Webinar slides

Now is the time: Seizing new opportunities to treat tobacco dependence

17th September 2024

Matthew Evison and Louise Ross

Consilient Health

Prescribing information is available by scanning the QR code, at the end of this presentation, and at:

https://www.quitsmokingsupport.co.uk/wpcontent/uploads/2024/07/Cytisine_UK_PI.pdf

Now is the time: Seizing new opportunities to treat tobacco dependence

17 September 2024 18:30 - 19:45

This webinar has been organised and funded by Consilient Heath (UK) Ltd and is intended for UK healthcare professionals and other relevant decision makers involved in the delivery of smoking cessation services

Promotional product information will be discussed at this webinar

Now is the time: Seizing new opportunities to treat tobacco dependence

A time of new opportunities?

- Range of treatments available
  - Nicotine Replacement Therapy
  - Cytisine (also known as cytisinicline)
  - Varenicline
  - Bupropion
  - e-cigarettes

- Government legislation and funding

Now is the time: Seizing new opportunities to treat tobacco dependence

Louise Ross
Clinical Consultant
National Centre for Smoking Cessation and Training

Professor Matthew Evison
Consultant Chest Physician, Wythenshawe Hospital

Housekeeping

- Cytisine prescribing and adverse event reporting information is available throughout the webinar – access via link in Q&A tab
- Audience cameras and microphones have been turned off
- Questions? Please use the “Q&A” tab – the chair will review and verbalise your questions to the speakers
- This webinar is being recorded. Consilient Health will look to make the recording available after the webinar on the Consilient Health website www.quitsmokingsupport.co.uk
- Certificate of attendance is available to download via a link in the Q&A tab

Now is the time: Seizing new opportunities to treat tobacco dependence

Professor Matthew Evison
Consultant in Respiratory Medicine
Manchester University NHS Foundation Trust
Clinical Lead for the Greater Manchester Make Smoking History Programme
@MatthewEvison1

UK-CYT-186d September 2024

Declarations

Honoraria:

AstraZeneca, Roche, Guardant 350, Consilient Health, Pfizer, BMS

Advisory Boards:

AstraZeneca, Abbie UK, AMBU

Objectives

- Setting the scene
  - The tobacco tragedy
  - What opportunities?
  - Why now? The turning tide

- **Nicotine Vapes**
- **Varenicline**
- **Cytisine**

- New national standards of care – BTS framework for inpatients

Cochrane Library

NICE
National Institute for Health and Care Excellence

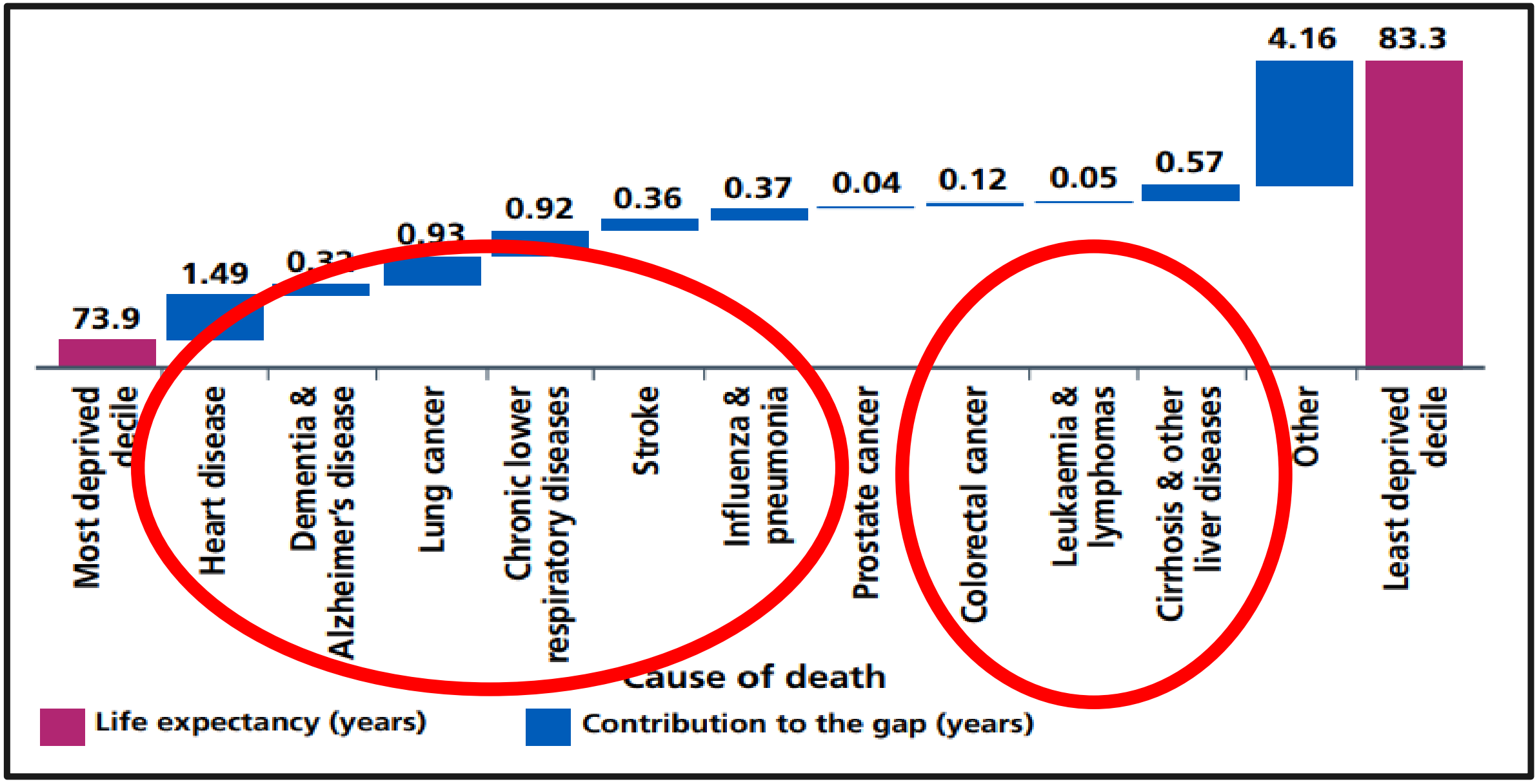
British Thoracic Society

Office for Health Improvement & Disparities

NHS

The scale of the tobacco pandemic……

- **Smoking tobacco is both uniquely addictive and uniquely dangerous**
- Two in three people that smoke tobacco will die prematurely as a direct result of the harms of tobacco
- For every person that dies a further thirty will suffer from the serious diseases of smoking
- In the UK, smoking tobacco has led to the death of more than 8 million people in the last 50 years
- Without urgent action a further 2 million will die in the next 50 years.
- Smoking disproportionately affects the poorest communities
- Manchester: population 500,000
- 8000 households (15,000 people) in Manchester would be lifted out of poverty if the cost of smoking was returned


73.9
1.49
0.32
0.93
0.92
0.36
0.37
0.04
0.12
0.05
0.57
4.16
83.3
Most deprived decile
Heart disease
Dementia & Alzheimer's disease
Lung cancer
Chronic lower respiratory diseases
Stroke
Influenza & pneumonia
Prostate cancer
Colorectal cancer
Leukaemia & lymphomas
Cirrhosis & other liver diseases
Other
Least deprived decile
Cause of death
Life expectancy (years)
Contribution to the gap (years)

REDUCING HEALTHCARE INEQUALITIES

The **Core20PLUS5** approach is designed to support Integrated Care Systems to drive targeted action in healthcare inequalities improvement

CORE20
The most deprived **20%** of the national population as identified by the Index of Multiple Deprivation

Target population

CORE20 PLUS 5

PLUS
ICS-chosen population groups experiencing poorer-than-average health access, experience and/or outcomes, who may not be captured within the Core20 alone and would benefit from a tailored healthcare approach e.g. inclusion health groups

Key clinical areas of health inequalities

1. **MATERNITY**
ensuring continuity of care for women from Black, Asian and minority ethnic communities and from the most deprived groups

2. **SEVERE MENTAL ILLNESS (SMI)**
ensure annual Physical Health Checks for people with SMI to at least, nationally set targets

3. **CHRONIC RESPIRATORY DISEASE**
a clear focus on Chronic Obstructive Pulmonary Disease (COPD), driving up uptake of Covid, Flu and Pneumonia vaccines to reduce infective exacerbations and emergency hospital admissions due to those exacerbations

4. **EARLY CANCER DIAGNOSIS**
75% of cases diagnosed at stage 1 or 2 by 2028

5. **HYPERTENSION CASE-FINDING**
and optimal management and lipid optimal management

SMOKING CESSATION
positively impacts all 5 key clinical areas

Cochrane Library

Cochrane Database of Systematic Reviews | Review - Intervention

Pharmacological and electronic cigarette interventions for smoking cessation in adults: component network meta-analyses

Nicola Lindson, Annika Theodoulou, José M Ordóñez-Mena, Thomas R Fanshawe, Alex J Sutton, Jonathan Livingstone-Banks, Anisa Hajizadeh, Sufen Zhu, Paul Aveyard, Suzanne C Freeman, Sanjay Agrawal, Jamie Hartmann-Boyce Authors' declarations of interest

Version published: 12 September 2023 Version history

High-certainty evidence that…

- ✓ **Nicotine vapes** (OR 2.37, 95% CI 1.73 to 3.24; 16 RCTs, 3828 participants) 

- ✓ **Varenicline** (OR 2.33, 95% CrI 2.02 to 2.68; 67 RCTs, 16,430 participants) 

- ✓ **Cytisine** (OR 2.21, 95% CrI 1.66 to 2.97; 7 RCTs, 3848 participants)* 

…were associated with higher quit rates than control.

Cochrane Evidence Synthesis and Methods ▶

E-cigarettes, varenicline and cytisine are the most effective stop-smoking aids, analysis of over 150,000 smokers reveals

- On average, for every 100 people trying to quit, around 14 are likely to succeed using an e-cigarette, varenicline or cytisine in any given quit attempt. This is compared to 6 in 100 who are likely to quit without using any aids.

