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Original article

Framework for Colorectal Cancer Health Needs Assessment in North and Central Asian Countries

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Abstract

Colorectal cancer (CRC) is the third leading cause for cancer worldwide. Prevalence of CRC is increasing in North and Central Asian Countries (NCAC). European guidelines encourage member countries to allocate resources for primary prevention of CRC through screening. Though, cost-effective screening is becoming a priority. A framework for health priority determination to prioritize CRC screening was developed. Public health websites were accessed to abstract epidemiologic data. The framework included prioritization by absolute risk (incidence, prevalence), relative risk (CRC ranking for national cancer deaths) and population attributable risk for the disease. Risk indicators were identified for the NCAC. Further detailed risk assessment scoring was completed to assess the CRC disease burden. Statistical analysis was performed for correlation. Variables included in risk assessment were population, life expectancy, gross national income per capita, percent GDP spent on health expenditure, total expenditure on health per capita, age standardized mortality to incidence ratio, cancer ranking by incidence and smoking prevalence. Risk assessment showed Kyrgyzstan, Georgia, Belarus and Armenia have more than expected CRC burden. Tajikistan, Turkmenistan and Latvia have lower than expected CRC burden. Conclusion: Identifying high CRC burden countries to prioritize screening is important. Uniform and comparable CRC risk indicators for the region is needed. Health need assessment and priority setting is important for better distribution of resources. Countries with lower risk score may implement preventive policy to reduce CRC risk factors and countries with higher risk could adapt mitigating policy for early diagnosis of CRC.

Keywords: ***colorectal neoplasms, developing countries, Asia, cancer screening, risk assessment***

Introduction

Colon and rectum cancers (CRC) rank third for cancer incidence accounting for 10.2% of all new cancers in 2018, with an age standardized rate of 235.7 disability adjusted life years (DALY) per 1,00,000 persons-years [1]. CRC is the second largest contributor to cancer-related deaths [2]. Traditionally high-income countries had higher burden of CRC in the world. Lately with economic and demographic transition, CRC burden is increasing in low- and middle-income countries (LMIC) including North and Central Asian Countries (NCAC) [3]. This could be related to ageing population, urbanization, increased prevalence of westernized diet, lifestyle risk factors including alcohol consumption, obesity and smoking [4,5]. Asia takes the lead in both incidence and mortality rates followed by Europe. The number of people diagnosed with colon and rectal cancer has doubled from 1990 to 2013; with most of the increase resulting from an aging and growing population. Nevertheless, 16% of this increase is independent of demographic changes. Almost 44% of global CRC related DALYs occur in developing countries [6].

CRC fulfills the criteria for gold standard for screening assessment. This includes, high incidence rate, long preclinical phase, recognizable and tractable precursor, and the correlation between the tumor stage and mortality rate. CRC screening had made a tremendous impact on its outcome [7]. Most high-income countries have some form of guideline-based screening program. On the other hand, few LMICs have a CRC screening program in place [8]. Furthermore, in many countries with screening programs, the implementation is localized and underutilized with uptake rates being suboptimal [9]. As a result, few data exist about the cost effectiveness, efficacy and sustainability of CRC screening program. Additionally, in LMIC, CRC prevention planning is based on competing disease burden, available resources and infrastructure. Screening by a low-cost test like fecal occult blood test (FOBT) or fecal immunochemical test (FIT) as compared to the gold standard of colonoscopy-based screening seems to be a better option [10].

World Health Organization (WHO) has a handbook on priority setting for national health policies and plans [11]. Priority setting is necessary especially in resource limited condition and where the intervention to outcome link is protracted. For a CRC screening to be effective and sustainable; multiple health, non-health and patient collaboration is required. (**Figure 1**) CRC screening is a multi-step process. In the first step an eligible patient is informed about the FIT/FOBT test. Further to facilitate screening test uptake, the test may have to be made available free of cost or at subsidized cost. A plan is required to follow up on the positive test results to have colonoscopy. Then if CRC is diagnosed, it requires appropriate treatment including possible surgery or chemotherapy. Most of these links should be working properly for the CRC screening to be effective. Hence, priority-setting exercise is needed for situation analysis that further aids the decision tool about CRC screening program. Situational analysis helps to assess and address the problem that may occur over time of plan implementation. Five key criteria are suggested for setting priorities in the health sector namely: 1] burden of the health issue; 2] effectiveness of the intervention; 3] cost of the intervention; 4] acceptability of the intervention and 5] fairness [11].

