

Korean Society for Health Promotion and Disease Prevention

2020년 대한임상건강증진학회 동계학술대회

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# 금연진료 및 심뇌혈관질환 예방

백 유 진 (한림의대)





**01** 흡연과 심뇌혈관질환 위험성

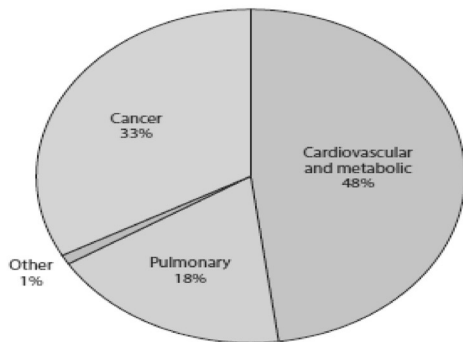
**02** 심뇌혈관질환 예방을 위한 금연상담

**03** 심뇌혈관질환에서 금연약물치료의 효과와 안전성

**01**

흡연과 심뇌혈관질환 위험성

## 담배는 암만 일으키나?



- 1965-2015년 사이, 직·간접흡연으로 2천 1백만 명 사망(美)
- 암보다 심혈관, 대사질환, 폐질환으로 더 많이 사망
- 신종담배?

US DHHS (Dep. Health Hum. Serv.). 2014. *The Health Consequences of Smoking—50 Years of Progress. A Report of the Surgeon General. Executive Summary.* Rockville, MD: US DHHS, Public Health Serv. Off. Surg. Gen.

## 흡연량 하루 1개비 미만에서의 질환별 사망률

Table 2. Smoking Status With All-Cause and Cause-Specific Mortality in the NIH-AARP Diet and Health Study Cohort<sup>a</sup>

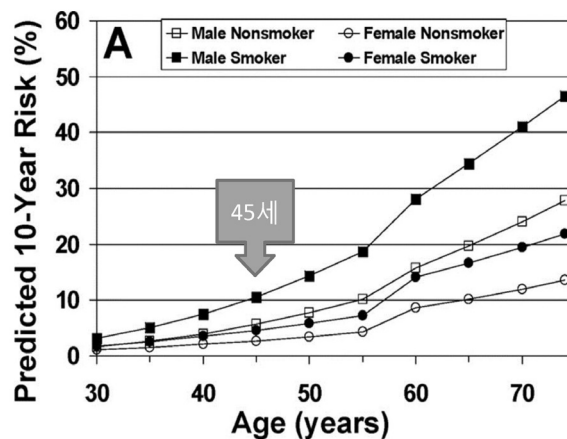
Character- istic	All Cause (n = 37 331)			All Cancer (n = 13 762)		Lung Cancer (n = 3801)		Cardiovascular Disease (n = 9496)		Respiratory Disease (n = 3139)	
	No.	No. (%)	HR (95% CI)	No.	HR (95% CI)	No.	HR (95% CI)	No.	HR (95% CI)	No.	HR (95% CI)
Smoking status and CPD at baseline (2004-2005 questionnaire)											
Never	111 473	9821 (9)	1 [Reference]	3468	1 [Reference]	253	1 [Reference]	2631	1 [Reference]	324	1 [Reference]
<1	1754	266 (15)	1.99 (1.76-2.25)	92	1.91 (1.55-2.35)	37	10.73 (7.59-15.15)	63	1.71 (1.33-2.21)	26	6.38 (4.27-9.51)
1-10	6627	1360 (21)	2.60 (2.45-2.75)	522	2.83 (2.58-3.11)	253	18.38 (15.42-22.91)	299	2.13 (1.89-2.40)	197	11.04 (9.23-13.19)
11-20	7721	1722 (22)	2.96 (2.81-3.11)	713	3.44 (3.17-3.74)	374	24.05 (20.46-28.26)	402	2.61 (2.34-2.90)	261	12.76 (10.81-15.05)
21-30	3329	900 (27)	3.57 (3.33-3.82)	390	4.40 (3.96-4.89)	228	34.54 (28.83-41.39)	195	2.89 (2.50-3.35)	136	15.52 (12.67-19.01)
>30	2906	854 (29)	3.91 (3.65-4.21)	370	4.80 (4.30-5.35)	212	36.83 (30.61-44.33)	179	3.05 (2.62-3.55)	151	20.17 (16.57-24.56)

JAMA Intern Med. 2017;177(1):87-95.

