

SUPPLEMENTARY MATERIAL

Occupational benzene exposure and colorectal cancer: a systematic review and meta-analysis

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Supplementary Table 1. Detailed search strategy used on the different databases.

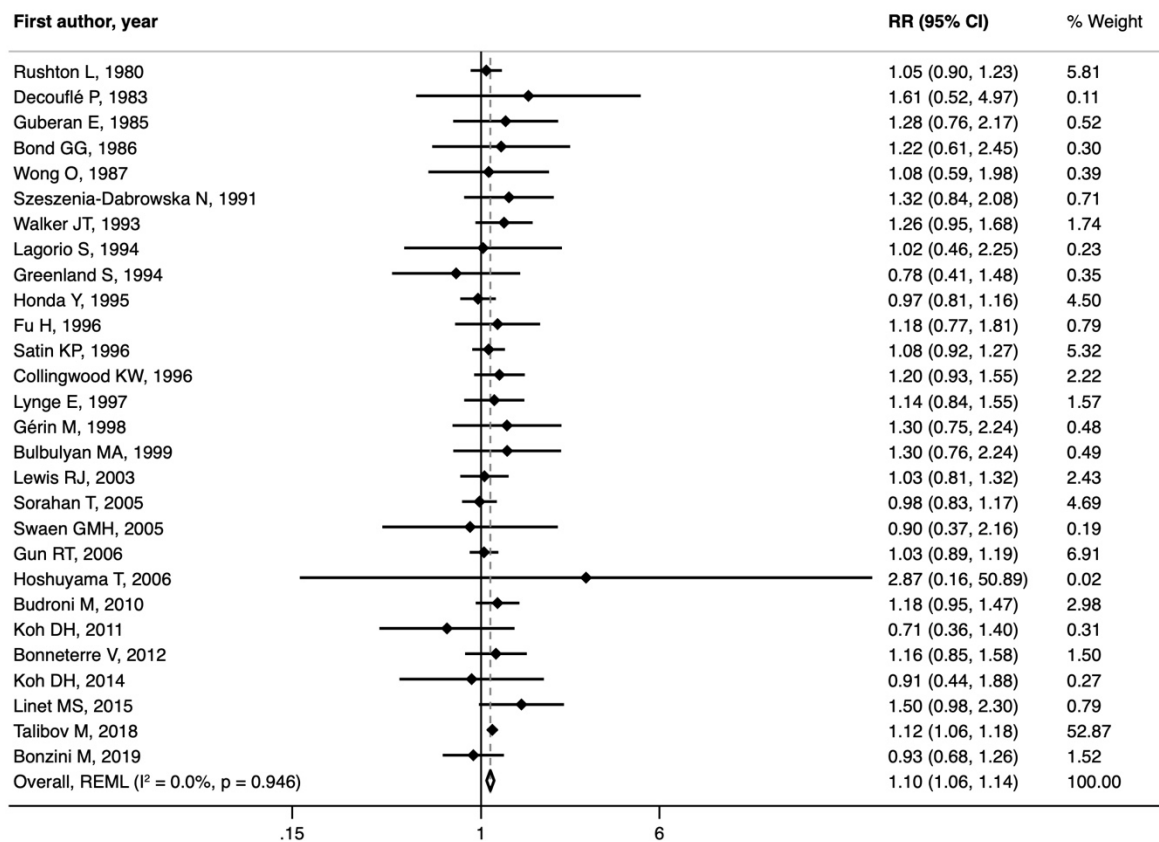
Database	Search string
Pubmed	<p><i>((("neoplasms"[Title/Abstract] OR "carcinoma"[Title/Abstract] OR "cancer"[Title/Abstract] OR "malignant"[Title/Abstract]) AND ("benzene"[Title/Abstract] OR "benzol"[Title/Abstract] OR ("cyclohexa-1"[All Fields] AND "3 5 triene"[Title/Abstract]) OR ("1"[All Fields] AND "3"[All Fields]) AND "5-cyclohexatriene"[Title/Abstract]) OR "cyclohexatriene"[Title/Abstract])) AND ((humans[Filter]) AND (english[Filter] OR french[Filter] OR german[Filter] OR italian[Filter] OR spanish[Filter])))</i></p>
Embase (Ovid)	<p><i>("benzene" or "benzol" or "cyclohexa-1,3,5-triene" or "1,3,5-cyclohexatriene" or "cyclohexatriene").tw. and ("neoplasms" or "carcinoma" or "cancer" or "malignant").tw. limit to ((behavioral & social sciences or clinical medicine or health professions or life sciences or medical humanities or nursing or patient education or public health or science) and original articles)</i></p>
Scopus	<p><i>((TITLE-ABS-KEY (benzene) OR TITLE-ABS-KEY (benzol) OR TITLE-ABS-KEY (cyclohexa-1,3,5-triene) OR TITLE-ABS-KEY (1,3,5-cyclohexatriene) OR TITLE-ABS-KEY (cyclohexatriene))) AND ((TITLE-ABS-KEY (neoplasms) OR TITLE-ABS-KEY (carcinoma) OR TITLE-ABS-KEY (cancer) OR TITLE-ABS-KEY (malignant))) AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re")) AND (LIMIT-TO (SUBJAREA , "MEDI") OR LIMIT-TO (SUBJAREA , "ENVI")) AND (LIMIT-TO (LANGUAGE , "English") OR LIMIT-TO (LANGUAGE , "German") OR LIMIT-TO (LANGUAGE , "Italian") OR LIMIT-TO (LANGUAGE , "French") OR LIMIT-TO (LANGUAGE , "Spanish")) AND (LIMIT-TO (SRCTYPE , "j")) AND (EXCLUDE (SUBJAREA , "BIOC") OR EXCLUDE (SUBJAREA , "EART") OR EXCLUDE (SUBJAREA , "ENGI") OR EXCLUDE (SUBJAREA , "CENG")) AND (EXCLUDE (SUBJAREA , "COMP") OR EXCLUDE (SUBJAREA , "MATH")) AND (EXCLUDE (LANGUAGE , "Portuguese") OR EXCLUDE (LANGUAGE , "Turkish")))</i></p>

