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RISK FACTORS

The effects of waterpipe tobacco smoking on health outcomes: a systematic review

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Background There is a need for a comprehensive and critical review of the literature to inform scientific debates about the public health effects of waterpipe smoking. The objective of this study was therefore to systematically review the medical literature for the effects of waterpipe tobacco smoking on health outcomes.

Methods We conducted a systematic review using the Cochrane Collaboration methodology for conducting systematic reviews. We rated the quality of evidence for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology.

Results Twenty-four studies were eligible for this review. Based on the available evidence, waterpipe tobacco smoking was significantly associated with lung cancer [odds ratio (OR) = 2.12; 95% confidence interval (CI) 1.32–3.42], respiratory illness (OR = 2.3; 95% CI 1.1–5.1), low birth-weight (OR = 2.12; 95% CI 1.08–4.18) and periodontal disease (OR = 3–5). It was not significantly associated with bladder cancer (OR = 0.8; 95% CI 0.2–4.0), nasopharyngeal cancer (OR = 0.49; 95% CI 0.20–1.23), oesophageal cancer (OR = 1.85; 95% CI 0.95–3.58), oral dysplasia (OR = 8.33; 95% CI 0.78–9.47) or infertility (OR = 2.5; 95% CI 1.0–6.3) but the CIs did not exclude important associations. Smoking waterpipe in groups was not significantly associated with hepatitis C infection (OR = 0.98; 95% CI 0.80–1.21). The quality of evidence for the different outcomes varied from very low to low.

Conclusion Waterpipe tobacco smoking is possibly associated with a number of deleterious health outcomes. There is a need for high-quality studies to identify and quantify with confidence all the health effects of this form of smoking.

Keywords Oesophageal neoplasms, infant, low birth-weight, lung neoplasms, hepatitis C, tobacco, waterpipe

Background

Tobacco smoking using waterpipe—also known as arguileh, hookah and shisha—is an older form of tobacco consumption traditional of the eastern Mediterranean region (Figure 1).[1] The waterpipe device indirectly heats the tobacco. The resulting

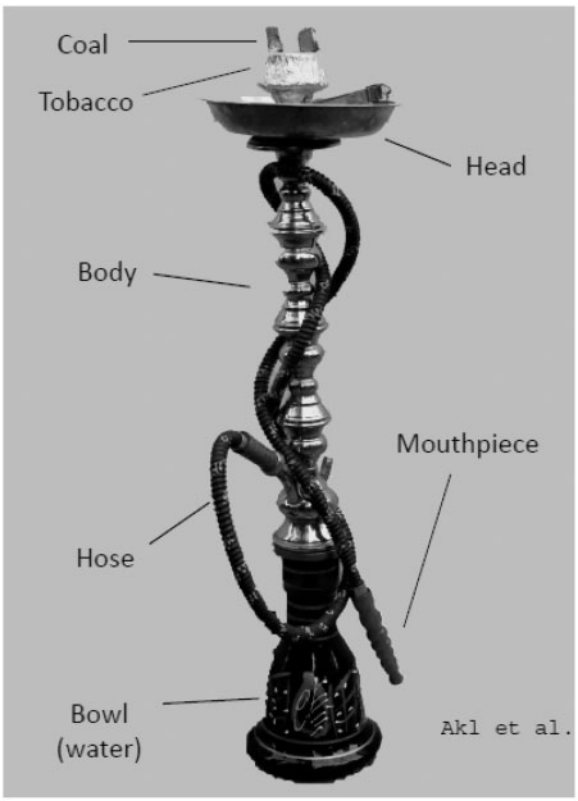

Figure 1 Annotated figure of a waterpipe device

smoke then passes through a column of water before being inhaled through the mouth using a pipe.[2] These two unique features of this form of smoking are assumed to minimize its tobacco-related health hazards. Also, waterpipe tobacco smoke is produced at a much lower temperature than cigarette smoke, suggesting that the toxins may be different for these different forms of tobacco smoking.[3] Another unique feature is the social nature of waterpipe smoking, whereby family members and friends may share the same device, which has been hypothesized to cause the transmission of communicable diseases.

Waterpipe tobacco smoking has been spreading globally at a remarkable pace.[4] Although its use in the eastern Mediterranean region has been, until recently, confined to adults, it is now gaining popularity among university students[5,6] and teenagers.[7–9] Waterpipe smoking is also spreading to Western countries such as Australia,[10] the UK,[11] Canada[12] and the USA,[13] where it is also affecting young people and adolescents.[14,15]

Waterpipe tobacco smoking is generally considered as a public health threat and the American Lung Association has recently called it the 'emerging deadly trend'.[2] In fact, waterpipe smoking has been suspected to be a risk factor for a number of tobacco-related diseases such as lung cancer,[16] oesophageal cancers,[17] cardiovascular disease[18] and adverse pregnancy outcomes.[19] In addition, the waterpipe device may expose its user (via its non-tobacco components) to metals and cancer-causing chemicals.[20,21] The potential association of waterpipe smoking with communicable diseases such as hepatitis C[22] and tuberculosis[23] (via its shared and repetitive use without proper sanitation) has also been investigated.

While one article reviewed the effects of waterpipe smoking on health outcomes,[24] we have identified no published systematic review or meta-analysis of the topic. The objective of this study was therefore to systematically review the medical literature for 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) assessing the association between waterpipe tobacco smoking and health outcomes. We excluded case reports, case series, outbreak investigations and abstracts. We also excluded studies assessing physiological outcomes [e.g. Forced Expiratory Volume in 1 Second (FEV1)], assessing waterpipe use for non-tobacco smoking purposes (e.g. marijuana smoking), not distinguishing waterpipe smoking from other forms of smoking, and not reporting any measure of association.

Search strategy

In June 2008, we electronically searched the following databases: MEDLINE (1950 onwards; access via OVID), EMBASE (1980 onwards; access via OVID) and ISI the Web of Science using a detailed search strategy with no language restrictions (Appendix 1). We designed the strategy based on a preliminary review of relevant articles, an extensive Internet search for waterpipe synonyms and the search strategy of a systematic review on interventions for waterpipe smoking cessation.[25] Two medical librarians reviewed and commented on the search strategy. We also reviewed the reference lists of included and relevant papers and used the 'Related Articles' feature in PubMed.

Selection process

Two reviewers independently screened the title and abstract of identified citations for potential eligibility using a standardized screening guide. We retrieved the full texts of citations judged potentially eligible by at least one reviewer. Then, two reviewers independently screened the full texts for eligibility using a standardized and pilot-tested form. They resolved their disagreements by discussion or by consulting a third reviewer.

Data abstraction

Two reviewers used a standardized and pilot-tested form to independently abstract data. They resolved their disagreements by discussion or by consulting a third reviewer. The abstracted data related to study design, population, exposure, outcomes, methodological features, results and funding. For exposure measurement, we assessed whether the instrument was standardized to measure the unique smoking patterns and characteristics of waterpipe smoking. We recorded the results of analyses restricted to waterpipe only smokers (i.e. people who smoked only waterpipe) as well as the results of analyses that included all waterpipe smokers (i.e. people who smoked waterpipe and other forms of tobacco). We recorded the effect measures derived from the regression models that adjusted for the maximum number of covariates. We rated the overall quality of evidence for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Appendix 2).[26]

Data analysis

We calculated the kappa statistic to evaluate the agreement between the two reviewers assessing full texts for eligibility. We conducted meta-analyses for the outcomes for which at least two studies reported effect estimates of their association with waterpipe tobacco smoking. When the authors reported odds ratios (ORs) for more than one analysis we selected the OR according to the following order: (i) analysis adjusted for other forms of tobacco smoking (choosing the one adjusting for the maximum number of confounders); (ii) analysis restricted to waterpipe only smokers; (iii) analysis not adjusted for other forms of tobacco smoking and not restricted to waterpipe only smokers. We used the ORs to calculate the corresponding ln(ORs) and standard errors. We then pooled, for each outcome, the ln(ORs) of eligible studies using the generic inverse variance and the random effects model in Review Manager Version 5.0.20. We measured homogeneity across study results using the I^2 statistic.[27] We checked for possible publication bias using inverted funnel plots.