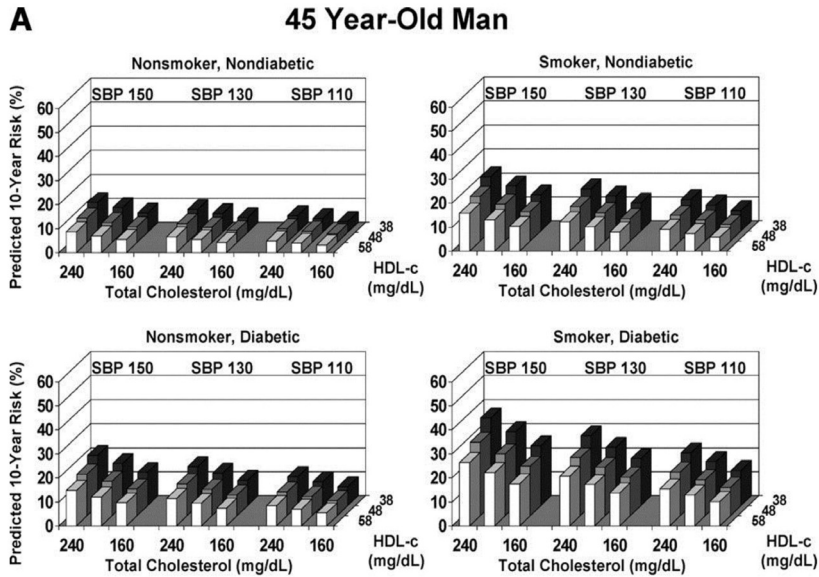
## Cardiovascular disease

- coronary heart disease
- congestive heart failure
- cerebrovascular disease
- intermittent claudication

## Framingham study(2009): CV risk profile

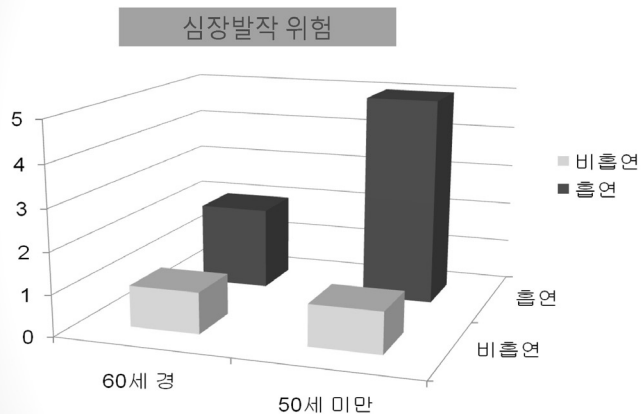


Circulation. 2009;120:384-390.



Circulation. 2009;120:384-390.

## 흡연 관련 심장발작 위험율은 젊은 흡연자에서 더 크다!



In the era of statins and reperfusion treatment, continuation of smoking is the strongest independent long-term predictor for recurrent MACE in young survivors of premature AMI.

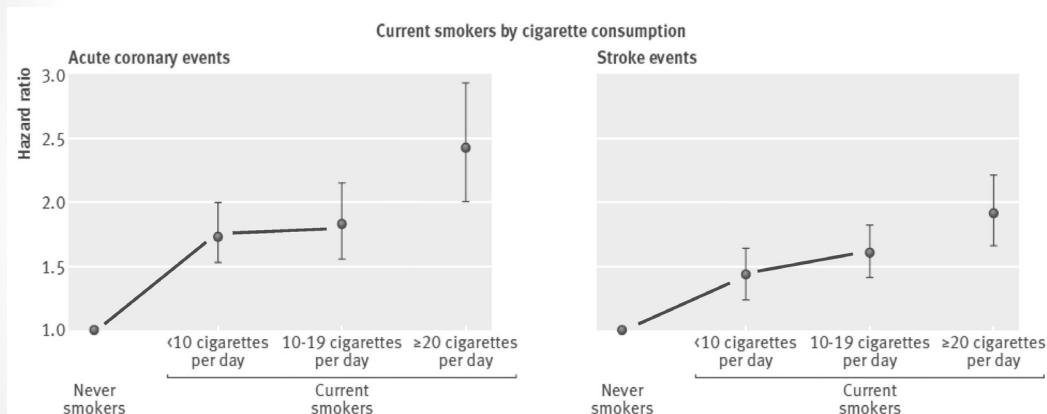
Am Heart J. 2015 Mar;169(3):356-62.

