

Heart Attack Day

May 24, 2018 Jamie Falk, BScPharm, PharmD



FACULTY/PRESENTER DISCLOSURE

Faculty: Jamie Falk

- Relationships with commercial interests:
 - -Not Applicable



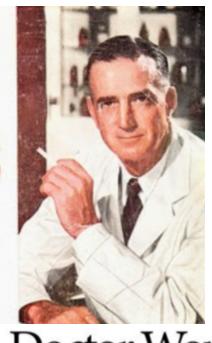
OUTLINE

- 1. Smoking is the worst thing in the world
- 2. Round 10 is slightly less brutal than Round 1
- Essential resources in a time of resource minimization
- 4. Does your NRT regimen do yoga?
- 5. NRT, NRPA, NDRI, NNT & TNT... are the benefits of cessation treatment dynamite?
- 6. Is trying to quit literally going to drive me crazy?
- 7. Can smoking cessation be heart breaking?
- 8. Sir, would you like to make that a combo?
- 9. Striking while the iron is hot
- 10. Just quit already... gradual vs. abrubt cessation



SHAME ON YOU

More Doctors
Smoke CAMELS
than any other
cigarette!





OH YEAH, RIGHT No Doctor Would Prescribe Tobacco, So Why Do Pharmacies Sell It?

It's time to end this practice.

SO, YOU KNOW, IT ALL BALANCES OUT

The Washington Post

Jan. 10, 2017

To Your Health

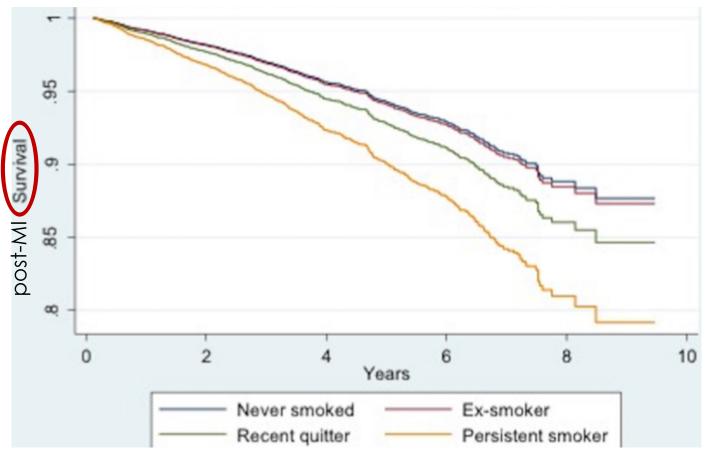
Smoking costs the world economy \$1 trillion per year, World Health Organization says

The world was gloomy before I won - there was no hope. Now the market is up nearly 10% and Christmas spending is over a trillion dollars!



WHAT'S SO BAD ABOUT SMOKING ANYWAY?

OK, NOW THIS IS PERSONAL



Cox proportional hazard regression survival curve



"MAN, I COULD KILL A HUMAN RIGHT NOW!"

AND...

for those who quit after an MI \rightarrow risk of \forall event = nonsmokers by 3 years

Ann Intern Med 2002; 137:494-500

BMJ Open 2017;7:e016874

SOME PEOPLE ARE TRYING REALLY HARD TO QUIT

May 9, 2013 (SACRAMENTO, Calif.) -- A California woman is so desperate to stop smoking she smacked a police officer.

Deputy Matt Campoy was leaving the county jail in Sacramento. He says Etta Lopez stepped right up and slapped him in the face.

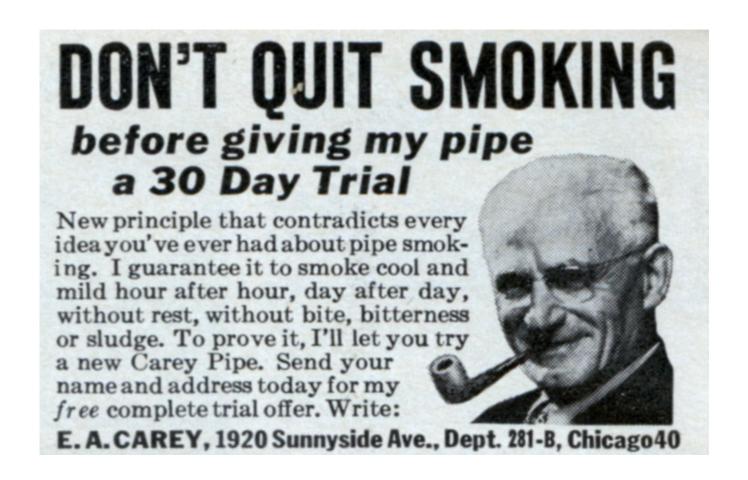
The officer says Lopez told him she knew she would be immediately arrested and tossed in jail. Lopez believes getting locked up is the only way she can quit smoking.

