



# Aktuelle Studien zur Gateway-Hypothese und zum Rauchstopp mittels E-Zigaretten

24. Vernetzungstreffen

Psychologische Aspekte der Tabakentwöhnung  
Neue Ergebnisse und Ansätze in der Tabakentwöhnung

3. Mai 2022

Prof. Dr. Reiner Hanewinkel

## Deklaration möglicher Interessenskonflikte

Ich habe nie Förderungen seitens der Suchtmittel- oder der pharmazeutischen Industrie angenommen.

Die eigenen Arbeiten, die ich in diesem Vortrag vorstellen werde, wurden durch das Bundesministerium für Gesundheit sowie die DAK finanziert.

## Die Gateway-Hypothese

Erste Vorstellung der **Gateway-Hypothese**  
1975 in **Science** durch Denise Kandel.

**Stufenmodell** das besagt, dass es eine  
zeitliche Abfolge des Erstkonsums von  
Drogen gibt.

Denise und ihr Mann Eric, Nobelpreisträger  
für Medizin, entwickelten die Hypothese  
weiter und publizierten neben Daten aus  
Beobachtungsstudien auch Daten zur  
**biologischen Plausibilität.**



Denise und Eric Kandel

Erste Publikation:  
Science 1975; **190**: 912-4

THE NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

SHATTUCK LECTURE

## A Molecular Basis for Nicotine as a Gateway Drug

Eric R. Kandel, M.D., and Denise B. Kandel, Ph.D.

### IMPLICATIONS FOR E-CIGARETTES

Our findings also provide initial biologic insights that may help inform the current debate about electronic e-cigarettes,<sup>27</sup> which have been promoted as a tool to stop smoking and reduce the harmful effects of combustible tobacco use in the population.<sup>28</sup> Although e-cigarettes eliminate some of the morbidity associated with combustible tobacco, they and related products are pure nicotine-delivery devices. They have the same effects on the brain as those reported here for nicotine, such as the acetylation of the *FOSB* promoter and the inhibition of HDAC, and they pose the same risk of addiction to other drugs and experiences.

Although the typical e-cigarette user has been described as a long-term smoker who is unable to stop smoking,<sup>28</sup> the use of e-cigarettes is increasing exponentially among adolescents and young adults.<sup>29</sup> Our society needs to be concerned about the effect of e-cigarettes on the brain, especially in young people, and the potential for creating a new generation of persons addicted to nicotine.<sup>29,30</sup> The effects we found in adult mice are likely to be even stronger in adolescent animals. Priming with nicotine has been shown to lead to enhanced cocaine-induced locomotor activity and increased initial self-administration of cocaine among adolescent, but not adult, rats.<sup>31,32</sup> Whether e-cigarettes will prove to be a gateway to the use of combustible cigarettes and illicit drugs is uncertain, but it is clearly a possibility.

Nicotine acts as a gateway drug on the brain, and this effect is likely to occur whether the exposure is from smoking tobacco, passive tobacco smoke, or e-cigarettes. More effective prevention programs need to be developed for all the products that contain nicotine, especially those targeting young people. Our data suggest that effective interventions would not only prevent smoking and its negative health consequences but also decrease the risk of progressing to illicit drug use and addiction.

N Engl J Med 2014;371:932-43

## Denkbare Übertragungsmechanismen



Sven Schneider

### 1. Sucht

Physische und psychische Abhängigkeit vom Nikotin

### 2. Erfahrung

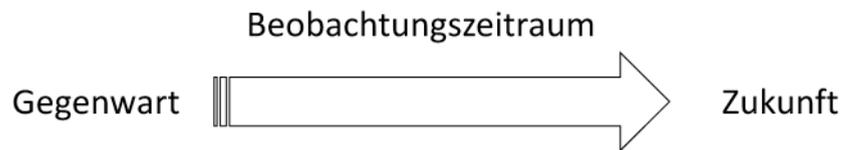
Habituelle und rituellen Vorgänge des Rauchens

### 3. Zugänglichkeit

Vertrieb über identische Verkaufsstätten

Nicotine Tob Res 2016; 18: 647-53

## Prospektive Kohortenstudie



Stichprobe:  
NIE-Raucher

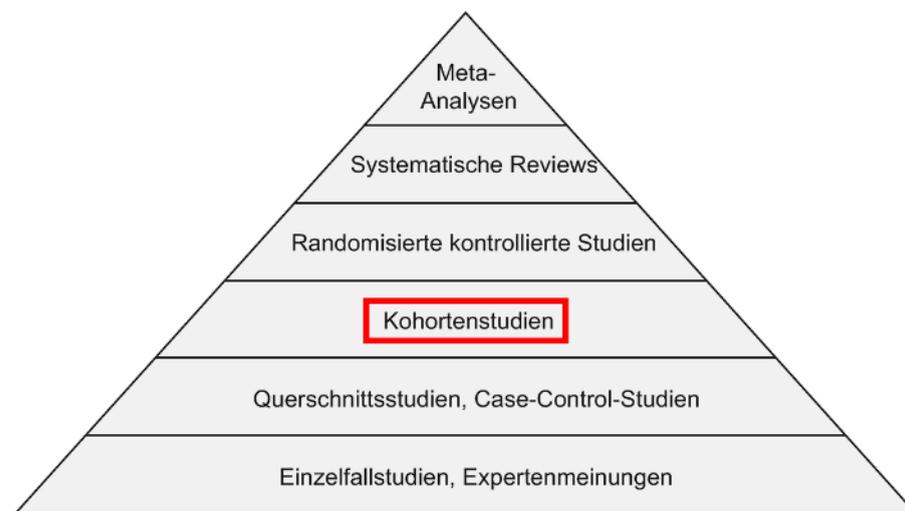
Einflussfaktoren:  
E-Zigarettenkonsum  
Soziodemografie  
Persönlichkeit  
...

