RESEARCH COMMUNICATION

Obesity and Kidney Cancer Risk in Women - a Meta-analysis (1992-2008)

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Abstract

We conducted a quantitative summary analysis to assess whether obesity carries higher relative risk in women than men. The studies included in this quantitative review were all cohort and case-control studies, which provided information on kidney cancer risk associated with obesity/overweight, published between 1992 and 2008. The details of studies have been identified through searches on the MEDLINE database. We first estimated the risk associated with a unit increase in BMI (1 kg/m^2) for individual studies using logit-linear model. After deriving the natural logarithm of the risk per unit of BMI for all studies, we calculated a pooled estimate and corresponding 95% confidence interval (CI) as a weighted average of the risk values obtained in individual studies, by giving a weight proportional to its precision. A total of 28 studies (15 cohort studies and 13 case-control studies) provided kidney cancer risk according to BMI in women. The relative risks (RR), which showed statistical significance, ranged from 1.04 to 1.12 per unit increase in BMI in various cohort studies. The pooled risk was 1.06 (95% CI=1.05-1.07) per unit increase in BMI based on cohort studies. Among all the studies, which reported association in both men and women, the pooled risk was slightly higher in women. In conclusion, the present analysis reported slightly a higher kidney cancer risk due to obesity in women than men. Increasing prevalence of obesity with higher proportion among women may be responsible for the rising incidence rates in women.

Key Words: Obesity - kidney cancer risk - meta-analysis

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Introduction

Kidney cancers, account for almost 2% of all cancers in women worldwide, with 80,000 new cases and 39,000 deaths from the disease occurring annually (Ferlay et al., 2004). Like in men, more than 80% of kidney cancers are renal cell carcinomas (RCC) originating from the renal parenchyma (Chow et al., 1999). Kidney cancer incidence rates are less than 5 per 10^2 women. These rates vary more than 5-fold worldwide and are highest in North America and Europe and lowest in Asian and Latin American countries (Curado et al., 2007).

Like in men, the incidence and mortality rates of this disease, particularly RCC, have been reported to be rising in women worldwide (Mathew et al., 2002; Perez-Farinos et al., 2006; Falebita et al., 2009) except in a few European countries (Levi et al., 2008). The increase in incidence is not fully explained by better diagnostic techniques (Hock et al., 2002). Studies have reported that the established risk factors such as smoking and obesity differ between men and women, with smoking being more important in men (Mclaughlin et al., 1995; Yuan et al., 1998). Several studies have reported higher kidney cancer risk due to obesity in women (Kriger et al., 1993; Mellengaard et al., 1995; Chow et al., 1996; Heath et al., 1997; Calle et al., 2003; Flaherty et al., 2005; Pischon et al., 2006; Chiu et al., 2006; Setiawan et al., 2007; Maso et al., 2007). Also, the prevalence of obesity has increased to epidemic proportion in recent decades in many populations with higher proportion of increase among women (Matsushita et al., 2008; Lilja et al., 2008; Wildman et al., 2008; Abubakari et al., 2008; Chen et al., 2009) and this increasing prevalence might therefore, at least, explain the increasing incidence of kidney cancer.

In a recent quantitative summary analysis by including cohort studies - in principle more valid study design among the observational studies – which were published during the past decade it is reported that 5% significantly increased risk for kidney cancer per unit of increase in body mass index (BMI) in men (Ildaphonse et al., 2009). In order to assess whether obesity carries higher risk in women, we conducted a similar quantitative summary analysis of kidney cancer risk according to BMI among women.

Materials and Methods

The studies included in this quantitative review were all cohort and case-control studies, which provided information on kidney cancer risk and obesity/overweight, published between 1992 and 2008. The details of studies have been identified through searches on the MEDLINE

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database, using keywords "kidney cancer", "renal cell carcinoma", "body mass index", "obesity" and "anthropometric factors". Papers were also searched among those quoted as references in the retrieved studies. We also identified previously published quantitative reviews to compare the present results. We considered mostly the studies of kidney parenchyma (ICD-10: C64). A description of the main characteristics such as the authors, year of publication, country, categories of BMI, the relative risk (RR) for cohort studies, the odds ratio (OR) for case-control studies and the corresponding 95% confidence intervals (CI), for different categories of BMI were obtained. We used the estimates adjusted for smoking and other confounding factors. If the RR or OR was expressed in more than one way, the estimate with greatest degree of controlling for confounders was used.

