.00		1.00		1.00	
nSES 3	2.18	(1.06–4.48)	2.00	(0.87–4.15)	2.24	(1.08–4.64)	1.79	(0.86–3.72)	2.51	(1.22–5.16)	1.71	(0.82–3.57)
nSES 2	2.34	(1.16–4.75)	2.05	(0.98–4.26)	2.24	(1.09–4.59)	1.65	(0.80–3.41)	2.45	(1.20–4.97)	1.39	(0.66–2.92)
nSES 1 (Lowest)	3.72	(1.86–7.43)	2.73	(1.30–5.71)	3.77	(1.87–7.60)	2.95	(1.46–5.96)	3.71	(1.85–7.44)	2.82	(1.38–5.75)
p value	0.0013		0.065		0.0013		0.0063		0.0026		0.0044	
Contribution to overall disparities			36%		-2%		28%		0%		33%	
By individual SES												
High	1.00		1.00		1.00		1.00		1.00		1.00	
Medium	1.31	(0.77–2.23)	1.15	(0.67–1.97)	1.29	(0.76–2.21)	1.01	(0.58–1.73)	1.13	(0.66–1.94)	0.69	(0.39–1.22)
Low	2.26	(1.44–3.54)	1.84	(1.16–2.92)	2.39	(1.50–3.81)	1.74	(1.11–2.72)	1.96	(1.23–3.12)	1.42	(0.90–2.26)
p value	0.0009		0.019		0.0005		0.016		0.0069		0.011	
Contribution to overall disparities			33%		-10%		41%		24%		67%	
Joint nSES and individual SES												
High/high	1.00		1.00		1.00		1.00		1.00		1.00	
High/medium	1.92	(0.85–4.36)	1.70	(0.75–3.88)	2.02	(0.89–4.61)	1.82	(0.80–4.15)	1.68	(0.74–3.83)	1.49	(0.65–3.44)
High/low	2.62	(1.21–5.66)	2.13	(0.97–4.67)	2.83	(1.30–6.16)	1.68	(0.77–3.67)	2.23	(1.02–4.89)	1.30	(0.59–2.88)
Low/high	2.32	(1.11–4.83)	1.91	(0.90–4.07)	2.39	(1.15–4.99)	1.85	(0.88–3.88)	2.20	(1.05–4.60)	1.91	(0.90–4.06)
Low/medium	2.05	(0.94–4.46)	1.58	(0.71–3.51)	1.99	(0.91–4.35)	1.16	(0.52–2.59)	1.70	(0.77–3.72)	0.70	(0.30–1.63)
Low/low	3.86	(2.02–7.37)	2.86	(1.45–5.67)	4.22	(2.16–8.23)	2.77	(1.45–5.33)	3.27	(1.69–6.34)	2.36	(1.22–4.58)
p value	0.0017		0.0497		0.001		0.012		0.0099		0.0028	
Contribution to overall disparities			35%		-13%		38%		21%		52%	

*Model 1: included SES measure, age at and year of diagnosis, and sex; Model 2: model 1 plus patient-related factors (marital status, private health insurance, place of residence and comorbidity); Model 3: model 1 plus lifestyle factors (smoking status, alcohol consumption, physical activity and BMI); Model 4: model 1 plus disease-related factors (stage at diagnosis, emergency presentation); Model 5: model 1 plus treatment-related factors (surgery, systemic therapy, radiation therapy); Final model: model 1 plus all factors with p value remain less than 0.15 in the full model stratified by stage at diagnosis after removal of non-significant variables

longer delay in getting adjuvant therapy after surgical resection due to lower adherence to effective therapy (Carethers and Doubeni 2020), and delaying adjuvant chemotherapy beyond 12 weeks post surgery was found to be associated with reduced survival for high-risk CRC patients (Biagi et al. 2011).

Our findings suggest that where people lived played a more important role than their education level in predicting CRC survival outcomes. The nSES variable used in this analysis is based on the smallest geographical unit for which a measure of SES from census data is available in Australia (Australian Bureau of Statistics 2013). It could be that nSES reflects access to cancer care and the quality of the care received (Ellis et al. 2018; Hill et al. 2010), and thus affects the outcomes of patients with both high and low education levels in the same neighbourhood. Timely and high-quality cancer care is a major prognostic factor, and this may be why our results indicate that nSES explains more of the survival disparities than individual patients' education level.

Survival disparities by SES may be partially attributable to the different screening patterns between population groups. Australia has a National Bowel Cancer Screening Program (NBCSP) which has been phased in since 2006 and reached full implementation in 2020 from which time all Australians aged 50–74 years are invited to screen biennially (Australian Institute of Health and Welfare 2019b). As of 2018, participation rates were lower for those living in the lowest socioeconomic areas (Australian Institute of Health and Welfare 2019b) which can often result in later stage at diagnosis. While our adjustment for cancer stage may account for some of the differences in screening participation, this adjustment was rather crude (Yu et al. 2005) and we are unable to control for possible within-stage survival differences for screen-detected versus symptomatic cancers (Lew et al. 2017). Nonetheless, as most of the participants in this study joined the cohort in 2008 and cancer diagnoses were up to 2013, the effect of screening on our survival results would be minimal.

