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Effectiveness Of Early Screening For Colorectal Cancer In Reducing Mortality Rates: A Systematic Review

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Abstract

Background:

Colorectal cancer (CRC) is a malignancy with mortality and incidence rates persisting to increase. It is one of the major reasons of cancer-related mortality. There is a progression in CRC therapeutic modalities; however, such modalities are inadequate to curb the increasing CRC burden. Screening has the ability to reduce CRC burden with a reduction in the CRC mortality rate. Hence, early detection can reduce the CRC burden and mortality while improving its survival.

Aim:

To assess the effectiveness of early screening of CRC on survival and mortality of the patients by reviewing the previous studies concerned with this subject.

Methods:

Electronic databases of scientific websites were explored using several related keywords to obtain articles related to our topic. The articles of interest were those focused on the impact of CRC screening on mortality and/or survival and published from 2016 to 2025. The eligible articles were original ones written in the English language and were available for full-text.

Results:

Eight studies met the determined criteria and were enrolled in the review. The studies were published between 2018 and 2025. The included populations in the studies were heterogeneous, but they all focused on one objective, which was the impact of CRC screening on survival and/or mortality.

Conclusion:

CRC early screening was effective in improving survival and reducing mortality related to CRC, even in advanced stages and metastasis. Also, there were some factors that could influence the survival of screened CRC patients that require further investigation.

Keywords: Effectiveness, CRC Screening, Mortality, Survival.

Introduction:

CRC is a multistep, complex, and multigenic illness with elusive etiology, although extensive research has been conducted **[1]**. However, its occurrence and progression are stated to be attributed to the genetic instability of key mutated genes **[2]**. CRC is a globally prevalent malignancy with mortality and incidence rates continuing to rise **[3, 4]**. It affects almost one million subjects each year and results in almost 500000 mortality cases annually **[5]**. Its incidence is rare before the age of 40 years; however, its incidence rapidly increases after the age of 45 years, with most cases diagnosed beyond the age of 50 **[5]**. CRC is one of the major reasons of cancer-related death, even if its incidence is reducing by almost 2% per year in subjects over 50 years old due to screening programs **[6]**.

CRC is commonly diagnosed at advanced stages due to inadequate screening programs and the high prevalence of common risk factors such as poor diet, smoking, and lack of physical activity **[7, 8]**. Screening has the ability to reduce CRC burden with a reduction of CRC mortality rate of 18-57% based on the screening test implemented **[9]**. Although there is a significant progression in therapeutic modalities, such efforts alone have proven to be inadequate to curb the increasing CRC burden **[1]**. Additionally, survival after diagnosis of CRC is highly stage-specific, ranging from over 90% of the localized condition to less than 15% of the fourth stage **[10]**. Therefore, risk reduction and early detection n can reduce the CRC burden **[1]**.

Screening methods are various and include multi-target stool DNA (mtsDNA) testing, sigmoidoscopy, fecal immunochemical test (FIT), and colonoscopy, which is the most invasive approach. Nonetheless, it is the most crucial tool for early screening because of its ability to provide pathology assessment, direct visualization, and removal of precancerous polyps **[1]**. Other screening modalities include CT colonography and capsule endoscopy, which have a role in detecting and removing precancerous lesions, leading to a reduction in cancer-related mortality **[5]**.

Screening is necessary to improve survival and reduce mortality as early symptoms of CRC aren't clear, and as a result, it is often detected in a late stage, which can reduce survival duration **[11]**. However, there are not enough studies focusing on the effectiveness of CRC screening on patients‘ survival and mortality. So, this systematic review was performed to evaluate the effectiveness of early screening of colorectal cancer on survival and mortality of the patients.

Method and search strategy:

The PRISMA checklist **[12]** was used to write this review. The electronic databases, including "PubMed, Science Direct, and Google Scholar", were explored to obtain related articles. The searching process was restricted to ten years of research from 2016 to 2025. For the searching process, several relevant terms were used, including "CRC, Survival, Mortality, Rate, Impact, Influence, Effect, Outcomes, Screening, Program, and Implementation." Such terms were used in various combinations to obtain all possible related studies.

