

# Incidence of colorectal cancer in Iran: A systematic review and meta-analysis

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**Background:** The incidence of colorectal cancer (CRC) is rising in Iran, but reports vary across different regions due to diverse methods and data sources. This study aimed to conduct a systematic review and meta analysis to provide an overview of the incidence rate of CRC and its trend among Iranians in various provinces. **Materials and Methods:** A comprehensive literature search based on the Preferred Reporting Items for Systematic Reviews and Meta Analyses checklist was performed using national and international databases for papers published up to December 2023. CRC incidence rates were extracted from the numbers, crude rates, and age standardized rates (ASRs). A meta analysis was conducted to calculate the incidence rate and 95% confidence intervals (CIs) in subgroups of sex and province. **Results:** The initial database search retrieved 1287 papers, with 47 studies meeting the inclusion criteria after further screening. Overall, the trend of CRC incidence has been increasing, although a different pattern was observed in 2008. The pooled incidence rate of CRC was 8.46 (95% CI: 7.16–9.86) per 100,000 population before the publication of the annual continuous reports of the Iranian National Cancer Registry. The latest national data (2014–2017) indicated an ASR of approximately 15 per 100,000 population. **Conclusion:** The incidence of CRC in Iran is lower than the global average. However, inconsistent cancer registration policies and gaps in registration have hindered the ability to establish a reliable trend of CRC incidence over time.

**Key words:** Colorectal cancer, incidence, Iran, meta-analysis, systematic review

**How to cite this article:** Rahimi F, Rezayatmand R, Tabesh E, Tohidinik HR, Hemami MR, Ravankhah Z, *et al.* Incidence of colorectal cancer in Iran: A systematic review and meta-analysis. *J Res Med Sci* 2024;29:65.

## INTRODUCTION

Cancer continues to be a formidable global health challenge, resulting in a staggering 10 million fatalities in the year 2022.<sup>[1]</sup> Among the various cancer types, colorectal cancer (CRC) has risen to prominence, ranking as the third most prevalent cancer worldwide in the same year. With a substantial count of 1,926,425 newly reported cases, CRC accounted for approximately 10% of all newly diagnosed cancers. Tragically, the gravity of CRC is further underscored by its designation as the second most fatal cancer, claiming the lives

of 904,019 individuals, representing around 9.3% of the total cancer-related deaths. The crude and age-standardized rates of CRC were reported at 24.4 and 18.4 per 100,000 in 2022.<sup>[1]</sup>

In 2022, the estimated number of new colorectal cancer cases varied across different regions. Asia reported the highest number of new cancer cases with 966,399 cases, followed by Europe with 538,262 cases, and Northern America with 183,973 cases. Latin America and the Caribbean had 145,120 cases, while Africa reported 70,428 cases, and Oceania had 22,243 cases.

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10.4103/jrms.jrms\_110\_23

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**Submitted:** 15-Feb-2023; **Revised:** 02-Jun-2024; **Accepted:** 18-Jun-2024; **Published:** 24-Oct-2024

Examining the crude incidence rates per 100,000 population, Europe had the highest rate at 72.0, followed by Oceania at 50.8, Northern America at 49.3, Latin America and the Caribbean at 2.8, Asia at 20.8, and Africa at 5. However, when considering the age-standardized rates, which adjust for differences in age distribution across populations, the rankings change. Oceania had the highest age-standardized rate at 31.1, followed by Europe at 30.5, Northern America at 27.2, Latin America and the Caribbean at 16.9, Asia at 15.6, and Africa at 8.2.<sup>[1]</sup>

Due to population growth, demographic changes, and Westernization of lifestyle habits, the global burden of CRC is increasing rapidly.<sup>[2]</sup> Although CRC is more prevalent in developed countries,<sup>[3]</sup> its incidence is rising in developing countries, with a higher proportion of cases among younger individuals.<sup>[4]</sup> CRC is a significant disease in Iran, but comprehensive studies on its occurrence and trends are lacking.

Rafiemanesh *et al.* used data from the national cancer registry system in Iran to evaluate CRC occurrence and morphology from 2003 to 2008.<sup>[5]</sup> Dolatkah *et al.* conducted a systematic review and meta-analysis of 39 studies from various regions of Iran, revealing age-standardized incidence rates of 8.16 and 6.17 per 100,000 person-years for males and females, respectively, with crude rates of 5.58 for males and 4.01 for females.<sup>[6]</sup> Dehghani *et al.* explored CRC incidence trends from 2003 to 2010, finding a significant increase in cases, with incidence rates rising from 6.22 to 9.99 per 100,000 persons in males and from 6.74 to 8.69 per 100,000 persons in females.<sup>[7]</sup> Danaei *et al.* reported ASRs of CRC based on reviews from Kerman, Yazd, and Qom.<sup>[8]</sup> Saadati *et al.* conducted a systematic review to investigate the incidence rate and risk factors of CRC in Iran, revealing variations across regions, populations, genders, age groups, and study years.<sup>[9]</sup>

Understanding the CRC incidence rate and its trend is crucial for preventive action planning. This study aims to systematically review and meta-analyze the incidence rate reported in studies until 2024. Unlike previous studies, this research reports CRC incidence at the provincial level, providing valuable insights specific to Iran. This approach acknowledges Iran's distinct demographic and lifestyle patterns, enabling the development of tailored prevention and intervention strategies. Expanding our understanding of CRC dynamics within Iran can drive informed efforts to mitigate its impact on public health.

## MATERIALS AND METHODS

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.

The Cochrane Library, Embase, and MEDLINE on Ovid were searched for epidemiologic studies reporting the incidence rate of CRC in Iran up to December 2023. Detailed search strategies are presented in Appendix 1. Additionally, two main databases of Iranian articles, the Scientific Information Database (SID) and the Islamic World Science Citation Center (ISC), as well as official cancer registry reports published by the Iran Ministry of Health, were included in the search. The review was limited to studies published in Persian and English between 2009 and 2023.

### Inclusion and exclusion criteria

In this study, the review process was carried out collaboratively by a multidisciplinary team. Two independent researchers were assigned to screen the articles, while two other authors provided oversight and monitoring to ensure accuracy and comprehensiveness. The initial screening involved evaluating the titles of the search results, followed by an assessment of the abstracts.

Selected articles had to meet the following criteria:

- The study was conducted at the national, regional, or provincial/city level, not limited to a specific facility like a hospital
- The study provided sufficient information on at least two indicators, including the number, crude incidence rate (CIR) and Age-Standardized Rate (ASR).

Articles were excluded if they met any of the following criteria:

- The study did not focus on the epidemiology of CRC among the average-risk population and was not presented as an original article
- The study primarily focused on biological events or mechanisms
- The study specifically discussed risk factors of CRC
- The population studied consisted of screened individuals
- The study design involved interventions.

To evaluate the quality of the included articles, we employed the Strengthening the Reporting of Observational Studies in Epidemiology checklist. This checklist was used to assess studies employing cohort, case-control, and cross-sectional designs. By applying this rigorous approach, we ensured the reliability and consistency of the selected studies in our review. The quality assessment indicated that most included articles had deficiencies in the methods and results sections. However, more than half of the articles achieved acceptable scores out of the 22 items reviewed. No study was excluded based on the quality assessment. Further information regarding this matter is provided in Appendix 2.

**Data analysis**

All incidence data were extracted from the articles and presented as Excel-based tables and figures. We assessed the heterogeneity between incidence rates using the  $I^2$  index, with values of 25%, 50%, and 75% representing low, moderate, and high levels of heterogeneity, respectively.<sup>[10]</sup> We also employed the  $Q$ -test for heterogeneity, considering a  $P < 0.1$  as statistically significant.

