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DISSERTATION

Efficacy of Emergency Department-Initiated Tobacco Control –  
Update of a Systematic Review and Meta-Analysis of  
Randomized Controlled Trials

zur Erlangung des akademischen Grades  
Doctor medicinae (Dr. med.)

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von

Christina Lemhöfer

aus Berlin

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## Zusammenfassung

**Einleitung:** Im Jahr 2012 wurde ein systematisches Review mit Meta-Analyse von sieben randomisierten kontrollierten Studien veröffentlicht, die die Effektivität einer qualifizierter Raucherberatung in Rettungsstellen (qRbR) untersuchte. Die Meta-Analyse konnte keinen Langzeiteffekt einer qRbR nachweisen. Das Ziel der jetzigen Studie war es daher, ein Update des systematischen Reviews mit Meta-Analyse durchzuführen.

**Methode:** Das Studienprotokoll wurde im Mai 2015 im internationalen Register für systematische Reviews (PROSPERO) registriert. Die Literaturrecherche erfolgte in sieben elektronischen Datenbanken. Eingeschlossen wurden randomisierte kontrollierte Studien mit Rettungsstellenpatienten, die eine qRbR erhielten. Zusätzlich musste mindestens ein deutscher, englischer oder spanischer Abstract vorhanden sein und das Publikationsdatum nach dem vierten Oktober 2010 liegen, dem Enddatum des vorherigen Reviews.

Primäre Zielgröße war die 7-Tage-Punkt-Prävalenz-Tabakabstinenz nach einem, drei, sechs und 12 Monaten Follow-up. Das relative Risiko (RR) für eine Tabakabstinenz nach einer qRbR (d.h. der Benefit einer qRbR) wurde für jede Studie und jeden Follow-up-Zeitpunkt einzeln, sowie gepoolt für jeden Follow-up-Zeitpunkt mittels Mantel-Haenszel-Relativen Risiken (MH-RRs) berechnet. Mittels linearer gemischter Modelle wurde zusätzlich der Langzeiteffekt der qRbR über alle Studien und alle Follow-up-Zeitpunkte hinweg kalkuliert. Abschließend wurden einzelne Sensitivitätsanalysen durchgeführt.

**Ergebnisse:** Die Literatursuche erbrachte zunächst 3723 Treffer, von denen, nach Prüfung der Ein- und Ausschlusskriterien, vier Studien mit insgesamt 1392 Teilnehmern in das Update eingeschlossen wurden. Eine Studie war lediglich als Abstract verfügbar. Somit lagen elf randomisierte kontrollierte Studien für die Meta-Analyse vor. Einen Monat nach einer qRbR ergab sich ein gepoolter Benefit von  $RR = 1.49$  (95% Konfidenzintervall (KI): 1.08, 2.05),  $p = 0,014$ , 3 Studien. Nach 3 Monaten betrug das  $RR=1.38$  (95%-KI: 1.12, 1.71),  $p=0,003$ , 9 Studien; nach 6 Monaten:  $RR=1.09$  (95%-KI: 0.84, 1.41),  $p = 0,54$ , 5 Studien und ein Jahr nach einer qRbR betrug das  $RR=1.26$  (95%-KI: 1.00, 1.59),  $p = 0,050$ , 3 Studien. Der kombinierte Langzeiteffekt über alle Follow-up-Zeitpunkte hinweg zeigte einen relativen Benefit von  $RR = 1.40$  (95%-KI: 1.06, 1.86),  $p = 0.023$ . Eine Subgruppenanalyse von acht Studien, mit motivierenden

Telefonanrufen nach der Rettungsstellenbehandlung, erbrachte einen gepoolten Benefit von  $RR = 1.39$  (95%-CI 1.00, 1.92),  $p = 0.048$ .

**Zusammenfassung:** Qualifizierte Raucherberatungen in der Rettungsstelle sind effektiv, um eine wiederholte Tabakabstinenz über sieben Tage für einen Zeitraum von bis zu 12 Monaten herbeizuführen. Da in Rettungsstellen Patienten einfach zu erreichen sind und viele der dort Vorstelligen rauchen, könnten solche Programme eine wichtige Strategie sein, um gerade diese Patienten zum Tabakverzicht zu motivieren. Eine besondere Bedeutung haben dabei qRbRs, bei denen zusätzlich motivierende Telefonanrufe nach der Rettungsstellenbehandlung stattfinden.

## Abstract

**Introduction:** In 2012 a systematic review and meta-analysis of seven randomized controlled trials was published evaluating the efficacy of emergency department initiated tobacco control (ETC). They showed only a short-term effect. Therefore the objective is to provide an update of the systematic review and meta-analysis determining the efficacy of ED-initiated tobacco control.

**Methods:** A literature search in 7 electronic databases was conducted after registration of the study protocol with the Prospero database in May 2015. Inclusion criteria were randomized controlled trials with ED patients of any age who were current smokers and who were offered a tobacco control intervention. A minimum requirement was the availability of an abstract in English or Spanish language. The publication date had to be after October 4<sup>th</sup>, 2010, the end date of the previous review.

The outcome parameter was point prevalence of the self-reported 7-days tobacco use abstinence at 1 to 12 months follow up. The proportion of tobacco abstinence was calculated for each study for each of the different follow-up times and pooled across studies using Mantel-Haenszel relative risks. To calculate the combined effect of ETC across all follow-up times generalized linear mixed effects models were used. In addition, sensitivity analyses were conducted.

**Results:** The literature search retrieved 3723 studies. After screening for inclusion criteria four new trials, 3 full texts and one abstract, with 1392 participants were included. Overall eleven studies were used for the update of the meta-analysis.

At 1 month follow up the point prevalence tobacco abstinence of ETC was RR = 1.49 (95% confidence interval (CI): 1.08, 2.05), p = 0,014, 3 studies. After 3 months follow up it resulted in RR=1.38 (95%-CI: 1.12, 1.71), p =0,003, 9 studies; after 6 months in RR=1.09 (95%-CI: 0.84, 1.41), p = 0,536, 5 studies and after one year in RR=1.26 (95%-CI: 1.00, 1.59), p = 0,050, 3 studies. The combined long-term effect of ETC over all follow up times showed RR = 1.40 (95%-CI: 1.06, 1.86), p = 0.023. Pooling the eight studies evaluating motivational interviewing on site versus booster phone call resulted in RR = 1.39 (95%-CI 1.00, 1.92), p= 0.048.

