The prediction of colorectal cancer: Perspective of smoking and socioeconomic influence of culture in East Java with SEM analysis

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ABSTRACT

Purpose: Colorectal cancer (CRC) is a global malignancy with 10.2% of cases, ranking third in worldwide cancer cases. According to Indonesia Health Research, CRC's prevalence has risen significantly, reaching 1, 8 per mile in 2018, and reports rising cancer cases in the past 5 years. This study explores the relationship model between smoking, socioeconomics, and CRC, considering cultural moderation.

Design/Methodology/Approach: Conducted as a retrospective study with 212 respondents, comprising 172 cases of left-sided colorectal cancer (left CRC) and 40 cases of right-sided colorectal cancer (right CRC) from three cultural areas. Structural Equation Modeling (SEM) employing Warp-PLS was utilized for data analysis.

Finding: A significant positive relationship was found between smoking and CRC prediction (β = 0,081, p-value = 0,040). This pattern also applies to socioeconomic status and CRC prediction (β = 0,311, p-value = <0,001). The influence of culture on both relationships is not the same. The relationship between smoking and CRC prediction is not influenced by culture (p-value = 0,318). Conversely, the relationship between socioeconomic status and CRC prediction is influenced by culture (β = 0,078, p = 0,047).

Conclusion: Poor smoking habits and weak economic conditions influence the prediction of CRC negatively in East Java Province. Unfavorable cultural practices further worsen the relationship between weak socioeconomic status and poor CRC prediction in East Java Province. Recommendations suggest that preventing adverse CRC outcomes can be achieved through smoking cessation and improving socioeconomic conditions. Preventive efforts to enhance socioeconomic conditions should consider local cultural nuances.

Research limitation: This research is limited to a population group in East Java Province, Indonesia, divided into three cultural areas: Mataraman, Arek, and Pendalungan.

Keywords: *CRC, Cancer, Culture, East Java, Smoking, Socioeconomic, SEM.*

1. INTRODUCTION

Colorectal cancer (CRC) ranks at the third in the malignancy disease in the world with 1,849,518 cases (10.2%). It is the second leading cause of death after lung cancer, with 880,792 cases (9.2%) (Bishehsari et al., 2018; Sung et al., 2021). Indonesian Health Research (*Riskesdas*) states that there has been an increase in cancer cases in the last 5 years in Indonesia, in 2013 as much as 1.4 per mile and increased to 1.8 per mile in 2018 (Kesehatan, 2018). The incidence of CRC in Indonesia, Globocan 2020, in men ranks number 2 after lung cancer and in general number 4 (Sung et al., 2021). Smoking, both active and passive, is one of the risk factors for CRC. The pathophysiology of smoking against the occurrence of colorectal cancer has been known through biomedical research, otherwise in epidemiological studies there is a difference in results. Research in Singapore shows smoking has a risk of CRC, OR = 1.43 in light smokers and 2.64 in heavy smokers (Tsong et al., 2007). Research in Thailand showed no significant

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association in smokers (OR = 1.67) and former smokers (OR = 1.34), with the incidence of CRC (Poomphakwaen, Promthet, Suwanrungruang, Kamsa-ard, & Wiangnon, 2015) as well as in Oman, OR = 1.62 (Mafiana et al., 2018). Model of Social Determinants of Cancer and Health Ecology illustrate the environmental factors that influence the prediction of cancer do not stand alone, but are also influenced by socioeconomic factors (Dahlgren & Whitehead, 2006; Hiatt & Breen, 2008). The influence of socioeconomic factors in several countries on the predictor of CRC was found to be different, for example the incidence of colorectal cancer in the USA and Canada was highest in low socioeconomic conditions (risk ratio (RR) 1.0-1.5), on the contrary the incidence of CRC in Europe was lowest at low socioeconomic status (RR 0.3-0.9) (Aarts, 2012). The right and left colon exhibit distinct molecular mechanisms in the pathophysiological processes of CRC. Similarly, both clinically and pathologically, right-sided CRC demonstrates poorer outcomes compared to the left side. The existence of these differences significantly influences the prognosis of right-sided and left-sided CRC (Cienfuegos et al., 2018; Mukund, Syulyukina, Ramamoorthy, & Subramaniam, 2020). The five-year survival rate of right-sided CRC is lower compared to left-sided CRC (55.2% vs. 59.7%) (Mangone et al., 2021). East Java is the largest province of Java in Indonesia which has an area of 47,995 km2, with a population of 41 million. The population spread over 38 counties and cities. East Java is divided into 2 main regions, namely East Java mainland and Madura islands (BPS, 2023). The incidence of cancer in East Java is 2.17 per mile, above the national rate of 1.4 per mile (Kesehatan, 2018). East Java is divided into ten cultural areas. The three major cultural areas groups include Mataraman culture, Arek culture, and Pendalungan culture (Zoebazary, 2017). The prediction of CRC is increasing in East Java, possibly due to uncontrolled risk factors. Controlled risk factors prevent the occurrence of colorectal cancer 30%-50% (Marmot, 2018). The results of studies in other countries show that the risk factors for CRC vary. Currently, it is still challenging to obtain a model of colorectal cancer (CRC) risk factors in Indonesia, particularly in East Java, as no prior research has been conducted. This is the basis for research on the influence of Mataraman culture, Arek culture, and Pendalungan culture on the occurrence of colorectal cancer in the perspective of smoking and socioeconomics.

