Appendix: Supplementary tables [posted as supplied by author]

Table A. Hazard ratios and 95% confidence intervals for the associations between subtypes of opium use in relation to overall mortality

Opium types	Number of participants (person years)	Number of deaths (Crude rate[1])	Cox HR	
			Unadjusted	Adjusted[2]
none	41,558 (196,825)	1,440 (731)	ref	ref
Any Type	8,487 (38,103)	705 (1,850)	2.26 (2.06 to 2.47)	1.86 (1.68 to 2.06)
Teriak only	7,308 (33,249)	605 (1,819)	2.21 (2.01 to 2.43)	1.83 (1.65 to 2.03)
Sukhteh only	6 (27)	0 (0)	-	-
Shireh only	721 (3,174)	66 (2,079)	2.65 (2.07 to 3.39)	2.19 (1.70 to 2.82)
Heroin only	4 (13)	3 (22,149)	34.0 (10.9 to 105)	25.4 (8.11 to 79.4)
Combinations[3]	359 (1,639)	31 (1,891)	2.28 (1.60 to 3.26)	1.78 (1.24 to 2.56)

[1] Crude death rate in 10^5 person years
[2] Adjusted for gender, ethnicity, education level, marital status, residential place, and cigarette smoking
[3] All two-way and three-way, and four-way combinations of opium use; the large majority (75%) were a combination of teriak and shireh use

Table B. Hazard ratios and 95% confidence intervals for opium cumulative use in relation to overall and cause-specific mortality in the Golestan Cohort Study

	Never users	Ex-users	Current users	Opium cumulative use in current opium users					
				1st quintile (≤1200)£	2nd quintile (1201-4696)£	3rd quintile (4697-12418)£	4th quintile (12419-30681)£	5th quintile (≥30682)£	*P* for trend¥
All causes									
N. of deaths	1,440	63	642	121	123	111	130	157	-
Cox HR€, all	ref	1.29 (1.00 to 1.67)	1.94 (1.75 to 2.16)	1.94 (1.61 to 2.35)	2.00 (1.65 to 2.41)	1.75 (1.43 to 2.13)	1.98 (1.64 to 2.39)	2.03 (1.70 to 2.43)	0.115
Cox HR, bef. dis.‡	ref	1.27 (0.98 to 1.65)	1.70 (1.52 to 1.90)	1.43 (1.14 to 1.79)	1.71 (1.39 to 2.10)	1.69 (1.36 to 2.08)	1.93 (1.60 to 2.33)	1.98 (1.65 to 2.39)	<0.001
Circulatory causes									
N. of deaths	738	38	297	58	63	50	68	58	-
Cox HR, all	ref	1.57 (1.12 to 2.20)	1.84 (1.58 to 2.14)	1.88 (1.43 to 2.46)	2.08 (1.60 to 2.71)	1.60 (1.19 to 2.15)	2.11 (1.63 to 2.74)	1.55 (1.17 to 2.06)	0.898
Cox HR, bef. dis.‡	ref	1.40 (0.98 to 1.99)	1.53 (1.30 to 1.80)	1.11 (0.78 to 1.59)	1.49 (1.09 to 2.03)	1.62 (1.19 to 2.20)	2.04 (1.57 to 2.64)	1.41 (1.04 to 1.91)	0.015
Cancer causes									
N. of deaths	312	8	129	17	21	19	28	44	-
Cox HR, all	ref	0.77 (0.38 to 1.57)	1.73 (1.37 to 2.18)	1.26 (0.77 to 2.07)	1.55 (0.99 to 2.44)	1.34 (0.83 to 2.15)	1.95 (1.30 to 2.92)	2.50 (1.77 to 3.54)	0.006
Cox HR, bef. dis.‡	ref	0.81 (0.39 to 1.64)	1.79 (1.41 to 2.26)	1.40 (0.85 to 2.30)	1.46 (0.91 to 2.35)	1.44 (0.88 to 2.34)	1.96 (1.31 to 2.94)	2.60 (1.82 to 3.72)	0.006
Respiratory causes									
N. of deaths	43	4	48	8	10	7	11	12	-
Cox HR, all	ref	2.02 (0.70 to 5.84)	4.05 (2.52 to 6.52)	3.74 (1.72 to 8.14)	4.61 (2.24 to 9.47)	3.10 (1.34 to 7.13)	4.63 (2.28 to 9.40)	4.19 (2.06 to 8.52)	0.541
Cox HR, bef. dis.‡	ref	2.01 (0.69 to 5.82)	3.85 (2.36 to 6.29)	2.54 (0.98 to 6.58)	5.65 (2.86 to 11.1)	2.38 (0.91 to 6.22)	4.05 (1.94 to 8.46)	4.51 (2.20 to 9.23)	0.365
Digestive causes									
N. of deaths	37	4	28	5	7	7	3	6	-
Cox HR, all	ref	3.01 (1.02 to 8.85)	3.14 (1.80 to 5.47)	2.79 (1.07 to 7.24)	4.25 (1.83 to 9.89)	4.09 (1.75 to 9.56)	1.67 (0.50 to 5.62)	2.96 (1.17 to 7.49)	0.489
Cox HR, bef. dis.‡	ref	3.06 (1.04 to 9.02)	3.16 (1.78 to 5.60)	3.05 (1.17 to 7.98)	3.88 (1.58 to 9.53)	5.26 (2.33 to 11.9)	0.56 (0.07 to 4.17)	3.37 (1.32 to 8.57)	0.369
Infectious causes									
N. of deaths	21	1	29	9	6	3	2	9	-
Cox HR, all	ref	1.37 (0.18 to 10.5)	6.05 (3.17 to 11.6)	9.94 (4.37 to 22.6)	6.56 (2.53 to 17.0)	3.17 (0.91 to 11.1)	2.09 (0.47 to 9.30)	8.12 (3.31 to 19.9)	0.650
Cox HR, bef. dis.‡	ref	1.25 (0.16 to 9.70)	5.23 (2.66 to 10.3)	8.21 (3.32 to 20.3)	5.47 (1.97 to 15.2)	2.21 (0.50 to 9.85)	3.87 (1.25 to 12.0)	6.37 (2.41 to 16.8)	0.834