Due to observed heterogeneity in the initial analyses, we applied random-effects models to pool the incidence estimates. Metaprop, a statistical procedure in the Stata package, was used to combine the incidence rates and calculate the pooled incidence of CRC and related 95% confidence intervals (CIs). The Freeman-Tukey double arcsine transformation was used to stabilize variances in the meta-analysis. We used the exact method (cimethod [exact] in Stata) to calculate the CIs of pooled estimates.

Meta-regression of log-transformed incidence estimates was performed to investigate sources of heterogeneity among studies, specifically examining sex, province, and publication year as potential moderator factors. For the province variable, we treated it as a categorical independent variable and applied dummy coding for each category, using the category with the highest number of studies as the reference contrast. Subgroup analysis was performed according to sex and province. A forest plot was employed

to illustrate the CRC incidence in individual studies, along with the pooled estimates and their corresponding 95% CIs. Stata 18 (Stata Corp, College Station, TX, USA) was used to analyze the data.

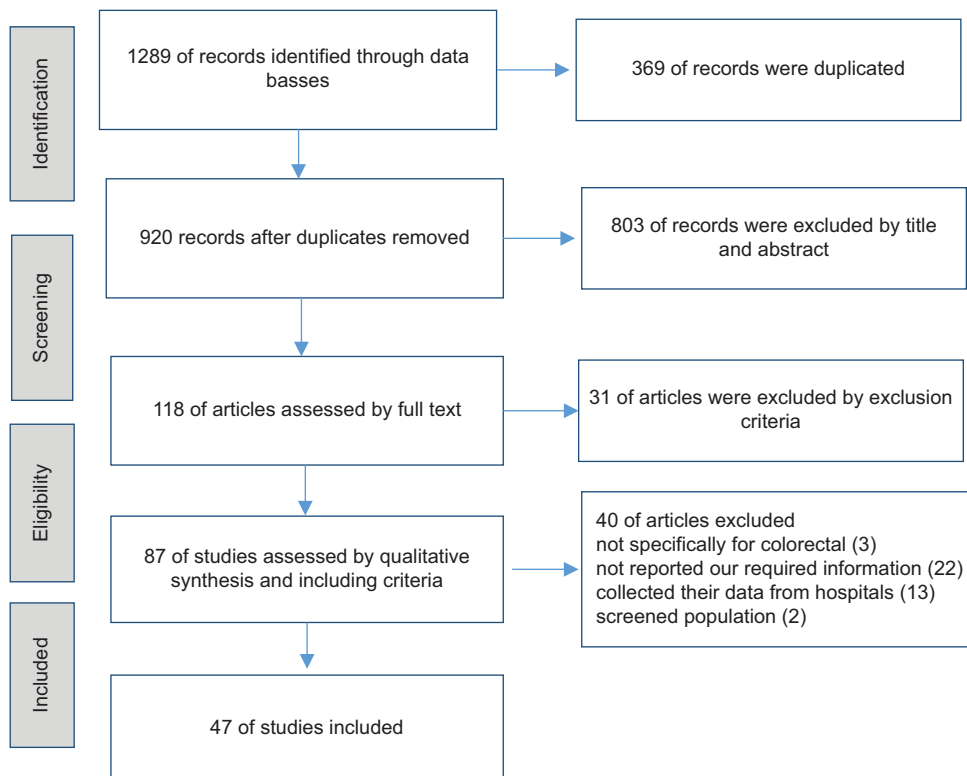
**RESULTS**

**Systematic review**

As shown in Figure 1, our search strategies yielded 1,289 results (9 from Cochrane, 691 from Ovid, 445 from Embase, 101 from SID, and 43 from ISC). After removing duplicates, 920 studies were identified. Title and abstract screening left 118 articles for full-text review. We excluded 71 articles for the following reasons: Not relevant (31), not specifically related to CRC (3), not reporting our required information (22), collecting data from hospitals (13), and reporting incidence in screened people (2). Ultimately, we included 47 articles, which are listed in Appendix 3.

Reviewed articles reported CRC incidence at national (15 articles), multi-provincial (2 articles), and provincial (29 articles) levels. The data collection periods ranged from 1991 to 2019, with study durations varying between 1 and 15 years.

At the national level, the data from the reviewed studies cover the years 2001-2017. Khanali and Kolahi (2021) reported the incidence of CRC in 2016;<sup>[11]</sup> however, this data,



**Figure 1:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart for systematic review of the incidence of colorectal cancer in Iran

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sourced from the VIZIT data visualization system, showed higher values than the published registry data and was thus excluded. Asgarian *et al.* reported the average incidence of CRC for 2004–2008.<sup>[12]</sup> Pourhoseingholi *et al.* found 21,543 CRC cases between 2005 and 2008 in Iran, with an incidence rate of 10.16 for males and 7.88 for females.<sup>[13]</sup> Roshandel *et al.* reported ASRs of 16.1 and 12.1 for males and females, respectively.<sup>[14]</sup> As shown in Table 1, the National Cancer Registration Program published reports for the years 2014 and 2017. The highest increase in incidence was observed in 2008, while in 2015, all indicators showed negative growth compared to the previous year.

All national-level data is depicted in Figure 2.

In multi-provincial studies, two were identified from the west and north of Iran. A study in the west, covering Hamedan, Ilam, Kurdistan, and Kermanshah provinces, reported a rise in new cancer cases from 65 in 2000 to 213 in 2005, with ASR increasing from 1.5 to 4.8 per 100,000 people. In the north, a study from Gilan, Mazandaran, and Golestan reported 3287 CRC cases from 2004 to 2009, with an ASR of about 10 per 100,000 people.

As shown in Table 2, the highest ASR for males and females was reported in Babol,<sup>[30]</sup> while the lowest was in Isfahan province in 2001 (0.42 and 0.56 per 100,000). In 2014 and 2015, based on national cancer registry reports, Semnan and Kurdistan had the highest and lowest ASRs for males and females, respectively.

Most reviewed studies considered periods of 1 year or 3–5 years, each accounting for 30% of all studies. More details can be found in Appendix 4.

### Results of meta-analysis

Twenty-two studies met the criteria for inclusion in the meta-analysis, but the study conducted in Babol<sup>[30]</sup> was excluded due to a significant discrepancy in the reported results. The pooled incidence of CRC from the remaining 21 studies was 8.46 (95% CI: 7.16–9.86) per 100,000 population. The incidence was moderately higher in men than in women. East Azerbaijan, Tehran, and Golestan had the highest incidences, while Kerman showed the lowest incidence of CRC in Iran [Table 3].

The meta-regression analysis was conducted to investigate the predictors of CRC incidence. The predictors examined include publication year, sex (female vs. male), and various provinces, with Isfahan serving as the reference category.

### Publication year

There is a significant positive association between publication year and CRC incidence (Beta = 0.04, 95% CI: 0.02–0.06,  $P < 0.001$ ). This suggests that the incidence of CRC has increased over the years.

### Sex (female vs. male)

The analysis did not find a significant difference in CRC incidence between females and males (Beta = 0.35, 95% CI: -1.45–2.15,  $P = 0.7$ ).

