Specialist Medical Review Council

Declaration and Reasons for Decisions

Section 196W
Veterans' Entitlements Act 1986

Re: Statements of Principles Nos. 53 and 54 of 2014
in respect of Malignant Neoplasm of the Prostate

Request for Review Declaration No. 30

APPENDICES

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APPENDIX A – META-ANALYSES

Tobacco smoking and prostate cancer incidence: a meta-analysis

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1. Background

This meta-analysis of the literature was conducted to inform the deliberations of the Specialist Medical Review Council (SMRC) as it considered an application for review of the contents of the Statement of Principles (SoPs) prepared by the Repatriation Medical Authority (RMA).

2. Methods

Three groups of studies were considered for inclusion in the meta-analyses conducted in this report:

Group 1 - The first group of studies that were considered for inclusion in the meta-analyses were those studies available to the RMA in 2014. The purpose of the meta-analyses on this group of studies was to determine the relationship between cigarette smoking and prostate cancer incidence through pooled quantitative analysis of studies, in a more precise way than any individual study. In the application for review, the applicant identified a literature review by Huncharek et al. [1] Huncharek et al. reviewed 16 studies in relation to smoking and prostate cancer incidence; 15 of these were available to the RMA. The one study not available to the RMA was by Allen et al. [2]. The Allen et al. study consisted of a sample of atomic-bomb survivors recruited from Nagasaki and Hiroshima, Japan. A different study by Kondo et al. [3] of atomic-bomb survivors recruited from Nagasaki, Japan, was available to the RMA that reported more comprehensive smoking dosage data than Allen et al. The RMA had available additional studies to Huncharek et al (refer to Table 2 to 7). Some of the additional studies available to the RMA were more recent than those reviewed by Huncharek et al.

Group 2 - the second group of studies that were considered for inclusion in the meta-analyses were those reviewed by Islami et al. [4]. Islami et al. considered some studies that were not available to the RMA. The purpose of the meta-analyses on this group of studies was to validate the Islami et al. findings.

Group 3 - the third group of studies included both available studies and the Islami et al. reviewed studies. The purpose of the meta-analyses on this group of studies was to determine if the outcome of the meta-analyses of the first group of studies, those available to the RMA in their 2014 review, would differ with the inclusion of more recently published data, from Group 2.

For all studies within the three groups identified above, data on incidence of prostate cancer were extracted by smoking status (i.e. never/former/current smoker) where possible. For each group of studies, the following comparisons for the association between cigarette smoking and prostate cancer incidence were conducted:

- “Ever”(Former + Current) with “Never” smokers
- “Current” with “Never” smokers
- “Current” with “Non-current”(Never + Former) smokers
- “Current” with “Ex” (Former) smokers

For each comparison of smoking status, the following six models of meta-analyses were conducted when possible:

- Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results
- Model **B** included studies with age-only adjusted data available
- Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates
- Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates
- Model **E** included studies with multivariate adjustment (highest number of covariates)

- Model **F** included studies with non-adjusted raw data

In addition to the main analyses, two other sets of meta-analyses were conducted to examine effects on the relationship between cigarette smoking and prostate cancer incidence. The first considered the effect of the amount of cigarette smoked (i.e. dosage) and the second considered the impact of the introduction of Prostate Specific Antigen (PSA) screening. The Islami et al. results were not validated for this analysis as there were no significant differences found in the main meta-analyses. Only model D and E were considered in these analyses as they represent the models that more comprehensively consider the impact of other covariates than the other models and no significant differences were found in the conclusions drawn between all the models from in the main analyses to warrant inclusion of them all in the secondary analyses.

Cigarette smoking dosage was inconsistently recorded among studies. The categories used in the meta-analysis outline described below were chosen to maximise the number of studies that could be included while still allowing for a dose-response relationship to be considered. Some studies were included that overlapped slightly (+/- 5 cigarettes per day or 5 pack years) other categories. Where this was the case, it is noted with the corresponding forest plot.

When considering the relationship between smoking dosage of cigarettes per day and prostate cancer incidence, the RMA considered the same studies that were considered by Islami et al., therefore, only a combined analyses was conducted (i.e., Group 3 - RMA + Islami et al. studies). The following comparisons for the association between cigarette smoking dosage and prostate cancer incidence were conducted:

- “Current” (<10 cigarettes/day) with “Never” smokers
- “Current” (10-19 cigarettes/day) with “Never” smokers
- “Current” (20+ cigarettes/day) with “Never” smokers

For Group 1 (RMA only studies) and Group 3 (RMA + Islami et al. studies), the following comparisons for the association between cigarette smoking cumulative dosage and prostate cancer incidence were conducted:

- “Current” (<20 pack/years) with “Never” smokers
- “Current” (20-40 pack/years) with “Never” smokers
- “Current” (40+ pack/years) with “Never” smokers

For groups 1 (RMA only studies) and 3 (RMA + Islami et al. studies), the following comparisons for cigarette smoking and prostate cancer incidence before and after the introduction of PSA screening were conducted:

- “Current” with “Never” smokers in studies with completed follow-up data before 1990
- “Current” with “Never” smokers in studies with completed follow-up data from 1990 onwards

The following table 1 is a summary of the meta-analyses conducted for this report:

Table 1 Summary of meta-analyses conducted for the studies available to the RMA and Islami et al.

	Ever Vs Never	Current Vs Never	Current Vs Non-current	Current Vs Ex	Current (<10 cigarettes/day) Vs Never	Current (10-19 cigarettes/day) Vs Never	Current (20+ cigarettes/day) Vs Never	Current (<20 pack/years) Vs Never	Current (20-40 pack/years) Vs Never	Current (40+ pack/years) Vs Never	Current Vs Never in studies with follow-up data before 1990	Current Vs Never in studies with follow-up data from 1990 onwards
Group 1: studies reviewed by RMA	**A, B, C, D, E, F**	**A, B, C, D, E, F**	**F**	**F**				**D, E**	**D, E**	**D, E**	**D, E**	**D, E**
Group 2: studies reviewed by Islami et al.	**A, B, C, D, E, F**	**A, B, C, D, E, F**	**F**	**F**								
Group 3: studies reviewed by RMA and Islami et al.	**A, B, C, D, E, F**	**A, B, C, D, E, F**	**F**	**F**	**D, E**	**D, E**	**D, E**	**D, E**	**D, E**	**D, E**	**D, E**	**D, E**

Note: Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with

age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data

Data extraction, treatment and statistical analysis

When reported, raw data (including number of prostate cancer cases and non-cases by smoking status) and adjusted data (including age-adjusted and multivariate-adjusted measures of risk, together with 95% confidence intervals (CIs)) were extracted. When it was not reported, the following data treatment decisions were made as suggested by Islami et al.:

1. For studies that reported on both former and current tobacco use, results on ever tobacco use were calculated by combining the results for former and current users. If studies only reported on current tobacco use, current users were considered as ever users.
2. When relative risk ratio (RR) and 95% CI for current or ever tobacco consumptions were not reported but RRs and 95% CIs for several categories of quantitative use among current users or among current and former users were available, a fixed effects meta-analytic approach was used to calculate the combined risk estimated for current or ever tobacco consumption, respectively.
3. If adjusted RRs were reported without 95% CIs, then the unadjusted 95% CIs were calculated using frequency distributions and the standard error of the unadjusted RR was multiplied by 1.5.
4. If 90% CIs were reported then they were converted to 95% CIs.

Information on author(s), year of publication, study design, location, participant group, age at entry, study period, length of follow-up, characteristics of smoking data collection, and adjustments used in the analysis, were also extracted (see tables 2 to 5). Risk of bias in each of the studies was assessed using the Quality Assessment tool [5]. The tool was adapted from the Newcastle-Ottawa tool for quality assessment of clinical cohort studies, nested case-control studies and case-control studies for use in the Prostate Cancer Foundation of Australia and Cancer Council Australia - *Development of Clinical Practice Guidelines for PSA Testing and Early Management of Test-Detected Prostate Cancer*. The number of low risk, moderate risk and high risk items, and overall risk of bias was determined for each study using this this tool and is presented in tables 2 to 5.

Results from studies reported by the same or similar authorship teams were scrutinised to determine if multiple publications reported on the same population, to ensure such studies were not combined in meta-analyses. When similar studies were identified, the study that included higher quality smoking variable data was included in the meta-analyses.

In all analyses, the main outcome (prostate cancer incidence) was treated as a binary outcome. Data were analysed using the OpenMeta[6] software, which is open-source software developed with funding from AHRQ (Agency for Healthcare Research and Quality), U.S. Department of Health and Human Services (grant number: R01HS018574[6]). If non-adjusted or adjusted risk estimates were not available, the summary non-adjusted risk estimates (Relative risks, including odds ratios (OR) and hazard ratios (HR)) and 95% CIs were calculated from the raw data available. When non-adjusted and adjusted risk estimates were used, the lower 95% CI was re-calculated based on the risk estimate and the upper 95% CI. Forest-plots were plotted using random effects models (DerSimonian-Laird method). Random-effects analyses were chosen as it was assumed that the effect would not be the same in all studies.

3. Results

Overview of meta-analyses

Tables 2 to 5 summarise 51 studies considered in the meta-analyses, with characteristics of the studies, risk of bias, and data for each of the smoking exposure measurements. Table 2 summaries the studies included in the meta-analyses for the association between ever cigarette smoking and prostate cancer incidence using “never” smokers as reference group. Table 3 summaries the studies included in the meta-analyses for the association between current cigarette smoking and prostate cancer incidence using “never” smokers as the reference group. Table 4 summaries

the studies included in the meta-analyses for the association between current cigarette smoking and prostate cancer incidence using non-current smokers as reference group. Table 5 summaries for the association between current cigarette smoking and prostate cancer incidence using former smokers as the reference group.

Table 6 summaries the studies included in the meta-analyses for the association between current cigarette smoking (<10, 10-15, 20 or more cigarettes per day) and prostate cancer incidence using "never" smokers as the reference group. Table 7 summarises the studies included in the meta-analyses for the association between current cigarette smoking (<20, 20 to 40, 40 or more pack years) and prostate cancer incidence using "never" smokers as reference group.

The meta-analyses in this report are reported on in eight sections (sections 3.1 to 3.8). Sections 3.1 to 3.3 report on the association between cigarette smoking and prostate cancer incidence. Section 3.1 reports on the meta-analyses of studies available to the RMA. Section 3.2 reports on the meta-analyses of studies reviewed by Islami et al. Section 3.3 reports on the meta-analyses of studies reviewed by both the RMA and Islami et al.

In sections 3.1 to 3.3, the meta-analyses are presented for the following comparisons for the association between cigarette smoking and prostate cancer incidence:

- "Ever" (Former + Current) with "Never" smokers
- "Current" with "Never" smokers
- "Current" with "Non-current" (Never + Former) smokers
- "Current" with "Ex" (Former) smokers

Each comparison is evaluated in up to six models (Figures A to F) to consider the impact of adjustment on the relationship between smoking and prostate cancer incidence.

Section 3.4 reports on the meta-analyses of the studies available to the RMA and Islami et al. for the association between cigarette smoking dosage (<10, 10-15, 20 or more cigarettes per day) and prostate cancer incidence.

Sections 3.5 and 3.6, report on the meta-analyses of the association between cigarette smoking cumulative dosage (<20 pack years, 20 to 40 pack years, 40 or more packs years) and prostate cancer incidence. Section 3.6 reports on the meta-analyses of the studies available to the RMA and section 3.7 reports on the meta-analyses of the studies available to the RMA and Islami et al.

Sections 3.8 and 3.9, report on the meta-analyses of the association between cigarette smoking and prostate cancer incidence considering the effect of Prostate Specific Antigen (PSA) screening. Section 3.8 reports on the meta-analyses of the studies available to the RMA and section 3.9 reports on the meta-analyses of the studies available to the RMA and Islami et al.

Table 2 Studies included in meta-analyses for the association between cigarette smoking ("ever" [former + current] smokers with "never" smokers) and prostate cancer incidence

First author	Year	Rev-RMA ID	Design	Location	Subjects	Data	Total cases	Total pop./ controls	PSA	Adjustment	Bias Risk	Never smoked/Non-smoker**		Ever (former + current)				
												Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI	
Adami [7]	1996	RIH-016355	Cohort	Sweden	Construction workers	B	2,368	135,006	>	A	H	39,636	682	*93,002	*1,686	*1.10	*1.02	*1.18
Alavanja [8]	2003	RO- 029275	Cohort	US	Pesticide applicators in Iowa & North Carolina	U^	566	55,332	>	A, E, R, Edu, PcaM, BM, D, VitSup, PA, CE	L	25,159	195	*24,052	*295	*1.34	*1.04	*1.73
Andersson	1996	RO- 012174	Case-control	Sweden	General population <80	N/A	256	252	>	A	H	86	68	*139	*167	*1.55	*1.12	*2.14
Bae [9]	2013	RI- 70206	Cohort	South Korea	General population	B	87	14,450	>	A	H	3,169	29	*10,891	*57	*0.65	*0.40	*0.90
Baglietto [10]	2006	IO	Cohort	Australia	General population	B	732	16,872	>	None	H	6,605	291	*9,534	*430	*0.94	*0.81	*1.07
Band	1999	RO- 017379	Case-control	Canada	General population ≥20	N/A	1516	4994	>	None	H	987	352	**3,920	**1,134	*0.85	*0.77	*0.95
Barba	2004	RO- 033231	Case-control	USA	General population	N/A	88	272	>	None	H	*77	*21	*195	*67	*1.19	*0.77	*1.84
Butler [11]	2009	RI- 065154	Cohort	Singapore	General Population 45-74	B	250	27,293	>	A, SDV, Edu, BioM, D	L	11,409	108	*15,634	*142	*0.95	*0.74	*1.16
Cerhan [12]	1997	RIH- 016660	Cohort	US	Men in Iowa 65 +	U	71	1050	>	A, BM, PA A	M	411	26	*568	*45	*1.70 *1.40	*1.14 *0.70	*2.53 *2.00
Darlington	2007	RO- 065148	case-control	Canada	General population in Ontario 50-84	N/A	752	1613	>	A, FHx, BM, Edu, O	H	373	158	*1,222	*587	*1.13	*0.93	*1.38
Dillner [13]	1998	RO- 16118	Nested	Finland	General population	B	165	290	>	None	H				109	0.79	0.50	1.24
Engeland [14]	1996	RIH- 009479	Cohort	Norway	General population	B	707	11,863	>	A	H	1,878	139	*9,278	*568	*1.00	*0.90	*1.30
Everatt [15]	2014	RO- 71303	Cohort	Lithuania	General population 40-59	B	336	6976	>	A, Edu, AC, BM A	M	1,997	137	*4,643	*199	*0.86 *0.86	*0.72 *0.71	*1.04 *1.04
Fincham	1990	RO- 007481	Case-control	Canada	General population ≥45	N/A	382	625	<	None	H	153	106	*472	*276	*0.90	*0.76	*1.07
Friedenreich	2003	RO- 030566	Case-control	Canada	General population in Alberta <80	N/A	988	1063	>	A	H	*318	*275	744	713	1.10	0.91	1.34
Furuya	1998	RO- 013932	Case-control	Japan	Patients in Chiba University Hospital	N/A	329	190	>	None	H	*90	*157	100	172	*0.99	*0.87	*1.13
Geybels [16]	2012	IO	Cohort	The Netherlands	General population 55-69	B	3,451	58,279	>	A, SM	M		492		*2,957	*1.01	*0.88	*1.13
Giles	2001	RO- 029017	Case-control	Australia	Australian citizens with a histopathologically confirmed diagnosis of adenocarcinoma ≤70	N/A	1476	1409	>	A, FHx, calendar year, study centre, country of birth	H	486	540	923	936	0.96	0.81	1.14
Giovannucci [17]	2007	RIH- 065156	Cohort	US	Health professionals *(see Giovannucci et al. 1999)*	U	3,544	47,750	>	A, PcaM, BM, Ht, PA, CB, E, D, VitSup	L					0.98	0.89	1.07
Giovannucci [18]	1999	RH- 017143	Cohort	US	Health professionals	U	1,369	47,781	>	A, BM, D	L		580		*789	*1.01	*0.92	*1.11
Gonzalez [19]	2007	IO	Cohort	US	General population 50-76	U^	832	35,244	>	A	H	13,211	303	*20,636	*516	*0.94	*0.82	*1.05
Gronberg [20]	1996	RO- 007192	Nested	Sweden	Unmatched twins	B	406	1,218	<	A	H	321	117	*738	*249	*0.95	*0.76	*1.18
Grundmark [21]	2011	IO	Cohort	Sweden	General population	B	208	2,045	>	None	H	449	69	*1388	*139	*0.67	*0.50	*0.83
Hakulinen [22]	1996	RO- S2.6	Cohort	Finland	"Cohort I" and "Cohort II"; General population	B	(1)209	(1)4,601	>	None	H	900	62	*3,492	*147	*0.63	*0.47	*0.84
							(II)109	(2)11,373		None		2,114	17	*9,150	*92	*1.25	*0.75	*2.09
Hayes	1994	RO- 003265	Case-control	USA	Black and White males in Atlanta, Detroit and New Jersey 40-79	N/A	981	1315	<	A, study site, race	H	**265	**174	**916	**709	*1.15	*0.96	*1.38

Table 2 Studies included in meta-analyses for the association between cigarette smoking ("ever" [former + current] smokers with "never" smokers) and prostate cancer incidence - continued

First author	Year	Rev-RMA ID	Design	Location	Subjects	Data	Total cases	Total pop./ controls	PSA	Adjustment	Bias Risk	Never smoked/Non-smoker**		Ever (former + current)				
												Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI	
Heikkila [23]	1999	RI- 018599	Nested	Finland	General population *(see Dillner et al. 1998)*	B	166	16,481 /300	<	None	H	188	114	112	52	*1.31	*0.87	*1.95
Heikkila [24]	2013	IO	12 studies	Europe	Data from 12 studies	N/A	865	116,056	>	A, SES, BM, AC	N/A	**83,805	**706	26,486	159	0.70	0.59	0.84
Helzlsouer [25]	2000	RO- 028981	Nested	US	General population	B	117	233	>	None	H	98	48	*135	*69	*1.03	*0.76	*1.39
Hiatt [26]	1994	RIH- 003316	Cohort	US	Health plan members	U^	238	43,432	<	A, E, AC, Edu	M	14,340	79	*25,960	*143	*1.10	*0.90	*1.40
Honda [27]	1988	RO- 003308	Case-control	US	General population <60	N/A	216	216	<	None	H	69	44	*146	*171	*1.39	*1.08	*1.78
Hsing	2000	RO- 029107	Case-control	China	Permanent residents in Shanghai without a history of any other cancer >18	N/A	238	471	>	None	H	174	100	*297	*138	*0.87	*0.71	*1.07
Huang	2003	RO- 028931	Case-control	USA	CLUE I and CLUE II cohort; General population	B	(I) 182	(I) 364	>	None	H	*125	*61	*239	*121	*1.02	*0.80	*1.32
							(II)142	(II) 284	>	None	H	*117	*55	*167	*87	*1.07	*0.81	*1.41
Hultdin [28]	2005	IO	Nested	Sweden	General population	U	254	514	>	None	H	230	115	*229	*124	*1.08	*0.79	*1.48
Karlsen [29]	2012	IO	Cohort	Denmark	General population	B	129	20,914	>	None	H	**12,954	**81	7,515	48	*1.00	*0.70	*1.43
Karppi [30]	2012	IO	Cohort	Finland	General population 42, 48, 54, or 60	B	68	997	>	None	H	**660	**57	269	11	*0.85	*0.76	*0.95
Karunasinghe [31]	2012	RO- 066733	Case-control	New Zealand	General population 40-81	B	275	441	>	None	H	273	127	168	140	1.79	1.32	2.44
Key	1997	RO- 012167	Case-control	UK	White male <75	N/A	328	328	>	None	H	82	79	*246	*249	*1.03	*0.86	*1.23
Kondo [3]	2013	RO- 70205	Cohort	Japan	Atomic-bomb survivors	B	631	18,409	>	A, SM, CE, AC	M	6,104	272	*11,674	*359	*0.69	*0.59	*0.81
Koutros [32]	2013	IO	Nested	US	General population 55-74	U^	1,122	1,112	>	None	H	313	398	*699	*623	*0.70	*0.58	*0.84
Le Marchand [33]	1994	RIH- 3179	Cohort	US	General Hawaiian population	B	198	8,881 of 20,316	>	A, E, I	M					*1.00	*0.70	*1.20
Lemogne [34]	2013	IO	Cohort	France	Workers in energy industry	U	412	10,506	>	A, O, AC, D, BM, PA, HS	L					*0.86	*0.73	*1.00
Lotufo [35]	2000	RIH- 28974	Cohort	US	Health professionals	U	996	22,071	>	A, Rx, PA, BM, Ht, AC	M	10,466	443	*10,523	*553	*1.10	*0.97	*1.28
Lumey	1997	RO- 011775	Case-control	US	White males	N/A	1,097	3,250	>	A, MS, O, AS, Edu, Religion	H	816	296	*2,434	*801	*0.90	*0.80	*1.01
Magura	2008	RO- 065151	Case-control	USA	General population from Meritcare hospital, North Dakota 50-74	N/A	312	319	>	None	H	146	130	*173	*182	*1.09	*0.93	*1.28
Mills [36]	1989	RIH- 003320	Cohort	US	Adventists	B	180	14,000	<	A	H		90		*82	*1.07	*0.74	*1.41
Murphy [37]	2013	RO- 70207	Case-control	US	Men from urology clinics	N/A	527	558	>	A, SDV, E, FHx, AC	M	281	233	*277	*293	*1.28	*1.00	*1.62
Nilsen [38]	2000	RIH- 029140	Cohort	Norway	General population	B	644	22,895	>	A	H	6,094	222	*12,388	*336	*0.97	*0.84	*1.12
Nomura [39]	2000	RI- 029108	Nested	US	Japanese Hawaiians	B	249	249 of 9413	>	A	H	98	87	*150	*162	*1.25	*0.93	*1.67
Norrish	1998	RO- 016995	Case-control	New Zealand	Male residents in Auckland 40-80	N/A	317	480	>	None	H	137	94	*342	*223	*0.97	*0.81	*1.17
Onitilo [40]	2013	IO	Cohort	US	Men from health clinics	B	3,432	33,832	>	None	H	389			921	**0.85	**0.76	**0.95

Park [41]	2007	IO	Cohort	US	Multiethnic general population >45	B	4,404	82,483	>	None	H	23,419	1,326	54,665	3,073	*0.99	*0.93	*1.06
Parker [42]	1999	RI- 017444	Cohort	US	Men in Iowa (see Putnam et al. 2000)	B	81	1,177	>	A	H		23		*58	*1.49	*1.02	*2.18

Table 2 Studies included in meta-analyses for the association between cigarette smoking ("ever" [former + current] smokers with "never" smokers) and prostate cancer incidence - continued

First author	Year	Rev-RMA ID	Design	Location	Subjects	Data	Total cases	Total pop./ controls	PSA	Adjustment	Bias Risk	Never smoked/Non-smoker**		Ever (former + current)				
												Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI	
Plaskon [43]	2003	RO-28497	Case-control	US	White & Black 40--64	N/A	753	703	>	A, E, FHx, PcaM	M	266	281	*437	*472	*1.1	*0.91	*1.33
Putnam [44]	2000	RH- 29009	Cohort	US	Men in Iowa	B	101	1,572	>	A	H		24		*77	*1.21	*0.83	*1.75
Rohan	1997	RO- 013929	Case-control	Canada	Recently diagnosed males from Ontario Cancer Registry and British Columbia Cancer Registry	N/A	408	407	>	A, study site	H	124	89	*274	*313	*1.57	*1.20	*2.05
Rohrmann [45]	2007	RIH-065219	Cohort	US	General population	U	(1)147	26,810	>	A	H	3,850	34	*19,504	*88	*1.16	*0.84	*1.6
							(2)351	28,292				5,688	94	*18,789	*213	*1.01	*0.83	*1.24
Rohrmann [46]	2013	RI- 065978	Cohort	Europe	General population	B	4,623	145,112	>	A, Ht, W, Edu, MS, PA	M		1,547		*3,076	*0.93	*0.89	*0.98
Ross (in Wald [47])	1990	RO- 7210	Cohort	US	Retirement community	B	138	5,106 of 13,987	<	A	H		56		*82	*0.82	*0.61	*1.09
Sawada [48]	2014	RI- 70208	Cohort	Japan	General population 40-69	B	913	48,218	>	A, SDV, BM, MS, AC, CB, D A, SDV	M	11,062	257	*36,252	*647	*0.80 *0.86	*0.72 *0.81	*0.89 *0.91
Severson [49]	1989	RIH-003251	Cohort	US	Japanese Hawaiians	B	174	7,999	<	A	H	2,341	63	*5,483	*111	*0.88	*0.65	*1.11
Shafique [50]	2012	RO- 066019	Cohort	Scotland	Two studies: (1) workers 21-75 (2) General Population	B	650	12,276	>	A, BM, SES, BioM	M	2,093	149	*10,182	*501	*0.94	*0.80	*1.10
Shafique [51]	2012	IO	Cohort	UK	General population *(see study 2 of Shafique et al. 2012)*	B	318	6,017	>	A, BioM, BM, AC, D, SES A, SES	M	1,026	68	*4,672	*250	*1.08 *1.17	*0.84 *0.94	*1.32 *1.45
Slattery	1993	RO- 003266	Case-control	USA	White male in Utah 45-74	N/A	362	685	<	None	H	**333	**167	**346	**191	*1.06	*0.90	*1.26
Stattin	2000	RO- 029289	Nested Case-referent	Sweden	General population from two counties 25-74	B	149	298	>	None	H							
Thompson [52]	1989	RIH- 003253	Cohort	US	White upper-middle class	B	54	1,776	<	A, CB, BM, D, BioM	L				11	1.3***	*0.70	*2.50
Veierod [53]	1997	RIH-16633	Cohort	Norway	General population	B	72	24,051	>	A	H		24		*45	*0.60	*0.30	*0.80
Villencuve	1999	RO- 018446	Case-control	Canada	General population from 8 provinces 50-74	N/A	1623	1623	>	(I) A, R	H	**344	**372	**1,261	**1,235	*0.92	*0.82	*1.03
										(II) A, R, BM, I, FHX, AC, D, race, yrs since quitting smoking, cigarette pack-years,	H	**304	**339	**1,093	**1,072	*0.67	*0.5	*0.9
Visvanathan [54]	2004	RI- 030795	Nested	US	General population *(see Helzlsouer et al. 2000)*	B	164	324 of 10,178	>	A	H	127	63	*197	*101	*0.99	*0.63	*1.36
Watters [55]	2009	RI- 065149	Cohort	US	Retirees 50-71	B	16,640	283,112	>	A, D, E, Edu, MS, Ht, BM, PA, FH, CB, PcaM, D A	L	80,283	5,512	*186,166	*11,128	*0.89 *0.87	*0.86 *0.84	*0.91 *0.89
Will [56]	1999	IO	Cohort	US	General population	U	2,523	305,065	<	A	H				1,256	1***	0.92	1.08

Zhang	2002	RO- 029063	Cohort	USA	White male from Framingham Study	B	100	912	>	None	H	**284	**43	**628	**57	*0.63	*0.44	*0.92

Abbreviations: ^follow-up less than 5 years, < = Last follow-up in 1989 or earlier, > Last follow-up after 1989, *Data calculated as suggested by Islami et al., ** Pooled results presented, ***Current (vs Ex & Never), A = Age, AC = Alcohol Consumption, B = Baseline, BioM = Biochemical Markers, BM = Body Mass Index, CB = Comorbidities, CE = Chemical Exposure, D = Diet variable, E = Ethnicity, Edu = Education, FHx = Family History of Prostate Cancer, H = High, HS = Health Status, Ht = Height, I = Income, IO = Study reviewed by Islami et al. only, IH = Study reviewed by Islami et al. and Huncharek et al., L = low, M = Moderate, MS = Marital Status, N/A = not applicable, O = Occupation, PA = Physical Activity, PcaM = Prostate Cancer Markers, R = Area of Residence, Rev = Study reviewed by, RH = Study available to the RMA and by Harcharek et al., RI = Study available to the RMA and by Islami et al., RIH = Study available to the RMA, Huncharek et al. and Islami et al., RO = Study available to the RMA Only, Rx = Medications, SDV = Study Design Variables, SES = Socio-Economic Status, SM = Smoking Markers, U= Updated Follow-Up Data, VitSup = Vitamin Supplementation, W = Weight

Table 3 Studies included in meta-analyses for the association between cigarette smoking ("current" smokers with "never" smokers) and prostate cancer incidence

First author	Year	Rev-RMA ID	Design	Location	Subjects	Data	Total cases	Total pop./ controls	PSA	Adjustment	Bias Risk	Never smoked/Non-smoker**		Current smoker				
												Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI	
Adami [7]	1996	RIH-016355	Cohort	Sweden	Construction workers	B	2,368	135,006	>	A	H	39,636	682	65,784	1,069	1.11	1.01	1.23
Alavanja [8]	2003	RO- 029275	Cohort	US	Pesticide applicators in Iowa & North Carolina	U^	566	55,332	>	A, E, R, Edu, PcaM, BM, D, VitSup, PA, CE	L	25,159	195	8,629	52	1.42	0.90	2.20
Andersson	1996	RO- 012174	Case-control	Sweden	General population <80	N/A	256	252	>	A	H	86	68	42	60	1.80	1.10	3.00
Bae [9]	2013	RI- 70206	Cohort	South Korea	General population	B	87	14,450	>	A	H	3,169	29	7,105	38	0.70	0.43	1.13
Baglietto [10]	2006	IO	Cohort	Australia	General population	B	732	16,872	>	None	H	6,605	291	2,379	76	*0.73	*0.56	*0.94
Band	1999	RO- 017379	Case-control	Canada	General population ≥20	N/A	1516	4994	>	None	H							
Barba	2004	RO- 033231	Case-control	USA	General population	N/A	88	272	>	None	H	*77	*21	*27	*13	*1.52	*0.84	*2.72
Butler [11]	2009	RI- 065154	Cohort	Singapore	General Population 45-74	B	250	27,293	>	A, SDV, Edu, BioM, D	L	11,409	108	9,862	73	0.88	0.65	1.19
Cerhan [12]	1997	RIH- 016660	Cohort	US	Men in Iowa 65 +	U	71	1050	>	A, BM, PA A	M	411	26	137	15	2.45 2.20	1.32 1.20	4.54 4.40
Darlington	2007	RO- 065148	case-control	Canada	General population in Ontario 50-84	N/A	752	1613	>	A, FHx, BM, Edu, O	H	373	158	270	133	1.20	0.90	1.70
Dillner [13]	1998	RO- 16118	Nested	Finland	General population	B	165	290	>	None	H							
Engeland [14]	1996	RIH- 009479	Cohort	Norway	General population	B	707	11,863	>	A	H	1,878	139	7,379	451	1.10	0.90	1.30
Everatt [15]	2014	RO- 71303	Cohort	Lithuania	General population 40-59	B	336	6976	>	A, Edu, AC, BM A	M	1,997	137	3,035	103	0.76 0.76	0.59 0.60	1.00 1.00
Fincham	1990	RO- 007481	Case-control	Canada	General population ≥45	N/A	382	625	<	None	H	153	106	155	93	*0.92	*0.74	*1.14
Friedenreich	2003	RO- 030566	Case-control	Canada	General population in Alberta <80	N/A	988	1063	>	None	H	*318	*275	*152	*139	*1.03	*0.89	*1.19
Furuya	1998	RO- 013932	Case-control	Japan	Patients in Chiba University Hospital	N/A	329	190	>	None	H							
Geybels [16]	2012	IO	Cohort	The Netherlands	General population 55-69	B	3,451	58,279	>	A, SM	M		492		1,084	0.98	0.82	1.18
Giles	2001	RO- 029017	Case-control	Australia	Australian citizens with a histopathologically confirmed diagnosis of adenocarcinoma ≤70	N/A	1476	1409	>	A, FHx, calendar year, study centre, country of birth	H	486	540	273	203	0.82	0.65	1.05
Giovannucci [17]	2007	RIH- 065156	Cohort	US	Health professionals *(see Giovannucci et al. 1999)*	U	3,544	47,750	>	A, PcaM, BM, Ht, PA, CB, E, D, VitSup	L					*0.98	*0.89	*1.07
Giovannucci [18]	1999	RH- 017143	Cohort	US	Health professionals	U	1,369	47,781	>	A, BM, D	L		580		112	1.04	0.85	1.27
Gonzalez [19]	2007	IO	Cohort	US	General population 50-76	U^	832	35,244	>	A	H	13,211	303	3,103	62	0.92	0.70	1.20
Gronberg [20]	1996	RO- 007192	Nested	Sweden	Unmatched twins	B	406	1,218	<	A	H	321	117	484	157	1.00	0.71	1.39
Grundmark [21]	2011	IO	Cohort	Sweden	General population	B	208	2,045	>	None	H	449	69	961	86	0.60	0.44	0.83
Hakulinen [22]	1996	RO- S2.6	Cohort	Finland	"Cohort I" and "Cohort II"; General population	B	(1)209	(1)4,601	>	None	H	900	62	2,410	99	*0.61	*0.45	*0.83
							(II)109	(2)11,373		None		2,114	17	5,117	36	*0.88	*0.49	*1.56
Hayes	1994	RO- 003265	Case-control	USA	Black and White males in Atlanta, Detroit and New Jersey 40-79	N/A	981	1315	<	A, study site, race	H	**265	**174	**398	**277	1.10	0.80	1.40

Table 3 Studies included in meta-analyses for the association between cigarette smoking ("current" smokers with "never" smokers) and prostate cancer incidence - continued

First author	Year	Rev-RMA ID	Design	Location	Subjects	Data	Total cases	Total pop./ controls	PSA	Adjustment	Bias Risk	Never smoked/Non-smoker**		Current smoker				
												Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI	
Heikkila [23]	1999	RI- 018599	Nested	Finland	General population *(see Dillner et al. 1998)*	B	166	16,481 /300	<	None	H	188	114	112	52	*1.31	*0.87	*1.95
Heikkila [24]	2013	IO	12 studies	Europe	Data from 12 studies	N/A	865	116,056	>	A, SES, BM, AC	N/A	**83,805	**706	26,486	159	0.70	0.59	0.84
Helzlsouer [25]	2000	RO- 028981	Nested	US	General population	B	117	233	>	None	H	98	48	17	10	1.22	0.50	2.98
Hiatt [26]	1994	RIH- 003316	Cohort	US	Health plan members	U^	238	43,432	<	A, E, AC, Edu	M	14,340	79	8,898	49	1.20	0.80	1.60
Honda [27]	1988	RO- 003308	Case-control	US	General population <60	N/A	216	216	<	None	H	69	44					
Hsing	2000	RO- 029107	Case-control	China	Permanent residents in Shanghai without a history of any other cancer >18	N/A	238	471	>	None	H	174	100	176	74	*0.81	*0.63	*1.04
Huang	2003	RO- 028931	Case-control	USA	CLUE I and CLUE II cohort; General population	B	(I) 182	(I) 364	>	None	H	*125	*61	*89	*48	*1.07	*0.79	*1.45
							(II)142	(II) 284	>	None	H	*117	*55	*31	*14	*0.97	*0.60	*1.58
Hultdin [28]	2005	IO	Nested	Sweden	General population	U	254	514	>	None	H	230	115	97	45	*0.93	*0.61	*1.41
Karlsen [29]	2012	IO	Cohort	Denmark	General population	B	129	20,914	>	None	H	**12,954	**81	7,515	48	*1.00	*0.70	*1.43
Karppi [30]	2012	IO	Cohort	Finland	General population 42, 48, 54, or 60	B	68	997	>	None	H	**660	**57	269	11	*0.85	*0.76	*0.95
Karunasinghe [31]	2012	RO- 066733	Case-control	New Zealand	General population 40-81	B	275	441	>	None	H							
Key	1997	RO- 012167	Case-control	UK	White male <75	N/A	328	328	>	None	H	82	79	55	56	*1.03	*0.81	*1.31
Kondo [3]	2013	RO- 70205	Cohort	Japan	Atomic-bomb survivors	B	631	18,409	>	A, SM, CE, AC	M	6,104	272	7,573	209	0.72	0.60	0.87
Koutros [32]	2013	IO	Nested	US	General population 55-74	U^	1,122	1,112	>	None	H	313	398	122	78	*0.50	*0.36	*0.69
Le Marchand [33]	1994	RIH- 3179	Cohort	France	Workers in energy industry	U	412	10,506	>	A, O, AC, D, BM, PA, HS	L							
Lemogne [34]	2013	IO	Cohort	US	General Hawaiian population	B	198	8,881 of 20,316	>	A, E, I	M					*0.70	*0.52	*0.88
Lotufo [35]	2000	RIH- 28974	Cohort	US	Health professionals	U	996	22,071	>	A, Rx, PA, BM, Ht, AC	M	10,466	443	2,313	96	*1.06	*0.83	*1.29
		RO- 011775								A, Rx						*1.10	*0.89	*1.36
Lumey	1997	RO- 065151	Case-control	US	White males	N/A	1,097	3,250	>	A, MS, O, AS, Edu, Religion	H	816	296	987	312	0.93	0.76	1.15
Magura	2008	RIH- 003320	Case-control	USA	General population from Meritcare hospital, North Dakota 50-74	N/A	312	319	>	None	H	146	130	34	56	*1.32	*1.08	*1.62
Murphy [37]	2013	RO- 70207	Case-control	US	Men from urology clinics	N/A	527	558	>	A, SDV, E, FHx, AC	M	281	233	157	160	*1.23	*0.93	*1.63
Nilsen [38]	2000	RIH- 029140	Cohort	Norway	General population	B	644	22,895	>	A	H	6,094	222	6,474	153	0.96	0.78	1.19
Nomura [39]	2000	RI- 029108	Nested	US	Japanese Hawaiians	B	249	249 of 9413	>	A	H	98	87	67	76	1.30	0.80	2.00
Norrish	1998	RO- 016995	Case-control	New Zealand	Male residents in Auckland 40-80	N/A	317	480	>	None	H	137	94	46	33	*1.03	*0.76	*1.39
Onitilo [40]	2013	IO	Cohort	US	Men from health clinics	B	3,432	33,832	>	None	H	389						
Park [41]	2007	IO	Cohort	US	Multiethnic general population >45	B	4,404	82,483	>	None	H	23,419	1,326	14,174	673	*0.84	*0.76	*0.92
Parker [42]	1999	RI- 017444	Cohort	US	Men in Iowa (see Putnam et al. 2000)	B	81	1,177	>	A	H		23		16	1.79	0.99	3.22

Table 3 Studies included in meta-analyses for the association between cigarette smoking ("current" smokers with "never" smokers) and prostate cancer incidence - continued

First author	Year	Rev-RMA ID	Design	Location	Subjects	Data	Total cases	Total pop./ controls	PSA	Adjustment	Bias Risk	Never smoked/Non-smoker**		Current smoker				
												Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI	
Plaskon [43]	2003	RO- 028497	Case-control	US	White & Balack 40--64	N/A	753	703	>	A, E, FHx, PcaM	M	266	281	115	123	1.40	1.00	2.00
Putnam [44]	2000	RH- 29009	Cohort	US	Men in Iowa	B	101	1,572	>	A	H		24		22	1.20	0.60	2.00
Rohan	1997	RO- 013929	Case-control	Canada	Recently diagnosed males from Ontario Cancer Registry and British Columbia Cancer Registry	N/A	408	407	>	A, study site	H	124	89	56	55	1.42	0.89	2.27
Rohrmann [45]	2007	RIH- 065219	Cohort	US	General population	U	(1)147	26,810	>	A	H	3,850	34	14,468	45	1.00	0.63	1.59
							(2)351	28,292				5,688	94	11,268	85	0.98	0.73	1.33
Rohrmann [46]	2013	RI- 065978	Cohort	Europe	General population	B	4,623	145,112	>	A, Ht, W, Edu, MS, PA	M		1,547		1,080	0.90	0.83	0.97
Ross (in Wald [47])	1990	RO- 7210	Cohort	US	Retirement community	B	138	5,106 of 13,987	<	A	H		56		9	0.90	0.40	1.80
Sawada [48]	2014	RI- 70208	Cohort	Japan	General population 40-69	B	913	48,218	>	A, SDV, BM, MS, AC, CB, D A, SDV	M	11,062	257	24,953	380	*0.79 *0.86	*0.68 0.81	*0.89 0.92
Severson [49]	1989	RIH- 003251	Cohort	US	Japanese Hawaiians	B	174	7,999	<	A	H	2,341	63	3,435	65	0.87	0.61	1.23
Shafique [50]	2012	RO- 066019	Cohort	Scotland	Two studies: (1) workers 21-75 (2) General Population	B	650	12,276	>	A, BM, SES, BioM	M	2,093	149	7,253	294	0.90	0.73	1.09
Shafique [51]	2012	IO	Cohort	UK	General population *(see study 2 of Shafique et al. 2012)*	B	318	6,017	>	A, BioM, BM, AC, D, SES A, SES	M	1,026	68	3,356	136	0.93 0.92	0.69 0.71	1.26 1.27
Slattery	1993	RO- 003266	Case-control	USA	White male in Utah 45-74	N/A	362	685	<	None	H							
Stattin	2000	RO- 029289	Nested Case-referent	Sweden	General population from two counties 25-74	B	149	298	>	None	H							
Thompson [52]	1989	RIH- 003253	Cohort	US	White upper-middle class	B	54	1,776	<	A, CB, BM, D, BioM	L				11	1.3***	*0.70	*2.50
Veierod [53]	1997	RIH- 016633	Cohort	Norway	General population	B	72	24,051	>	A	H		24		25	*0.50	*0.20	*0.80
Villencuve	1999	RO- 018446	Case-control	Canada	General population from 8 provinces 50-74	N/A	1623	1623	>	(I) A, R	H							
										(II) A, R, BM, I, FHX, AC, D, race, yrs since quitting smoking, cigarette pack-years,	H							
Visvanathan [54]	2004	RI- 030795	Nested	US	General population *(see Helzlsouer et al. 2000)*	B	164	324 of 10,178	>	A	H	127	63	34	14	0.82	0.39	1.71
Watters [55]	2009	RI- 065149	Cohort	US	Retirees 50-71	B	16,640	283,112	>	A, D, E, Edu, MS, Ht, BM, PA, FH, CB, PcaM, D A	L	80,283	5,512	29,309	1,446	0.85 0.83	0.80 0.79	0.90 0.88
Will [56]	1999	IO	Cohort	US	General population	U	2,523	305,065	<	A	H				1,256	1***	0.92	1.08
Zhang	2002	RO- 029063	Cohort	USA	White male from Framingham Study	B	100	912	>	None	H							

Abbreviations: ^follow-up less than 5 years, < = Last follow-up in 1989 or earlier, > Last follow-up after 1989, *Data calculated as suggested by Islami et al., ** Pooled results presented, ***Current (vs Ex & Never), A = Age, AC = Alcohol Consumption, B = Baseline, BioM = Biochemical Markers, BM = Body Mass Index, CB = Comorbidities, CE = Chemical Exposure, D = Diet variable, E = Ethnicity, Edu = Education, FHx = Family History of Prostate Cancer, H = High, HS = Health Status, Ht = Height, I = Income, IO = Study reviewed by Islami et al. only, IH = Study reviewed by Islami et al. and Huncharek et al., L = low, M = Moderate, MS = Marital Status, N/A = not applicable, O = Occupation, PA = Physical Activity, PcaM = Prostate Cancer Markers, R = Area of Residence, Rev = Study reviewed by, RH = Study

available to the RMA and by Harcharek et al., RI = Study available to the RMA and by Islami et al., RIH = Study available to the RMA, Huncharek et al. and Islami et al., RO = Study available to the RMA Only, Rx = Medications, SDV = Study Design Variables, SES = Socio-Economic Status, SM = Smoking Markers, U= Updated Follow-Up Data, VitSup = Vitamin Supplementation, W = Weight

Table 4 Studies included in meta-analyses for the association between cigarette smoking ("current" with "non-current" (never + former) smokers) and prostate cancer incidence

First author	Year	Rev-RMA ID	Design	Location	Subjects	Data	Total cases	Total pop./ controls	PSA	Adjustment	Bias Risk	Non-Current		Current smoker				
												Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI	
Adami [7]	1996	RIH-016355	Cohort	Sweden	Construction workers	B	2,368	135,006	>	None	H	66,854	1299	65,784	1,069	*0.84	*0.77	*0.91
Alavanja [8]	2003	RO- 029275	Cohort	US	Pesticide applicators in Iowa & North Carolina	U^	566	55,332		None	L	40,582	438	8,629	52	*0.56	*0.42	*0.75
Andersson	1996	RO- 012174	Case-control	Sweden	General population <80	N/A	256	252	>	None	H	183	175	42	60	*1.20	*0.99	*1.46
Bae [9]	2013	RI- 70206	Cohort	South Korea	General population	B	87	14,450	>	None	H	6,955	48	7,105	38	*0.78	*0.51	*1.19
Baglietto [10]	2006	IO	Cohort	Australia	General population	B	732	16,872	>	None	H	13,760	645	2,379	76	*0.69	*0.55	*0.87
Band	1999	RO- 017379	Case-control	Canada	General population ≥20	N/A	1516	4994	>	None	H							
Barba	2004	RO- 033231	Case-control	USA	General population	N/A	88	272	>	None	H	245	75	27	13	*1.39	*0.85	*2.26
Butler [11]	2009	RI- 065154	Cohort	Singapore	General Population 45-74	B	250	27,293	>	None	L	17,181	177	9,862	73	*0.72	*0.55	*0.95
Cerhan [12]	1997	RIH- 016660	Cohort	US	Men in Iowa 65 +	U	71	1050	>	None	M	842	56	137	15	*1.58	*0.92	*2.72
Darlington	2007	RO- 065148	case-control	Canada	General population in Ontario 50-84	N/A	752	1613	>	None	H	1325	612	270	133	*1.05	*0.90	*1.22
Dillner [13]	1998	RO- 16118	Nested	Finland	General population	B	165	290	>	None	H							
Engeland [14]	1996	RIH- 009479	Cohort	Norway	General population	B	707	11,863	>	None	H	3,777	256	7,379	451	*0.91	*0.78	*1.05
Everatt [15]	2014	RO- 71303	Cohort	Lithuania	General population 40-59	B	336	6976	>	None	M	3,605	233	3,035	103	*0.54	*0.43	*0.68
Fincham	1990	RO- 007481	Case-control	Canada	General population ≥45	N/A	382	625	<	None	H	470	289	155	93	*0.99	*0.82	*1.18
Friedenreich	2003	RO- 030566	Case-control	Canada	General population in Alberta <80	N/A	988	1063	>	None	H	911	849	152	*139	*0.99	*0.87	*1.13
Furuya	1998	RO- 013932	Case-control	Japan	Patients in Chiba University Hospital	N/A	329	190	>	None	H							
Geybels [16]	2012	IO	Cohort	The Netherlands	General population 55-69	B	3,451	58,279	>	None	M		2,365		1,084			
Giles	2001	RO- 029017	Case-control	Australia	Australian citizens with a histopathologically confirmed diagnosis of adenocarcinoma ≤70	N/A	1476	1409	>	None	H	1135	1273	273	203	*0.81	*0.72	*0.90
Giovannucci [17]	2007	RIH- 065156	Cohort	US	Health professionals (see Giovannucci et al. 1999)	U	3,544	47,750	>	None	L							
Giovannucci [18]	1999	RH- 017143	Cohort	US	Health professionals	U	1,369	47,781	>	None	L	1,257			112			
Gonzalez [19]	2007	IO	Cohort	US	General population 50-76	U^	832	35,244	>	None	H	30,744	757	3,103	62	*0.82	*0.63	*1.05
Gronberg [20]	1996	RO- 007192	Nested	Sweden	Unmatched twins	B	406	1,218	<	None	H	575	209	484	157	*0.92	*0.77	*1.10
Grundmark [21]	2011	IO	Cohort	Sweden	General population	B	208	2,045	>	None	H	1,410	155	961	86	*0.83	*0.64	*1.07
Hakulinen [22]	1996	RO- S2.6	Cohort	Finland	"Cohort I" and "Cohort II"; General population	B	(1)209	(1)4,601	>	None	H	1,982	110	2,410	99	*0.75	*0.58	*0.98
							(II)109	(2)11,373		None		6,147	73	5,117	36	*0.60	*0.40	*0.89