2. METHODS

2.1. Concept

This study uses a case control design. There are two variables independent (smoking and socialeconomics), one dependent variable (colorectal cancer), and one moderator variable (culture). The data that has been collected is carried out the fitness of models and hypothesis tests. The inclusion criteria consist of CRC diagnosis with adeno carcinoma histopathology examination (sufferer / case), age 40 to 70 years, resident dan born in East Java. The exclusion criteria consist of dementia, suffering breast cancer, prostate cancer and cervix cancer.

2.2. Smoking

Smoking is the activity of deliberately smoking a cigarette (active) or being in the same room with an active smoker (passive). There are 4 data from smoking variables, among them are smoking status, early smoking age, passive smoking and type of cigarette. Where it falls on the ordinal variable scale, with the highest score indicates poor smoking behavior.

2.3. Socialeconomics

Socialeconomis is environmental conditions around the patient and control. This variable consists of 4 data, including CRC knowledge, income, poverty, and education. Where it falls on the ordinal variable scale, with the highest value indicating poor economic conditions.

2.4. Colorectal Cancer (CRC)

Colorectal cancer is a malignancy that originates in the colonic mucosa and rectum. Diagnosis of CRC is ascertained by histopathological examination of adeno carcinoma. Where it falls on the ordinal variable scale, with colorectal cancer patients on the right side (CRC Right), including cancer of the cecum (C18.0), Vermiform Appendix (C18.1), ascending colon (C18.2), hepatic flexure (C18.3), and transverse colon (C18.4), are assigned a value of 2. Meanwhile, patients on the left side (CRC Left), comprising cancer of the splenic flexure (C18.5), descending colon (C18.6), sigmoid colon (C18.7), rectosigmoid (C19), and rectum (C20), are assigned a value of 1.

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2.5. Culture

Culture serves as a moderating factor in this study and is inherent to the research individuals, unalterable, encompassing three main cultural areas present in East Java Province, Indonesia. It falls within the nominal variable, where the number 1 represents Arek culture, the number 2 represents Mataraman culture, and the number 3 represents Pandalungan culture.

2.6. Ethics

The Committee ensures that this research adheres to ethical guidelines, emphasizing voluntary participation, informed consent, data security, confidentiality, and sensitivity to cultural aspects. Approval was granted after a thorough consideration of the ethical implications of the proposal, demonstrating alignment with ethical standards and a commitment to safeguarding participant rights and well-being. On June 14, 2022, the Ethics Committee at Saiful Anwar General Hospital in Malang, East Java, Indonesia, meticulously reviewed and approved this research proposal titled "Predictive Model of Colorectal Cancer Risk Factors in the Perspective of Cultural Dietary Patterns, Smoking, and Socioeconomic Factors in East Java".

2.7. Statistic

The sample selection method employs non-random sampling (purposive sampling), selecting all subjects meeting the criteria from several hospitals in East Java, including RSUD (General Hospital) dr. Saiful Anwar Malang, RSUD dr. Soetomo Surabaya, RSUD dr. M Soewandi Surabaya, RSUD dr. M IskakTulungagung, and RSUD dr. SoebandiJember. According to Hair, Hult, Ringle, and Sarstedt (2017) the sample size should ideally reach 100 or more. In this study, there are 4 items related to smoking, 6 items for socioeconomic questions, and 1 each for cultural and cancer diagnosis questions, resulting in a minimum required sample size of 180. Before conducting the analysis, it is necessary to check the model variables and perform prerequisite tests. Variable model checks are carried out by analyzing the model using the WarpPLS 7.0 application. The analysis involves testing outer weight, collinearity (VIF) on formative variables (smoking and socioeconomic), and reflective variables (culture and CRC). This is followed by testing outer loading factors, namely average variance extracted (AVE), and composite reliability (Hair et al., 2017). After the variable model check, the next step is to perform prerequisite tests, namely the Goodness of Fit (GoF) with a minimum of two model fit indicators such as Sympson's paradox ratio (SPR), R-squared contribution ratio (RSCR), Statistical suppression ratio (SSR), and Nonlinear bivariate causality direction ratio (NLBCDR). These indicators are used to evaluate the quality of the model (Kenny, 2020). Subsequently, the SEM model test is conducted using the WarpPLS 7.0 application, where this test can be performed to determine the relationship values between independent and dependent variables in the previously designed model. The established relationship comprises a single model, where the model illustrates the overall relationship of the variable set with colorectal cancer (CRC) as the focal point of the relationship, and culture as the moderating point for the entire cultural group. This can be understood as follows:

