



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,²⁷ which have been promoted as a tool to stop smoking and reduce the harmful effects of combustible tobacco use in the population.²⁸ 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,²⁸ the use of e-cigarettes is increasing exponentially among adolescents and young adults.²⁹ 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.^{29,30} 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.^{31,32} 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

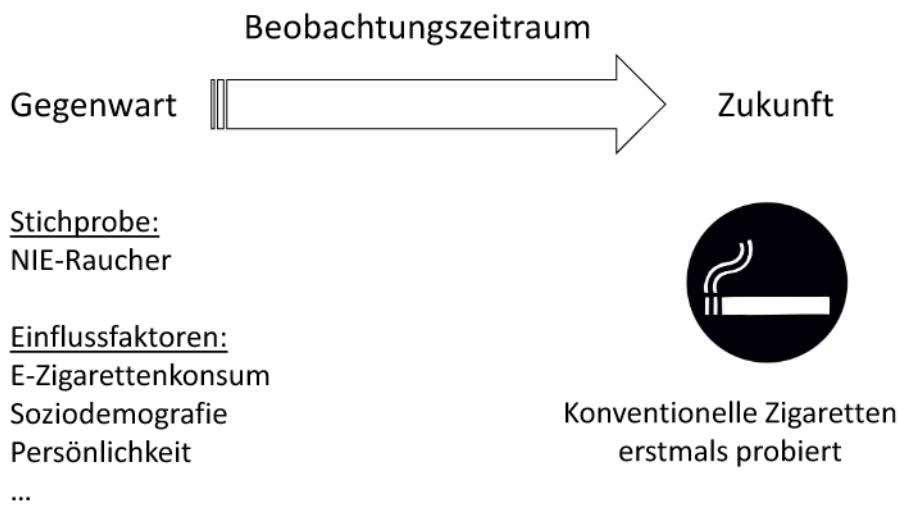
1. Sucht
Physische und psychische Abhängigkeit vom Nikotin

