# Temporal and spatial analyses of colorectal cancer incidence in Yogyakarta, Indonesia: a cross-sectional study

**Juan Adrian Wiranata,[1,2] Herindita Puspitaningtyas,[3] Susanna Hilda Hutajulu,[4] Jajah Fachiroh,[5] Nungki Anggorowati,[6] Guardian Yoki Sanjaya,[7] Lutfan Lazuardi,[7] Patumrat Sripan[8]**

*[1]Academic Hospital; [2]Master Program in Clinical Epidemiology; [3]Doctorate Program of Health and Medical Science, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta; [4]Division of Hematology and Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta, Indonesia; [5]Department of Histology and Cell Biology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta; [6]Department of Anatomical Pathology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta, Indonesia; [7]Department of Health Policy and Management, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia; [8]Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand*

Correspondence: Susanna Hilda Hutajulu, Division of Hematology and Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta, Indonesia.
Tel./Fax: +62.274.553122
E-mail: susanna.hutajulu@ugm.ac.id

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## Abstract

We aimed to explore the district-level temporal dynamics and sub-district level geographical variations of colorectal cancer (CRC) incidence in the Special Region of Yogyakarta Province. We performed a cross-sectional study using data from the Yogyakarta population-based cancer registry (PBCR) comprised of 1,593 CRC cases diagnosed in 2008-2019. The age-standardized rates (ASRs) were determined using 2014 population data. The temporal trend and geographical distribution of cases were analysed using joinpoint regression and Moran's *I* statistics. During 2008-2019, CRC incidence increased by 13.44% annually. Joinpoints were identified in 2014 and 2017, which were also the periods when annual percentage change (APC) was the highest throughout the observation periods (18.84). Significant APC changes were observed in all districts, with the highest in Kota Yogyakarta (15.57). The ASR of CRC incidence per 100,000 person-years was 7.03 in Sleman, 9.20 in Kota Yogyakarta, and 7.07 in Bantul district. We found a regional variation of CRC ASR with a concentrated pattern of hotspots in the central sub-districts of the catchment areas and a significant positive spatial autocorrelation of CRC incidence rates in the province (I=0.581, p<0.001). The analysis identified four high-high clusters sub-districts in the central catchment areas. This is the first Indonesian study reported from PBCR data, showing an increased annual CRC incidence during an extensive observation period in the Yogyakarta region. A heterogeneous distribution map of CRC incidence is included. These findings may serve as basis for CRC screening implementation and healthcare services improvement.

## Introduction

Colorectal cancer (CRC) is the third most prevalent malignancy and the second leading cause of cancer death worldwide, with the Asian population ranking first in terms of the incidence and mortality (Ferlay *et al.*, 2020). In Indonesia, 34,189 new cases of CRC were estimated in 2020, making it the country's fourth most prevalent cancer incidence, and the CRC mortality rate the fifth largest in the world by reaching 6.7 deaths per 100,000 person-years (Ferlay *et al.*, 2020). According to the Indonesian Ministry of Health (MoH), the Special Region of Yogyakarta Province, one of 34 provinces in Indonesia, is the province with the highest cancer prevalence (MoH, 2019). Data from the hospital-based cancer registry (HBCR) at the top referral hospital in the region (Dr Sardjito Hospital) showed that CRC incidence ranked second only to breast cancer. The CRC cases were dominated by males (54.0%), adults of productive age (20-69 years) (62.3%), and advanced tumours (49.7%) (Jogja Cancer Registry, 2022). Exploration of CRC trend and geographical variation in this population are of utmost importance regarding its high cancer prevalence.

In exploring the dynamics of cancer burden, joinpoint regression is a recognized, valuable tool for concluding changes in trends over time (Arnold *et al.*, 2017; Sarakarn *et al.*, 2017; Sung *et al.*, 2019). This analysis has been extensively used to characterize long-term cancer incidence and mortality trends and advocate policy changes to promote cancer control and prevention programs (Jemal *et al.*, 2008). Trend analysis using population-wide data from population-based cancer registries (PBCRs) has been commonly used in cancer epidemiology, which may provide essential cues for the public, policymakers, and researchers in identifying the timing and extent of changes in the time series. Many studies have measured disparities in CRC geographically. Identifying areas with a concentrated cancer burden can potentially increase the efficiency of CRC prevention and control (Wheeler & Basch, 2017). For these purposes, previous studies have successfully demonstrated spatial variability of CRC linked to socioeconomics and environmental risks, including investigating spatial autocorrelation using Local Moran's *I* statistics (Dadashi *et al.*, 2021; Halimi *et al.*, 2020), and determining local coefficient with Geographically Weighted Regression (GWR) (Mansori *et al.*, 2019; Thatcher *et al.,* 2021). Access to health facilities and exposure to the environment, such as poor air quality, traffic emission, heavy metal contamination (Wang *et al.*, 2017), water pollution (Fathmawati *et al.*, 2017), urbanity status, poverty rates, unemployment and crime have been explored (Soffian *et al*., 2021).

Cancer registry data are important for estimating cancer indicators in temporal and geospatial analyses. HBCR is essential in providing actual and high-quality cancer data for quality-of-care improvement (Mohammadzadeh *et al.*, 2017), and can be used for the above-mentioned purposes. However, by design, it is unable to provide the actual profile of the current cancer burden in the population due to the absence of systematic ascertainment of cancer reporting as served in PBCRs (Bray *et al.*, 2014; Jensen *et al.*, 1991). Besides, heterogeneous performance of HBCRs in various countries exists (Mohammadzadeh *et al.*, 2017). PBCRs are more regulated and have a standardized data quality parameter to ensure their comparability (Bray *et al.*, 2014).

