

## Observational Study

## Prevalence of colorectal neoplasms in young, average risk individuals: A turning tide between East and West

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### Abstract

#### AIM

To determine the prevalence of colorectal neoplasia in average risk persons 40-59 years of age in Israel and to compare the results with other populations.

#### METHODS

We reviewed the results of asymptomatic average-risk subjects, aged 40 to 59 years, undergoing their first screening colonoscopy between April 1994 and January 2014. The detection rates of adenoma, advanced adenoma (AA) and colorectal cancer (CRC) were determined in the 40's and 50's age groups by gender. The prevalence of lesions was compared between age groups. After meticulous review of the literature, these

results were compared to published studies addressing the prevalence of colorectal neoplasia in similar patient groups, in a variety of geographical locations.

### RESULTS

We included first screening colonoscopy results of 1750 individuals. The prevalence of adenomas, AA and CRC was 8.3%, 1.0% and 0.2% in the 40-49 age group and 13.7%, 2.4% and 0.2% in the 50-59 age group, respectively. Age-dependent differences in adenoma and AA rates were significant only among men ( $P < 0.005$ ). Literature review disclosed 17 relevant studies. As expected, in both Asian and Western populations, the risks for overall adenoma and advanced adenoma was significantly higher in the 50's age group as compared to the 40's age group in a similar fashion. The result of the current study were similar to previous studies on Western populations. A substantially higher rate of adenoma, was observed in studies conducted among Asian populations in both age groups.

### CONCLUSION

The higher rate of colorectal neoplasia in Asian populations requires further investigation and reconsideration as to the starting age of screening in that population.

**Key words:** Colonoscopy; Adenoma; Colorectal cancer; Average risk; Young; Asian; Western

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**Core tip:** This research focuses on evaluating detection rates of colorectal neoplasia among average risk individuals aged 40-59 years and comparing the detection rates between the fifth and sixth decades. In this prospective study of first screening colonoscopy from 1750 consecutive average risk subjects aged 40-59, we found that the prevalence of colorectal neoplasia is age and gender dependent. In addition we did an extensive search of the literature that revealed a markedly higher adenoma detection rate among Asians, and in particular Koreans compares to Western populations.

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## INTRODUCTION

Colorectal cancer (CRC) is the third leading cause of cancer mortality in the Western world<sup>[1,2]</sup>, with an estimated lifetime risk of 5%-6%. Approximately 70%

of patients who develop CRC are considered "average risk"<sup>[3]</sup>. The incidence and mortality rates of CRC increase after 50 years of age, the time that screening should be initiated. Only a small number of studies focusing on the prevalence of adenomas among persons younger than 50 years have been published and revealed variable results.

The aim of this study was to determine the prevalence of colorectal neoplasia in average risk persons in the fifth and sixth decades and to compare it to other populations from various geographical areas.

## MATERIALS AND METHODS

### Study design

Between April 1994 and June 2014, we have been prospectively collecting and documenting the results of screening colonoscopies carried out by several senior gastroenterologists from the Division of Gastroenterology at the Tel-Aviv Medical Center (TASMC). In addition to endoscopic reports, all participants were interviewed by the physician regarding symptoms, details of recent laboratory tests, and any personal or family history. The collected data were entered into a computerized database. Consecutive first screening colonoscopy of asymptomatic average-risk (*i.e.*, no personal or family history of colorectal CRC or CRC related syndrome) subjects aged 40-59 years old at the time of colonoscopy were included.

Individuals were excluded if they reported a personal history of colorectal adenoma or carcinoma at any time; if they had a family history of colorectal adenoma or carcinoma (one first-degree relative aged < 70, or two or more family relatives at any age); if they reported symptoms suggestive of neoplasia (rectal bleeding, change in bowel habit, abdominal pain, or unexplained weight loss during the previous 6 mo); or if they had a positive fecal occult blood test (FOBT), or laboratory abnormalities, such as iron-deficiency anemia. Other exclusion criteria were inflammatory bowel disease (IBD) or severe co-morbidity (*e.g.*, malignancy, significant cardio-pulmonary, renal or hepatic diseases). Mild complaints (such as chronic constipation without a recent change in bowel habit, or minor anal or abdominal discomfort, such as flatulence or bloating) were not regarded as neoplasia-related symptoms and were not considered to be exclusion criteria. Written informed consent was obtained from all participants. The study was approved by the TASMC Helsinki Committee. Colonoscopy was performed according to the usual protocol in our institute, as previously described<sup>[4]</sup>.