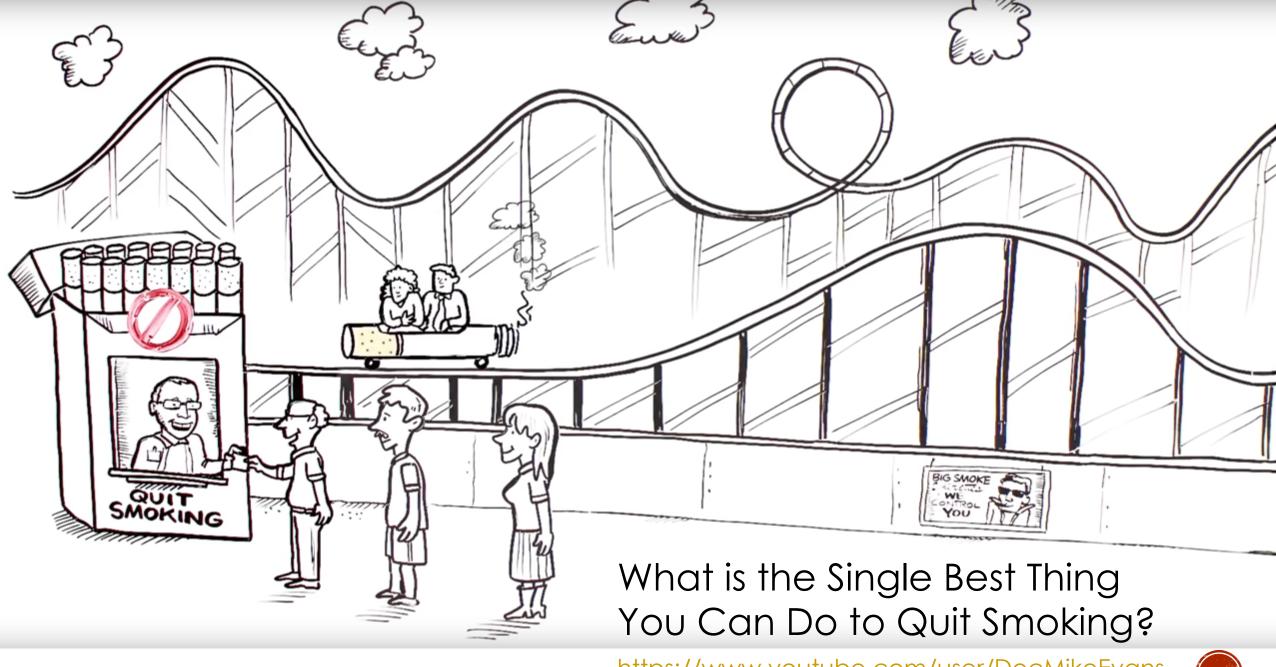
Lopez is charged with assaulting an officer. She is in jail, where no cigarettes are allowed.

www.abc7chicago.com



SOME ARE NOT...

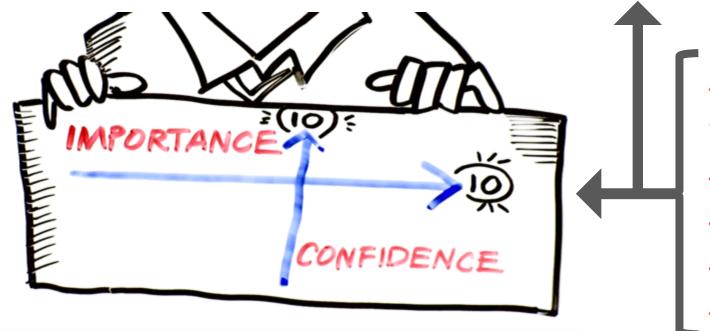






SELF-EFFICACY

"Your job is to be honest. My job is to see if I can move your scores towards 10."