Eligibility criteria:

During the searching procedure, all the titles and abstracts were revised thoroughly to prevent missing potential studies, and the related ones were included for further stages. The findings were examined to preclude duplicates and articles published before 2016 to reduce the frequency of the studies. Original

articles written in the English language and reporting survival and or mortality related to CRC screening were considered for eligibility. The next step involved studies focused on CRC screening, but didn't focus on the outcomes of screening regarding survival and/or mortality. Articles from all countries and even different patient populations were eligible. Articles available for abstracts only and weren't available for the full-text, and those that reported incomplete data were excluded. The scheme of the eligibility is displayed in figure 1.

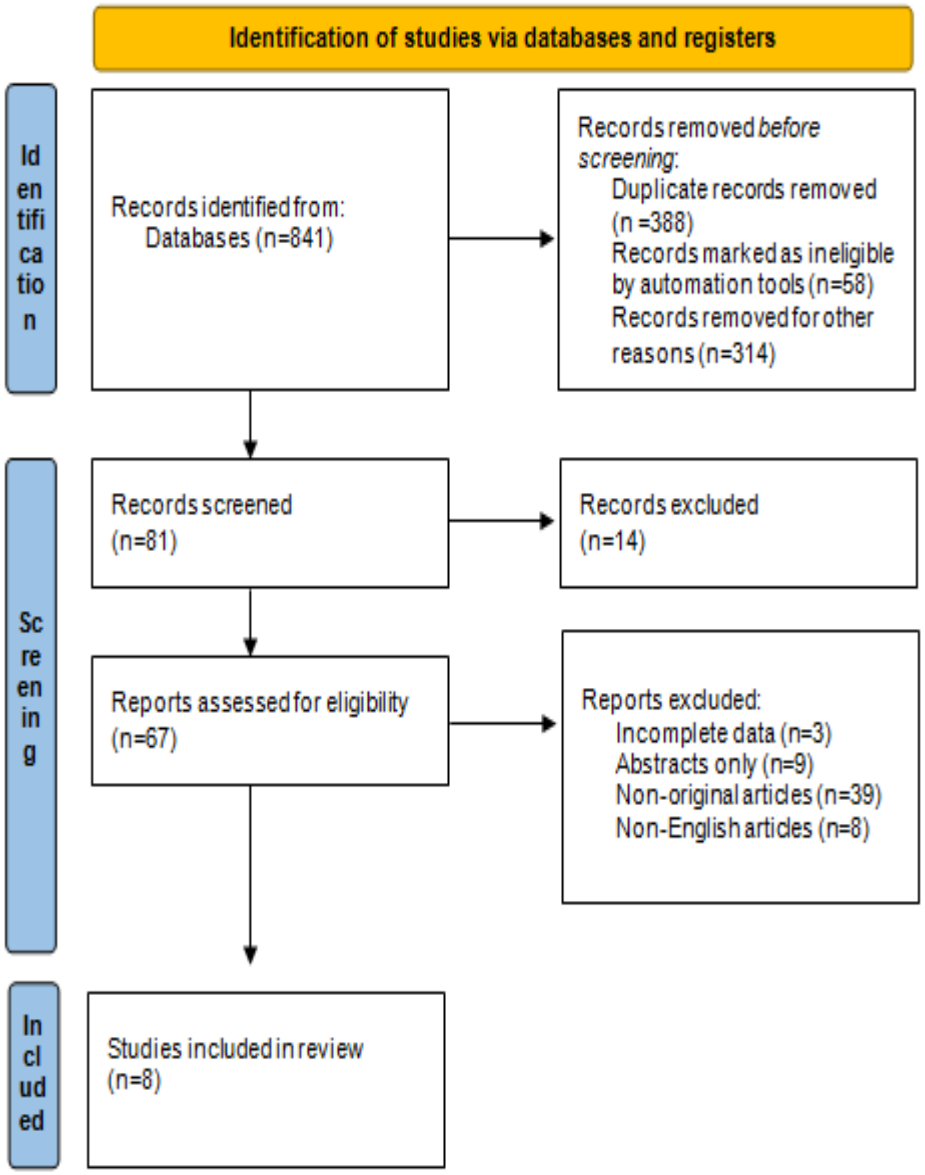

Fig 1: Eligibility Scheme

Data review and analysis:

The first step involved reviewing the abstracts of each included study to determine the data of interest for further extraction. The next step was reviewing the full-text for data extraction using a pre-designed Excel sheet. The extracted data was then revised to ensure its accuracy, and then transferred to a pre-designed table and summarized under four major titles.