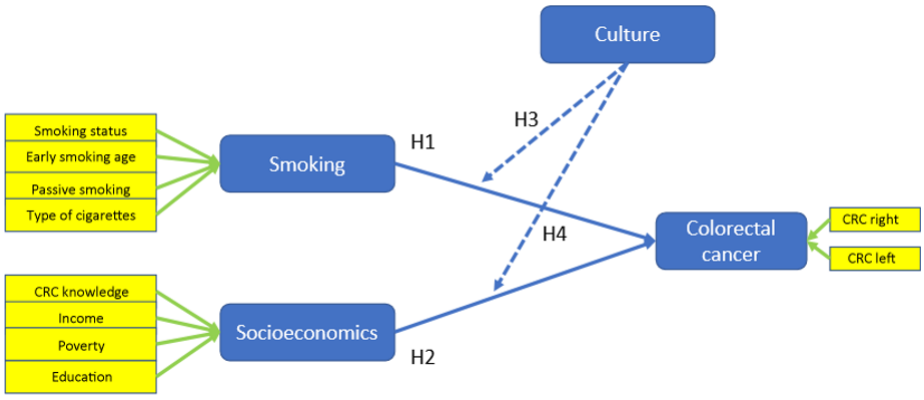

Figure 1. Relationship models using SEM with WarpPLS.

Note: The Figure 1 above illustrates the proposed hypothesis structure layout in the SEM model to be conducted. It outlines the SEM relationship model between the independent variables, smoking and socioeconomic status, and the dependent variable, colorectal cancer (CRC). This is moderated by cultural factors in East Java Province, including Mataraman, Arek, and Pendalungan.

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And the hypothesis is:
H_1: Smoking is positively associated with CRC prediction in East Java Province (Direct path).
H_2: Socioeconomic is positively associated with CRC prediction in East Java Province (Direct path).
H_3: Culture is positively moderation associated Smoking with CRC prediction in East Java Province (Indirect path).
H_4: Culture is positively moderation associated Socioeconomic with CRC prediction in East Java Province (Indirect path).

3. RESULTS

3.1. Characteristic of Study

In Table 1, the distribution of Colorectal Cancer (CRC) Patients among Hospitals in the Region is depicted. The table depicts the number of CRC patients treated at various hospitals in the region, including SaifulAnwal General Hospital Malang, Iskak General Hospital Tulungagung, patients of RSAL (Marine Forces Hospital) Ramelan, RS DKT (Army Hospital) Jember, and other hospitals. SaifulAnwal General Hospital Malang is treating 96 patients with CRC, accounting for 55% of the total number of CRC patients in the region. Similarly, Iskak General Hospital Tulungagung is treating 31 patients, representing 18% of the total number of CRC patients. RSAL Ramelan is treating 20 patients (11%), DKT Hospital Jember is treating 11 patients (6%), and other hospitals are treating 17 patients (10%).

Table 1. Spread of colorectal patients.

Hospital	n	%
SaifulAnwal General Hospital Malang	96	55%
Iskak General Hospital Tulungagung	31	18%
RSAL Ramelan	20	11%
DKT Hospital Jember	11	6%
RSLainnya	17	10%

Table 2 provides various statistics related to the demographic and health characteristics of the study population. It includes the average age of individuals from three different cultural groups, the percentage of individuals who smoke and the kind of smoke they consume and their socioeconomic. It also reports the percentage of individuals with cancer and their CRC status. This information can help understand the health profile of the study population and inform public health interventions.

Table 2. Characteristic data of the control and sample groups.

Age average	Y.o		Deviation standard
Arek	54.4		9.22
Mataraman	53.6		
Pendalungan	51.4		
Cultural group	n	%	
Arek culture			
Male	47	12%	
Female	46	12%	
Mataraman culture			
Male	40	10%	
Female	30	8%	
Pendalungan culture			
Male	26	7%	
Female	23	6%	
Total	212	55%	
CRC status	n	%	
CRC right	40	19%	
C18.0 Caecum	10	5%	