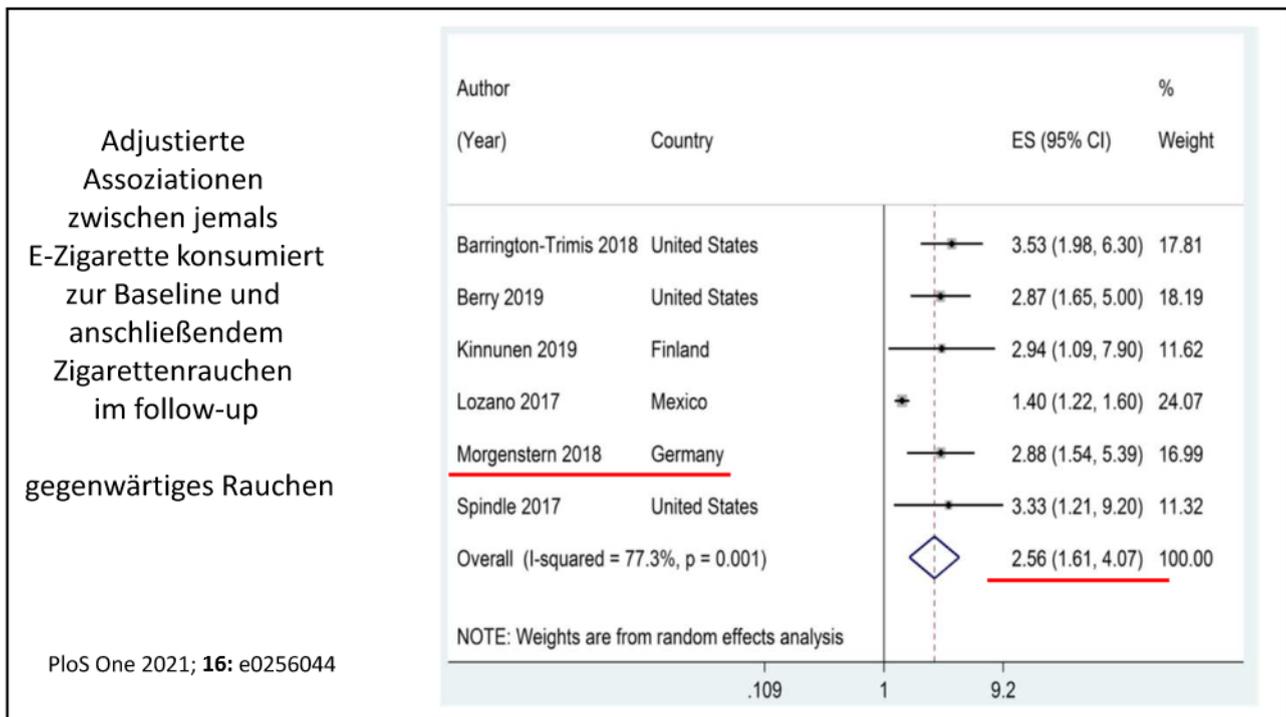
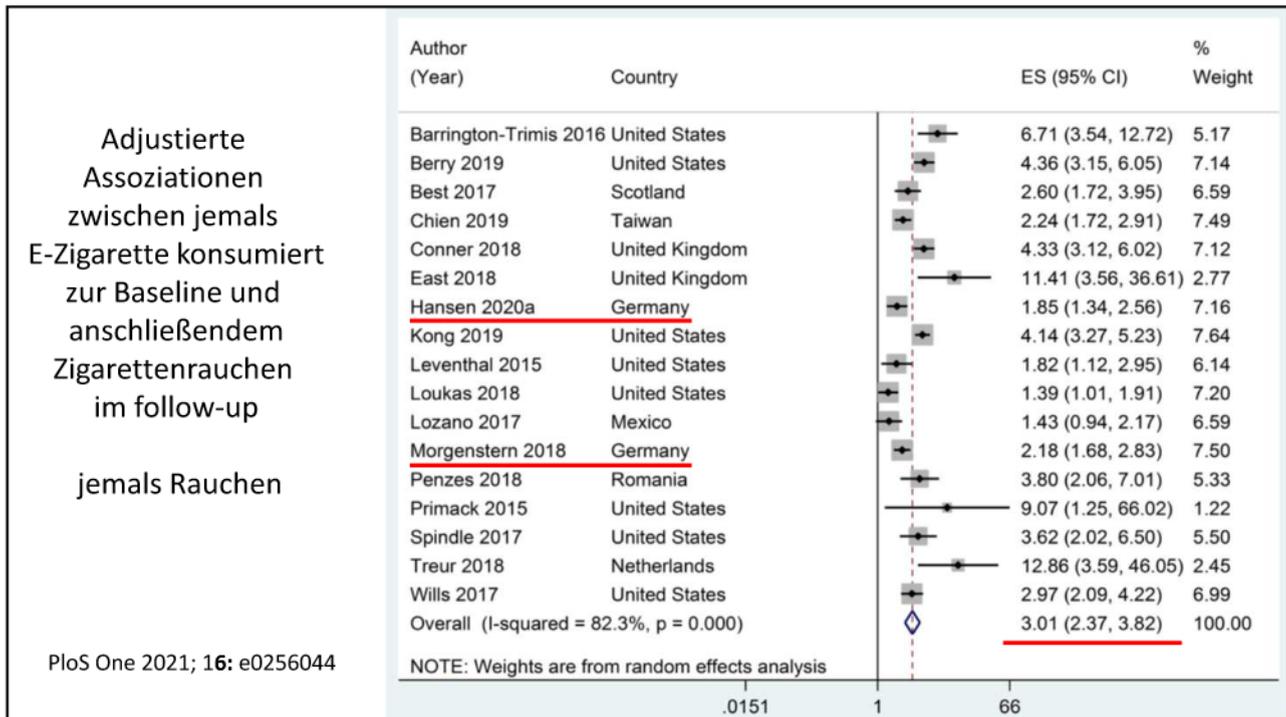