## 연도별 심근경색 기여율\_나이는 젊어지고, 흡연은 더욱 중요해졌다.

Variable	1995-1999	2000-2004	2005-2009	2010-2014	P value
Number	725	953	1081	1153	NA
Age	63.6 ± 12.2	61.5 ± 13.2	60.6 ± 12.9	60.3 ± 12.7	<0.001
Sex (males)	69%	67.6%	66.9%	68.2%	0.8
Diabetes mellitus	24.6%	25.4%	23.9%	30.6%	0.002
Hypertension	56.7%	66.7%	69.7%	77.3%	<0.001
Current smoker	27.7%	31.6%	42.3%	45.4%	<0.001
Hyperlipidemia	18%	21.5%	20.4%	22.2%	0.4
Renal insufficiency	4.8%	5.4%	4.5%	6.3%	0.3
Obesity	31.6%	36.8%	37.9%	39.6%	0.007

International Journal of Cardiology 248 (2017) 69-72

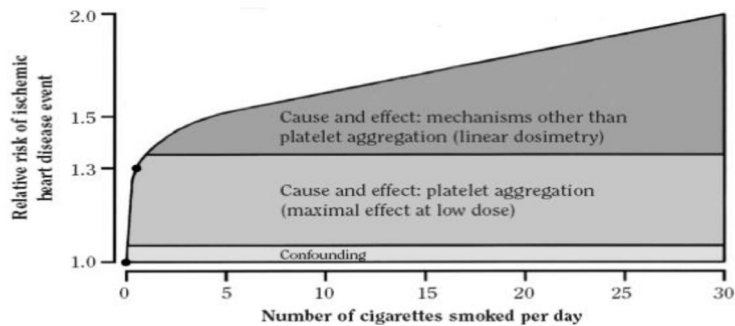
## 하루 10개비 미만과 0개비의 심뇌혈관질환 발생위험도(>65)



Impact of smoking and smoking cessation on cardiovascular events and mortality among older adults: meta-analysis. BMJ 2015;350:h1551

## 흡연량과 허혈성 심혈관 질환의 관계

- 소량의 흡연도 허혈성 심혈관 질환의 위험을 크게 증가(BMJ, 2018)
- 담배를 줄여도 사망위험을 크게 줄이지 못함(USPSTF, 2010)
- 심장질환 동반자는 단 1개비의 흡연도 허용이 되지 않음



USPSTF, 2010

## 완전 금연 vs 불완전 금연

■관상동맥질환에 미치는 영향

- 하루 1개비(CPD) 라도 관상동맥질환 발생 up !
- 48% 관상동맥질환 발생 증가
- 28% 뇌졸중 발생 증가
- 여성: 57%, 31% 로 남성보다 위험
- 하루 20개비 피는 사람의 40-50% 정도의 위험도

Low cigarette consumption and risk of coronary heart disease and stroke: meta-analysis of 141 cohort studies in 55 study reports. BMJ 2018;360:j3984 |