Ask - about tobacco use every visit

Advise - to quit

Assess - willingness to quit

Assist - implement plan

Arrange - follow-up



For us:

- www.can-adaptt.net
- PACT SK/MB http://www.makeapact.ca/

guidelines algorithms tools

For them:

- Smokers' Helpline: https://www.smokershelpline.ca
- Run to quit: https://www.runtoquit.com
- On the Road to Quitting:
 https://www.canada.ca/en/health canada/services/publications/healthy-living/road-quitting guide-becoming-non-smoker.html
- Local smoking cessation programs
 - https://wellnessinstitute.ca/smoking-cessation/
 - http://www.wrha.mb.ca/community/primarycare/files/He althMgmt-GroupProgram-Guide.pdf

You

resources:

WE'VE GOT A FEW OPTIONS





Providing Leadership in Tobacco Reduction

About MANTRA

MANTRA Resources

QUIT Resourc

Cessation Counseling

Quit to Win

Workplace Programs

Student Programs

Printed Material for Cessation

Aboriginal Resources

Resources for Health Professionals & Community Members

Cessation Medications

Hospitals

Health Insurance Plans

Province of Manitoba

In Manitoba, there is a variety of resources and progavailable to reduce tobacco use among a numb populations. MANTRA has compiled a list of Man specific resources for people looking to quit smokin those who want to help people quit.

CESSATION COUNSELING

Smoker's Helpline and Smoker's Helpline Online

Manitoba Quits

Break It Off Website and App

Tobacco Dependence Clinic

Individual or Group Quit Smoking Assistance

Commit to Quit

Regional Pulmonary Rehabilitation Program

LGBTTQ

Your nurse, doctor or pharmacist

P: (866) 366-3667 www.smokershelpline

 A free confidential tollhelp line staffed with traprofessionals who can advice and support in a judgmental manner.

QUIT TO WIN

Walk or Run to Quit

First Week Challenge

Get help to quit smoking to walk or run 5 km. Wall running can help you ow withdrawals and cravings cutting down or quitting s gets better, when you qu and get active, you'll have a chance to win \$1000!

There are supportive training programs available at a cost or a free train on your own option. For more information visit www.runtoquit.com

CESSATION COUNSELING

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Manitoba Quits

Break It Off Website and App

Tobacco Dependence Clinic

Individual or Group

Quit Smoking Assistance

Commit to Quit

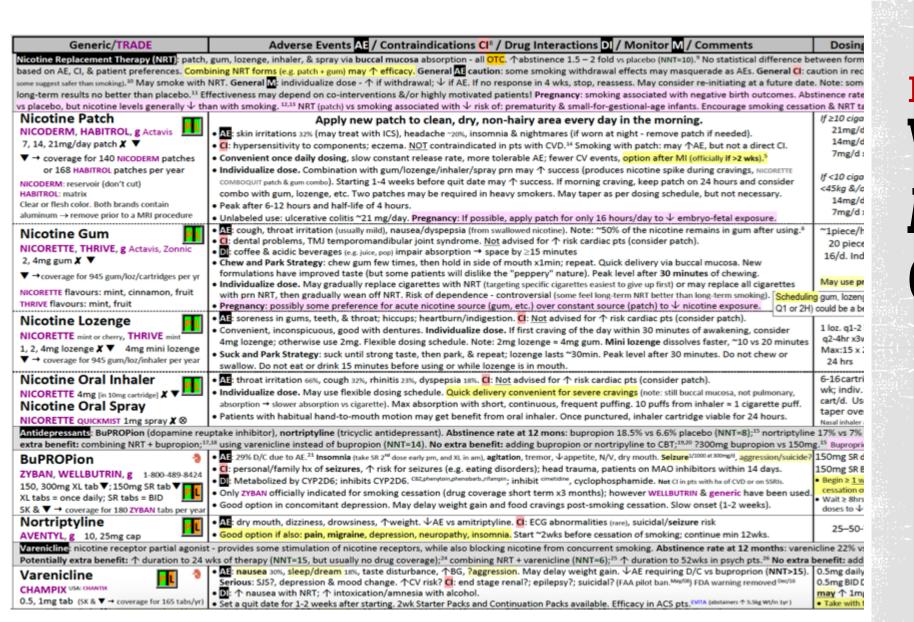
Regional Pulmonary Rehabilitation Program

LGBTTQ

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 A free confidential toll-free help line staffed with trained professionals who can offer advice and support in a nonjudgmental manner.

