Other Therapies for Smoking Cessation and e-cigarrette

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Outline

- Pharmacotherapies for smoking cessation
- Addressing problems encountered by former smokers
- E-cigarette

Pharmacotherapies for Smoking Cessation

Five first line medications

- Bupropion hydrochloride
- Nicotine gum
- Nicotine inhaler
- Nicotine nasal spray
- Nicotine patch

New emerging therapy

- Varenicline

Second line Pharmacotherapies

- Nortriptyline hydrochloride
- Clondine hydrochloride

Effectiveness for Various Medications Compared to Placebo at 6-months post-quit (*n=86 studies)*

Medication	**Estimated OR (95% CI)**	**Abstinence rate (95% CI)**
Placebo	1.0	13.8
Monotherapies		
Varenicline (2 mg/day)	3.1 (2.5, 3.8)	33.2 (28.9, 37.8)
Bupropion SR	2.0 (1.8, 2.2)	24.2 (22.2, 26.4)
Clonidine	2.1 (1.2, 3.7)	25.0 (15.7, 37.3)
Nicotine patch (6–14 weeks)	1.9 (1.7, 2.2)	23.4 (21.3, 25.8)
Nortriptyline	1.8 (1.3, 2.6)	22.5 (16.8, 29.4)
Nicotine gum (6–14 weeks)	1.5 (1.2, 1.7)	19.0 (16.5, 21.9)
Combination therapies		
Patch (long-term; 14 weeks) + ad lib NRT (gum or spray)	3.6 (2.5, 5.2)	36.5 (28.6, 45.3)
Patch + bupropion SR	2.5 (1.9, 3.4)	28.9 (23.5, 35.1)
Patch + nortriptyline	2.3 (1.3, 4.2)	27.3 (17.2, 40.4)

Am J Prev Med 2008;35(2):158–176)

When to Use Second-line Agents

- Contraindications for first-line medications
- When first-line medications are not helpful

RCT with Nortriptyline

- 255 smokers for 12 weeks

→ Abstinence rate

28% of 86 participants receiving bupropion SR

25% of 80 participants receiving nortriptyline

15% of 89 participants receiving placebo

→ The rate of depression

bupropion SR–treated group : 27.0%

nortriptyline-treated group : 12.5%

Arch Intern Med 2005 Oct 24;165(19):2286-92.

Nortriptyline Hydrochloride

- Contraindication : risk of arrythmia
- Adverse effects : dry mouth, sedation, diarrhea or constipation, fatigue
- Dosage : 75 – 100 mg/day
- Duration : 12 weeks

JAMA 2000 ; 283: 3243 -3253

Clondine Hydrochloride

- Contraindication : rebound hypertension
- Adverse effects :

  → dose-dependent side-effects : particularly dry mouth and sedation.

  → drowsiness, dizziness, fatigue, postural hypotension
- Dosage : 0.15 - 0.75mg/kg/day
- Duration : 3-10 weeks

Cochrane Database Syst Rev. 2004;CD000058

JAMA 2000 ; 283: 3243 -3253

Addressing Problems Encountered by Former Smokers

- Lack of support for cessation
- Negative mood or depression
- Strong or prolonged withdrawal symptoms
- Relapse
- Weight gain

Relapse

- Warning against high risk situations

→ Social settings previously associated with smoking

→ Alcohol

- Encourage
- Reassure that quitting may take multiple attempts
- Intensive counseling
- Long term therapy (6 months or more) by bupropion, varenicline, and nicotine replacement can be helpful for persistent withdrawal symptoms.

Weight gain

- In the first few weeks, 1-2 kilogram
- Followed by 2-3 kilogram over the next several months
- Reduce vital capacity

Measures for Weight gain

- Physical activity
- Heathy diet & active lifestyle
- Low calories substitutes such as sugarless chewing gum, vegetable, or mints
- Bupropion, nicotine gum

  → delay weight gain.

