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# Sex and Gender in Tobacco Reduction - The State of the Evidence

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# Sex and Gender in Tobacco Reduction- The state of the evidence

Speaker: Iris Torchalla & Chizimuzo Okoli

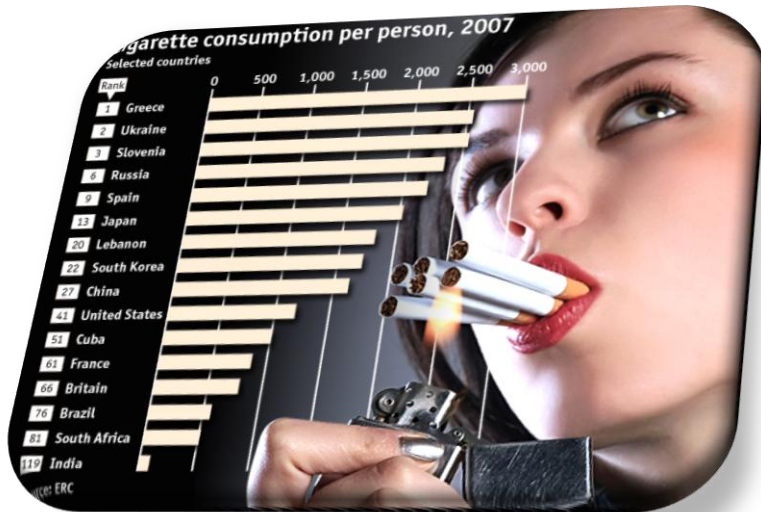
Date: April 19<sup>th</sup> 2012

iTAG 2012 Annual Spring Meeting

# Outline

- Global prevalence, risk, and mortality from smoking
- Gender/Sex specific diseases associated with tobacco use
- Gender/Sex specific reasons for smoking
- Gender/Sex specific factors in treating tobacco use

# Global prevalence, risk, and mortality from smoking



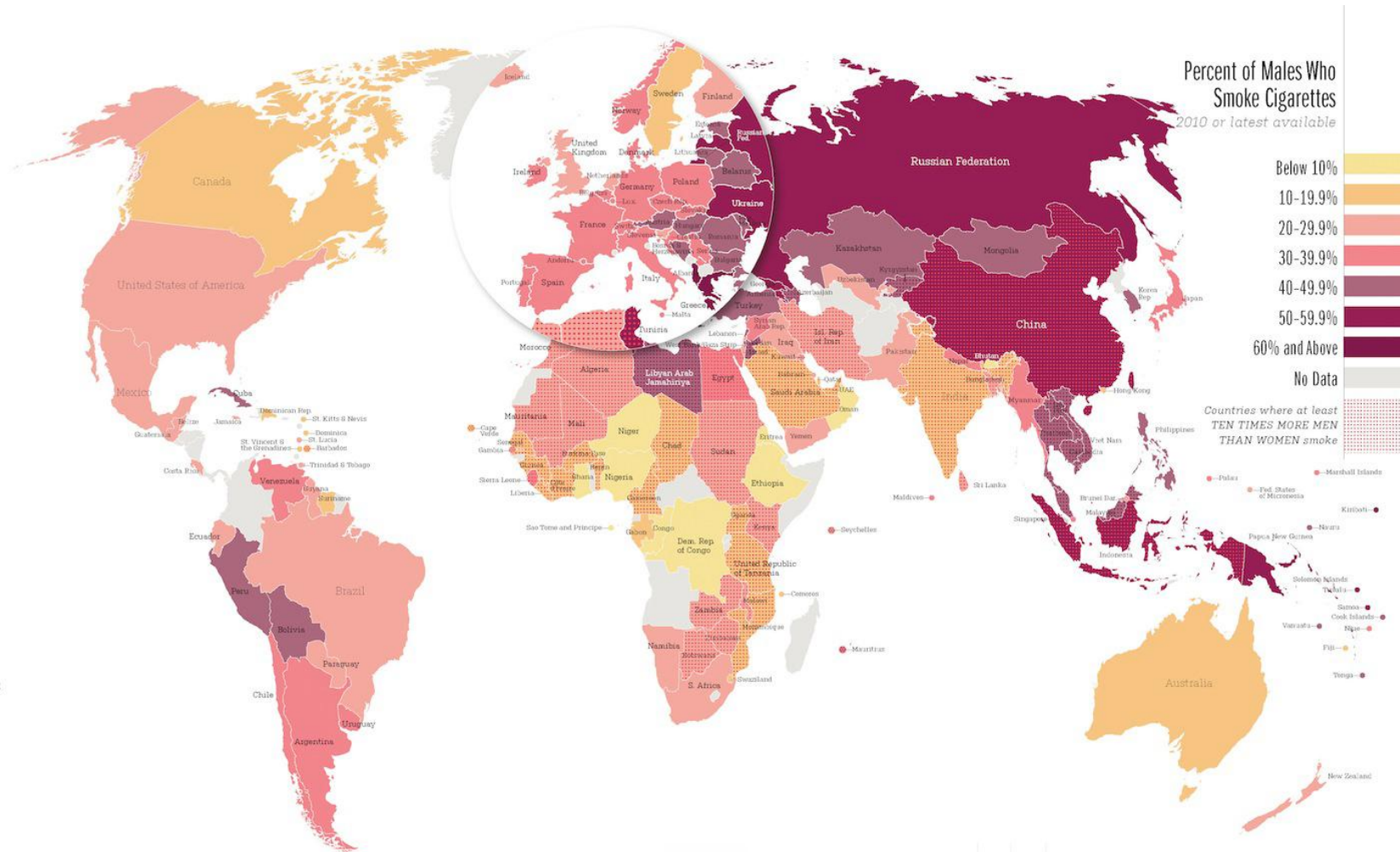
*“Cigarettes are like women. The best ones are thin and rich.”*