€ All Cox HRs are adjusted for gender, ethnicity, education level, marital status, residential place, and cigarette smoking

‡ Excluding subjects who started opium use after being diagnosed with a serious disease (ischemic heart disease, cerebrovascular accidents, hypertension, or diabetes mellitus)

£ Quantities in parentheses are the cumulative opium use amounts in nokhod-days unit

¥ P for trend is calculated by assigning consecutive integers to quintiles of cumulative opium use in current opium users

Table C. Estimated hazard ratios for all cause and cause-specific mortality in ever opium user groups in total and also after excluding events that happened in first 6, 12, 18, and 24 months of follow up.

	Adjusted Cox HRs in opium users	Adjusted Cox HRs in opium users after excluding deaths happened in first							
		6 months		12 months		18 months		24 months	
		No.*	Cox HR (95%CI)	No.*	Cox HR (95%CI)	No.*	Cox HR (95%CI)	No.*	Cox HR (95%CI)
All causes	1.86 (1.68 to 2.06)	1977	1.84 (1.65 to 2.05)	1772	1.81 (1.62 to 2.03)	1552	1.81 (1.60 to 2.05)	1319	1.85 (1.62 to 2.11)
Circulatory causes	1.81 (1.56 to 2.09)	980	1.86 (1.59 to 2.16)	867	1.83 (1.55 to 2.15)	769	1.88 (1.58 to 2.23)	654	1.99 (1.65 to 2.40)
Cancer causes	1.61 (1.28 to 2.03)	416	1.51 (1.19 to 1.92)	373	1.43 (1.11 to 1.84)	321	1.39 (1.05 to 1.82)	271	1.43 (1.06 to 1.94)
Respiratory causes	3.78 (2.36 to 6.04)	86	3.59 (2.19 to 5.88)	79	3.54 (2.11 to 5.93)	70	3.86 (2.22 to 6.70)	62	3.15 (1.76 to 5.66)
Digestive causes	3.12 (1.82 to 5.37)	67	3.07 (1.77 to 5.31)	60	2.96 (1.66 to 5.29)	52	3.08 (1.65 to 5.75)	44	2.99 (1.51 to 5.90)
Infectious causes	5.47 (2.87 to 10.4)	47	5.45 (2.81 to 10.6)	45	5.20 (2.65 to 10.2)	37	4.56 (2.17 to 9.59)	34	5.02 (2.31 to 10.9)

* The number of outcomes

Table D Hazard ratios (95% confidence interval) for the association between opium use and overall mortality, after adjusting for several alternative covariates.

