

Comparison of Colorectal Cancer Prognosis Between Developed and Developing Countries: A Literature Review

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Background Colorectal cancer incidence is globally ranked third in men and second in women. This highlights the need to effectively screen and manage colorectal cancer to achieve a better prognosis and prevent mortality and morbidity. Screening and management are not uniform worldwide, and it is affected by the economy of individual countries. In this context, we aimed to explore the prognosis of colorectal cancer in developed and developing countries and look for the factors affecting the prognosis.

Material and Methods This study was conducted in accordance with the “Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) Guidelines. Online databases such as PubMed, EBSCOHost, and EZproxy were searched comprehensively using the keywords. Eligible studies were selected. The countries included in the study were grouped into developed and developing countries based on the Gross Domestic Product (GDP). The factors affecting the prognosis reported in the studies were analyzed and concluded.

Results Reports from 8 developed and 8 developing countries were included in this study. The prognosis in developed countries ranged from 50% to 70%, and in developing countries, it ranged from 16% to 87.5%. Health care spending in developed countries was higher compared to developing countries. Developed countries had good screening systems in place, while that was lacking in developing countries due to inadequate resources.

Conclusion The range of prognosis among developed countries is narrower than those in developing countries. A

Kasturi Subramaniam¹,
Jeevan Shetty¹,
Thirupathi Rao¹,
Venkatesh R Naik¹

¹ Perdana University-Royal
College of Surgeon's in Ireland
School of Medicine (PU-RCSI)

Correspondence to:

Venkatesh R Naik
Perdana University-Royal
College of Surgeon's in
Ireland School of Medicine
(PU-RCSI), Perdana
University, Kuala Lumpur,
Malaysia

venkatesh@perdanauniversit.edu.my

better prognosis can be achieved by implementing total mesorectal excision (TME) and more effective screening strategies. More health care spending and including Non-Biological factors like unmarried, health insurance, lower education level during the staging of the disease, will significantly help in predicting a more accurate prognosis.

Keywords: *'developed countries', 'developing countries', 'prognosis', 'survival rate', 'colorectal neoplasm.'*

Background

The word cancer is derived from the Greek word "Carcinos", which means crab. Hippocrates coined it as the cut surface of cancer looked like a crab with the tumor extensions looking like its numerous legs. Cancer generally affects older people. There are a variety of cancers described, each with its own behavior.

Cancer occurs when the epithelial cells start dividing abnormally in the body and invades the surrounding tissues. It can also spread to the other parts of the body through the blood and lymphatic systems.¹ Age, genetics, and lifestyle are major risk factors in developing cancer. The World Cancer Research Fund states that colorectal cancer is globally ranked third in men and second in women in terms of disease occurrence.² With a global mortality rate of 880,792 according to the World Health Organization (WHO) global overview, colorectal cancer has shown to be a significant burden on countries in terms of economy and finance.³

According to the World Cancer Report 2014, more than 65% of new colorectal cancer cases occurred in countries with high or very high human development index (HDI). Men in Central Europe and the Republic of Korea showed the highest incidence.⁴ The Human Development Index (HDI) is a summary measure of average achievement in key dimensions of human development: a long and healthy life, being knowledgeable, and having a decent living standard.⁵ Developed countries are countries in the top quartile in the HDI distribution, those in the bottom

three quartiles are developing countries.⁶ Countries with high GDP are considered developed, and countries with low GDP are considered developing countries. Studies have shown that there was a significant correlation between reduced deaths and the level of Gross Domestic Product Expenditure on Health (GDPEH) of each nation.⁷

Developed and Developing countries are terms used to categorize countries based on the infrastructure and facilities and provide for their citizens. According to the United Nations, there is no clear-cut definition.⁷ What is accepted and used by the United Nations, World health organization, and other world governing bodies is a classification based on the Human Development Index (HDI).⁸

Total health spending is growing faster than GDP, increasing more rapidly in low and middle-income countries (close to 6% on average) than in high-income countries (4%).⁸ Inpatient and outpatient curative care and dispense of medicines and medical supplies account for more than 70% of health spending.⁸ Total healthcare spending is strongly related to GDP.⁸ Countries with more money tend to spend more on health care facilities for their population.⁸

Since colorectal cancer is the leading cause of death worldwide, it is essential to have effective screening and management protocols to achieve a better prognosis and to reduce mortality and morbidity. Screening and management are not uniform worldwide, and it is affected by the economy of individual

countries.⁸ We wanted to look deeper into what might affect the prognosis of colorectal cancer in different countries. In this context, we aimed to explore the prognosis of colorectal cancer in developed and developing countries and look for the factors affecting the prognosis. This, with the hope of helping the countries to acquire and adopt the best practices within the available resources for a better outcome in colorectal cancer survival rate.