American Tobacco Company advertising slogan, US, circa 1970



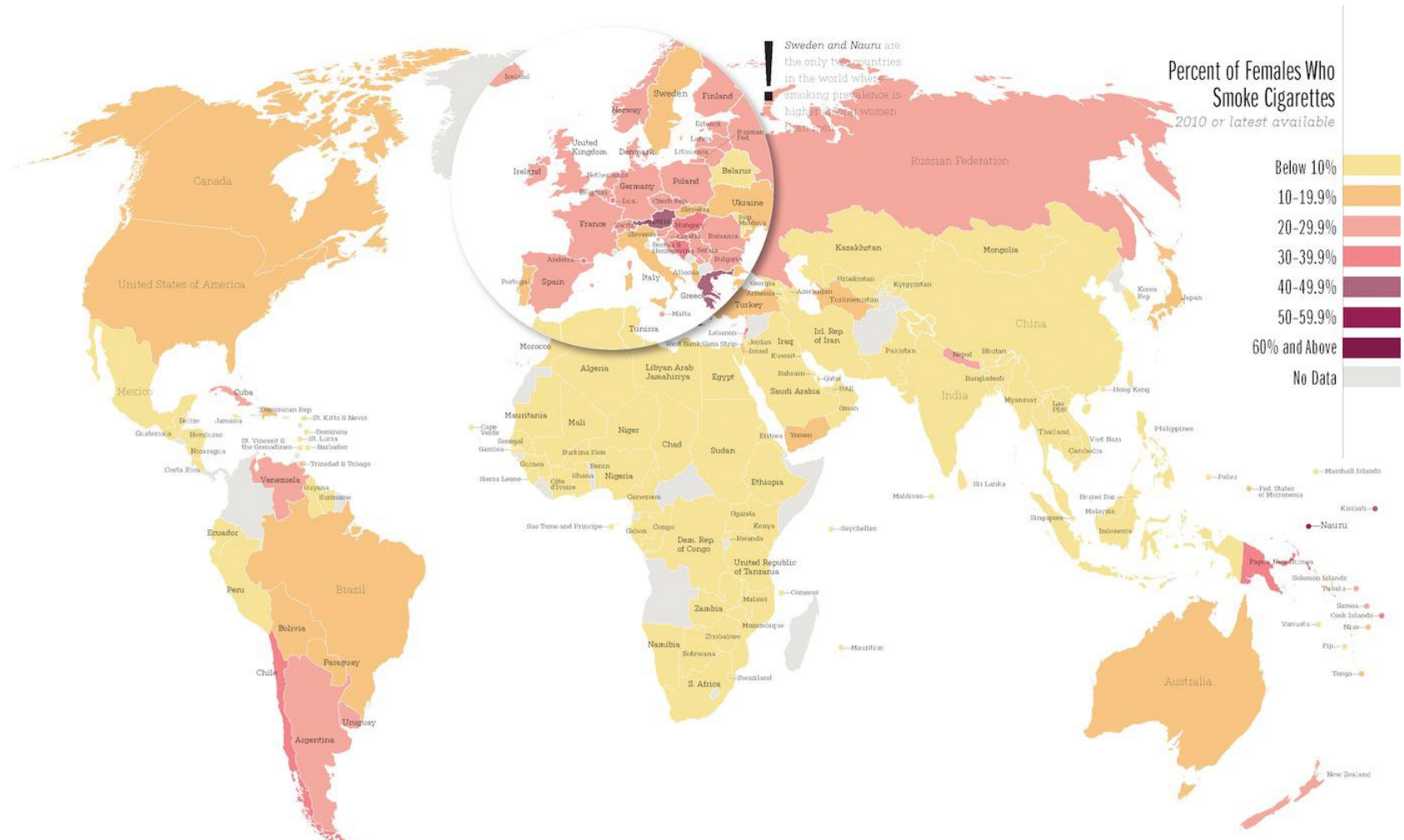
*“I’m no cowboy and I don’t ride horseback, but I like to think I have the freedom the Marlboro man exemplifies. He’s the man who doesn’t punch a clock. He’s not computerized. He’s a free spirit.”*

