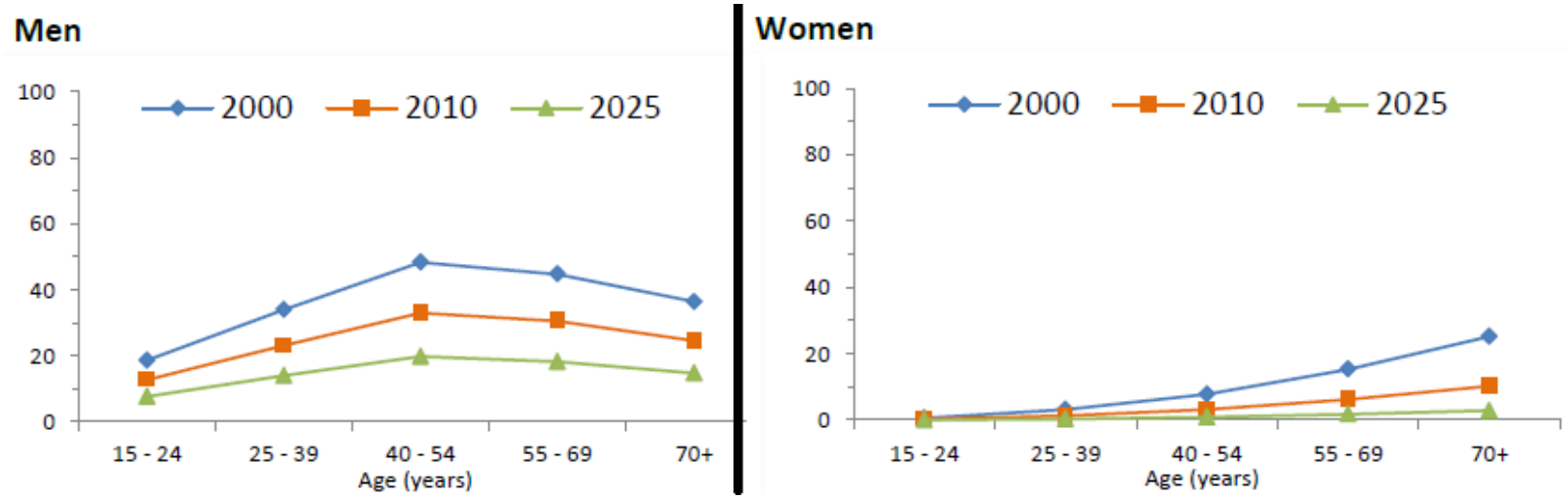
Smoking cessation

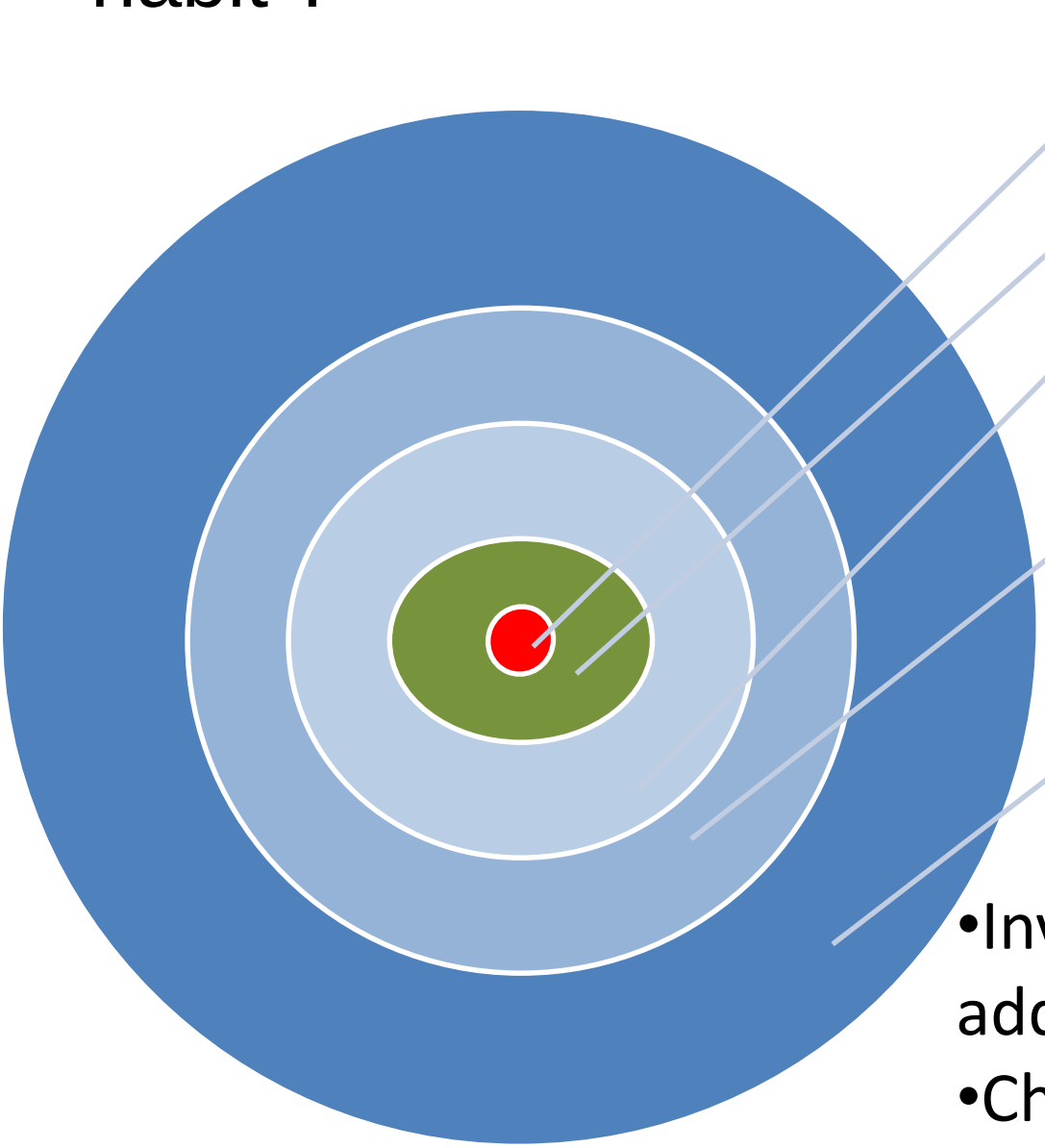
Survey name	Survey year	Age (years)	Smokeless use		Tobacco type	Current use		Daily use	
			Men	Women		Men	Women	Men	Women
Global Adult Tobacco Survey (GATS) - India	2009-10	15+	32.9	18.4	Tobacco smoking	24.3	2.9	18.3	2.4
National Family Health Survey (NFHS)	2005-06	15-49	36.9	9.0	Tobacco smoking	. . .	1.4	. . .	1.4
The extent, pattern and trends of drug abuse in India. National s	2000-01	12-60	. . .	. . .	Any tobacco use	55.8	. . .	. . .	. . .
National Family Health Survey (NFHS)	1998-99	15+	28.3	12.4	Tobacco smoking	29.4	2.5	. . .	. . .

- WHO estimates that about 13% of India's population smoke. Far fewer women than men use tobacco.



In 2010, WHO estimates that about 13% of India's population smoked (approximately 111,856,400 persons). If tobacco control efforts continue at the same intensity, WHO projects that in 2025 around 8% of the population (approximately 83,514,000 persons) will be smokers.

Smoking – An addictive behaviour or casual habit ?