2. Erfahrung
Habituelle und rituellen Vorgänge des Rauchens

3. Zugänglichkeit
Vertrieb über identische Verkaufsstätten

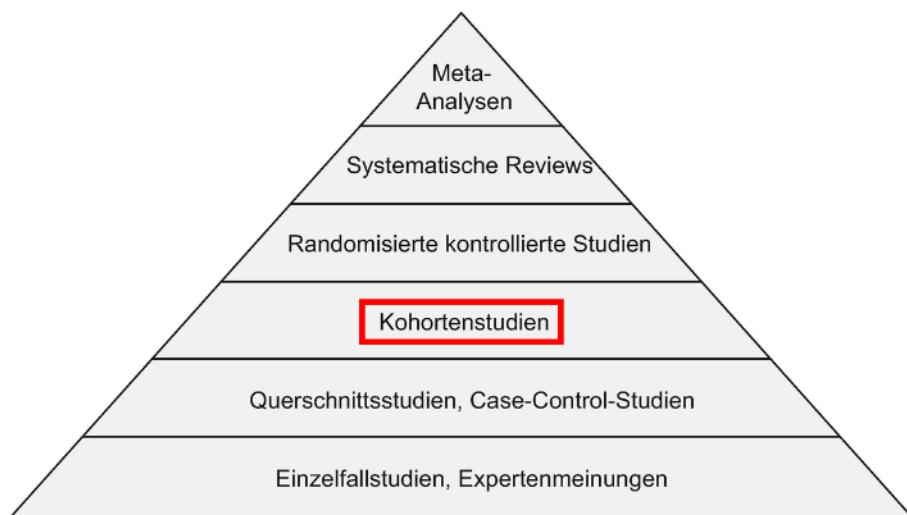
Nicotine Tob Res 2016; 18: 647-53

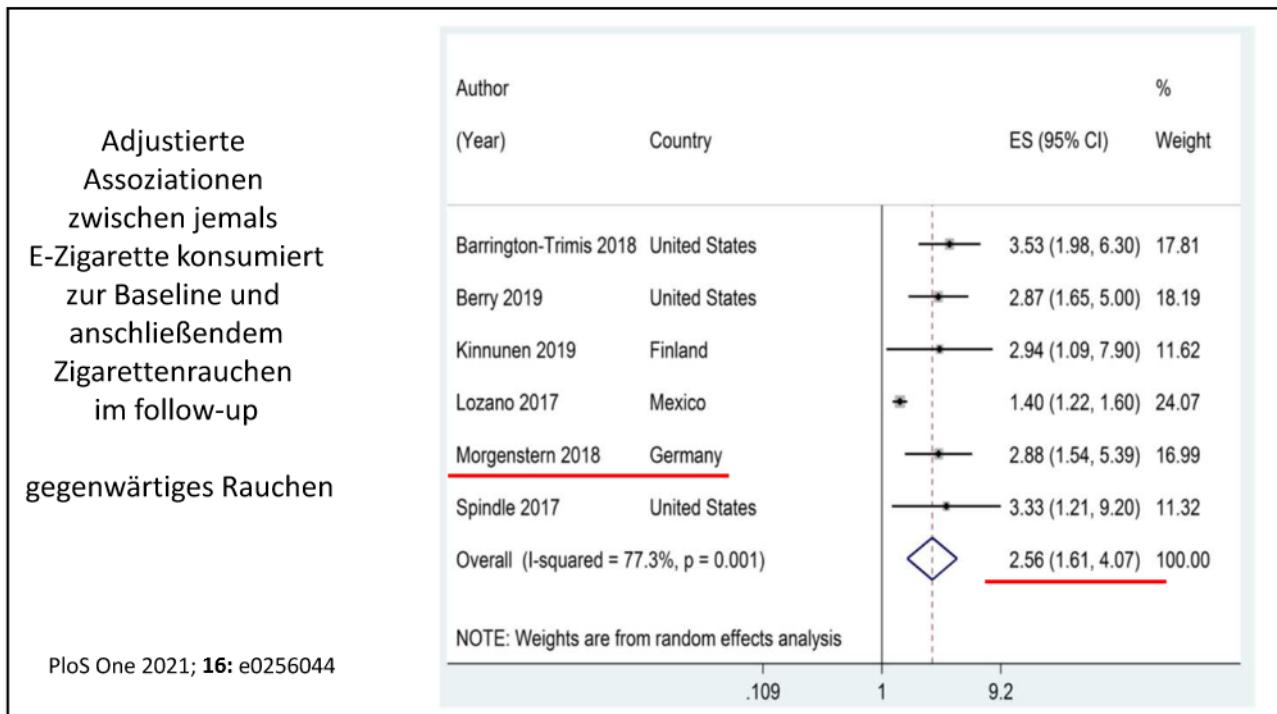
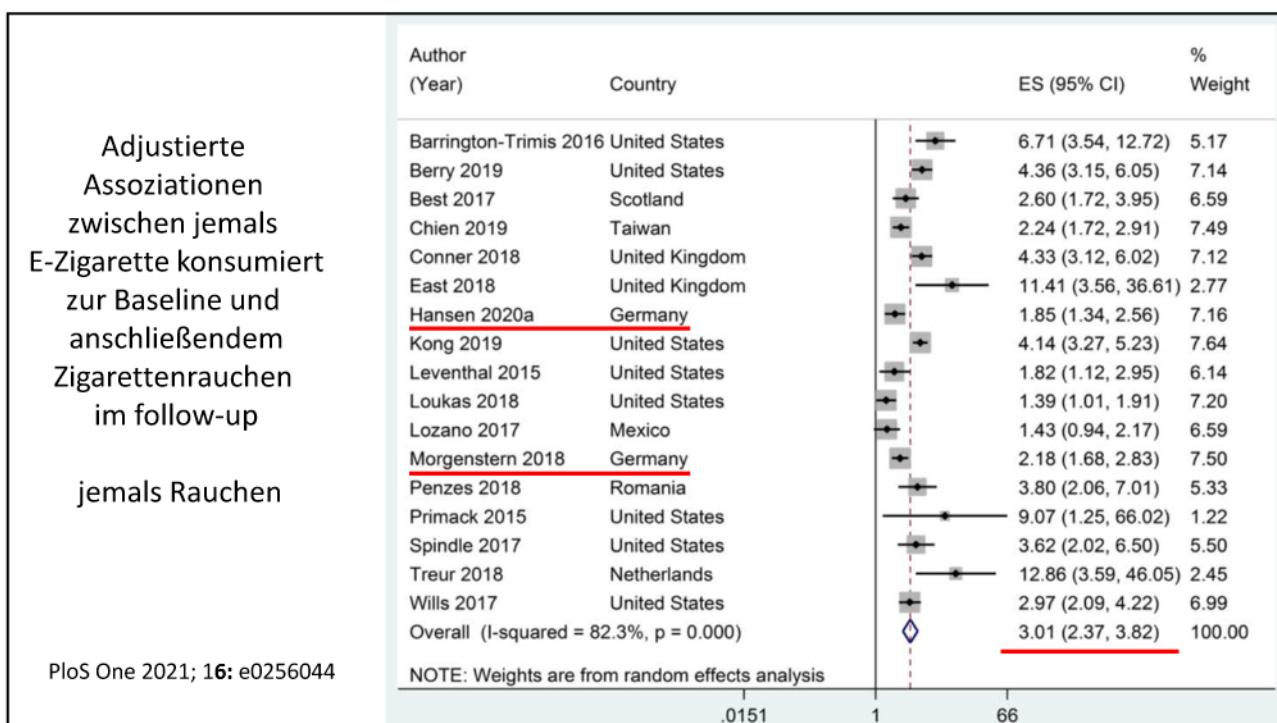
Prospektive Kohortenstudie