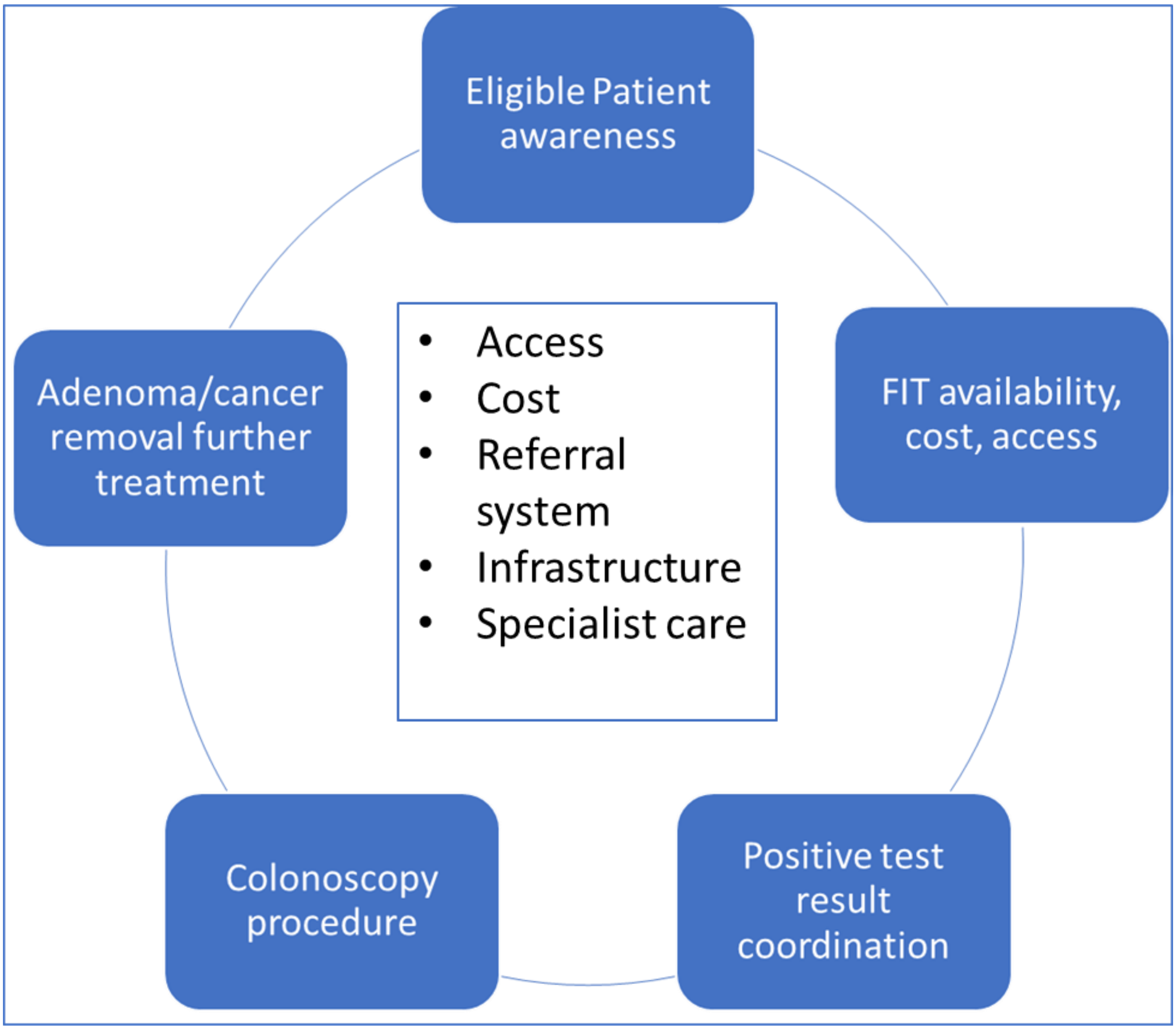

Figure 1: Intervention to outcome in colorectal cancer screening

Of the criteria suggested, the burden of the health issue, e.g. CRC, could be assessed using a health need assessment (HNA) approach. This provides us with magnitude, severity and urgency of the matter. HNA utilizes epidemiological, qualitative and comparative methods to describe health problem of a population. It describes the patterns of disease in a population (at local, regional or national) level while especially highlighting the areas of unmet need to avoid disparity, misallocation, inequity, inefficiency and unnecessary cost [11]. Traditionally, this approach has been done qualitatively, in local or regional level and seldom for a national population. HNA is a form of risk assessment wherein a risk for higher than expected disease burden is identified. Though risk assessment for decision making has a long history, the field of risk assessment as a science has developed more recently in 30-40 years [12]. Hence, we have tried to develop a framework for quantitative health priority determination by risk assessment score to prioritize CRC screening for NCAC. This would help us identify NCAC with higher than expected CRC burden that may need more urgent action in form of implementing a screening program or improving CRC related infrastructure. The framework includes prioritization by absolute risk (incidence, prevalence), relative risk (CRC ranking for national cancer deaths) and population attributable risk for the disease.

Materials and Methods

(I) Data source: We evaluated CRC risk indicators that may be helpful in assessing the CRC disease burden and the infrastructure available for CRC screening and treatment. Most of the data about the included indicators are available through public health agency (PHA). The data for the risk indicator and risk assessment was derived from International Cancer Control Partnership (ICCP) 2020 cancer country profiles and 2019 WHO report on the global tobacco epidemic [13-15]. The ICCP is a collaboration to support, develop and implement national cancer control plan. The study is a non-human subject research and based on publicly available anonymized database and hence exempted from ethical compliance.

(II) Risk indicators: The important CRC burden risk indicators identified were: 1) Cancer as percent of non-communicable disease (NCD) premature deaths 2) Population attributable fractions