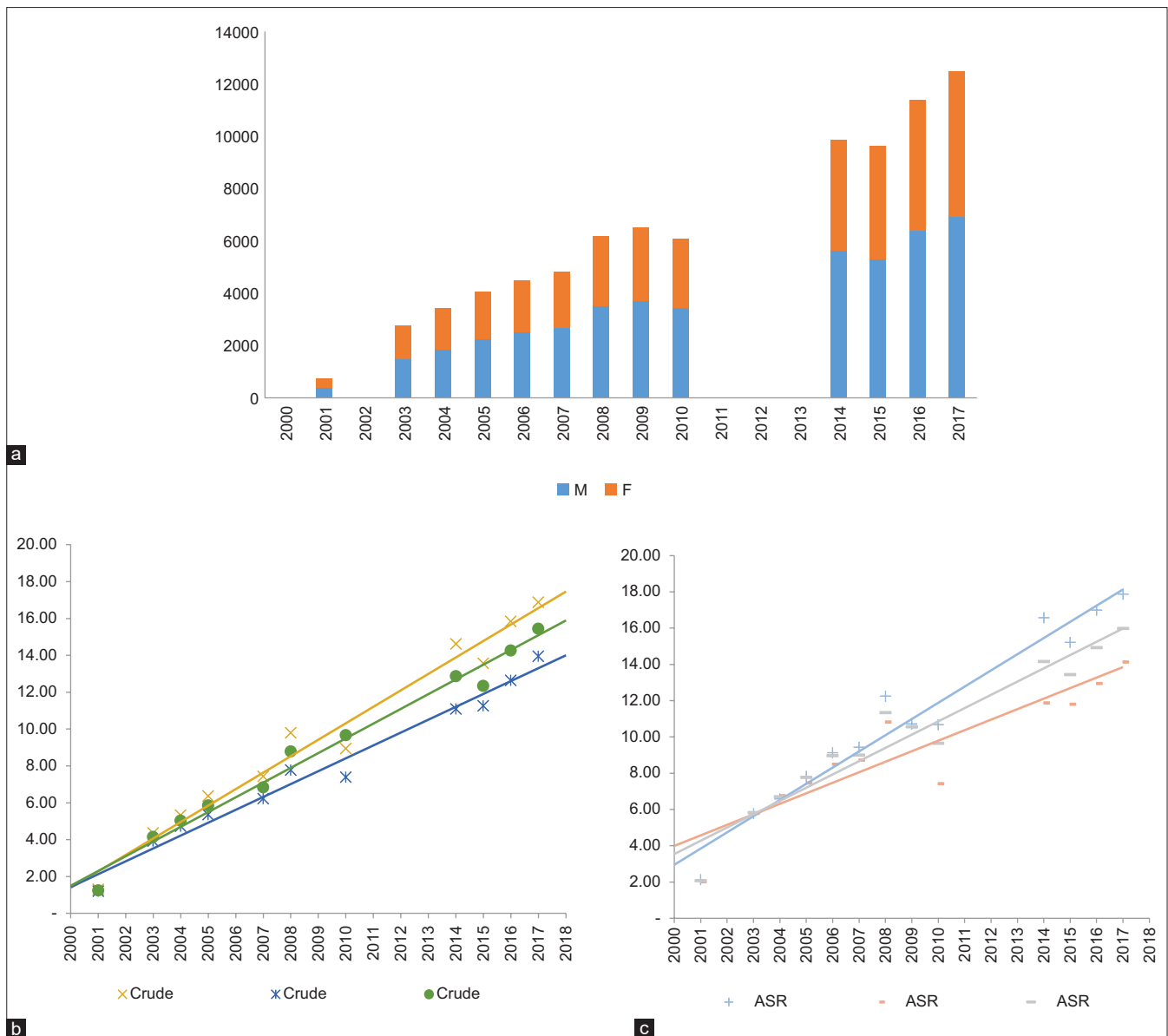
### Province

East Azerbaijan, Golestan, Hamadan and Markazi: Significantly higher incidence compared to Isfahan ( $P < 0.05$ ). Other provinces such as Kerman, Gilan, Kermanshah, Khuzestan, Kurdistan, Mazandaran, Qom, Tehran, and Yazd did not show a statistically significant difference compared to Isfahan.

**Table 1: Colorectal cancer incidence rate in Iran (at the national level)**

Year	n			Crude (100,000)			ASR (100,000)			Reference
	Male	Female	Total	Male	Female	Total	Male	Female	Total	
2001	379	344	723	1.3	1.2	1.25	2.12	2	2.06	[16]
2003	1490	1269	2759	4.37	3.92	4.145	5.50–6.22	5.40–6.74	5.45–6.48	[10,13,14,21]
2004	1849	1558	3407	5.33	4.73	5.03	6.38–6.75	6.64–6.94	6.67–6.7	[11,14,21]
2005	2255	1801	4056	6.37	5.36	5.865	7.23–8.19	7.40–7.56	7.68–7.9	[11,14,20,21]
2006	2526*	1967	4493	-	-	-	9.11	8.17–8.79	8.95	[14,21,56]
2007	2679	2127	4887	7.44	6.23	6.835	9.42	8.705	8.99	[14,21,56]
2008	3527	2658	6185 7774	9.8	7.78	8.79	12.242	10.815	11.336 12.7	[12-14,18-21,25]
2009	3727	2783	6210	-	-	-	10.11–11.3	9.87–10.9	9.99–11.1	[16,17,21]
2010	3443	2641	6084	8.8–9.1	7.1–7.7	8.25–11.1	9.99–11.28	5.62–8.69	8.45–11.1	[15,16,21]
2014	5644	4217	9861	14.62	11.09	12.87	16.57	11.86	14.15	
2015	5299	4337	9636	13.57	11.27	12.34	15.21	11.79	13.43	
2016	6413	4983	11,396 11,558	15.84	12.64	14.26	16.98	12.93	14.92 15.1	[25]
2017	6929	5563	12,492	16.89	13.96	15.45	17.87	14.12	15.97	

\*All blue color data extracted from the annual report of the Iranian National Population-based cancer registry.<sup>[58]</sup> ASR=Age-standardized rate



**Figure 2:** Trend of national colorectal cancer (CRC) burden in Iran between 2001 and 2017. (a) Number of colorectal cancer cases in Iran between 2001 and 2017. (b) Crude incidence rate (CIR) of CRC in Iran. (c) Age-standardized rate of CRC in Iran

The meta-regression did not suggest sex as a source of heterogeneity (p-value = 0.7). However, publication year (p-value<0.001) and province were significantly related to the heterogeneity in the overall colorectal cancer incidence [Table 4].

There was considerable heterogeneity among the studies ( $I^2 = 99.2\%$ ) both overall [Figure 3] and in subgroup analyses [Appendixes 5 and 6].

## DISCUSSION

This systematic review and meta-analysis aimed to report the CRC incidence rate and its trend in Iran, including provincial-level data where available. The pooled incidence rate was found to be 8.46 per 100,000 population. However,

there was considerable heterogeneity between different provinces. The pooled incidence rate relates to studies reporting provincial-level CRC incidence from 1991 to 2019. Based on the latest national cancer registry reports (2014–2017), the CRC incidence rate, with a mean ASR approaching 15 per 100,000, reflects a similar increasing trend reported by Dolatkah *et al.*<sup>[6]</sup> and Dehghani *et al.*<sup>[7]</sup> However, due to inconsistent cancer registration policies over time, this trend should be interpreted with caution.

The first annual national cancer registry report was published in 2006, followed by another in 2007. Subsequent reports from 2014 to 2017 have been issued with a lag of about 5 years. No CRC incidence data were available for the period between 2011 and 2013.