We first estimated the OR or RR associated with a unit increase in BMI (1 kg/m^2) for individual studies where the results were reported in categories of BMI. To treat BMI as a continuous exposure variable, its value was set at the midpoint of each category. For upper and lower open-ended categories of BMI, we assigned a value following the algorithms suggested by II'yasova et al. (2005). We subtracted the midpoint BMI of reference category from the midpoint BMI of all other categories. The natural logarithm of OR for the corresponding reference category was set to zero (corresponding to OR=1).

The OR associated with a unit increase in BMI was estimated using logit-linear (linear-logistic) model: $\phi(x, z) = \alpha + \beta x + \chi' z$; where 'x' is BMI, 'z' is the vector of confounders, and 'ϕ' is the log odds of being a case in the study versus being a control. The estimate ('β') [OR or RR=exp (β)] is computed using the weighted least squares method given by Greenland and Longnecker (1992).

After deriving the natural logarithm of the RR per unit of BMI for all the studies, we calculated a pooled estimate RRsum (RRsum and corresponding 95% CI) as a weighted average of the RRs (RRi), by giving a weight proportional to its precision (i.e., to the inverse of the variance of the RRi) [i.e. RR_{sum}=sum (weight$_i$ x ln RR_i)/sum (weight$_i$)]. To assess the consistency of findings among studies, we calculated test for heterogeneity using general variance-based method. i.e. Q= sum [weight$_i$ x(ln RR_{sum}–ln $RR_i)^2$]. Q is referred to the chi-square distribution with degrees of freedom equal to the number of studies minus 1. When the chi-square p-value is less than 0.1, we excluded studies with a high value of [weight$_i$ x (ln RR_{sum}– ln $RR_i)^2$] and then calculated RRsum and the corresponding 95% CI assuming a fixed-effect model (Petiti, 2000). Estimates based on cohort and case-control studies separately and combined were computed. The results of the meta-analysis along with the individual studies were presented graphically (forest plot), plotting RR and the respective 95% CI. The estimation was carried out using SAS programming language and the plotting was carried out using the Graph pad software.

Results

During 1992-2008, a total of 28 studies (15 cohort studies and 13 case-control studies) that provided kidney cancer risk according to BMI in women. A description of the main characteristics and results of each study are presented in Tables 1-2. Majority of the cohort studies (Hiatt et al., 1994; Prineas et al., 1997; Bjorge et al., 2004; Flaherty et al., 2005; Lindgren et al., 2005; Lukanova et al., 2006; Pischoon et al.,2006; Luo et al., 2007;Reeves et al., 2007; Setiawan et al., 2007; Adams et al., 2008; Song et al., 2008) and all case-control studies in the present review are based on incident cases of kidney cancer. Majority of the case-control studies are population–based (Kriger et al., 1993; Chow et al., 1996; Shapiro et al., 1999; Hu et al., 2003; Chiu et al., 2006; Pan et al., 2006) and a few studies are hospital-based (Benhamou et al., 1993; Maso et al., 2007).

In the majority of the cohort studies, height and weight for calculating BMI were obtained using self-administered questionnaire (Heath et al., 1997; Prineas et al., 1997; Calle et al., 2003; Flaherty et al., 2005; Lindgren et al., 2005; Pischon et al., 2006; Lukanova et al., 2006; Setiawan et al., 2007; Reeves et al., 2007; Adams et al., 2008; Song et al., 2008) except in a few studies where these variables were obtained through measurements (Bjorge et al., 2004; Luo et al., 2007). The ages of kidney cancer cases were between 20 and 79 in most of the studies (McCredie et al., 1992; Lindblad et al., 1994; Mellengaard et al., 1995; Chow et al., 1996; Heath et al., 1997; Yuan et al., 1998; Shapiro et al., 1999; Bjorge et al., 2004; Pischon et al., 2006; Pan et al., 2006; Maso et al., 2007). A few studies limited their ages between 40-64 years (Mclaughlin et al., 1992; Prineas et al., 1997; Hu et al., 2003; Flaherty et al., 2005; Chiu et al., 2006; Lukanova et al., 2006; Setiawan et al., 2007; Reeves et al., 2007; Luo et al., 2007; Song et al., 2008; Adams et al., 2008). Some studies provided only the mean age among cases and the same was between 50 to 64 years (Hiatt et al., 1994; Lindblad et al., 1994; Yuan et al., 1998; Calle et al., 2003; Bjorge et al., 2004; Lindgren et al., 2005; Song et al., 2008).