### Literature review

English language medical literature searches for human studies were performed through June 2015 using "screening", "colonoscopy", and "average risk" as keywords. Articles describing the prevalence of

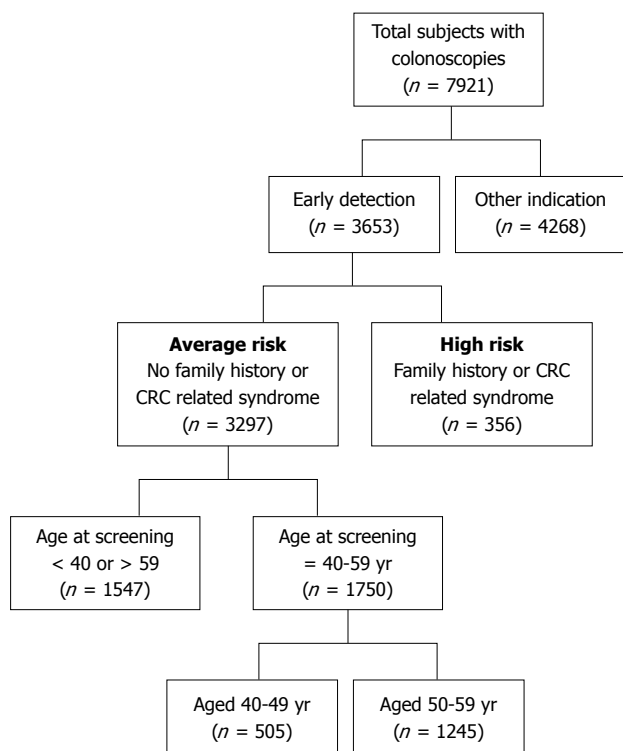


Figure 1 Flow chart for selection of study population.

colorectal neoplasia during screening colonoscopy among asymptomatic persons in their fifth and sixth decades were used to compare the current report.

### Statistical analysis

Statistical analyses were performed using IBM SPSS 21.0 software. The statistical significance level was set to 0.05. The prevalence of lesions was presented as proportions with 95%CI. Age was considered as a categorical variable, divided into two groups (40-49, 50-59 years). Pearson's  $\chi^2$  tests and student's *t*-test were used for comparison of lesion prevalence according to sex and age group.

## RESULTS

Data were collected from a total of 7921 subjects who underwent colonoscopy of which 3653 were primary screening procedures. After exclusion of subjects aged above 59 or below 40 years at the time of the procedure, there were 1750 eligible subjects for final analysis (Figure 1).

The mean age of the subjects was  $51.9 \pm 5.1$  years and men comprised 52.3% of the study population. There were 505 subjects aged 40-49 (mean age  $45.3 \pm 2.8$  years) of whom 278 (55.0%) were men. In the 50-59 age group (mean age  $51.9 \pm 5.09$ ), there were 1245 screenees, of whom 916 (51.2%) were men. Demographic features are shown in Table 1.

All lesions were sampled and sent for pathological examination. If more than one lesion was detected, the colonoscopic findings were classified according to the

