بسم الله الرحمن الرحيم



Ref:

Epidemiology of pancreatic cancer

Dr MM.Malekzadeh

Mashhad, MUMS

Imam Reza Hospital



Ref:

Content

- Global incidence and prevalence
- National and subnational incidence and prevalence
- Non-genetic risk factor of pancreatic cancer
  - Gender
  - Smoking
  - Diabetes
  - Obesity
  - Alcohol
  - Opium



Ref:

Global prevalence and incidence

- The past two decades: doubling in the annual number of PC
  - Aging of world population
  - Improved diagnosis
  - Increased prevalence of risk factors (especially, in high- income nations)
- Age standardized incidence rates:
  - 5.0 per 100,000 person- years in 1990
  - 5.7 (5.6–5.8) per 100,000 person- years in 2017.



Ref:Alison P.Klein 2021, Nature gastro

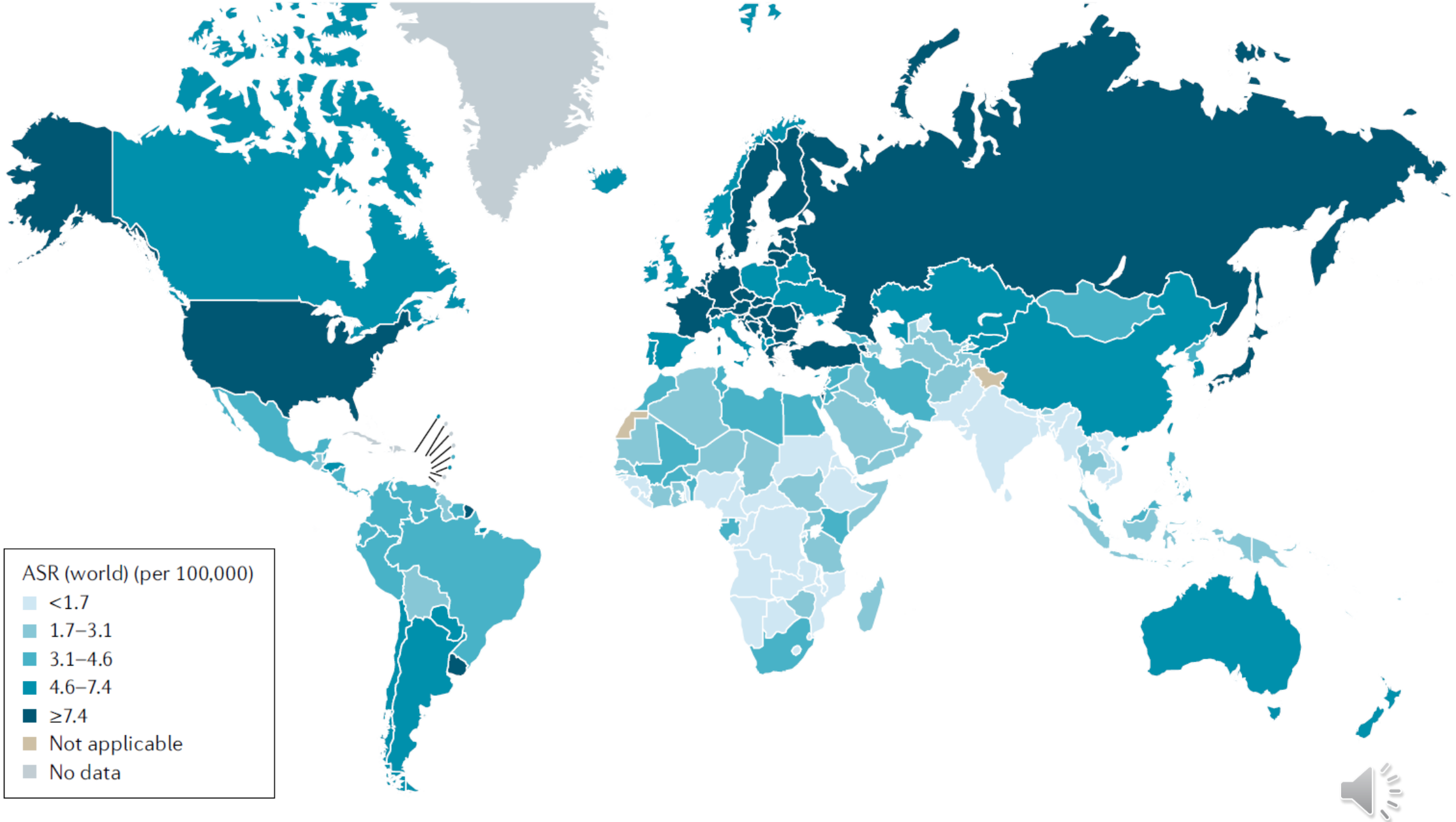


Fig. 1 | **Incidence of pancreatic cancer.** Age-standardized incidence rates (ASR) of pancreatic cancer across the globe in 2020. Figure adapted with permission from REF.[5], International Agency for Research on Cancer (accessed 14 April 2021).

