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The Association between Metabolic Syndrome and Colorectal Neoplasm: Systemic review and Meta-analysis

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Abstract

Background—There has been constant speculation about the association between metabolic syndrome (MetS) and colorectal neoplasia (CN); however, the published results are conflicting. The aims of this study are to systematic search, and assess literature to determine the available evidence on the association between these two conditions.

Methods—Meta-analysis was conducted based on relevant studies identified through a systematic literature review from PubMed, OvidSP and Cochrane database during January 1980 to July 2011. A combined analysis was performed, followed by a subgroup analyses stratified by the study design, type of colorectal lesions and gender. Publication bias was assessed using the Begg's and Egger's tests and visual inspection of funnel plot.

Results—Eighteen studies were included in the final analysis. Overall, MetS was associated with 34% increase in the risk of CN (summary RR - 1.34, 95% CI 1.24–1.44). The association between MetS and CN was found to be statistically significant in separate analysis for both case-control studies (summary RR -1.58, 95% CI 1.44–1.79) and cohort studies (summary RR – 1.21, 95% CI 1.13–1.29). The association remained significant when analyses were restricted by type of colorectal lesions (colorectal cancer: RR – 1.30, 95% CI 1.18–1.43; colorectal adenoma: RR – 1.37, 95% CI 1.26–1.49). Further subgroup analysis by gender showed significant association between MetS and CN in both male and female population.

Conclusion—Our meta-analysis showed significant association between presence of MetS and CN. These results may help in identifying high risk individuals at early stage that might benefit from targeted CRC screening intervention.

BACKGROUND

Colorectal cancer (CRC) is the third most common cancer diagnosed and the third leading cause of cancer death in the United States. The mortality rate from CRC has been declining for the past two decades, possibly because of early detections of precancerous polyps/ adenomas or even CRC through screening colonoscopy [1, 2]. Despite the success of screening colonoscopy for colorectal cancer prevention, it is still of importance to

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understand the risk factors and associated conditions for CRC since they form an integral part in the management and screening paradigm.

The metabolic syndrome (MetS) is a constellation of interrelated risk factors including high blood pressure, increased waist circumference, high triglyceride, low high-density lipoprotein and impaired glucose, which confer an increased likelihood of atherosclerotic cardiovascular disease and increase in mortality [3, 4]. The overall incidence and prevalence of MetS in the United States are on the rise with the obesity epidemic [5, 6]. There are several reports demonstrating the increasing risks of several types of malignancies including CRC in subjects with MetS. Though exact mechanism of these associations remains unclear, it is plausible that alterations in cytokines and signaling pathways place these subjects at risk for cancer development [7]. Despite the possible link between MetS and CRC, the results from several reports were quite inconclusive [8–12]. Some demonstrated increased in incidence of colorectal adenoma or cancer in individuals with MetS, while others did not [8–12]. In order to address this issue, we performed a systematic review and meta-analysis focusing on the question of whether the presence of MetS is associated with colorectal neoplasia (CN).

METHODS

Search Strategy and selection criteria

We identified studies by literature search of all languages from PubMed, OvidSP and Cochrane database from January 1, 1980 through June 30, 2011. The search term comprised the following keywords: metabolic syndrome, insulin resistance, metabolic abnormalities, colorectal neoplasm, colorectal cancer, colonic adenoma, adenomatous polyps, and colon cancer. We interrogated references of all the articles to further identify additional studies that were not originally included during the initial search. Only publications that fulfilled the following criteria were selected for meta-analysis: (i) the study subjects were adult (≥ 18 years old), and (ii) they reported an estimate of relative risk (RR) of colorectal neoplasia (defined as colorectal adenoma or adenocarcinoma or both) in individuals with MetS. For this study, we selected all the publications with various definitions of MetS from the following panels/organization including the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) [3], World Health Organization [13], International Diabetes Federation [14], and the American Heart Association [15]. In the circumstance when the reports did not clearly outline the definition of MetS being used, the relative risk (RR) of CN in individuals with more than or equal to three metabolic abnormalities (based on Adult Treatment Panel III) was considered in the analysis. Only publications with case-control or cohort study designs were included. If multiple studies were found on same population or subpopulation, only estimates from the most recent reports were considered in the final analysis.

Data extraction

Information extracted from the extensive review of each publication include: publication data [first author's last name and first name initials, year of publication and country of the population studied], type of study design, number of cases and controls (for case-control studies), number of exposed and unexposed (for cohort studies), definitions of metabolic syndrome, risk estimates with their corresponding confidence intervals (CIs), and all the covariates (if any) being used in the multivariate analyses and modeling. Odds ratios from case-control studies were considered as estimate of relative risk [16]. Two independent reviewers reviewed the studies and any discrepancies regarding inclusion/exclusion or risk estimates were resolved by consensus. The agreement between reviewers for inclusion/exclusion of studies was assessed using Cohen's kappa coefficient [17].

Assessment of methodological quality

The Newcastle-Ottawa Scale was used for assessment of methodological quality of all the publications that were included in our meta-analysis. The scales allocate stars, maximum of nine, for quality of selection, comparability, exposure and outcome of study participants [18].