*some of the cytisine trials included in the Cochrane review used doses not consistent with UK product licence

BMJ Open Respiratory Research

'The dark before the dawn': the 2021 British Thoracic Society Audit of the treatment of tobacco dependency in acute trusts

Nikesh Devani ,[1] Zaheer Mangera,[2] Howard Smith,[3] Jessica Gates ,[4] Arran Woodhouse,[5] Duncan Fullerton,[6] Aravind Ponnuswamy,[7] Matthew Evison [8]

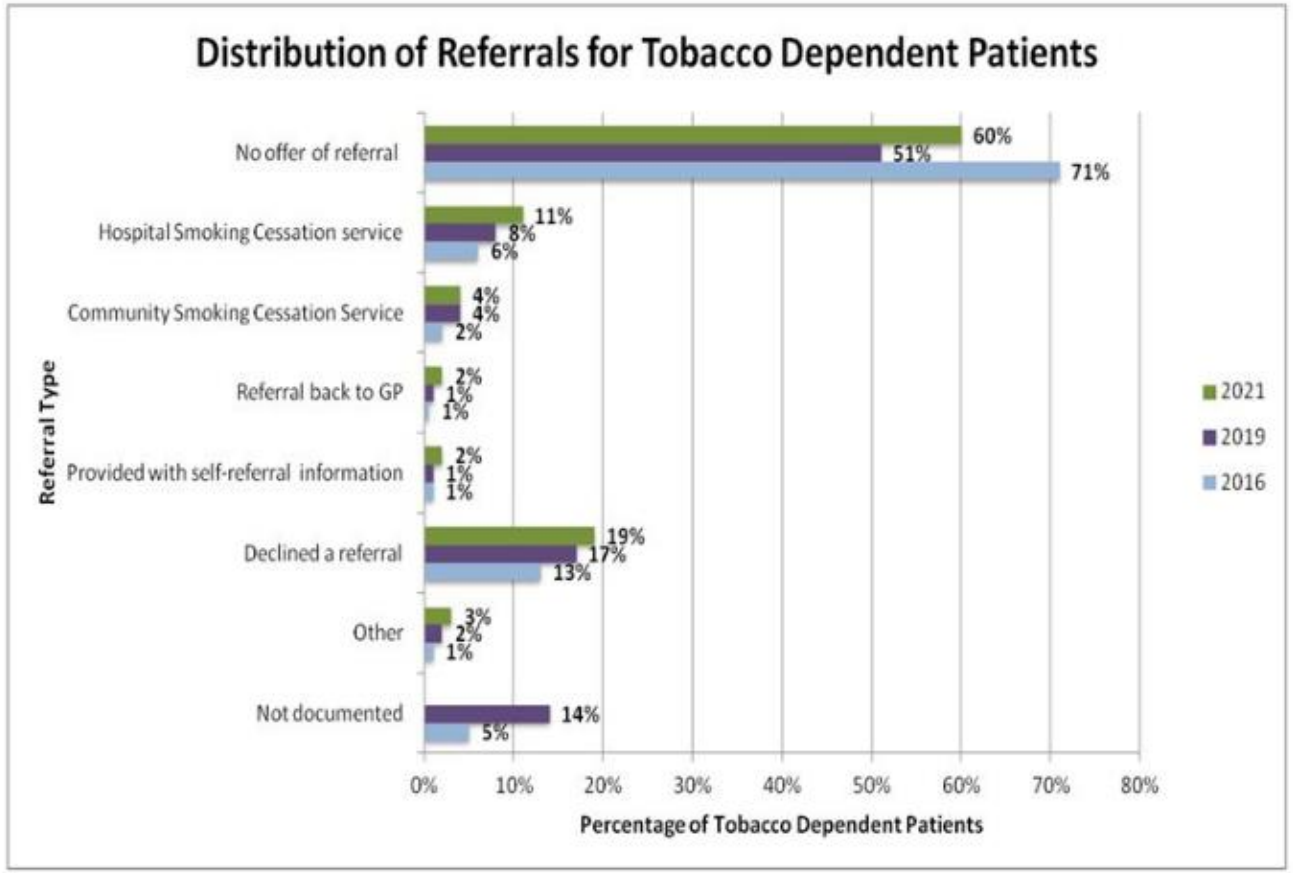


Table 2 Provision of evidence-based interventions for treating tobacco dependency during an acute care hospital admission

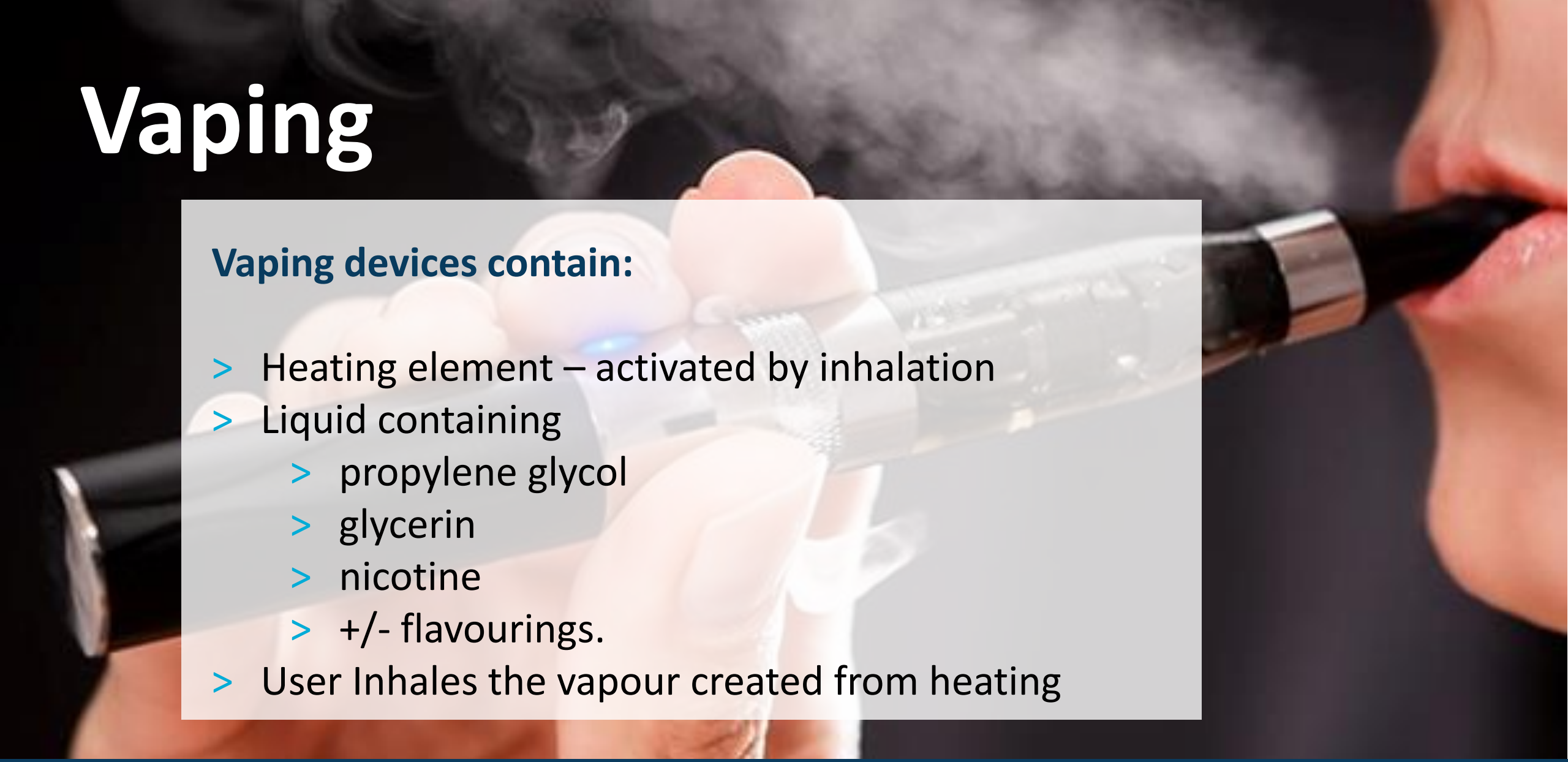
	No of patients
Provision of pharmacotherapy as inpatient	
Single agent NRT	331 (13.8%)
Combination NRT	117 (5%)
Varenicline	3 (0.1%)
Buproprion	0 (0%)
Offered but declined	333 (13.9%)
Provision of pharmacotherapy on discharge	
Single agent NRT	167 (7%)
Combination NRT	65 (2.7%)
Varenicline	2 (0.08%)
Buproprion	0
Attendance at follow-up after discharge	
Hospital stop smoking service	42 (1.9%)
Community stop smoking service	29 (1.2%)
Patient did not attend	56 (2.3%)
No-follow-up arrangement made	696 (29%)
Patient declined follow-up	300 (12.5%)
Not possible to ascertain	1274 (53.1%)

NRT, nicotine replacement therapy.

MAKE SMOKING HISTORY

A deep-dive into vaping

Vaping



Vaping devices contain:

- Heating element – activated by inhalation
- Liquid containing
  - propylene glycol
  - glycerin
  - nicotine
  - +/- flavourings.
- User Inhales the vapour created from heating

Sources of evidence to evaluate vaping…

- Randomised controlled trials

- Systematic reviews & meta-analyses

- Cochrane reviews

A systematic review prepared and supervised by a Cochrane Review Group that identifies, appraises & synthesizes all the empirical evidence that meets pre-specified eligibility criteria to answer a specific research question. CRs use explicit, systematic methods to minimise bias & produce more reliable findings to inform decision-making. CRs are updated to reflect the findings of new evidence when it becomes available.

- NICE Guidelines

Evidence-based recommendations developed by independent committees, including professionals and lay members, and consulted on by stakeholders.