RESEARCH ARTICLE

Editorial Process: Submission:06/12/2022 Acceptance:11/02/2022

Pancreatic Cancer in Iran - Result of the Iranian National Cancer Registry Program

Saba Alvand[1]*, Gholamreza Roshandel[2], Peyman Nejat[3], Hossein Poustchi[1]

Abstract

Objective: In this article, we aimed to report the incidence rate of PC at the national and regional levels of Iran from 2014 to 2017 for the first time based on the IARC protocols. **Methods:** The data was recruited from the Iranian national program of cancer registry, a national cancer registry program reformed in 2014 after including cancer diagnosis based on clinical judgment and death certificates. This registry includes data from the pathology laboratories and clinical sectors included with death certificates from 60 medical universities in 31 provinces of Iran. Age-standardized incidence rates were calculated at the national and regional levels. **Results:** From 2014 to 2017, 8851 new cases (males=60.46%) were diagnosed, with a mean age of 66.2 ± 19.6. Forty-one percent of the patients were diagnosed by microscopic verification, and 51% were diagnosed based on clinical judgment without microscopic verification and death certificates. The age-standardized incidence rate was measured as 3.45 per 100,000 in 2017, with the highest rates in individuals older than 85 (30.91 per 100,000), and the provinces of Qom, Tehran, and Isfahan recorded the highest incidence rates with 3.87, 3.85, and 3.66 per 100,000 respectively. **Conclusions:** PC incidence in Iran is still lower than in western countries. However, the incidence from 2014 to 2017 is higher than previous national and regional reports and should not be overlooked. Improvement in the national cancer registry program and documentation may be reasons for this difference.

Keywords: Incidence- Iran- pancreatic neoplasms- registries

Epidemiology of PC in Iran

- Iran national cancer registry by Alvand, 2022
  - The age-standardized incidence rate: **3.45** per 100,000 in 2017
  - The highest rates: age> than 85 (30.91 per 100,000)
  - Highest rate in provinces of Qom, Tehran, and Isfahan rates (3.87, 3.85, and 3.66 per 100,000 respectively)
- Masoompour, 2011
  - Overall incidence of pancreatic cancer in southern Iran was 1.18 in males and 0.84 in females in 100,000 in 2002.
  - The incidence was increasing during study period