Cohort studies

Of the 15 cohort studies that investigated the association between BMI and kidney cancer risk after adjusted for age, smoking and other confounding factors, 11 studies reported a significant increased risk (RR ranged from 1.04 to 1.12) (Moller et al.,1994; Heath et al.,1997; Prineas et al.,1997; Calle et al., 2003; Bjorge et al., 2004; Flaherty et al., 2005; Pischon et al., 2006; Luo et al., 2007; Setiawan et al., 2007; Song et al.,2008; Adams et al.,2008), and the remaining studies reported increased risk with borderline significance (RR ranged from 1.02 to 1.05) (Hiatt et al.,1994; Flaherty et al., 2005; Lindgren et al.,2005; Lukanova et al., 2006; Reeves et al.,2007). The risk per unit increase in BMI could not be estimated in one study, as BMI category was not specified (Moller et al.,1994) and thus excluded the study for assessing the heterogeneity between studies. Significant association was observed in all the 6 studies that reported dose-response relationship between BMI and kidney cancer risk (Calle et al., 2003; Bjorge et al.,2004; Flaherty et al.,2005; Luo et al., 2007; Setiawan et al., 2007; Adams et al., 2008). No heterogeneity between the cohort studies was observed

Table 1. Association Between Body Mass Index and Kidney Cancer Risk in Women (Cohort Studies)

Author/Country	Category comparison	BMI[1] as a Category		BMI[1] as a Continuous Variable	
		RR	95% CI	RR	95% CI
Adams et al., 2008	22.5-25.0 vs. 18.5-22.5	1.11	0.74-1.65	1.05	1.03-1.08
USA	25.0-27.5 vs. 18.5-22.5	1.57	1.07-2.29		
	27.5-30.0 vs. 18.5-22.5	1.60	1.05-2.44		
	30.0-35.0 vs. 18.5-22.5	2.16	1.47-3.17		
	>35.0 vs. 18.5-22.5	2.59	1.70-3.96		
Song et al., 2008	23.0-24.9 vs. 18.5-22.5	1.64	0.66-4.06	1.12	1.03-1.21
Korea	25.0-26.9 vs. 18.5-22.5	2.16	0.88-5.30		
	27.0-29.9 vs. 18.5-22.5	2.12	0.81-5.58		
	>30.0 vs. 18.5-22.5	3.25	0.95-11.1		
Reeves et al., 2007	25.0-27.4 vs. 22.5-24.9	1.10	0.94-1.28	1.05	0.97-1.18
UK	27.5-29.5 vs. 22.5-24.9	1.19	0.99-1.44		
	vs. 22.5-24.9	1.52	1.31-1.77		
Setiawan et al., 2007	25.0-30.0 vs. <25.0	2.03	1.31-3.15	1.09	1.04-1.15
USA	>30.0 vs. <25.0	2.27	1.37-3.74		
Luo et al., 2007	25.0-29.9 vs. <25.0	1.30	1.00-1.80	1.04	1.02-1.07
USA	30.0-34.9 vs.<25.0	1.60	1.10-2.30		
	>35.0 vs. <25.0	1.80	1.20-2.70		
Lukanova et al., 2006	22.9-25.9 vs. 18.5-22.8	0.76	0.21-2.75	1.03	0.88-1.21
Sweden	>26.0 vs. 18.5-22.8	1.26	0.44-4.10		
Pischon et al., 2006	21.8-23.7 vs. <21.8	1.48	0.73-3.01	1.08	1.02-1.15
Europe	23.8-25.9 vs. <21.8	1.39	0.69-2.80		
	26.0-29.0 vs. <21.8	1.99	1.03-3.88		
	>29.1 vs. <21.8	2.25	1.14-4.44		
Lindgren et al., 2005	25.3-28.2 vs. <25.3	1.06	0.50-2.25	1.05	0.97-1.13
Finland	28.2-31.6 vs. <25.3	1.35	0.66-2.78		
	≥31.6 vs. <25.3	1.63	0.81-3.27		
Flaherty et al., 2005	22.0-24.9 vs. <22.0	1.30	0.90-2.00	1.09	1.05-1.15
USA	25.0-27.9 vs. <22.0	1.60	0.90-2.50		
	28.0-29.9 vs. <22.0	2.20	1.20-4.10		
	≥ 30.0 vs. <22.0	2.70	1.60-4.40		
Bjorge et al., 2004	25.0-29.9 vs. 18.5-24.9	1.21	1.21-1.45	1.04	1.03-1.05
Norway	>30.0 vs. 18.5-24.9	1.66	1.66-2.06		
Nicodemus et al.,2004	22.9-25.0 vs. < 22.9	0.80	0.38-1.65	1.10	1.04-1.16
USA	25.0-27.4 vs. < 22.9	1.46	0.77-2.74		
	27.4-30.6 vs. < 22.9	1.87	1.02-3.41		
	>30.6 vs. < 22.9	2.49	1.39-4.40		
Calle et al., 2003	25.0-29.9 vs. 18.5-24.9	1.33	1.08-1.63	1.10	1.02-1.19
USA	30.0-34.9 vs. 18.5-24.9	1.66	1.23-2.24		
	35.0-34.9 vs. 18.5-24.9	1.70	0.94-3.05		
	>40 vs. 18.5-24.9	4.75	2.50-9.04		
Heath et al., 1997	22.0-27.2 vs. 19.1-21.9	1.50	0.90-2.60	1.07	1.04-1.13
USA	27.3-32.2 vs. 19.1-21.9	2.50	1.40-4.40		
	≥32.3 vs. 19.1-21.9	3.10	1.50-6.40		
Primer et al.,1997 USA	>28.3 vs. <24.3	2.80	1.34-5.70	1.06	1.01-1.13
Prineas et al.,1997	24.3-28.3 vs. <24.3	2.36	1.13-4.93	1.09	1.06-1.12
USA	>28.3 vs. <24.3	2.77	1.34-5.70		
Hiatt et al., 1994 USA	> 27.8 vs. ≤21.8	1.20	0.40-4.30	1.02	0.93-1.13
Moller et al., 1994 Denmark	Obesity vs. normal[2]	2.00	1.50-2.60		
	Heterogeneity p-value =0.081		Summary RR	1.06	1.05-1.07