- Real world data e.g. Office for National Statistics

Randomised trial of vaping vs nicotine replacement therapy

Methods

- UK NHS stop smoking services
- NRT (patient choice) for up to 3 months vs an e-cigarette starter pack (a second-generation refillable e-cigarette with one bottle of 18 mg/L nicotine)
- Weekly behavioural support for at least 4 weeks

Follow-up study: £65/QALY cost-effectiveness

Results

- 886 participants
- **1-year abstinence rate 9.9% in the NRT group**
- **1-year abstinence rate 18.0% in the vaping group**
- RR 1.83; 95% CI 1.30 to 2.58; p<0.001
- Among participants with 1-year abstinence, those in the vaping group were more likely than those in the NRT group to use their assigned product at 52 weeks (80% vs 9%)
- Throat or mouth irritation was reported more frequently in the vaping group (65.3% vs 51.2%)
- Nausea more frequently reported in the NRT group (37.9% vs 31.3%)
- The vaping group reported greater declines in the incidence of cough and phlegm

Hajek P *et al*. *N Engl J Med* 2019;380:629–37

Cochrane Living Systematic Review Sept 23:
'Nicotine e-cigarettes help people stop smoking'

September 2023

There is high certainty evidence that vaping is an effective treatment for tobacco dependence using an outcome measure of long-term abstinence (at least 6 months).

✓ Nicotine vapes are more effective than NRT

(quit rates 50% higher than NRT, RR 1.63, 95% CI 1.30-2.04)

✓ Nicotine vapes are more effective than no pharmacotherapy

(quit rates 2.5 times higher, RR 2.66, 95% CI 1.52-4.65).

✓ No evidence of harm from vaping was detected with a follow-up period of two years.

NICE National Institute for Health and Care Excellence

NICE guideline

Tobacco: preventing uptake, promoting quitting and treating dependence

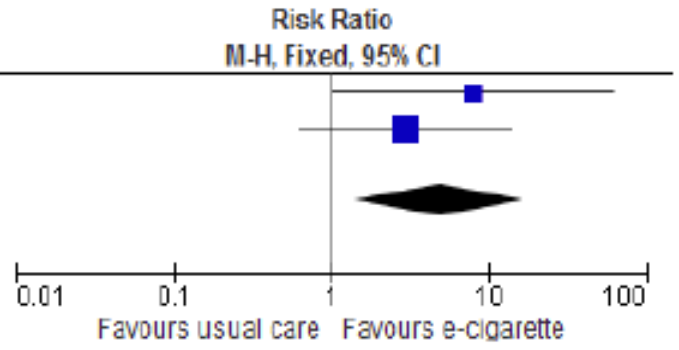
NICE guideline
Published: 30 November 2021
www.nice.org.uk/guidance/ng209

- ✓ A systematic review and network meta-analysis on the effectiveness of vaping to achieve abstinence from smoking tobacco
- ✓ Pre-defined primary outcome of abstinence at 6 months.
- ✓ Nicotine vapes are more effective at achieving abstinence at 6 months versus non-nicotine vaping (RR 2.02, 95%CI 0.97-4.21, p0.06, two trials, 489 participants)
- ✓ Nicotine vapes are more effective then usual care (RR 4.92, 95%CI 1.43-16.91, p=0.01, two trials, 1239 participants).
- ✓ A benefit from combining NRT with vaping over NRT alone (RR 1.77, 95%CI 1.07-2.94, two trials, 520 participants).

Figure 19: E-cigarette vs usual care

Study or Subgroup	E-cigarette Events	E-cigarette Total	Usual care Events	Usual care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Halpern 2018	12	1199	1	813	37.3%	8.14 [1.06, 62.45]
Holliday 2019	6	40	2	40	62.7%	3.00 [0.64, 13.98]
Total (95% CI)		**1239**		**853**	**100.0%**	**4.92 [1.43, 16.91]**
Total events	18		3			

Heterogeneity: Chi² = 0.63, df = 1 (P = 0.43); I² = 0%
Test for overall effect: Z = 2.53 (P = 0.01)



Real-world data

- Vaping has consistently been shown to be a popular stop smoking intervention in the UK.
- In 2017, it was estimated that in the UK 50,700 smokers had quit smoking as a result of using vapes as an alternative method of delivering nicotine.
- In 2020, 27.2% of smokers in the UK used vaping as their chosen quit aid

  15.5% for NRT

  4.4% for varenicline.

- The 2021 Public Health England commissioned report on vaping products found that vaping was the most popular aid used by people trying to quit smoking, and the highest quit rates (74%) were seen when the quit attempt involved using a licensed medicine and a vaping product consecutively.

So why is there even a debate?

- What are the harms of vaping?

Smoking

ORIGINAL ARTICLE

Pro-inflam
condensat

Aaron Scott,[1] Sel
Rahul Y Mahida,
Robert Foronjy,[4]

Respiratory research
Original article

Chronic electronic cigarette exposure in mice induces features of COPD in a nicotine-dependent manner

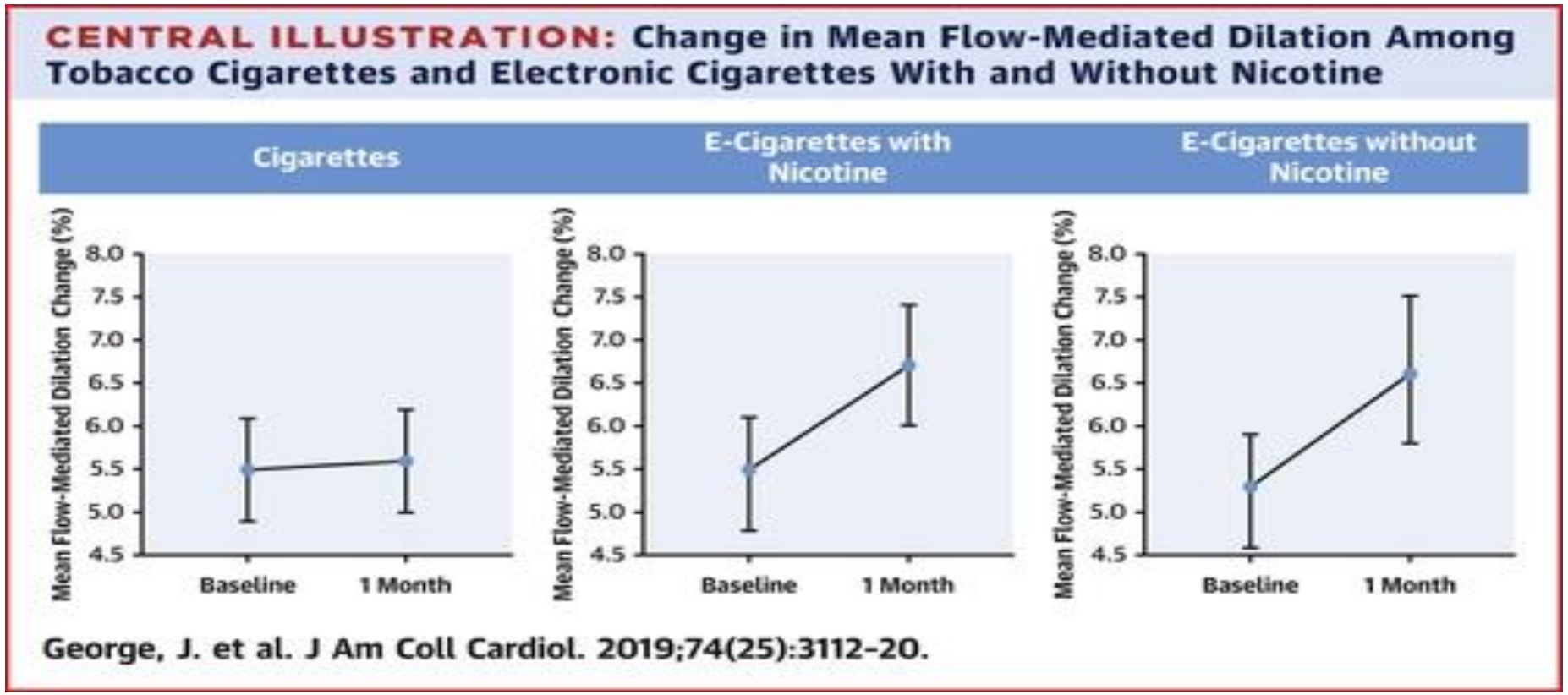
Itsaso Garcia-Arcos [1, 2], Patrick Geraghty [1, 2], Nathalie Baumlin [3], Michael Campos [3], Abdoulaye Jules Dabo [1, 2], Bakr Jundi [4], Neville Cummins [5], Edward Eden [5], Astrid Grosche [3], Matthias Salathe [3], Robert Foronjy [1, 2]

Correspondence to Dr Robert Foronjy, Division of Pulmonary and Critical Care Medicine, SUNY Downstate Medical Center, Brooklyn, NY 11203, USA; Robert.Foronjy@downstate.edu

'Harms' without comparison to the harms caused by tobacco smoke
Translational research without real-world relevant outcomes

Cardiovascular Effects of Switching From Tobacco Cigarettes to Electronic Cigarettes

- Present the harms of tobacco smoke in direct comparison with harms of vaping ……..
- 1% improvement in FMD = 13% reduction in risk of cardiovascular event



Smoking tobacco creates poor vascular health. Switching from smoking tobacco to vaping significantly and immediately improves vascular health. Nicotine is not the cause of poor vascular health.

Jacob George et al. *J Am Coll Cardiol* 2019; 74:3112-3120.

JACC JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Is vaping safe? NO. But it's substantially less harmful than smoking tobacco

"There is conclusive evidence that completely substituting combustible tobacco with vaping nicotine liquid reduces users' exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes"

US National Academy of Academy of Science, Engineering and Medicine

"Vaping is estimated to be 95% less harmful than smoking tobacco"

The Royal College of Physicians

Long term: E-cigarettes have been in widespread use for less than a decade. We lack long term evidence on harms, which may yet emerge and continued vigilance is crucial.

Medium term: Bio marker studies suggest "*Long-term NRT-only and EC-only use, but not dual use with cigarettes, is associated with substantially reduced levels of measured carcinogens and toxicants relative to cigarette-only smoking*." Users of EC and NRT had similar levels of measured toxicants.

Short term: RCT show little risk from EC when used short term for smoking cessation. A recent Cochrane review *"did not detect evidence of harm from nicotine EC, but longest follow-up was two years*."