Statistical analysis

The heterogeneity of all the publications was evaluated with Cochran's *Q*-test and I^2-statistic [19]. Summaries of relative risk (RR) estimates were evaluated using both fixed- and random-effects methods. Initial analysis including all the studies was performed to look for association between MetS and CN. Many subgroup analyses stratified by study design (case-control or cohort), type of neoplasm (adenoma or cancer or both), gender (men or women), potential confounding factors (such as smoking) and by definition of MetS (ATP III or other definitions) were carried out to account for different forms of possible bias. Further sensitivity analyses were performed by excluding studies with Newcastle – Ottawa Scale score of less than six. Publication bias was assessed by construction and visual inspection of funnel plot. Additional tests including Egger's and Begg and Mazumdar tests were used [20, 21]. The *p* value of <0.05 indicated statistical significance. All analyses were performed using Comprehensive Meta-analysis Version 2 (Biostat, Englewood, New Jersey).

RESULTS

Study characteristics

We initially identified 3,717 studies, either in full publications or abstract forms, using the methodology and the search terms described above. After title (excluding 3605) and abstract (excluding 78) review, 34 publications were considered to be relevant to our study subject. All references from these publications were further reviewed and additional three studies that were pertinent to our study were included. Out of the 37 studies, 19 were excluded as they did not meet the specific study criteria. As such, eighteen studies were included for final analyses. The observed Cohen's kappa for the agreement between reviewers was 0.84. Of these, 10 were cohort and 8 were case-control studies. Four studies were conducted in the United States, five in Europe, and nine in Asia. The schematic diagram of the study selection is shown in Figure 1. Details of these studies have been described in Tables 1, 2 and 3.

Overall analyses on the association of metabolic syndrome and colorectal neoplasia (CN)

Due to evidence of heterogeneity of the 18 studies (*Q*= 59.59, *p* value for heterogeneity = 0.001, I^2=51.3%), random-effect model was considered for summary RR. The overall RR (in 703,992 subjects from 18 studies) for CN (adenoma or colon cancer) associated with MetS was 1.34 (95% CI 1.24–1.44) (Figure 2 and Table 4). The association between MetS and CN was found to be higher in case-control (n = 8 studies, summary RR - 1.58, 95% CI 1.44–1.73) compared to cohort studies (n = 10 studies, summary RR – 1.21, 95% CI 1.13–1.29). Further subgroup analysis by gender showed significant association between MetS and CN in both males (n = 13 studies, summary RR – 1.31, 95% CI 1.19–1.44) and females (n = 10 studies, summary RR – 1.32, 95% CI 1.11–1.56). We also performed analysis of studies that controlled for smoking status separately to evaluate the confounding effect of smoking on MetS and CN association. Analysis of 11 studies that controlled for smoking status still showed significant association between MetS and CN (summary RR – 1.30, 95% CI 1.20–1.41).

Overall analyses on the association of metabolic syndrome and colorectal adenoma

There were 8 publications (3 cohort and 5 case-control studies) determining the association between MetS and colorectal adenoma. A pooled analysis of these 8 studies (21,474 subjects) demonstrated that the RR for colorectal adenoma in those with MetS was 1.37 (95% CI 1.26–1.49) (Figure 3 and Table 4).

Overall analyses on the association of metabolic syndrome and colorectal cancer

Ten studies involving 687,413 individuals provided data that allowed us to obtain the RR for colorectal cancer in those with MetS (Figure 4 and Table 4). The RR of colorectal cancers among those with MetS was 1.30 (95% CI 1.18–1.43).

Publication quality and bias

The Newcastle-Ottawa Scale to assess the publication quality revealed that the ten cohort studies averaged 7.2 stars and the eight case-control studies averaged 8.1 stars. (Tables 5 and 6). Visual inspection of funnel plot (Figures 5A, 5B, and 5C) and further evaluation with Egger's or Begg and Mazumdar tests (overall CN: Begg and Mazumdar test – $p = 0.49$, Egger's test – $p = 0.13$; colonic adenoma: Begg and Mazumdar test – $p = 0.33$, Egger's test – $p = 0.45$; and colon cancer: Begg and Mazumdar test – $p = 0.56$, Egger's test – $p = 0.31$) did not show evidence of publication bias.

DISCUSSION

To our knowledge this is the first meta-analysis that showed association between MetS (using various definitions) and CN. Further, no gender difference for such association was demonstrated.

Previous reports have found the individual component of MetS, notably impaired fasting glucose to be associated with the risk of CN [22, 23]. Yuhara et al. reported the significantly higher risk of colon cancer in diabetes patients (RR 1.38, 95% CI 1.26–1.51) compared to controls, after adjusting for potential confounders such as smoking status and subjects' body mass index [23]. However, the link between CN and other components of MetS (such as hypertension, hypertriglyceridemia and low HDL) yielded inconclusive results [9, 24, 25]. Since the presence of MetS is closely related to obesity, several meta-analysis studies have found the significant association between the risk of colon cancer in obese subjects [22, 26]. Larsson et al. showed that the RR for colon cancer in obese men and women was 1.30 (95% CI 1.25–1.35) and 1.12 (95% CI 1.07–1.18), respectively.