George Weissman, Former President and CEO, Philip Morris USA, 1978



source: Tobacco Atlas, 4th edition; tobaccoatlas.org

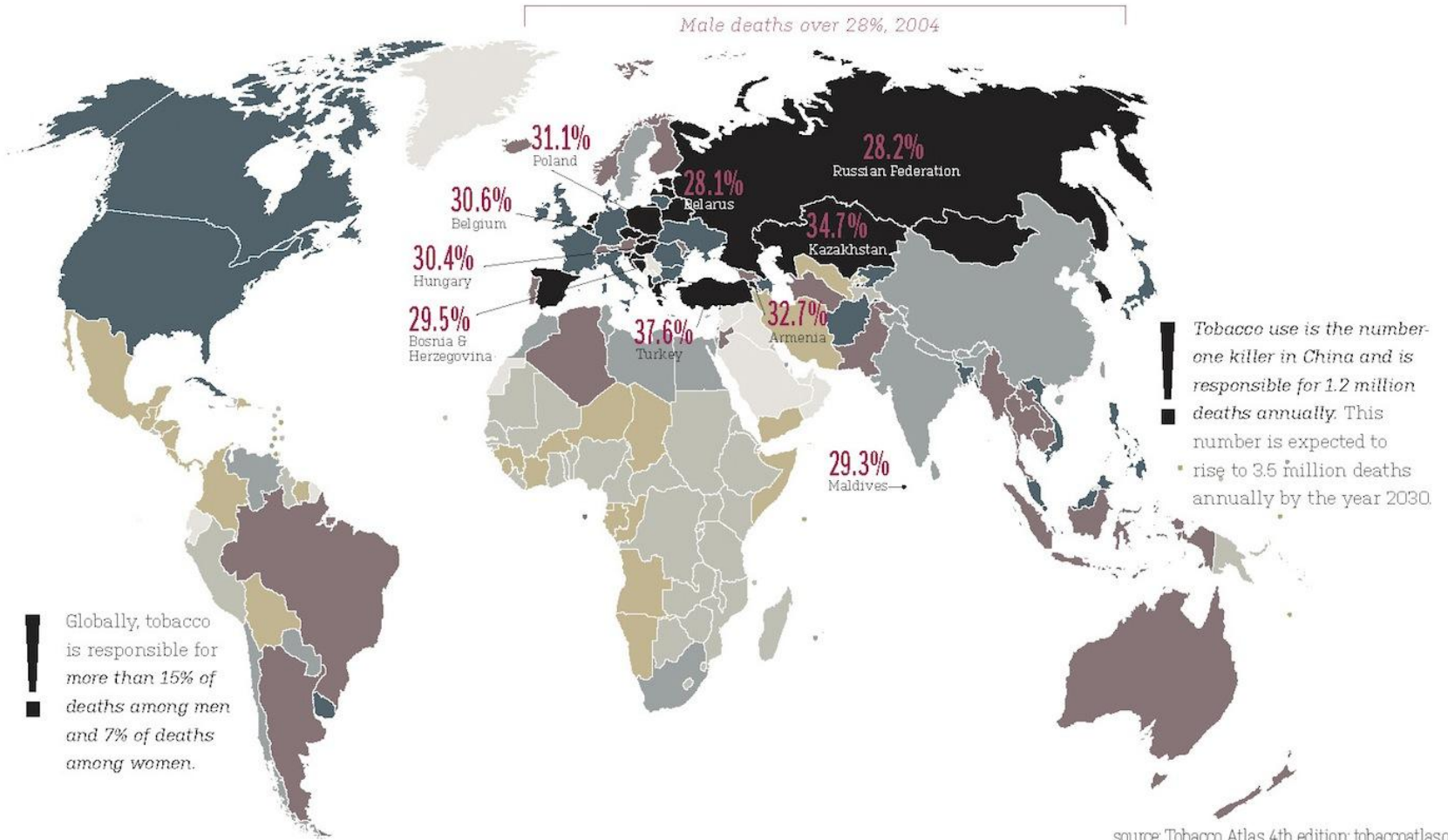
800 million adult men worldwide smoke cigarettes. **Almost 20% of the world's adult male smokers live in high-income countries, while over 80% are in low- and middle-income countries.**