Research and analysis

Nicotine vaping in England: 2022 evidence update main findings

Published 29 September 2022

Vaping: the theory

- *Dramatically reduce / remove the harms of smoking tobacco*

- In the short and medium term, **vaping poses a small fraction of the risks of smoking**
- Vaping is not risk-free, particularly for people who have never smoked
- Significantly lower exposure to harmful substances from vaping compared with smoking, as shown by biomarkers associated with the risk of cancer, respiratory and cardiovascular conditions
- No significant increase of toxicant biomarkers after short-term second hand exposure to vaping among people who do not smoke or vape
- In stop smoking services in 2020 to 2021, quit attempts involving a vaping product were associated with the highest success rates (64.9% compared with 58.6% for attempts not involving a vaping product)

‘Epidemic’ of vaping-induced lung injury

In the US

> No regulation of e-cigarettes in the US

> All cases linked to oil solvent

> CBD oil, butane hash oil, vitamin E oil

In the UK

> Heavily regulated e-cigarette market

> No cases of death/illness

> Yellow card reporting system

> 62 reports in 10 years from 3 million vapers

> (paracetamol = 100,000 hospital admissions per year)

> (1 million deaths from tobacco in the same time frame)

Vaping products are tightly regulated in the UK by tobacco product regulations that were adopted from the European Tobacco Products Directive and consumer product regulations.

Advice:

> Buy from a licensed vendor

> Do not buy illicit liquids

> Do not buy liquids abroad

Nicotine or tobacco abstinence?

Rachael L. Murray[1,2], Matthew Evison[3] and Matthew E. Callister[4]

[1]Academic Unit of Lifespan and Population Health, School of Medicine, University of Nottingham, Nottingham, UK. [2]SPECTRUM consortium, Edinburgh, UK. [3]Wythenshaw Hospital, Manchester University NHS Foundation Trust, Manchester, UK. [4]Leeds Teaching Hospitals NHS Trust, Leeds, UK.

Corresponding author: Rachael L. Murray (rachael.murray@nottingham.ac.uk)

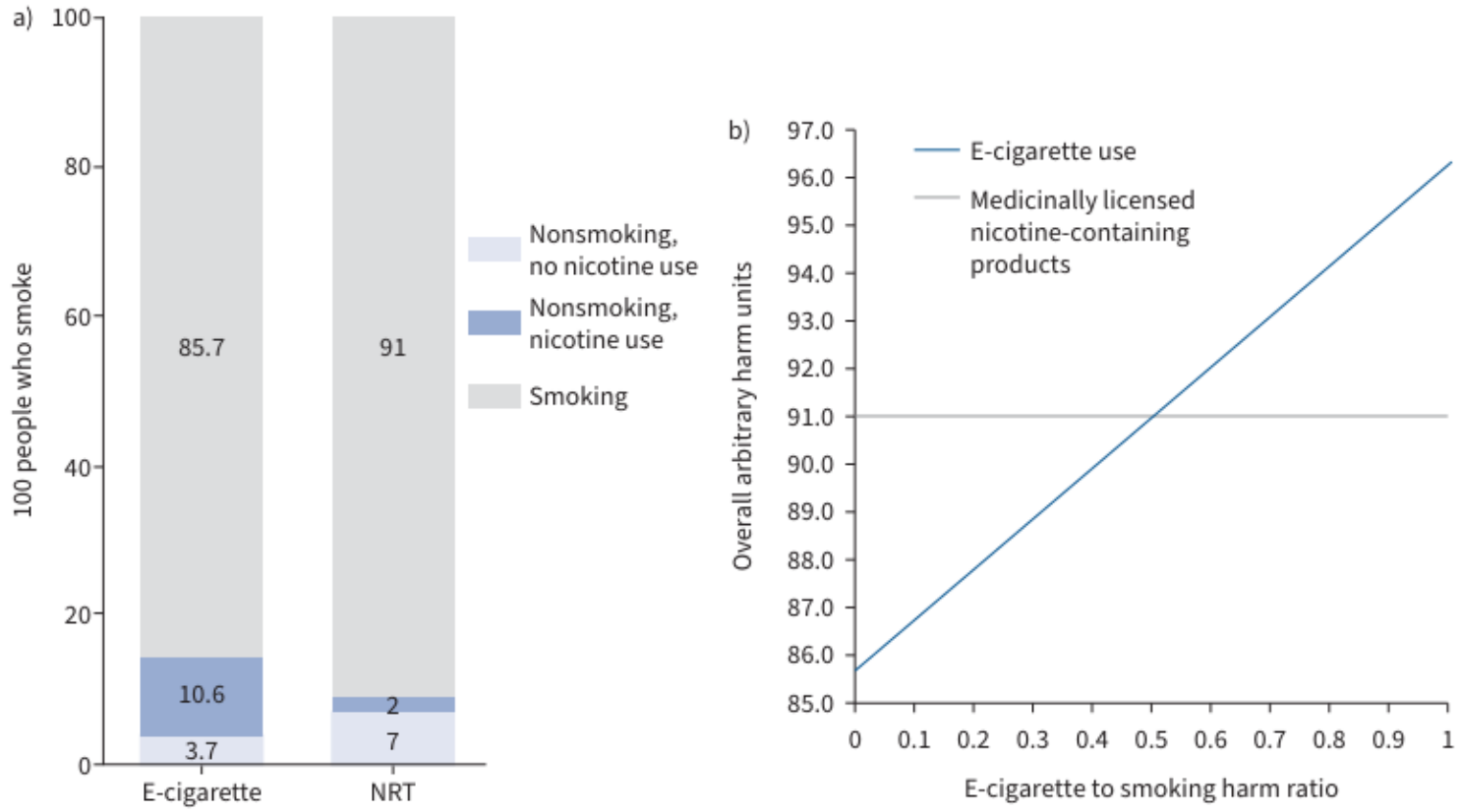


FIGURE 1 a) Anticipated absolute effects of e-cigarette use *versus* nicotine replacement therapy (NRT); reproduced from Hanewinkel *et al.* [1]. b) Overall net population harm caused by the use of e-cigarettes *versus* medicinally licensed nicotine-containing products according to e-cigarette to smoking harm ratio.

Accurate & consistent information to patients dependent on tobacco……..

Vaping

Fact: Tobacco is uniquely deadly and is the single most important disease to address to improve population health, respiratory health and inequalities

Fact: Nicotine vapes are an effective treatment for tobacco dependency & are one component of a comprehensive patient-centred treatment plan

Fact: Nicotine vapes are not risk free but are a fraction of the risk of smoking tobacco and leads to substantial net harm reduction

Fact: Nicotine vapes are solely a treatment for tobacco dependency and have no place in society for children young adults or adults that do not smoke.

Fact: Mice shouldn’t vape

A deep-dive into varenicline

Varenicline – medications that act on the nicotinic receptor

‘Breaks the addiction to nicotine’

- Dual agonist and antagonist to the nicotine receptor
- Agonist = dopamine release and relief from cravings
- Antagonist = prevents dopamine release from nicotine when smoking
- Takes away the pleasure of smoking and the positive reinforcement of the addiction

- 0.5 mg once daily, day 1–3
- 0.5 mg twice daily, day 4–7
- 1 mg twice daily, day 8+
- 12-week course
- Patient needs additional nicotine in the initial stage
- Aims to gradually reduce nicotine use as medication takes effect
- Set a quit date

Can be extended to 24 weeks if high risk of relapse, eg multiple previous quit attempts

What are the benefits of varenicline?

Varenicline is an effective treatment for tobacco addiction increasing the chance of abstinence by over **200%** vs placebo (RR 2.24, 95% CI 2.06–2.43) *(based on 27 trials with 12,625 patients)*.

Cahill K *et al*. *Cochrane Database Syst Rev* 2016;2016(5):CD006103

OR = odds ratio

Varenicline is more effective than bupropion. Smokers are approximately **40%** more likely to stop with varenicline vs bupropion (RR 1.39, 95% CI 1.25–1.54) *(based on 5 trials with 5,887 patients).*

Cahill K *et al*. *Cochrane Database Syst Rev* 2016;2016(5):CD006103

Varenicline and behavioural support is the most effective combination to treat tobacco addiction in a meta-analysis of 115 trials and 57,000 patients. Smokers are approximately **60%** more likely to stop smoking with varenicline and behavioural support than with bupropion (OR 1.56, 95% CI 1.07–2.34) and NRT (OR 1.65, 95%CI 1.10–2.12).

Windle SB *et al*. *Am J Prev Med* 2016; 51(6):1060–71

Cochrane Database of Systematic Reviews 2016

- Randomised controlled trials with a minimum 6-month follow up.
- Number needed to treat (NNT) derived from pooled difference between placebo and treatment quit rates.

	NNT to achieve additional long-term quitter vs placebo
NRT	23 (95% CI 20–25)
Bupropion	22 (95% CI 18–28)
Varenicline	11 (95% CI 9–13)

Cahill K *et al*. Nicotine receptor partial agonists for smoking cessation. *Cochrane Database Syst Rev* 2016;(5):CD006103.

Conclusions of NICE technology appraisal 2007

- Varenicline is superior to NRT and bupropion in achieving continuous abstinence (over a lifetime horizon varenicline dominated bupropion and NRT – it was **cheaper and more effective** – in all sensitivity analysis).
- Varenicline should normally be provided in conjunction with counselling and support, but if such support is refused or is not available, **this should not preclude treatment** with varenicline.
- When NICE recommends a treatment 'as an option', the NHS must make sure it is available. **This means that, if the doctor responsible for a patient's care thinks that varenicline is the right treatment for smoking cessation, it should be available for use, in line with NICE's recommendations.**

NICE. *Varenicline for smoking cessation. Technology appraisal guidance 123 [TA123].* London: NICE. 2007.

EAGLES trial

- Largest trial of smoking cessation pharmacotherapy
- Study requested and co-designed with the FDA
- 140 centres, 16 countries, 5 continents
- Double-blind, triple dummy, placebo-controlled, randomised trial
- Smokers aged 18–75, at least 10 cigarettes per day (cpd)
- 12 weeks of treatment + 12 weeks of further follow up (24-week trial)
- Total 15 clinic visits – 10 minutes of smoking cessation advice
- **8,144 participants randomised**

Anthenelli RM *et al*. *The Lancet* 2016;387(10037):2507–20.