Results:

Based on the criteria of eligibility, a total of eight articles were enrolled **[13-20] (Table 1).** The enrolled studies were published between 2018 and 2025. Three studies didn't state the study design **[14, 19, 20]**, whereas the remaining five study designs included retrospective **[13]**, nested case-control **[15]**, nationwide registry-based data **[16]**, retrospective observational, population-based **[17]**, and prospective **[18]**.

The studies were conducted on varied populations from different countries, included Chinese CRC patients **[13, 19]**, Iraqi CRC patients **[14]**, Korean cancer free subjects **[15]**, CRC patients who developed metachronous metastasis from Netherlands **[16]**, CRC cases and CRC modality cases from Belgium **[17]**, patients treated for CRC from Denmark **[18]**, and CRC patients from Spain **[20]**.

The objectives of the studies were to identify the outcomes and/or the impact of CRC screening on survival and/ or mortality; however, variations in the establishment of the study were found. One study compared screening and non-screening groups **[13]**, one assessed the impact of applying an early screening program for two years **[14]**, and one identified the implementation of a national screening program **[15]**. Also, comparisons were made between screen-detected and not screen-detected cases **[17]**, the effect of a six-year screening program by comparing CRC cases and mortality cases **[17]**, the adoption of CRC screening **[18]**, the impact of the screening program on five-year survival **[19]**, and a comparison between screening and non-screening groups **[20]**.

The stages of CRC patients varied between studies; one study focused on stage III only **[13]**, four studies involved cases with stages I-IV **[14, 17, 18, 19]**, two studies enrolled cases with stages I-III **[16, 20]**, whereas one study didn't report the stages of CRC **[15]**.

The findings regarding CRC screening and impact on survival revealed that screening was linked with better five-year OS (P=0.005), and a trend to improved DFS in stage III, but with a non-significant impact (P=0.06) **[13]**. The five-year OS (35.4%) of another study and the median duration of OS (19.2months) after metastasis were considerably higher for screen-detected primary tumors (P<0.0001) **[16]**. The five-year relative survival was found to be significantly greater for screen-detected (93.8%) patients compared to non-screened and screening interval cases **[17]**. One study reported that DFS at five and ten years was greater in screening patients (P<0.01) **[20]**.

Another study revealed that screening for two years resulted in a high survival rate (92.77%) compared to mortality (7.23%), revealing that early screening reduced the mortality rates **[14]**. The odds of CRC mortality for screened patients were low (OR 0.74), revealing the protective role of screening for mortality **[15]**.

The improved survival was studied in one research by the evaluation of 30 and 90 days mortality and it was found that mortality at these time intervals were reduced in the screen-detected patients (HR 0.4, P<0.01 for both) based on the basic model of analysis, whereas the advanced model revealed that only 90 days mortality was considerably reduced in the screen-detected patients (HR0.5, P=0.01) **[18]**. Another study demonstrated that the annual percentage changes of the survival rates elevated rapidly after screening program implementation, but in a non-significant trend **[19]**.

Regarding the factors affecting the survival and/or mortality, it was found that screening was a protective factor and determinant for OS (HR 0.5, P=0.002) and DFS (HR 0.6, P=0.04) in stage III **[13]**. One study revealed that CRC mortality was reduced with the increased number of screenings; however, such findings were related to those aged 50-79 years, whereas the findings for those aged 75-79 weren't significant, and those aged ≥80 years reported opposite results **[15]**. Among metastasis patients, screening of the primary tumor was a protective factor and determinant for OS after metastasis (HR 0.7) **[16]**. Regarding gender impact, one study revealed that the impact of CRC screening for six years resulted in a reduction of CRC incidence, especially among males, with a reduction in mortality in men two years following screening implementation **[17]**. Reduced CRC survival (HR 1.46) and all-causes survival (HR 1.37) were significantly linked with non-participation in the screening program. Additionally, delayed screening was linked with poor cancer-specific survival (HR = 2.93) and all-causes survival (HR = 3.29) **[19]**. One study revealed that significant variations were found between those who underwent screening and those who didn't regarding survival among those with stage I and III; DFS in stage I and III at five (P<0.001) and ten years (P = 0.002) were considerably greater in the screening patients **[20]**.