source: Tobacco Atlas 4th edition, tobaccoatlas.org

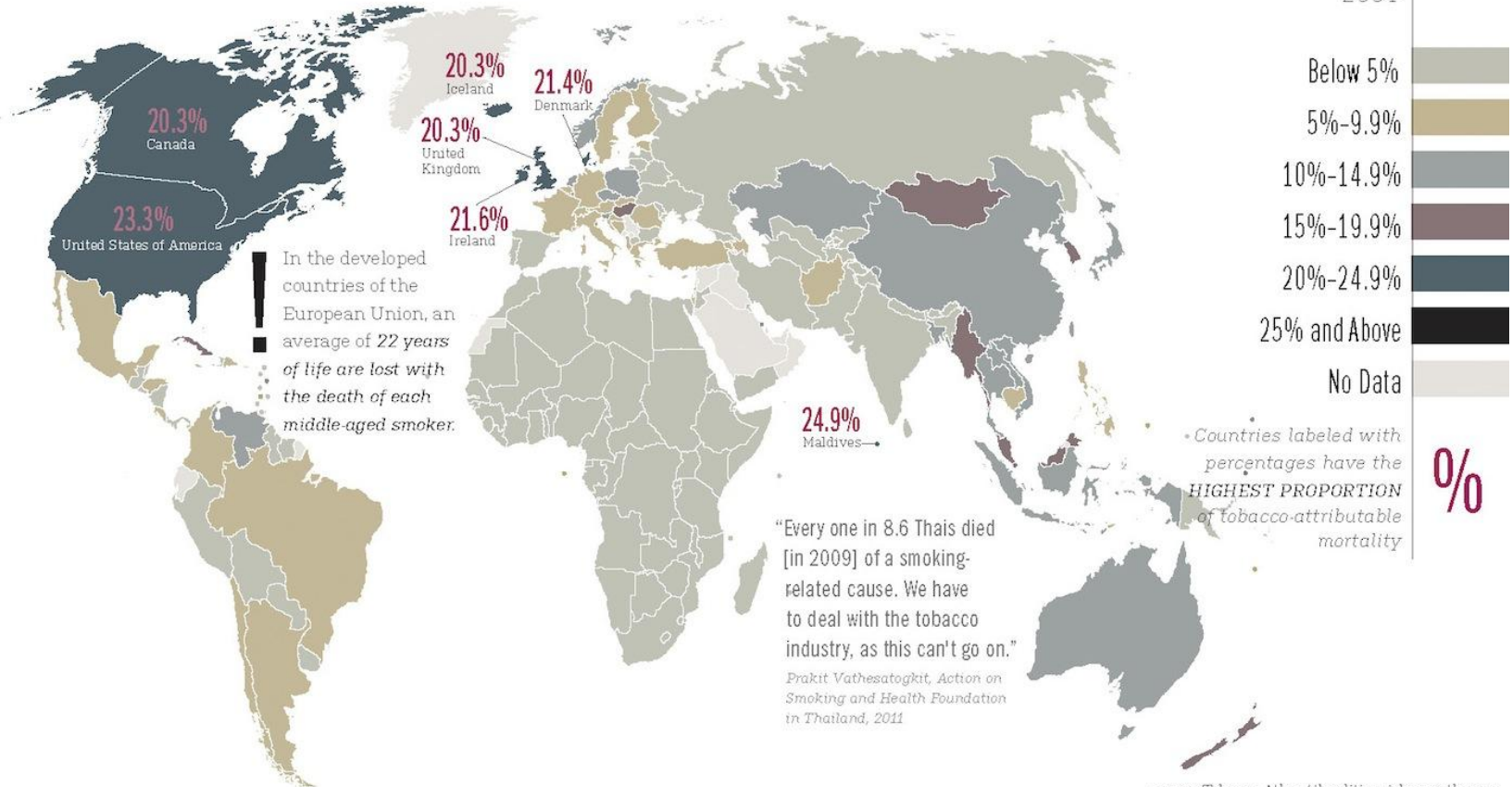
Nearly 200 million adult women smoke worldwide

# Male Deaths



# Female Deaths

Female deaths over 20%, 2004



source: Tobacco Atlas, 4th edition; tobaccoatlas.org



# Global Mortality Estimates

- In 2011, tobacco use killed almost 6 million people (80% of deaths occurring in low-and middle-income countries)
- Tobacco use is responsible for up to 15% of all deaths among men and 7% of all deaths among women globally (smoking also causes almost 80% of male and nearly 50% of female lung cancer deaths)
- Approximately 600, 000 nonsmokers died in 2011 from involuntary exposure to secondhand smoke.

“Tobacco caused 100 million deaths during the twentieth century, and if current trends continue, approximately 1 billion people will die during the twenty–first century because of tobacco use”

# Gender/Sex specific diseases associated with tobacco use

- #1 Lung cancer
- #2 Ischemic heart disease
- #3 Chronic airways obstruction<sup>1</sup>



## Cancers<sup>1</sup>

Bronchus	Lung,
Esophagus	Lip, Oral cavity/pharynx
Cervix uteri	Larynx, trachea
Stomach <sup>2</sup>	Urinary bladder
Leukemia <sup>2</sup>	Colon <sup>2</sup>
Kidney,	Pancreas
other urinary	Liver <sup>2</sup>

## Cardiovascular disease<sup>1</sup>

Ischemic heart disease  
Cerebrovascular disease  
Rheumatic heart disease  
Atherosclerosis  
Hypertension  
Aortic aneurysm  
Pulmonary heart disease  
Other arterial disease

## Respiratory disease<sup>1</sup>

Chronic airways obstruction  
Asthma  
Bronchitis/emphysema  
Pneumonia/influenza  
Respiratory tuberculosis

## Paediatric disease<sup>1</sup>

Low birth weight  
Respiratory conditions-newborn  
Respiratory distress syndrome  
Sudden Infant Death Syndrome

