CARDIOVASCULAR & RESPIRATORY HEALTH IMPACT OF WATERPIPE SMOKING

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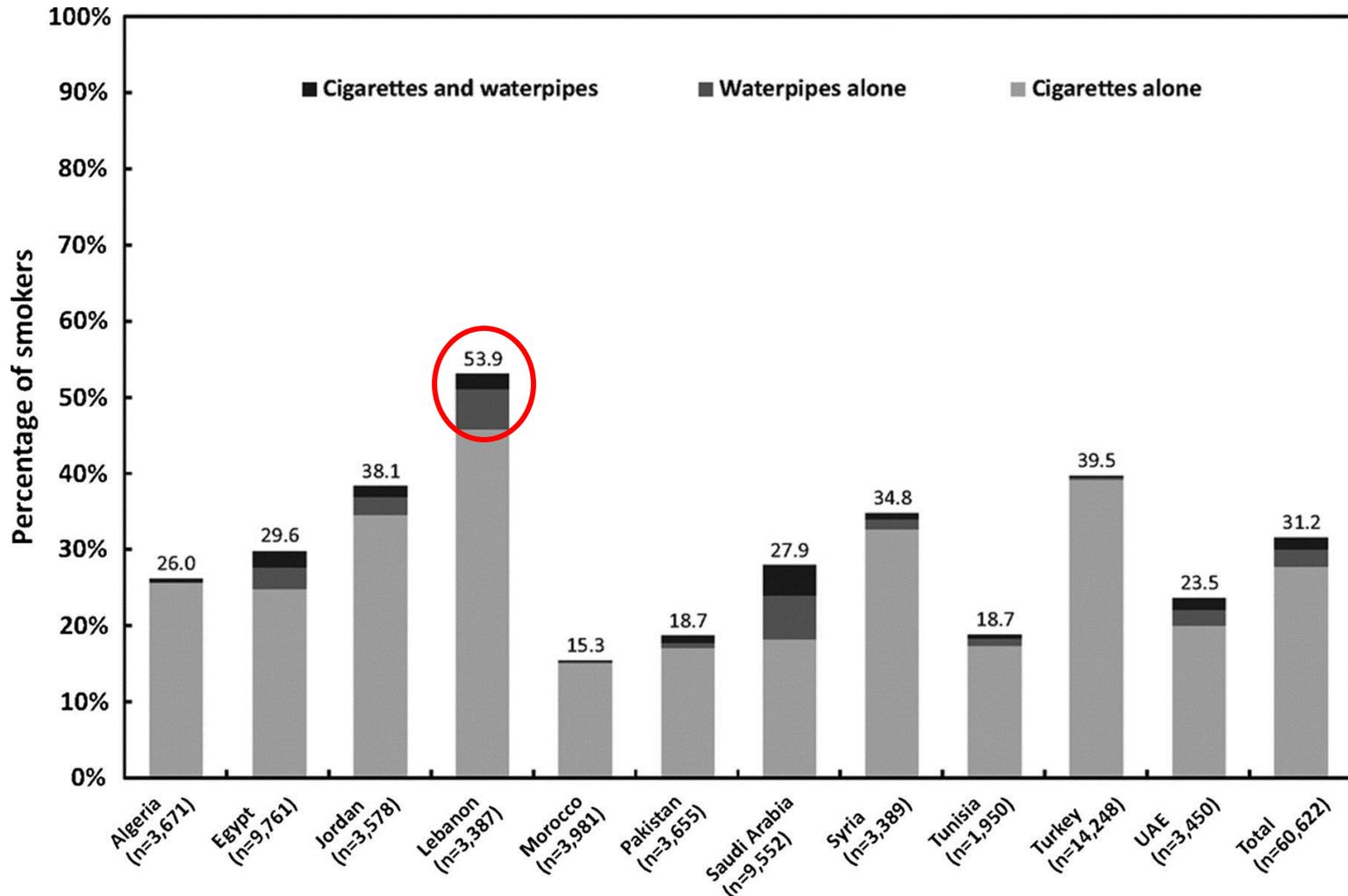American University of Beirut

OUTLINE

I. WPS EPIDEMIOLOGY

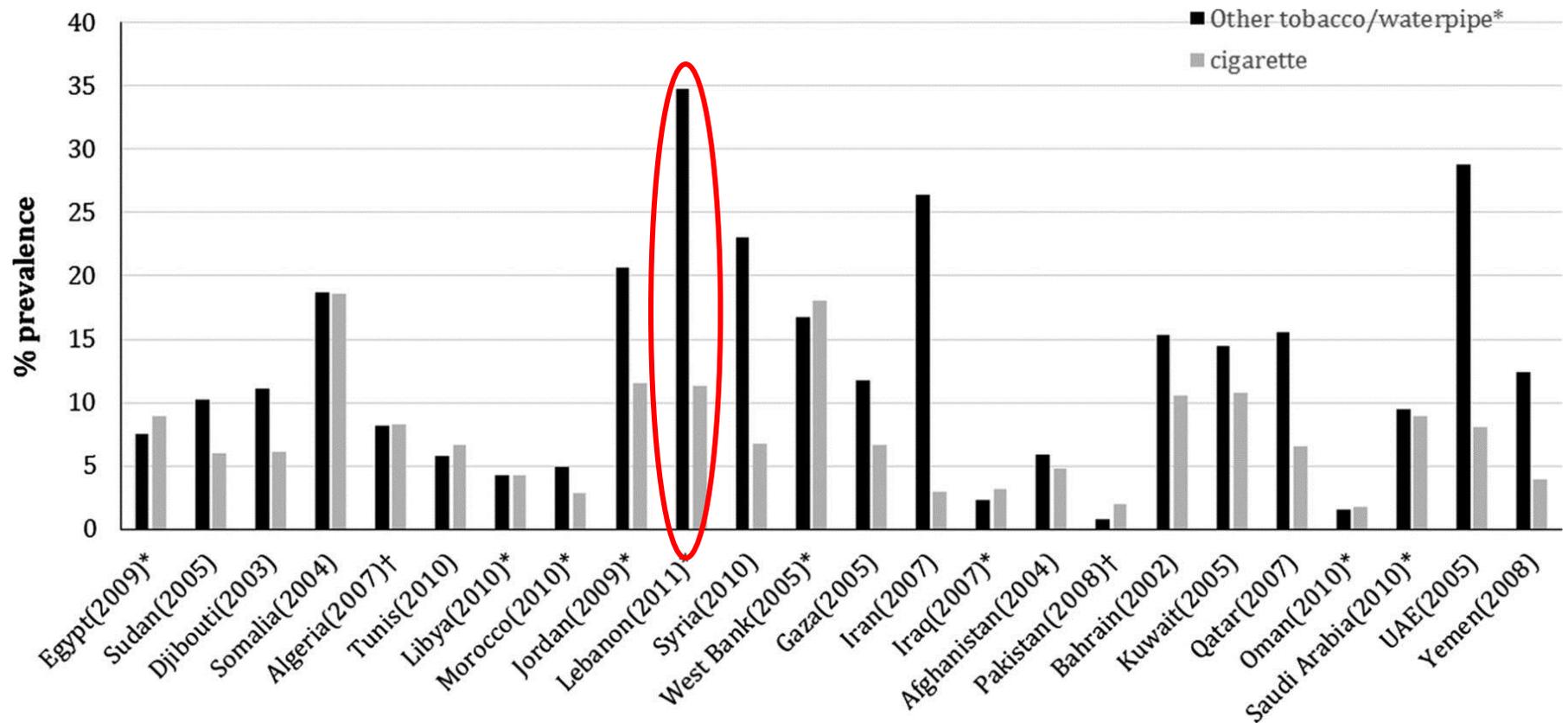**Smoking behaviours among representative samples of individuals <u>aged ≥40 years</u> (62 086) from 10 Arab countries & Pakistan.**

Adel Khattab et al. Respiratory Medicine 2012;106:s16-s24

I. WPS EPIDEMIOLOGY
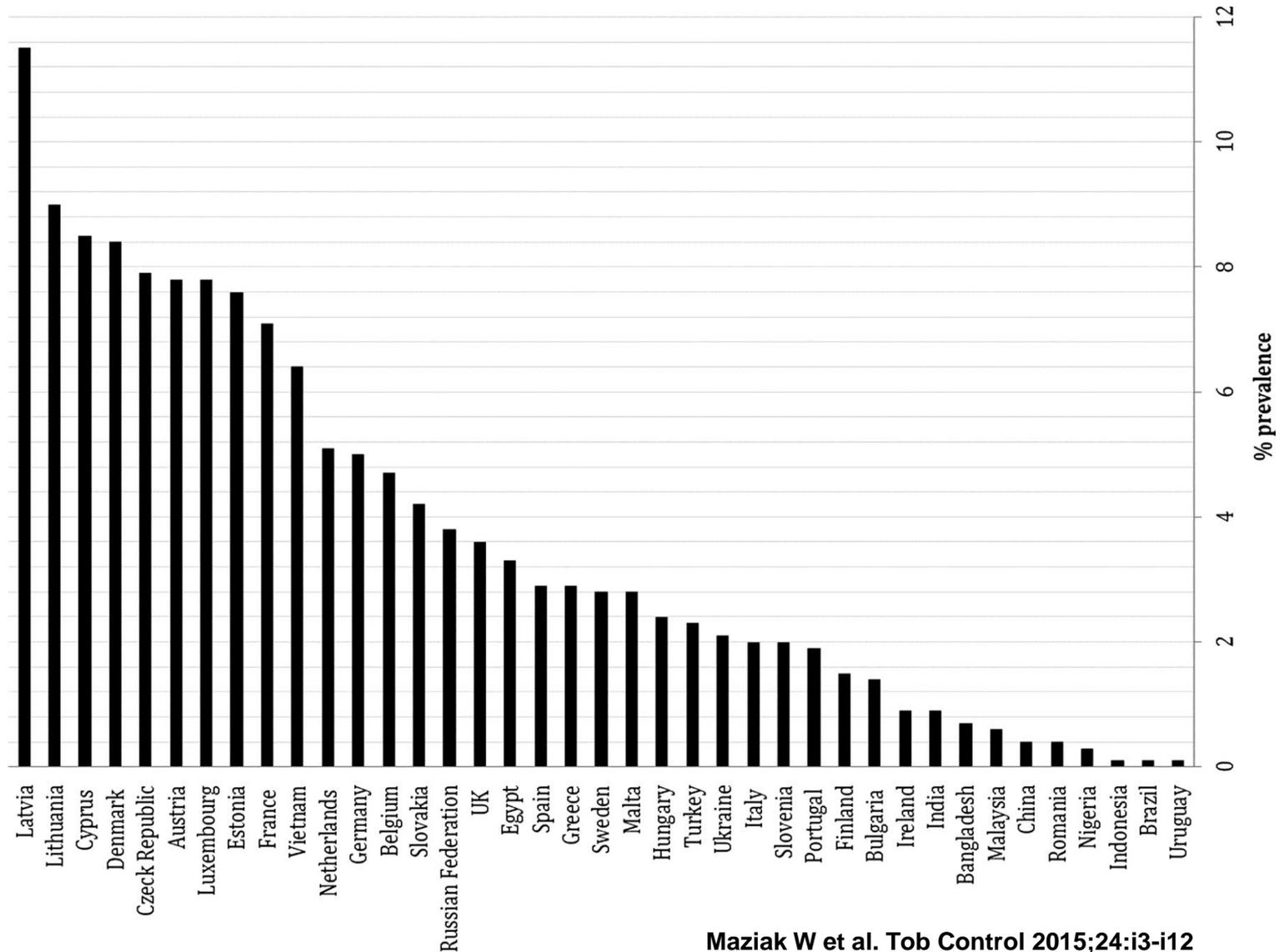
Global Youth Tobacco Survey (GYTS):

Current other tobacco/waterpipe vs. cigarette smoking in adolescents 13–15 year-old

Maziak W, et al. Tob Control 2015;24:i3–i12

I. WPS EPIDEMIOLOGY

Global prevalence of current waterpipe smoking among persons aged ≥15 years.45.

Maziak W et al. Tob Control 2015;24:i3-i12

II. WPS AND CORONARY ARTERY DISEASE

A hospital-based study among 7930 patients hospitalized with Acute Coronary Syndrome in 65 hospitals from 6 Arab countries (Bahrain, KSA, Qatar, Oman, UAE and Yemen)

➢ Exclusive WP smokers had 1.8 times the odds of hospital mortality (age and sex-adjusted) compared to non-smokers

➢ Exclusive WP smokers had twice the rate of recurrent ischemia (26.9%) compared to cigarette smokers (14.1%).

Al Suwaidi et al J Postgrad Med J 2012;88:566–74

II. WPS AND CORONARY ARETRY DISEASE

The Iranian Golestan Cohort cross-sectional analysis (n=50,045):

- **Heavy WP smokers** (>180WP-years n=25) had 3.75 the odds of **self-reported HD** compared to never smokers
- Moderate to heavy WP users (>50WP-years n=120) had 1.83 the odds of self-reported HD compared to low/never smokers
- Strength: Community-based with little overlap between cigarette and WPS
- Limitations: 1) Recall bias (self-reported HD)

    2) low number of WP smokers (N=525, 1%)

    3) Did not adjust for important risk factors ex: hyperlipidemia and Family history of HD

Tobacco use*	All participants (%)	HD cases (%)	Participants without HD (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)†
Water-pipe smoking					
Ever versus never use					
Never	49489 (98.9)	2990 (98.1)	46499 (99.0)	Reference	Reference
Ever	525 (1.1)	51 (1.9)	474 (1.0)	1.67 (1.25 to 2.24)	1.09 (0.80 to 1.48)
Moderate-high versus never-low use					
≤50 water-pipe-years	49894 (99.8)	3022 (99.4)	46872 (99.8)	Reference	Reference
>50 water-pipe-years	120 (0.2)	19 (0.6)	101 (0.2)	2.92 (1.78 to 4.77)	1.83 (1.10 to 3.07)
Cumulative use					
Never	49489 (98.9)	2990 (98.3)	46499 (99.0)	Reference	Reference
≤50 water-pipe-years	405 (0.8)	32 (1.0)	373 (0.8)	1.33 (0.93 to 1.91)	0.87 (0.60 to 1.28)
50.1–100	52 (0.1)	6 (0.2)	46 (0.1)	2.03 (0.86 to 4.74)	1.25 (0.52 to 3.03)
100.1–180	43 (0.1)	5 (0.2)	38 (0.1)	2.05 (1.03 to 2.80)	1.49 (0.57 to 3.87)
>180	25 (0.1)	8 (0.3)	17 (0.04)	6.39 (2.65 to 15.41) p trend: <0.001	3.75 (1.52 to 9.22) p trend: 0.04

WP-years= WP smoked per day X smoking duration

II. WPS AND CORONARY ARTERY DISEASE

Another community-based study from Bangladesh showed increased risk of heart disease in waterpipe smokers included significant concurrent cigarette smoking:

1) The Health Effects of Arsenic Longitudinal Study (HEALS) (N=20,033) Bangladesh

➢ Women who ever smoked WP had 2.81 the risk of death from any cause compared to non-WPS

➢ Heavy male smokers (WPS >5 /day) had increased risk of death from any cause (HR=1.35) and from ischemic heart disease (HR=1.96) compared to non-WPS.

