Chapter 23 Colorectal Cancer in the Arab World



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23.1 Status of CRC in Arab Countries

23.1.1 Incidence

According to the most recent GLOBOCAN report, Colorectal Cancer (CRC) is considered the third most commonly diagnosed cancer and the second leading cause of cancer-related death worldwide. It accounted for almost 1.8 million new cases, and 860,000 deaths in 2018. It is expected that the global CRC burden will increase by 60% by 2030 [1]. The global incidence and mortality of CRC vary according to the geographical areas and countries, which could be attributed to existing risk factors, ethnicity, comprehensiveness of cancer registries, availability of screening facilities and management protocols [2].

Fortunatly, the CRC incidence and CRC-related death is declining in the western countries [1]. On the other hand, there has been an obvious and rapid rise of CRC incidence and mortality across many developed countries in Asia, Eastern Europe and South America [3]. The Arab population is no exception, although the figures reported for colorectal cancer among Arabs are much lower than that for developed countries, yet the incidence of colorectal cancer in the Arab countries is increasing in the past ten years [4].

The Arab world has a population of >300 million people distributed among 22 countries delimited by Lebanon and Syria to the north, Morocco to the west, Yemen to the south, and Iraq to the east. It includes the 7 Gulf Cooperation Council (GCC) member countries, including Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates, and Yemen.

A rapid revolution and modernization have happened in this region at all levels, which cumulatively led to major changes in the disease burden profile where Non-Communicable Diseases exert a huge burden. That is mainly attributed to increased incidence of obesity, physical inactivity, stressful busy life, smoking, and dietary habits, which correlated with a dramatic increase in cancer incidence over the past 10 years [5].

Focusing on Colorectal Cancer (CRC), the incidence and mortality of CRC among Arabs have obviously increased in the last decade. For example, in the GCC countries, CRC is considered the second most common cancer among both genders with reported 2.3 fold and a 2.7 fold increase in newly diagnosed cases of CRC among male and female, respectively [4]. A similar trend has been reported from other Arab countries (Table 23.1).

From table 23.1, Comoros reported the least CRC Age-Standardized Rate (ASR) (4.5/100,000) of both genders among Arab countries, while Gaza Strip reported the maximum ASR (18.6/100,000). It is very noticeable from the GLOBOCAN report that there is a multi-fold increase in the ASR in this region compared to previously reported ASR in the region [4, 6–9].

The National Health Services in the GCC countries and the World Cancer Research Fund Report (WCRF) and the American Institute for Cancer Research (AICR) have linked this increase to the drastic changes in the lifestyle and food consumption patterns such as high daily calorie intake, increased consumption of carbohydrates and sedentary lifestyle plus increased sitting time regardless of physical activity. These factors have synergized with the genetic factors of cancer among Arabs and resulted in a noticeable increase in the incidence of cancer. In fact, studies in food consumption patterns have confirmed the high consumption of this diet that is considered a high-risk dietary profile for cancer in general and CRC specifically [4, 10]. A comprehensive longitudinal study is needed to evaluate the detailed dietary profile and sedentary lifestyle of Arabs and evaluate their correlation with CRC incidence.

23.1.2 Clinicopathological Parameters

23.1.2.1 Age

CRC tends to occur at a younger age among Arabs compared to western population. The median age for CRC among Arabs is found to be 60+/- 15 compared to the average age of 70 years in Westernized countries. The population structure of Arabs might explain this finding as the majority of the Arab population are in this age group [7, 9, 11-16] but more studies are needed to find out if this is a real increase in the incidence in this age group or is it the population structure effect.

Table 23.1 Estimated age-standardized incidence rates of Colorectal Cancer in 2020 across all ages in Arab countries compared to non-Arab countries

