# The current evidence base for smoking cessation treatment in smokers with COPD

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# Disclosures

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None.

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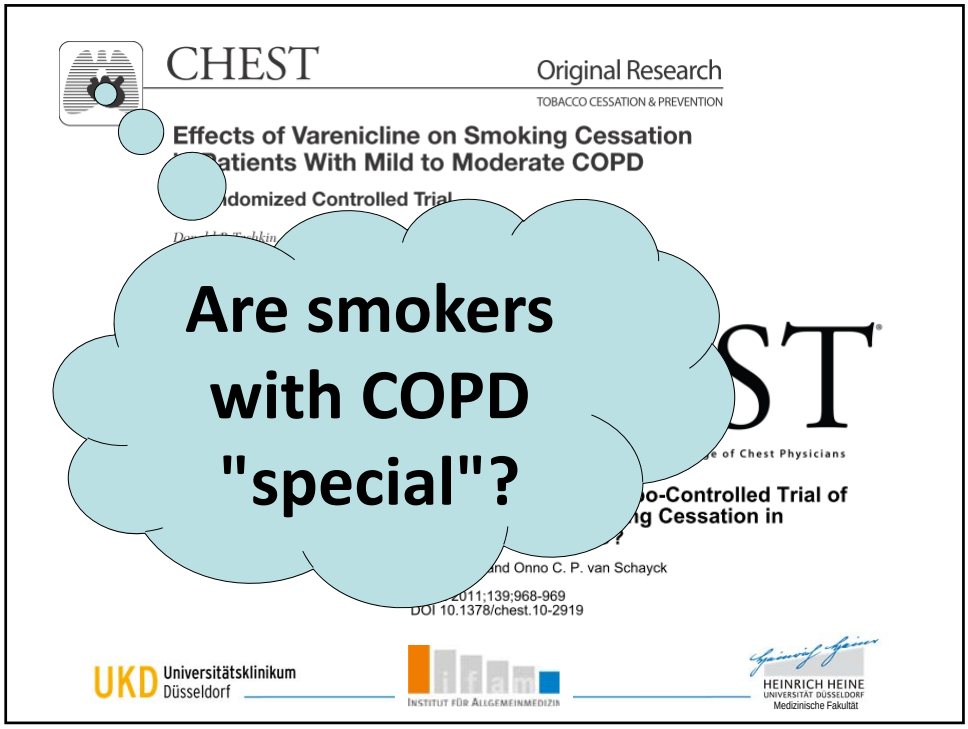
None, but DK received an unrestricted grant from Pfizer in 2009 for an investigator-initiated trial on the effectiveness of practice nurse counselling and varenicline for smoking cessation in primary care (Dutch Trial Register NTR3067).




## Tobacco as risk factor for COPD

- Tobacco smoking = most important risk factor for development and progression of COPD
  - population attributable fraction (PAF) ~85%
- Smoking cessation = only treatment to reduce accelerated decline in lung function, also ….
- … positive effect on treatment outcome, e.g., response to bronchodilators

[www.goldcopd.com; Jiménez-Ruiz, ERJ 2015]

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# COPD and quitting tobacco

Respiration

Clinical Investigations

Respiration
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**Do We Need Tailored Smoking Cessation Interventions for Smokers with COPD? A Comparative Study of Smokers with and without COPD Regarding Factors Associated with Tobacco Smoking**

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# COPD and quitting tobacco

Compared with the "general" smoking population, smokers with COPD….

- \> smoke tobacco
- \> concerned about health and risks of smoking
- = motivation to quit
- >= attempts to quit
- >= use of evidence-based quitting aids
- \> depression
- \> cigarette dependence
- < self-efficacy
- < **chance to successfully quit smoking**

[van Eerd, Respiration 2015; Shahab, Thorax 2006; Wagena, Arch Intern Med 2005; Vozoris, Resp Med 2011]

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# Difference in success rate: example from the varenicline trials

**non-COPD smokers**

week 9-12 abstinence (primary outcome)

placebo = 18%

[Jorenby, JAMA 2006; Gonzales, JAMA 2006]

