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Miscellaneous

The effects of waterpipe tobacco smoking on health outcomes: an updated systematic review and meta-analysis

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Abstract

Background and aims: A systematic review conducted in 2008 found significant associations between waterpipe tobacco smoking and lung cancer, respiratory disease, periodontal disease and low birthweight. Since then, a number of relevant studies have been published. The objective of this study was to update the systematic review on the effects of waterpipe tobacco smoking on health outcomes.

Methods: In May 2015 we electronically searched the following databases with no date restrictions: MEDLINE, EMBASE and the ISI Web of Science using a detailed search strategy with no language restrictions. We also screened the references' lists of the included studies. We included cohort, case-control and cross-sectional studies, and excluded case reports, conference abstracts, editorials and reviews. We excluded studies not conducted in humans, assessing physiological outcomes, not distinguishing waterpipe tobacco smoking from other forms of smoking or not reporting association measures. We assessed risk of bias for each included study and conducted meta-analyses for each of the outcomes of interest.

Results: We identified 50 eligible studies. We found that waterpipe tobacco smoking was significantly associated with: respiratory diseases [COPD; odds ratio (OR) = 3.18, 95% confidence interval CI = 1.25, 8.08; bronchitis OR = 2.37, 95% CI = 1.49, 3.77; passive waterpipe smoking and wheeze OR) = 1.97, 95% CI = 1.28, 3.04]; oral cancer OR = 4.17, 95% CI = 2.53, 6.89; lung cancer OR = 2.12, 95% CI = 1.32, 3.42; low birthweight (OR = 2.39, 95% CI = 1.32, 4.32); metabolic syndrome (OR 1.63–1.95, 95% CI = 1.25, 2.45); cardiovascular disease (OR = 1.67, 95% CI = 1.25, 2.24); and mental health (OR 1.30–2.4,

95% CI = 1.20, 2.80). Waterpipe tobacco smoking was not significantly associated with: oesophageal cancer (OR = 4.14, 95% CI = 0.93, 18.46); worse quality of life scores [standardized mean difference (SMD) = −0.16, 95% CI = −0.66, 0.34]; gastric carcinoma (OR = 2.16, 95% CI = 0.72, 6.47); bladder cancer (OR = 1.25, 95% CI = 0.99, 1.57); prostate cancer (OR = 7.00, 95% CI = 0.90, 56.90); hepatitis C infection (OR = 0.98, 95%0.80, 1.21); periodontal disease (OR = 3.00, 5.00); gastro-oesophageal reflux disease (OR = 1.25, 95% CI = 1.01, 1.56); nasopharyngeal carcinoma (OR = 0.49, 95% CI = 0.20, 1.23); bladder cancer (OR = 1.25, 95% CI = 0.99, 1.57); infertility (OR = 2.50, 95% CI = 1.00, 6.30); and mortality (OR = 1.15, 95% CI = 0.93, 1.43).

Conclusions: There is accumulating evidence about the association of waterpipe tobacco smoking with a growing number of health outcomes.

Key words: Waterpipe tobacco smoking, health effects, systematic review

Key Messages

- Waterpipe tobacco smoking is likely associated with oral cancer and lung cancer.
- It is also likely associated with respiratory diseases, low birthweight, metabolic syndrome, cardiovascular disease and mental health.
- Waterpipe tobacco smoking is likely not associated with oesophageal cancer, gastric carcinoma, bladder cancer or prostate cancer.
- It is also likely not associated with hepatitis C infection, periodontal disease, gastro-oesophageal reflux disease, infertility or mortality.

Background

The past decade has witnessed a steady increase in waterpipe tobacco smoking, especially among the younger age groups.[1,2] A systematic review found that school and university students have the highest prevalence of waterpipe tobacco smoking across countries.[3] In the Global Adult Tobacco Survey[4,5] conducted in 13 low- and middle-income countries, the prevalence of waterpipe use among men was highest in Vietnam (13%) and Egypt (6.2%). Among women, waterpipe use was highest in Russia (3.2%) and Ukraine (1.1%). Even though the Middle Eastern youth are affected the most by the waterpipe smoking epidemic, over the past two decades many studies have reported increase in waterpipe use among youth in North America and Europe.[6–9]

We systematically reviewed the literature in 2008 and found significant associations between waterpipe tobacco smoking and a number of health outcomes.[10] For example, waterpipe tobacco smoking was associated with increased odds of lung cancer [odds ratio (OR) = 2.12] and respiratory disease (OR = 2.30). We also found evidence suggesting clinically significant association with periodontal disease (OR = 3–5) and low birthweight (OR = 2.12).