Limitation: **99% of WP smokers also smoked cigarette or beedi concurrently**, making it impossible to isolate the effect of WPS

….and hospital-based study from Lebanon

2) Cross-sectional study among 1210 patients undergoing coronary angiography at 4 Lebanese hospitals:

➢ 2.95 times the odds of severe coronary artery stenosis (>70%) determined by angiography in heavy WP smokers compared to non-smokers (95% CI: 1.04 -8.33)

➢ **Significant concurrent (29%) or prior (12%) cigarette smoking**

Wu et al PLOS 2013

Sibai AM Atherosclerosis 2014;234:454–60

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I. WPS AND CAD EVIDENCE

1. Limitations

1) Cross-sectional studies

2) Concurrent cigarette smoking

3) Lack of adjustment for important confounders

4) Selection hospital-based samples

I. WPS AND CAD EVIDENCE

2. Objectives

1) Evaluate the association of **exclusive waterpipe smoking** with cardiovascular and pulmonary disease in a **community-based sample**

2) Validate a survey tool for assessment of WPS

3) Establish a **well-characterized** cohort for **prospective evaluation** of health outcomes

STUDY DESIGN

Hypothesis

➢ Waterpipe smoking is associated with validated markers/predictors of cardiovascular and pulmonary disease

1) Observational Cross-sectional Study

2) Compares markers of cardiovascular and respiratory disease in **exclusive** WP smokers and never smokers

3) Recruited from the **community**

STUDY OUTCOMES

PRIMARY OUTCOME

- **Coronary Artery Calcium (CAC) score** (expressed as % predicted)
    - A validated predictor of cardiovascular events (infarction and death)
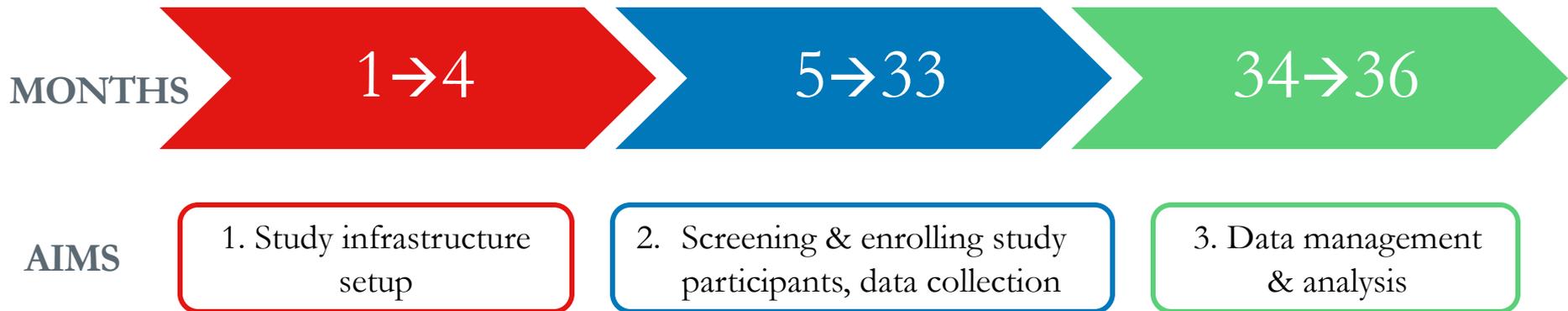   - Independent of other risk factors and the Framingham risk score
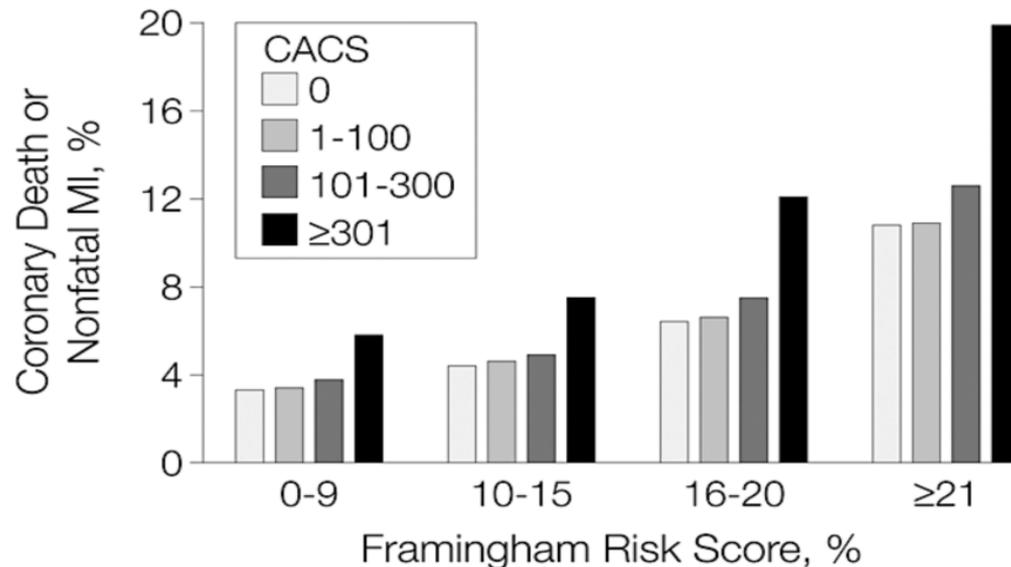
Predicted 7-Year Event Rates From COX Regression Model for CHD Death or Nonfatal Myocardial Infarction for Categories of FRS or CACS
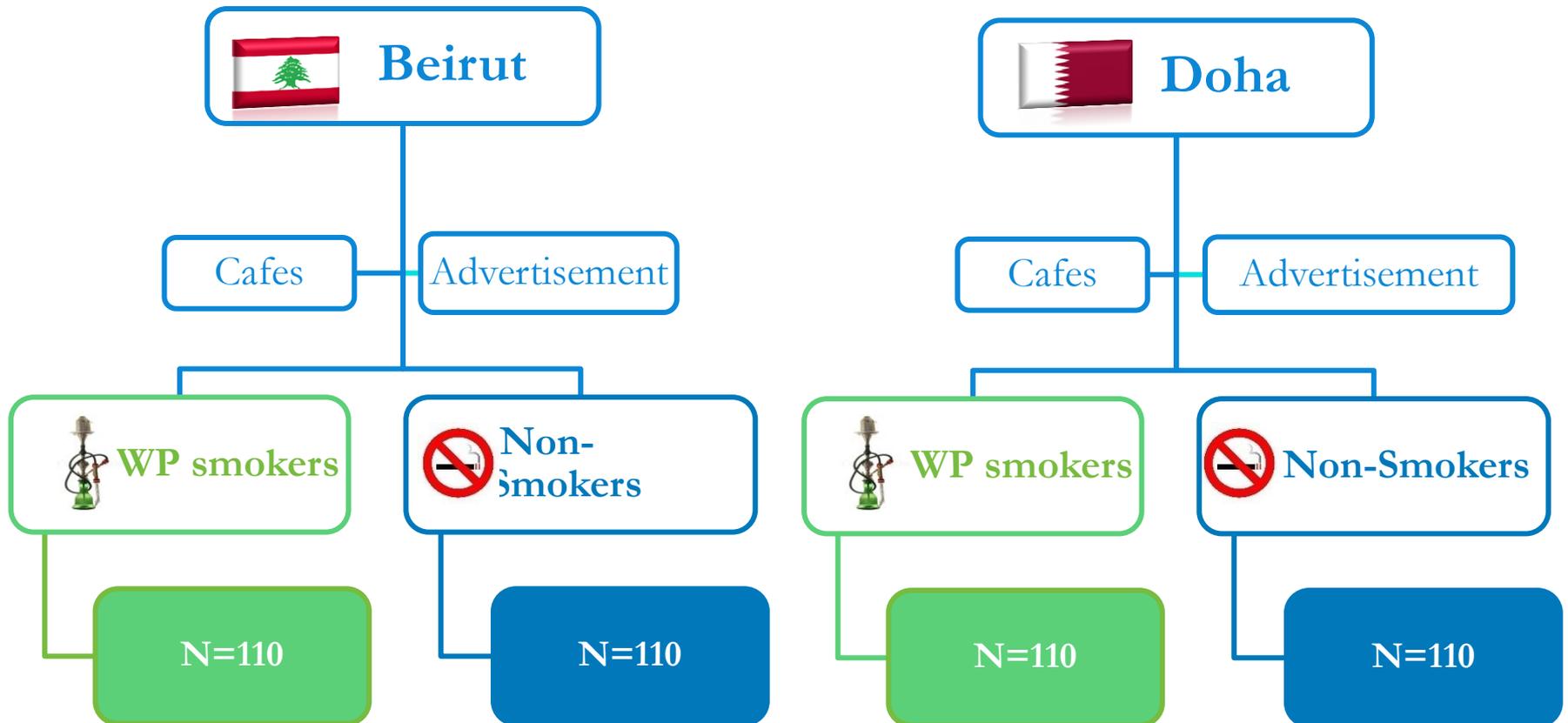
STUDY OUTCOMES

SECONDARY OUTCOMES

- **Arterial stiffness:** Augmentation index & Carotid-femoral pulse wave velocity
  - Predictors of incident hypertension, coronary heart disease and mortality

- **Volumetric Lung Analysis:** Quantitative % Emphysema
  - Correlates with emphysema on autopsy, predicts lung function decline in smokers

- **Measures of airway obstruction**: FVC, FEV1, FEV1/FVC ratio & airway resistance (impulse oscillometry)

- **Metabolic markers:** LDL, HDL, Triglyceride

- **Inflammatory markers**: C-reactive protein (CRP); (IL-6); ICAM and fibrinogen
  - Markers of vascular inflammation
  - predictors of cardiovascular events and mortality

- **Oxidative stress marker:** Urinary isoprostanes

- Urine microalbumin

- Serum cotinine level

STUDY TIMELINE: 3 YEARS
EXTENDED FOR A 4TH YEAR

MONTHS	1→4	5→33	34→36
AIMS	1. Study infrastructure setup	2. Screening & enrolling study participants, data collection	3. Data management & analysis

STUDY SITES & SAMPLE

```
        Beirut                              Doha

   Cafes    Advertisement            Cafes    Advertisement

WP smokers   Non-                 WP smokers   Non-Smokers
             Smokers

  N=110        N=110               N=110         N=110
```

STUDY SAMPLE

1. Inclusion & Exclusion Criteria

Recruitment checklist

☐ **WATER PIPE SMOKERS**

Yes	No	Inclusion Criteria
		Age >= 40 years old
		Smoking water pipe daily for more than 10 years
		Non-cigarette and non-cigar smokers

Yes	No	Exclusion Criteria
		Current pregnancy*
		Non-smoking pulmonary disease** (asthma, bronchiectasis, fibrosis)
		Diabetes
		Renal failure

*Pregnant women can be identified but cannot be enrolled in the study while pregnant
**Smoking related lung disease can be included (COPD, chronic bronchitis, emphysema, & lung cancer)

☐ **CONTROLS**

Yes	No	Inclusion Criteria
		Age >= 40 years old
		Never smokers (waterpipe, cigarette and cigar)

Yes	No	Exclusion Criteria
		Current pregnancy*
		Non-smoking pulmonary disease** (asthma, bronchiectasis, fibrosis)
		Diabetes
		Renal failure

*Pregnant women can be identified but cannot be enrolled in the study while pregnant
**Smoking related lung disease can be included (COPD, chronic bronchitis, emphysema, & lung cancer)

CHECK IF: **ALL** *inclusion* criteria are checked "yes" and **ALL** of *exclusion* criteria are answered "no"

Participants should abstain from smoking for 6 hours prior to testing, be fasting, avoid exercise the day of the assessment, healthy (no infection symptoms, flu, fever)

STUDY SAMPLE

2. Recruitment Strategies

Faced with many difficulties, a variety of recruitment strategies were adopted:

1. Approach smokers in cafes directly

2. Social media

   https://www.aub.edu.lb/fm/studies/waterpipe

   https://www.facebook.com/Waterpipestudy

   @waterpipe_study

3. Posters   /   Flyers   /   Summary Cards

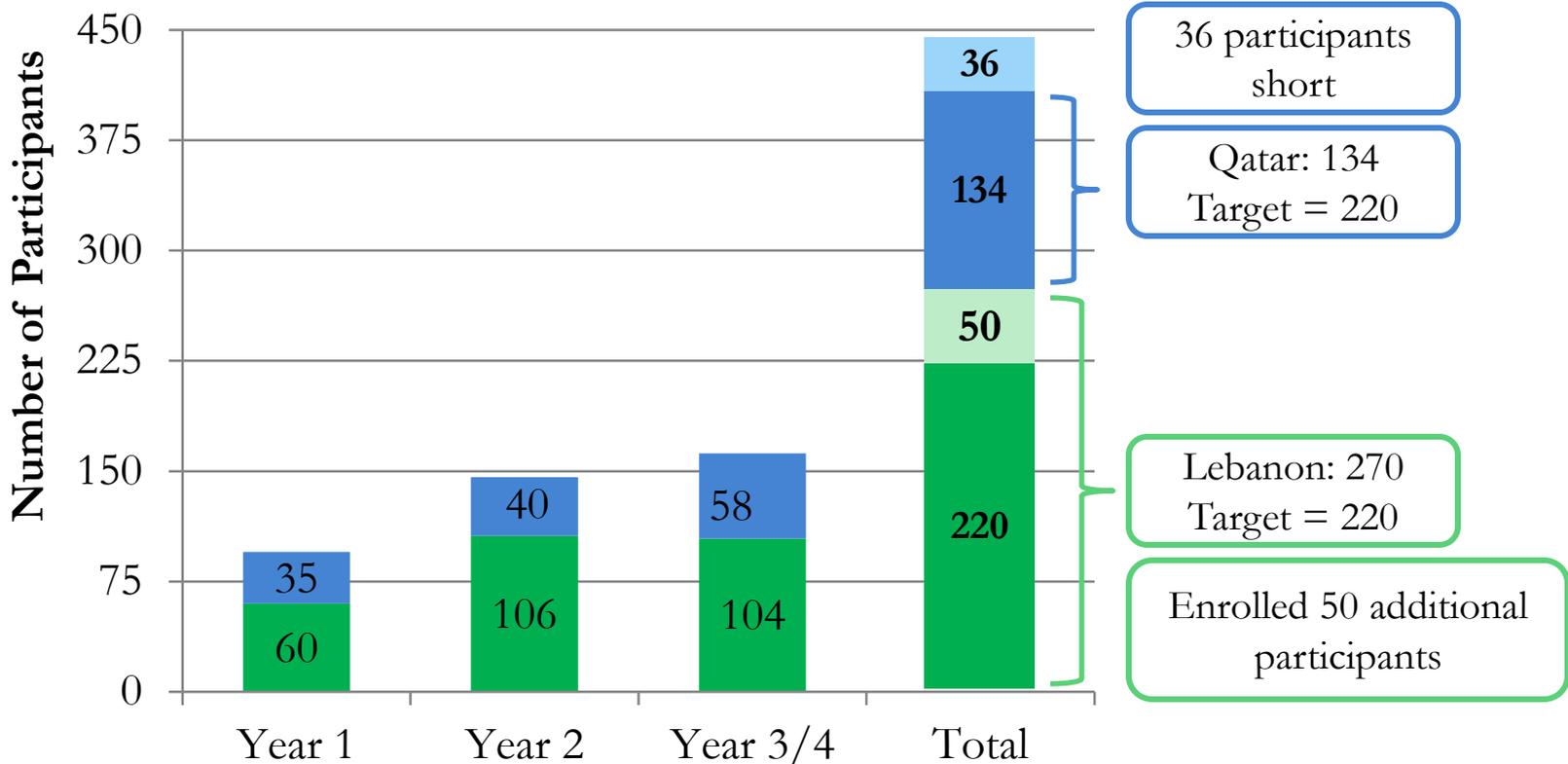4. Newspaper advertisement

STUDY SAMPLE

Started enrolment: Jan 2014   Sept 2013

Completed enrolment: Mar 2017   June 2016
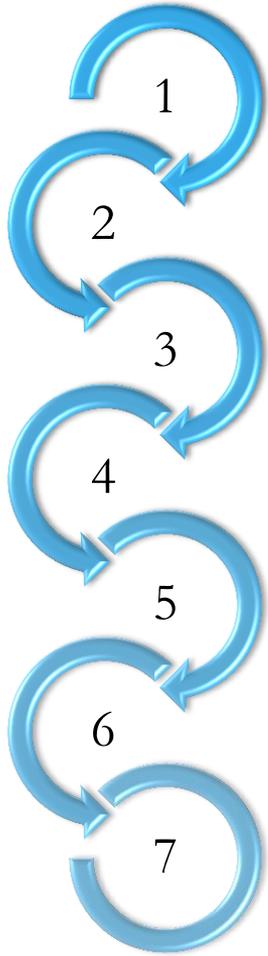
STUDY SAMPLE

2. Recruited participants

Lebanon

AGE	SMOKERS	CONTROLS	TOTAL
40-49	38	40	57
50-59	65	60	103
60-69	20	26	41
70+	11	8	19
Total	136	134	**270**

Qatar

AGE	SMOKERS	CONTROLS	TOTAL
40-49	54	**46**	**77**
50-59	13	16	25
60-69	1	1	2
70+	1	2	2
Total	69	65	**134**

TOTAL: 404

STUDY PROCEDURES

1. **Informed Consent**

2. **Waterpipe Smoking & Health Status Questionnaires**

3. **Measure Height, weight and blood pressure**

4. **Tonometry N=404**

5. **Chest CT scan N=351**

6. **Blood and Urine Sampling for Biomarkers N=404**

7. **Pulmonary Function Testing: Spirometry +IOS***
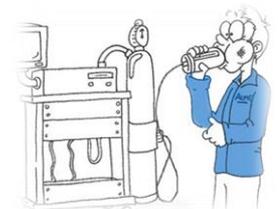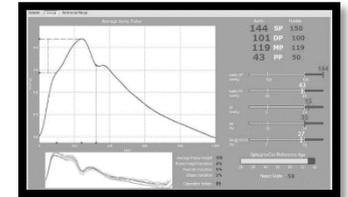
*Impulse Oscilometry performed only in Beirut N= 210

All testing and procedures were harmonized at both site

Original Research

Validation of an Arabic version of an instrument to measure waterpipe smoking behavior

S. Abou Arbid [a], A. Al Mulla [b], B. Ghandour [a], N. Ammar [a], M. Adawi [b], R. Daher [c], N. Younes [b], H.A. Chami [a,d,*]