Results

Figure 2 shows the study flow. We included 23 reports on: lung cancer ($n = 6$),[16,28–32] bladder cancer

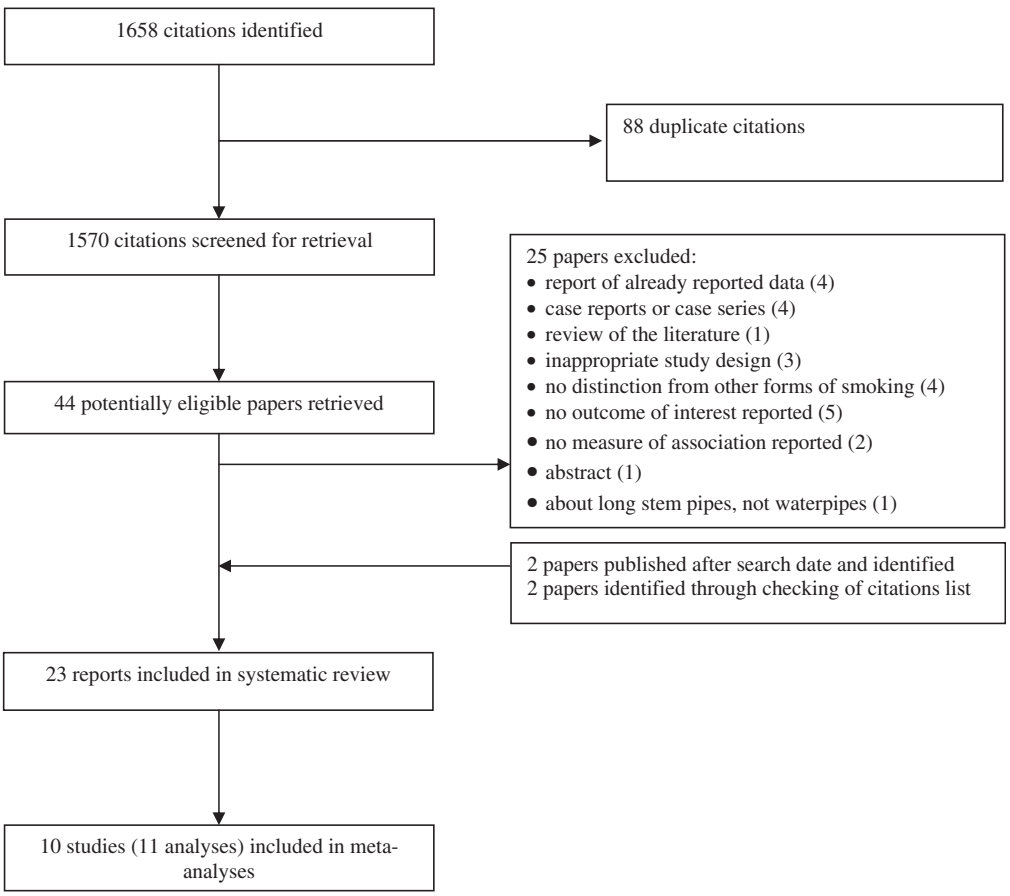

Figure 2 Study flow diagram

($n=1$),[33] oesophageal cancers ($n=1$),[17] nasopharyngeal cancer ($n=1$),[34] dysplasia of the oral mucosa ($n=1$),[35] pregnancy outcomes ($n=3$),[19,36,37] periodontal disease ($n=5$),[38–42] hepatitis C infection ($n=3$),[22,43,44] respiratory illness ($n=1$)[45] and infertility ($n=1$).[46] Agreement between reviewers for study eligibility was excellent (kappa = 0.963).

Lung cancer

Five of the six included studies were case–control studies assessing lung cancer diagnosis,[16,28–31] and one was a retrospective cohort study assessing lung cancer mortality (Table 1).[32] One was conducted in Northern India,[28] one was conducted in Tunisia,[31] whereas rule four reported data from the same population in China. While in the recent global epidemic the tobacco is processed and flavoured and indirectly heated by the charcoal, in most of the included studies (conducted in China and India) the tobacco is 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% confidence interval (CI) 1.32–3.42; $I^2=0\%$] (Figure 3). We judged the overall quality of evidence to be very low (Appendix 3). The calculated crude relative risk (RR) for the association with lung cancer mortality was 4.39 (3.82–5.04). We judged the overall quality of evidence to be very low (Appendix 3). A sensitivity analysis restricted to studies with no major methodological limitations, included the study by Hsairi *et al.*[31] for which the OR was 3.0 (95% CI 1.2–7.6).

Bladder cancer

The one included case–control study[33] reported a potentially protective association between waterpipe tobacco smoking and bladder cancer diagnosis of 0.8 (95% CI 0.2–4.0) (Table 1). A stratified analysis by the amount of cigarette smoking suggested a potential interaction between waterpipe and cigarette smoking but the CI overlapped and no interaction test was reported. An interaction test we ran was statistically not significant ($P=0.55$). We judged the overall quality of evidence to be very low (Appendix 3).

Oesophageal cancer

The one study assessing oesophageal cancer diagnosis was a case–control study (Table 1).[17] The reported OR for the association of waterpipe tobacco smoking with oesophageal cancer diagnosis was 1.85 (95% CI 0.95–3.58). We judged the overall quality of evidence to be low (Appendix 3).

Nasopharyngeal cancer

The one included study was a case–control study (Table 1). The OR for the association of waterpipe tobacco smoking with nasopharyngeal cancer was 0.49 (95% CI 0.20–1.23). We judged the overall quality of evidence to be very low (Appendix 3).

Oral dysplasia

The one included study was a cross-sectional study that recruited exclusively subjects who practiced 'takhzeen al-qat', i.e. a practice that is distinct from waterpipe smoking and consists of chewing a green-leaved plant for its stimulant effect (Table 1).[35] The OR for the association of waterpipe tobacco smoking with dysplasia of the oral mucosa on chewing side was 8.33 (95% CI 0.78–9.47). There were no events observed in either group on non-chewing side. We judged the overall quality of evidence to be very low (Appendix 3).

Pregnancy outcomes

Of the three included studies, two were retrospective cohort studies[19,36] and one was a case–control study (Table 2).[37] All three studies assessed low birth-weight. One study also reported on Apgar score, pulmonary problems, malformations and perinatal complications.[19] The pooled OR for the association of waterpipe tobacco smoking with low birth-weight was 2.12 (95% CI 1.08–4.18; $I^2=0\%$) (Figure 4). The reported OR for the association of waterpipe tobacco smoking with newborn pulmonary problems was 3.65 (95% CI 1.52, 8.75). The associations were not significant for Apgar scores at 1 and 5 min, malformations or perinatal complications. We judged the overall quality of evidence for pregnancy outcomes to be low (Appendix 3).

Periodontal disease

Of the five included studies,[38–42] four were conducted in the same (or in a subgroup of the same) group of participants (Table 3).[39–42] These four studies were cross-sectional and evaluated the same outcome (i.e. periodontal disease) using different outcome measurement (periodontal bone height loss, plaque index and gingivitis, deepening of the sulci or pockets, vertical periodontal bone loss). We did not pool the four related studies evaluating periodontal disease as their data were derived from the same participants. Their results were consistent in showing a statistically significant association of waterpipe tobacco smoking with periodontal disease (OR = 3–5). We judged the overall quality of evidence to be low (Appendix 3).

The fifth included study was a cohort study with 7 days follow-up after surgical removal of mandibular third molars and evaluated the outcome of dry socket.[38] 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. The reported RR for the association of waterpipe tobacco smoking

Table 1 Characteristics of included studies assessing the effect of waterpipe tobacco smoking on cancer outcomes

Study	Population	Exposure	Outcomes	Methodological features	Results
Qiao[16] • Study design: case–control study • Funding: China State Science and Technology Commission; and the US National Cancer Institute grant	• Setting and period: Gejiu city, Yunnan Province, China, interviews conducted in 1985 • Cases: 107 lung cancer cases in males 35–80 years old reported to Labor Protection Institute of the Yunnan Tin Corporation (YTC) during 1967–84 • Controls: 107 controls chosen systematically by selecting every 20th person from the list of all living past or present workers of the YTC; one control per case	• Type: Chinese water pipes, cigarettes • Measurement tool: self-developed questionnaire, no standardization reported; cumulative consumption calculated as pipe years • Exposure levels: Cases: mean pipe years = 177 (range 0–560); Controls: mean pipe years = 122 (range 0–480)	Lung cancer diagnosis • Measurement tool: detected by radiology and confirmed by histology or cytology • Blinding of outcome adjudicator: not reported	• Selection bias: series of incident cases but unclear whether all incident cases reported, controls were selected from the same study base as cases • Information bias: objective outcome evaluation: yes; standardized exposure measurement: no. Surrogates were interviewed for 10% of cases and 6% of controls • Confounding: matching for age; adjustment for age; no adjustment reported for radon • Participation rate: not reported	OR compared with never smoking: • 1.9 (95% CI 0.4–9.4) (waterpipe only smoking) • 2.1 (95% CI 0.5–9.1) (waterpipe and cigarette smoking) • 0.9 (95% CI 0.1–5.4) (cigarette only smoking) Statistically significant dose response to water pipe smoking OR=3.4 (1.3–8.1) by quarter of pipe-years
Lubin[29] • Study design: case–control study • Funding: China Science and Technology Commission; and the US National Cancer Institute • Unclear whether this is a report on a subpopulation of Qiao[18]	• Setting and period: Gejiu city, Yunnan Province, China, study conducted in 1985 • Cases: 74 lung cancer cases in males with mean age 62 years (range 35–80) alive at the time of the study reported to Labor Protection Institute of the YTC during 1981–84 • Controls: 74 controls chosen from the list of all living past or present workers of the YTC; one control per case	• Type: Chinese water pipes, cigarettes • Measurement tool: self-developed questionnaire, no standardization reported; cumulative consumption calculated as pipe years • Exposure levels of included subjects: number of pipe years (cases/controls): 0 (6/16); 1–114 (18/23); 115–220 (21/15); ⩾220 (29/20)	Lung cancer diagnosis • Measurement tool: cases confirmed by an independent panel of pathologists, clinicians and cytologists • Blinding of outcome adjudicator: not reported	• Selection bias: series of incident cases but unclear whether all incident cases reported; excluded those who had died by the time of the study; controls were selected from the same study base as cases • Information bias: objective outcome evaluation: yes; standardized exposure measurement: no; validated confounder measurement (arsenic): no • Confounding: matching for age (within 5-year age groups) • Participation rate: not reported • Data were sparse and authors were unable to adjust for important confounding factors	OR compared with no tobacco smoking: • 3.6 (waterpipe only smoking) • 1.2 (cigarette only smoking) • 3.5 (mixed smoking)