3 % quit rate un-aided

30 % with optimal Rx

32 % took help to quit

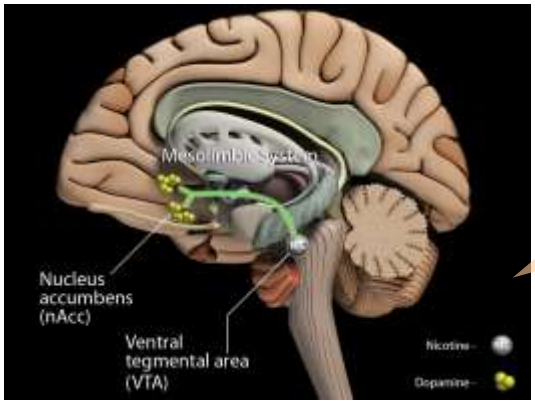
50 % tried to quit

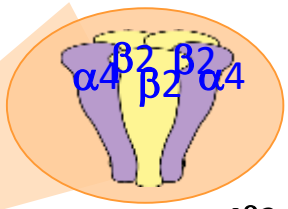
70 % want to quit

- Involuntary nature of the addiction !
- Chronic relapsing disorder

Mechanism of Addiction

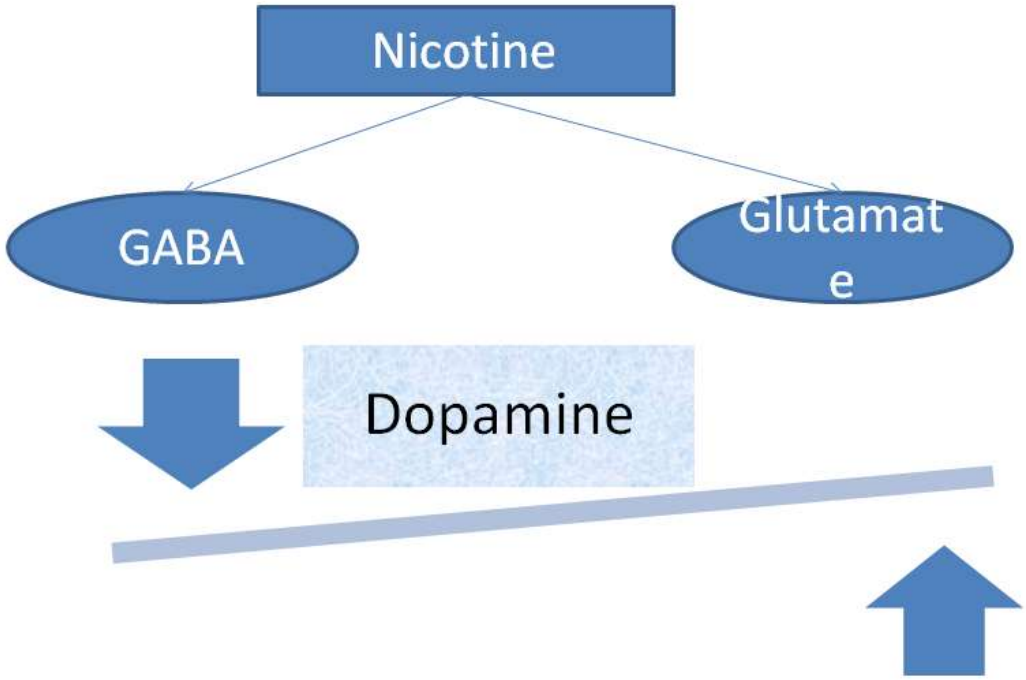
- Inhalation of cigarette smoke carries the nicotine to the lungs from where it is rapidly absorbed and transported to brain.





α4β2 nicotinic acetylcholine receptor (nAChR)

- Nicotine binds preferentially to nAChRs in the central nervous system; one key area is the α4β2 nicotinic receptor in the VTA
- After nicotine binds to the α4β2 nAChR in the VTA, dopamine is released in the nAcc which is believed to be linked to reward centers.



- Nicotine desensitizes GABAergic neurons, which inhibits Dopa release.
- There is no desensitization of neurons that release Glutamate, which augments Dopa release.
- Chronic use ⇒ further addiction

- As nicotine levels fall in blood, the nAchr revert to their steady state, this leads to decrease in dopamine levels.
- This fall in dopamine levels causes a variety of psychological and physical conditions- “withdrawal syndrome “
- The smoker craves nicotine to release more Dopamine, thus restoring pleasure and calmness.

Is there an age for quitting smoking ?

AMERICAN JOURNAL OF
Preventive Medicine

RESEARCH ARTICLE

Cigarette Smoking and Mortality in Adults Aged 70 Years and Older: Results From the NIH-AARP Cohort

Sarah H. Nash, PhD,[1,2] Linda M. Liao, PhD,[2] Tamara B. Harris, MD,[3] Neal D. Freedman, PhD[2]

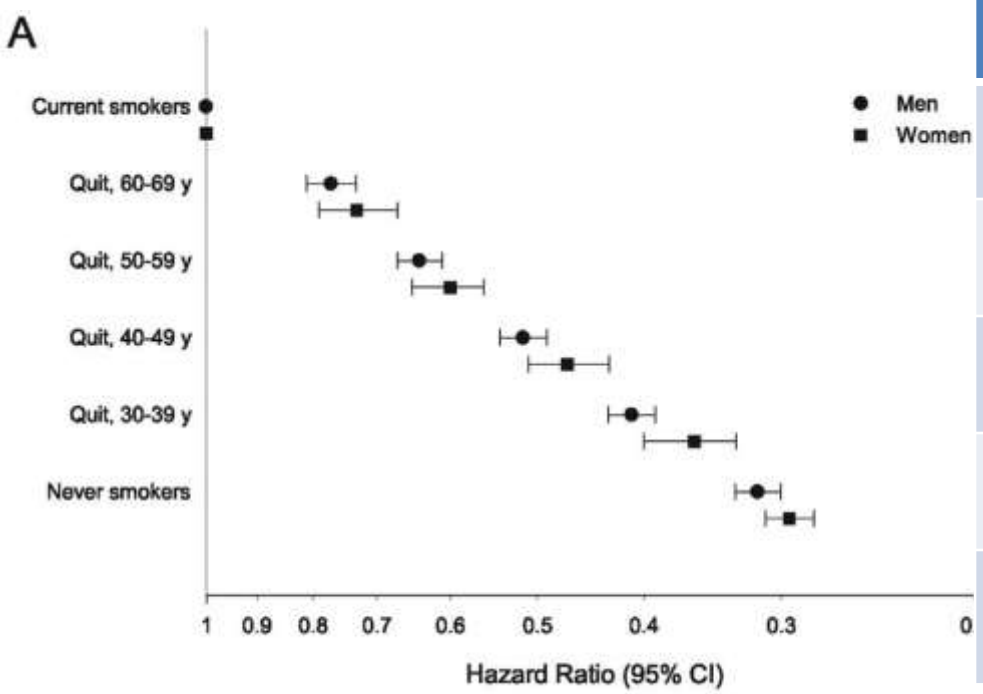
Introduction: Tobacco use remains a leading modifiable cause of cancer incidence and premature mortality in the U.S. and globally. Despite increasing life expectancy worldwide, less is known about the effects of cigarette smoking on older populations. This study sought to determine the effects of smoking on mortality in older age.

Methods: Associations of mortality with self-reported age at smoking cessation, age at smoking initiation, and amount smoked after age 70 years were examined in 160,113 participants of the NIH-AARP Diet and Health Study aged >70 years. Participants completed a questionnaire detailing their smoking use in 2004–2005, and were followed for mortality through December 31, 2011. Analyses were conducted between 2014 and 2016.

Results: Relative to never smokers, current smokers were more likely to die during follow-up (hazard ratio, 3.18; 95% CI=3.04, 3.31). Furthermore, former smokers had lower risks than current smokers (hazard ratios for quitting between ages 30–39, 40–49, 50–59, and 60–69 years were 0.41 [95% CI=0.39, 0.43], 0.51 [95% CI=0.49, 0.54], 0.64 [95% CI=0.61, 0.67], and 0.77 [95% CI=0.73, 0.81], respectively). Among current smokers, mortality was inversely associated with age at initiation, but directly associated with the number of cigarettes smoked per day at age >70 years.

Conclusions: As among younger people, lifetime cigarette smoking history is a key determinant of mortality after age 70 years.

Am J Prev Med 2016;▮(▮):▮▮▮–▮▮. Published by Elsevier Inc. on behalf of American Journal of Preventive Medicine



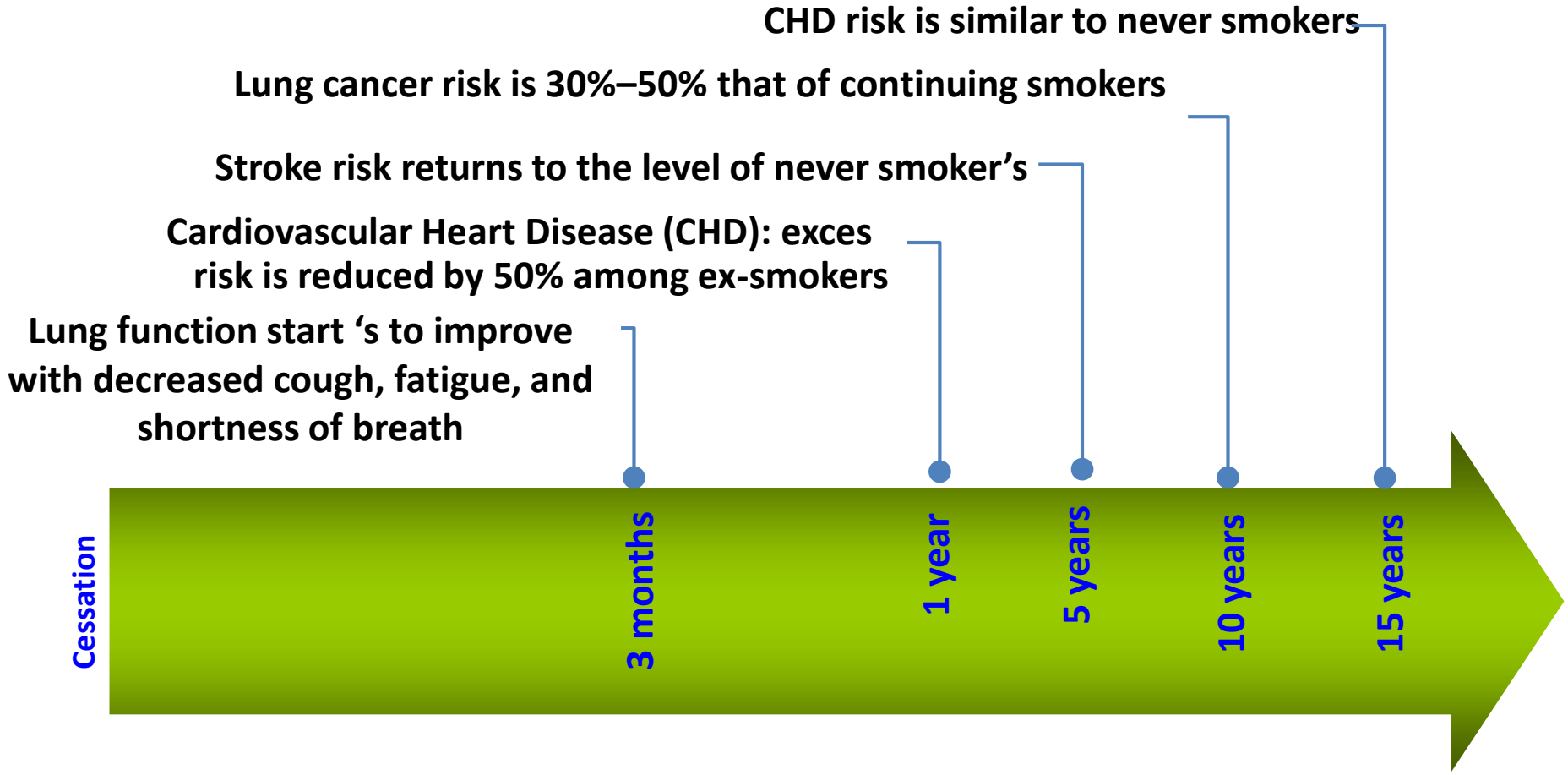
Age of quitting	HR
Non smoker	0.32 ,95% CI0.30, 0.33
30-39	0.41, 95% CI0.39, 0.43
40-49	0.51,95% CI0.49,0.54
50-59	0.64 ,95% CI0.61, .67
60-69	0.77,95% CI0.73,0.81