Stufen wissenschaftlicher Evidenz

Kausale Aussagen allein aufgrund der Ergebnisse von Kohortenstudien sind nicht möglich





**Kovariaten,
die statistisch kontrolliert wurden**

Morgenstern et al.
Dtsch Arztbl 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
Ängstlichkeit
Hoffnungslosigkeit
Extraversion
soziale Vertraglichkeit
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 SCALE¹

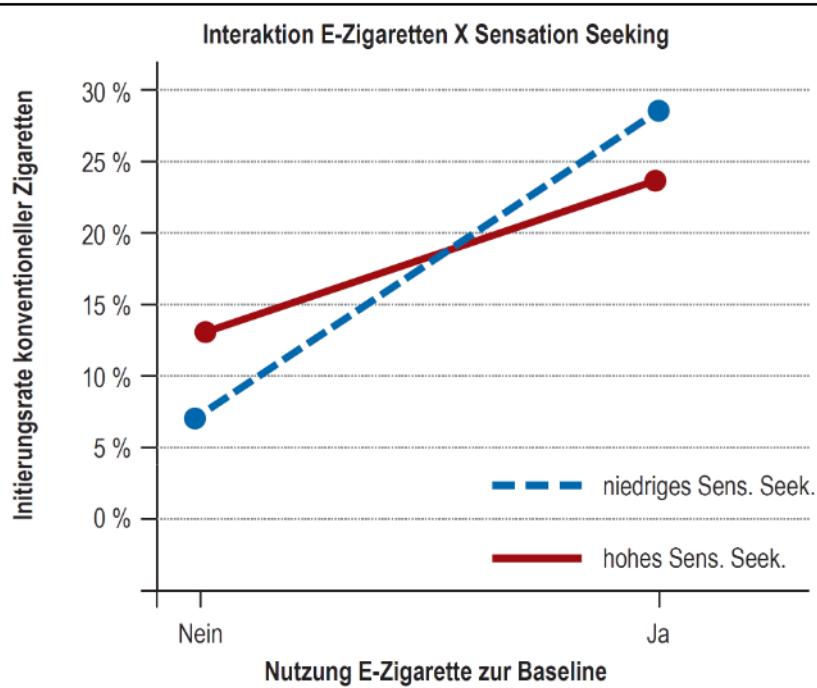
MARVIN ZUCKERMAN

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.



Nicotine & Tobacco Research, 2022, 366–371<https://doi.org/10.1093/ntr/ntab166>

Original Investigation

Received December 14, 2020; Editorial Decision August 6, 2021; Accepted August 10, 2021



Original Investigation

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

Ann-Kathrin Seidel PhD¹, Matthias Morgenstern PhD¹, Artur Galimov MD^{2,✉}, Anya Pedersen PhD³, Barbara Isensee PhD¹, Michaela Goecke MA⁴, Reiner Hanewinkel PhD^{1,✉}

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

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- (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 Rauchstopp hilfe

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Our Cochrane Review is out! 😊
cochranelibrary.com/cdsr/doi/10.10...