Table 1 Group size, mean age and male percentage according to age study group

Age study group	40-49 yr	50-59 yr	Total
Number of subjects	505	1245	1750
Mean age (yr) at colonoscopy (SD)	45.30 (2.81)	54.64 (2.83)	51.94 (5.09)
Male percentage (%)	55	51.2	52.3

most advanced lesion, *e.g.*, adenocarcinoma, adenoma, hyperplastic or inflammatory polyp. Advanced neoplasia was defined as any adenoma measuring more than 10 mm, or with villous or tubulovillous histology, adenoma with high-grade dysplasia, or cancer<sup>[5,6]</sup>. Of the 1750 study subjects, 212 (12.1%) were found to have one or more colorectal neoplasia (non-advanced adenoma 10.4%; advanced 2.0%; invasive cancer 0.2%). The prevalence of colorectal neoplasia in the two age brackets according to gender is illustrated in Table 2. Among the 40-49 year age group, 43 (8.5%) individuals had adenomas (7.5% non-advanced, 1% advanced). Among the 50-59 year age group, 174 (13.7%) individuals had adenomas (11.6% non-advanced, 2.4% advanced,  $P = 0.01$  and  $0.06$  respectively). A total of four (0.2%) cases of adenomas with high-grade dysplasia were detected all of which were in the 50's age group. Four (0.2%) CRC cases were detected (three in the 40's and one in the 50's year groups). The increased prevalence of neoplastic findings among the 50's age group was significant only among men for both adenomatous polyps and advanced adenoma ( $P = 0.001$  and  $0.005$ , respectively). No differences were observed for women ( $P = 0.435$  and  $0.744$ , respectively). The difference in CRC prevalence rate between the age and gender groups didn't reach statistical significance most probably due to the small sample size.

Literature review disclosed 17 relevant studies (Table 3). The adenoma detection rate (ADR) and advanced lesion in each study is depicted in Figures 2 and 3, respectively. As expected, in both Asian and Western populations, the risks for overall adenoma and advanced adenoma was significantly higher in the 50's age group as compared to the 40's age group in a similar fashion (Table 4).

The most prominent observation is the markedly higher ADR among Asians, and in particular Koreans for both age groups (OR = 2.56, 95%CI: 2.04-2.51; and OR = 2.64, 95%CI: 2.09-2.23, in the 40's and 50's age groups, respectively,  $P < 0.0001$ ). This difference between Western and Asian studies is significantly diminished in both age groups with regard to advanced adenoma and CRC rates. The prevalence of advanced lesions had a narrower range between studies (range between 1.1% to 3.7% in the 40's group and between 1.5% to 7.5% in the 50's age group), and in contrast to ADR, the detection rate of advanced lesions was significantly lower in the Asian

**Table 2** Comparison of detection rates of neoplastic findings on primary screening between subjects aged 40-49 and subjects aged 50-59 years, according to gender *n* (%)

Gender finding type	40-49 yr	50-59 yr	Total	<i>P</i> value <sup>1</sup>	OR (95%CI)
All					
Total colonoscopies	505	1245	1750		
Adenomatous polyps	42 (8.3)	170 (13.7)	212 (12.1)	0.002	1.74 (1.22-2.49)
Advanced adenoma	5 (1.0)	30 (2.4)	35 (2.0)	0.060	2.47 (0.95-6.40)
Cancer	1 (0.2)	3 (0.2)	4 (0.2)	1.000	1.22 (0.13-11.73)
Men					
Total colonoscopies	278	638	916		
Adenomatous polyps	23 (8.3)	106 (16.6)	129 (14.1)	0.001	2.21 (1.37-3.55)
Advanced adenoma	1 (0.4)	22 (3.4)	23 (2.5)	0.005	9.89 (1.33-73.76)
Cancer	1 (0.4)	2 (0.3)	3 (0.3)	1.000	0.87 (0.08-9.65)
Women					
Total colonoscopies	227	607	834		
Adenomatous polyps	19 (8.4)	64 (10.5)	83 (10.0)	0.435	1.29 (0.76-2.21)
Advanced adenoma	4 (1.8)	8 (1.3)	12 (1.4)	0.744	0.75 (0.22-2.50)
Cancer	0 (0.0)	1 (0.2)	1 (0.1)	1.000	1

<sup>1</sup> $\chi^2$  statistical comparison of distribution of selected findings.