Few temporal analyses have been performed to evaluate the cancer burden in Indonesia (Gondhowiardjo *et al.*, 2021; Tjindarbumi & Mangunkusumo, 2002). Furthermore, these studies did not report the cancer incidence due to being performed in a hospital-based setting and did not focus on any specific cancer type. Information about cancer geographical variation in Indonesia is also very limited. One spatial study in Yogyakarta Province described the geographical variance of cancer incidence, including CRC, for cases diagnosed in 2019-2020 at the district level (Solikhah *et al.*, 2022). This study did not describe temporal trends nor sub-district level variance and only collected data from four hospital-based registries. Accordingly, our study aimed to analyse the temporal dynamics and identify CRC incidence variations and clusters in the sub-district level of Yogyakarta Province for cases diagnosed in an extensive period (2008-2019) using PBCR data.

## Materials and Methods

### Study design, area, and population

A cross-sectional design was used to examine CRC incidence in patients residing ≥6 months in the Special Region of Yogyakarta Province, Indonesia. The province comprises five districts and 78 sub-districts covering an area of 3,186 km² and with a population of 3,677 million in 2021. All data of CRC cases were obtained from the Yogyakarta PBCR, which has three catchment districts, namely Sleman, Kota Yogyakarta, and Bantul. In 2021, these three districts had a population of 1.088 million, 0.415 million and 0.956 million, respectively, while the administrative area covered by each district is 574.8 km², 32.5 km² and 506 km², respectively. Sleman and Bantul districts comprise a total of 17 sub-districts each, while Kota Yogyakarta comprises 14 sub-districts (Figure 1).

### Data source, variables and measurement

The Yogyakarta PBCR is part of the national PBCR network, which includes 14 vertical-level referral hospitals. The network was established in 2016 by the MoH and initiated data collection in the same year. It collects information from various levels of healthcare facilities, including the vertical and district referral hospitals, public and private pathology laboratories, oncology clinics and primary health centres. Information from the sources was collected from the patients' medical records and examination results, such as radiology and anatomical pathology reports. To date it has collected data from 18,992 cancer cases diagnosed from January 2008 to mid-2020.

The registered data were classified into three parts. Part I included patient demography, including medical record number, name, identity number, permanent resident address, sex, religion, marital status, ethnicity, occupation, age of diagnosis and date of birth. Part II included clinical data such as tumour topography, morphology and behaviour according to the International Classification of Disease-Oncology (ICD-O), basis of diagnosis, tumour extent [according to the surveillance, epidemiology, and end results (SEER) program summary staging manual], stage, metastasis and treatments. Part III included data summary and follow-up such as physicians' records, examination results, date of first identification, date of last contact and patients' vital status. These variables are defined according to CanReg5, an open-source tool developed by the International Agency for Research on Cancer (IARC) specially designed to input, store, check, and analyze population-based cancer registry data, which has been adopted for the Indonesian cancer registry (version 5.00.40).

The present study included all primary CRC cases (n=1,604) from the PBCR database, defined as C18.0-9, C19.9 and C20.9 according to the ICD-10 codes. We focused on data from patients diagnosed in 2008-2019. Data extraction was done between May and July 2022. The main variables included permanent address, year of diagnosis and sex; data with incomplete addresses were excluded (n=6 or 0.4%). Additional variables with coding completeness of ≥80% were also extracted to describe characteristics of the cases, including age, religion, marital status, tumour site, stage and morphology types. Because cases of age <20 years were relatively few (n=5 or 0.3%), they were also excluded. Finally, 1,593 data were included for temporal and spatial analyses.

## Data analysis

Population data for Sleman, Kota Yogyakarta and Bantul Districts were obtained at sub-district levels as provided by the Indonesian Central Bureau of Statistics. The numbers of populations from each sub-districts in 5-year age increments (up to 79 and ≥80 years of age) were used to calculate the age-specific risk of CRC in the population. The World Standard Population was used as a weights reference in computing the age-standardized incidence rates (ASR) (Boyle & Parkin, 1991). ASR is reported per 100,000 person-years and provided for both sexes (male and female) separately due to the disparity of cancer susceptibility in each sex (Kim *et al.*, 2018). The ASRs of 2008–2019 were determined using population data from 2014, which is the central year of the study. Joinpoint regression employing a permutation test (Gillis & Edwards, 2019) was then performed to identify the dynamic changes of ASRs within the observation years. It models the time sequence using a few continuous linear segments, which are then joined at points that indicate the year in which a statistically significant shift in the rate trend occurred (Xu *et al.*, 2020). With the assumption that the time data can be divided into subsets. the jointpoint method thus enables the identification of a point within a linear trend when a change takes place.

We obtained the shapefile for the base maps of the three districts from the basic geospatial information (Informasi Geospasial Dasar) provided by the Geospatial Information Agency (Badan Informasi Geospasial) of Indonesia made available for public for use, adaptation and distribution as a website (https://tanahair.indonesia.go.id/). We generated a map of the CRC ASR patterns at the sub-district level based on sex for descriptive data visualization. The area with the highest case density (4th quartile) was determined a hotspot, with the remaining areas categorized as coldspots. Clinical characteristics of the subjects were expressed as median with standard error (SE) for continuous variables and numbers for categorical variables. Chi-square analyses with 95% confidence interval (CI) were performed to determine the statistical differences (p<0.05) among cases located in hotspots and coldspots.

The Global Moran's *I* statistic was used to determine spatial autocorrelation or global clustering in the pattern of CRC ASR at the sub-district level (Goodchild, 1986). Analysis with Local Indicators of Spatial Association (LISA) (Anselin *et al.*, 1996) was used to identify local statistically significant clusters and outliers. The LISA statistic may identify four types of spatial clusters or outliers. These include a high-high (HH) cluster (defined as a high ASR sub-district located adjacent to similarly high ASR subdistricts), low-low (LL) cluster (defined as alow ASR sub-district located adjacent to similarly low ASR sub-districts), high-low (HL) outlier (defined as a high ASR sub-district located adjacent to low ASR sub-districts) ot low-high (LH) outlier (defined as a low ASR sub-district located adjacent to high ASR sub-districts). Using the LISA analysis, a map was generated to identify statistically significant sub-districts.