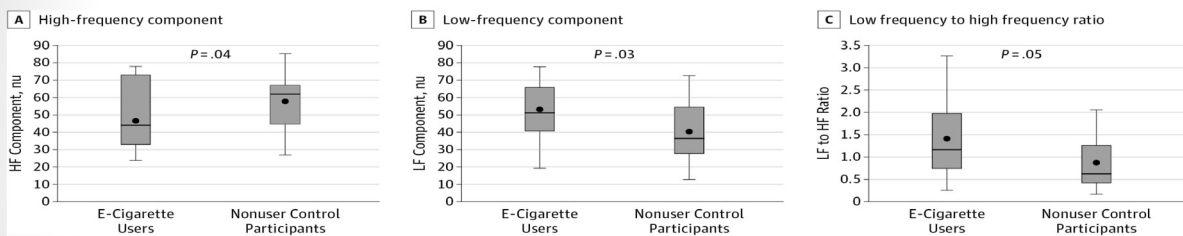
## 전자담배와 혈관내피손상

- **Conclusion 7-1.**
- 전자담배의 에어로졸은 급성기 혈관내피 기능 손상을 일으킨다.
- 에어로졸의 장기영향은 알 수 없다.

Public Health Consequences of E-Cigarettes  
(2018) Consensus Study Report

### From: Increased Cardiac Sympathetic Activity and Oxidative Stress in Habitual Electronic Cigarette Users : Implications for Cardiovascular Risk

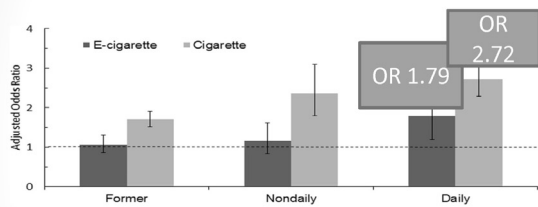
JAMA Cardiol. 2017;2(3):278-284. doi:10.1001/jamacardio.2016.5303



#### Figure Legend:

Heart Rate Variability ComponentsA, The high-frequency (HF) component, an indicator of vagal activity, was significantly decreased in the e-cigarette users compared with nonuser control individuals (mean [SEM], 46.5 [3.7] nu vs 57.8 [3.6] nu,  $P = .04$ ). B and C, The low-frequency (LF) component (mean [SEM], 52.7 [4.0] nu vs 39.9 [3.8] nu,  $P = .03$ ), and the LF to HF ratio (1.37 [0.19] vs 0.85 [0.18],  $P = .05$ ), were significantly increased in the e-cigarette users compared with nonuser controls, consistent with sympathetic predominance. These findings were present even in the absence of recent e-cigarette use, as verified by the absence of detectable nicotine in the plasma.

## 전자담배, 일반담배의 심근경색 발생율: 단면연구 (2018)



Nevertheless, this finding remains controversial, because of concerns about reverse causality based on the possibility that after having a myocardial infarction smokers switched to e-cigarettes, which would induce a spurious association between e-cigarette use and myocardial infarction.

Am J Prev Med 2018;55(4):455-461.

## 전자담배 사용\_뇌졸중: 2020

Current sole combustible cigarette users vs. Non-smokers<sup>a</sup>

Current sole combustible cigarette users vs. Non-smokers<sup>b</sup>

Current sole combustible cigarette users vs. Non-smokers<sup>c</sup>

Current sole e-cigarette users vs. Non-smokers<sup>a</sup>

Current sole e-cigarette users vs. Non-smokers<sup>b</sup>

Current sole e-cigarette users vs. Non-smokers<sup>c</sup>

Current e-cigarette users who were former combustible cigarette users vs. Non-smokers<sup>a</sup>

Current e-cigarette users who were former combustible cigarette users vs. Non-smokers<sup>b</sup>

Current e-cigarette users who were former combustible cigarette users vs. Non-smokers<sup>c</sup>

Current dual users vs. Non-smokers<sup>a</sup>

Current dual users vs. Non-smokers<sup>b</sup>

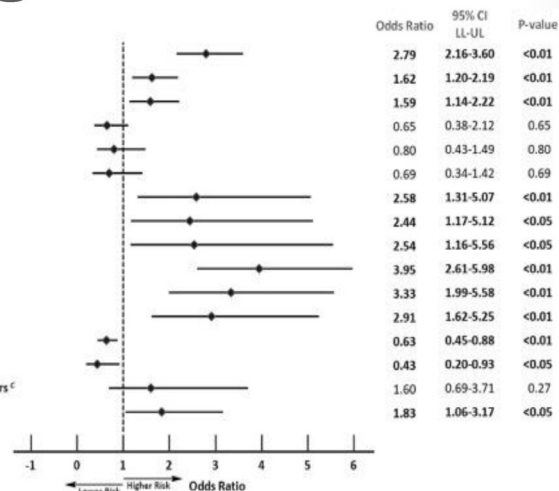
Current dual users vs. Non-smokers<sup>c</sup>