Several molecular mechanisms have been proposed regarding higher risk of CN in those with MetS including the role of oxidative stress [7], insulin growth factor-1 (IGF-1) [27], and inflammatory cytokines [28]; all of which are increased in those with MetS [7]. Higher level of reactive oxygen species found in those with MetS might lead to DNA damage and thus place subjects at risk for CN development [7]. IGF-1 has been shown to increase cellular turnover and inhibits apoptosis. It also leads to increase production of vascular endothelial growth factor which supports tumor growth [29, 30]. In individuals with MetS, hyperinsulinemia either due to obesity or impaired fasting glucose leads to increase in IGF-1 and possibly increases the carcinogenic effects. These effects of IGF-1 have been studied selectively on colonic mucosa in many in-vitro studies [31, 32] and their implications were evident in many clinical studies looking at colon cancer risk in diabetes patients [33, 34]. Other potential mechanisms for development of CN in MetS individuals is likely mediated through inflammatory cytokines, especially tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) [35, 36]. The role of IL-6 in activation of signal transducers and activators of transcription factors (such as STAT1 and STAT3), via Janus kinases has been

thought to be representing the neoplastic effects and cancer development [28, 37]. Similarly TNF – α works through the AP-1 and NF-κB signaling pathways to stimulate cell proliferation and survival leading to cancer development [38].

Despite the strength of meta-analysis, our study also has several limitations. It did not take into account of other possible confounding factors which might be associated with the risk of CN, for example, dietary patterns, family history of colon cancer, and alcohol use. Such data are either incomplete or lacking from the original publications which were included in this analysis. Our study does not provide any insight regarding genetic or socioeconomic risk factors which might have influence on development of CN in MetS individuals. Lastly, we included all studies with various definitions of MetS that were endorsed by different panels/organizations. However, when we conducted separate analysis for studies that only used the widely accepted definition (ATP III) or its modified version, we still found the significant association exists between MetS and CN (7 studies, summary RR – 1.37, 95% CI 1.19–1.58).

In conclusion, we found the significant association between MetS and colonic neoplasia. Given the rising in epidemic of MetS worldwide [5, 6], healthcare provider should be more vigilant and adhere with colon cancer screening guideline in subjects with MetS.

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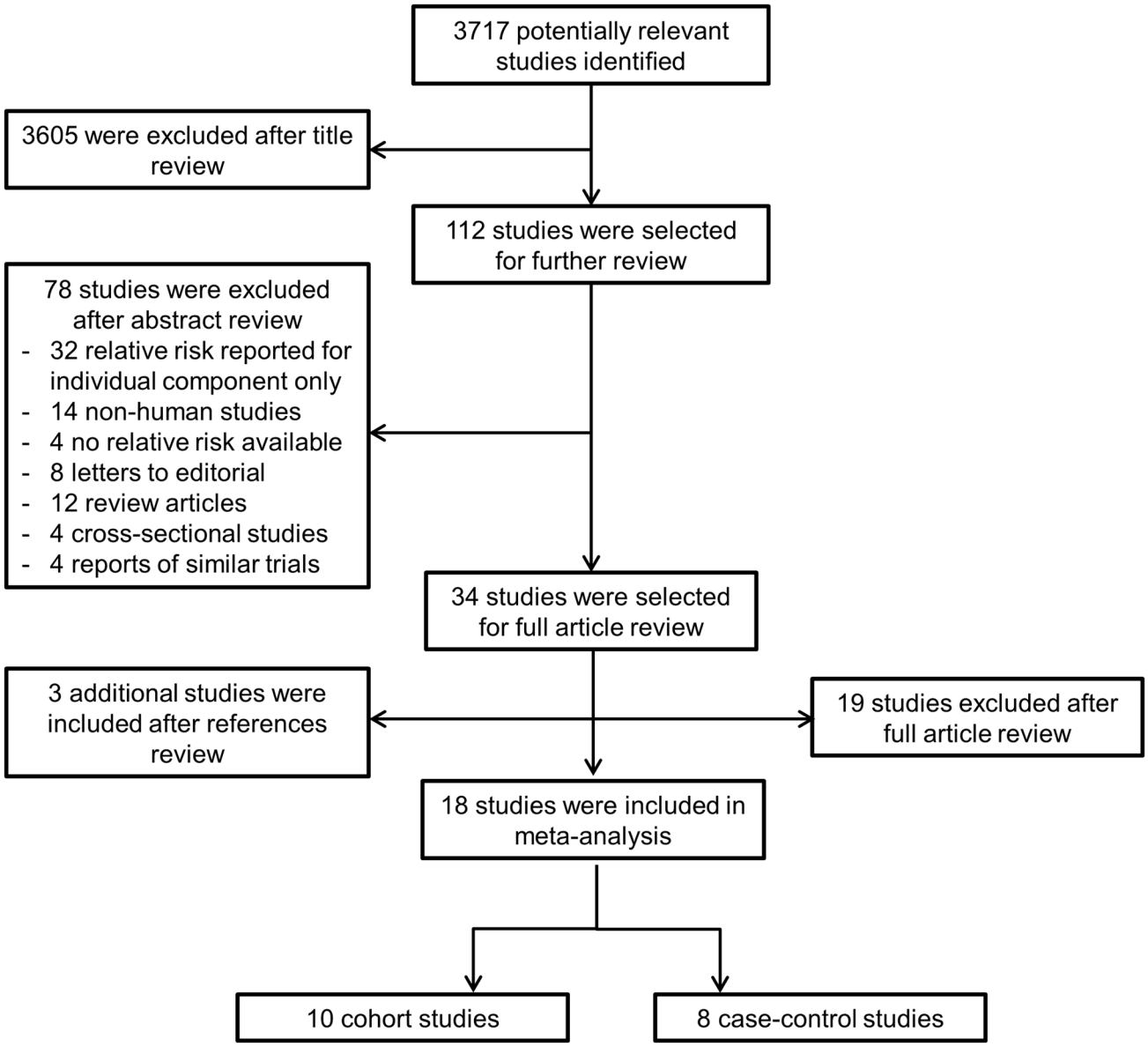