Statistical analysis was performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). The temporal trend was observed using the Joinpoint Regression program, version 4.9.1.0 (SEER, USA). Data visualization was performed using the Quantum Geographic Information System (QGIS), desktop version 3.26, a GIS open-source software. Global Moran's *I* analysis was conducted using the spdep package (Bivand & Wong, 2018), whereas LISA analysis was performed using the rgeoda package (Anselin & Li, 2022); both performed using R statistical software version 4.2.2 (https://www.r-project.org/).

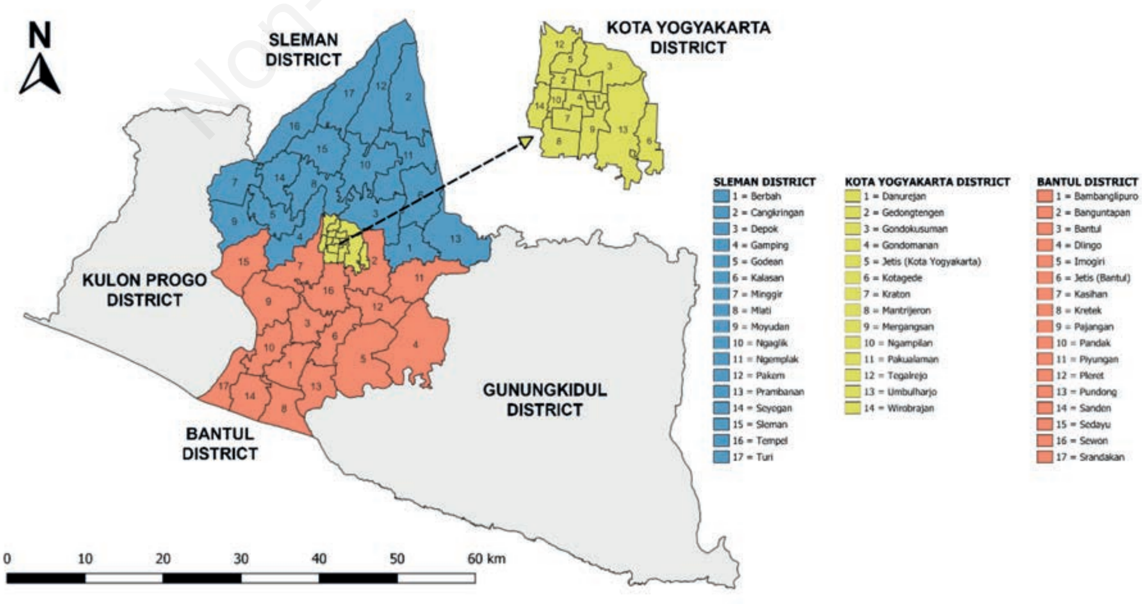


**Figure 1. Districts and sub-districts in the Special Region of Yogyakarta Province.**

## Results

Data were collected from the Yogyakarta PBCR database for 1,593 CRC cases diagnosed from 1 January 2008 to 31 December 2019. There were 684 residents from the Sleman District, 328 from the Kota Yogyakarta District, and 581 from the Bantul District (Supplementary Material 1). There were 865 (54.3%) males and 728 (45.7%) females. The median age was 58±18 years old, with 405 cases (25.42%) of early-onset CRC (EO-CRC) (Table 1). The peak incidence of CRC in the population is within the age group 65-69 years old in males (ASR=30.44; SE=2.93) and 60-64 years old in females (ASR=21.35; SE=2.01) (Figure 2). Most cases were Muslims (n=1,131; 71.0%) and married (n=1,175; 73.8%). More cases were diagnosed with colon cancer (n=904; 56.8%), with the most common morphology type being adenocarcinoma (n=1,007; 63.2%). Among cases observed, most subjects presented at advanced stages (n=189; 11.9%) (Table 1).

In total, 514 cases (32.2%) were identified in the CRC hotspot in the three districts. Analysis showed similar distributions of EO-CRC cases, religion, marital status, stage, and morphology sub-types in the hotspots and cold spots (all p-values > 0.05). In the hotspot, we observed significantly more cases compared to the coldspot (n=315; 61.3% and n=591; 54.8%; p=0.014), despite similar proportions of CRC in both groups (Table 1). Figure 3 shows temporal trends of CRC cases. During 2008-2019, CRC incidence in the three districts increased 13.4% on an annual basis (95% CI: 11.06-15.86; p<0.001). The average annual changes of CRC incidence were similar among males and females (annual percent change/APC=12.93; 95% CI: 9.33-16.64 and APC=14.07; 95% CI: 10.73-17.90, p=0.628). Joinpoints were identified in 2014 and 2017, which were also the periods when APC was the highest throughout the observation period (APC=18.84; 95% CI: -7.39-52.51). Significant APC changes were observed in all districts, with the highest observed in Kota Yogyakarta (APC=15.57; 95% CI:10.18-21.22; p<0.001), followed by Sleman (APC=8.03; 95% CI: 4.20-12.00; p<0,001) and Bantul (APC=8.0; 95% CI: 4.12-11.94; p<0.001).

The ASR of CRC incidence was 7.03 in Sleman, 9.20 in Kota Yogyakarta, and 7.07 in Bantul District. The highest CRC incidence was observed in the Umbulharjo (ASR=12.32), while the lowest was in the Gedongtengen (ASR=3.00), both located in Kota Yogyakarta District (Table 2). The highest ASR in males was observed in Pakualaman (ASR=16.86), Kota Yogyakarta, while the lowest was in Tempel, Sleman (ASR=3.28). The highest incidence in females was in Bantul, Bantul District (ASR=11.84), while the lowest was in Gedongtengen, Kota Yogyakarta (ASR=0.96).

