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Mini lecture
Waterpipe tobacco smoking and gastric cancer risk among Vietnamese men

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PLOS ONE

RESEARCH ARTICLE

Waterpipe Tobacco Smoking and Gastric Cancer Risk among Vietnamese Men

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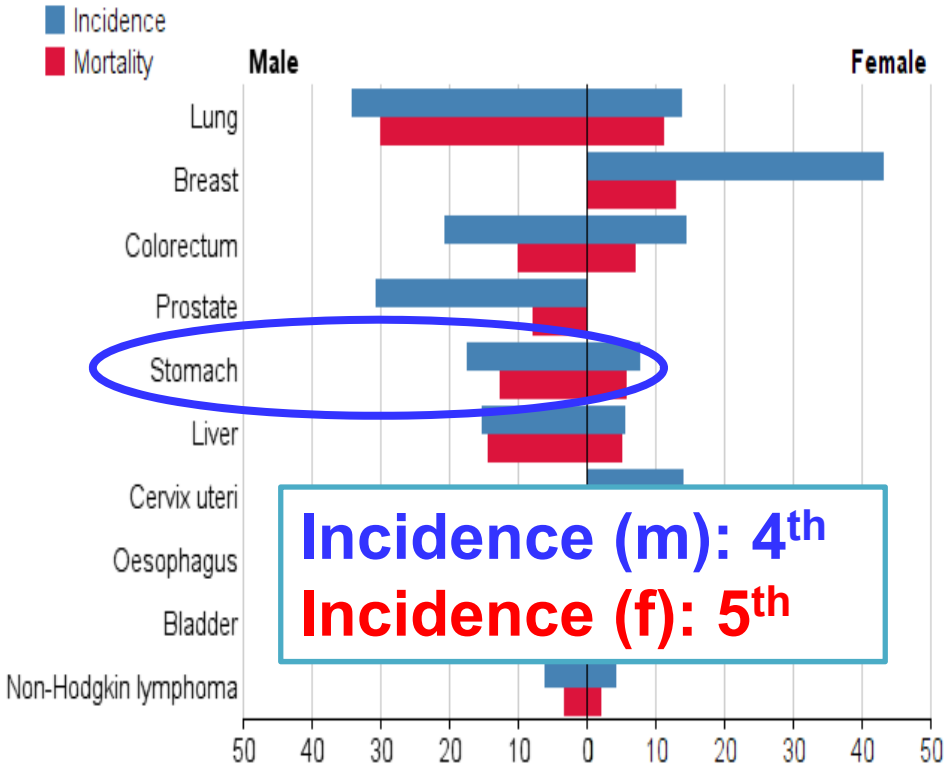
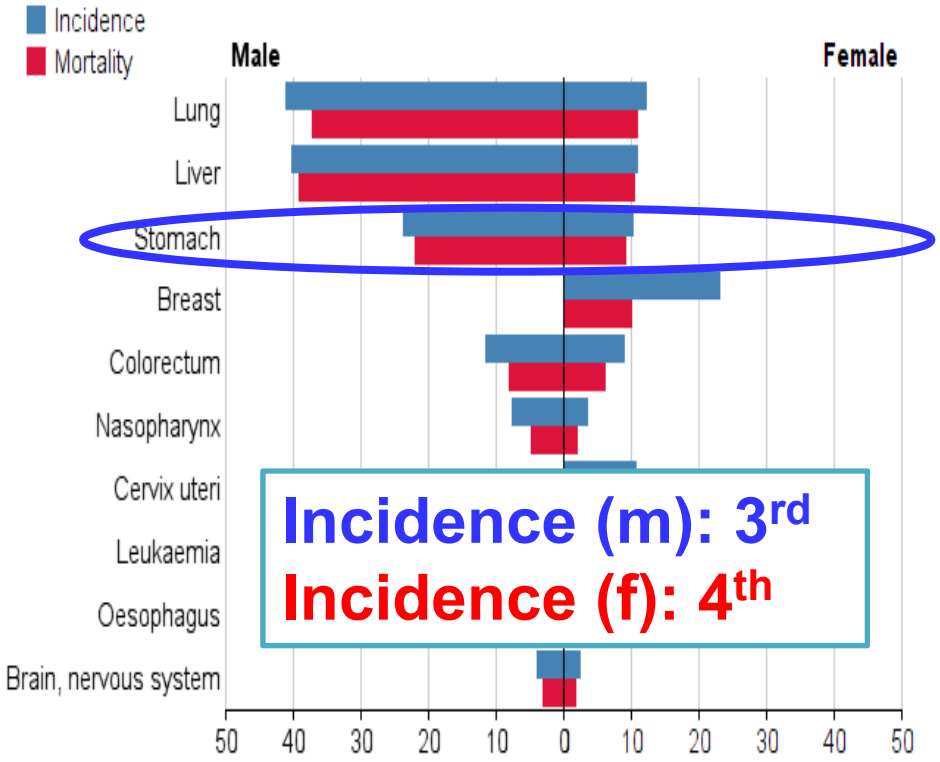
Epidemiology of Gastric Cancer