Hayes	1994	RO- 003265	Case-control	USA	Black and White males in Atlanta, Detroit and New Jersey 40-79	N/A	981	1315	<	None	H	783	*606	398	277	*0.94	*0.84	*1.05

Table 4 Studies included in meta-analyses for the association between cigarette smoking ("current" with "non-current" (never + former) smokers) and prostate cancer incidence - continued

First author	Year	Rev-RMA ID	Design	Location	Subjects	Data	Total cases	Total pop./ controls	PSA	Adjustment	Bias Risk	Non- Current		Current smoker				
												Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI	
Heikkila [23]	1999	RI- 018599	Nested	Finland	General population (see Dillner et al. 1998)	B	166	16,481 /300	<	None	H	188	114	112	52	*0.84	*0.64	*1.10
Heikkila [24]	2013	IO	12 studies	Europe	Data from 12 studies	N/A	865	116,056	>	None	N/A			26,486	159	*0.71	*0.60	*0.85
Helzlsouer [25]	2000	RO- 028981	Nested	US	General population	B	117	233	>	None	H	216	107	17	10	*1.12	*0.67	*1.87
Hiatt [26]	1994	RIH- 003316	Cohort	US	Health plan members	U^	238	43,432	<	None	M	31,402	173	8,898	49	*1.00	*0.73	*1.37
Honda [27]	1988	RO- 003308	Case-control	US	General population <60	N/A	216	216	<	None	H							
Hsing	2000	RO- 029107	Case-control	China	Permanent residents in Shanghai without a history of any other cancer >18	N/A	238	471	>	None	H	295	164	176	74	*0.83	*0.66	*1.04
Huang	2003	RO- 028931	Case-control	USA	CLUE I and CLUE II cohort; General population	B	(I) 182	(I) 364	>	None	H	275	134	89	48	*1.07	*0.82	*1.40
							(II)142	(II) 284	>	None	H	253	128	31	14	*0.93	*0.59	*1.46
Hultdin [28]	2005	IO	Nested	Sweden	General population	U	254	514	>	None	H	362	194	97	45	*0.91	*0.70	*1.19
Karlsen [29]	2012	IO	Cohort	Denmark	General population	B	129	20,914	>	None	H	12,954	81	7,515	48	*1.02	*0.72	*1.46
Karppi [30]	2012	IO	Cohort	Finland	General population 42, 48, 54, or 60	B	68	997	>	None	H	660	57	269	11	*0.49	*0.26	*0.93
Karunasinghe [31]	2012	RO- 066733	Case-control	New Zealand	General population 40-81	B	275	441	>	None	H							
Key	1997	RO- 012167	Case-control	UK	White male <75	N/A	328	328	>	None	H	273	272	55	56	*1.01	*0.83	*1.24
Kondo [3]	2013	RO- 70205	Cohort	Japan	Atomic-bomb survivors	B	631	18,409	>	None	M	10,205	422	7,573	209	*0.68	*0.57	*0.80
Koutros [32]	2013	IO	Nested	US	General population 55-74	U^	1,122	1,112	>	None	H	890	943	122	78	*0.76	*0.63	*0.91
Le Marchand [33]	1994	RIH- 3179	Cohort	France	Workers in energy industry	U	412	10,506	>	None	L							
Lemogne [34]	2013	IO	Cohort	US	General Hawaiian population	B	198	8,881 of 20,316	>	None	M							
Lotufo [35]	2000	RIH- 28974	Cohort	US	Health professionals	U	996	22,071	>	None	M	18,676	900	2,313	96	*0.87	*0.71	*1.07
Lumey	1997	RO- 011775	Case-control	US	White males	N/A	1,097	3,250	>	None	H	2,263	785	987	312	*0.93	*0.83	*1.05
Magura	2008	RO- 065151	Case-control	USA	General population from Meritcare hospital, North Dakota 50-74	N/A	312	319	>	None	H	285	256	34	56	*1.32	*1.09	*1.58
Mills [36]	1989	RIH- 003320	Cohort	US	Adventists	B	180	14,000	<	None	H	169			3			
Murphy [37]	2013	RO- 70207	Case-control	US	Men from urology clinics	N/A	527	558	>	None	M	401	366	157	160	*1.06	*0.93	*1.21
Nilsen [38]	2000	RIH- 029140	Cohort	Norway	General population	B	644	22,895	<	None	H	12,008	405	6,474	153	*0.71	*0.59	*0.85
Nomura [39]	2000	RI- 029108	Nested	US	Japanese Hawaiians	B	249	249 of 9413	<	None	H	181	173	67	76	*1.09	*0.90	*1.31
Norrish	1998	RO- 016995	Case-control	New Zealand	Male residents in Auckland 40-80	N/A	317	480	>	None	H	433	284	46	33	*1.06	*0.80	*1.39
Onitilo [40]	2013	IO	Cohort	US	Men from health clinics	B	3,432	33,832	>	None	H							
Park [41]	2007	IO	Cohort	US	Multiethnic general population >45	B	4,404	82,483	>	None	H	63,910	3,726	14,174	673	*0.82	*0.76	*0.89

Parker [42]	1999	RI- 017444	Cohort	US	Men in Iowa (see Putnamet al. 2000)	B	81	1,177	>	None	H		65		16			

Table 4 Studies included in meta-analyses for the association between cigarette smoking ("current" with "non-current" (never + former) smokers) and prostate cancer incidence - continued

First author	Year	Rev-RMA ID	Design	Location	Subjects	Data	Total cases	Total pop./ controls	PSA	Adjustment	Bias Risk	Non- Current		Current smoker				
												Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI	
Plaskon [43]	2003	RO- 028497	Case-control	US	White & Balack 40--64	N/A	753	703	>	None	M	588	630	115	123	*1.00	*0.87	*1.14
Putnam [44]	2000	RH- 29009	Cohort	US	Men in Iowa	B	101	1,572	<	None	H		79		22			
Rohan	1997	RO- 013929	Case-control	Canada	Recently diagnosed males from Ontario Cancer Registry and British Columbia Cancer Registry	N/A	408	407	>	None	H	342	347	56	55	*0.98	*0.80	*1.20
Rohrmann [45]	2007	RIH- 065219	Cohort	US	General population	U	(1)147	26,810	>	None	H	8,886	77	14,468	45	*0.36	*0.25	*0.52
							(2)351	28,292		None		13,209	222	11,268	85	*0.45	*0.35	*0.58
Rohrmann [46]	2013	RI- 065978	Cohort	Europe	General population	B	4,623	145,112	>	None	M	3,543			1080			
Ross (in Wald [47])	1990	RO- 7210	Cohort	US	Retirement community	B	138	5,106 of 13,987	<	None	H	129			9			
Sawada [48]	2014	RI- 70208	Cohort	Japan	General population 40-69	B	913	48,218	>	None	M	22,361	524	24,953	380	*0.66	*0.57	*0.75
Severson [49]	1989	RIH- 003251	Cohort	US	Japanese Hawaiians	B	174	7,999	<	None	H	4,389	109	3,435	65	*0.77	*0.57	*1.04
Shafique [50]	2012	RO- 066019	Cohort	Scotland	Two studies: (1) workers 21-75 (2) General Population	B	650	12,276	>	None	M	5,022	356	7,253	294	*0.59	*0.51	*0.68
Shafique [51]	2012	IO	Cohort	UK	General population *(see study 2 of Shafique et al. 2012)*	B	318	6,017	>	None	M	2,342	182	3,356	136	*0.54	*0.44	*0.67
Slattery	1993	RO- 003266	Case-control	USA	White male in Utah 45-74	N/A	362	685	<	None	H							
Stattin	2000	RO- 029289	Nested Case-referent	Sweden	General population from two counties 25-74	B	149	298	>	None	H	245	118	53	31	*0.85	*0.63	*1.15
Thompson [52]	1989	RIH- 003253	Cohort	US	White upper-middle class	B	54	1,776	<	None	L				11	1.30	*0.70	*2.50
Veierod [53]	1997	RIH- 016633	Cohort	Norway	General population	B	72	24,051	<	None	H		465		25			
Villencuve	1999	RO- 018446	Case-control	Canada	General population from 8 provinces 50-74	N/A	1623	1623	>	None	H							
Visvanathan [54]	2004	RI- 030795	Nested	US	General population *(see Helzlsouer et al. 2000)*	B	164	324 of 10,178	>	None	H	290	150	34	14	*0.86	*0.54	*1.35
Watters [55]	2009	RI- 065149	Cohort	US	Retirees 50-71	B	16,640	283,112	>	None	L	237,140	15,194	29,309	1,446	*0.78	*0.74	*0.82
Will [56]	1999	IO	Cohort	US	General population	U	2,523	305,065	<	None	H				1,256	1.00	0.92	1.08
Zhang	2002	RO- 029063	Cohort	USA	White male from Framingham Study	B	100	912	>	None	H							

Abbreviations: ^follow-up less than 5 years, < = Last follow-up in 1989 or earlier, > Last follow-up after 1989, *Data calculated as suggested by Islami et al., H = High, IO = Study reviewed by Islami et al. only, IH = Study reviewed by Islami et al. and Huncharek et al., L = low, M = Moderate, N/A = not applicable, Rev = Study reviewed by, RH = Study available to the RMA and by Harcharek et al., RI = Study available to the RMA and by Islami et al., RIH = Study available to the RMA, Huncharek et al. and Islami et al., RO = Study available to the RMA Only, U= Updated Follow-Up Data

Table 5 Studies included in meta-analyses for the association between cigarette smoking ("current" with "ex" (former) smokers) and prostate cancer incidence

First author	Year	Rev-RMA ID	Design	Location	Subjects	Data	Total cases	Total pop./ controls	PSA	Adjustment	Bias Risk	Ex- smoker		Current smoker				
												Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI	
Adami [7]	1996	RIH-016355	Cohort	Sweden	Construction workers	B	2,368	135,006	>	None	H	27,218	617	65,784	1,069	*0.72	*0.65	*0.80
Andersson	1996	RO- 029275	Case-control	Sweden	General population <80	N/A	256	252	>	None	H	97	107	42	60	*1.12	*0.91	*1.38
Alavanja [8]	2003	RO- 012174	Cohort	US	Pesticide applicators in Iowa & North Carolina	U^	566	55,332	>	None	L	15,423	243	8,629	52	*0.39	*0.29	*0.52
Bae [9]	2013	RI- 70206	Cohort	South Korea	General population	B	87	14,450	>	None	H	3,786	19	7,105	38	*1.07	*0.62	*1.85
Baglietto [10]	2006	IO	Cohort	Australia	General population	B	732	16,872	>	None	H	7,155	354	2,379	76	*0.66	*0.51	*0.84
Band	1999	RO- 017379	Case-control	Canada	General population ≥20	N/A	1516	4994	>	None	H							
Barba	2004	RO- 033231	Case-control	USA	General population	N/A	88	272	>	None	H	168	54	27	13	*1.34	*0.81	*2.21
Butler [11]	2009	RI- 065154	Cohort	Singapore	General Population 45-74	B	250	27,293	>	None	L	5,772	69	9,862	73	*0.62	*0.45	*0.86
Cerhan [12]	1997	RIH- 016660	Cohort	US	Men in Iowa 65 +	U	71	1050	>	None	M	431	30	137	15	*1.52	*0.84	*2.74
Darlington	2007	RO- 065148	case-control	Canada	General population in Ontario 50-84	N/A	752	1613	>	None	H	952	454	270	133	*1.02	*0.87	*1.20
Dillner [13]	1998	RO- 16118	Nested	Finland	General population	B	165	290	>	None	H							
Engeland [14]	1996	RIH- 009479	Cohort	Norway	General population	B	707	11,863	>	None	H	1,899	117	7,379	451	*0.99	*0.81	*1.21
Everatt [15]	2014	RO- 71303	Cohort	Lithuania	General population 40-59	B	336	6976	>	None	M	1,608	96	3,035	103	*0.58	*0.44	*0.76
Fincham	1990	RO- 007481	Case-control	Canada	General population ≥45	N/A	382	625	<	None	H	317	183	155	93	*1.03	*0.84	*1.25
Friedenreich	2003	RO- 030566	Case-control	Canada	General population in Alberta <80	N/A	988	1063	>	None	H	544	537	152	*139	*0.96	*0.84	*1.10
Furuya	1998	RO- 013932	Case-control	Japan	Patients in Chiba University Hospital	N/A	329	190	>	None	H							
Geybels [16]	2012	IO	Cohort	The Netherlands	General population 55-69	B	3,451	58,279	>	None	M		1,873		1,084			
Giles	2001	RO- 029017	Case-control	Australia	Australian citizens with a histopathologically confirmed diagnosis of adenocarcinoma ≤70	N/A	1476	1409	>	None	H	649	733	273	203	*0.80	*0.72	*0.90
Giovannucci [17]	2007	RIH- 065156	Cohort	US	Health professionals *(see Giovannucci et al. 1999)*	U	3,544	47,750	>	None	L							
Giovannucci [18]	1999	RH- 017143	Cohort	US	Health professionals	U	1,369	47,781	>	None	L		677		112			
Gonzalez [19]	2007	IO	Cohort	US	General population 50-76	U^	832	35,244	>	None	H	17,533	454	3,103	62	*0.78	*0.60	*1.01
Gronberg [20]	1996	RO- 007192	Nested	Sweden	Unmatched twins	B	406	1,218	<	None	H	254	92	484	157	*0.92	*0.74	*1.15
Grundmark [21]	2011	IO	Cohort	Sweden	General population	B	208	2,045	>	None	H	427	53	961	86	*0.74	*0.54	*1.03
Hakulinen [22]	1996	RO- S2.6	Cohort	Finland	"Cohort I" and "Cohort II"; General population	B	(1)209	(1)4,601	>	None	H	1,082	48	2,410	99	*0.93	*0.66	*1.30
							(II)109	(2)11,373		None		4,033	56	5,117	36	*0.51	*0.34	*0.77
Hayes	1994	RO- 003265	Case-control	USA	Black and White males in Atlanta, Detroit and New Jersey 40-79	N/A	981	1315	<	None	H	518	432	398	277	*0.90	*0.81	*1.01

Table 5 Studies included in meta-analyses for the association between cigarette smoking ("current" with "ex" (former) smokers) and prostate cancer incidence - continued

First author	Year	Rev-RMA ID	Design	Location	Subjects	Data	Total cases	Total pop./ controls	PSA	Adjustment	Bias Risk	Ex- smoker		Current smoker		RR/OR	CI	
												Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)			
Heikkila [23]	1999	RI- 018599	Nested	Finland	General population (see Dillner et al. 1998)	B	166	16,481 /300	<	None	H			112	52			
Heikkila [24]	2013	IO	12 studies	Europe	Data from 12 studies	N/A	865	116,056	>	None	N/A			26,486	159			
Helzlsouer [25]	2000	RO- 028981	Nested	US	General population	B	117	233	>	None	H	118	59	17	10	*1.11	*0.65	*1.90
Hiatt [26]	1994	RIH- 003316	Cohort	US	Health plan members	U^	238	43,432	<	None	M	17,062	94	8,898	49	*1.00	*0.71	*1.41
Honda [27]	1988	RO- 003308	Case-control	US	General population <60	N/A	216	216	<	None	H							
Hsing	2000	RO- 029107	Case-control	China	Permanent residents in Shanghai without a history of any other cancer >18	N/A	238	471	>	None	H	121	64	176	74	*0.86	*0.65	*1.13
Huang	2003	RO- 028931	Case-control	USA	CLUE I and CLUE II cohort; General population	B	(I) 182	(I) 364	>	None	H	150	73	89	48	*1.07	*0.80	*1.44
							(II)142	(II) 284	>	None	H	136	73	31	14	*0.89	*0.56	*1.43
Hultdin [28]	2005	IO	Nested	Sweden	General population	U	254	514	>	None	H	132	79	97	45	*0.85	*0.63	*1.14
Karlsen [29]	2012	IO	Cohort	Denmark	General population	B	129	20,914	>	None	H			7,515	48			
Karppi [30]	2012	IO	Cohort	Finland	General population 42, 48, 54, or 60	B	68	997	>	None	H			269	11			
Karunasinghe [31]	2012	RO- 066733	Case-control	New Zealand	General population 40-81	B	275	441	>	None	H							
Key	1997	RO- 012167	Case-control	UK	White male <75	N/A	328	328	>	None	H	191	193	55	56	*1.00	*0.81	*1.24
Kondo [3]	2013	RO- 70205	Cohort	Japan	Atomic-bomb survivors	B	631	18,409	>	None	M	4,101	150	7,573	209	*0.76	*0.62	*0.94
Koutros [32]	2013	IO	Nested	US	General population 55-74	U^	1,122	1,112	>	None	H	577	545	122	78	*0.80	*0.67	*0.96
Le Marchand [33]	1994	RIH- 3179	Cohort	France	Workers in energy industry	U	412	10,506	>	None	L							
Lemogne [34]	2013	IO	Cohort	US	General Hawaiian population	B	198	8,881 of 20,316	>	None	M							
Lotufo [35]	2000	RIH- 28974	Cohort	US	Health professionals	U	996	22,071	>	None	M	8,210	457	2,313	96	*0.76	*0.61	*0.94
Lumey	1997	RO- 011775	Case-control	US	White males	N/A	1,097	3,250	>	None	H	1447	489	987	312	*0.95	*0.84	*1.08
Magura	2008	RO- 065151	Case-control	USA	General population from Meritcare hospital, North Dakota 50-74	N/A	312	319	>	None	H	139	126	34	56	*1.31	*1.07	*1.61
Mills [36]	1989	RIH- 003320	Cohort	US	Adventists	B	180	14,000	<	None	H		79		3			
Murphy [37]	2013	RO- 70207	Case-control	US	Men from urology clinics	N/A	527	558	>	None	M	120	133	157	160	*0.96	*0.82	*1.13
Nilsen [38]	2000	RIH- 029140	Cohort	Norway	General population	B	644	22,895	<	None	H	5,914	183	6,474	153	*0.77	*0.62	*0.95
Nomura [39]	2000	RI- 029108	Nested	US	Japanese Hawaiians	B	249	249 of 9413	<	None	H	83	86	67	76	*1.04	*0.84	*1.29
Norrish	1998	RO- 016995	Case-control	New Zealand	Male residents in Auckland 40-80	N/A	317	480	>	None	H	296	190	46	33	*1.07	*0.81	*1.42
Onitilo [40]	2013	IO	Cohort	US	Men from health clinics	B	3,432	33,832	>	None	H							
Park [41]	2007	IO	Cohort	US	Multiethnic general population >45	B	4,404	82,483	>	None	H	40,491	2,400	14,174	673	*0.81	*0.75	*0.88
Parker [42]	1999	RI- 017444	Cohort	US	Men in Iowa (see Putnam et al. 2000)	B	81	1,177	>	None	H		42		16			

Table 5 Studies included in meta-analyses for the association between cigarette smoking ("current" with "ex" (former) smokers) and prostate cancer incidence - continued

First author	Year	Rev-RMA ID	Design	Location	Subjects	Data	Total cases	Total pop./ controls	PSA	Adjustment	Bias Risk	Ex- smoker		Current smoker				
												Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI	
Plaskon [43]	2003	RO- 028497	Case-control	US	White & Balack 40--64	N/A	753	703	>	None	M	322	349	115	123	*0.99	*0.86	*1.15
Putnam [44]	2000	RH- 29009	Cohort	US	Men in Iowa	B	101	1,572	<	None	H		55		22			
Rohan	1997	RO- 013929	Case-control	Canada	Recently diagnosed males from Ontario Cancer Registry and British Columbia Cancer Registry	N/A	408	407	>	None	H	218	258	56	55	*0.91	*0.74	*1.12
Rohrmann [45]	2007	RIH- 065219	Cohort	US	General population	U	(1)147	26,810	>	None	H	5,036	43	14,468	45	*0.37	*0.24	*0.56
							(2)351	28,292		None		7,521	128	11,268	85	*0.45	*0.34	*0.59
Rohrmann [46]	2013	RI- 065978	Cohort	Europe	General population	B	4,623	145,112	>	None	M		1,996		1,080			
Ross (in Wald [47])	1990	RO- 7210	Cohort	US	Retirement community	B	138	5,106 of 13,987	<	None	H		73		9			
Sawada [48]	2014	RI- 70208	Cohort	Japan	General population 40-69	B	913	48,218	>	None	M	11,299	267	24,953	380	*0.65	*0.56	*0.76
Severson [49]	1989	RIH- 003251	Cohort	US	Japanese Hawaiians	B	174	7,999	<	None	H	2,048	46	3,435	65	*0.85	*0.58	*1.23
Shafique [50]	2012	RO- 066019	Cohort	Scotland	Two studies: (1) workers 21-75 (2) General Population	B	650	12,276	>	None	M	2,929	207	7,253	294	*0.59	*0.50	*0.70
Shafique [51]	2012	IO	Cohort	UK	General population *(see study 2 of Shafique et al. 2012)*	B	318	6,017	>	None	M	1,316	114	3,356	136	*0.49	*0.38	*0.62
Slattery	1993	RO- 003266	Case-control	USA	White male in Utah 45-74	N/A	362	685	<	None	H							
Stattin	2000	RO- 029289	Nested Case-referent	Sweden	General population from two counties 25-74	B	149	298	>	None	H							
Thompson [52]	1989	RIH- 003253	Cohort	US	White upper-middle class	B	54	1,776	<	None	L				11			
Veierod [53]	1997	RIH- 016633	Cohort	Norway	General population	B	72	24,051	<	None	H		20		25			
Villencuve	1999	RO- 018446	Case-control	Canada	General population from 8 provinces 50-74	N/A	1623	1623	>	None	H							
Visvanathan [54]	2004	RI- 030795	Nested	US	General population *(see Helzlsouer et al. 2000)*	B	164	324 of 10,178	>	None	H	163	87	34	14	*0.84	*0.52	*1.34
Watters [55]	2009	RI- 065149	Cohort	US	Retirees 50-71	B	16,640	283,112	>	None	L	156,857	9,682	29,309	1,446	*0.81	*0.77	*0.85
Will [56]	1999	IO	Cohort	US	General population	U	2,523	305,065	<	None	H				1,256			
Zhang	2002	RO- 029063	Cohort	USA	White male from Framingham Study	B	100	912	>	None	H							

Abbreviations: ^follow-up less than 5 years, < = Last follow-up in 1989 or earlier, > Last follow-up after 1989, *Data calculated as suggested by Islami et al., H = High, IO = Study reviewed by Islami et al. only, IH = Study reviewed by Islami et al. and Huncharek et al., L = low, M = Moderate, N/A = not applicable, Rev = Study reviewed by, RH = Study available to the RMA and by Harcharek et al., RI = Study available to the RMA and by Islami et al., RIH = Study available to the RMA, Huncharek et al. and Islami et al., RO = Study available to the RMA Only, U= Updated Follow-Up Data

Table 6 Studies included in meta-analyses for the association between cigarette smoking by dosage (<10, 10-19, 20 or more cigarettes/day) ("current" smokers with "never" smokers) and prostate cancer incidence

First author	Year	Rev-RMA ID	Adjustment	Never smoked/Non-smoker**		<10 cigarettes/day					10-19 cigarettes/day					20+ cigarettes/day					Reported categories
				Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI		Non-cases (n)	Cases (n)	RR/OR	CI		Non-cases (n)	Cases (n)	RR/OR	CI		Cigarettes/day ([ł]gram/day) ([ħ]pack/day)
Adami [7]	1996	RIH-016355	A	39,636	682	46,818	741	*1.08	*1.00	*1.17	54,962	698	*1.11	*1.03	*1.21	2,527	38	1.00	0.72	1.38	1-4, 5-14, 15-24, >25
Alavanja [8]	2003	RO- 029275	A, E, R, Edu, PcaM, BM, D, VitSup, PA, CE	25,159	195																
Andersson	1996	RO- 012174	A	86	68	*76	*104	*1.72	*1.19	*2.50	18	18	1.20	0.60	2.60	30	37	1.50	0.90	2.70	≤5, 6-10, 11-15, >15
Bae [9]	2013	RI- 70206	A	3,169	29	1,229	6	0.65	0.27	1.57	3,810	16	0.55	0.30	1.01	5,686	35	*0.79	*0.51	*1.24	1-10, 11-20, 21-30, ≥31
Baglietto [10]	2006	IO	None	6,605	291																
Band	1999	RO- 017379	None	987	352																
Barba	2004	RO- 033231	None	*77	*21																
Butler [11]	2009	RI- 065154	A, SDV, Edu, BioM, D	11,409	108		59	1.08	0.79	1.49		57	0.99	0.71	1.37		26	0.71	0.46	1.10	<13, 13-22, ≥23
Cerhan [12]	1997	RIH- 016660	A A, BM, PA	411	26												9	2.70 2.90	1.20 1.30	6.00 6.70	<20, ≥20
Darlington	2007	RO- 065148	A, FHx, BM, Edu, O	373	158																
Dillner [13]	1998	RO- 16118	None																		
Engeland [14]	1996	RIH- 009479	A	1,878	139																
Everatt [15]	2014	RO- 71303	A	1,997	137																
Fincham	1990	RO- 007481	None	153	106	151	86	*0.89	*0.71	*1.11	117	71	*0.92	*0.73	*1.17	*200	*110	*0.87	*0.70	*1.07	1-10, 11-20, 21-30, 30+
Friedenreich	2003	RO- 030566	A	*318	*275																
Furuya	1998	RO- 013932	None	*90	*157																
Geybels [16]	2012	IO	A, SM		492																
Giles	2001	RO- 029017	A, FHx, calendar year, study centre, country of birth	486	540											320	304	0.93	0.75	1.16	≤15, 16-20. >20
Giovannucci [17]	2007	RIH- 065156	A, PcaM, BM, Ht, PA, CB, E, D, VitSup																		
Giovannucci [18]	1999	RH- 017143	A, BM, D		580																
Gonzalez [19]	2007	IO	A	13,211	303																
Gronberg [20]	1996	RO- 007192	A	321	117	293	112	1.06	0.77	1.45	191	66	0.96	0.66	1.39	132	33	0.72	0.43	1.15	1-9, 10-19, ≥20
Grundmark [21]	2011	IO	None	449	69																
Hakulinen [22]	1996	RO- S2.6	None	900	62	1,320	52	*0.59	*0.41	*0.84	726	34	*0.69	*0.46	*1.04	310	13	*0.62	*0.35	*1.12	1-14[ł], 15-25[ł], >25[ł]
			None	2,114	17	1,311	15	*1.42	*0.71	*2.83	2,330	14	*0.75	*0.37	*1.52	1,009	7	*0.86	*0.36	*2.08	
Hayes	1994	RO- 003265	A, study site, race	**265	**174	**39	**27	0.90	0.50	1.60	**88	**60	1.00	0.70	1.60	**270	**190	*1.14	*0.89	*1.45	<10, 10-19, 20-39, 40+

Table 6 Studies included in meta-analyses for the association between cigarette smoking by dosage (<10, 10-19, 20 or more cigarettes/day) ("current" smokers with "never" smokers) and prostate cancer incidence - continued

First author	Year	Rev-RMA ID	Adjustment	Never smoked/Non-smoker**		<10 cigarettes/day					10-19 cigarettes/day					20+ cigarettes/day					Reported categories
				Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI		Non-cases (n)	Cases (n)	RR/OR	CI		Non-cases (n)	Cases (n)	RR/OR	CI		Cigarettes/day ([l]gram/day) ([H]pack/day)
Heikkila [23]	1999	RI- 018599	None	188	114																
Heikkila [24]	2013	IO	A, SES, BM, AC	**83,805	**706																
Helzlsouer [25]	2000	RO- 028981	None	98	48																
Hiatt [26]	1994	RIH- 003316	A, E, AC, Edu	14,340	79											4,560	25	1.90	1.20	3.10	<1[H], >1[H]
Honda [27]	1988	RO- 003308	None	69	44																
Hsing	2000	RO- 029107	None	174	100																
Huang	2003	RO- 028931	None	(I) *125	(I) *61																
				(II) *117	(II) *55																
Hultdin [28]	2005	IO	None	230	115																
Karlsen [29]	2012	IO	None	**12,954	**81																
Karppi [30]	2012	IO	None	**660	**57																
Karunasinghe [31]	2012	RO- 066733	None	273	127																
Key	1997	RO- 012167	None	82	79																
Kondo [3]	2013	RO- 70205	A, SM, CE, AC	6,104	272																
Koutros [32]	2013	IO	None	313	398																
Le Marchand [33]	1994	RIH- 3179	A, O, AC, D, BM, PA, HS					*0.90	*0.60	*1.40			*1.00	*0.70	*1.60			*1.00	*0.60	*1.60	1-10, 11-20, >20
Lemogne [34]	2013	IO	A, E, I																		
Lotufo [35]	2000	RIH- 28974	A, Rx, PA, BM, Ht, AC	10,466	443											1,498	61	1.07	0.82	1.41	<20, ≥20
		RO- 011775	A, Rx															1.10	0.84	1.44	
Lumey	1997	RO- 065151	A, MS, O, AS, Edu, Religion	816	296	61	26	1.19	0.71	1.98	451	162	1.08	0.84	1.39	*475	*124	*0.75	*0.59	*0.95	<10. 10-20. 21-39, ≥40
Magura	2008	RIH- 003320	None	146	130																
Murphy [37]	2013	RO- 70207	A, SDV, E, FHx, AC	281	233																
Nilsen [38]	2000	RIH- 029140	A	6,094	222	5,303	140	*0.94	*0.77	*1.14	2,028	51	1.37	1.00	1.88	2,210	45	1.27	0.91	1.76	1-8, 9-10, 11-15, >15
Nomura [39]	2000	RI- 029108	A	98	87																
Norrish	1998	RO- 016995	None	137	94																
Onitilo [40]	2013	IO	None	389																	
Park [41]	2007	IO	None	23,419	1,326	4,355	264	*1.07	*0.93	*1.23	5,497	277	*0.89	*0.78	*1.02	4,322	132	*0.54	*0.45	*0.65	<10, 10-19, >20
Parker [42]	1999	RI- 017444	A		23												7	1.90	0.80	4.50	<20, ≥20
Plaskon [43]	2003	RO- 028497	A, E, FHx, PcaM	266	281	75	91	1.10	0.80	1.60	230	216	1.00	0.80	1.30		165	*1.40	*1.05	*1.87	1-10, 11-20,21-30, 31-40, 41-60, >60
Putnam [44]	2000	RH- 29009	A		24												7	1.60	0.70	3.90	<20, ≥20

Table 6 Studies included in meta-analyses for the association between cigarette smoking by dosage (<10, 10-19, 20 or more cigarettes/day) ("current" smokers with "never" smokers) and prostate cancer incidence - continued

First author	Year	Rev-RMA ID	Adjustment	Never smoked/Non-smoker**		<10 cigarettes/day					10-19 cigarettes/day					20+ cigarettes/day					Reported categories
				Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI		Non-cases (n)	Cases (n)	RR/OR	CI		Non-cases (n)	Cases (n)	RR/OR	CI		Cigarettes/day ([l]gram/day) ([H]pack/day)
Rohan	1997	RO-013929	A, study site	124	89																
Rohrmann [45]	2007	RIH- 65219	A	3,850	34		5	0.52	0.20	1.33		23	1.03	0.60	1.79		17	1.38	0.75	2.54	<10, 10-19, ≥20
				5,688	94		10	1.12	0.58	2.15		49	0.95	0.67	1.35		26	1.01	0.65	1.57	
Rohrmann [46]	2013	RI- 065978	A, Ht, W, Edu, MS, PA		1,547		420	0.97	0.87	1.08		365	0.90	0.80	1.01		131	0.87	0.73	1.05	1-14, 15-24, ≥25
Ross (in Wald [47])	1990	RO- 7210	A		56		30	0.90				24	0.70				22	0.70			1-10, 11-20, >20
Sawada [48]	2014	RI- 70208	A, SDV, BM, MS, AC, CB, D	11,062	257																
Severson [49]	1989	RIH- 03251	A	2,341	63																
Shafique [50]	2012	RO-066019	A, BM, SES, BioM	2,093	149																
Shafique [51]	2012	IO	A, BioM, BM, AC, D, SES	1,026	68																
Slattery	1993	RO-003266	None	**333	**167																
Stattin	2000	RO-029289	None																		
Thompson [52]	1989	RIH-003253	A, CB, BM, D, BioM																		
Veierod [53]	1997	RIH- 16633	A		24		11	0.50	0.30	1.10											0-10, ≥11
Villencuve	1999	RO-018446	(I) A, R	**344	**372	173	185	1.00	0.80	1.30	367	389	0.90	0.80	1.20	*721	*661	*0.85	*0.74	*0.99	1-9,10-19,20-29,30+
			(II) A, R, BM, I, FHX, AC, D, race, yrs since quitting smoking, cigarette pack-years	**304	**339	137	162	0.80	0.50	1.40	321	343	0.70	0.40	1.30	*635	*567	*0.6	*0.39	*0.90	1-9,10-19,20-29,30+
Visvanathan [54]	2004	RI- 030795	A	127	63																
Watters [55]	2009	RI- 065149	A, D, E, Edu, MS, Ht, BM, PA, FH, CB, PcaM, D A	80,283	5,512		2,433	0.93 0.95	0.89 0.90	0.98 0.99		3,680	0.90 0.90	0.87 0.86	0.94 0.93		5,015	*0.87 *0.83	*0.84 *0.81	*0.90 *0.86	1-10, 11-20, 21-30, 31-40, 41-60, >60
Will [56]	1999	IO	A																		
Zhang	2002	RO-029063	None	**284	**43	186	18	*0.67	*0.40	*1.13	174	13	*0.53	*0.29	*0.96	268	26	*0.67	*0.42	*1.07	<10, 10-19, 20+

Abbreviations: A = Age, AC = Alcohol Consumption, B = Baseline, BioM = Biochemical Markers, BM = Body Mass Index, CB = Comorbidities, CE = Chemical Exposure, D = Diet variable, E = Ethnicity, Edu = Education, FHx = Family History of Prostate Cancer, HS = Health Status, Ht = Height, I = Income, IO = Study reviewed by Islami et al. only, IH = Study reviewed by Islami et al. and Huncharek et al., MS = Marital Status, N/A = not applicable, O = Occupation, PA = Physical Activity, PcaM = Prostate Cancer Markers, R = Area of Residence, Rev = Study reviewed by, RH = Study available to the RMA and by Harcharek et al., RI = Study available to the RMA and by Islami et al., RIH = Study available to the RMA, Huncharek et al. and Islami et al., RO = Study available to the RMA Only, Rx = Medications, SDV = Study Design Variables, SES = Socio-Economic Status, SM = Smoking Markers, VitSup = Vitamin Supplementation, W = Weight

Table 7 Studies included in meta-analyses for the association between cigarette smoking by cumulative dosage (<20, 20 to 40, 40 or more pack years) ("current" smokers with "never" smokers) and prostate cancer incidence

First author	Year	Rev-RMA ID	Adjustment	Never smoked/Non-smoker**		<20 pack years					20 to 40 pack years					40+ pack years					Reported categories
				Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI		Non-cases (n)	Cases (n)	RR/OR	CI		Non-cases (n)	Cases (n)	RR/OR	CI		Pack-years (ǂgram-years)
Adami [7]	1996	RIH-016355	A	39,636	682																
Andersson	1996	RO- 029275	A																		
Alavanja [8]	2003	RO- 012174	A, E, R, Edu, PcaM, BM, D, VitSup, PA, CE	25,159	195																
Bae [9]	2013	RI- 70206	A	3,169	29	5,111	24	*0.70	*0.45	*1.10	3,662	21	0.75	0.43	1.29	1,490	8	0.55	0.25	1.19	1-10, 11-15, 16-20, 21-34, ≥35
Baglietto [10]	2006	IO	None	6,605	291																
Band	1999	RO- 017379	None	987	352																
Barba	2004	RO- 033231	None	*77	*21																
Butler [11]	2009	RI- 065154	A, SDV, Edu, BioM, D	11,409	108																
Cerhan [12]	1997	RIH- 016660	A	411	26		14	1.30	0.70	2.50							16	2.00	1.10	3.80	<31, 31-55, >55
Darlington	2007	RO- 065148	A, FHx, BM, Edu, O	373	158	385	189	1.20	0.90	1.50	391	191	1.20	0.90	1.50	387	174	1.10	0.80	1.40	0-20, 21-43, >43
Dillner [13]	1998	RO- 16118	None																		
Engeland [14]	1996	RIH- 009479	A	1,878	139																
Everatt [15]	2014	RO- 71303	A, Edu, BM, AC A	1,997	137	1,211	48	*0.78 *0.78	*0.57 *0.58	*1.07 *1.06	810 810	18 18	0.50 0.49	0.30 0.30	0.81 0.81						<10, 10-19, 20-29, ≥30
Fincham	1990	RO- 007481	None	153	106																
Friedenreich	2003	RO- 030566	A	*318	*275																
Furuya	1998	RO- 013932	None	*90	*157																
Geybels [16]	2012	IO	A, SM		492																
Giles	2001	RO- 029017	A, FHx, calendar year, study centre, country of birth	486	540	290	316	1.01	0.81	1.26	292	294	0.92	0.73	1.15	332	316	0.96	0.77	1.20	<15, 15-35, >35
Giovannucci [17]	2007	RIH- 065156	A, PcaM, BM, Ht, PA, CB, E, D, VitSup																		
Giovannucci [18]	1999	RH- 017143	A, BM, D		580																
Gonzalez [19]	2007	IO	A	13,211	303																
Gronberg [20]	1996	RO- 007192	A	321	117																
Grundmark [21]	2011	IO	None	449	69																
Hakulinen [22]	1996	RO- S2.6	None	900	62	1,333	52	*0.58	*0.41	*0.83											1-199 ǂ, 200-499 ǂ, ≥500 ǂ
			None	2,114	17	3,176	14	*0.55	*0.27	*1.11											
Hayes	1994	RO- 003265	A, study site, race	**265	**174	**256	**180	1.10	0.80	1.40	**322	**248	1.10	0.90	1.50	**308	**270	1.20	0.90	1.60	<20. 20-44, >44

Table 7 Studies included in meta-analyses for the association between cigarette smoking by cumulative dosage (<20, 20 to 40, 40 or more pack years) ("current" smokers with "never" smokers) and prostate cancer incidence - continued

First author	Year	Rev-RMA ID	Adjustment	Never smoked/Non-smoker**		<20 pack years					20 to 40 pack years					40+ pack years					Reported categories
				Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI		Non-cases (n)	Cases (n)	RR/OR	CI		Non-cases (n)	Cases (n)	RR/OR	CI		Pack-years ([1]gram-years)
Heikkila [23]	1999	RI- 018599	None	188	114																
Heikkila [24]	2013	IO	A, SES, BM, AC	**83,805	**706																
Helzlsouer [25]	2000	RO- 028981	None	98	48																
Hiatt [26]	1994	RIH- 003316	A, E, AC, Edu	14,340	79																
Honda [27]	1988	RO- 003308	None	69	44																
Hsing	2000	RO- 029107	None	174	100																
Huang	2003	RO- 028931	None	(I) *125	(I) *61																
				(II) *117	(II) *55																
Hultdin [28]	2005	IO	None	230	115																
Karlsen [29]	2012	IO	None	**12,954	**81																
Karppi [30]	2012	IO	None	**660	**57																
Karunasinghe [31]	2012	RO- 066733	None	273	127																
Key	1997	RO- 012167	None	82	79																
Kondo [3]	2013	RO- 70205	A, SM, CE, AC	6,104	272																
Koutros [32]	2013	IO	None	313	398																
		RIH- 3179																			
Le Marchand [33]	1994	IO	A, O, AC, D, BM, PA, HS					*0.90	*0.50	*1.50			*0.70	*0.40	*1.20			*1.20	*0.80	*1.80	1-22, 23-44, ≥45
Lemogne [34]	2013	RIH- 28974	A, E, I					0.76	0.55	1.05											<20, ≥20
Lotufo [35]	2000	RO- 011775	A, Rx, PA, BM, Ht, AC	10,466	443		236	1.20	1.02	1.41		129	0.96	0.78	1.17		126	1.14	0.93	1.40	0.25-19, 20-39, ≥40
		RO- 065151	A, Rx					1.22	1.04	1.43			0.98	0.81	1.19			1.18	0.97	1.44	
Lumey	1997	RIH- 003320	A, MS, O, AS, Edu, Religion	816	296																
Magura	2008	RO- 70207	None	146	130																
Murphy [37]	2013	RIH- 029140	A, SDV, E, FHx, AC	281	233																
Nilsen [38]	2000	RI- 029108	A	6,094	222	4,457	84	*0.90	*0.71	*1.15	2,049	58	1.24	0.92	1.67						1-10, 11-17, 18-25, >25
Nomura [39]	2000	RO- 016995	A	98	87	16	20	1.40	0.70	2.90											1-30, >30
Norrish	1998	IO	None	137	94																
Onitilo [40]	2013	IO	None	389																	
Park [41]	2007	RI- 017444	None	23,419	1326																
Parker [42]	1999	RO- 028497	A		23																
Plaskon [43]	2003	RH- 29009	A, E, FHx, PcaM	266	281	185	197	*0.92	*0.69	*1.22	149	145	*1.05	*0.78	*1.40	103	140	1.60	1.10	2.20	≤10, 11-20, 21-30, 31-40, >40
Putnam [44]	2000	RH	A		24		29	1.70	1.00	3.00							22	1.40	0.80	2.50	<25, 25-50, >50

Table 7 Studies included in meta-analyses for the association between cigarette smoking by cumulative dosage (<20, 20 to 40, 40 or more pack years) ("current" smokers with "never" smokers) and prostate cancer incidence - continued

First author	Year	Rev-RMA ID	Adjustment	Never smoked/Non-smoker**		<20 pack years					20 to 40 pack years					40+ pack years					Reported categories
				Non-cases (n)	Cases (n)	Non-cases (n)	Cases (n)	RR/OR	CI		Non-cases (n)	Cases (n)	RR/OR	CI		Non-cases (n)	Cases (n)	RR/OR	CI		Pack-years ([t]gram-years)
Rohan	1997	RO- 013929	A, study site	124	89	9	5	0.77	0.25	2.41	14	16	1.59	0.72	3.50	32	32	1.39	0.79	2.46	≤15.6, >15.6 and ≤37.6, >37.6
Rohrmann [45]	2007	RIH- 065219	A	3,850	34																
				5,688	94																
Rohrmann [46]	2013	RI- 065978	A, Ht, W, Edu, MS, PA		1,547																
Ross (in Wald [47])	1990	RO- 7210	A		56																
Sawada [48]	2014	RI- 70208	A, SDV, BM, MS, AC, CB, D	11,062	257		53	0.67	0.49	0.91		194	0.84	0.70	1.02		133	0.80	0.65	1.00	0-20, 20-40, >40
			A, SDV					0.70	0.52	0.95			0.83	0.69	1.01			0.79	0.64	0.98	
Severson [49]	1989	RIH- 003251	A	2,341	63																
Shafique [50]	2012	RO- 066019	A, BM, SES, BioM	2,093	149																
Shafique [51]	2012	IO	A, BioM, BM, AC, D, SES	1,026	68																
Slattery	1993	RO- 003266	None	**333	**167																
Stattin	2000	RO- 029289	None																		
Thompson [52]	1989	RIH- 003253	A, CB, BM, D, BioM																		
Veierod [53]	1997	RIH- 016633	A		24																
Villencuve	1999	RO- 018446	(I) A, R	**344	**372	*684	*734	*0.97	*0.84	*1.12	281	272	0.90	0.70	1.10	280	225	0.80	0.60	1.00	1-9, 10-24, 25-39, ≥40
			(II) A, R, BM, I, FHX, AC, D, race, yrs since quitting smoking, cigarette pack-years	**304	**339	588	642	*0.85	*0.68	*1.06	255	231	0.70	0.50	0.90	250	198	0.60	0.50	0.80	
Visvanathan [54]	2004	RI- 030795	A	127	63																
Watters [55]	2009	RI- 065149	A, D, E, Edu, MS, Ht, BM, PA, FH, CB, PcaM, D	80,283	5,512																
Will [56]	1999	IO	A																		
Zhang	2002	RO- 029063	None	**284	**43																