- Questionnaire:

    WPS Intensity: WP/day

    WPS Pattern of use: daily/occasional

    WPS Duration

    WPS Extent: Waterpipe-years

- Serum Cotinine

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PRIMARY OUTCOME ANALYSIS - 345 Participants

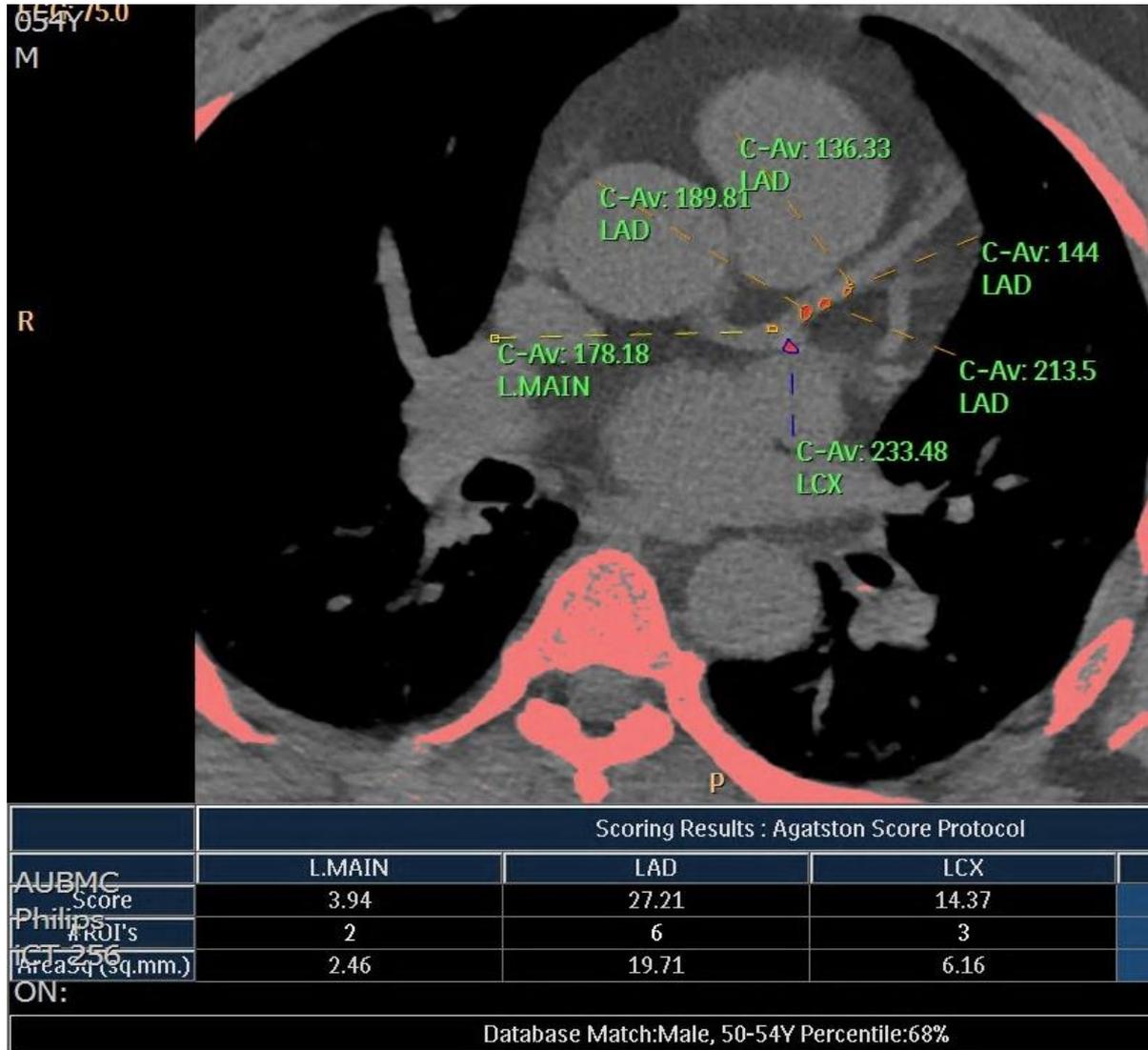(Excluded 6 participants with coronary artery stents)

Sample Characteristics

	WPS Smokers (n=175)	Never smokers (n=170)
Study Site		
Beirut (n=218)	62.9%	63.5%
Doha (n=127)	37.1%	36.5%
Age (Years), *Mean (SD)*	53.7 (9.4)	53.8 (8.7)
Females	33.1%	31.8%
BMI (kg/m^2), *Mean (SD)*	29.7 (4.6)	28.8 (5.1)
Cholesterol		
LDL	125.4 (31.5)	127.7 (32)
HDL	47.0 (12.2)	49.5 (13.3)
Lipid Lowering Medications	**13.1%**	**6.5%**

Sample Characteristics

	WPS Smokers (n=175)	Never smokers (n=170)
Cardiovascular disease		
Prevalent CVD	2.3%	2.4%
Family history of CVD	**57.7%**	**42.2%**
SBP	124.8 (16.4)	128.0 (15.9)
Hypertension	15.4%	14.7%
Anti-hypertensive	17.7	15.9
Consume Alcohol Regularly	6.3%	4.7%
Consume Caffeinated Beverages	**99.4%**	**89.4%**
Exercise Regularly	32.6%	35.3%
Cotinine	**142 (317)**	**1.5 (8.5)**
Waterpipes Smoked/day, *Mean (SD)*	2.3 (1.7)	-
Duration of waterpipe smoking (Years), *Mean (SD)*	27.9 (11.3)	-
Exposed to Second hand smoking	-	**44.9%**

CAC MEASURMENT

	L.MAIN	LAD	LCX	
Scoring Results : Agatston Score Protocol				
Score	3.94	27.21	14.37	
#ROI's	2	6	3	
AreaSq (sq.mm.)	2.46	19.71	6.16	

Database Match:Male, 50-54Y Percentile:68%

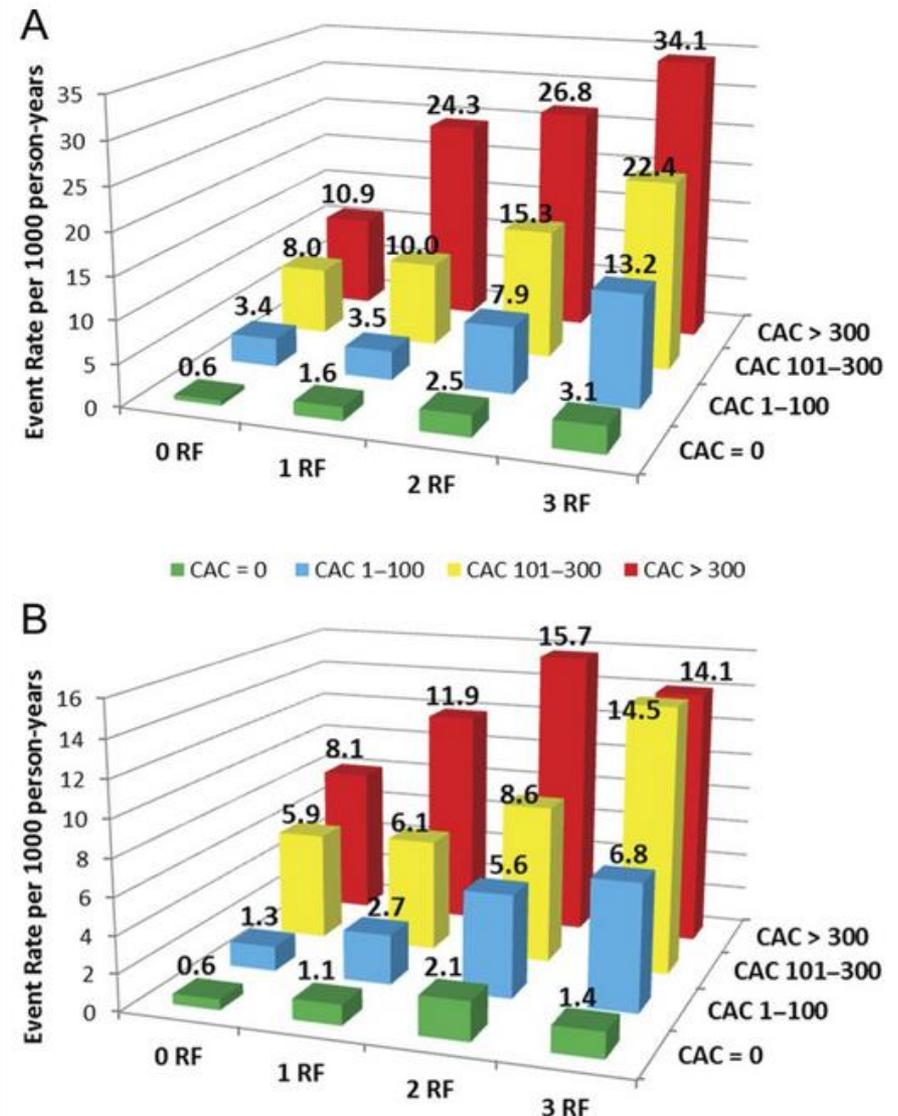## WHY IS CORONARY ARTERY CALCIUM SCORE IMPORTANT?

Individuals with 0 Risk Factors and CAC>100 or >300 had >3 the risk of CHD events of individuals with 3RF and CAC=0

CAC score is a reliable non-invasive test for predicting the risk of future cardiovascular events

Total (*A*) and hard (*B*) coronary heart disease event rates with increasing CAC score according to risk factor (RF) burden (Risk Factors (RF) included : Diabetes, HTN, Cholesterol, current smoking and family history of CHD).
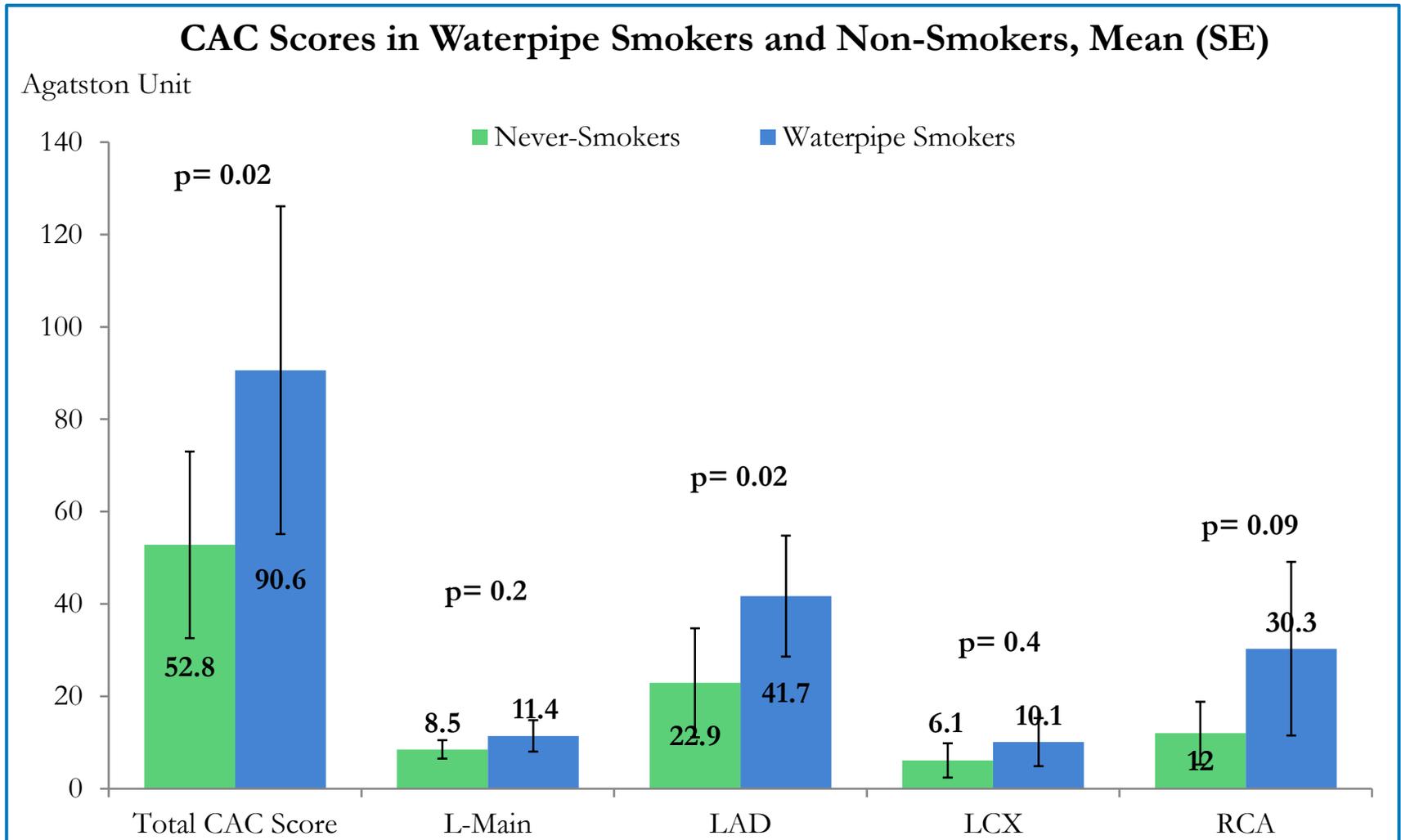
≋ CHEST™