Age-standardized rate (incidence and mortality), Worldwide 2012



Age-standardized rate (incidence and mortality), Vietnam 2012



Data source: GLOBOCAN 2012

Epidemiology of Gastric Cancer

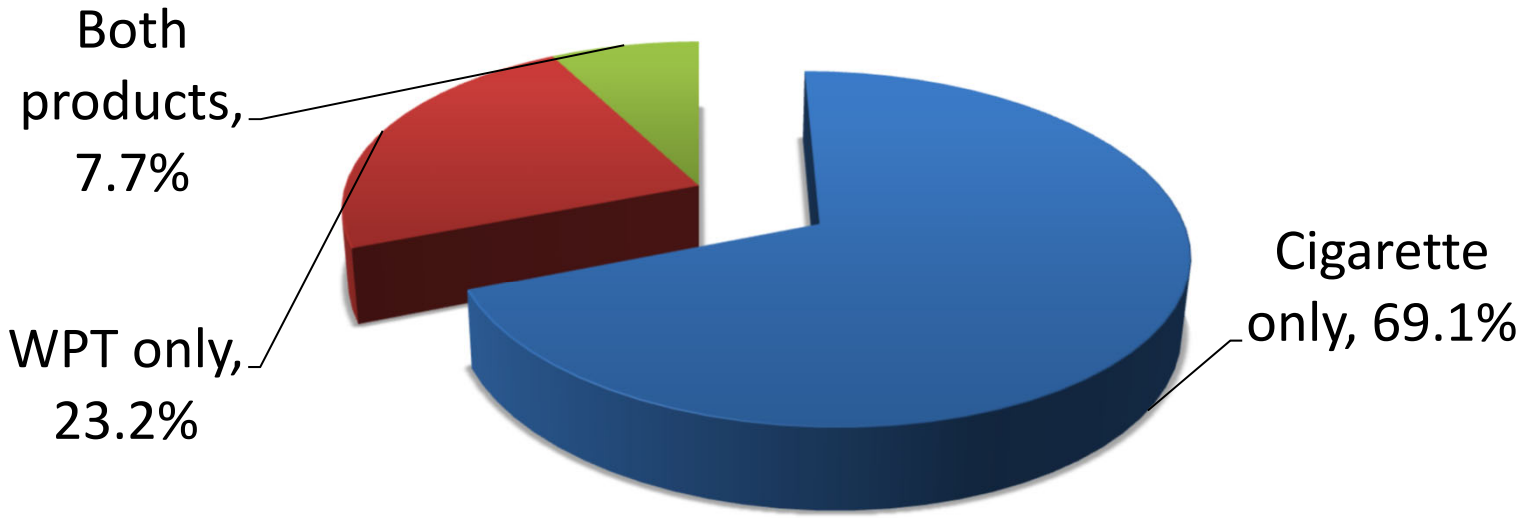
- Environmental and lifestyle factors are major contributors to the etiology of GC.
  - ✓ Helicobacter pylori: ↑ (OR: 1.7~6.0) HCCG, Gut 2001
  - ✓ Salt and salty foods: ↑ (OR: 1.01~5.2)

    WCRF/AICR 2007
  - ✓ Fruits and vegetables: ↓ (OR: 0.58~0.69 for fruits/ 0.3~1.7 for vegetables) IARC 2003
  - ✓ Alcohol drinking: RR=1.07 (95%CI =1.01-1.13)

    Tramacere, Annals of Oncology 2012
  - ✓ Tobacco smoking: ↑ (OR: 1.4~2.6) IARC 2004