Abbreviations: A = Age, AC = Alcohol Consumption, B = Baseline, BioM = Biochemical Markers, BM = Body Mass Index, CB = Comorbidities, CE = Chemical Exposure, D = Diet variable, E = Ethnicity, Edu = Education, FHx = Family History of Prostate Cancer, HS = Health Status, Ht = Height, I = Income, IO = Study reviewed by Islami et al. only, IH = Study reviewed by Islami et al. and Huncharek et al., MS = Marital Status, N/A = not applicable, O = Occupation, PA = Physical Activity, PcaM = Prostate Cancer Markers, R = Area of Residence, Rev = Study reviewed by, RH = Study available to the RMA and by Harcharek et al., RI = Study available to the RMA and by Islami et al., RIH = Study available to the RMA, Huncharek et al. and Islami et al., RO = Study available to the RMA Only, Rx = Medications, SDV = Study Design Variables, SES = Socio-Economic Status, SM = Smoking Markers, VitSup = Vitamin Supplementation, W = Weight

3.1 Meta-analyses of studies available to the RMA for the association between cigarette smoking and prostate cancer incidence

Table 8 Summary of studies available to the RMA included in meta-analyses (Models A to F) for the association between cigarette smoking ("ever" [former + current] smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A	Model B	Model C	Model D	Model E	Model F
Honda	1988	√					√
Mills	1989	√	√	√	√		
Severson	1989	√	√	√	√		√
Thompson	1989	√		√	√	√	
Fincham	1990	√					√
Ross	1990	√	√	√	√		
Slattery	1993	√					√
Hayes	1994	√		√	√	√	√
Hiatt	1994	√		√	√	√	√
Le Marchand	1994	√		√	√	√	
Adami	1996	√	√	√	√		√
Andersson	1996	√	√	√	√		√
Engeland	1996	√	√	√	√		√
Gronberg	1996	√	√	√	√		√
Hakulinen (1)	1996	√					√
Hakulinen (2)	1996	√					√
Cerhan	1997	√	√	√	√	√	√
Key	1997	√					√
Lumey	1997	√		√	√	√	√
Rohan	1997	√		√	√	√	√
Veierod	1997	√	√	√	√		
Dillner [c]	1998	√					
Furuya	1998	√					√
Norrish	1998	√					√
Band	1999	√					√
Giovannucci [d]	1999	√		√	√	√	
Heikkila [c]	1999						√
Parker [a]	1999						
Villencuve	1999	√		√	√	√	√
Helzlsouer [b]	2000						
Hsing	2000	√					√
Lotufo	2000	√	√	√	√	√	√
Nilsen	2000	√	√	√	√		√
Nomura	2000	√	√	√	√		√
Putnam [a]	2000	√	√	√	√		
Stattin	2000						
Giles	2001	√		√	√	√	√
Zhang	2002	√					√
Alavanja	2003	√		√	√	√	√
Friedenreich	2003	√	√	√	√		√
Huang (1)	2003	√					√
Huang (2)	2003	√					√
Plaskon	2003	√		√	√	√	√
Barba	2004	√					√
Visvanathan [b]	2004	√	√	√	√		√
Darlington	2007	√		√	√	√	√
Giovannucci [d]	2007						
Rohrmann (1)	2007	√	√	√	√		√
Rohrmann (2)	2007	√	√	√	√		√
Magura	2008	√					√
Butler	2009	√		√	√	√	√
Watters	2009	√	√	√	√	√	√
Karunasinghe	2012	√					√
Shafique	2012	√		√	√	√	√
Bae	2013	√	√	√	√		√
Murphy	2013	√		√	√	√	√
Rohrmann	2013	√		√	√	√	
Everatt	2014	√	√	√	√	√	√
Kondo	2014	√		√	√	√	√

Sawada	2014	√		√	√	√	√

Note:[a, b, c, d] were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data

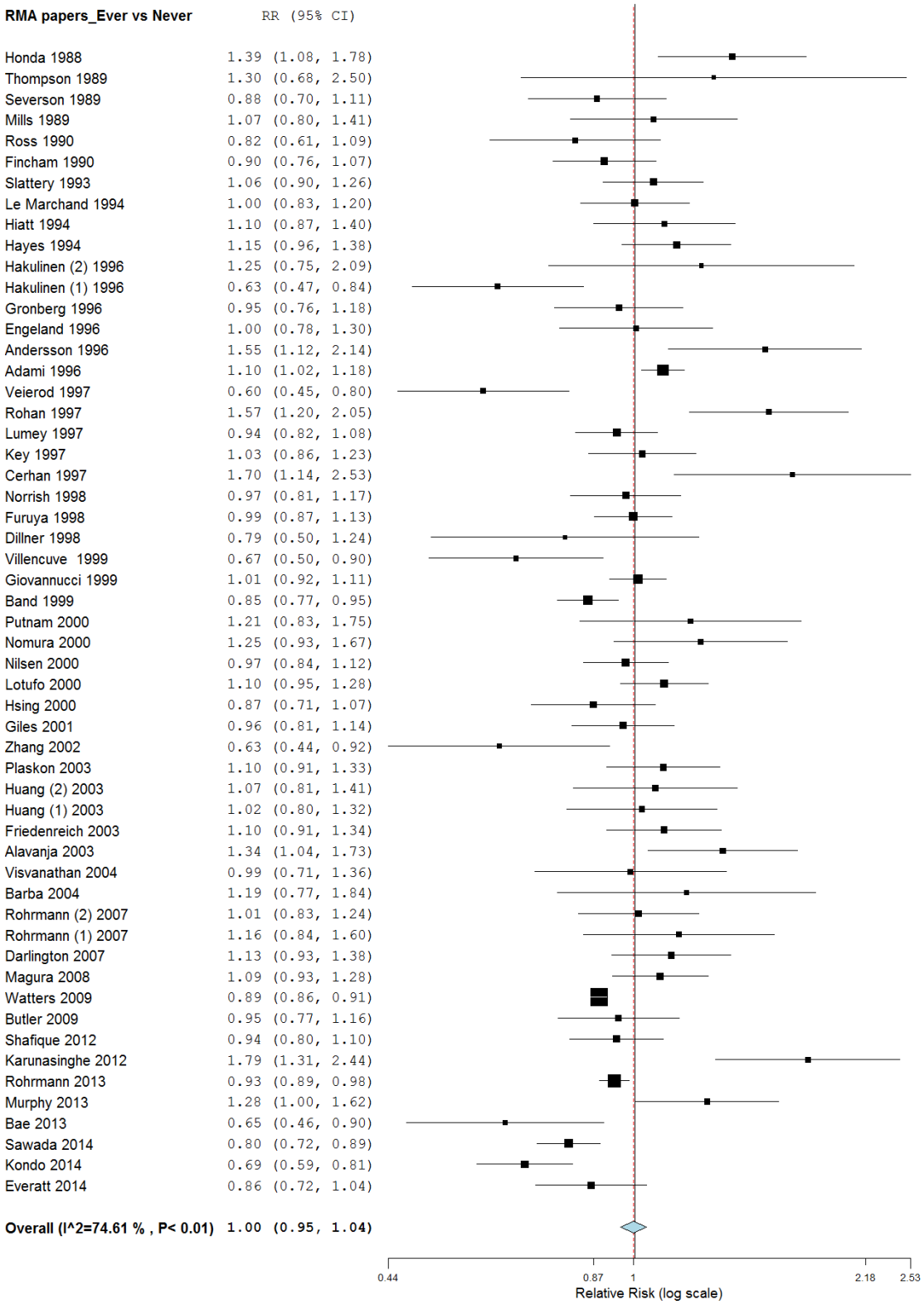


Figure 1A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies available to the RMA includes studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results (Model A)

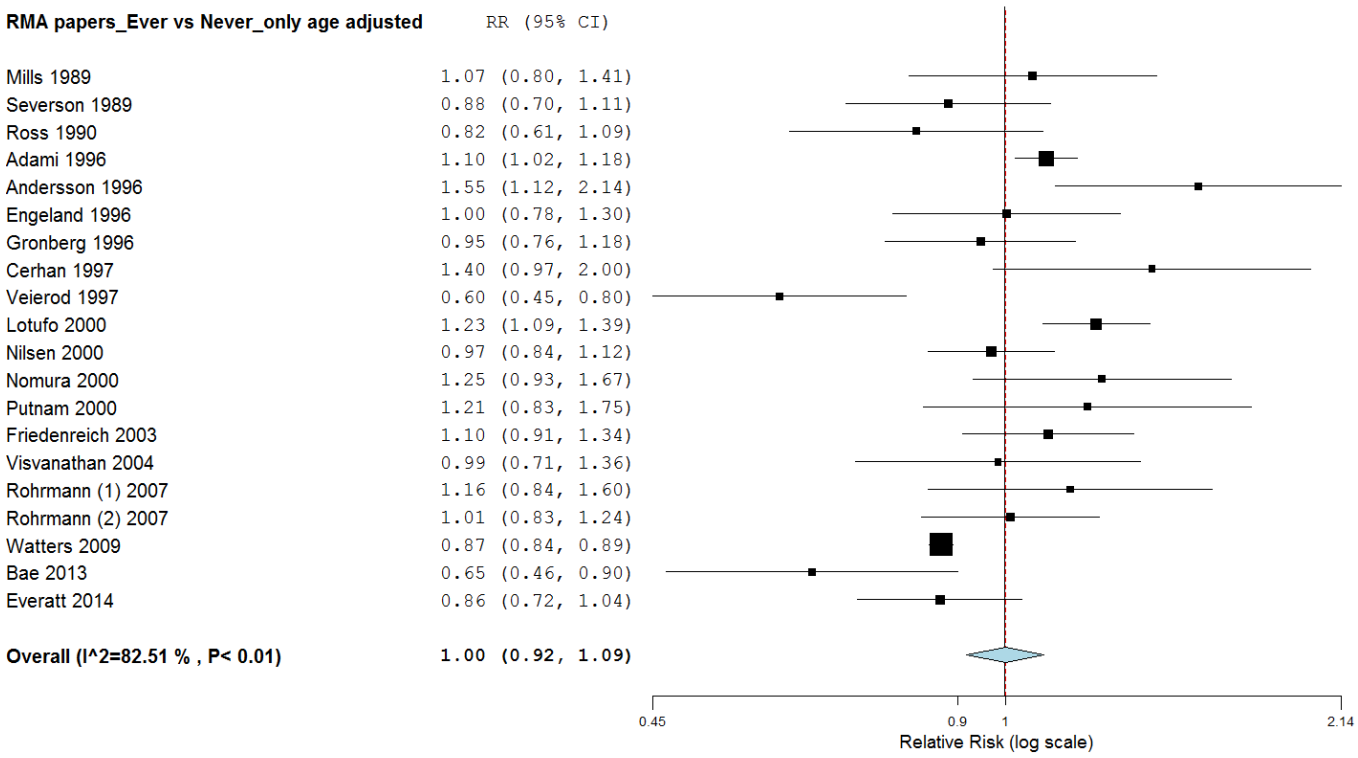


Figure 1B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies available to the RMA includes studies with age-only adjusted data available (Model B)

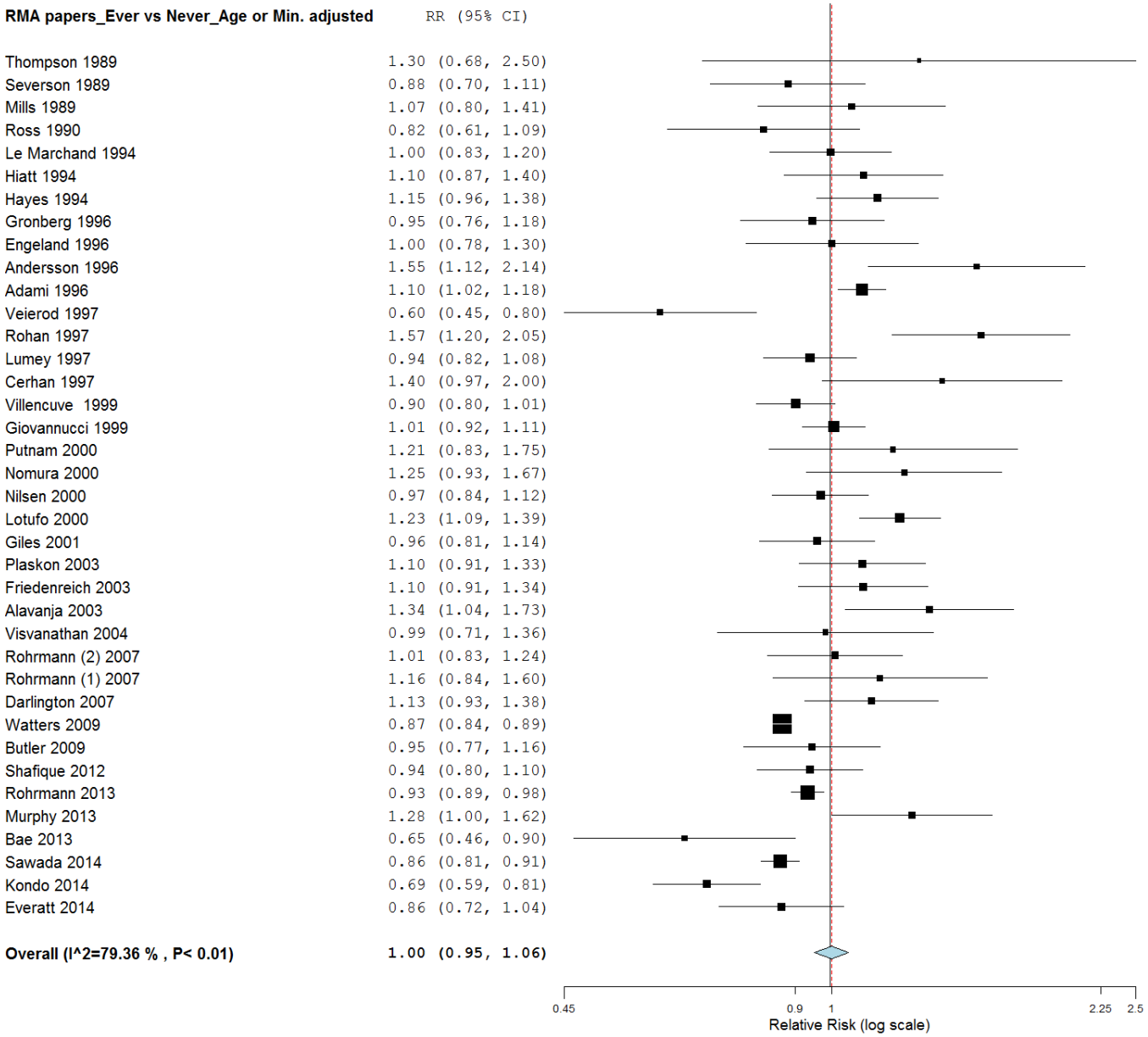


Figure 1C: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies available to the RMA includes studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates (Model C)

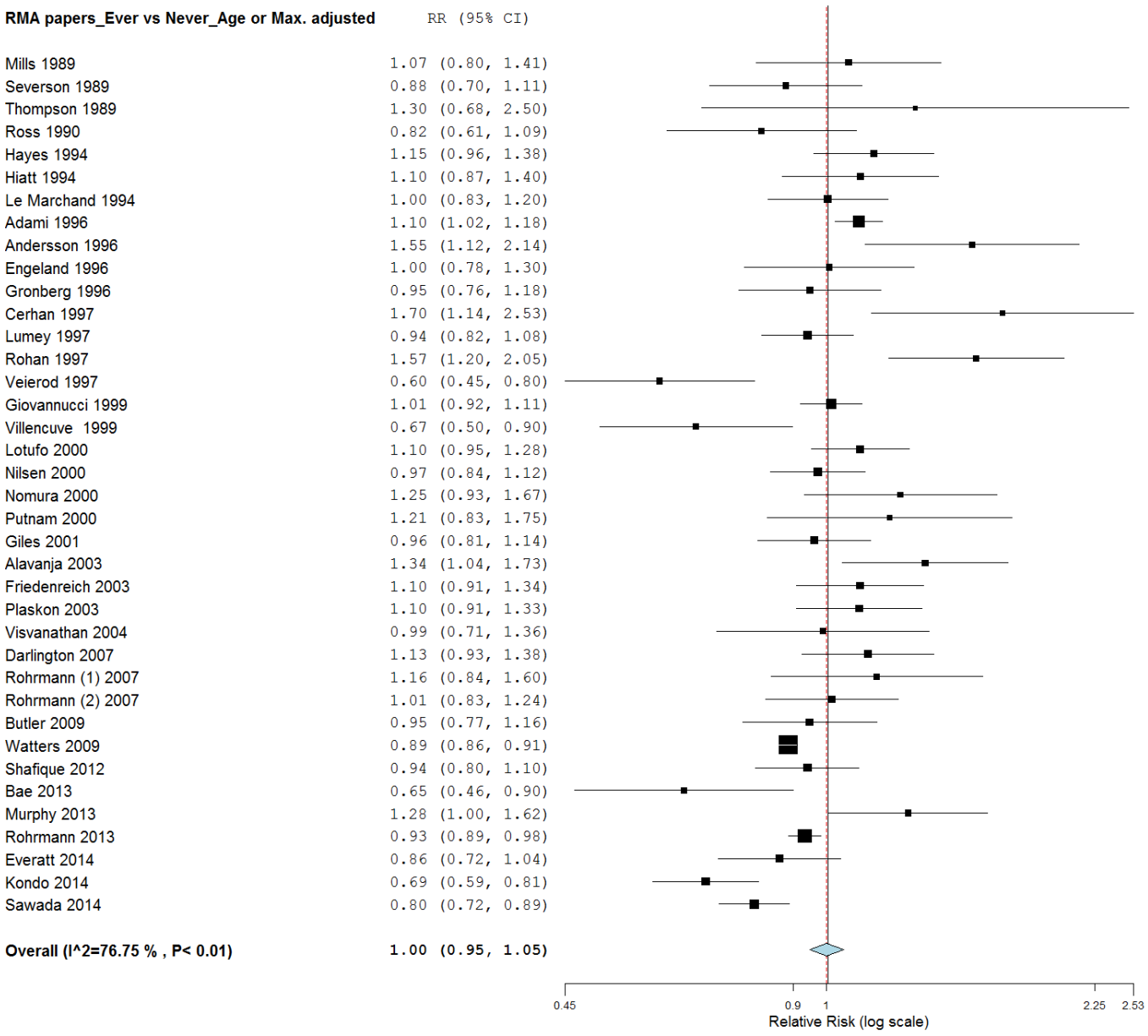


Figure 1D: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies available to the RMA includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)

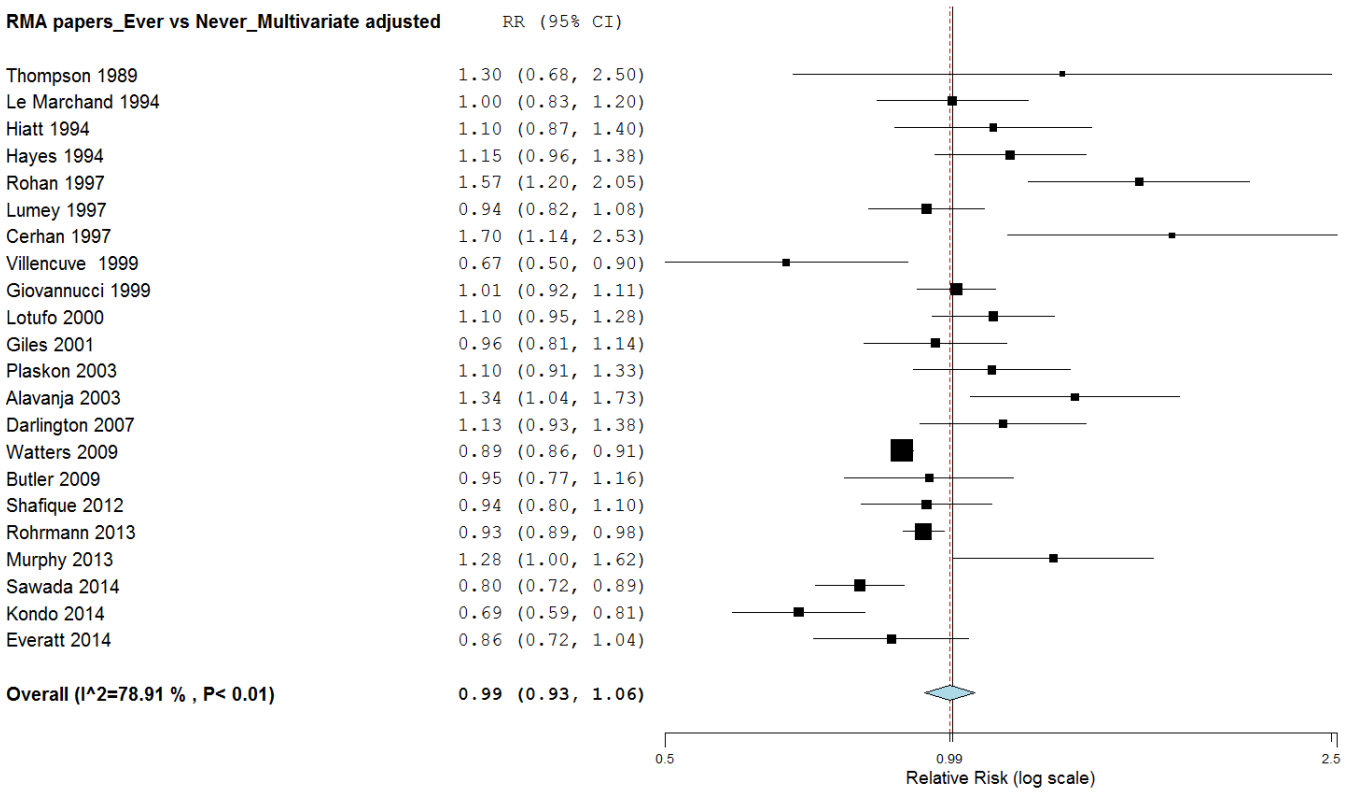


Figure 1E: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies available to the RMA includes studies with multivariate adjustment (highest number of covariates) (Model E)

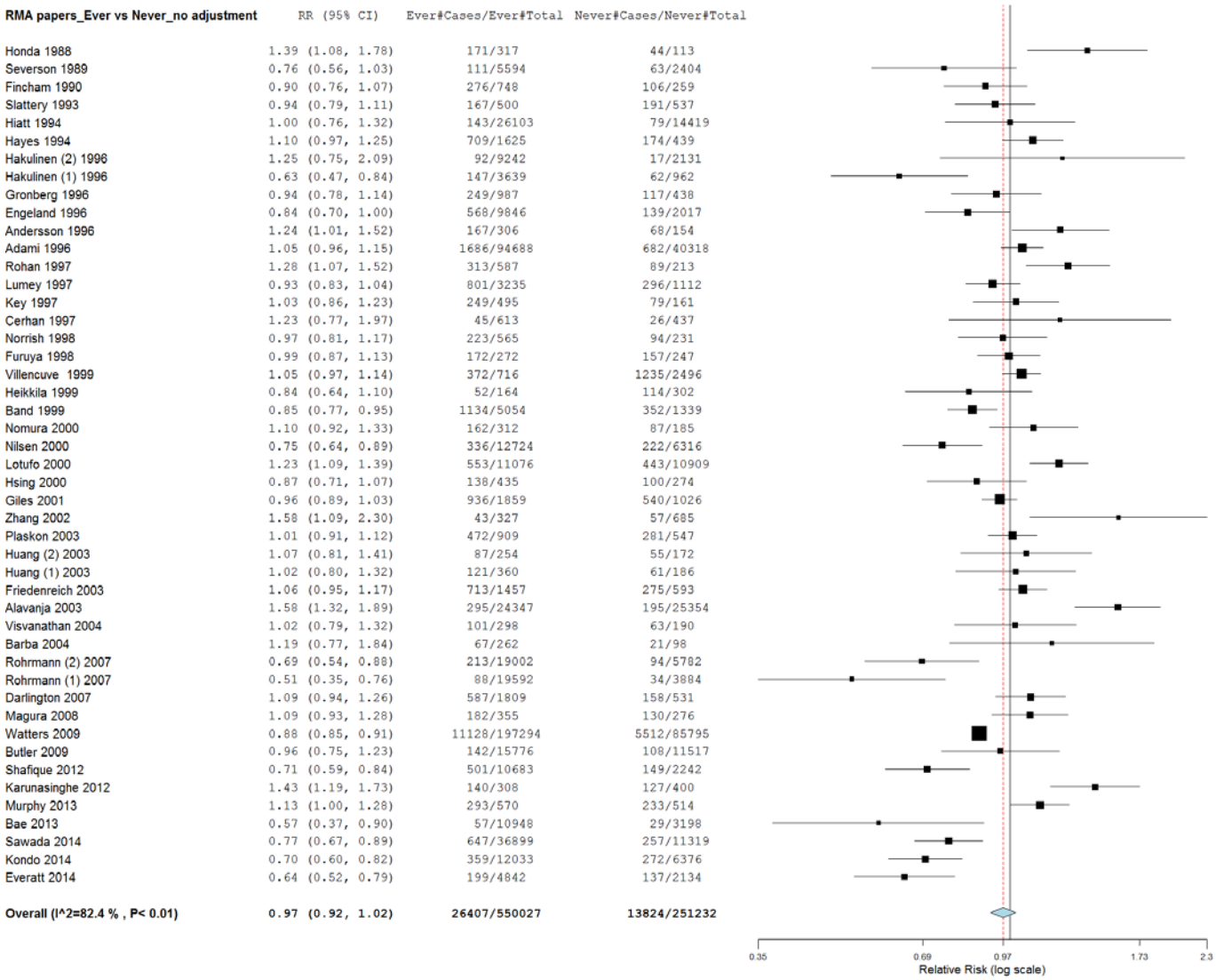


Figure 1F: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies available to the RMA includes studies with non-adjusted raw data (Model F)

Table 9 Summary of studies available to the RMA included in meta-analyses (Models A to F) for the association between cigarette smoking ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A	Model B	Model C	Model D	Model E	Model F
Honda	1988						
Mills	1989	√	√	√	√		
Severson	1989	√	√	√	√		√
Thompson	1989	√		√	√	√	
Fincham	1990	√					√
Ross	1990	√	√	√	√		
Slattery	1993						
Hayes	1994	√		√	√	√	√
Hiatt	1994	√		√	√	√	√
Le Marchand	1994						
Adami	1996	√	√	√	√		√
Andersson	1996	√	√	√	√		√
Engeland	1996	√	√	√	√		√
Gronberg	1996	√	√	√	√		√
Hakulinen (1)	1996	√					√
Hakulinen (2)	1996	√					√
Cerhan	1997	√	√	√	√	√	√
Key	1997	√					√
Lumey	1997	√		√	√	√	√
Rohan	1997	√		√	√	√	√
Veierod	1997	√	√	√	√		
Dillner [c]	1998						
Furuya	1998						
Norrish	1998	√					√
Band	1999						
Giovannucci [d]	1999	√		√	√	√	
Heikkila [c]	1999	√					√
Parker [a]	1999						
Villencuve	1999						
Helzlsouer [b]	2000						
Hsing	2000	√					√
Lotufo	2000	√	√	√	√	√	√
Nilsen	2000	√	√	√	√		√
Nomura	2000	√	√	√	√		√
Putnam [a]	2000	√	√	√	√		
Stattin	2000						
Giles	2001	√		√	√	√	√
Zhang	2002						
Alavanja	2003	√		√	√	√	√
Friedenreich	2003	√					√
Huang (1)	2003	√					√
Huang (2)	2003	√					√
Plaskon	2003	√		√	√	√	√
Barba	2004	√					√
Visvanathan [b]	2004	√	√	√	√		√
Darlington	2007	√		√	√		√
Giovannucci [d]	2007						
Rohrmann (1)	2007	√	√	√	√		√
Rohrmann (2)	2007	√	√	√	√		√
Magura	2008	√					√
Butler	2009	√		√	√	√	√
Watters	2009	√	√	√	√	√	√
Karunasinghe	2012						
Shafique	2012	√		√	√	√	√
Bae	2013	√	√	√	√		√
Murphy	2013	√		√	√	√	√
Rohrmann	2013	√		√	√	√	
Everatt	2014	√	√	√	√	√	√
Kondo	2014	√		√	√	√	√

Sawada	2014	√		√	√	√	√

Note:[a, b, c, d] were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data

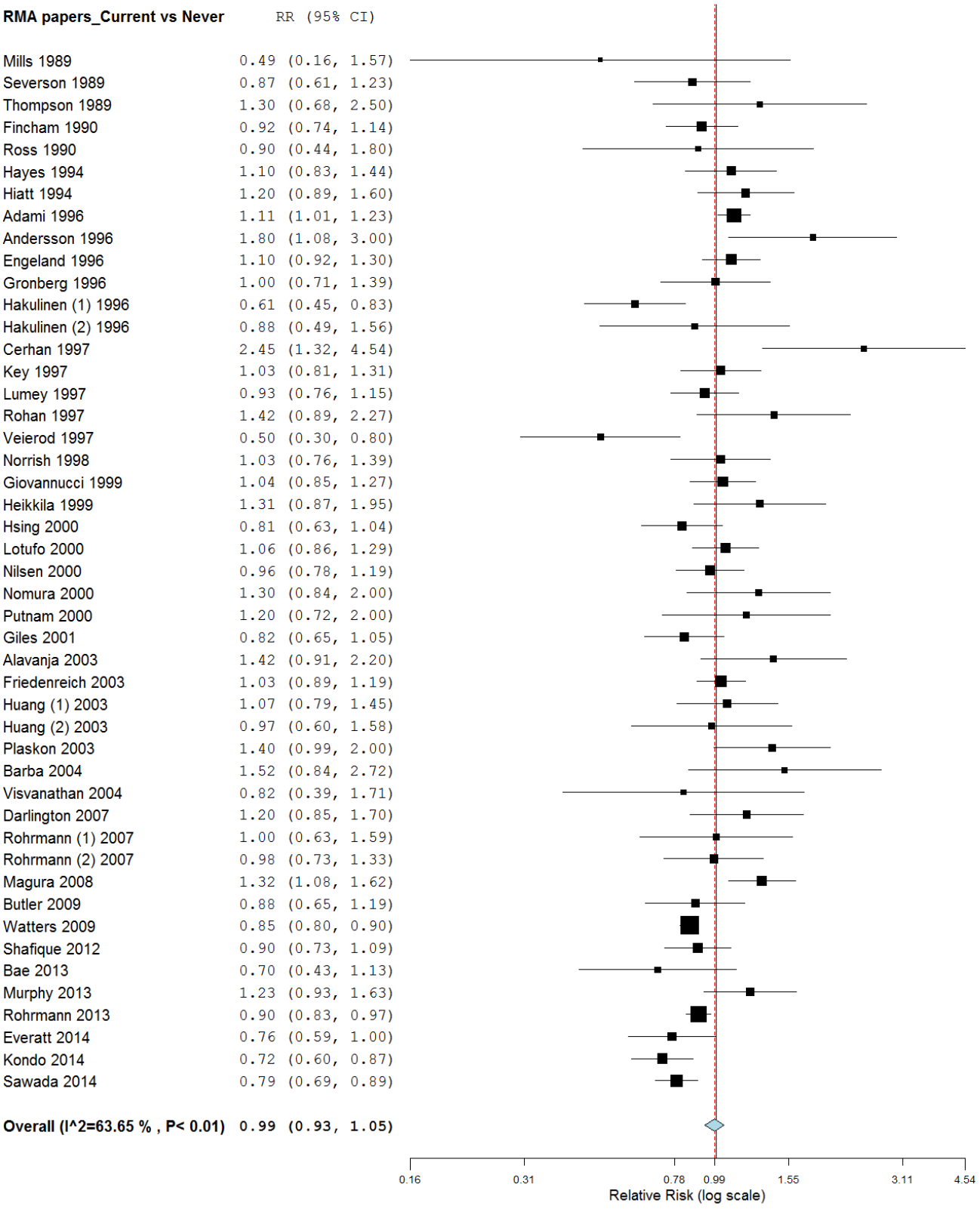

RMA papers_Current vs Never
RR (95% CI)
Mills 1989 0.49 (0.16, 1.57)
Severson 1989 0.87 (0.61, 1.23)
Thompson 1989 1.30 (0.68, 2.50)
Fincham 1990 0.92 (0.74, 1.14)
Ross 1990 0.90 (0.44, 1.80)
Hayes 1994 1.10 (0.83, 1.44)
Hiatt 1994 1.20 (0.89, 1.60)
Adami 1996 1.11 (1.01, 1.23)
Andersson 1996 1.80 (1.08, 3.00)
Engeland 1996 1.10 (0.92, 1.30)
Gronberg 1996 1.00 (0.71, 1.39)
Hakulinen (1) 1996 0.61 (0.45, 0.83)
Hakulinen (2) 1996 0.88 (0.49, 1.56)
Cerhan 1997 2.45 (1.32, 4.54)
Key 1997 1.03 (0.81, 1.31)
Lumey 1997 0.93 (0.76, 1.15)
Rohan 1997 1.42 (0.89, 2.27)
Veierod 1997 0.50 (0.30, 0.80)
Norrish 1998 1.03 (0.76, 1.39)
Giovannucci 1999 1.04 (0.85, 1.27)
Heikkila 1999 1.31 (0.87, 1.95)
Hsing 2000 0.81 (0.63, 1.04)
Lotufo 2000 1.06 (0.86, 1.29)
Nilsen 2000 0.96 (0.78, 1.19)
Nomura 2000 1.30 (0.84, 2.00)
Putnam 2000 1.20 (0.72, 2.00)
Giles 2001 0.82 (0.65, 1.05)
Alavanja 2003 1.42 (0.91, 2.20)
Friedenreich 2003 1.03 (0.89, 1.19)
Huang (1) 2003 1.07 (0.79, 1.45)
Huang (2) 2003 0.97 (0.60, 1.58)
Plaskon 2003 1.40 (0.99, 2.00)
Barba 2004 1.52 (0.84, 2.72)
Visvanathan 2004 0.82 (0.39, 1.71)
Darlington 2007 1.20 (0.85, 1.70)
Rohrmann (1) 2007 1.00 (0.63, 1.59)
Rohrmann (2) 2007 0.98 (0.73, 1.33)
Magura 2008 1.32 (1.08, 1.62)
Butler 2009 0.88 (0.65, 1.19)
Watters 2009 0.85 (0.80, 0.90)
Shafique 2012 0.90 (0.73, 1.09)
Bae 2013 0.70 (0.43, 1.13)
Murphy 2013 1.23 (0.93, 1.63)
Rohrmann 2013 0.90 (0.83, 0.97)
Everatt 2014 0.76 (0.59, 1.00)
Kondo 2014 0.72 (0.60, 0.87)
Sawada 2014 0.79 (0.69, 0.89)
Overall (I^2=63.65 % , P< 0.01) 0.99 (0.93, 1.05)
0.16
0.31
0.78
0.99
1.55
3.11
4.54
Relative Risk (log scale)

Figure 2A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies available to the RMA includes studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results (Model A)

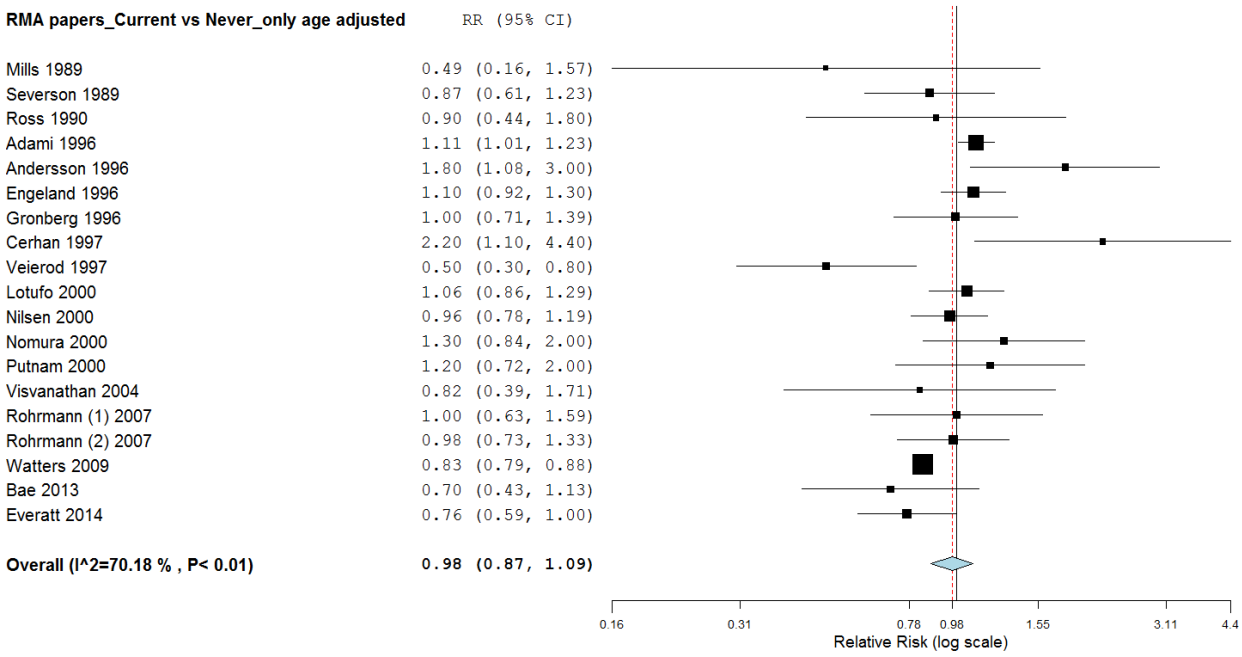


Figure 2B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies available to the RMA includes studies with age-only adjusted data available (Model B)

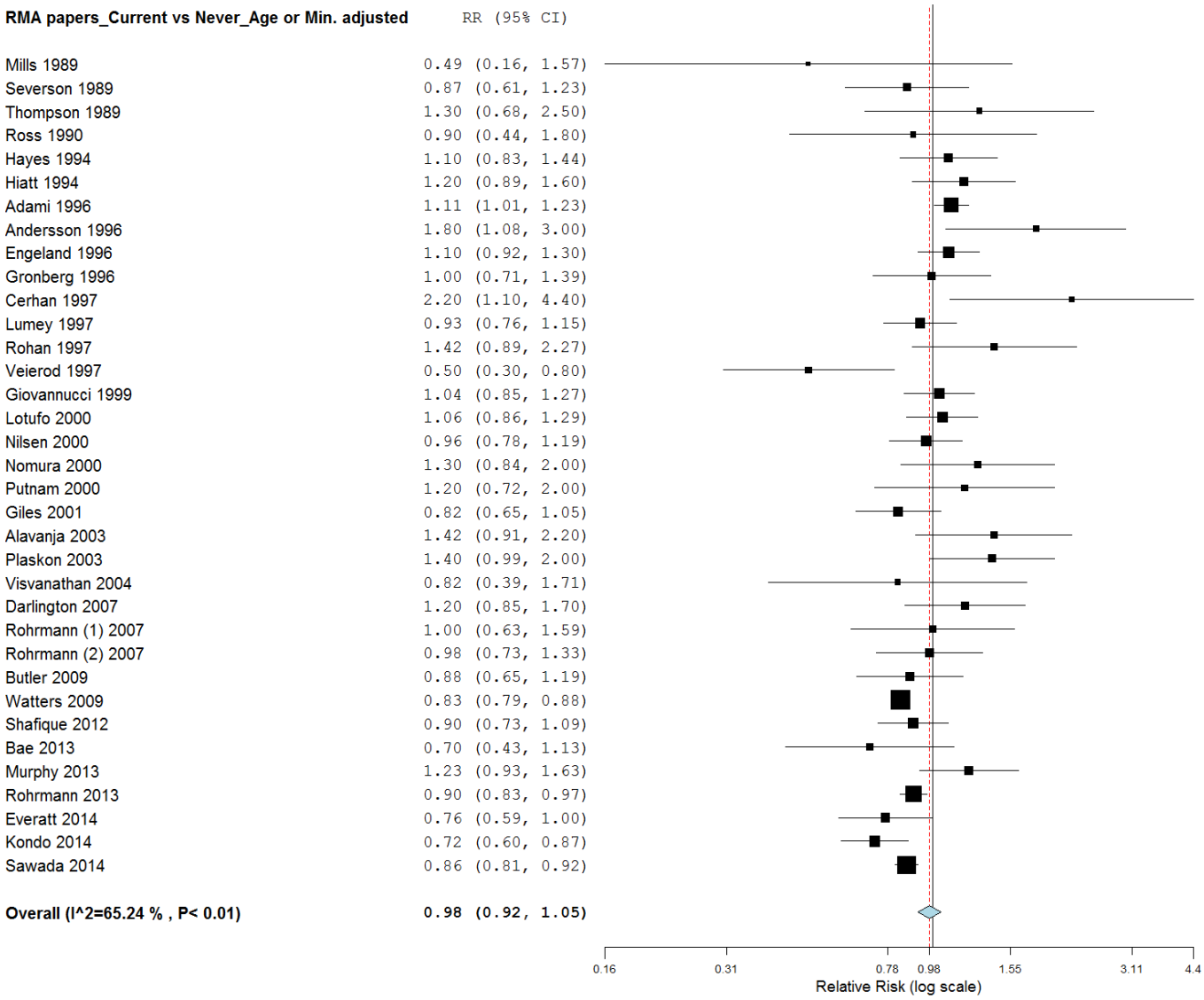


Figure 2C: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies available to the RMA includes studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates (Model C)

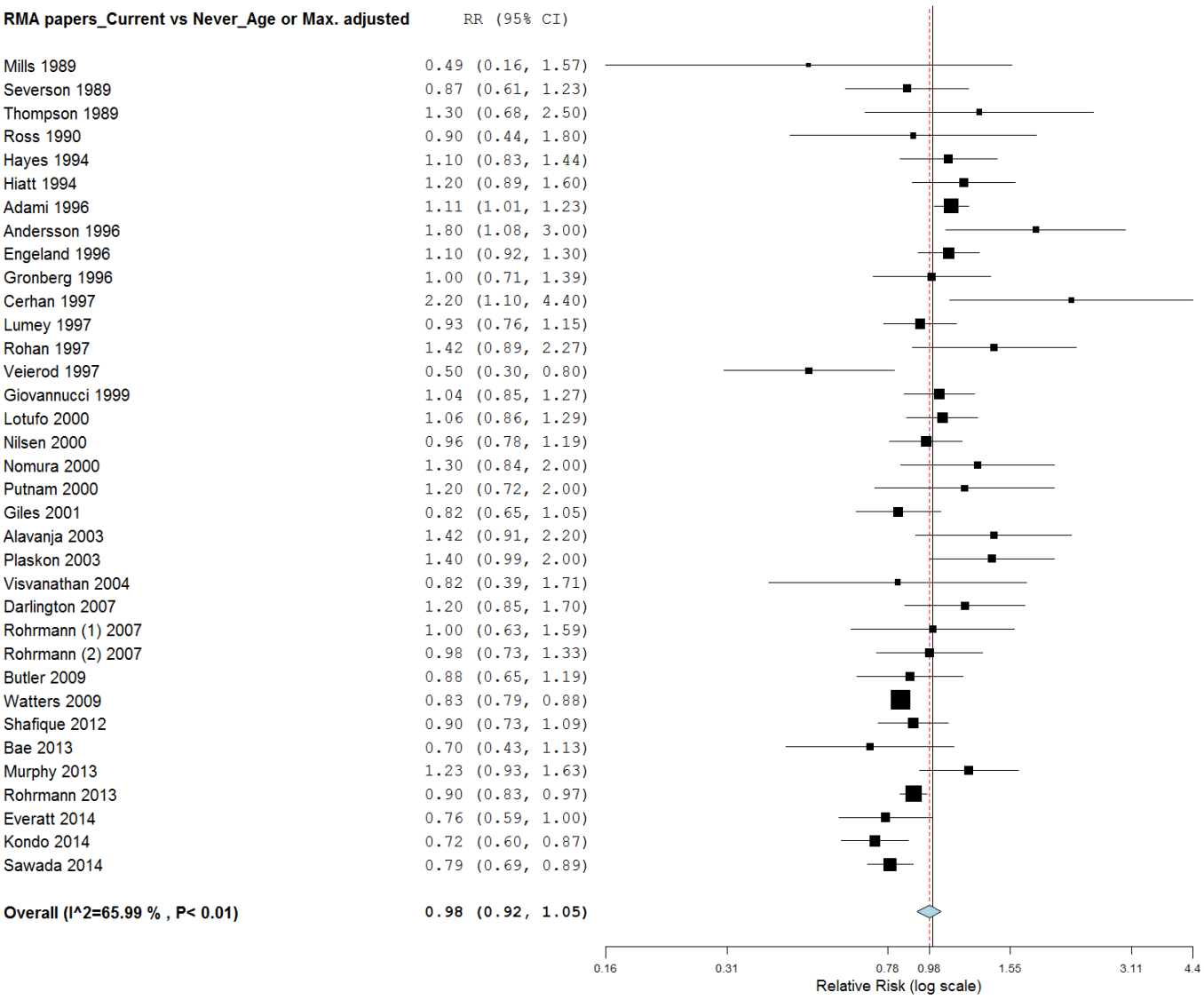


Figure 2D: Forest plot of pooled results reflecting risk of prostate cancer incidence among “current” smokers versus “never” smokers in studies available to the RMA includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)