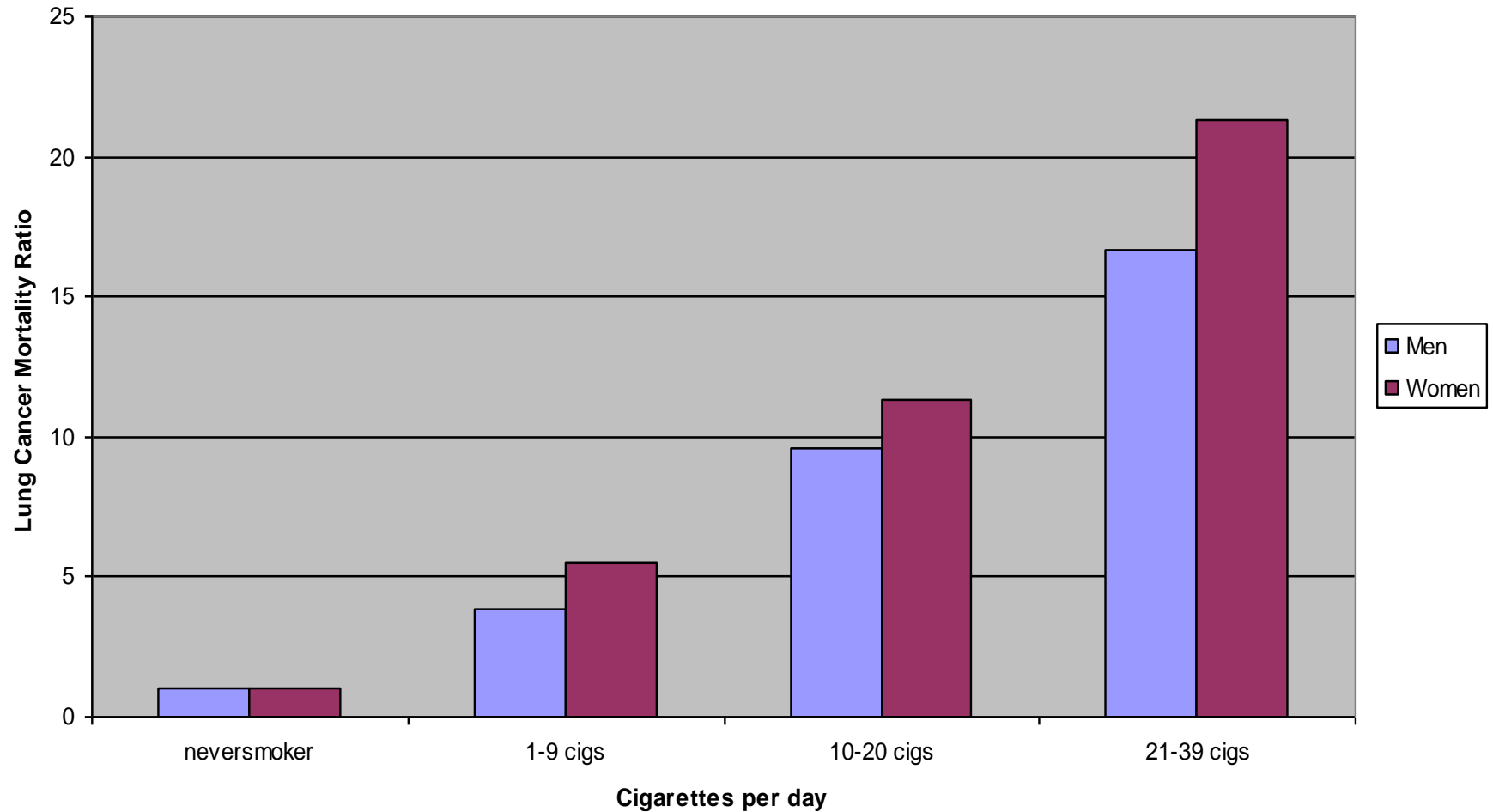
## Reproductive Problems<sup>2</sup>

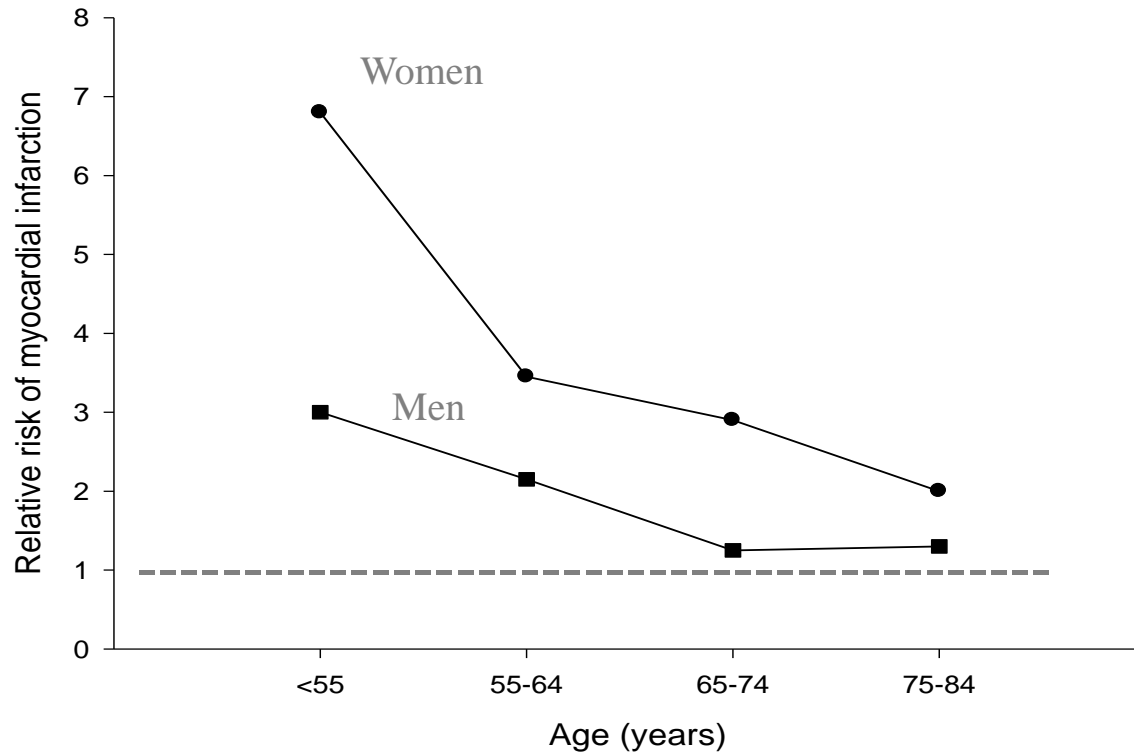
Reduced fertility  
Spontaneous Abortion  
Placental abruption