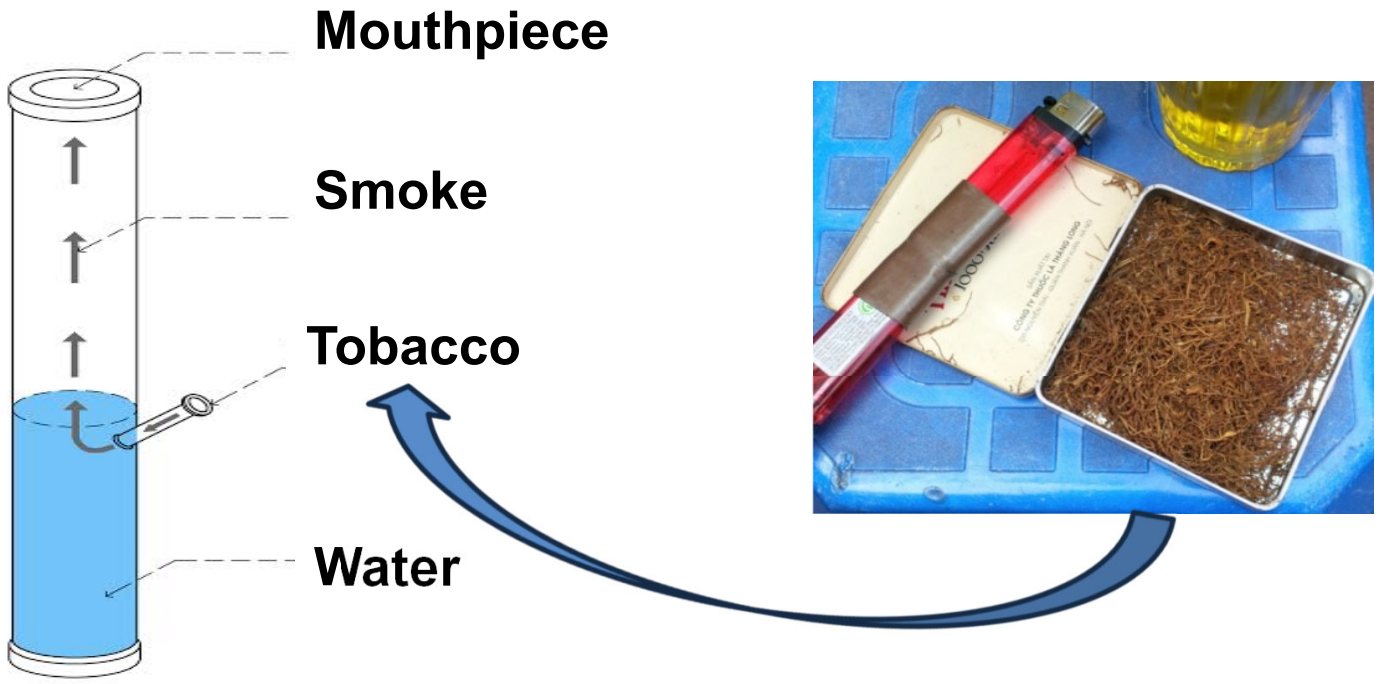
Waterpipe tobacco (WPT) smoking is the second common form of tobacco use in Vietnam

Prevalence of male smokers: **51.2%**



Vietnam National Health Survey in 2001-2002
*(*Xuan et al., *Pre Chronic Dis 2013)*

Vietnamese/Chinese waterpipe



Chinese waterpipe (WP): "BONG" WP

- Started in China during the Ming Dynasty (16th century)
- Made of bamboo, metal or glass and used in other countries as Laos, Myanmar and Vietnam

Hookah vs Vietnamese/Chinese WPT smoking

- **Similarity:** Smoke is passed through a column of water before being inhaled.
- **Differences**

	Hookah	Vietnamese type
Tobacco	Flavored tobacco	Sundried processed tobacco
Heat source	Burning charcoal	Fire, no charcoal
Smoking duration	45-60 min	Less than 5 min

Hookah smoke contains more toxicant and carcinogen than cigarette smoke

	Compared to cigarette	Components
Hookah smoke	Higher level of carcinogen and toxicant (Maziak, *Cancer Epidemiol 2013)* • Nicotine: 1-3 times • CO: 6-15 times • PAHs: 8-15 times benzo(a)pyrene • Formaldehydes: 6-9 times • Heavy metals: As, Cr, lead...	• Burning charcoal ✓ 90% CO ✓ 75-92% PAHs (Monzer, *Food Chem Toxicol 2008)* • Flavored tobacco ✓ ↑ 60% aldehydes ✓ Chemical composition (Rashidi, *Food Chem Toxicol 2006)*
Chinese WPT smoke	Higher level of CO *(She, Chest 2014)*	