The available evidence at that time did not allow ruling out or confirming an association between waterpipe tobacco smoking and bladder cancer, nasopharyngeal cancer, oesophageal cancer, oral dysplasia and infertility. Since then, newly published studies have addressed some of these outcomes (e.g. oesophageal carcinoma)[11–12] as well as additional outcomes [e.g. quality of life, cardiovascular diseases, gastro-oesophageal reflux disease (GERD)].[13–17] Therefore, the objective of this study was to update our systematic review of the medical literature on the effects of waterpipe tobacco smoking on health outcomes.

Methods

Eligibility criteria

We included observational studies (i.e. cohort studies, case-control studies and cross-sectional studies). The exposure of interest was waterpipe tobacco smoking and the outcomes of interest were any health outcomes. We excluded: case reports; case series; outbreak investigations; and abstracts. We also excluded studies: assessing waterpipe use for non-tobacco smoking purposes (e.g. marijuana smoking and other recreational drug use); not distinguishing waterpipe tobacco smoking from other forms of smoking; assessing physiological [e.g. forced expiratory volume in 1 s (FEV1)] or other surrogate outcomes (e.g., artery occlusion); and not reporting any measure of association.

Search strategy

In May 2015, we updated the literature search originally conducted in June 2008. We used the OVID interface to electronically search MEDLINE (1950 onwards) and EMBASE (1980 onwards). We also searched the ISI Web of Science. Appendix 1 & Appendix 2 (available as Supplementary data at *IJE* online) presents our detailed search strategy. We designed the search strategy based on extensive internet search for waterpipe synonyms, and the search strategy used by Akl *et al.*[10] The strategy consisted of the synonyms for waterpipe (e.g. 13 synonyms in the Medline strategy) but did not include any study design filter and was not restricted to any language. Two medical librarians reviewed and provided input on the search strategy. Additional search strategies included: (i) a review of the reference lists of included studies; (ii) the use of the 'Related citations' feature in PubMed; and (iii) an ongoing surveillance of the literature in place while updating the manuscript.

Selection process

Teams of two reviewers independently screened the title and abstract of identified citations for potential eligibility. We acquired the full texts of citations judged as potentially eligible by at least one of two reviewers. Next, two reviewers used a standardized and pilot-tested form to independently screen each full text for eligibility. Disagreements were resolved by discussion or by consulting a third reviewer.

Data abstraction

Teams of two reviewers used a standardized and pilot-tested form to independently abstract data. Disagreements were resolved by discussion or by consulting a third reviewer. Data abstracted from individual studies included information about study design, population, exposure, outcomes, methodological features, results and funding.

Risk of bias assessment

We have assessed the risk of bias of all the included studies based on the following four commonly used criteria: selection bias; information bias; confounding; and completeness of data. The risk of bias was rated as 'high' in studies that failed three or more of these criteria, 'moderate' in studies that failed one or two criteria and 'low' in studies that failed none of them. To assess selection bias, we reviewed sampling of participants, their recruitment and their representativeness. We have assessed information bias for measurement of exposure and outcome with regard to using validated tools with adequate evidence of validation provided. Confounding assessment was based on whether authors reported controlling for relevant confounders with adequate details (e.g. in the design phase through matching and/or in the analysis through adjustment). Completeness of data was based on whether authors provided information about missing data and participation rate (Appendix 3 & Appendix 4, available as Supplementary data at *IJE* online).

Data analysis

Agreement between the reviewers was calculated using Cohen's kappa statistic. We conducted meta-analyses for the outcomes for which at least two studies reported effect estimates of their association with waterpipe tobacco smoking. When a study reported more than one relevant effect estimate, we selected the one that adjusted for the maximum number of confounders, particularly for other forms of tobacco smoking.