[1]BMI, body mass index; [2]Category not specified

(p=0.475). The pooled risk estimate was 1.06 (95% CI: 1.05-1.07) per unit increase in BMI (Table 1 and Figure 1).

Case-control studies

Of the 13 case-control studies that investigated the association between BMI and kidney cancer risk after adjusted for age, smoking and other confounding factors, 9 studies reported a significant increased risk (OR ranged from 1.06-1.17) (Mclaughlin et al.,1992; Kriger et al.,1993; Lindblad et al.,1994; Mellengaard et al., 1995; Chow et al., 1996; Shapiro et al., 1999; Hu et al., 2003; Chiu et al., 2006; Pan et al., 2006), and the remaining studies reported increased risk with borderline significance (OR ranged from 1.04-1.09) (McCredie et al., 1992; Benhamou et al., 1993; Yuan et al., 1998; Maso et al., 2007). Risk per unit increase in BMI could not be estimated in one study, as BMI category was not specified (Benichou et al., 1998) and thus excluded the study for assessing the heterogeneity between studies. Of the 3 studies (McCredie and Stewart 1992; Pan et al., 2006; Maso et al., 2007) that reported dose-response relationship

Table 2. Association Between Body Mass Index and Kidney Cancer Risk in Women (Case-control Studies)

Author/Country	Category comparison	BMI[1] as a Category		BMI[1] as a Continuous Variable	
		RR	95% CI	RR	95% CI
Maso et al., 2007[2]	25-29.99 vs. <25	1.21	0.82-1.79	1.04	0.99-1.10
Italy	>30 vs. <25	1.57	0.78-3.18		
Chiu et al., 2006[3]	21.18-23.01 vs. ≤21.17	0.50	0.20-1.10	1.07	1.03-1.11
USA	23.02-25.59 vs. ≤21.17	1.30	0.60-2.70		
	25.60-28.26 vs. ≤21.17	1.70	0.80-3.60		
	> 28.27 vs. ≤21.17	1.90	0.90-4.20		
Pan et al., 2006	25-29.99 vs. 18.5-25.0	1.68	1.24-2.27	1.09	1.05-1.13
Canada	>30.0 vs. 18.5-25.0	2.56	1.82-3.58		
Hu et al., 2003	25.0-29.99 vs. <18.5-24.99	1.50	1.20-1.90	1.07	1.05-1.09
Canada	30.0-34.99 vs. <18.5-24.99	2.50	1.90-3.40		
	35.0-39.99 vs. <18.5-24.99	2.70	1.70-4.40		
	≥ 40.00 vs. <18.5-24.99	3.80	2.30-6.40		
Shapiro et al., 1999	23.35-26.04 vs.<23.35	3.10	1.10-8.30	1.10	1.02-1.20
USA	26.05-30.08 vs.<23.35	3.00	1.10-8.00		
	>30.08 vs. <23.35	3.30	1.20-8.70		
Yuan et al., 1998	22.0-24.0 vs. <22.0	1.70	1.10-2.50	1.06	0.98-1.14
USA	24.0-26.0 vs. <22.0	1.50	0.96-2.30		
	26.0-28.0 vs. <22.0	1.30	0.70-2.20		
	28.0-30.0 vs. <22.0	2.30	1.00-4.20		
	30.0-32.0 vs. <22.0	4.00	2.30-7.00		
Chow et al., 1996[5]	26.89-28.45 vs. 26.75	1.40	0.60-2.90	1.13	1.05-1.20
USA	28.46-30.57 vs. 26.75	1.40	0.60-3.00		