Non-smokers vs. Current sole combustible cigarette users<sup>c</sup>

Current sole e-cigarette users vs. Current sole combustible cigarette users<sup>c</sup>

Current e-cigarette users who were former combustible cigarette users vs. Current sole combustible cigarette users<sup>c</sup>

Current dual users vs. Current sole combustible cigarette users<sup>c</sup>

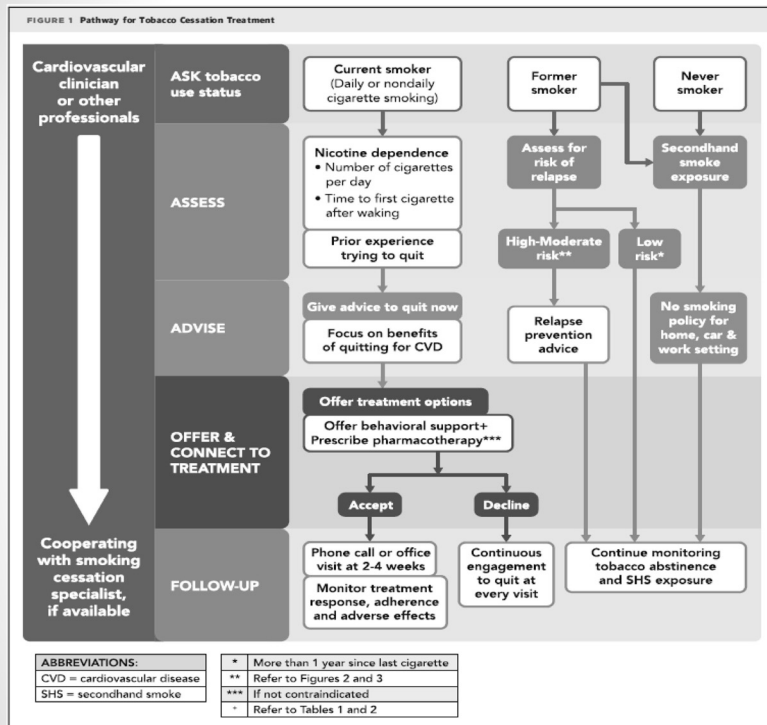


Pooled data (2016–2017) were analyzed from the Behavior Risk Factor Surveillance System, a nationally representative, cross-sectional telephone survey, in 2019. The sample size was 161,529 participants aged 18–44 years.

Risk of Stroke With E-Cigarette and Combustible Cigarette Use in Young Adults. AJPM 2020

## 02

### 심뇌혈관질환 예방을 위한 금연상담



출처: A Report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents: 2018 ACC Expert Consensus Decision Pathway on Tobacco Cessation Treatment:

## CVD (-) 환자에서 금연시 사망위험 감소효과(20%)

### All cause mortality

Smoking cessation<sup>1</sup>

Blood pressure<sup>2</sup>

Cholesterol<sup>3</sup>

Reduction in all cause mortality between approximately 15 to 20%

### Mortality due to CVD

Smoking cessation<sup>1</sup>

Blood pressure<sup>2</sup>

Cholesterol<sup>3</sup>

Reduction in mortality due to CVD approximately 25 to 35%

0.1 0.4 0.7 1.0 1.3 1.6 1.9

1. Kawachi, 1993. 2. Lievre, 2000. (Beta blockers and diuretics) 3. Vrcer, 2003 (Statins)

## CVD (+) 환자에서 금연시 사망위험 감소효과(36%)

### All cause mortality

Smoking cessation<sup>1</sup>

Blood pressure<sup>2a</sup>

Blood pressure<sup>2b</sup>

Cholesterol<sup>3</sup>

Cholesterol<sup>4</sup>

Reduction in all cause mortality between approximately 12 to 36%.