Whole-cell pertussis vaccine in early infancy for the prevention of allergy in children
Cochrane Review, Jennifer Rawley, Christopher G. Doherty, James Vistis, Elizabeth Peat, Schmid, Pruzek-Rosicka
Last published: 06 December 2014. © 2014 The Authors. Cochrane Database of Systematic Reviews Ltd. Published by John Wiley & Sons, Ltd.

Sep 15, 2021

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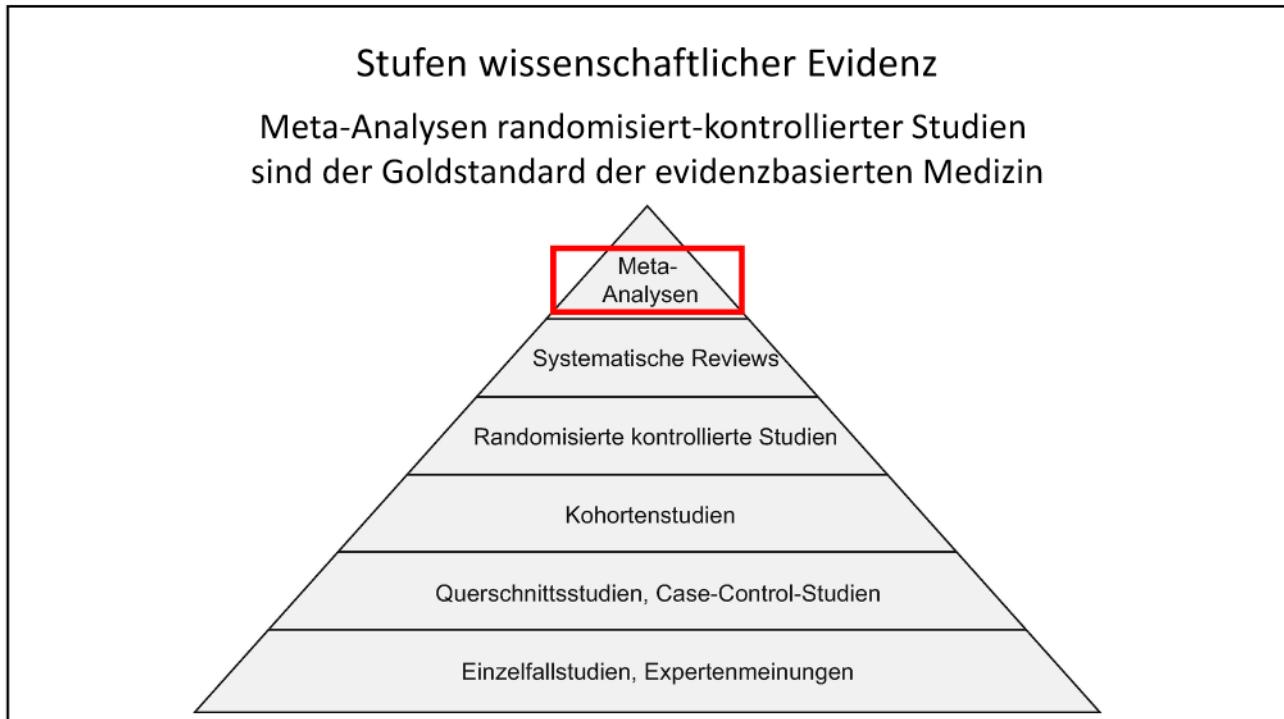
(Stage filter not available for Subtopic view)

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- ▷ [Interventions to prevent tobacco use \(10\)](#)
- ▷ [Interventions to reduce harm in people who use tobacco \(5\)](#)
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112 Reviews

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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

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Background

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Abstract

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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.

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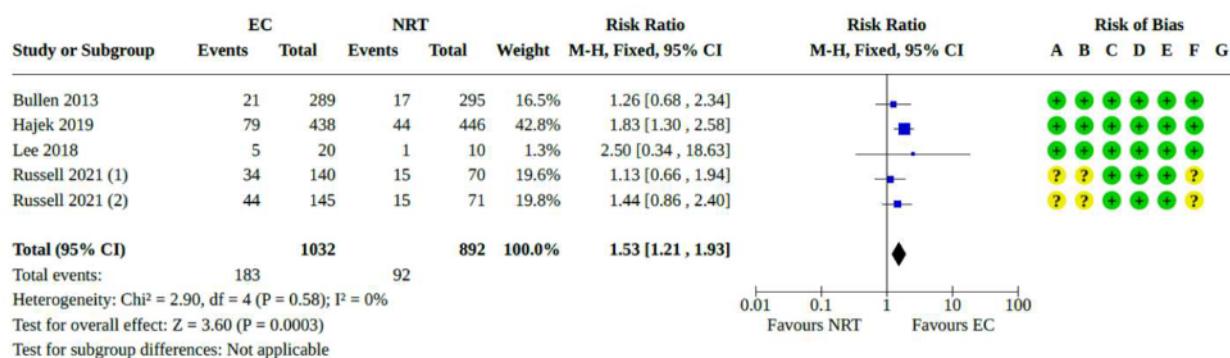
Vergleich: E-Zigarette vs. Nikotinersatz (September 2021)