**Conclusions:** This review and meta-analysis strengthens the evidence for the beneficial impact of smoking cessation in the emergency department setting. Especially approaches including booster sessions after the initial contact in the emergency

department seem to be an effective intervention. It could be an important strategy to motivate also hard-to-reach smokers to tobacco cessation.

## Eidesstattliche Versicherung

„Ich, Christina Lemhöfer, geborene Funke, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: *„Efficacy of Emergency Department-Initiated Tobacco Control – Update of a Systematic Review and Meta-Analysis of Randomized Controlled Trials“* selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.

Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren beruhen, sind als solche in korrekter Zitierung (siehe „Uniform Requirements for Manuscripts (URM)“ des ICMJE -[www.icmje.org](http://www.icmje.org)) kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) entsprechen den URM (s.o) und werden von mir verantwortet.

Mein Anteil an der ausgewählten Publikation entspricht dem, der in der untenstehenden gemeinsamen Erklärung mit dem Betreuer, angegeben ist.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§156,161 des Strafgesetzbuches) sind mir bekannt und bewusst.“

Datum

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Unterschrift

## **Ausführliche Anteilserklärung an der erfolgten Publikation**

Christina Lemhoefer, Gwen Lisa Rabe, Jürgen Wellmann, Steven L Bernstein, Ka Wai Cheung, William J. McCarthy, Susanne Vahr Lauridsen, Claudia Spies, Bruno Neuner, *Efficacy of Emergency Department-Initiated Tobacco Control – Update of a Systematic Review and Meta-Analysis of Randomized Controlled Trials*, Preventing chronic disease, 2017

Beitrag im Einzelnen):

- Festlegung von Ein- und Ausschlusskriterien sowie der Suchwörter für das systematische Review (zusammen mit BN, JW und GLR)
- Durchführung des systematischen Reviews in sieben elektronischen Datenbanken sowie in unveröffentlichter Literatur (unabhängig von und parallel zu GLR)
- Dokumentation der Ergebnisse, Zusammenstellung der gemeinsamen Excel-Datenbank, händische Suche nach Duplikaten, Mitarbeit bei der Erstellung der finalen ‚Rohtreffer‘-Datenbank (unabhängig von und parallel zu BN)
- Prüfung der Ein- und Ausschlusskriterien und damit Auswahl der relevanten Studien für das systematische Review (unabhängig von und parallel zu GLR)
- Datenextraktion (unabhängig von und parallel zu GLR) anhand des PROSPERO-Protokolls einschließlich einer
- Qualitativen Bewertung der relevanten Studien mit dem EPHPP (Effective Public Health Practice Project) Tool (unabhängig von und parallel zu SVL)
- Erstellung der Tabellen mit den Ergebnissen des systematischen Reviews (zusammen mit GLR, BN, WMC, SVL)
- Meta-Analyse mit unterstützt und nachvollzogen (zusammen mit JW und BN)
- Artikel geschrieben (Kommentare, Korrekturen und Ergänzungen durch alle Autoren)

Unterschrift, Datum und Stempel des  
betreuenden Hochschullehrers

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Unterschrift der Doktorandin

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**Journal Data Filtered By: Selected JCR Year: 2015 Selected Editions: SSCI  
Selected Categories: 'PUBLIC, ENVIRONMENTAL & OCCUPATIONAL  
HEALTH' Selected Category Scheme: WoS  
Rang Nr. 32 von 153**

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
1	Lancet Global Health	1,379	14.722	0.008420
2	Annual Review of Public Health	4,631	10.240	0.007260
3	TOBACCO CONTROL	6,340	6.321	0.019200
4	EPIDEMIOLOGY	10,988	6.075	0.024310
5	AMERICAN JOURNAL OF PUBLIC HEALTH	32,270	4.138	0.064430
6	JOURNAL OF EPIDEMIOLOGY AND COMMUNITY HEALTH	12,440	3.865	0.020540
7	JOURNAL OF ADOLESCENT HEALTH	11,470	3.838	0.025140
8	NICOTINE & TOBACCO RESEARCH	7,482	3.811	0.023250
9	SCANDINAVIAN JOURNAL OF WORK ENVIRONMENT & HEALTH	4,429	3.793	0.006140
10	AIDS PATIENT CARE AND STDS	3,035	3.578	0.007100
11	HEALTH EXPECTATIONS	1,932	3.207	0.004110
12	JOURNAL OF HEALTH AND SOCIAL BEHAVIOR	6,483	3.190	0.006380
13	AIDS AND BEHAVIOR	6,847	3.063	0.024690
14	PREVENTION SCIENCE	2,510	2.926	0.006310
15	SOCIAL SCIENCE & MEDICINE	34,360	2.814	0.051470
16	Population Health Metrics	993	2.768	0.005570
17	International Journal of Public Health	1,766	2.754	0.005500
18	EUROPEAN JOURNAL OF PUBLIC HEALTH	4,513	2.751	0.012230
19	Globalization and Health	967	2.540	0.004250
20	Critical Public Health	709	2.530	0.002070
21	HEALTH & PLACE	4,396	2.441	0.012810
22	QUALITY OF LIFE RESEARCH	9,395	2.429	0.017550
23	Administration and Policy in Mental Health and Mental Health Services Research	1,502	2.415	0.004240
24	International Journal for Equity in Health	1,356	2.378	0.005010
25	PSYCHIATRIC SERVICES	8,356	2.335	0.013870
26	HEALTH EDUCATION & BEHAVIOR	3,342	2.312	0.004530
27	International Journal of Health Geographics	1,596	2.270	0.004320
28	LGBT Health	112	2.261	0.000680
29	RISK ANALYSIS	6,134	2.225	0.010320
30	STUDIES IN FAMILY PLANNING	1,513	2.192	0.002160
31	Translational Behavioral Medicine	538	2.189	0.002800
32	Preventing Chronic Disease	3,280	2.170	0.012020
33	ACCIDENT ANALYSIS AND PREVENTION	10,191	2.070	0.020930
34	AMERICAN JOURNAL OF COMMUNITY PSYCHOLOGY	4,387	2.068	0.005000

# **Efficacy of Emergency Department-Initiated Tobacco Control – Update of a Systematic Review and Meta-Analysis of Randomized Controlled Trials**