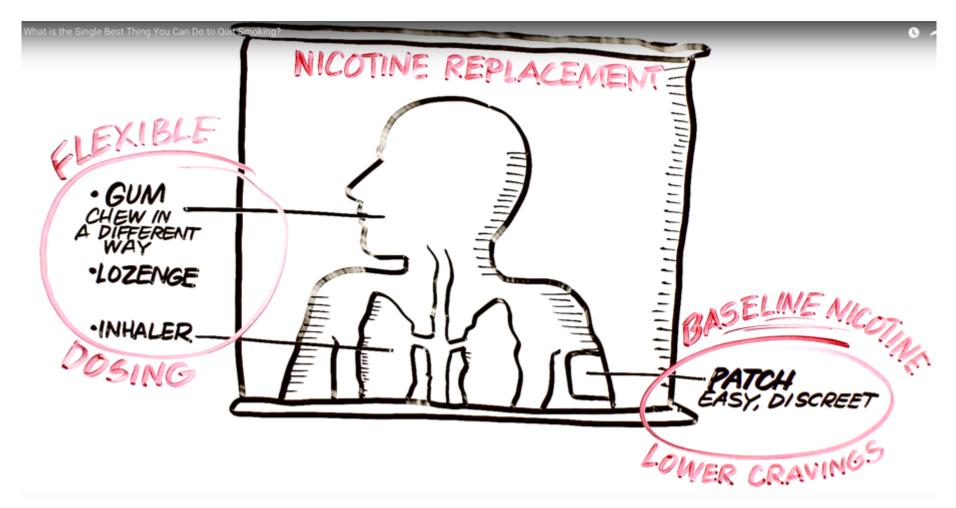




pharmacotherapy: WE'VE GOT A FEW OPTIONS

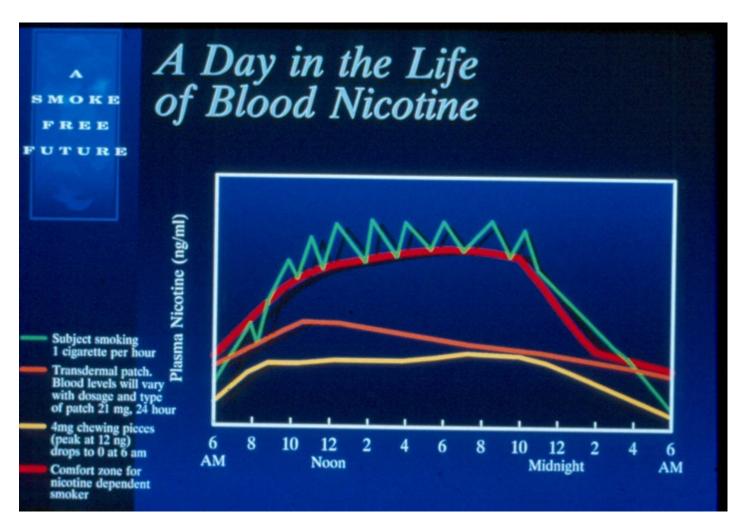


NICOTINE REPLACEMENT THERAPY (NRT)





WHAT'S THE RIGHT DOSE?



i.e.Whatever it takes

↑ abstinence 1.5-2X vs. placebo (NNT=10-17)

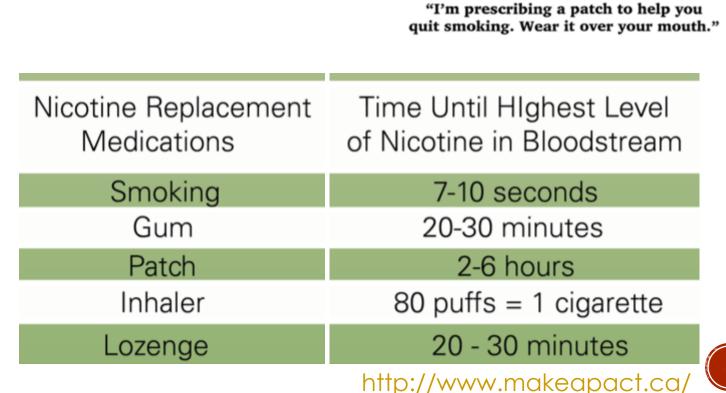
(no statistical difference between formulations)



UNREGIMENTED REGIMENS

- Patch alone, 24 hrs
- Patch alone, off at night
- Oral alone, scheduled
- Oral alone, prn
- Patch + scheduled oral
- Patch + prn oral

* Technically (statistically), combo NRT > single NRT (NNT = 20)?



NRT CONSIDERATIONS

	pros	cons		
patch	Once daily Discreet Preferred post-MI?	Slow to start Skin irritation (32%)		
gum	Flexible dosing Easy to disguise	Chew + park Dental issues, dentures Cough, throat irritation, dyspepsia		
lozenge	Flexible dosing Easy to disguise	Suck + park Cough, throat irritation, dyspepsia		
inhaler/spray	Quickest delivery Hand-to-mouth	Cough, throat irritation, dyspepsia Cost (>2X other oral)		