	30.58-33.74 vs. 26.75	2.60	1.30-5.20		
	33.75-36.46 vs. 26.75	1.90	0.80-4.70		
	≥ 36.47 vs. 26.75	3.80	1.70-8.40		
Mellengaard et al., 1995[4]	29.2-32.2 vs. <29.2	1.20	0.90-1.70	1.1	1.06-1.13
Australia, Denmark,	32.2-36.9 vs. <29.2	1.80	1.30-2.40		
Germany, Sweden, USA	>36.9 vs. <29.2	2.50	1.80-3.50		
Lindblad et al., 1994[4]	22.6-24.6 vs. <22.6	1.62	0.79-3.33	1.08	1.04-1.12
Western Europe	24.7-27.9 vs. <22.6	2.22	1.06-4.63		
	>27.9 vs. <22.6	2.40	1.12-5.16		
Benhamou et al.,1993 France	≥27.0 vs. <20.0	3.50	1.00-11.8	1.09	0.98-1.20
Krieger et al., 1993 Canada	≥23.0 vs. <19.7	2.50	1.40-4.60	1.17	1.05-1.25
McCredie et al.,1992[5]	21.21-30.79 vs. <27.21	1.20	0.80-2.00	1.04	0.99-1.04
Australia	>30.79 vs. <27.21	1.30	0.80-2.10		
Mclaughlin et.al.,1992[5]	24.5-27.4 vs. <24.4	2.00	0.50-8.20	1.06	1.02-1.11
China	27.5-30.6 vs. <24.4	1.10	0.20-4.90		
	>30.6 vs. <24.4	3.30	0.70-15.1		
	Heterogeneity p-value =0.0643		Summary OR	1.07	1.06-1.08

[1]BMI: body mass index; [2]BMI at age 30 years; [3]BMI at age 40 years; [4]used maximal weight for BMI; [5]kg/m$^{1.5}$

between the BMI and kidney cancer risk, significant association was observed in 2 studies (McCredie and Stewart 1992; Pan et al., 2006). No heterogeneity between the case-control studies was observed (p=0.78). The pooled risk estimate was 1.07 (95% CI: 1.06-1.08) per unit increase in BMI (Table 2 and Figure 1).

Kidney cancer risk according to BMI among women in comparison with men

A total of 9 cohort studies and 13 case-control studies that provided kidney cancer risk in both gender and the risk per unit increase in BMI for these studies is provided in Table 3. Of the 9 cohort studies, 5 studies showed higher risk in women than men (Heath et al., 1997; Calle et al., 2003; Flaherty et al., 2005; Pischon et al., 2006; Setiawan et al., 2007) and one study showed almost similar risk in both gender (Adams et al., 2008). The pooled risk based on all cohort studies was 1.05 (95% CI: 1.04-1.06) and 1.04 (95% CI: 1.03-1.05) in women and men respectively. Of the 13 case-control studies, 5 studies reported higher risk (Kriger et al., 1993; Mellengaard et al., 1995; Chow et al.,1996; Chiu et al., 2006; Maso et al., 2007) and 4 studies reported almost similar risk in both gender (Mclaughlin et al.,1992; Lindblad et al.,1994; Hu et al., 2003; Pan et al., 2006). The pooled risk based on all the above case-control studies was same in men and women (OR=1.07, 95%CI: 1.06-1.08).