Check for updates

The Association of Water-Pipe Smoking and Coronary Artery Calcium in a Community-Based Sample
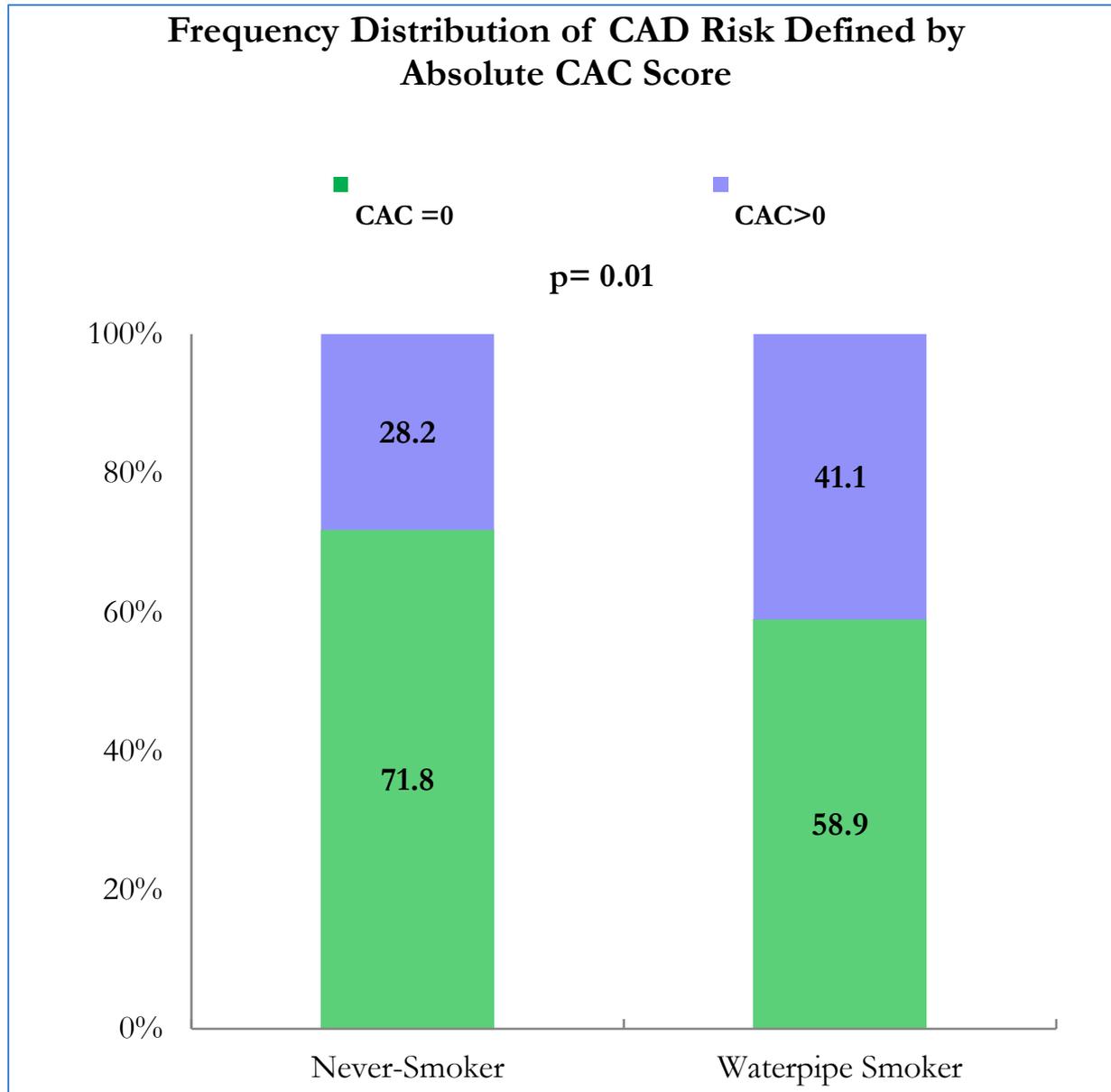
Hassan A. Chami, MD; Hussain Isma'eel, MD; Hani Tamim, PhD; Marwa Adawi, MPH; Mariam Al Kuwari, MD; and Ahmad Al Mullah, MD
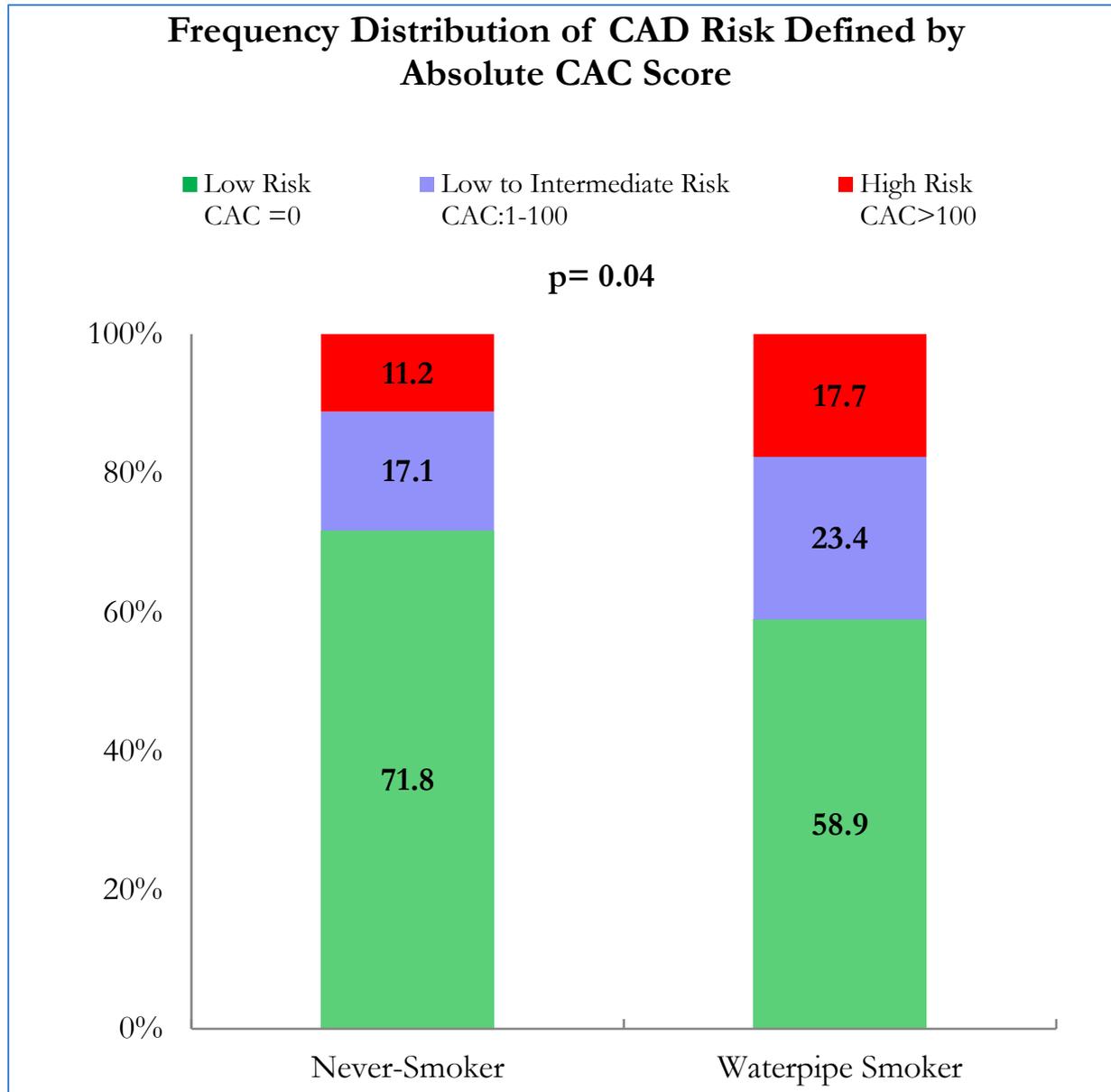
Coronary Artery Calcium Score among WP Smokers and Never Smokers

CAC Scores in Waterpipe Smokers and Non-Smokers, Mean (SE)

Agatston Unit

Legend: ■ Never-Smokers ■ Waterpipe Smokers

- Total CAC Score: Never-Smokers 52.8, Waterpipe Smokers 90.6, p= 0.02
- L-Main: Never-Smokers 8.5, Waterpipe Smokers 11.4, p= 0.2
- LAD: Never-Smokers 22.9, Waterpipe Smokers 41.7, p= 0.02
- LCX: Never-Smokers 6.1, Waterpipe Smokers 10.1, p= 0.4
- RCA: Never-Smokers 12, Waterpipe Smokers 30.3, p= 0.09

Coronary Artery Calcification among WP Smokers and Never Smokers

Frequency Distribution of CAD Risk Defined by Absolute CAC Score

CAC =0   CAC>0

p= 0.01

Risk Category	Never-Smoker	Waterpipe Smoker
CAC>0	28.2	41.1
CAC =0	71.8	58.9

Coronary Artery Disease Risk among WP Smokers and Never Smokers

Frequency Distribution of CAD Risk Defined by Absolute CAC Score

Legend:
- Low Risk CAC =0 (green)
- Low to Intermediate Risk CAC:1-100 (purple)
- High Risk CAC>100 (red)

p= 0.04

Never-Smoker: 71.8 (Low Risk), 17.1 (Low to Intermediate Risk), 11.2 (High Risk)

Waterpipe Smoker: 58.9 (Low Risk), 23.4 (Low to Intermediate Risk), 17.7 (High Risk)

Coronary Artery Disease Risk among WP Smokers and Never Smokers

Frequency Distribution of CAD Risk Defined by %Predicted CAC Score Adjusted for Age, Sex & Race

Legend:
- Low Risk (CAC<25%)
- Low to Intermediate Risk (CAC:25-49%)
- Intermediate Risk (CAC:50-74%)
- High risk (CAC≥75%)

$p = 0.003$

Never-Smoker:
- High risk: 8.9
- Intermediate Risk: 10.7
- Low to Intermediate Risk: 8.9
- Low Risk: 71.6

Waterpipe Smoker:
- High risk: 21.7
- Intermediate Risk: 14.9
- Low to Intermediate Risk: 5.7
- Low Risk: 57.7

Predictors of Coronary Artery Disease Risk Defined by CAC Score

Ref CAC =0	Presence of CAC		CAC 1-100		CAC >100	
	Adjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Waterpipe Smoking	**2.20 (1.2-4.01)**	**0.01**	**1.97 (1.07-3.63)**	**0.03**	**2.45 (1.08-5.56)**	**0.03**
Age	1.18 (1.11 – 1.23)	<0.01	1.14 (1.09-1.20)	<0.001	1.25 (1.18-1.32)	<0.001
Sex	0.15 (0.07-0.31)	<0.01	0.13 (0.06-0.31)	<0.001	0.07 (0.03-0.19)	<0.001
Family history of Heart Disease	2.58 (1.44-4.63)	0.001	2.24 (1.21-4.15)	0.01	3.33 (1.43-7.74)	0.005
Study Site			1.27 (0.62-2.59)	0.52	4.72 (1.47-15.18)	0.01
Lipid lowering meds	2.16 (0.92-5.09)	0.08				
Alcohol	3.60 (1.11-11.66)	0.03				
Caffeine	0.35 (0.10-1.22)	0.10				

Regression model accounted stepwise for: age (ref male); sex; BMI; site (ref Qatar); alcohol; caffeine; exercise; systolic blood pressure; high-density lipoprotein, total cholesterol, lipid lowering medications anti-hypertensive medications and family history of heart disease.

ASSOCIATION OF WATERPIPE SMOKING WITH CAC CATEGORY
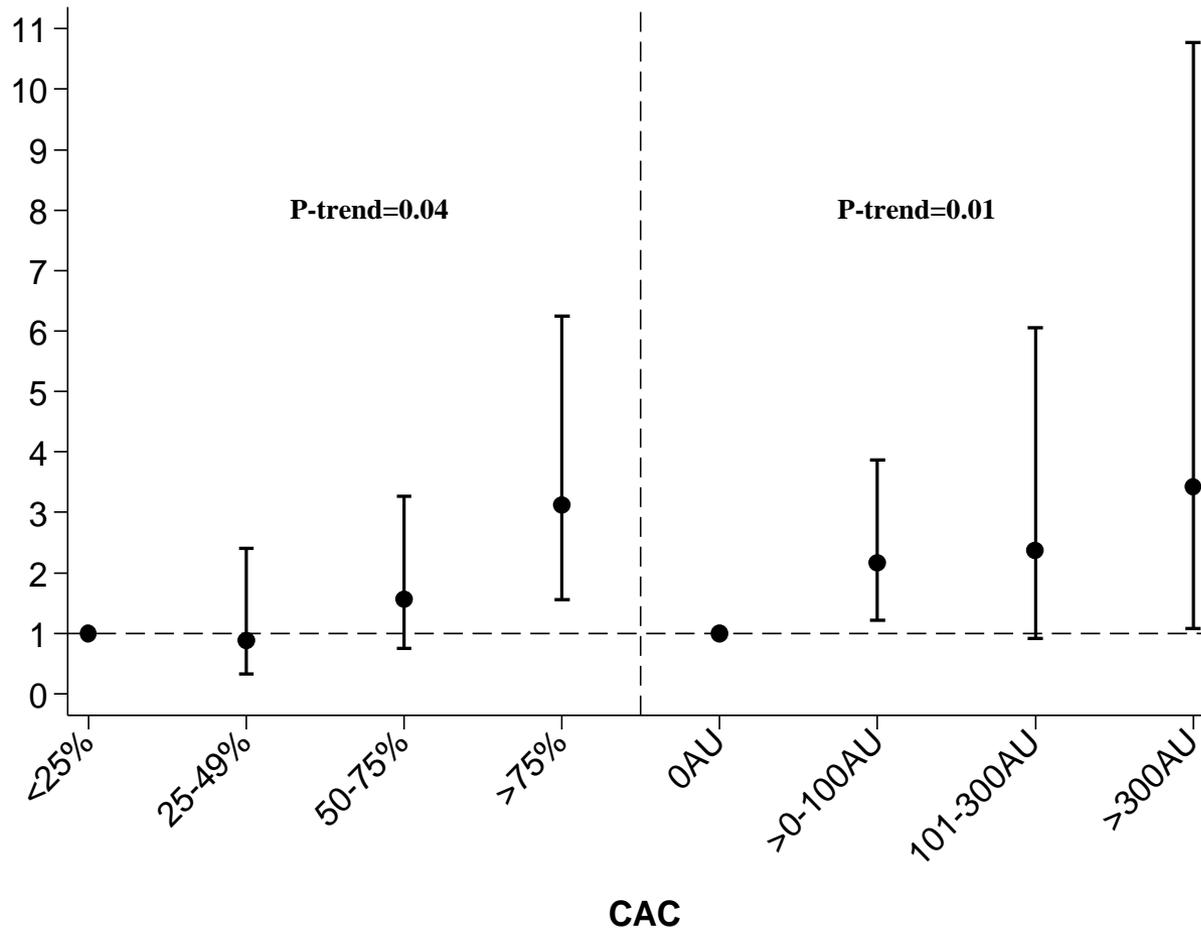
Regression models accounted stepwise for: age; sex; BMI; study site; alcohol consumption; caffeine consumption; exercise; systolic blood pressure; high-density lipoprotein, total cholesterol, lipid lowering medication; anti-hypertensive medications and family history of heart disease.

ASSOCIATION OF CAC WITH WATERPIPE SMOKING EXTENT

	Log (CAC +1)		MESA CHD risk	
	β (95% CI)	P-value	β (95% CI)	P-value
Waterpipe Smoking duration	0.17 (0.05-0.29)	**0.03**	1.69 (1.32-2.05)	**<0.001**
Waterpipe smoked per day	0.09 (-.11 – 0.20)	**0.09**	0.74 (0.35-1.13)	**<0.001**
Waterpipe-years	0.04 (0.003-0.07)	**0.03**	0.37 (0.25-2.05)	**<0.001**

Regression model accounted stepwise for: age (ref male); sex; BMI; site (ref Qatar); alcohol; caffeine; exercise; systolic blood pressure; high-density lipoprotein, total cholesterol, lipid lowering medications anti-hypertensive medications and family history of heart disease.

MESA 10-years CHD risk accounts for age, sex, race/ethnicity, diabetes, current smoking, high-density lipoprotein, total cholesterol, systolic blood pressure, family history of heart attack (in parent/sibling/child), anti-hypertensive or lipid lowering medication use and coronary artery calcium score.
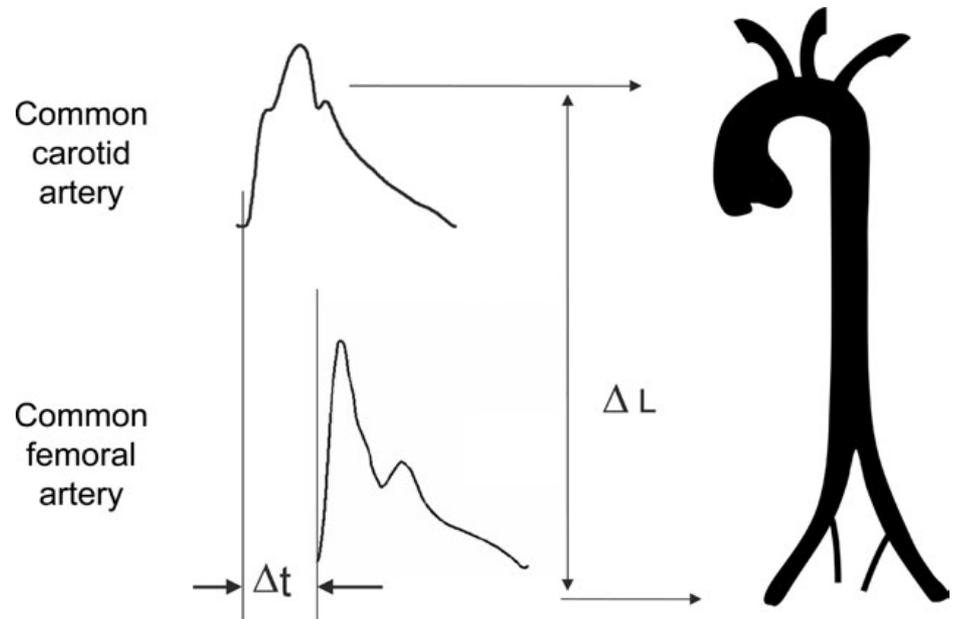
CONCLUSION 1