SMOKING CESSATION

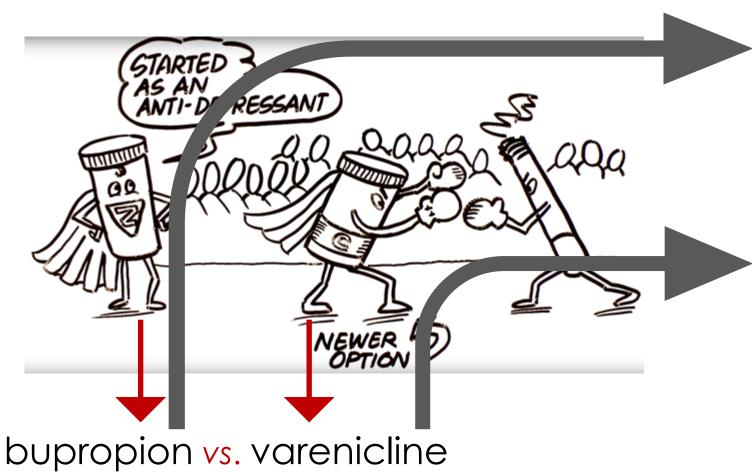
						Coverage	
Generic Name	Brand Name	Strength	Usual Dosing	Cost	Per Unit Cost	Pharmacare	NIHB
Nicotine Replaceme	ent Therapy						
Nicotine Patch	Generic (TEVA)	21mg, 14mg, 7mg	21mg/d x 6wk 14mg/d x 2wk 7mg/d x 2wk	\$160/10 week treatment	\$16/7 patches (all strengths)	N	Y ⁴
	Habitrol	21mg, 14mg, 7mg	21mg/d x 4wk 14mg/d x 2wk 7mg/d x 2wk	\$162/8 week treatment	\$20/7 patches (all strengths)	N	Y ⁴
	Nicoderm	21mg, 14mg, 7mg	21mg/d x 6wk 14mg/d x 2wk 7mg/d x 2wk	\$273/10 week treatment	\$27/7 patches (all strengths)	N	Y ⁴
Nicotine Gum	Generic (TEVA)	2mg	12 pcs/day	\$17 /110 pcs		N	Y ⁴
	Thrive	4mg	12 pcs/day	\$32 /108 pcs		N	Y ⁴
	Nicorette	2mg	12 pcs/day	\$34/ 105 pcs		N	Y ⁴
	Nicorette	4mg	12 pcs/day	\$34/ 105 pcs		N	Y ⁴
Nicotine Inhaler	Nicorette	Cartridge	Maximum 12/ day	\$34/ 42 re	efill cartridges	N	Y ⁴

I'LL TAKE NICOTINE FOR \$16-34, ALEX

945 gum pieces/yr945 inhaler cartridges/yr140-168 patches/yr



NON-NICOTINE OPTIONS



 Dopamine reuptake inhibitor → ↓ symptoms of nicotine withdrawal (e.g. anxiety & irritability)

\$85/12 wk course

 Nicotine partial receptor agonist acts like a weaker kind of nicotine & blocks nicotine from getting to the nicotine receptors

\$334/12 wk course

HOW DO THEY COMPARE CLINICALLY?

ABSTINENCE RATES (@1yr)

NNT

bupropion vs. placebo

8-10

varenicline vs. placebo

8

varenicline vs. bupropion

14

varenicline vs. NRT

21

bupropion vs. NRT

No difference



Original Investigation

Effects of Nicotine Patch vs Varenicline vs Combination Nicotine Replacement Therapy on Smoking Cessation at 26 Weeks

A Randomized Clinical Trial

JAMA 2016;315(4):371-379



- Non-ACS patients (n=1086)
- Intervention:
 - nicotine patch only
 - varenicline only
 - nicotine patch + nicotine lozenge
- Abstinence @ 26 wks...
 - * All interventions similar

+ 6 counseling sessions

ADVERSE EVENTS (~NNH):

NRT > V... rash = 5

V > **NRT...** nausea = **5**

insomnia = 10

vivid dreams = 15

sleepiness = 10

MY TOP "MENTIONABLE" SIDE EFFECTS

VARENICLINE

- Nausea (up to 1/3)
- Insomnia
- Abnormal dreams
- Aggression?

BUPROPION

- Insomnia (up to 1/3)
- Agitation
- Nausea/↓ appetite
- Seizure (~1/1000)





ON A RELATED NOTE...

FDA revises description of mental health side effects of the stopsmoking medicines Chantix (varenicline) and Zyban (bupropion) to reflect clinical trial findings

[12-16-2016] Based on a U.S. Food and Drug Administration (FDA) review of a large clinical trial that we required the drug companies to conduct, we have determined the risk of serious side effects on mood, behavior, or thinking with the stop-smoking medicines Chantix (varenicline) and Zyban (bupropion) is lower than previously suspected. The risk of these mental health side effects is still present, especially in those currently being treated for mental illnesses such as depression, anxiety disorders, or schizophrenia, or who have been treated for mental illnesses in the past. However, most people who had these side effects did not have serious consequences such as hospitalization. The results of the trial confirm that the benefits of stopping smoking outweigh the risks of these medicines.