WPT smoking and health effects

- **Chinese/Vietnamese WPT smoking and lung cancer**
  - ✓ OR: 1.8~3.6, no significant; 3 case-control studies in China
  - ✓ Crude RR=4.39, 95%CI=3.82-5.04; a cohort study on Chinese WPT smoking with lung cancer mortality

    (Elie et al., *IJE 2010)*
  - ✓ Crude OR=6.21, p<0.001; a case-control study in Vietnam

    (Anh et al., *J Med Information 1999*)
- **Hookah smoking and cancers**
  - ✓ Lung cancer: OR=3.0, 95%CI=1.2-7.6; a case-control study in Tunisia

    (Elie et al., *IJE 2010)*
  - ✓ Oral cancer: OR=4.4, 95%CI=2.3-8.4; a cross-sectional study in India

    (Dangi et al., *Tob Induc Dis 2012*)
  - ✓ Oesophageal cancer: OR=1.85, 95%CI=1.41-2.44; a case-control study in Kashmir, India

    (Dar et al., *BJC 2012*)

WPT smoking and Gastric Cancer

Place, Year	Study design	Result (Non vs Hookah smokers)
Northeast Iran Shakeri, *IJC 2013*	Case-control study 309 cases and 613 controls	OR=1.1 95%CI=0.3-3.3
Northwest Iran Sadjad, *IJC 2014*	Cohort study 928 Helicobacter pylori infected but otherwise healthy subjects	RR=3.4 95%CI=1.7-7.1

*** Regarding Vietnamese WPT, its association with gastric cancer risk has NOT been studied.**

Objectives

- Our study aimed to clarify the association between Vietnamese WPT smoking and gastric cancer risk among men.

Study design

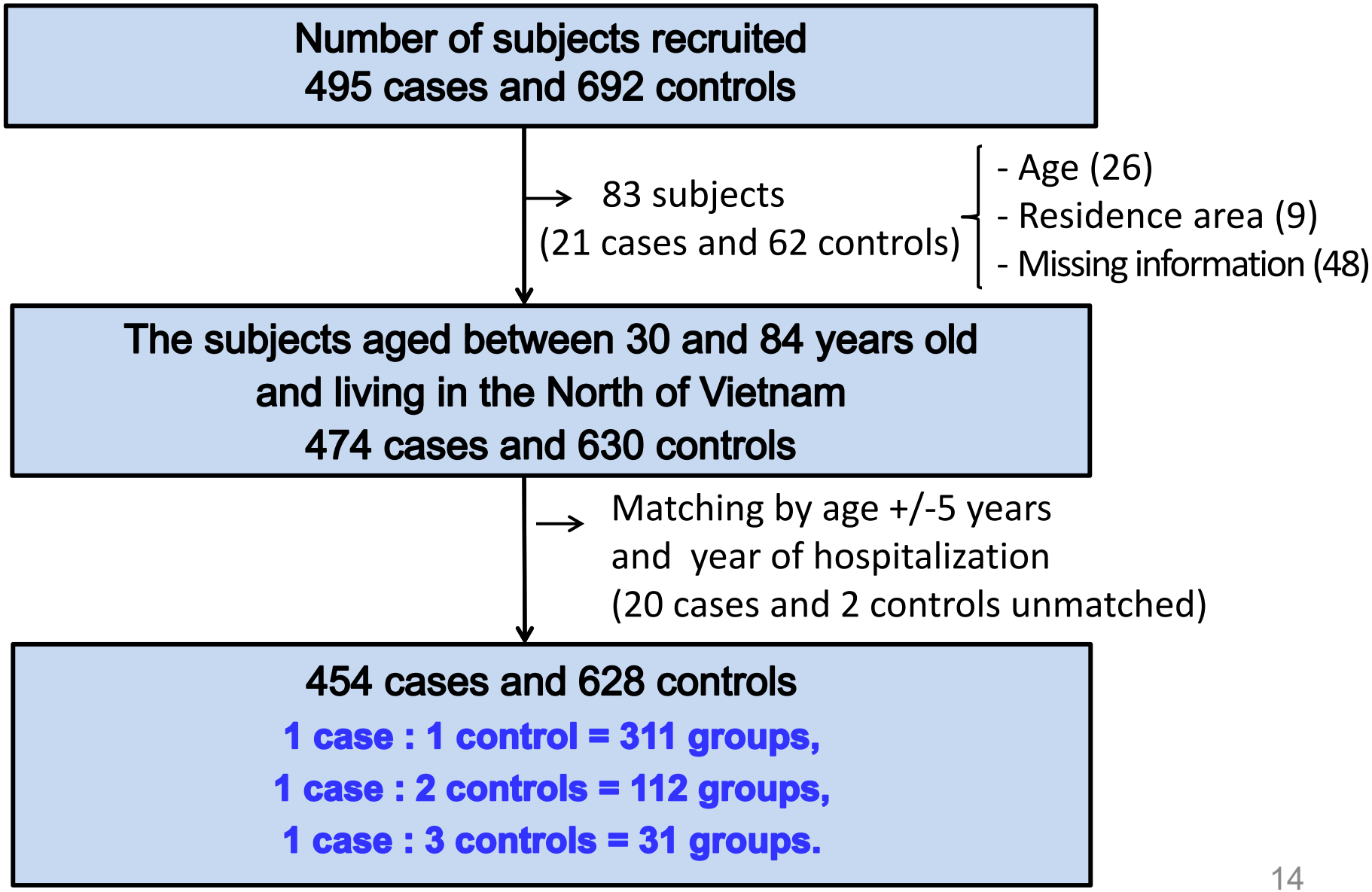
- A hospital-based case-control study
- Study places: three hospitals in Hanoi city, Vietnam