Discussion

The results of this meta-analysis indicated an increased kidney cancer risk with increased BMI in women. In a recent quantitative summary analysis by including 13 cohort studies, which were published during the past decade, it is reported that 5% increased risk for kidney cancer per unit of increase in BMI in men (Ildphonse et

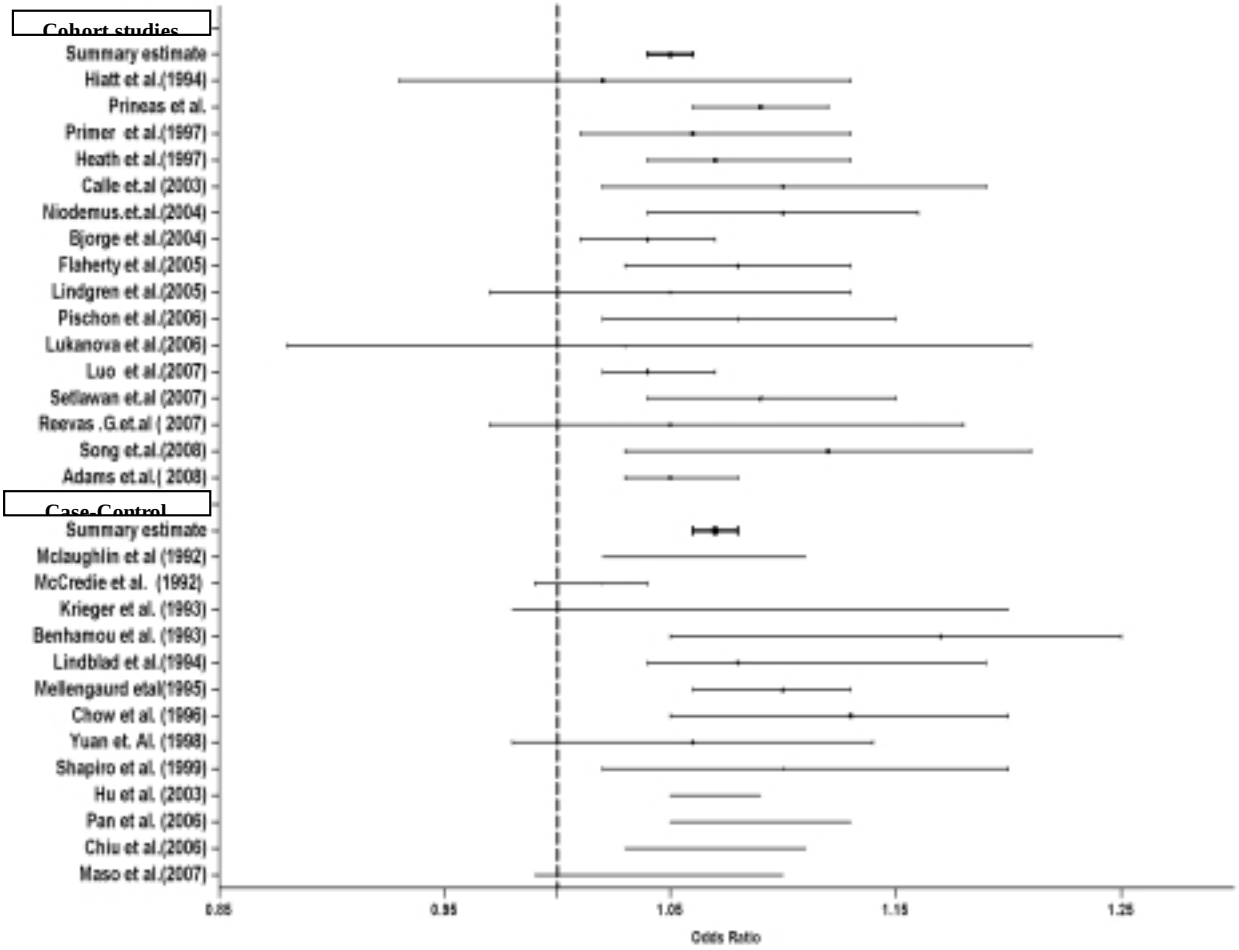

Figure 1: Results of the Reanalysis and Summary Analysis of Published Studies on the Association between Body Mass Index (BMI) and Kidney Cancer Risk among Women. Relative risk per unit increase in BMI (1 kg/m^2) and 95% confidence intervals (CI)