Figure 1.
Flowchart of study selection

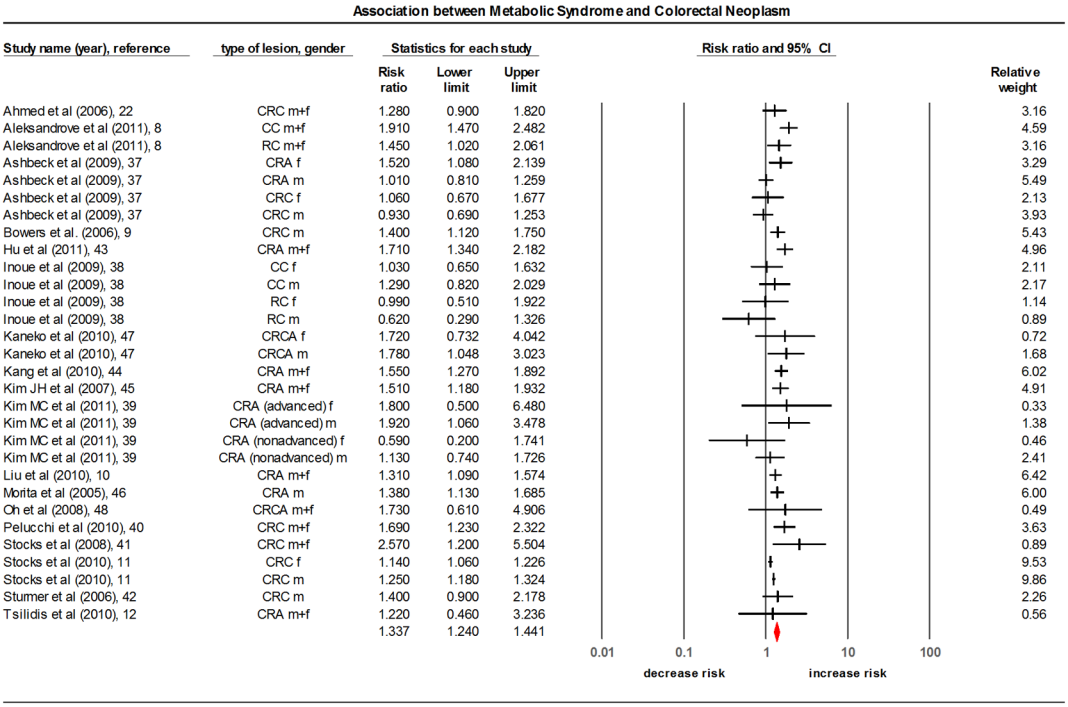

Figure 2.

Forest plot: Association between metabolic syndrome and colorectal neoplasm (adenoma and cancer combined). CRN – colorectal neoplasm; CRC – colorectal cancer; CC – colon cancer; RC – rectal cancer; CRA – colorectal adenoma; CRCA – colorectal cancer and adenoma; m – male; f – female.

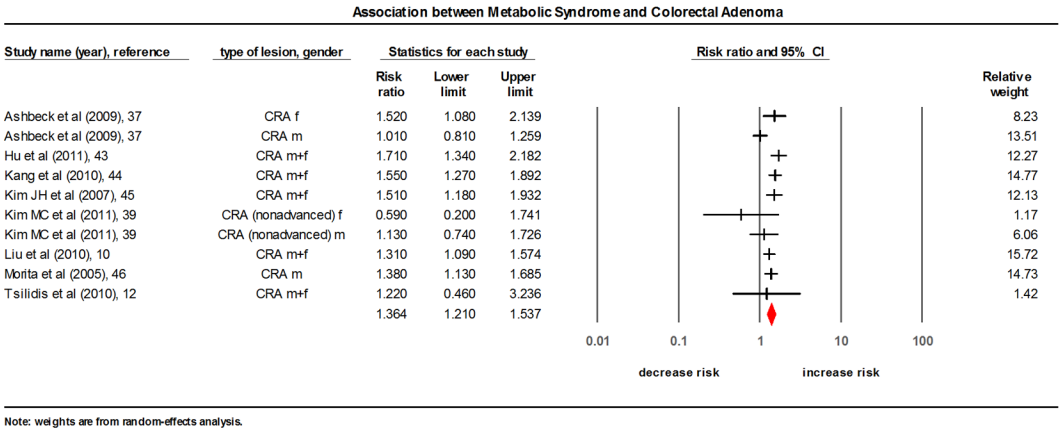

Figure 3.