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Age average	Y.o		Deviation standard
C18.2 column asending	22	10%	
C18.3.flexura hepatic	1	0%	
C18.4 column tranversum	7	3%	
CRC LEFT	172	81%	
C18.6 column desending	9	4%	
C18.7 kolon sigmoid	34	16%	
C19 rektosigmoid	37	17%	
C20 rectum	92	43%	
Total	212	100%	
Smoke status	n	%	
Not smoke	96	45%	
Ex smoker	23	11%	
Rare smoker	36	17%	
Active smoker	57	27%	
Total	212	100%	
Early smoke	n	%	
Not smoke	96	45%	
> 22 th	25	12%	
15-22 th	28	13%	
< 15 th	63	30%	
Total	212	100%	
Pasive smoker	n	%	
Not smoke	96	45%	
Rare	23	11%	
Usually	24	11%	
Everyday	69	33%	
Total	212	100%	
Kind of smoke	n	%	
Not smoke	96	45%	
Whithe smoke	22	10%	
Ceruttu	16	8%	
Cigarette	78	37%	
Total	212	100%	
Socioeconomic			
Knowledge	n	%	Deviation standard
Low	132	62%	3.38
Middle low	16	8%	
Middle up	22	10%	
High	42	20%	
Total	212	100%	
Income			
≤ $90	106	50%	
$91 - $132	57	27%	
$133 - $219	33	16%	
$220 - $442	16	8%	
Total	212	100%	
Poverty			Deviation standard
Low	102	48%	5.02

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Age average	Y.o		Deviation standard
Middle low	66	31%	
Middle up	32	15%	
High	12	6%	
Total	212	100%	
Education level			
Under and elementary school	57	27%	
Junior high school	41	19%	
Senior high school	68	32%	
University	46	22%	
Total	212	100%	

The table presents data on the mean age of individuals within three distinct cultural groups: Arek, Mataraman, and Pendalungan. The highest average age is noted in the Arek group at 54.4 years, followed by the Mataraman group with an average of 53.6 years and the lowest in the Pendalungan group with an average of 51.4 years. Within the Arek culture group, there were 47 males (12%) and 46 females (12%), totaling 93 individuals. The Mataraman culture group consisted of 40 males (10%) and 30 females (8%), amounting to 70 individuals. Meanwhile, the Pendalungan culture group included 26 males (7%) and 23 females (6%), totaling 49 individuals.

The percentage and count of individuals based on CRC status, categorized into rigthCRC group and leftCRC Group. The CRC status data reveals that out of the total 212 cases, 40 individuals (19%) have CRC on the right side, distributed as follows: Caecum (C18.0) with 10 cases (5%), ascending colon (C18.2) with 22 cases (10%), flexura hepatica (C18.3) with 1 case (0%), and transverse colon (C18.4) with 7 cases (3%). The majority of CRC cases, 172 individuals (81%), occur on the left side, including descending colon (C18.6) with 9 cases (4%), sigmoid colon (C18.7) with 34 cases (16%), rektosigmoid (C19) with 37 cases (17%), and rectum (C20) with 92 cases (43%).

The smoking status within the study population, totaling 212 individuals. In terms of current smoking habits, 96 individuals (45%) are categorized as Not Smoke, 23 individuals (11%) as Ex Smoker, 36 individuals (17%) as Rare Smoker, and 57 individuals (27%) as Active Smoker. The provided socioeconomic data outlines the poverty levels within the study population. 102 individuals (48%) are categorized as having low poverty status, while 66 individuals (31%) fall into the middle-low poverty category. Additionally, 32 individuals (15%) are classified as middle-high poverty, and 12 individuals (6%) are designated as high poverty.

3.2. Analysis of Study

The analysis of this study was conducted using the warpPLS application, which consists of two steps: prerequisites test and conducting the PLS analysis.

3.3. Prerequisites Test

The analysis of this study was conducted using the warpPLS application, which consists of two steps: testing the prerequisites and conducting the PLS analysis.

Based on Table 3, there are three variables that do not meet the criteria and, therefore, must be excluded from the analysis, namely X1.1 (smoking status) and X1.4 (cigarette type), as they do not meet the requirement to have a VIF value below 5 with a P-Value < 0.05. Specifically, X1.1 (smoking status) has a VIF value of 15.177 and a P-Value < 0.001, while X1.4 (cigarette type) has a VIF value of 8.361 and a P-Value < 0.001. This exclusion is necessary as these two variables could introduce errors or lead to misinterpretation during the analysis process. Thus, the table is revised as follows:

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Table 3. The factor loading test results were used to determine the qualifying indicators for the variable.

Variable		Type of variable	Outer weight	VIF	P value	Outer loading	AVE	Composite reliability	P value	Qualification
Culture		Reflective				1.000	1.000	1.000	<0.001	Qualify
Smoke	X1.1	Formative	0.362	15.177	<0.001					Unqualify
	X1.2	Formative	0.320	4.033	<0.001					Qualify
	X1.3	Formative	0.165	1.103	<0.001					Qualify
	X1.4	Formative	0.334	8.361	<0.001					Unqualify
Social economic	X2.1	Formative	0.254	1.145	<0.001					Qualify
	X2.2	Formative	0.341	1.430	<0.001					Qualify
	X2.3	Formative	0.366	1.587	<0.001					Qualify
	X2.4	Formative	0.371	1.657	<0.001					Qualify
CRC	Y1.1	Reflective				1.000	1.000	1.000	<0.001	Qualify
Moderation	Culture x smoke (Y2.1)	Reflective				1.000	1.000	1.000	<0.001	Qualify
	Culture x socioeconomic (Y2.2)	Reflective				1.000	1.000	1.000	<0.001	Qualify

Table 4. The variables determined after filtering out unqualified indicator variables.