As a result of our review of the large clinical trial, we are removing the *Boxed Warning*.

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

Lancet 2016; 387: 2507-20 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

Lancet 2016; 387: 2507-20

CAUTIOUS REASSURANCE

- Who? \rightarrow n=8144 (~50/50 psych/non-psych cohort)
 - Psychiatric cohort: only ~50% on psych meds,
 depression/anxiety scores borderline, stable X 6 months

What?

placebo vs. nicotine patch (21 mg/d with taper) vs. varenicline (1 mg BID) vs. bupropion (150 mg BID)
 X 12 wks

Results:

- → Cessation rates @24 wks: no difference
- Neuropsychiatric | adverse events

	Non-psychiatric cohort* (n=3984)			Psychiatric cohort* (n=4074)				
	Varenicline	Bupropion	Nicotine patch	Placebo	Varenicline	Bupropion	Nicotine patch	Placebo
	(n=990)	(n=989)	(n=1006)	(n=999)	(n=1026)	(n=1017)	(n=1016)	(n=1015)
Primary composite neuropsychiatric endpoint	13 (1.3%)	22 (2.2%)	25 (2.5%)	24 (2·4%)	67 (6.5%)	68 (6.7%)	53 (5·2%)†	50 (4.9%)
Estimated primary composite neuropsychiatric adverse events (% [95% CI])	1·25%	2·44%	2·31%	2·52%	6·42%	6.62%	5·20%	4.83%
	(0·60 to 1·90)	(1·52 to 3·36)	(1·37 to 3·25)	(1·58 to 3·46)	(4·91 to 7·93)	(5.09 to 8.15)	(3·84 to 6·56)	(3.51 to 6.16)

IF MY PATIENT IS NAUSEOUS, CAN THEY USE 1/2 DOSE?

Test for overall effect: Z = 4.99 (P < 0.00001)

CDSR 2016, Issue 5. Art. No.: CD006103

Analysis 7.2. Comparison 7 Variations in usage, Outcome 2 Non-standard dose varenicline versus placebo at 52 weeks.

Study or subgroup	Varenicline	Control	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI		M-H,Fixed,95% CI
I Low-dose varenicline vs plac	cebo at 52 weeks				
Nakamura 2007 (I)	51/155	35/154	-	58.7 %	1.45 [1.00, 2.09]
Niaura 2008 (2)	35/160	12/160		20.0 %	2.92 [1.57, 5.41]
Nides 2006 (3)	7/126	6/123		10.1 %	1.14 [0.39, 3.29]
Oncken 2006 (4)	48/259	5/129		11.2 %	4.78 [1.95, 11.72]
Subtotal (95% CI)	700	566	•	100.0 %	2.08 [1.56, 2.78]
Total events: 141 (Varenicline)	, 58 (Control)				
Heterogeneity: $Chi^2 = 9.44$, d	$f = 3 (P = 0.02); I^2 = 6$	8% NN '	Γ = 10 4		



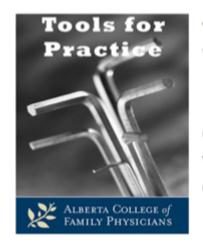
THE CV SAGA CONTINUES?

Risk of serious adverse cardiovascular events associated with varenicline: a systematic review and meta-analysis

1 2.4 CV events/1000 patients

Reviewed: July 26, 2016 Evidence Updated: New evidence





Varenicline and Cardiovascular Risk – Is the Cure Worse than the Affliction?

Clinical Question: Does smoking cessation with varenicline (Champix®) increase the risk of cardiovascular disease (CVD)?

Bottom Line: Varenicline does not appear to increase the risk of cardiovascular events over placebo or other smoking cessation drugs. Smoking cessation is the most effective intervention to reduce CVD risk. Varenicline is at least as good as other medications for cessation and may be slightly better.

But then...