  National Cancer Hospital, Viet Duc Surgery Hospital, and Bach Mai General Hospital
- Data collection period: Feb 2003 – Apr 2011
  - ✓ Period 1: February 2003 – August 2006
  - ✓ Period 2: September 2006 – November 2007
  - ✓ Period 3: November 2010 – April 2011

Study subjects

- Patients, men who had undergone surgery
- **Cases:** diagnosed as primary gastric cancer histopathologically
- **Controls:** not have any cancer, matched with case for age +/- 5 years and the calendar year of hospitalization
- **Inclusion criteria**
  - ✓ Age: 30-84 years old
  - ✓ Residential area: The North Vietnam
  - ✓ Smoking information was available

Process of subject selection



Data collection

- **Structured Questionnaire**
  - ✓ Socio-demographic factors
  - ✓ Cancer history of subjects and their family
  - ✓ Tobacco smoking, alcohol drinking and dietary habits
- **Definition of smokers**
  - ✓ Never smokers were those who never smoked or smoked less than 1 year and <100 cigarettes/WPTs in their lifetime.
  - ✓ Smokers who have smoked cigarette/WPT regularly for at least 1 year
    - ❑ Ex-smokers who had smoked but quit at least 1 year before the onset of disease
    - ❑ Others were current smokers

Statistical analysis

- Odds ratios, 95% confidence intervals (CI) and p for trend were obtained using conditional logistic regression model.
- Adjusted for potential confounding factors:
  - ✓ Age (continuous variable)
  - ✓ Education (<6 / 6-9 / 10-12 / >12 / unknown)
  - ✓ Residential area (Hanoi/Red River Delta/others)
  - ✓ Frequency of salted processed meats and fish intake (never or rarely / monthly / daily or weekly / unknown)
  - ✓ Frequency of citrus fruits and raw vegetables consumption (tertiles based on their distributions in control group)
- P for homogeneity was estimated using the likelihood ratio test.

The effects of socioeconomic status on gastric cancer risk

Variables	Controls		GC cases		OR (95%CI)	P for homogeneity
	n	%	n	%		
Total	**628**	**100**	**454**	**100**		
Education (years)					*P for trend = 0.003*	
<6	57	9.1	56	12.3	1.0	0.034
6-9	282	44.9	223	49.1	0.7 (0.5-1.1)	
10-12	180	28.7	116	25.6	0.6 (0.4-1.0)	
>12	106	16.9	57	12.6	0.5 (0.3-0.8)	
Unknown	3	0.5	2	0.4	0.5 (0.1-3.3)	
Occupation						
Retirant	166	26.4	83	18.3	1.0	0.006
Farmer	138	22.0	138	30.4	2.0 (1.3-2.9)	
Factory worker	31	4.9	20	4.4	1.4 (0.7-2.6)	
Office worker	33	5.3	15	3.3	0.8 (0.4-1.7)	
Free labor and others	75	11.9	43	9.5	1.1 (0.7-1.9)	
Unknown	185	29.5	155	34.1	1.8 (0.8-3.9)	
Refrigerator						
No	248	39.5	219	48.2	1.0	0.002
Yes	339	54.0	199	43.8	0.6 (0.5-0.8)	
Unknown	41	6.5	36	7.9	0.9 (0.5-1.4)	