JAMA 2000 ; 283: 3244 -3254

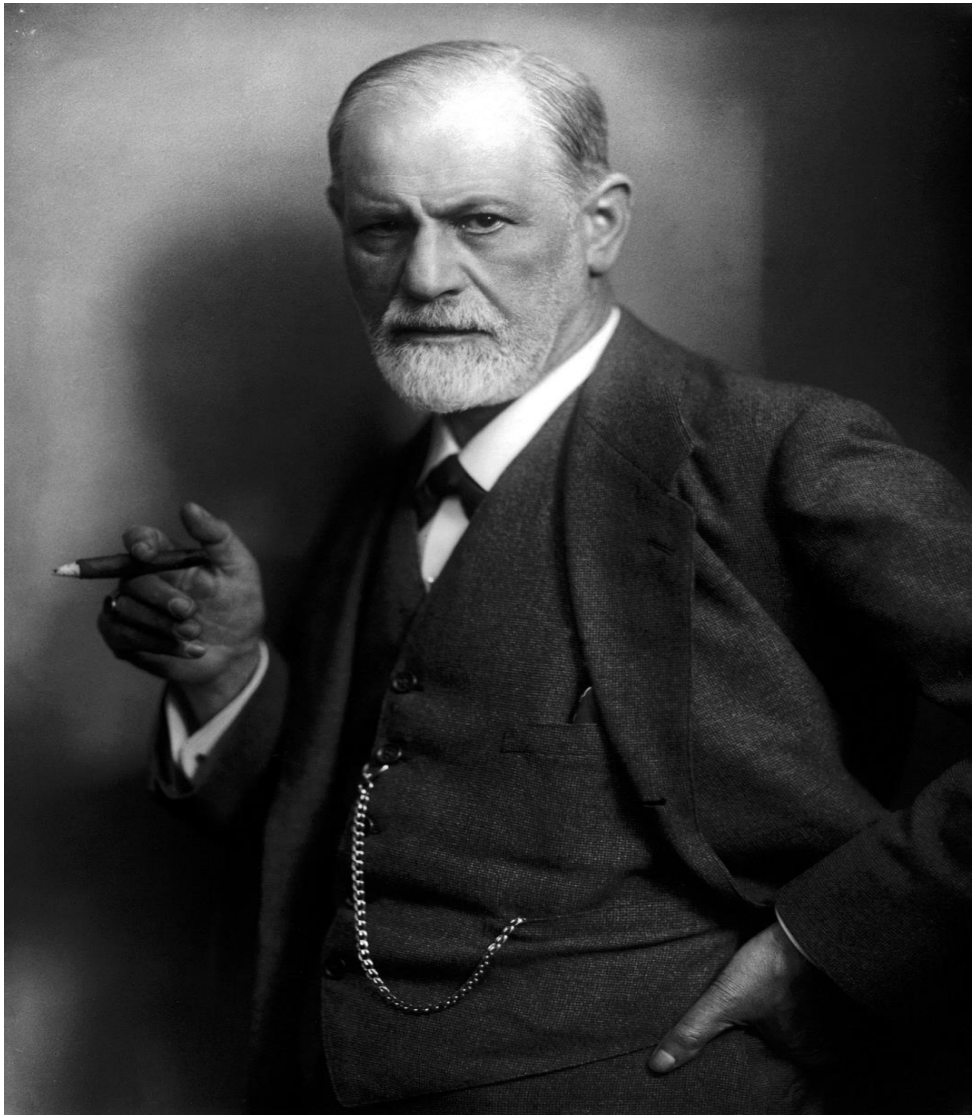
Depression

- In patients with a history of depression

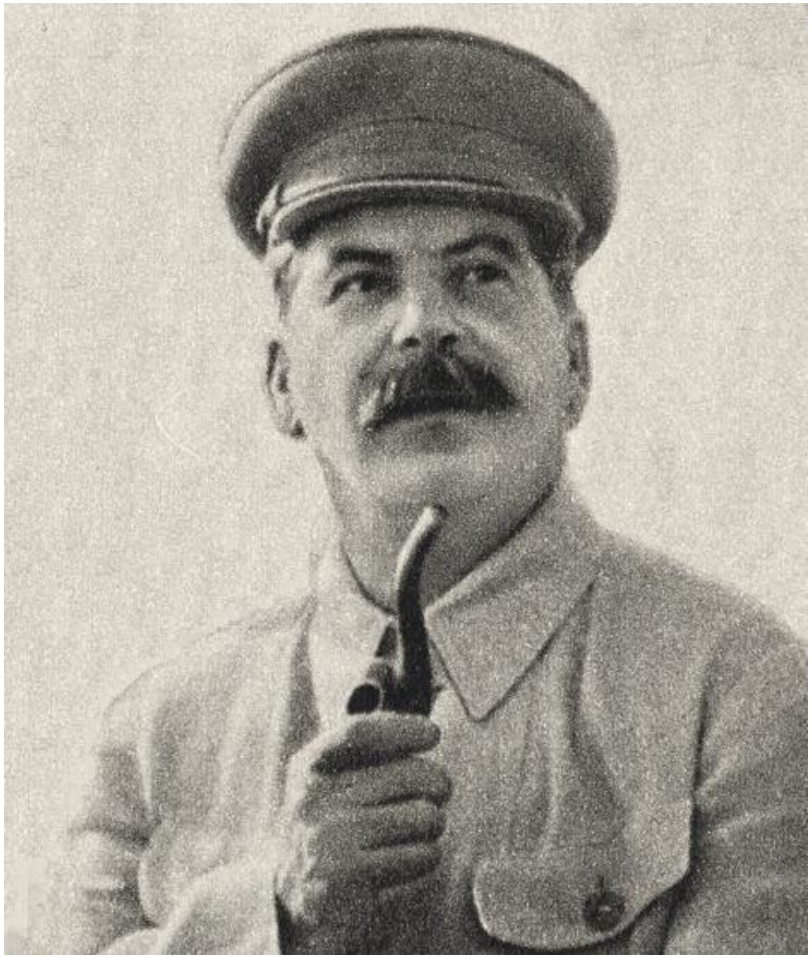
→ Nortriptyline

- Counselling
- Appropriate medication
- Referral to a specialist

Historical Victims to smoking



Sigmund Freud suffered from oral cancer caused by smoking.
His doctor assisted Freud's death in September 1939.