Supplementary Table 2. Modified version of the Newcastle-Ottawa Scale (NOS) used for quality assessment of included studies, with scores for individual items reported in bold in parentheses.

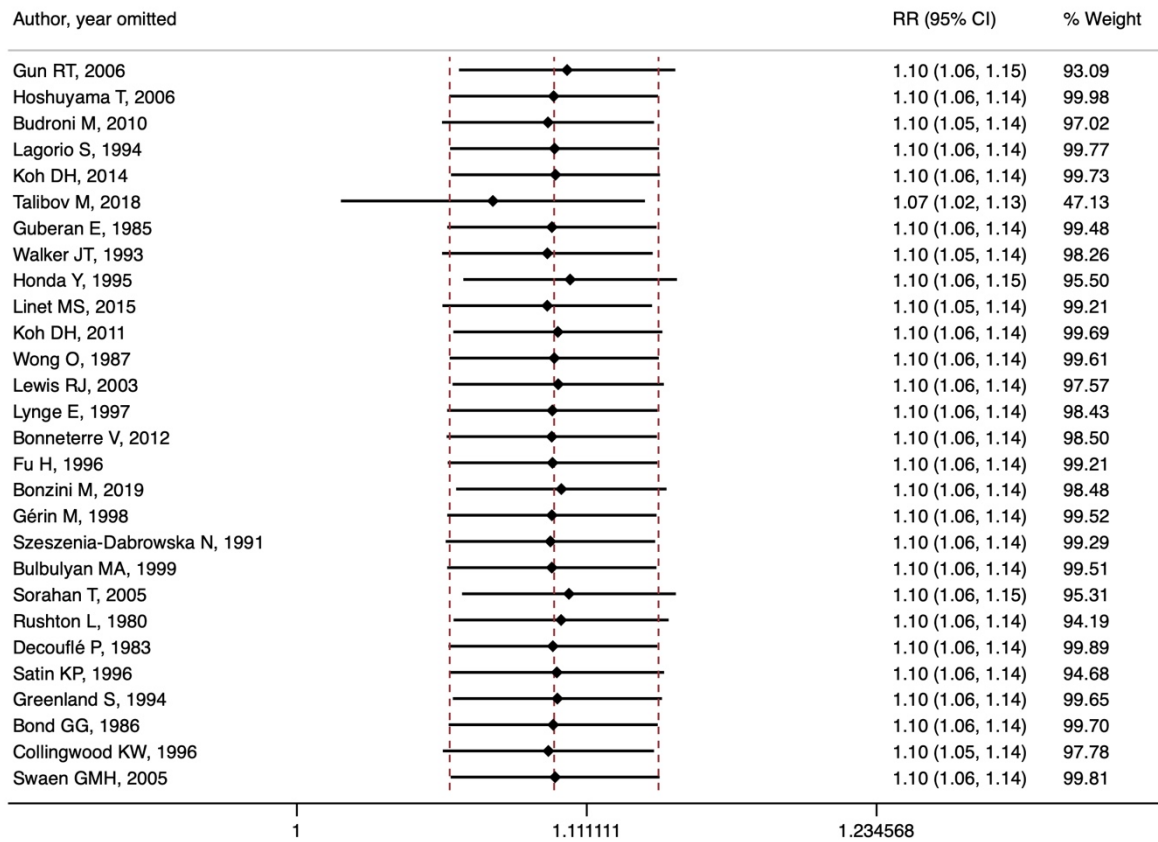
CASE CONTROL STUDIES (maximum score: 9)
<p>Selection</p> <p>1) Is the case definition adequate? a) yes, with independent validation (1) b) yes, eg record linkage (1) or based on self-reports (0.5) c) no description (0)</p> <p>2) Representativeness of the cases a) consecutive or obviously representative series of cases (1) b) potential for selection biases or not stated (0)</p> <p>3) Selection of Controls a) community controls (1) b) hospital controls (0.5) c) no description (0)</p> <p>4) Definition of Controls a) no history of disease (endpoint) (1) b) no description of source (0)</p>
<p>Comparability</p> <p>1) Comparability of cases and controls on the basis of the design or analysis a) study controls for age, gender, province (0) b) study controls for age, gender, province +smoking (1) c) study controls for age, gender, province +smoking + other additional factors (2)</p>
<p>Exposure</p> <p>1) Ascertainment of exposure a) secure record (eg surgical records) (1) b) structured interview where blind to case/control status (1) c) interview not blinded to case/control status (0.5) d) written self-report or medical record only (0.5) e) no description (0)</p> <p>2) Same method of ascertainment for cases and controls a) yes (1) b) no (0)</p> <p>3) Non-Response rate a) one or both groups, <10% (1) b) one or both groups, 10-40% (0.5) c) one or both groups, >40 (0) d) no statement (0)</p>
COHORT STUDIES (maximum score: 10)
<p>Selection</p> <p>1) Representativeness of the exposed cohort a) truly representative of the average exposed workers' population (2) b) somewhat representative of the average exposed workers' population (1) c) selected group of users eg nurses, volunteers (0.5) d) no description of the derivation of the cohort (0)</p> <p>2) Selection of the non-exposed cohort a) drawn from the same community as the exposed cohort (1) b) drawn from a different source (0.5) c) no description of the derivation of the non-exposed cohort (0)</p> <p>3) Ascertainment of exposure a) secure record (eg surgical records) (1) b) structured interview (1)</p>