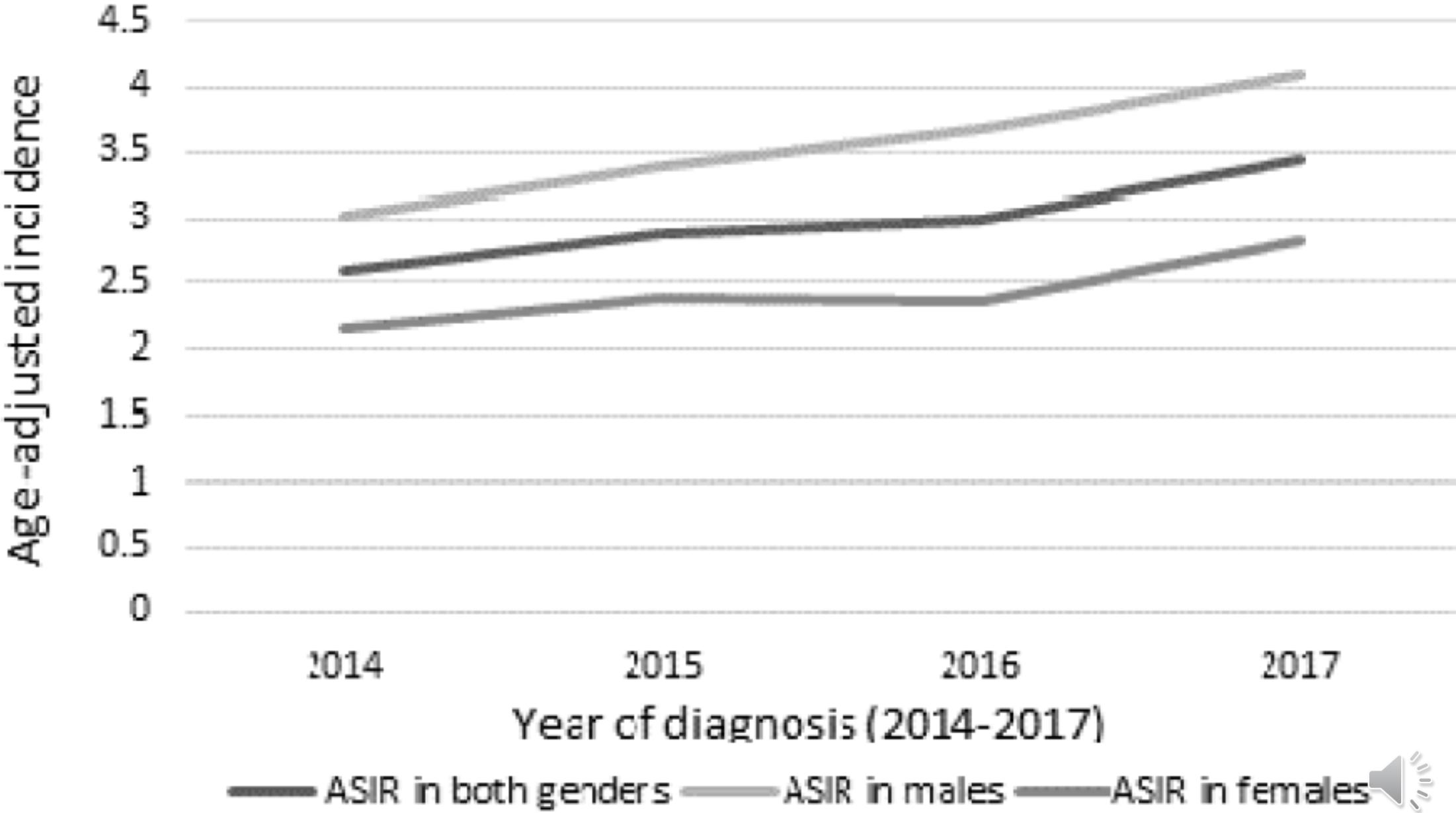
Ref:Siri 2020

Iranian national cancer registry

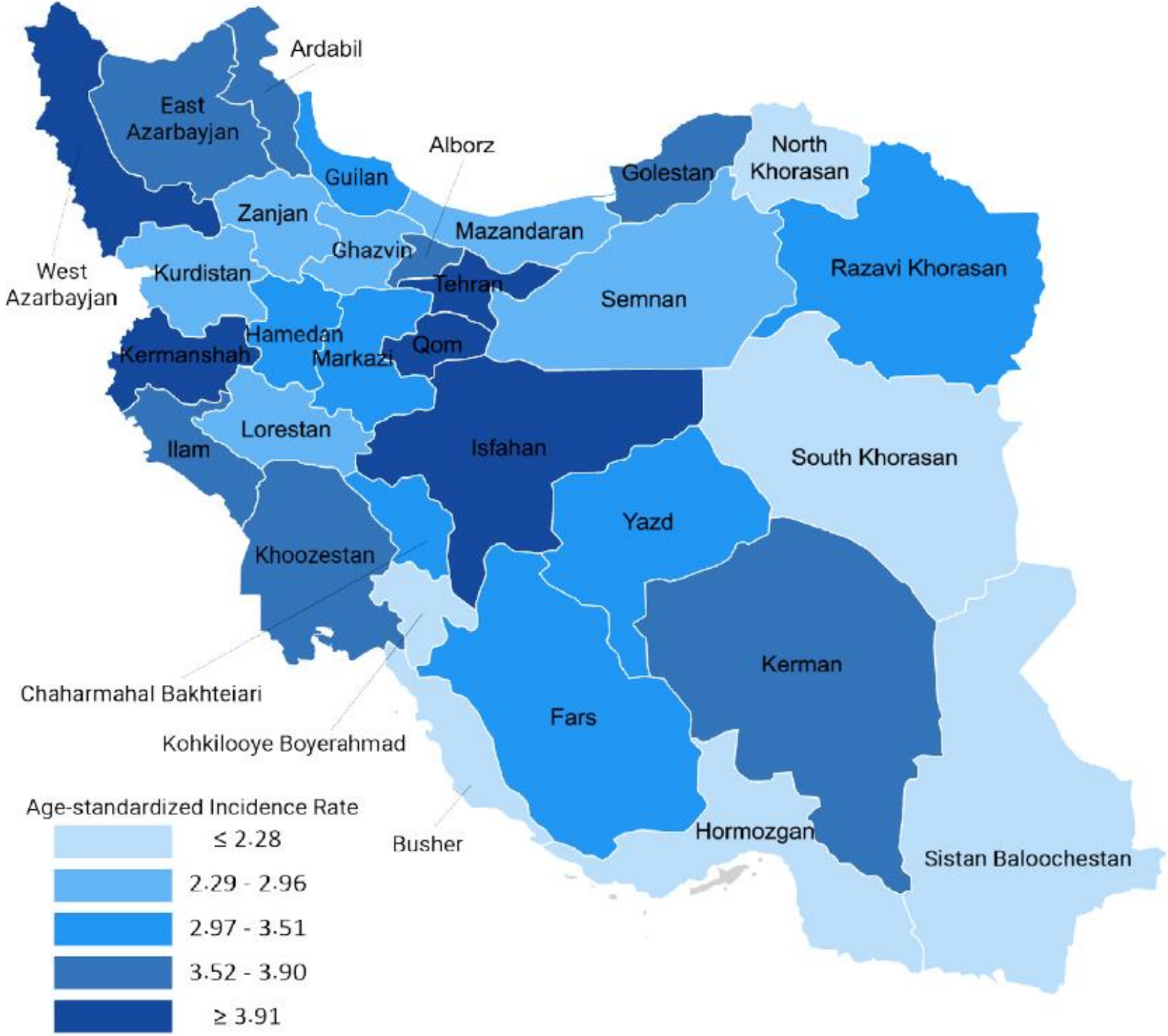
- Incidence of PC in Iran is lower than in western countries
- The incidence grown dramatically in recent years because:
  - The aging of the population,
  - Rise in risk factors
  - Improvement in cancer registry documentation
  - Improvement in pancreatic cancer diagnosis.

