



OPIUM CONSUMPTION

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TO HUMANS

Table S1.6.2E Exposure assessment quality of mechanistic studies on opium exposure

Reference and outcome	Type of study	Type of assessment	Exposure assessment relative to outcome	Could the “unexposed” reference group include exposed?	Definition of opium exposure	Intensity of exposure	Duration of exposure	Cumulative exposure	Temporality of opium use relative to study outcome	Type of opium exposure	Method of exposure	Co-exposures collected in paper ^a	Exposure assessment methods
Abedi-Ardekani et al. (2011) <i>TP53</i> mutation in oesophageal squamous cell carcinomas	Exposed/Unexposed comparison of cases from Nasrollahzadeh et al. (2008) i.e. from Golestan case-control study	Structured & validated questionnaire (GSCQ)	Retrospective	No	Undefined “Use”	No info	Undefined	No	No info probably past	Undefined subjects used “various forms (smoking or chewing)”	Undefined	Tobacco use (smoking or chewing) ever/never alcohol Farming/raising animals Time to drink after pouring hot tea	Structured questionnaire obtaining detailed information on opium use characteristics. But combined to “use” “never use”
Asgary et al. (2008)	Cross sectional study (Exposed/unexposed comparison)	Structured interview	Unclear (cross-sectional)	Possibly, as they were just “non-addicts”	Undefined “opium addicted men”	No info	Duration of addiction	No info	Recent	Undefined	Smoke Ingest	Smoking tobacco (restricted to tobacco smokers)	Trained nurse interviewed the men about opium and tobacco use. Urinary morphine was assessed
Ayatollahi-Mousavi et al. (2016) Immune function, with and without fungal infection	Cross sectional study (Exposed/unexposed comparison)	Questionnaire	Unclear (cross-sectional)	Possibly, as just defined as “non-addicts” and data not presented for controls	Undefined “addicted to opium”	No info	At least 3 years	No info	Recent	Undefined	Smoke <i>n</i> = 28 Ingest <i>n</i> = 8	Smoking (assumed tobacco) Medicine use (unspecified)	Questionnaire about smoking and narcotic drug use with no details
Dwivedi et al. (2019) Cardiometabolic profile, oxidative stress	Cross sectional study (Exposed/unexposed comparison)	Undefined/unclear	Unclear (cross-sectional)	Probably, as comparison group were addict’s attendees, possible bystander exposure at home?	100 mg/day opiate consumption for a minimum of 1-year abuse and dependence as per ICD 10 classification 1992	Unclear Minimum 100 mg/day consumption	Partial Minimum 1-year abuse and dependence (ICD-10)	No info	Recent	Combined Used pure opium, opium husk, and heroin	Undefined	Smoking tobacco (prob current only) Chewing tobacco (prob current only) Excluded multiple substance abuse.	“Chronic opiate abusers” diagnosed with ICD-10, recruited from de-addiction clinic. Controls were their attendees. No information about how intensity, type of opium or tobacco exposure was collected
Ghazavi et al. (2013b) Cytokines	Cross sectional study (Exposed/unexposed comparison)	Probably Questionnaire	Unclear (cross-sectional)	No; urine drug testing to ensure no morphine	Defined DSM-IV and consumption > 2 g of opium per day for at least 1 year	Range 2–3 g/d	> 1 year	No info	Recent	Raw (Teriak but only in the title and intro as translation for opium)	Smoked	Tobacco smoking Addicts known to abuse alcohol were excluded Urine testing for range of drugs	No details were given about how the opium history was obtained
Ghazavi et al. (2013a) Serum markers of inflammation and oxidative stress	Cross sectional study (Exposed/unexposed comparison)	Probably Questionnaire	Unclear (cross-sectional)	No; urine drug testing to ensure no morphine	Defined DSM-IV and consumption > 2 g of opium per day for at least 1 year	Range 2–3 g/d	> 1 year	No info	Recent	Raw (Teriak but only in the title and intro as translation for opium)	Smoked	Tobacco smoking Addicts known to abuse alcohol were excluded Urine testing for range of drugs	No details were given about how the opium history was obtained
Hashemipour et al. (2013) Cytology of oral mucosa	Cross sectional study (Exposed/unexposed comparison)	Questionnaire	Unclear (cross-sectional)	No; no use of any smoked material for 1 year	Defined Addict based on DSM-IV-TR criteria and using at least 4 g opium per day during three or more of the last six years	Precise 4 groups: < 5 g, 5–7 g, 7–10 g > 10 g per d	Probably Lifetime opium use history Duration in years in results	No info	Recent (use in last 6 months) but could have been much longer	Undefined	Smoke	Smoking tobacco (cigarettes per day and years) Alcohol users excluded	Questionnaire. No details of questions or whether administered or self-completed
Kadivar & Attar (2008) Cell proliferation	Cross sectional study (Exposed/unexposed comparison)	Undefined/unclear	Unclear (cross-sectional)	Possibly, as comparison group were just “non-addicts” with 0 years of opium addiction	Undefined “opium addict”	No info	Lifetime opium use history Duration in years in results	No	Recent	Undefined	Undefined	Smoking tobacco	No details given
Mohammadi et al. (2016) Clinical and	Case series	Patient records	Unclear (cross-sectional)	Possibly, as comparison group were just non-addicts	Undefined “Patients who used opium”	No info	Undefined	No info	No info	Undefined	Undefined but most common route was injection but	Alcohol Yes/No	Investigation of HIV patients. 5/99 participants used opium and no details of type/usage