**COPD smokers**

week 9-12 abstinence (primary outcome)

placebo = 9%

[Tashkin, Chest 2011]

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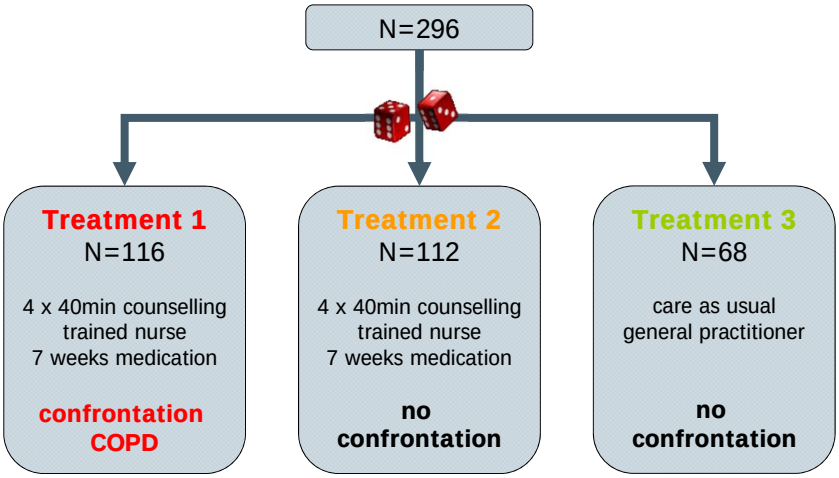
# Example: COSMO trial [Kotz, ERJ 2009] (Confroting SMOkers with COPD) trial



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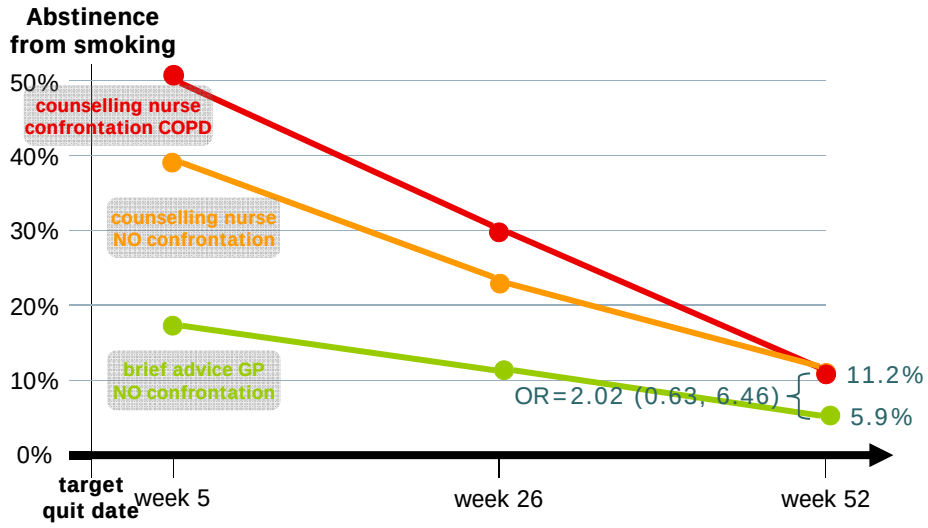
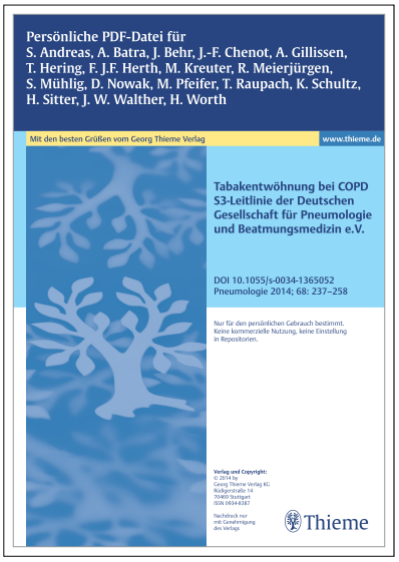
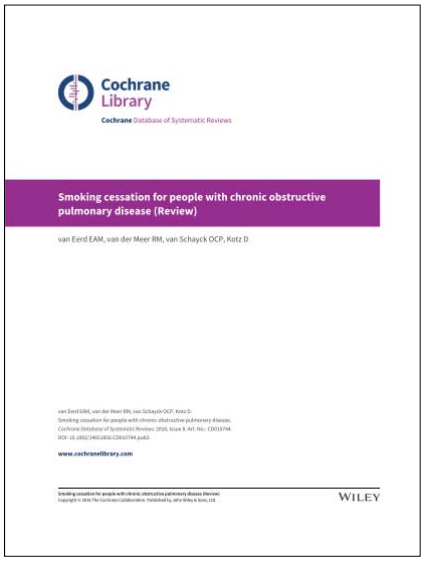