Short title: Efficacy of ED-initiated tobacco control

Christina Lemhoefer MD<sup>1</sup>, Gwen Lisa Rabe MD<sup>2</sup>, Jürgen Wellmann PhD<sup>3</sup>, Steven L Bernstein MD PhD<sup>4</sup>, Ka Wai Cheung MD MPH<sup>5</sup>, William J. McCarthy PhD<sup>6</sup>, Susanne Vahr Lauridsen MEd, PhD stud<sup>7</sup>, Claudia Spies MD<sup>1</sup>, Bruno Neuner MD MSc<sup>1</sup>

## **Institutions:**

<sup>1</sup>Charité – Universitätsmedizin Berlin, Department of Anesthesiology and Intensive Care Medicine, Berlin, Germany

<sup>2</sup>Krankenhaus der Augustinerinnen, Department of Internal Medicine, Cologne, Germany

<sup>3</sup>Institute of Epidemiology and Social Medicine, University of Münster, Münster, Germany

<sup>4</sup>Department of Emergency Medicine, Yale University School of Medicine; Yale Cancer Center; Department of Health Policy, Yale School of Public Health, New Haven, CT, US

<sup>5</sup>Department of Emergency Medicine, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada

<sup>6</sup>University of California Los Angeles (UCLA), Center for Cancer Prevention and Control Research, Fielding School of Public Health and Jonsson Comprehensive Cancer Center, Los Angeles, US

<sup>7</sup>University Hospital of Copenhagen, Rigshospitalet, Department of Urology, Copenhagen, Denmark

Corresponding author:

Bruno Neuner MD MSc

Charité – Universitätsmedizin Berlin

Department of Anesthesiology and Intensive Care Medicine

Campus Virchow Klinikum and Campus Charité Mitte

Charitéplatz 1

10117 Berlin, Germany

Tel.: ++ 49 – 30 – 450 – 531026

E-Mail: bruno.neuner@charite.de

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## **ABSTRACT**

**Introduction:** A 2012 systematic review and meta-analysis of randomized controlled trials on emergency department-initiated tobacco control (ETC) showed only short-term efficacy. Therefore, the aim of this study was to update this topic.

**Methods:** After registration of the study protocol on the International prospective register of systematic reviews (PROSPERO) in May 2015, literature search involved 7 databases and grey literature sources. Relevant outcome was the point prevalence of tobacco use abstinence at 1, 3, 6, or 12 months follow-up. The relative risk (RR) of tobacco use abstinence post ETC was calculated at each follow-up time separately for each study and pooled, at different follow-up times, by Mantel-Haenszel relative risks. The effect of ETC on combined point prevalence tobacco use abstinence across all follow-up times was calculated using generalized linear mixed effects models.

**Results:** The literature update retrieved four additional studies, one published as an abstract, with 1,392 participants overall. These results were pooled with those of the seven studies included in the previous review with 1,986 participants overall. The 1-month follow-up point prevalence abstinence of ETC resulted in RR = 1.49 (95% confidence interval (CI): 1.08, 2.05), 3 studies; 3-months results: RR=1.38 (95%-CI: 1.12, 1.71), 9 studies; 6-months results: RR=1.09 (95%-CI: 0.84, 1.41), 5 studies; and 12-months results: RR=1.26 (95%-CI: 1.00, 1.59), 3 studies; respectively. The effect on combined point prevalence abstinence was RR = 1.40 (95%-CI: 1.06, 1.86),  $p = 0.023$ .

**Conclusions:** Emergency department-initiated tobacco control is effective in promoting repeated tobacco use abstinence up to 12 months follow-up. ETC may be a critically important public health strategy for engaging hard-to-reach smokers in tobacco use cessation.

## **INTRODUCTION**

In 1998, a task force of the Society for Academic Emergency Medicine (SAEM) published recommendations for screening and intervention activities in emergency departments (EDs) including smoking cessation counseling (1,2). In 2006, a panel convened by the American College of Emergency Physicians called on emergency care providers to routinely screen ED patients for their smoking status and to initiate smoking cessation counseling and/or referral to outpatient treatment (3). These ED-initiated tobacco control (ETC) services are meant to reduce the enormous burden of tobacco-related diseases by using the teachable moment of the ED visit to motivate smokers to quit (3,4).

Although there are several compelling arguments for such services, including high smoking prevalence rates in ED patients (5-7), the hard-to-reach nature of their typical patients and the high credibility of EDs regarding preventive and health promoting services (8), the benefit of ETC is unclear: A 2008 systematic review of smoking cessation interventions in the ED (9) identified seven studies with only one of them reporting a significant intervention benefit.

Likewise, a systematic review and meta-analysis published in 2012 and covering publications through October 2010 found a clear point prevalence abstinence advantage of ETC over usual care at only one month post ETC, and a nonsignificant effect ( $p=.08$ , seven studies) for a cumulative point prevalence abstinence benefit of ETC over all follow-up points (1,3,6, and 12 months post ETC) (10). In 2014, a systematic review identified 13 randomized controlled trials (RCTs) with 11 of them reporting no significant differences between study groups (11). While there exists compelling evidence on the efficacy of tobacco control interventions in other medical settings (12,13), the efficacy of ETC with regard to cessation rates for periods exceeding 1 month has yet to be demonstrated. Therefore, the objective of the present study was to provide an update of the systematic review and meta-analysis of RCTs published by Rabe et al. (10) in 2012.

## **METHODS**

### **Data sources**

This systematic review and meta-analysis updates a previous review and includes publications appearing after October 2010 (10). Inclusion criteria, quality assessment and analysis methods were identical to those used in the previous review (10) and specified in advance and documented in a protocol in compliance with the ‘Preferred Reporting Items for Systematic Reviews and Meta-Analyses’ (PRISMA) Statement (14). Details of the protocol for this systematic review were registered on PROSPERO in May 2015 and can be accessed at [http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42015020581](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015020581).

Inclusion criteria were randomized controlled trials with ED patients of any age who were current smokers and who were offered a tobacco control intervention. The tobacco control intervention was defined according to the 2006 joint statement of emergency medicine organizations (3) as preventive services such as screening and brief interventions delivered in the emergency department to promote smoking cessation. The outcome, – usually evaluated as self-reported 7-days tobacco use abstinence (point prevalence tobacco abstinence) –, had to be measured at least once during follow-up. Studies had to be accessible and published at least as an abstract in English or Spanish after October 4<sup>th</sup>, 2010, the end date of the previous review (10).