Forest plot: Association between metabolic syndrome and colorectal adenoma. CRA – colorectal adenoma; m – male; f – female

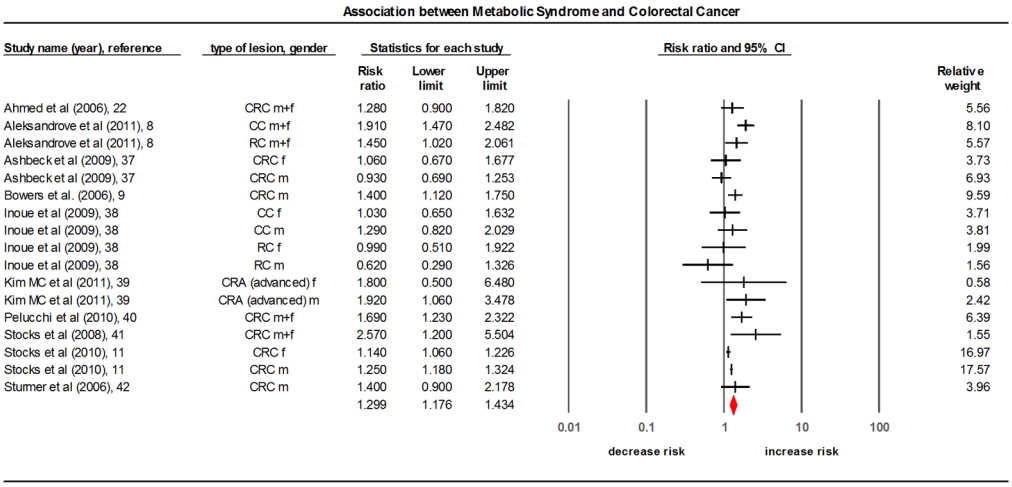

Figure 4.

Forest plot: Association between metabolic syndrome and colorectal cancer. CRC – colorectal cancer; CC – colon cancer; RC – rectal cancer; CRA – colorectal adenoma; m – male; f – female.

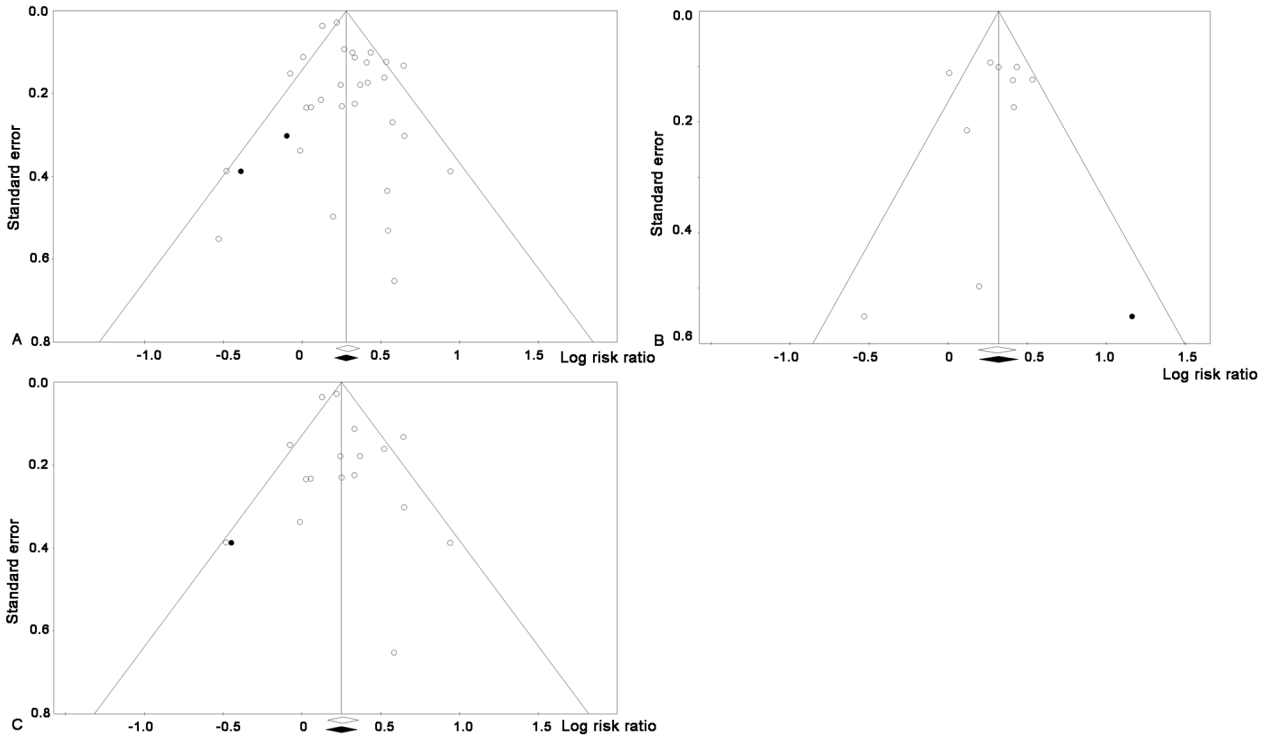

Figure 5.
Funnel plots for publication bias
(a) Metabolic syndrome and colorectal neoplasm (adenoma and cancer combined)
(b) Metabolic syndrome and colorectal adenoma
(c) Metabolic syndrome and colorectal cancer