The geographical distribution of the CRC according to LISA was similar when considering the male or female populations separately and when combined as shown in Figure 4. The hotspots was mainly concentrated in the centre of the region. Four of the ten sub-districts in Kota Yogyakarta District (Gondomanan, Mergangsan, Umbulharjo, and Wirobrajan) and one sub-district in Bantul District (Bantul) were consistently recognized as hotspots both for the male and female populations, as well as combined. Meanwhile, Danurejan (Kota Yogyakarta District), considered a hotspot for the male and female populations, was no longer included in the highest quartile when combining both populations. On the contrary, Depok (Sleman District) and Srandakan (Bantul District), recognized as hotspots when only considering the male or female population, remained in the highest quartile when combining both populations.

The global spatial autocorrelation analysis of the cumulative CRC ASR of incidence in Sleman, Kota Yogyakarta, and Bantul between 2008 and 2019 showed a Moran's $I$ of 0.205 (z=2.534; p<0.001), a positive spatial autocorrelation which indicates geographically adjacent ASR values of a Sub-District tended to be similar. The LISA analysis revealed the presence of four HH clusters, which included the Kasihan Sub-district of the Bantul District and the Mantrijeron, Mergangsan and Pakualaman Sub-districts of the Kota Yogyakarta District. It also revealed five LL clusters. A group of four such clusters were seen in the southeast of the catchment area, which included the Prambanan Sub-district of the Sleman District and the Piyungan, Pleret and Dlingo Sub-districts of the Bantul District. One LL cluster located in the northwest of

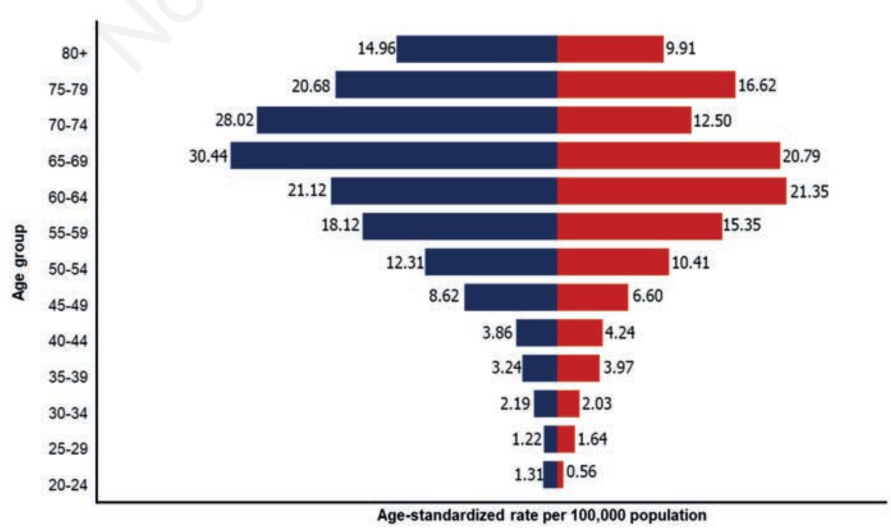


**Figure 2. Incidence rate of colorectal cancer in Sleman, Kota Yogyakarta and Bantul.**

the catchment area was the Seyegan sub-district of the Sleman District. Two spatial outliers were located in the Gedongtengen and Gondokusuman Sub-districts of the Kota Yogyakarta District (Figure 5).

## Discussion

The current findings based on PBCR data demonstrate a consistent increase in the incidence trend from CRC from 2008-2019 in all three districts of interest and shows the unequal distribution and considerable regional variation of CRC in of the study area. CRC tends to stand out more in the central sub-districts than in the peripheral bordering sub-districts. The Global Moran's *I* and z-score in this study (I=0.205; z=2.534) indicate statistically significant positive spatial autocorrelation, which is higher compared to other studies that also have investigated CRC clustering, *e.g.*, in north-eastern Iran (I=0.057; z=1.549) (Goshayeshi *et al*., 2019), and mainland Portugal (z=–0.46 for men and –0.34 for women) (Roquette *et al*., 2019). This finding suggests that CRC incidence in the location of our study appeared more clustered.

The highest APC was found in the Kota Yogyakarta District (15.6%), where the hotspot distribution is centred and several high-high clusters located. This is in accordance with the fact that it not only has the highest population density but also is the smallest district in the province. In addition, the increased accessibility through national universal health coverage and the close distance to the health facilities facilitate access to proper screening and diagnostic examination, which has also been observed by others (Musoke *et al.*, 2014). This condition might not apply to the other two districts which have more extensive areas and lower population density. Remarkably, our findings differ from a very recent report by Solikhah *et al.* (2022) that shows a very high CRC burden in the Sleman District (crude rate=332 per 100,000 population at risk). The discrete method of this study and the use of hospital-based registries may explain its different results from ours.

Previous studies indicated that CRC incidence is increasing alongside socioeconomic advancement and urbanization (Wen *et al.*, 2018). Many modifiable risk factors such as sedentary lifestyles and