The systematic search was conducted by one reviewer (CL) in 7 electronic databases:

MEDLINE, The Cochrane Library, EMBASE, PsycINFO, LILACS, and the citation indexes of the ISI Web of knowledge.

The International Clinical Trial Register was screened for unpublished studies. The Conference Proceedings Citation Index) contains grey literature and unpublished studies as well. Furthermore, we screened the references of the included studies to identify additional potentially relevant studies.

The following search terms were used:

(Smok\* AND Emergency OR Tobacco AND Emergency OR Nicotine AND Emergency OR Cigarette\* AND Emergency) AND (Control OR Intervention\* OR Counseling OR Counselling OR Assistance OR Treat\* OR Prevention OR Promotion\* OR Referral\* OR Cessation) AND (randomized OR randomly OR control\* OR trial\* OR controlled study OR investigation OR prospective OR longitudinal OR pilot).

### **Study selection**

The period of the literature search was between October 4, 2010 and May 15, 2015.. We included RCTs that examined the efficacy of smoking cessation interventions in ED patients of any age. Smoking cessation interventions according to the American College of Emergency Physicians statement (3) were motivational interviewing or counseling on site in combination with referral to outpatient treatments or to telephone quitlines. The treatment in the control group could be usual care (brochures, self-help material, information leaflets on state smokers' quitlines, or any less intensive program such as brief advice only, or no material / advice at all. Tobacco use abstinence had to be evaluated at least once during follow-up. Relevant outcome measures were defined as point prevalence tobacco use abstinence (16) at all available follow-up times.

We excluded studies with patients from outpatient settings, with relatives or visitors of ED patients or studies in hospitalized patients.

Relevant text was imported into Reference Manager 12.0. After automated duplicate removal, two reviewers (CL and GR) independently screened titles and abstracts of all remaining search results for relevance. In a second step, the full texts of potentially relevant studies were assessed for eligibility. Any disagreement between reviewers was resolved in discussion with a third reviewer (BN).

## **Data extraction**

Two investigators (CL and BN) extracted relevant information on study design and outcomes independently. The following data were extracted:

- Setting: Kind of Emergency Department, localization, annual patient census,
- Participants: Total number, number in each study arm, age and gender distribution,
- Smoking-related variables: smoking definition, screening instruments, biologic validation), use of other biological marker,
- Nature of smoking cessation intervention and type of treatment in the control group,
- Follow-up: time in months, number of follow-up contacts, absolute number and percentage of participants lost to follow-up, number of abstinent smokers (or other outcomes) at each follow-up.

Risk of bias was assessed independently by two reviewers (CL and BN) employing the Quality Assessment Tool for Quantitative Studies developed by the Effective Public Health Practice Project (EPHPP, McMaster University, Ontario, Canada) (17). The tool includes the following six component ratings: selection bias, study design, confounders, blinding, data collection methods and withdrawals and dropouts. Combined component ratings resulted in a global rating of either “strong”, “moderate” or “weak”. Potential publication bias was assessed by a funnel plot, using the longest follow-up observations in each study.

## **Data synthesis**

Although the number of follow-up contacts varied between studies, all studies reported abstinence rates at either 1, 3, 6, or 12 months follow-up. Study participants not reached at follow-up were assumed to be current smokers. The proportion of tobacco abstainers in both study arms was calculated for each study for each of the different follow-up times. The first analysis across studies consisted of pooling the relative ‘risk of abstinence’ (representing the

relative benefit of the smoking cessation counseling, i.e. the ratios of the proportions of abstainers in the treatment group to the proportions of abstainers in the control group) across studies using Mantel-Haenszel relative risks. However, our main meta-analysis utilized the individual study results for each follow-up. In order to account for heterogeneity between studies as well as for repeated measurements within studies, generalized linear mixed models (GLMM) (18,19) were used with 7-days point prevalence tobacco use abstinence at all follow-up times as the outcome. More specifically, random intercepts were used to model variability in smoking status across studies as a function of ETC/no ETC treatment in interaction with time of assessment. A log link and a binomial error distribution were used to estimate the log odds of relative risks; exponentiation was then used to report the relative risks and their 95 percent confidence intervals. The variance-covariance matrix used reflected the fact that outcomes were highly correlated across different follow-up times within each study, because the repeated assessments of smoking behavior involved the same participants. The final GLMM was set up with four fixed effects (the intercept, the treatment effect, the effect of time, and their interaction). Additionally, sensitivity analyses were run in subgroups, e.g. involving those studies that featured motivational interviewing on site in combination with booster phone calls. A p-value of  $p < 0.05$  was defined as statistically significant.

## **RESULTS**

The electronic literature search initially identified 3,723 studies. Of these, 2,532 remained after manual and automatic duplicate removal. A further 2,504 studies did not meet the inclusion criteria. Of the remaining 28 publications, 24 were excluded for other reasons (see Figure 1), including one qualitative study and two quasi-randomized controlled trials with a phased intervention versus usual care (20-22).



Four studies consisting of three full text articles and one abstract with 1,392 participants were added to the systematic review and meta-analysis (23-26). Follow-up time varied between 1 and 12 months.

### **Results of eligible studies**

Details of the included studies are given in Table 1. All newly retrieved studies featured motivational interviewing / cessation advice on site with three out of the four studies also featuring additional booster phone calls. Anders et al. (23) tested the feasibility and effectiveness of a brief advice on site in combination with proactive phone calls. An external cessation phone counseling service delivered these calls within two weeks after the brief advice. Additionally, up to six cognitive-behavioral therapy sessions, either telephone-based or involving in-person treatment as well as nicotine patches, were provided gratis. Control group participants received one session of personalized cessation advice and printed self-help material. Follow-up occurred 3 months later. In both of their studies, Bernstein et al. (24,25) tested a combination of motivational interviewing on-site together with follow-up phone calls within three days. Additionally, study participants were offered written informational material and NRT gratis for up to six weeks. The comparison condition included brochure/quitline information only. Biochemically confirmed tobacco use abstinence rate at 3 months was the primary endpoint. The 2015 study additionally evaluated abstinence rates at 12 months (25). Cheung et al. (26) explored a brief intervention on site followed by referral to a provincial telephone quitline. Abstinence rates were evaluated at 1, 3, 6 and 12 months follow-up.