Konventionelle Zigaretten  
erstmals probiert

## Stufen wissenschaftlicher Evidenz

Kausale Aussagen allein aufgrund der Ergebnisse  
von Kohortenstudien sind nicht möglich





## Kovariaten, die statistisch kontrolliert wurden

Morgenstern et al.  
Dtsch Arztebl Int 2018; **115**: 243-8

### Studienvariable zur Baseline

#### Soziodemografie

Geschlecht weiblich

Alter > 15

Bundesland Niedersachsen

Schulart kein Gymnasium

Migrationshintergrund

Schulabschluss der Eltern

SES

#### Persönlichkeit

Sensation Seeking

Impulsivität

Angstlichkeit

Hoffnungslosigkeit

Extraversion

soziale Verträglichkeit

Gewissenhaftigkeit

Neurotizismus

Offenheit

#### Substanzkonsum

E-Zigaretten jemals

Alkohol jemals

Rauschtrinken jemals

Cannabis jemals

andere illegale Drogen jemals

## Kritische Fragen:

Weist diese Assoziation nicht lediglich auf Jugendliche hin, die ohnehin ein höheres Risiko haben, mit dem Rauchen zu beginnen?

Würden diese Jugendliche nicht früher oder später auch ohne vorherige E-Zigaretten-Erfahrung mit dem Rauchen beginnen?

=

*„common liability“-Hypothese*

*Journal of Consulting Psychology*  
1964, Vol. 28, No. 6, 477-482

## DEVELOPMENT OF A SENSATION-SEEKING SCALE <sup>1</sup>

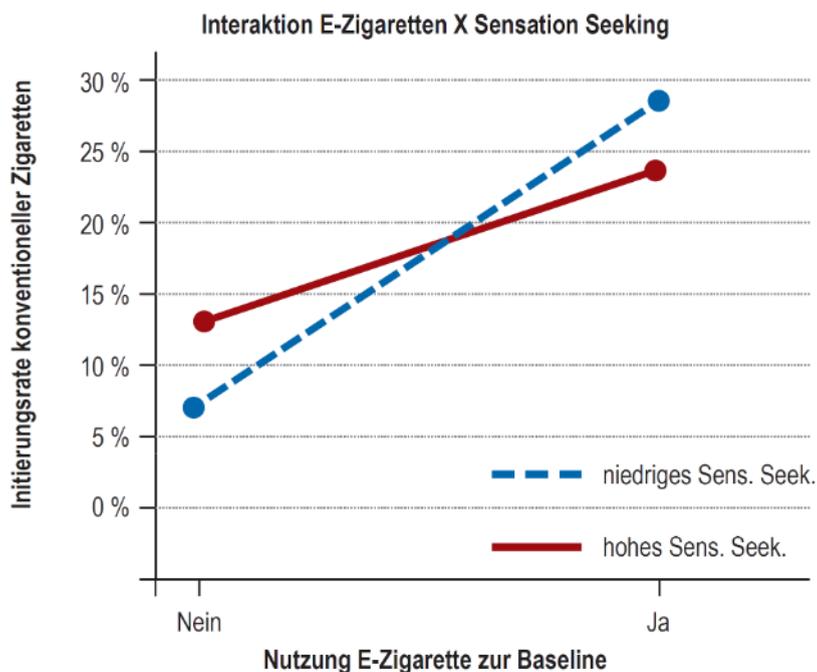
MARVIN ZUCKERMAN

*Department of Endocrinology and Reproduction, Albert Einstein Medical Center, Philadelphia*

ELIZABETH A. KOLIN, LEAH PRICE, AND INA ZOOB

*Adelphi College*

This article reports the development of a Sensation-Seeking Scale (SSS) designed to quantify the construct: "optimal stimulation level." Items were written, using the construct as a guide, and given to undergraduates. The items were factor analyzed. A general factor was found and the item-factor correlation pattern was similar in males and females. In another sample, satisfactory reliability for the SSS was obtained and it was found to be positively correlated with field independence as measured by the Embedded Figures Test. In a third sample, nonsignificant correlations between SSS and Howard's Stimulus Seeking Maze tests were found. A significant negative correlation between SSS and anxiety, as measured by the Multiple Affect Adjective Check List was obtained.





Original Investigation

## Use of Electronic Cigarettes as a Predictor of Cannabis Experimentation: A Longitudinal Study Among German Youth

Ann-Kathrin Seidel PhD<sup>1</sup>, Matthis Morgenstern PhD<sup>1</sup>, Artur Galimov MD<sup>2,\*</sup>, Anya Pedersen PhD<sup>3</sup>, Barbara Isensee PhD<sup>1</sup>, Michaela Goecke MA<sup>4</sup>, Reiner Hanewinkel PhD<sup>1,\*</sup>

<sup>1</sup>Institute for Therapy and Health Research, IFT-Nord, Kiel, Germany; <sup>2</sup>Department of Preventive Medicine, Institute for Health Promotion and Disease Prevention Research, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA; <sup>3</sup>Clinical Psychology and Psychotherapy, Department of Psychology, University of Kiel, Kiel, Germany; <sup>4</sup>Federal Centre for Health Education, Cologne, Germany

Corresponding Author: Reiner Hanewinkel, PhD, Institute for Therapy and Health Research, IFT-Nord, Harmsstr. 2, D-24114 Kiel, Germany. Telephone: +494315702920; Fax: +494315702929; E-mail: [hanewinkel@ift-nord.de](mailto:hanewinkel@ift-nord.de)



- (1) Kohortenstudien aus Asien, Europa, Nord- und Mittelamerika geben Hinweise, dass Jugendliche, die vorher E-Zigaretten probiert haben, später häufiger Tabak konsumieren.
- (2) Die signifikante Interaktion zwischen dem E-Zigarettenkonsum und dem Persönlichkeitsmerkmal „Sensation Seeking“ stützt die Annahmen der Gateway-Hypothese und widerspricht der Alternativhypothese.
- (3) Epidemiologische Beobachtungsstudien zeigen Assoziationen auf, aber keine unmittelbare Kausalität.