Variable		Type of variable	Outer weight	VIF	P value	Outer loading	AVE	Composite reliability	P Value	Qualification
Culture		Reflective				1.000	1.000	1.000	<0.001	Qualify
Smoke	X1.2	Formative	0.32	4.033	<0.001					Qualify
	X1.3	Formative	0.165	1.103	<0.001					Qualify
Socioeconomic	X2.1	Formative	0.254	1.145	<0.001					Qualify
	X2.2	Formative	0.341	1.430	<0.001					Qualify
	X2.3	Formative	0.366	1.587	<0.001					Qualify
	X2.4	Formative	0.371	1.657	<0.001					Qualify
CRC	Y1.1	Reflective				1.000	1.000	1.000	<0.001	Qualify
Moderation	Culture x Smoke (Y2.1)	Reflective				1.000	1.000	1.000	<0.001	Qualify
	Culture x Socioeconomic (Y2.2)	Reflective				1.000	1.000	1.000	<0.001	Qualify

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After that, the input variables in the application are reduced by the two unqualified variables. Subsequently, the analysis is conducted again, and the results are obtained as shown in Table 4. This table provides an overview of various variables in the analysis, including VIF, P-Value, Outer Loading, AVE (Average Variance Extracted), and Composite Reliability. The Culture variable is reflective with an outer weight of 1.000, VIF of 1.000, and P-Value <0.001, qualifying for further analysis. The Smoking variable (X1.2 and X1.3) is formative, displaying outer weights, VIF values, and P-Values that all qualify for continued analysis. Similarly, the Socioeconomic variable (X2.1 to X2.4) exhibits formative characteristics with Outer Loading, VIF, and P-Value meeting the criteria for further analysis. The Colorectal Cancer (CRC) variable and Moderation variables (Culture x Smoking and Culture x Socioeconomic) are reflective, each meeting the criteria for Outer Loading, VIF, and P-Value. These results indicate that the variables in the analysis have acceptable levels of reliability and validity, supporting their inclusion in further assessments.
The next step is to test the model fit by checking at least 5 significant indicators, such as:

Table 5. The model fit results were used to determine the goodness of fit (GoF) for the model used.

Model fit and quality indices	Qualification
Average path coefficient (APC)=0,238, P<0,001	Qualify
Average R-squared (ARS)=0,151, P<0,001	Qualify
Average adjusted R-squared (AARS)=0,146, P<0,001	Qualify
Average block VIF (AVIF)=1,095, acceptable if <= 5, ideally <= 3,3	Ideally
Average full collinearity VIF (AFVIF)=1,342, acceptable if <= 5, ideally <= 3,3	Ideally
TenenhausGoF(GoF)=0,324, small >= 0,1, medium >= 0,25, large >= 0,36	Medium
Sympson's paradox ratio (SPR)=1,000, acceptable if >= 0,7, ideally = 1	Ideally
R-squared contribution ratio (RSCR)=1,000, acceptable if >= 0,9, ideally = 1	Ideally
Statistical suppression ratio (SSR)=0,636, acceptable if >= 0,7	Acceptable
Nonlinear bivariate causality direction ratio (NLBCDR)=0,818, acceptable if >= 0,7	Acceptable

Based on Table 5. the analysis of model fit can be show by the SPR value is 1, indicating an ideal indicator, and the NLBCDR value is 0.818, falling within the accepted category. Therefore, it can be concluded that the model created meets the requirements for conducting PLS analysis.

3.4. PLS Analysis

The following are the results of PLS analysis using the WarpPLS application, from the hypothesis path created, there are three significant paths and one un-significant path at a significance level of 5%, as explained below:

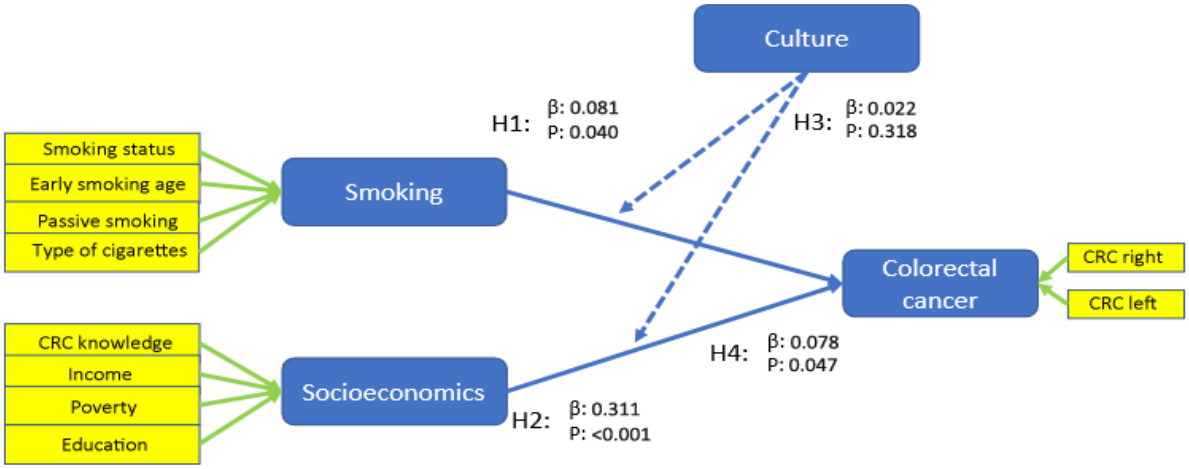

Figure 2. Results of relationship analysis using SEM with WarpPLS.

Note: Figure 2 above illustrates the layout of the hypothesis structure and the values of the relationship generated in the conducted SEM model. It explains the SEM relationship model between the independent variables, smoking, and socioeconomic status, and the dependent variable, colorectal cancer (CRC). Moderation is carried out by cultural factors in East Java Province, involving Mataraman, Arek, and Pendalungan.

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The Figure 2 or Table 6 includes four hypotheses (H_1-H_4) testing the relationship between several variables and CRC. The first three hypotheses test the direct pathways between smoking and socioeconomic status, each towards CRC. H_1 shows a significant positive relationship between smoking and CRC with sig 0,040 < α 0,05. H_2 shows a significant positive relationship between socioeconomic status and CRC with sig 0.001 < α 0.05. The last three hypotheses (H_3-H_4) test the indirect pathways through the mediation of cultural moderation of smoking habits and socioeconomic status, respectively, towards CRC. H_3 is non-significant with sig 0.318 > α 0.05, while H_4 is significant with sig 0.047 < α 0.05.

Table 6. The path model testing results were obtained using SEM with Warp-PLS.

Path	Type path	β	P-values	Signification
H_1: Smoking -> CRC	Direct path	0.081	0.040	Significant
H_2: Socioeconomic -> CRC	Direct path	0.311	<0.001	Significant
H_3: Culture moderation smoking habit -> CRC	Indirect path	0.022	0.318	Unsignificant
H_4: Culture moderation social economic -> CRC	Indirect path	0.078	0.047	Significant

4. DISCUSSION

4.1. Asociation of Smoking with CRC

Hypothesis H_1, which posits a positive association between smoking habits and CRC prediction in East Java Province (Direct Path), yields significant results with a P-value= 0,040 <α 0,05. This indicates a positive relationship with a coefficient value of β = 0,081. This value is solely derived from the sub-variables of age at first smoking (X1.2) and passive smoking (X1.3), while the sub-variables of smoking status (X1.1) and cigarette type (X1.4) are not yet eligible for analysis. As a result, the prognosis of CRC deteriorates with increasingly detrimental smoking behavior. The early age of smoking initiation and exposure to passive smoke become crucial determining variables in this context. The severity of colorectal cancer outcomes is intricately linked to the negative impact of smoking habits, where both the early age of smoking initiation and exposure to passive smoke play pivotal roles as significant factors in East Java.

Subsequently, Hypothesis H_3, which suggests that smoking habits positively moderation between culture and CRC prediction in East Java Province (Indirect Path), indicates that the culture variable is not yet robust enough to moderate or strengthen the relationship between smoking factors and the occurrence of CRC in East Java Province with P-value= 0,318 <α 0,05 and β = 0,022.

The meta-analysis conducted by Botteri et al. (2020), involving a total of 106 studies and 40,719 cancer cases, indicates that smoking is directly associated with an increased risk of colorectal cancer, while quitting smoking may reduce the risk of colorectal cancer. This study also examines the relationship between smoking and alcohol consumption with the risk of colorectal cancer (CRC) based on molecular subtypes and pathological pathways. The study results show that smoking (P-value = <0.001) and alcohol consumption (P-value = <0.012) are associated with a higher risk of CRC, particularly in CRC with high Microsatellite Instability (MSI), BRAF mutation, KRAS wild-type, and high CpG island methylator phenotype (CIMP).