For continuous outcomes using different scales, we calculated the standardized mean difference (SMD) for each study and then pooled across eligible studies using the inverse variance method. For dichotomous outcomes, we used the reported ORs to calculate the Natural logarithm of odds ratios (ln(ORs)) and standard errors. We then pooled the ln(ORs) across eligible studies using the inverse variance method. We used fixed-effects models when pooling only two studies, and used the random-effects model in all other cases. We measured heterogeneity across studies using the I^2 statistic. We considered heterogeneity to be high when I^2 was greater than 50%. We used Review Manager software Version 5.0.2 for all analyses.

Results

Search results

Appendix 1 shows the study flow. Out of 360 full texts assessed, we excluded 301, with reasons for exclusion provided in Appendix 1. Of the 50 included studies, 24 were identified by the original search and 26 were identified by the update. Agreement between reviewers for study eligibility was excellent (kappa = 0.94 and 0.80 for the two teams).

The included studies assessed the associations between waterpipe tobacco smoking and the following outcomes: respiratory diseases ($n = 9$); quality of life ($n = 2$); oesophageal cancer ($n = 3$); gastric carcinoma ($n = 3$); oral cancer ($n = 3$); bladder cancer ($n = 2$); nasopharyngeal cancer ($n = 1$); lung cancer ($n = 6$); prostate cancer ($n = 1$); colorectal cancer ($n = 1$); pregnancy outcomes ($n = 3$); periodontal disease ($n = 6$); hepatitis C infection ($n = 3$);

infertility ($n = 1$); metabolic syndrome ($n = 1$); gastro-oesophageal reflux disease (GERD) ($n = 1$); cardiovascular diseases ($n = 2$); mental health ($n = 1$); and mortality outcomes ($n = 1$)

Methodological features

Risk of bias assessment

Out of the 50 included studies, only 8 studies were assessed to have selection bias and/or report insufficient information about the sampling techniques, and 16 studies reported the participation rate. There was no agreement across studies on a standardized way to measure exposure to waterpipe tobacco smoking, and this was the main reason for heterogeneity in the meta-analysis. There was agreement across studies on the need to adjust for potential confounders such as age, gender, education and other forms of tobacco use.

Evidence synthesis

Respiratory diseases

Nine studies evaluated the association between waterpipe tobacco smoking and respiratory disease. Five studies assessed the association between waterpipe tobacco smoking and chronic obstructive pulmonary disease (COPD) (four cross-sectional studies and one case-control) (Table 1; Appendix 3: Table 1 & Figure 1).[5,19–23] The pooled odds ratios for the association of waterpipe tobacco smoking and COPD was OR = 3.18, (95% CI = 1.25, 8.08; $I^2 = 95\%$). Two studies assessed the association between waterpipe tobacco smoking and bronchitis (two cross-sectional studies) (Table 1; Appendix 3: Table 1 & Figure 2).[23,25] The pooled odds ratios for the association of waterpipe tobacco smoking and bronchitis was OR = 2.37, (95% CI = 1.49, 3.77).

Two cross sectional studies[18,24] evaluated the association between passive waterpipe tobacco smoking and respiratory illness (defined as nasal congestion and wheezing) (Table 1; Appendix 3: Table 1 & Figure 3). The pooled odds ratio for the association of passive waterpipe tobacco smoking and respiratory illness was 1.97 (95% CI = 1.28, 3.04).

Quality of life

Two cross-sectional studies evaluated the association between waterpipe tobacco smoking and quality of life[13,26] (Table 1; Appendix 3: Table 2 & Figure 4). One found that waterpipe smokers have a poorer respiratory quality of life, using the Clinical COPD Questionnaire (CCQ) and the MRC dyspnoea scale.[26] Another found that waterpipe smokers have a higher risk for poorer health-related quality of life with regard to physical function, bodily pain, general health, mental health, vitality and social function on the Short Form Health Survey (SF-36).[13] They also found a higher risk on the Mental Component Score (MCS) and Physical Component Score (PCS). The pooled standardized mean difference (SMD) was -0.16 (95% CI = −0.66, 0.34; $I^2 = 93\%$).