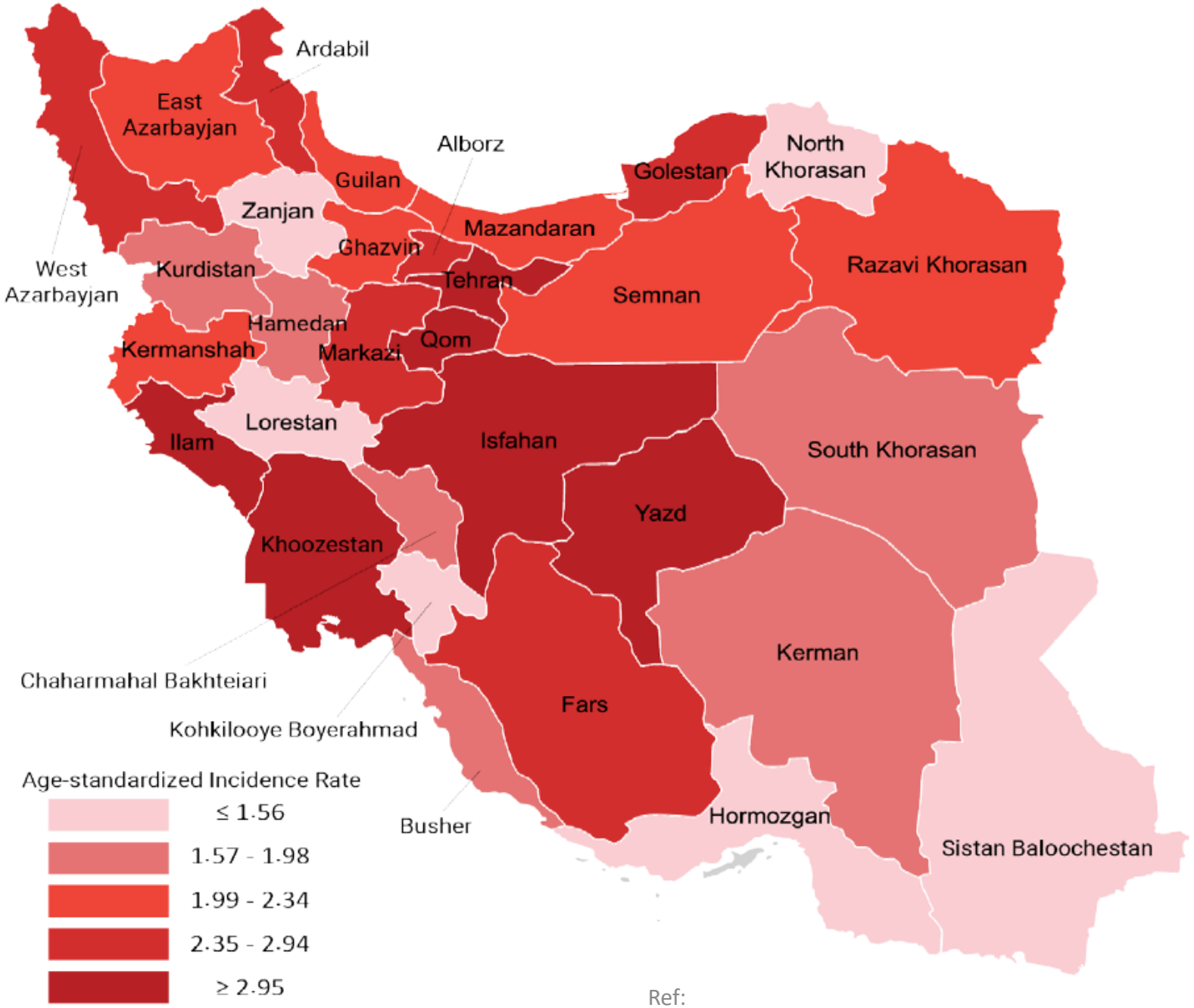


Ref:


Age-adjusted incidence
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
2014
2015
2016
2017
Year of diagnosis (2014-2017)
ASIR in both genders
ASIR in males
ASIR in females

Ref:


Ardabil
East Azarbayjan
Alborz
Guilan
Golestan
North Khorasan
Zanjan
Mazandaran
Ghazvin
Razavi Khorasan
West Azarbayjan
Kurdistan
Tehran
Semnan
Hamedan
Qom
Kermanshah
Markazi
Lorestan
Ilam
Isfahan
South Khorasan
Yazd
Khoozestan
Kerman
Chaharmahal Bakhteiari
Fars
Kohkilooye Boyerahmad
Busher
Hormozgan
Sistan Baloochestan
Age-standardized Incidence Rate
≤ 2.28
2.29 - 2.96
2.97 - 3.51
3.52 - 3.90
≥ 3.91


Ardabil
East Azarbayjan
Alborz
Guilan
Golestan
North Khorasan
Zanjan
Mazandaran
Ghazvin
West Azarbayjan
Kurdistan
Tehran
Semnan
Razavi Khorasan
Hamedan
Qom
Kermanshah
Markazi
Lorestan
Ilam
Isfahan
South Khorasan
Yazd
Khoozestan
Kerman
Chaharmahal Bakhteiari
Fars
Kohkilooye Boyerahmad
Busher
Hormozgan
Sistan Baloochestan
Age-standardized Incidence Rate
≤ 1.56
1.57 - 1.98
1.99 - 2.34
2.35 - 2.94
≥ 2.95

Ref:

Cigarette smoking

- Well established risk factor
- A meta-analysis : odds ratio of 1.74 (95% CI 1.61–1.87) for current smoker compared to never smoker
- Dose-dependent
- As the patient stop smoking the risk decreases



Ref: Klein, 2021

Diabetes mellitus

- Both a risk factor for pancreatic cancer and a consequence of cancer
- Longstanding diabetes (>3 years) has been associated with a **1.5–2.4- fold** increased risk of pancreatic cancer
- Patient with new- onset diabetes
  - 1% of patient with newly diagnosed DM will develop PC in 3 years (mayo clinic study)
  - Another study showed lower risk of 0.3% (US Department of Veteran Affairs)
- The prevalence of diabetes has increased globally:
  - From 4.3% in 1980 to 9.0% in 2014 in men, and from 5.0% to 7.9% in women.
  - Explain the increase of incidence of PC despite a decreasing prevalence of cigarette smoking.