<p>c) written self-report (0.5) d) no description (0)</p> <p>4) Demonstration that outcome of interest was not present at start of study a) yes (1) b) no (0)</p>
<p>Comparability</p> <p>1) Comparability of cohorts on the basis of the design or analysis a) study controls for age, gender, province (0) b) study controls for age, gender, province +smoking (1) c) study controls for age, gender, province +smoking + other additional factors (2)</p>
<p>Outcome</p> <p>1) Assessment of outcome a) independent blind assessment (1) b) record linkage (1) c) self-report (0.5) d) no description (0)</p> <p>2) Was follow-up long enough for outcomes to occur a) yes (average 15 years) (1) b) no (0)</p> <p>3) Adequacy of follow up of cohorts a) complete follow up - all subjects accounted for (> 90%) (1) b) subjects lost to follow up unlikely to introduce bias - small number lost – 60-90 % follow up, or description provided of those lost) (0.5) c) follow up rate < 60% and no description of those lost (0) d) no statements (0)</p>

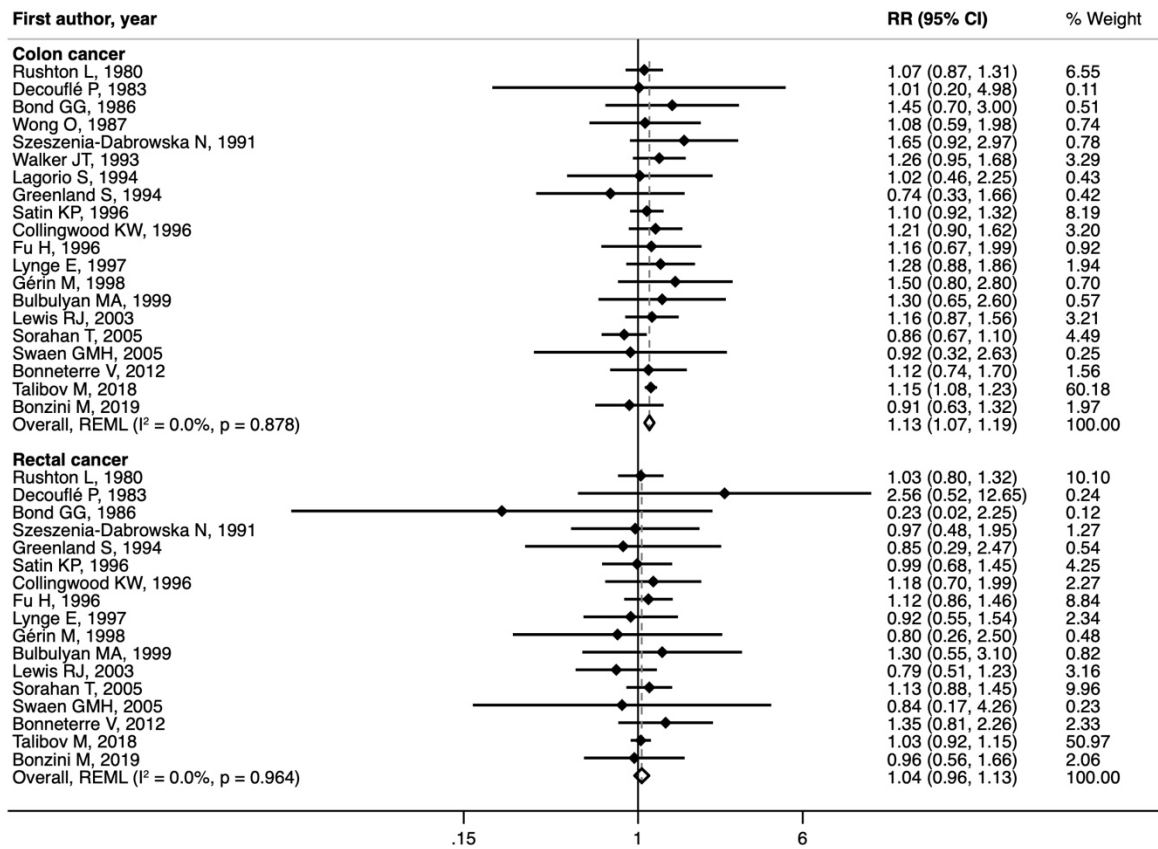
Supplementary Figure 1. Results of the meta-analysis on the association between occupational benzene exposure and colorectal cancer incidence and mortality combined, with restricted maximum likelihood method.



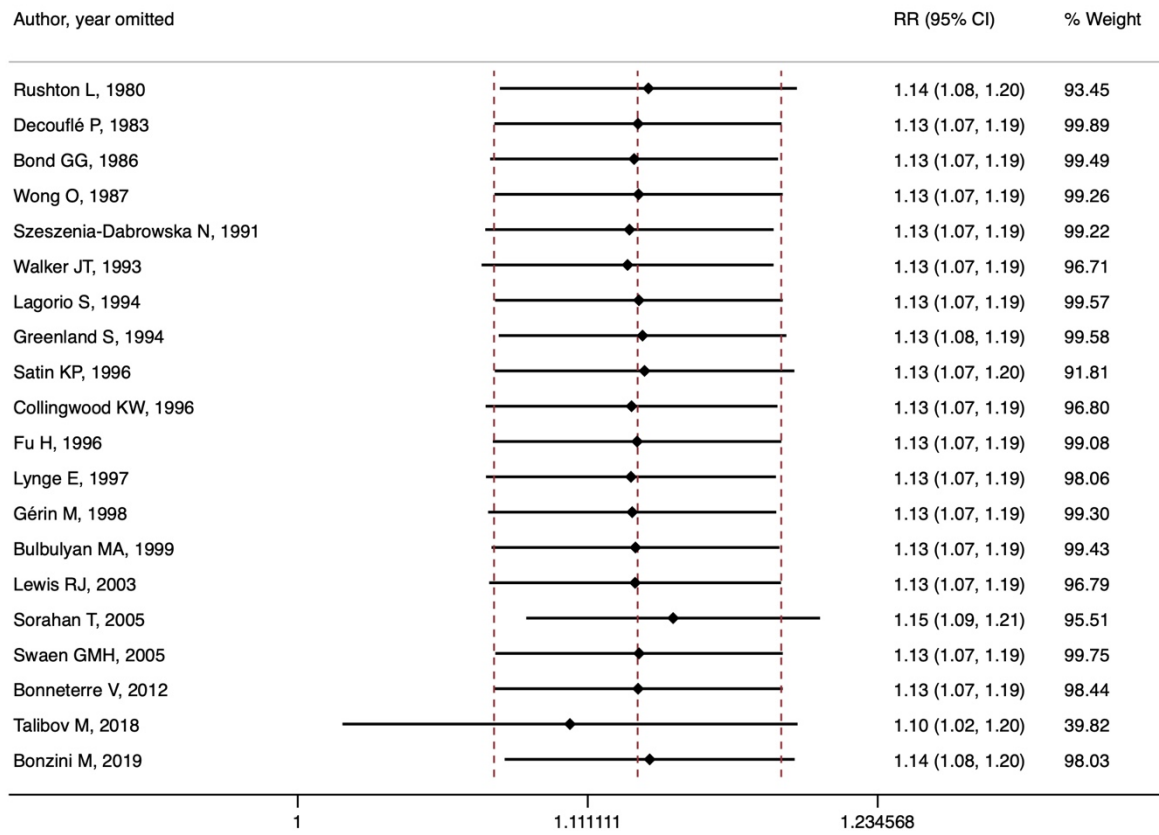
Supplementary Figure 2. Leave-one-out meta-analysis for the association between occupational benzene exposure and colorectal cancer incidence and mortality combined.