Andreas, Pneumologie 2014




van Eerd, Cochrane 2016

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## Take home message

High quality evidence that that a **combination** of **behavioural support** and **pharmacotherapy** is effective in helping smokers with COPD to quit smoking

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Cochrane Library
Cochrane Database of Systematic Reviews

## Methods

van Eerd, 2016

- Smokers with COPD
- Behavioural support and/or pharmacotherapy
- >=6 months prolonged abstinence
- Randomised controlled trials

➢ 16 RCTs

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# Main findings

Cochrane Database of Systematic Reviews
van Eerd, 2016

Only 2 recent (<10y) trials assessing intensive behavioural support vs. usual care/brief advice/no support

1. **High intensity vs. usual care** [Lou, BMC Fam Prac 2013]
   RR=25.38 (95%CI=8.03-80.22)

Methodological comments

- Chinese setting
- large study: 3,562 patients, 7 + 7 health care centres (**clustering**)
- very intensive support: weekly/monthly (at home)
  GP intervention + monthly group sessions **for 24 months**
- primary outcome: abstinence from week 24 to 30
- unclear measurement of abstinence (e.g., increase in prolonged abstinence over time)
- exceptionally high quit rates: **46 % vs. 3%**

# Main findings

Cochrane Database of Systematic Reviews
van Eerd, 2016

Only 2 recent (<10y) trials assessing intensive behavioural support vs. usual care/brief advice/no support

2. **High intensity vs. brief advice** [Chen, Exp Ther Med 2014]
   RR=2.18 (95%CI=1.05-4.09)

Methodological comments

- Chinese setting
- low sample size (N=85)
- very intensive support: face-to-face counselling by trained physicians, in person + 9 phone calls over 5 months
- primary outcome: prolonged abstinence **week 4 to month 6**
- exceptionally high quit rate: **40% vs. 19%**

# Main findings

Cochrane Library
Cochrane Database of Systematic Reviews
van Eerd, 2016

Only 4 placebo-controlled trials (5 comparisons)

- 1 **NRT sublingual tablet*** RR=2.60 (95%CI=1.29-5.24)
- 1 **varenicline*** RR=3.34 (95%CI=1.88-5.92)
- 2 **bupropion** pooled RR=2.03 (95%CI=1.26-3.28)
- 1 **nortriptyline** RR=2.54 (95%CI=0.87-7.44) N.S.

*high quality

In all studies: pharmacotherapy combined with high intensity behavioural support!

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# Main findings

Cochrane Library
Cochrane Database of Systematic Reviews
van Eerd, 2016

Only 4 placebo-controlled trials (5 comparisons)

**Pooled (N=1,429) RR=2.53 (95%CI=1.83-3.50)**

"…no convincing evidence for preferring any particular form of behavioural or pharmacological treatment."