Cancer outcomes

Oesophageal cancer

Three case-control studies evaluated the association between waterpipe tobacco smoking and oesophageal cancer: one from Iran and two from Kashmir (Table 1; Appendix 3: Table 3 & Figure 5).[11,12,27] The pooled odds ratios for the association of waterpipe tobacco smoking with oesophageal cancer was OR = 4.14 (95% CI = 0.93, 18.46). The level of statistical heterogeneity was high ($I^2 = 96\%$).

Gastric carcinoma

Two case-control studies and one prospective cohort study evaluated the association between waterpipe tobacco smoking and gastric carcinoma (Table 1; Appendix 3: Table 3 & Figure 6).[29–31] Both studies were from Iran. The pooled odds ratio for the association of waterpipe tobacco smoking with gastric carcinoma was OR = 2.16 (95% CI = 0.72, 6.47). The level of statistical heterogeneity was high ($I^2 = 61\%$). One case-control study reported only means, so was not included in the meta-analysis.[31] It reported higher frequency of waterpipe smoking among those with gastric carcinoma (mean = 3 ± 1.6) compared with healthy controls (mean = 2 ± 1.1; P-value = 0.4).

Oral cancer

Three cross-sectional studies evaluated the association between waterpipe tobacco smoking and oral cancer: one from Yemen and one from India.[41–43] The pooled odds ratio for the association of waterpipe tobacco smoking with oral cancer was OR = 4.17 (95% CI = 2.53, 6.89) (Table 1; Appendix 3: Table 3 & Figure 7).

Bladder cancer

Two case-control studies evaluated the association between waterpipe tobacco smoking and bladder cancer, both of which were conducted in Egypt[32,33] (Table 1; Appendix 3: Table 3 & Figure 8). The pooled odds ratios for the association of waterpipe tobacco smoking with bladder cancer was OR = 1.25 (95% CI = 0.99, 1.57).

Table 1. Summary of studies published on health outcomes of waterpipe tobacco smoking between 1990 and 2015[¶]

ID	Study	Design	Participants(*N*)	Outcome	Reported OR (95% CI)
Respiratory diseases					
1	Tamim 2003[18]	Cross-sectional	143	Wheezes/passive	2.30 (1.10, 5.10)
2	Mohammed 2013[5]	Cross-sectional	788	COPD	2.60 (0.60, 11.50)
3	Mohammed 2008[19]	Cross-sectional	77	COPD	N/A
4	Tageldine 2012[20]	Cross-sectional	61551	COPD	1.42 (1.12, 1.80)
5	Salameh 2012[21]	Case-control	211 cases 527 controls	Bronchitis	6.40 (2.55, 16.11)
6	Waked 2011[22]	Cross-sectional	425	COPD	2.53 (1.83, 3.50)
7	Waked 2009[23]	Cross-sectional	1268315	Bronchitis	1.95 (0.96, 8.08)
8	Mohammed 2014[24]	Cross-sectional	2734	Wheezes/passive	2.05 (1.01, 4.17)
9	She 2014[25]	Cross-sectional	1238	COPD	10.61 (6.89, 16.34)
Quality of life					
10	Tavafian 2009[13]	Cross-sectional	1675	Quality of life	Physical 2.15 (1.56, 2.96) Mental 1.88 (1.36, 2.60)
11	Joseph 2012[26]	Cross-sectional	2201	Quality of life	N/A
Cancers					
12	Malik 2010[27]	Case-control	135 cases 195 controls	Ooesophageal	21.44 (11.63, 39.54)
13	Dar 2012[11]	Case-control	702 cases 1663 controls	Ooesophageal	1.85 (1.41, 2.44)
14	Nasroallahzadeh 2008[12]	Case-control	300 cases 571 controls	Ooesophageal	1.69 (0.76, 3.77)
15	Hosseini 2009[28]	Case-control	300 cases 571 controls	Prostate	7.00 (0.90, 56.9)
16	Sadjadi 2014[29]	Cohort	928	Gastric	3.44 (1.66, 7.11)
17	Shakeri 2013[30]	Case-control	309 cases 613 controls	Gastric	1.10 (0.30, 3.30)
18	Karajibani 2014[31]	Case-control	50 cases 46 controls	Gastric	N/A
19	Zheng 2012[32]	Case-control	1886 cases 2716 controls	Bladder	Urothelial carcinoma: 1.30 (1.00, 1.80) SCC: 1.20 (0.80, 1.70)
20	Bedwani 1997[33]	Case-control	151 cases 157 controls	Bladder	0.80 (0.20, 4.00)
21	Qiao 1989[34]	Case-control	107 cases 107 controls	Lung	1.90 (0.40, 9.40)
22	Lubin 1990[35]	Case-control	74 cases 74 controls	Lung	3.60
23	Lubin 1992[36]	Case-control	427 cases 1011 controls	Lung	1.80 (0.80, 4.20)
24	Hsairi 1993[37]	Case-control	110 cases 110 controls	Lung	3.00 (1.20, 7.6)
25	Gupta 2001[38]	Case-control	265 cases 525 controls	Lung	1.94 (0.85, 4.44)
26	Hazelton 2001[39]	Cohort	1289 WP only 2306 WP/cigarettes 8416 non-smokers	Lung	RR 4.39 (3.82, 5.04)