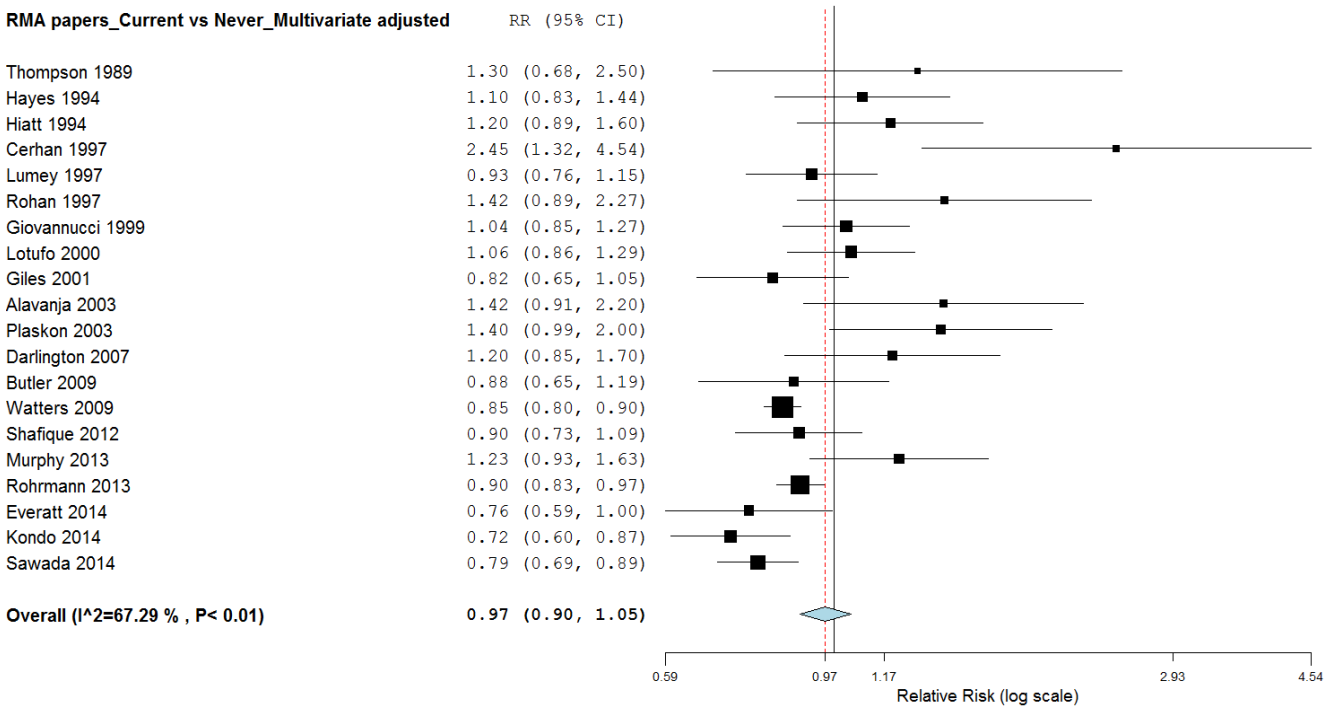


Figure 2E: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies available to the RMA includes studies with multivariate adjustment (highest number of covariates) (Model E)

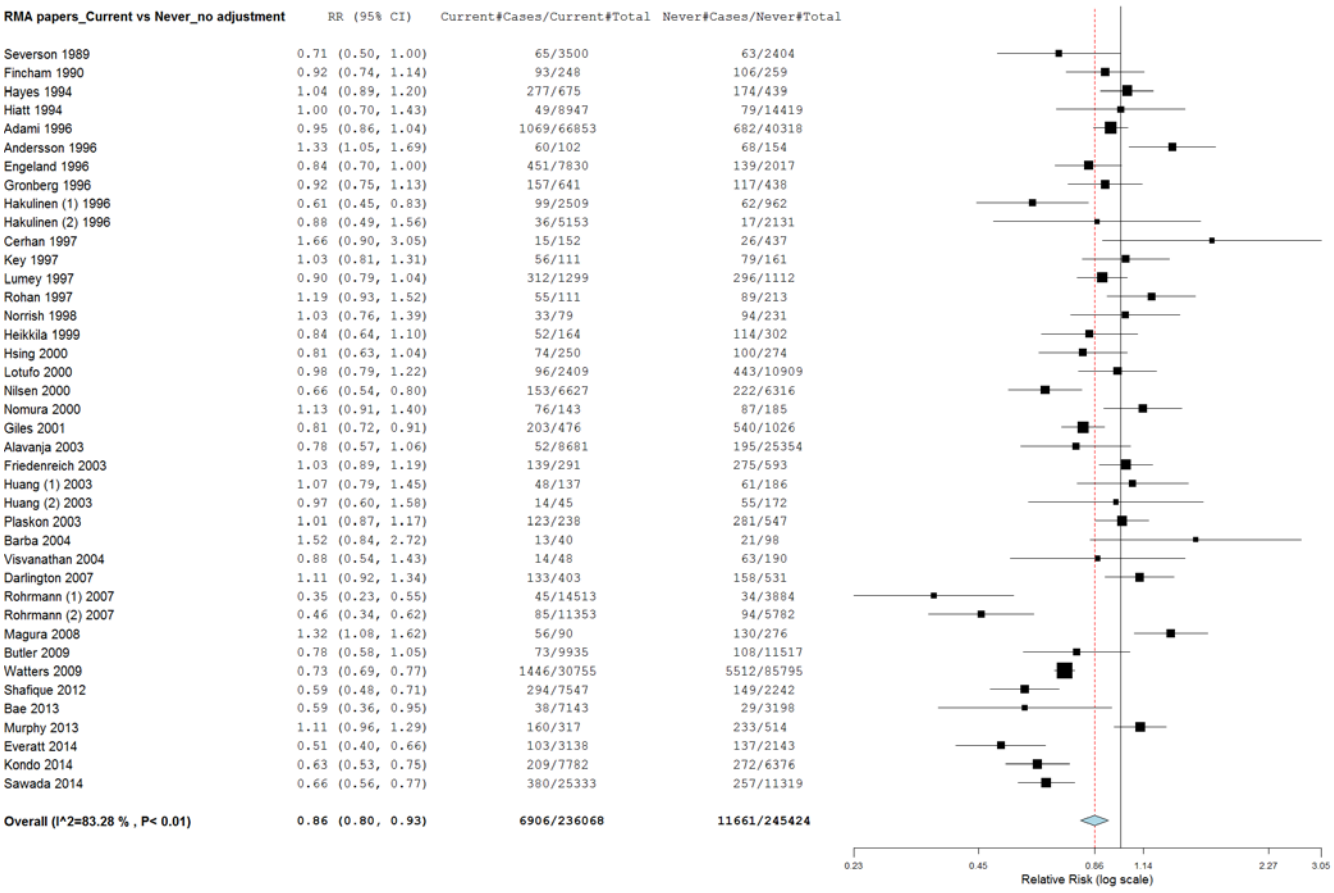


Figure 2F: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers available to the RMA includes studies with non-adjusted raw data (Model F)

Table 10 Summary of studies available to the RMA included in meta-analyses (Models A to F) for the association between cigarette smoking ("current" with "non-current" (never + ex) smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D*	Model E*	Model F
Honda	1988						
Mills	1989						
Severson	1989						√
Thompson	1989						
Fincham	1990						√
Ross	1990						
Slattery	1993						
Hayes	1994						√
Hiatt	1994						√
Le Marchand	1994						
Adami	1996						√
Andersson	1996						√
Engeland	1996						√
Gronberg	1996						√
Hakulinen (1)	1996						√
Hakulinen (2)	1996						√
Cerhan	1997						√
Key	1997						√
Lumey	1997						√
Rohan	1997						√
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						√
Band	1999						
Giovannucci [d]	1999						
Heikkila [c]	1999						√
Parker [a]	1999						
Villencuve	1999						
Helzlsouer [b]	2000						
Hsing	2000						√
Lotufo	2000						√
Nilsen	2000						√
Nomura	2000						√
Putnam [a]	2000						
Stattin	2000						√
Giles	2001						√
Zhang	2002						
Alavanja	2003						√
Friedenreich	2003						√
Huang(1)	2003						√
Huang(2)	2003						√
Plaskon	2003						√
Barba	2004						√
Visvanathan [b]	2004						√
Darlington	2007						√
Giovannucci [d]	2007						
Rohrmann (1)	2007						√
Rohrmann (2)	2007						√
Magura	2008						√
Butler	2009						√
Watters	2009						√
Karunasinghe	2012						
Shafique	2012						√
Bae	2013						√
Murphy	2013						√
Rohrmann	2013						

Everatt	2014						√
Kondo	2014						√
Sawada	2014						√

Note:[a, b, c, d] were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; * Risk estimates not available for "current" with "non-current" comparison

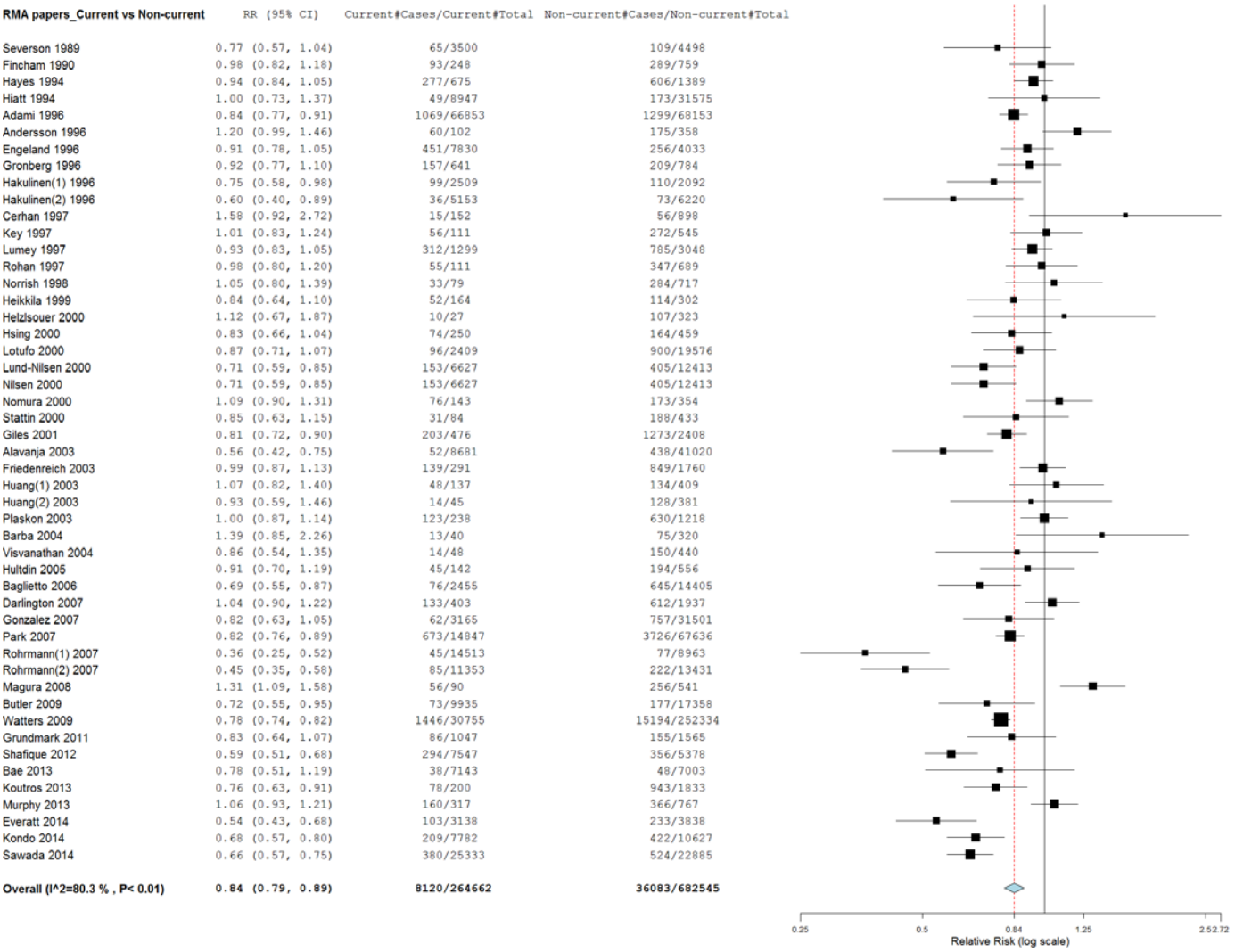


Figure 3A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" with "non-current" (never + ex) smokers available to the RMA includes studies with non-adjusted raw data (Model F)

Table 11 Summary of studies available to the RMA included in meta-analyses (Models A to F) for the association between cigarette smoking ("current" with "ex" (former) smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D*	Model E*	Model F
Honda	1988						
Mills	1989						
Severson	1989						√
Thompson	1989						
Fincham	1990						√
Ross	1990						
Slattery	1993						
Hayes	1994						√
Hiatt	1994						√
Le Marchand	1994						
Adami	1996						√
Andersson	1996						√
Engeland	1996						√
Gronberg	1996						√
Hakulinen (1)	1996						√
Hakulinen (2)	1996						√
Cerhan	1997						√
Key	1997						√
Lumey	1997						√
Rohan	1997						√
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						√
Band	1999						
Giovannucci [d]	1999						
Heikkila [c]	1999						
Parker [a]	1999						
Villencuve	1999						
Helzlsouer [b]	2000						
Hsing	2000						√
Lotufo	2000						√
Nilsen	2000						√
Nomura	2000						√
Putnam a	2000						
Stattin	2000						
Giles	2001						√
Zhang	2002						
Alavanja	2003						√
Friedenreich	2003						√
Huang(1)	2003						√
Huang(2)	2003						√
Plaskon	2003						√
Barba	2004						√
Visvanathan [b]	2004						√
Darlington	2007						√
Giovannucci d	2007						
Rohrmann (1)	2007						√
Rohrmann (2)	2007						√
Magura	2008						√
Butler	2009						√
Watters	2009						√
Karunasinghe	2012						
Shafique (RMA)	2012						√
Bae	2013						√
Murphy	2013						√
Rohrmann	2013						

Everatt	2014						√
Kondo	2014						√
Sawada	2014						√

Note:[a, b, c, d] were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; * Risk estimates not available for "current" with "ex" comparison

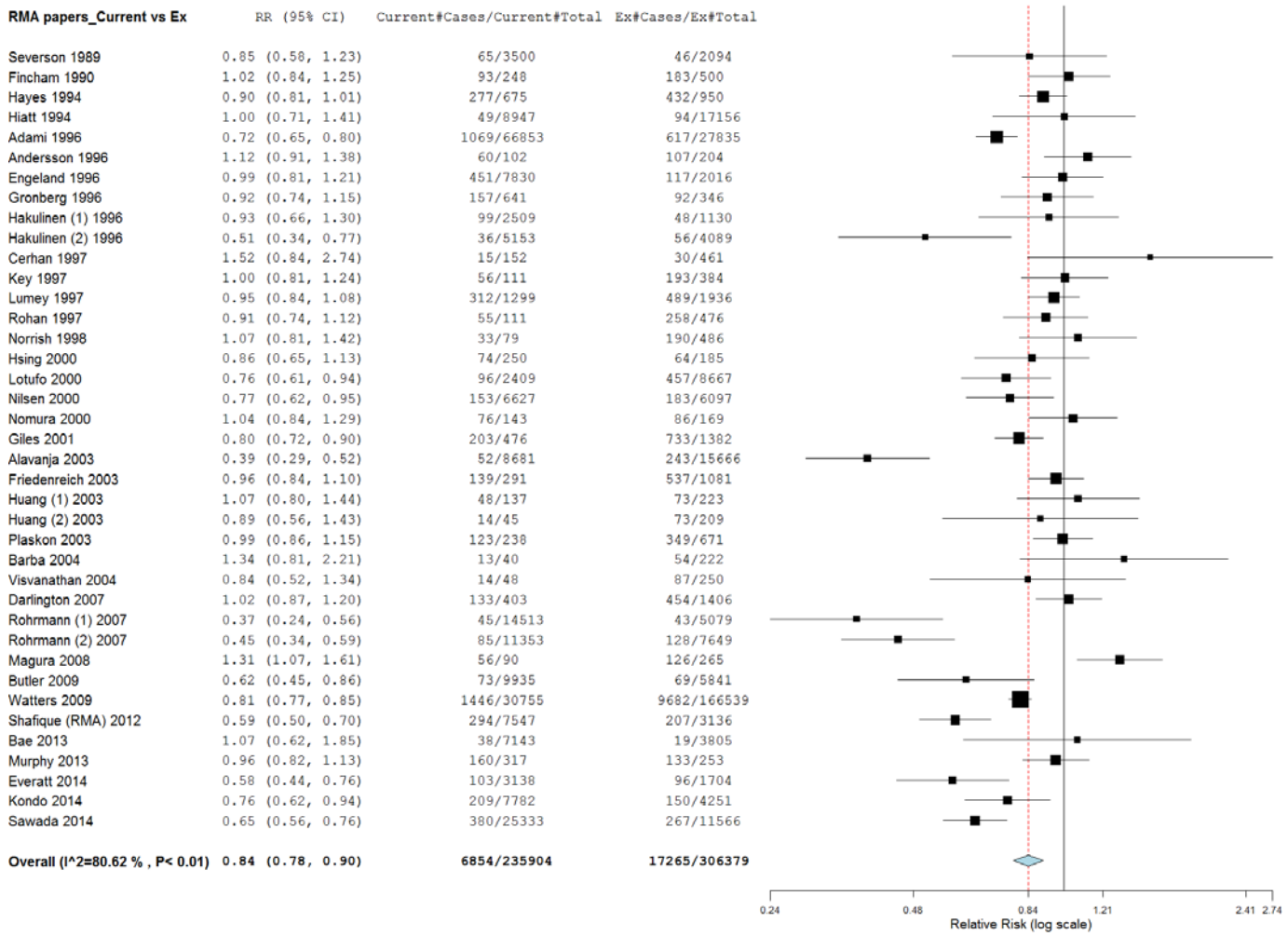


Figure 4A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" with "ex" (former) smokers available to the RMA includes studies with non-adjusted raw data (Model F)

3.2 Meta-analyses of studies considered by Islami et al. for the association between cigarette smoking and prostate cancer incidence

Table 12 Summary of studies considered by Islami et al. included in meta-analyses (Models A to F) for the association between cigarette smoking ("ever" [former + current] smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A	Model B	Model C	Model D	Model E	Model F
Mills	1989	√	√	√	√		
Severson	1989	√	√	√	√		√
Thompson	1989	√		√	√	√	
Hiatt	1994	√		√	√	√	√
Le Marchand	1994	√		√	√	√	
Adami	1996	√	√	√	√		√
Engeland	1996	√	√	√	√		√
Cerhan	1997	√	√	√	√	√	√
Veierod	1997	√	√	√	√		
Heikkila	1999	√					√
Parker	1999	√		√	√		
Lotufo	2000	√	√	√	√	√	√
Nomura	2000	√	√	√	√		√
Visvanathan	2004	√	√	√	√		√
Rohrmann (1)	2007	√	√	√	√		√
Rohrmann (2)	2007	√	√	√	√		√
Giovannucci	2007	√		√	√		
Butler	2009	√		√	√	√	√
Watters	2009	√	√	√	√	√	√
Shafique (Islami)	2012	√		√	√	√	√
Bae	2013	√	√	√	√		√
Rohrmann	2013	√		√	√	√	
Sawada	2014	√		√	√	√	√
Will	1999	√	√	√	√		
Nilsen (as Lund-Nilsen)	2000	√	√	√	√		√
Hultdin	2005	√					√
Baglietto	2006	√					√
Gonzalez	2007	√	√	√	√		√
Park	2007	√					√
Grundmark	2011	√					√
Geybels	2012	√		√	√	√	
Karppi	2012	√					√
Heikkila	2013	√		√	√	√	√
Koutros	2013	√					√
Lemogne	2013	√		√	√	√	
Karlsen	2012	√					√
Onitilo	2013	√					

Note:[a, b, c, d] were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data

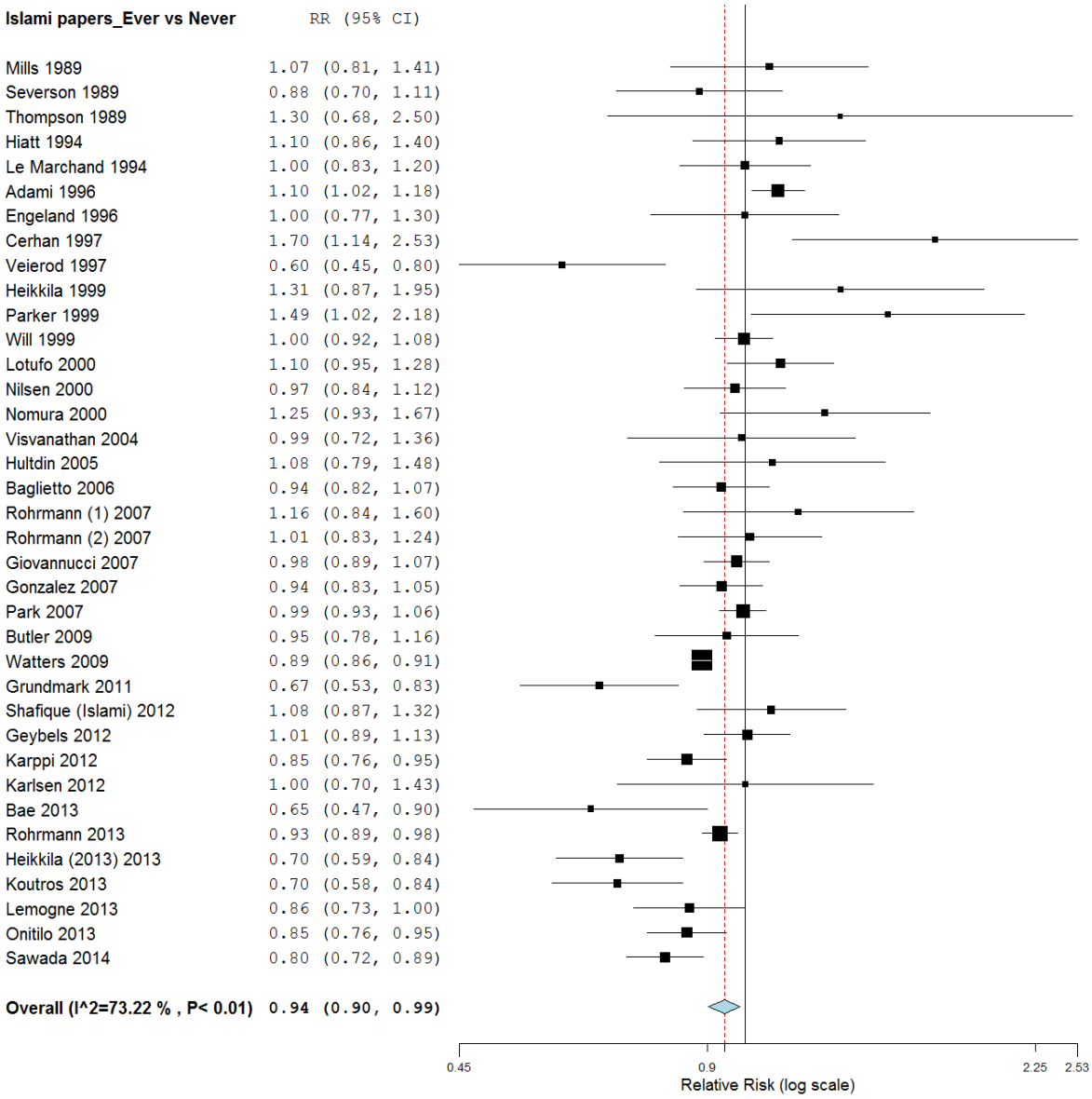


Figure 5A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies considered by Islami et al. includes studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results (Model A)

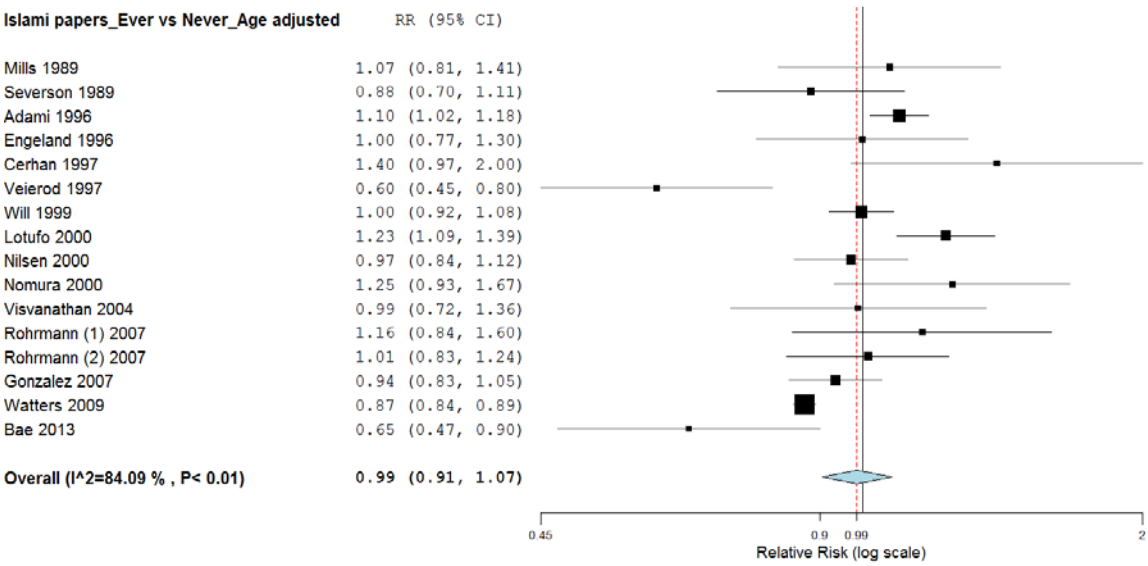


Figure 5B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies considered by Islami et al. includes studies with age-only adjusted data available (Model B)

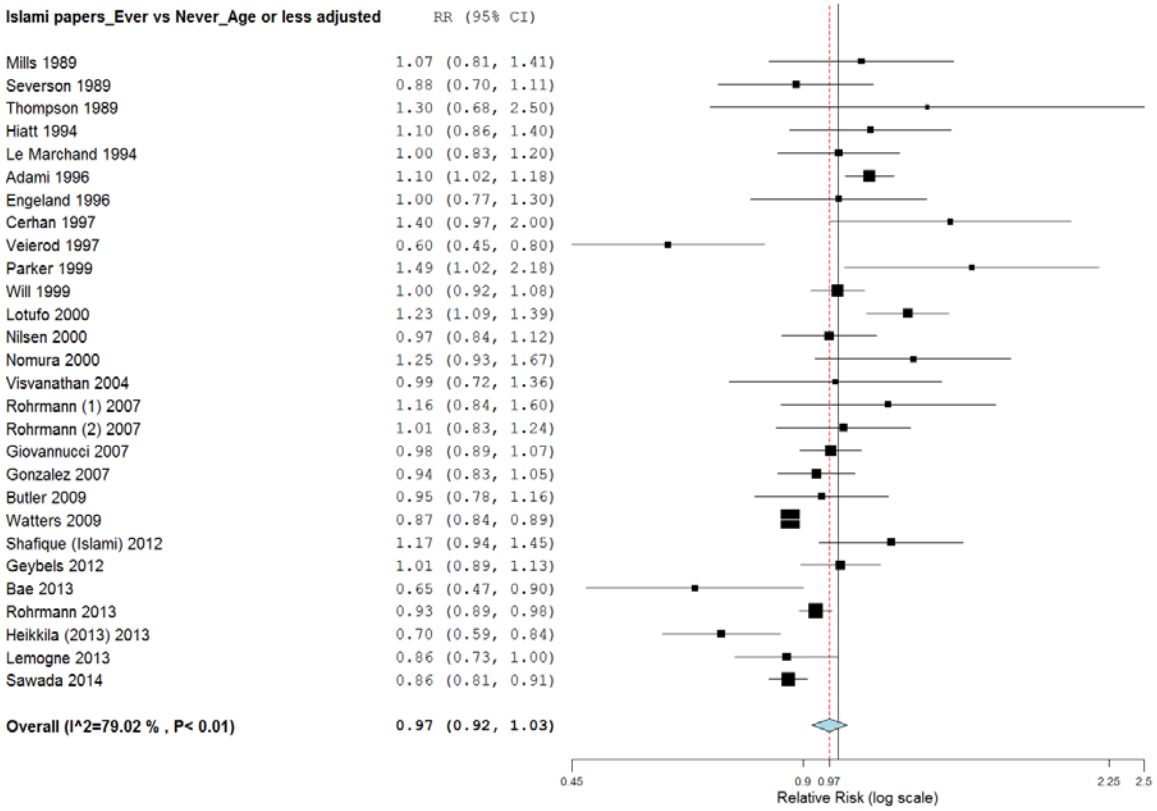


Figure 5C: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies considered by Islami et al. includes studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates (Model C)

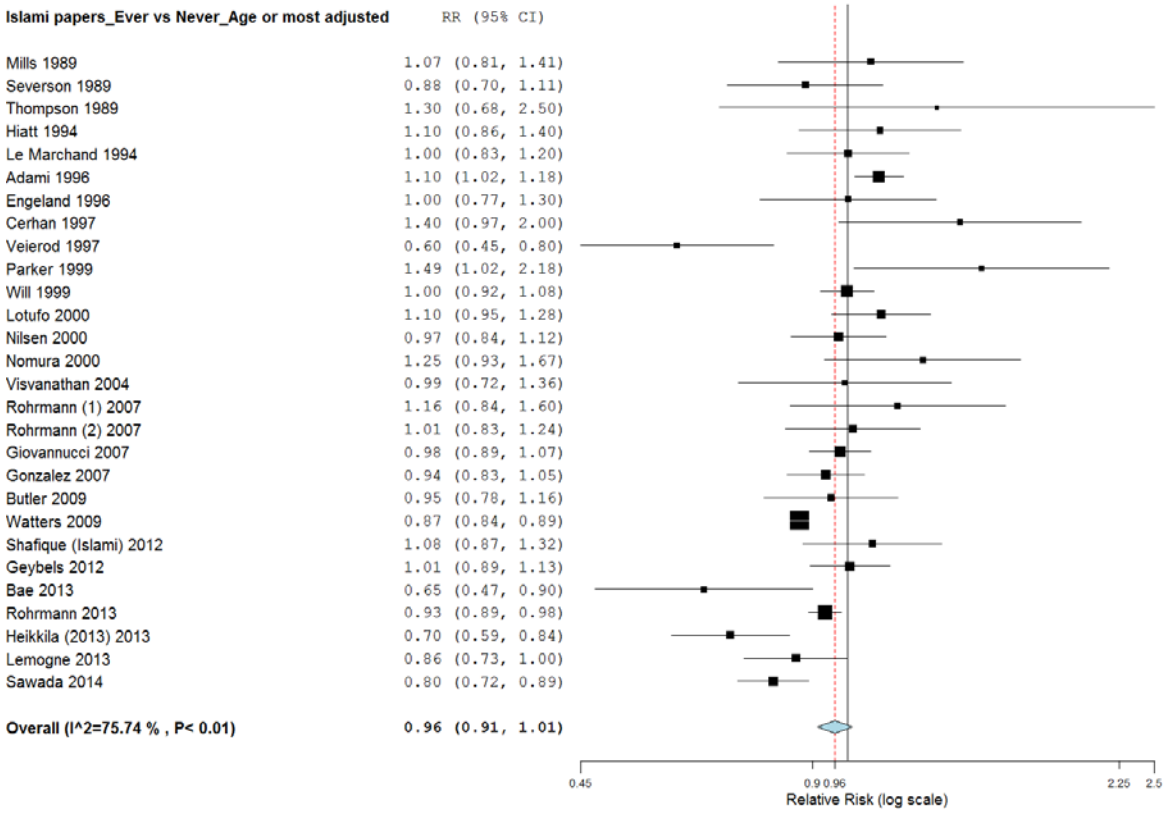


Figure 5D: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies considered by Islami et al. includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)

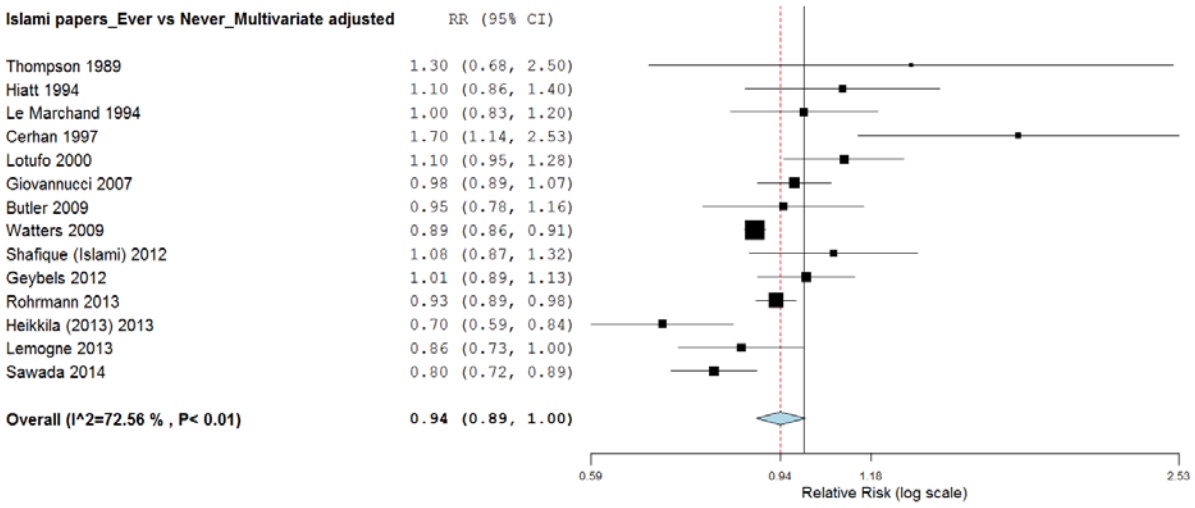


Figure 5E: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies considered by Islami et al. includes studies with multivariate adjustment (highest number of covariates) (Model E)

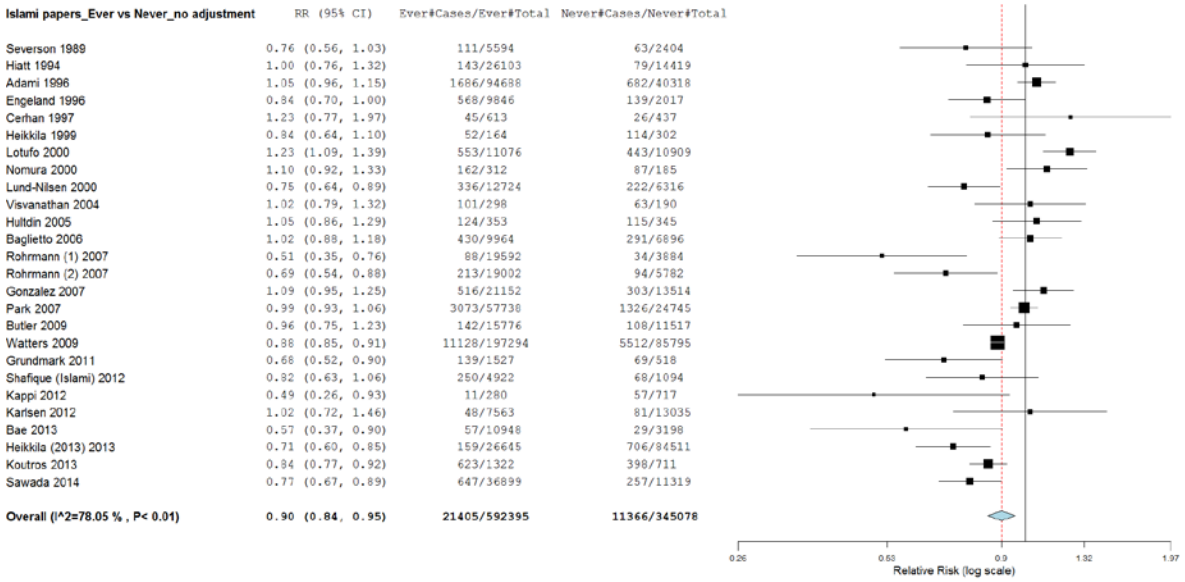


Figure 5F: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies considered by the Islami et al. includes studies with non-adjusted raw data (Model F)

Table 13 Summary of studies considered by *Islami et al.* included in meta-analyses (Models A to F) for the association between cigarette smoking ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A	Model B	Model C	Model D	Model E	Model F
Mills	1989	√	√	√	√		
Severson	1989	√	√	√	√		√
Thompson	1989	√		√	√	√	
Hiatt	1994	√		√	√	√	√
Le Marchand	1994						
Adami	1996	√	√	√	√		√
Engeland	1996	√	√	√	√		√
Cerhan	1997	√	√	√	√	√	√
Veierod	1997	√	√	√	√		
Heikkila	1999	√					√
Parker	1999	√	√	√	√		
Lotufo	2000	√	√	√	√	√	√
Nomura	2000	√	√	√	√		√
Visvanathan	2004	√	√	√	√		√
Rohrmann (1)	2007	√	√	√	√		√
Rohrmann (2)	2007	√	√	√	√		√
Giovannucci	2007	√		√	√	√	
Butler	2009	√		√	√	√	√
Watters	2009	√	√	√	√	√	√
Shafique (Islami)	2012	√		√	√	√	√
Bae	2013	√	√	√	√		√
Rohrmann	2013	√		√	√	√	
Sawada	2014	√		√	√	√	√
Will	1999	√	√	√	√		
Nilsen (as Lund-Nilsen)	2000	√	√	√	√		√
Hultdin	2005	√					√
Baglietto	2006	√					√
Gonzalez	2007	√	√	√	√		√
Park	2007	√					√
Grundmark	2011	√					√
Geybels	2012	√		√	√	√	
Karppi	2012	√					√
Heikkila	2013	√		√	√	√	√
Koutros	2013	√					√
Lemogne	2013	√		√	√	√	
Karlsen	2012	√					√
Onitilo	2013						

Note:[a, b, c, d] were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data

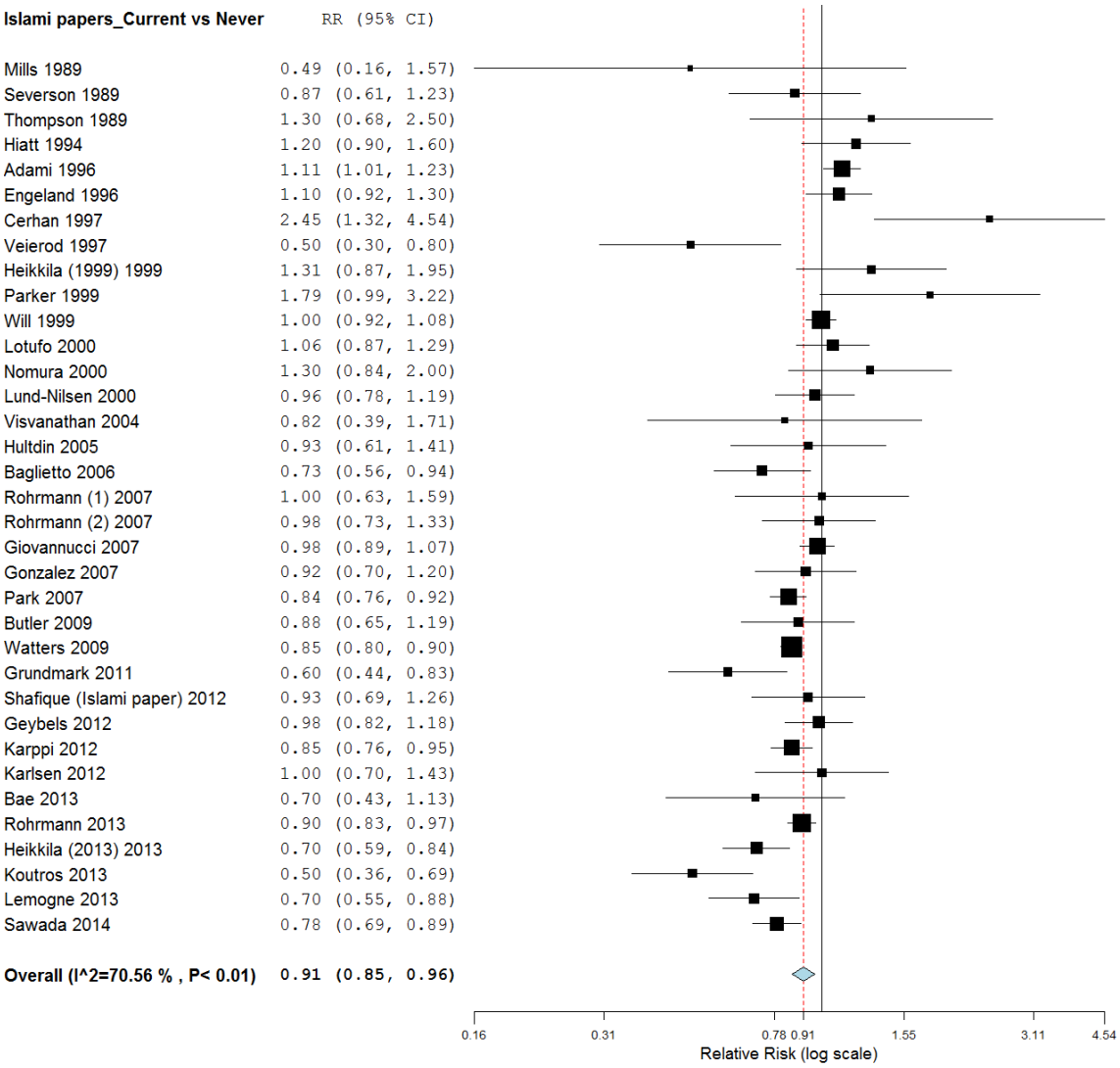


Figure 6A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies considered by Islami et al. includes studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results (Model A)

Note: Comparison of these results to those reported by Islami et al. (Supplementary Figure 5) revealed three differences. Firstly, Islami et al. inconsistently used the age adjusted RR for Cerhan (1997) whereas they used the multivariate adjusted RR (when available) for all other studies. This meta-analysis used the multivariate adjusted RR for Cerhan (1997) in this model as it was available. Secondly, the Supplementary Table 1A reported by Islami et al. reported different values to their Supplementary Figure 5 for Veierod (1997). This meta-analysis used the value from Islami et al. Supplementary Table 1A. Lastly, Supplementary Table 1A reported by Islami et al. reported the Karlsen (2012) study, but did not include this study in their meta-analysis (Supplementary Figure 5). The Karlsen (2012) study was included in this meta-analysis. Therefore, the results of this meta-analysis included 35 studies whereas the Islami et al. meta-analysis (as shown in Supplementary Figure 5) included 34 studies.