Table 1: Summary of the extracted data

Author and Publication year	Study design	Population characteristics	Results and main findings
Chen et al 2025 [13]	Retrospective	-Chinese population -N=4104 patients *Screening group=137 *Nonscreening group= 3967 -Stage III CRC	*Cancer identification by screening was linked with better five-year OS (P=0.005) and a tendency to improved DFS (P=0.064). *Based on multivariate analysis, screening was a protective factor for OS (HR: 0.517; P 0.002) and DFS (HR: 0.683; P 0.040).
Olwiwi & Aboud 2025 [14]	-----	-Iraq -N=166 patients -Applying the program for early screening of CRC for 2 years -Stages: I-IV	*Mortality rate was 7.23%, whereas the survival rate during the two days was 92.77% * Early diagnosis screens for cancer and lowers death rates.
Lee et al 2024 [15]	Nested case-control	-Korea -N=5944540 cancer-free subjects -Korean National screening program -Stage:--------	*Subjects who had been screened revealed an OR of 0.74 for CRC-specific mortality. *CRC mortality reduced as the screenings increased. *Similar results were discovered for those aged 50–79 years, whereas the results for 75–79 years subjects were not significant. *Those aged ≥ 80 years had the opposite findings.
Hamers et al 2024 [16]	Nationwide registry-based data	-Netherlands -N=794 patients who developed metachronous metastasis *Screen detected=152 *Not screen detected=642 -CRC screening following meachronous metastasis -Stage: I-III	*Median OS and five-year OS following metastasis were greater for screen-detected cases (38.3 months) (35.4%) vs. non-screen-detected primary tumors (19.2 months) (18.8%) (P< 0.0001). *Multivariate analysis revealed an association between the screening of the primary tumor and OS following metastasis that remained significant (HR 0.70).
Tran et al 2023 [17]	Retrospective, observational, population-based	-Belgium -N=69834 *CRC cases=55688 *CRC mortality=14146 -Six-year screening program -Stages: *Early stages (I-II) *advanced stages (III-IV)	* CRC screening considerably reduced CRC incidence, especially that of advanced-stage CRCs, with a more impact in men. *Mortality began to decline in males two years following screening. *The 5-year relative survival was considerably greater in screen-detected (93.8%) and lower in screening non-subjects CRCs (61.9%) vs. screening interval cancers (67.6%) and CRCs in never-invited cases (66.7%).
Wilhelmsen et al, 2021 [18]	Prospective	-Denmark -N=5348 patients treated for CRC *Screened=1813 *Non-screened=3535 -Implementation of screening for CRC -Stages: I-IV	* The adjusted risk of 30 and 90 days mortality was declined in the screen-detected cases (HR = 0.43, P<0.01) and (HR = 0.45, P<0.01), respectively. *In the advanced model, only 90 days total mortality was declined in the screen-detected cases (HR 0.59, P=0.01).

Li et al 2019 [19]	-------	-Chinese -N=18592 patients -Screening program for 5-year survival -Stages: I-IV	*The annual percentage changes of rates of survival elevated faster following screen, but with a non-significant trend. *Multivariate analysis suggested that cases who did not undergo the screening had considerably lower cancer survival (HR = 1.46) and all-causes survival (HR = 1.37). *Delayed screening was linked with poor cancer survival (HR = 2.93) and all-causes survival (HR = 3.29).
Cienfuegos et al 2018 [20]	------	-Spain -N=1580 patients *Screening group=250 *Non-screening group=1330 -Stages: I-III	*DFS at five and ten years was greater in the screening category (P< 0.01). *Significant variations were found between the two categories regarding stage I and III tumors. *DFS in stage I& III at five years (P< 0.001) and ten years (P=0.002) was greater in the screening categories.

CRC; Colorectal cancer, OS; Overall survival, DFS; Disease-free survival, HR; Hazard ratio.

Discussion:

CRC is the third greatest reason of mortality regarding cancer-related causes in the United States **[21]** and the leading cause of global cancer mortality **[22]**. More than 85% of CRC cases are found to be advanced, leading to their 5-year survival rate being poor 50% **[23],** despite the active implementation of surgery, chemotherapy, and targeted therapy **[22]**. In the mid-1990s, CRC screening was mandatory for all individuals aged 50 years and older; consequently, CRC incidence and related mortality with later onset CRC among this population have steadily reduced over the previous two decades. However, the worrying trend of occurrence among subjects younger than 50 years old has been steadily rising **[24, 25]**. Therefore, early detection and screening of CRC can greatly improve the prognosis of the disease. The United States encourages people to participate in CRC screening as the incidence of CRC evelates year by year **[26]**. However, the effectiveness of CRC screening on survival and mortality is insufficiently studied; therefore, this review was established to identify the effectiveness of early screening of CRC on the survival and mortality of patients.