Stalin suffered from atherosclerosis from his heavy smoking. He suffered a severe heart attack in 1945. Stalin died of cerebral hemorrhage on 5 March 1953, at the age of 74.

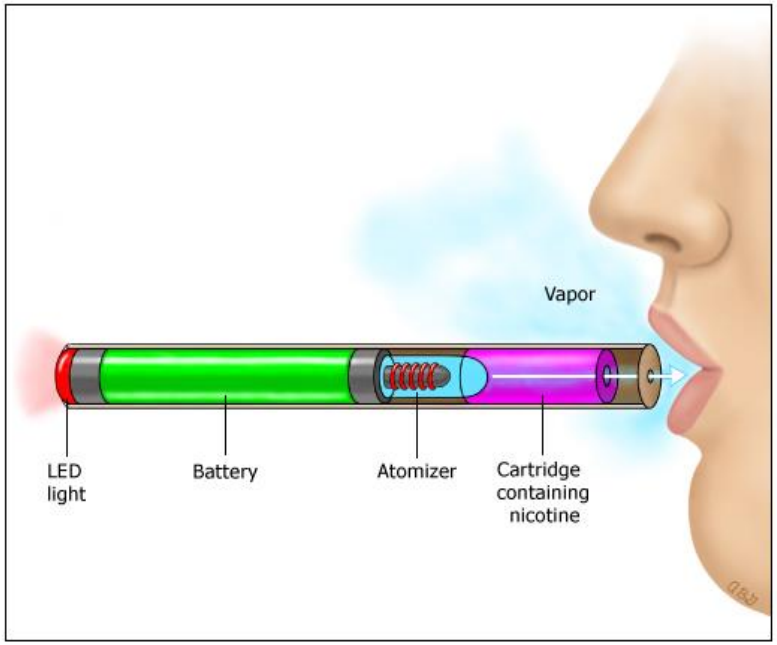
Churchill was a victim of clinical depression. His mental capacity was reduced because of the ten strokes he suffered from during the period 1949–1963. On 1965, Churchill suffered a severe stoke and died at his London home.