(continued)

Table 1 Continued

Study	Population	Exposure	Outcomes	Methodological features	Results
Lubin[30] • Study design: case–control study • Funding: not reported	• Setting and period: Gejiu city, Yunnan Province, China • Cases: 427 male lung cancer patients, mean age 63 years (range 35–75); reported between 1984 and 1988 to the Cancer Registry of the Labor Protection Institute of YTC or to the Gejiu City Cancer Registry; 339 from Yunnan Tin Corporation and 88 from Gejiu City • Controls: 1011 male controls, two controls per case, mean age 62 years (range 35–75), 770 from YTC and 241 from Gejiu city	• Type: Chinese waterpipe, cigarettes • Measurement tool: self-developed standardized structured questionnaire, no standardization reported; consumption calculated as pipe years • Exposure levels of included subjects: mean duration of pipe only smoking is 41 years	Lung cancer diagnosis • Measurement tool: confirmed by independent panel of pathologists, clinicians, radiologists and cytologists • Blinding of outcome adjudicator: not reported	• Selection bias: series of incident cases, controls were community based and selected from the same study base as cases; • Information bias: objective outcome evaluation: yes; standardized exposure measurement: no • Confounding: matching for age (within 5-year age groups); adjustment for age, number of years of work underground, source of subject, type of respondent • Participation rate: 72% for cases, 88% for controls	OR compared with no smoking: • 1.8 (95% CI 0.8–4.2) (waterpipe only smoking) • 2.6 (95% CI 1.1–6.2) (cigarette only) ORs for pipe users show increasing trend with increased duration of use (test for trend statistically significant)
Hsairi[31] • Study design: case–control study • Funding: not reported	• Setting and period: Ariana, Tunis, December 1988 to May 1989 • Cases: 110 lung cancer patients; epidermoid (56%), anaplastic small cell (17%), undifferentiated (13%), adenocarcinoma (12%), anaplastic large cell (3%), • Controls: 110 residents of the same area	• Type: waterpipe, pipe, inhaled tobacco, cannabis • Measurement tool: self-developed tool, no standardization reported • Exposure levels of included subjects: not reported	Lung cancer diagnosis • Measurement tool: histologically confirmed in 70% of cases, 'very probable' in 30% of cases based on clinical, radiological and endoscopic suspicion • Blinding of outcome adjudicator: not reported	• Selection bias: series of incident cases, controls were community based and selected from the same study base as cases. • Information bias: objective outcome evaluation: yes; standardized exposure measurement: no • Confounding: matching for age, sex, consumption of cigarettes per day; adjustment for age, sex, cigarette consumption, occupational risks • Participation rate: not reported	OR compared with no smoking: • 3.0 (95% CI 1.2–7.6)[a]
Gupta[28] • Study design: case–control study • Funding: International Agency	• Setting and period: Northern India; recruitment, January 1995 to June 1997	• Type: cigarettes, bidis, hookah • Measurement tool: self-developed tool, no standardization	Lung cancer diagnosis • Measurement tool: detected by radiology	• Selection bias: series of hospital based incident cases, community-based controls selected from the same study base as cases	OR compared with no smoking: • 1.94 (95% CI 0.85–4.44) (hookah smoking) in men

(continued)

Table 1 Continued

Study	Population	Exposure	Outcomes	Methodological features	Results
for Research on Cancer, Lyon France; and the International cancer related technology transfer fellowship award	• Cases: 265 incident cases of lung cancer • Controls: 525 visitors and attendants of the patients; two controls per case • Participants were 85% male, of different religions, ages ranging from <50 to >70 living in rural or urban areas	reported; cumulative consumption calculated as pack-year equivalent of cigarettes (1 hookah = 4 cigarettes) stratified in four groups (0–9; 10–19; 20–29; 30+) • Exposure levels of included subjects: incompletely reported	and confirmed by histology or cytology • Blinding of outcome adjudicator: not reported	• Information bias: objective outcome evaluation: yes; standardized exposure measurement: no • Confounding: matching for age and sex; adjustment for age, and education. No adjustment for any confounding factor including other forms of tobacco consumption • Participation rate: not reported • Missing data: 54.3% for exposure	• Numbers for women were too small to derive stable risk estimates
Hazelton[32] • Study design: retrospective cohort study • Funding: National Institute of Health	• Setting and period: Gejiu city, Yunnan Province, China, 12 years follow-up (1976–88) • Exposed: 1289 male waterpipe-only smokers and 2306 male waterpipe and cigarette smokers • Non-exposed: 8416 males	• Type: Chinese waterpipe, cigarette • Measurement tool: not reported, calculated as cumulative exposure and categorized into quartiles of liang/month year • Measurement time points: every 5 years • Exposure levels of included subjects: cumulative dose quartiles: 0 ($n = 8416$), 0.16–4.44 ($n = 877$), 4.44–6.25 ($n = 888$), 6.25–9.21 ($n = 906$), 9.21–82.19 ($n = 924$)	Lung cancer mortality • Measurement tool: not reported • Blinding of outcome adjudicator: not reported • Incidence: 7%	• Selection bias: smokers were representative of the study base, non-smokers selected from the same community as smokers • Information bias: unlikely for mortality outcome; standardized exposure measurement: no • Confounding: no adjustment (no adjusted RR reported; crude RR calculated from reported data) • Participation rate: not reported • 8% lost to follow-up	• RR compared with no smoking = 4.39 (95% CI 3.82–5.04) (water pipe smoking)
Bedwani[33] • Study design: case–control study • Funding: National Research Council-Applicazioni cliniche della ricerca oncologica (CNR-ACRO Project); and Italian	• Setting and period: Greater Alexandria, Egypt; study conducted, January 1994 to July 1996 • Cases: 151 male incident cases of invasive bladder cancer with median age 61 years (range 31–74) admitted to a network of	• Type: waterpipe, cigarette, hashish • Measurement tool: self-developed structured questionnaire; standardization not reported; participants categorized as ever smokers and never	Bladder cancer diagnosis • Measurement tool: centrally reviewed histopathological diagnosis • Blinding of outcome	• Selection bias: hospital-based cases of bladder cancer confirmed within the year preceding interview, hospital-based controls selected from the same study base as cases. Selection related to exposure status (in the case of	OR compared with never smoking: • 0.8 (95% CI 0.2–4.0) (waterpipe smoking) • 5.4 (95% CI 2.4–12.1) (<20/day cigarette smoking)

(continued)