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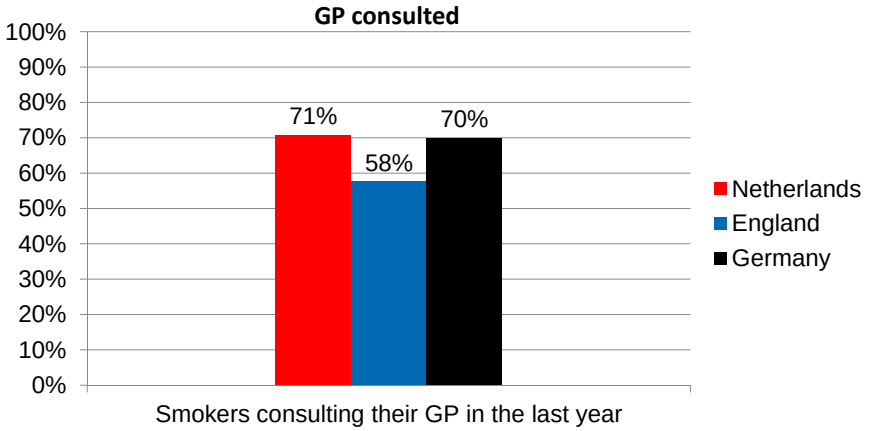
# Unfortunately…

Evidence-based guideline

Evidence-based practice

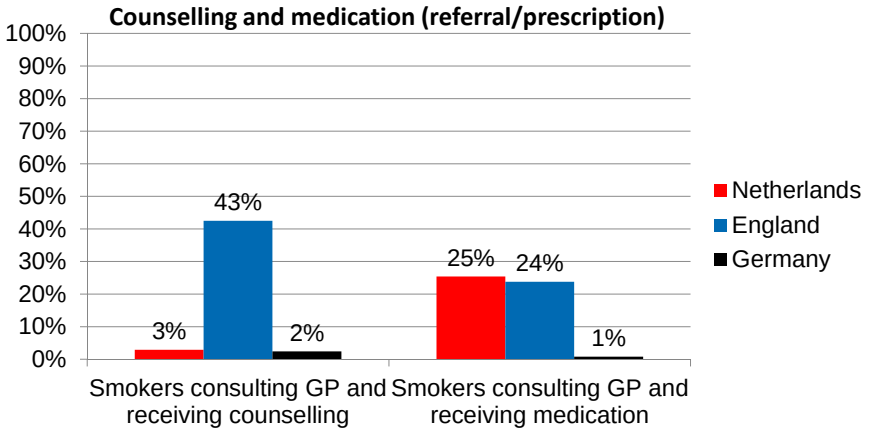
# GP performance NL vs. E vs. GER




Smokers consulting their GP in the last year

[Kotz, Eur J Gen Prac 2013; www.debra-study.info]

# GP performance NL vs. E vs. GER




[Kotz, Eur J Gen Prac 2013; www.debra-study.info]

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**Tabakentwöhnung bei COPD S3-Leitlinie der Deutschen Gesellschaft für Pneumologie und Beatmungsmedizin e.V.**

Andreas, Pneumologie 2014

**Empfehlung E3**

Allen COPD-Patienten, die ihren Tabakkonsum beenden wollen, soll eine Tabakentwöhnung mit medikamentöser und psychosozialer Unterstützung angeboten werden (▶ **Tab. 12**). ↑↑

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# Opt-in approach

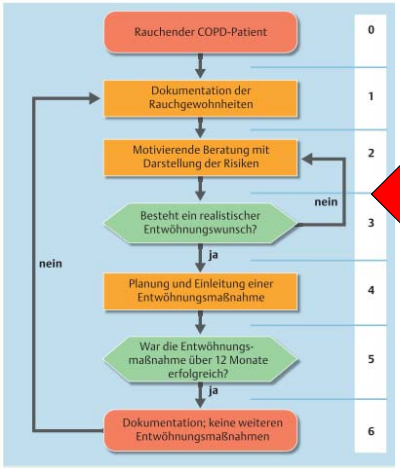


**Abb. 3** Flussdiagramm für das Management rauchender Patienten/innen mit COPD.

S3-Leitlinie Pneumologie

[Andreas, Pneumologie 2014]

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# Who is ready?