Summary

- Consider second-line agents when first-line medications are contraindicated or not helpful.
- Available second-line agents are nortriptyline and clondine.
- Bupropion and nortriptyline should be considered in a patient with a history of depression.
- Long term therapy (6 months or more) for smokers with persistent withdrawal symptoms.

E-cigarrette

E-cigarette



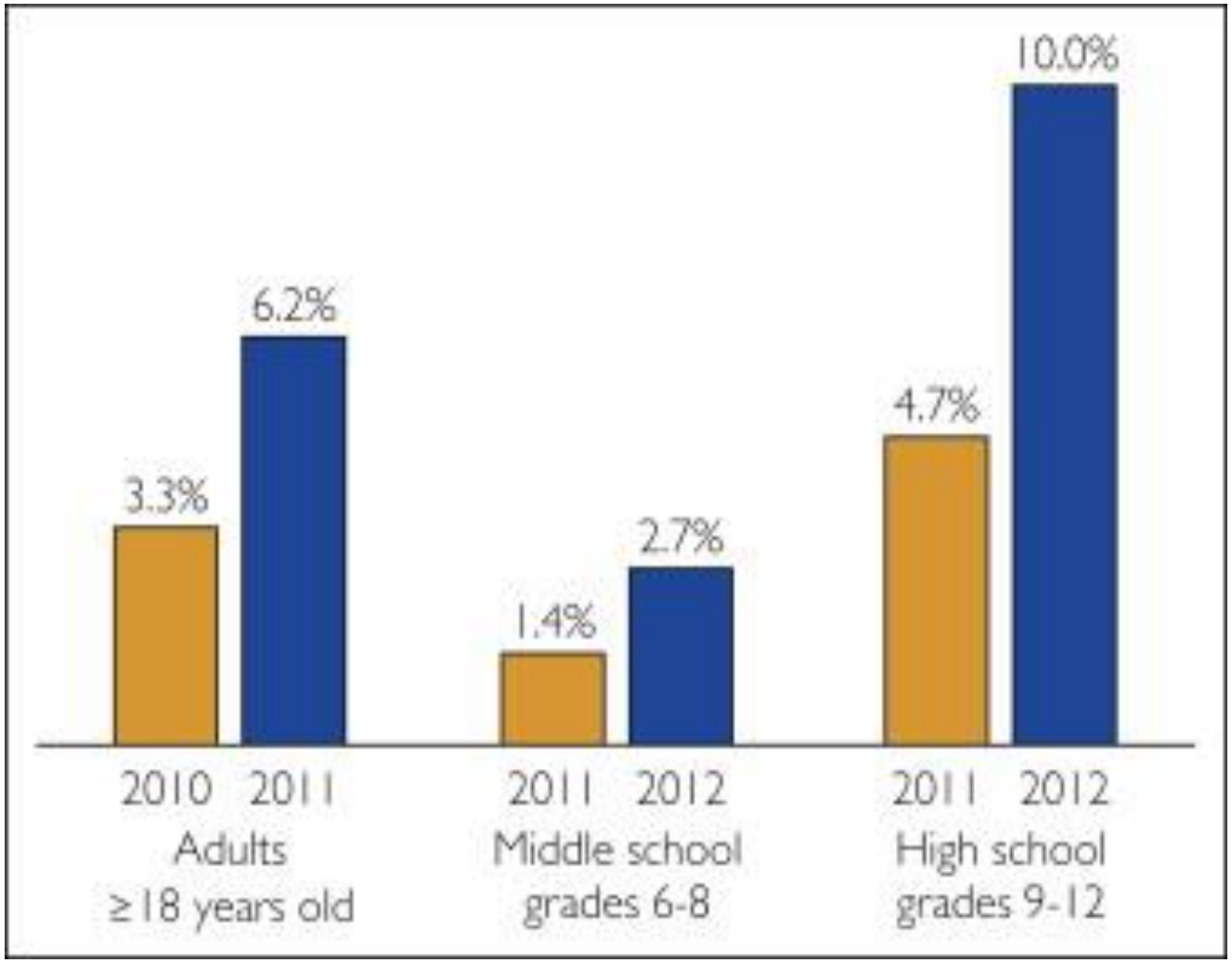
- E-cigarettes were invented in 2003 in China and entered the United States and European markets in 2006

Problems Regarding e-cigarette

- Ever use of e-cigarettes increased from 3.3 to 8.5 % of all adults between 2010 and 2013,

  King BA et al, Nicotine Tob Res 2015; 17: 219

- A majority of e-cigarette users perceive them to be a tool to quit or reduce their smoking.
- Most e-cigarette users are cigarette smokers.
- FDA does not regulate their manufacturing or sales.