**Table 3** Studies reporting detection rates of adenoma and advanced lesion among average risk individuals aged 40-49 and 50-59 years

Ref.	Country of origin	Year published	Number of subjects in age group	
			40-49 yr	50-59 yr
Western origin				
de Jong <i>et al</i> <sup>[17]</sup>	the Netherlands	2005	90	36
Regula <i>et al</i> <sup>[8]</sup>	Poland	2006	2392	37313
Boursi <i>et al</i> <sup>[18]</sup>	Israel	2009	262	672
Current study	Israel	-	505	1245
Strul <i>et al</i> <sup>[4]</sup>	Israel	2006	183	409
Imperiale <i>et al</i> <sup>[6]</sup>	United States	2002	906	1533
Thoma <i>et al</i> <sup>[19]</sup>	United States	2010	247	747
Rundle <i>et al</i> <sup>[20]</sup>	United States	2008	553	352
Studies of Western origin (8)			5138	40774
Asian origin				
Hemmasi <i>et al</i> <sup>[21]</sup>	Iran	2014	333	407
Chiu <i>et al</i> <sup>[22]</sup>	Taiwan (China)	2005	654	592
Chiu <i>et al</i> <sup>[23]</sup>	Taiwan (China)	2008	4161	4211
Liu <i>et al</i> <sup>[24]</sup>	Taiwan (China)	2005	2656	1903
Choe <i>et al</i> <sup>[25]</sup>	South Korea	2006	1875	1587
Hong <i>et al</i> <sup>[26]</sup>	South Korea	2010	1049	712
Kim <i>et al</i> <sup>[27]</sup>	South Korea	2013	4550	4436
Chung <i>et al</i> <sup>[28]</sup>	South Korea	2009	1930	2716
Park <i>et al</i> <sup>[29]</sup>	South Korea	2009	1057	1207
Ko <i>et al</i> <sup>[30]</sup>	South Korea	2012	1200	1038
Studies of Asian origin (9)			19465	18807
All studies (17)			24603	59581

population (OR = 0.79, 95%CI: 0.72-0.86, *P* < 0.0001; and OR = 0.78, 95%CI: 0.63-0.97, *P* = 0.027). The rate of CRC ranged from 0% to 0.7% in the 40's age group and 0.1% to 0.9% in the 50's age group. The differences between Asian and Western populations in CRC rate were not statistically significant.

**Table 4** Odds ratio for colorectal neoplasia detection among individuals aged 50-59 years compared to those aged 40-49 according to country of origin

Finding	OR (95%CI)	<i>P</i> value <sup>1</sup>
Studies of Western origin		
Overall adenomas	1.7 (1.53-1.88)	< 0.0001
Advanced adenoma	2.34 (1.95-2.81)	< 0.0001
Cancer	2.33 (1.45-3.75)	< 0.0001
Studies of Asian origin		
Overall adenomas	1.99 (1.89-2.09)	< 0.0001
Advanced adenoma	2.36 (2.05-2.72)	< 0.0001
Cancer	3.88 (2.41-6.23)	< 0.0001
Total		
Overall adenomas	1.25 (1.20-1.30)	< 0.0001
Advanced adenoma	2.65 (2.38-2.94)	< 0.0001
Cancer	3.39 (2.45-4.68)	< 0.0001

<sup>1</sup> $\chi^2$  statistical comparison of distribution of selected findings.

## DISCUSSION

Overall, the 50 year age group had higher rate of colorectal neoplasia as compared to the 40 year age group, similar to all studies across the world. There is a significant increased risk for colorectal neoplasia, in both age groups, between Western and Asian origins.

The differences between the two age brackets are statistically significant among men only. It is consistent with previous studies which found that women have a lower risk for colorectal neoplasia across all age groups<sup>[7]</sup>. Regula *et al*<sup>[8]</sup> and Ferlitsch *et al*<sup>[9]</sup> observed that men tend to develop advanced adenomas a decade earlier than women. The current study is limited to subjects younger than 60 years which can explain the lack of difference among women.