Population	Country	Both gender	Female	Male
Arab Population	Comoros	4.5	5.2	3.7
	South Sudan	5.7	5.1	6.3
	Egypt	6.1	6.2	5.8
	Sudan	6.3	6	6.6
	Djibouti	6.9	5.9	7.8
	Mauritania	7.2	6.1	8.6
	Iraq	8.7	6.9	10.8
	Somalia	9.3	8.6	10.1
	Oman	9.9	7.7	11.2
	Yemen	10.7	9.5	12
	Morocco	11.3	9.9	12.9
	Lebanon	12.2	9.5	15.2
	Kuwait	12.5	11.9	13.1
	Tunisia	12.7	11.7	14
	United Arab Emirates	13.1	17.3	11.5
	Bahrain	13.9	14.6	13.7
	Saudi Arabia	13.9	10.9	16.1
	Algeria	15.3	14.2	16.5
	Libya	15.7	15.1	16.7
	Qatar	15.7	20.6	13.6
	Jordan	17.7	18.4	17.2
	Gaza Strip and West Bank	18.6	16.7	20.7
Non-Arab Population	Democratic Republic of Korea	18.8	15.9	22.8
	Malaysia	19.6	18	21.2
	Turkey	20.6	16.2	26.2
	United States of America	25.6	22.9	28.7
	Germany	25.8	21.8	30.4
	Sweden	27.8	25.2	30.5
	France	30.1	24.9	36.3
	Canada	31.2	27.9	34.7
	Singapore	33	27.4	38.6
	United Kingdom	34.1	29	40
	Japan	38.5	30.5	47.3
	Islamic Republic of Iran	13.9	11.9	15.9

Data Source: Arnold M, Rutherford M, Lam F, Bray F, Ervik M, Soerjomataram I (2019). ICBP SURVMARK-2 online tool: International Cancer Survival Benchmarking. Lyon, France: International Agency for Research on Cancer. Available from: http://gco.iarc.fr/survival/survmark, accessed [05/Feb/2021]

23.1.2.2 Stage

Most CRC clinicopathological studies in the region reported an advanced stage (stage III and IV) cancer at diagnosis. Majority of CRC patients are diagnosed late when the tumor has already grown into a clinically detectable size causing alarming symptoms and signs [7, 9, 11–16]. It has been attributed mainly to lack of screening, poor awareness of the disease early symptoms and disconnected healthcare system. These patients either have ignored their symptoms since they are non-specific, or the primary care providers do not have high suspicion for cancer for such symptoms.

23.1.2.3 Lateralization

There are no consistent findings on the lateralization of CRC among the Arab population. Majority of studies of CRC in Arab countries found that the most affected site is the rectum, followed by sigmoid and distal colon. This is similar to reports from western and regional countries [7, 9, 11–17]. In fact, there is a noticeable shift toward proximal colon cancer in western countries which has been explained by the high success rate of CRC screening for detection of rectal and distal colon tumors, leaving the proximal colon cancer undetected till late in the disease [1, 18, 19].

23.1.3 Survival and Mortality

The CRC survival rate is lower in Arab countries compared to western countries. This is mainly because the majority of patients are detected late in an advanced stage due to lack of screening and poor awareness of signs and symptoms [9, 20]. The Age-standardized mortality rate in the Arab population compared to non-Arab countries is listed in Table 23.2 (constructed from Globocan 2018 report).

Egypt has the least estimated age-standardized mortality among Arab population (3.4) and Gaza strip has the highest among all Arab countries (11.2).

Prognosis of CRC that is diagnosed at a late stage is unfavorable with very limited treatment options available. The 5-years survival of CRC is highly dependent on the stage of the disease, being 95% for stage I CRC and decreasing to 70% for stage IV CRC [21]. This explains the relatively low survival rate of CRC among Arabs compared to western countries [16, 20, 22].

Table 23.2 Estimated age-standardized mortality rates of colorectal cancer in 2020 across all ages in Arab countries compared to non-Arab countries

	ized mortality rates in 2020, Colore		Female	Mala
Population	Country	Both gender		Male
Arab Population	Egypt	3.4	3.4	3.3
	Sudan	3.9	3.6	4.2
	South Sudan	4.5	4	5.1
	Djibouti	5.3	4.6	6.1
	Iraq	5.4	4.4	6.8
	Mauritania	5.4	4.6	6.5
	Oman	5.7	4.5	6.2
	Morocco	6.2	5.4	7.2
	Tunisia	6.4	5.6	7.3
	Kuwait	6.6	6.1	7
	Lebanon	6.7	5	8.8
	United Arab Emirates	6.9	8.7	6.2
	Bahrain	7.1	7.5	6.8
	Saudi Arabia	7.3	5.6	8.7
	Somalia	7.7	7.1	8.4
	Yemen	7.7	6.9	8.6
	Syrian Arab Republic	8.2	7.2	9.4
	Algeria	8.3	7.7	9
	Qatar	9	10.9	8
	Jordan	9.6	9.6	9.7
	Libya	10.2	9.8	11
	Gaza Strip and West Bank	11.2	9.9	12.7
Non-Arab Population	Canada	9.9	8	12
	United States of America	8	6.7	9.4
	Germany	9.9	7.3	12.9
	Turkey	10.1	7.8	13
	Malaysia	10.2	9.4	11
	France	10.4	8.1	13.3
	Sweden	10.8	9.7	12.1
	Democratic Republic of Korea	10.9	8.7	13.5
	United Kingdom	11.4	9.6	13.5
	Japan	11.6	8.9	14.7
	Singapore	16.2	12.8	19.8
	Islamic Republic of Iran	7.3	6.3	8.3