This study has many strengths, such as the comprehensive inclusion of prospective data on patient and lifestyle variables from a large contemporary Australian cohort (Banks et al. 2008), and the ability to investigate a range of prognostic factors. Additionally, our analysis assessed these socioeconomic disparities at both individual and neighbourhood-levels separately and jointly, as has been previously recommended (Wallner and Griggs 2018). However, there are some potential limitations. First, the study population was limited to the participants in the 45 and Up Study, a cohort which has been shown to be older and more educated than the general population (Banks et al. 2008), so our results may not be representative of the entire NSW population. However prior studies have indicated that there is little evidence of bias in the association between nSES and cancer survival in this cohort (Creighton et al. 2018), and reasonable estimates of relative differences can be obtained (Mealing et al. 2010). Second, variables related to care coordination, or the quality of care were not available, each of which is potentially an important determinant of survival. Third, although individual's educational attainment is a widely used SES measure, using it alone has limitations, e.g., the older patients in our cohort were over-represented among those classified as less educated. Finally, coverage of radiation therapy may be incomplete as not all radiation therapy is captured in the MBS claims records for public patients in public hospitals (Australian Institute of Health and Welfare 2019a), and this information is limited in the hospital admission records (Goldsbury et al. 2012).

Our study was performed using data that pre-dates the COVID-19 pandemic. In Australia, as in other countries, one concern is that health service disruptions will have long term implications for cancer outcomes and that the pandemic will exacerbate pre-existing inequalities in outcomes. Although the NBCSP did not pause operations in Australia, indications of a drop in colonoscopy procedures during April–May 2020 were noted (Cancer Australia 2020). Our findings suggest that disparities in outcomes are in part driven by SES-related factors, particularly for rectal cancer. If SES-related factors prove to be important in determining cancer outcomes in the context of crisis-related health services disruptions, then addressing the impact of disparities in rectal cancer outcomes might be an important focus area for longer-term crisis mitigation planning (Carethers et al. 2020). Future policy decisions will need to consider ways in which disparities can be reduced and our work can help inform decisions that may relate to resource allocation or awareness program coverage, guided by the contribution of the various demographic and geographical factors.

As has been found previously (Beckmann et al. 2016; Kelsall et al. 2009; Stanbury et al. 2016a; b; Yu et al. 2005; Yu et al. 2008), our study showed that even in Australia, a country with a universal healthcare system, there are observed survival disparities by socioeconomic level. Our study goes beyond those previous studies by providing detailed analyses of contributing factors and the magnitude of their contribution. The approach used in this study to investigate underlying mechanisms for survival disparities could be a useful tool for improving our understanding of the underlying reasons for survival disparities. The approach can be applied to other cancer types both in Australia and in other countries. Using these findings, policy-driven and evidence-informed interventions could be developed to reduce SES-driven disparities and improve survival. These

interventions could include encouraging lifestyle changes to reduce risky behaviours, improving participation in early detection programs, and ensuring delivery of high-quality treatments in concordance with treatment guidelines regardless of patient's socioeconomic level or where they live (Bergin et al. 2020; Carethers and Doubeni 2020; te Marvelde et al. 2019). The latter may require policy considerations regarding alternative funding models to support cancer patients with low SES. In addition, for rectal cancer further work is required to understand the remaining differences and how they can be addressed so that all rectal cancer patients have the best possible survival outcomes.

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Author contributions XQY conceived the original research idea with input from DLO'C. XQY performed the data analysis and wrote the initial draft of this paper. DG, EF, CEK, KC and DLO'C revised the manuscript critically. DG made significant contributions to the description of data sources and variables to be used in the analysis. All authors approved the final version of this paper.

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Availability of data and material Data underlying this article may be shared on request to the corresponding author with approval from the NSW Population & Health Services Research Ethics Committee.

Code availability Not applicable.

Declarations

Conflict of interest KC is co-principal investigator of an investigator-initiated trial of cytology and primary HPV screening in Australia ("Compass"), which is conducted and funded by the VCS Foundation, a government-funded health promotion charity. VCS has received equipment and a funding contribution for the Compass trial from Roche Molecular Systems and Ventana USA. However neither KC, nor her institution on her behalf (Cancer Council NSW) has received direct or indirect funding from industry for Compass or any other project. No other conflict of interests is declared.

Ethics approval The 45 and Up Study was approved by the University of NSW Human Research Ethics Committee (HREC 05035/HREC 10186). This analysis was covered by ethics approval from the NSW Population and Health Services Research Ethics Committee (HREC/14/CIPHS/54).

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