**Table 1** Baseline characteristics of included smokers ($n = 1272$)

| | Included smokers |
|---|---|
| MTSS score, % (*n*) | |
| 1: 'I don't want to stop smoking' | 18.7 (238) |
| 2: 'I think I should stop smoking but don't really want to' | 31.6 (402) |
| 3: 'I want to stop smoking but haven't thought about when' | 18.1 (230) |
| 4: 'I really want to stop smoking but I don't know when I will' | 16.3 (207) |
| 5: 'I want to stop smoking and hope to soon' | 8.6 (109) |
| 6: 'I really want to stop smoking and intend to in the next 3 months' | 3.3 (42) |
| 7: 'I really want to stop smoking and intend to in the next month' | 3.5 (44) |
| Stage of Change, % (*n*) | |
| Precontemplation | 75.0 (883) |
| Contemplation | 21.3 (251) |
| Preparation | 3.7 (43) |

[Hummel, Eur J Publ Health 2016]

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# Not ready ≠ not willing

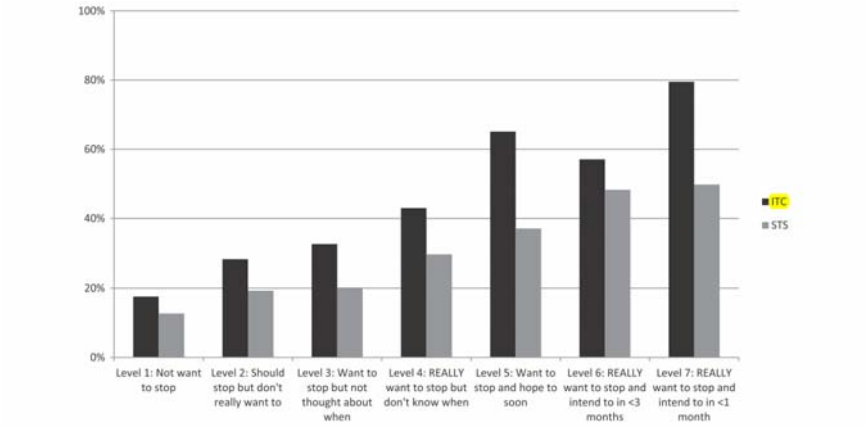


**Figure 1** Percentage of smokers who made a quit attempt in the next 12 months in the current Dutch sample [International Tobacco Control (ITC) Survey; black bars] and in the next 6 months in the initial English validation sample [Smoking Toolkit Study (STS); grey bars], stratified by MTSS score

[Hummel, Eur J Publ Health 2016]

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Addiction
SSA Society for the Study of Addiction
FOR DEBATE
doi:10.1111/add.12734

## It's time to change the default for tobacco treatment

**Kimber P. Richter[1,2] & Edward F. Ellerbeck[1,2]**

Department of Preventive Medicine and Public Health, University of Kansas Medical Center, Kansas City, Kansas, USA[1] and Kansas University Cancer Center, Kansas City, Kansas, USA[2]

[Richter, Addiction 2015]

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# Opt-in approach

- Current default = "opt-in" approach
  - default during consultation = NO treatment
  - patients often do not ask for help,
    physicians often do not pro-actively offer help
  - before offering help: physicians ask about readiness
    > provide treatment only to those ready to quit

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# Opt-out approach

- New default = "opt-out approach" [Richter, Addiction 2015]
  - offer evidence-based treatment **opportunistically to all tobacco smokers**,
    … independent of their reason of consultation
    … without screening for readiness

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# Opt-out approach

**Syst. review "opportunistic advice"** [Aveyard, Addiction 2012]

Effects on quit attempts

- compared with **no intervention**:
  - advice to quit: RR 1.24 (95%CI 1.16–1.33)
  - offering behavioural support: RR 2.17 (95%CI 1.52–3.11)
  - offering NRT: RR 1.68 (95%CI 1.48–1.89)
- compared with **advice to quit**:
  - offering behavioural support: RR 1.69 (95%CI 1.24–2.31)
  - offering NRT: 1.39 (95%CI 1.25–1.54)

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# Opt-in > opt-out approach

**Opportunities opt-out (opportunistic physician advice)**

- more effective at triggering attempts [Aveyard, Addiction 2012]
- larger target group (all smokers, irrespective of motivation)
- easier and less time consuming for physicians to apply
- as a consequence: (potentially)
  - brief advice more often applied by physicians
  - more smoking patients consulting physician attempt to quit
  - more us of evidence-based treatments to aid next attempt