Table 1

Characteristics of studies providing colorectal cancer risk [8, 9, 11, 24, 39–44]

Cohort studies					
Author, year, country, reference	**Study population**	**Definition of MetS**	**type of lesion, sex, RR, 95% CI**	**Controlled variables**	**Study characteristics[+]**
Ahmed *et al.*, 2006, USA [24]	14,109 individuals from Atherosclerosis Risk in Communities (ARIC) multicenter cohort study	AHA	CRC m+f – 1.28, 0.9–1.7 CRC m – 1.31, 0.9–1.9 CRC f – 1.29, 0.8–2.0	Age, gender, physical activity, NSAIDs, aspirin use, smoking, alcohol	Age group – 45–64 male – 45.6% Smoking (current) – 25.2% Alcohol use (current) – 56.3%
Bowers *et al.*, 2006, Finland [9]	28,983 Finnish male smokers	≥ 3 metabolic abnormalities	CRC m-1.40, 1.12–1.74 CC m- 1.58, 1.18–2.10 RC m- 1.20, 0.85–1.68	Age, smoking, total cholesterol	Age (mean) – 57.0 male – 100% Smoking – 100% Alcohol use – n/a
Inoue *et al.*, 2009, Japan [40]	27,724 general Japanese population	AHA	CC m – 1.29, 0.82–2.02 CC f – 1.03, 0.65–1.65 RC m – 0.62, 0.29–1.34 RC f – 0.99, 0.51–1.92	Age, smoking, alcohol intake, serum cholesterol	Age (mean) men – 56.5 ± 8.2 women – 55.5 ± 8.1 male – 34.4% Smoking (past or current) – 27.7% Alcohol use (≥ 150 g/week) – 16.5 %
Stocks *et al.*, 2010, Norway, Austria, Sweden [11]	578,700 general population	≥ 3 metabolic abnormalities	CRC m – 1.25, 1.18–1.32 CRC f – 1.14, 1.06–1.22 CC m – 1.28, 1.20–1.38 CC f – 1.12, 1.03–1.23 RC m – 1.20, 1.10–1.31 RC f- 1.16, 1.02–1.32	Age, smoking and individual components of metabolic abnormalities	Age (mean) men – 43.9 ± 11.1 women – 44.1 ± 12.3 male – 50.1% Smoking (past or current) – 55.2% Alcohol use – n/a
Sturmer *et al.*, 2006, USA [44]	22,071 healthy male physician	ATP III	CRC m – 1.4, 0.9–2.1	Age, exercise, smoking, alcohol use, NSAIDs	Age (mean) – 53.8 ± 9.5 male – 100% Smoking (past or current) – 50.5% Alcohol use (≥ twice/week) – 60%
Ashbeck *et al.*, 2009, USA [39]	2392 individuals from Wheat Bran Fiber trial and the Ursodeoxycholic Acid trial	ATP III	CRA m – 1.01, 0.81–1.26 CRA f – 1.52, 1.08–2.13 CRC m - 0.93, 0.69–1.25 CRC f - 1.06, 0.67–1.69	Age	Age (mean) men – 66 women – 65.7 male – 67.3% Smoking (past or current) – 66.5% Alcohol use – men – 10.0 g/day women – 3.3 g/day
Kim MC *et al.*, 2011, Korea [41]	3430 general Korean population	ATP III	CRA (advanced) m-1.92, 1.06–3.47 CRA (advanced) f- 1.80, 0.50–6.45	Age	Age (mean) men – 48.4 women – 47.9 male – 66% Smoking (past or current) – 57.8% Alcohol use – 69.4%

Case-control studies						
Author, year, country, reference	**Study population (cases & controls)**	**Controls Matched for**	**Definition of MetS**	**type of lesion, sex, RR, 95% CI**	**Controlled variables**	**Study characteristics[+]**
Aleksandrove *et al.*, 2011, Denmark, France, Germany, Greece, Italy, Spain, Netherland, UK [8]	CC -689 cases and 689 controls RC – 404 cases and 404 controls	Age, sex, study center, menopause status, menstrual cycle, HRT	ATP III	CC m+f – 1.91, 1.47–2.42 CC m – 1.70, 1.15–2.50 CC f – 2.25, 1.55–3.26 RC m+f – 1.45, 1.02–2.06 RC m – 1.35, 0.83–2.21 RC f – 2.03, 1.14–3.62	Dietary consumption	Age (mean) CC cases – 58.8 ± 7.3 RC cases – 58.1 ± 7.0 male – CC cases – 45.3% RC cases – 54.2% Smoking – CC cases – 23.7% RC cases – 27.7% Alcohol use –CC cases – 7.9 g/day RC cases – 11.9 g/day
Pelucchi *et al.*, 2010, Italy [42]	CC - 1378 cases, RC - 878 cases, 4661 controls	study center	IDF	CRC m+f – 1.69, 1.23–2.33 CRC m – 2.09, 1.38–3.18 CRC f – 1.15, 0.68–1.94 CC m+f – 1.71, 1.17–2.50 CC m – 2.15, 1.31–3.53 CC f – 1.17, 0.64–2.14 RC m+f – 1.82, 1.19–2.79 RC m – 2.19, 1.29–3.73 RC f – 1.14, 0.53–2.46	Age, sex, education, smoking, alcohol, occupation, physical activity	Age (median) – CC cases –61 RC cases – 61 Controls - 57 male – CC cases – 56.6% RC cases – 60.4% Controls – 50.7% Smoking — n/a Alcohol use – n/a
Stocks *et al.*, 2008, Sweden [43]	306 cases, 595 controls	Age, sex, blood sample date and fasting time	WHO	CRC m+f – 2.57, 1.20–5.52 CRC m – 1.57, 0.53–4.70 CRC f – 4.16, 1.30–13.3	none	Age (median) men CRC cases – 59.8 women CRC cases – 59.7 male – CRC cases – 40.8% Smoking – n/a Alcohol use – n/a