# E-Zigaretten als Rauchstopphilfe

The screenshot shows the homepage of the Cochrane Tobacco Addiction website. At the top, there is a navigation bar with links for 'Cochrane Library', 'Cochrane.org', and 'Admin'. The main header features the Cochrane Tobacco Addiction logo and the tagline 'Trusted evidence. Informed decisions. Better health.' A search bar is located to the right of the logo. Below the header is a blue navigation menu with links for 'About us', 'News', 'Priority setting', 'Our Reviews', 'Resources', and 'Join Cochrane'. The main content area includes a welcome message: 'Welcome to the Cochrane Tobacco Addiction Group's website'. A photograph of five team members is displayed, with a white text box overlaid on it containing the URL 'https://tobacco.cochrane.org/'. To the right of the photo is a dark blue box stating 'We are part of Cochrane Public Health and Health Systems'. Below this is a 'Tweets by @CochraneTAG' section, featuring a tweet from Gladymar Pérez Ch. (@gladymar85) announcing a Cochrane Review on pertussis vaccine in early infancy for the prevention of allergy in children, dated Sep 15, 2021.



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Our Reviews
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## Our reviews

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### Our reviews

Find a list of the topics that our reviews fall under below and navigate these to link to our reviews in the Cochrane Library:

### Our Reviews

Full list
By Subtopic
New - Updated

(Stage filter not available for Subtopic view)

**By subtopic:**

- ▶ [Interventions at the population level \(18\)](#)
- ▶ [Interventions to help smokers and other tobacco users to quit \(69\)](#)
- ▶ [Interventions to prevent tobacco use \(10\)](#)
- ▶ [Interventions to reduce harm in people who use tobacco \(5\)](#)
- ▶ [Other reviews managed by the Tobacco Addiction Group \(8\)](#)
- ▶ [The effects of quitting smoking \(2\)](#)

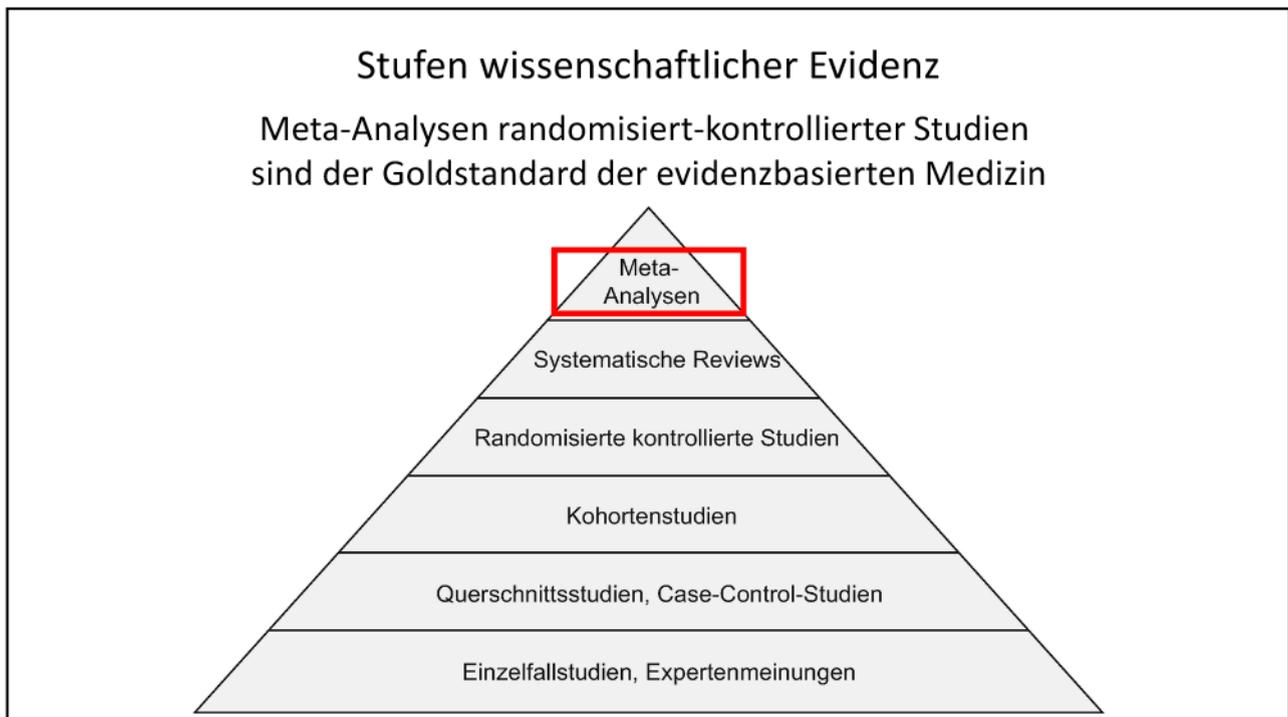
# 112 Reviews

### Related Resources

#### What is a Cochrane Review?

Cochrane Reviews investigate the effects of interventions for prevention, treatment and rehabilitation in a healthcare setting. They are designed to facilitate the choices that doctors, patients, policy makers and others face in health care.  
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Cochrane Database of Systematic Reviews | [Review - Intervention](#)