**Table 2: Incidence of colorectal cancer in Iran (at the provincial level)**

Province	Study	Duration	Number	Crude (100,000)	ASR (100,000)	Reference
West of Iran	Abdifard <i>et al.</i> , 2013	2000–2005	65 (2000) 213 (2005)		1.3, 1.5, 2.4, 3.3, 4.6, 5.8 (male) 1.8, 2.1, 1.5, 2.9, 4.6, 3.8 (female)	[26]
Kermanshah					0.6, 1.2, 3.7, 4.1, 4.5, 7.7 (male) 0.8, 2.2, 2.9, 2.8, 4.1, 4.7 (female)	
Kordestan					2.4, 1.9, 2.9, 3.7, 3.8, 5.6 (male) 2.9, 3.2, 1.0, 3.3, 5.5, 2.5 (female)	
Ilam					0.0, 0.5, 2.8, 1.2, 3.3, 2.9 (male) 0.0, 1.9, 1.5, 1.7, 0.9, 1.3 (female)	
Hamedan					1.4, 1.7, 0.7, 2.8, 5.5, 4.6 (male) 2.3, 1.3, 0.5, 2.8, 5.2, 4.6 (female)	
North of Iran	Salehiniya <i>et al.</i> , 2016	2004–2009	3287		10.60 (male) 10.09 (female)	[27]
Gilan			1529		13.50 (male) 13.14 (female)	
Mazandaran			1329		10.46 (male) 9.94 (female)	
Golestan			529		7.83 (male) 7.2 (female)	
Markazi (Arak)	Moradzadeh and Mirgaloybaya 2022	2009–2014	40, 32, 56, 54, 56, 50 (male) 29, 26, 40, 48, 54, 48 (female)	13, 10.4, 18.4, 17.9, 18.5, 16.6 (male) 9.7, 8.7, 13.5, 16.3, 18.4, 16.3 (female)	15.2, 12.2, 20.9, 17.9, 18.7, 18.4 (male) 11.3, 9.4, 14.1, 16.1, 17.9, 15.5 (female)	[28]
Markazi	Taheri <i>et al.</i> , 2021	2010–2014			10.4, 15.8, 17, 21.8, 15 (male) 8.2, 9.8, 16.5, 16.3, 15 (female)	[49]
East Azerbaijan	Somi MH <i>et al.</i> , 2009	2006–2007	125 (≥65 years)	2.23 (male, 15–44 years) 28.89 (male, 45–64 years) 65.13 (male, ≥65 years) 2.64 (female, 15–44 years) 24.47 (female, 45–64 years) 43.46 (female, ≥65 years)	63.02 (male, ≥65 years) 43.51 (female, ≥65 years)	[31]
	Somi MH <i>et al.</i> , 2014	2007–2011	201 (male) 165 (female)	11.5 (male) 9.22 (female)	11.2 (male) 8.93 (female)	[32]
	Somi MH <i>et al.</i> , 2018	2015–2016	366 (male) 299 (female)	18.7 (male) 15.4 (female)	18.2 (male) 13.7 (female)	[33]
Fars	Masoompour <i>et al.</i> , 2016	2007–2010		7.21 (male) 5.64 (female)	9.57 (male) 7.49 (female)	[34]
	Hassanzade <i>et al.</i> , 2011	2008–2009	157 (male) 118 (female)		11.43 (male) 9.12 (female)	[35]
Golestan	Roshandel <i>et al.</i> , 2012	2004–2008	345 (male) 266 (female)	8.34 (male) 6.54 (female)	12.4 (male) 9.5 (female)	[36]
	Hasanpour-Heidari <i>et al.</i> , 2019	2004–2013	52, 52, 78, 88, 75, 103, 92, 125, 110, 128 (male) 41, 43, 54, 72, 58, 87, 76, 93, 84, 104 (female)	6.47, 6.39, 9.43, 10.46, 8.79, 12.01, 10.6, 14.03, 12.15, 13.81 (male) 5.19, 5.37, 6.64, 8.7, 6.9, 10.3, 8.88, 10.61, 9.41, 11.33 (female)	9.2, 9.1, 15, 14.5, 12.2, 16.6, 14.8, 19.2, 14.8, 19.2 (male) 7.6, 8.3, 9, 12.6, 9, 14.2, 12.4, 13.4, 11.9, 14.1 (female)	[37]
	Ghasemi-Kebria	2004–2018	32,764	8.6 (2004) 16.0 (2018)	15.6 (M) 11.9 (F)	[39]
Hamadan	Zahedi <i>et al.</i> , 2015	2004–2009	215 (female)		6.02 (female)	[38]
	Halimi <i>et al.</i> , 2020	2007–2014	805	45.89		[39]

Contd...

**Table 2: Contd...**

Province	Study	Duration	Number	Crude (100,000)	ASR (100,000)	Reference
Isfahan	Rejali <i>et al.</i> , 2018	2000–2011	75, 9, 33, 27, 44, 143, 190, 204, 236, 238, 217, 238 (male) 69, 11, 27, 18, 22, 112, 117, 165, 176, 178, 169, 184 (female)		3.51, 0.42, 1.52, 1.3, 2.16, 6.91, 8.96, 9.78, 10.97, 11.43, 10.42, 11.56 (male) 3.17, 0.56, 1.27, 0.85, 1.04, 5.42, 5.54, 7.58, 8.36, 8.39, 7.97, 8.92 (female)	[40]
Kerman	Shahesmaeili <i>et al.</i> , 2018	2014		6.34 (male) 5.14 (female)	10.0 (male) 7.7 (female)	[41]
	Haghdoost <i>et al.</i> , 2011	1991–2002	275 (male) 277 (female)	2.1 (male) 2.2 (female)	5.0 (male) 5.3 (female)	[42]
	Keyghobadi <i>et al.</i> , 2015	2004–2009	299 (male) 291 (female)		5.43, 4.34, 5.47, 5.11, 4.83, 8.58 (female)	[43]
Kermanshah	Najafi <i>et al.</i> , 2011	1993–2007	394 (male) 271 (female)		3.5, 5.2, 3.1, 4.5, 4.6, 2, 4.4, 5.8, 2.8, 3.6, 6.1, 4.9, 6, 5.6, 5.7	[44]
Khuzestan	Talaiezhadeh <i>et al.</i> , 2013	2002–2009	627 (male) 475 (female)	4.32 (male) 3.45 (female)	6.32 (male) 5.72 (female)	[45]
	Amoori <i>et al.</i> , 2014	2004–2008		8.8 (male) 7 (female)	11.6 (male) 10 (female)	[46]
	Rostami <i>et al.</i> , 2023	2011–2019	1821	40.18		[47]
Kurdistan	Hosseini <i>et al.</i> , 2019	2010–2015	154, 192, 122 (male) 114, 100, 96 (female)	9.85, 12.28, 7.8 (male) 7.44, 6.52, 6.26 (female)	11.58, 14.58, 9.18 (male) 8.68, 7.58, 7.3 (female)	[48]
Mazandaran	Hedayatzadeh-Omran <i>et al.</i> , 2020	2015	201 (male) 157 (female)		10.86 (male) 8.47 (female)	[50]
Mazandaran (Babol)	Nikbakht <i>et al.</i> , 2015	2007–2012	134 (male) 103 (female)		7.7 in 2007 14.6 in 2012	[29]
	Amiri <i>et al.</i> , 2022	2008–2017	117, 38, 118, 43, 63, 50, 40, 56, 47, 96 (male) 96, 37, 95, 36, 42, 39, 28, 39, 41, 93 (female)		334.70, 99.64, 312.19, 141.17, 162.41, 156.43, 120.28, 146.03, 140.30, 302.41 (all)	[30]
Qom	Rafieemanesh <i>et al.</i> , 2016	2004–2008	28, 29, 34, 46, 42 (male) 15, 15, 13, 26, 32 (female)		7.62, 6.97, 8.4, 10.79, 10.12 (male) 5.75, 4.35, 3.71, 7.34, 8.86 (female)	[51]
Semnan (Shahroud)	Fateh and Emamian, 2013	2001–2010		7.24 (male) 6.98 (female)	8.39 (male) 8.15 (female)	[52]
Tehran	Rasaf <i>et al.</i> , 2012	2007	420 (male) 342 (female)	10.535 (male) 8.958 (female)	8.603 (male) 7.164 (female)	[53]
	Looha <i>et al.</i> , 2020	2006–2015			5.9, 9.28, 20.94, 17.52, 17.79, 15.02, 17.09, 26.37, 25.9, 19.14 (male) 5.17, 7.93, 15.12, 14.14, 12.6, 10.74, 14.02, 18.6, 17.59, 15.02 (female)	[54]
Yazd	Vakili <i>et al.</i> , 2014	2004–2009	367		6.1, 6.9, 7.9, 9.6, 9.9 (male) 5.2, 5.1, 7.5, 10.4, 6 (female)	[55]