al., 2009). In the present similar analysis, by including 15 cohort studies, a slightly increased pooled risk (6%) was observed in women. Several studies have reported higher kidney cancer risk due to obesity in women than men (Kriger et al., 1993; Mellengaard et al., 1995; Chow et al.,1996; Heath et al., 1997; Calle et al., 2003; Flaherty et al., 2005; Chiu et al., 2006; Pischon et al., 2006; Maso et al., 2007; Setiawan et al., 2007). The present meta

Table 3. Association between Body Mass Index and Kidney Cancer Risk: Women vs. Men (ORs and 95%CIs)

Study type	Author, year	Country	Women		Men	
Cohort studies	Adams et al., 2008	USA	1.05	1.03-1.08	1.05	1.03-1.07
	Setiawan et al., 2007	USA	1.09	1.04-1.15	1.04	0.98-1.09
	Lukanova et al., 2006	Sweden	1.03	0.88-1.21	1.06	0.98-1.14
	Pischon et al., 2006	Europe	1.06	1.02-1.15	1.03	0.96-1.08
	Flaherty et al., 2005	USA	1.09	1.05-1.15	1.04	0.94-1.15
	Bjorge et al., 2004	Norway	1.04	1.03-1.06	1.05	1.03-1.07
	Calle et.al., 2003	U.S	1.10	1.02-1.19	1.02	0.99-1.05
	Heath et al., 1997	USA	1.07	1.04-1.13	1.06	1.02-1.10
	Hiatt et al.,1994	USA	1.02	0.93-1.13	1.05	0.95-1.16
Case-control studies	Maso et al., 2007	Italy	1.04	0.99-1.10	1.03	0.98-1.08
	Chiu et al., 2006	USA	1.07	1.03-1.11	1.05	1.00-1.10
	Pan et al., 2006	Canada	1.09	1.05-1.13	1.09	1.06-1.13
	Hu et al., 2003	Canada	1.07	1.05-1.09	1.07	1.05-1.09
	Shapiro et al., 1999	USA	1.10	1.02-1.20	1.15	1.06-1.25
	Yuan et al., 1998	USA	1.06	0.98-1.14	1.11	1.01-1.21
	Chow et al., 1996	USA	1.13	1.05-1.20	1.04	0.98-1.10
	Mellengaard et al.,1995	Western world	1.11	1.05-1.18	1.08	1.05-1.12
	Lindblad et al., 1994	Western Europe	1.08	1.04-1.12	1.08	0.96-1.22
	Benhamou et al., 1993	France	1.09	0.98-1.20	1.11	1.04-1.75
	Krieger et al., 1993	Canada	1.17	1.05-1.25	1.05	0.97-1.10
	McCredie et al., 1992	Australia	1.04	0.99-1.04	1.10	1.04-1.17
	Mclaughlin et.al., 1992	China	1.06	1.02-1.11	1.06	1.02-1.11

analysis supports this result. It is reported that the prevalence of obesity has increased to epidemic proportion in recent decades in many populations with higher proportion of increase among women (Abubakari et al., 2008; Lilja et al., 2008; Matsushita et al., 2008; Wilman et al., 2008; Chen et al., 2009) and this increasing prevalence might therefore, at least, explain the increasing incidence of kidney cancer.

In the present review, higher risks were observed in most of the case-control studies compared to the cohort studies with a wider variation in the risks (OR ranged from 1.04-1.17). This points to the presence of selection bias in case-control studies. Moreover, odds ratios always show slightly overestimated figures than risk ratios. These might be the reasons for higher risks reported in case-control studies.