Mayo Clin Proc 2015 Jan;90(1):128-34.

Toxic Components of Cigarrette

- 7000 compounds with at least 70 carcinogens

  → form aldehyde

  → benzene

  → nitrosamine

  → free radicals

  → heavy metals

  → toxic gases

Toxic materials in E-cigarette

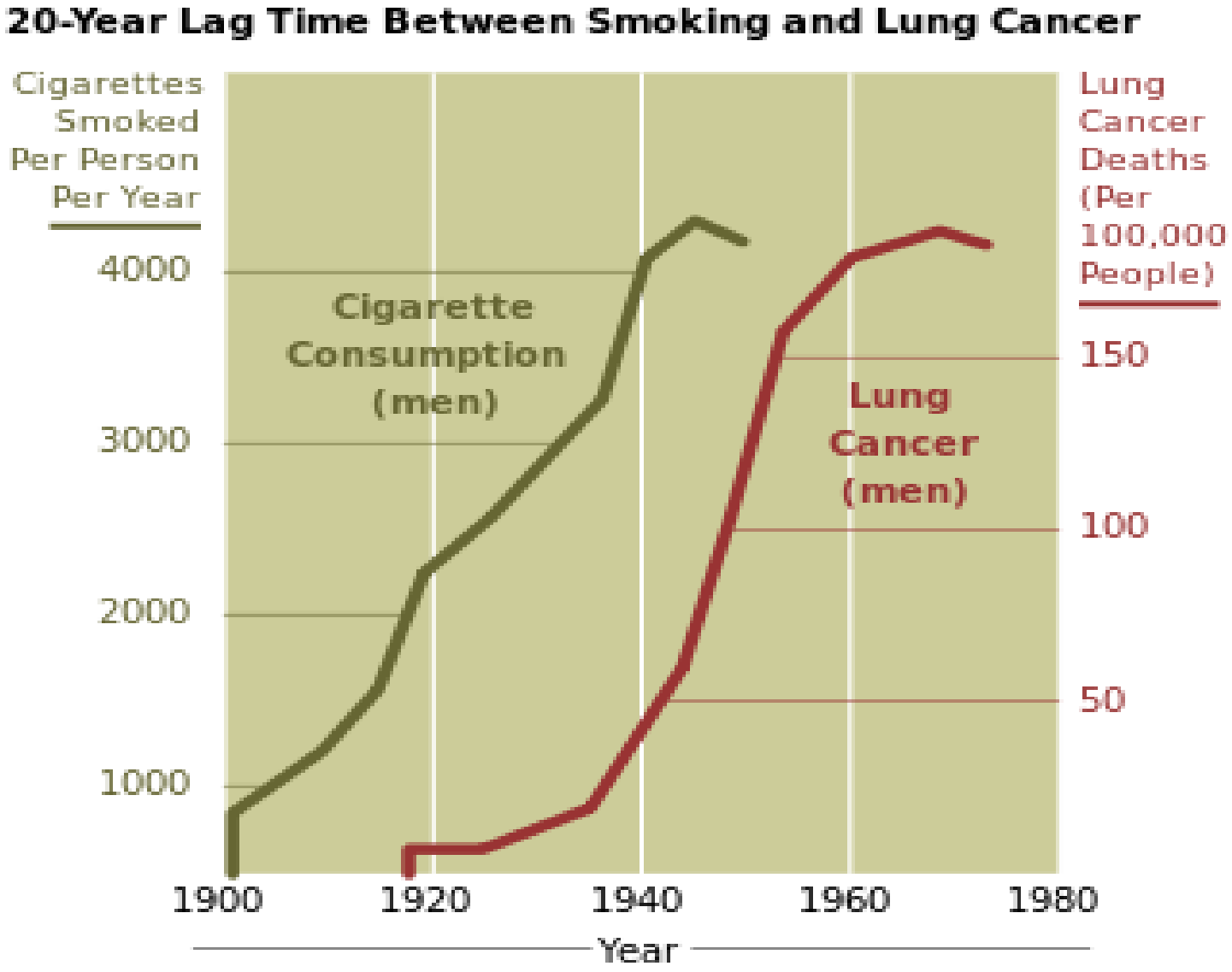
- Nicotine
- Propylene glycol
- Flavoring agents