The number and the proportion of abstinent smokers at follow-up in the included studies are reported in Table 2. The proportion of abstinent smokers varied between 4.5% and 34.6%. In two studies, smokers in the intervention group showed higher abstinence rates compared with smokers in the control group (24,25). Anders et al. (23) additionally demonstrated that all

participants in the intervention group consented to a faxed referral, of whom 13.5% attended treatment sessions, while control group treatment attendance was 2.7%. Cheung et al. (26) found that 16 /27 (59.3%) participants in the intervention group accepted a referral to the quitline. Six participants were reached, but only five were enrolled in the program and only two completed the program.

### **Risk of bias Assessment**

The EPHPP “Quality Assessment Tool for Quantitative Studies” was used to assess the risk of bias associated with the three newly included full text studies. Two studies received a ‘moderate’ rating (23,25), and one study a ‘weak’ rating (24) (Table 4 supplement). The study by Cheung et al. (26) could not be assessed due to unavailable information necessary for the application of the EPHPP tool.

### **Update of the systematic review and meta-analysis**

When adding the evidence of the newly retrieved studies to the evidence from the previous meta-analysis (10), pooled results at one month after ETC ( $p=0.014$ ) and at three months after ETC ( $p=0.003$ ) were statistically significant (see Table 3). At 12 months follow-up, the pooled results were not significant ( $p= 0.050$ ). Pooling all available evidence across all follow-up assessment periods through May 2015, the cumulative point prevalence abstinence of ETC compared to control yielded a relative benefit of  $RR = 1.40$  (95% confidence interval (CI) 1.06, 1.86),  $p=0.023$ , 11 studies. Excluding the study by Cheung et al, which was reported as an abstract only, the cumulative point prevalence abstinence of ETC compared to control condition was  $RR = 1.36$  (95% CI 1.00, 1.85),  $p=0.047$ ,  $n = 10$  studies. Pooling the eight studies evaluating motivational interviewing on site versus booster phone calls (23-25,27-31) resulted in a comparable point prevalence abstinence relative risk of  $RR = 1.39$  (95%-CI 1.00, 1.92),  $p= 0.048$ . Further sensitivity analyses revealed that pooling only the four newly retrieved studies

(see Tables 1-2) from this update, the cumulative point prevalence abstinence of ETC compared to control condition was  $RR = 1.57$  (95%-CI 0.59, 4.17),  $p = 0.24$ . When pooling the four studies with biochemically confirmed smoking outcomes (24,25,27,28) the cumulative point prevalence abstinence of ETC was  $RR = 1.34$  (95%-CI 0.91, 1.97),  $p = 0.10$ .

Figure 2 presents a funnel plot of the relative risks for the benefit of ETC vs. control condition, using the longest follow-up observations in each study. The y-axis represents the log of the standard error of the last assessment in each study while the x-axis represents the log of the relative risk for each study. The funnel plot, based on 11 observations, was found not to be significantly asymmetric by the Peters funnel plot test ( $t(11) = -0.57$ ,  $P = 0.58$ ) (32). There are overall more studies with positive results ( $RR > 1$ ,  $n = 7$ ), some of them with large standard deviations; however, studies with negative results ( $RR < 1$ ,  $n = 4$ ) show both large and small standard deviations.

## **DISCUSSION**

### **Main findings**

This update of a systematic review and meta-analysis of RCTs evaluating the efficacy of tobacco control measures in an emergency department setting reveals an overall benefit of emergency department-initiated tobacco control (ETC) over control condition on repeated 7-days point prevalence abstinence at 1, 3, 6, and 12 months follow-up. At 1 and 3 months-follow-up, the pooled 7-day point-prevalence abstinence was higher in the ETC group compared with usual care. Eight (23-25,27-31) out of 11 studies overall evaluated motivational interviewing on site combined with proactive booster telephone calls. Pooling these studies, ETC showed increased cumulatively assessed point prevalence abstinence compared to the control condition.

### **Strengths and limitations**

The quality standard of the systematic review was similar to that of Rabe et al. (10): The literature search encompassed the seven most relevant major electronic databases including unpublished studies. The methodological quality and the risk of bias were determined for all studies included in this review. The statistical approach replicated that used in our earlier systematic review. We conservatively assumed that all participants lost to follow-up were smoking at follow-up. There was admittedly some heterogeneity in the intervention strategies used between studies. However, all but one of the newly retrieved studies and eight out of eleven of the studies included in the review investigated the impact of the combination of motivational interviewing / strong advice to quit either on site or through proactive telephone calls delivered promptly after the ED treatment. In three out of four of the newly retrieved studies, study participants received nicotine patches free of charge. Heterogeneity mainly occurred regarding the provision of self-help / informational material and brochures and referral to telephone quitlines. This heterogeneity was taken into consideration when calculating the overall effect of ETC through our statistical approach. This approach allowed for variance between studies as well as variation within studies over time and may therefore satisfactorily reflect the true variability of intervention conditions in clinical practice. The funnel plot, used to evaluate potential risk of publication bias, showed that 4 (36%) studies with negative results (odds ratios for the ETC effect  $< 1$ ) were indeed published, although most (64%) of the eligible studies were found to have positive results. The overall shape of the plot appears fairly symmetric (with predictably greater heterogeneity of effect sizes among the smaller studies as reflected in the expected inverted funnel shape (33)). This lack of funnel plot asymmetry was confirmed statistically. Despite the foregoing, publication bias cannot be ruled out as the explanation for these data, but seems unlikely. Pooling results of the newly retrieved studies shows an effect size larger than that found by the previous meta-analysis (10). Thus, the more impressively significant results of the current update are attributable to both the increased cumulative sample

size made possible by the addition of the newly retrieved studies and to the larger effect sizes reported by these recent studies. Abstinence rates at 6 months and 12 months, in the newly retrieved studies with larger sample sizes (see Table 3) compared favorably to the results of the previous meta-analysis (10, Table 3, page 648). One possible reason for this improvement might be the more consistent delivery of NRT in the more recent trials. Not all studies biologically validated the smoking outcomes. The pooled result on cumulative point prevalence abstinence of ETC in studies with validated tobacco abstinence was slightly weaker (RR = 1.34) compared to the pooled result of all available studies (RR = 1.40). Although several studies that examined the issue of self-reported smoking validity concluded that self-reported smoking history was accurate (34,35), our finding may indicate social desirability bias in the non-validated studies and thus a slight overestimation of the true effect of ETC.