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# Opt-in > opt-out approach

**Threats opt-out approach**

- what to offer opportunistically?
- needs to create impact: [Kotz, Addiction 2015; Rigotti, Arch Int Med 2011]
  - infrastructure for behavioural support
  - reimbursement of treatments [Kaper, Addiction 2005; Kaper, Addiction 2006]

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# Discussion

- COPD smokers are a special subgroup of the total smoking population; **in this subgroup…**
- Combination of intensive behavioural support and pharmacotherapy is effective
  - future research: combination brief advice + pharmacotherapy (more likely to be implemented)
- No evidence for effectiveness of single behavioural support in EU health care context
- Opt-out approach (offering treatment opportunistically) reaches more smokers

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# Discussion

**All COPD smokers should be offered a combination of behavioural support and pharmacotherapy opportunistically (opt-out)!**

To create impact, structural changes are needed in the current healthcare system

- complete reimbursement of evidence-based behavioural support and pharmacotherapy
- build nationwide network of smoking cessation clinics (similar to UK Stop Smoking Services)

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DEBRA Deutsche Befragung zum Rauchverhalten

**DEBRA symposium 30 June 2017**

Theme: tobacco smoking and e-cigarette use in Germany: findings from a new national survey (DEBRA) in an international perspective.

**Düsseldorf, 30 June 2017, 12.00-16.30h**

Keynote lecture: Prof. Robert West, University College London

**Free registration: www.debra-study.info**

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Download today's presentation at

**www.daniel-kotz.de**

**Tab. 8** Pharmakotherapie bei Tabakentwöhnung.

| Wirkstoff | Applikationsform | Dosierungen | Besonderheiten |
|---|---|---|---|
| Nikotin | Pflaster | 3 Stärken (unterschiedlich je nach Hersteller) über 16 oder 24 Stunden anwendbar | Kombinationstherapie mit anderen Nikotinersatzpräparaten möglich. UAW: Hautreaktion |
| | Kaugummi | 2 mg, 4 mg maximal 25 Stück (2 mg) bzw. 15 Stück (4 mg)/Tag | problematisch bei Zahnprothesen-Trägern 4 mg: insbesondere zur Verhinderung einer Gewichtszunahme und bei starken Rauchern (>20/Tag). UAW: Sodbrennen, Mundreizung |
| | Sublingualtablette | 2 mg maximal 30 Stück / Tag | UAW: Mundreizung |
| | Lutschtablette | 1 mg, 2 mg, 4 mg max. 30 Stück / Tag (2 mg Tbl.) | UAW: Mundreizung |
| | Inhaler | Patrone mit 10 mg 6–maximal 12 Patronen tgl. | UAW: Reizung Atemwege |
| Vareniclin | Tablette | 0,5 mg 1 × tgl. für 3 Tage 0,5 mg 2 × tgl. für 4 Tage danach Rauchstop danach 1 mg 2 × tgl. für mindestens 11 Wochen | UAW: Übelkeit, lebhafte Träume evtl. erhöhte Depressivität, erhöhte Suizidalität, evtl. erhöhtes kardiovaskuläres Risiko |
| Bupropion | Tablette | 150 mg 1 × tgl. für 7 Tage, danach Rauchstop, danach 150 mg 2 × tgl. Gesamt-Behandlungsdauer: 8 Wochen | UAW: zerebrale Krampfanfälle (Häufigkeit 1:1000), Übelkeit, Schlafstörungen |

UAW: unerwünschte Arzneimittelwirkung.
Anmerkung: Nikotin-Nasenspray ist in Deutschland nur über die internationale Apotheke erhältlich. Trotz bestehender Arzneimittel-Zulassung wurde es vom Hersteller aufgrund zu geringer Umsätze vom Markt genommen.