  - cinnamaldehyde, diacetyl and acetyl propionyl
- Toxic metal : tin, cadmium, nickel, lead
- Other compounds : tobacco-specific nitrosamines, carbonyl compounds, and phenolic compounds

Comparison with cigarette

Toxin	Conventional cigarette (μg/cigarette in mainstream smoke)	Electronic cigarette (μg per 15 puffs)	Average ratio (conventional: electronic)
Carbonyl compounds			
formaldehyde	1.6–52	0.20–5.61	9
acetaldehyde	52–140	0.11–1.36	450
acrolein	2.4–62	0.07–4.19	15
Toluene	8.3–70	0.02–0.63	120
Nitrosamines			
N′-nitrosonornicotine	0.005–0.19	0.00008–0.00043	380
NNK	0.012–0.11	0.00011–0.00283	40

Annals ATS 2014 ; 11: 2: 236-242


20-Year Lag Time Between Smoking and Lung Cancer
Cigarettes Smoked Per Person Per Year
4000
3000
2000
1000
Cigarette Consumption (men)
Lung Cancer (men)
Lung Cancer Deaths (Per 100,000 People)
150
100
50
1900
1920
1940
1960
1980
Year

NIH.svg

Adverse Effects of E-cigarette

- Nicotine exposure

→ experienced users : longer puffs and intensive use

- Vapor exposure by propylene glycol

→ probable human carcinogen

→ forms the carcinogens such as formaldehyde and acetaldehyde

- Compared to conventional cigarette : low level of nitrosamines, metals, and phenolic compounds

Public Health Concern about E-cigarette

- Serve as a gateway to conventional smoking
- Reglamorize smoking & renewed acceptance of smoking
- Perpetuate nicotine dependence by decreasing incentives for smoking cessation

Annals ATS 2014 ; 11: 2: 236-242

Benefits of E-cigarette

- One randomized controlled trial in New Zealand
- 657 smokers were randomized

  → 289 to nicotine e-cigarettes

  → 295 to nicotine patches

  → 73 to placebo e-cigarettes
- Abstinence rate at 6 months,

  → 7.3% (21 of 289) with nicotine e-cigarettes,

  → 5.8% (17 of 295) with patches,

  → 4.1% (3 of 73) with placebo e-cigarettes.

Bullen C et al, Lancet 2013 Sept 7

Benefits of E-cigarette

- E-cigarettes appear to help smokers unable to stop smoking.

McRobbie H et al. Cochrane Database Syst Rev. 2014;12:CD010216.

- Harm reduction or cessation of smoking

→ Few studies

→ Not scientifically proven

→ E-cigarettes are not approved by US FDA for smoking cessation

Am J Respir Crit Care Med 190; 6: 611–618, 2014

An Official Statement

(E-cigarette Working Group, American Heart Association, Forum of International Respiratory Societies)

- The health risks of electronic cigarettes have not been scientifically studied.
- The addictive power of nicotine and its untoward effects should not be underestimated.
- Second-hand exposure cannot be excluded.
- The benefits of e-cigarettes have not been scientifically proven.
- E-cigarettes should be regulated

Circulation. 2014; 130: 1418-1436

Int J Tuberc Lung Dis 2014,18(1):5–7

Am J Respir Crit Care Med 190; 6: 611–618, 2014

Summary

- E-cigarettes expose users to nicotine as well as heated and aerosolized propylene glycol and glycerol.
- Public health concerns

→ Include their potential to increase tobacco products.

→ Re-normalize tobacco use in places where cigarette smoking is not acceptable.

→ Accidental nicotine poisoning in children.

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