Study in investigating of relationship between smoking and the risk of colorectal cancer (CRC), while taking into account various factors such as sex, age, and the anatomical subsite of the cancer. The study observed that both male and female smokers had higher prediction of CRC in comparison to non-smokers, and smoking was associated with an increased risk of left colon and rectal cancer in both sexes. Although the association between smoking and right colon cancer was not statistically significant for men, women who had ever smoked showed a 20% higher risk of right colon cancer. Moreover, the study noted that smoking dose and duration were directly linked to CRC risk, with no significant differences observed between sexes. Based on the results, smoking was identified as an important risk factor for CRC, particularly for left colon and rectal cancer. As a consequence, it is recommended that both male and female smokers be encouraged to quit smoking to minimize their risk of developing CRC(Gram, Park, Wilkens, Haiman, & Le Marchand, 2020).

Research on the impact of smoking status (active smokers) affecting the prognosis of CRC remains challenging to obtain. The available research focuses on the influence of smoking duration on patient survival. Patients who smoked for more than 30 years have the highest risk of mortality (HR = 1.14; p = 0.0076)(Huang et al., 2023).

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The carcinogenic mechanisms of smoking influencing the occurrence of CRC are demonstrated through the MSI-high pathway. This is evidenced in a case-control study involving 2,444 cases and 2,475 controls. Smokers with CRC have a higher MSI-high (OR = 2.79, 95% CI: 1.86–4.18) compared to MSS (Microsatellite Stability) (OR = 1.41, 1.14–1.75, p-heterogeneity (p-het) = 0.001). The carcinogenesis process occurs through the sessile serrated pathway(Amitay et al., 2020).

Right-sided colon cancer has a poorer prognosis than left-sided colon cancer. Differences between the right and left colon include their molecular carcinogenesis processes. The right colon follows the MSI-high pathway and mismatch repair-deficient tumors (dMMR), while the left colon follows the chromosomal instability-high (CIN-high) pathway. A cohort study in the USA shows a median survival of 78 months for right-sided colon cancer and 89 months for left-sided colon cancer(Baran et al., 2018).

Smoking is associated with a poor prognosis in CRC patients, as explained above. Smoking causes CRC through the MSI-high pathway. The right colon, which has a poor prognosis, undergoes one of its molecular carcinogenesis processes through MSI-high. This explains how smoking leads to a poor prognosis in CRC. Therefore, SEM methods can be used to assess the prognosis in CRC.

4.2. Asociation of Socioeconomic with CRC

This study is the first to investigate the relationship between socioeconomic status and the prognosis of CRC in East Java. The research also compares three cultural backgrounds, namely Arek, Mataraman, and Pandalungan. Structural Equation Modeling (SEM) is employed to analyze these relationships.

In the association of socioeconomic factors with CRC in Hypothesis H_2, which posits a positive association between Socioeconomic factors and CRC prediction in East Java Province (Direct Path), significant results are observed with P-value <0,001 <α 0,05 and a coefficient of β = 0.311. This finding is supported by all sub-variables: Knowledge (X2.1), Monthly Salary/Wage/Income (X2.2), Poverty (X2.3), and Education (X2.3). Subsequently, Hypothesis H_4, which suggests that socioeconomic habits positively moderation between culture and CRC prediction in East Java Province (Indirect Path), indicates that the culture variable is yet enough to moderate or strengthen the relationship between socioeconomic factors and the occurrence of CRC in East Java Province with P-value= 0,047 <α 0,05 and β = 0,078.

A positive relationship implies that the better the socio-economic conditions, the better the predicted prognosis of CRC. Conversely, a negative relationship signifies that the better the economic conditions, the worse the predicted prognosis of CRC.

An aligned positive relationship is evident in a cohort study in the UK that observed the prognosis or mortality events of CRC patients over 15 years by linking them to their socio-economic conditions. The research findings indicate that in lower socio-economic conditions, mortality rates increase (low education P-value= 0,005; manual occupation= 0,011; renting residence P-value= <0.001, and the most deprived environment P-value= <0.001) (Sturley, Norman, Morris, & Downing, 2023).

Income (socioeconomic status) influences good health outcomes for several reasons: first, sufficient income allows for access to quality basic needs, such as nutritious and safe food; second, it facilitates access to healthcare services, especially through convenient transportation, enabling early disease detection and therapy; third, it affects educational attainment, leading to better knowledge about CRC; fourth, social status within society influences ease of access to healthcare services and other essential needs (Chokshi, 2018; Darin-Mattsson, Fors, & Kåreholt, 2017; Galobardes, Shaw, Lawlor, Lynch, & Smith, 2006; Konradsen et al., 2020).

Good socioeconomic conditions are associated with sedentary culture and low physical activity (Yin et al., 2017). This condition results in obesity, a known risk factor for CRC (Ye, Xi, Huang, & Xu, 2020). The average obesity rate in the Arek cultural background is 13.5%, exceeding the East Java average of 10.87. This explains that the better the socio-economic conditions, the worse the predicted prognosis of CRC.

According to Onyoh et al. (2019) socioeconomic factors and inequities such as poverty and lack of insurance have an impact, especially the out-of-pocket expenses associated with the increasing cost of chemotherapy, making it very difficult for those in need to access screening, care, and further management of CRC.