Table 1 Continued

Study	Population	Exposure	Outcomes	Methodological features	Results
Association for Cancer Research	general and teaching hospitals. • Controls: 157 males admitted for acute, non-neoplastic, non-urinary tract, non-smoking-related conditions, median age 50 years (range 32–74) • 39 female cases and 30 female controls were excluded because 'only one female case was a smoker'	smokers. Age at starting, duration of habit, average daily consumption extracted from history but not reported • Exposure levels of included subjects: not reported	adjudicator: not reported	females and patients with non-smoking-related conditions) • Information bias: objective outcome evaluation: yes; standardized exposure measurement: no • Confounding: adjustment for age, education, type of house, history of schistosomiasis, high-risk occupation, tobacco smoking • Participation rate: >95% of eligible subjects participated in the interview	• 7.6 (95% CI 3.4–16.8) for ⩾20/day cigarette smoking
Nasrollahzadeh[17] • Type of design: case–control study • Funding: Digestive Disease Research Center: Tehran University of Medical Sciences (DDRC/TUMS); and National Cancer Institute at National Institute of Health	• Setting and period: Atrak Clinic in Gonbad City, eastern Golestan Province of Iran, December 2003 to June 2007 • Cases: 300 oesophageal squamous cell carcinoma cases, 50% males, mean age 64.5 years • Controls: 571 controls, two population-based matched control subjects per case for 90% of cases	• Type: hookah, cigarettes, nass chewing, opium • Measurement tool: self-developed questionnaire, tested for reliability and validity, cumulative consumption calculated as hookah-years and categorized into never users, ⩽32 hookah-years, >32 hookah-years • Exposure levels of included subjects: median of 32 hookah-years	Oesophageal squamous cell carcinoma diagnosis • Measurement tool: histopathologically confirmed • Blinding of outcome adjudicator: not reported	• Selection bias: series of incident cases (70% of incident cases registered with local cancer registry were referred to the Atrak Clinic), controls were selected from the same study base as cases • Information bias: objective outcome evaluation: yes; standardized exposure measurement: yes • Confounding: matching for age, sex, residence; adjustment for education, ethnicity, other types of tobacco use, total intake of fruit and vegetables • Participation rate: not reported	OR compared with no smoking: • 1.85 (95% CI 0.95–3.58) (hookah smoking) • 1.69 (95% CI 0.76–3.77) (hookah only smoking) • 1.50 (95% CI 0.92–2.43) (cigarette only smoking) • Test for trend significant for intensity ($P=0.03$) but not for duration, total amount, or age started)
Feng[34] • Study design: case–control study • Funding: Association for International Cancer Research	• Setting and period: five hospitals in Algeria, Morocco, and Tunisia, January 2002 to March 2005 • Cases: 636 incident cases of nasopharyngeal cancer	• Type: cigarette, shisha, snuff, cannabis • Measurement tool: interviews, self-developed questionnaire, no standardization reported;	Nasopharyngeal carcinoma • Measurement tool: cases identified by clinician in the Oncology and	• Selection bias: series of hospital-based incident cases (2001–04), controls were hospital-based or friends and family of cases, and recruited from the same study base as cases	OR compared with never smoking: 0.49 (95% CI 0.20–1.23) (ever shisha smoking)

(continued)

Table 1 Continued

Study	Population	Exposure	Outcomes	Methodological features	Results
	• Controls: 615 controls [patients hospitalized for non-cancer diseases (61%) and friends and family of non-cancer patients (39%)]	participants categorized as ever smokers and never smokers. Ages of starting, and quitting daily consumption extracted from history but not reported • Exposure levels of included subjects: not reported	radiotherapy departments • Blinding of outcome adjudicator: not reported	• Information bias: objective outcome measurement: yes, standardized exposure measurement: no • Confounding: matching for hospital, age, sex, household type (urban/rural); adjustment for age • Participation rate: >90%	
Ali[35] • Study design: cross-sectional study • Funding: not reported	• Setting and period: Yemen; period not reported • Population: Yemeni volunteers (27 men and six women) all chewers of al-qat, mean age 38.5 years (range 22–58), all of them free from any systematic diseases. 11 waterpipe smokers, 11 cigarette smokers, 11 non-smokers	• Type: cigarette smoking, waterpipe smoking • Measurement tool: interviews, standardization not reported, subjects categorized as heavy cigarette smokers (>20/day), non-smokers and waterpipe smokers • Exposure levels of included subjects: not reported	Dysplasia of oral mucosa diagnosis • Measurement tool: histopathological examination of buccal mucosa biopsies • Blinding of outcome adjudicator: not reported	• Selection bias: volunteer recruitment into the study • Information bias: objective outcome measurement: yes, standardized exposure measurement: no • Confounding: no matching or adjustment in the analysis reported • Participation rate: not reported	OR compared with no smoking: • 8.33 (95% CI 0.78–9.47) (waterpipe smoking) Results are restricted to the chewing side; no events in either group on non-chewing side. OR calculated from reported numbers

[a]Ninety five percent adjusted OR and CI reported as 5.7 (1.2–7.6). As the effect estimate was not consistent with the position of the lower and upper borders of the CI and given the unadjusted OR was 4.8, and as we were unable to contact the authors, we used OR = 3.0 which we calculated based on the CI of 1.2–7.6.

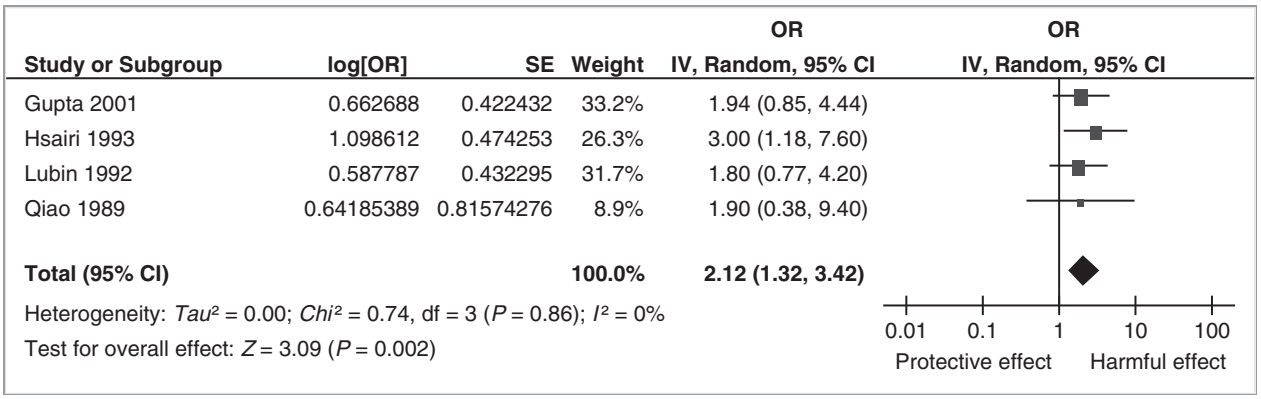

Figure 3 Association between waterpipe tobacco smoking and lung cancer

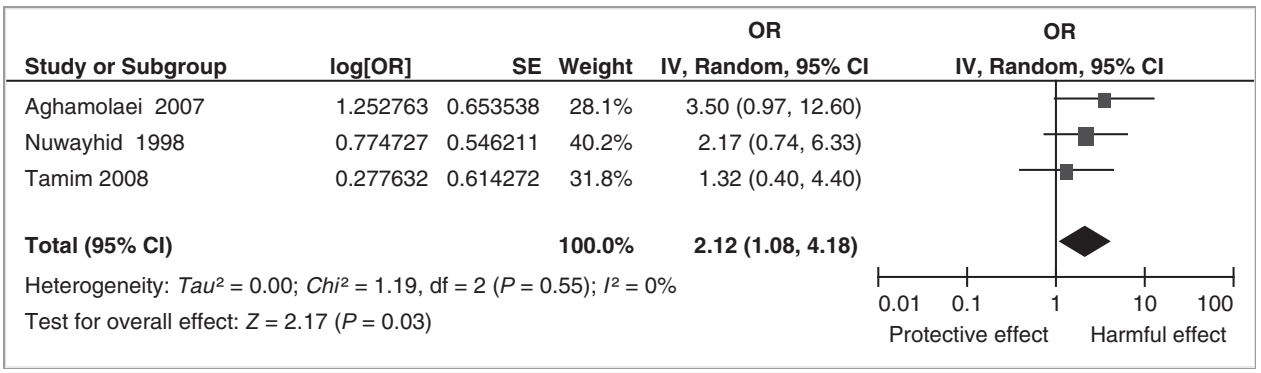

Figure 4 Association between waterpipe tobacco smoking and low birth-weight

with dry socket was 3.7 ($P = 0.001$). We judged the overall quality of evidence to be low (Appendix 3).

Infectious disease

We identified three studies on hepatitis C. The three cross-sectional studies were conducted in Egypt and restricted to male participants exposed to group waterpipe tobacco smoking (Table 4).[22,43,44] The pooled OR for the association of group waterpipe tobacco with hepatitis C was 0.98 (95% CI 0.80–1.21; $I^2 = 0\%$) (Figure 5). We judged the overall quality of evidence to be very low (Appendix 3).

We did not identify any eligible study assessing the association between waterpipe smoking and the transmission of tuberculosis. We did identify two reports of outbreak investigations suggesting an association between tuberculosis and sharing tobacco waterpipe[23] and marijuana waterpipe.[47]

Respiratory illness

One cross-sectional study evaluated the association between waterpipe smoking and respiratory illness (defined as perennial rhinitis and including nasal congestion and wheezing) (Table 5).[45] The study reported significant association of waterpipe tobacco smoking (OR = 2.3; 95% CI 1.1–5.1) and of waterpipe and/or cigarette smoking (OR = 2.5; 95% CI 1.6–3.8) with respiratory illness. We judged the overall quality of evidence to be very low (Appendix 3).