Apr 1, 2018 Am J Respir Crit Care Med 2018;197(7):913–922

Cardiovascular and Neuropsychiatric Events after Varenicline Use for Smoking Cessation

Observational study of 56,851 varenicline users

The incidence of cardiovascular events was 34%

higher in the risk compared with the control interval

= 1 4 CV events/1000 patients over the 12 wk exposure interval

But finally, Apr 9, 2018... JAMA Intern Med 2018;178(5):622-631

Cardiovascular Safety of Varenicline, Bupropion, and Nicotine Patch in Smokers

A Randomized Clinical Trial (i.e. EAGLES → + 28 more wks of CV follow-up)

Bottom line: smoking cessation treatments did not 1 risk of serious CV events (caveat: in mostly low-CV risk patients, mean age 48)

WOULD LIKE TO MAKE THAT A COMBO? (i.e. ARE 2 BETTER THAN 1)



- NRT + NRT → Maybe
- Bupropion + NRT → Maybe
- Varenicline + bupropion → NO
- Varenicline + NRT → Yes? (NNT=6) → Why?

What about prolonged treatment?

Varenicline X 24 wks vs. 12 wks → NNT = 15





Cochrane Database of Systematic Reviews

Interventions for smoking cessation in hospitalised patients (Review)

Rigotti NA, Clair C, Munafò MR, Stead LF CDSR 2012, Issue 5. Art. No.: CD001837

STRIKING WHILE THE IRON IS HOT

Authors' conclusions

High intensity behavioural interventions that begin during a hospital stay and include at least one month of supportive contact after discharge promote smoking cessation among hospitalised patients. The effect of these interventions was independent of the patient's admitting diagnosis and was found in rehabilitation settings as well as acute care hospitals. There was no evidence of effect for interventions of lower intensity or shorter duration. This update found that adding NRT to intensive counselling significantly increases cessation rates over counselling alone. There is insufficient direct evidence to conclude that adding bupropion or varenicline to intensive counselling increases cessation rates over what is achieved by counselling alone.



Manitoba Acute Coronary Syndrome (ACS) Network

Recommended Standards for the Evaluation/Treatment of Suspected Cardiac Chest Pain

Discharge practices:

- ACS patients who are current smokers will be offered Nicotine Replacement Therapy (NRT) to start while in hospital to manage nicotine withdrawal.
- ACS patients who are current smokers will be provided referral for smoking cessation counseling after discharge. *If unavailable in your community consider referral to smoker's Helpline* (www.smokershelpline.ca).

NRT Decision Tree (SBGH), 2014:

⇒ Cardiac patients: NRT should be used with caution in patients in the immediate postmyocardial infarction period, those with a serious arrhythmia, and with unstable angina

WRHA Management of Tobacco Use and Dependence Clinical Practice Guideline, 2013: Abstinence without NRT is preferred, but NRT may be safer than continued use

Intensive Smoking Cessation Intervention Reduces Mortality in High-Risk Smokers With Cardiovascular Disease* CHEST 2007; 131:446–452

BEYOND SIMPLY MANAGING IN-HOSPITAL WITHDRAWAL

- Mhos
 - n=209 smokers after CCU admission
- What?
 - usual care: counseling and printed educational material provided prior to hospital discharge
 - intensive treatment: a minimum of 12 wks of behavior modification counseling and individualized pharmacotherapy (NRT and/or bupropion) at no cost

Results at 2 yrs: •17% ARR in hospitalization (NNT = 6)

■ 9% ARR in mortality (NNT = 11)

Despite abstinence rates of <40%

(context: ASA provides a 1.4% reduction (NNT 72) in mortality in a similar population and time frame)



HOW ABOUT VARENICLINE? THE EVITA STUDY Circulation

Circulation 2016;133(1):21-30

- In-hospital ACS patients (n=302)
 Varenicline vs. placebo X 12 wks
 - Efficacy @ 24 wks:
 - 7-day point-prevalence abstinence:
 ARR=15%, NNT=7
 - Continuous abstinence: 35% vs. 25% →
 ARR=10% (but p=0.08)
 - Harms
 - No ↑ in major harms (including CV) 30-d after treatment d/c
 - Common adverse events
 - Nausea, insomnia, nightmares
 - → NNH for each = ~20



Received 46 min of counselling

So, a vote of confidence for varenicline post-ACS

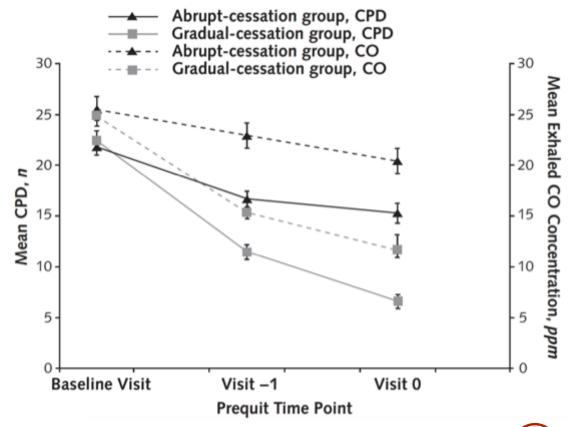
JUST QUIT ALREADY...