In a community-based sample of asymptomatic individuals and after adjustment for confounders, **exclusive waterpipe smokers had a higher CAD risk compared to non-smoker,** measured by the presence and extent of CAC
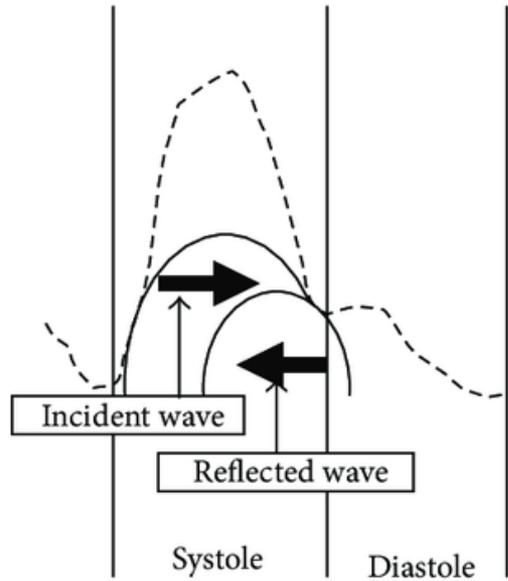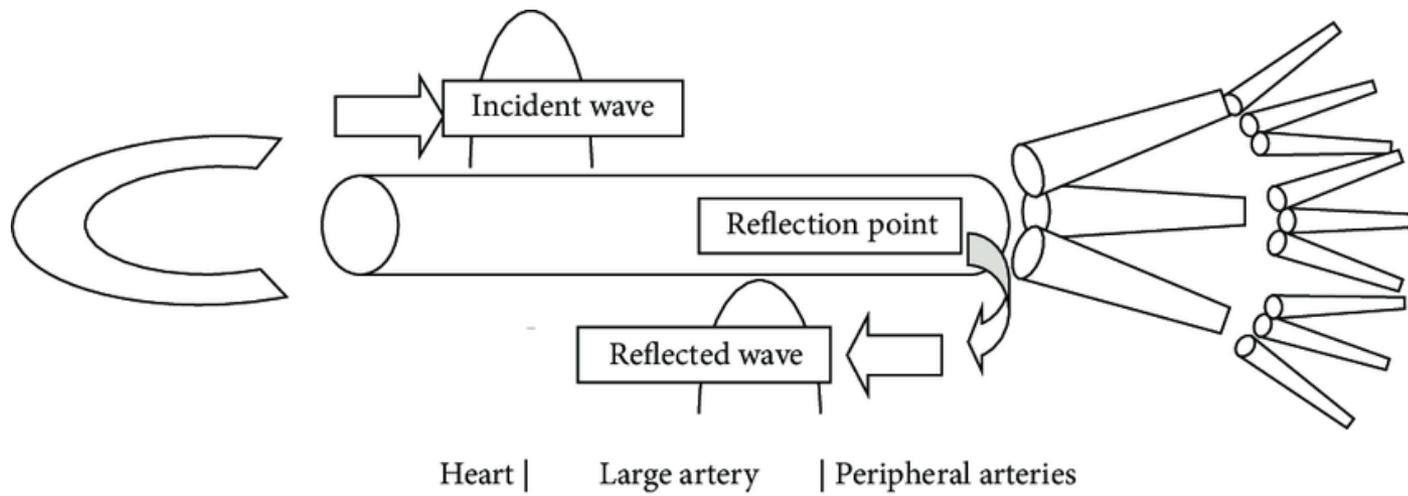
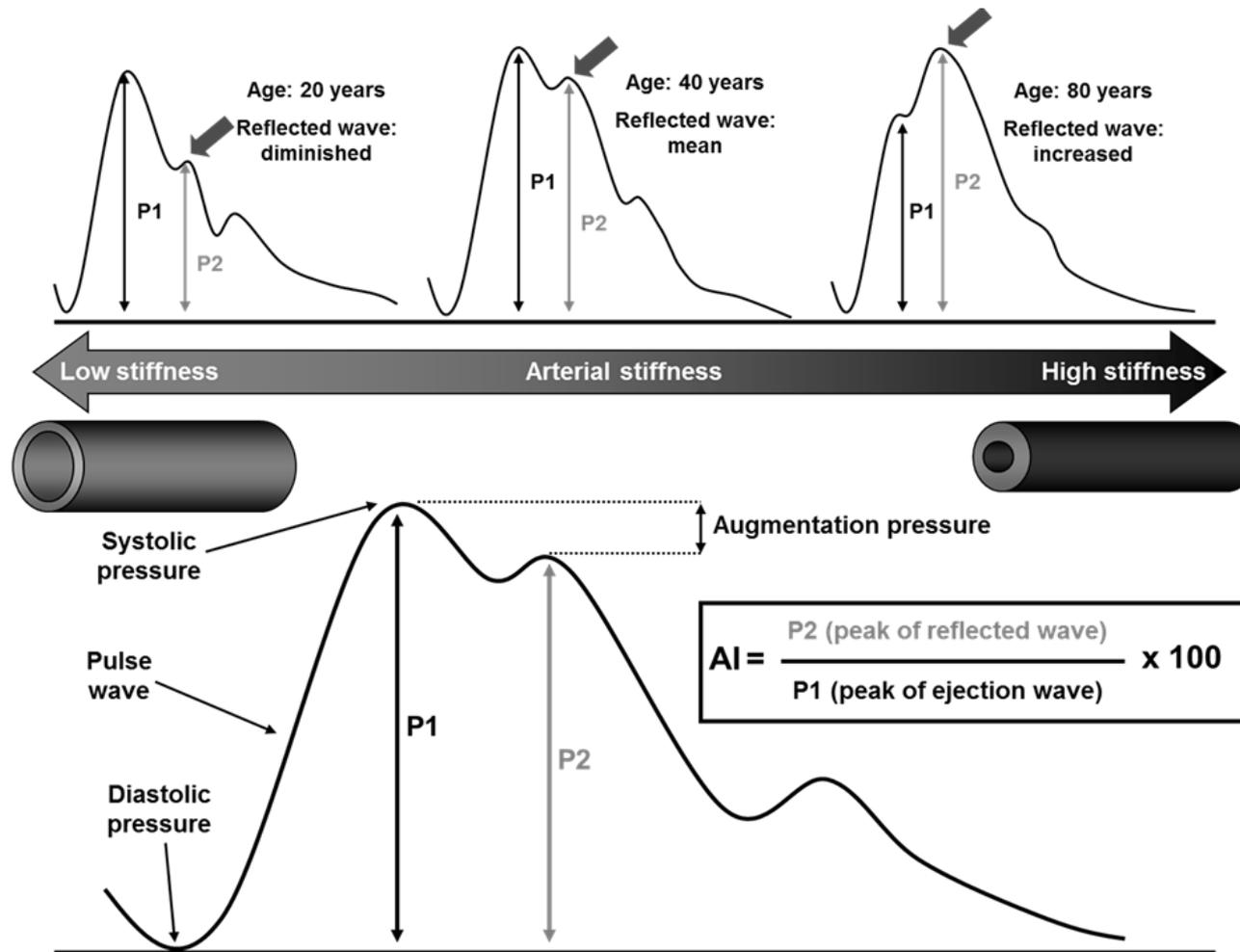# III. WPS AND ARTERIAL STIFFNESS

CF-PWV MEASUREMENT

$$PWV = D \text{ (m)} / \Delta t \text{ (s)}$$

Common carotid artery

Common femoral artery

ΔL

Δt

Time delay between the feet of the two pulse waveforms obtained at the carotid and femoral artery sites

Foot-to-foot velocity method

Incident wave

Reflection point

Reflected wave

Heart | Large artery | Peripheral arteries

Incident wave

Reflected wave

Systole   Diastole

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AP = P2-P1

AI = P2/P1

AIx = AP/PP

$$AI = \frac{P2 \text{ (peak of reflected wave)}}{P1 \text{ (peak of ejection wave)}} \times 100$$

Fonseca et al World journal of cardiovascular disease 2014

IMPORTANCE OF THE AUGMENTATION INDEX

➢ Measure of arterial stiffness

➢ Associated with cardiovascular risk

➢ Predicts the presence and severity of coronary artery disease (CAD)

	Quartile I	Quartile II	Quartile III	Quartile IV
■ % CAD	57.1	71.2	81.8	91.7
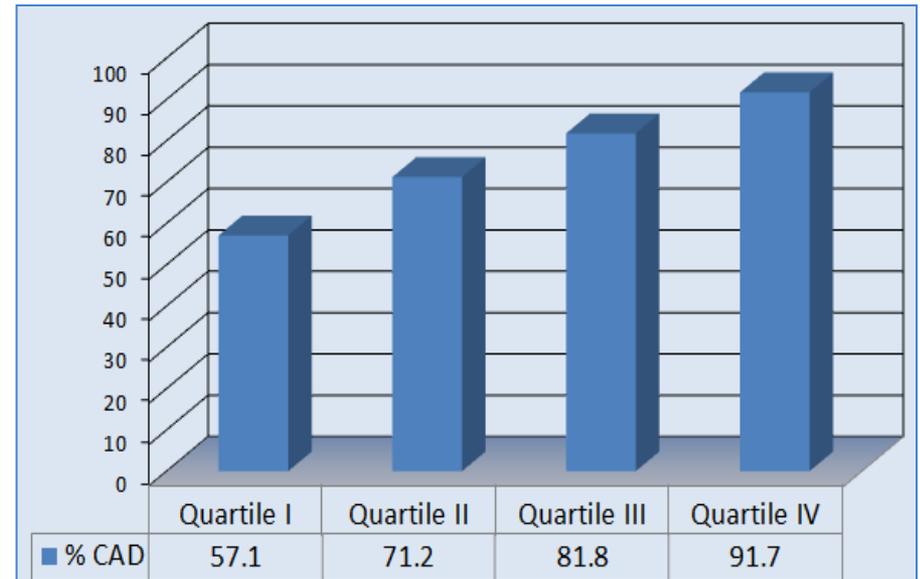
AIx and presence of CAD in younger patients (up to 60 years of age). AIx, 17 to 9, 10 to 21, 22 to 28, and 29 to 60 in quartiles 1, 2, 3, and 4, respectively.

Nürnberger J Journal of hypertension. 2002;20(12):2407-14
Weber et al. 2004. *Circulation*. 2004;109:184-189

Acute Effect of Hookah Smoking on Arterial Stiffness and Wave Reflections in Adults Aged 18 to 34 Years of Age

Mary Rezk-Hanna, PhD[a,b,*], Lynn Doering, PhD[b], Wendie Robbins, PhD[b], Linda Sarna, PhD[b], Robert M. Elashoff, PhD[c], and Ronald G. Victor, MD[a,**]
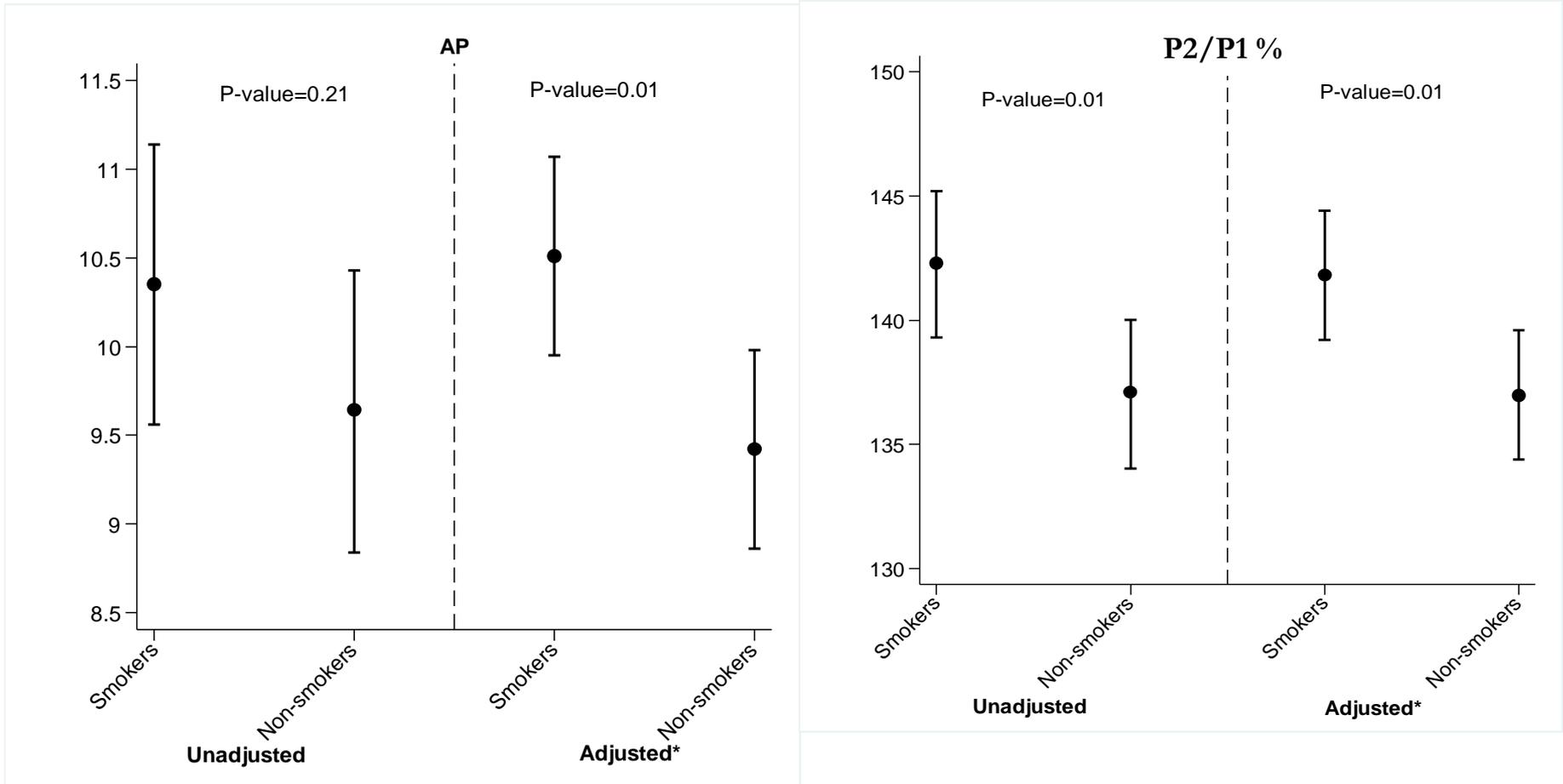
Hemodynamics, brachial blood pressure, indexes of vascular stiffness and exposure biomarkers responses to acute hookah smoking

Variable	Pre-Hookah	Post-Hookah	p Value
Heart rate (beats·min^{-1})	64 ± 1	80 ± 2	<0.001
Respiratory rate (breath·min^{-1})	17 ± 0	19 ± 1	<0.001
Brachial blood pressure (mm Hg)			
Systolic	115 ± 1	123 ± 2	<0.001
Diastolic	68 ± 1	73 ± 1	<0.001
Pulse pressure	47 ± 1	51 ± 2	<0.001
Mean	84 ± 1	90 ± 1	<0.001
Indices of vascular stiffness			
Carotid-femoral pulse wave velocity (m/s^{-1})	7.59 ± 0.15	8.25 ± 0.16	<0.001
Augmentation index (%)	13.68 ± 11.87	19.12 ± 11.63	0.034
Aortic blood pressure (mm Hg)			
Systolic	101 ± 1	108 ± 2	<0.001
Diastolic	70 ± 1	73 ± 2	<0.001
Pulse pressure	32 ± 1	35 ± 1	0.035
Mean	80 ± 1	85 ± 1	<0.001
Exposure biomarkers			
Expired carbon monoxide (ppm)	3.23 ± 0.27	28.67 ± 1.67	<0.001
Plasma nicotine (ng/ml)	0.57 ± 0.05	5.57 ± 0.98	<0.001

Data are reported as mean ± SE.

Pulse Wave Velocity

Augmentation Index

Central Aortic Systolic BP

Central Aortic Diastolic BP
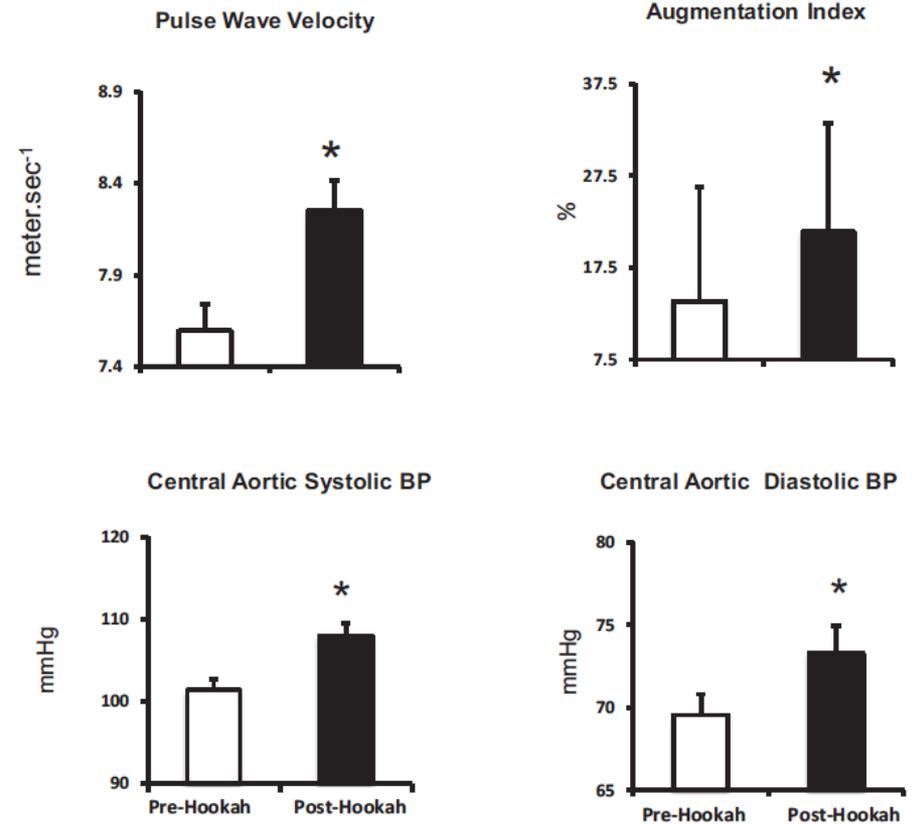
AUGMENTATION INDEX IN WPS (205) AND NON-SMOKERS (199)

AP

P-value=0.21   P-value=0.01

P2/P1 %

P-value=0.01   P-value=0.01

Adjusted stepwise for: Age; sex; body-mass index; study site; alcohol consumption; caffeine consumption; regular exercise; systolic blood pressure; high-density lipoprotein, cholesterol, lipid lowering medication; anti-hypertension medications, family history of heart disease, and tonometry heart rate.