The findings in an Israeli population are comparable with observations from previous studies conducted in the West, indicating that age and male gender are the most important risk factors for the development of colorectal adenomas. A review of studies from Western

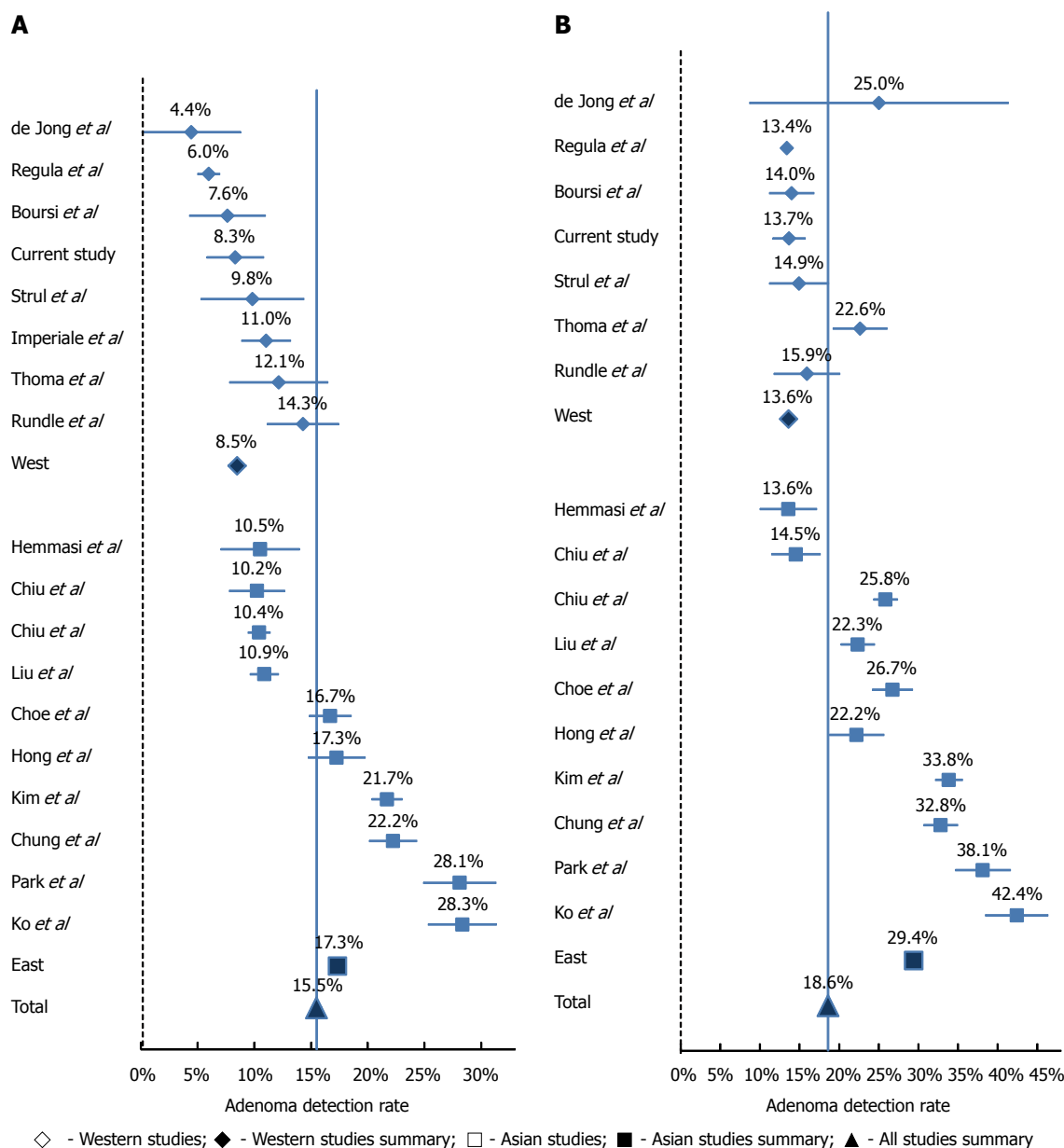


Figure 2 Overall adenoma detection rate in 40's (A) and 50's (B) age groups.

countries, including Israel, revealed heterogeneity in the prevalence rates of adenomas and advanced adenomas. ADR and the detection of advanced adenomas were slightly lower in Israel than in other countries. Various factors might explain these discrepancies, mainly differences in genetic and environmental backgrounds. The use of different study design is another possible explanation.