Cox Regression Model	Cox HRs in opium users (95% CI)
Unadjusted model	2.26 (2.06 to 2.47)
Adjusted Model 1: Adjusted for sex, residential place, ethnicity, marital status, education level, cigarette smoking	1.86 (1.68 to 2.06)
Adjusted Model 2: model 1 plus adjustment for body mass index (kg/(cm)^2) as categorical variable (WHO classification)	1.82 (1.64 to 2.02)
Adjusted Model 3: model 1 plus adjustment for body mass index (kg/(cm)^2) as continuous variable	1.84 (1.65 to 2.04)
Adjusted Model 4: model 1 plus adjustment for height (cm) as a continuous variable	1.86 (1.68 to 2.06)
Adjusted Model 5: model 1 plus adjustment for alcohol consumption	1.87 (1.68 to 2.07)
Adjusted Model 6: model 1 plus adjustment for composite wealth score	1.81 (1.64 to 2.01)
Adjusted Model 7: model 1 plus adjustment for intake of fruits and vegetables	1.88 (1.69 to 2.08)
Adjusted Model 8: model 2 plus adjustment for alcohol consumption	1.82 (1.64 to 2.02)
Adjusted Model 9: model 8 plus adjustment for composite wealth score	1.79 (1.61 to 1.98)
Adjusted Model 10: model 9 plus adjustment for intake of fruits and vegetables	1.81 (1.63 to 2.01)

Table E. Hazard ratios and 95% confidence intervals for the association between methods of opium use (smoking, ingestion, or both) and overall and cause-specific mortality in Golestan Cohort Study

Routes of opium administration	Cox HR			
	Unadjusted	Adjusted[€]		
	Overall	Overall	Males	Females
All deaths				
Smoking	2.01 (1.80 to 2.26)	1.68 (1.48 to 1.90)	1.50 (1.29 to 1.73)	2.02 (1.61 to 2.54)
Ingestion	2.55 (2.24 to 2.91)	2.08 (1.81 to 2.40)	1.76 (1.48 to 2.09)	2.92 (2.31 to 3.69)
Both ways	2.85 (2.20 to 3.70)	2.34 (1.80 to 3.06)	2.06 (1.52 to 2.80)	3.47 (2.03 to 5.93)
Circulatory deaths				
Smoking	2.02 (1.72 to 2.37)	1.75 (1.48 to 2.08)	1.47 (1.20 to 1.80)	2.45 (1.81 to 3.31)
Ingestion	2.11 (1.73 to 2.57)	1.83 (1.48 to 2.26)	1.54 (1.19 to 1.99)	2.56 (1.80 to 3.65)
Both ways	2.21 (1.47 to 3.31)	1.93 (1.27 to 2.92)	1.64 (1.02 to 2.66)	2.99 (1.32 to 6.76)
Cancer deaths				
Smoking	1.82 (1.41 to 2.34)	1.48 (1.13 to 1.95)	1.56 (1.13 to 2.15)	1.35 (0.77 to 2.37)
Ingestion	2.14 (1.58 to 2.90)	1.67 (1.21 to 2.31)	1.76 (1.21 to 2.58)	1.45 (0.75 to 2.79)
Both ways	3.24 (1.93 to 5.45)	2.55 (1.49 to 4.35)	2.66 (1.48 to 4.77)	2.14 (0.52 to 8.81)
Respiratory deaths				
Smoking	3.44 (2.00 to 5.90)	2.42 (1.34 to 4.36)	1.76 (0.85 to 3.63)	3.87 (1.50 to 10.0)
Ingestion	7.89 (4.70 to 13.0)	5.35 (3.05 to 9.36)	3.38 (1.67 to 6.86)	10.4 (4.49 to 23.9)
Both ways	12.6 (5.88 to 26.9)	8.44 (3.77 to 18.9)	6.36 (2.48 to 16.3)	15.4 (3.43 to 69.1)
Digestive deaths				
Smoking	2.91 (1.57 to 5.39)	2.26 (1.16 to 4.40)	2.19 (1.01 to 4.75)	2.48 (0.68 to 9.02)
Ingestion	5.81 (3.15 to 10.7)	4.64 (2.37 to 9.10)	4.40 (1.96 to 9.87)	5.13 (1.56 to 16.9)
Both ways	5.84 (1.79 to 19.0)	4.59 (1.36 to 15.5)	5.82 (1.66 to 20.4)	-
Infectious deaths				
Smoking	5.53 (2.85 to 10.7)	4.66 (2.24 to 9.71)	3.06 (1.26 to 7.46)	6.37 (1.92 to 21.2)
Ingestion	8.83 (4.38 to 17.8)	7.02 (3.21 to 15.3)	4.52 (1.66 to 12.3)	11.2 (3.68 to 34.1)
Both ways	6.74 (1.57 to 28.9)	5.53 (1.23 to 24.8)	2.68 (0.33 to 21.5)	17.6 (2.17 to 142)

[€] Adjusted for gender, ethnicity, education level, marital status, residential place, and cigarette smoking