(continued)

Table 1. Continued

ID	Study	Design	Participants(*N*)	Outcome	Reported OR (95% CI)
Respiratory diseases					
27	Feng 2009[40]	Case-control	636 cases 615 controls	Nasopharyngeal	0.49 (0.20, 1.23)
28	Ali 2007[41]	Cross-sectional	33	Oral	8.33 (0.78, 9.47)
29	Dangi 2012[42]	Cross-sectional	761	Oral	4.42 (2.32, 8.41)
30	Schmidt-Westhausen 2014[43]	Cross-sectional	162	Oral	4.35 (1.73, 10.93)
31	Nikbakht 2015[44]	Cross-sectional	120	Colorectal	N/A
Pregnancy outcomes					
32	Nuwayhid 1998[45]	Retrospective cohort	895	Low birthweight	2.17 (0.74, 6.33)
33	Aghamolaei 2007[46]	Case-control	60 cases 60 controls	IUGR	3.50 (1.1, 12.6)
34	Tamim 2008[47]	Retrospective cohort	1391	Low birth weight	1.20 (0.60, 2.20)
35	Eftekhar 2007[48]	Case-control	60 cases 60 controls	IUGR	3.50 (1.10, 12.60)
Periodontal disease					
36	Natto 2005[49, 50,†]	Cross-sectional	355	Periodontal disease	3.50 (1.6, 7.6)
37	Natto 2004[51]	Cross-sectional	244	Periodontal disease	N/A
38	Baljoon 2005[52]	Cross-sectional	262	Periodontal disease	2.90 (1.20, 7.00)
39	Al-Belasy 2004[53]	Cohort	100	Dry socket	RR 3.00 (*P*-value 0.001)
Infectious diseases					
40	Habib 2001[54]	Cross-sectional	1827	HCV	1.10 (0.7, 1.5)
41	Medhat 2002[55]	Cross-sectional	2717	HCV	0.90 (0.4, 2.0)
42	El-Sadawy 2004[56]	Cross-sectional	782	HCV	1.02 (0.64, 1.62)
Infertility					
43	Inhorn 1994[57]	Case-control	45	Infertility	2.50 (1.0, 6.3)
Digestive/GIT diseases					
44	Shafique 2012[58]	Cross-sectional	30–75	Metabolic syndrome	Hypertriglycaemia 1.63(1.25, 2.10) Hypergylcaemia 1.82 (1.37, 2.41) Hypertension 1.95 (1.52, 2.45)
45	Islami 2014[17,†]	Cross-sectional	75	GERD	1.34 (1.02, 1.75)
Cardiovascular disease					
46	Al-Suwaidi 2012[14]	Cohort	7939	ACS	N/A
47	Islami 2012[16,†]	Cross-sectional	75	CVD	3.75 (1.52, 9.22)
Mental health					
48	Primack 2013[59]	Cross-sectional	100891	Mental health	1.40 (1.30, 1.50)
Mortality					
49	Wu 2013[15]	Cohort	11746	Mortality	HR 1.15 (0.93, 1.43)

[¶]Excluding studies that did not fulfill the eligibility criteria.

WP, waterpipe; HCV, hepatitis C virus; RR, risk ratio; SCC, squamous cell carcinoma; N/A, not available; IUGR, intrauterine growh retardation; GIT, gastro-intestinal tract; ACS, acute coronary syndrome; CVD, cardiovascular disease.