(PAFs) related to tobacco, alcohol and obesity, 3) Availability of population-based cancer registry (PBCR), 4) Number of surgeons, 5) Number of public cancer centers per 10,000 cancer patients, 6) Cervical cancer screening available, if available is it organized, 7) Cervical cancer screening available with or without a defined referral system, 8) Smoking prevalence of the population and 9) FIT availability at PHC. 'The PAF is an epidemiologic measure widely used to assess the public health impact of exposures in populations. PAF is defined as the fraction of all cases of a particular disease or other adverse condition in a population that is attributable to a specific exposure [16].'

(III) Methodology for risk assessment: From the identified CRC burden risk indicators, few indicators termed 'variables' were included in the further risk assessment scoring. For calculating the quantitative risk assessment score, we first calculate the mean and standard deviation (SD) for each variable from the pooled countries' data. Further a standard score (Z score) is calculated for each variable for each country i.e., how far is the value of each country from the mean of all the countries. Hence prior risk indicators with 'yes/no' answers and variables with missing data for some countries were excluded from the risk assessment score. The assessment included variables from different domains such as demographic (population factors), social (social determinants of health), economic (infrastructure capability and feasibility assessment), CRC risk factors and CRC disease burden in each country. Ideally 2-3 indicators are included from each domain for good representation of the domain in final assessment. Because of paucity of indicators, we included 1-2 variables from each domain. Statistical analysis is performed for correlation to confirm, that the indicators are not very closely related thus augmenting the final score. The linearity of the variable is assigned by the epidemiological knowledge of the variable if it increases or decreases the risk burden. For example, the linearity of score is positive for life expectancy since CRC burden would increase with increased life expectancy. On the other hand, the linearity of score is negative for cancer ranking since higher the cancer rank (12th or 22nd), lower would be the CRC burden.