AUGMENTATION INDEX & PWV IN WPS AND NON-SMOKERS
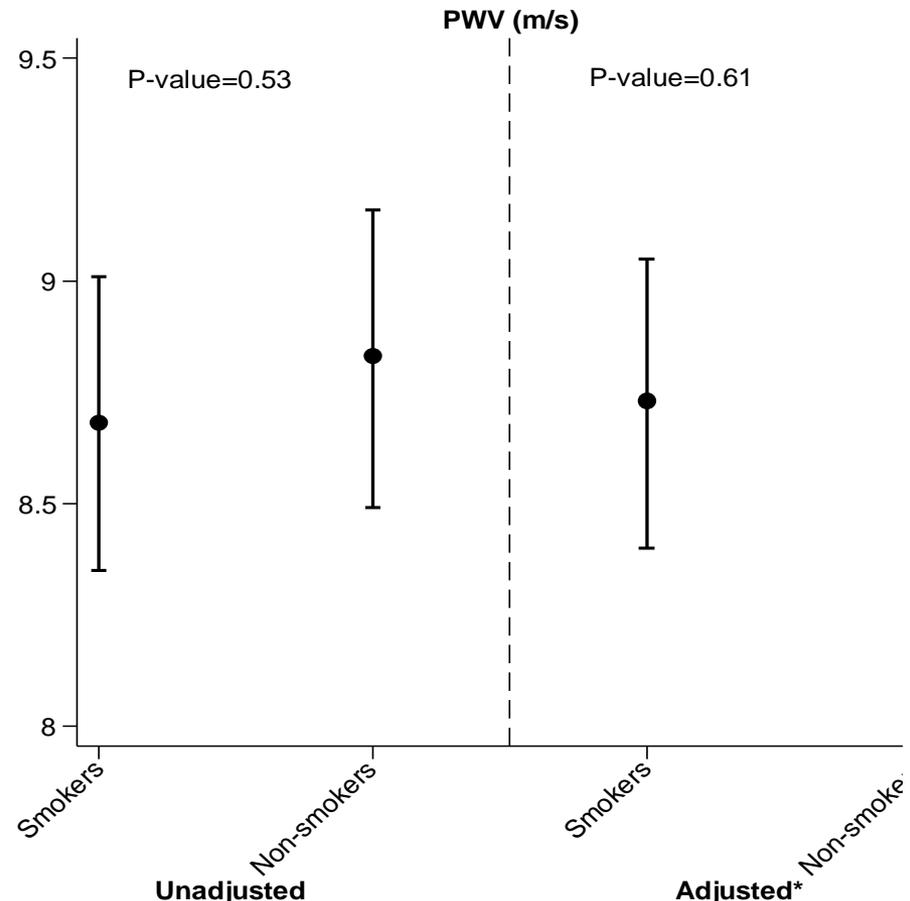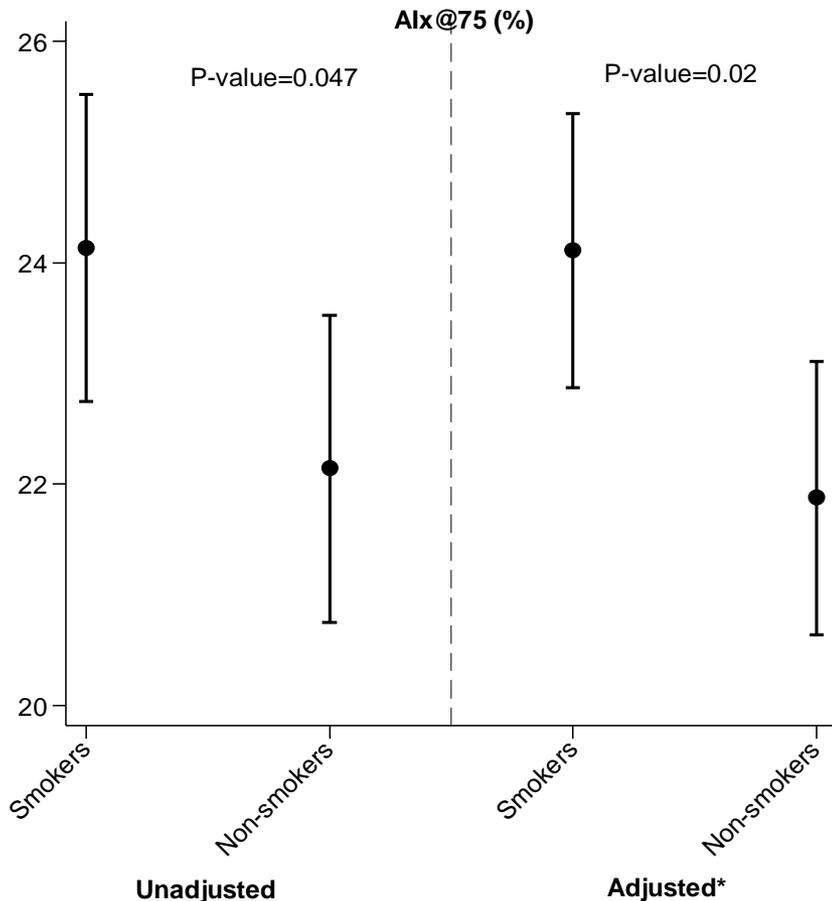
Adjusted stepwise for: Age; sex; body-mass index; study site; alcohol consumption; caffeine consumption; regular exercise; systolic blood pressure; high-density lipoprotein, cholesterol, lipid lowering medication; anti-hypertension medications, family history of heart disease, and tonometry heart rate.

ASSOCIATION OF ARTERIAL STIFNESS WITH WATERPIPE SMOKING EXTENT

	AP (mmHg)		AIx (%)		AIx@75 (%)		P2/P1 (%)		PWV (m/s)	
	β (95 % CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value	β (95 % CI)	p-value
Waterpipe Smoking (Yes/No)	1.04 (0.26;1.81)	**0.01**	2.52 (0.82;4.21)	**0.004**	2.31 (0.604.03)	**0.01**	4.74 (1.17;8.31)	**0.01**	-0.004 (-0.45;0.45)	0.98
Waterpipe-years (by 10 units)	0.13 (0.06;0.20)	**0.001**	0.30 (0.13;0.47)	**<0.001**	0.28 (0.11;0.45)	**0.002**	0.64 (0.29;1.00)	**<0.001**	-0.005 (-0.05;0.04)	0.82
Waterpipes smoked per day	0.48 (0.15;0.81)	**0.005**	1.04 (0.53;1.56)	**<0.001**	0.94 (0.24;1.65)	**0.009**	2.35 (0.83;3.86)	**0.003**	-0.09 (-0.22;0.05)	0.22
Waterpipe smoking duration (years)(by 10 units)	0.34 (0.08;0.61)	**-0.01**	0.80 (0.22;1.39)	**0.01**	0.74 (0.15;1.35)	**0.01**	1.59 (0.36;2.81)	0.01	0.049 (-0.10;0.20)	0.53
Cotinine levels (by 100 units)	0.24 (0.05;0.42)	**0.01**	0.51 (0.11;0.91)	**0.01**	0.56 (0.15;0.97)	**0.01**	0.92 (0.11;1.74)	**0.03**	-0.04 (-0.15;0.07)	0.46

Adjusted stepwise for: Age; sex; body-mass index; study site; alcohol consumption; caffeine consumption; regular exercise; systolic blood pressure; high-density lipoprotein, cholesterol, lipid lowering medication; anti-hypertension medications, family history of heart disease, and tonometry heart rate.

CONCLUSION 2

In a community-based sample and after adjustment for confounders, **asymptomatic exclusive WPS had increased augmentation index compared to non-smokers**

IV. WPS AND LUNG FUNCTION

Table 3 Long-term effect of waterpipe smoking on pulmonary function

Study	Population	WP quantity	Tobacco type	Included only healthy participants?	Comparison	Diff in FEV₁%pred*	Diff in FVC %pred*	Diff in FEV₁/FVC %*	Diff in FEF25–75% pred*
Boskabady 2012[61]	371 men, 301 women, average ages in 30s and 40s	Average (Avg) 1.17 (±0.53) WP smoked per week	Unspecified	Yes	WP vs non-smokers	−14.6	−21.9	NE	−13.8
					WP vs cigarette (normal inhalation)	−3.83 (NS)	−7.03	NE	−13.0
Ben Saad 2013[63]	142 men age 35–60 years	Avg 36 (±22) WP-years	Tabamel (sweetened tobacco)	Yes	WP vs cigarette	+24.0	+14.0	+13.0	NE
Ben Saad 2011[62]	110 men, age 20–60 years	Median 14 WP-years 14	Unspecified	Yes	WP vs reference values	†	†	†	†
Mutairi 2006[64]	139 men, 13 women, age 24–65 years	unspecified	Moassal,	Yes	WP vs cigarette	−1.1 (NS)	NE	+0.5‡ (NS)	NE
					WP vs non-smokers	−12.2 (NS)	NE	−2.5‡ (NS)	NE
Aydin 2004[65]	25 persons average age 49.2 (±12.2) years	Avg 23.7 (±8.3) years smoking 1–2 times/day	Unspecified	Yes	WP vs passive cigarette smokers	−2.5 (NS)	+0.9 (NS)	−5.6‡	−7.2 (NS)
Kiter 2000[66]	397 men, age 18–85 years	Average 37 (±42) Jurak-years	Jurak (tobacco-fruit mixture)	No	WP vs non-smokers	−6.5	−5.86 (NS)	−3.02‡	−8.63
					WP vs cigarette	+3.01	−0.5 (NS)	+4.49‡	+5.08
Mohammad 2013[67]	788 women, age 44 + years	Unspecified	Unspecified	No	WP vs cigarette	+5.3 (NS)	NE	+0.1 (NS)	NE
					WP vs non-smokers				
She 2014[69]	1238, mostly men, age 40+ years	Average 28 (±11.2) years of 17.9 (±8.9) g tobacco/day	Chinese WP tobacco	Yes	WP vs non-smokers	−9.4	+6.1	−12.1	NE
					WP vs cigarette	−4.0	+7.1	−8.0	NE
					WP passive vs never-passive	−9.0	−6.6	−4.5	NE
					WP passive vs cigarette-passive	−6.9	−5.5	−3.0	NE
Al-Fayez 1988[70]	441 men, 154 women smokers, 878 total participants, men 20–59 years, women 17–59 years	Not reported	Jurak (tobacco-fruit mixture)	Yes	WP smokers vs non-smokers				
					Males	−0.54 L	−0.43 L	−4.6	NE
					Females	−0.41 L	−0.19 L	−11.42	NE
Boskabady 2014[71]	§	§	§	§	§	§	§	§	§
Layoun 2014[21]	87 men, 45 women, avg age 33.4 (±13.29) years, exclusive WP smokers	Avg 11.12 (±17.27) WP/ week	Moassal	No	WP vs non-smokers	−4.4 (NS)	−9.1	+5.56	NE
					WP vs cigarette	+1.63 (NS)	−2.28 (NS)	+4.28	NE

Primarily community-based

Limitations: Cross sectional, lack of standardized WPS assessment or spirometric methods not clearly defined, no adjustment for confounding

El Zaatari ZM et al Tob Control 2015;24:i31

CHEST

Effects of Water-Pipe Smoking on Lung Function

A Systematic Review and Meta-analysis

Dany Raad, MD; Swarna Gaddam, MBBS, MPH; Holger J. Schunemann, MD, PhD, FCCP; Jihad Irani, MD, MPH; Philippe Abou Jaoude, MD; Roland Honeine, MD; and Elie A. Akl, MD, PhD, MPH

FEV$_1$

Forest plot for FEV$_1$:

Study or Subgroup	Waterpipe smoking Mean	SD	Total	No tobacco smoking Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Al Fayez 1988 A[18]	86.31	5.71	252	88.43	6.4	164	29.7%	-0.35 [-0.55, -0.16]
Al Fayez 1988 B[18]	82.39	6.63	92	87.06	9.08	119	19.7%	-0.57 [-0.85, -0.30]
Al Mutairi 2006[16]	89.8	18	77	102	39.55	16	6.7%	-0.53 [-1.07, 0.02]
Aydin 2004[19]	97.5	5.2	14	100	4.9	11	3.2%	-0.48 [-1.28, 0.33]
Kiter 2000[17]	88.63	19.14	82	93.6	15.48	117	19.1%	-0.29 [-0.57, -0.01]
Koseoglu 2006[21]	105.8	19	20	103.6	12.7	15	4.6%	0.13 [-0.54, 0.80]
Mohammad 2008[20]	83.5	17.79	77	94.08	13.65	100	17.2%	-0.68 [-0.98, -0.37]
Total (95% CI)			614			542	100.0%	-0.43 [-0.58, -0.29]

Heterogeneity: Tau² = 0.01; Chi² = 7.85, df = 6 (P = 0.25); I² = 24%
Test for overall effect: Z = 5.72 (P < 0.00001)

Favors no tobacco smoking   Favors waterpipe smoking

FEV$_1$/FVC
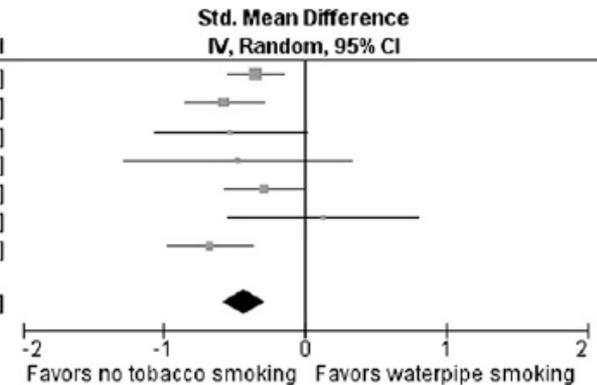
Forest plot for FEV$_1$/FVC:

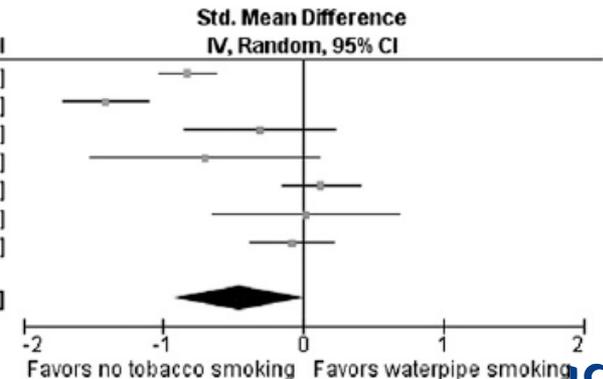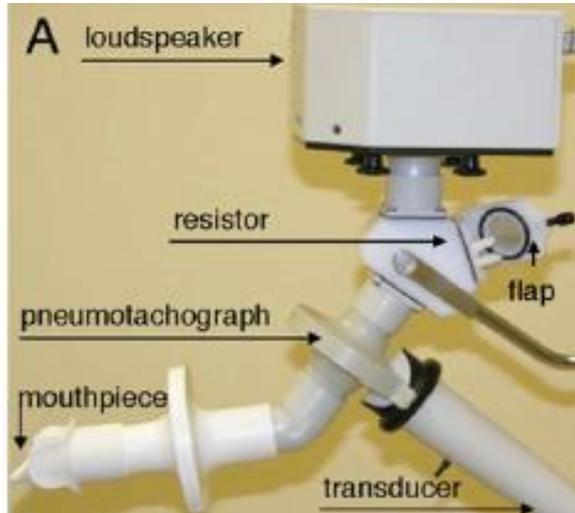| Study or Subgroup	Waterpipe smoking Mean	SD	Total	No tobacco smoking Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Al Fayez 1988 A[18]	81.6	4.92	252	86.2	6.4	164	16.1%	-0.83 [-1.03, -0.62]
Al Fayez 1988 B[18]	75.14	6.05	92	86.52	9.27	119	15.5%	-1.41 [-1.72, -1.11]
Al Mutairi 2006[16]	89.54	8.5	77	92	3.25	16	13.6%	-0.31 [-0.85, 0.23]
Aydin 2004[19]	82.1	8.5	14	87.7	6.5	11	11.1%	-0.70 [-1.52, 0.11]
Kiter 2000[17]	98.16	13.28	82	96.82	8.19	117	15.7%	0.13 [-0.16, 0.41]
Koseoglu 2006[21]	82.1	4.9	20	82	6.3	15	12.4%	0.02 [-0.65, 0.69]
Mohammad 2008[20]	80.51	11.27	77	81.24	6.87	100	15.6%	-0.08 [-0.38, 0.22]
Total (95% CI)			614			542	100.0%	-0.46 [-0.93, 0.01]