The diagnosis of CRC during screening prior to the progression of symptoms displayed considerably improved outcomes. Cancers identified in screening revealed a 74% reduction in CRC-related mortality compared to those diagnosed after the onset of symptoms **[27]**. In our review, we found that some studies assessed mortality rates and survival rates at different durations; however, all the studies revealed that CRC screening improved survival, including overall survival and DFS at 30 and 90 days, two, five, and ten years, and screening was a protective factor for mortality even among those with stage III CRC and metastasis. Such findings indicate that CRC screening was effective in improving the survival of patients and reducing their mortality.

Furthermore, we found that screening was a protective factor of mortality and determinant for OS, DFS for those with stage III **[13]**, determinant for OS among patients with metastasis **[16]**, and it was linked with DFS in stage I and III at five and ten-years survival **[20]**, whereas non-involvement in screening was linked with reduced survival **[19]**. All such findings confirm the significant role of screening in improving survival and reducing mortality of CRC patients.

The management of stage III CRC, where the cancer invades the regional lymph nodes, involves a multimodal approach integrating procedure and systemic chemotherapy **[5]**. We found in one of the included studies that CRC screening tended to improve DFS in stage III patients, although this improvement wasn't significant **[13]**. The stage IV of CRC is characterized by distant metastasis, and this stage is managed by systemic therapy to prolong

the survival **[5]**. However, we also found that five-year OS and the median duration of OS were improved even after metastasis for those who underwent screening and reported screen-detected primary tumor **[16]**.

There was a lack of review and literature reporting the factors influencing survival among screened patients. However, we could detect some factors by reviewing the enrolled studies. We found that the survival and/or mortality of CRC was influenced by the number of screenings in specific age populations **[15]**, delayed screening **[19]**, and male gender **[17]**. The increase in the number of screenings was linked with reduced mortality among those aged 50-79 years old, indicating that both the number of screenings and age of the patients affected the outcomes of the patients **[15]**. It was stated that socioeconomic status was found to be linked with high changes in mortality differences between different populations **[28]**. However, none of the included studies reported the impact of socioeconomic status on survival or mortality among screened patients.

It was stated that early screening for CRC shouldn't be delayed **[11]**. This was in agreement with our findings, as one study revealed that delayed screening was linked with poor cancer survival and all-cause survival, leading to a higher mortality rate **[19]**. Furthermore, we found that the incidence of CRC and its mortality was reduced, especially among males compared to females **[17]**, which may indicate the role of gender in survival among screened patients. Also, this may indicate that survival among the screened patients may be influenced by sex chromosomes, which indicate genetic involvement in survival.

Similar to our findings, a previous analysis of 58 organized CRC screening programs from 22 countries revealed that a CRC screening program for more than five years was linked with a declining of CRC mortality; screening longer duration was linked with a greater reduction in the pooled age-standardized mortality ratio. On the other hand, in the pooled age-standardized mortality ratio became non-significant when the screening was implemented for less than 5 years **[29]**.

One analysis included 16 case-control and 13 cohort studies that enrolled 4713778 subjects, revealing that colonoscopy was linked with a 52% relative risk reduction in CRC incidence and 62% relative risk reduction in CRC mortality. Such findings indicated improvement in the survival rate and a reduction in CRC incidence. Further analysis demonstrated that the impact of colonoscopy was the same on people below and above 50 years **[22]**.

Conclusion:

The present review revealed that CRC early screening was effective in improving survival and reducing mortality related to CRC. CRC screening was also effective and beneficial for those with stage III CRC and those who experienced metastasis, and improved their survival. Additionally, we could identify a few factors that could influence the survival of screened CRC patients, including the number of screenings, age, gender, and time of screening. However, such factors require further investigation due to the lack of studies reporting such influencing factors.

Limitations, strengths, and recommendations:

The limitations of this review include the heterogeneity of the studied populations between the included studies and the lack of focus on the factors influencing survival and mortality among screened patients. The strength of this review was that it was the first review to report the factors influencing the survival of screened patients. Therefore, further studies are highly recommended.

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