Materials and Methods

A systematic search of the peer-reviewed journals from the databases was carried out to answer the following key research questions:

- What is the prognosis of colorectal cancer in specific developed countries?
- What is the prognosis of colorectal cancer in specific developing countries?
- What are the factors affecting the prognosis of colorectal cancer in the said countries?

Inclusion criteria: This study included all journal publications related to the prognosis of colorectal cancer. All articles used are in English, published between 2009 to 2019. Journals were obtained from databases subscribed to by our library. The papers were selected depending on the availability of relevant information.

Exclusion Criteria

Papers not in English, papers published before 2009 or after 2019, non-availability of full free-text, papers that do not address our research questions, and Papers which are not from the countries included in our list or which do not include the countries from our list in their research.

EBSCOHost, EZproxy, and PubMed databases were used to search for papers. The following search terms "prognosis of colorectal cancer" OR "survival rate of colorectal cancer" OR "5-year survival of colorectal cancer" OR "factors affecting the prognosis of colorectal cancer" OR "prognostic factor of colorectal cancer" AND "developed countries" OR "developing countries" were used to look for relevant articles. Countries were classified as developed and developing concerning the UN World Economic Situation and Prospects 2014.⁹

Process of selecting relevant studies

All the articles retrieved through search criteria were reviewed for the study scope by closely examining the objectives of the study. After applying the inclusion and exclusion criteria to the retrieved articles from the database and eliminating papers not meeting the criteria, 8 papers were shortlisted to be included in the study. Figure 1 depicts the process of identifying, screening, and choosing the eligible articles suitable using the PRISMA guidelines.