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laboratory profiles of HIV patients											various drugs included		
Nabati et al. (2013) Cytokines in addict/non addict participants’ plasma and lymphocytes cultured with and without opium	Cross sectional study (Exposed/unexposed comparison)	Probably Questionnaire	Unclear (cross-sectional)	No	Defined opium-addict, consumption > 0.5 g of opium per day for at least 1 year	Unclear Must have been collected but data not presented	Undefined	No info	Recent	Undefined	Smoked	Excluded if: Cigarette smokers; or Consumption of other components of opium (Heroin, morphine, etc.)	No details were given about how the opium history was obtained
Saadat et al. (2012) Cytokine levels in patients with coronary artery disease	Cross sectional study (Exposed/unexposed comparison)	Undefined/unclear	Unclear (cross-sectional)	Possibly, as just specifies “non-addicted”	Undefined “opium addiction”	No info	Undefined	No info	Recent	Raw	Smoked	Tobacco; all participants were current smokers	No details were given about how the opium history was obtained
Safarinejad et al. (2013a) Sperm, oxidative stress	Cross sectional study (Exposed/unexposed comparison)	Questionnaire Biomarkers	Unclear (cross-sectional)	Possibly, they did test urine of all subjects for opioids but results not presented	Defined DSM-IV-TR opium addiction Also opioid positive urine	Precise Nokhods/day (0.1935 g) Heroin mg/d	Lifetime opium use Months of dependence	No info	Recent	Raw Prepared Both Inject	Smoke Ingest Both Inject Other - sniffing/snorting	Smoking tobacco Alcohol (dependency) Chemical exposure (unclear) Other dugs use tested in urine	Could be questionnaire or interview. Opium use validated by opioid in urine but results not presented and no individual results for opium only presented
Salarian et al. (2018) Serum markers of inflammation and oxidative stress before and after methadone treatment	Cross sectional study (Exposed/unexposed comparison) (baseline data from intervention study)	Clinical interview Biomarkers	Cross-sectional	No; Urine test negative for opioids for all comparison subjects	Defined DSM-IV-TR opium addiction at least 1 year of opium use; at least 1 g opium [per day]*? Opioid-positive urine test	Unclear	Partial (> 1 year)	No info	Recent	Undefined	Smoke Ingest Both?	Smoking tobacco (average 1.31 pack per d)*	Data collected at clinical interview. Opium use validated by opioid in urine
Shojaeepour et al. (2018) Oxidative stress in lead-adulterated opium-users	Cross sectional study (Exposed/unexposed comparison)	Questionnaire Interview Biomarkers	Retrospective	Yes (healthy controls with no occupational contact with lead)	Undefined “opium addict”	No info	Undefined	No info	Recent (admitted to hospital with symptoms of lead poisoning due to consumption of lead-adulterated opium)	Undefined	Smoke Ingest Both	Tobacco smoking	Data collected by questionnaire. Unclear if opium use was validated

^a Tobacco use, alcohol, household fuel, diet, occupation. If these were stated as being assessed in the study they are listed here, whether or not they were used in analyses.

*[The Working Group noted that the paper did not provide a time for the use and felt it was most likely that this was 1 g opium per day.]

**[The Working Group noted that the paper described the average smoking by participants as being “1.31 pack per year” but it was more likely that it would be 1.31 packs a day.]

d, day; ICD, International Classification of Diseases.

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