## Nicotine replacement therapy versus control for smoking cessation

✉ [Jamie Hartmann-Boyce](#), [Samantha C Chepkin](#), [Weiyu Ye](#), [Chris Bullen](#), [Tim Lancaster](#) Authors' declarations of interest

Version published: 31 May 2018 [Version history](#)

<https://doi.org/10.1002/14651858.CD000146.pub5>

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[Abstract](#)

[Plain language summary](#)

[Authors' conclusions](#)

### Hauptergebnis aus 136 Studien mit 64.640 Personen

„Es gibt qualitativ hochwertige Evidenz dafür, dass alle zugelassenen Formen der Nikotinersatztherapie... Menschen, die einen Rauchstoppversuch unternehmen, helfen können, ihre Chancen auf eine erfolgreiche Raucherentwöhnung zu erhöhen.

Nicotinersatztherapie erhöht die Rate des Aufhörens um 50 bis 60 %, unabhängig vom Setting, und es ist sehr unwahrscheinlich, dass weitere Untersuchungen unser Vertrauen in die Schätzung des Effekts ändern werden.“

## Von 100 Rauchern sind tabakfrei:

	Kontrolle	Nikotinersatz
Alle Studien	10,5	16,2 (95% KI: 15,6-16,8)
Minimale behaviorale Unterstützung	4,0	6,2 (95% KI: 6,0-6,4)
Intensive behaviorale Unterstützung	15,0	23,2 (95% KI: 22,4-24,2)

6 bis 24 Monate nach Ende der Behandlung



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Cochrane Database of Systematic Reviews | [Review - Intervention](#)

## Electronic cigarettes for smoking cessation

✉ Jamie Hartmann-Boyce, Hayden McRobbie, Ailsa R Butler, Nicola Lindson, Chris Bullen, Rachna Begh, Annika Theodoulou, Caitlin Notley, Nancy A Rigotti, Tari Turner, Thomas R Fanshawe, Peter Hajek Authors' declarations of interest

Version published: 14 September 2021 [Version history](#)

<https://doi.org/10.1002/14651858.CD010216.pub6>

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### Abstract

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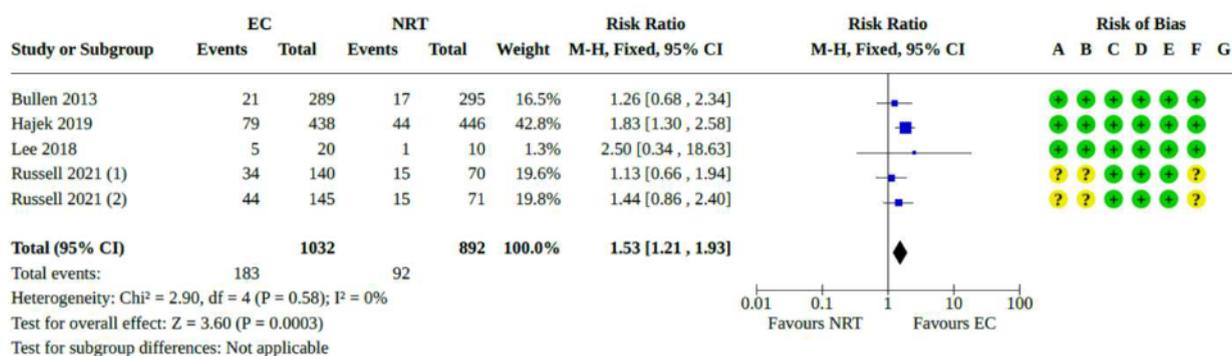
## Vergleich: E-Zigarette vs. Nikotinersatz (September 2021)

4 Studien

1.924 Personen

Katamnese: 6 bis 12 Monate nach Ende der Behandlung

### Analysis 1.1. Comparison 1: Nicotine EC versus NRT, Outcome 1: Smoking cessation



### Von 100 Rauchern sind tabakfrei:

*Cochrane-Review vom April 2021 (3 Studien)*

Nikotinersatz

6

E-Zigarette

10 (95% KI: 8-14)

*Cochrane-Review vom September 2021 (4 Studien)*

Nikotinersatz

6

E-Zigarette

9 (95% KI: 7-12)

6 bis 12 Monate nach Ende der Behandlung



WAIT A  
MINUTE

Wurden seit Einführung der E-Zigarette vor etwa  
15 Jahren weltweit tatsächlich lediglich vier  
randomisiert-kontrollierte Studien zu dieser  
Fragestellung publiziert?

Wirklich nur alle drei bis vier Jahre eine Studie?

*Das ist korrekt.*

Stimmt es, dass eine dieser vier Studien lediglich als Abstract einer Tagungspräsentation vorliegt?

*Stimmt.*

**Russell 2021** *{published and unpublished data}*

Russell C, McKeganey N, Katsampouris E, Satchwell A, Haseen F. A randomised community-based trial of a closed-system pod e-vapour product and nicotine replacement therapy for cigarette abstinence and reduction. Society for Research on Nicotine and Tobacco (SRNT) 2021 Annual Meeting February 24-27 2021 virtual:PH-353 p230.

Ist die Aufnahme eines Konferenzvortrags in ein Cochrane-Review problematisch?