ASR=Age-standardized rate

Meta-analysis revealed considerable heterogeneity in incidence rates across different studies and geographic areas. Lower CRC incidence rates have been reported in southern Iran compared to the north and central regions,<sup>[6,33,42]</sup> likely due to differences in genetics, diet, environmental exposures, socioeconomic status, and CRC screening rates.<sup>[58-60]</sup>

In pooled data, the incidence of CRC was moderately higher in men. A study found higher CRC incidence in females

from 2003 to 2006, but males had higher incidence rates until 2010, with similar rising trends in both genders.<sup>[7]</sup> National data indicated a 30% higher ASR in males and nearly 25% higher CRC incidence in males compared to females.<sup>[59]</sup>

While the overall CRC incidence in Iran is lower than the global average due to lifestyle factors and a younger population, some provinces have incidence rates close

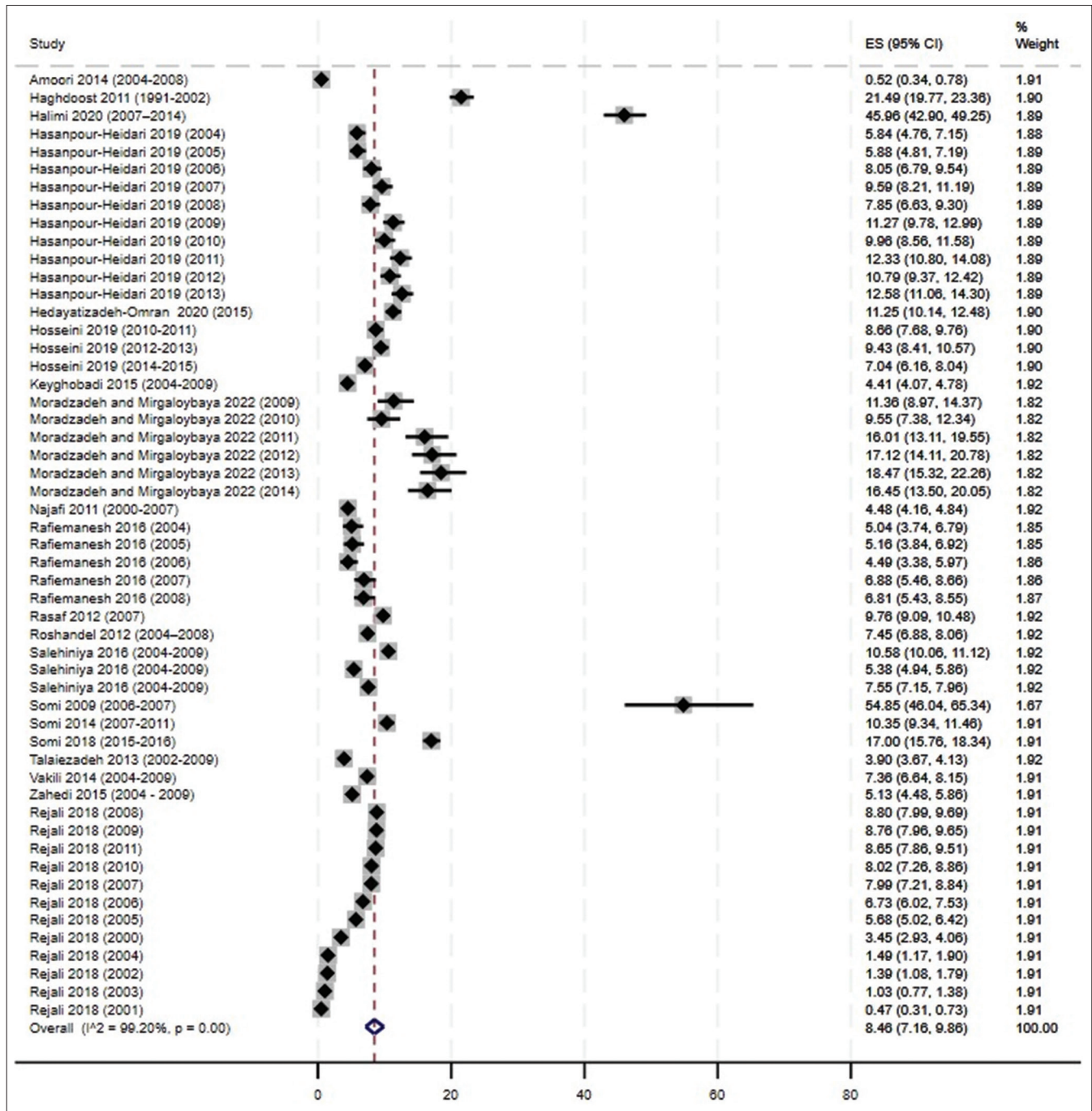


Figure 3: Forest plot for Meta-analysis of incidence of colorectal cancer in Iran (per 100,000 population)

to the global average. Iran is among the countries with a high incidence in the Eastern Mediterranean Region.<sup>[61]</sup> The increasing CRC incidence in Asia is attributed to overpopulation, aging populations, and a westernized dietary lifestyle.<sup>[62]</sup>

Inconsistent registration policies over time and incomplete implementation across the country may have resulted in statistics that do not accurately reflect the real incidence of the disease. Although articles were searched up to 2023,

the latest statistics are from 2017, and recent cancer registry data are lacking. This gap in data challenges timely policy decisions.