[†]Indicates two studies from the same population, thus grand total = 50 studies

Nasopharyngeal cancer

One case-control study evaluated the association between waterpipe tobacco smoking and nasopharyngeal cancer in Tunisia, Morocco and Ira[40] (Table 1; Appendix 3, Table 3). The OR for the association of waterpipe tobacco smoking with nasopharyngeal cancer was 0.49 (95% CI = 0.20, 1.23).

Lung cancer

Five of six eligible studies were case-control studies measuring lung cancer diagnosis,[34,36,38,60,61] and one was a retrospective cohort study measuring lung cancer mortality[39] (Table 1; Appendix 3: Table 3 & Figure 9). One was conducted in Northern India, one was conducted in Tunisia and four reported data from the same population in China. Although nowadays waterpipe tobacco is processed, flavoured and indirectly heated by charcoal, in most of the included studies (those conducted in China and India) tobacco was typically unprocessed and burned directly by charcoal.

The pooled OR for the association of waterpipe tobacco smoking with lung cancer diagnosis was 2.12 (95% CI = 1.32, 3.42; $I^2 = 0\%$) (Table 1; Appendix 3: Table 3 & Figure 9). The calculated crude risk ratio (RR) for the association with lung cancer mortality was 4.39 (3.82–5.04). A sensitivity analysis restricted to one study with no major methodological limitations produced an OR of 3.00 (95% CI = 1.20, 7.60).[60]

Prostate cancer

One case control study assessed the association between waterpipe tobacco smoking and prostate cancer.[28] A sample of 137 male participants from Northern Iran, who were histologically confirmed with prostate cancer, were included in the study. The OR for the association between waterpipe tobacco smoking and prostate cancer was 7.00 (95 % CI = 0.90, 56.90) (Table 1; Appendix 3, Table 3).

Colorectal cancer

One cross-sectional study assessed the association between waterpipe smoking and colorectal cancer,[44] A sample of 120 participants who were recorded on the cancer registry centre of Babol were contacted to fill in a survey about demographics and risk factors including waterpipe use. Among waterpipe smokers, 22.70% of men and 15.80% of women were diagnosed with colorectal-cancer (Table 1; Appendix 3, Table 3).

Pregnancy outcomes

Two retrospective cohort studies and two case-control studies evaluated the association between waterpipe tobacco smoking and pregnancy outcomes[45–48] (Table 1; Appendix 3: Table 4 & Figure 10). One study also reported Apgar score, pulmonary problems, malformations and perinatal complications.[46] The pooled OR for the association of waterpipe tobacco smoking with low birthweight was 2.39 (95% CI = 1.32, 4.32; $I^2 = 0\%$). The reported OR for the association of waterpipe tobacco smoking with newborn pulmonary problems was OR = 3.65 (95% CI = 1.52, 8.75). The associations were not significant for Apgar scores at 1 min and 5 min, malformations or perinatal complications.

Periodontal disease

Of the five studies that evaluated the association between waterpipe tobacco smoking and periodontal disease,[49–53] four were cross-sectional studies conducted in the same (or in a subgroup of the same) group of participants[49–52] (Table 1; Appendix 3, Table 5). These four studies assessed periodontal disease using different measures (periodontal bone height loss, plaque index and gingivitis, deepening of the sulci or pockets, vertical periodontal bone loss). We did not pool data from the four related studies as they were derived from the same participants. Their results consistently showed a significant association of waterpipe tobacco smoking with periodontal disease (OR ranging 3.00–5.00).

The fifth study was a cohort study with 7 days' follow-up after surgical removal of mandibular third molars, and evaluated the outcome of dry socket.[53] The reported RR for the association of waterpipe tobacco smoking with dry socket was 3.70 ($P = 0.001$). Dry socket, or alveolar osteitis, is the most common complication following tooth extractions. It is caused by the dislodgement of the blood clot at the site of the tooth extraction, exposing underlying bone and nerves and causing increasing pain.