*Ich persönlich finde ja, da...*

- (1) ein Abstract nur wenige Hundert Wörter umfasst und dieser Umfang nicht ausreicht, um die Arbeit bewerten zu können.*
- (2) bislang kein rigoroses peer review stattfand, dem entscheidenden Instrument der Qualitätssicherung in der Biomedizin.*

**PH-353****A RANDOMISED COMMUNITY-BASED TRIAL OF A CLOSED-SYSTEM POD E-VAPOUR PRODUCT AND NICOTINE REPLACEMENT THERAPY FOR CIGARETTE ABSTINENCE AND REDUCTION**

Christopher Russell, Neil McKeganey, Evangelos Katsampouris, Alex Satchwell, Farhana Haseen, Centre for Substance Use Research, Glasgow, United Kingdom.

**Significance:** E-cigarettes are the most commonly used method of quitting smoking in the United Kingdom. This study assessed the effectiveness of a closed-system pod e-vapour product and nicotine replacement therapy for reducing and replacing conventional cigarettes. **Methods:** Established daily cigarette smokers aged 18 years and older were recruited in London, United Kingdom and randomised to receive a three-month free provision of either (i) over-the-counter nicotine replacement therapies (NRTs); or (ii) a closed system pod e-vapour product (*myblu*<sup>TM</sup>) containing either nicotine salt e-liquid pods (NSPs) or (iii) freebase nicotine e-liquid pods (FBNPs). Participants in each of the two e-cigarette groups were given a primary device, a backup device, and reimbursement for retail purchases of up to 12 e-liquid pods (six packs of x2 pods) per month for three months. Participants were encouraged to use their assigned e-vapour product and to choose and change flavours and nicotine concentrations of their assigned e-liquid pods as they wished. Online surveys administered at study enrolment and then at one, two, three, and six-months post-enrolment assessed self-reported past 30-day consumption of conventional cigarettes and use of NRTs and assigned e-vapour products. Participants who were lost-to-follow-up were considered to be smoking at the level indicated at study enrolment. **Results:** A total of 426 participants were randomised and completed the enrolment assessment. The six-month retention rate was 85.8% in the NRT group, 85.5% in the *myblu* plus NSPs group, and 73.6% in the *myblu* plus FBNPs group. The six-month past 30-day cigarette abstinence rate was 21.3% in the NRT group (30 of 141 participants), 30.3% in the *myblu* plus NSPs group (44 of 145 participants), and 24.3% in the *myblu* plus FBNPs group (34 of 140 participants). Among participants who were not abstinent at six-months, total past 30-day cigarette consumption at six-months was significantly lower than at study enrolment in all three groups, with the magnitude of reduction observed to be comparable across groups (NRT group,  $n = 111$ ,  $M = 174.1$  fewer cigarettes pp/p.m,  $SE = 19.1$ ; *myblu* plus NSPs group,  $n = 101$ ,  $M = 156.3$  fewer cigarettes pp/p.m,  $SE = 19.9$ ; *myblu* + FBNPs group,  $n = 106$ ,  $M = 140.3$  fewer cigarettes pp/p.m,  $SE = 19.4$ ). **Conclusions:** The *myblu* pod e-vapour product was at least as effective as nicotine replacement therapy for yielding cigarette abstinence among adult established daily smokers, and a significant reduction in cigarette consumption among those who did not achieve abstinence.

FUNDING: E-cigarette/Alternative nicotine products industry

**Editorial****Journal policy on research funded by the tobacco industry**

Fiona Godlee, Ruth Malone, Adam Timmis, Catherine Otto, Andrew Bush, Ian Pavord, Trish Groves

As editors of the *BMJ*, *Heart*, *Thorax* and *BMJ Open*, we have decided that the journals will no longer consider for publication any study that is partly or wholly funded by the tobacco industry. Our new policy is consistent with those of other journals including *PLoS Medicine*, *PLoS One*, *PLoS Biology*;<sup>1</sup> *Journal of Health Psychology*;<sup>2</sup> journals published by the American Thoracic Society;<sup>3</sup> and the *BMJ's* own *Tobacco Control*.<sup>4</sup>

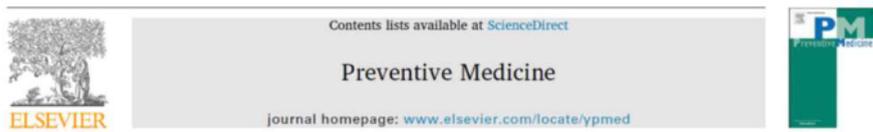
BMJ Dezember 2013

## Financial Conflicts of Interest and Stance on Tobacco Harm Reduction: A Systematic Review

Am J Pub Health 2019; **109**: e1-e8

Yogi H. Hendlin, PhD, Manali Vora, BDS, MPH, Jesse Elias, MA, and Pamela M. Ling, MD, MPH

Preventive Medicine 119 (2019) 124–131



Review Article

A conflict of interest is strongly associated with tobacco industry–favourable results, indicating no harm of e-cigarettes

Charlotta Pisinger<sup>a,b,\*</sup>, Nina Godtfredsen<sup>c,d</sup>, Anne Mette Bender<sup>e</sup>

<sup>a</sup> Center for Clinical Research and Prevention, Bispebjerg and Frederiksberg Hospital, The Capital Region of Denmark, Hovedvejen, Entrance 5, Nordre Fasanvej 57, DK-2000 Frederiksberg, Denmark

<sup>b</sup> University of Copenhagen, Faculty of Health Sciences, Department of Public Health, Denmark

<sup>c</sup> Department of Pulmonary Medicine, Hvidovre University Hospital, Hvidovre, Denmark

<sup>d</sup> Institute of Clinical Medicine, University of Copenhagen, Denmark

<sup>e</sup> University of Copenhagen, Faculty of Health Sciences, Department of Public Health, Section of Social Medicine, Denmark



Stimmt es, dass von den vier Studien lediglich eine einzige einen signifikanten Unterschied der Interventionen nahelegt?