EAGLES trial: Neuropsychiatric safety outcomes

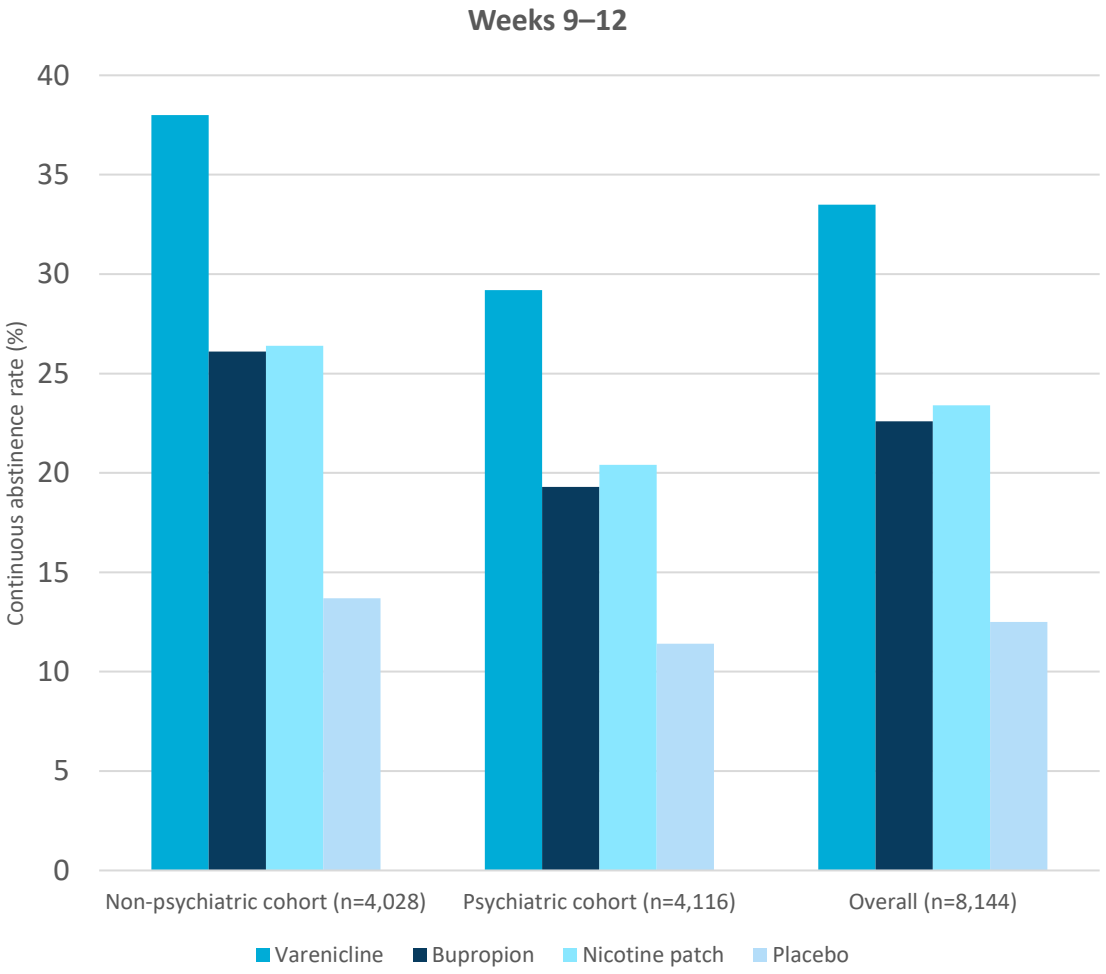
- Psychiatric vs non psychiatric cohorts
- Psychiatric illness stable for 3 months – no medication changes
- Psychiatric illness stratified as mood, anxiety, psychotic, personality
- Clearly defined composite outcome – 16 neuropsychiatric symptoms
- ‘Neuropsychiatric adverse event interview’ – 25 questions
- Healthcare professional interview if ‘Yes’ to any question
- 8,000 patients to estimate a 75% increase in neuropsychiatric adverse event rate within +1.59% or –1.59%

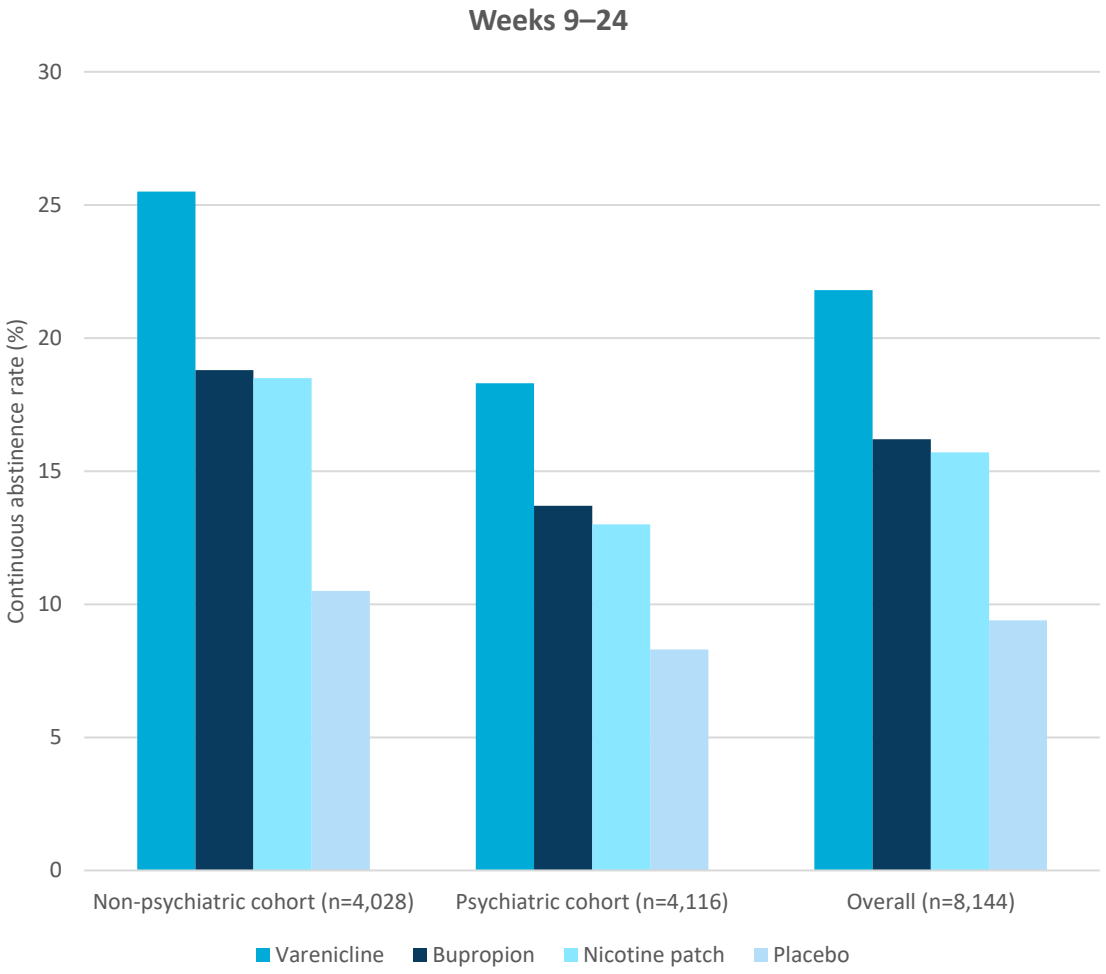
Anthenelli RM *et al*. *The Lancet* 2016;387(10037):2507–20.


THE LANCET

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

Which medication worked best?





Anthenelli RM *et al*. *The Lancet* 2016;387(10037):2507–20.

Outcomes of EAGLES trial: Neuropsychiatric adverse events

- **There is no increased risk of moderate to severe neuropsychiatric adverse events with varenicline (EAGLES study 2016, *The Lancet*).**
- The act of stopping smoking carries a small risk of moderate to severe neuropsychiatric events and this is **regardless of the treatment used**.
- The risk is higher in those with a history of psychiatric illness (5%) versus those without (2%). **Advise patients to seek help in the event of a neuropsychiatric event.**
- In the long term, stopping smoking improves mental health disease, eg stopping smoking is more effective than antidepressants in treating depression.

Anthenelli RM *et al*. *The Lancet* 2016;387(10037):2507–20.

Common side effects

Very common:

- **Vivid dreams**
- **Nausea (take with food and water)**
- Sleep disturbance
- Headaches
- Nasopharyngitis

Dose can be reduced to 0.5 mg twice daily if intolerable side effects

Considerations

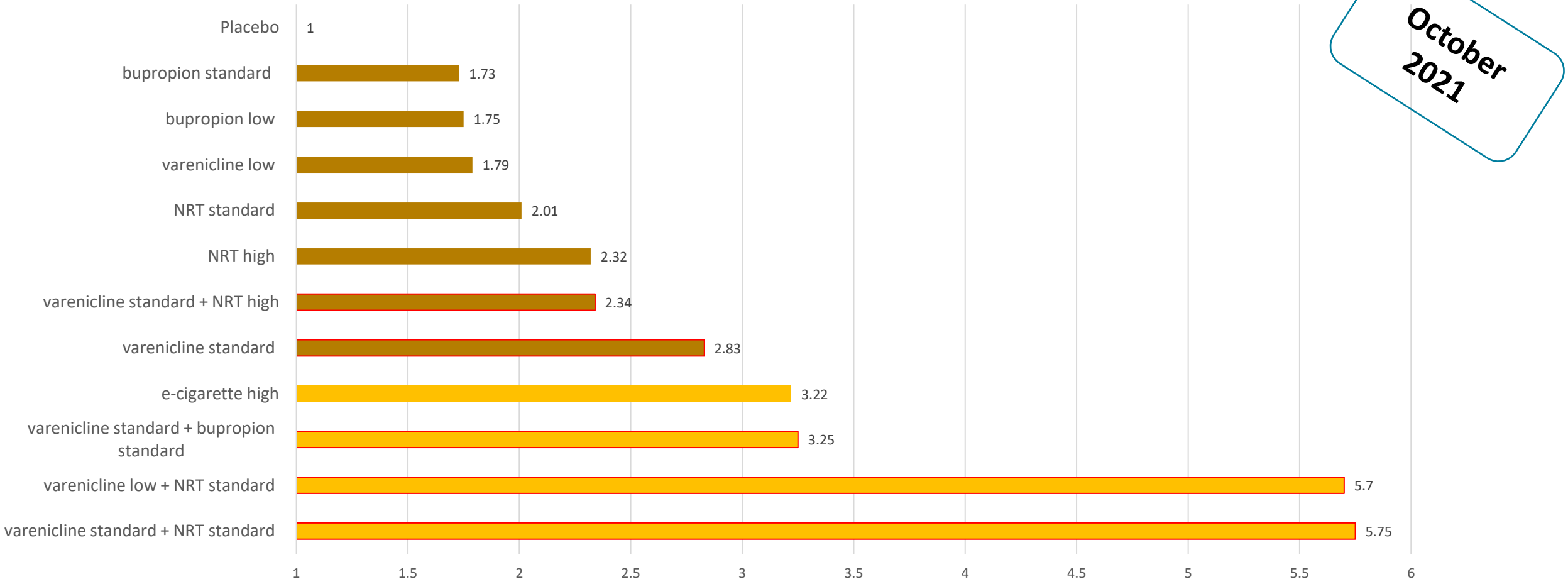
- Contraindications: hypersentivity to active ingredient or excipients
- Pregnancy: preferrable to avoid
- Breastfeeding: consider risk:benefit
- End-stage renal failure (eGFR <10mL/min/1.73m^2): not recommended
- Mental health illness is NOT a Contraindication (is under Special Warnings & Precautions)