- Relative to current smokers, the risk of all-cause mortality was lowest among former smokers who quit at age 30–39 years
- The benefits of quitting at an older age were lower, although still substantial.

Quitting at Any Age May Increase Life Expectancy

- For participants who quit smoking in their 60s,the protective effect of smoking cessation on mortality was most evident for death from heart attack, stroke, and respiratory infection.

Potential Health Benefits of Quitting Smoking



1. USDHHS. The Health Benefits of Smoking Cessation: http://profiles.nlm.nih.gov/NN/B/B/C/T/.
2. American Cancer Society. Guide to Quitting Smoking. Available at: http://www.cancer.org.

Approach to a quit attempt

- At least 70% of smokers see a physician each year.
- Smokers cite a physician's advice to quit as an important motivator for attempting to stop smoking.
- Most smokers are interested in quitting, clinicians and health systems are in frequent contact with smokers, and clinicians have high credibility with smokers.

80 % DIDN'T receive a physician counseling at their visit

Therefore all clinicians are in a position to intervene with patients who use tobacco.

Kreuter MW, Arch Fam Med. 2000 May;9(5):426-33.

The “5 A’s” of smoking cessation

Recommend the use of approved medication, except where contraindicated	Explain how these medications increase quitting success and reduce withdrawal symptoms.

Provide practical counseling (problem-solving/skills training).	***Abstinence.*** Striving for total abstinence is essential. Not even a single puff after the quit date. ***Past quit experience.*** Identify what helped and what hurt in previous quit attempts. Build on past success. ***Anticipate triggers or challenges in upcoming attempt.*** Discuss challenges/triggers and how patient will successfully overcome them (e.g., avoid triggers, alter routines). ***Alcohol.*** Since alcohol is associated with relapse, the patient should consider limiting/abstaining from alcohol while quitting. (Note that reducing alcohol intake could precipitate withdrawal in alcohol dependent persons.) ***Other smokers in the household.*** Quitting is more difficult when there is another smoker in the household. Patients should encourage housemates to quit with them or not smoke in their presence.

Approaches to Therapy of Tobacco Dependence

Components of Tobacco Dependence	Treatment Approaches to Therapy
Physiological	Pharmacotherapy
Psychological	Pharmacotherapy/ Behavioral Counseling
Behavioral*	Behavioral Counseling

* Behavioral components include triggers and stressors such as alcohol, prior severe withdrawal symptoms, work and family issues, driving, living with another smoker, etc.

Behavioral counseling

- **Clinician counseling**
- **Group programs**
- **Telephone counseling — reactive vs proactive**
- **Web-interventions**
- **Text messaging**
- **Phone apps**
- **Self-help**

Physician advice for smoking cessation (Review)

We defined trials where advice was provided (with or without a leaflet) during a single consultation lasting less than 20 minutes plus up to one follow-up visit as minimal intervention. A trial was defined as intensive when the intervention involved a greater time commitment at the initial consultation, the use of additional materials other than a leaflet, or more than one follow-up visit. We

(2004)	2003, •31,000 smokers.		to 2.05	NS
		•With follow up provided	•2.55 (2.04 to 3.19)	
		Intensive vs Non-intensive	OR 1.24, 95% CI 1.02 to 1.50	edit

This meta analysis suggests a small but significant benefit for simple physician advice and may be increased by providing a follow up. Whenever possible an intensive session should be used.

Behavioral counseling

- **Clinician counseling**
- **Group programs**
- **Telephone counseling — reactive vs proactive**
- **Web-interventions**
- **Text messaging**
- **Phone apps**
- **Self-help**

Group programs

- Lies between self-help methods with minimal therapist contact and intensive individual counselling/therapy
- gives people who smoke the opportunity to share problems and experiences with others attempting to quit.
- Behavioural interventions typically include such methods as coping and social skills training, contingency management, self control, and cognitive-behavioural interventions.

	Population	Intervention	Outcome
			Quit rate
Stead, L. F. and T. Lancaster (2005).	•13 trials, •4375	•Group vs self help	•OR 1.98 [1.60, 2.46]
‘’	5 trials 788	•Group vs individual therapy	•1.01 [0.77, 1.32]
’’ Stead, L. F., et al. (2015)	3 trials 1051	•Group + NRT vs NRT	•1.08 [0.88, 1.31]
	47 trials 18000		•RR 1.17, 95% CI 1.11 to 1.24
		•Group programme vs brief intervention	NA
	8 trials 1040	•Group versus no intervention controls	2.71 [1.84, 3.97]

- Group programs are almost twice as effective as self help programs and no intervention at all.
- No evidence that they are better than individual therapy, or physician advice.
- They have a small but statistically significant benefit as an add on to NRT.

Behavioral counseling

- **Clinician counseling**
- **Group programs**
- **Telephone counseling — reactive vs proactive**
- **Web-interventions**
- **Text messaging**
- **Phone apps**
- **Self-help**

- EBM Telephone counseling can increase the quit rates when added on to standard physician advice.
-

Study	Pop	Follow up	Quit rates	
Borland, R., et al. (2008)	N=1039	3 mo	12.3 vs 6.9	OR 1.92 CI 1.17-3.13
		12 mo	6.5 VS 2.6	OR 2.86 CI .94-8.71

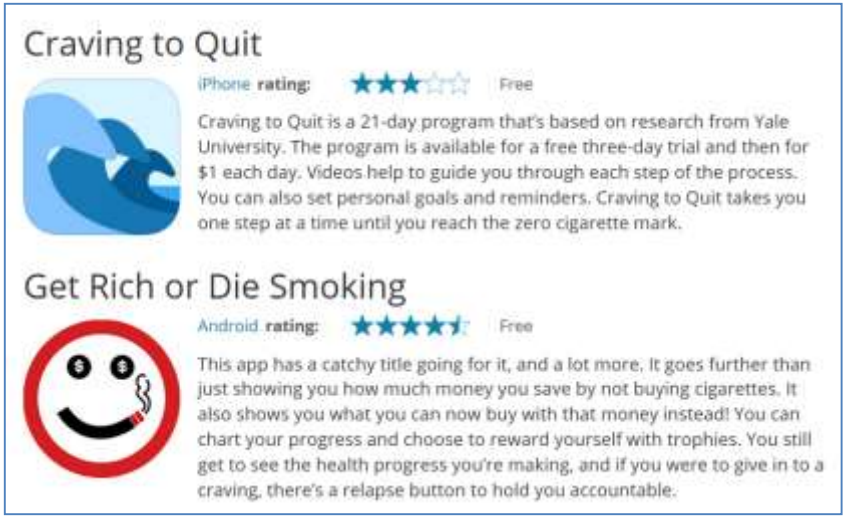
Borland, R., Fam Pract. 2008 Oct;25(5):382-9

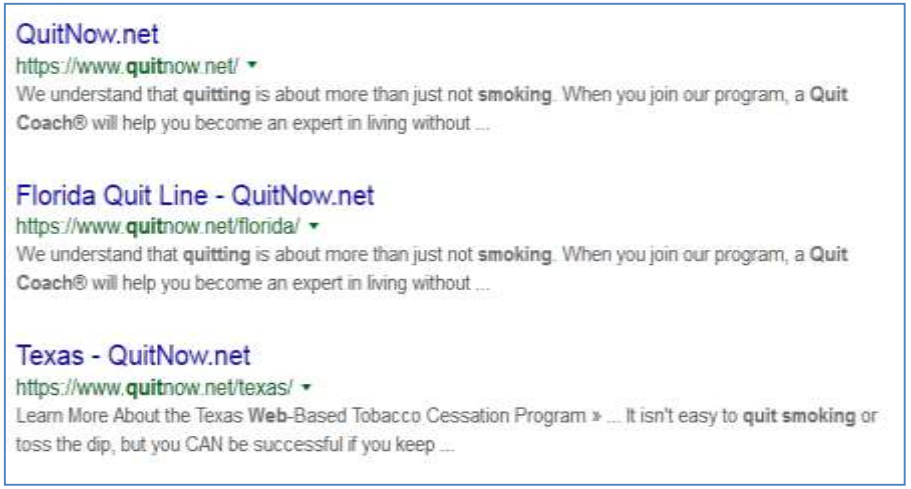
- *Proactive counseling*, in which calls t o smokers are initiated by a counselor according to a prearranged schedule and
- *Reactive counseling*, provided by quitlines, in which all calls to counsellors are smoker initiated

Behavioral counseling

- **Clinician counseling**
- **Group programs**
- **Telephone counseling — reactive vs proactive**
- **Web-interventions**
- **Text messaging**
- **Phone apps**
- **Self-help**

- Web-based/text based/phone apps are smoking cessation tools that may assist in smoking cessation.
- Evidence shows them to be slightly more effective than self-help and no intervention in quitting smoking.