**Table 1. Characteristics of colorectal cancer in Sleman, Kota Yogyakarta and Bantul.**

| Characteristic | Total number (%) or median (IQR) | Hotspot number (%) or median (IQR) | Coldspot number (%) or median (IQR) | p |
|---|---|---|---|---|
| Cases | 1,593 (100) | 514 (32.18) | 1,079 (67.82) | |
| Age in years | 58.00 (18.00) | 58.00 (18.00) | 58.00 (18.00) | |
| Age at diagnosis | | | | 0.565 |
| <50 years | 405 (25.42) | 126 (24.51) | 279 (25.86) | |
| ≥50 years | 1,188 (74.58) | 388 (75.49) | 800 (74.14) | |
| Sex | 0.821 | | | |
| Male | 865 (54.30) | 277 (53.89) | 588 (54.49) | |
| Female | 728 (45.70) | 237 (46.11) | 491 (45.51) | |
| Religion | | | | 0.323 |
| Islam | 1,131 (71.00) | 349 (67.90) | 782 (72.47) | |
| Catholic | 87 (5.46) | 36 (7.00) | 51 (4.73) | |
| Protestant | 62 (3.89) | 20 (3.89) | 42 (3.89) | |
| Hindu | 1 (0.06) | 0 (0.00) | 1 (0.09) | |
| Buddhist | 3 (0.19) | 1 (0.19) | 2 (0.19) | |
| Other | 309 (19.40) | 108 (21.01) | 201 (18.63) | |
| Marital status | | | | 0.279 |
| Married | 1,175 (73.76) | 365 (71.01) | 810 (75.07) | |
| Divorced or widowed | 65 (4.08) | 24 (4.67) | 41 (3.80) | |
| Single | 33 (2.07) | 14 (2.72) | 19 (1.76) | |
| Unknown | 320 (20.09) | 111 (21.60) | 209 (19.37) | |
| Tumour site | | | | 0.014* |
| Colon | 904 (56.75) | 315 (61.28) | 591 (54.77) | |
| Rectum | 687 (43.13) | 199 (38.72) | 488 (45.23) | |
| Stage | | | | 0.274 |
| I | 52 (3.26) | 15 (2.92) | 37 (3.43) | |
| II | 84 (5.27) | 26 (5.06) | 58 (5.38) | |
| III | 94 (5.90) | 34 (6.61) | 60 (5.56) | |
| IV | 189 (11.86) | 73 (14.20) | 116 (10.75) | |
| Unknown | 1,174 (73.70) | 366 (71.21) | 808 (74.88) | |
| Morphological subtype | | | | 0.731 |
| Adenocarcinoma NOS | 1,007 (63.21) | 329 (64.01) | 678 (62.84) | |
| Neoplasm, malignant | 319 (20.03) | 105 (20.43) | 214 (19.83) | |
| Mucinous adenocarcinoma | 80 (5.02) | 28 (5.45) | 52 (4.82) | |
| Signet ring cell carcinoma | 26 (1.63) | 7 (1.36) | 19 (1.76) | |
| Other | 161 (10.11) | 45 (8.75) | 116 (10.75) | |

CRC, colorectal cancer; IQR, Interquartile range; NOS, not otherwise specified;*statistically significant.

unhealthy diets relate to urban living (Katsidzira *et al.*, 2019). In fact, the three districts studied have shown significant urbanization during the recent decades, with the majority of sub-districts displaying 2-5% and >5% urbanization rates during the 1990-2010 period and urbanization levels >50% in 2010 (Setyono *et al.*, 2016). Dietary consumption patterns possibly also play a role in the unequal distribution of CRC incidence between districts of interest. Data collected in 2018 (Central Bureau of Statistics of Kota Yogyakarta, 2018) showed that Kota Yogyakarta District has higher exposure to fast foods, instant drinks, cigarettes and tobacco products and lower consumption of fruits and vegetables (Mahfouz *et al.*, 2014) compared to the other two districts. Although information on the rate of physical activity of the observed population is currently unavailable, routine government surveillance have demonstrated an increase in the prevalence of obesity in the urban population in Yogyakarta Province (39.7% in 2018 *vs* 30.7 % in 2013) (Central Bureau of