From a public health point-of-view, a measure of continuous tobacco use abstinence would provide more unambiguous evidence of long-term ETC efficacy than the point prevalence abstinence used here (15,13). However, insisting on strictly continuous abstinence may unfairly classify too many successes as relapses (15,36). It is common research practice to assess 7-days-point-prevalence-rates supported by a negative biochemical test (15) since these are regarded as valid, replicable outcome measures and less likely to be biased by faulty recall or social desirability.

This meta-analysis showed a non-monotonic attenuation of the ETC effect over twelve month.

We believe that the apparent drop in effect size at six months was artifactual and not representative of the 12 months trend. Of six studies pooled at six months, three (26,30,37) showed negative results. Two of these studies (30,37) reported no 12 months results. The third study (26) found an advantage of ETC over the control condition at 1 and 3 months but not thereafter. Thus, the attenuation at 6 months was driven by two studies with 6-months-only results and by one very small study, which attenuated the pooled 12 months results negligibly.

However, a drop-off of intervention effect over time is characteristic of most interventions designed to reduce psychoactive drug use (38) or tobacco use (36). Absent changes in the conditions that gave rise to smoking in the first place, relapse appears to be the rule. Even if tobacco abstinence is time-limited, there is nonetheless significant benefit to the smoker's lung health in having enjoyed a substantial respite from smoking's daily assault on normal physiological functioning (39). Moreover, previous experience with quitting seems to predispose to further attempts to quit (36).

### **What this update adds**

This review and meta-analysis strengthen and extend the evidence for the beneficial impact of smoking cessation in the emergency department setting. The addition of the most recent studies has enriched the portfolio of novel approaches, especially in regard to booster sessions after the initial contact in the emergency department. Anders et al. (23) used cessation services offering two proactive telephone calls within two weeks post-ED treatment. A comparable approach was chosen by Cheung et al. (26) as well as Bernstein et al. (24,25) who referred patients to a telephone quitline service. Such services have shown their feasibility and effectiveness in tobacco control in other settings, such as primary care practices (40). They might reduce the workload of EDs that do not have such follow-up services available. Anders (23) and Bernstein (24,25) provided NRT gratis to their patients. Participants with higher nicotine dependence were less likely to benefit from exposure to tobacco counseling in EDs or other settings (28,41-43). Additionally, providing NRT during the cessation counseling (alone or in combination with other pharmacologic strategies) increased quit attempts and abstinence rates in specific patients' groups (44,45). As there were no individual data available and thus no information on the actual use of NRT in the specific study populations in this systematic review and meta-analysis, it was

not possible to identify the attributable benefit of NRT provided gratis on near-term and long-term cessation outcomes.

### **Future directions**

This meta-analysis suggests that cessation counseling initiated in the ED is effective in promoting repeated tobacco abstinence. Because of their high reach and the high percentage of ED patients who smoke, EDs may play an important population-level role in motivating patients to quit smoking (3). EDs are especially important venues for reaching young and uninsured persons, who appear disproportionately in EDs. The credibility of ED staff regarding prevention and health promotion is high and the teachable moment represented by an ED-based intervention is a persuasive argument for supporting such services (46). The core curriculum of emergency medicine now incorporates knowledge on tobacco epidemiology and motivational interviewing techniques as outlined in the joint statement of Emergency Medicine Organizations in 2006 (3). Acknowledgment of the role of EDs in promoting preventive and health promoting services is changing and ED staff members readily accept that the ED encounter may provide a “teachable moment” for encouraging smoking cessation (21,22). More knowledge is needed on how to incorporate ETC into clinical routine efficiently. Facilitators to implementing a multifaceted smoking cessation intervention in an ED were context-specific training, a systematic approach to assessment and action as well as reminder tools (20,22,47). Routine use of computerized decision support systems helped nurses and physicians to implement tobacco cessation treatment and further referral in a pediatric ED (48). In the clinical setting, a best practice alert appearing when patients were coded as smokers in the electronic health record were effective in motivating physicians to order tobacco cessation treatment medication and to refer their patients to a telephone quitline (49). Such devices and approaches may help to further integrate tobacco control services in EDs into clinical routine.

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**Table 1:** Results of the data extraction involving the four studies retrieved by the systematic review

<b>Year of publication, Authors / Country</b>		<b>2011 Anders et al. / US</b>	<b>2011, Bernstein et al. / US</b>	<b>2013, Cheung et al. / Canada</b>	<b>2015, Bernstein et al. / US</b>
<b>No. of participants randomized // Intervention / Control group (Target group)</b>		221 // 111 / 110 (Adults)	338 // 170 / 168	53 // 27 / 26 (Adults)	780 // 388 / 390 (Adults)
<b>Setting / Size of yearly patient load</b>		Urban ED / 48,000	Urban ED / 90,000	Urban ED	Urban ED / 90,000
<b>Smoking definition</b>		Answer 'Yes' to the question: “Do you smoke tobacco?” with smoking intensity $\geq 1$ cigarette / day	> 100 cigarettes in lifetime AND current daily or occasional smokers with a mean consumption $\geq 10$ cigarettes/smoking day	Tobacco use within the last 30 days	> 100 cigarettes in lifetime AND current or occasional smokers with a mean consumption > 5 cigarettes/day
<b>Treatment in the intervention group</b>	Advice / MI on site	×	×	×	×
	Follow-up calls	×	×		×
	NRT for free	×	×		×
	Brochure		×		×

<b>Treatment in the control group</b>	1) Personalized advice to quit smoking by an advanced practice nurse	Brochure with general information about smoking	Usual practice only	1) Brochure with general information about smoking cessation
	2) Self-help material + brochure with contact information for cessation a program	cessation and contact information for smoking cessation programs		2) Telephone number of the state Smokers' Quitline
<b>Definition of tobacco use abstinence</b>	Self-reported 7-days tobacco use abstinence	Self-reported 7-days tobacco use abstinence, verified by exhaled carbon monoxide and salivary cotinine	30-day tobacco point prevalence abstinence	Self-reported 7-days tobacco use abstinence, verified by exhaled carbon monoxide measurement

ED = Emergency department; MI = Motivational interviewing; NRT = Nicotine replacement therapy; QL = Quitline; AHA = American Heart Association.