Drug interactions

No clinically meaningful interactions

Systematic review and network meta-analysis: Effectiveness of treatments for tobacco dependency 2021

(Wide confidence intervals in yellow, varenicline in red frame)



Comparative clinical effectiveness and safety of tobacco cessation pharmacotherapies and electronic cigarettes: a systematic review and network meta-analysis of RCTs, Thomas et al 2021

A deep-dive into cytisine


Cytisine

INTRODUCTION

- Cytisine is a plant-based, naturally occurring chemical found in plants like Laburnum
- Cytisine is a **nicotine analogue:** it is a partial agonist at the nicotine receptor in the brain and can therefore alleviate withdrawal and cravings to smoke (like varenicline)
- Strong evidence base across multiple RCTs, meta-analyses and Cochrane database review
- Established in routine clinical care in mainland Europe for many decades

Key Advantages of Cytisine:

- ✓ Plant based, naturally occurring chemical
- ✓ Robust evidence of effectiveness
- ✓ 25-day course can be provided in a single prescription / supply
- ✓ Potential cost saving versus other treatment courses
- ✓ Less side effects compared to other nicotine analogues

Courtney RJ et al. JAMA 2021 326(1)56-64

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Placebo-Controlled Trial of Cytisine for Smoking Cessation

Robert West, Ph.D., Witold Zatonski, M.D., Magdalena Cedzynska, M.A., Dorota Lewandowska, Ph.D., M.D., Joanna Pazik, Ph.D., M.D., Paul Aveyard, Ph.D., M.D., and John Stapleton, M.Sc.

Single-centre, placebo controlled RCT (UK)

Primary outcome: 12 month sustained abstinence

740 participants

Cytisine more effective than placebo p=<0.001

Increased GI adverse events with cytisine than placebo (5.7% higher rate)

Outcome	Cytisine (N=370)	Placebo (N=370)	Percentage-Point Difference (95% CI)	Relative Rate (95% CI)†
	percent (number)			
Primary outcome: abstinence for 12 mo	8.4 (31)	2.4 (9)	6.0 (2.7–9.2)‡	3.4 (1.7–7.1)
Abstinence for 6 mo	10.0 (37)	3.5 (13)	6.5 (2.9–10.1)‡	2.9 (1.5–5.3)
Point prevalence at 12 mo	13.2 (49)	7.3 (27)	5.9 (1.6–10.3)§	1.8 (1.2–2.8)

MAKE SMOKING HISTORY

Clinical effectiveness: Cytisine vs placebo
Meta-analysis

Cytisine vs placebo

8 trials: 7 with extractable data

2x high quality studies

RR 1.57, 1.42-1.74 (7 studies)

RR 3.29, 1.84-5.90 (2x high quality studies)

No difference in overall adverse event profile

Increased GI symptoms specifically with Cytisine (RR 1.76, 1.28-2.42)

Hajek P et al Thorax 2013;68: 1037–1042.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 18, 2014 VOL. 371 NO. 25

Cytisine versus Nicotine for Smoking Cessation

Natalie Walker, Ph.D., Colin Howe, Ph.D., Marewa Glover, Ph.D., Hayden McRobbie, M.B., Ch.B., Ph.D., Joanne Barnes, Ph.D., Vili Nosa, Ph.D., Varsha Parag, M.Sc., Bruce Bassett, B.A., and Christopher Bullen, M.B., Ch.B., Ph.D.

Open-label, non-inferiority RCT (New Zealand)

Cytisine (25 days) vs NRT (8 weeks)

Primary outcome: continuous abstinence at 1 month

40% vs 31%

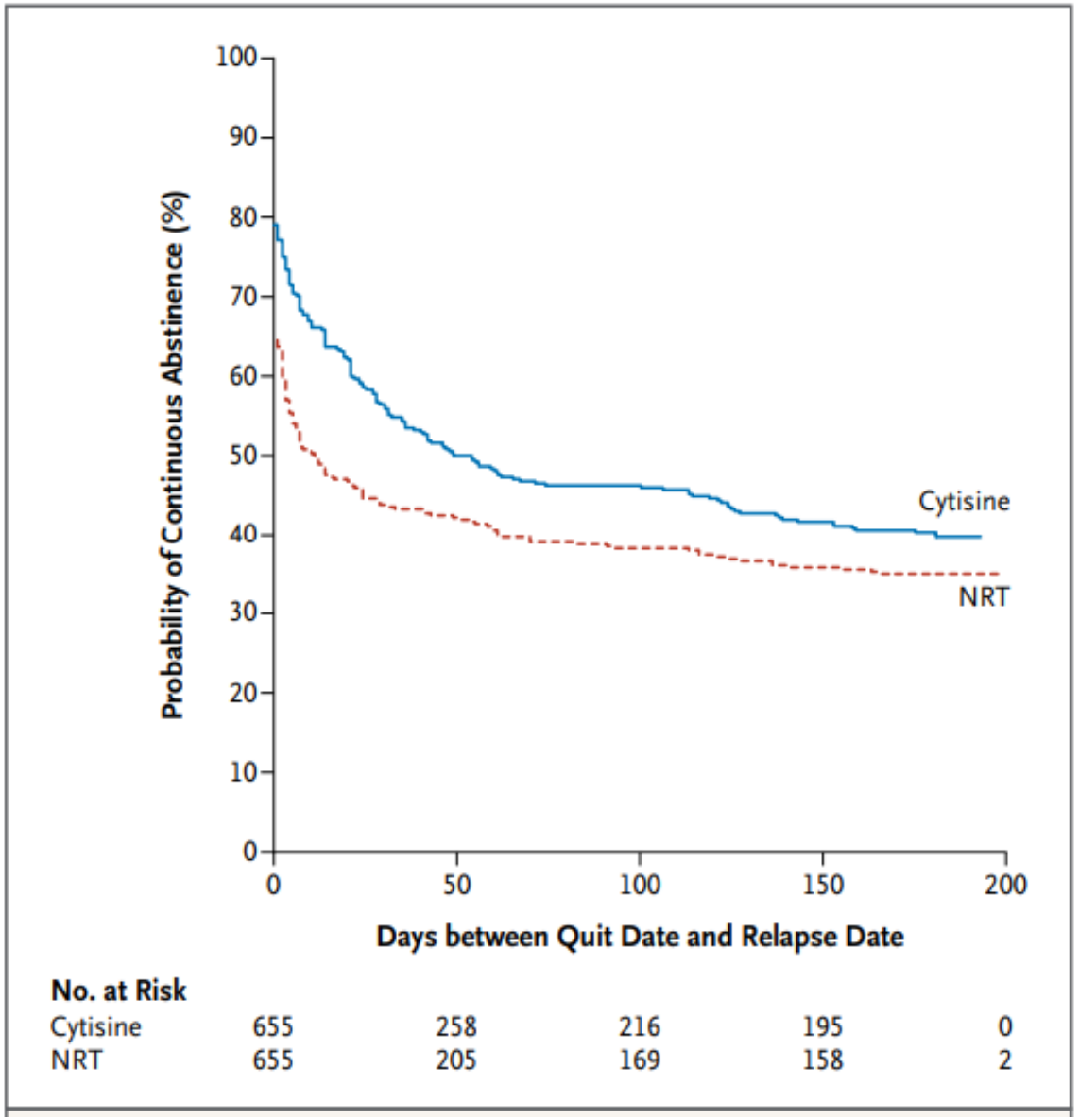
RR 1.3, 1.1-1.5, p=<0.001

Cytisine Number Needed to Treat = 11

Higher adverse events Cytisine

(nausea, vomiting, sleep disturbance)

Cytisine is non-inferior, possibly superior



JAMA Network™

QUESTION Is cytisine noninferior to varenicline regarding smoking cessation?

CONCLUSION The clinical trial findings failed to demonstrate noninferiority of cytisine compared with varenicline regarding smoking cessation in adult daily smokers.

POPULATION

742 Women
710 Men

Adult daily smokers willing to make a quit attempt

Mean age: **43** years

LOCATIONS

Australia

INTERVENTION

1452 Patients randomized
1108 Patients completed final follow-up

725

Cytisine

1.5-mg capsules taken 6 times daily initially, then reduced over 25-day course

727

Varenicline

0.5-mg tablets titrated to 1 mg twice daily for 12 weeks

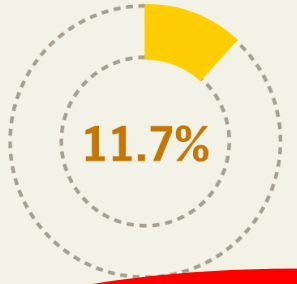
PRIMARY OUTCOME

6-month continuous abstinence verified using carbon monoxide breath test at 7-month follow-up, and noninferiority set at 5%

FINDINGS

6-month biochemically verified continuous abstinence rate

Cytisine
85 of 725 patients



Varenicline
97 of 727 patients

Cytisine was not noninferior to varenicline:
between-group difference, **−1.62%**
(1-sided 97.5% CI, −5.02% to ∞)

Courtney RJ, McRobbie H, Tutka P, et al. Effect of cytisine vs varenicline on smoking cessation: a randomized clinical trial. *JAMA*. Published July 6, 2021. doi:10.1001/jama.2021.7621

Summary of the evidence for cytisine

- ✓ Cytisine is a highly effective treatment for tobacco dependency
- ✓ Probably more effective than NRT
- ✓ Probably not as effective as varenicline when given as 25 days vs 84 days varenicline
- ✓ Less side effects than varenicline

West R et al. N Engl J Med 2011;365:1193-2000, Hajek P et al Thorax 2013;68: 1037–1042.
Walker N et al. N Engl J Med 2014;371:2353-62. Courtney RJ et al. JAMA 2021 326(1)56-64

Prescribing & Supplying Cytisine

Cytisine is now available in the UK as a prescription only medication.