1. Makomaski Illing EM, Kaiserman, MJ. *Can J Public Health* 2004;95:38-44.

2. Ghadirian, P (for Health Canada). *Sleeping with a Killer: The Effects of Smoking on Human Health*. Health Canada. Sept. 2002.

# Lung cancer risk may be higher in women, both among smokers (shown here) and nonsmokers





## Relative risk of myocardial infarction for current smokers compared with never smokers, by sex

Prescott et al. (1998) Smoking and risk of myocardial infarction in women and men: longitudinal population study. *Brit Med J* 316: 1043-1047

# Disease risk I

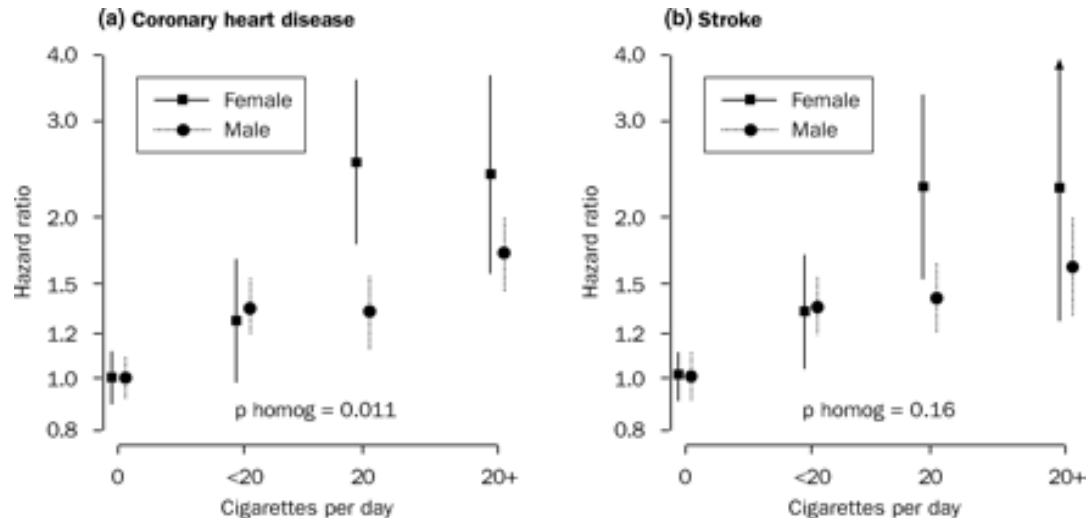
Meta-analyses examining the risk for a variety of diseases associated with smoking in English language studies:

- For smokers of  $<20$  cigarettes per day, the rate ratio point estimate was 1.42 for males and 1.77 for females.
- For smokers of  $\geq 20$  cigarettes per day, the point estimate was 1.95 for males and 2.75 for females.
- The increase in risk from low to high levels of smoking was greater for females than for males.

# Disease risk II

Meta-analyses examining the risk for cardiovascular diseases associated with smoking in Asian and Australian/New Zealand (ANZ) studies

- Lower mean daily cigarette consumption among females (10 in Asia; 15 in ANZ) compared with males (16 and 20, respectively)
- For both CHD and stroke, hazard ratios comparing smokers of  $\geq 20$  cigarettes per day with non-smokers were higher for women than men.



# Gender/Sex specific reasons for smoking



# Sex differences in factors which influence tissue response to nicotine (pharmacodynamics)

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## Influence of Gender and Sex Hormones on Nicotine Acute Pharmacological Effects in Mice

M. IMAD DAMAJ

Department of Pharmacology and Toxicology, Medical College of Virginia of Virginia Commonwealth University, Richmond, Virginia  
Received April 12, 2000; accepted September 10, 2000 This paper is available online at <http://jpet.aspetjournals.org>

- Female mice less sensitive to the acute effects of nicotine
- Progesterone and 17 $\beta$ -estradiol were found to block nicotine's antinociception in mice. Testosterone failed to do so.
- Progesterone and 17 $\beta$ -estradiol blocked nicotine activation of  $\alpha 4\beta 2$  neuronal acetylcholine nicotinic receptors expressed in oocytes.