**Table 2:** Number and proportion of abstinent smokers at follow-up; results of the four studies retrieved by the systematic review

Year of publication, authors	Type of group	No. of randomized participants	Number and proportion of abstinent smokers at follow-up			
			1 month	3 months	6 months	12 months
2011, Anders et al.	Intervention	111		5 (4.5%)		
	Control	110		8 (7.3%)		
2011, Bernstein et al.	Intervention	170		25 (14.7)		
	Control	168		22 (13.2)		
2013, Cheung et al.	Intervention	27	7 (25.9%)	8 (29.6%)	6 (22.2%)	4 (14.8%)
	Control	26	4 (15.4%)	4 (15.4%)	9 (34.6%)	7 (26.9%)
2015, Bernstein et al.	Intervention	388		47 (12.1%)		62 (16.0%)
	Control	390		19 (4.9%)		45 (11.5%)

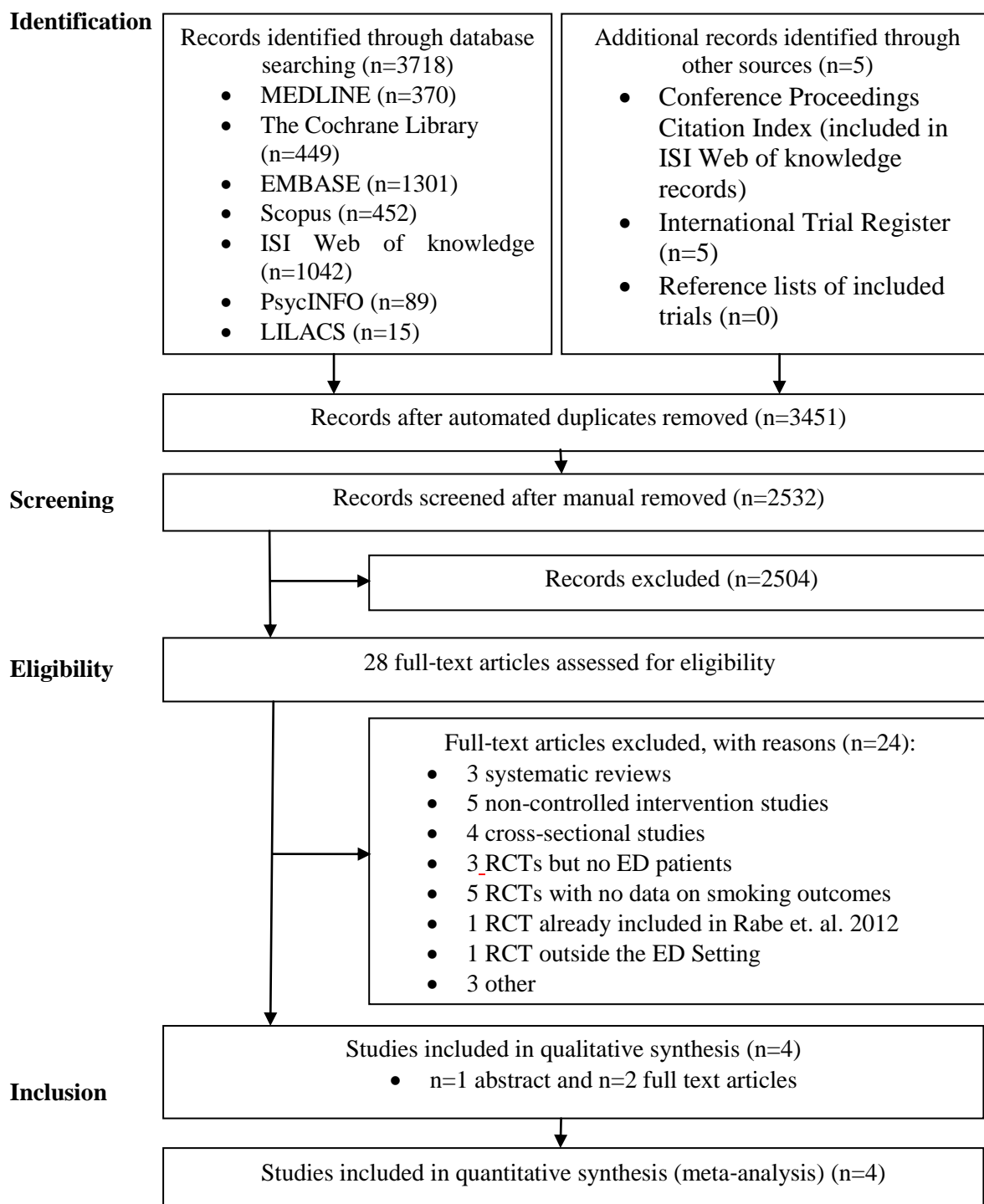
**Table 3:** Benefit of emergency department-initiated tobacco control versus control condition on tobacco use abstinence (Mantel-Haenszel relative risks), results of individual studies and meta-analyses, stratified by follow-up time, n= 11 studies

Year of publication, first author	Relative risks (95% confidence intervals) and p-values at follow-up			
	1 month	3 months	6 months	12 months
2000, Antonacci			0.33 (0.01 – 7.74) <sup>a</sup>	
2000, Richman		1.14 (0.36 – 3.57)		
2007, Horn			0.83 (0.05 – 12.77)	
2007, Schiebel		2.00 (0.20 – 20.33)	9.00 (0.52 – 156.91) <sup>a</sup>	
2008, Bock	1.64 (1.04 – 2.56)	1.35 (0.86 – 2.12)	1.04 (0.64 – 1.68)	
2008, Boudreaux		1.86 (0.25 – 13.91)		
2009, Neuner	1.30 (0.79 - 2.15)	1.13 (0.75 – 1.69)	1.14 (0.81-1.61)	1.25 (0.91 – 1.72)
2011, Anders		0.62 (0.21 – 1.83)		
2011, Bernstein		1.12 (0.66 – 1.91)		
2013, Cheung	1.69 (0.56 – 5.08)	1.93 (0.66 – 5.63)	0.64 (0.27 – 1.55)	0.55 (0.18 – 1.66)
2015, Bernstein		2.49 (1.49 – 4.16)		1.38 (0.97 – 1.98)
Meta analyses <sup>§</sup>	1.49 (1.08 – 2.05) p = 0.014	1.38 (1.12 – 1.71) p = 0.003	1.09 (0.84 -1.41) p = 0.536	1.26 (1.00 – 1.59) p = 0.050