The findings indicate a considerable increase in CRC incidence in Iran over the 15-year study period, although it remains lower than in developed countries. The inconsistency in cancer registration policies and non-registration in some years complicates the assessment of a reliable trend in CRC incidence in Iran. The existing lag in publishing CRC



**Table 3: Pooled incidence rates and 95% confidence intervals of colorectal cancer in Iran in different subgroups**

Groups	Number of records	Incidence per 100,000 (95% CI)	I <sup>2</sup> (%)	P-value of Q-test
Total		8.46 (7.16–9.86)	99.2	<0.01
Men		9.28 (7.87–10.81)	98.04	<0.01
Women		7.64 (5.96–9.51)	99.8	<0.01
Provinces				
Hamadan	2	12.91 (12.02–13.85)	NA	NA
Kermanshah	1	4.48 (4.16–4.84)	NA	NA
Kurdistan	3	8.34 (7.0–9.8)	NA	NA
Khuzestan	2	3.27 (3.08–3.47)	NA	NA
Kerman	2	6.29 (5.9–6.68)	NA	NA
Golestan	12	8.72 (7.27–10.31)	95.42	<0.01
Mazandaran	2	8.06 (7.68–8.45)	NA	NA
Tehran	1	9.76 (9.09–10.48)	NA	NA
Markazi	6	14.63 (11.83–17.73)	81.95	<0.01
Qom	5	5.66 (4.72–6.68)	53.08	0.07
Isfahan	12	4.51 (2.66–6.84)	99.27	<0.01
Gilan	1	10.58 (10.06–11.12)	NA	NA
East Azerbaijan	3	23.44 (13.1–36.76)	NA	NA
Yazd	1	7.36 (6.64–8.15)	NA	NA

\*Proportion of total variance due to between study variance. NA=Not available; CI=Confidence interval

**Table 4: Meta-regression analysis of the predictors of colorectal cancer incidence\***

	Beta	95% CI	P
Publication year	0.04	0.02–0.06	<0.001
Sex (female vs. male)	0.35	-1.45–2.15	0.7
Province			
Isfahan	Reference		
East Azerbaijan	1.76	0.82–2.71	<0.01
Gilan	1.06	-0.46–2.59	0.17
Golestan	0.85	0.26–1.45	0.01
Hamadan	1.44	0.32–2.55	0.01
Kerman	0.98	-0.14–2.10	0.08
Kermanshah	0.20	-1.32–1.73	0.79
Khuzestan	-0.95	-2.06–0.17	0.09
Kurdistan	0.82	-0.12–1.77	0.09
Mazandaran	0.92	-0.19–2.04	0.10
Qom	0.43	-0.35–1.20	0.28
Tehran	0.98	-0.54–2.50	0.20
Yazd	0.70	-0.82–2.22	0.36
Markazi	1.37	0.64–2.10	<0.001

\*Logarithmic transformation of CRC incidence. CI=Confidence interval; CRC=Colorectal cancer

statistics hinders timely policy decisions to combat disease prevalence.

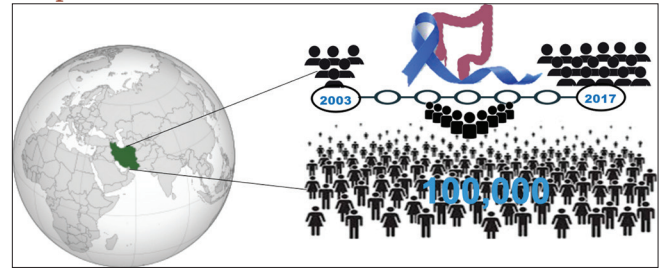
**Acknowledgments**

Research ethical approval was given by the research ethics committee of Isfahan University of Medical Sciences, Isfahan, Iran (IR.MUI.RESEARCH.REC.1398.257). This study has used secondary data from published articles so it was not possible to identify the patients from the data, directly or indirectly.

**Financial support and sponsorship**

Nil.

**Graphical abstract**



**Conflicts of interest**

There are no conflicts of interest.

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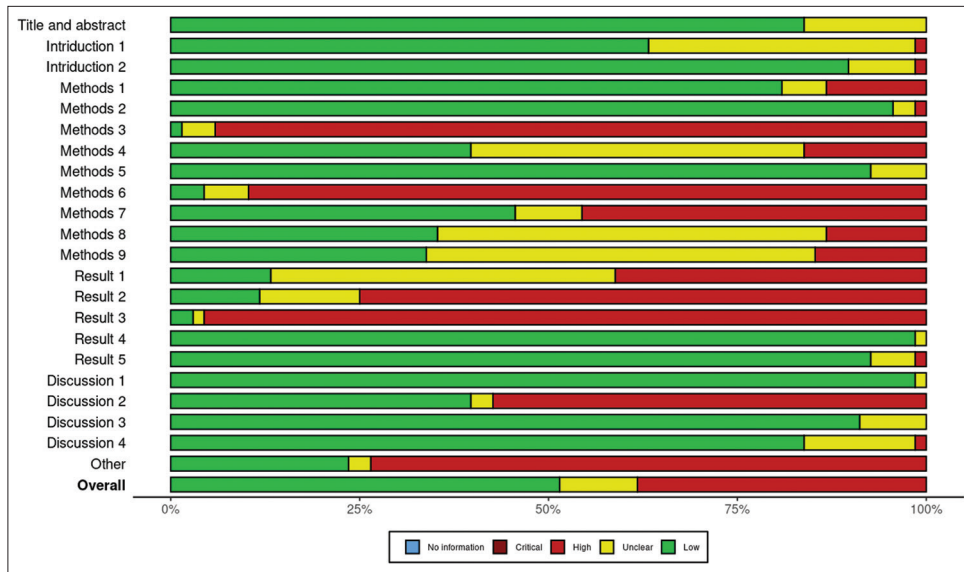
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**Appendix 1: Search strategies for systematic review of incidence of colorectal cancer in iran**

Databases	Search queries
Cochrane	1) epidemi* OR incidence* OR prevalence* 2) colorectal 3) Cancer OR neoplasm*OR tumor* OR carcinoma* 4) Iran 5) #1 AND #2 AND #3 AND #4
Medline by Ovid	1) Incidence*.mp. [mp=tx, bt, ti, ot, ab, ct, sh, kw, nm, hw, fx, kf, ox, px, rx, an, ui, ds, on, sy] 2) Prevalence*.mp. [mp=tx, bt, ti, ot, ab, ct, sh, kw, nm, hw, fx, kf, ox, px, rx, an, ui, ds, on, sy] 3) Epidemi*.mp. [mp=tx, bt, ti, ot, ab, ct, sh, kw, nm, hw, fx, kf, ox, px, rx, an, ui, ds, on, sy] 4) Colorectal.mp. [mp=ti, ot, ab, tx, ct, sh, kw, nm, hw, fx, kf, ox, px, rx, an, ui, sy] 5) cancer OR neoplasm*OR tumor* OR carcinoma*).mp. [mp=ti, ot, ab, tx, ct, sh, kw, nm, hw, fx, kf, ox, px, rx, an, ui, sy] 6) epidemi* OR incidence* OR prevalence*).mp. [mp=ti, ot, ab, tx, ct, sh, kw, nm, hw, fx, kf, ox, px, rx, an, ui, sy] 7) Iran.mp. [mp=tx, bt, ti, ot, ab, ct, sh, kw, nm, hw, fx, kf, ox, px, rx, an, ui, ds, on, sy] 8) 1 OR 2 OR 3 OR 6 9) 4 and 5 10) 8 and 9 and 7
Embase	1) epidemi* OR incidence* OR prevalence* 2) colorectal 3) cancer* OR neoplasm*or tumor* OR carcinoma* 4) iran