(IV) Statistical analyses: To test the correlation between the indicators we performed a pairwise correlation. A total of 15 continuous variables were included in a correlation coefficient matrix with a pre-specified .05 significance level. The analyses were performed in STATASE-15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC). The indicators included in the final scoring are:

- ***Demographic:*** population, life expectancy
- ***Social:*** Gross national income per capita (international dollars), Percent Gross domestic product (GDP) spent on health expenditure,
- ***Economic:*** Total expenditure on health per capita (international dollars)
- ***CRC burden:*** Age standardized mortality to incidence ratio, Cancer ranking by incidence
- ***CRC risk factors:*** Smoking prevalence

Results and Discussion

Demographics

Table 1 summarizes the current CRC incidence and mortality in NCAC, and Table 2 provides information about current socio-demographic setting in NCAC. Table 3 provides information about the CRC risk indicators. Number of surgeons per 10,000 population and cancer centers per 10,000 cancer patients could be optimum standard measures to compare infrastructure amongst NCAC. This variable was not available for all the countries and hence was not included the risk score.

Table 1: Current CRC incidence and mortality in North and Central Asian countries 1

Country	Age standardized Mortality rates	Age standardized incidence rates	Age standardized mortality to incidence ratio	Cancer ranking by incidence
	Total	Total		Total
Armenia	12.4	19.9	0.62	3
Azerbaijan	7.1	10.2	0.70	4
Belarus	15.1	31.8	0.48	1
Estonia	12.5	29.2	0.43	2
Georgia	5.7	8.7	0.66	4
Kazakhstan	10.5	15.4	0.68	4
Kyrgyzstan	5.7	7.3	0.78	13**
Latvia	12.8	33	0.39	1
Lithuania	12.8	27.2	0.47	1
Moldova	18.7	34.2	0.55	1
Russia	14.7	26.7	0.55	2
Tajikistan	3.1	4.0	0.78	22**
Turkmenistan	3.7	6.0	0.62	16**
Ukraine	15.1	25.8	0.59	1
Uzbekistan	3.8	6.3	0.60	4

1. Global cancer observatory. https://gco.iarc.fr/ (Accessed 03/24/2020).
The data points marked * were the data that were not available through Globacon 2018 and was obtained from WHO cancer mortality database with International Agency for Research on Cancer (IARC) 2015 database. Though the rates are age standardized per 100,000, it is difficult to state how comparable are these data with Globacon 2018. Countries with CRC ranking based on incidence for countries Kyrgyzstan, Tajikistan and Turkmenistan has been derived from different data source (marked **) and hence may not be comparable to the other country ranking for CRC. For some countries the ranking were separate for colon cancer and rectal cancer while for some it was combined as colorectal cancer which additionally adds to the limitation of this data point. The country ranking by incidence is mapped by number of cases and excludes non-melanoma skin cancer.

Table 2: Current Socio-demographic setting in North and Central Asian countries [1,2]

Country	Population	Life expectancy (yrs.)	Gross national income per capita (international dollars)	Total expenditure on health per capita (international dollars)	% GDP spent on health expenditure	Health care system type (UHC)
Armenia	2,925,000	74.8	8,140	362	4.5	Public/Private (yes)
Azerbaijan	9,725,000	73.1	16,180	1,047	6.0	Public/Private Mandatory health insurance (yes)
Belarus	9,480,000	74.2	16,940	1,031	5.7	Universal Government Funded (yes)
Estonia	1,312,000	77.8	24,230	1,668	6.4	Universal Government Funded (yes)
Georgia	3,925,000	72.6	7,040	628	7.4	Public/Private (no)
Kazakhstan	17,988,000	71.1	20,570	1,068	4.4	Public/Private (no)
Kyrgyzstan	5,956,000	71.4	3,070	215	6.5	Public/Private (no_
Latvia	1,971,000	75.0	22,970	940	5.9	Public (yes)
Lithuania	2,908,000	75.0	24,500	1,718	6.5	Public/Private Compulsory Health Insurance (no)
Moldova	4,060,000	71.5	5,190	514	10.3	Public/Private Universal healthcare system(yes)
Russia	143,965,000	71.9	23,200	1,836	7.1	Public/Private Federal compulsory medical insurance fund (yes)
Tajikistan	8,735,000	70.8	2,500	185	6.9	Public/Private (no)
Turkmenistan	5,663,000	68.2	12,920	320	2.1	Public mostly (no)
Ukraine	44,439,000	72.5	8,960	584	7.1	Public mostly (yes)
Uzbekistan	31,447,000	72.3	5,340	340	5.8	Public mostly (no)