Data Source: Arnold M, Rutherford M, Lam F, Bray F, Ervik M, Soerjomataram I (2019). ICBP SURVMARK-2 online tool: International Cancer Survival Benchmarking. Lyon, France: International Agency for Research on Cancer. Available from: http://gco.iarc.fr/survival/survmark, accessed [05/Feb/2021]

23.2 CRC Screening in the Arab Region

23.2.1 Status of CRC Screening in the Arab Region and Barriers to Its Implementation

Screening is known to be the most powerful intervention to reduce the incidence and mortality of cancer [23]. In fact, the nationwide screening programs implemented in the western courtiers have resulted in a noticeable reduction in both incidence and mortality rate of the screened cancers [1].

Unfortunately, there is no established CRC screening program in most of the Arab countries, and even in those countries that have established such a program as a trial at a smaller scale, for instance, in the UAE, the uptake is very low [24]. The barriers were studied and collectively listed as system based and patients' based barriers. The system based barriers include lack of resources, disintegrated medical systems and lack of test recommendation to patient by the treating physicians. Patients based barriers include unawareness of symptoms and risk factors of CRC, lack of knowledge of screening tests and their significance, embarrassment from doing the test and stigma about being diagnosed with cancer [4, 24-30]. A study from UAE reported that almost 95% of participants were not advised to do the CRC screening by their physicians [31]. This necessitates significant efforts to be directed toward increasing the awareness of both patients and healthcare providers, primary healthcare providers specifically, about the suspicious symptoms and the significance of early detection and screening. Furthermore, primary healthcare providers should be involved in the CRC screening program construction as they are the ones who can reach people and advocate for such campaigns.

In parallel to these findings, Arab Americans were found to have low adherence to CRC screening in the USA compared to Americans from other ethnic groups as well. The same local cultural, religious, and familiarity barriers do exist in the Arab American population despite being in a non-Arab country with well-established screening programs. Poor communication with the healthcare providers was highlighted as a major factor either due to language and culture barriers or distrust of the western recommendation. Other significant factors are costs and inaccurate understanding of risk factors [29, 32]. Such sociocultural barriers necessitate innovative awareness campaigns for Arabs to correct misconceptions and stress on the cost-effectiveness of screening programs. Furthermore, statistics of CRC status in the country and symptoms of the disease should be clearly communicated with people to influence their uptake of the screening program.

23.2.2 How to Improve CRC Screening in Arab Region

Every country has its own cancer burden that necessitates the construction of a cancer control plan with goals and objectives tailored to the available infrastructures and resources. In general, cancer screening programs are constructed either to

target the whole population or high-risk group specifically. There are so many determinants for such a decision. Since the number of CRC among Arabs is relatively low compared to western nations, a screening program targeting high-risk groups would be a suitable starting step. Large-scale nationwide screening is expensive and needs a well-built infrastructure which is not the case in most of the Arab countries.

The reported insufficient screening uptake and poor awareness of CRCs among Arabs reflect the need for the involvement of all stakeholders; primary healthcare providers, ministry of health, media sector, schools, Non-Governmental Organizations, etc. Primary healthcare providers should be aware of the gap in knowledge in the population and work hard to ensure proper understanding of issues related to the risk of CRC and the usefulness of the screening programs [33]. Nongovernmental and governmental organizations should be involved to spread awareness and correct misconceptions and negative attitudes related to the disease and the screening program. Media is a very powerful platform to spread awareness where it should be extensively used to stress on the significance of screening, increase awareness of the risk factors, CRC signs and symptoms. In fact, a study conducted in UAE showed that 66% of participants claimed that their main source of cancer information is media channels [31]. The other significant hallmark of successful screening program is the preparation of a strong and connected healthcare infrastructure in order to handle suspicious and confirmed cases systematicly and offer the needed management plans promptly.