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*TM) 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/pm, SE = 19.1; *myblu* plus NSPs group, n = 101, M = 156.3 fewer cigarettes pp/pm, SE = 19.9; *myblu* + FBNPs group, n = 106, M = 140.3 fewer cigarettes pp/pm, 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*,¹ *Journal of Health Psychology*,² journals published by the American Thoracic Society,³ and the *BMJ*'s own *Tobacco Control*.⁴

BMJ Dezember 2013

AJPH OPEN-THEMED RESEARCH

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



Contents lists available at ScienceDirect
Preventive Medicine
journal homepage: www.elsevier.com/locate/ypmed



Review Article

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



Charlotta Pisinger^{a,b,*}, Nina Godtfredsen^{c,d}, Anne Mette Bender^e

^a Center for Clinical Research and Prevention, Bispebjerg and Frederiksberg Hospital, The Capital Region of Denmark, Hovedvejen, Entrance 5, Nørre Fasanvej 57, DK-2000 Frederiksberg, Denmark

^b University of Copenhagen, Faculty of Health Sciences, Department of Public Health, Denmark

^c Department of Pulmonary Medicine, Hvidovre University Hospital, Hvidovre, Denmark

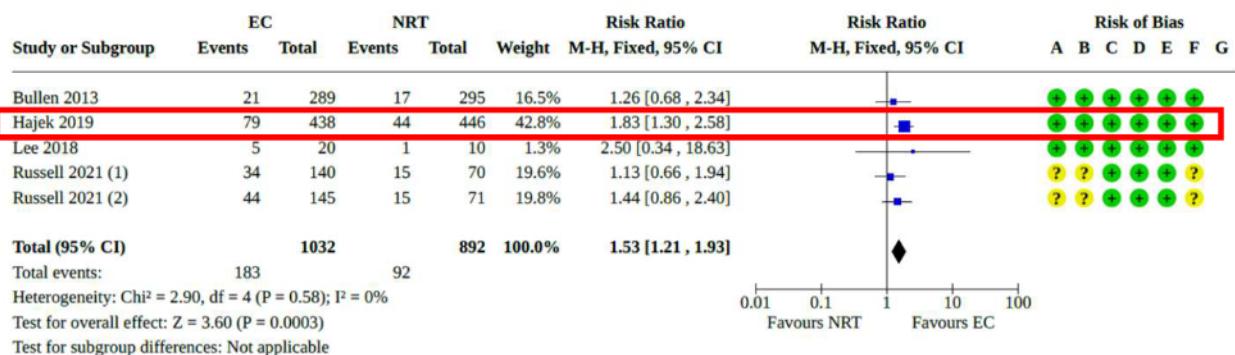
^d Institute of Clinical Medicine, University of Copenhagen, Denmark