- ✓ Each tablet contains 1.5mg of cytisine.
- ✓ One pack of Cytisine contains 100 tablets
- ✓ A complete treatment course is 25 days
- ✓ Cytisine should be taken with water
- ✓ The dose of cytisine starts at 6 tablets per day
  - (1 tablet every 2 hours)
- ✓ The dose gradually reduces over the treatment course
- ✓ The aim is to reduce the number of cigarettes smoked as cytisine take effect and help control the urges to smoke. Ideally, this is on **Day 5 of cytisine**

Days of treatment	1st to 3rd			4th to 12th									13th to 16th				17th to 20th				21st to 25th				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
Recommended dosing	1 tablet every 2 hours			1 tablet every 2.5 hours									1 tablet every 3 hours				1 tablet every 5 hours				1–2 tablets a day				
Maximum daily dose	6 tablets			5 tablets									4 tablets				3 tablets				2 tablets				

contraindications

- Allergy to cytisine or any other ingredient
- Pregancy & breastfeeding
- Unstable angina
- Recent myocardial infarction
- Significant cardiac arrythmia
- Recent stroke
- Current treatment with TB antibiotics – not recommended

CAUTIONS

Caution in prescribing in (lack of clinical data):

- Not recommended in <18 yrs or >65 yrs
- Renal impairment
- Liver impairment

Refer to full SPC before prescribing
https://www.medicines.org.uk/emc/product/15789

SIDE EFFECTS

Very common:

- change in appetite (mainly increase), weight gain
- dizziness, irritability, mood changes, anxiety, sleep disorders (insomnia, drowsiness, lethargy, abnormal dreams, nightmares), headaches
- tachycardia
- hypertension
- dry mouth, diarrhoea, nausea, changes flavour, heartburn, constipation, vomiting, abdominal pain
- rash
- myalgia
- fatigue

Most side effects occur at the beginning of the therapy and resolve along with its duration.

These symptoms are also common when anybody stops smoking (withdrawal symptoms), regardless of treatment with cytisine

Healthcare professionals are encouraged to report suspected side effects via the Yellow Card scheme, https://yellowcard.mhra.gov.uk/

Cytisine in hospitalised patients (BTS & Greater Manchester approach)

- ✓ Cytisine is a highly effective treatment for tobacco dependency
- ✓ Hospitalised patients that smoke should be considered for treatment with cytisine by doctors, prescribing nurses and tobacco dependency specialists
- ✓ The initiation of combination NRT at the point of admission is a standard of care across the country for any patients that smokes (immediate treatment of nicotine withdrawal)
- ✓ Cytisine can be started as an inpatient and NRT used to provide the additional nicotine in the early stages of treatment that continued smoking would normally provide, aiming to stop NRT on day 5
- ✓ Ongoing smoking or NRT use beyond day 5 of cytisine treatment ***could*** risk adverse symptoms of nicotine excess but there is also a risk of relapse without adequate nicotine treatment

A standardised & structured intervention: The BTS framework

A new standard of care

Treating tobacco dependence in patients admitted to hospital leads to substantial benefits for both the individual and the healthcare system and is now **a standard of care in the NHS**

Maximising every hospital admission

•Every hospital admission is a real opportunity to help patients manage their tobacco dependence

•The Framework describes a series of interventions, starting upon admission, that will help patients to manage their tobacco dependence

•Aim is to add as many blocks as possible to a tobacco dependent patient's treatment and care; no single building block is more important than another.

•Not every patient will accept every intervention but the more building blocks that are used as part of managing their tobacco dependence the more likely they will:

- control their withdrawal symptoms and urges to smoke
- maximise chance of a smoke-free hospital admission
- start on journey to achieving long term abstinence from tobacco

British Thoracic Society

The Framework: Block by Block

Block 1 - Screen for tobacco dependence

- Ask every patient if they smoke
- Record ‘Tobacco dependency’ as an active disease in the medical history
- Ensure any electronic systems for recording smoking status & supporting referral to the specialist tobacco dependency team are completed

Block 2: **Advise on the role of nicotine**

- Nicotine drives the dependency to tobacco but it is NOT the cause of the harms of smoking
- The harms of smoking come from thousands of toxic chemicals produced when tobacco is burnt to create smoke
- Keeping these poisonous chemicals out of the body during this hospital admission will help acutely unwell patients recover more quickly
- Nicotine withdrawal can be unpleasant and it is important to provide nicotine in safe, alternative ways to help alleviate this
- Being smoke-free does not have to mean being nicotine-free both during a hospital admission and beyond

The Framework: Block by Block

Block 3 - Initiate combination NRT as soon as possible

- Use the Rapid Inpatient NRT Prescribing Protocol and prescribe a 25mg/16hour nicotine patch plus a short acting nicotine product (inhalator/lozenge/mouth spray)
- The most serious risk of relapsing back to smoking is prescribing an insufficient dose of NRT and not adequately addressing the patient's withdrawal symptoms and urges to smoke

Block 4 - Complete a referral to an on-site tobacco dependency advisor (TDA)

- Refer all patients with tobacco dependence to the TDA team unless they opt out or ensure automated referral processes to the TDA team when the patient is recorded as tobacco dependent, allowing them to opt out at first approach by the TDA
- Advise on the benefits of working with specialist advisors
- If no on-site team is available, complete an onward referral to local community services to provide ongoing treatment & support after discharge

The Framework: Block by Block

Block 5 - Provide accurate and consistent information about vaping

- Nicotine vapes deliver high dose short-acting nicotine which can help to alleviate withdrawal and urges to smoke
- Vaping is an effective treatment for tobacco dependency
- Inpatients should be advised to switch entirely to vaping (and NRT) to maximise the harm reduction, both during the admission and after discharge

The Framework: Block by Block

Block 6 - Discuss. Offer and prescribe nicotine analogue medications

- Nicotine analogue medications (varenicline, cytisine) are highly effective treatments and can be discussed & commenced at the point of admission or during the admission

- Combination therapies (e.g. NRT and varenicline) are as effective if not more effective than single therapies and support abstinence in the unique environment of the inpatient setting

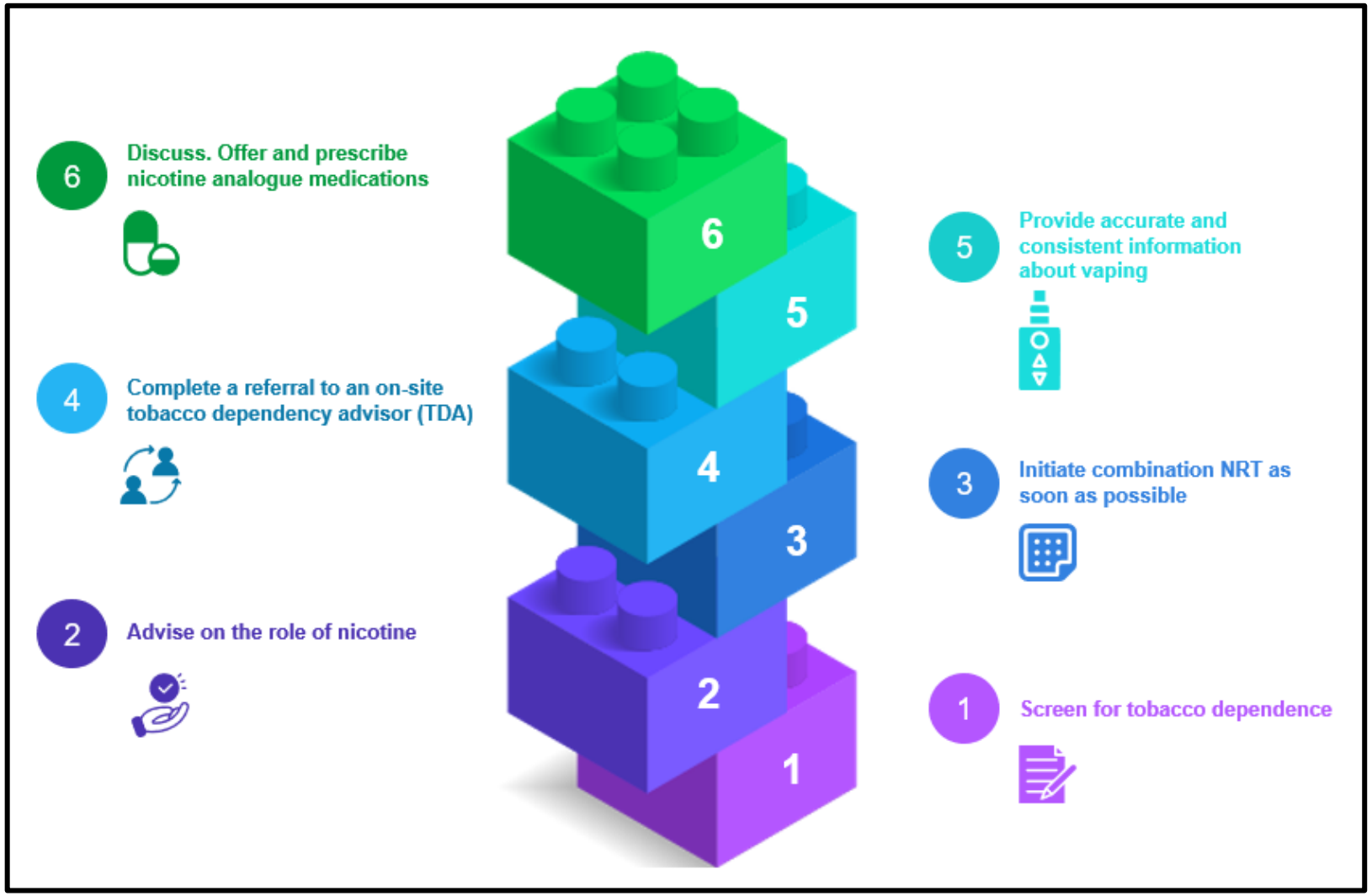
A standardised & structured intervention