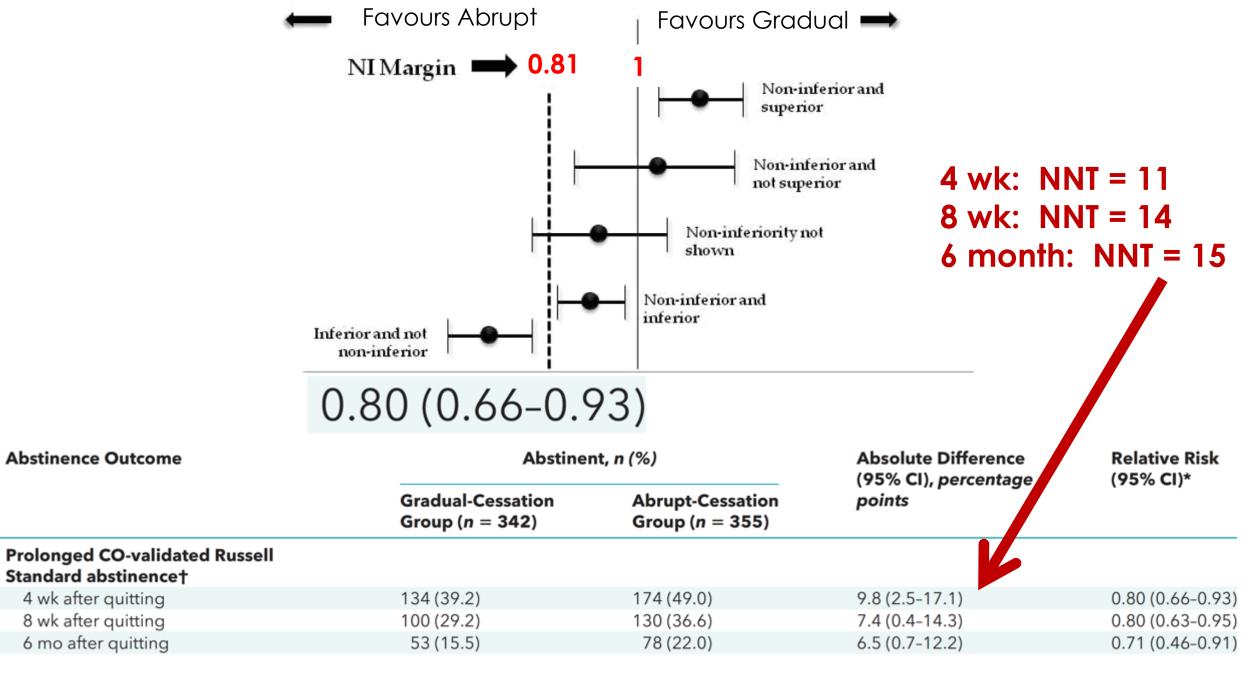
Annals of Internal Medicine

Gradual Versus Abrupt Smoking Cessation A Randomized, Controlled Noninferiority Trial

- n = 697 (median age 49 yrs, 20 cigs/day)
 - Efficacy @ 4 wks, 8 wks, 6 months
 - Randomized (not blinded) to:
 - Gradual Cessation (over 2 wks)
 - Abrupt Cessation
 - Non-inferiority trial (margin: RR of 0.81)
 - NRT available to both groups (~80-90% used)

Figure 2. Prequit exhaled CO concentration and CPD, by trial group.





OUTLINE

- 1. Smoking is the worst thing in the world → there's some truth to that
- 2. Round 10 is slightly less brutal than Round 1
 → each attempt is a step... support them through the journey
- 3. Essential resources in a time of resource minimization

 → many resources exist... help them navigate through what may work for them
- 4. Does your NRT regimen do yoga? → flexibility and buy-in are key
- 5. NRT, NRPA, NDRI, NNT & TNT... are the benefits of cessation treatment dynamite?
 → none of them are incredible, but they're all somewhat effective... what does the patient want?
- 6. Is trying to quit literally going to drive me crazy? → No, not likely from varenicline anyway.
- 7. Can smoking cessation be heart breaking?
 → varenicline is unlikely to cause CV events. If it does, the risk is very small.
- 8. Striking while the iron is hot \rightarrow a present and motivated patient is likely worth the time
- 9. Sir, would you like to make that a combo? → adding more is often not much better
- 10. Just quit already... gradual vs. abrubt cessation → put your money on the cold turkey