** P for trend was estimated excluding unknown group.*

Lai et al., PLOS ONE | DOI:10.1371/journal.pone.0165587 November 1, 2016

The effects of dietary factors on gastric cancer risk

Variables	Controls		GC cases		OR (95%CI)*	P for homogeneity
	n	%	n	%		
Total	**628**	**100**	**454**	**100**		
Frequency of salted processed meats and dried fish intake					*P for trend = 0.105*	
Never or rarely use	210	33.4	143	31.5	1.0	0.070
Monthly	338	53.8	220	48.5	0.9 (0.7-1.2)	
Daily/weekly	78	12.4	90	19.8	1.5 (1.0-2.2)	
Unknown	2	0.3	1	0.2	0.8 (0.1-9.6)	
Frequency of citrus fruits consumption					*P for trend = 0.002*	
T1	212	33.8	187	41.2	1.0	0.007
T2	206	32.8	161	35.5	0.9 (0.7-1.3)	
T3	208	33.1	104	22.9	0.6 (0.4-0.8)	
Unknown	2	0.3	2	0.4	1.1 (0.1-7.8)	
Frequency of raw vegetables consumption					*P for trend = 0.756*	
T1	257	40.9	176	38.8	1.0	0.204
T2	173	27.6	151	33.3	1.2 (0.9-1.6)	
T3	198	31.5	126	27.8	0.9 (0.7-1.3)	
Unknown	0	0.0	1	0.2	-	

- *T1-T3: Tertile of frequency of citrus fruits consumptions (T1 <0.17, 0.17≤T2 <0.6, T3 ≥0.6), and of raw vegetables consumptions (T1=0, 0<T2<0.08, T3≥0.08)*
- *P for trend was estimated excluding unknown group.*

Lai et al., PLOS ONE | DOI:10.1371/journal.pone.0165587 November 1, 2016

An increased risk of GC in current WPT smokers

Variables	Controls		GC cases		OR (95%CI)*	P for homogeneity
	n	%	n	%		
Total	**628**	**100**	**454**	**100**		
Cigarette smoking						
Never	238	37.9	168	37.0	1.0	0.547
Ex-smoker	117	18.6	94	20.7	1.2 (0.9-1.7)	
Current smoker	273	43.5	192	42.3	1.1 (0.8-1.4)	
Water-pipe tobacco smoking						
Never	388	61.8	219	48.2	1.0	<0.001
Ex-smoker	69	11.0	56	12.3	1.5 (1.0-2.4)	
Current smoker	171	27.2	179	39.4	1.8 (1.3-2.4)	
Alcohol drinking						
Never	194	30.9	121	26.7	1.0	0.605
Some times	222	35.4	175	38.6	1.0 (0.7-1.4)	
Daily	210	33.4	156	34.4	1.1 (0.8-1.6)	
Unknown	2	0.3	2	0.4	1.4 (0.1-17)	

** OR and corresponding 95%CI were adjusted for the effects of age, education, residential area, intake of salted processed meats and dried fish, citrus fruits and raw vegetables consumption.*

Lai et al., PLOS ONE | DOI:10.1371/journal.pone.0165587 November 1, 2016

Characteristics of study subjects regarding smoking status

Variable	Mean (SD)	
	Controls	GC cases
Current cigarette smoking only		
No. cigarettes per day	10.6 (7.1)	9.1 (6.9)
Current WPT smoking only		
No. WPTs per day	9.2 (6.2)	11.3 (7.8)
Years of smoking	29.4 (13.3)	34.3 (12.6)
Age at starting to smoke	29.4 (14.3)	26.7 (11.0)