BTS Clinical Statement

Medical management of inpatients with tobacco dependency

Sanjay Agrawal ,[1] Matthew Evison,[2,3] Sachin Ananth,[4] Duncan Fullerton,[5] Helen McDill,[6] Melanie Perry,[7] Jacqueline Pollington,[8] Louise Restrick,[9] Elspeth Spencer,[10] Ameet Vaghela[11]

https://www.brit-thoracic.org.uk/quality-improvement/clinical-statements/medical-management-of-inpatients-with-tobacco-dependency/



British Thoracic Society

Conclusions

- A unique and critically important moment……
- We have an **opportunity** and a **responsibility** to provide patients with tobacco dependence access to the most effective treatments
  - ……..at every touch point with the healthcare system
  - ……equitably
  - ……at scale
  - ……as a standard of care

- We must
  - **Breakdown the myths and lies about vaping**
  - **Embed varenicline and cytisine as fundamental components of all tobacco dependency treatment programmes**

Questions

Dr Matthew Evison
@MatthewEvison1

‘There is no good reason why a switch from tobacco products to less harmful nicotine delivery systems should not be encouraged. Smoking-related deaths after the year 2000 would fall steadily and substantially if this can be achieved. There is no compelling objection to the recreational and even addictive use of nicotine provided it is not shown to be physically, psychologically, or socially harmful to the use or to others.’

The Lancet 1991

Questions?

Cytisine prescribing and adverse event reporting information for is available via link in Q&A tab

Smoking Cessation Services: where are we now?

Louise Ross, Clinical Consultant, NCSCT

NCSCT

UK-CYT-186c September 2024

Declaration

- Louise Ross (lou.ross@ncsct.co.uk) was the Stop Smoking Service Manager for Leicester City Council. She is a clinical consultant for the NCSCT, Smoking Cessation Lead for Smoke Free Digital Home - Smoke Free (smokefreeapp.com) and Chair and mental health lead for the New Nicotine Alliance http://nnalliance.org/
- Consilient Health

The NCSCT and its staff have a clear policy not to engage in work or conversation with companies who receive funding or backing from organisations related to the tobacco industry.

350 people aged 18-25 start smoking regularly in the UK every day [1]

New ring-fenced funding has been made available to local authorities to tackle smoking, especially in the most disadvantaged areas [2]

NCSCT resources

- Commissioning, Delivery and Monitoring Guidance 2024
- Gold Standard guide to every aspect of local Stop Smoking Services
- Local Stop Smoking Services and support: commissioning, delivery and monitoring guidance (ncsct.co.uk)

NCSCT training

- Free online training
- Register for an account and you're ready to go
- Very Brief Advice
- Practitioner training
- Specialist modules on mental health, pregnancy, smokefree homes and vaping
- Stop-smoking medications: NRT, varenicline, Cytisine and Zyban

Are you able to get prescription-only medication to your service users?

Some areas have successfully got Cytisine and varenicline on their local formularies; others have not.

This needs to be driven by local health leaders – no one will do it for you!

Failure to get medications on the formulary causes frustration to patients and means that people keep smoking for longer than they should.

Implementing change in Local Stop Smoking Services

- If you do what you've always done, you get what you've always got
- Listen to what people say about how they want to quit
- Consider digital as an adjunct
- Swap to Stop scheme
- Confidence about Cytisine

New treatments: gaining confidence

- Most people who smoke are looking for the Holy Grail, the Magic Solution
- There IS no magic, but you can inspire them to put all their trust in the treatment plan you devise for them
- Ask each service user for honest feedback – make it safe for them to tell you the truth
- Use lessons learned from your clients to grow your confidence in what works

Developing confidence in Cytisine

- We know that Cytisine works because we have the trial data [3-6]
- What we want to know more about is how effective it can be when used in our SSSs
- The health community is watching closely to see results
- It's being piloted in acute care, but we need *community* results
- Every service user who quits with Cytisine will inspire others to do the same

Summary

- People who smoke often search for something new, something they haven't tried before.
- Cytisine is a new and important tool in our toolbox
- It's effective, well-tolerated and cost-effective [7,8]

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1. Smokefree Action Coalition cdn.smokefreeaction.org.uk
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6. Walker N, Howe C, Glover M et al. Cytisine versus Nicotine for Smoking Cessation. N Engl J Med 2014;371:2353-62
7. NICE. 2024 exceptional surveillance of tobacco: preventing uptake, promoting quitting and treating dependence (NICE guideline NG209) https://www.nice.org.uk/guidance/ng209/evidence
8. AMWSG cytisinicline (cytisine) https://awttc.nhs.wales/accessing-medicines/medicine-recommendations/cytisinicline-cytisine/

Further resources on Cytisine

https://www.ncsct.co.uk/publications/category/cytisine

- Briefing document
- Dosing guide
- Cytisine specific Product Characteristics
- Template for getting Cytisine approved by Medicines Management

NCSCT

NATIONAL CENTRE FOR SMOKING CESSATION AND TRAINING

Questions?

Cytisine prescribing and adverse event reporting information for is available via link in Q&A tab

To contact Consilient Health

- Visit the Consilient Health website www.quitsmokingsupport.co.uk for more information on Cytisine
  - Consilient Health will look to make the recording available after the webinar on www.quitsmokingsupport.co.uk

- Contact
  - Lesley Tew 07786 194 842 ltew@consilienthealth.com
  - Grant McCalman 07825 537 321 gmaccalman@consilienthealth.com
  - Medical Information 0203 751 1888 drugsafety@consilienthelath.com

- Don’t forget to download your attendance certificate from the Q&A tab before leaving the webinar

Cytisine 1.5mg Tablets Prescribing Information

Please refer to the Summary of Product Characteristics for full details.

Product name: Cytisine 1.5mg tablets Composition: 1.5mg of cytisine **Indication:** Smoking cessation and reduction of nicotine cravings in smokers willing to stop. Treatment goal is the permanent cessation of use of nicotine-containing products. **Posology and administration: Adults:** One pack (100 tablets) is sufficient for a complete treatment course of 25 days: Day 1-3: 1 tablet every 2 hours (maximum 6 per day); Day 4-12: 1 tablet every 2.5 hours (maximum 5 per day); Day 13-16: 1 tablet every 3 hours (maximum 4 per day); Day 17-20: 1 tablet every 5 hours (maximum 3 per day); Day 21-25: 1-2 tablets a day (maximum 2 per day). Stop smoking no later than 5th day of treatment; continuing smoking may aggravate adverse reactions. In case of treatment failure, discontinue; may be resumed after 2 to 3 months. **Special populations:** *Renal or hepatic impairment:* no clinical experience; not recommended. *Elderly (over 65 years):* limited clinical experience; not recommended. *Paediatric population (under 18 years):* Safety and efficacy not established; not recommended. **Method of administration:** Orally with water. **Contraindications:** Hypersensitivity to active substance or excipients; unstable angina; recent myocardial infarction or stroke; clinically significant arrhythmias; pregnancy and breastfeeding. **Warnings and precautions (see SPC for full details):** Only for patients with serious intention of weaning off nicotine. Patient should be aware that simultaneous smoking or use of nicotine-containing products could lead to aggravated adverse reactions of nicotine. Use with caution in: ischemic heart disease, heart failure, hypertension, pheochromocytoma, atherosclerosis and other peripheral vascular diseases, gastric and duodenal ulcer, gastroesophageal reflux disease, hyperthyroidism, diabetes and schizophrenia. Polycyclic aromatic hydrocarbons in tobacco smoke induce metabolism by CYP 1A2 (and possibly CYP 1A1). Stopping smoking may slow metabolism and raise blood levels of such drugs. Potentially clinically important if narrow therapeutic window, e.g. theophylline, tacrine, clozapine, ropinirole. Levels of products partly metabolised CYP1A2 e.g. imipramine, olanzapine, clomipramine, fluvoxamine, may also increase; data are lacking, clinical significance unknown. Limited data indicate metabolism of flecainide and pentazocine may be induced by smoking. Be aware of serious neuropsychiatric symptoms in patients attempting to quit smoking, with or without treatment, including: depressed mood, rarely including suicidal ideation and suicide attempt; exacerbation of underlying psychiatric illness (e.g. depression) - take care in these patients and advise accordingly. (See Pregnancy). **Pregnancy**: Contraindicated. Women of childbearing potential must use highly effective contraception. If on systemically acting hormonal contraceptives, add a second barrier method. **Breast-feeding:** Contraindicated. **Fertility:** No data available. **Undesirable effects: Very Common (≥ 1/10):** change in appetite (mainly increase), weight gain, dizziness, irritability, mood changes, anxiety, sleep disorders (insomnia, drowsiness, lethargy, abnormal dreams, nightmares), headaches, tachycardia, hypertension, dry mouth, diarrhea, nausea, changes flavour, heartburn, constipation, vomiting, abdominal pain (especially in the upper abdomen), rash, myalgia, fatigue **Common (≥1/100 to <1/10):** difficulty in concentration, slow heart rate, abdominal distension, burning tongue, malaise. **Uncommon (≥1/1000 to <1/100):** dyspnea. See SPC for full list of Uncommon undesirable effects. **NHS Price:** £115.00 per box of 100 tablets. **Legal Classification:** POM **MA numbers:** PL 51228/0001 **Marketing Authorisation Holder:** Bonteque Consulting Ltd, 29 Westcott Crescent, Hanwell, W7 1PL, United Kingdom. **Further information is available on request from:** Consilient Health (UK) Ltd, No.1 Church Road, Richmond upon Thames, Surrey TW9 2QE or drugsafety@consilienthealth.com. **Job Code:** UK-CYT-162 **Date of preparation of PI:** July 2024

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/.

Adverse events should also be reported to Consilient Health (UK) Ltd, No. 1 Church Road, Richmond upon Thames, Surrey TW9 2QE UK or drugsafety@consilienthealth.com