23.3 CRC in Arab: Hereditary, Familial, or Sporadic?

The mode of presentation of CRC follows one of three patterns: sporadic, inherited, and familial.

- Sporadic CRC is the most common and accounts for approximately 70–75% of all diagnosed CRCs. It is characterized by an absence of family history. Early onset CRC cases in Arabs are thought to be sporadic, which necessitates further research to decipher the main molecular, environmental, and behavioral mechanisms.
- Inherited CRC represents only 10% of all diagnosed CRCs. Patients usually are diagnosed with inherited syndromes that predispose them to develop CRC. The inherited syndromes are divided into two categories, polyp associated syndromes such as Familial Adenomatous Polyposis (FAP), MUTYH-Associated Polyposis (MAP) and hamartomatous polyposis syndromes and non-polyp associated syndromes such as Lynch syndrome (HNPCC). Having a family member with CRC due to any of these syndromes necessitates early screening and sometimes prophylactic procedures for all people in the family who are at risk to reduce their chance of developing CRC.

• The third and least well-understood pattern is known as "familial" CRC, which accounts for up to 25% of cases. In this category, the CRC patients have a family history of CRC, but there is no clear pattern that is consistent with any of the known inherited syndromes. If a family member developed a familial CRC, it increases the risk of other members to develop CRC up to 1.7-fold, especially if the affected person is below the age of 55.

Unfortunately, data about the pattern of CRC and the molecular characteristics from Arab countries is scarce. That could be explained by the retrospective nature of the majority of the available studies where molecular markers and detailed family history are not routinely available. Furthermore, until recently, suspicious hereditary CRC cases are identified through the application of specific clinical criteria listed in the Amsterdam and Bethesda guidelines without the use of a laboratory-based screening test [34]. Therefore, there is not enough molecular or genetic data to determine the pattern and molecular signatures of CRC among Arabs, which is a fertile area for future research.

23.3.1 Biological Markers

The development of colorectal cancer is an accumulative process that necessitates a sequence of genetic mutations and epigenetic events at different sites that transforms the cells into cancerous cells [35]. There are several mutations that have been investigated and found to play a role in the initiation of CRC. Some of them have reached the clinic as biological markers for personalized medicine and prognosis prediction, such as mutations in KRAS, BRAF, and MMR, which are critical genes that are involved in cell proliferation, angiogenesis, cell motility and apoptosis. In fact, clinical evaluation and consideration of these genetic markers along with other clinicopathological parameters have revolutionized CRC management and improved patient outcome and prognosis. For example, KRAS-wild CRC showed 40–60% good response to anti-EGFR agents such as cetuximab. While KRAS mutant CRC and extended RAS family mutant tumors do not respond to anti-EGFR agents. Understanding the status of these biological markers in the Arab population is crucial to compare with other non-Arab populations and support international guidelines.

23.3.1.1 KRAS

It is the Kirsten Rat Sarcoma (KRAS) gene, one of the commonly mutated oncogenes that has been linked to CRC. The KRAS protein is involved in signaling pathways that play a major role in cell proliferation, differentiation, and apoptosis. KRAS testing is now considered as part of the standard of care of metastatic CRC being recommended by international guidelines. The frequency of KRAS in the

Arab population has been found to range from 30% to 50%, which is similar to reported data from western population. Majority of KRAS mutations occur in codon 12, which is found to be the same among Arab, Middle Eastern and Western populations [36–43]. KRAS mutant tumors are claimed to be associated with a more advanced stage CRC. Studies from the Arab world in patients at different stages of CRC did not find such association [43]. Therefore, the prognostic value of KRAS mutation was conflicting among studies. It has been associated with poor prognosis and outcome regardless of the stage of the tumor in a study done in Saudi Arabia [43], but it did not show that association in other studies. This could be explained by the variation in study design, especially study parameters that are related to sample size, ethnic group, modality of testing the KRAS mutation and timing of the reported tumor stage, whether the reported stage was at the time of diagnosis or at the time of data collection.