## 2. Sex differences which lead to systemically higher or lower plasma nicotine levels (pharmacokinetics)

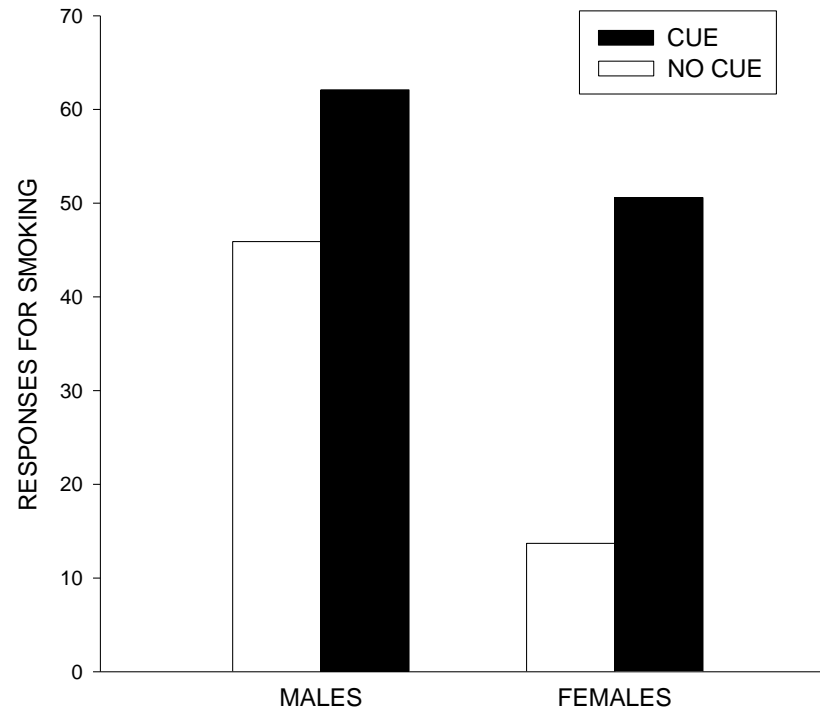
JOURNAL OF WOMEN'S HEALTH & GENDER-BASED MEDICINE  
Volume 11, Number 2, 2002  
© Mary Ann Liebert, Inc.

### Gender Differences in Tobacco Smoking: Higher Relative Exposure to Smoke Than Nicotine in Women

M.V. ZEMAN, M.Sc., L. HIRAKI, B.Sc., and E.M. SELLERS, M.D., Ph.D.

- No significant difference was found in the number of cigarettes per day or CO levels between the sexes.
- Females had significantly lower nicotine levels than males ( $16.9 \pm 0.6$  vs.  $21.1 \pm 0.07$ ,  $p < 0.01$ )
- Female heavy smokers demonstrated higher  $-\log$  nicotine/CO values (a representation of cost of smoking) compared with male heavy smokers ( $0.1 \pm 0.02$  vs.  $0.02 \pm 0.01$  mg/L ppm,  $p < 0.05$ ).

# Sex/Gender Differences in non-pharmacological stimuli and drug (i.e., conditioned responses)



- Removal of lit cigarette cue decreases smoking reinforcement (VR) more in women than in men.

# Biopsychosocial (i.e., gender) factors which differentiate men and women

## Common reasons boys start smoking:

- peer pressure
- misconceptions that smoking is cool or enhances popularity
- easy access to tobacco products
- cigarette pricing
- tobacco marketing.

## Common reasons young women start smoking

- Association with others (parents and friends) who smoke
- Concern with weight, body image, or social acceptance
- Interest in rebelling or stating individuality
- Reaction to positive image of smoking in magazines, movies, and youth culture
- Influence from cigarette marketing campaigns targeting women

# Gender/Sex specific factors in treating tobacco use



# Nicotine Replacement Therapy Outcome

Two meta-analyses examining nicotine replacement therapy (NRT) for smoking cessation → Women less successful than men.

1. Cepeda-Benito et al. (2004) → 21 RCTs with different NRT products:
  - NRT more effective than placebo at each follow-up for men.
  - Benefits for women clearly evident only at 3- and 6-month.
    - at 6 month only in combination with high-intensity counselling.
  - At 12 month, NRT was not superior to placebo for women, regardless of counselling intensity.
  - Effect sizes decreased over time for both men and women, but the decline was statistically significant only for women.

# Nicotine Patch Therapy Outcome

2. Perkins & Scott (2008) → 14 RCTs with nicotine patch:
  - 6-months abstinence rates for NRT versus placebo were 20.1% versus 10.8% for men, and 14.7% versus 10.1% for women.
  - Increase in quitting due to nicotine versus placebo was only about half as large in women as in men (ORs: 2.2 versus 1.6).
  - NNTs: 10 for men and 19 for women → almost twofold increase in the estimated number needed to treat for women relative to men to get one additional long-term abstinent ex-smoker.