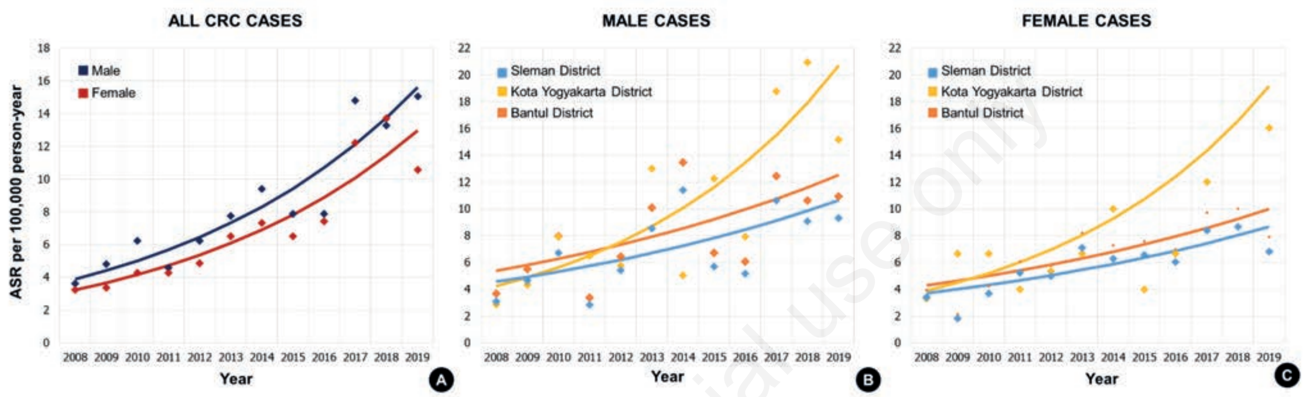


**Figure 3. Temporal dynamics of the colorectal cancer incidence using Joinpoint regression analysis from 2008-2019.**

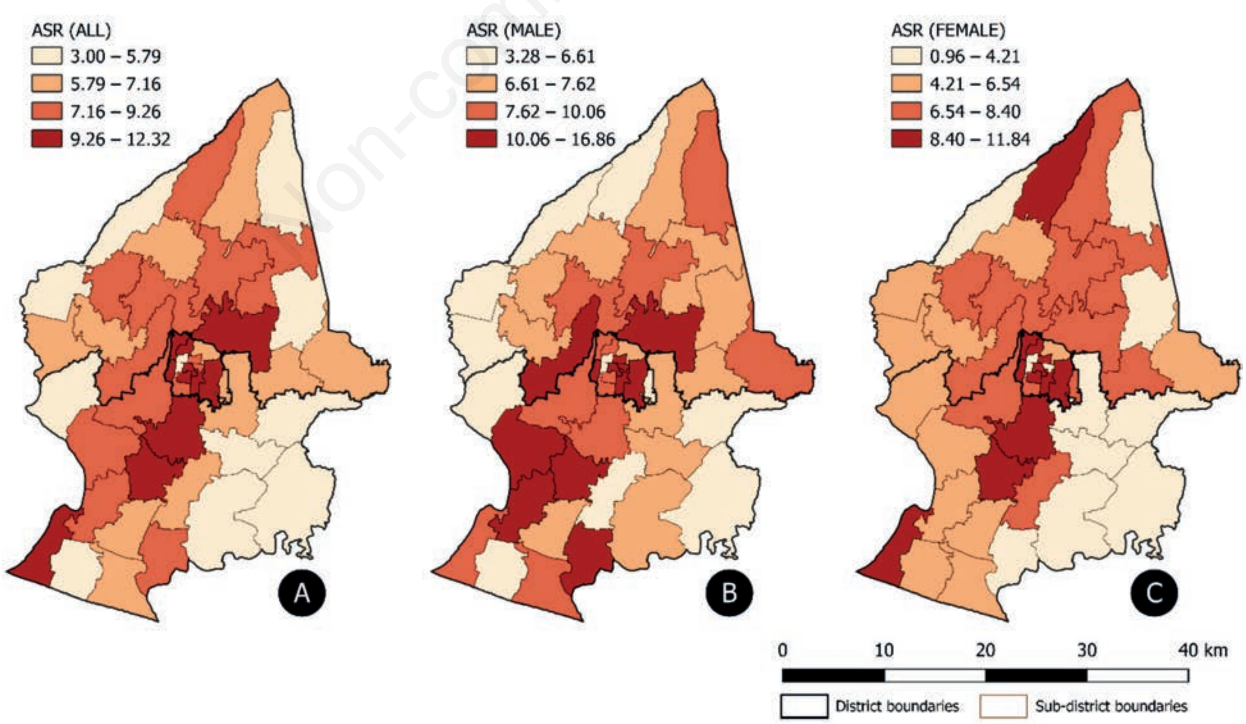


**Figure 4. Geographic variation of the age-standardized colorectal cancer incidence rate by sub-district in Sleman, Kota Yogyakarta and Bantul.**

Statistics, 2018). The higher proportion of colon cancer in the hotspots, which mainly comprise the sub-districts of Kota Yogyakarta, despite the relatively similar characteristics of subjects among hotspots and coldspots, suggests the possibility of other specific geographical factors that were not captured in this study.

Living in an industrial area has also been indicated to affect the incidence of CRC by exposure to air and water pollutants (García-Pérez *et al.*, 2020). In recent years, the transition of agricultural land into industrial areas has been widespread in Yogyakarta, primarily in urban areas. With the majority of agricultural units conducted on a small scale with minimal contribution of the agricultural sector to the whole province's economy, economic pressures have made many households sell their agricultural land, which later changed into many other functions, including industrial areas (Prihatin, 2015). Nitrate contamination of drinking water and associated health concerns are among the most common problems adversely affecting groundwater quality worldwide. Most anthropogenic sources of nitrate penetrate into the groundwater through agricultural activities (fertilizers and livestock waste) and urban activities (sewage systems and septic tank drainages) (Badeenezhad *et al.*, 2019). Higher nitrate concentration in drinking water has been observed to increase the risk of CRC (Schullehner *et al.*, 2018). Supporting this finding, a previous study in Yogyakarta Province showed that nitrate concentration in wells tended to increase from time to time, with the highest median nitrate water content in the Kota Yogyakarta District compared with the other two districts (Fathmawati *et al.*, 2017). This fact may correlate with our findings demonstrating the highest CRC ASR ranking of sub-districts from Kota Yogyakarta District.

Another concern linked to CRC risk includes particulate matter with diameters of less than 2.5 $\mu$m ($PM_{2.5}$) and less than 10 $\mu$m ($PM_{10}$) suspended in the air (World Health Organization, 2013). Anthropogenic sources of this kind of air pollution include diesel or gasoline combustion engines, coal burning, energy generation from households and industrial activities, pavement erosion, brakes and tire abrasion and agriculture. The International Agency for Research on Cancer has classified PM as a carcinogen based on evidence from numerous sources that long-term exposure of this kind causes lung cancer (International Agency for Research on Cancer, 2010). Exposure to $PM_{2.5}$ and $PM_{10}$ might increase the incidence (Coleman *et al.*, 2020) and mortality of CRC (Guo *et al.*, 2020). Gastrointestinal cancer would be linked to the gastrointestinal tract by transfer from bronchioles and alveolar spaces via mucociliary clearance (Munkholm & Mortensen, 2014).

A local study in the Yogyakarta Province has highlighted that sub-districts in the Kota Yogyakarta District have the highest $PM_{10}$ concentration compared to other districts. The presence of numerous economic centres and other public facilities requiring transportation in the Kota Yogyakarta District might be responsible for high $PM_{10}$ production. Green open spaces that can reduce the impact of air pollution are also lacking in this district (Basuki & Saptutyningsih, 2012).

The role of lead in CRC carcinogenesis has been put forward by Sohrabi *et al.* (2018) after they found a higher lead level in CRC tissue compared with healthy tissue. Soils in residential and recreational sites are reported to have a high lead content, which might be explained by traffic emissions and industrial activities; in addition house paint often contains lead (Wang *et al.*, 2017). Kota Yogyakarta District has a significantly higher lead concentration in soil compared to neighbouring districts' areas (Sekarningsih *et al.*, 2021), a fact that may partially explain the high CRC ranking in certain of its sub-districts. Although high CRC screening rates may increase the CRC incidence owing to early disease detection, this may not be applied to our population. The CRC screening programme is not widely available and relatively high in cost, while low awareness of this possibility affects access. The high personal cost of examination (79.5%) and fear (58.5%) are other factors leading to people's reluctance to screening (Abdullah *et al.*, 2009). The low level of public knowledge regarding the risks and symptoms of CRC and screening programmes is another obstacle to screening efforts (Lee, 2018). Discovery and awareness of CRC spatial patterns can provide valuable information for policymakers in the implementation of screening programmes for at-risk populations.