PRISMA FLOW CHART

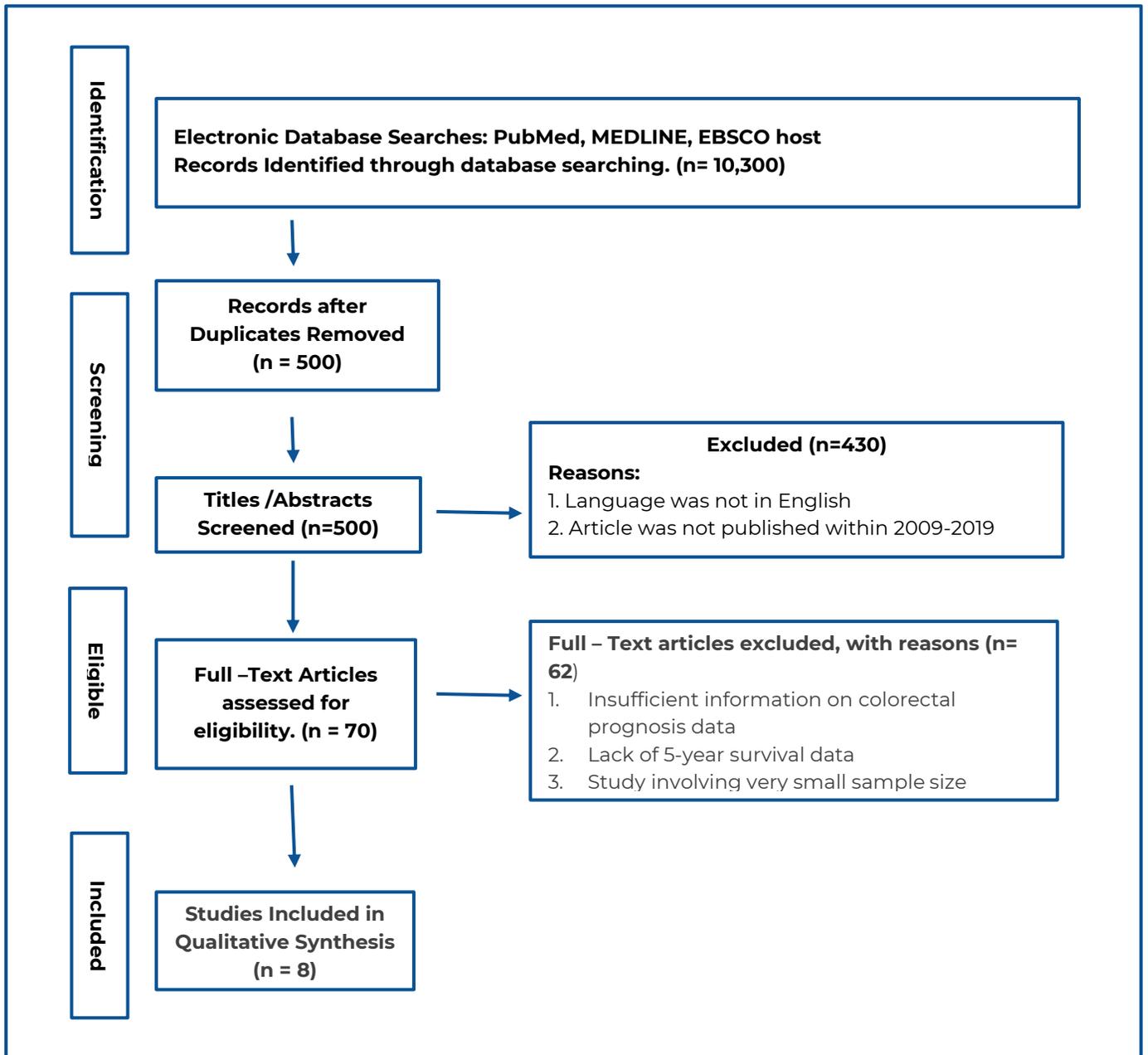


Figure 1 PRISMA flow diagram, including database searches, the number of abstracts screened, and the full texts retrieved.

Results

Eight studies, including the OECD, Health-at-a-glance report were selected as they were meeting our inclusion, exclusion criteria and addressed our study objectives. We selected data from 16 countries. Eight countries are developed, and the remaining eight are developing countries.

Table 1 shows the list of developed countries selected in this study. Countries namely Australia, Denmark, United Kingdom, Sweden, Poland, Canada, Norway, and the United States are developed countries situated in the West and have a predominantly Caucasian population. These countries belong to the OECD (Organisation for Economic Co-operation and Development) countries with a higher GDP and spend more money on their health care systems.¹⁰ They have a robust health insurance system for their citizens. The health insurance system is mainly from the taxes collected.¹⁰ The 5-year survival of patients with colorectal cancer between 2008 to 2013 in these countries ranges from 50% in Poland to 70% in Australia.¹⁰

Table 1. Colorectal cancer prognosis in developed countries

Article Title	Country	The 5-year survival rate of colorectal cancer (%)
OECD, Health at a glance 2015.10.	Australia	70.0
	Denmark	62.0

United Kingdom	56.0
Sweden	64.0
Poland	50.0
Canada	63.0
Norway	63.0
United States	64.0

Table 2 shows the list of developing countries selected in this study. Countries like Korea, Ghana, Gaza Strip, Malaysia, China, Turkey, Saudi Arabia, and Taiwan were analyzed. There was a variety of ethnicity in these countries, including Asians and Middle Easterners. The 5-year survival of colorectal cancer in these countries ranged from a low 16% in Ghana to a soaring 87.5% in Turkey. This list of countries is scattered worldwide and does not have much in common except that they fall under developing countries. This is based on GDP. Countries with lower GDP spent less on health care facilities.⁸ “Out of pocket spending” is more prevalent in these countries, reflecting on the disease prognosis and outcome.⁸

Table 2. Colorectal cancer prognosis in developing countries

Article Title	Country	The 5-year survival rate of colorectal cancer (%)
OECD (2015), Health at a glance 2015.10	Korea	72.0