Pharmacotherapy

- First line
  - nicotine gum
  - nicotine patch
  - nicotine lozenge
  - nicotine nasal spray
  - nicotine inhaler
  - bupropion
  - varenicline
  - combinations
- Second line
  - clonidine
  - nortriptyline

NRT

- Rationale

- After a puff nicotine is rapidly absorbed from the lungs, in 10-20 s.
- Faster than IV administration !!!

- The rapidity of rise helps to titrate the level of nicotine related effects and produces rapid behavioral reinforcement.

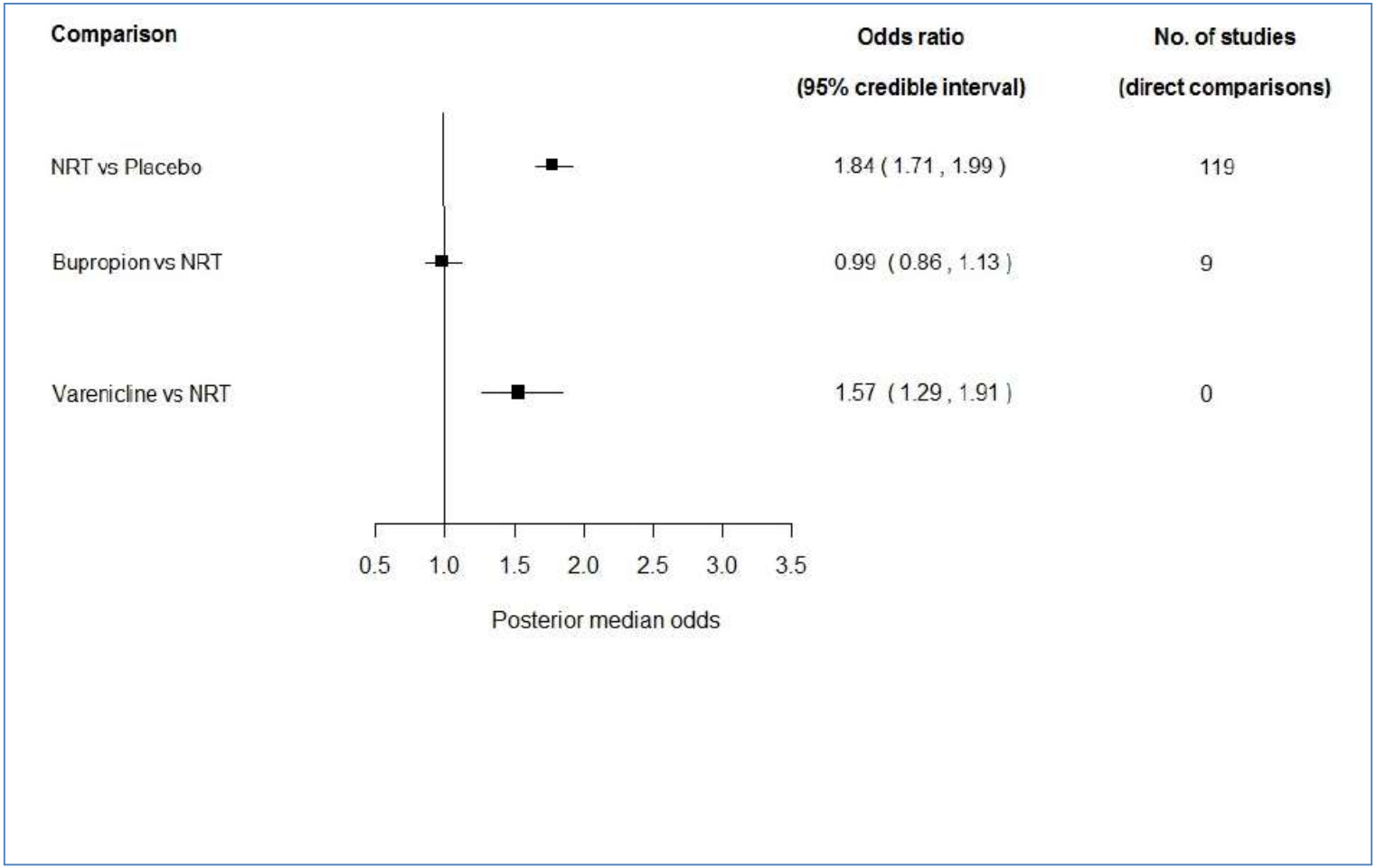
- Absorption of nicotine from all NRTs is slower and the increase in blood levels is more gradual than from smoking. This results in low abuse liability of NRTs

Type of nicotine administration[a]	C_{max}[b] ng ml^{-1}	T_{max}[b,c] min	Bioavailability %
Smoking (one cigarette, 5 min) (~2 mg/cigarette[d])	15–30 (venous)	5–8 (venous)	80–90 (of inhaled nicotine)
	20–60 (arterial)	3–5 (arterial)	
Nasal spray 1 mg	5–8 (venous)	11–18 (venous)	60–80
	10–15 (arterial)	4–6 (arterial)	
Gum (30 min, total dose in gum)			
2 mg	6–9	30	78
4 mg	10–17	30	55
Inhaler 4 mg released (one 10 mg cartridge, 20 min)	8.1	30	51–56
Lozenge (20–30 min)			
2 mg	4.4	60	50
4 mg	10.8	66	79
Transdermal patch (labeled dose)			
15 mg/16 h (Nicotrol)	11–14	6–9 h	75–100
14 mg/24 h (Nicoderm)	11–16	4–7 h	
21 mg/24 h (Nicoderm)	18–23	3–7 h	68

- The long-acting, slow-onset nicotine patch is the primary NRT to control baseline nicotine withdrawal symptoms [6]. Adding a short-acting form of NRT (lozenge,
- gum, inhaler, or nasal spray) helps to control cravings and withdrawal symptoms during the day on an as-needed basis.

Efficacy

- Evidence shows NRT to be superior to placebo, increasing quit rates by approximately twofold.
- Among the first line Rx, direct comparison between NRT and Bupropion showed no difference in efficacy.
- Varenicline was associated with higher smoking cessation rates compared with single forms of NRT and bupropion, but similar rates with combination NRT.



Cahill K; Cochrane Database Syst Rev(5): Cd009329. 2013

- Trials comparing the different types of NRT, generally show a similar efficacy.

	Trial	Pop	Outcome
Stead, L. F., et al. (2008)	Inhaler vs Patch	N=222	0.59 ; 95% CI 0.22,1.18
	Nasal spray vs Patch	N =1272	.90; CI 0.64,1.27
Hajek, P., et al. (1999)	Gum vs Patch vs Spray vs Inhaler	N= 127 N=124 N=126 N=127	P= NS for quit rates among the groups

Combination Cessation Pharmacotherapy Versus Monotherapy Group Comparisons at Study Endpoints, Point-Prevalence Abstinence

	One Week Post-Quit			Eight Weeks Post-Quit			Six Months Post-Quit		
Comparison[a]	Abstinence Rate, %	OR (95% CI)	P Value	Abstinence Rate, %	OR (95% CI)	P Value	Abstinence Rate, %	OR (95% CI)	P Value
Patch+Lozenge Vs.	48.0	1[Reference]		44.8	1[Reference]		26.9	1[Reference]	
Bupropion Only	38.3	0.66 (0.46-0.94)	.021	27.7	0.45 (0.31-0.65)	<.001[b]	16.8	0.54 (0.35-0.82)	.004[b]
Nicotine Lozenge	38.7	0.67 (0.47-0.96)	.027	28.0	0.47 (0.33-0.68)-	<.001[b]	19.9	0.67 (0.45-1.01)	.057
Nicotine Patch	45.0	0.89 (0.63-1.24)	.484	28.4	0.47 (0.33 0.68)	<.001[b]	17.7	0.56 (0.37-0.85)	.006[b]

Study	Pop	Intervention	Outcome
Cahil et all 2013 Meta-analysis	3 Trials	Combination NRT vs NRT patch	1.43, 95 CI (1.08,1.91)
	1 Trial	Combination NRT vs NRT gum	1.63, 95 CI (1.21,2.2)
Smith SS et all RCT 2010	N=1346	Combination NRT vs NRT	combination significantly increased abstinence compared with monotherapies

Adverse effects

- GI A/E- nausea, vomiting, abdominal pain, diarrhea,
- The risks associated with NRT in patients with cardiac disease is low and are much less than the risks of continued smoking.
- The benefits of nicotine medication to promote smoking abstinence or cessation far outweigh the risks in cardiovascular disease patients.

NRT after ACS

Am J Cardiol. 2012 Oct 1;110(7):968-70. doi: 10.1016/j.amjcard.2012.05.028. Epub 2012 Jun 20.