Infertility

One case–control study evaluated the association between waterpipe smoking and male factor infertility (based on semen analysis) (Table 5).[46] The reported OR for the association of waterpipe tobacco smoking with male factor infertility was not statistically significant (OR = 2.5; 95% CI 1.0–6.3). We judged the overall quality of evidence to be very low (Appendix 3).

Discussion

We systematically reviewed the medical literature for the effects of waterpipe tobacco smoking on health outcomes. Based on the available evidence, waterpipe tobacco smoking was significantly associated with lung cancer, respiratory illness, low birth-weight and periodontal disease. It was not significantly associated with bladder cancer, nasopharyngeal cancer, oesophageal cancer, oral dysplasia or infertility but the CIs did

Table 2 Characteristics of included studies assessing the effect of waterpipe tobacco smoking on pregnancy outcomes

Study	Population	Exposure	Outcomes	Methodological features	Results
Nuwayhid[19] • Study design: retrospective cohort study • Funding: Hariri Foundation; and University Research Board at the American University of Beirut	• Setting and period: hospitals in Lebanon; 1993 and 1995 • Participants: pregnant women delivering in hospitals. 106 narghile smokers (mean age 27.6 years), 277 cigarette smokers (mean age 29.1) and 512 non-smokers (mean age 28.5)	• Type of exposure: narghile, cigarettes • Measurement tool: interviews, standardization not reported; categorized into <1 vs ⩾1 per day; and started smoking during first vs second or third trimester • Measurement time points: not reported • Exposure levels of included subjects: <1 per day ($n=38$); ⩾1 per day ($n=67$) per day; first trimester ($n=78$); second or third trimester ($n=25$)	Low birth-weight, Apgar score <7 (1 and 5 min), pulmonary problems, malformations, perinatal complications • Measurement tool: medical records; low birth-weight defined as a birth weight <2500 g • Blinding of outcome adjudicator: not reported	• Selection bias: unclear whether sample is representative (data collection in a few number of hospitals) • Information bias: objective outcome measurement: yes but based on medical records, standardized exposure measurement: no • Confounding: adjustment for age, hospital location, gestational age, exposure to passive smoking, and previous low birth-weight • Participation rate: not reported • <10% missing data	OR for narghile smoking compared with no smoking • low birth-weight =2.17 (95% CI 0.74–6.33) • low birth-weight = 2.36 (95% CI 0.52–10.73) (<1/day) • low birth-weight = 2.07 (95% CI 0.54–7.94) (⩾1/day) • low birth-weight = 2.93 (95% CI 0.97–8.83) (narghile smoking started in first trimester) • Test for trend for low birth-weight not significant for intensity ($P<0.18$) • Apgar score <7 at 1 min = 1.73 (95% CI 0.73–4.14) • Apgar score <7 at 5 min = 3.39 (95% CI 0.54–21.42) • Pulmonary problems = 3.65 (95% CI 1.52–8.75) • Malformations = 2.01 (95% CI 0.59–6.88) • Perinatal complications =1.67 (95% CI 0.82–3.41) OR for cigarette smoking compared with no smoking • Low birth-weight = 2.00 (95% CI 0.96–4.20) • low birth-weight = 2.25 (95% CI 1.04–4.86) (narghile smoking started in first trimester) • Apgar score <7 at 1 min = 1.59 (95% CI 0.82–3.07) • Apgar score <7 at 5 min = 2.62 (95% CI 0.56–12.29) • Pulmonary problems = 1.76 (0.80–3.87) • Malformations = 1.36 (0.49–3.80) • Perinatal complications = 1.50 (0.87–2.57)

(continued)

Table 2 Continued

Study	Population	Exposure	Outcomes	Methodological features	Results
Aghamolaei[37] • Study design: case–control study • Funding: not reported	• Setting and period: Shariati Hospital of Bandar Abbas, South of Iran; period not reported • Cases: 60 Intra-uterine growth retardation infants • Controls: 60 normal birth infants • Included subjects: all term infants with gestational age 37–42 weeks; 29 males and 31 females in each group. 'None of included mothers smoked and used alcohol during pregnancy and none of them had diabetes'	• Type: hookah smoking by mother • Measurement tool: structured questionnaire administered to mothers, standardization not reported • Exposure levels of included subjects: not reported	Intra uterine growth retardation (IUGR) • Definition: term infants with a birth-weight <2500 g • Measurement tool: birth weight determined up to 10 min of delivery using a digital baby scale • Blinding of outcome adjudicator: not reported	• Selection bias: series of incident cases of IUGR in maternity wards, controls selected from the same study base as the cases • Information bias: objective outcome measurement: yes, standardized exposure measurement: no • Confounding: explored 18 potential risk factors and adjusted for maternal work, hypertension, antenatal care • Participation rate: not reported	• OR for hookah smoking during pregnancy compared with no hookah smoking during pregnancy = 3.5 (95% CI 1.1–12.6)
Tamim[36] • Study design: retrospective cohort study • Funding: Lebanese National Council for Scientific Research; the Medical Practice Plan; and the University Research Board at the American University of Beirut	• Setting and period: six major hospitals in greater Beirut, Lebanon, August 2000 to August 2003 • Population: 378 singleton newborns to women exclusive narghile smokers, 929 singleton newborns to women exclusive cigarette smokers, 84 singleton newborns to women smoking both types of tobacco, 7201 singleton newborns to women non-smokers	• Type: narghile, cigarettes • Measurement tool: interviews, questionnaire pilot tested; narghile smokers categorized into ⩽1 vs >1 per day; categorized into <1 vs ⩾1 per day; and started smoking during first vs second or third trimester • Measurement time points: not reported • Exposure levels of included subjects: ⩽1 per day (n=233); >1 per day (n = 145); first trimester (n = 309); second or third trimester (n = 69)	Low birth-weight • Measurement tool: data collection from obstetric and nursery charts, low birth-weight defined as ⩽2500 g • Blinding of outcome adjudicator: not reported	• Selection bias: sample representative of populations of six major hospitals in Greater Beirut • Information bias: objective outcome measurement: yes but based on medical records, standardized exposure measurement: no (pilot tested only) • Confounding: adjustment for maternal/paternal education, mother's working status, mother's age, parity, diabetes, bleeding, pregnancy hypertensive disorders, gestational age, and passive smoking • Participation rate: not reported	OR for narghile only smoking compared with no smoking • low birth-weight = 1.32 (95% CI 0.39–4.40) (OR pooled for ⩽1 day and >1 day) • low birth-weight = 0.7 (95% CI 0.3–1.6) (⩽1 day) • low birth-weight = 2.4 (95% CI 1.2–5.0) (>1 day) • low birth-weight = 1.2 (95% CI 0.6–2.2) (narghile smoking started in first trimester) • OR for cigarette only smoking compared with no smoking = 1.32 (95% CI 0.91–1.90)

Table 3 Characteristics of included studies assessing the effect of waterpipe tobacco smoking on periodontal disease

Study	Population	Exposure	Outcomes	Methodological features	Results
Natto[39] • Study design: cross-sectional study • Funding: Ministry of Health in Saudi Arabia; and Saudi Arabian Cultural Bureau Office in Bonn	• Setting and period: Jeddah, Saudi Arabia, period not reported • Participants: 355 volunteers, 28% females, mean age 36.9 years (range 17–60), having 20 teeth and not pregnant	• Type: waterpipe, cigarettes • Measurement tool: standardized questionnaire administered in interviews, standardization not reported; calculated as run-years (product of waterpipe runs per day with years of smoking; a run is the completion of the waterpipe smoking until the tobacco is burnt); heavy exposure was defined as $\geqslant$40 run-years • Exposure levels of included subject: mean exposure of 56.8 run-years for waterpipe smokers	Periodontal disease measured as periodontal bone height loss • Measurement tool: digital panoramic radiographs. Bone loss defined as bone height $\leqslant$70%. Mean bone height per individual is the ratio of the periodontal bone height to the root length • Blinding of outcome adjudicator: yes	• Selection bias: volunteers recruited by newspaper announcements • Information bias: objective outcome measurement: yes, standardized exposure measurement: no • Confounding: adjustment for age only • Participation rate: not reported	OR compared with no smoking • 3.5 (95% CI 1.6–7.6) (waterpipe only smoking) • 1.0 (95% CI 0.3–3.1) (light waterpipe only smoking) • 7.5 (95% CI 3.0–18.3) (heavy waterpipe only smoking) • The association between waterpipe smoking and bone height remained statistically significant after controlling for 'education as a surrogate for socio-economic standard and other variables' • Differences between light and heavy exposures were statistically significant ($P < 0.001$)
Natto[40] • Study design: cross-sectional study • Funding: not reported	• Setting and period: Western part of Saudi Arabia, period not reported • Participants: 244 volunteers, 34% females, mean age 37.4 years (range 25–70), having 20 teeth and not pregnant	• Type: waterpipe, cigarettes • Measurement tool: standardized questionnaire administered in interviews, standardization not reported; calculated as run-years (product of waterpipe runs per day with years of smoking; a run is the completion of the waterpipe smoking until the tobacco is burnt) • Exposure levels of included subject: not reported	Periodontal disease measured as plaque index and gingivitis • Measurement tool: Plaque: clinical examination, presence of visible dental plaque was recorded according to the criteria of Silness and Loe • Blinding of outcome adjudicator: not reported	• Selection bias: 244 of the 355 volunteers participating in another study[38] volunteered for a clinical examination • Information bias: objective outcome measurement: yes, standardized exposure measurement: no • Confounding: adjustment for age, dental care habit • Participation rate: 68%	• There was an overall significant association between smoking and plaque index and gingival index. No effect estimates reported