Heterogeneity: Tau² = 0.35; Chi² = 73.17, df = 6 (P < 0.00001); I² = 92%
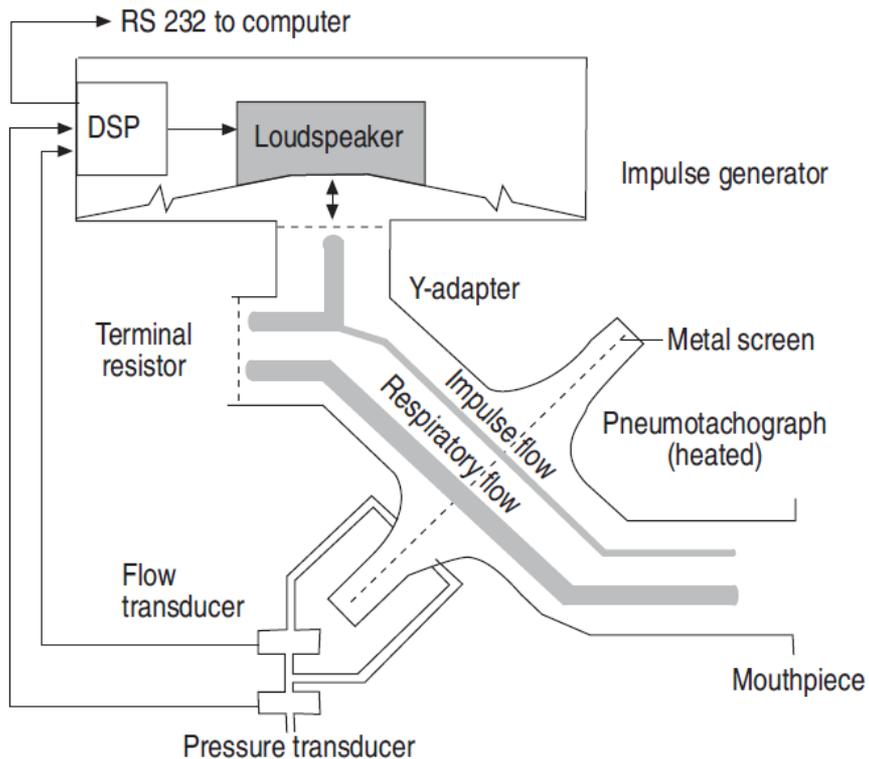Test for overall effect: Z = 1.93 (P = 0.05)

Favors no tobacco smoking   Favors waterpipe smoking

Raad D et al. Chest 2011;139:764-774

45

IMPULSE OSCILLOMETRY

A simple, non-invasive technique that assesses the mechanical properties of the lungs during normal breathing

IOS TECHNIQUE

- **Brief oscillating sound waves at multiple frequencies are generated through a loudspeaker at the mouth.**

  The waves propagate across the airways resulting in distension and recoil of the elastic components of the lungs.

  Reflected waves are detected by flow and pressure transducers and are analyzed to calculate airway resistance (R) and reactance (X)

IOS DETECTS COPD SEVERITY
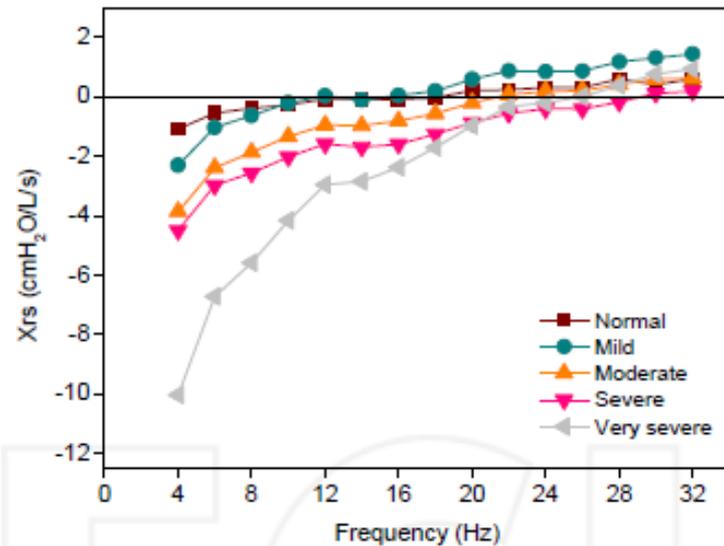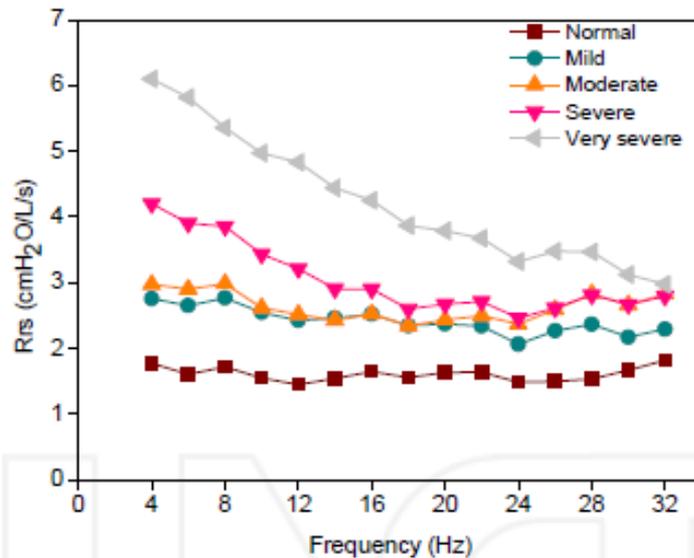
IOS detects patients with varying degrees of COPD

Di Mango et al. 2006

IOS DETECTS EARLY RESPIRATORY DYSFUNCTION
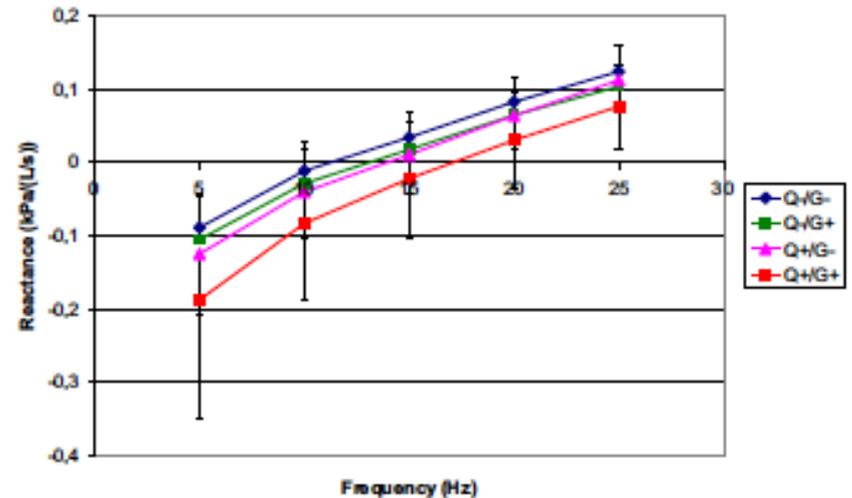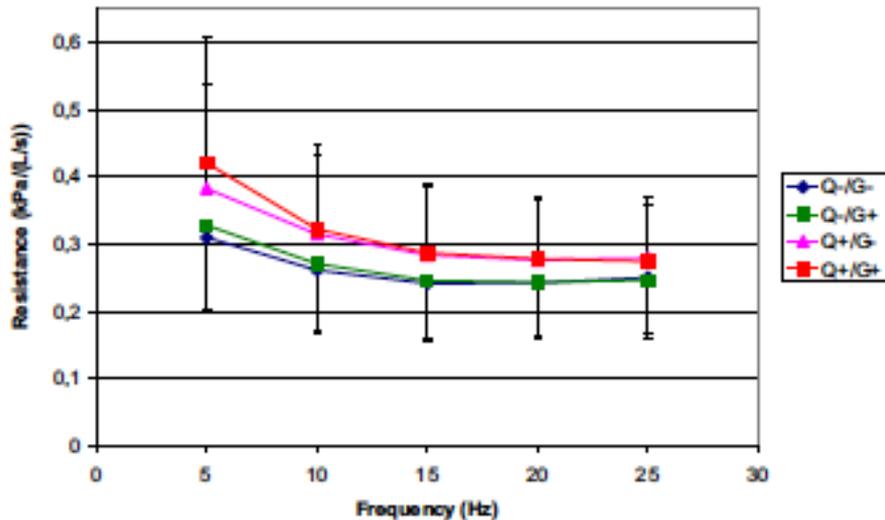
IOS is highly sensitive for detecting early changes in respiratory function
Even when spirometry s normal

Q: questionnaire
G: GOLD spirometry

Frantz, S., et al. Respir Med, 2012. 106(8): p. 1116-23

Spirometry Measures in WPS and non-smokers
N=210

Forced Vital Capacity % Predicted, Mean
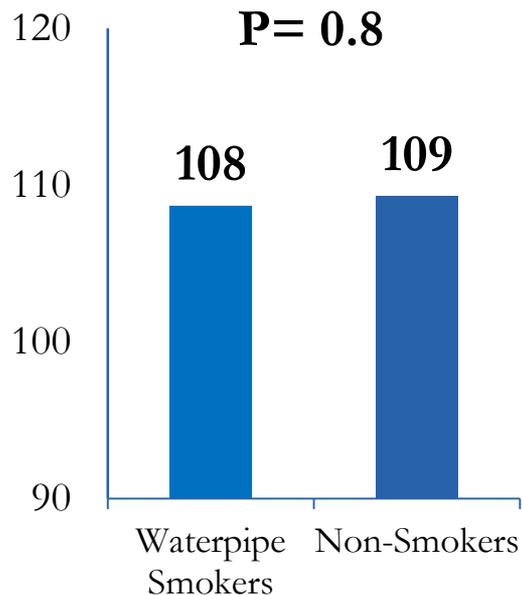
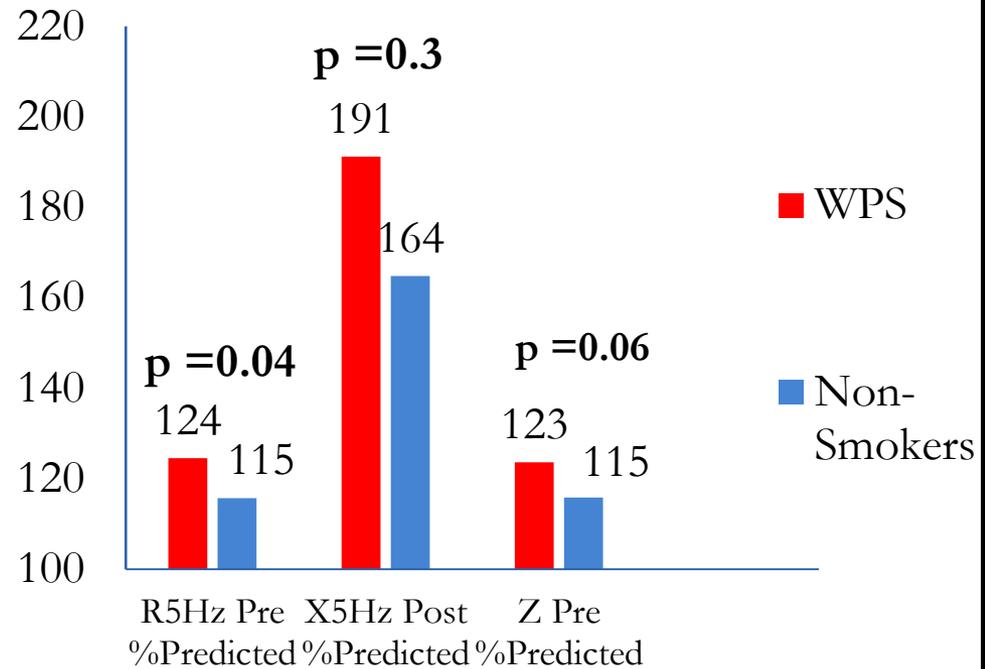**Forced Expiratory Volume 1 % Predicted, Mean**

FEV1/FVC< 70%

P= 0.8

108 109

P= 0.6

109 108

P= 0.3

2.2 5.9
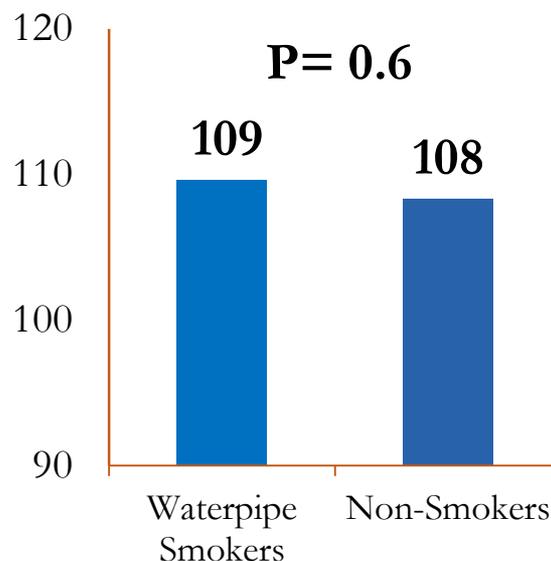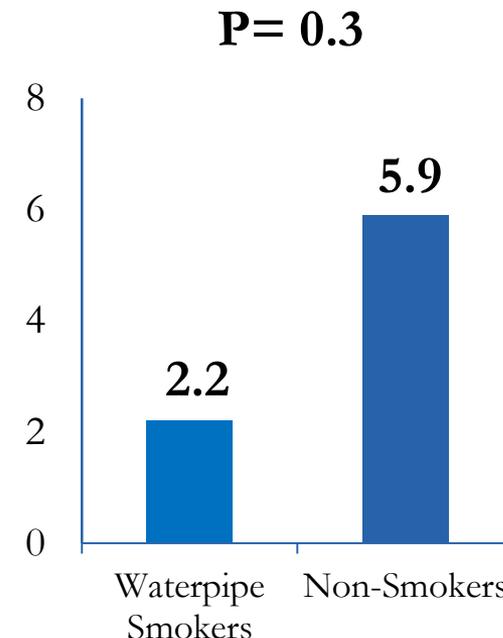
	WSP	Non-smokers	P-value
Cough	0	0	-
Dyspnea	2 (2.2%)	0	0.4
Emphysema	1 (1.1%)	0	0.2
COPD	0	0	-

IMPULSE OSCILLOMETRY IN WPS AND NON-SMOKERS (N=210)

Measured (kPa/L/s) Mean (SD)
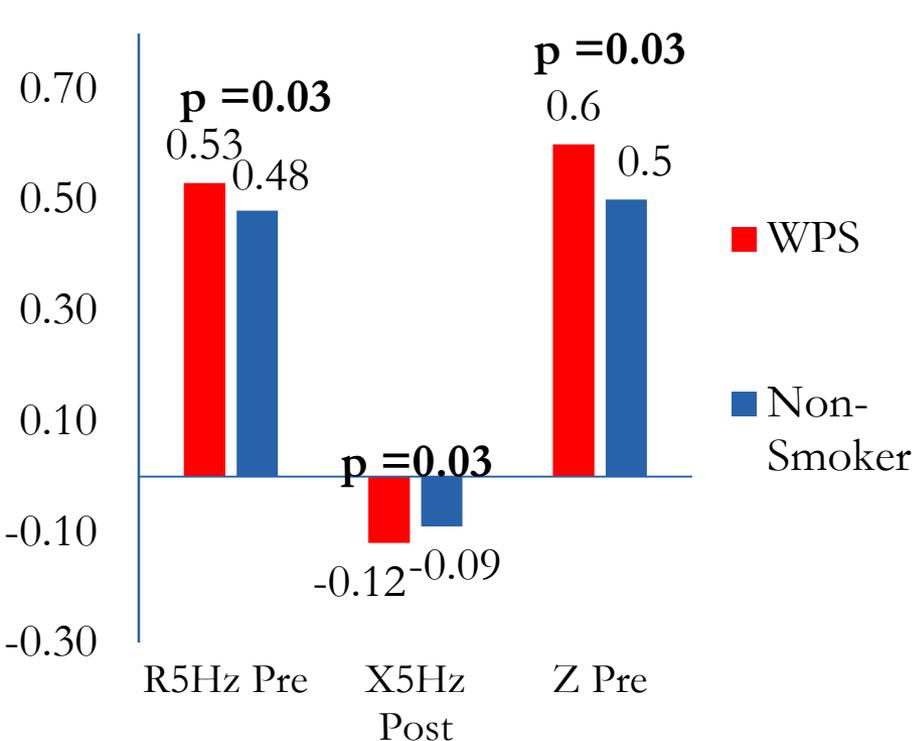
% Predicted, Mean (SD)