Ref: Klein, 2021

Body mass index

- Increased weight or BMI has been shown to increase the risk of pancreatic cancer
- relative risk of pancreatic cancer in individuals with a BMI of >30 kg/m2 Vs. BMI of <23 kg/m2: 1.72 (95% CI 1.19–2.4)
- The global prevalence of obesity has tripled since 1975, which will probably lead to an increasing burden of pancreatic cancer



Ref: Klein, 2021

Alcohol

- Alcohol intake, particularly heavy alcohol intake, is associated with pancreatic cancer risk
- Pooled analysis showed a relative risk of 1.22 (95% CI 1.03–1.45) of pancreatic cancer (drink>30 g/d Vs. nondrinker)



Ref: Klein, 2021

Pancreatitis

- Pancreatitis is a risk factor for pancreatic cancer
  - Inflammation and damage can lead to the development of cancer
- A pooled analysis within the PanC4 consortium showed that 6% of patients with pancreatic cancer reported a history of pancreatitis compared with 1% of control individuals
- A recent diagnosis of pancreatitis (<1 year) was associated with an odds ratio of **21.35** (95% CI 12.03–37.86) for pancreatic cancer
- Whereas individuals diagnosed with pancreatitis >2 years previously had an odds ratio for pancreatic cancer of **2.71** (95% CI 1.96–3.74)



Ref: Klein, 2021

Allergy

- Individuals with a personal history of allergies have been shown to be protected against pancreatic cancer
  - Active immune system might have increased anti-tumour immunity
- A 2005 meta- analysis of 14 studies:
  - Relative risk of **0.83** (95% CI 0.68–0.80) for pancreatic cancer in individuals with a history of allergy compared to those without



Ref: Klein, 2021

Microbiota

- A meta-analysis demonstrated that periodontal disease and tooth loss is associated with **a 50–70%** increased risk of pancreatic cancer
- The oral microbiota has been associated with future risk of pancreatic cancer
  - *Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans*
  - in 361 individuals who developed pancreatic cancer and 371 matched controls
- Infection with *Helicobacter pylori* has also been associated with pancreatic cancer in some studies.
- Further studies are needed to determine if inconsistency in the results



Ref: Klein, 2021

Environmental factors

- One study in Mayo clinic showed that patient with PC had more environmental exposure than matched control:
  - Pesticides (OR 1.21, 95% CI 1.02–1.44)
  - Asbestos (OR 1.54, 95% CI 1.23–1.92)
  - Benzene (OR 1.70, 95% CI 1.23–2.35)
  - Chlorinated hydrocarbons (OR 1.63, 95% CI 1.32–2.02).
  - However, this study was based on retrospective self- reported lifetime exposures and differential recall between cases and controls might have led to biased associations.
- One Spanish study
  - 118 patients with pancreatic cancer and 339 hospital- based controls
  - Association was found between the risk of pancreatic cancer and the **levels of lead, nickel, selenium, cadmium** and arsenic in toenail samples.
- Further studied should be done



Ref: Klein, 2021

Table 1 | **Pancreatic cancer risk factors**

Risk factor	Associated risk of pancreatic cancer	Refs
Cigarette smoking	~1.7-fold increased risk compared with never smokers	13–16
Obesity	~1.6-fold increased risk in individuals with obesity compared with those with normal weight	39,40,42
Alcohol use	1.6-fold increased risk in those consuming >6 drinks per day compared with those consuming >1 drink per day	45–49
New-onset diabetes	<0.3–0.8% of patients with new-onset diabetes develop pancreatic ductal adenocarcinoma within 3 years of diabetes diagnosis	31–33
Long-standing diabetes	1.5–2-fold increased risk of pancreatic cancer for individuals with diabetes of >3 years in duration	26–30
Family history of pancreatic cancer	Twofold increased risk in individuals with a single family member with pancreatic cancer compared with the general population; sevenfold increased risk in individuals with multiple family members with pancreatic cancer compared with the general population	78
Pancreatitis	Twofold to threefold increased risk in individuals with long-standing chronic pancreatitis	50–52
Allergy	25% lower risk of developing pancreatic cancer	53–56



opium

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Opium use as an independent risk factor for pancreatic cancer: A case-control study

Ahmad Naghibzadeh-Tahami [a], Maryam Marzban [b], Vahid Yazdi-Feyzabadi [c], Zaher Khazaei [d], Mohammad Javad Zahedi [e], Vahid Moazed [f], Ali Akbar Haghdoost [g,*]

[a] Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran
[b] The Persian Gulf Tropical Medicine Research Center, The Persian Gulf Biomedical Sciences Research Institute, Bushehr University of Medical Sciences, Bushehr, Iran
[c] Health Services Management Research Center, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran
[d] Social Determinants of Health Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran
[e] Gastroenterology and Hepatology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
[f] Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences Kerman, Iran
[g] Modeling in Health Research Center, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran

Ref:

Research Article

Cancer Epidemiology, Biomarkers & Prevention

Opium Use and Risk of Pancreatic Cancer: A Prospective Cohort Study

Shirin Moossavi[1], Mehdi Mohamadnejad[1], Akram Pourshams[1], Hossein Poustchi[1], Farhad Islami[2], Maryam Sharafkhah[1], Babak Mirminachi[1], Siavosh Nasseri-Moghaddam[1], Shahryar Semnani[3], Ramin Shakeri[1], Arash Etemadi[4], Shahin Merat[1], Masoud Khoshnia[3], Sanford M. Dawsey[4], Paul D. Pharoah[5], Paul Brennan[6], Christian C. Abnet[4], Paolo Boffetta[7], Farin Kamangar[8], and Reza Malekzadeh[1]

Abstract

Background: We examined the association between opium consumption and pancreatic cancer incidence in a large-scale prospective cohort of the general population in northeastern Iran.

Methods: A total of 50,045 adults were systematically followed up (median of 7.4 years), and incident cases of pancreatic cancer were identified. Self-reported data on opium consumption was collected at baseline. Cumulative use (-year) was defined as number of nokhods (a local unit, approximately 0.2 g) of opium consumed per day multiplied by number of years consuming. Adjusted HRs and 95% confidence intervals (CIs) for the association between opium consumption and pancreatic cancer were calculated using Cox proportional hazards regression models.

Results: Overall, 54 confirmed cases of pancreatic cancer were identified. Opium use of more than 81 nokhod-years (high cumulative use), compared with never use, was strongly associated with pancreatic cancer even after adjustments for multiple potential confounding factors [HR = 3.01; 95% CI, 1.25–7.26]. High cumulative consumption of opium was significantly associated with risk of pancreatic cancer after adjusting for cumulative dose of cigarette smoking [HR = 3.56; 95% CI, 1.49–8.50]. In a sensitivity analysis, we excluded participants (including 2 pancreatic cancer cases) who were recruited within the first 5 years of starting opium consumption; high cumulative use of opium was still associated with pancreatic cancer risk [HR = 2.75; 95% CI, 1.14–6.64].

Conclusions: Our results showed a positive association between opium consumption and pancreatic cancer.

Impact: This is the first prospective large-scale study to show the association of opium consumption with pancreatic cancer as a risk factor. *Cancer Epidemiol Biomarkers Prev; 27(3); 268–73. ©2017 AACR.*

Downloaded from http://aacrjournals.org/cebp/article-pdf/27/3/268

Table 2. HR (95% CI) for pancreatic cancer according to opium consumption

	Opium use				
		Low-dose opium use		High-dose opium use	
Index	**None**	**<81 Nokhod-year**	***P***	**≥81 Nokhod-year**	***P***
No. of cases (patients)	37	9		8	
Person-year	296,781	45,006		11,107	
HR (95% CI) (model 1)	Ref.	1.44 (0.68–3.04)	0.337	4.49 (2.00–1.07)	**<0.001**
HR (95% CI) (model 2)	Ref.	1.20 (0.55–2.63)	0.642	3.43 (1.44–8.18)	**0.005**
HR (95% CI) (model 3)	Ref.	1.16 (0.52–2.55)	0.718	3.13 (1.30–7.61)	**0.011**
HR (95% CI) (model 4)	Ref.	1.10 (0.49–2.44)	0.819	2.92 (1.20–7.12)	**0.019**

NOTE: Cox HR adjusted for age, sex (model 1); further adjusted for cigarette smoking status (never, ever) and alcohol consumption (never, ever) (model 2); cigarette smoking status was modeled as never, former, or current (model 3); further adjusted for type 2 diabetes mellitus and BMI (model 4).
Significant *p* values are in bold.