Risk reduction is greatest with smoking cessation

0.1 0.4 0.7 1.0 1.3 1.6 1.9

1. Critchley, 2003. 2. BPLTTC, 2003. (a. ACE Inhibitor b. Calcium antagonist) 3. Vrcer, 2003. (Statins) 4. CTT, 2005. (Statins)

## 한국남성에서 금연시 심,뇌혈관질환 감소율

- 지속 흡연자와 비교하여

- 금연시 허혈성 뇌졸중 발생위험도 : 0.66
- 금연시 지주막하 출혈 발생위험도 : 0.58
- 금연시 심근경색 : 0.43

Stroke. 2008;39:2432

## 심뇌혈관질환 흡연자의 상담

- 직접 흡연, 간접흡연 모두 혈관내벽에 이상을 초래하여 혈관수축, 동맥경화, 심근경색, 중풍을 일으킬 수 있다.
- 금연시 심혈관질환은 1년 내에 절반으로 감소한다.
- 15년이 지나면 비흡연자와 동일한 위험성으로 감소한다.
- 금연은 관상동맥질환을 36% 가량 감소시키는데 이는 재발을 줄이는데 쓰는 약물(스타틴, 베타차단제, ACEI) 과 함께 사용하면 효과적이다.
- 금연을 시도할 때는 1개비의 흡연도 용납되지 않는다.
- 바레니클린은 심장혈관 이상 등의 부작용이 증가하지 않으며 심혈관질환자에서 비교적 안전하게 처방할 수 있고 가장 효과적인 금연약제다.

## 액상형 전자담배를 환자와 상담하기

**TABLE 10** Guidance for Clinicians' Discussions of E-Cigarettes With Patients

**Recommendations:**

- Emphasize to smokers the importance of the goal of *complete* cessation of all combustible tobacco products. Even a single cigarette per day increases cardiovascular risk.
- Recommend that smokers use evidence-based, FDA-approved smoking cessation aids, which are known to be safe and effective.
- Clinicians should be prepared to discuss the evidence about e-cigarettes' risks and benefits with patients who ask about them.

**Points to cover in a discussion with a patient who asks about e-cigarettes:**

- E-cigarettes are devices that heat a nicotine-containing liquid, producing an aerosol that differs from the smoke produced by burning tobacco.
- E-cigarettes contain chemicals in addition to nicotine, including propylene glycol, glycerin, and flavoring chemicals that may pose a risk.
- Because they do not burn tobacco, e-cigarettes expose the user to fewer and lower levels of toxic compounds than smoking a cigarette does.
- Therefore, if used as a complete substitute for combustible tobacco products, e-cigarettes are expected to be less harmful than smoking combustible tobacco products in the short-term, but their long-term safety is uncertain.
- Because e-cigarettes are new products, scientific information about their health effects and effectiveness to help smokers quit is limited and rapidly evolving. They are not currently approved by the FDA as safe and effective cessation aids.
- E-cigarettes vary considerably in their design, in the contents of the e-liquids, and in nicotine and toxicant delivery to the user.

**If smoker chooses to use e-cigarettes, provide evidence-based advice:**

- Switch completely to e-cigarettes. Avoid dual use of both combustible tobacco products and e-cigarettes.
- The eventual goal is cessation of e-cigarettes as well as combustible cigarettes, because of uncertainty about e-cigarettes' long-term health risks. After stopping combustible tobacco, plan to taper off e-cigarettes.
- Heed safety instructions. Choose products with child-proof packaging to minimize the risk of nicotine poisoning of children. Follow instructions for device maintenance, battery recharging, and storage to minimize the risk of explosion.
- Avoid using e-cigarettes around children.

FDA = U.S. Food and Drug Administration.