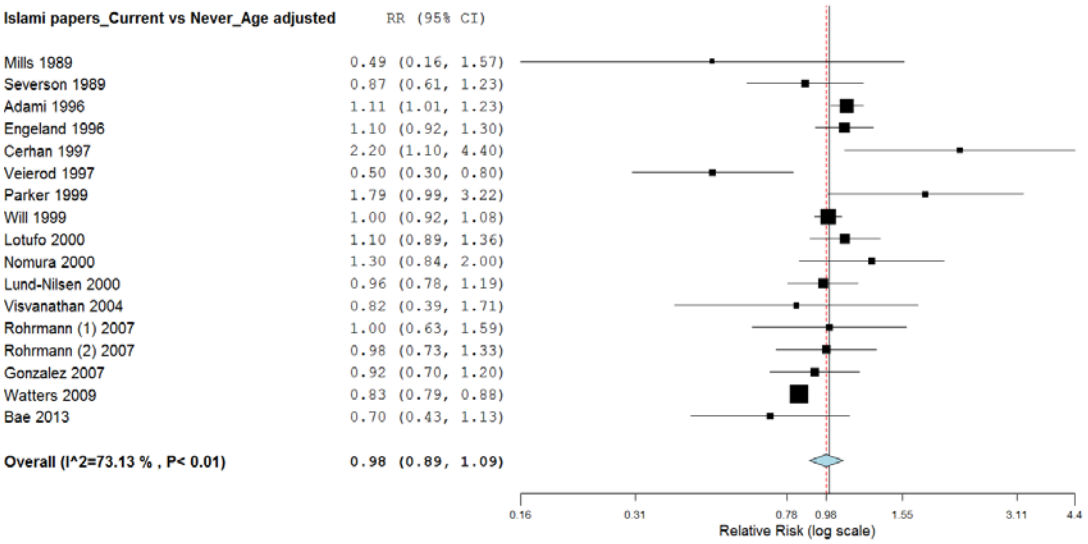


Figure 6B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies considered by Islami et al. includes studies with age-only adjusted data available (Model B)

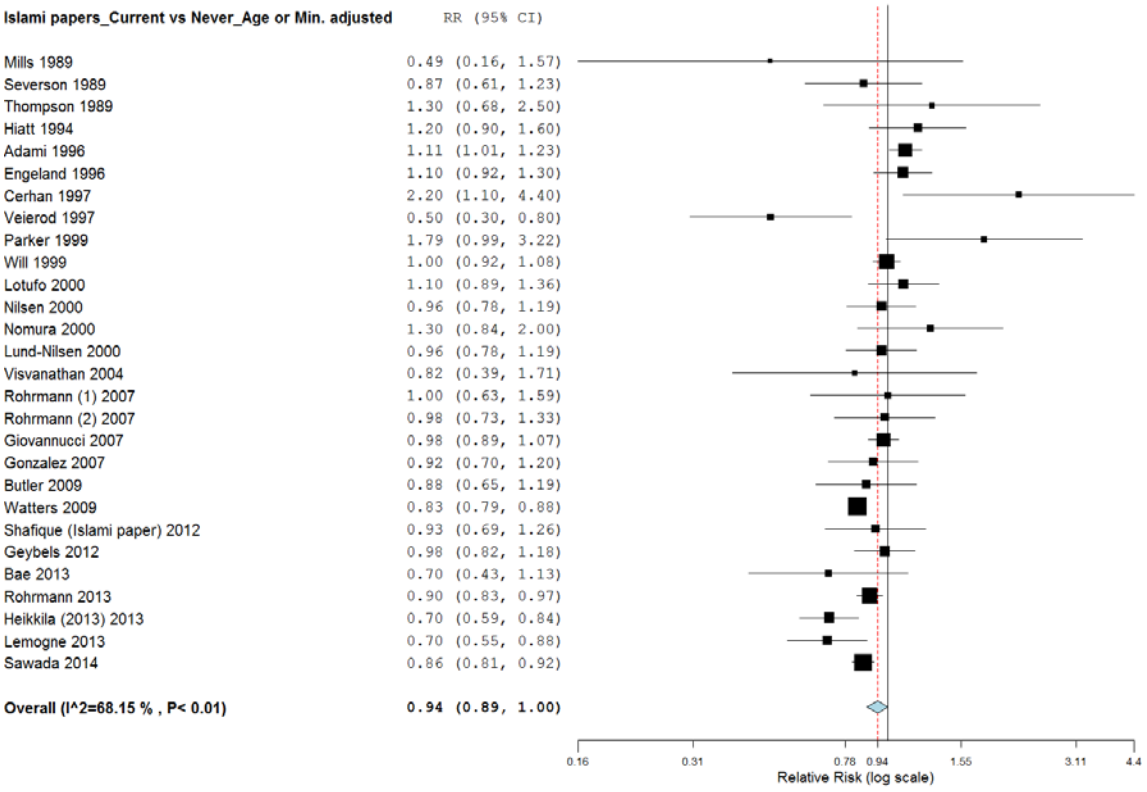


Figure 6C: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies considered by Islami et al. includes studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates (Model C)

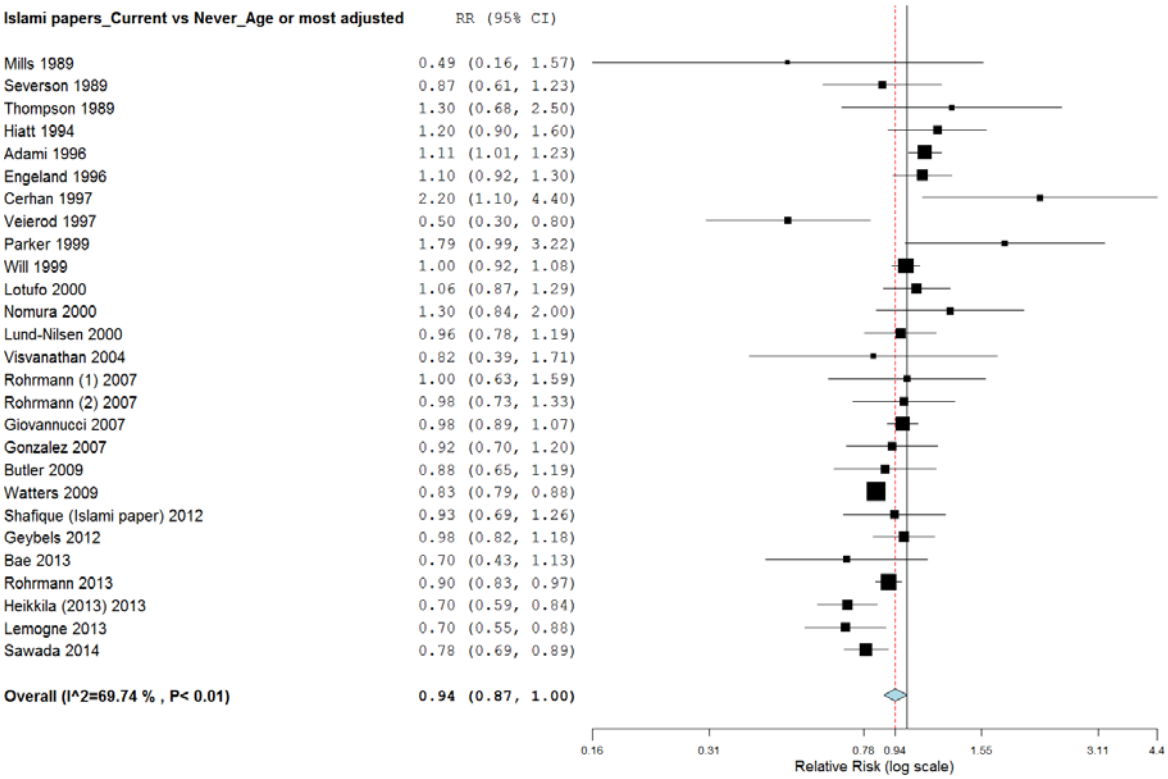


Figure 6D: Forest plot of pooled results reflecting risk of prostate cancer incidence among “current” smokers versus “never” smokers in studies considered by Islami et al. includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)

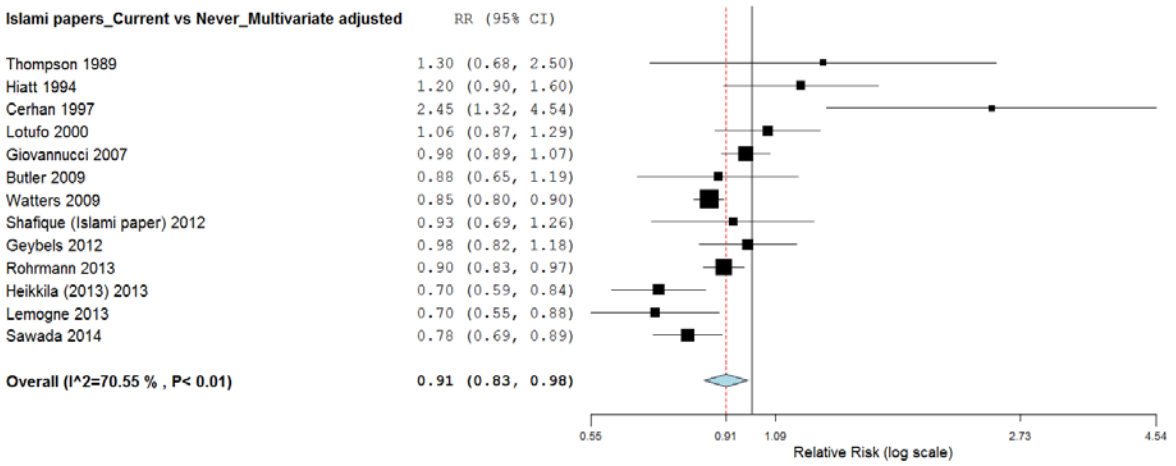


Figure 6E: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies considered by Islami et al. includes studies with multivariate adjustment (highest number of covariates) (Model E)

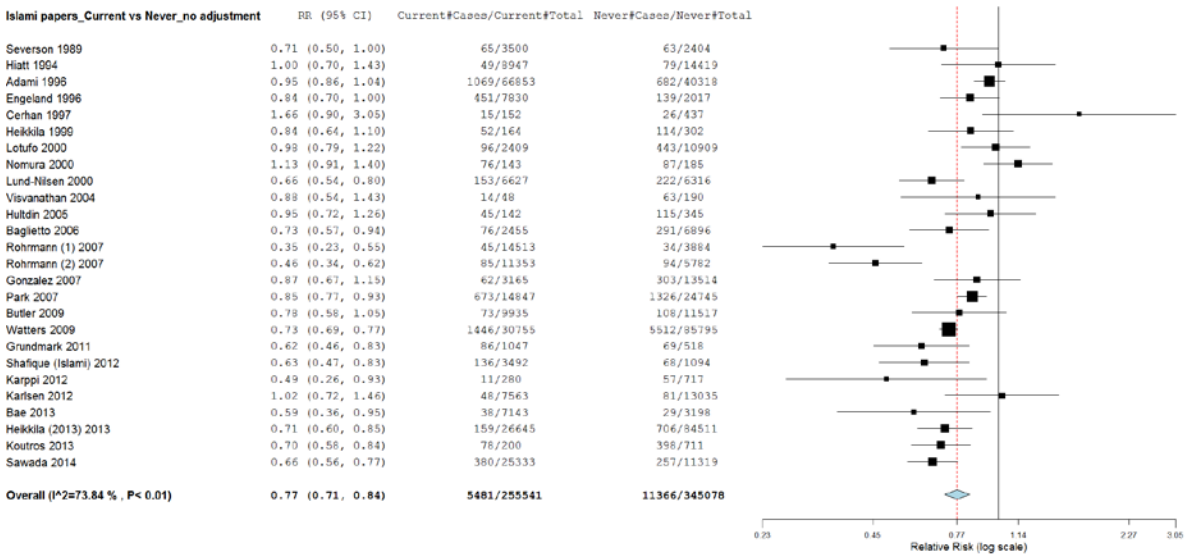


Figure 6F: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers considered by Islami et al. includes studies with non-adjusted raw data (Model F)

Table 14 Summary of studies considered by *Islami et al.* included in meta-analyses (Models A to F) for the association between cigarette smoking ("current" with "non-current" (never + ex) smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D*	Model E*	Model F
Mills	1989						
Severson	1989						√
Thompson	1989						
Hiatt	1994						√
Le Marchand	1994						
Adami	1996						√
Engeland	1996						√
Cerhan	1997						√
Veierod	1997						
Heikkila	1999						√
Parker	1999						
Will	1999						
Nilsen (as Lund-Nilsen)	2000						√
Lotufo	2000						√
Nomura	2000						√
Visvanathan	2004						√
Hultdin	2005						√
Baglietto	2006						√
Rohrmann (1)	2007						√
Rohrmann (2)	2007						√
Giovannucci	2007						
Gonzalez	2007						√
Park	2007						√
Butler	2009						√
Watters	2009						√
Grundmark	2011						√
Shafique	2012						√
Karlsen	2012						√
Karppi	2012						√
Heikkila	2013						√
Koutros	2013						√
Bae	2013						√
Rohrmann	2013						
Sawada	2014						√

Note:[a, b, c, d] were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Risk estimates not available for "current" with "non-current" comparison

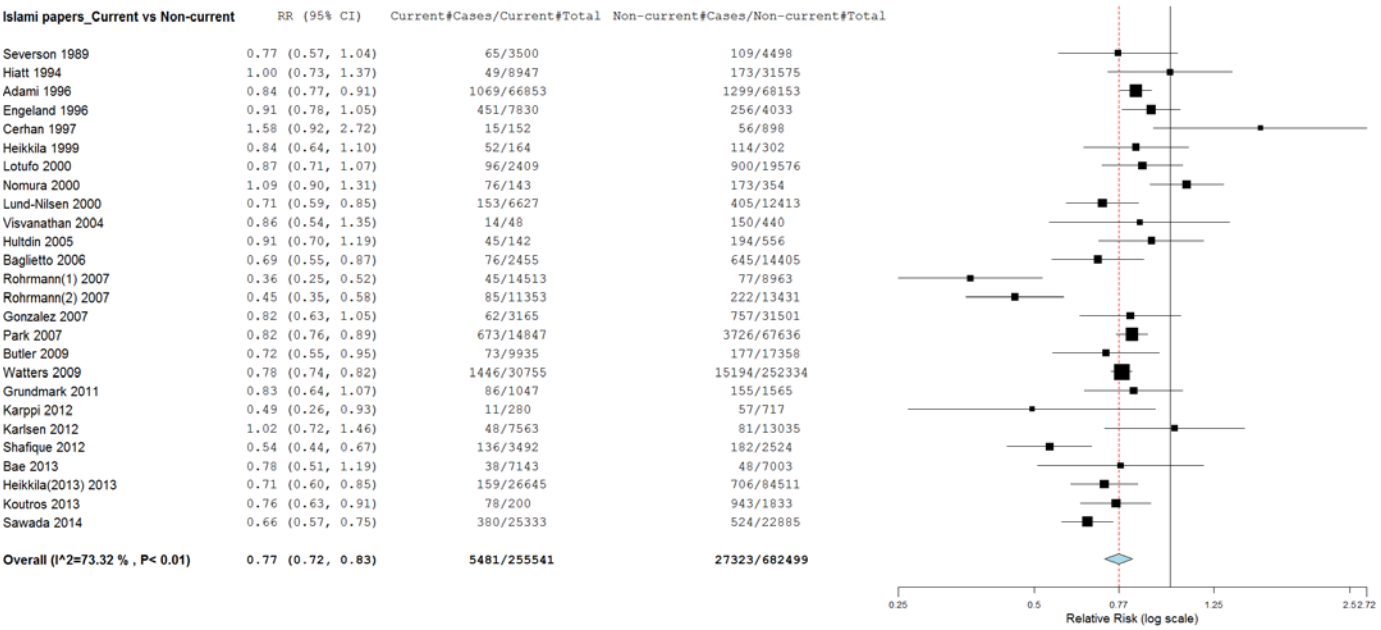


Figure 7A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" with "non-current" (never + ex) smokers considered by Islami et al. includes studies with non-adjusted raw data (Model F)

Table 15 Summary of studies considered by *Islami et al.* included in meta-analyses (Models A to F) for the association between cigarette smoking ("current" with "ex" (former) smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D*	Model E*	Model F
Mills	1989						
Severson	1989						√
Thompson	1989						
Hiatt	1994						√
Le Marchand	1994						
Adami	1996						√
Engeland	1996						√
Cerhan	1997						√
Veierod	1997						
Heikkila	1999						
Parker	1999						
Will	1999						
Nilsen (as Lund-Nilsen)	2000						√
Lotufo	2000						√
Nomura	2000						√
Visvanathan	2004						√
Hultdin	2005						√
Baglietto	2006						√
Rohrmann (1)	2007						√
Rohrmann (2)	2007						√
Giovannucci	2007						
Gonzalez	2007						√
Park	2007						√
Butler	2009						√
Watters	2009						√
Grundmark	2011						√
Shafique (Islami)	2012						√
Karlsen	2012						
Karppi	2012						
Heikkila	2013						
Koutros	2013						√
Bae	2013						√
Rohrmann	2013						
Sawada	2014						√

Note:[a, b, c, d] were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; * Risk estimates not available for "current" with "ex" comparison.

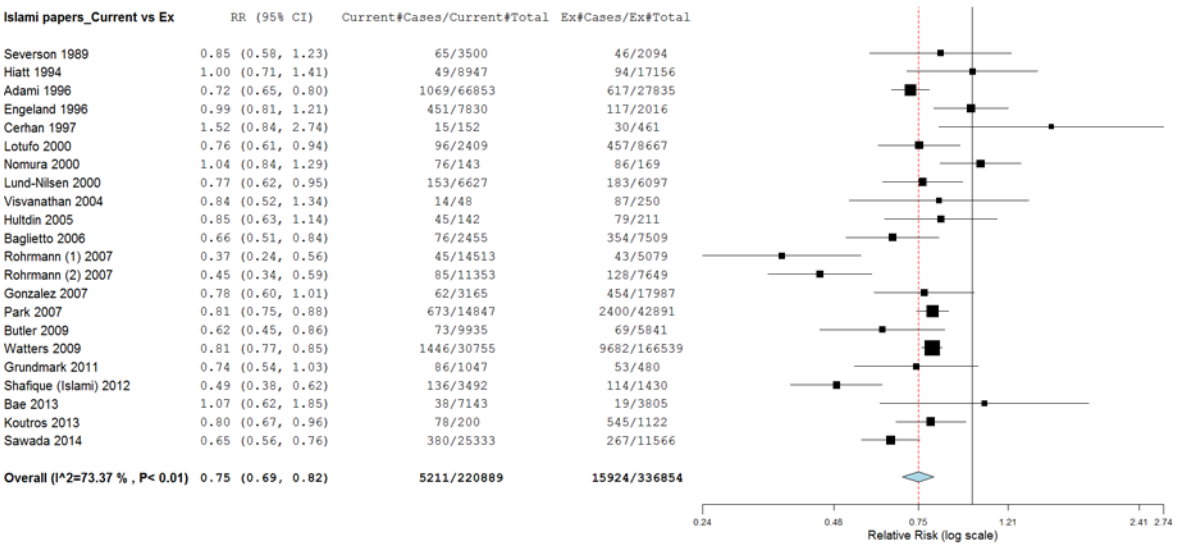


Figure 8A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" with "ex" (former) smokers considered by Islami et al. includes studies with non-adjusted raw data (Model F)

3.3 Meta-analyses of studies available to the RMA and Islami et al. for the association between cigarette smoking and prostate cancer incidence

Table 16 Summary of studies available to the RMA and Islami et al. included in meta-analyses (Models A to F) for the association between cigarette smoking ("ever" [former + current] smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A	Model B	Model C	Model D	Model E	Model F
Honda	1988	√					√
Mills	1989	√	√	√	√		
Severson	1989	√	√	√	√		√
Thompson	1989	√		√	√	√	
Fincham	1990	√					√
Ross	1990	√	√	√	√		
Slattery	1993	√					√
Hayes	1994	√		√	√	√	√
Hiatt	1994	√		√	√	√	√
Le Marchand	1994	√		√	√	√	
Adami	1996	√	√	√	√		√
Andersson	1996	√	√	√	√		√
Engeland	1996	√	√	√	√		√
Gronberg	1996	√	√	√	√		√
Hakulinen (1)	1996	√					√
Hakulinen (2)	1996	√					√
Cerhan	1997	√	√	√	√	√	√
Key	1997	√					√
Lumey	1997	√		√	√	√	√
Rohan	1997	√		√	√	√	√
Veierod	1997	√	√	√	√		
Dillner [c]	1998	√					
Furuya	1998	√					√
Norrish	1998	√					√
Band	1999	√					√
Giovannucci [d]	1999	√		√	√	√	
Heikkila [c]	1999						√
Parker [a]	1999						
Villencuve	1999	√		√	√	√	√
Helzlsouer [b]	2000						
Hsing	2000	√					√
Lotufo	2000	√	√	√	√	√	√
Nilsen	2000	√	√	√	√		√
Nomura	2000	√	√	√	√		√
Putnam [a]	2000	√	√	√	√		
Stattin	2000						
Giles	2001	√		√	√	√	√
Zhang	2002	√					√
Alavanja	2003	√		√	√	√	√
Friedenreich	2003	√	√	√	√		√
Huang (1)	2003	√					√
Huang (2)	2003	√					√
Plaskon	2003	√		√	√	√	√
Barba	2004	√					√
Visvanathan [b]	2004	√	√	√	√		√
Darlington	2007	√		√	√	√	√
Giovannucci [d]	2007						
Rohrmann (1)	2007	√	√	√	√		√
Rohrmann (2)	2007	√	√	√	√		√
Magura	2008	√					√
Butler	2009	√		√	√	√	√
Watters	2009	√	√	√	√	√	√
Karunasinghe	2012	√					√
Shafique [e] (RMA)	2012	√		√	√	√	√
Shafique [e] (Islami)	2012						
Bae	2013	√	√	√	√		√

Murphy	2013	√		√	√	√	√
Rohrmann	2013	√		√	√	√	
Everatt	2014	√	√	√	√	√	√
Kondo	2014	√		√	√	√	√
Sawada	2014	√		√	√	√	√
Will	1999	√	√	√	√		
Hultdin	2005	√					√
Baglietto	2006	√					√
Gonzalez	2007	√	√	√	√		√
Park	2007	√					√
Grundmark	2011	√					√
Geybels	2012	√		√	√	√	
Karppi	2012	√					√
Heikkila	2013	√		√	√	√	√
Koutros	2013	√					√
Lemogne	2013	√		√	√	√	
Karlsen	2012	√					√
Onitilo	2013	√					

Note:[a, b, c, d,e] were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data

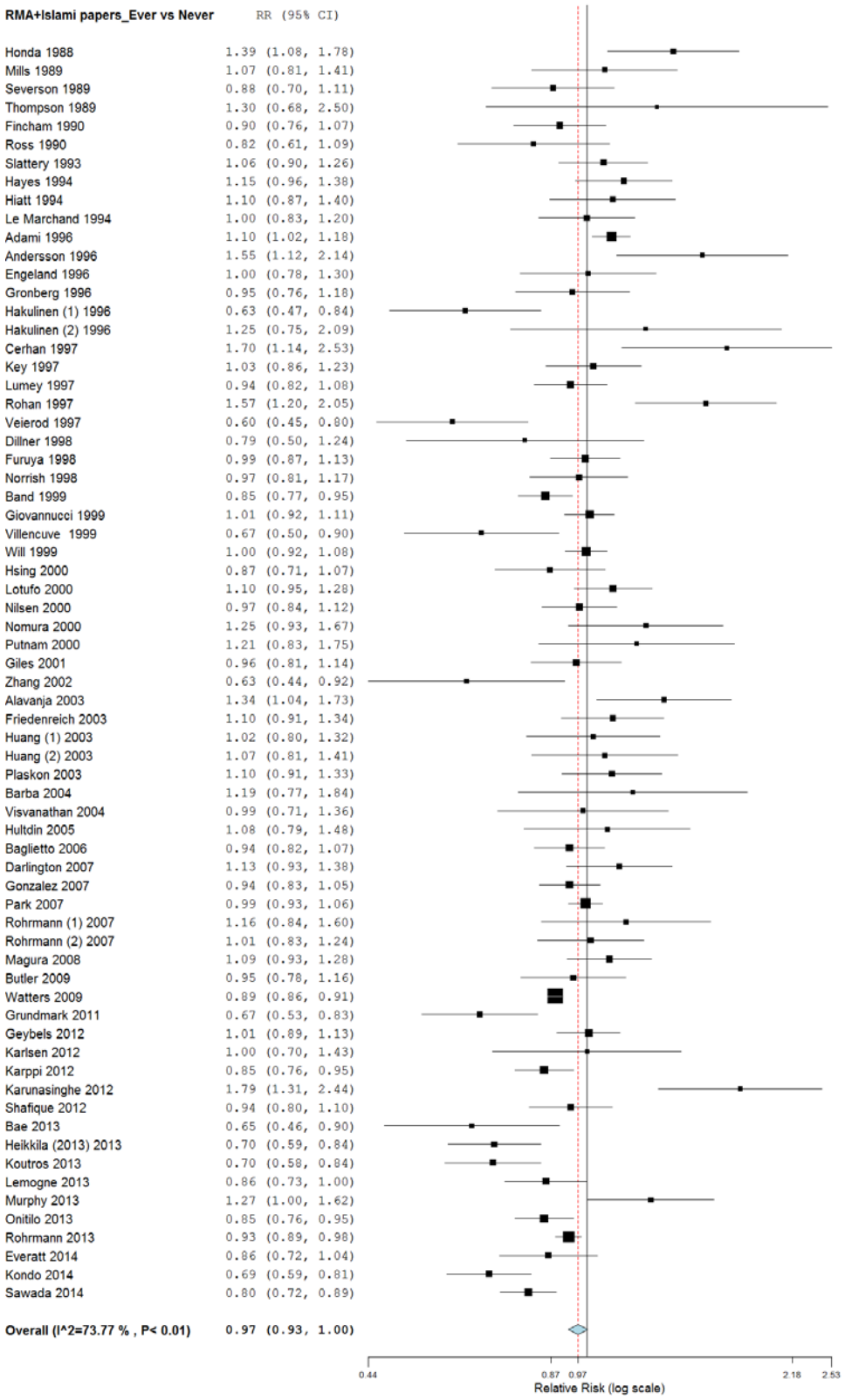


Figure 9A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results (Model A)

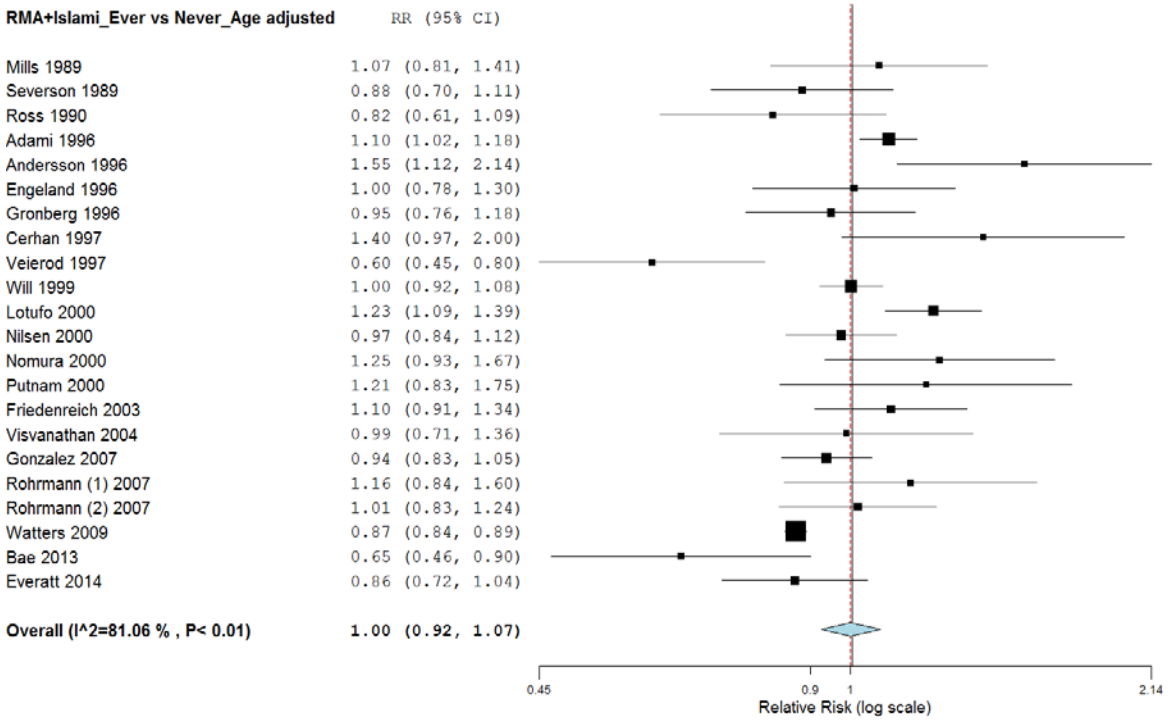


Figure 9B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with age-only adjusted data available (Model B)

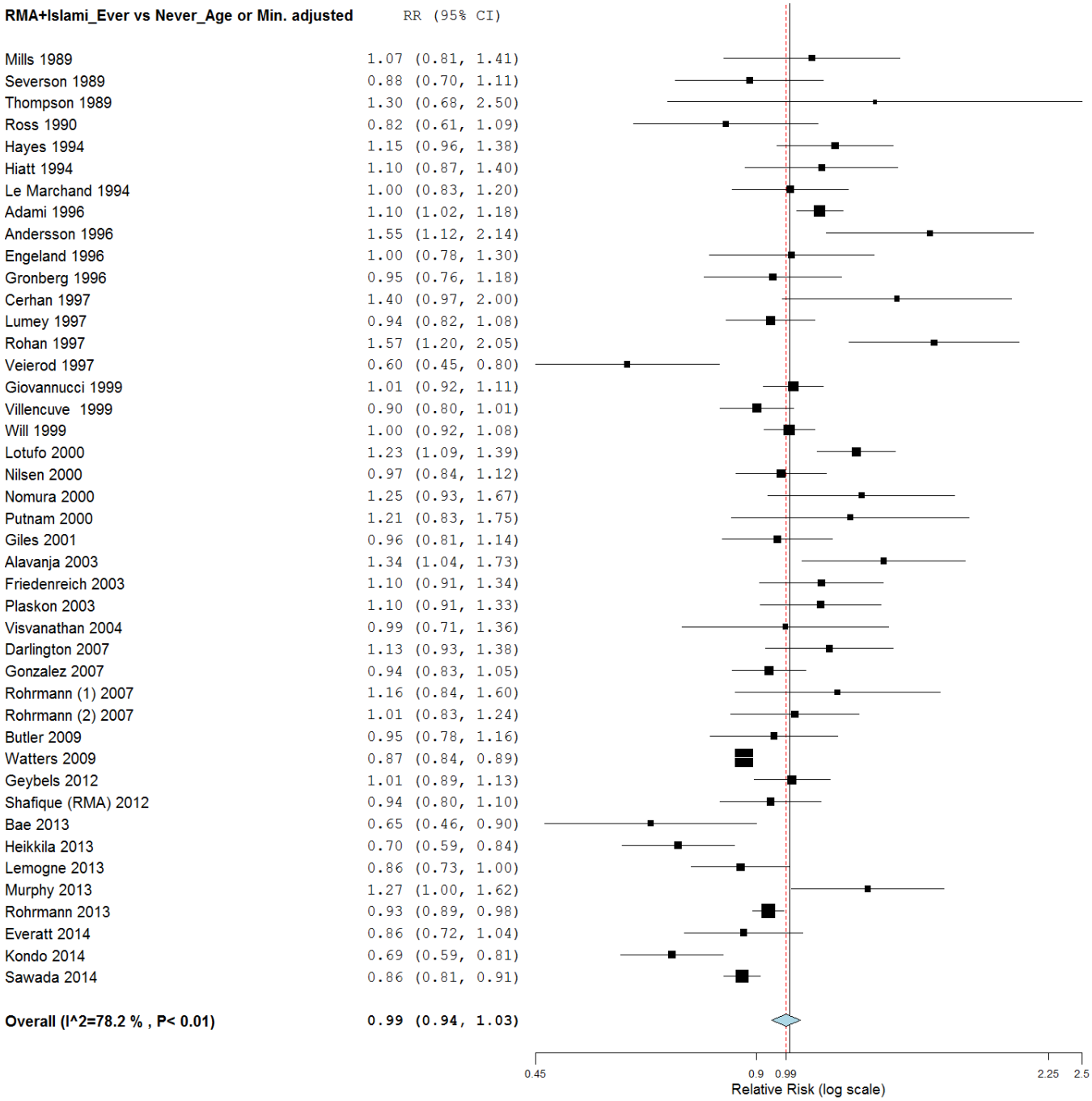


Figure 9C: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates (Model C)

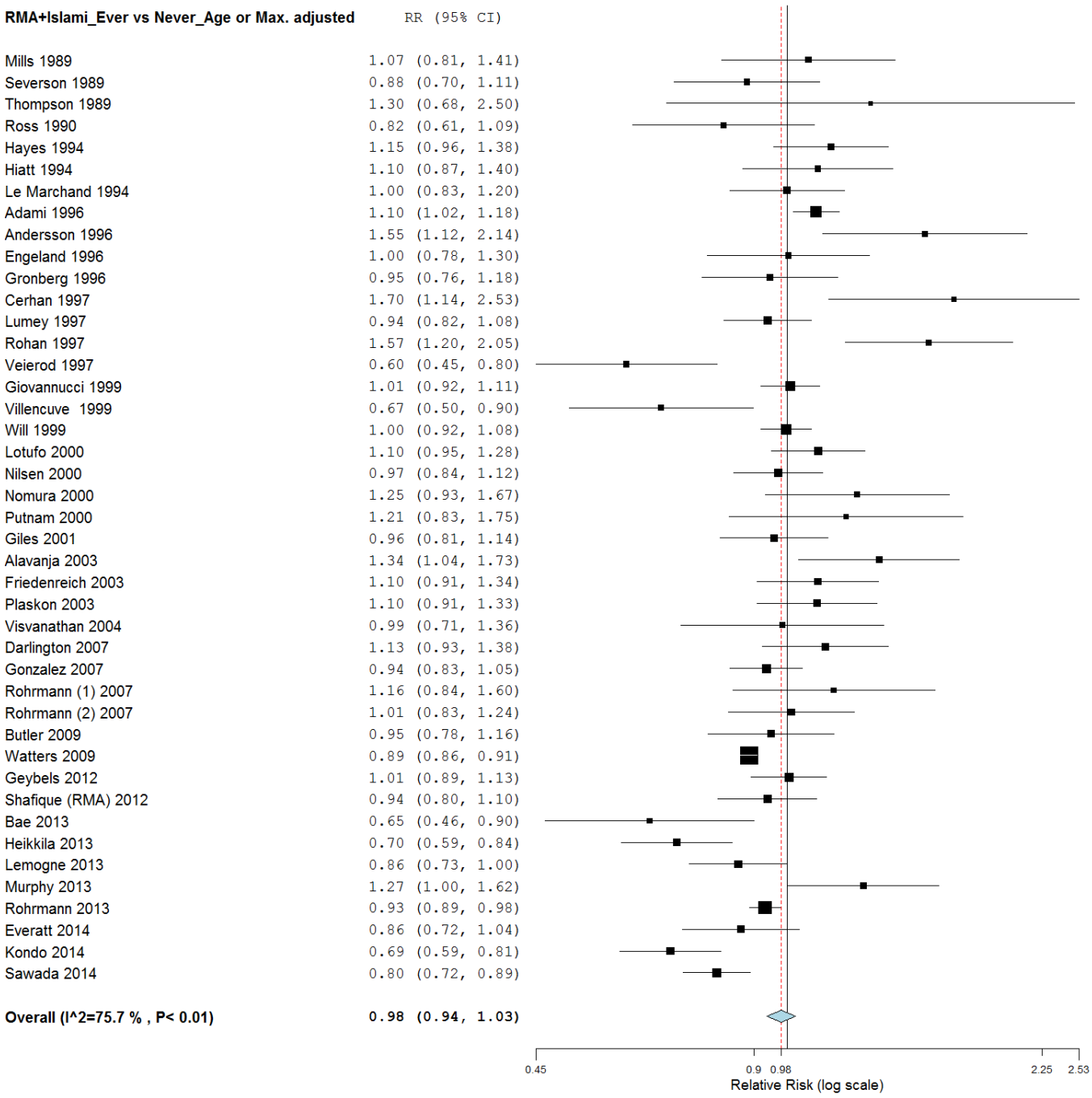


Figure 9D: Forest plot of pooled results reflecting risk of prostate cancer incidence among “ever” [former + current] smokers versus “never” smokers in studies available to the RMA and Islami et al. includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)

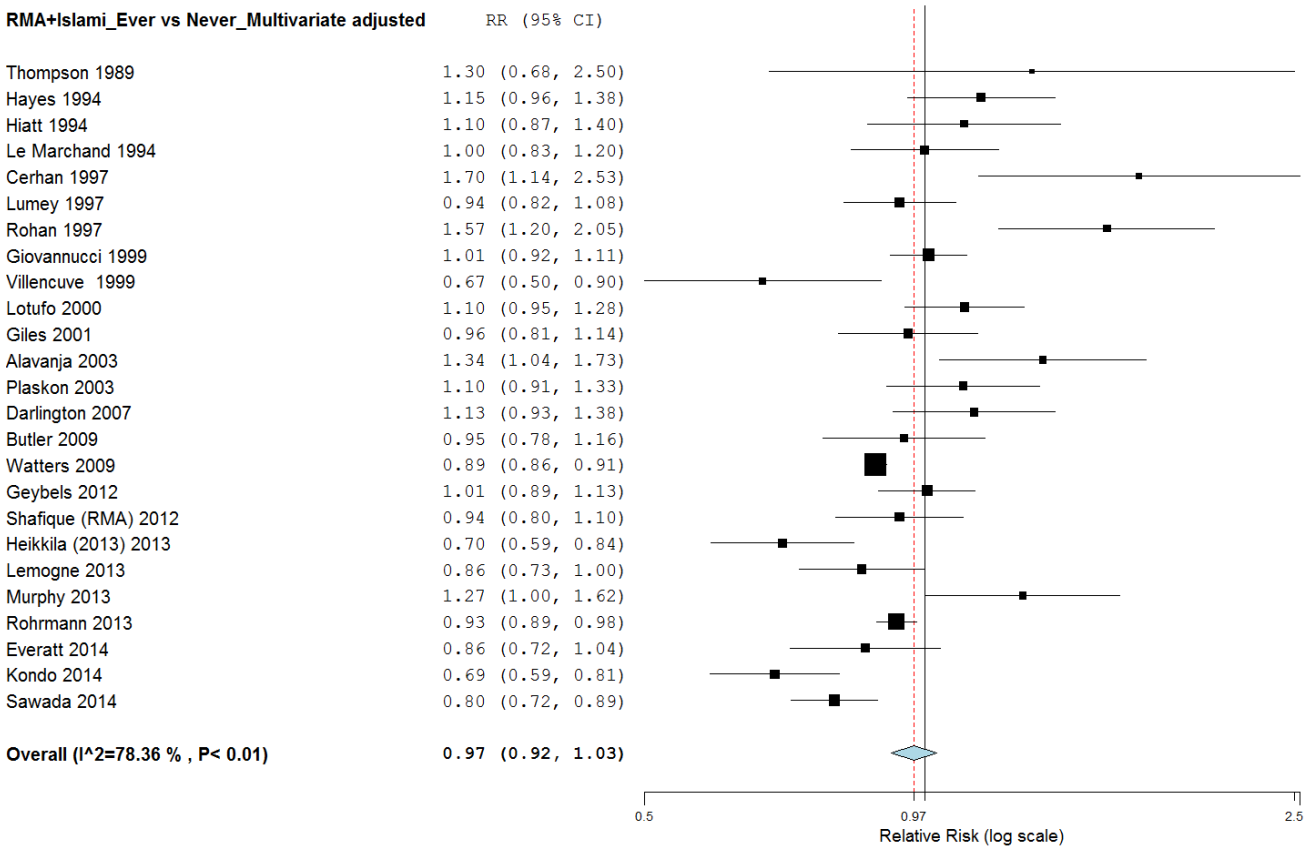


Figure 9E: Forest plot of pooled results reflecting risk of prostate cancer incidence among “ever” [former + current] smokers versus “never” smokers in studies available to the RMA and Islami et al. includes studies with multivariate adjustment (highest number of covariates) (Model E)

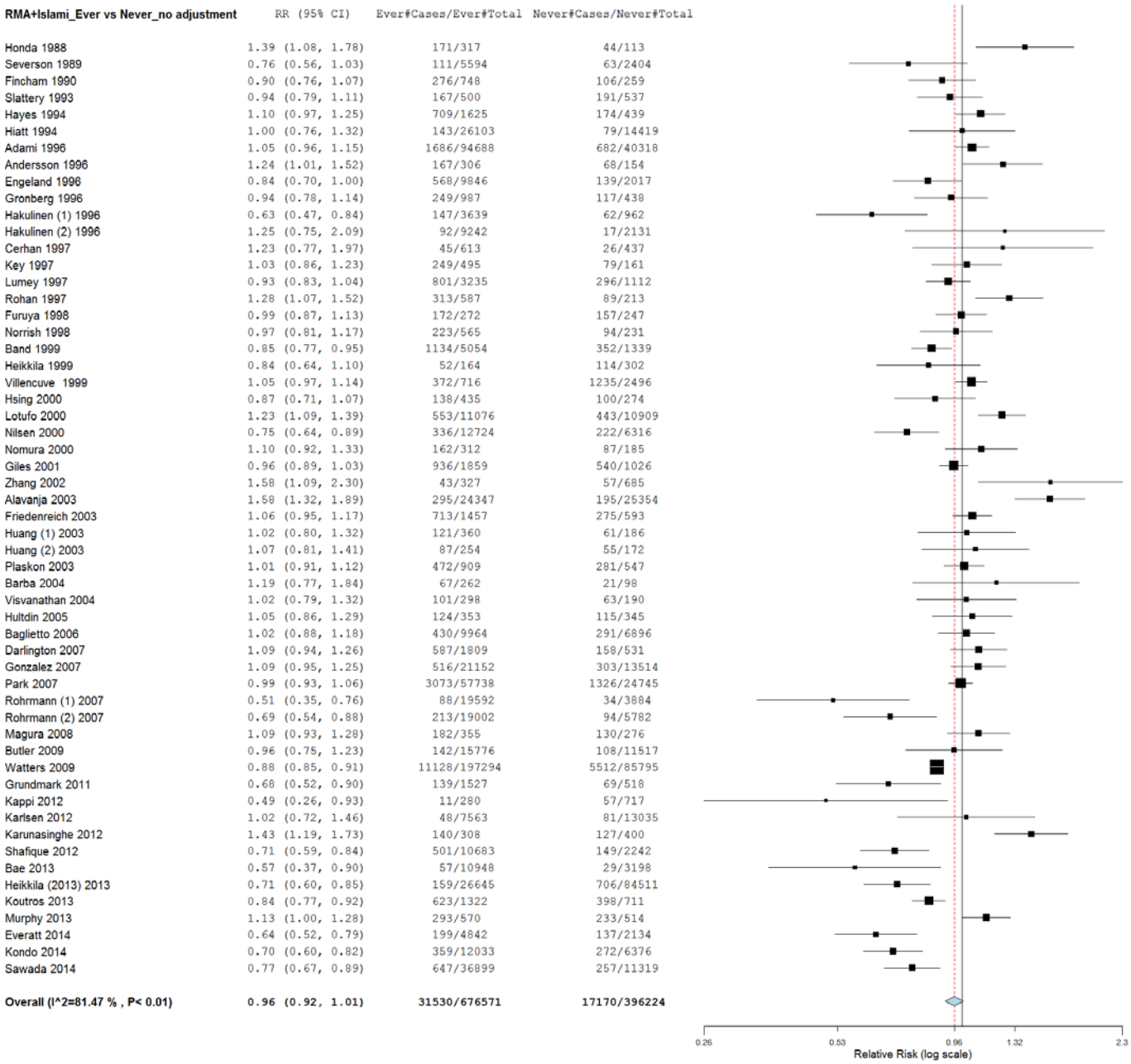


Figure 9F: Forest plot of pooled results reflecting risk of prostate cancer incidence among "ever" [former + current] smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with non-adjusted raw data (Model F)

Table 17 Summary of studies available to the RMA and Islami et al. included in meta-analyses (Models A to F) for the association between cigarette smoking ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A	Model B	Model C	Model D	Model E	Model F
Honda	1988						
Mills	1989	√	√	√	√		
Severson	1989	√	√	√	√		√
Thompson	1989	√		√	√	√	
Fincham	1990	√					√
Ross	1990	√	√	√	√		
Slattery	1993						
Hayes	1994	√		√	√	√	√
Hiatt	1994	√		√	√	√	√
Le Marchand	1994						
Adami	1996	√	√	√	√		√
Andersson	1996	√	√	√	√		√
Engeland	1996	√	√	√	√		√
Gronberg	1996	√	√	√	√		√
Hakulinen (1)	1996	√					√
Hakulinen (2)	1996	√					√
Cerhan	1997	√	√	√	√	√	√
Key	1997	√					√
Lumey	1997	√		√	√	√	√
Rohan	1997	√		√	√	√	√
Veierod	1997	√	√	√	√		
Dillner [c]	1998						
Furuya	1998						
Norrish	1998	√					√
Band	1999						
Giovannucci [d]	1999	√		√	√	√	
Heikkila [c]	1999	√					√
Parker [a]	1999						
Villencuve	1999						
Helzlsouer [b]	2000						
Hsing	2000	√					√
Lotufo	2000	√	√	√	√	√	√
Nilsen	2000	√	√	√	√		√
Nomura	2000	√	√	√	√		√
Putnam [a]	2000	√	√	√	√		
Stattin	2000						
Giles	2001	√		√	√	√	√
Zhang	2002						
Alavanja	2003	√		√	√	√	√
Friedenreich	2003	√					√
Huang (1)	2003	√					√
Huang (2)	2003	√					√
Plaskon	2003	√		√	√	√	√
Barba	2004	√					√
Visvanathan [b]	2004	√	√	√	√		√
Darlington	2007	√		√	√		√
Giovannucci [d]	2007						
Rohrmann (1)	2007	√	√	√	√		√
Rohrmann (2)	2007	√	√	√	√		√
Magura	2008	√					√
Butler	2009	√		√	√	√	√
Watters	2009	√	√	√	√	√	√
Karunasinghe	2012						
Shafique [e] (RMA)	2012	√		√	√	√	√
Shafique [e] (Islami)	2012						
Bae	2013	√	√	√	√		√
Murphy	2013	√		√	√	√	√
Rohrmann	2013	√		√	√	√	
Everatt	2014	√	√	√	√	√	√

Kondo	2014	√		√	√	√	√
Sawada	2014	√		√	√	√	√
Will	1999	√	√	√	√		
Hultdin	2005	√					√
Baglietto	2006	√					√
Gonzalez	2007	√	√	√	√		√
Park	2007	√					√
Grundmark	2011	√					√
Geybels	2012	√		√	√	√	
Karppi	2012	√					√
Heikkila	2013	√		√	√	√	√
Koutros	2013	√					√
Lemogne	2013	√		√	√	√	
Karlsen	2012	√					√
Onitilo	2013						

Note:[a, b, c, d] were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data

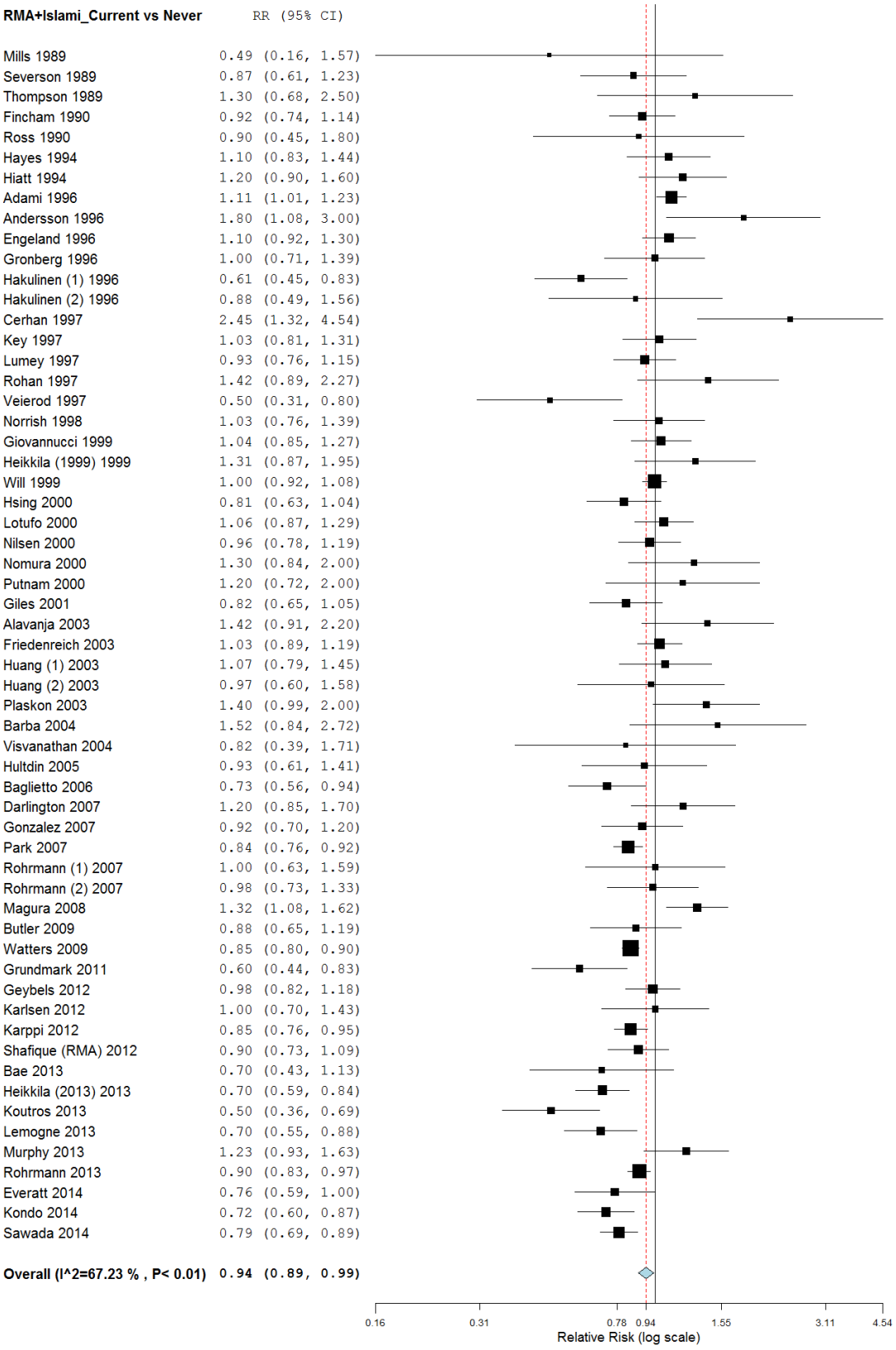


Figure 10A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results (Model A)