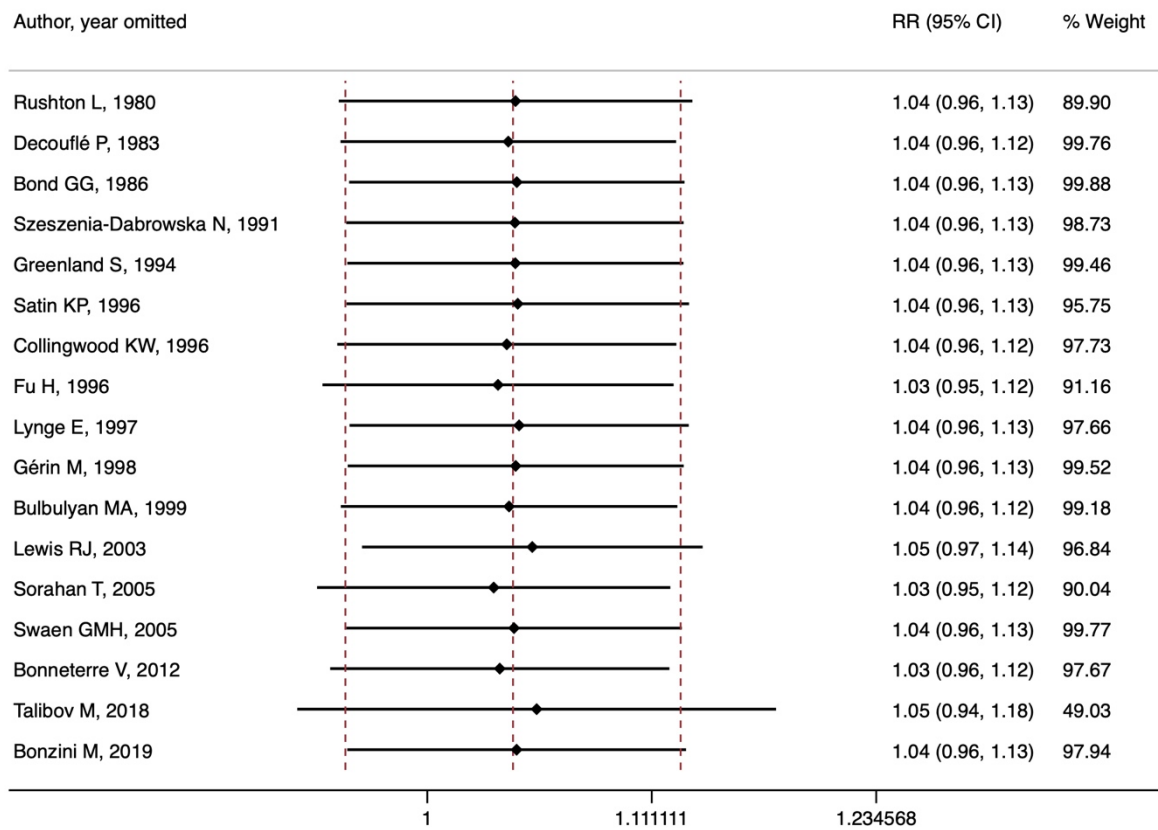
Supplementary Figure 3. Results of the meta-analysis on the association between occupational benzene exposure and colon and rectal cancer incidence and mortality combined, with restricted maximum likelihood method.



Supplementary Figure 4. Leave-one-out meta-analysis for the association between occupational benzene exposure and colon cancer incidence and mortality combined.



Supplementary Figure 5. Leave-one-out meta-analysis for the association between occupational benzene exposure and rectal cancer incidence and mortality combined.



Supplementary Figure 6. Contour-enhanced funnel plot to explore small-study effect for incidence (figure A, top) and mortality (figure B, bottom) of colorectal cancer.