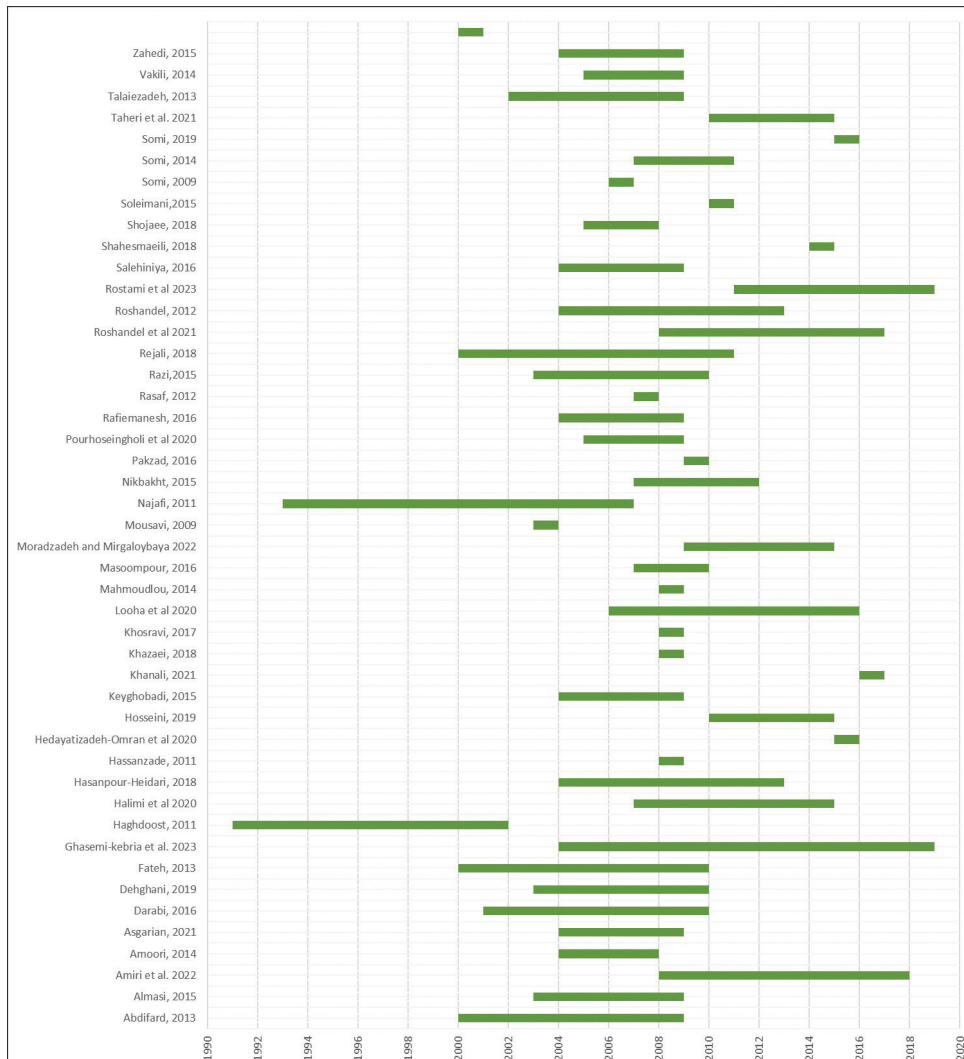


**Appendix 2: Quality check of reviewed articles by STORB Checklist**

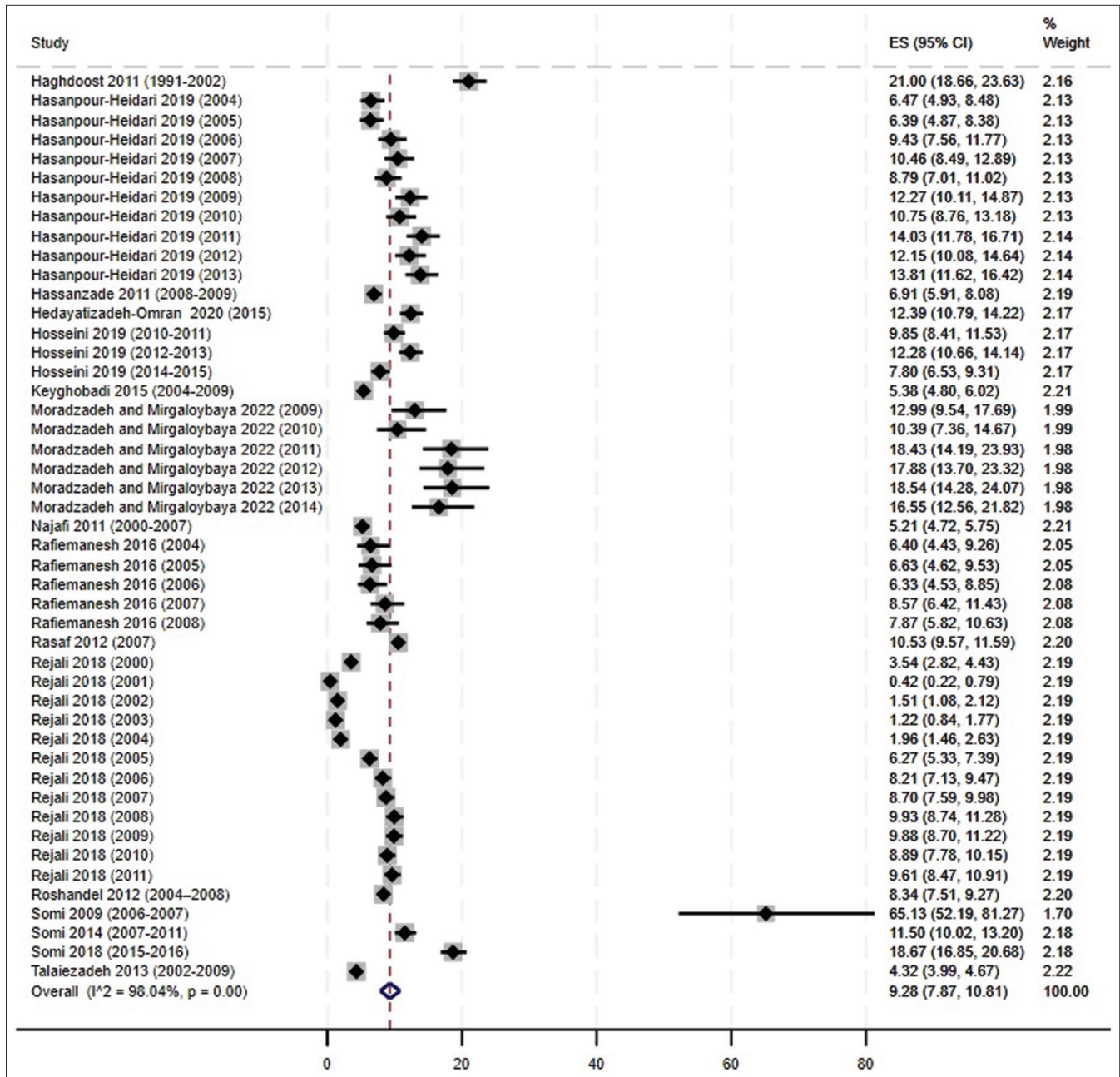
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**Appendix 3: Information of included studies in systematic review**