Association of IOS measures with Waterpipe Smoking Extent

| IOS Parameters		R5Hz Pre	R5Hz Pre, % predicted	X5Hz Pre	X5Hz Pre, % predicted	Z Pre	Z Pre, % predicted
Waterpipe-year (by 10 years)	β (95 %CI)	0.007 (0.001; 0.01)	0.009 (-0.001;0.02)	-0.002 (-0.005;0.0)	0.02 (-0.02; 0.05)	0.007 (0.001;0.01)	0.002 (-0.007;0.01)
	p-value	**0.02**	0.09	0.10	0.3	**0.01**	0.6
Duration of Waterpipe Smoking (years)	β (95 %CI)	0.04 (0.01; 0.08)	0.05 (0.001;0.10)	0.01 (-0.02;0.006)	0.14 (0.01; 0.27)	0.05 (0.01;0.08)	0.01 (-0.03;0.06)
	p-value	**0.01**	**0.05**	0.3	**0.03**	**0.004**	0.5

% Predicted for age, sex, race, and height

CONCLUSION 3

Apparently healthy, largely asymptomatic exclusive waterpipe smokers from the community have **impaired lung function assessed by IOS** compared to non-smokers

V. WPS AND COPD
SPIROMETRY
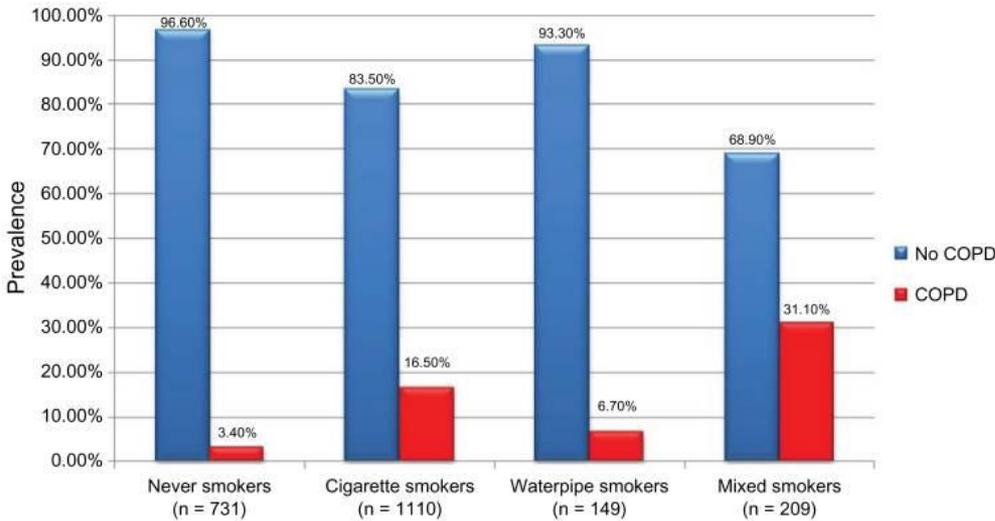
Independent variables in logistic regression model[a]	OR[a]	95% CI
Dependent variable = COPD		
Older age group[b]	1.05	1.04–1.06
Region		
Mount Lebanon vs Beirut	0.84	0.58–1.22
North Lebanon vs Beirut	0.97	0.62–1.52
South Lebanon vs Beirut	0.80	0.48–1.31
Bekaa plain vs Beirut	1.59	1.01–2.51
Cigarette smoking	4.88	3.37–7.06
Water-pipe smoking	2.53	1.83–3.50

- Cross-sectional community based study N=2201
- GOLD Spirometry definition of COPD FEV1/FVC<70%
- Adjusted for possible confounders: including age and cigarettes smoking

Waked M et al Clin Epidemiol 2011;3:315–23.

- Similar association with the Chinese waterpipe OR =10.62

She J et al. Chest 2014;146:924–31.

V. WPS AND COPD
CHRONIC BRONCHITIS

- **"Chronic cough with sputum production for >3 consecutive months per year for > 2 years"**

- **Cross-sectional questionnaire-based studies adjusting for cigarette smoking**

- Adjusted OR=1.42, 95% CI 1.12-1.8

  Tageldin MA, et al. Respir Med 2012;106(Suppl 2):S25–32

- Adjusted OR= 1.89, 95% CI 1.16-3.07

  Waked M, et al East Mediterr Health J 2009;15:432–42.

- Adjusted OR=5.65 in >20 WP-years

  Salameh P, et al. East Mediterr Health J 2012;18:996–1004

V. WPS AND COPD
QUANTITATIVE EMPHYSEMA
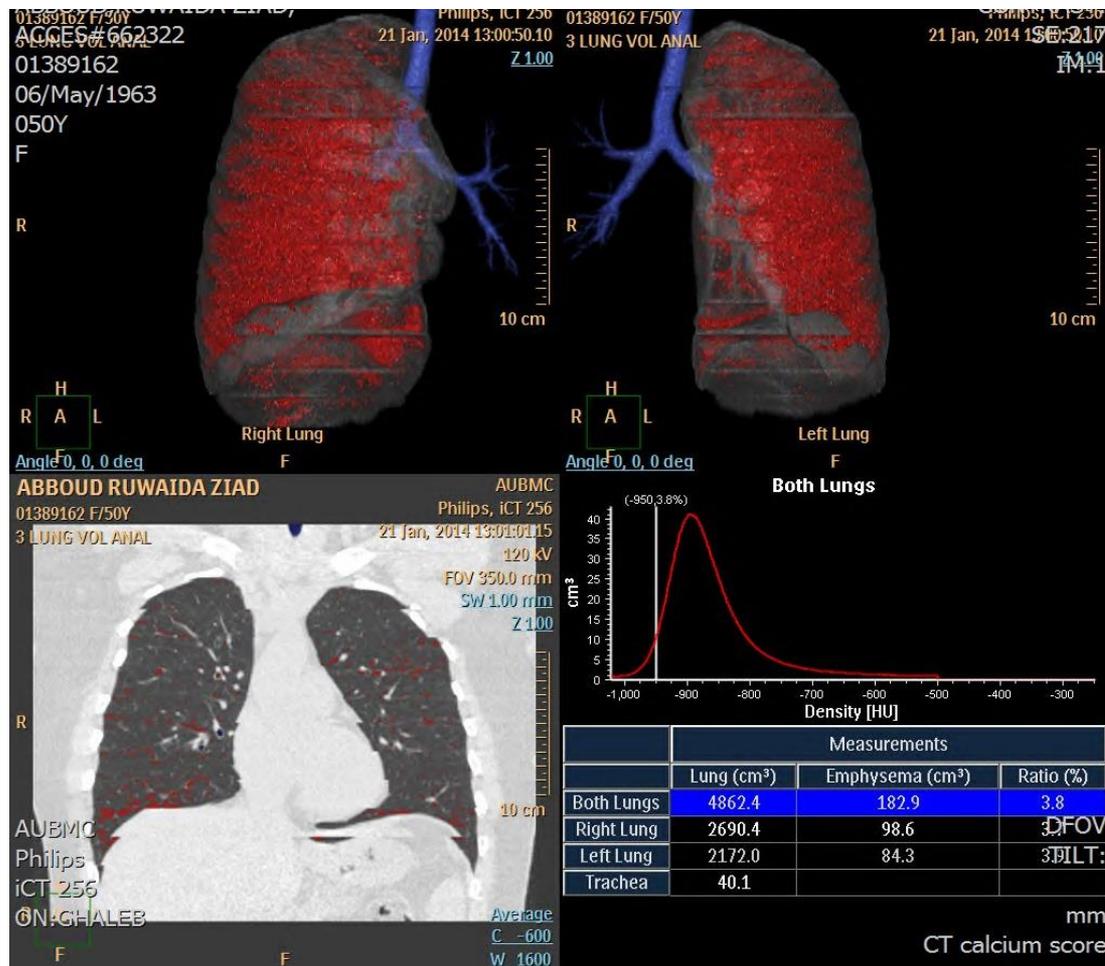
- Measured using quantitative analysis of lung CT images
- Measures volume of low density pixels <950 HU
- Correlated with extent of emphysema on surgical lung specimen

Gevenois PA et al AJRCCM 1995:152:653-7

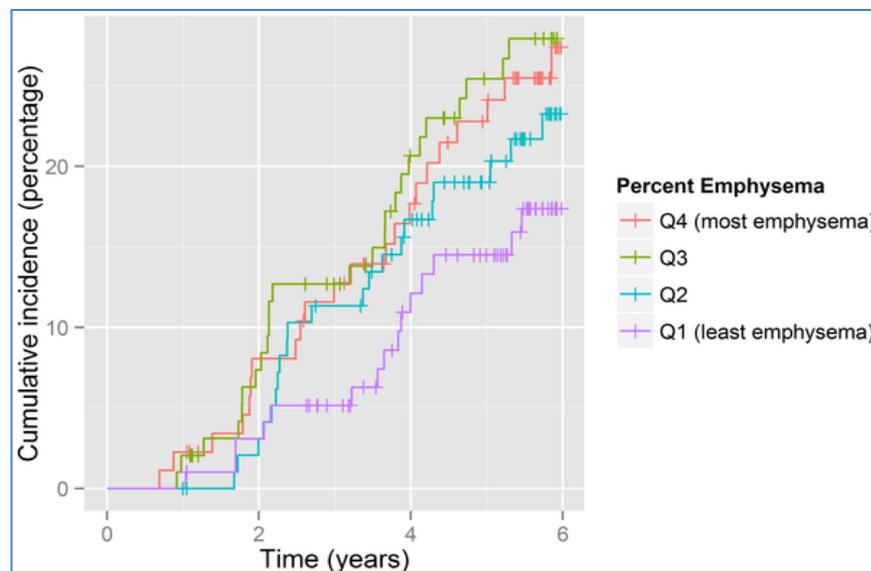# IMPORTANCE OF % EMPHYSEMA

Percent emphysema predicts:

1. Mortality in patients with COPD

2. Hospitalization in older smokers

3. Incident airway obstruction in older smoker
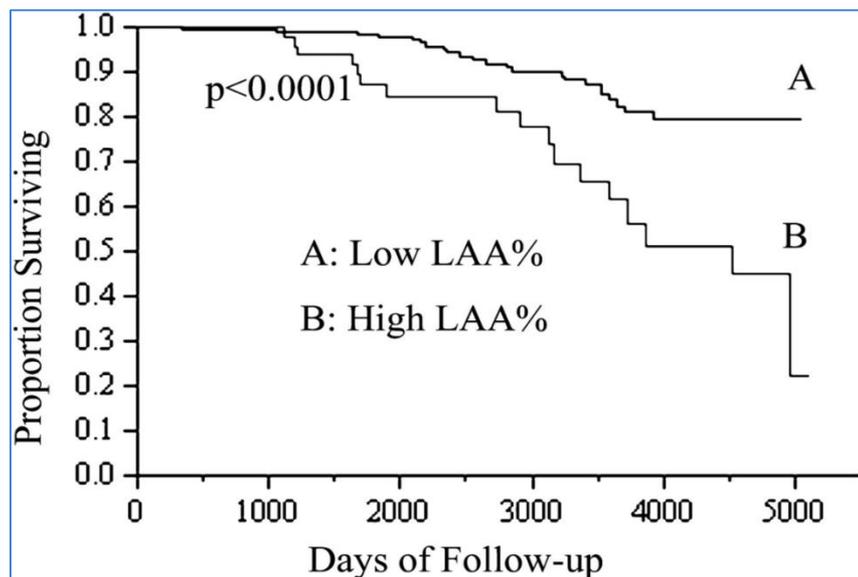
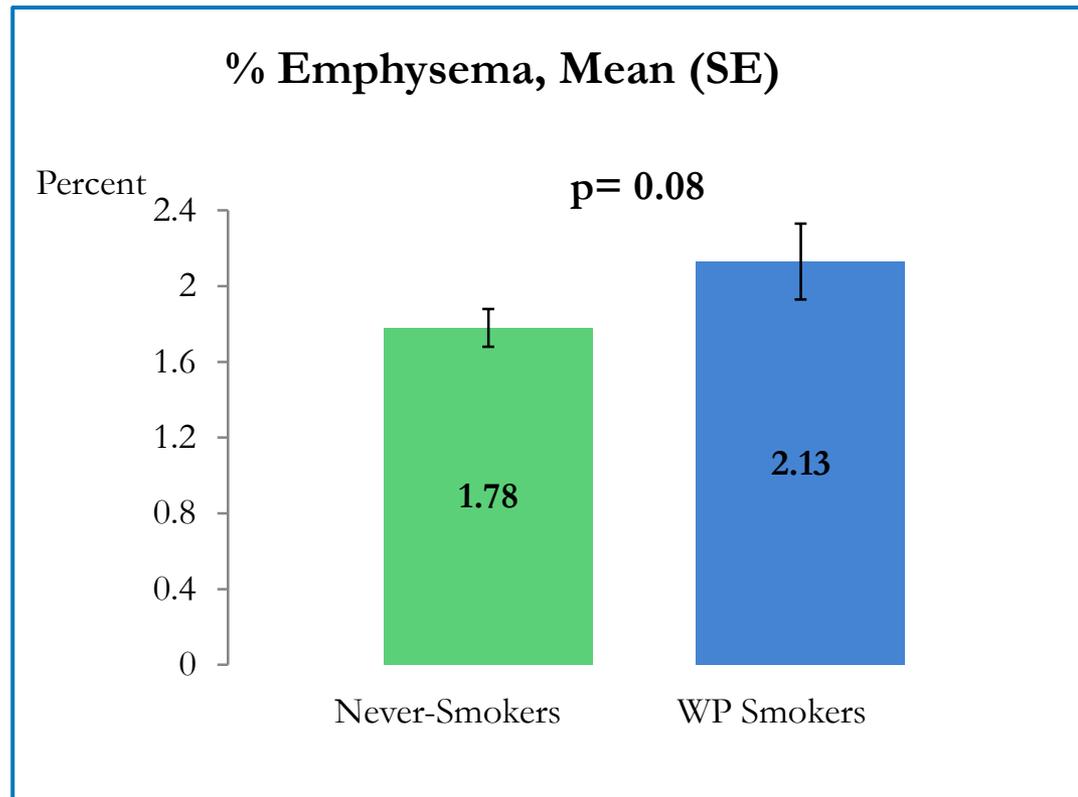Kaplan-Meier survival curve for patients with COPD stratified by %LAA

LAA% = the percentage of the lung field occupied by low attenuation areas.

Incidence plot of time to first hospitalization by % emphysema in older smokers

Haruna et al. Chest. 2010;138(3):635-640

McAllister et al. (2014). PLoS ONE 9(4): e93221.

Emphysema in WP Smokers and Non-Smokers (N=334)

Excluded 17 inadequate CT

% Emphysema, Mean (SE)

Percent

p= 0.08

Never-Smokers: 1.78
WP Smokers: 2.13

ASSOCIATION OF EMPHYSEMA WITH WATEPIPE SMOKING AND ITS EXTENT

	% Emphysema	
	β* (95 % CI)	p-value
Waterpipe Smoking (Yes/No)	0.30 (0.03 ; 0.57)	**0.03**
Waterpipes smoked per day	0.07 (-0.02 ; 0.16)	0.13
Waterpipe smoking duration (by 10 years)	0.10 (0.004 ; 0.19)	**0.04**
Cotinine levels (by 100 units)	0.11 (0.02 ; 0.19)	**0.01**

* Adjusted stepwise for: Age; sex; body-mass index; study site

CONCLUSION 4

Exclusive waterpipe smoking and its extend are associated with **extent of emphysema assessed quantitatively on chest CT** in largely asymptomatic individuals from the community

LIMITATIONS

Cross sectional design

No prospective studies

Second-hand smoking

FUTURE DIRECTION

- **Metabolic markers:** LDL, HDL, Triglyceride

- **Inflammatory markers**: C-reactive protein (CRP); (IL-6); ICAM and fibrinogen

  - Markers of vascular inflammation

  - predictors of cardiovascular events and mortality

- **Oxidative stress marker:** Urinary isoprostanes

- Urine microalbumin

THANK YOU!

NPRP No.: 5-9753216

GENETIC REPOSITORY PROJECT

- We collected genetic material from peripheral blood samples on 231 participants in Beirut and 27 in Doha.

- Extracted DNA and cell preserved **for RNA**

- **Objective** Explore the effect of waterpipe smoking on gene expression and the interaction of waterpipe smoking with genetic variant/predictors of disease.

- **Specific Aim:** perform whole-exome sequencing (WES) of DNA from blood of waterpipe smokers and non-smokers to uncover variants that may be associated with increased risk of disease phenotypes.

LUNG CANCER

- Several methodologically limited case-control studies and on cohort support and association between **WP** smoking and lung **CA**

- **Greater risk noted among former Lebanese waterpipe smokers, association became non-significant after adjusting for confounders**

- **4 times greater risk in Indian male heavy WP smokers adjusting for age.**

- **Chinese study did not control for confounders.**