[+]Age in years, proportion of male, smoking, and alcohol use

AHA: American Heart Association; ATP: Adult Treatment Panel; IDF: International Diabetes Federation; WHO: World Health Organization; CRC: Colorectal cancer; CC: colon cancer; RC: rectal cancer; CRA: colorectal adenoma, t: total for both genders, m: male; f: female; NSAIDs: Non-steroidal anti-inflammatory drugs; HRT: Hormone replacement therapy

Table 2

Characteristics of studies providing colorectal adenoma risk [10, 12, 39, 41, 45–48]

Cohort studies					
Author, year, country, reference	**Study population**	**Definition of MetS**	**type of lesion, sex, RR, 95% CI**	**Controlled variables**	**Study characteristics[+]**
Ashbeck *et al.*, 2009, USA [*][39]	2392 individuals from Wheat Bran Fiber trial and the Ursodeoxycholic Acid trial	ATP III	CRA m – 1.01, 0.81–1.26 CRA f – 1.52, (1.08–2.13)	age and study	Age (mean) men – 66 women – 65.7 male – 67.3% Smoking (past or current) – 66.5% Alcohol use – men – 10.0 g/day women – 3.3 g/day
Kim MC *et al.*, 2011, Korea [*][41]	3430 general Korean population	ATP III modified for region	CRA (advanced) m-1.92, 1.06–3.47 CRA (advanced) f- 1.80, 0.50–6.45 CRA (nonadvanced) m – 1.13, 0.74–1.72 CRA (nonadvanced) f – 0.59, 0.20–1.75	Age	Age (mean) men – 48.4 women – 47.9 male – 66% Smoking (past or current) – 57.8% Alcohol use – 69.4%
Liu *et al.*, 2010, China [10]	4872 general Chinese population	AHA	CRA m+f – 1.31, 1.09–1.57 CRA m – 1.44, 1.16–1.80 CRA f – 1.04, 0.74–1.46	Age, gender, smoking, alcohol	Age (mean) – 49.6 ± 11.7 male – 57.4% Smoking (past or current) – 34.7% Alcohol use (past or current) – 35.4%

Case-control studies						
Author, year, country, reference	**Study population (cases & controls)**	**Controls Matched for**	**Definition of MetS**	**type of lesion, sex, RR, 95% CI**	**Controlled variables**	**Study characteristics[+]**
Kang *et al.*, 2010, Korea [46]	1122 cases, 1122 controls	Age, sex	ATP III modified for region	CRA m+f – 1.55, 1.27–1.90	none	Age (mean) cases – 56.0 ± 7.8 male – 77.2% Smoking (current) – cases – 25.0% controls – 20.2 Alcohol use (>140 g/week) – cases – 17.5% controls – 16.0%
Kim JH *et al.*, 2007, Korea [47]	731 cases, 1800 controls	Nonpolyp/cancer controls	ATP III modified for region	CRA m+f – 1.51, 1.18–1.93	Age, gender, smoking, alcohol	Age (mean) cases – 53.6 ± 7.6 controls – 51.0 ± 7.9 male – cases – 86.8% controls – 72.2% Smoking – cases – 31% controls – 23% Alcohol use (>40 g/d) – cases – 59% controls – 48%
Morita *et al.*, 2005, Japan [48]	756 cases and 1751 controls male	Not mentioned	IDF	CRA m – 1.38, 1.13–1.69	Age, hospital	Age group – cases – 49–57 controls – 44–59 male – 100% Smoking – n/a Alcohol use n/a

Case-control studies						
Author, year, country, reference	**Study population (cases & controls)**	**Controls Matched for**	**Definition of MetS**	**type of lesion, sex, RR, 95% CI**	**Controlled variables**	**Study characteristics[+]**
Tsilidis *et al.*, 2010, USA [12]	132 cases, 260 controls	Age, sex, race, date of blood draw, fasting	≥ 3 metabolic abnormalities	CRA m+f – 1.22, 0.46–3.20	smoking, hormone use, NSAIDs	Age (mean) cases – 55.2 ± 10.0 male – cases – 50% Smoking (past or current) – cases – 57.6% controls – 45.8% Alcohol use cases – 7.5 g/day controls – 6.7 g/day
Hu *et al.*, 2011, Taiwan [45]	397 cases, 2709 controls	Nonpolyp/cancer controls	ATP III modified for region	CRA m+f – 1.71, 1.34–2.17	Age, sex, smoking, drinking	Age (mean) cases – 51.5 ± 11.4 controls – 46.5 ± 10.5 male – cases – 76.3% controls – 56.1% Smoking – cases – 48.1% controls – 26.9% Alcohol use (>1 drink/week) – cases – 30.6% controls – 26.8%

[+]Age in years, proportion of male, smoking, and alcohol use

[*]Ashbeck et al. and Kim MC et al. provided RR for both adenoma and cancer separately.