However, different findings were reported by Savijärvi, Seppä, Malila, Pitkäniemi, and Heikkinen (2019) a study that analyzed the incidence of colon and rectal cancer in Finland between 1976 and 2014, with a focus on the association with education level and socioeconomic status. The study found that the incidence of colon cancer was

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higher among individuals with higher levels of education, particularly among men, but there was no significant difference for rectal cancer. Trends in the incidence of colon cancer by education level varied over time, and the differences between groups decreased in recent years. The study also found that the incidence of colon cancer was higher among individuals with higher socioeconomic status, particularly among men, with the largest differences observed in distal colon cancer. However, the differences between socioeconomic groups were smaller in women.

4.3. Moderation of Culture with CRC

The cultural variable is a moderation variable, which affects (strengthen or weaken) the relationship between the independent and dependent variables. In hypothesis H_3: Culture is positively moderating the association between smoking habit and CRC prediction in East Java Province (Indirect Path), the relationship is not significant with P-value 0.318 < α 0.05 and a coefficient of β = 0.022. This indicates that the cultural variable has no relationship with the relationship between smoking and CRC. In the next hypothesis, H_4: Culture is positively moderating the association between socio-economic status and CRC prediction in East Java Province (Indirect Path), the relationship is significant with P-value 0.047 < α 0.05 and a coefficient of β = 0.078, and it strengthens the existing relationship. Overall, the results obtained are relatively different from one another. Treatment plans for different races and cultures vary, for example, Hispanic patients are less likely to receive surgery compared to White patients, while Asian patients are more likely to receive chemotherapy. Patients listed as "Other" in the race/ethnicity category are also less likely to receive surgery and chemotherapy. Therefore, the characteristics of each ethnicity differ significantly in terms of habits and physiological adaptation (Tramontano et al., 2020). Culture should also enhance the strength of community groups. A meta-analysis study shows that several studies have reported that peer support can significantly increase the awareness and intention to receive colorectal cancer screening in ethnic minorities and is an ideal choice for promoting the screening among ethnic minorities, especially in diverse communities. Peer support intervention is recommended to promote the implementation of screening in Asian Americans, where they mostly build their communities more intimately. The concept of peer counseling is worth promoting, such as church-based peer counseling programs, but the challenges obtained require enhanced management to maintain sustainability (Hu, Wu, Ji, Fang, & Chen, 2020).

5. CONCLUSION

The article discusses the association between smoking , socioeconomic factors, colorectal cancer (CRC) prediction, and moderation by culture in East Java Province. The study found a positive association between smoking habit and CRC prediction in men in East Java Province. The meta-analysis conducted by Botteri et al. (2020) also supports this finding, demonstrating that smoking is associated with an increased risk of CRC, while smoking cessation may reduce the risk. Moreover, smoking and alcohol consumption are associated with a higher risk of CRC, particularly with MSI-high, BRAF-mut, KRAS-wt, and CIMP-high CRC. The study results also indicate that smoking is associated with a higher risk of cancer that develops through traditional or serrated pathological pathways. The study recommends that both male and female smokers be encouraged to quit smoking to minimize their risk of developing CRC. The study also found a positive association between social economic factors and CRC prediction in East Java Province. Socioeconomic factors and inequities such as poverty and lack of insurance have an impact on the predicting of CRC, especially the out-of-pocket expenses associated with the increasing cost of chemotherapy, making it very difficult for those in need to access screening, care, and further management of CRC. However, different findings were reported by Savijärvi et al. (2019) who found that the prediction of colon cancer was higher among individuals with higher levels of education, particularly among men, but there was no significant difference for rectal cancer. The study also found that the prediction of colon cancer was higher among individuals with higher socioeconomic status, particularly among men, with the largest differences observed in distal colon cancer. However, the differences between socioeconomic groups were smaller in women.In conclusion, the study provides evidence that smoking and unfavorable socioeconomic conditions are factors exacerbating CRC in the East Java Province. Detrimental cultural practices further compound the weakened socioeconomic relationships with the severity of CRC. The study recommends that individuals should be encouraged to quit smoking and address socioeconomic factors to minimize their risk of developing CRC. Cultural factors must be considered in preventing adverse CRC incidence, particularly in conditions of weak socioeconomic status. Further research is needed to confirm these findings and to investigate other potential risk factors for CRC prediction.

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The Ethical Committee of the General Hospital Dr. Saiful Anwar Malang, Indonesia has granted approval for this study on 14 June 2022 (Ref. No. 400/116/K. 3/102.7/2022).

TRANSPARENCY
The authors confirm that the manuscript is an honest, accurate, and transparent account of the study; that no vital features of the study have been omitted; and that any discrepancies from the study as planned have been explained. This study followed all ethical practices during writing.

COMPETING INTERESTS
The authors declare that they have no competing interests.

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