SD, standard deviation

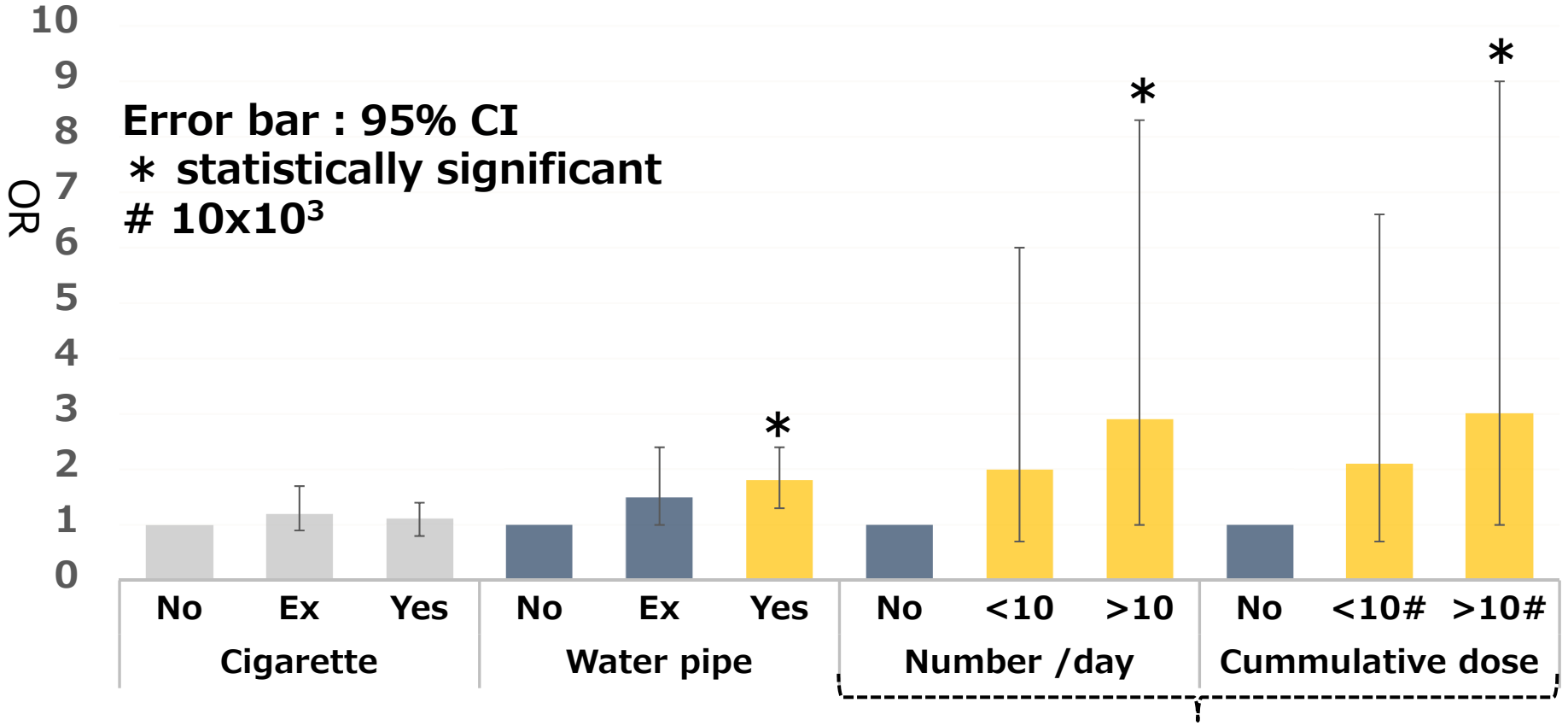
Association of WPT smoking and GC risk after excluding cigarette smokers

Variables	Controls		GC cases		OR (95%CI)*	P for homogeneity
	n	%	n	%		
Total	**105**	**100**	**88**	**100**		
Waterpipe tobacco only					*P for trend = 0.024*	
Never	71	67.6	45	51.1	1.0	0.055
Ex-smoker	9	8.6	8	9.1	1.2 (0.3-4.1)	
Current smoker	25	23.8	35	39.8	2.7 (1.2-6.5)	
Daily frequency					*P for trend = 0.144***	
Never	71	67.6	45	51.1	1.0	0.317
<10	11	10.5	13	14.8	2.0 (0.7-6.0)	
≥10	13	12.4	19	21.6	2.9 (1.0-8.3)	
Unknown	1	1.0	3	3.4	7.9 (0.6-104)	
Cumulative frequency					*P for trend = 0.284***	
Never	71	67.6	45	51.1	1.0	0.554
<10,000	10	9.5	11	12.5	2.1 (0.7-6.6)	
≥10,000	12	11.4	18	20.5	3.0 (1.0-9.0)	
Unknown	3	2.9	6	6.8	3.9 (0.8-20)	

- *OR and corresponding 95%CI were adjusted for the effects of age, education, residential area, intake of salted processed meats and dried fish, citrus fruits and raw vegetables consumption.*
- *P for trend was estimated excluding unknown group.*