Effect of nicotine replacement therapy on cardiovascular outcomes after acute coronary syndromes.

Woolf KJ[1], Zabad MN, Post JM, McNitt S, Williams GC, Bisognano JD.

One-year outcomes and adjusted odds ratios (95% confidence intervals)*

Outcome	NRT	Control	OR (95% CI)
Composite†	53 (29%)	149 (31%)	0.89 (0.61–1.30)
Death	7 (4%)	24 (5%)	0.80 (0.33–1.91)
Myocardial infarction	8 (4%)	23 (5%)	0.90 (0.40–2.06)
Repeat revascularization	18 (10%)	58 (12%)	0.77 (0.44–1.36)
Hospitalization‡	41 (22%)	104 (22%)	1.01 (0.66–1.53)

- NRT use was not associated with an increased risk of adverse cardiovascular events in the first year after ACS.

Contraindications

Absolute	Relative
• 2 weeks before and 2 weeks after free flap surgery	Patients who may continue to use tobacco if not prescribed NRT • immediate (within 2 weeks) post myocardial infarction period • serious arrhythmias • unstable angina pectoris • Hemodynamically unstable
• Patients who due to the severity of illness and circumstances of care, do not have the option to use tobacco products and are comfortable without NRT • immediate (within 2 weeks) post myocardial infarction period • serious arrhythmias • unstable angina pectoris • Hemodynamically unstable	

Dosing

Product	Nicotine Patch	Nicotine Gum	Nicotine Lozenge	Nicotine Nasal Spray	Nicotine Inhaler
Brand Name /Generic Available	Nicoderm CQ® Habitrol Generic	Nicorette® Generic	COMMIT®	Nicotrol NS®	Nicotrol® Inhaler
Product Strength	21 mg 14 mg 7 mg	2 mg 4 mg	2 mg 4 mg	10 mg/ml	10 mg/ cartridge
Dosing	1 patch / 24 hours **11+ cigarettes per day**, use 21 mg for 4-6 wks, 14 mg for 2-4 wks, 7 mg for 2-4 wks. **6-10 cigarettes per day**, use 14 mg for 4-6 wks, 7 mg for 2-4 wks.	Use 4 mg **for 20 or more cigarettes /day**. Use 1 piece every 1-2 hrs. Maximum 24 pieces/day. Taper as comfortable.	Use 1 2-mg piece every 1 to 2 hrs. Use 4mg with **20+ cigarettes/ day**. Maximum 24 per day.	1-2 doses/hour Dose = 1 spray per nostril Do not exceed 5 doses/hr or 40 doses/day For heavier smokers	6-16 cartridges/day. Taper as comfortable
Time to peak Plasma level	5-10 hours	20-30 minutes	20-30 minutes	5-7 minutes	15 minutes
Possible Adverse Reactions	*Mild skin reactions (rotate site, use 1% cortisone cream) *If vivid dreams or sleep disturbance, remove at night	*Mouth soreness *Hiccups *Indigestion *Jaw ache (Avoid constant chewing; park between cheek and gums)	*Headache *Insomnia *Nausea, indigestion *Hiccups	*nose, throat or eye irritation (usually short term) *Higher dependence potential compared to other NRT	*Mouth or throat irritation, cough (usually short term). Use proper technique - like sucking on a straw.
Instructions for Use	Apply 1 patch to healthy, clean, dry hairless skin such as upper arm, lower back or hip. Remove after waking and replace daily.	Chew gum until a peppery taste and slight tingle occurs, and park between cheek and gum. Chew again when taste fades, then park in another area of mouth. Use for 30 minutes.	Allow lozenge to dissolve slowly over 20-30 minutes without chewing or swallowing. Occasionally move lozenge from one side of mouth to the other.	Blow nose if not clear. Insert bottle tip as far as comfortable, angling toward wall of nostril. Do not sniff while spraying.	Pull top off. Press cartridge firmly until seal breaks. Align marks to close. Inhale using a short puffing or sipping action. Do not inhale into lungs. Contains about 200 puffs.

Vernaciline

- Varenicline is an $\alpha 4\beta 2$ nicotinic receptor partial agonist,
- dual agonist and antagonist activities.
- results in both a lesser amount of dopamine release from the VTA at the nAcc as well as the prevention of nicotine binding at the $\alpha 4\beta 2$ receptors.
- Therefore ;
  - partial stimulation - reduces withdrawal symptoms
  - Blocking the nicotine- reduces rewarding aspect of nicotine

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Articles

Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial

Study	Pop/ no of studies	Comparator	Outcome
Anthenelli, R. M., et al. 2016 RCT	N = 8144	Vernaciline vs placebo	2·74 (2·28–3·30)p<0·0001
		Vernaciline vs Bupropion	1·45 (1·24–1·70)p<0·0001
		Vernacilline vs NRT	1·52 (1·29–1·78)p<0·0001

Dosage

- 0.5 mg daily for three days, then 0.5 mg twice daily for four days, and then 1 mg twice daily for the remainder of a 12-week course.

Adverse effects

- Nausea
- Neuro-psychiatric AE
  - Post marketing surveillance had found an increased rate of suicidal/self harm events with Vernaciline, prompting FDA warning.
  - The EAGLE trial did not find any significant increase in AE among first line agents/placebo.

FDA Removes Warnings on Smoking-Cessation Medication

DECEMBER 16, 2016

Colleen Hall

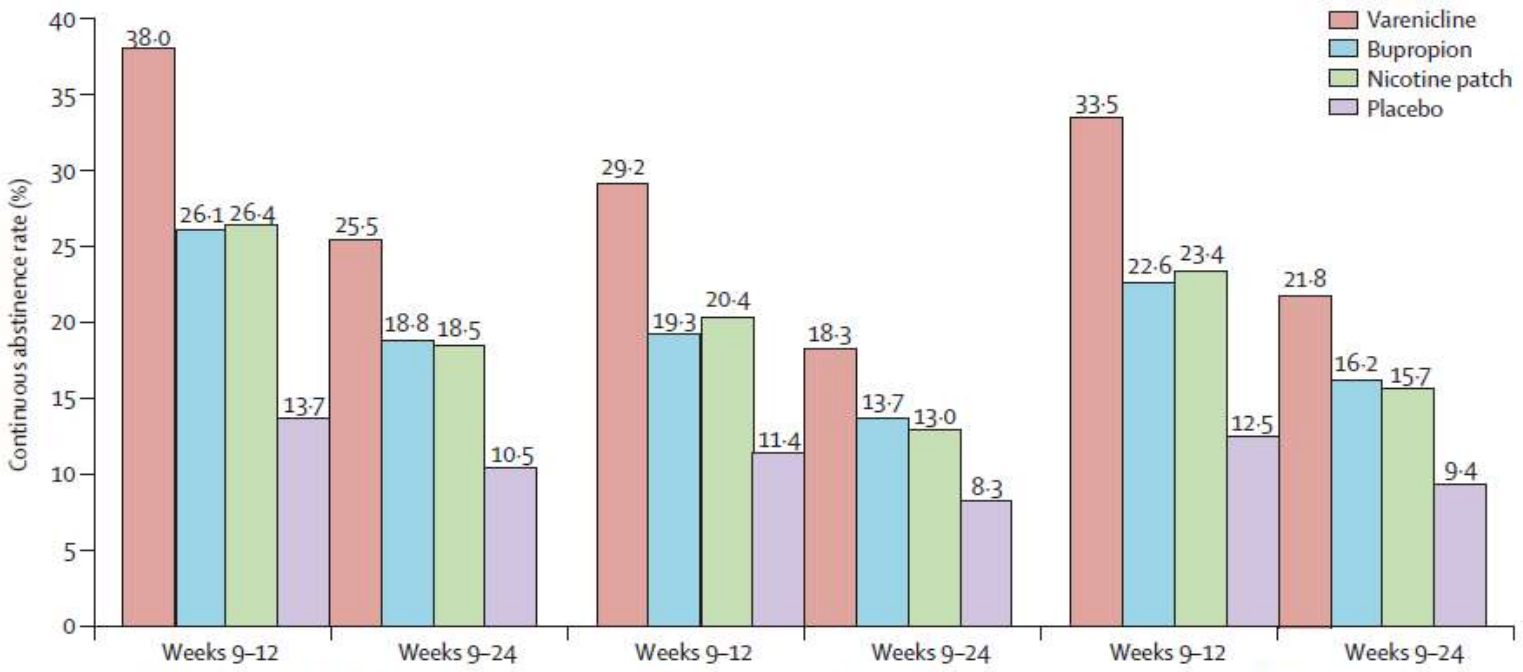
- Cardio-vascular events
- Data from randomized trials and meta-analyses do not clearly confirm or refute this association, however available data indicate the risk is minimum.

	Pop		Outcome
Prochaska JJ 2012 Meta-analysis	22 Trials N=9232	cardiovascular serious adverse events	risk difference, 0.27% (95% CI -0.10 to 0.63 P = 0.15
Rigotti NA 2010	RCT 714 smokers Stable CVD	• varenicline (1 mg twice daily) or placebo • CV events & Mortality	7.1% versus 5.7%; difference, 1.4%; 95% CI, -2.3 to 5.0 NS

Prochaska JJ ;BMJ. 2012 May 4;344:e2856
Circulation. 2010 Jan 19;121(2):221-9.