The major strength of the present analysis is that several cohort studies were included, as cohort studies are in principle the most valid study design in observational studies. A total of 15 cohort studies were included in the present analysis as against 3 by Bergstrom et al. (2001). In the present analysis we observed a lower risk (RR=1.06) with a narrow 95% confidence interval (95% CI: 1.04-1.07) as against the previous review (RR=1.07; 95%CI: 1.04-1.09) (Bergstrom et al., 2001).

Another strength of the present analysis was that the individual studies were controlled for a varying degree of confounders. Even though cigarette smoking is consistently reported with an increased risk of kidney cancer (Hu et al., 2003; Flaherty et al., 2005; Pan et al., 2006; Pischon et al., 2006) smoking was not adjusted in four studies (McCredie and Stewart 1992; Shapiro et al., 1999; Lindgren et al., 2005; Adams et al., 2008). Prevalence of smoking may be low in these populations and thus the reason for not being included as a confounder. Other confounders included in various studies were hypertension (Chow et al., 1996; Heath et al., 1997; Shapiro et al., 1999; Flaherty et al., 2005; Lindgren et al., 2005; Chiu et al., 2006; Luo et al., 2007; Setiawan et al., 2007), socio-economic status (Reeves et al.,2007; Song et al., 2008), alcohol use (Calle et al., 2003; Hu et al., 2003; Pan et al., 2006; Pischon et al., 2006; Reeves et al., 2007; Setiawan et al., 2007; Song et al., 2008), family history of kidney cancer (Chiu et al.,2006; Maso et al., 2007), physical activity (Calle et al., 2003; Pan et al., 2006; Pischon et al., 2006; Setiawan et al., 2007; Reeves et al., 2007; Song et al., 2008), energy intake (Calle et al., 2003; Chiu et al., 2006; Pan et al., 2006; Luo et al., 2007), meat intake (Hu et al., 2003; Chiu et al., 2006), fruits and vegetables intake (Calle et al., 2003; Hu et al., 2003; Chiu et al., 2006; Pan et al., 2006), use of hormone replacement therapy (Calle et al., 2003; Pischon et al., 2006; Reeves et al., 2007), oral contraceptive use (Luo et al., 2007) and diabetes mellitus (Shapiro et al., 1999).

There can be several arguments in favour of a causal relationship between obesity and the occurrence of kidney cancer. Similar to the risk observed in men (Ildaphonse et al., 2009), an increased risk was observed in all the studies in which we performed a meta-analysis. In addition to the consistency and strength of association, a dose-response relationship was observed in most of the studies. Further a biologic plausibility exists, as obesity might be associated with increased risk of kidney cancer through several hormonal mechanisms (Hall et al., 1994; Frystyk et al., 1995; Kellerer et al., 1995; Moyad 2001). Obesity could also have other effects on the kidneys. Obese individuals have been reported to have higher glomerular filtration rate and renal plasma flow independent of hypertension, which may increase risk for kidneys damage (Hall et al., 1994; Ribstein et al., 1995), and therefore make the kidney more susceptible to carcinogens.

The main limitation of summary analysis concerns the possibility that the included studies may be a biased sample of studies in general, since findings of no association are more likely to be unpublished. Another concern is that not all published studies during the period 1992-2008, provided results that could be included in the summary analysis as the specific categories of BMI was not provided (Moller et al., 1994; Mellengaard et al., 1994; Benichou et al., 1998; Nicodemus et al., 2004; Pan et al., 2004; VanDijk et al., 2004; Spyridopoulos et al., 2007). However, all these studies were also reported an increased risk with increased BMI.

Another potential limitation of the present findings is that majority of the studies in the summary analysis used height and weight using self-administered questionnaire. Although such data have been shown to be quite accurate, obese subjects in general under-report, their weight more than non-obese subjects while underweight subjects overestimate their body size. This might lead to non-differential misclassification, which, if anything, only underestimates the true association between obesity and kidney cancer risk and therefore cannot explain the finding of a positive association (Rothman and Greenland 1998). The possibility of differential misclassification (recall bias -i.e. case subjects might report their weight differently than control subjects) may be possibility in the case-control studies, but the consistency of findings from the cohort studies and the case-control studies is a strong argument against recall bias.

In conclusion, the pooled analysis reported a slightly higher kidney cancer risk due to obesity in women than men. Increasing prevalence of obesity with higher proportion among women may be responsible for the rising incidence rates in women.

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