Andreas, Pneumologie 2014

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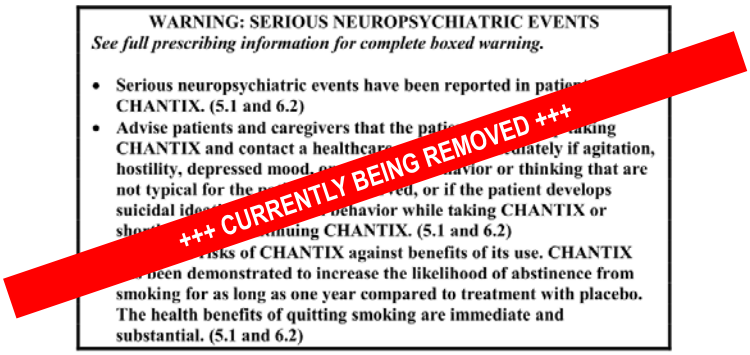
# Varenicline: safety

- FDA "black box" waring (strongest warning)



**WARNING: SERIOUS NEUROPSYCHIATRIC EVENTS**

***See full prescribing information for complete boxed warning.***

- **Serious neuropsychiatric events have been reported in patie… CHANTIX. (5.1 and 6.2)**
- **Advise patients and caregivers that the pati… taking CHANTIX and contact a healthcar… diately if agitation, hostility, depressed mood, … havior or thinking that are not typical for the p… red, or if the patient develops suicidal ide… behavior while taking CHANTIX or sho… nuing CHANTIX. (5.1 and 6.2)**

**…isks of CHANTIX against benefits of its use. CHANTIX …been demonstrated to increase the likelihood of abstinence from smoking for as long as one year compared to treatment with placebo. The health benefits of quitting smoking are immediate and substantial. (5.1 and 6.2)**



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# Findings in context

**Cardiovascular risk (in general population)**

- increased risk reported in one meta-analysis (Singh, Can Med Assoc J 2011)
- **no** increased risk in three more recent meta-analyses (Prochaska, BMJ 2012; Cahill, JAMA 2014; Sterling J Am Heart Assoc 2016)
- ... and in a network meta-analysis (Mills, Circulation 2014)
- ... and within the FDA's Mini-Sentinel Program (Toh, JAMA Intern Med 2013)

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# Findings in context

**Neuropsychiatric risk (in general population)**

- three systematic reviews / meta-analyses found **no** increased risk

  (Cahill, JAMA 2014; Hughes, Nicotine Tob Res 2015; Pfizer 2015)

- ... as did two cohort studies in CPRD regarding depression, suicidal thoughts, and self-harm (Gunnell, BMJ 2009; Thomas, BMJ 2013)
- ... and the other observational studies (Meyer, Addiction 2013; Pasternak, Addiction 2013; Buggy, Drug Safety 2013)

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Articles

## Cardiovascular and neuropsychiatric risks of varenicline: a retrospective cohort study

Daniel Katz, Wolfgang Viechtbauer, Colin Simpson, Onno C P van Schayck, Robert West, Aziz Sheikh

**Interpretation** Varenicline does not seem to be associated with an increased risk of documented cardiovascular events, depression, or self-harm when compared with NRT. Adverse events that do not come to attention of general practitioners cannot be excluded. These findings suggest an opportunity for physicians to prescribe varenicline more broadly, even for patients with comorbidities, thereby helping more smokers to quit successfully than do at present.

*Lancet Respir Med* 2015
Published Online
September 7, 2015
http://dx.doi.org/10.1016/S2213-2600(15)00320-3

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# Apply opportunistic approach

**5A approach**

- **A**sk about tobacco use
- **A**dvise to quit
- **A**ssess willingness to quit
- **A**ssist in quit attempt
- **A**rrange follow-up

[Fiore, Am J Prev Med 2008]

**ABC/3A/VBA approach**

- **A**sk about tobacco use
- give **B**rief advice how best to quit
- offer evidence-based **C**essation support
  - stop-smoking consultation
- no assessment of willingness!
  - can put patient on defensive
  - costs valuable time

[McRobbie, N Z Med J 2008; elearning.ncsct.co.uk/vba]

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Cochrane Library
Cochrane Database of Systematic Reviews

# Main findings

van Eerd, 2016

<u>Only 2 recent (<10y) trials assessing intensive behavioural support vs. usual care/brief advice/no support</u>

- 1 **"smoker's lung" vs. usual care** RR=1.98 (95%CI=0.74-5.31) (Brandt, Lancet 1997)

Methodological comments

- small sample size (N=48)
- lack of blinding
- old study (awareness of association smoking <> COPD)

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