(continued)

Table 3 Continued

Study	Population	Exposure	Outcomes	Methodological features	Results
Natto[41] • Study design: cross-sectional study • Funding: Ministry of Health in Saudi Arabia; and Saudi Arabian Cultural Bureau Office in Bonn	• Setting and period: Jeddah, Saudi Arabia, period not reported • Population: 262 volunteers, 35% females, mean age 36.5 (range 17–60). Participants were required to have 20 teeth and not be pregnant. 51 citizens with periodontal disease and 211 citizens without periodontal disease	• Type: waterpipe, cigarettes • Measurement tool: standardized questionnaire administered in interviews, standardization not reported; calculated as run-years (product of waterpipe runs per day with years of smoking; a run is the completion of the waterpipe smoking until the tobacco is burnt); heavy exposure was defined as ⩾40 run-years • Exposure levels of included subject: mean exposure of 35.8 run-years for waterpipe smokers	Periodontal disease measured as deepening of the sulci or pockets • Measurement tool: clinical examination probing the depth of the sulci or pockets with a 2-mm graduated periodontal probe; periodontal disease defined as ⩾10 sites with a probing depth ⩾5 mm • Blinding of outcome adjudicator: not reported	• Selection bias: 262 of the 355 volunteers participating in another study[18] volunteered for a clinical examination • Information bias: objective outcome measurement: yes, standardized exposure measurement: no • Confounding: adjustment for age only • Participation rate: 74%	OR compared with no smoking • 5.1 (95% CI 2.0–13.5 (waterpipe only smoking) • 8.2 (95% CI 2.9–22.9) (heavy waterpipe smoking) • 2.9 (95% CI 1.7–4.8) (light waterpipe smoking) • 3.8 (95% CI 1.3–11.0) (cigarette only smoking) • 5.0 (95% CI 1.6–16.2), $P < 0.001$ (heavy cigarette only smoking) • 1.5 (95% CI 1.1–2.0), $P < 0.001$ (light cigarette only smoking) • Differences between light and heavy exposure were statistically significant
Baljoon[42] • Study design: cross-sectional study • Funding: Ministry of Health in Saudi Arabia; and Saudi Arabian Cultural Bureau Office in Bonn	• Setting and period: Jeddah, Saudi Arabia, period not reported • Population: 103 volunteers with vertical periodontal bone loss and 159 individuals without vertical periodontal bone loss	• Type: waterpipe, cigarettes • Measurement tool: standardized questionnaire administered in interviews, standardization not reported; calculated as run-years (product of waterpipe runs per day with years of smoking; a run is the completion of the waterpipe smoking until the tobacco is burnt); heavy exposure was defined as ⩾40 run-years	Periodontal disease measured as vertical periodontal bone loss • Measurement tool: intra-oral radiographs; vertical periodontal bone loss defined as one-sided bone resorption of the interdental marginal bone ⩾2 mm that had a typical angulation towards either the mesial or distal aspect of the root • Blinding of outcome adjudicator: yes	• Selection bias: 262 of the 355 volunteers participating in another study,[51,52] volunteered to participate in this study • Information bias: objective outcome measurement: yes, standardized exposure measurement: no • Confounding: adjustment for age only • Participation rate: 74%	OR compared with no smoking • 2.9 (95% CI 1.2–7.0) (waterpipe only smoking) • 43.3 (95% CI 12.1–71.6) (heavy waterpipe smoking) • 0.6 (95% CI 0.3–1.4) (light waterpipe smoking) • 6.6 (95% CI 2.6–17.1) (cigarette only smoking) • 18.3 (95% CI 6.2–53.9), $P < 0.001$ (heavy cigarette only smoking)

(continued)

Table 3 Continued

Study	Population	Exposure	Outcomes	Methodological features	Results
		• Exposure levels of included subject: mean exposure of 56.8 run-years for waterpipe smokers			• 1.3 (95% CI 0.5–3.4), $P < 0.001$ (light cigarette only smoking) • Differences between light and heavy exposures were statistically significant ($P < 0.001$)
Al-Belasy[38] • Study design: cohort study with 7 days follow-up after surgical removal of mandibular third molars • Funding: not reported	• Setting and period: Mansoura Egypt, January 2000 to February 2002 • Exposed: 100 male shisha smokers, mean age 28.7 years (range 22–39), 100 male cigarette smokers, mean age 28.7 years (range 20–38) • Non-exposed: 100 males non-smokers, mean age 27.7 years (range 20–37) • Included subjects were required to be healthy not taking medications at the time of the study and with unilateral high mesoangular impactions with exposed occlusal surfaces. Patients with recent antibiotic use or the medial need for antibiotic prophylaxis were excluded	• Type: shisha, cigarettes • Measurement tool: self-report, standardization not reported • Measurement time points: on day of the surgery, on the first and second post-operative days • Exposure levels of included subjects: not reported	Dry socket • Measurement tool: clinical diagnosis on the basis of constant radiating pain not relieved by the analgesic, accompanied by a denuded socket or necrotic clot and a fetid smell • Blinding of outcome adjudicator: not reported	• Selection bias: only healthy patients not taking medications were included, non-smokers selected from the same community as smokers • Information bias: objective outcome measurement: yes, standardized exposure measurement: no; same duration follow-up for both groups • Confounding: no matching or adjustment in the analysis reported • Participation rate: not reported • Attrition rate: not reported	• 'Shisha smokers had three times the risk of non-smokers for developing dry socket' (RR = 3.7; $P = 0.001$); trend of developing dry socket with frequency of shisha smoking was statistically significant ($P = 0.001$) • Compared with non-smokers, shisha smokers who smoked the day of surgery or the first day after surgery had a significantly increased incidence of dry socket (day 0, $P = 0.001$; day 1, $P = 0.005$)

Table 4 Characteristics of included studies assessing the effect of waterpipe tobacco smoking on hepatitis C infection

Study	Population	Exposure	Outcomes	Methodological features	Results
Habib[22] • Study design: cross-sectional study • Funding: Hepatitis C Prevention Project (USAID grant)	• Setting and period: Aghour El Soughra, a rural village in Nile Delta, in 1997 • Population: male village inhabitants screened for Hepatitis C. Four-hundred and fifty-five tested positive for Hepatitis C and 1372 tested negative for Hepatitis C (study also recruited females but restricted goza analysis to males)	• Type: Group goza smoking (assessed in men only) • Measurement tool: questionnaire, standardization not reported • Exposure levels of included subjects: not reported	Hepatitis C infection • Measurement tool: second generation Enzyme Immunoassay (Abbott HCV EIA 2.0) • Blinding of outcome adjudicator: not reported	• Selection bias: sample was 'systematically selected' • Information bias: objective outcome measurement: yes, standardized exposure measurement: no • Confounding: adjustment for age, sex, marital status, education, history of invasive medical procedures and dental procedures • Participation rate: half of households selected • 0.15% missing data • Two subjects (goza smokers) excluded for age <20 years • It is not clear how female subjects were dealt with in the regression analyses	• OR for group goza smoking compared with non-group goza smoking = 1.1 95% CI (0.7–1.5) (males ⩾20 years old)
Medhat[44] • Study design: cross-sectional study • Funding: Hepatitis C Prevention Project [USAID grant]	• Setting and period: Community in Upper Egypt, period not reported. • Population: male village inhabitants screened for Hepatitis C. 308 tested positive for Hepatitis C and 2409 tested negative for Hepatitis C (study also recruited females but restricted goza analysis to males)	• Type: group goza smoking (assessed in men only) • Measurement tool: questionnaire, standardization not reported • Exposure levels of included subjects: not reported	Hepatitis C infection • Measurement tool: second generation Enzyme Immunoassay (Abbott HCV EIA 2.0). Of the 523 participants, 514 with positive anti-HCV test results were tested for HCV RNA by a one-step reverse transcriptase-polymerase chain reaction method • Blinding of outcome adjudicator: not reported	• Selection bias: sample represents 62.8% of village inhabitants • Information bias: objective outcome measurement: yes, standardized exposure measurement: no • Confounding: adjustment for age, injection history, hospital or clinical experiences, dental treatments, obstetric exposures (women ⩾20 years), sharing razors within family (males only), circumcision, shaving at community barber (men only), ear piercing	• OR for group goza smoking compared with non-group goza smoking = 0.9 (0.4–2.0) (males ⩽30 years old) • OR for group goza smoking compared with non-group goza smoking = 0.8 (0.5–1.2) (males >30 years old)