## 03

### 심뇌혈관질환에서 금연약물치료의 효과와 안전성

## 바레니클린 심장부작용 위험성 ↓ !

- **Comparative Safety of Smoking Cessation Pharmacotherapies During a Government-Sponsored Reimbursement Program (Nicotine Tob Res. 2020 Jun 2;ntaa100. doi: 10.1093/ntr/ntaa100.)**
- **Results:** 116,442 participants were included. Compared to NRT, varenicline was associated with a 10% one-year relative risk decrease of cardiovascular hospitalization [Adjusted Risk Ratio (RR) = 0.90, 95% Confidence Interval (CI): (0.82-1.00)], a 20% one-year relative risk decrease of neuropsychiatric hospitalization [RR: 0.80, CI: (0.7 -0.89)], and a 19% one-year relative risk decrease of mortality [RR: 0.81, CI: (0.71-0.93)]. We found no significant association between NRT and bupropion for cardiovascular hospitalizations, neuropsychiatric hospitalizations, or mortality.

## EAGLES 연장 연구\_심혈관계 부작용 (RCT)

▶ 흡연자에서 바레니클린, 부프로피온 및  
니코틴 패치의 심혈관계 안전성: 무작위 임상시험

**Cardiovascular Safety of Varenicline, Bupropion, and Nicotine Patch in Smokers: A Randomized Clinical Trial.**

Benowitz NL, Pipe A, West R, et al. Cardiovascular Safety of Varenicline, Bupropion, and Nicotine Patch in Smokers. JAMA Intern Med. 2018;178(5):622-631.

## 주요 사항 EAGLES 연장 연구\_심혈관계 부작용

- ▶ 치료 및 추적 관찰 동안, 주요 심혈관계 사건의 발생률은 낮았으며(MACE <0.5%), 투여군 간의 유의한 차이를 보이지 않음

	발생률, n(%)			
	바레니클린 (n=2016)	부프로피온 (n=2006)	니코틴 대체요법(NRT) (n=2022)	위약 (n=2014)
	주요 심혈관계 사건 (MACE)			
☑ 치료 기간 동안	1 (<0.1)	2 (0.1)	1 (<0.1)	4 (0.2)
☑ 30일 추적 관찰 기간 동안	1 (<0.1)	2 (0.1)	2 (0.1)	4 (0.2)
☑ 연구 종료 시점*	3 (0.1)	9 (0.4)	6 (0.3)	8 (0.4)

Adapted from Benowitz NL, et al. 2018

Ref. Benowitz NL, Pipe A, West R, et al. Cardiovascular Safety of Varenicline, Bupropion, and Nicotine Patch in Smokers. JAMA Intern Med. 2018;178(5):622-631.

## 심혈관질환자 금연약제 추천(외래, 입원)

Recommended Pharmacotherapy		
	OUTPATIENT WITH STABLE CVD	INPATIENT WITH ACS
<b>1<sup>st</sup> Line Therapy</b>	Varenicline OR combination NRT*	<i>In-hospital to relieve nicotine withdrawal:</i> Nicotine patch OR combination NRT*  <i>At discharge:</i> Combination NRT OR varenicline†
<b>2<sup>nd</sup> Line Therapy</b>	Bupropion OR single NRT product	<i>At discharge:</i> Single NRT product
<b>3<sup>rd</sup> Line Therapy</b>	Nortriptyline‡	Bupropion§
<b>If single agent is insufficient to achieve abstinence</b>	Combine categories of FDA-approved drugs: • Varenicline + NRT (single agent) • Varenicline + bupropion • Bupropion + NRT (single agent)	(n/a)

†Some committee members planning to use varenicline would start it in-hospital; others would not start until discharge. Regardless, continue nicotine patch or short-acting form for 1 week to manage nicotine withdrawal symptoms during up-titration of varenicline dose.

<https://www.acc.org/~/media/Non-Clinical/Files-PDFs-Excel-MS-Word-etc/Guidelines/2018/Tobacco-Cessation-Clinician-ToolFINAL112918-UPLOADED-Dec-5-2018.pdf>



## 이번 시간에 배운 내용을 요약해 볼까요?

- 흡연은 심혈관질환의 가장 큰 위험요인이며 젊은 층과 여성에서 특히 위험하다.
- 전자담배도 단기적으로 심혈관건강에 부정적인 영향을 미치며 장기 영향은 아직 알 수 없다.
- 금연상담시 1개비도 안된다는 메시지를 전달하라.
- 금연약물은 CVD 환자에서 안전하고 효과가 확립되어 있으며 특히 바레니클린이 가장 효과적이다.