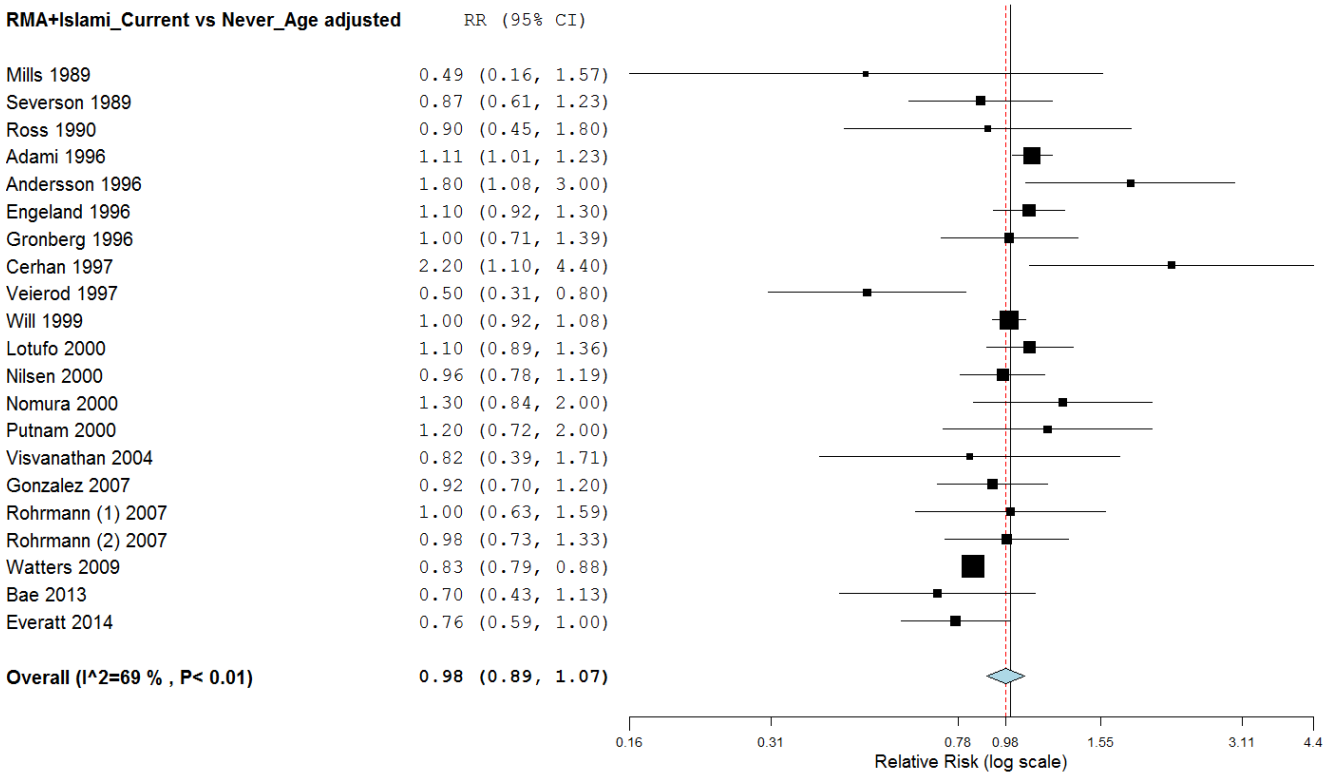


Figure 10B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with age-only adjusted data available (Model B)

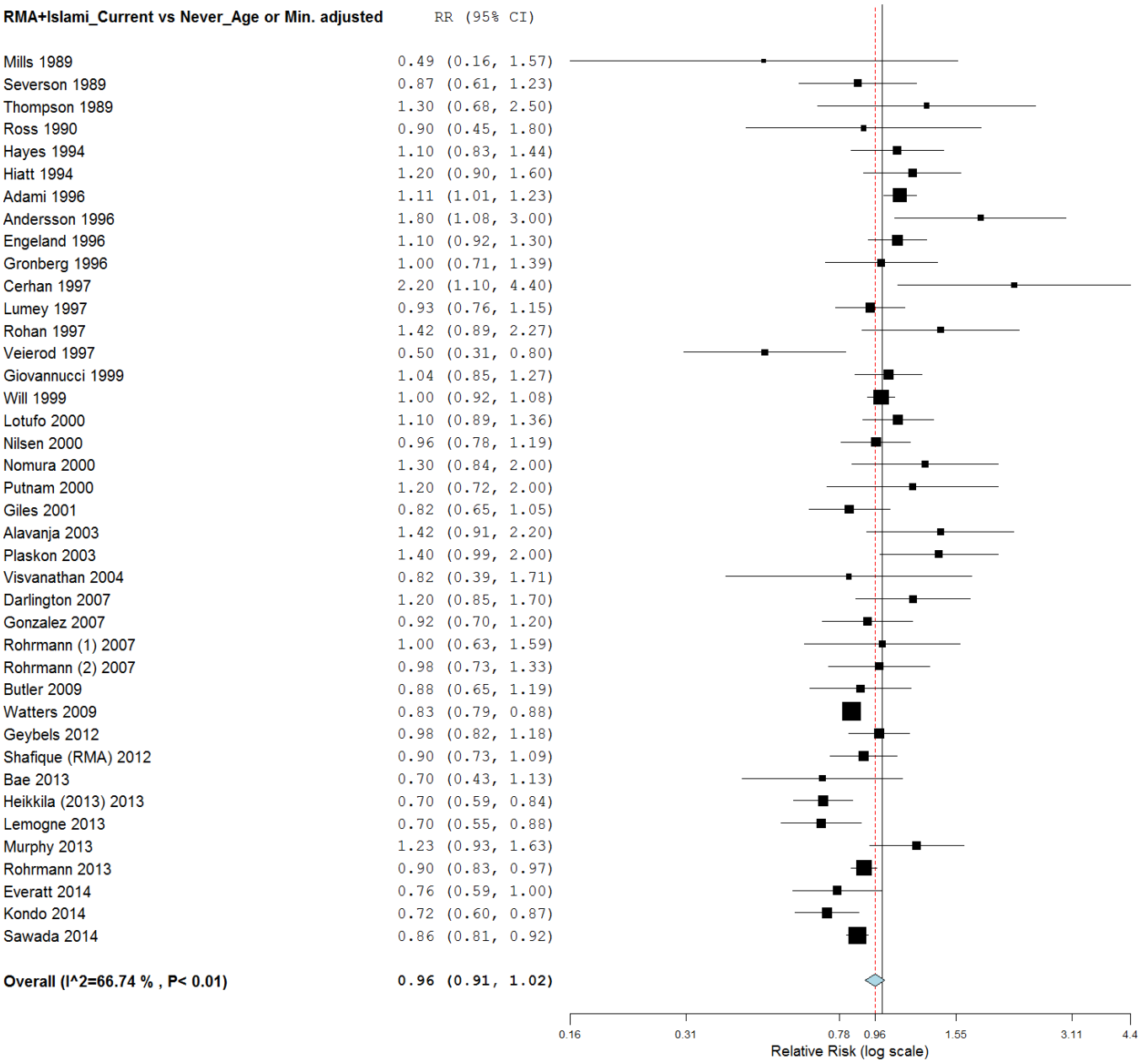


Figure 10C: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates (Model C)

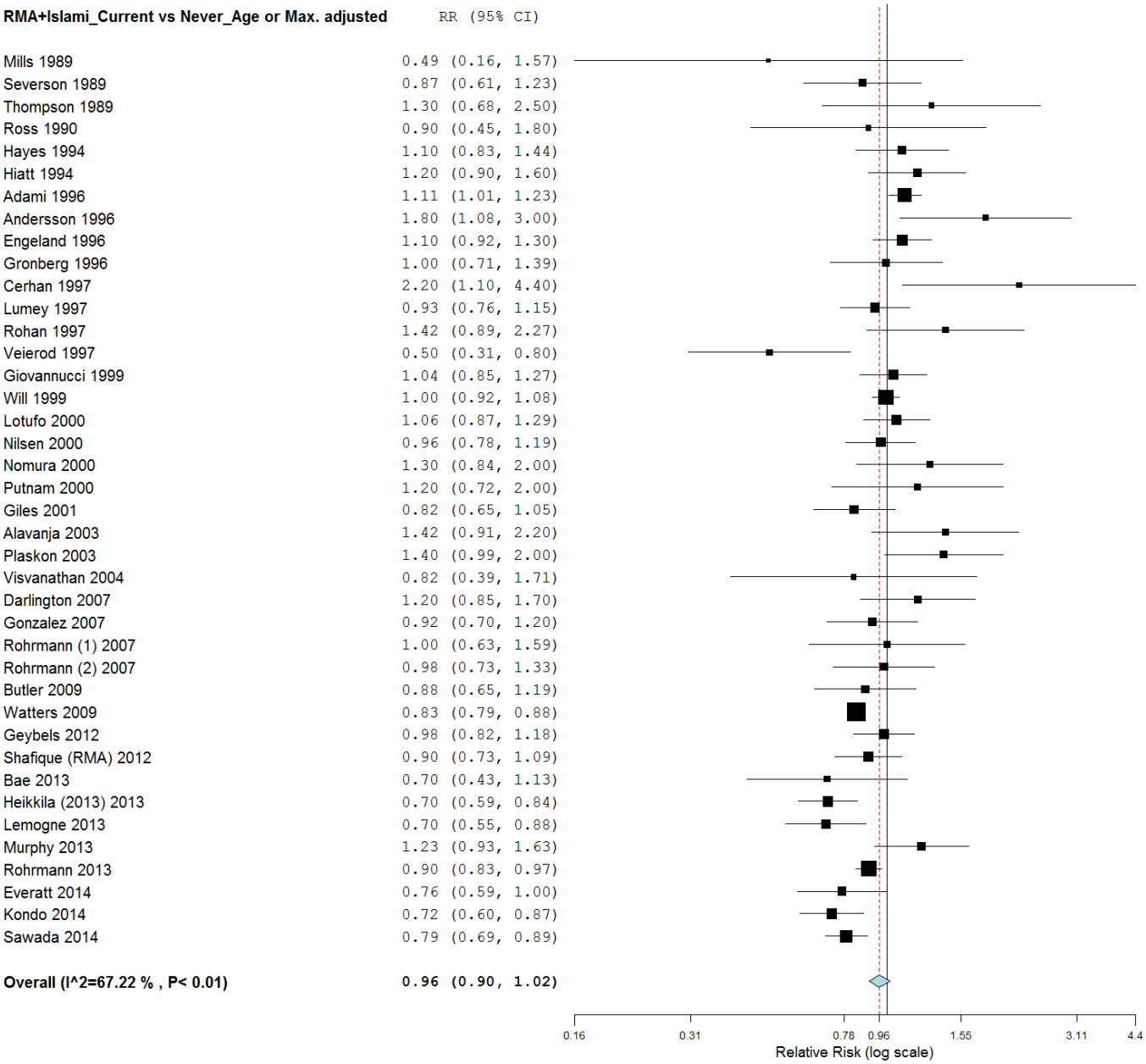


Figure 10D: Forest plot of pooled results reflecting risk of prostate cancer incidence among “current” smokers versus “never” smokers in studies available to the RMA and Islami et al. includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)

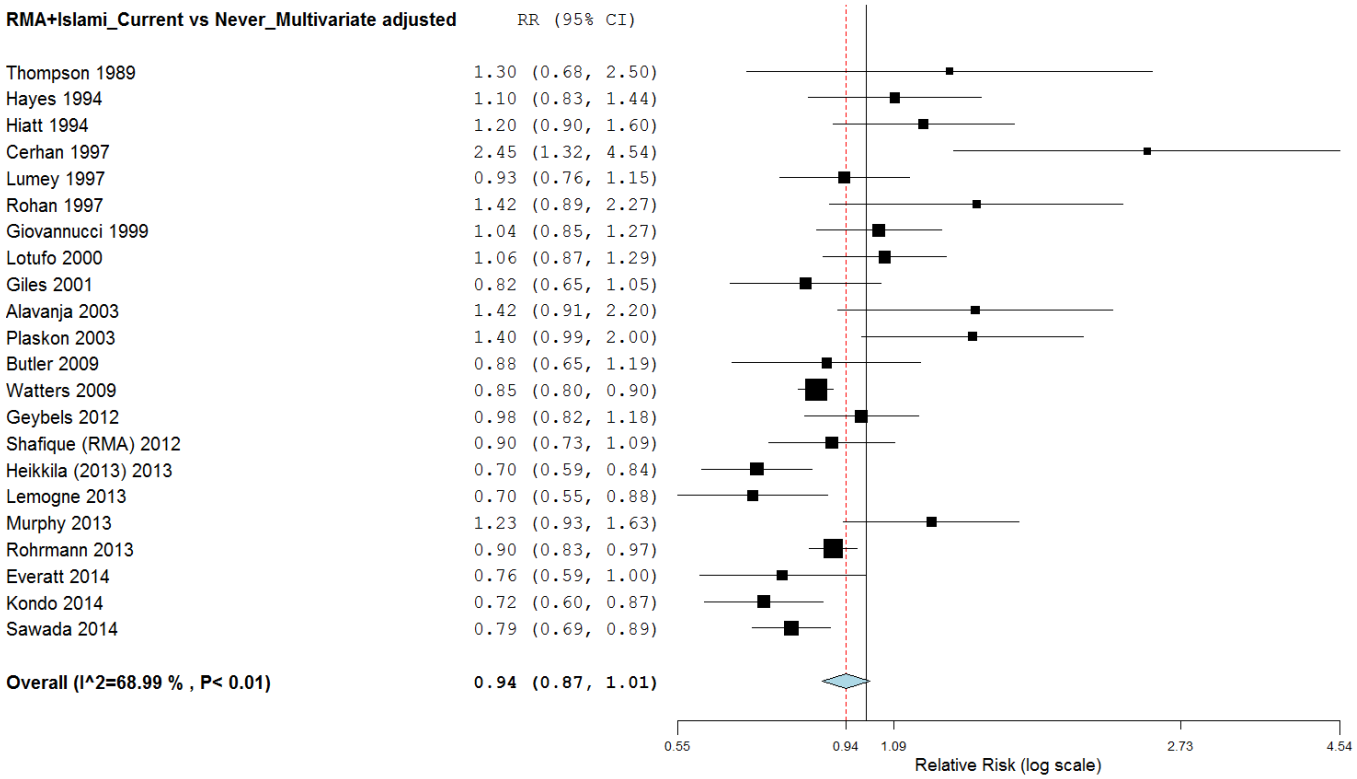


Figure 10E: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with multivariate adjustment (highest number of covariates) (Model E)

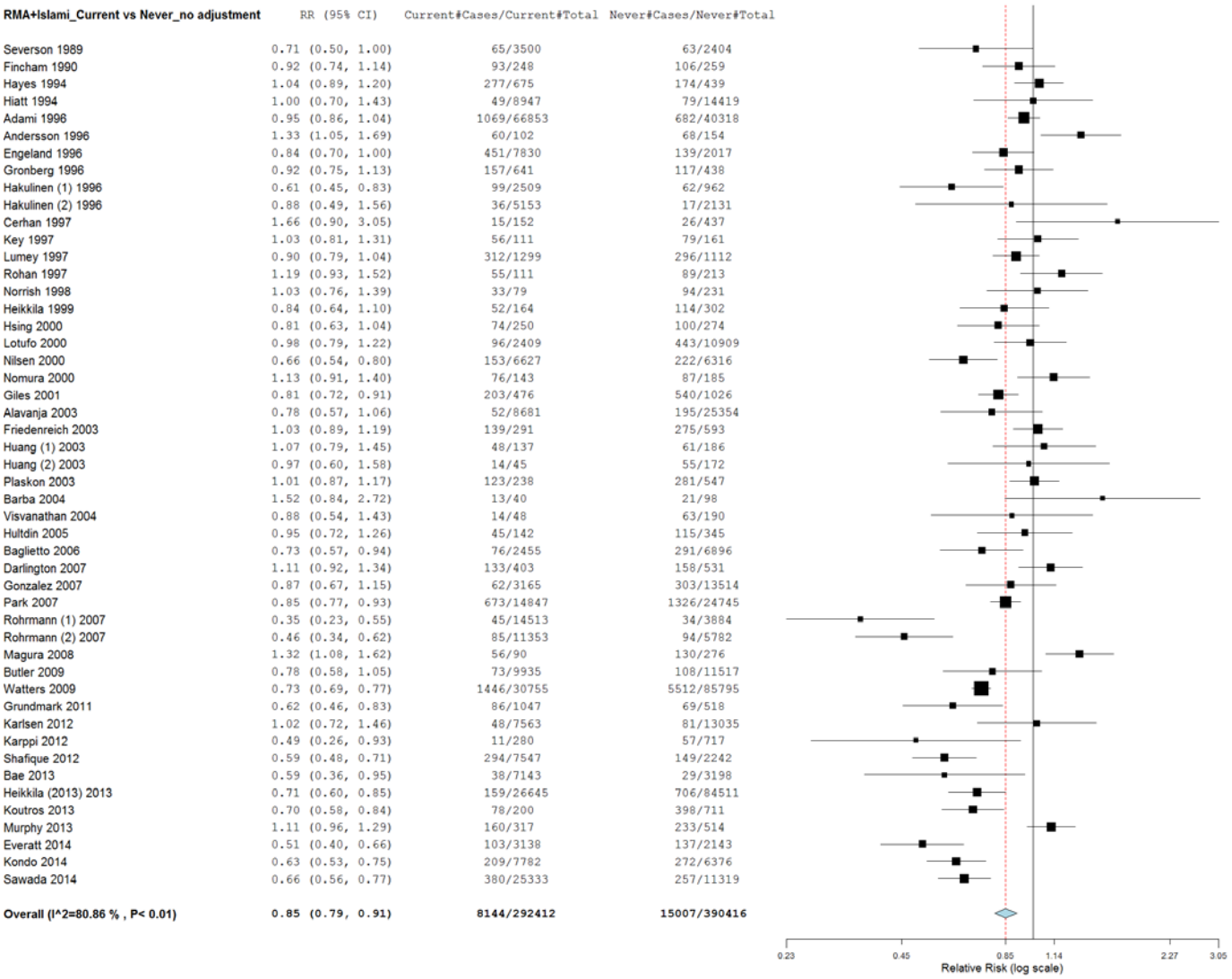


Figure 10F: Forest plot of pooled results reflecting risk of prostate cancer incidence among “current” smokers versus “never” smokers available to the RMA and Islami et al. includes studies with non-adjusted raw data (Model F)

Table 18 Summary of studies available to the RMA and Islami et al. included in meta-analyses (Models A to F) for the association between cigarette smoking ("current" with "non-current" (never + ex) smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D*	Model E*	Model F
Honda	1988						
Mills	1989						
Severson	1989						√
Thompson	1989						
Fincham	1990						√
Ross	1990						
Slattery	1993						
Hayes	1994						√
Hiatt	1994						√
Le Marchand	1994						
Adami	1996						√
Andersson	1996						√
Engeland	1996						√
Gronberg	1996						√
Hakulinen (1)	1996						√
Hakulinen (2)	1996						√
Cerhan	1997						√
Key	1997						√
Lumey	1997						√
Rohan	1997						√
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						√
Band	1999						
Giovannucci [d] (RMA)	1999						
Heikkila [c]	1999						√
Parker [a]	1999						
Will	1999						
Villencuve	1999						
Helzlsouer [b]	2000						
Hsing	2000						√
Lotufo	2000						√
Nilsen	2000						√
Nomura	2000						√
Putnam [a]	2000						
Stattin	2000						√
Giles	2001						√
Zhang	2002						
Alavanja	2003						√
Friedenreich	2003						√
Huang(1)	2003						√
Huang(2)	2003						√
Plaskon	2003						√
Barba	2004						√
Visvanathan [b]	2004						√
Hultdin	2005						√
Baglietto	2006						√
Darlington	2007						√
Giovannucci [d] (RMA, Islami)	2007						
Rohrmann (1)	2007						√
Rohrmann (2)	2007						√
Gonzalez	2007						√
Park	2007						√
Magura	2008						√
Butler	2009						√

Watters	2009						√
Grundmark	2011						√
Karunasinghe	2012						
Shafique [e] (RMA)	2012						√
Shafique [e] (Islami)	2012						
Karlsen	2012						√
Karppi	2012						√
Heikkila	2013						√
Koutros	2013						√
Bae	2013						√
Murphy	2013						√
Rohrmann	2013						
Everatt	2014						√
Kondo	2014						√
Sawada	2014						√

Note:[a, b, c, d] were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; * Risk estimates not available for "current" with "non-current" comparison

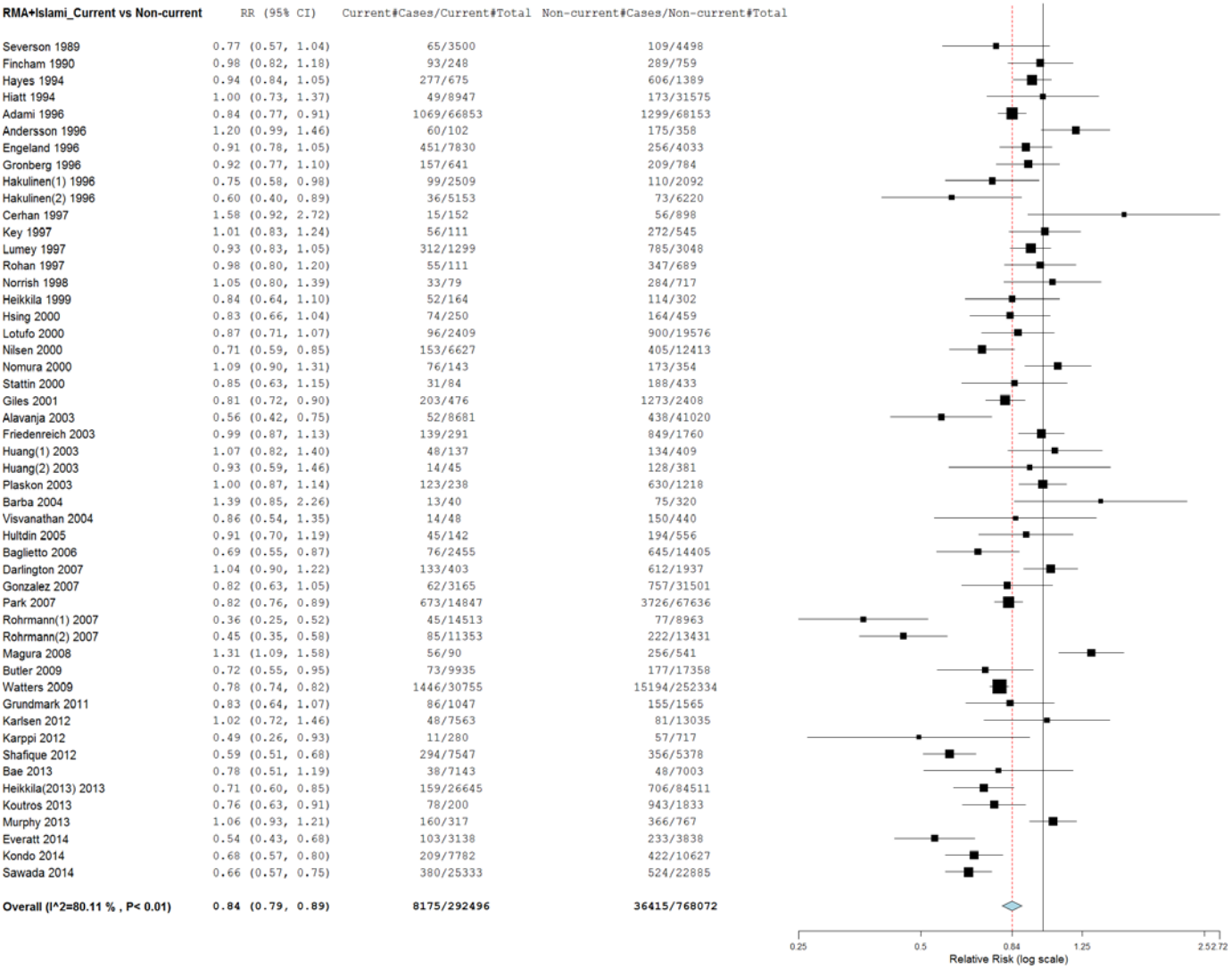


Figure 11A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" with "non-current" (never + ex) smokers available to the RMA and Islami et al. includes studies with non-adjusted raw data (Model F)

Table 19 Summary of studies available to the RMA and Islami et al. included in meta-analyses (Models A to F) for the association between cigarette smoking ("current" with "ex" (former) smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D*	Model E*	Model F
Honda	1988						
Mills	1989						
Severson	1989						√
Thompson	1989						
Fincham	1990						√
Ross	1990						
Slattery	1993						
Hayes	1994						√
Hiatt	1994						√
Le Marchand	1994						
Adami	1996						√
Andersson	1996						√
Engeland	1996						√
Gronberg	1996						√
Hakulinen (1)	1996						√
Hakulinen (2)	1996						√
Cerhan	1997						√
Key	1997						√
Lumey	1997						√
Rohan	1997						√
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						√
Band	1999						
Giovannucci [d] (RMA)	1999						
Heikkila [c]	1999						
Parker [a]	1999						
Will	1999						
Villencuve	1999						
Helzlsouer [b]	2000						
Hsing	2000						√
Lotufo	2000						√
Nilsen	2000						√
Nomura	2000						√
Putnam [a]	2000						
Stattin	2000						
Giles	2001						√
Zhang	2002						
Alavanja	2003						√
Friedenreich	2003						√
Huang(1)	2003						√
Huang(2)	2003						√
Plaskon	2003						√
Barba	2004						√
Visvanathan [b]	2004						√
Hultdin	2005						√
Baglietto	2006						√
Darlington	2007						√
Rohrmann (1)	2007						√
Rohrmann (2)	2007						√
Giovannucci [d] (RMA, Islami)	2007						
Gonzalez	2007						√
Park	2007						√
Magura	2008						√
Butler	2009						√
Watters	2009						√
Grundmark	2011						√

Karunasinghe	2012						
Shafique [e] (RMA)	2012						√
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Heikkila	2013						
Koutros	2013						√
Bae	2013						√
Murphy	2013						√
Rohrmann	2013						
Everatt	2014						√
Kondo	2014						√
Sawada	2014						√

Note:[a, b, c, d] were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the *lowest* number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the *highest* number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; * Risk estimates not available for "current" with "ex" comparison.

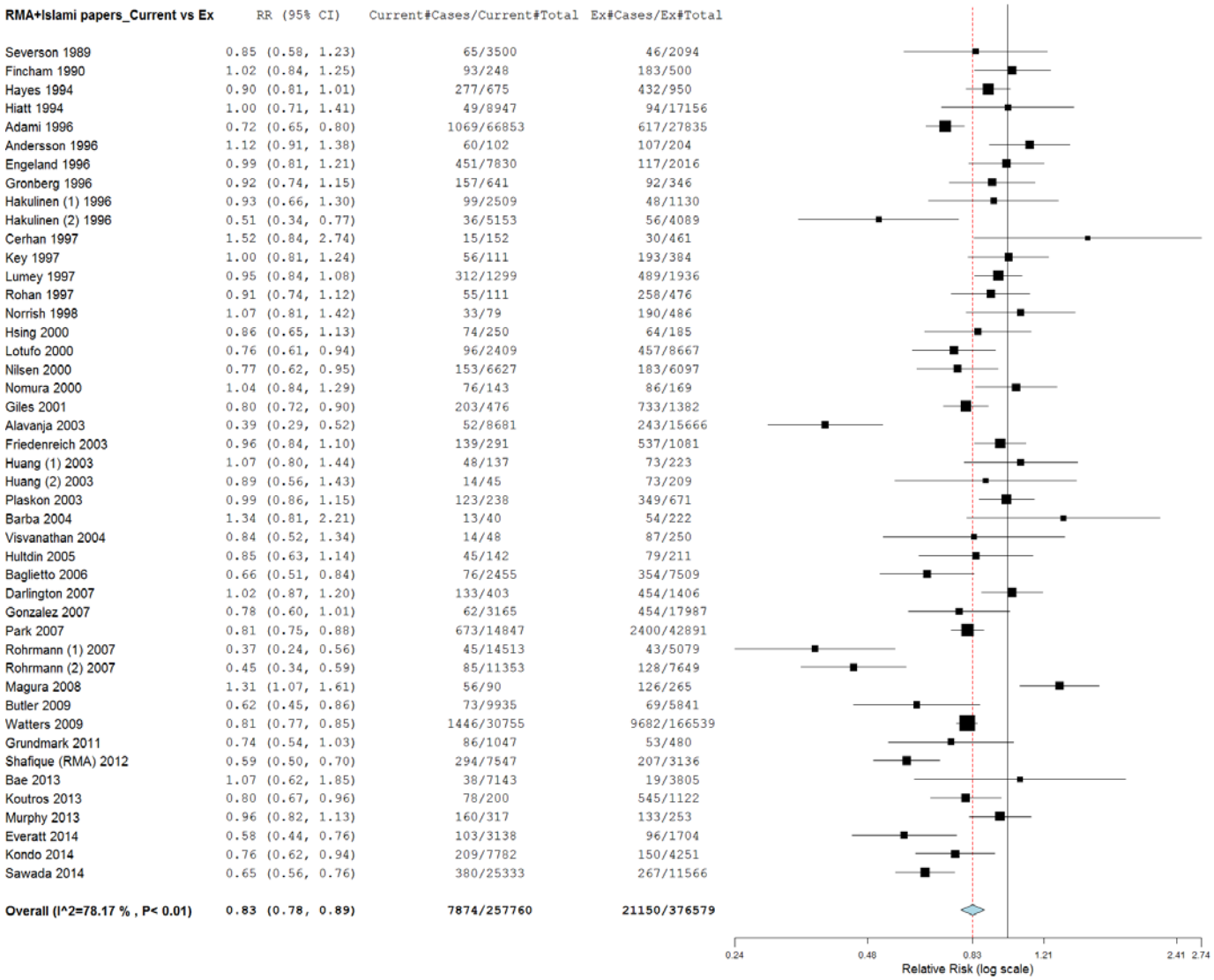


Figure 12A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" with "ex" (former) smokers available to the RMA and Islami et al. includes studies with non-adjusted raw data (Model F)

3.4 Meta-analyses of studies considered by RMA and Islami et al. for the association between cigarette smoking by dosage (<10, 10-19, 20 or more cigarettes per day) and prostate cancer incidence

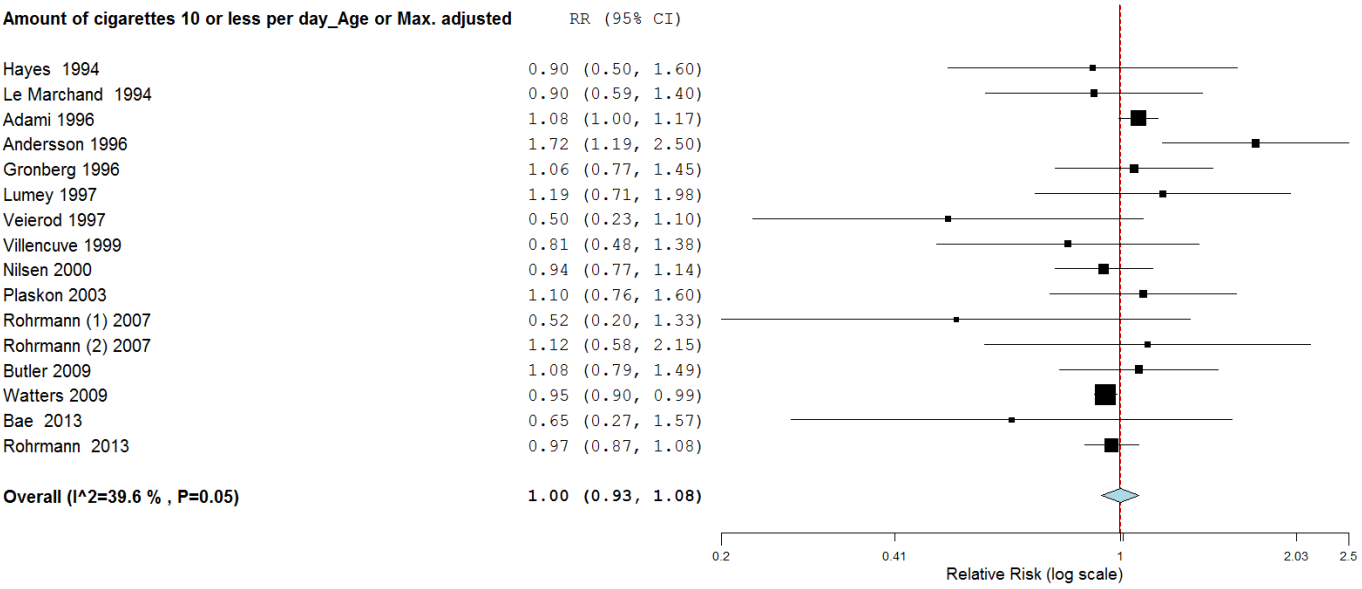
Table 20 Summary of studies considered by RMA and Islami et al. included in meta-analyses (Models D and E) for the association between smoking <10 cigarettes per day ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Honda	1988						
Mills	1989						
Severson	1989						
Thompson	1989						
Fincham	1990						
Ross	1990						
Slattery	1993						
Hayes	1994				√	√	
Hiatt	1994						
Le Marchand	1994				√	√	
Adami	1996				√		
Andersson	1996				√		
Engeland	1996						
Gronberg	1996				√		
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997						
Key	1997						
Lumey	1997				√	√	
Rohan	1997						
Veierod	1997				√		
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999						
Heikkila [c]	1999						
Parker [a]	1999						
Villencuve	1999				√	√	
Will	1999						
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000						
Nilsen	2000				√		
Nomura	2000						
Putnam [a]	2000						
Stattin	2000						
Giles	2001						
Zhang	2002						
Alavanja	2003						
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003				√	√	
Barba	2004						
Visvanathan [b]	2004						
Darlington	2007						
Hultdin	2005						
Baglietto	2006						
Giovannucci [d] (RMA, Islami)	2007						
Rohrmann (1)	2007				√		
Rohrmann (2)	2007				√		
Gonzalez	2007						
Park	2007						
Magura	2008						
Butler	2009				√	√	
Watters	2009				√	√	
Grundmark	2011						
Karunasinghe	2012						

Shafique [e] (RMA)	2012						
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Heikkila	2013						
Koutros	2013						
Lemogne	2013						
Bae	2013				√		
Murphy	2013						
Rohrmann	2013				√	√	
Everatt	2014						
Kondo	2014						
Sawada	2014						

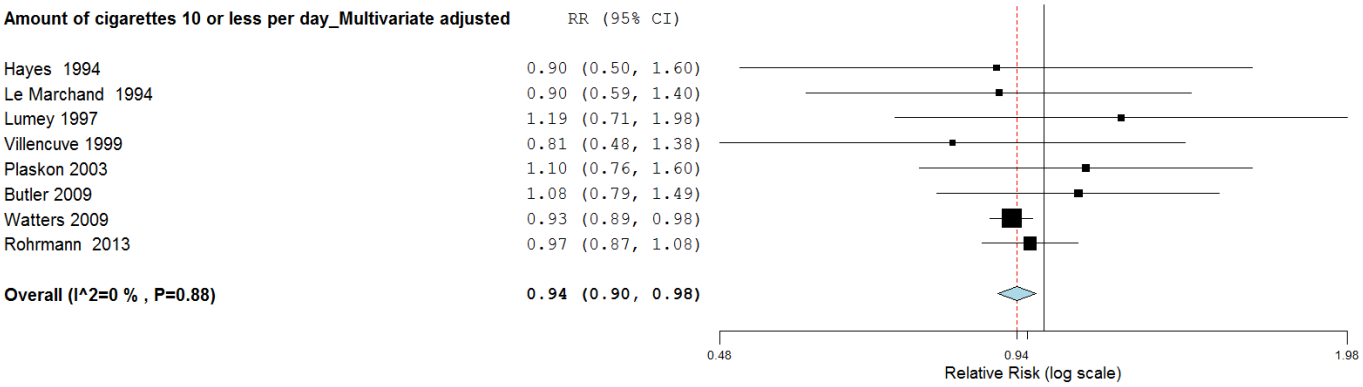
Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Only the most parsimonious models was chosen for this subgroup analysis.

The studies available to the RMA and Islami et al for the association between smoking 10 or less cigarettes per day ("current" smokers versus "never" smokers) and prostate cancer incidence were the same, therefore separate analyses of RMA only papers and RMA +Islami et al. papers were not conducted.



Note: Adami 1996, including 1-4 and 5-14 cigarettes per day
Andersson 1996, including <5 and 6-10 cigarettes per day
Butler 2009, <13 cigarettes per day

Figure 13A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" <u>≤10 cigarettes per day</u> smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)



Note: Butler 2009, <13 cigarettes per day

Figure 13B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" <10 cigarettes per day smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with multivariate adjustment (highest number of covariates) (Model E)

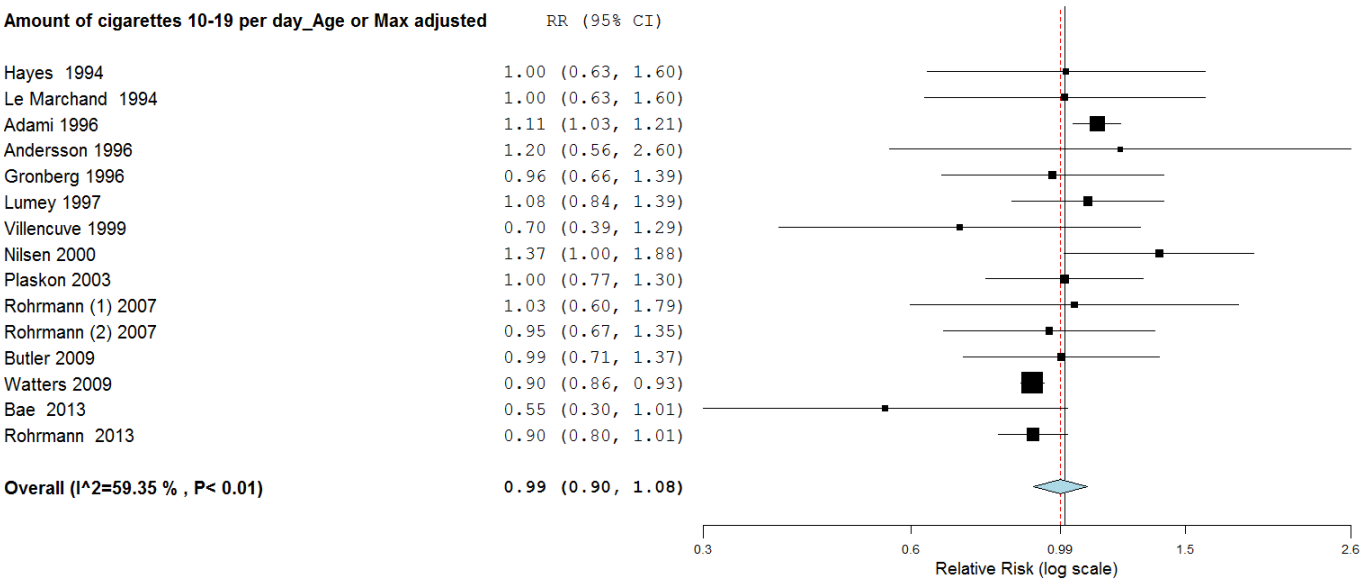
Table 21 Summary of studies considered by RMA and Islami et al. included in meta-analyses (Models D and E) for the association between smoking 10-19 cigarettes per day ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Honda	1988						
Mills	1989						
Severson	1989						
Thompson	1989						
Fincham	1990						
Ross	1990						
Slattery	1993						
Hayes	1994				√	√	
Hiatt	1994						
Le Marchand	1994				√	√	
Adami	1996				√		
Andersson	1996				√		
Engeland	1996						
Gronberg	1996				√		
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997						
Key	1997						
Lumey	1997				√	√	
Rohan	1997				√		
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999						
Heikkila [c]	1999						
Parker [a]	1999						
Will	1999						
Villencuve	1999				√	√	
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000						
Nilsen	2000				√		
Nomura	2000						
Putnam a	2000						
Stattin	2000						
Giles	2001						
Zhang	2002						
Alavanja	2003						
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003				√	√	
Barba	2004						
Visvanathan [b]	2004						
Hultdin	2005						
Baglietto	2006						
Darlington	2007						
Giovannucci [d] (RMA, Islami)	2007						
Rohrmann (1)	2007				√		
Rohrmann (2)	2007				√		
Gonzalez	2007						
Park	2007						
Magura	2008						
Butler	2009				√	√	
Watters	2009				√	√	
Grundmark	2011						

Karunasinghe	2012						
Shafique [e] (RMA)	2012						
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Geybels	2012						
Heikkila	2013						
Koutros	2013						
Lemogne	2013						
Bae	2013				√		
Murphy	2013						
Rohrmann	2013				√	√	
Everatt	2014						
Kondo	2014						
Sawada	2014						

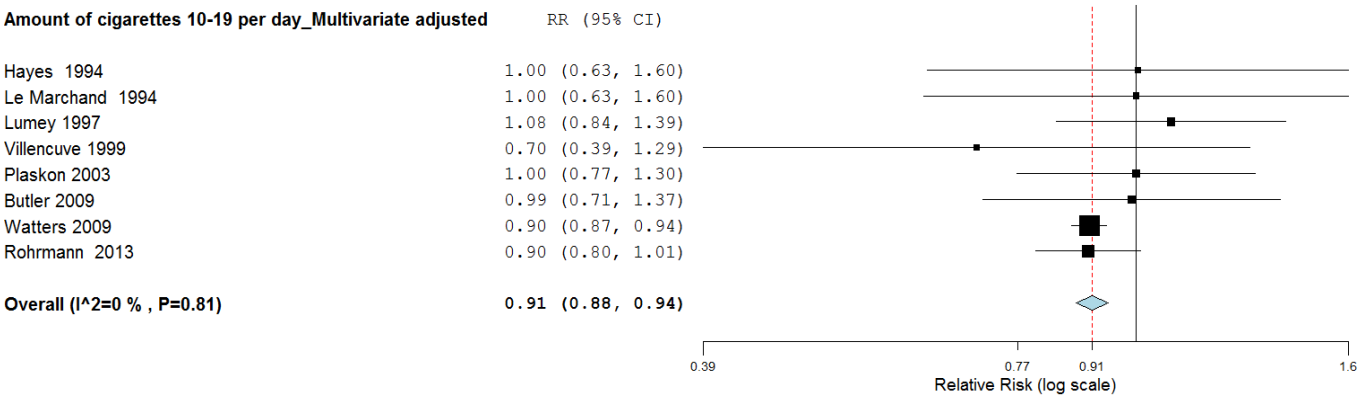
Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Only the most parsimonious models was chosen for this subgroup analysis.

The studies available to the RMA and Islami et al for the association between smoking 10-19 cigarettes per day ("current" smokers versus "never" smokers) and prostate cancer incidence were the same, therefore separate analyses of RMA only papers and RMA +Islami et al. papers were not conducted.