Author	Place	Duration	Reference
<b>National studies</b>			
Mousavi <i>et al.</i> , 2009	Iran	2003–2006	[12]
Mahmoudlou <i>et al.</i> , 2014	Iran	2008	[13]
Almasi <i>et al.</i> , 2015	Iran	2003–2009	[14]
Razi S <i>et al.</i> , 2015	Iran	2003–2009	[15]
Soleimani <i>et al.</i> , 2015	Iran	2010	[16]
Darabi <i>et al.</i> , 2016	Iran	2001–2010	[17]
Pakzad <i>et al.</i> , 2016	Iran	2009	[18]
Khosravi Shadmani <i>et al.</i> , 2017	Iran	2008	[19]
Khazaei <i>et al.</i> , 2018	Iran	2008	[20]
Shojaee <i>et al.</i> , 2018	Iran	2005–2008	[21]
Dehghani <i>et al.</i> , 2019	Iran	2003–2010	[22]
Khanali <i>et al.</i> , 2021	Iran	2000 and 2016	[23]
Asgarian <i>et al.</i> , 2021	Iran	2004–2008	[24]
Pourhoseingholi <i>et al.</i> , 2020	Iran	2005–2008	[25]
Roshandel <i>et al.</i> , 2021	Iran	2008–2025	[26]
<b>Multi-provincial studies</b>			
Abdifard <i>et al.</i> , 2013	West of Iran	2000–2005	[27]
Salehiniya <i>et al.</i> , 2016	North of Iran	2004–2009	[28]
<b>Provincial studies</b>			
Moradzadeh and Mirgaloybaya 2022	Arak	2009–2014	[29]
Nikbakht <i>et al.</i> , 2015	Babol	2007–2012	[30]
Amiri <i>et al.</i> , 2022	Babol	2008–2017	[31]
Somi MH <i>et al.</i> , 2009	East Azerbaijan	2006–2007	[32]
Somi MH <i>et al.</i> , 2014	East Azerbaijan	2007–2011	[33]
Somi MH <i>et al.</i> , 2018	East Azerbaijan	2015–2016	[34]
Masoompour <i>et al.</i> , 2016	Fars	2007–2010	[35]
Hassanzade <i>et al.</i> , 2011	Fars	2008–2009	[36]
Roshandel <i>et al.</i> , 2012	Golestan	2004–2008	[37]
Hasanpour-Heidari <i>et al.</i> , 2019	Golestan	2004–2013	[38]
Ghasemi-kebria <i>et al.</i> , 2023	Golestan	2004–2018	[39]
Zahedi <i>et al.</i> , 2015	Hamadan	2004–2009	[39]
Halimi <i>et al.</i> , 2022	Hamadan	2007–2014	[40]
Rejali <i>et al.</i> , 2018	Isfahan	2000–2011	[41]
Shahesmaeili <i>et al.</i> 2018	Kerman	2014	[42]
Haghdoost <i>et al.</i> 2011	Kerman	1991–2002	[43]
Keyghobadi <i>et al.</i> 2015	Kerman	2004–2009	[44]
Najafi <i>et al.</i> , 2011	Kermanshah	1993–2007	[45]
Talaiezhadeh <i>et al.</i> , 2013	Khuzestan	2002–2009	[46]
Amoori <i>et al.</i> , 2014	Khuzestan	2004–2008	[47]
Rostami <i>et al.</i> , 2023	Khuzestan	2011–2019	[48]
Hosseini <i>et al.</i> , 2019	Kurdistan	2010–2015	[49]
Taheri <i>et al.</i> , 2021	Markazi (Arak)	2010–2014	[50]
Hedayatizadeh-Omran <i>et al.</i> , 2020	Mazandaran	2014, 2015	[51]
Rafiemanesh <i>et al.</i> , 2016	Qom	2004–2008	[52]
Fateh and Emamian, 2013	Semnan	2001–2010	[53]
Rasaf <i>et al.</i> , 2012	Tehran	2007	[54]
Looha <i>et al.</i> , 2021	Tehran	2006–2015	[55]
Vakili <i>et al.</i> , 2014	Yazd	2004–2009	[56]

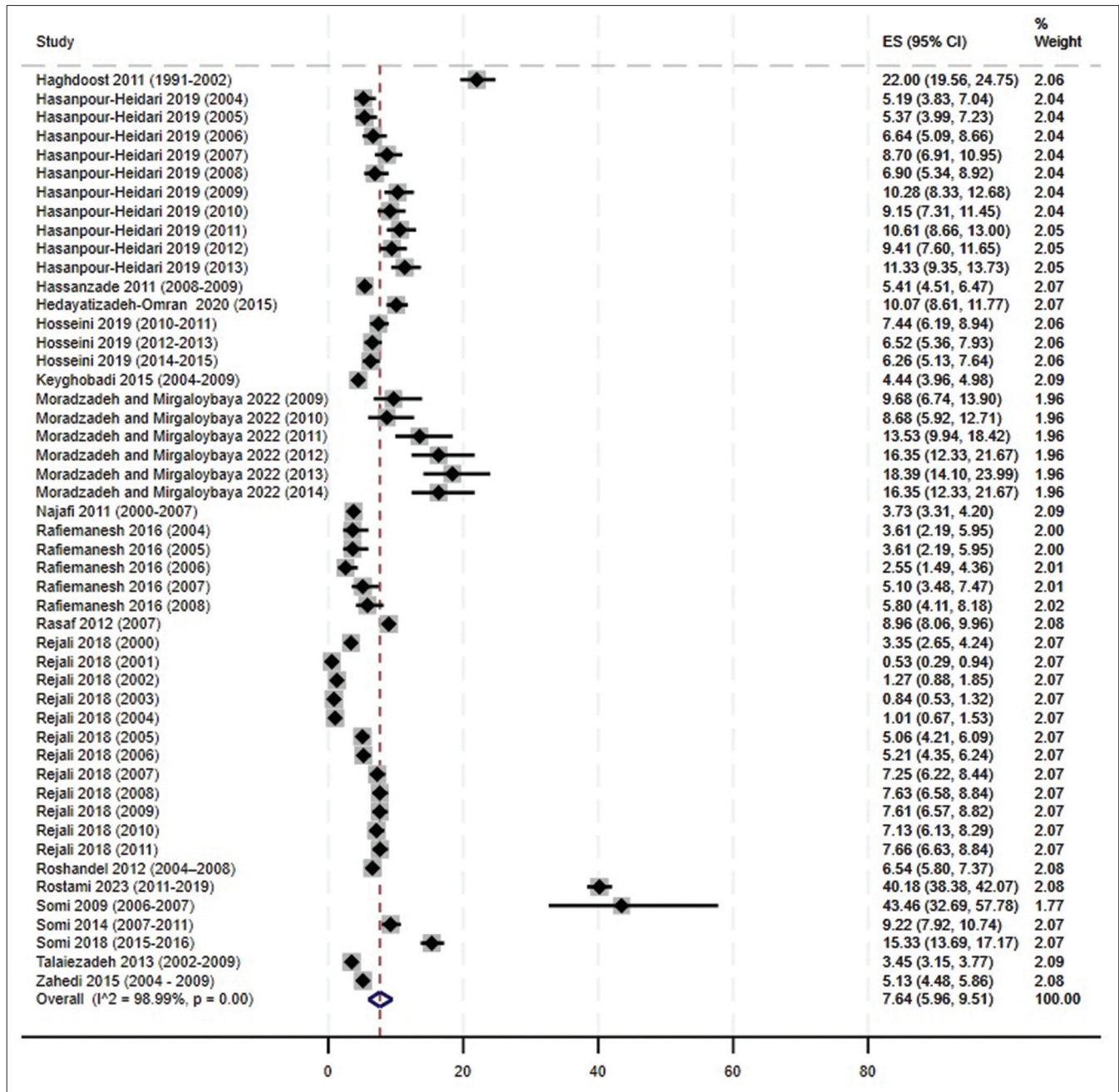


Appendix 4: The study duration of included articles in systematic review of incidence of colorectal cancer in Iran



Appendix 5: Forest plot for meta-analysis of incidence of colorectal cancer in men in Iran (per 100,000 population)

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Appendix 6: Forest plot for meta-analysis of incidence of colorectal cancer in women in Iran (per 100,000 population)

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