1. https://www.who.int/countries (accessed 03/26/2020).
2. World Life Expectancy. https://www.worldlifeexpectancy.com/ (accessed 03/26/2020).
GDP Gross domestic product, UHC Universal health coverage

Table 3: CRC risk indicators*

	Cancer as % of NCD premature deaths (2016)	PAFs (population attributable fractions): Tobacco (2017)	PAFs (population attributable fractions): Obesity (2012)	Availability of population-based cancer registry (PBCR)	Number of surgeons per 10,000 cancer patients	Number of Public cancer centers per 10,000 cancer patients	Cervical cancer screening available/ organized	Cervical cancer screening available, defined referral system	FIT/FOBT generally available at Primary Health Center	Smoking prevalence on the population (%)
Armenia	50.7	28.4	5.5	Yes (2019)	1144.3 (2014)	n/a	Yes	Yes	Yes	27.7
Azerbaijan	31.1	24.8	2.6	Yes (2019)	NA	1.7	No	Yes	No	24.0
Belarus	29.2	29.5	5.9	Yes (2019) high quality	1520.1	2.6	Yes	Yes	Yes	29.6
Estonia	37.5	26.9	5.0	Yes (2019) high quality	246.6	2.6	Yes	Yes	Yes	24.7
Georgia	25.8	24.5	3.3	Yes	NA	n/a	Yes	Yes	No	31.0
Kazakhstan	26.1	25.2	4.5	Yes	NA	6.2	Yes	Yes	Yes	22.4
Kyrgyzstan	19.2	17.4	3.5	Yes	2853.7	3.1	No	No	No	25.7
Latvia	33.9	25.8	5.8	Yes (2019) high quality	866.8	4.1	Yes	Yes	Yes	23.3
Lithuania	34.8	26.0	6.4	Yes (2019) high quality	1485.5	3.7	Yes	Yes	Yes	29.0
Moldova	27.5	NA	NA	Yes	368.4	0.7	Yes	Yes	Yes	25.3
Russia	33.3	26.8	7.0	Yes (2019) high quality	439.0	0.2	Yes	Yes	Yes	29.0
Tajikistan	22.6	13.3	2.6	Yes	2350.9	3.6	No	No	No	6.3
Turkmenistan	20.9	16.3	2.2	Yes	2697.3	8.6	Yes	Yes	Yes	3.4
Ukraine	30.4	28.0	5.7	Yes (2019) high quality	NA	1.6	Yes	Yes	No	22.8
Uzbekistan	15.4	13.8	3.0	Yes	NA	6.3	No	Yes	No	14.4

* The data for the table is derived from The International Cancer Control Partnership (ICCP) 2020 cancer country profiles. The data was accessed on 04/24/2020 from website https://www.iccp-portal.org/. The information about smoking prevalence was obtained from 2019 WHO report on the global tobacco epidemic.

CRC risk factors, incidence and mortality patterns are undergoing transition in the region. Another case control study from south-east Serbia looking at the CRC risk factors found a significant increased risk with smoking (OR=2.13, P=0.0004), BMI between 25-30 (OR=2.45, P=0.0004), alcohol (OR=8.73, P<0.0001), excessive red meat consumption (P<0.0001), excessive intake of dairy products (P<0.0001), family history of gastrointestinal malignant tumors (OR=3.99, P<0.0001) and an income exceeding twice the subsistence minimum (OR=5.34, P<0.0001). Most of the risk factors are similar to those seen in resource rich countries [17]. Further analyses suggest primary or secondary prevention (intervening at proximal determinant) with screening in high income countries and primary prevention (intervening at distal determinants) like risk factor reduction (smoking, diet, obesity) for CRC prevention is more beneficial for resource limited countries [18]. Hence, smoking prevalence was included as an indicator in our risk assessment and found to be an important contributor in risk score for CRC burden in NCAC. Consequently, countries with lower than expected CRC burden may intervene to decrease CRC risk factors (smoking, obesity). An interesting study with the PREVENT software model showed that CRC incidence can be decreased in Latvia by intervening to decrease weight to optimum body mass index (BMI) in males and increasing physical activity in females [19].