Note: Adami 1996, including 5-14 and 15-24 cigarettes per day.
Andersson 1996, 11-15 cigarettes per day
Butler 2009, 13-22 cigarettes per day
Lumey 1997, 10-20 cigarettes per day
Rohrmann 2013, 15-24 cigarettes per day

Figure 14A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" 10-19 cigarettes per day smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)



Note: Lumey 1997, 10-20 cigarettes per day
Rohrmann 2013, 15-24 cigarettes per day

Figure 14B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" 10-19 cigarettes per day smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with multivariate adjustment (highest number of covariates) (Model E)

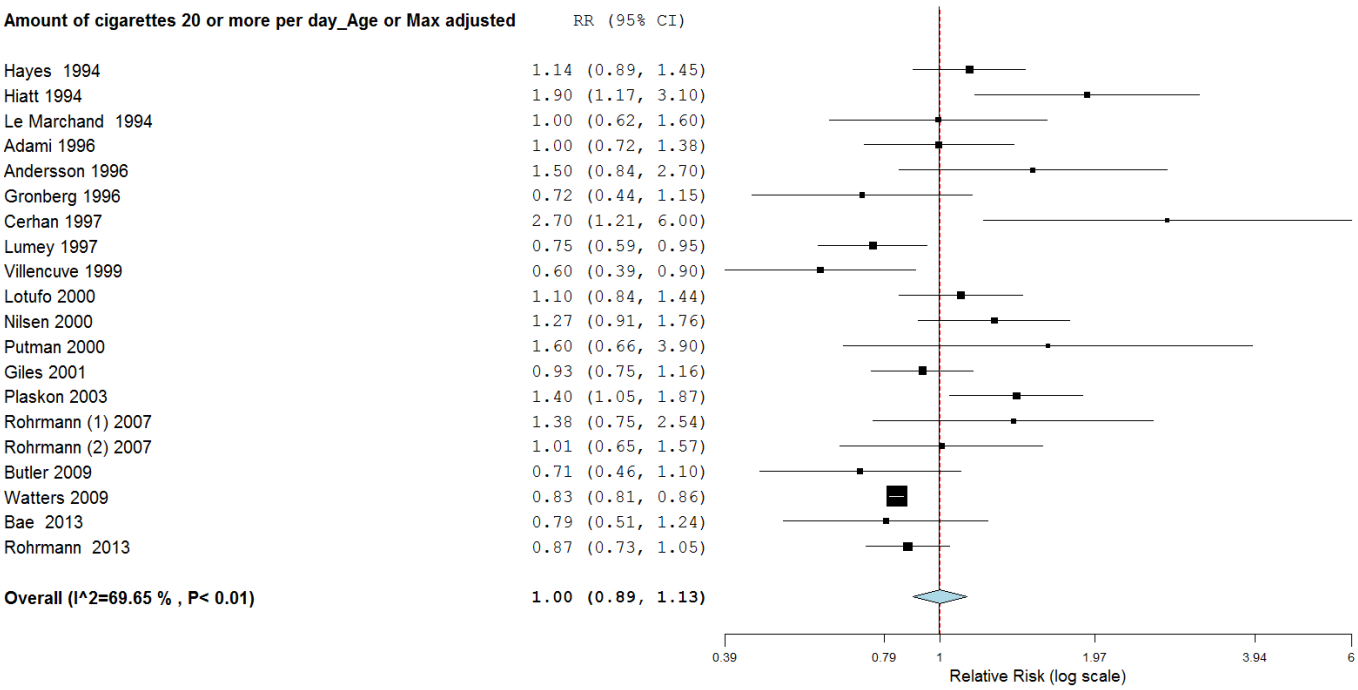
Table 22 Summary of studies considered by RMA and Islami et al included in meta-analyses (Models D and E) for the association between smoking 20 or more cigarettes per day ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Honda	1988						
Mills	1989						
Severson	1989						
Thompson	1989						
Fincham	1990						
Ross	1990						
Slattery	1993						
Hayes	1994				√	√	
Hiatt	1994				√	√	
Le Marchand	1994				√	√	
Adami	1996				√		
Andersson	1996				√		
Engeland	1996						
Gronberg	1996				√		
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997				√	√	
Key	1997						
Lumey	1997				√	√	
Rohan	1997						
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999						
Heikkila [c]	1999						
Parker [a]	1999						
Will	1999						
Villencuve	1999				√	√	
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000				√	√	
Nilsen	2000				√		
Nomura	2000						
Putnam [a]	2000				√		
Stattin	2000						
Giles	2001				√	√	
Zhang	2002						
Alavanja	2003						
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003				√	√	
Barba	2004						
Visvanathan [b]	2004						
Hultdin	2005						
Baglietto	2006						
Darlington	2007						
Giovannucci [d] (RMA, Islami)	2007						
Rohrmann (1)	2007				√		
Rohrmann (2)	2007				√		
Gonzalez	2007						
Park	2007						
Magura	2008						
Butler	2009				√	√	
Watters	2009				√	√	
Grundmark	2011						
Karunasinghe	2012						

Shafique [e] (RMA)	2012						
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Heikkila	2013						
Koutros	2013						
Lemogne	2013						
Bae	2013				√		
Murphy	2013						
Rohrmann	2013				√	√	
Everatt	2014						
Kondo	2014						
Sawada	2014						

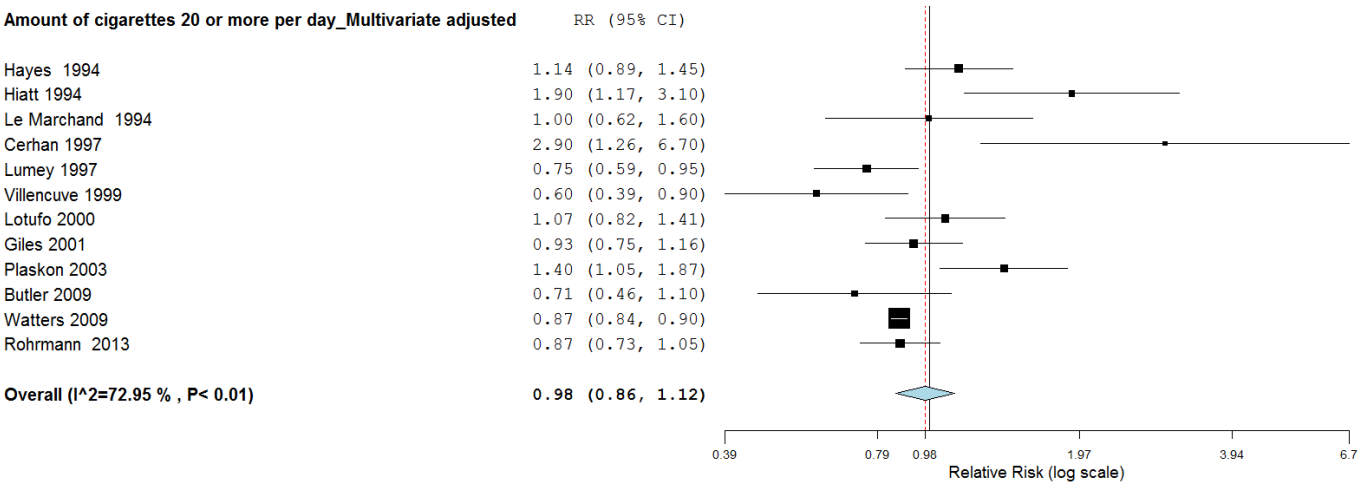
Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Only the most parsimonious models was chosen for this subgroup analysis;

The studies available to the RMA and Islami et al for the association between smoking <20 cigarettes per day ("current" smokers versus "never" smokers) and prostate cancer incidence were the same, therefore separate analyses of RMA only papers and RMA +Islami et al papers were not conducted.



Note: Andersson 1996, >15 cigarettes per day
Lumey 1997, >20 cigarettes per day
Villencuve 1999, including 20-29 and 30+ cigarettes per day
Nilsen 2000, >15 cigarettes per day
Giles 2001, >20 cigarettes per day

Figure 15A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" 20 or more cigarettes per day smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)



Note: Lumey 1997, >20 cigarettes per day
Villencuve 1999, including 20-29 and 30+ cigarettes per day
Giles 2001, >20 cigarettes per day

Figure 15B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" 20 or more cigarettes per day smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with multivariate adjustment (highest number of covariates) (Model E)

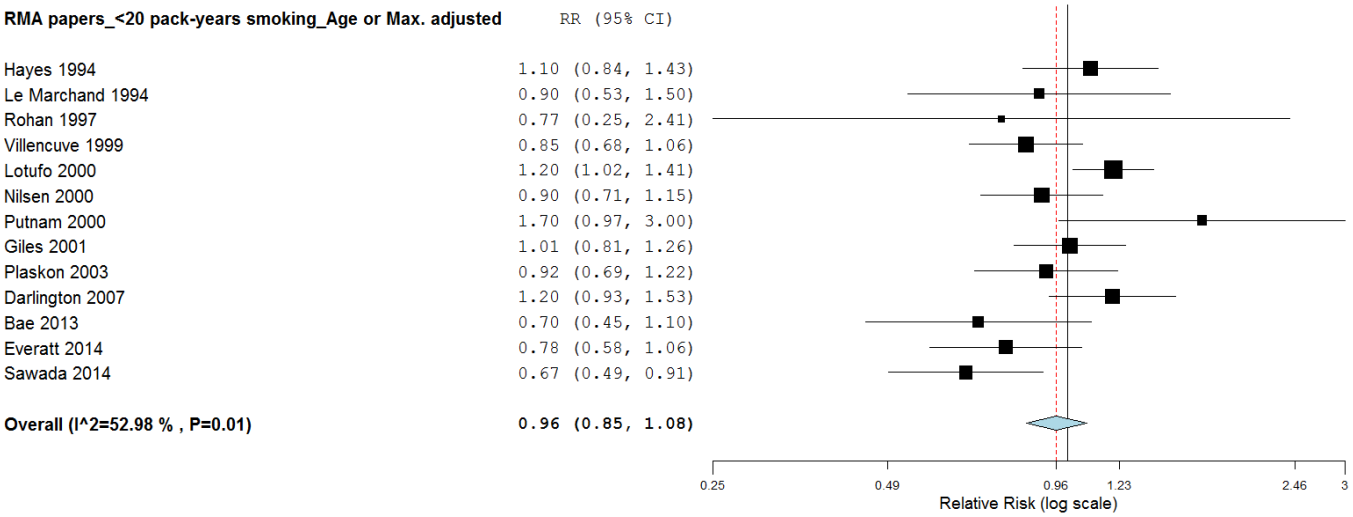
3.5 Meta-analyses of studies available to the RMA only for the association between cigarette smoking by cumulative dosage (<20, 20 to 40, 40 or more pack years) and prostate cancer incidence

Table 23 Summary of studies available to the RMA only included in meta-analyses (Models D and E) for the association between smoking < 20 pack-years ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Honda	1988						
Mills	1989						
Severson	1989						
Thompson	1989						
Fincham	1990						
Ross	1990						
Slattery	1993						
Hayes	1994				√	√	
Hiatt	1994						
Le Marchand	1994				√	√	
Adami	1996						
Andersson	1996						
Engeland	1996						
Gronberg	1996						
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997						
Key	1997						
Lumey	1997						
Rohan	1997				√	√	
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999						
Heikkila [c]	1999						
Parker [a]	1999						
Will	1999						
Villencuve	1999				√	√	
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000				√	√	
Nilsen	2000				√		
Nomura	2000						
Putnam [a]	2000				√		
Stattin	2000						
Giles	2001				√	√	
Zhang	2002						
Alavanja	2003						
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003				√	√	
Barba	2004						
Visvanathan [b]	2004						
Hultdin	2005						
Baglietto	2006						
Darlington	2007				√	√	
Giovannucci [d] (RMA, Islami)	2007						
Rohrmann (1)	2007						
Rohrmann (2)	2007						
Magura	2008						
Gonzalez	2007						
Park	2007						
Butler	2009						
Watters	2009						
Grundmark	2011						
Karunasinghe	2012						

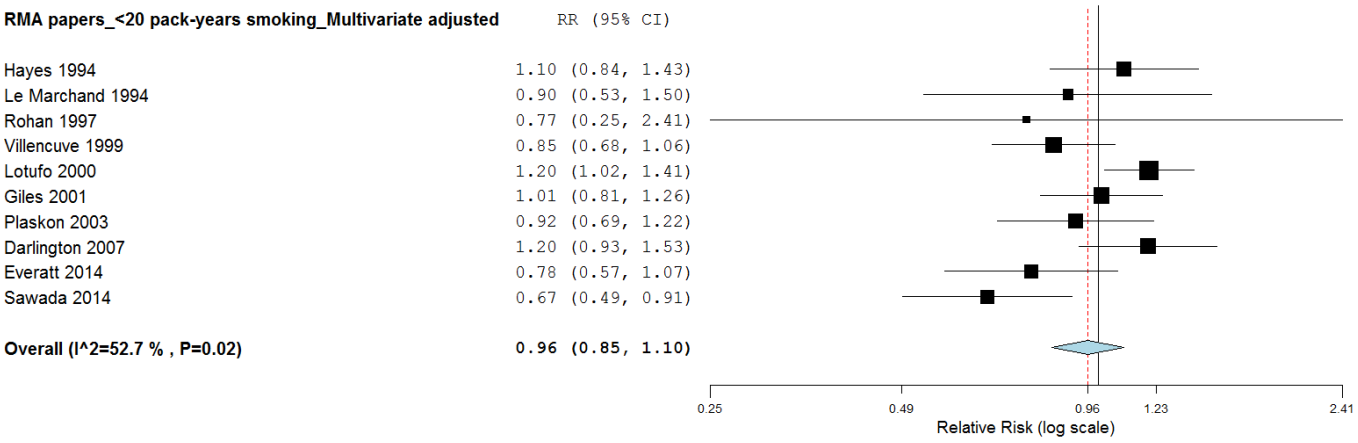
Shafique [e] (RMA)	2012						
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Heikkila	2013						
Koutros	2013						
Lemogne	2013						
Bae	2013				√		
Murphy	2013						
Rohrmann	2013						
Everatt	2014				√	√	
Kondo	2014						
Sawada	2014				√	√	

Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Only the most parsimonious models was chosen for this subgroup analysis.



Note: Le Marchand 1994, 1-22 pack-years
Rohan 1997, ≤15.6 pack-years
Villencuve 1999, including 1-9 and 10-24 pack-years
Putnam 2000, <25 pack-years
Giles 2001, <15 pack-years
Darlington 2007, 0-20 pack-years

Figure 16A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers (<20 pack years) versus "never" smokers in studies available to the RMA only includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)



Note: Le Marchand 1994, 1-22 pack-years
Rohan 1997, ≤15.6 pack-years
Villencuve 1999, including 1-9 and 10-24 pack-years
Giles 2001, <15 pack-years
Darlington 2007, 0-20 pack-years

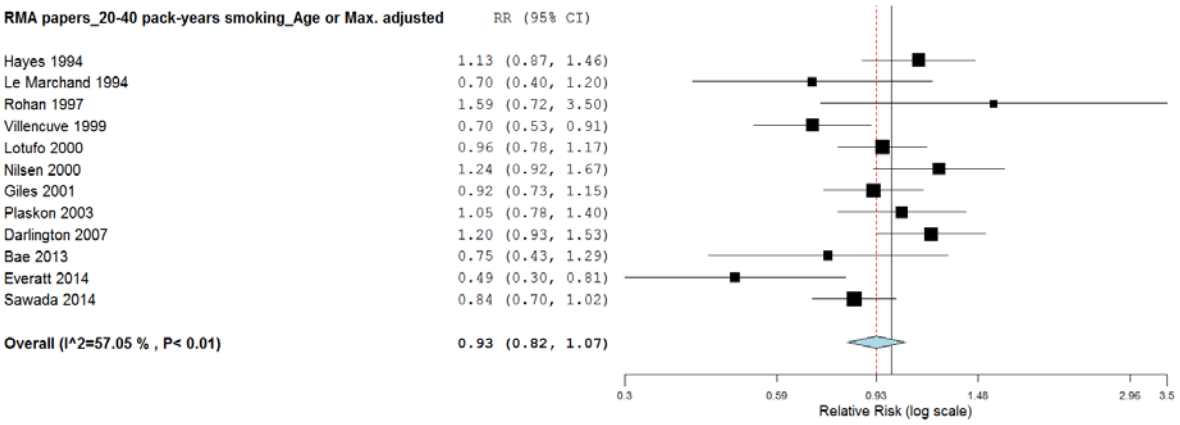
Figure 16B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers (< 20 pack years) smokers versus "never" smokers in studies available to the RMA only includes studies with multivariate adjustment (highest number of covariates) (Model E)

Table 24 Summary of studies available to the RMA only included in meta-analyses (Models D and E) for the association between smoking 20 to 40 pack years ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Honda	1988						
Mills	1989						
Severson	1989						
Thompson	1989						
Fincham	1990						
Ross	1990						
Slattery	1993						
Hayes	1994				√	√	
Hiatt	1994						
Le Marchand	1994				√	√	
Adami	1996						
Andersson	1996						
Engeland	1996						
Gronberg	1996						
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997						
Key	1997						
Lumey	1997						
Rohan	1997				√	√	
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999						
Heikkila [c]	1999						
Parker [a]	1999						
Villencuve	1999				√	√	
Will	1999						
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000				√	√	
Nilsen	2000				√		
Nomura	2000						
Putnam [a]	2000						
Stattin	2000						
Giles	2001				√	√	
Zhang	2002						
Alavanja	2003						
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003				√	√	
Barba	2004						
Visvanathan [b]	2004						
Hultdin	2005						
Baglietto	2006						
Darlington	2007				√	√	
Giovannucci [d] (RMA, Islami)	2007						
Rohrmann (1)	2007						
Rohrmann (2)	2007						
Gonzalez	2007						
Park	2007						
Magura	2008						
Butler	2009						
Watters	2009						
Grundmark	2011						
Karunasinghe	2012						

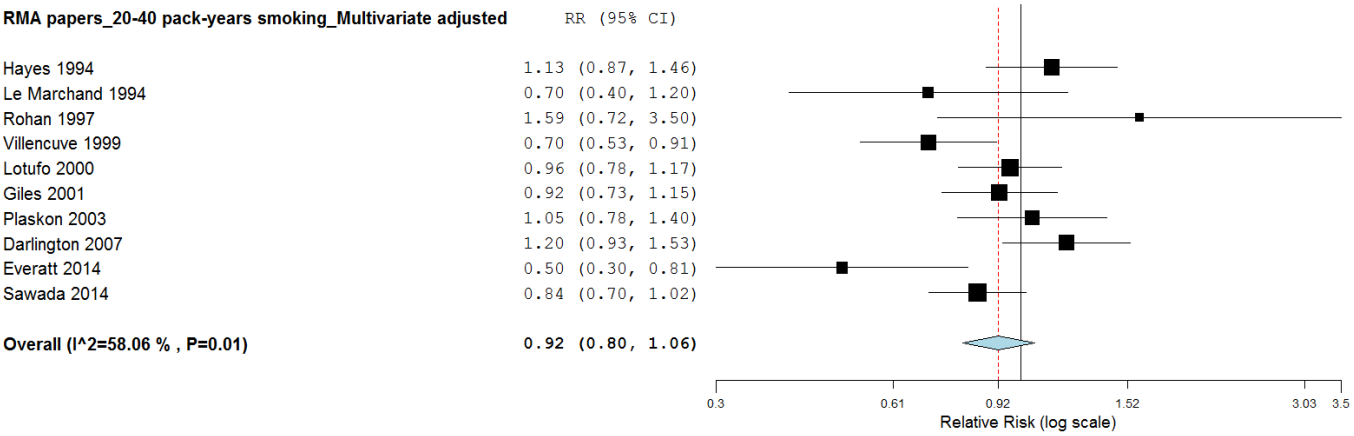
Shafique [e] (RMA)	2012						
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Geybels	2012						
Heikkila	2013						
Koutros	2013						
Lemogne	2013						
Bae	2013				√		
Murphy	2013						
Rohrmann	2013						
Everatt	2014				√	√	
Kondo	2014						
Sawada	2014				√	√	

Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Only the most parsimonious models was chosen for this subgroup analysis.



Note: Hayes 1994, 20-44 pack-years
Le Marchand 1994, 23-44 pack-years
Rohan 1997, >15.6 and ≤37.6 pack-years
Villencuve 1999, 25-39 pack-years
Nilsen 2000, 18-25 pack-years
Giles 2001, 15-35 pack-years
Darlington 2007, 21-43 pack-years
Everatt 2014, 20-29 pack-years

Figure 17A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers (20 to 40 pack years) smokers versus "never" smokers in studies available to the RMA only includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)



Note: Hayes 1994, 20-44 pack-years
Le Marchand 1994, 23-44 pack-years
Rohan 1997, >15.6 and ≤37.6 pack-years
Villencuve 1999, 25-39 pack-years
Giles 2001, 15-35 pack-years
Darlington 2007, 21-43 pack-years
Everatt 2014, 20-29 pack-years

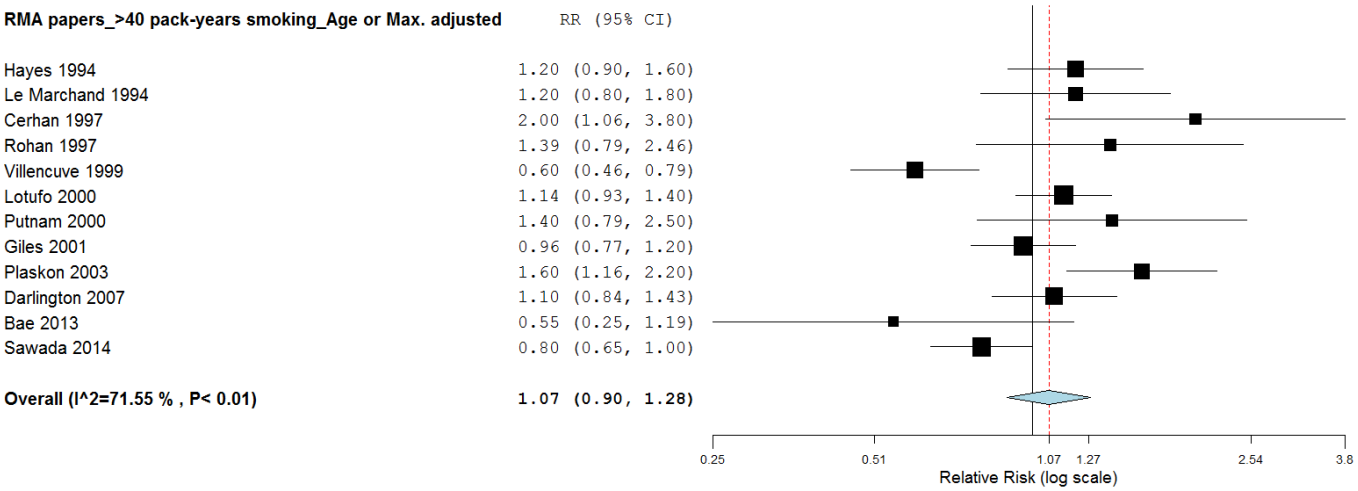
Figure 17B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers (20 to 40 pack years) versus "never" smokers in studies available to the RMA only includes studies with multivariate adjustment (highest number of covariates) (Model E)

Table 25 Summary of studies available to the RMA only included in meta-analyses (Models D and E) for the association between smoking 40 or more pack years ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Honda	1988						
Mills	1989						
Severson	1989						
Thompson	1989						
Fincham	1990						
Ross	1990						
Slattery	1993						
Hayes	1994				√	√	
Hiatt	1994						
Le Marchand	1994				√	√	
Adami	1996						
Andersson	1996						
Engeland	1996						
Gronberg	1996						
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997				√		
Key	1997						
Lumey	1997						
Rohan	1997				√	√	
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999						
Heikkila [c]	1999						
Parker [a]	1999						
Villencuve	1999				√	√	
Will	1999						
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000				√	√	
Nilsen	2000						
Nomura	2000						
Putnam [a]	2000				√		
Stattin	2000						
Giles	2001				√	√	
Zhang	2002						
Alavanja	2003						
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003				√	√	
Barba	2004						
Visvanathan [b]	2004						
Hultdin	2005						
Baglietto	2006						
Darlington	2007				√	√	
Giovannucci [d] (RMA, Islami)	2007						
Rohrmann (1)	2007						
Rohrmann (2)	2007						
Gonzalez	2007						
Park	2007						
Magura	2008						
Butler	2009						
Watters	2009						
Grundmark	2011						
Karunasinghe	2012						
Shafique [e] (RMA)	2012						

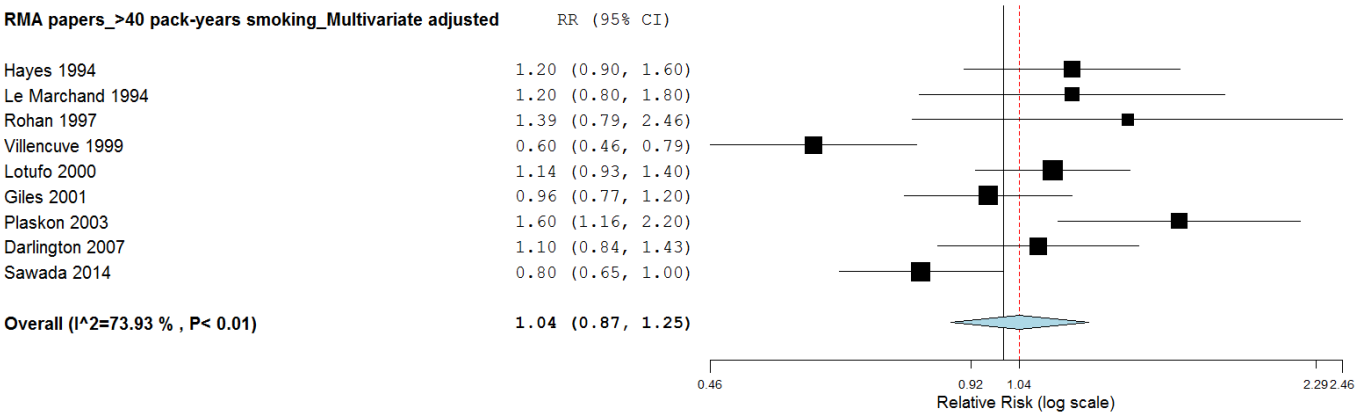
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Geybels	2012						
Heikkila	2013						
Koutros	2013						
Lemogne	2013						
Bae	2013				√		
Murphy	2013						
Rohrmann	2013						
Everatt	2014						
Kondo	2014						
Sawada	2014				√	√	

Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Only the most parsimonious models was chosen for this subgroup analysis.



Note: Hayes 1994, >44 pack-years
Le Marchand 1994, 45+ pack-years
Cerhan 1997, >55 pack-years
Rohan 1997, >37.6 pack-years
Villencuve 1999, 40+ pack-years
Giles 2001, >35 pack-years
Darlington 2007, >43 pack-years
Bae 2013, ≥35 pack-years

Figure 18A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers (40 or more pack years) smokers versus "never" smokers in studies available to the RMA only includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)



Note: Hayes 1994, >44 pack-years
Le Marchand 1994, 45+ pack-years
Rohan 1997, >37.6 pack-years
Villencuve 1999, 40+ pack-years
Giles 2001, >35 pack-years
Darlington 2007, >43 pack-years

Figure 18B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers (40 or more pack years) versus "never" smokers in studies available to the RMA only includes studies with multivariate adjustment (highest number of covariates) (Model E)

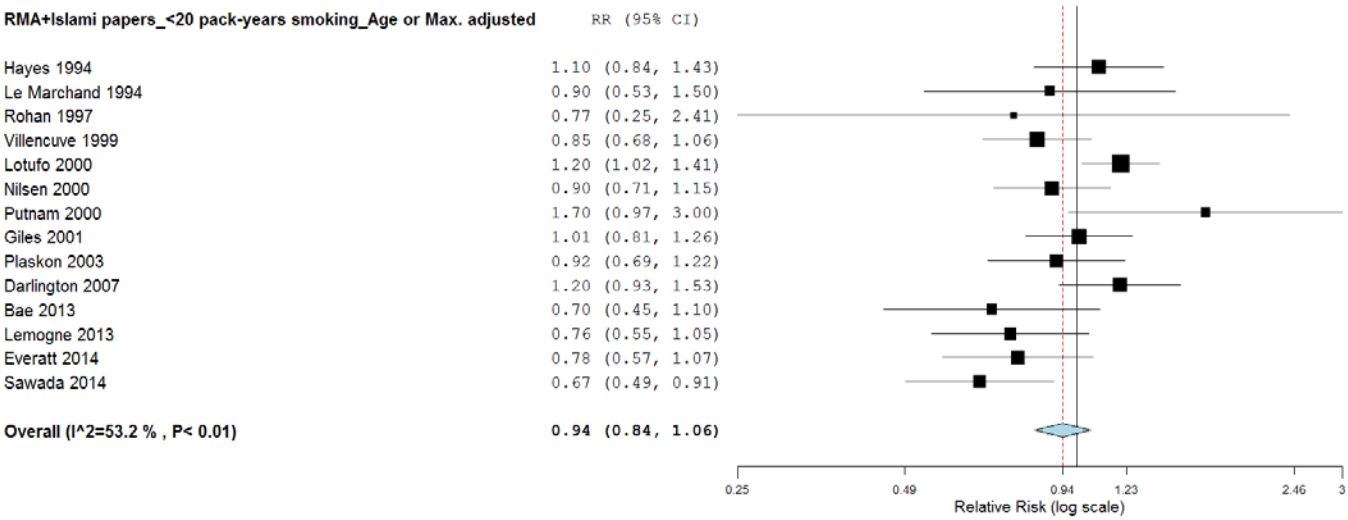
3.6 Meta-analyses of studies available to the RMA and Islami et al. for the association between cigarette smoking by cumulative dosage (<20, 20 to 40, 20 or more pack years) and prostate cancer incidence

Table 26 Summary of studies available to the RMA and Islami et al. included in meta-analyses (Models D and E) for the association between smoking <20 pack-years ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Honda	1988						
Mills	1989						
Severson	1989						
Thompson	1989						
Fincham	1990						
Ross	1990						
Slattery	1993						
Hayes	1994				√	√	
Hiatt	1994						
Le Marchand	1994				√	√	
Adami	1996						
Andersson	1996						
Engeland	1996						
Gronberg	1996						
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997						
Key	1997						
Lumey	1997						
Rohan	1997				√	√	
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999						
Heikkila [c]	1999						
Parker [a]	1999						
Will	1999						
Villencuve	1999				√	√	
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000				√	√	
Nilsen	2000				√		
Nomura	2000						
Putnam [a]	2000				√		
Stattin	2000						
Giles	2001				√	√	
Zhang	2002						
Alavanja	2003						
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003				√	√	
Barba	2004						
Visvanathan [b]	2004						
Hultdin	2005						
Baglietto	2006						
Darlington	2007				√	√	
Rohrmann (1)	2007						
Rohrmann (2)	2007						
Giovannucci [d] (RMA, Islami)	2007						
Gonzalez	2007						
Park	2007						
Magura	2008						
Butler	2009						
Watters	2009						
Grundmark	2011						
Karunasinghe	2012						

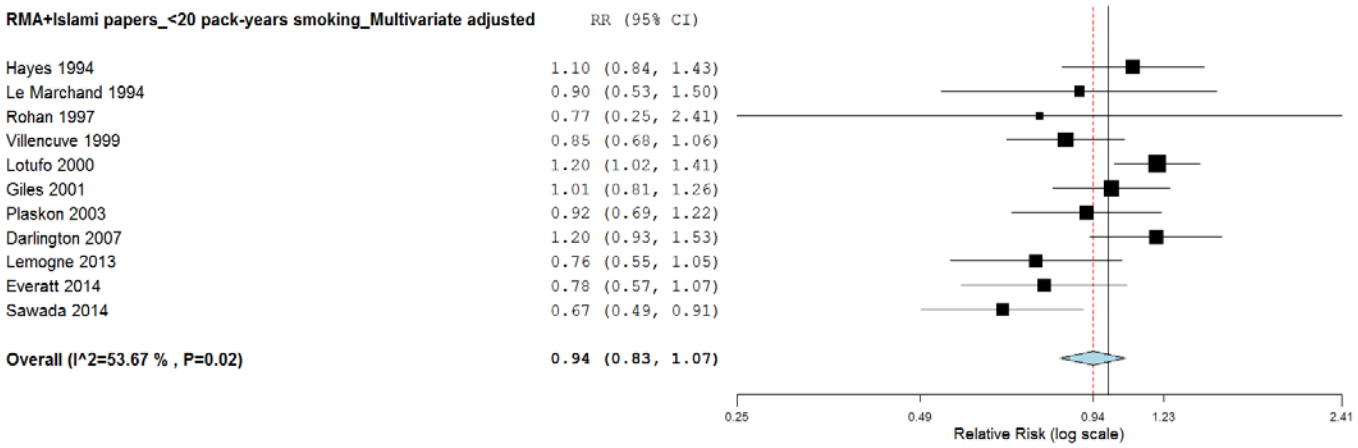
Shafique [e] (RMA)	2012						
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Heikkila	2013						
Koutros	2013						
Lemogne	2013				√	√	
Bae	2013				√		
Murphy	2013						
Rohrmann	2013						
Everatt	2014				√	√	
Kondo	2014						
Sawada	2014				√	√	

Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data



Note: Le Marchand 1994, 1-22 pack-years
Rohan 1997, ≤15.6 pack-years
Villencuve 1999, including 1-9 and 10-24 pack-years
Putnam 2000, <25 pack-years
Giles 2001, <15 pack-years
Darlington 2007, 0-20 pack-years

Figure 19A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers (<20 pack-years) versus "never" smokers in studies available to the RMA and Islami et al. includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)



Note: Le Marchand 1994, 1-22 pack-years
Rohan 1997, ≤15.6 pack-years
Villencuve 1999, including 1-9 and 10-24 pack-years
Giles 2001, <15 pack-years
Darlington 2007, 0-20 pack-years

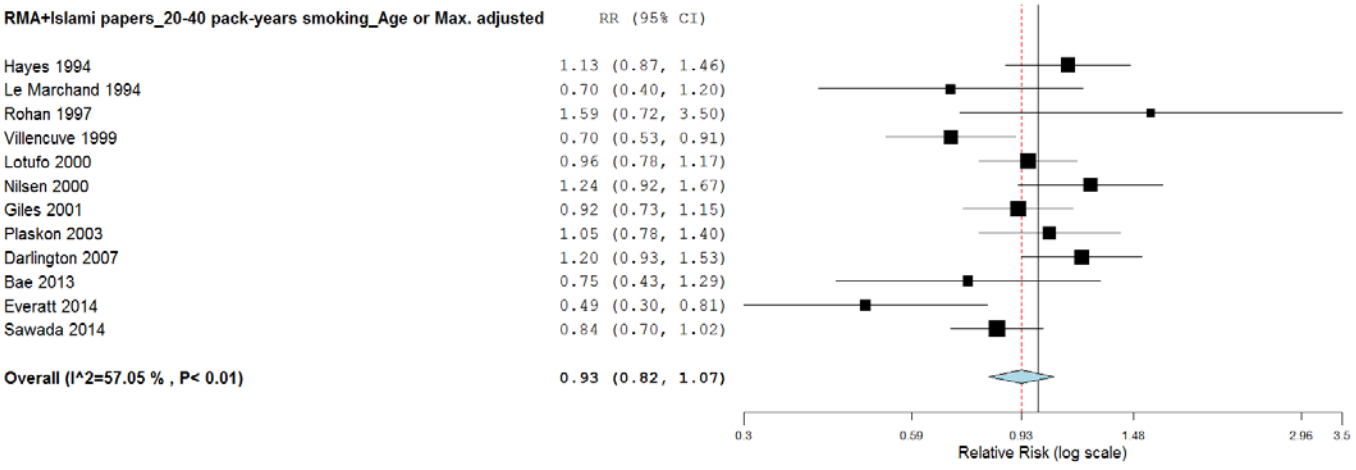
Figure 19B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers (<20 pack-years) smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with multivariate adjustment (highest number of covariates) (Model E)

Table 27 Summary of studies available to the RMA and Islami et al. included in meta-analyses (Models D and E) for the association between smoking 20 to 40 pack-years ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Honda	1988						
Mills	1989						
Severson	1989						
Thompson	1989						
Fincham	1990						
Ross	1990						
Slattery	1993						
Hayes	1994				√	√	
Hiatt	1994						
Le Marchand	1994				√	√	
Adami	1996						
Andersson	1996						
Engeland	1996						
Gronberg	1996						
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997						
Key	1997						
Lumey	1997						
Rohan	1997				√	√	
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999						
Heikkila [c]	1999						
Parker [a]	1999						
Villencuve	1999				√	√	
Will	1999						
Putnam [a]	2000						
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000				√	√	
Nilsen	2000				√		
Nomura	2000						
Stattin	2000						
Giles	2001				√	√	
Zhang	2002						
Alavanja	2003						
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003				√	√	
Barba	2004						
Visvanathan [b]	2004						
Hultdin	2005						
Baglietto	2006						
Darlington	2007				√	√	
Rohrmann (1)	2007						
Rohrmann (2)	2007						
Giovannucci [d] (RMA, Islami)	2007						
Gonzalez	2007						
Park	2007						
Magura	2008						
Butler	2009						
Watters	2009						
Grundmark	2011						
Karunasinghe	2012						

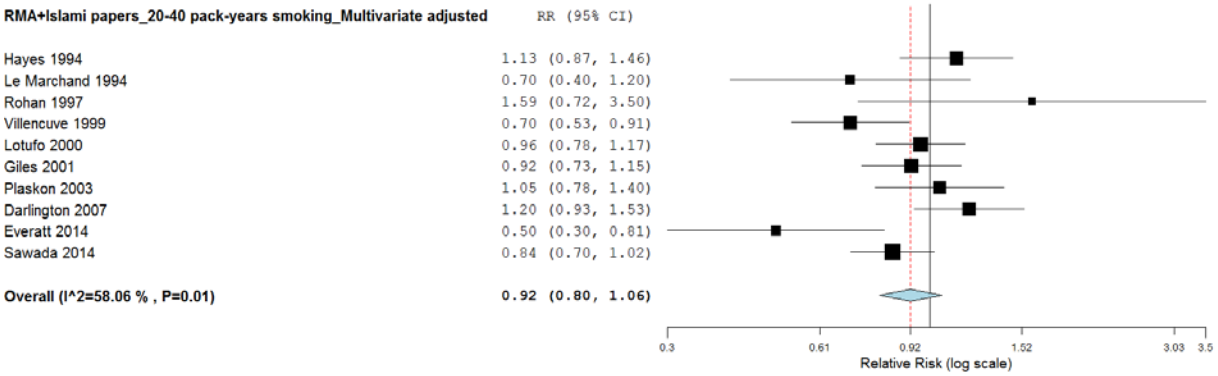
Shafique [e] (RMA)	2012						
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Geybels	2012						
Heikkila	2013						
Koutros	2013						
Lemogne	2013						
Bae	2013				√		
Murphy	2013						
Rohrmann	2013						
Everatt	2014				√	√	
Kondo	2014						
Sawada	2014				√	√	

Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Only the most parsimonious models was chosen for this subgroup analysis.



Note: Hayes 1994, 20-44 pack-years
Le Marchand 1994, 23-44 pack-years
Rohan 1997, >15.6 and ≤37.6 pack-years
Villencuve 1999, 25-39 pack-years
Nilsen 2000, 18-25 pack-years
Giles 2001, 15-35 pack-years
Darlington 2007, 21-43 pack-years
Everatt 2014, 20-29 pack-years

Figure 20A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers (20 to 40 pack-years) smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)



Note: Hayes 1994, 20-44 pack-years
Le Marchand 1994, 23-44 pack-years
Rohan 1997, >15.6 and ≤37.6 pack-years
Villencuve 1999, 25-39 pack-years
Giles 2001, 15-35 pack-years
Darlington 2007, 21-43 pack-years
Everatt 2014, 20-29 pack-years

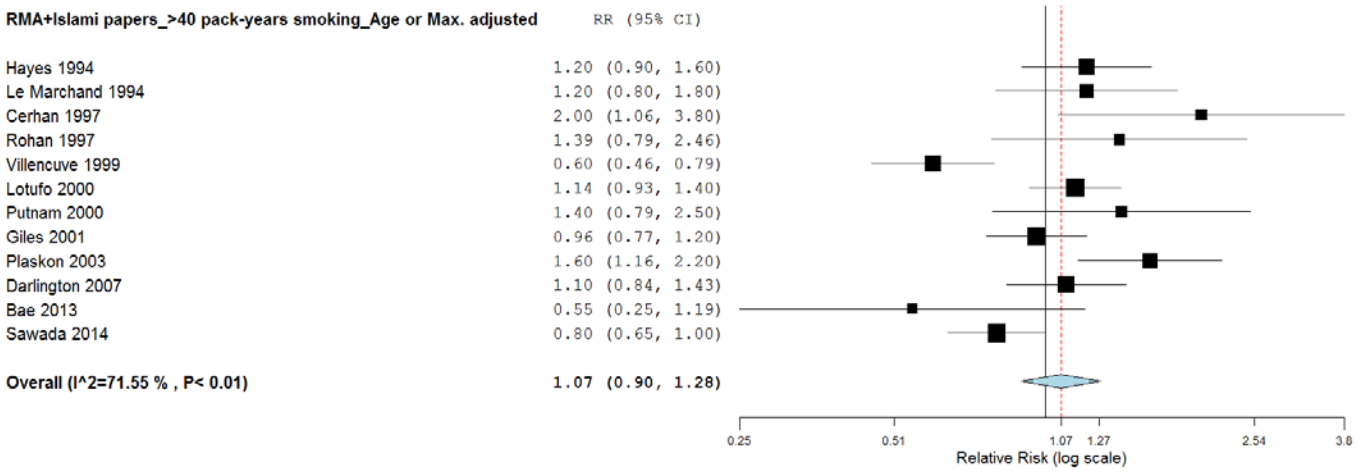
Figure 20B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers (20 to 40 pack-years) versus "never" smokers in studies available to the RMA and Islami et al. includes studies with multivariate adjustment (highest number of covariates) (Model E)

Table 28 Summary of studies available to the RMA and Islami et al. included in meta-analyses (Models D and E) for the association between smoking 40 or more pack-years ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Honda	1988						
Mills	1989						
Severson	1989						
Thompson	1989						
Fincham	1990						
Ross	1990						
Slattery	1993						
Hayes	1994				√	√	
Hiatt	1994						
Le Marchand	1994				√	√	
Adami	1996						
Andersson	1996						
Engeland	1996						
Gronberg	1996						
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997				√		
Key	1997						
Lumey	1997						
Rohan	1997				√	√	
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999						
Heikkila [c]	1999						
Parker [a]	1999						
Villencuve	1999				√	√	
Will	1999						
Putnam [a]	2000				√		
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000				√	√	
Nilsen	2000						
Nomura	2000						
Stattin	2000						
Giles	2001				√	√	
Zhang	2002						
Alavanja	2003						
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003				√	√	
Barba	2004						
Visvanathan [b]	2004						
Hultdin	2005						
Baglietto	2006						
Darlington	2007				√	√	
Rohrmann (1)	2007						
Rohrmann (2)	2007						
Giovannucci [d] (RMA, Islami)	2007						
Gonzalez	2007						
Park	2007						
Magura	2008						
Butler	2009						
Watters	2009						
Grundmark	2011						
Karunasinghe	2012						

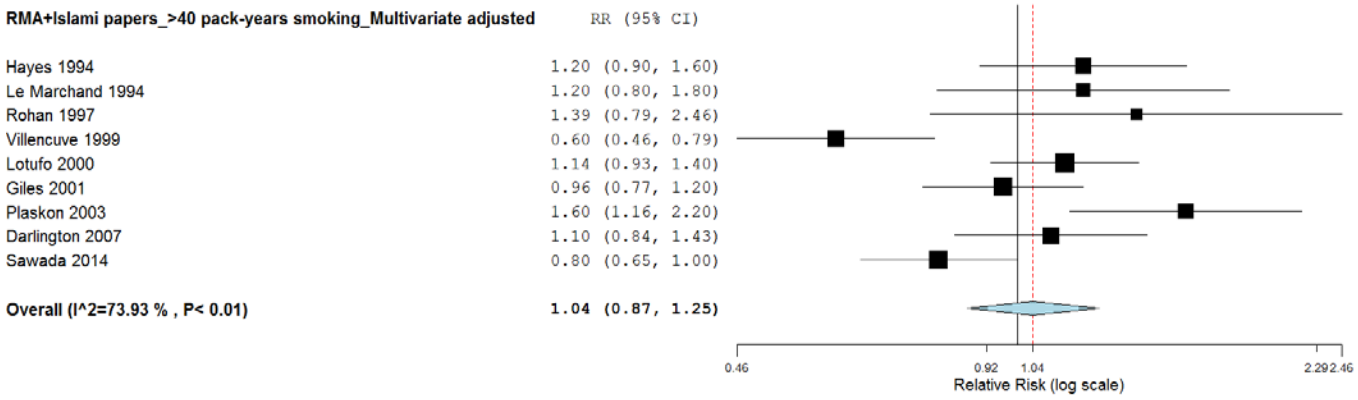
Shafique [e] (RMA)	2012						
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Geybels	2012						
Heikkila	2013						
Koutros	2013						
Lemogne	2013						
Bae	2013				√		
Murphy	2013						
Rohrmann	2013						
Everatt	2014						
Kondo	2014						
Sawada	2014				√	√	

Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Only the most parsimonious models was chosen for this subgroup analysis.



Note: Hayes 1994, >44 pack-years
Le Marchand 1994, 45+ pack-years
Rohan 1997, >37.6 pack-years
Villencuve 1999, 40+ pack-years
Cerhan 1997, >55 pack-years
Giles 2001, >35 pack-years
Darlington 2007, >43 pack-years
Bae 2013, ≥35 pack-years

Figure 21A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers (40 or more pack-years) smokers versus "never" smokers in studies available to the RMA and Islami et al. includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)



Note: Hayes 1994, >44 pack-years
Le Marchand 1994, 45+ pack-years
Rohan 1997, >37.6 pack-years
Villencuve 1999, 40+ pack-years
Giles 2001, >35 pack-years
Darlington 2007, >43 pack-years

Figure 21B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers (40 or more pack-years) versus "never" smokers in studies available to the RMA and Islami et al. includes studies with multivariate adjustment (highest number of covariates) (Model E)

3.7 Meta-analyses of studies available to the RMA only for the association between cigarette smoking and prostate cancer incidence considering the effect of prostate specific antigen (PSA) screening

Table 29 Summary of studies with completed follow-up before 1990 available to the RMA only included in meta-analyses (Models D and E) for the association between cigarette smoking ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Studies with completed follow-up before 1990							
Honda	1988						
Mills	1989				√		
Severson	1989				√		
Thompson	1989				√	√	
Ross	1990				√		
Hayes	1994				√	√	
Hiatt	1994				√	√	
Le Marchand	1994						
Gronberg	1996				√		
Heikkila [c]	1999						
Will	1999						
Studies with completed follow-up from 1990 onwards							
Fincham	1990						
Slattery	1993						
Adami	1996						
Andersson	1996						
Engeland	1996						
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997						
Key	1997						
Lumey	1997						
Rohan	1997						
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999						
Parker [a]	1999						
Villencuve	1999						
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000						
Nilsen	2000						
Nomura	2000						
Putnam [a]	2000						
Stattin	2000						
Giles	2001						
Zhang	2002						
Alavanja	2003						
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003						
Barba	2004						
Visvanathan [b]	2004						
Hultdin	2005						
Baglietto	2006						
Darlington	2007						
Giovannucci [d] (RMA, Islami)	2007						
Rohrmann (1)	2007						
Rohrmann (2)	2007						
Gonzalez	2007						
Park	2007						
Magura	2008						
Butler	2009						
Watters	2009						

Grundmark	2011						
Karunasinghe	2012						
Shafique [e] (RMA)	2012						
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Geybels	2012						
Heikkila	2013						
Koutros	2013						
Lemogne	2013						
Bae	2013						
Murphy	2013						
Rohrmann	2013						
Everatt	2014						
Kondo	2014						
Sawada	2014						

Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Only the most parsimonious models was chosen for this subgroup analysis; *Only the most parsimonious models was chosen for this subgroup analysis.