*Auch dies ist zutreffend.*

### Analysis 1.1. Comparison 1: Nicotine EC versus NRT, Outcome 1: Smoking cessation



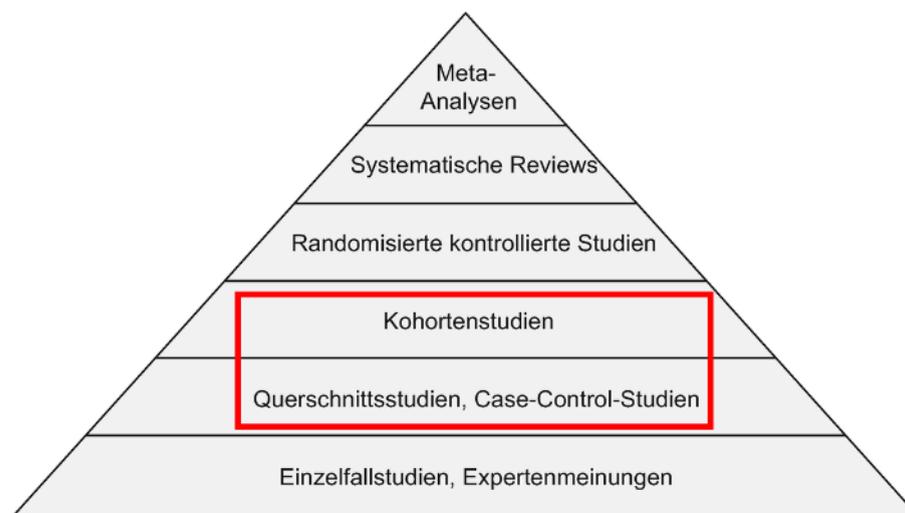
### Kritische Punkte der Hajek 2019 Studie

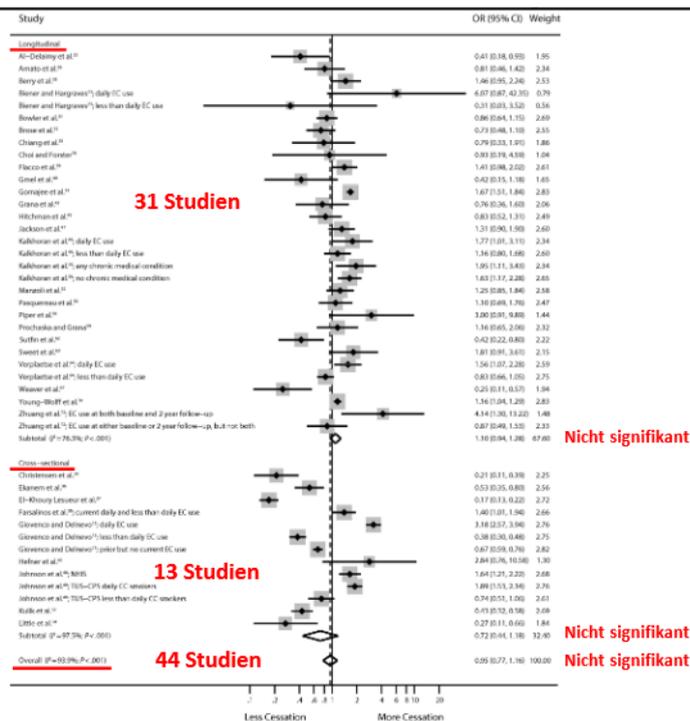
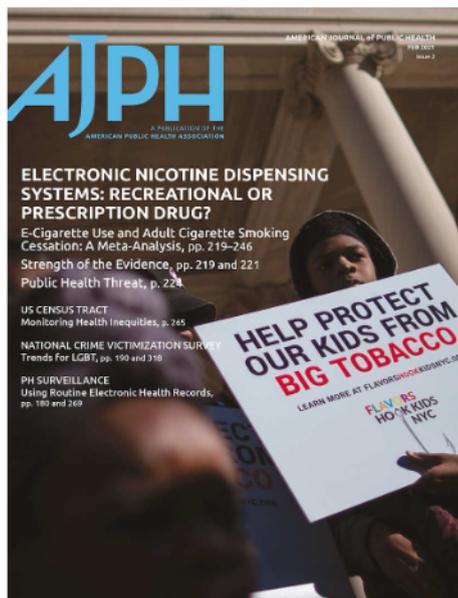
- (1) 75% der Teilnehmer hatte schon vor Studienbeginn vergeblich versucht, sich mit Hilfe von NRT das Rauchen abzugewöhnen.
- (2) Iatrogener Effekt größer als therapeutischer Effekt: 18% der E-Zigaretten-Gruppe stellte das Rauchen ein, aber 25% initiierte Dual Use.

NEJM 2019; 380: 1973

Kommen Beobachtungsstudien  
zu einem anderen Ergebnis?

Zur Erinnerung





Wie ist es um die Nikotinabstizienz bestellt?



## E-cigarettes and nicotine abstinence: a meta-analysis of randomised controlled trials

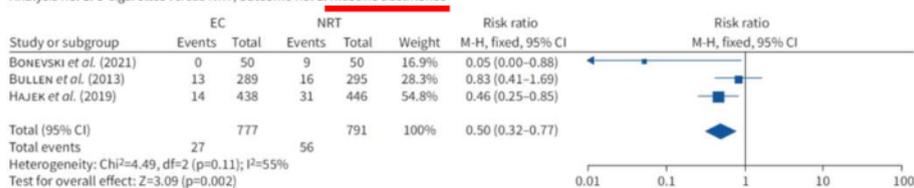
Reiner Hanewinkel <sup>1</sup>, Kathrin Niederberger<sup>2,3</sup>, Anya Pedersen <sup>2</sup>, Jennifer B. Unger <sup>4</sup> and Artur Galimov <sup>4</sup>

<sup>1</sup>Institute of Therapy and Health Research, IFT-Nord, Kiel, Germany. <sup>2</sup>Clinical Psychology and Psychotherapy, Dept of Psychology, Kiel University, Kiel, Germany. <sup>3</sup>Institute of Medical Psychology and Medical Sociology, University Medical Center Schleswig-Holstein, Kiel University, Kiel, Germany. <sup>4</sup>Institute for Health Promotion and Disease Prevention Research, Dept of Population and Public Health Sciences, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA.