Table 3

Characteristics of studies providing the risk for colorectal adenoma and cancer combined [49, 50]

Cohort studies					
Author, year, country, reference	**Study population**	**Definition of MetS**	**type of lesion, sex, RR, 95% CI**	**Controlled variables**	**Study characteristics[+]**
Kaneko *et al.*, 2010, Japan [49]	727 general Japanese population	Japanese ministry of health, labor and welfare	CRCA m – 1.784, 1.048–3.036 CRCA f – 1.727, 0.732–4.072	Age, dietary intake	Age (mean) – 61.71 male – 62.2% Smoking (current) – 40.4% Alcohol use (current) – 49.7%
Oh *et al.*, 2008, Korea [50]	200 general Korean population	IDF modified for region	CRCA m+f – 1.73, 0.61–4.84	Age, sex, smoking	Age (mean) – 50.9 ± 8.5 male – 66.5% Smoking (current) – 36% Alcohol use (current) – 43%

[+]Age in years, proportion of male, smoking, and alcohol use CRCA - colorectal cancer and adenoma

Table 4

Summary RR estimates and 95% CIs for subgroup analyses

	No. of studies	*Q*	*P*-heterogeneity	I^2 Statistics %	Summary RR (95% CI)
Total	18	59.59	<0.01	51.3	1.34 (1.24–1.44)
Subgroup					
Lesion *					
Colorectal cancer	10	35.69	<0.01	55.2	1.30 (1.18–1.43)
Colorectal adenoma	8	16.35	0.06	44.9	1.37 (1.26–1.49)
Cancer + adenoma	2	0.01	0.99	0.0	1.76 (1.16–2.66)
Study type					
Cohort study	10	25.77	0.17	22.4	1.21 (1.16–1.26)
Case-control study	8	6.58	0.58	0.0	1.58 (1.44–1.73)
Gender					
Male	13	26.54	0.05	39.7	1.27 (1.21–1.33)
Female	10	26.62	0.01	51.2	1.32 (1.11–1.56)
Confounding factor					
Smoking	11	24.46	0.04	42.8	1.24 (1.19–1.29)
Definition of MetS					
ATP III/modified ATP III	7	31.30	<0.01	58.5	1.37 (1.19–1.58)
Others	11	21.98	0.11	31.7	1.23 (1.19–1.29)

* 2 studies provided RR for both adenoma and cancer separately, so total number of studies by type of lesion does not equal 18.

Table 5

Newcastle – Ottawa quality scale for cohort studies

	Selection (score)				Comparability (score)	Outcome (score)			Total score
	Representative of exposed cohort	Selection of nonexposed cohort	Ascertainment of exposure	Absence of outcome at start of study	Control for age or other factors	Assessment of outcome	Follow-up period (more than 10 years)	Adequacy of follow up	
Ahmed *et al.*, 2006[24]	1	1	1	1	2	1	1	0	8
Bowers *et al.*, 2006[9]	1	1	1	1	2	1	1	0	8
Inoue *et al.*, 2009[40]	1	1	1	1	2	1	1	1	9
Stocks *et al.*, 2010[11]	1	1	1	1	2	1	1	0	8
Sturmer *et al.*, 2006[44]	0	1	0	1	2	1	1	0	7
Ashbeck *et al.*, 2009[39]	1	1	1	1	2	1	0	0	7
Kim MC *et al.*, 2011[41]	1	1	1	0	1	1	0	0	5
Liu *et al.*, 2010[10]	1	1	1	1	2	1	0	0	7
Kaneko *et al.*, 2010[49]	1	1	1	0	2	1	0	0	6
Oh *et al.*, 2008[50]	1	1	1	1	2	1	0	0	7
									Average 7.20

Table 6

Newcastle – Ottawa quality scale for case-control studies

	Selection (Score)				Comparability (Score)	Exposure (Score)			Total score
	Case definition	Representative of cases	Selections of controls	Definition of controls	Control age or other additional factors	Ascertainment of exposure	Same method of ascertainment for participants	Nonresponse rate	
Aleksandrove *et al.*, 2011[8]	0	1	1	1	2	1	1	1	8
Pelucchi *et al.*, 2010[42]	0	1	0	0	2	0	1	1	5
Stocks *et al.*, 2008[43]	0	1	1	1	2	1	1	1	8
Kang *et al.*, 2010[46]	1	1	1	1	2	1	1	1	9
Kim JH *et al.*, 2007[47]	1	1	1	1	2	1	1	1	9
Morita *et al.*, 2005[48]	1	1	1	1	2	1	1	1	9
Tsilidis *et al.*, 2010[12]	1	1	1	0	2	1	1	1	8
Hu *et al.*, 2011[45]	1	1	1	1	2	1	1	1	9
									Average 8.12