23.3.1.2 BRAF

BRAF is another attributed genetic marker for the initiation of CRC. The BRAF gene encodes a protein that is part of the Ras-Raf-MEK-ERK [44]. The frequency of BRAF mutation among Arabs with CRC was found to range from 2.4% to 4%, which is similar to nearby Asian and Middle Eastern countries, 4.9%, 4.6%, respectively, but lower than that reported from western countries (9.2%) [38, 39, 45].

The BRAF and KRAS mutations were not significantly associated with any clinicopathological parameters, tumor lateralization, gender, age, compared to western countries, which were significantly associated with right-side tumor, female gender and metastatic tumor. This could be explained by the small sample size again from Arab studies and the method used to test these molecular markers [37, 38].

23.3.1.3 PIK3CA

This gene plays a role in the cell survival signaling pathway. Mutations in this gene have been found to be similar in Arabs and Western countries, which is about 12–13% [36, 38, 46].

23.3.1.4 APC

The tumor suppressor gene APC plays an important role in CRC development. The absence of the APC protein leads to the accumulation of beta-catenin in the cytoplasm, resulting in constitutive transcriptional activation of TCF-responsive genes, which enhances tumor progression [47]. The frequency from the pooled results in Middle Eastern countries is (33%), which is consistent with the frequency rate in

Asian countries (32.4%), but it is lower than the frequency rate in Western countries (44.8%) [38, 48].

23.3.1.5 Mismatch Repair (MMR) Genes

A mutation in Mismatch Repair (MMR) genes (MLH1, MSH2, MSH6, and PMS2) is linked to the most common hereditary autosomal dominant CRC syndrome "Lynch syndrome (LS). The presence of Microsatellite Instability (MSI) is the hallmark of this syndrome. Several studies from the Middle East reported LS families, and the clinical features of these families appear to be similar to those seen in Western families. About 0.9% of newly diagnosed CRC in Saudi Arabia has LS, which is similar to other countries [49–51]. Siraj et al. reported 11.2% of CRC in Saudi Arabia patients to have MSI high that was related to LS [51], compared to 9.4% found in the CRC population from UAE [52] and 11.6% from Israeli Arabs [53]. It is worth mentioning that MSI high is not only correlated to LS but also has been found in 10% of sporadic CRC. The presence of a hotspot mutation in the BRAF oncogene with the MSI indicates a sporadic tumor because the BRAF mutation is never detected in LS [52]. MSI in sporadic CRC was associated with more proximal, poorly differentiated tumors and young male predominance [52, 54]. More studies are needed among Arabs in the genetic predisposition of CRC as early identification of individuals at high risk would allow earlier screening, intervention and subsequently improve outcomes.

23.3.1.6 Consensus Molecular Subtypes of CRC

Recent studies have evaluated the Consensus Molecular Subtypes (CMS) of CRC tumors and if there are any differences in these signatures related to the age of onset, the anatomical location or the prognosis. Interestingly, a CMS classification system has been constructed, which divided the CRC into four distinct subtypes, CMS1 (Microsatellite Instability Immune), CMS2 (Canonical), CMS3 (Metabolic), and CMS4 (Mesenchymal) [55]. These subtypes differ in their clinical, genetic and biological signatures and subsequently treatment response. Since the construction of this CMS classification in 2015, it has been implemented largely in basic and clinical cancer research but not yet integrated into clinical practice [56, 57]. More intensive research projects with multidisciplinary collaboration are required in order to decipher the correlation between these classifications and other clinicopathological parameters before integrating them into routine clinical practice. There are no studies conducted on the prevalence of CMS subtypes among Arabs yet. In fact, Korphaisarn, et al. analyzed them among different populations and concluded that there is a substantial variation by geographic region [58]. Further studies are needed in global populations to understand the pattern and validate their findings which ultimately might add a new transcriptomic dimension for CRC management strategy.