The current study included real average population as they were all asymptomatic subjects with no family history of CRC. Other studies, like the landmark study of Regula *et al*<sup>[8]</sup>, included patients with a family history of CRC.

Herein, it can be confirmed that CRC screening in the West should begin earlier than the age of 50.

During our review of the literature we detected a secondary important finding regarding a significantly

increased ADR among Asians, and in particular from the Far East, as compared to those from Western countries. This observation is consistent with reports showing an increase in CRC in eastern countries<sup>[10]</sup> which is considered the result of rapid economic development and life style modification. Shin *et al*<sup>[11]</sup> reported a rapid increase in CRC incidence in Korea between 1999-2009 in both men and women. Although in part attributed to the introduction of colorectal cancer screening, they concluded that transition in risk factors (*e.g.*, alcohol consumption, obesity and increased meat consumption) also has a significant role in the increase of CRC incidence.

Interestingly, despite the increased overall adenoma rate in Asian countries, the prevalence of advanced adenomas did not increase in similar proportions, and were even lower than in the West. This observation



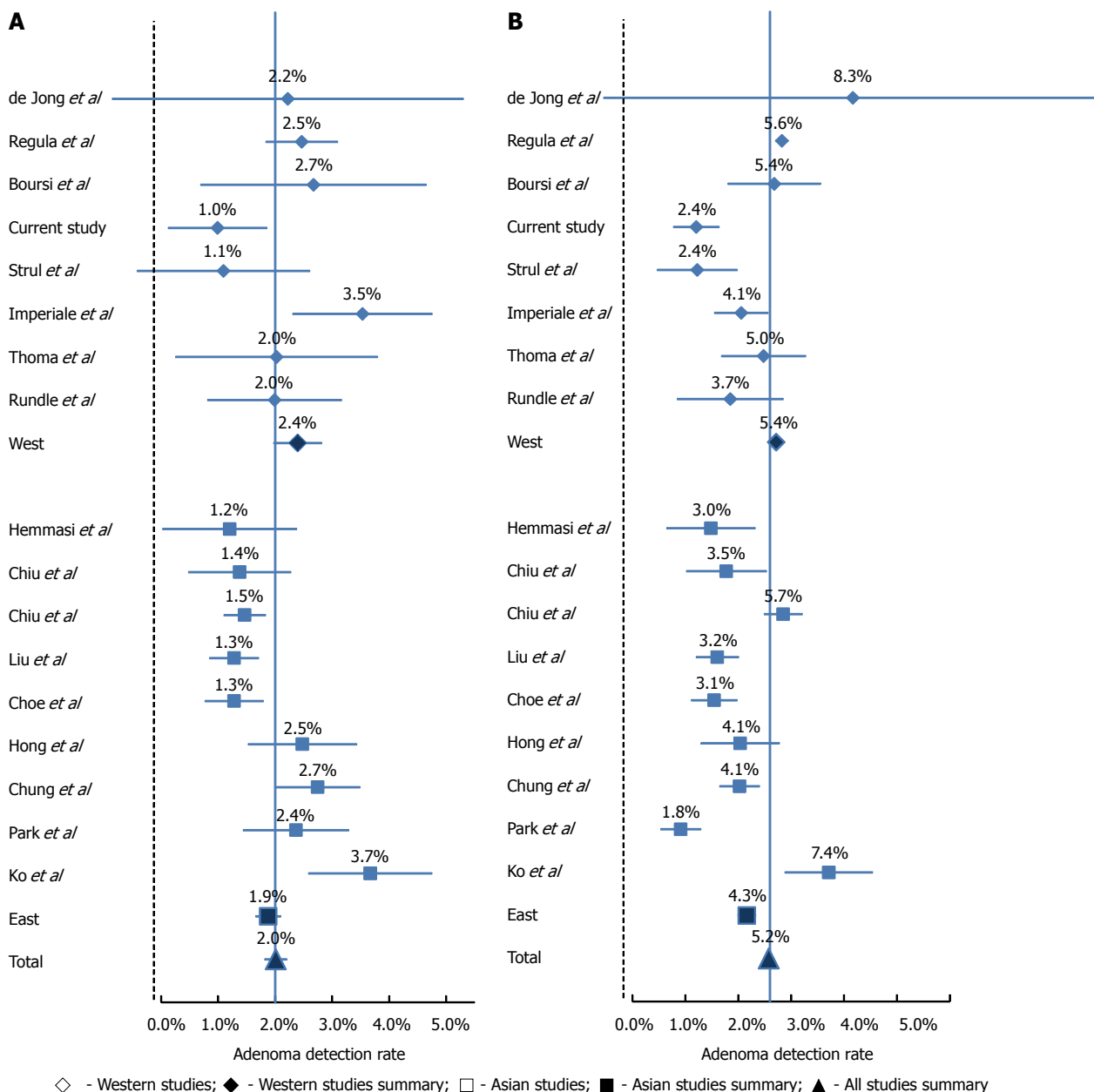


Figure 3 Advanced adenoma detection rate in 40's (A) and 50's (B) age groups.

suggests a slower rate of adenoma progression in Eastern Asia which may be due to genetic and/or environmental factors.

The high rates of colorectal neoplasia in East Asia population, is of great significance regarding immigrants from these countries to the West and specifically the United States. Ladabaum and colleagues<sup>[12]</sup> calculated CRC incidence rates in foreign-born Asian ethnic subgroups in California and found significant impacts of nativity and residence in an ethnic enclave on CRC incidence, suggesting a substantial effect of acquired environmental factors. In contrast to other minorities, such as African Americans, studies regarding the rate of polyps among East Asian immigrants aged 40-59 in the United States is limited, while there is a lot of information about the poor adherence of

this population to CRC screening programs. In fact, Asian Americans have been described as one of the underrepresented and hard-to-reach populations<sup>[13]</sup>. Several studies have found that Asian Americans have lower CRC screening rates than non-Hispanic white Americans<sup>[14,15]</sup>. Moreover, Oh *et al*<sup>[16]</sup> described lower rates of CRC screening knowledge and uptake among Korean Americans compared to Asian Americans as a whole.