^e 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



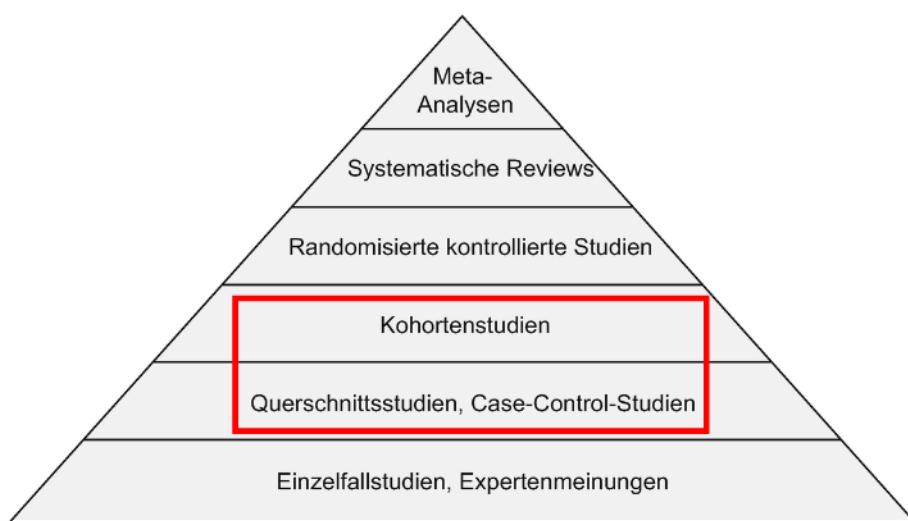
Kritische Punkte der Hajek 2019 Studie

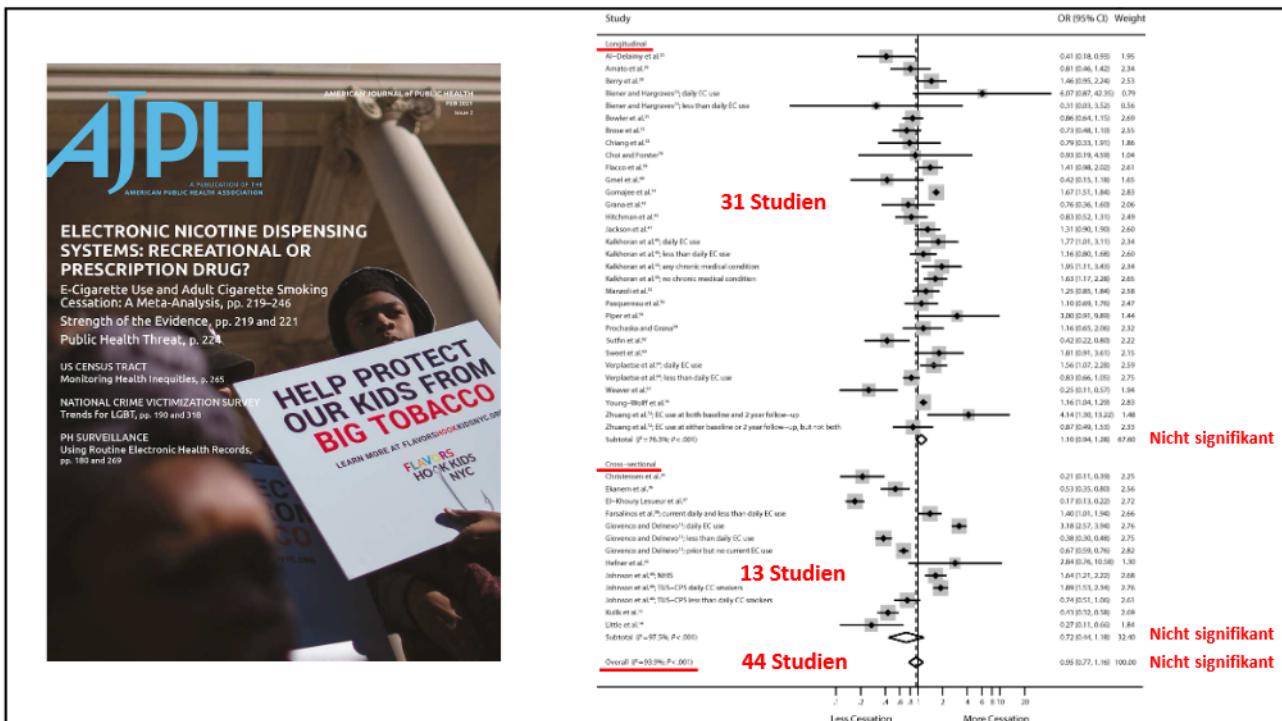
- (1) *75% der Teilnehmer hatte schon vor Studienbeginn vergeblich versucht, sich mit Hilfe von NRT das Rauchen abzugewöhnen.*
- (2) *Iatrogener Effekt größer als therapeutischer Effekt: 18% der E-Zigaretten-Gruppe stellte das Rauchen ein, aber 25% initiierte Dual Use.*

NEJM 2019; 380: 1973

Kommen Beobachtungsstudien zu einem anderen Ergebnis?

Zur Erinnerung





Wie ist es um die Nikotinabstinenz bestellt?