<sup>a</sup> 0.5 added to all cells of the 2 × 2 table in calculating the relative risks to avoid degeneracy caused by sampling zero counts; <sup>b</sup> Mantel-Haenszel relative risk; a p-value < 0.05 was defined as statistically significant

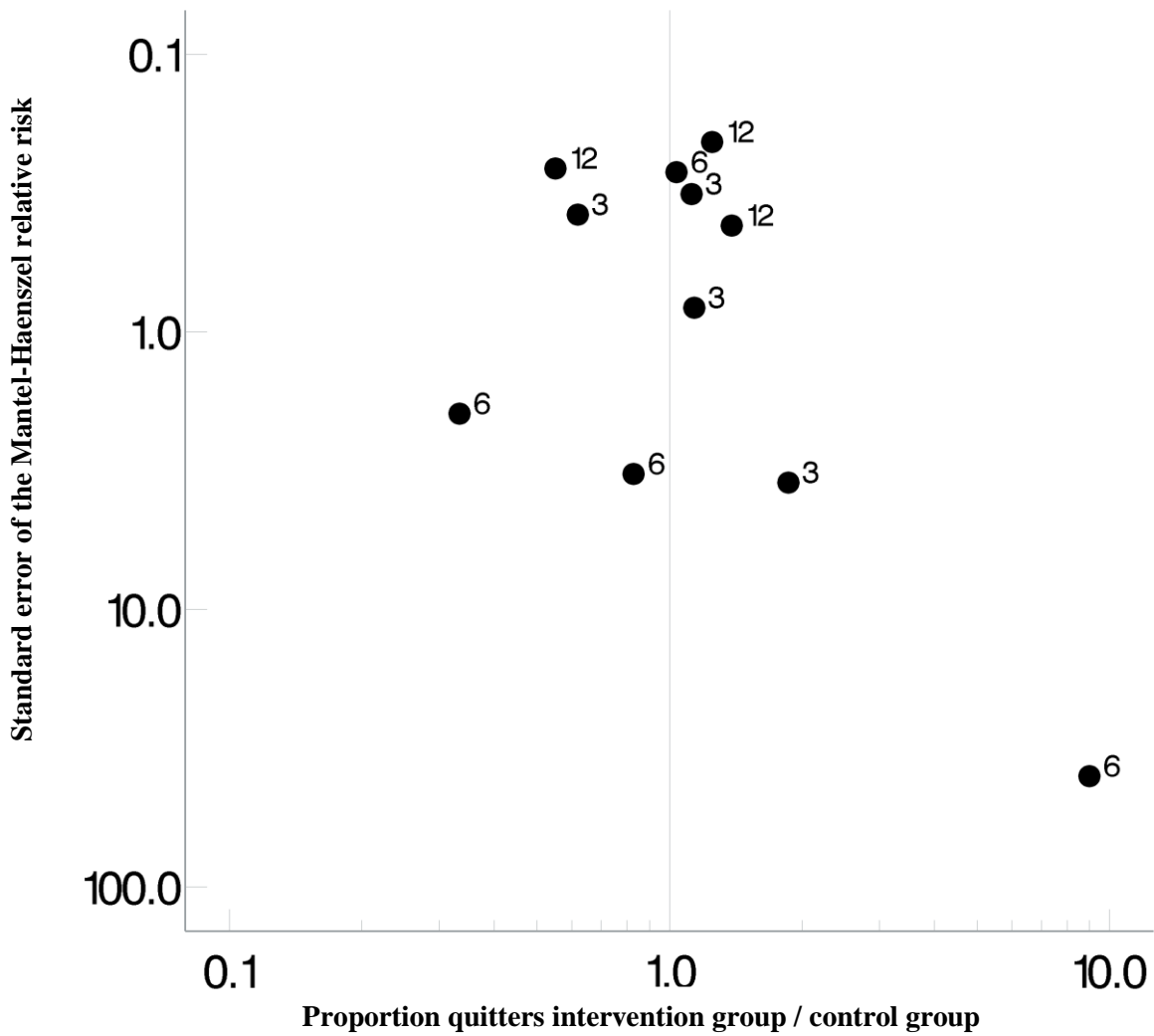


**Figure 1:** Flow chart showing the literature search in 7 electronic databases and the sequential study selection process



MEDLINE = Medical Literature Analysis and Retrieval System Online of the United States National Library of Medicine; EMBASE = Excerpta Medica database; PsycINFO = literature database of the American Psychological Association; LILACS = Literatura Latino-Americana e do Caribe em Ciências da Saúde (Literature in the Health Sciences in Latin America and the Caribbean); RCT = randomized controlled tri

**Figure 2:** Funnel plot showing the effect estimates (Mantel-Haenszel relative risks / benefits of emergency department–initiated tobacco control) on the x-axis and the standard errors of the effect estimates on the y-axis, using the last follow-up observation in n = 11 studies.



Superscript numbers represent the follow-up month; both axes are log-10 scales.

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

## Publikationsliste

*Christina Lemhöfer*

Christina Lemhoefer, Gwen Lisa Rabe, Juergen Wellmann, Steven L Bernstein, Ka Wai Cheung, William J. McCarthy, Susanne Vahr Lauridsen, Claudia Spies, Bruno Neuner, *Efficacy of Emergency Department-Initiated Tobacco Control – Update of a Systematic Review and Meta-Analysis of Randomized Controlled Trials*, Preventing chronic disease, 2017

Impact Faktor 2,170

Valle C., Sperr M., Lemhöfer C., Bartel K., Schmitt-Sody M.: *Beeinflusst sportliche Aktivität die Revisionsrate nach Knieendoprothese? Analyse eines 12 Jahres Follow Up*, Sportverl Sportschad 2017; 31(2)

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Schmitt-Sody M., Valle C., Lemhöfer C., Pilger-Lampersberger V.: *Rehabilitation nach operativen Eingriffen am Sprunggelenk*. [www.my-medibook.de](http://www.my-medibook.de), 2016

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