In conclusion, the detection rates of colorectal neoplasms among asymptomatic average-risk subjects in this study were compatible with previous results of Western origin, confirming the current guidelines to begin screening for CRC at the age of 50. The substantial differences between Western and East Asian populations in terms of overall adenoma and advanced adenoma

detection rates mandate further investigation and imply the need for specific screening recommendation for this population.

## COMMENTS

### Background

Colorectal cancer (CRC) is the third leading cause of cancer mortality in the Western world and approximately 70% of patients who develop CRC are considered "average risk". According to previous studies, the incidence and mortality rates of CRC increase after 50 years of age, and therefore screening should be initiated at this age. However, only few studies focused on the prevalence of adenomas among persons younger than 50 years and those that have been published revealed variable results.

### Research frontiers

As the rate of CRC increases over time, it is important to re-evaluate and examine the detection rates of screening colonoscopy among average-risk individuals to better determine the recommended age to begin screening. It is of no less importance to search for CRC risk factors including gender and origin.

### Innovations and breakthroughs

The present study confirms the current guidelines to begin screening for CRC at the age of 50. Environmental factors such as diet and lifestyle are known to have a significant effect on risk for CRC. The substantial differences between Western and East Asian populations in terms of overall adenoma and advanced adenoma detection rates observed in this study is a clear proof that such factors should be taken into consideration.

### Applications

The results of this study mandate further investigation and imply the need for specific screening recommendation for the Asian population especially among immigrants to western countries.

### Terminology

CRC is the third leading cause of cancer mortality in the Western world. As in most cancers the best treatment is detection and removal of premalignant lesions by colonoscopy. Currently the recommended age for screening is 50 years in which these lesion start to develop.

### Peer-review

This is an interesting and well-designed study, addressing the issue of CRC screening in two year groups, 40-50 and 50-59, in an Israeli population. The results are comparable with studies conducted in the West, but interestingly with a slightly lower prevalence rate of adenomas and advanced adenomas in Israel.

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