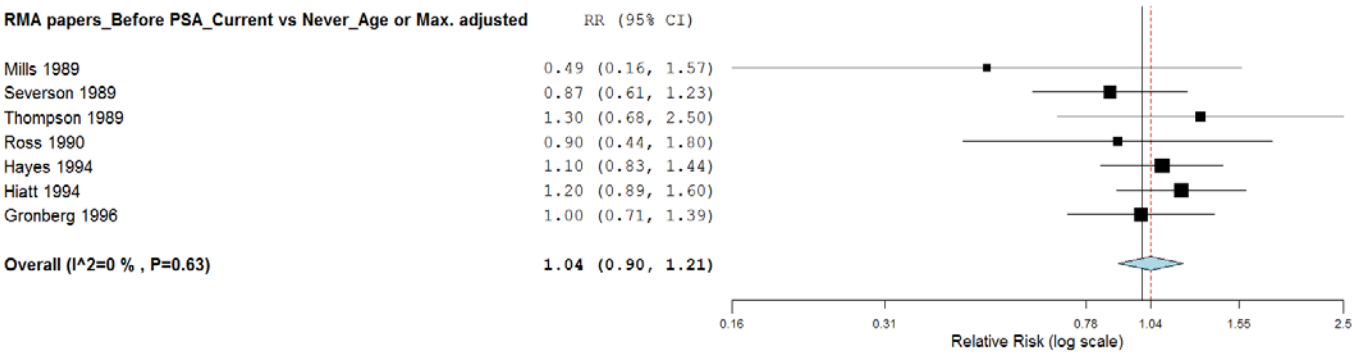


Figure 22A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies with completed follow-up before 1990 available to the RMA includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)

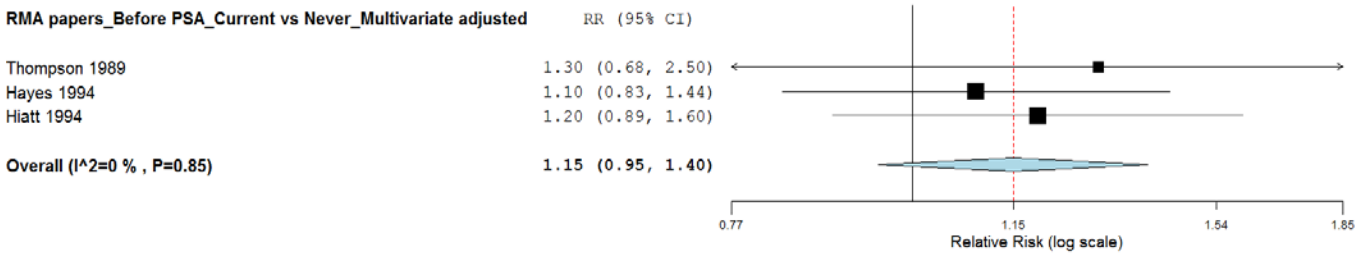


Figure 22B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies with completed follow-up before 1990 available to the RMA includes studies with multivariate adjustment (highest number of covariates) (Model E)

Table 30 Summary of studies with completed follow-up from 1990 onwards available to the RMA included in meta-analyses (Models D and E) for the association between cigarette smoking ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Studies with completed follow-up before 1990							
Honda	1988						
Mills	1989						
Severson	1989						
Thompson	1989						
Ross	1990						
Hayes	1994						
Hiatt	1994						
Le Marchand	1994						
Gronberg	1996						
Heikkila [c]	1999						
Will	1999						
Studies with completed follow-up from 1990 onwards							
Fincham	1990						
Slattery	1993						
Adami	1996				√		
Andersson	1996				√		
Engeland	1996				√		
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997				√	√	
Key	1997						
Lumey	1997				√	√	
Rohan	1997				√	√	
Veierod	1997				√		
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999				√	√	
Parker [a]	1999						
Villencuve	1999						
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000				√	√	
Nilsen	2000				√		
Nomura	2000				√		
Putnam [a]	2000				√		
Stattin	2000						
Giles	2001				√	√	
Zhang	2002						
Alavanja	2003				√	√	
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003				√	√	
Barba	2004						
Visvanathan [b]	2004				√		
Hultdin	2005						
Baglietto	2006						
Darlington	2007				√	√	
Rohrmann (1)	2007				√		
Rohrmann (2)	2007				√		
Giovannucci [d] (RMA, Islami)	2007						
Gonzalez	2007						
Park	2007						
Magura	2008						
Butler	2009				√	√	
Watters	2009				√	√	

Grundmark	2011						
Karunasinghe	2012						
Shafique [e] (RMA)	2012				√	√	
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Geybels	2012						
Heikkila	2013						
Koutros	2013						
Lemogne	2013						
Bae	2013				√		
Murphy	2013				√	√	
Rohrmann	2013				√	√	
Everatt	2014				√	√	
Kondo	2014				√	√	
Sawada	2014				√	√	

Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Only the most parsimonious models was chosen for this subgroup analysis.

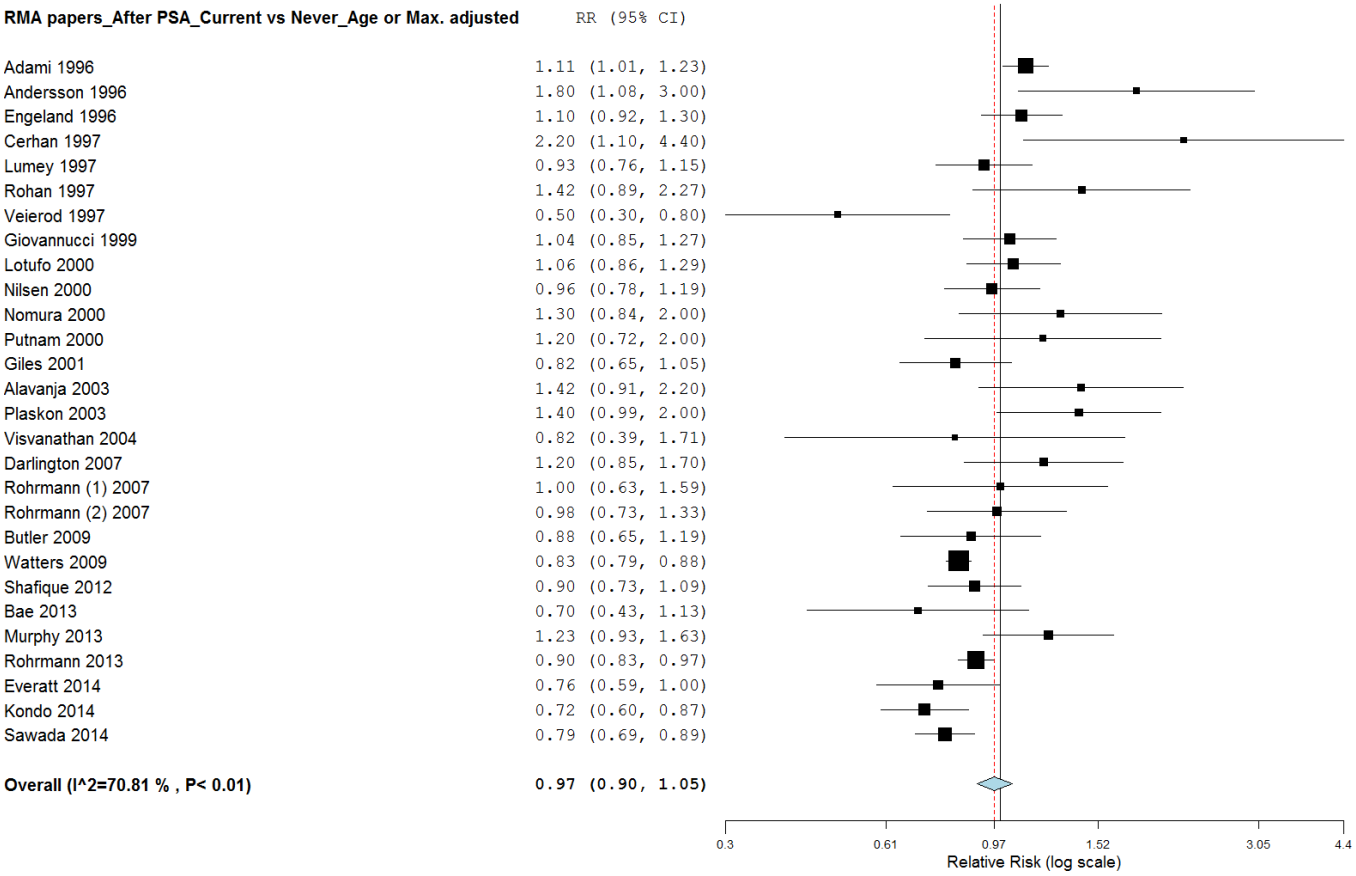


Figure 23A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies with completed follow-up from 1990 onwards available to the RMA includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)

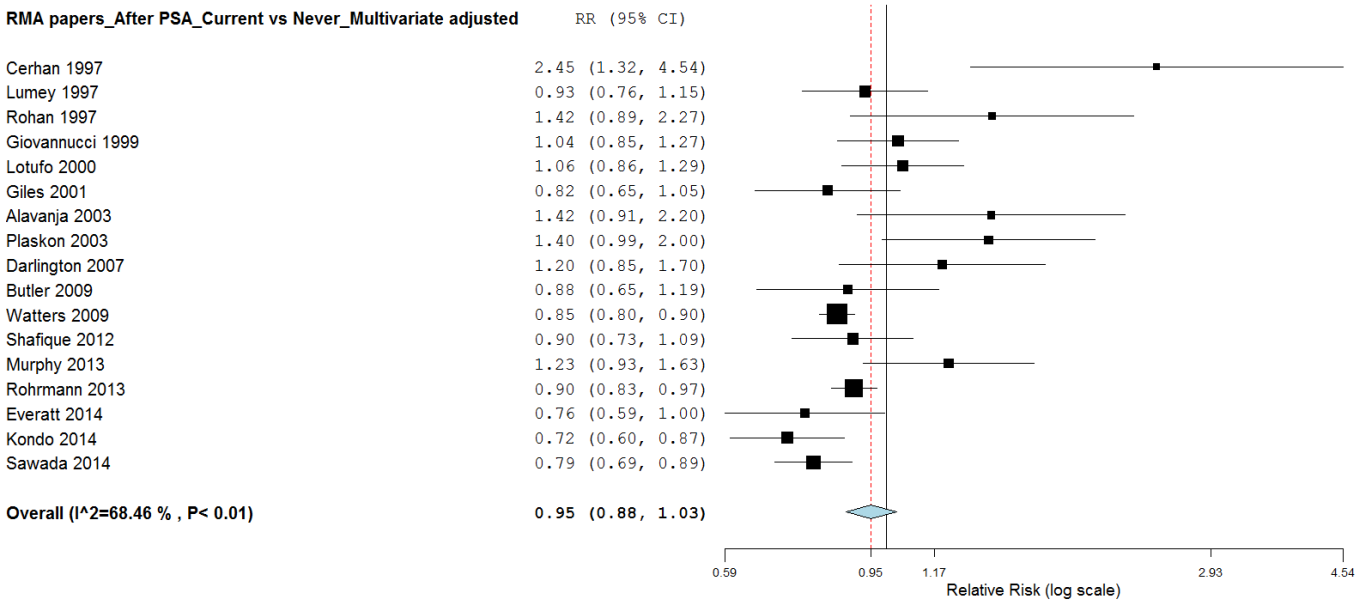


Figure 23B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies with completed follow-up from 1990 onwards available to the RMA includes studies with multivariate adjustment (highest number of covariates) (Model E)

3.8 Meta-analyses of studies available to the RMA and Islami et al. for the association between cigarette smoking and prostate cancer incidence considering the effect of prostate specific antigen (PSA) screening

Table 31 Summary of studies with completed follow-up before 1990 available to the RMA and Islami et al. included in meta-analyses (Models D and E) for the association between cigarette smoking ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Studies with completed follow-up before 1990							
Honda	1988						
Mills	1989				√		
Severson	1989				√		
Thompson	1989				√	√	
Ross	1990				√		
Hayes	1994				√	√	
Hiatt	1994				√	√	
Le Marchand	1994						
Gronberg	1996				√		
Heikkila [c]	1999						
Will	1999				√		
Studies with completed follow-up from 1990 onwards							
Fincham	1990						
Slattery	1993						
Adami	1996						
Andersson	1996						
Engeland	1996						
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997						
Key	1997						
Lumey	1997						
Rohan	1997						
Veierod	1997						
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999						
Parker [a]	1999						
Villencuve	1999						
Putnam [a]	2000						
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000						
Nilsen	2000						
Nomura	2000						
Stattin	2000						
Giles	2001						
Zhang	2002						
Alavanja	2003						
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003						
Barba	2004						
Visvanathan [b]	2004						
Hultdin	2005						
Baglietto	2006						
Darlington	2007						
Rohrmann (1)	2007						
Rohrmann (2)	2007						
Giovannucci [d] (RMA, Islami)	2007						
Gonzalez	2007						
Park	2007						
Magura	2008						
Butler	2009						
Watters	2009						

Grundmark	2011						
Karunasinghe	2012						
Shafique [e] (RMA)	2012						
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Geybels	2012						
Heikkila	2013						
Koutros	2013						
Lemogne	2013						
Bae	2013						
Murphy	2013						
Rohrmann	2013						
Everatt	2014						
Kondo	2014						
Sawada	2014						

Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Only the most parsimonious models was chosen for this subgroup analysis.

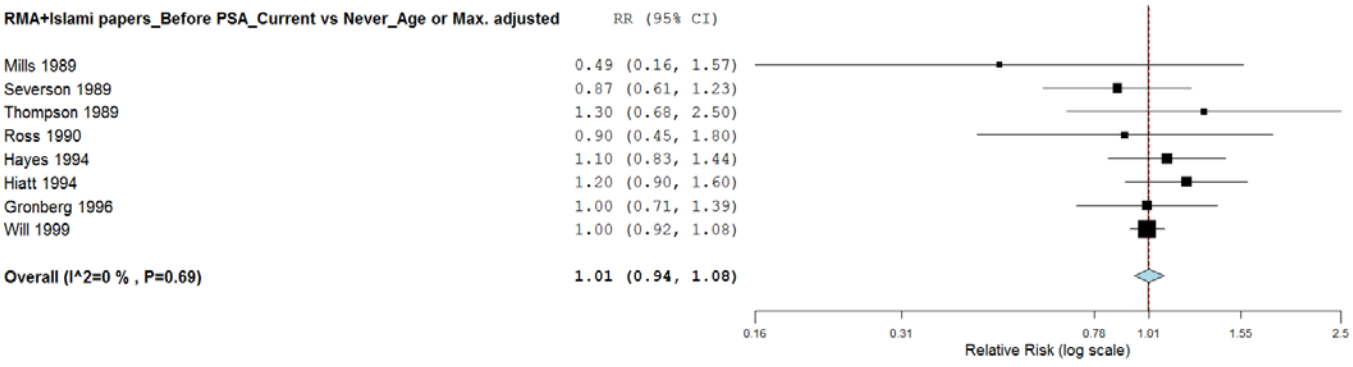


Figure 24A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies with completed follow-up before 1990 available to the RMA and Islami et al. includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)

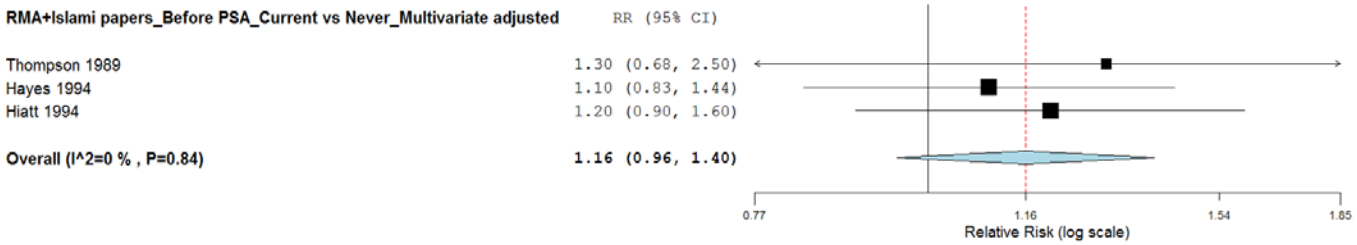


Figure 24B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies with completed follow-up before 1990 available to the RMA and Islami et al. includes studies with multivariate adjustment (highest number of covariates) (Model E)

Table 32 Summary of studies with completed follow-up from 1990 onwards available to the RMA and Islami et al. included in meta-analyses (Models D and E) for the association between cigarette smoking ("current" smokers versus "never" smokers) and prostate cancer incidence

Studies		Model A*	Model B*	Model C*	Model D	Model E	Model F*
Studies with completed follow-up before 1990							
Honda	1988						
Mills	1989						
Severson	1989						
Thompson	1989						
Ross	1990						
Hayes	1994						
Hiatt	1994						
Le Marchand	1994						
Gronberg	1996						
Heikkila [c]	1999						
Will	1999						
Studies with completed follow-up from 1990 onwards							
Fincham	1990						
Slattery	1993						
Adami	1996				√		
Andersson	1996				√		
Engeland	1996				√		
Hakulinen (1)	1996						
Hakulinen (2)	1996						
Cerhan	1997				√	√	
Key	1997						
Lumey	1997				√	√	
Rohan	1997				√	√	
Veierod	1997				√		
Dillner [c]	1998						
Furuya	1998						
Norrish	1998						
Band	1999						
Giovannucci [d] (RMA)	1999				√	√	
Parker [a]	1999						
Villencuve	1999						
Helzlsouer [b]	2000						
Hsing	2000						
Lotufo	2000				√	√	
Nilsen	2000				√		
Nomura	2000				√		
Putnam [a]	2000				√		
Stattin	2000						
Giles	2001				√	√	
Zhang	2002						
Alavanja	2003				√	√	
Friedenreich	2003						
Huang(1)	2003						
Huang(2)	2003						
Plaskon	2003				√	√	
Barba	2004						
Visvanathan [b]	2004				√		
Hultdin	2005						
Baglietto	2006						
Darlington	2007				√	√	
Rohrmann (1)	2007				√		
Rohrmann (2)	2007				√		
Giovannucci [d] (RMA, Islami)	2007						
Gonzalez	2007				√		
Park	2007						
Magura	2008						
Butler	2009				√	√	
Watters	2009				√	√	

Grundmark	2011						
Karunasinghe	2012						
Shafique [e] (RMA)	2012				√	√	
Shafique [e] (Islami)	2012						
Karlsen	2012						
Karppi	2012						
Geybels	2012				√	√	
Heikkila	2013				√	√	
Koutros	2013						
Lemogne	2013				√	√	
Bae	2013				√		
Murphy	2013				√	√	
Rohrmann	2013				√	√	
Everatt	2014				√	√	
Kondo	2014				√	√	
Sawada	2014				√	√	

Note: a, b, c, d, e were paired papers in which data were from the same cohorts; √ study included in meta-analysis model. Studies were excluded due to missing relevant data; Model **A** included studies with adjusted data (highest number of covariates) when available or, when not available, the unadjusted results; Model **B** included studies with age-only adjusted data available; Model **C** included studies with age-only adjustment when available or, when not available, the results for which age was adjusted with the lowest number of additional covariates; Model **D** included studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates; Model **E** included studies with multivariate adjustment (highest number of covariates); Model **F** included studies with non-adjusted raw data; *Only the most parsimonious models was chosen for this subgroup analysis.

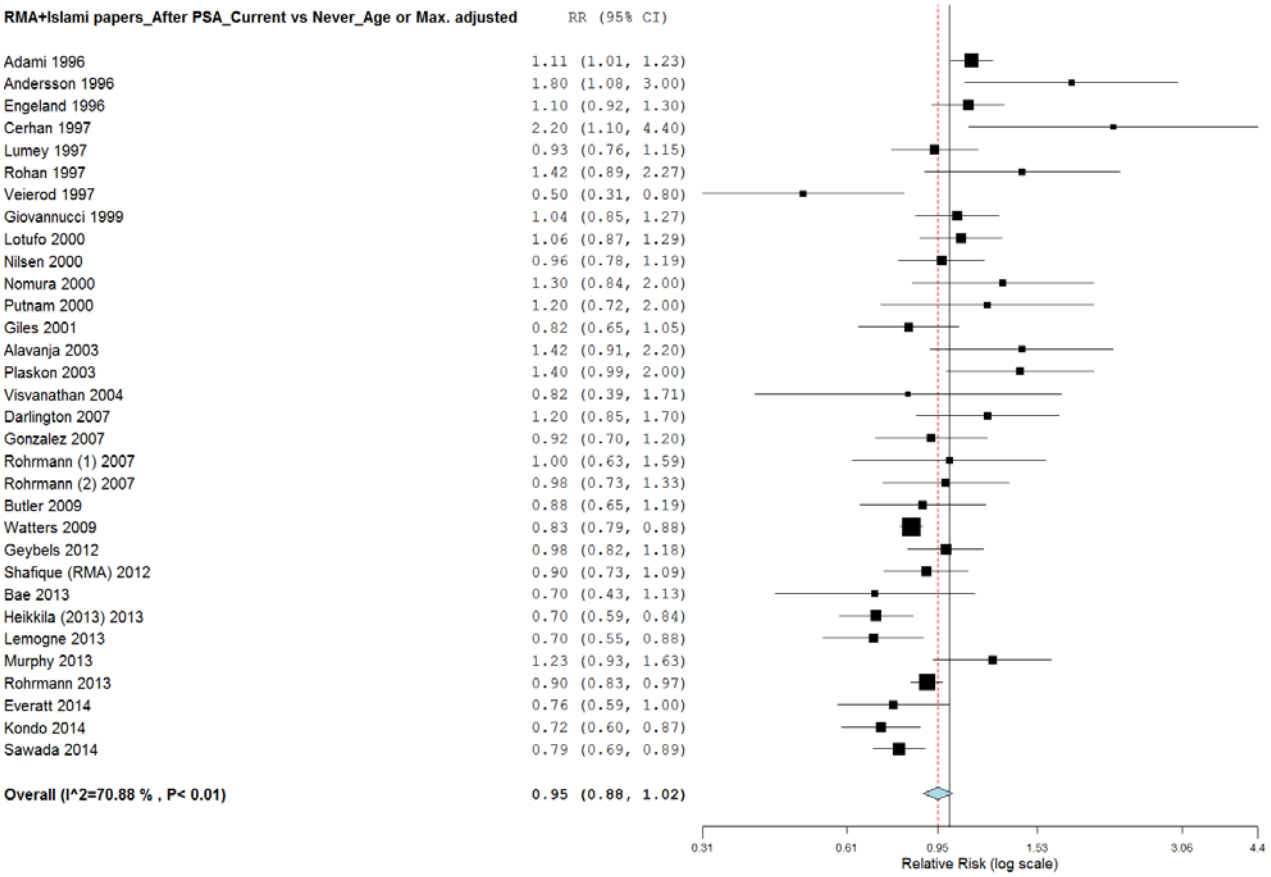


Figure 25A: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies with completed follow-up from 1990 onwards available to the RMA and Islami et al. includes studies with age only adjustment when available or, when not available, the results for which age was adjusted with the highest number of additional covariates (Model D)

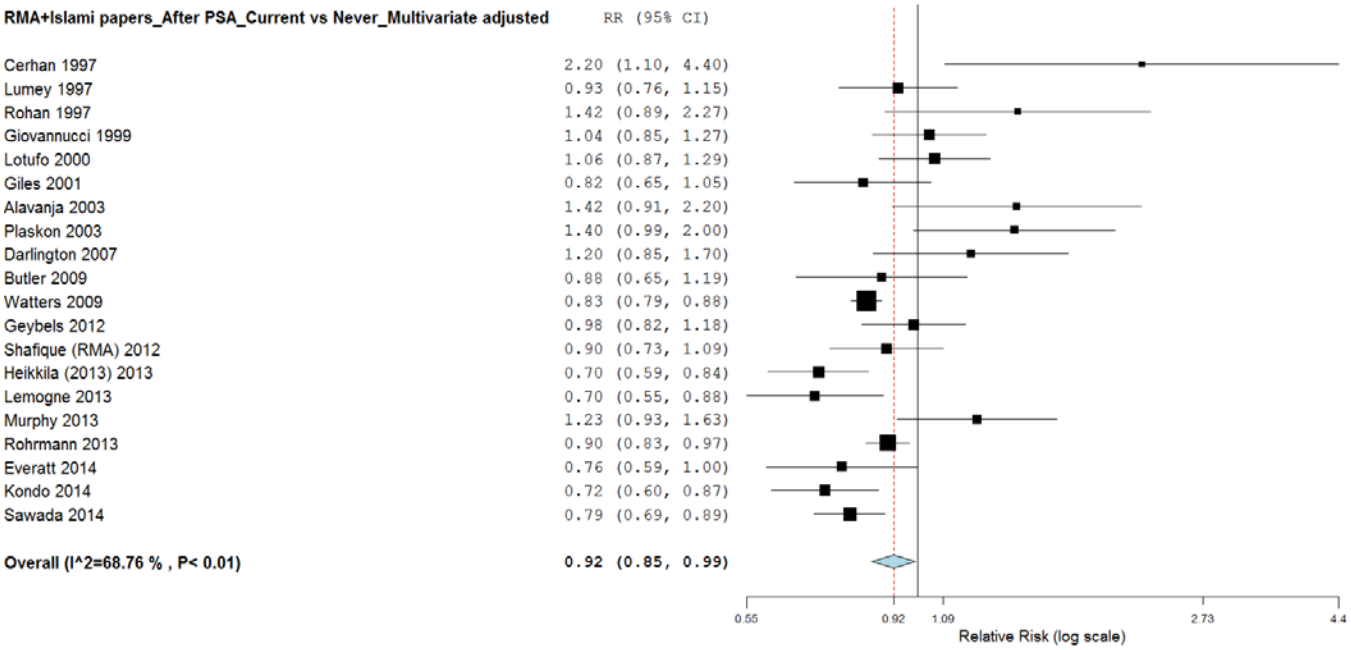


Figure 25B: Forest plot of pooled results reflecting risk of prostate cancer incidence among "current" smokers versus "never" smokers in studies with completed follow-up from 1990 onwards available to the RMA and Islami et al. includes studies with multivariate adjustment (highest number of covariates) (Model E)

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APPENDIX B: TABLES OF MORTALITY STUDIES

Table 1 Studies with data on the risk of prostate cancer death in men diagnosed with prostate cancer and who were current smokers

First author & year	RMA ID	Country	Cohort subjects	Number of deaths from prostate cancer among current smokers	Total number of current smokers	Adjustment[a]	Smoking data[b]	RR[c]	95% CI[d]
Kenfield 2011[20]	065041	USA	Health professionals	41	277	A D BM T P	U	**1.61**	**1.11-2.32**
Merrick 2004[27]	030797	USA	Patients underwent brachytherapy	1	51*	None	B	1.82*	0.11-28.72*
Meyer 1999[28]	029071	Canada	General population 45+	9	68	A G TS O	B	2.0	0.9-4.5

a Confounders controlled for in smoking results: A = age; BM = Body Mass Index; C = comorbidities; D = diet; E = education; F = Family history; G = Cancer grade; H = height; M = marital status; P = physical activity; R = race; T= PSA screening test, TS= T stage; W = weight; O = other.

b Smoking data collection: B = at study baseline; U = updated data collected during study.

c RR = relative risk v never-smokers, except where indicated.

d CI = confidence interval.

* calculated

Table 2 Studies with data on the association between cigarette smoking ("current" smokers with "never" smokers) and prostate cancer mortality risk

First author & year	RMA ID	Country	Cohort subjects	Total prostate cancer mortality cases	Adjustment[a]	Smoking data[b]	Current smokers			
							Category	cases	RR[c]	95% CI[d]
Carstenen 1987[29]	003249	Sweden	General population 18+	193*	None	B		72*	0.9	0.7-1.3
Rohrmann 2007[14]	065219	USA	General population	1) 217*	A	U	Total	104	0.93	0.67-1.29
							<10 cigs/d	*21*	*1.11*	*0.67-1.84*
							10-19 cigs/d	*49*	*0.85*	*0.57-1.25*
							20+ cigs/d	*34*	*0.95*	*0.62-1.47*
				2) 164*			Total	59	1.25	0.84-1.87
							<10 cigs/d	*31*	*1.12*	*0.44-2.28*
							10-19 cigs/d	*23*	*1.11*	*0.7-1.77*
							20+ cigs/d	*20*	*1.58*	*0.94-2.64*
Akiba 1990[30]	007148	Japan	General population 40+	147*	None	B	Total	108	1.1	0.7-1.5
							1-4 cigs/d	***8***	***3.1***	***1.4-6.4***
							5-14 cigs/d	*50*	*1*	*0.7-1.6*
							15-24 cigs/d	*42*	*0.9*	*0.6-1.4*
							25-34 cigs/d	*3*	*0.8*	*0.2-2.1*
							35+ cigs/d	*5*	*3*	*1.0-7.1*
Hsing 1991[31]	003309	USA	Veterans	4607	A	B	Total	1407	**1.18**	**1.09-1.28**
							1-9 cigs/d	*260*	*1.11*	*0.97-1.27*
							10-20 cigs/d	*695*	***1.15***	***1.05-1.27***
							21-39 cigs/d	*374*	***1.23***	***1.09-1.38***
							>39 cigs/d	*78*	***1.51***	***1.20-1.90***
Lotufo 2000[12]	28974	US	Physicians	113	A BM H P O (alcohol, aspirin assignment and beta-carotene assignment)	U	Total	11	1.23	0.63-2.41
							<20 cigs/d	*4*	*1.25*	*0.45-3.49*
							20+ cigs/d	*7*	*1.22*	*0.54-2.74*
Adami 1996[6]	016355	Sweden	Construction workers	709*	A	B		343	**1.26**	**1.06-1.50**
Rohrmann 2012[5]	065978	Europe	General population	432*	H W E M P	B	Total	121	1.27[j]	0.98-1.65
							1-14 cigs/d	*40*	*1.19[j]*	*0.82-1.73*
							15-24 cigs/d	*40*	*1.31[j]*	*0.90-1.91*
							25+ cigs/d	*21*	***1.81[j]***	***1.11-2.93***

Table 2 Studies with data on the association between cigarette smoking ("current" smokers with "never" smokers) and prostate cancer mortality risk (continued)

First author & year	RMA ID	Country	Cohort subjects	Total prostate cancer mortality cases	Adjustment[a]	Smoking data[b]	Current smokers			
							Category	cases	RR[c]	95% CI[d]
Batty 2008[32]	052193	UK	Govt employees 40-69	484	A BM P M H C O(employment grade, forced expiratory volume in 1s)	B	Total	184	**1.3**[j]	**1.01-1.69**
Coughlin 1996[33]	016621	USA	White & black men 35+	826	A R	B	Total	312	**1.31**[g]	**1.13-1.52**
							1-15 cigs/d	*79*	*1.54*	*NR*
							16-25 cigs/d	*102*	*1.27*	*NR*
							26-35 cigs/d	*58*	*1.23*	*NR*
							36-45 cigs/d	*57*	*1.5*	*NR*
							46+ cigs/d	*16*	*1.22*	*NR*
Rodriguez 1997[34]	010918	USA	White & black men 30+	1748	A D F R O	B	Total	339	**1.34**	**1.16-1.56**
							<10 cigs/d	*42*	*1.33*	*0.96-1.83*
							10-19 cigs/d	*74*	***1.58***	***1.23-2.03***
							20 cigs/d	*108*	***1.38***	***1.10-1.71***
							21+ cigs/d	*107*	*1.25*	*1.00-1.57*
Eichholzer 1999[35]	017003	Switzerland	General population in Basel	30	None	B		12	1.38*	0.67-2.85*
Giovannucci 2007[9]	065156	USA	Health professionals 40-75	NR[h]	A BM H P F C D(tomato source) O	B		NR[h]	**1.41**[k]	**1.04-1.91**
Weinmann 2010[24]	065153	USA	White and Black men died of prostate adenocarcinoma (note: case-control study)	768	A R T O(health plan, number of months in health plan, reference date)	B		125	**1.5**	**1.1-2.0**
Giovannucci 1999[36]	017143	USA	Health professionals 40-75	103*	A D F R	U		11	1.58	0.81-3.10
Kenfield 2011[20]	065041	USA	Health professionals	524	A D BM T P	U	Total	41	**1.61**	**1.11-2.32**
							0-39 pack-years	*17*	*1.72*	*0.96-3.08*
							40+ pack-years	*17*	***1.82***	***1.03-3.20***
Watters 2009[4]	065149	USA	Retirees 50-71	394*	A R E M H W P F T D C	B		64	1.69	1.25-2.27
Hsing 1990[31]	003310	USA	White male 35+	149	A	B	Total	91[l]	**1.8**	**1.1-2.9**
							Occasional and ex	*52*	***1.9***	***1.1-3.3***
							1-19 cigs/d	*12*	*1.6*	*0.8-3.3*
							20-29 cigs/d	*11*	*1.7*	*0.8-3.5*
							30+ cigs/d	*3*	*1.4*	*0.4-4.4*

Table 2 Studies with data on the association between cigarette smoking ("current" smokers with "never" smokers) and prostate cancer mortality risk (continued)

First author & year	RMA ID	Country	Cohort subjects	Total prostate cancer mortality cases	Adjustment[a]	Smoking data[b]	Current smokers			
							Category	cases	RR[c]	95% CI[d]
Merrick 2004[27]	030797	USA	Patients underwent brachytherapy	5*	None	B		1	1.82*	0.11-28.72*
Meyer 1999[28]	029071	Canada	General population 45+	32	A G TS O	B		9	2.0	0.9-4.5
Daniell 1995[37]	016339	USA	Community hospital patients	57*	None	B		25*	2.14*[m]	1.34-3.42
Tverdal 1993[37]	026034	Norway	General population 35-49	32*	A C P BM H	B	Total *<10 cigs/d* *10-19 cigs/d* *20+ cigs/d*	15* *7* *5* *3*		Relative risk per 10 cigarettes: 0.6 (0.3-1.4)

a Confounders controlled for in smoking results: A = age; BM = Body Mass Index; C = comorbidities; D = diet; E = education; F = Family history; G = Cancer grade; H = height; M = marital status; P = physical activity; R = race; T= PSA screening test, TS= T stage; W = weight; O = other.
b Smoking data collection: B = at study baseline; U = updated data collected during study.
c RR = relative risk v never-smokers, except where indicated.
d CI = confidence interval.
e Dose data = dose response data reported for at least 3 levels of consumption.
f Precise number not reported.
g Result for current smokers at baseline v former & never-smokers.
h NR = not reported.
i NC = not calculable from available data.
j Hazard ratio reported
k Includes current and past smoking within past 10 years
l ever used cigarettes
m smokers vs non-smokers
* calculated

Table 3 Studies with data on the association between cigarette smoking ("current" smokers with "never" smokers) and prostate cancer recurrence

First author & year	RMA ID	Country	Cohort subjects	Total alive prostate cancer cases	Total recurrent cases	Adjustment[a]	Smoking data[b]	Current smokers			
								categories	cases	RR[c]	95% CI[d]
Moreira 2010[39]	065785	USA	Men underwent radical prostatectomy but not hormone or radiation therapy	1267	NR[h]	A R BM T G O	B		NR[h]	1.12[j]	0.89-1.44
Joshu 2011[22]	065158	USA	Men underwent radical prostatectomy but not hormone or radiation therapy	1416	106*	A R F T BM G O	U	5 yrs before prostatectomy	9	1.19[j]	0.55-2.57
								1 yr after prostatectomy	8	**2.31[j]**	**1.05-5.10**
Kenfield 2011[20]	065041	USA	Health professionals	3633	878	A D BM T P	U	Total	51	**1.61**	**1.16-2.22**
								0-39 pack-years	*23*	***2.13***	***1.24-3.64***
								40+ pack-years	*21*	*1.48*	*0.88-2.48*
Pickles 2004[21]	030796	Canada	Patients treated with curative external beam radiation therapy	601	NR[h]	G T TS	B		NR[h]	**1.68**	**1.11-2.56**
Merrick 2004[27]	030797	USA	Patients underwent brachytherapy	544	22	None	B		7	2.83*	0.93-8.67*

a Confounders controlled for in smoking results: A = age; BM = Body Mass Index; C = comorbidities; D = diet; E = education; F = Family history; G = Cancer grade; H = height; M = marital status; P = physical activity; R = race; T= PSA screening test, TS= T stage; W = weight; O = other.
b Smoking data collection: B = at study baseline; U = updated data collected during study.
c RR = relative risk v never-smokers, except where indicated.
d CI = confidence interval.
e Dose data = dose response data reported for at least 3 levels of consumption.
f Precise number not reported.
g Result for current smokers at baseline v former & never-smokers.
h NR = not reported.
i NC = not calculable from available data.
j Hazard ratio reported
k Includes current and past smoking within past 10 years
l ever used cigarettes
* calculated

Table 4 Studies with data on the association between cigarette smoking ("current" smokers with "never" smokers) and disease stage

First author & year	RMA ID	Country	Cohort subjects	Disease stage	Total cases at this stage	Adjustment[a]	Smoking data[b]	Current smokers		
								cases	RR[c]	95% CI[d]
Giovannucci 1999[36]	017143	USA	Health professionals 40-75	Distant metastatic	152*	A D F R	U	13	1.23	0.67-2.24
Kenfield 2011[20]	065041	USA	Health professionals	T1^	2731*	None	U	108*	1	
				T2	1890*			128*	**1.33***	**1.17-1.51***
				T3 or T4	217*			23*	**2.82***	**1.85-4.31***
				M1 and/or N1	251*			18*	**1.79***	**1.13-2.84***
Watters 2009[4]	065149	USA	Retirees 50-71	Nonadvanced	14810*	A R E M H W P F T D C	B	1255	0.82[j]	0.77-0.88
				Advanced	1830*			191	1.04[j]	0.88-1.24
Giovannucci 2007[9]	065156	USA	Health professionals 40-75	T1 or T2 and N0, M0^	2161	A BM H P F C D O	B	NR[h]	0.88[k]	0.77–1.01
				T3a and N0, M0	345			NR[h]	1.11[k]	0.82-1.52
				T3b or T4 or N1 or M1	523			NR[h]	1.14[k]	0.90-1.45
Daniell 1995[36]	016339	USA	Community hospital patients	A^^	124	None	B	36*	1	
				B	111			22	0.75*	0.53-1.08*
				C	41			9	0.75*	0.39-1.44*
				D1	37			12	1.13*	0.62-2.06*
				D2	46			17	1.29*	0.78-2.14*
Kobrinsky 2003[23]	028875	USA	General population	Local	1944*	None	B	308	1	
				Metastatic	279*			68	**1.53**	**1.17-2.02**
				Regional	88*			23	**1.83**	**1.09-3.06**
Merrick 2004[27]	030797	USA	Patients underwent brachytherapy	Low risk *(Gleason score ≤6, PSA ≤10 ng/ml, T1c-T2a^)*	219	None	B	38	1	
				Intermediate risk *(Gleason score≥7, or PSA>10ng/ml, or ≥T2b)*	231			38	0.99*	0.75-1.31*
				High risk *(two or three of the intermediate risk criteria)*	132			22	1.06*	0.70-1.62*
Pickles 2004[21]	030796	Canada	Patients treated with curative external beam radiation therapy	T1^	93*	None	B	6	1	
				T2	304*			35	1.10*	0.94-1.28*
				T3	180*			41	**1.37***	**1.12-1.68***
				T4	14*			5	**3.64***	**1.18-11.17***

Table 4 Studies with data on the association between cigarettes smoking ("current" smokers with "never" smokers) and disease stage (continued)

First author & year	RMA ID	Country	Cohort subjects	Disease grade	Total cases at this stage	Adjustment[a]	Smoking data[b]	Current smokers		
								cases	RR[c]	95% CI[d]
Hussain 1992[40]	017448	USA	Patients with adenocarcinoma of prostate	A^^	11*	None	B	7	1	
				B	60*			28	0.90*	0.74-1.10*
				C	32*			16	1.16*	0.65-2.06*
				D	158*			110	1.02*	0.93-1.12*
Rohrmann 2012[5]	065978	Europe	General population	Localised	1516*	H W E M P	B	361	0.86	0.75-0.99
				Advanced	808*			216	1.05	0.87-1.27

a Confounders controlled for in smoking results: A = age; BM = Body Mass Index; C = comorbidities; D = diet; E = education; F = Family history; G = Cancer grade; H = height; M = marital status; P = physical activity; R = race; T= PSA screening test, TS= T stage; W = weight; O = other.

b Smoking data collection: B = at study baseline; U = updated data collected during study.

c RR = relative risk v never-smokers, except where indicated.

d CI = confidence interval.

e Dose data = dose response data reported for at least 3 levels of consumption.

f Precise number not reported.

g Result for current smokers at baseline v former & never-smokers.

h NR = not reported.

i NC = not calculable from available data.

j Hazard ratio reported

k Includes current and past smoking within past 10 years

l ever used cigarettes

* calculated

^ TNM staging system

^^ Whitmore-Jewett staging system

Table 5 Studies with data on the association between cigarettes smoking ("current" smokers with "never" smokers) and disease grade

First author & year	RMA ID	Country	Cohort subjects	Disease stage or grade	Total cases at this stage	Adjustment[a]	Smoking data[b]	Current smokers		
								cases	RR[c]	95% CI[d]
Plakson 2003[16]	028497	USA	White & Black 40-64	Less aggressive	498*	A R F P O	U	81	1.4	1.0-2.0
Spitz 2000[41]	028975	USA	Patients underwent radical prostatectomy	Gleason score ≤ 7 (3+4) Gleason score of 7 (4+3)	83 20	None	B	3* 1*	NC[e]	

a Confounders controlled for in smoking results: A = age; F = Family history; P = physical activity; R = race; O = other.
b Smoking data collection: B = at study baseline; U = updated data collected during study.
c RR = relative risk v never-smokers, except where indicated.
d CI = confidence interval.
e NC = not calculable from available data

APPENDIX C: THE CONSTITUTED COUNCIL AND LEGISLATIVE FRAMEWORK OF THE REVIEW

The Specialist Medical Review Council

1. The composition of each Review Council changes from review to review depending on the issues relevant to the particular Statement/s of Principles under review. When a review is undertaken three to five Councillors selected by the Convener constitute the Council.

2. The Minister must appoint one of the Councillors to be the Convener. If the Council does not include the Convener, the Convener must appoint one of the Councillors selected for the review to preside at all meetings as Presiding Councillor.

3. Professor Charles Guest, the Convener of the SMRC presided for this review. Professor Guest is Chief Health Officer of Victoria, with academic affiliations at the University of Melbourne, Monash University and the Australian National University.

4. The other members of the Council were:
   - Professor Bruce Armstrong who is a leading cancer researcher. He is an Emeritus Professor in the School of Public Health at the University of Sydney and an Adjunct Professor in the School of Population Health at the University of WA. Among others, he has previously been Director of Research at the Sydney Cancer Centre, Head of the School of Public Health at the University of Sydney, Director of Research and Registers at Cancer Council NSW, Deputy Director of the International Agency for Research on Cancer and Professor of Epidemiology and Cancer Research at the University of WA.

   - Associate Professor Michael Izard who is Clinical Associate Professor with Sydney Medical School and Clinical Senior Lecturer at the Australian School of Advanced Medicine and Macquarie University.

The Legislation

5. The legislative scheme for the making of Statements of Principles is set out in Parts XIA and XIB of the VEA. Statements of Principles operate as templates. They are determined by the RMA, and set out those criteria (conditions or exposures), known as factors, that must as a minimum exist before it can be said that an injury, disease or death can be connected with service, on either or both of the two statutory tests, the reasonable hypothesis test and the balance of probabilities test. Statements of Principles are ultimately applied by decision-makers in determining individual claims for benefits under the VEA and the Military Rehabilitation and Compensation Act 2004 (the MRCA).

APPENDIX D

TABLE 1 - RELEVANT SMSE AND NEW INFORMATION

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See also the reference list at Appendix A

APPENDIX D

Table 2 – Material available to the RMA

Australian Government
Repatriation Medical Authority

MALIGNANT NEOPLASM OF THE PROSTATE

RMA ID Number	Reference List for # 042 as at 9 April 2014
113	Lanes SF, Cohen A, Rothman KJ, Dreyer NA, et al (1990). Mortality of cellulose fiber production workers. Scand J Work Environ Health, 16(4): 247-51.
769	Smith PG, Doll R (1982). Mortality Among Patients with Ankylosing Spondylitis after a Single Treatment Course with X-Rays. BMJ, 284(6314): 449-60.
1991	Keller JE, Howe HL (1994). Case-control studies of cancer in Illinois farmers using data from the Illinois state cancer registry and the US census of agriculture. European J Cancer, 30A(4): 469-73.
2999	Hirayama T (1990). Life-Style and Mortality - a large scale census-based cohort study in Japan. J Wahrendorf (Ed). Contributions to Epidemiology and Biostatistics, 6: 1-138. Karger, Basel.
3011	Weir JM, Dunn JE Jr (1970). Smoking and mortality: A prospective study. Cancer, 25(1): 105-12.
3015	Siemiatycki J, Krewski D, Franco E, Kaiseman M (1995). Associations between cigarette smoking and each of 21 types of cancer: A multi-site case-control study. Int J Epidemiol, 24: 504-14.
3023	Garfinkel L (1980). Cancer mortality in nonsmokers: Prospective study by the American Cancer Society. JNCI, 65(5): 1169-73.
3025	Wigle DT, Mao Y, Grace M (1980). Relative importance of smoking as a risk factor for selected cancers. Can J Public Health, 71(4): 269-75.
3081	Blair A, Dosemeci M, Heineman EF (1993). Cancer and other causes of death among male and female farmers from twenty-three states. Am. Journal of Industrial Med, 23: 729-742.
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3174	Giovannucci E, Rimm EB, Colditz GA, Stampfer MJ, et al (1993). Article - A prospective study of dietary fat and risk of prostate cancer. J Nat Can Institute, 85(19): 1571-9.
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3236	MacLennan R, Smith P (1994). Veterans and agent orange: Health effects of herbicides used in Vietnam. Report prepared for Department of Veteran Affairs commenting on the NAS report.
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3238	Rogers J, McCredie M, Lalak A, Frydenberg M, et al (1995). Prostate cancer - Forum. Cancer Forum, 19(1): 5-35.
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Appendix A

Information received in relation to investigation 042-09 concerning malignant neoplasm of the prostate as at 9 April 2014

[nb this information supplements the list of information received as at 5 September 2005 (1387852R) and previously provided to the SMRC]

1. Submissions

1.1 RMA medical researcher briefing paper 'Malignant neoplasm of the prostate', Volume 1, August 2005 (13110699R);
1.2 RMA medical researcher briefing paper 'Malignant neoplasm of the prostate', Volume 2, August 2005 (13110700R);
1.3 RMA medical researcher briefing paper 'Malignant neoplasm of the prostate', Volume 3, August 2005 (13110701R);
1.4 XXXXXXXXXXXXXXXXXX (request for investigation) (1412356R);
1.5 XXXXXXXXXXXXXXXXXX (request for investigation) (1412352R);
1.6 XXXXXXXXXXXXXXXXXXXX (request for investigation) (1412353R);
1.7 XXXXXXXXXXXXXXXXXX (request for investigation) (1412354R);
1.8 XXXXXXXXXXXXXXX, email, 27 May 2013 (1310019R);
1.9 XXXXXXXXXXXXXXXXXXX (request for investigation) (1390829R);
1.10 XXXXXXXXXXXXXXXXXXX submission, 9 January 2014 (143515R);

2. Other information

2.1 SMRC Requests for Review Declaration No. 17, 16 August 2012 (1379598R);
2.2 SMRC Requests for Review Reasons for Decision, 16 August 2012 (1379599R).