Infectious disease

Three cross-sectional studies evaluated the association between waterpipe tobacco smoking and hepatitis C.[54–56] The three studies were conducted in Egypt and included male participants exposed to group waterpipe tobacco smoking (Table 1; Appendix 3: Table 6 & Figure 11). The pooled OR for the association of group waterpipe smoking with hepatitis C was 0.98 (95% CI = 0.80, 1.21).There were no eligible studies assessing the association between waterpipe tobacco smoking and the transmission of tuberculosis. The two reports that we found of outbreak investigations suggested an association between tuberculosis and sharing tobacco waterpipes and marijuana waterpipes.[62,63]

Infertility

One case-control study evaluated the association between waterpipe smoking and male factor infertility (based on

semen analysis)[57] (Table 1; Appendix 3, Table 7). The reported OR for the association of waterpipe tobacco smoking with male factor infertility was OR = 2.50 (95% CI = 1.00, 6.30).

Metabolic syndrome

One cross-sectional study evaluated the association between waterpipe tobacco smoking and metabolic syndrome.[58] Waterpipe smokers were significantly more likely to have hypertriglyceridaemia (OR 1.63, 95% CI = 1.25, 2.10), hyperglycaemia (OR 1.82, 95% CI = 1.37, 2.41), hypertension (OR 1.95, 95% CI = 1.51, 2.51) and abdominal obesity (OR 1.93, 95% CI = 1.52, 2.45 (Table 1; Appendix 3, Table 8).

Gastro-oesophageal reflux disease

One cross-sectional study evaluated the association between waterpipe tobacco smoking and gastro-oesophageal reflux disease (GERD).[17] The reported odds ratio for the association of waterpipe tobacco smoking with having any gastro-oesophageal reflux disease symptom was 1.25 (95% CI = 1.01, 1.56) (Table 1; Appendix 3, Table 8).

Cardiovascular disease

Two cross-sectional studies evaluated the association between waterpipe tobacco smoking and cardiovascular disease.[14,16] In one study, the reported odds ratio for the association between waterpipe tobacco smoking and heart disease was 1.67 (95% CI = 1.25, 2.24). The other study was based on data obtained from a population based cohort study conducted in the Golestan province in Iran, and included individuals between 40 and 75 years old. The reported OR for the association between waterpipe tobacco smoking and heart disease was 3.75 (95% CI = 1.55, 9.22) (Table 1; Appendix 3, Table 8).

Mental health

One cross-sectional study, conducted among institutions participating in the national college health assessment of the American College Health Association, evaluated the association between waterpipe tobacco smoking and mental health.[59] All mental health diagnoses were significantly associated with increased rates of waterpipe tobacco smoking, with ORs ranging from 1.30 to 2.40 (Table 1; Appendix 3, Table 8).

Mortality outcomes

One cohort study associated waterpipe tobacco smoking with mortality outcomes.[15] The first study, by Fen Wu *et al.*, found that waterpipe tobacco smoking was significantly associated with increased risk of mortality from all causes (HR = 1.15; 95% CI 0.93, 1.43), cancer (HR = 1.30; 95% CI = 0.78, 2.18) and ischaemic heart disease (HR = 1.20, 95% CI = 0.87, 1.67) (Table 1; Appendix 3, Table 8).

Discussion

We systematically reviewed the medical literature for the effects of waterpipe tobacco smoking on health outcomes. We found that waterpipe tobacco smoking was associated with respiratory diseases (COPD, bronchitis and wheeze due to exposure to passive waterpipe smoking), oral cancer, lung cancer, low birthweight, metabolic syndrome, cardiovascular disease and mental health. The existing evidence suggested no association with oesophageal cancer, gastric carcinoma, bladder cancer, prostate cancer, hepatitis C infection, periodontal disease, gastro-oesophageal reflux disease, nasopharyngeal carcinoma, bladder cancer, infertility or mortality.