Risk scoring and assessment

Table 4 provides the risk scoring for NCAC. The risk assessment shows difference in CRC burden amongst the NCAC. Armenia, Belarus, Georgia and Kyrgyzstan have high burden with risk scores ranging from 2-5. Though Latvia and Lithuania have some CRC burden, the risk score is mitigated by expenditure on health and improved mortality to incidence ratio because of CRC screening. On the other hand, Tajikistan with some risk factors had most of its score decreased by the CRC mortality ranking of 22nd indicating a very low CRC burden. Thus, the risk score can be used as an arbitrary measure to evaluate inter regional variability in CRC burden. Please refer to Supplementary material A for detailed risk assessment scores. On correlation testing, age standardized mortality to incidence ratio is statistically corelated with life expectancy. Please refer to Supplementary material B for correlation testing.

Table 4: Risk assessment Z score

Country	Z score Population	Z score Life Expectancy	Z score Gross national income per capita (international dollars)	Z score % GDP spent on health expenditure	Z score Total expenditure on health per capita (international dollars)	Z score Age standardized mortality to incidence ratio	Z score Cancer ranking by incidence	Z score Smoking prevalence	Total Score
Tajikistan	0	-1	1	0	1	2	-3	-2	-2
Turkmenistan	0	0	0	2	1	0	-2	-2	-1
Latvia	0	1	-1	0	0	-2	1	0	-1
Moldova	0	-1	1	-2	1	0	1	0	0
Kazakhstan	0	-1	-1	1	0	1	0	0	0
Russia	3	-1	-1	-1	-2	0	1	1	0
Uzbekistan	0	0	1	0	1	0	0	-1	1
Azerbaijan	0	0	0	0	0	1	0	0	1
Ukraine	1	-1	1	-1	0	0	1	0	1
Estonia	-1	2	-1	0	-1	1	1	0	1
Lithuania	0	1	-1	0	-2	1	1	1	1
Kyrgyzstan	0	-1	1	0	1	2	-1	0	2
Georgia	0	0	1	-1	0	1	0	1	2
Belarus	0	1	0	0	0	-1	1	1	2
Armenia	0	1	1	1	1	0	0	1	5

Since CRC screening in resource limited countries necessitates planning based on competing disease burden and resources available, different approaches could be utilized for prioritization. Country level CRC health needs assessment using epidemiologic quantitative risk assessment is one of the modalities that could be used for assessing each countries' screening needs. An ideal risk assessment would be able to assess the disparities related to CRC burden. If the indicators are not related, it may suggest the domain with major effect on this risk score. The risk assessment scores depend upon the variables included. Hence selecting the appropriate variables that would depict the true disease burden is important. Further the validity and uniformity of the variables is also important. Mortality to incidence is a variable signifying the mortality rates among those diagnosed with CRC. With screening program implementation, since more CRC are diagnosed in earlier stage with better outcomes, the mortality to incidence rate decreases. Kyrgyzstan, Georgia, Belarus and Armenia have more than expected CRC burden. Tajikistan, Turkmenistan and Latvia have lower than expected CRC burden. No population-based risk assessment studies have been done. A geospatial risk assessment study evaluated cervical cancer screening and treatment based on distance and time of travel to health facility. The study found fewer women completed screening or followed up on abnormal screening if the distance and time of travel to health facility was higher [20].

Epidemiology is integrated with risk assessment process to assist in identifying and evaluating disease burden. This plays an integral role in the formulation of health policy and regulation [21]. The article by Aven T. gives details about the concept of risk assessment and recent advances in the field of risk assessment [12]. Countries found to have high a CRC burden in risk assessment should have a higher priority for CRC screening implementation. This risk-based approach may help resource-limited countries to allocate resources appropriately. A previous similar indicator study, with English abstract and non-English full article, suggested a score card with seven indicators including gross national product, scientific production, smoking rate, breast screening participating rate, all cancer mortality rate (male population), 5 years relative survival for colorectal cancer and life expectancy at birth. Similarly, a validated and uniform set of public health indicators may help in formulating policy for cancer control [22].