Bupropion

- Only antidepressant used for smoking cessation.
- Mechanism of action
  - Noradrenergic and dopamine reuptake inhibitor
  - non competitive antagonist of nicotinic acetylcholine receptors.
- diminish the reinforcing properties of nicotine.



OR (95% CI) p value	Weeks 9–12	Weeks 9–24	Weeks 9–12	Weeks 9–24	Weeks 9–12	Weeks 9–24
Primary comparisons						
Varenicline *vs* placebo	4·00 (3·20–5·00) p<0·0001	2·99 (2·33–3·83) p<0·0001	3·24 (2·56–4·11) p<0·0001	2·50 (1·90–3·29) p<0·0001	3·61 (3·07–4·24) p<0·0001	2·74 (2·28–3·30) p<0·0001
Bupropion *vs* placebo	2·26 (1·80–2·85) p<0·0001	2·00 (1·54–2·59) p<0·0001	1·87 (1·46–2·39) p<0·0001	1·77 (1·33–2·36) p<0·0001	2·07 (1·75–2·45) p<0·0001	1·89 (1·56–2·29) p<0·0001
Secondary comparisons						
Nicotine patch *vs* placebo	2·30 (1·83–2·90) p<0·0001	1·96 (1·51–2·54) p<0·0001	2·00 (1·56–2·55) p<0·0001	1·65 (1·24–2·20) p=0·0007	2·15 (1·82–2·54) p<0·0001	1·81 (1·49–2·19) p<0·0001
Varenicline *vs* nicotine patch	1·74 (1·43–2·10) p<0·0001	1·52 (1·23–1·89) p=0·0001	1·62 (1·32–1·99) p<0·0001	1·51 (1·19–1·93) p=0·0008	1·68 (1·46–1·93) p<0·0001	1·52 (1·29–1·78) p<0·0001
Bupropion *vs* nicotine patch	0·98 (0·80–1·20) p=0·8701	1·02 (0·81–1·28) p=0·8645	0·94 (0·75–1·16) p=0·5467	1·07 (0·83–1·39) p=0·5824	0·96 (0·83–1·11) p=0·5797	1·04 (0·88–1·24) p=0·6002
Varenicline *vs* bupropion	1·77 (1·46–2·14) p<0·0001	1·49 (1·20–1·85) p=0·0003	1·74 (1·41–2·14) p<0·0001	1·41 (1·11–1·79) p=0·0047	1·75 (1·52–2·01) p<0·0001	1·45 (1·24–1·70) p<0·0001

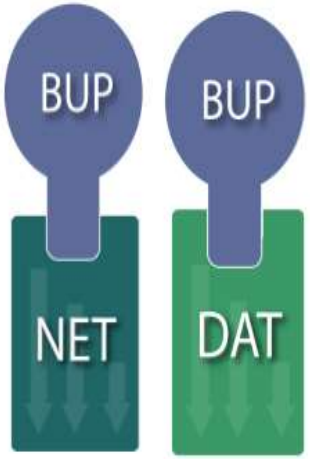
Dosage

	Pop	Intervention	Outcome
Hughes JR et all 2014	**3 Trials N= 2042**	**300 mg/day versus 150 mg/day**	**Risk 1.08 [0.93, 1.26]**

- Benefits of bupropion in improving abstinence rates are not immediate, and take several weeks or longer to be evident.
- it is started one week before a smoker's target quit date
- Treatment is continued for at least 12 weeks.
- Dosage is 150 mg/day for three days, then 150 mg twice a day thereafter.

Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial

EAGLES trial comparing varenicline, bupropion, and the nicotine patch with placebo found no difference in adverse psychiatric effects, leading FDA to withdraw the backbox warning.



Restlessness

Activation

Tremors

Insomnia

Nausea

Seizure

Janicak, P G., Marder S R.; Pavuluri M N. Principles and Practice of Psychopharmacotherapy. 5th ed. Philadelphia: LWW.2010.

PSYCHOPHARMACOLOGY INSTITUTE

Nortriptyline	• Meta-analysis • NT vs Placebo • 6 Trials, N=975	RR 2.03, 95% CI 1.48 to 2.78	• significant benefit of over placebo
	• Meta-analysis • NT vs NT+NRT • 4 Trials, N =1644	RR1.21, 95%CI 0.94 to 1.55	• No benefit
MAO-I	• Moclobemide (1 Trial) • Selegiline (4 Trials) • N= 827	RR 1.29, 95% CI 0.93 to 1.79	• No benefit
Venlafaxine	• RCT	RR 1.22, 95% CI 0.64 to 2.32,	• No benefit
St John's wort	• Meta-analysis • 2 Trials N= 261,	RR 0.81, 95% CI 0.26 to 2.53	• No benefit

Clonidine	• 6 Study	RR 1.63; 95% CI 1.22 to 2.18,	• Significant benefit • Sedation and postural hypotension
Cytisine (alpha2beta 4 rch partial agonist)	• 8 Study •	RR1.57 95% CI 1.42 to 1.74	• Significant benefit • Few adverse effects • Cheap
St John's wort	• Meta-analysis • 2 Trials N= 261,	RR 0.81, 95% CI 0.26 to 2.53	• No benefit

Nicotine Vaccine

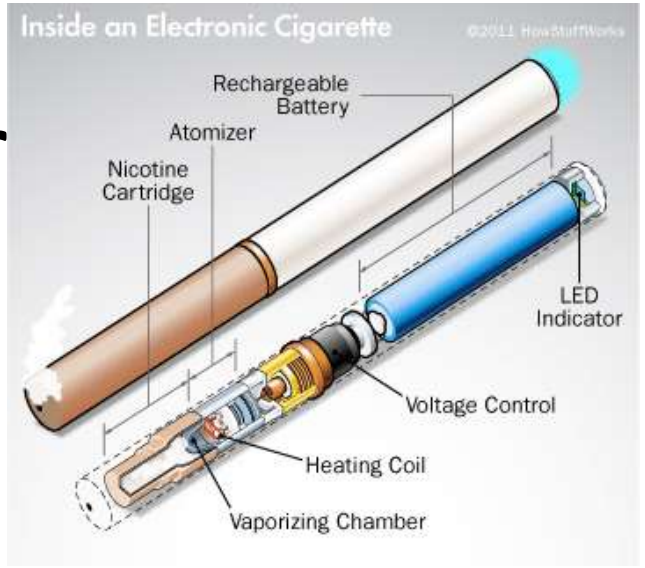
- Body to generate specific anti-nicotine antibodies.
- The antibody binds to nicotine that reaches the bloodstream from smoking cigarettes. The resulting nicotine-antibody complex is too large to cross the blood-brain barrier.
- By blocking nicotine's access to the brain, the smoker derives less satisfaction when they smoke a cigarette.
- It is hypothesized that vaccines may help smokers to quit, and may help former smokers not to relapse

- Nabi Pharmaceuticals' NicVax showed promising results in Phase II trails in 2005
- However Phase III trials in 2009 didn’t show any long term benefit.
- The vaccines were reported to have few adverse effects.

E cigarettes

- invented by Chinese pharmacist Hon Lik
- e-cigarette smoking or "vaping”
- Battery-powered device that converts liquid nicotine into a mist, or vapor, that the user inhales.