Cigarette smoking is known to be a major cause of respiratory diseases through promoting lung function loss and decreasing lung function rates.[64–66] In a similar manner, waterpipe smoking was associated with significant reduction in forced expiratory volume in 1 s (FEV-1) and forced vital capacity (FVC), by 4.04% and 1.38% respectively, compared with non waterpipe smokers.[67] This suggests an obstructive mechanism, as was similarly reported by Chaouchi *et al.* who have shown that chronic use of a waterpipe with one or more smoking sessions per day can lead to COPD.[68] This result is also in agreement with the reported estimates that tobacco smoking increases the risks of death from lung cancer or COPD by 20-fold.[6] Another mechanism for the effect of waterpipe smoking on respiratory outcomes was found to be through the damage that it causes to the lung parenchyma and the associated inflammation of the airways.[69,70]

Tobacco was found to be a source of 69 carcinogens and has been widely associated with increasing the risk of developing cancers and malignancies.[6,71] Thus, strong associations have been established between cigarette smoking and different cancers, particularly in the lungs and the digestive system.[65,66,72–75] These results can also be extended to include waterpipe smoking, as has been reported by a study of 56 chronic Pakistani waterpipe smokers that found markedly increased levels of carcinoembryonic antigen (CEA) as compared with non-smokers ($P < 0.0001$).[76] CEA is known to be elevated in lung, pancreatic, uterus and breast cancers as well as in cases of chronic inflammation. Other studies also reported increased risk of carcinogenesis among waterpipe smokers due to genotoxic and clastogenic components in the waterpipe smoke, such as

tar and polycyclic aromatic hydrocarbons.[69,77] This likely explains the association between waterpipe tobacco smoking and cancers outside the lung such as prostate cancer, an association previously shown between cigarette smoking and prostate cancer.[78,79] There is also evidence that smoking induces hormonal changes in men that could affect the risk of prostate cancer.[80]

The effects of tobacco on atherosclerosis have been attributed to various mechanisms that promote atherosclerosis and endothelial dysfunction.[6,81] Cigarette smoking has been associated with cardiovascular disease through promoting atherosclerosis and being highly dose related.[81–83] Similarly, a comparative double-blinded study done on 37 waterpipe smokers who reported smoking a waterpipe 2–5 times/month showed increased mean (± SEM) plasma nicotine concentration (3.6 ± 0.7 ng/ml) and heart rate (8.6 ± 1.4 bpm) as compared with placebo (0.1 ± 0.0 ng/ml; 1.3 ± 0.9 bpm), indicating that the effects of waterpipe smoking on cardiovascular outcomes are mediated by its nicotine content.[84] Some studies also attributed the deleterious effects of waterpipe smoking on cardiovascular disease to in vivo oxidation injury and systemic inflammation that increases the likelihood of atherosclerosis and arrhythmia.[85–87]

Strengths and limitations

To our knowledge, no systematic reviews have been conducted on the association between waterpipe smoking and health outcomes since our earlier review in 2010. Further strengths of the review include adhering to the Cochrane Collaboration methodology, which is considered the gold standard for systematically reviewing literature, using a sensitive search strategy and conducting screening and data extraction independently and in duplicate.

The confidence in the effects estimates in this systematic review is affected by a number of limitations. Indeed, five out of 11 meta-analyses suffered from a high degree of heterogeneity, namely oesophageal carcinoma, gastric carcinoma, low birthweight, COPD and quality of life. Also, Appendix 3 shows the methodological limitations of the included studies. Most of the studies used non-validated tools for measurement of waterpipe tobacco exposure, which is a major limitation given that the practice of waterpipe tobacco smoking can vary widely according to the quantity of tobacco used, the frequency and the length of the session.

We were not able to conduct meta-analyses for all outcomes. One reason was the high level of heterogeneity, as was the case for the quality of life outcome. Another reason was that we could not pool several outcomes derived from the same study, as was the case for the metabolic syndrome, nasopharyngeal carcinoma, gastro oesophageal reflux disease, mental health and mortality outcomes.

Additional research implications of our findings include the need for more research on this topic using validated tools for measurement of both the exposure and the outcome of interest. There is also a need to investigate the effect of second-hand exposure due to the amount of smoke generated by a waterpipe.

Our findings have both clinical and public health implications. Our findings reinforce the message that all forms of smoking are unsafe, and clinicians should be clear about delivering this unified message to patients. Given the available evidence, public health agents and policy makers need not wait for more evidence to enact and implement laws, and develop public health programmes to reduce waterpipe tobacco use, particularly among youth. This is particularly relevant given the emerging evidence that waterpipe tobacco smoking may predict cigarette initiation and thus serve as a gateway to cigarette smoking.[88]

Supplementary Data

Supplementary data are available at *IJE* online.

Conflict of interest: None.

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