Lai et al., PLOS ONE | DOI:10.1371/journal.pone.0165587 November 1, 2016

Gastric cancer risk by smoking



Water pipe tobacco

Lai et al. (PLOS ONE 2016)

Association of WPT smoking and GC risk after excluding cigarette smokers (cont)

Variables	Controls		GC cases		OR (95%CI)*	P for homogeneity
	n	%	n	%		
Total	**105**	**100**	**88**	**100**		
Smoking duration (years)					*P for trend = 0.154*	
Never	71	67.6	45	51.1	1.0	0.515
<20	7	6.7	7	8.0	1.3 (0.4-4.6)	
20-29	6	5.7	9	10.2	2.4 (0.6-10.2)	
30 or more	18	17.1	22	25.0	2.7 (0.9-8.0)	
Unknown	3	2.9	5	5.7	2.9 (0.5-15.8)	
Starting age for WPT smoking (years)					*P for trend = 0.249*	
<25	10	9.5	18	20.5	3.7 (1.2-11.3)	0.103
25 or more	18	17.1	20	22.7	1.9 (0.8-4.7)	
Never	71	67.6	45	51.1	1.0	
Unknown	6	5.7	5	5.7	1.5 (0.4-6.2)	

- *OR and corresponding 95%CI were adjusted for the effects of age, education, residential area, intake of salted processed meats and dried fish, citrus fruits and raw vegetables consumption.*
- *P for trend was estimated excluding unknown group.*

Lai et al., PLOS ONE | DOI:10.1371/journal.pone.0165587 November 1, 2016

Combined effects of WPT smoking and cigarette smoking on gastric cancer risk

Cigarette smoking	WPT smoking	Controls		GC cases		OR (95%CI)*
		n	%	n	%	
Never	Never	111	30.6	65	23.3	1.0
	Current	48	13.2	64	22.9	**2.7 (1.5-4.8)**
Current	Never	128	35.3	85	30.5	1.5 (0.9-2.4)
	Current	76	20.9	65	23.3	1.6 (0.9-2.9)

** OR and corresponding 95%CI were adjusted for the effects of age, education, residential area, intake of salted processed meats and dried fish, citrus fruits and raw vegetables consumption.*

Lai et al., PLOS ONE | DOI:10.1371/journal.pone.0165587 November 1, 2016

Discussion

- A significant increase of GC risk among current WPT smokers (OR=1.8, 95%CI=1.3-2.4), after excluding cigarette smokers (OR=2.7, 95%CI=1.2-6.5)

Our findings are consistent with the result of Hookah smoking in Iranian study (RR=3.4, 95%CI=1.7-7.1)

Sadjadi et al., *IJC 2014*

- GC risk tend to increase with the daily frequency, duration, and early start of WPT smoking, but not significant among exclusively WPT smokers.

Vietnamese WPT smoke may have similar carcinogenic effects as well as Arabian WPT

- Vietnamese WPT smoke may contain high level of PAHs and other carcinogens

  The report by She et al. (2014) showed that the water of Chinese WPT contains high level of PAHs and heavy metals.

- Smoking duration of Vietnamese WPT per day

✓ Duration of smoking sessions: 5 min

✓ Median frequency of smoking per day

among exclusively WPT smokers: 10 times

Equivalent to one session of Arabian WPT (45-60 min)

Limitations

(1) Insufficient information on tumor location of GC

- Most of GC in this study might be antral GC
  - ✓ Approximately 50.2% GC cases had information on tumor site, in which 82% cases were antral GC.
  - ✓ The risk of antral GC in current WPT smokers (OR=1.7, 95%CI=1.2-2.6) was similar to that of all GC cases (OR=1.8, 95%CI=1.3-2.4)
- No differences in the effect of smoking regarding to tumor location

Chow 1999, Sasazuki 2002, Sung 2007, Maziak 2013

Limitations (cont)

(2) No data on histological type of GC

- A hospital-based case-control study in Japan showed no significant difference between intestinal and diffuse types regarding the association of cigarette smoking with GC risk.

Inoue et al., *IJC 1999*

- A cross-sectional study in Hanoi, Vietnam 2010-2012 reported most of Vietnamese GCs were intestinal type (82.7%).

Anh and Tho, *Practical Medicine 2013*

Conclusion

- Water-pipe tobacco smoking was positively associated with gastric cancer risk among Vietnamese men

- First hospital-based case-control study on the association between water-pipe tobacco smoking and gastric cancer risk in Viet Nam