

# Colorectal cancer

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## Description of condition and intervention

Colorectal cancer (CRC) is a disease in which malignant (cancer) cells form in the tissues of the colon or the rectum. CRC is a very heterogeneous disease that is caused by the interaction of genetic and environmental factors. CRC develops through gradual accumulation of genetic and epigenetic changes which leads to the transformation of normal colonic mucosa into invasive cancer. Most CRC develops from adenomas (adenoma-carcinoma sequence), and the neoplastic transformation time is considered approximately 10-15 years, which represents the available time to detect and remove these adenomas before their progression to invasive carcinoma (Binefa et al 2014).

Globally, CRC is the third most diagnosed malignancy and the second leading cause of cancer death (Anania et al 2019). Colorectal cancer is the fourth leading cause of death in men (7.6%) and the third in women (8.6%) (Keum & Giovannucci 2019). The GLOBOCAN report 2020 estimated that there were 1931590 (10%) incident cases and 935173 (9.4%) deaths from colorectal cancer. The World Health Organization estimates an increase of 77% in the number of newly diagnosed cases of CRC and an increase of 80% in deaths from CRC by 2030. The risk factors for CRC include a diet low in fruit and vegetables, excessive intake of red meat and saturated fat, alcohol intake, a sedentary lifestyle, tobacco and being overweight (Binefa et al 2014).

Colorectal screening is done by Fecal occult blood test, Sigmoidoscopy, Colonoscopy, Virtual colonoscopy, Double contrast barium enema (DCBE) and DNA stool test. Diagnosis of colorectal cancer is done by Colonoscopy, Biopsy, Biomarker testing of the tumor, Blood tests,

Computed tomography (CT or CAT) scan, positron emission tomography (PET) or PET-CT scan, and magnetic resonance imaging (MRI). Standard treatments for colorectal cancer are surgery, chemotherapy and radiotherapy which may be used in combination to treat patients (Johdi, Sukor 2020).

We assessed the effects and costs for following interventions in this evidence brief:

*Treatment of colorectal cancer: Confirmatory colorectal cancer diagnostics and staging*

*Treatment of early-stage colorectal cancer: Stage I & Stage II*

*Palliative care for late-stage colorectal cancer: Stage III & Stage IV*

## International guidelines

Organization	Indications/recommendations	Applicability in LIC & Lower MIC settings

## Intervention attributes

### Type of interventions

Colorectal cancer confirmation is a type of diagnostic intervention. The rest of the interventions are considered as curative category.

### Delivery platform

The interventions involving diagnostics and treatment of colorectal cancer including treatment of various stages of this cancer and palliative care may be delivered at the referral and specialty hospital.

## Equity

In addition to considerations like cost-effectiveness and health systems factors, dimensions of equity can be relevant for priority setting. The opportunity for a long and healthy life varies according to the severity of a health condition that individuals might have, so there are inequities in individuals' opportunities for long and healthy lives based on the health conditions they face. Metrics used to estimate the severity of illness at an individual level can be used to help prioritize those with less opportunity for lifetime health. FairChoices: DCP Analytics Tool uses Health adjusted age of death (HAAD), which is a metric that estimates the number of years lived from birth to death, discounting years lived with disability. A high HAAD thus represents a disease less severe in terms of lifetime health loss, while a low HAAD represents a disease that is severe on average, causing early death or a long period of severe disability. It is also possible to estimate the distribution of HAAD across individuals with a health condition. FairChoices shows for each intervention an average HAAD value of the conditions that are affected by respective interventions that have health effects. Additionally, a plot shows HAAD values for around 290 conditions (Johansson KA et al 2020).

## Time dependence

Moderate level of urgency. Treatment outcomes not highly affected by some days of delay.

## Population in need of interventions

Treated population: All incident cases of colorectal cancer stratified by the stage-wise distribution in the age-group 30 to 69 years are the treated population.

Affected population: The affected population for this intervention includes males and females diagnosed with colon/rectum cancer, age 30-69. The affected fraction of 9.8% is estimated over time with the help of a Markov trace, using transition probabilities from a modelling study by Ralaidovy AH et al 2018. The geometric mean calculated was used as an annual estimate. Most cases had colon cancer (58.7 %), while 41.3% had rectal cancer. Source: NCD Countdown appendix

## Disease state addressed

The included interventions target colon and rectum cancer.

## Intervention effect and safety

Table 1: Effect and safety of treatment for colorectal cancer

Effect of intervention		Certainty of evidence
Mortality (due to condition)  Stage 1 Stage 2 Stage 3 Stage 4	Relative reduction in mortality consistent with OneHealth Tool effect sizes, dependent on stage at diagnosis (Liu, 2014; Frazier, 2000; Wu, 2006; Chadder, 2016): 94.4% decrease 94.4% decrease 91.4% decrease 36.7% decrease  The mortality reduction is the weighted effect of stage 1 and 2 effect sizes = 94.4%. RRR = $94.4\% \times 9.8\% = 9.3\%$ (Source NCD Countdown appendix)	See appendix

## Model assumptions

Table 2: Summary of model parameters and values used in FairChoices – DCP Analytical Tool

Category	Model parameter	Notes
Intervention	1. Treatment of colorectal cancer: Confirmatory colorectal cancer diagnostics and staging 2. Treatment of early-stage colorectal cancer: Stage I & Stage II 3. Palliative care for late-stage colorectal cancer: Stage III & Stage IV	
Cost calculation		

Treated population	Incidence of colorectal cancer	Global Burden of Disease Study 2019
Gender	Male & female	
Age	30 to 69 years	
Treated fraction		We take treated fraction as 1 (all incident cases of colon and rectum cancer)
Stage 1	0.051	
Stage 2	0.203	
Stage 3	0.5	
Stage 4	0.246	
Effect calculation		
Affected population	Those with condition	
Affected gender	Male & female	
Affected fraction age	30 to 69 years	
Affected fraction		
Early-stage colorectal cancer treatment	0.098	
Comparison	No intervention	
Mortality Reduction (RRR)		Table 1
Early-stage colorectal cancer treatment	0.093	

## Intervention cost

The average 1-year patient cost cost for colorectal cancer diagnostics is estimated to be RM 1414.25, in 2013 Malaysian Ringgit (Azzani M et al 2016). The cost was calculated as a weighted average of the diagnostics cost for patients in Stage I stage II, Stage III, and Stage IV of colorectal cancer. The total treatment expenditure for colorectal cancer: Stage I stage II, Stage III, and Stage IV is estimated at THB 82,214, THB159547, THB183037, THB 195364 in 2013 Thai baht ((Sermisri et al, 2014). The cost for palliative care was estimated to be 64.36 USD per capita in 2016 in low-income countries (LIC) (Source: DCP3 Volume 9).

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## Appendix

### Literature Review for effectiveness & safety

This literature search is an example of Level 1 search for intervention inputs taken from DCP3 or generated in an ad hoc manner (e.g., quick google search found one study of cervical cancer screening cost-effectiveness that was used to create an effectiveness parameter for that intervention).

Level of evidence of efficacy studies:

1. low (expert opinions, case series, reports, low-quality case control studies)
2. moderate (high quality case control studies, low quality cohort studies)
3. high (high quality cohort studies, individual RCTs)
4. very high (multiple RCTs, metaanalysis, systematic review, clinical practice guidelines).