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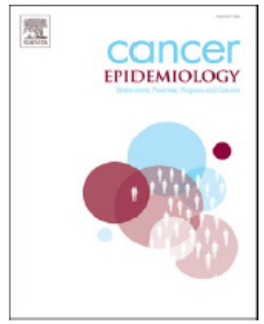



Opium consumption and pancreatic cancer: A meta-analysis

Irena Ilic [a,*], Milena Ilic [b]

[a] Faculty of Medicine, University of Belgrade, Belgrade, Serbia
[b] Department of Epidemiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

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Meta-analysis

ABSTRACT

Pancreatic cancer represents a serious public health problem worldwide. Due to its high mortality, efforts on identifying risk factors are very important since only a few risk-related factors have been well established. The present study aimed to address this knowledge gap by estimating the risk of pancreatic cancer associated with opium use. We performed a thorough literature search of PubMed, Web of Science and Scopus, which yielded 3 case-control and 1 cohort study which were included in the analysis. A meta-analysis was conducted using the DerSimonian and Laird inverse-variance approach as the random effects method. The pooled risk ratio for pancreatic cancer in opium users was significantly increased (RR=1.98, 95 % CI 1.33–2.96, p = 0.0008) compared to never users. Subgroup analyses identified a significantly increased risk for pancreatic cancer in men (RR=1.74, 95 % CI 1.22–2.47, p = 0.002), in persons who consumed both raw teriak and refined shireh opium

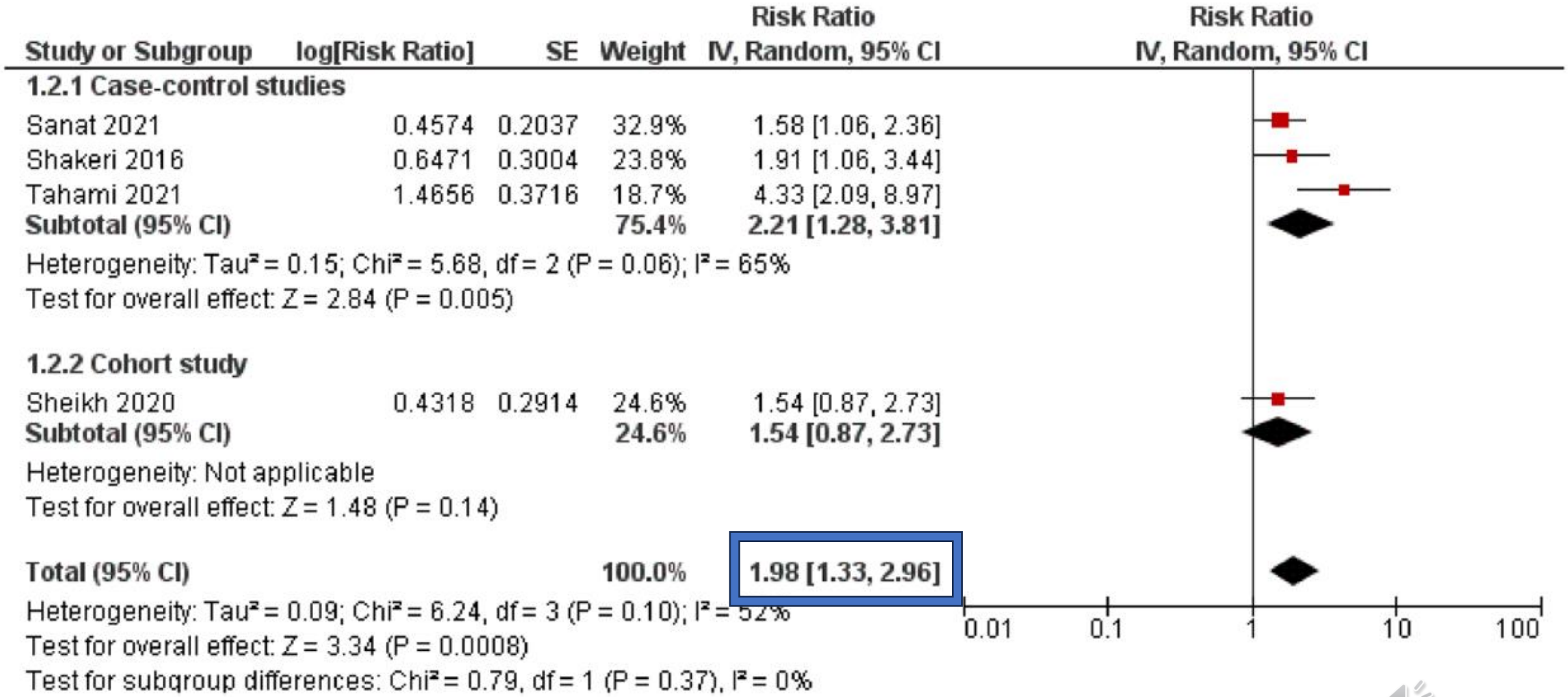

Fig. 2. Forest plot of the association between opium use and risk for pancreatic cancer.

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Thanks for your attention



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