Francis Agyemang-Yeboah, et al. ¹¹	Ghana	16.0
Chiara Panato, et al. I. 2018. ¹²	GAZA Gaza Strip	50.2
Sajesh K. Veettil, et al. 2017. ¹³	Malaysia	53.0
Lei Zhang, et al. I. 2019. ¹⁴	China	77.0
Erhan Akgun, et al. I. 2015. 15	Turkey	87.5
Nasser Alsanea, et al. 2015. ¹⁶	Saudi Arabia	44.6
Chao-Hsien LEE, et al. 2018. ¹⁷	Taiwan	63.0

Discussion

The OECD member countries are considered as developed countries.¹⁰ They spent an average of 12.6 % of their GDP (Gross Domestic Product) on health care services. Of this 61% was from the government coffers and the rest was by private spending.¹⁰ The developing countries spent an average of 4 to 5 % of their GDP on health care services of this 20 to 33% is sponsored by the government.¹⁸ From this data, it can be observed that developed countries spent more GDP on health services than developing countries. This, in turn, translates into better health care for their citizens. The health Insurance system is robust in developed nations, but it is more of “Out of Pocket” spending in developing countries.⁸

Cost-of-illness (COI) studies provide information on a specific disease's economic burden from a societal, public payer, family, or individual perspective. COI

becomes important in countries when there is more “Out of Pocket” spending rather than Health Insurance coverage. COI studies aim to evaluate the disease-related health care costs and the overall costs to society, including medical and non-medical expenses.¹⁹ For example, the annual cost of treatment for colorectal cancer was €3165, and the total cost as % of GDP/capita was 16% for colorectal cancer in Hungary, a developing country.²⁰

We observed a range of prognoses among developed countries; however, the gap was narrower in these countries compared to those in developing countries. This may be mainly due to more standardized screening and treatment practices in developed countries. Among the developed countries, Australia has shown to have the best prognosis. During the 1982-1986 period, the 5-year survival rate of colorectal cancer patients in Australia was 48% for men and 50% for women.²¹ Since then, Australia has changed its clinical practice guidelines on colorectal cancer.

According to the Clinical Practice Guidelines for the Prevention, Early Detection, and Management of Colorectal Cancer by the Australian Cancer Council, Australia implemented several practices to increase the detection rate of colorectal cancer. As primary prevention, the guideline recommends giving aspirin 100-300mg/day for a minimum of 2.5 years starting at the ages between 50-70 years.²¹ As for high-risk patients such as those with Lynch syndrome, it is recommended to start aspirin therapy from the start of their colonoscopy screening from the age of 25 years.²¹ A population screening for those

with average risk includes an immunochemical fecal occult blood test every two years from 50 to 74.²¹ To increase the detection rate, those with Familial Adenomatous Polyposis start their screening regime at 10-15 years of age or earlier if there are any gastrointestinal symptoms. As for Juvenile Polyposis Syndrome, colonoscopy begins at 12-15 years of age, done every 1-3 years. Apart from that, intensive follow-up after post-curative surgeries, regular carcinoembryonic antigen (CEA) Titters, and CT-scan are done with the aim of early detection of recurrence.²²

Among the developed countries, in Norway, both colon and rectal cancer incidence has been increasing for many decades, but the rectal cancer rates have leveled off since the 1990s.²³ Of particular note is the increased survival and declining mortality from rectal cancer in both sexes, and the mortality is now nearly half of what it used to be.²³ The most important determinants are probably the national introduction of total mesorectal excision in the early 1990s, increasing specialization treatment, and use of preoperative radiation.²³

Another developed country included in the study is Denmark. It has been recognized for decades that Danish colorectal cancer patients have an inferior prognosis than neighboring countries.²⁴ Danish government started several national initiatives in the mid-1990s to overcome this poor outcome. Danish government's extensive and profound focus on rectal cancer management by implementing total mesorectal excision

(TME) helped decrease the local recurrence rate.²⁴ Other essential elements the government focused on in the management of rectal cancer, which helped to enhance the survival rate, include efficient T-staging by use of magnetic resonance imaging (MRI) and use of neoadjuvant chemo-radiotherapy.²⁴