The risk indicators selected for this review are feasible, available from most Public health websites and is across a variety of domains (socio economic factors, life expectancy, CRC burden, CRC risk factors, CRC screening and treatment infrastructure) making the risk score comparable between the different NCAC. Some additional variables that may have been good indicators were number of surgeons per 10,000 population, number of endoscopy facilities and cancer centers per 100,000 persons, though the data is not available for all the countries. Different risk tools exist to predict individualized risk for CRC, intervals for CRC screening and need for further testing [23-26]. Though few risk tools could help assess and mitigate population level CRC burden. For most countries, the risk assessment score is not contributed entirely by one to two variables. Both Georgia and Latvia have screening program. However, Georgia has high age standardized mortality to incidence ratio and smoking prevalence with higher than expected CRC burden suggesting barriers to screening. Armenia has risk factors contributed by each domain that adds up to the high score of five. Estonia with high life expectancy and CRC prevalence negated its effect by high expenditure on health.

Study limitation

The data points obtained from PHA have limitations associated with the sources they were derived from. Most data are not recent. Data collection process for the included indicators may vary amongst NCAC. This leads to discrepancies in data interpretation. One of the major discrepancies for the variables exist for the derivation of smoking prevalence. The WHO 2017 data is an estimated data for smoking prevalence and the Health System Performance Assessment Survey is an actual survey data from 2016 to determine population smoking prevalence. For some countries, smoking prevalence is from more recent survey data. Some countries have no CRC related data. Some of the countries considered are also part of Eurasian countries. Like ecological studies, wherein the unit of study is not a person but a whole population; these risk score testing may give spurious results [27]. Nevertheless, they are beneficial to assess unmet health needs.

Conclusions

Numerous countries are exploring the options to introduce organized CRC screening program. Cost and cost-effectiveness assessments are becoming a priority in initiating and then sustaining a cancer-screening program. The EU-TOPIA (Towards improved screening for breast, cervical and colorectal cancer in all of Europe) project is planned to evaluate the harms and benefits of CRC screening programs to reduce the disparities in screening strategies [28]. Identifying high-risk countries to prioritize screening is important for most efficient allocation of limited health care resources. Uniform and comparable CRC risk indicators for the region is needed. Health need assessment and risk assessment are important for better distribution of resources and informed decision-making. Further research is needed to evaluate the cancer screening implementation based on risk assessment. For policy implications, countries with lower risk score may implement preventive policy to reduce risk factors and countries with higher risk could adapt mitigating policy for early diagnosis of CRC.

Ethics approval and consent to participate

Not applicable: The study is a non-human subject research and based on publicly available anonymized database and hence exempted from ethical compliance.

List of abbreviations

CRC: Colorectal cancer
DALY: Disability adjusted life years
FOBT: Fecal occult blood test
FIT: Fecal immunochemical test
GDP Gross domestic product
HNA Health need assessment
ICCP: International Cancer Control Partnership,
LMIC: Low- and middle-income countries
NCAC: North and Central Asian Countries
NCD Non-communicable disease:
PHA: Public health agency
PAF: Population attributable fractions
PBCR: Population-based cancer registry
SD: Standard deviation
UHC: Universal health coverage
WHO: World Health Organization
Z score Standard score

Data Availability

All data is from publicly available database and links to website is provided in reference

Conflicts of Interest

The author declares that there is no conflict of interest regarding the publication of this paper.

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Authors' contributions

Rebecca Pratiti: Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Writing original draft, Writing -review and editing. Dr. Olga Santiago and Dr. Carlos Rios Bedoya helped with the statistical analysis.

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Supplementary Materials

Supplementary material A has detailed risk assessment scores. Supplementary material B shows statistical correlation testing of the included variables in risk assessment.

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