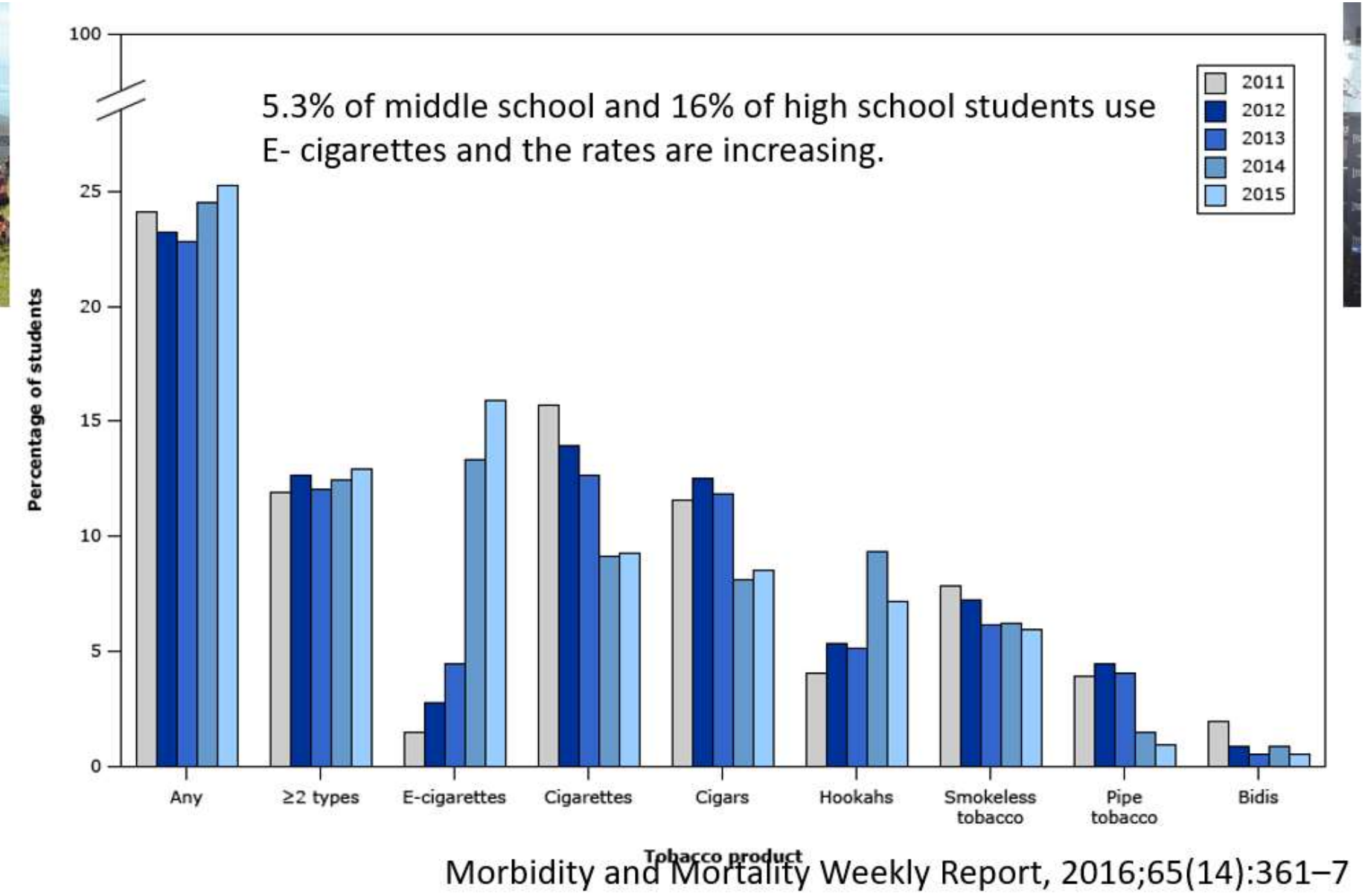
Inside a E- cigar



- Contains
  - **A**tomizer with vaporization chamber - heating element
  - **B**attery-usually a Li
  - **C**artridge- “smoke juice’’-Nicotine(0 to 36mg/Ml) with propylene glycol(food additive-95%) and flavor-mint, chocolate, coffee !
- User activates a pressure sensor by inhaling, causing the heating element to atomize the liquid solution
- The e-liquid reaches a temperature of 100-250 °C within a chamber to create an aerosolized vapor which the user inhales

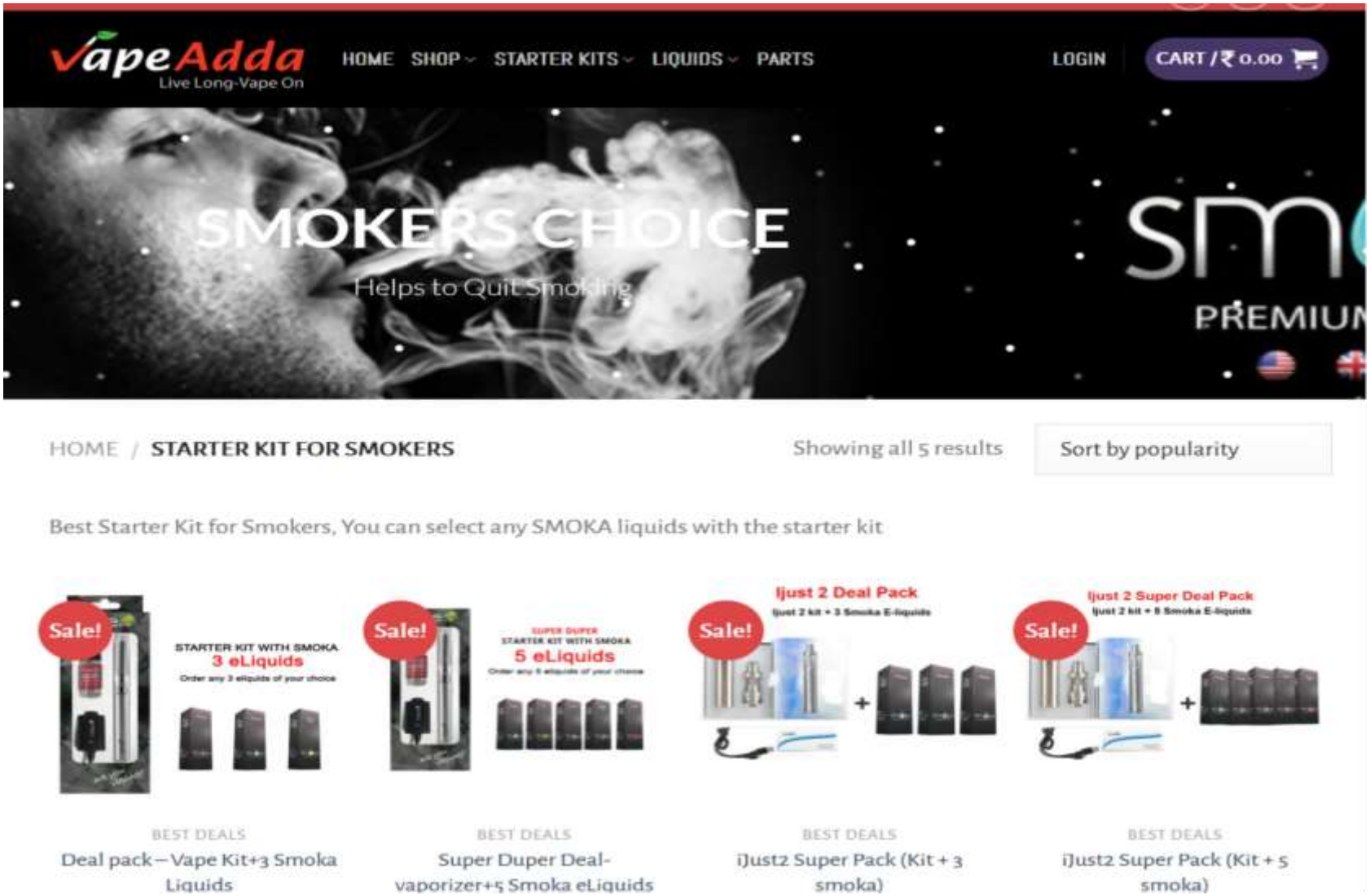
- The user changes the cartridge
  once depleted of the fluid.
- Comes in variety of shapes, sizes and tech, low resistance coils to create more vapor !
- The toxicity of the contents varies from 13-807 fold lower than conventional cigarette
- Toxicity dependent on voltage used !

Kosmider L ;Nicotine Tob Res. 2014 Oct;16(10):1319-26.



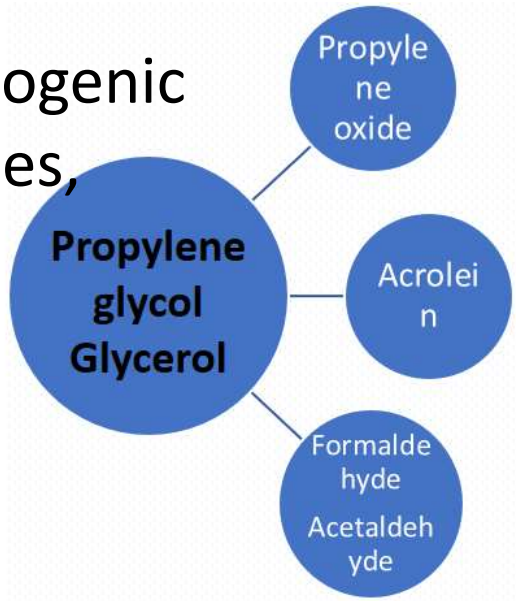
Morbidity and Mortality Weekly Report, 2016;65(14):361–7

Indian scenario



Adverse effects

- Nicotine exposure — Nicotine exposure from e-cigarette use.
- Vapor exposure-
  - Sparse data available safety or the carcinogenic effects of propylene glycol or glycerol when heated and inhaled for longer durations.
  - Metabolites at high temp are carcinogenic
  - Others- tobacco-specific nitrosamines, carbonyl compounds, metals, and phenolic compound



Propylene glycol	1. Animal studies show safe for adults 2. desiccation effect- dry throat and mouth 3. Can induce/exacerbate rhinitis, asthma, eczema, and allergic symptoms in children
Glycerol	1. Low risk 2. Long term risk unknown
Acrolein	1. Lung cancer 2. Levels lower than conventional cigarette • 60 % reduction in those who continued to smoke • 80% reduction those who quit
Tobacco-specific nitrosamines or polycyclic aromatic hydrocarbons	1. Carcinogen 2. Levels NIL to 1000 times lower than Cigarette
Metals	1. 10 to 50 times below the levels allowed in inhalation medicines—Negligible