The use of 12 years of CRC incidence data from the PBCR that has regional coverage guarantees the accuracy of the present study. Case finding and data collection process were done with a standardized process, involving multi-layer verifications, to ensure data coverage and quality, meeting the standards set for the Cancer Incidence in 5 Continents (CI5) programme. In general, the Yogyakarta PBCR data used in our study have minimal percentage of unknown age at diagnosis (0.03%), ill-defined sites (0.78%) and unknown primary sites (2.06%) (Supplementary Material 2). This study also has some limitations. PBCR data in Bantul District currently have 60.24% of morphology verification, which is lower than that recommended by the World Health Organization (>75%), unlike Sleman and Kota Yogyakarta that have 78.07% and 78.96%, respectively. Another limitation is the fact that the PBCR does not cover 100% of the patients so we may have missed some CRC cases. Nonetheless, the detection of hot and cold spot areas should not be affected by this condition.

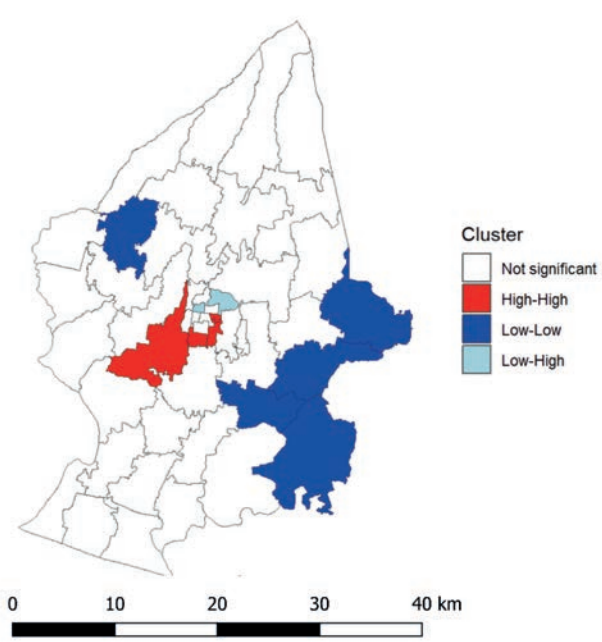


**Figure 5. The geographical distribution of the various cluster characteristics by sub-district in Sleman, Kota Yogyakarta and Bantul.**

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**Table 2. Colorectal cancer data by sub-district in Sleman, Kota Yogyakarta and Bantul.**