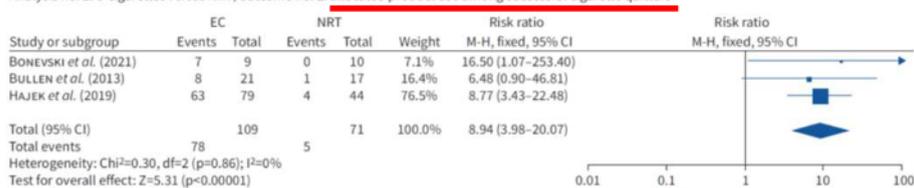
Corresponding Author: Reiner Hanewinkel (hanewinkel@ift-nord.de)

Eur Respir Rev 2022; 31: 210215

### Analysis no. 1: e-cigarettes versus NRT; outcome no. 1: nicotine abstinence



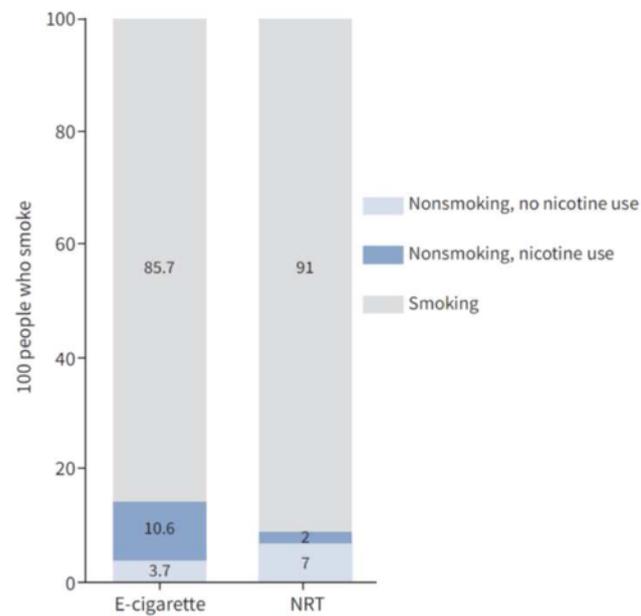
### Analysis no. 2: e-cigarettes versus NRT; outcome no. 2: allocated product use among successful cigarette quitters



### Analysis no. 3: e-cigarettes versus NRT; outcome no. 3: smoking cessation



## Antizipierte absolute Effekte



MEDIZIN

Originalarbeit

## Effektivität von E-Zigaretten bei der Tabakentwöhnung

Ein Vergleich mit Nikotinersatztherapie und keiner Nutzung evidenzbasierter Unterstützung in der deutschen Bevölkerung

Daniel Kotz, Sarah Jackson, Jamie Brown, Sabrina Kastaun

	E-Zigarette	Nikotinersatz	
Tabakfrei	15,6% (17 von 109)	13,8% (12 von 87)	nicht signifikant
Nikotinfrei	5,5% (6 von 109)		
Dual Use	19,3% (21 von 109)		

# Wie viele Personen schaffen es ohne Hilfsmittel, den Nikotinkonsum einzustellen?



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## Physician advice for smoking cessation

✉ [Lindsay F Stead](#), [Diana Buitrago](#), [Nataly Preciado](#), [Guillermo Sanchez](#),  
[Jamie Hartmann-Boyce](#), [Tim Lancaster](#) Authors' declarations of interest

Version published: 31 May 2013 [Version history](#)

<https://doi.org/10.1002/14651858.CD000165.pub4>

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### Abstract

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### Background

Healthcare professionals frequently advise people to improve their health

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[Am score](#) 82      **Used in 44 guidelines**

---

**Abstract**

[Plain language summary](#)

[Authors' conclusions](#)

[Background](#)

[Objectives](#)

### Von 100 Rauchern sind nikotinfrei:

Ohne Hilfsmittel	2-3
Kurzer ärztlicher Ratschlag	4-6

42 RCTs  
31.000 Raucher  
Mindestens 6 Monate nach Ende der Behandlung



### Von 100 Rauchern sind nikotinfrei:

Ohne Hilfsmittel	2-3
E-Zigarette	3-4
Kurzer ärztlicher Ratschlag	4-6
Nikotinersatz	6-7
Nikotinersatz <u>plus</u> intensive behaviorale Unterstützung	20-22

Mindestens 6 Monate nach Ende der Behandlung



- (1) 44 Beobachtungsstudien sprechen insgesamt nicht für die Wirksamkeit der E-Zigarette als Rauchstopphilfe.
- (2) Lediglich 4 RCTs wurden bislang publiziert.
- (3) Ein einziges RCT deutet eine Überlegenheit der E-Zigarette an.
- (4) Dieses singuläre Ergebnis konnte bislang nicht repliziert werden.
- (5) Definiert man Suchtfreiheit als primären Endpunkt der RCTs, ist die E-Zigarette der Nikotinersatztherapie signifikant unterlegen und unterscheidet sich nicht von der Nikotinentwöhnung ohne Hilfsmittel.
- (6) Aufgrund der geringen Anzahl an Studien ist diese Einschätzung lediglich moderat-sicher.

*Danke*  
für Ihre Aufmerksamkeit!

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