# Bupropion Outcome

Meta-analyses examining bupropion for smoking cessation  
→ 12 RCT's with Bupropion 300mg SR versus Placebo:

- Both women and men benefited from bupropion as compared to placebo.
- Women and men benefited equally from bupropion treatment, no sex differences were found in its effectiveness.
- However, women were less likely than men to quit smoking, regardless of treatment type.

# Women-specific interventions

Treatment models	Treatment components
Weight concerns/weight gain are greater in women than in men	<ul style="list-style-type: none"><li>• Behavioural strategies to prevent weight gain;</li><li>• Medications to prevent weight gain;</li><li>• Cognitive strategies to reduce weight and body image concerns.</li></ul>
Negative affect/depression present special challenges for women	Strategies to reduce /cope with negative affect: <ul style="list-style-type: none"><li>• behavioural (e.g., exercise);</li><li>• coping skills /stress management training</li><li>• medication (e.g., bupropion)</li></ul>
The psychological aspects of smoking and the cues associated with smoking present special challenges for women	<ul style="list-style-type: none"><li>• Cognitive-behavioural strategies to manage situations which trigger craving.</li><li>• Medication to reduce the rewarding effects of nicotine: Naltrexone</li></ul>
Nicotine withdrawal is higher during the luteal than during the follicular phase of the menstrual cycle	Scheduling the quit date according to the menstrual cycle



# Women-specific interventions

Treatment models	Treatment components
<ul style="list-style-type: none"><li>• Certain sociocultural populations are hard to reach.</li><li>• Treatment needs to account for their characteristics.</li><li>• Counselors must be able to communicate with them and act as role models.</li></ul>	<ul style="list-style-type: none"><li>• Peer lay counselors who share commonalities with the target group (e.g. language, culture, attitudes, beliefs).</li><li>• Socioculturally adapted materials and components</li></ul>
<p>Women receiving health services may be specifically receptive for proactive smoking cessation intervention.</p>	<ul style="list-style-type: none"><li>• Brief motivational interventions (counseling plus telephone calls / letters).</li><li>• Additionally: tailored/gendered booklets, video/poster exposure.</li><li>• Or: mailings / telephone calls only (no face-to-face contact).</li></ul>

# Outcomes

- **Programs addressing exercise, weight gain/-concerns:** Promising results, at least in the short term.
- **Mood management / stress management :** no significant main effect, especially when compared to contact-matched programs. Counselling x medication effects possible.
- **Matching the quit date to the menstrual cycle:** no consistent effects.
- **Peer counselling:** preliminary promising results.
- **Interventions without face-to-face contact:** no medium- and long-term effects reported.
- **Brief interventions in public health clinics:** significantly higher medium-term abstinence rates compared to usual care

# Conclusions

- Women-specific tobacco programs help women stop smoking.
- The choice of treatment for an individual smoker can be guided by client's preferences.
- Health care providers should be encouraged to address women's smoking proactively and in any setting.
- Future research:
  - Identify those elements that are essential for designing women-specific smoking cessation programs.
  - Develop more creative and multifaceted women-specific programs, addressing the full range mechanisms relevant for women's smoking behaviour.

## Description of study

Author (Year)	Design	Sample size	Components	% Quit at EOT
Rose & Hamilton, (1978)	RCT	1445	Quit advice from Physician	31.8%*
Li, et al., (1984)	RCT	576	Behavioural Counseling	8.4%*
Burling et al., (1991)	RCT	39	Relapse Prevention + Nicotine fading + Contingency management	26.3%*
Pallonen et al., (1994)	RCT	265	Self-help manual	25%*
Jenkins et al., (1997)	Pre-Post	2714	Media led anti-tobacco interventions	7.2%
Kalman et al., (2001)	RCT	36	Individuals counseling + Nicotine Patch + substance use counselling	16.6%
Stanton et al., (2004)	RCT	561	Video + nicotine patch + support material	16.5%*
Harding, Bensley, & Corigan, (2005)	Cohort	69	Behavioural counselling + peer support + Nicotine replacement	64%
Loke & Lam (2005)	RCT	758	Advice on encouraging husbands to quit	6.1%
Richmond et al., (2006)	Cohort	30	Behavioural counselling + Nicotine replacement + Bupropion	37%
Gershon Grand et al., (2007)	Cohort	231	Behavioural counselling + Nicotine replacement + Bupropion	36.4%

# Discussion

- Associations with Sex & Gender:
  - No study specifically designed the intervention with sex or gender in consideration.
  - No study examined sex or gender differences in outcomes among men
  - Three studies were ‘men-centred’ – two examined expectant fathers, and one study addressed ‘gay’ men.
- Associations with smoking cessation :
  - The most effective studies utilized combinations of behavioural counselling, nicotine replacement therapy and peer support.

# Future directions

- Need for studies examining sex and gender differences in smoking cessation outcomes.
- Development of ‘women- centred’ and ‘men-centred’ interventions, tailored appropriately to the targetted male and female populations.
- Further exploration of gendered factors associated with smoking cessation interventions and outcomes.