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TO HUMANS

Table S1.6.2A Exposure assessment quality of studies on cancer of the oesophagus and opium consumption

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 ^a	Type of opium exposure	Method of exposure	Co-exposures collected in paper ^b
Sheikh et al. (2020)	Golestan Cohort study	Structured & validated questionnaire (GCSQ)	Prospective	Yes. Includes those who used for < 6 months and/or < 1 × per week	Defined (used opium at least once per week for at least 6 months)	Precise nokhod/d d/wk	Lifetime opium use history	Yes Nokhod- years	Past Combined	Raw Prepared Dross $(n = 6)$ Combined Other heroin $(n = 4)$	Smoke Ingest Both smoke and ingest	Smoking tobacco cumulative pack years Hookah use ever/never Chewing tobacco (nass) cumulative nass years Alcohol ever/never Food quality household fuel
Khademi et al. (2012) Mortality from all cancers, oesophagus, stomach, lung and other cancers	Golestan Cohort Study	Structured & validated questionnaire (GSCQ)	Prospective	Yes. Includes those who used for < 6 months and/or < 1 × per week	Defined (used opium at least once per week for at least 6 months)	Precise nokhod/d d/wk	Lifetime opium use history	Yes Nokhod- days	Past Combined	Raw Prepared Dross $(n = 6)$ Combined Other heroin $(n = 4)$	Smoke Ingest Both smoke and ingest	Smoking tobacco Alcohol Both ever/never
Malekzadeh et al. (2013) Malignant GI mortality	Golestan Cohort Study	Structured & validated questionnaire (GSCQ)	Prospective	Yes. Includes those who used for < 6 months and/or < 1 × per week	Defined (used opium at least once per week for at least 6 months)	Precise nokhod/d d/wk	Lifetime opium use history	Yes Nokhod- days	Past Combined	Raw Prepared Dross $(n = 6)$ Combined Other heroin $(n = 4)$	Smoke Ingest Both smoke and ingest	Smoking tobacco Alcohol Both ever/never
Shakeri et al. (2012)	Case control (Golestan case control study)	Structured & validated questionnaire (GCSQ)	Retrospective	Yes. Includes those who used for < 6 months and/or < 1 × per week	Defined (used opium at least once per week for at least 6 months)	Precise number of times/day, assumes 1 nokhod each time	opium use	Yes in the community study) No in the hosp study)	Combined	Raw Prepared Dross (none) Combined Other heroin (none)	Smoke Ingest Both smoke and ingest	Smoking tobacco Hookah tobacco Chewing tobacco (nass) Alcohol Food Other (age, sex, place of residence, education, ethnicity)
Nasrollahzadeh et al. (2008)	Case control (Golestan case control study)	Structured & validated questionnaire (GCSQ)	Retrospective	Yes. Includes those who used for < 6 months and/or < 1 × per week	Defined (used opium at least once per week for at least 6 months)	Precise nokhod/d d/wk	Lifetime opium use history	Yes Nokhod- years	Combined	Raw Prepared Dross (none) Combined Other heroin (none)	Smoke Ingest Both smoke and ingest	Smoking tobacco Hookah tobacco Chewing tobacco (nass) Alcohol Food Other (age, sex, place of residence, education, ethnicity)
Bakhshaee et al. (2017)	Case control	Interview (not clear how systematic)	Retrospective	Yes. Includes those who used for < 1 year and/or < 1 × per day	Defined (used opium at least once per day for a minimum of one year)	Undefined	Undefined	No	Combined	Undefined	"Snuffing" presumably smoking	Smoking tobacco
Pournaghi et al. (2019)	Case control	Structured interview/ questionnaire	Retrospective	No, "never consumption"	Undefined "drug use" with opium then specified	Imprecise (overlapping categories) number of times consumed per day ≤ 1 , 1–3, versus ≥ 3	Duration of use presented in 10-year groups	No	Recent Past	Undefined	Smoke Ingest	Smoking tobacco Hookah tobacco Alcohol Other: age, sex, place of residence

^a Indicates proximity of assessed exposures to the time of cancer occurrence: response options are "recent," "past," "combined," "no info".

^b Tobacco use, alcohol, household fuel, diet, tea temperature, occupational exposures and other co-exposures included in the study are listed here.

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d, day; GI, gastrointestinal; wk, week.

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