(continued)

Table 4 Continued

Study	Population	Exposure	Outcomes	Methodological features	Results
				(females only), tattoo, cautery • Participation rate: 6033 (53.7%) of the 11 227 village inhabitants were included in the study • It is not clear how female subjects were dealt with in the regression analyses	
El-Sadawy[43] • Study design: cross-sectional study • Funding: not reported	• Setting and period: Urban and rural areas of Sharkia Governorate, Egypt; period not reported • Population: male village inhabitants screened for hepatitis C. 217 tested positive for Hepatitis C and 565 tested negative for Hepatitis C (study also recruited females but restricted goza analysis to males)	• Type: Group goza smoking (assessed in men only) • Measurement tool: specifically designed questionnaire; pilot tested before survey for reliability • Exposure levels of included subjects: not reported	Hepatitis C infection • Measurement tool: antibody to HCV assessed by MEIA and HCV RNA tested by real-time PCR • Blinding of outcome adjudicator: not reported	• Selection bias: used 'stratified random sampling, which included systematic sampling • Information bias: objective outcome measurement: yes; however, while 25.8% tested positive by MEIA, 7.66% test positive by PCR; standardized exposure measurement: no (pilot tested only) • Confounding: unclear whether reported results were adjusted for potential confounders • Participation rate not reported • Missing data not reported	• OR for group goza smoking compared with non-group goza smoking =1.02 (0.64–1.62) (males)

MEIA, micro-particle enzyme immunoassay; PCR, polymerase chain reaction.

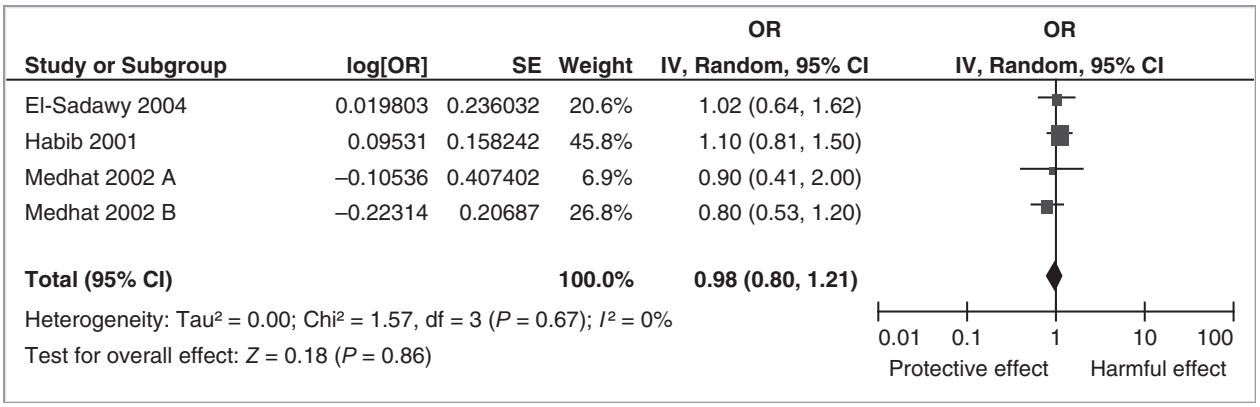

Figure 5 Association between waterpipe tobacco smoking and hepatitis C infection

not exclude important associations. Smoking waterpipe in groups was not significantly associated with hepatitis C infection. The overall quality of evidence varied from very low to low.

To our knowledge, this is the first meta-analysis of studies assessing the association of waterpipe smoking with health outcomes. While Knishkowy *et al*.[24] reviewed the health effects of waterpipe tobacco smoking, they did not use systematic methods, formally evaluate the quality of the evidence or use statistical methods to pool the results across studies. The main strength of our study is the use of the Cochrane Collaboration methodology for conducting systematic reviews, i.e. using a very sensitive and comprehensive search strategy, a duplicate and independent selection process, a duplicate and independent data abstraction process, and a rigorous appraisal of the methodological quality of included studies. We also used the GRADE approach to rate the overall quality of evidence for each outcome.

For most of the outcomes of interest the evidence was either lacking, indirect or of lower quality. In terms of indirectness, lung cancer studies were conducted mostly in China and India where tobacco is typically unprocessed and burned directly by charcoal. The practice of waterpipe smoking that is involved in the recent global epidemic involves tobacco that is processed and flavoured and indirectly heated by the charcoal. In terms of quality, the one methodological study limitation that affected our rating of the quality of evidence for most outcomes was measurement bias, which has been reported in similar systematic reviews.[48] In fact, only one study used a standardized exposure measurement tool in spite of the fact that the practice of waterpipe smoking can vary widely. Variables include the quantity of tobacco used, the type of tobacco used, the concomitant use of other substances, the frequency of smoking sessions, and the length of sessions, the number of years of smoking. In addition, no study reported using a standardized measurement tool for other forms of tobacco smoking in spite of the variety of these forms and the need to account for passive smoking and past smoking history.

The other methodological study limitation that affected our rating of the quality of evidence for many outcomes was the inappropriate handling of confounding, particularly for other forms of tobacco smoking and for factors such as radon exposure among miners as a risk factor for lung cancer. Furthermore, although many studies reported separate ORs for waterpipe and cigarette smoking, none reported tests for interactions between these two forms of smoking. This type of information is needed given that a significant proportion of waterpipe smokers also smoke cigarettes.[11,49]

In spite of the many methodological study limitations for lung cancer and pregnancy outcomes, the findings showed consistency (i.e. the low heterogeneity) across studies. Similarly, the lack of association between smoking waterpipe in groups and hepatitis C infection was characterized by the consistency across studies and a relatively narrow CI. These findings are consistent with current pathophysiological knowledge of the spread of hepatitis C by blood-to-blood contact. While the lack of evidence for an association between waterpipe smoking with bladder cancer, nasopharyngeal cancer, oral dysplasia and infertility could reflect a true absence of association, it could also be explained by lack of power to detect any existing association given their relatively wide CIs. Indeed, the lack of studies and of insufficient data on such long-term health effects is related to the short epidemiological time frame of the recent waterpipe epidemic.

The one study that reported on coronary heart disease was excluded because of its publication exclusively as an abstract.[18] The quality of the evidence from that study was very low and the OR was 2.2 (95% CI 0.9–5.4) for ever smokers and 0.7 (95% CI 0.3–1.9) for current smokers compared with never smokers.

Table 5 Characteristics of included studies assessing the effect of waterpipe tobacco smoking on other outcomes

Study	Population	Exposure	Outcomes	Methodological features	Results
Tamim[45] • Study design: cross-sectional study • Funding: not reported	• Setting and period: students in the second and third intermediate classes from five primary schools in Greater Beirut area, in April 2000 • Population: 625 students with mean age 13 years (range 10–15). 143 students (85 males) reported respiratory tract symptoms, 482 students (237 males) reported no symptoms	• Type: second-hand exposure to cigarettes, narghile • Measurement tool: questionnaire, standardization not reported • Exposure levels of included subjects: not reported	Respiratory illness throughout the year (not seasonal) including nasal congestion or wheezing • Measurement tool: questionnaire assessing clinical condition throughout the year • Blinding of outcome adjudicator: not reported	• Selection bias: sample representative of populations of the five primary schools • Information bias: objective outcome measurement: no, standardized exposure measurement: no • Confounding: no matching or adjustment in the analysis reported • Participation rate: not reported	OR compared with no exposure at home • 2.3 95% CI (1.1–5.1) (narghile only exposure) • 2.5 (1.6–3.8) (narghile and/or cigarette exposure) • 3.2 (1.9–5.4) (cigarette only exposure)
Inhortn[46] • Study design: case–control study Funding: National Science Foundation, the Fulbright Institute for International Education, the US Department of Education Fulbright-Hays Doctoral Dissertation Research Abroad Program and the Soroptimists International Founder Region Fellowship Program	• Setting and period: infertility clinic of the University of Alexandria's Shatby Hospital, the public obstetrics/gynaecology teaching hospital, rural areas of the northwestern Nile Delta region, Egypt; October 1988 to December 1989 • Cases: husbands of 40 female patients of the university infertility clinic who were diagnosed of male-factor infertility (problems of semen and sperm) • Controls: husbands of 90 fertile female patients of the university hospital • Participants: 15–45 years old, lower and lower-middle socio-economic classes	• Type: husbands' waterpipe and cigarette smoking behaviours • Measurement tool: interviews, self-developed semi-structured questionnaire, no standardization reported; participants categorized as regular smokers and never smokers • Exposure levels of included subjects: not reported	Couple infertility associated with male-factor infertility • Measurement tool: medical records of semen analyses • Blinding of outcome adjudicator: not reported	• Selection bias: prevalent cases of infertility, controls were hospital-based and recruited from the same study base as cases • Information bias: objective outcome measurement: yes, standardized exposure measurement: no (second-hand information) • Confounding: matching for age group, socio-economic class; adjustment for cigarette smoking, tea drinking, marital duration, husband's age, husband's education • Participation rate: >98%	OR compared with never smoking: 2.5 (1.0–6.3) (regular waterpipe smoking)

This study indicates the need for more research, as the World Health Organization (WHO) has already advised.[50] The overall quality of evidence for the different outcomes was mostly low, limiting our confidence in the results. There is a need for high-quality cohort studies to identify and quantify with confidence all the health effects of waterpipe smoking and to explore its interaction with other forms of smoking. The high quality of future studies will depend on the use of standardized exposure measurement tools,[49] another area of research need.