23.4 Early Onset Colorectal Cancer (EOCRC) in Arabs

Early Onset Colorectal Cancer (EOCRC) is defined as a colorectal cancer that is diagnosed before the screening age, i.e., < 50 years of age. As stated earlier, there was a noticeable decrease in incidence of adult-onset CRC (> 50 years) by 2% per year in the western countries compared to an annual increase of 1.5% per year among patients 20 to 49 years old. In fact, there is a prediction that by 2030 in the USA, 10% of all colon and 22% of all rectal cancers are expected to be diagnosed in patients <50 years old [4]. Almost all reports on CRC in the Arab region reported predominant young age at diagnosis, even younger than western population at diagnosis. 17-38% of CRC patients diagnosed in Arab were younger than 40 years old [6, 7, 20, 54, 59–62]. This increase in EOCRC incidence has not been fully understood till now. A key question in understanding the factors responsible for increasing incidence of EOCRC is whether EO- and LO-CRC are the same disease, or if EOCRC is caused by unique underlying biological pathways that synergize with different risk factors. It was strongly believed that EOCRC is highly linked to genetic factors and hereditary familial syndrome. Surprisingly, recent evidence do not support this belief. Genetic risk assessment of a cohort of young CRC patients revealed that only 1 in 5 of these patients do carry a germline genetic mutation and about 25% of them had a firstdegree relative with CRC. The remaining majority of patients are sporadic [63, 64].

Retrospective studies to understand sporadic EOCRC revealed distinctive histologic features in terms of the anatomical location of the tumor and stage at diagnosis compared to late-onset CRC and inherited EOCRC. Sporadic young-onset CRC has been found to present at advanced stages and often in the distal colon and the rectum. Several studies have shown that sporadic EOCRC exhibit mucinous and signet ring features or poorly differentiated histology. Furthermore, they usually present with metastasis at diagnosis and are shown to have early disease recurrence and subsequently lower survival [63–65]. At the molecular level, investigation is going on to decipher its molecular profile. The most recent findings showed that sporadic EOCRC is associated with a higher percentage of synchronous and metachronous tumors [66]. The genetic profile of this cancer entity is different as well, where most of these tumors are microsatellite and chromosomal stable (MACS), lack DNA repair mechanism abnormalities and have significantly fewer BRAF and APC mutations than late-onset CRC [38, 66, 67]. More studies are needed to understand the molecular and clinicopathological signatures of EOCRC among Arabs in order to construct the best preventive and intervention measures.

23.5 Cancer Genetic Counseling in Arabs

As discussed earlier, hereditary cancer occurs in high frequency in several Arab populations due to high rates of consanguinity; 25–60% of consanguineous marriages among Arabs [33]. In fact, a comprehensive genetic study conducted in Saudi

Arabia on children with cancer found that 4 in 10 children with cancer have hereditary cancer syndrome. They reported 38% consanguinity among the studied group. Unfortunately, there are a smaller number of studies on familial and hereditary cancer among the Arab population. Several initiatives have been initiated from many Arab countries, such as the Saudi Human Genome Project (SGHP) and similar programs in Qatar, Egypt, and the United Arab Emirates aiming to understand the genetic profile and distribution of cancer among their population.

At the same time, healthcare planners envisioned the huge demand for familial cancer genetic counseling in the Arab world and worldwide in general [33]. The definition of Genetic counseling is a "process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease" [68]. These facilities provide screening, monitoring and offer prophylactic interventions to reduce the risk of cancer development.

It is true that these facilities have been found to positively reduce the cost of care and improve the cancer awareness and care satisfaction among patients and their relatives, but they have raised few other negative issues related to the psychological distress of doing the genetic test, misinterpretation of genetic results and sometimes unnecessary interventions [33, 69]. Therefore, professionally trained personnel are needed to run these clinics in order to overcome these challenges. Genetic counselors must successfully communicate risk perception to their patients and to provide significant levels of long-term psychosocial support to patients and their families.

Such clinics were established in several Arab countries such as in Saudi Arabia [33], Oman [70] and others. They have constructed guidelines and recommendations for different types of cancer [33]. These clinics receive referrals for patients who are genetically high-risk in order to do the needed genetic or clinical screening and proper counseling and interventions. Such genetic counseling and prophylactic intervention coupled with increase in public awareness of risk factors, signs, and symptoms will collectively help in reducing the impact of CRC in the societies.

23.6 Conclusion

The burden of CRC is increasing worldwide. There is an unmet need for primary and secondary prevention measures in Arab countries. Cancer prevention programs should be implemented within an organized program with all infrastructure and resources tailored to ensure offering a comprehensive cancer care through all steps of the cancer continuum. Cost-effectiveness studies of either high-risk population or nationwide screening options are needed by every country to tackle their own cancer burden.

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