| No | Sub-district | All cases | | | | Male | | | | Female | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N | ASR | SE | Rank | N | ASR | SE | Rank | N | ASR | SE | Rank |
| 1 | Berbah | 34 | 6.68 | 1.26 | 26 | 18 | 6.84 | 1.67 | 34 | 16 | 6.57 | 1.69 | 24 |
| 2 | Cangkringan | 17 | 5.50 | 1.54 | 38 | 13 | 8.43 | 2.46 | 21 | 4 | 2.87 | 1.44 | 46 |
| 3 | Depok | 109 | 9.62 | 0.94 | 11 | 62 | 10.83 | 1.40 | 8 | 47 | 8.25 | 1.23 | 14 |
| 4 | Gamping | 72 | 8.75 | 1.07 | 14 | 44 | 10.7 | 1.65 | 9 | 28 | 6.82 | 1.32 | 23 |
| 5 | Godean | 41 | 6.25 | 1.04 | 32 | 25 | 7.51 | 1.53 | 26 | 16 | 5.00 | 1.27 | 33 |
| 6 | Kalasan | 36 | 5.28 | 0.90 | 41 | 24 | 7.47 | 1.56 | 28 | 12 | 3.02 | 0.89 | 44 |
| 7 | Minggir | 19 | 5.39 | 1.41 | 40 | 8 | 4.63 | 1.67 | 42 | 11 | 6.10 | 2.00 | 27 |
| 8 | Mlati | 64 | 7.83 | 1.02 | 20 | 36 | 8.64 | 1.48 | 20 | 28 | 7.16 | 1.40 | 21 |
| 9 | Moyudan | 21 | 6.19 | 1.53 | 34 | 11 | 6.54 | 2.08 | 37 | 10 | 5.69 | 1.92 | 31 |
| 10 | Ngaglik | 66 | 7.77 | 0.98 | 21 | 35 | 8.10 | 1.40 | 23 | 31 | 7.51 | 1.37 | 17 |
| 11 | Ngemplak | 41 | 7.87 | 1.27 | 19 | 20 | 7.54 | 1.73 | 25 | 21 | 8.30 | 1.84 | 13 |
| 12 | Pakem | 24 | 6.99 | 1.54 | 25 | 12 | 7.01 | 2.09 | 32 | 12 | 6.88 | 2.03 | 22 |
| 13 | Prambanan | 31 | 6.51 | 1.22 | 29 | 22 | 8.92 | 1.92 | 19 | 9 | 4.22 | 1.43 | 36 |
| 14 | Seyegan | 33 | 7.33 | 1.33 | 24 | 14 | 6.63 | 1.84 | 36 | 19 | 7.97 | 1.87 | 16 |
| 15 | Sleman | 35 | 6.10 | 1.03 | 35 | 20 | 7.14 | 1.61 | 31 | 15 | 5.02 | 1.32 | 32 |
| 16 | Tempel | 18 | 3.21 | 0.90 | 46 | 9 | 3.28 | 1.12 | 48 | 9 | 3.18 | 1.09 | 43 |
| 17 | Turi | 23 | 7.50 | 1.56 | 23 | 8 | 5.58 | 2.00 | 39 | 15 | 9.39 | 2.45 | 10 |
| 18 | Danurejan | 20 | 9.26 | 2.50 | 12 | 10 | 10.14 | 3.23 | 11 | 10 | 8.69 | 2.77 | 12 |
| 19 | Gedongtengen | 5 | 3.00 | 1.25 | 48 | 4 | 5.32 | 2.7 | 40 | 1 | 0.96 | 0.96 | 48 |
| 20 | Gondokusuman | 24 | 6.58 | 1.37 | 27 | 11 | 6.67 | 2.07 | 35 | 13 | 6.51 | 1.86 | 25 |
| 21 | Gondomanan | 17 | 11.87 | 3.12 | 4 | 8 | 12.06 | 4.3 | 6 | 9 | 11.66 | 3.93 | 3 |
| 22 | Jetis (Yogyakarta) | 24 | 9.68 | 2.07 | 10 | 11 | 9.88 | 3.04 | 14 | 13 | 9.68 | 2.78 | 9 |
| 23 | Kotagede | 16 | 6.25 | 1.49 | 33 | 7 | 5.04 | 1.95 | 41 | 9 | 7.27 | 2.50 | 19 |
| 24 | Kraton | 20 | 9.74 | 2.34 | 9 | 7 | 7.69 | 2.98 | 24 | 13 | 11.49 | 3.28 | 4 |
| 25 | Mantrijeron | 26 | 8.44 | 1.72 | 15 | 14 | 9.35 | 2.55 | 17 | 12 | 7.22 | 2.12 | 20 |
| 26 | Mergangsan | 32 | 11.89 | 2.08 | 3 | 15 | 12.51 | 3.36 | 4 | 17 | 11.71 | 2.90 | 2 |
| 27 | Ngampilan | 7 | 4.40 | 1.65 | 44 | 4 | 5.72 | 2.95 | 38 | 3 | 3.69 | 2.15 | 41 |
| 28 | Pakualaman | 10 | 9.26 | 3.41 | 13 | 8 | 16.86 | 6.11 | 1 | 2 | 3.40 | 2.42 | 42 |
| 29 | Tegalrejo | 33 | 10.40 | 1.87 | 6 | 15 | 9.63 | 2.51 | 15 | 18 | 11.35 | 2.73 | 5 |
| 30 | Umbulharjo | 66 | 12.32 | 1.47 | 1 | 35 | 13.58 | 2.35 | 3 | 31 | 11.13 | 2.07 | 7 |
| 31 | Wirobrajan | 28 | 12.02 | 2.29 | 2 | 17 | 15.66 | 3.86 | 2 | 11 | 8.76 | 2.72 | 11 |
| 32 | Bambanglipuro | 26 | 6.36 | 1.43 | 30 | 15 | 7.15 | 1.90 | 29 | 11 | 5.71 | 1.78 | 30 |
| 33 | Banguntapan | 52 | 5.83 | 0.81 | 36 | 33 | 7.49 | 1.33 | 27 | 19 | 4.18 | 0.98 | 37 |
| 34 | Bantul | 64 | 11.05 | 1.47 | 5 | 30 | 10.08 | 1.90 | 12 | 34 | 11.84 | 2.10 | 1 |
| 35 | Dlingo | 11 | 3.11 | 0.99 | 47 | 6 | 3.41 | 1.42 | 47 | 5 | 2.88 | 1.36 | 45 |
| 36 | Imogiri | 31 | 5.43 | 1.04 | 39 | 19 | 6.96 | 1.61 | 33 | 12 | 3.74 | 1.13 | 40 |
| 37 | Jetis (Bantul) | 34 | 6.35 | 1.18 | 31 | 13 | 4.55 | 1.32 | 43 | 21 | 8.17 | 1.85 | 15 |
| 38 | Kasihan | 66 | 8.36 | 0.98 | 16 | 36 | 9.35 | 1.60 | 16 | 30 | 7.47 | 1.40 | 18 |
| 39 | Kretek | 23 | 6.55 | 1.75 | 28 | 13 | 8.37 | 2.48 | 22 | 10 | 4.97 | 1.70 | 34 |
| 40 | Pajangan | 20 | 7.57 | 1.56 | 22 | 13 | 10.43 | 2.95 | 10 | 7 | 4.83 | 1.94 | 35 |
| 41 | Pandak | 40 | 8.26 | 1.41 | 17 | 26 | 10.97 | 2.23 | 7 | 14 | 5.71 | 1.58 | 29 |
| 42 | Piyungan | 15 | 3.26 | 0.93 | 45 | 9 | 3.88 | 1.33 | 45 | 6 | 2.76 | 1.14 | 47 |
| 43 | Pleret | 21 | 5.66 | 1.20 | 37 | 13 | 7.14 | 2.02 | 30 | 8 | 4.08 | 1.47 | 39 |
| 44 | Pundong | 27 | 7.96 | 1.71 | 18 | 20 | 12.11 | 2.76 | 5 | 7 | 4.14 | 1.58 | 38 |
| 45 | Sanden | 14 | 4.97 | 1.29 | 43 | 5 | 4.03 | 1.84 | 44 | 9 | 5.97 | 2.00 | 28 |
| 46 | Sedayu | 19 | 5.06 | 1.12 | 42 | 7 | 3.78 | 1.45 | 46 | 12 | 6.15 | 1.82 | 26 |
| 47 | Sewon | 85 | 9.87 | 1.12 | 8 | 45 | 10.06 | 1.53 | 13 | 40 | 9.76 | 1.58 | 8 |
| 48 | Srandakan | 33 | 10.19 | 2.09 | 7 | 15 | 8.95 | 2.39 | 18 | 18 | 11.31 | 2.81 | 6 |

N, number; ASR, age-adjusted standardized rate.

## Conclusions

Our findings demonstrate a heterogeneous distribution map of CRC incidence in the Yogyakarta Province during the period 2008-2019. However, some of these patterns need more detailed exploration to understand the reasons behind higher incidence in some sub-districts compared to others. It is essential to further study the risk factors and the availability and performance of current health services. These findings should stimulate similar research in other Indonesian regions, especially in the other 13 regions appointed by the Indonesian Health Ministry as regional cancer registry data centres. A nationwide investigation may provide better and more comprehensive data for calling for actions in various levels of authority in performing CRC screening programs and further promotion of healthcare services to provide better management for patients with CRC.

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*Online supplementary material:*
*Appendix 1. Flowchart of case recruitment process.*
*Appendix 2 Parameter of data quality of colorectal cancer in Sleman, Kota Yogyakarta and Bantul Districts.*