The study also has important implications for public health practice. Public health policy makers have to deal with suggestive but generally weak evidence of the association of waterpipe tobacco smoking with deleterious health outcomes. One approach could be to prioritize public health resources to deal with other public health crises (such as youth cigarette smoking) for which the evidence is much stronger, while awaiting further evidence regarding waterpipe smoking. Another approach could be to devote the necessary resources to control at a relatively early stage the rapid growth of the waterpipe trend. Whatever the decision policy makers make, it should be based on an objective consideration of the current available evidence in the proper public health context.

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KEY MESSAGES

- Waterpipe tobacco smoking is possibly associated with a number of deleterious health outcomes including lung cancer, respiratory illness, low birth-weight and periodontal disease.
- There is a need for higher quality evidence to determine with confidence all the health effects of waterpipe tobacco smoking

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Appendix 1 Electronic search strategies

MEDLINE (1950 onward)

Waterpipe*.mp.
''water pipe*''.mp.
shisha*.mp.
sheesha*.mp.
hooka*.mp.
huqqa*.mp.
guza*.mp.
goza*.mp.
narghil*.mp.
nargil*.mp.
arghil*.mp
argil*.mp
(hubbl* adj3 bubbl*).mp.
or/1–13

EMBASE (1988 onward)

Waterpipe*.mp.
''water pipe*''.mp.
shisha*.mp.
sheesha*.mp.
hooka*.mp.
huqqa*.mp.
guza*.mp.
goza*.mp.
narghil*.mp.
nargil*.mp.
arghil*.mp
argil*.mp
(hubbl* adj3 bubbl*).mp.
or/1-13

ISI the Web of Science

(waterpipe* OR ''water pipe*'' OR shisha* OR sheesha* OR hooka* OR huqqa* OR guza* OR goza* OR narghil* OR nargil* OR argil* OR arghil* OR (hubbl* SAME bubbl*)) AND (smoking OR smoke OR health OR disease OR cancer* OR malignan* OR lung* OR pulmonary OR heart OR cardiac OR vascular OR stroke) (in Title or Topic)

Appendix 2 GRADE approach for rating the quality of evidence

Quality is first assigned based on study design	Quality of evidence	Quality is lowered if[a]	Quality is raised if[a]
Randomized trials →	4 = High	Limitations of design	Large effect
		−1 Serious	+ 1 Large
		−2 Very serious	+ 2 Very large
	3 = Moderate	Inconsistency	Dose response
		−1 Serious	+ 1 Evidence of a gradient
		−2 Very serious	
		Indirectness	All plausible confounding
Observational study →	2 = Low	−1 Serious	+ 1 Would reduce a demonstrated effect, or
		−2 Very serious	
		Imprecision	+ 1 Would suggest a spurious effect when results show no effect
		−1 Serious	
	1 = Very low	−2 Very serious	
		Publication bias	
		−1 Likely	
		−2 Very likely	

The quality of evidence reflects the extent of confidence that an estimate of effect is correct.
[a]1, move up or down one grade (for example from high to intermediate); 2, move up or down two grades (for example from high to low).

Factors that lower the quality of evidence

(1) Limitations of design
- Selection bias
- Measurement bias for risk factor (validity of risk factor measurement instrument, blinding of risk status data collector and blinding of risk status adjudicator)
- Measurement bias for outcome (validity of outcome measurement instrument, blinding of outcome data collector and blinding outcome adjudicator)
- Inappropriate handling of confounding (stratification, adjustment)

- Attrition (for cohort studies)

(2) Inconsistency
Inconsistency in the estimates of the association across studies (i.e. heterogeneity) suggests true differences in underlying cause–effect relationship that may arise from differences in:
- populations (e.g. different association in populations with differing other specific exposures or other genetic profiles);
- risk factor (e.g. larger association with higher exposure or different associations with varying forms of the same exposure);
- outcomes (e.g. different associations with different length of follow-up because of diminishing or increasing association with time).

When heterogeneity exists, but investigators fail to identify a plausible explanation, the quality of evidence should be downgraded by one or two levels, depending on the magnitude of the inconsistency in the results.

(3) Indirectness
The question being addressed by the authors of a systematic review is different from the available evidence regarding:
- population (e.g. general population vs population of miners);
- risk factor (e.g. cigarette use vs pipe use);
- outcome (e.g. intra-uterine growth vs low birth-weight)

(4) Imprecision
Results are imprecise when studies include relatively few patients and few events and thus have wide CIs around the estimate of the effect. The 95% CI (or alternative estimate of precision) around the pooled or best estimate of association includes both negligible association and appreciable benefit or appreciable harm.

(5) Publication bias
Publication bias is a systematic underestimate or an overestimate of the underlying beneficial or harmful effect due to the selective publication of studies (publication bias). That is, investigators fail to report studies they have undertaken (typically those that show no effect).

Factors that increase the quality of evidence

(1) Large magnitude of effect
When methodologically strong observational studies yield large or very large and consistent estimates of the magnitude of association, we may be confident about the results. The larger the magnitude of effect, the stronger becomes the evidence.

(2) Dose–response gradient
A gradient dose–response may increase our confidence in the findings and thus enhance the assigned quality of evidence.

(3) Plausible confounding, which would reduce a demonstrated effect
On occasion, all plausible confounders or biases from observational studies would result in an underestimate of the association estimate. If, for instance, only sick patients have an exposure, yet they still fare better, it is likely that the exposure effect is even larger than the data suggest.

Appendix 3 Rating the quality of evidence for different association using the GRADE framework

Outcome	Factors lowering the rating of quality	Factors raising the rating of quality	Final rating
Lung cancer diagnosis	Limitations of design: four of five studies did not appropriately deal with confounding Indirectness: most studies likely used unprocessed tobacco burned directly by charcoal	Dose response: two studies reported statistically significant dose–response relationships in terms of the total amount of exposure and duration of exposure	Very low
Lung cancer mortality	Limitations of design: included study did not appropriately deal with confounding Indirectness: study likely used unprocessed tobacco burned directly by charcoal	None	Very low
Bladder cancer diagnosis	Limitations of design: use of prevalent cases Imprecision	None	Very low
	None		Low

(continued)

Oesophageal cancer	Imprecision	Dose response: the included study reported statistically significant dose response relationship in terms of intensity of use	
Nasopharyngeal cancer	Limitations of design: investigators used matching and adjusted the analysis for a number of confounding factors but not for other types of smoking Imprecision	None	Very low
Oral dysplasia	Limitations of design: not reporting dealing with confounding factors; also the analysis was stratified by chewing side (i.e. analysis of outcome occurring on the chewing side separate from the analysis of outcome occurring on the non-chewing side) Imprecision	None	Very low
Pregnancy outcomes	None	None	Low
Periodontal disease	Limitations of design: included studies partially dealt with confounding factors (three adjusted for age only and one adjusted for age and dental care habit)	Dose response: two studies found a statistically significant dose response relationship in terms of total amount of exposure	Low
Dry socket	Limitations in design: study did not adequately deal with confounding factors	Dose response: statistically significant dose response relationship in terms of total amount of exposure	Low
Hepatitis C infection	Limitations in design: study reported discrepancies between the results of MEIA and PCR	None	Very low
Respiratory illness	Limitations in design: study did not adequately deal with confounding factors	None	Very low
Infertility	None Imprecision	None	Very low

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Commentary: The waterpipe—a global epidemic or a passing fad

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Six years ago, we published in *Tobacco Control* the first comprehensive review about the waterpipe (also known as shisha, hookah, arghile and narghile) in response to what seemed to be a burgeoning global