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

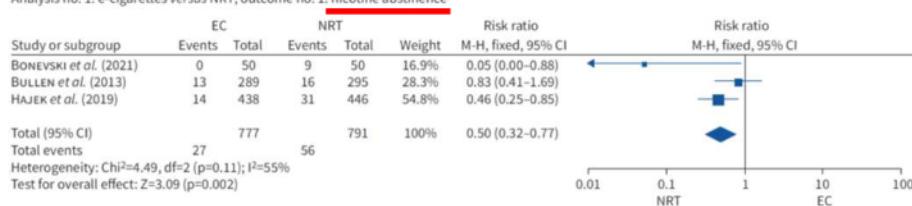
Reiner Hanewinkel ¹, Kathrin Niederberger ^{2,3}, Anya Pedersen ², Jennifer B. Unger ⁴ and Artur Galimov ⁴

¹Institute of Therapy and Health Research, IFT-Nord, Kiel, Germany. ²Clinical Psychology and Psychotherapy, Dept of Psychology, Kiel University, Kiel, Germany. ³Institute of Medical Psychology and Medical Sociology, University Medical Center Schleswig-Holstein, Kiel University, Kiel, Germany. ⁴Institute 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.

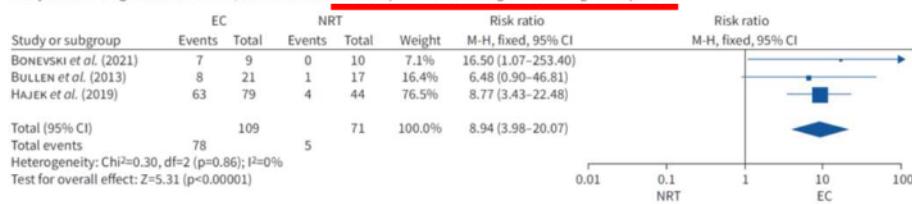
Corresponding Author: Reiner Hanewinkel (hanewinkel@ift-nord.de)

Eur Respir Rev 2022; 31: 210215

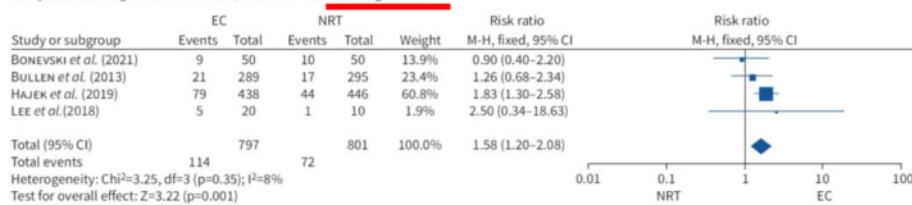
Analysis no. 1: e-cigarettes versus NRT; outcome no. 1: nicotine abstinence



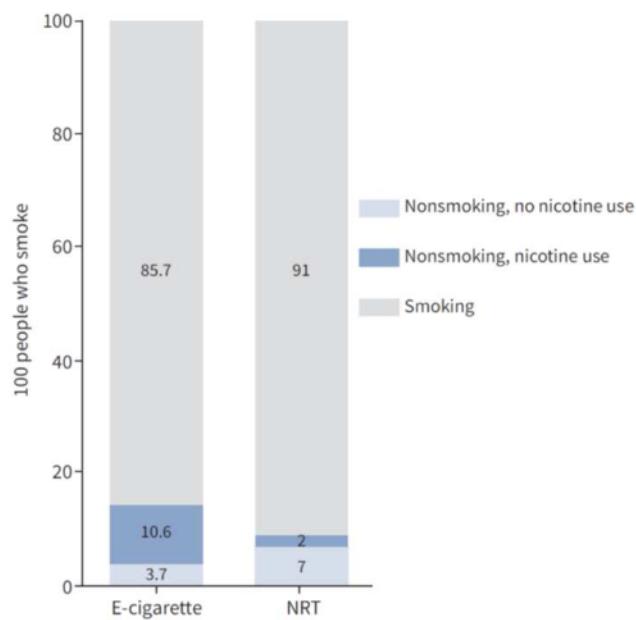
Analysis no. 2: e-cigarettes versus NRT; outcome no. 2: allocated product use among successful cigarette quitters



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 Rauchstopp hilfe.
- (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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