Feng, Z; Proceedings of the National Academy of Sciences. 103 (42): 15404–15409

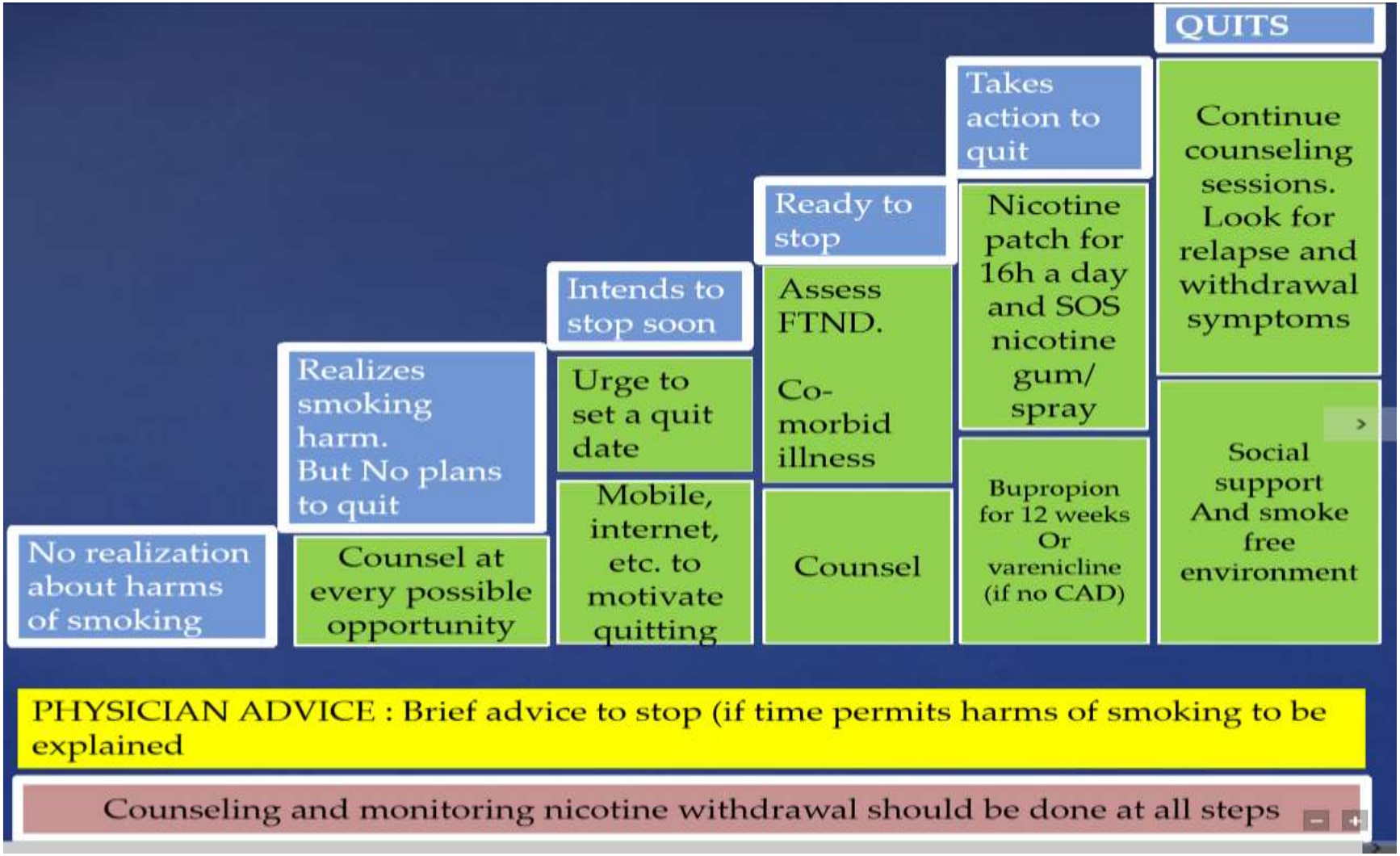
ROLE IN SMOKING CESSATION

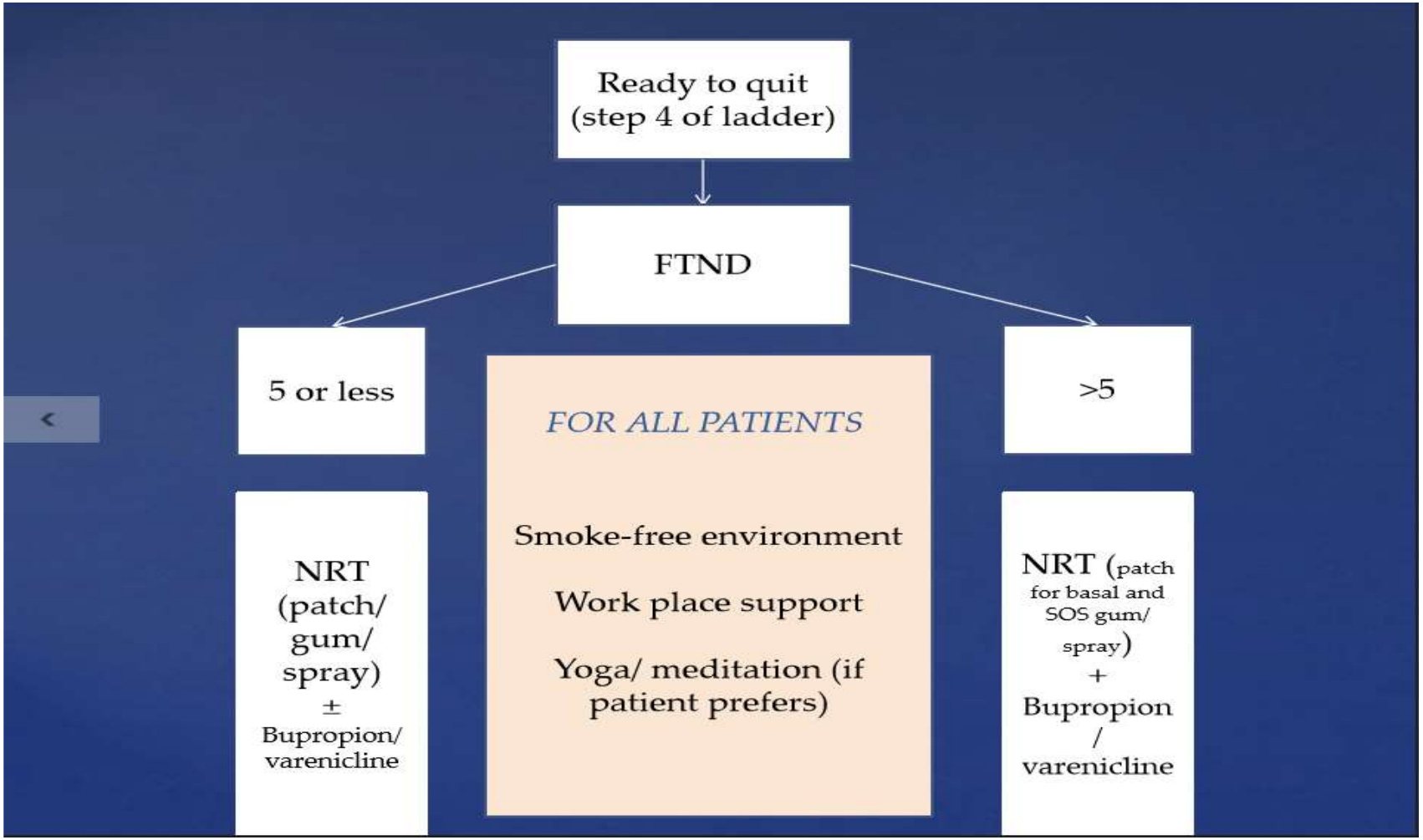
- “Tobacco harm reduction”
  - smokers who are unwilling or unable to quit may switch to nicotine containing e-cigarettes and diminish their overall morbidity related to components found in tobacco smoke, i.e., carcinogens while maintaining their addiction to nicotine.
- “smoking cessation/reduction aids”
  - studies limited and heterogeneous with conflicting results.

Study	Pop	Intervention	Outcome Abstinence rates
Bullen C et all 2013	RCT Smokers N= 657	E-cig (16MG)vs Nicotine patch(21MG) vs Placebo E-cig	1. not statistically significant. 2. e-cigarettes were at least as effective as patches. 3. Quit rates lower for study
Caponnetto P et all 2013,ECLAT Study	RCT Smokers N=300	E-Cig(7.2) vs E-Cig (5.4) vs E-Cig (placebo)	1. No difference in quit rates between E-Cig after 24wk 2. 26 % sustained quit rates at week 52 using E-cig
Adriaens K et all 2014	RCT Unwilling to quit	E-Cig (2^{nd} gen) vs No e-cig	1. Significant reduction in smoking at 8 mo. 2. Significant reduction cigarette craving and withdrawal symptoms

Bullen C ; Lancet. 2013;382(9905):1629.
Caponnetto P; PLoS One. 2013; 8(6): e66317.
Adriaens K ;Int J Environ Res Public Health. 2014 Nov; 11(11): 11220–11248.

- E-cig have a role in smoking cessation with similar efficacy as NRT, and comparable adverse effects.
- Can reduce tobacco attributable morbidity and mortality.
- More studies required.


QUITS
Takes action to quit
Ready to stop
Intends to stop soon
Realizes smoking harm. But No plans to quit
No realization about harms of smoking
Continue counseling sessions. Look for relapse and withdrawal symptoms
Nicotine patch for 16h a day and SOS nicotine gum/ spray
Assess FTND.
Co-morbid illness
Urge to set a quit date
Counsel at every possible opportunity
Mobile, internet, etc. to motivate quitting
Counsel
Bupropion for 12 weeks Or varenicline (if no CAD)
Social support And smoke free environment
PHYSICIAN ADVICE : Brief advice to stop (if time permits harms of smoking to be explained
Counseling and monitoring nicotine withdrawal should be done at all steps


Ready to quit
(step 4 of ladder)
FTND
5 or less
>5
FOR ALL PATIENTS
Smoke-free environment
Work place support
Yoga/ meditation (if patient prefers)
NRT (patch/ gum/ spray) ± Bupropion/ varenicline
NRT (patch for basal and SOS gum/ spray) + Bupropion / varenicline