Among the developing countries analyzed, Turkey showed a significantly positive 5-year survival rate of 87.5%.¹⁵ In Turkey, colorectal cancer is the third most common cancer following lung cancer and breast cancer.²⁵ According to the Turkey Cancer Control Programme 2013-2018, there is 1.7 times increase in the risk of developing colorectal cancer in patients with a family history of colorectal cancer in comparison to the general population.^{26,24} In patients with a family history of colorectal cancer, screening starts at the age of 40, or 5 years before the age of diagnosis in the said relative, whichever comes first. Screening includes a fecal occult blood test every two years, with colonoscopy is done every ten years.²⁶

Saudi Arabia, which also falls under the developing countries category, has a relatively low survival rate of 44.6%.¹⁶ It has been reported that colorectal cancer presents at a younger age in Saudis, especially in women.¹⁶ This has a significant implication for decisions about the threshold age for screening. The average survival rate has increased but is still much lower than in developed countries. Compared with developed countries, the lower overall 5-year survival is due to lack of screening, a higher proportion of advanced-stage cancer at presentation,

lack of specialized care outside the major cities, and a higher percentage of rectal cancer cases.¹⁶

Colorectal cancer is the third most common cancer in females and the second most common cancer in males in Malaysia, a developing country also included in this study. It is causing a substantial economic burden on the health care sector, which is likely to increase over time, owing to the current colorectal cancer incidence trend. Malaysian government spends an average of between 2.8 to 3.7 % of GDP on the health care of its citizens.¹⁸ With the improving socioeconomic status and an increasingly westernized lifestyle in developing countries in Asia, including Malaysia, it could be expected to be associated with an increased incidence of colorectal cancer.¹¹ Malaysians have higher spending ability, which enhances the prevalence of obesity, the practice of a westernized diet, and tobacco smoking. All these in combination or independently impact the increased incidence of colorectal cancer and its prognosis.^{11,9,13} In Malaysia, about 80% of colorectal cancer cases are diagnosed in people aged more than 50 years; the increase in their population's aging trend can further increase the prevalence.¹³

Looking at Ghana with the lowest 5-year survival of 16.0%, followed by the Gaza strip at 50.2%, among the developing countries, the factors affecting their prognosis are inevitable. In Ghana, the lack of modern infrastructures for cancer care and the inaccessibility to curative treatment added with the lack of education and late

presentation lead to its bad prognosis.¹¹ In the Gaza strip, the isolation of their citizens due to the Gaza Strip's closure policy for security reasons is causing the cancer patients who are living there not to get adequate cancer care. On top of that, multiple antineoplastic medications are not allowed to patients due to prohibition.¹²

Even though regular prompt screening and reasonable care to the patient available in most developed countries brings a better outcome, but, many other factors play a significant role. Studies have shown that the outcome of CRC is determined by various factors, including the American Joint Committee on Cancer AJCC staging, tumor location, and neoadjuvant/adjuvant chemotherapy. Along with all these factors, socioeconomic status (SES) is also an important prognostic factor of CRC.²⁷ Studies have shown that married individuals possess a better prognosis for major causes of death than those who are single, separated, widowed, or divorced. These authors also found that insured patients have the best overall survival rate compared to uninsured patients.²⁷ They concluded that unmarried, Medicaid, lower education level, and Non-Hispanic Black CRC patients are at a greater risk.²⁷

Thus, the evolution of multiple factors and their impact on colon cancer led to a term Non-Biological Factor (NBF) -staging, which was proposed as an independent prognostic factor in colon cancer.²⁸ Effect of NBFs on the survival of colon cancer necessitates further clinical attention. Moreover, incorporating NBF-stage into

the AJCC TNM staging system is essential for prognostic prediction and clinical guidance of adjuvant chemotherapy in stage II and III colon cancer.²⁸

In conclusion, colorectal cancer prognosis and survival depend on multiple factors. The spending ability of individual countries plays a crucial impact on mortality and morbidity. A better prognosis can be achieved by implementing total mesorectal excision (TME) and more effective screening strategies. More health care spending and including non-biological factors like unmarried, health insurance, and lower education level during the staging of the disease will significantly help in predicting a more accurate prognosis. We also recommend the implementation of screening and management strategies used in Australia and Turkey into other countries as the survival rates in both these countries improved after they changed their strategy.

Conflict of Interest

None

Acknowledgment

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