COPD
ALTBEWÄHRTES UND NEUES
12.11.2024

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Leiter Pneumologie und Schlafmedizin KSM

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Altbewährtes und Neues

- Chronisch obstruktive Pneumopathie COPD
  - Epidemiologie
  - GOLD
  - Exazerbationen
- Tabakrauch vs Tabakerhitzen vs e-Zigaretten
- Fragen/Diskussion

2

COPD verstehen

COPD - eine chronische Erkrankung, die nicht zu unterschätzen ist

COPD = Chronisch-obstruktive Lungenerkrankung.

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COPD ist die **dritthäufigste Todesursache** weltweit[1]

~384 Millionen sind weltweit an COPD erkrankt[2]

Exazerbationen führen zu:
- **Verschlechterung des Gesundheitsstatus**[3]
- **Angstzuständen und Depressionen**[4]
- **Erhöhtem Mortalitätsrisiko**[5]

In der Schweiz:
- Geschätzte **400.000 Personen** mit einer diagnostizierten COPD[6]
- Ca. **2,6% der jährlichen Hospitalisationen**[7]
- Ca. **50% der Todesfälle** innerhalb der Atemwegserkrankungen[8]

COPD = Chronisch-obstruktive Lungenerkrankung.
1. World Health Organization. The top 10 causes of death. 2020;1-9. Available from https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death (letzter Zugriff: Juli 2024). 2. Adeloye D, et al. J Glob Health. 2015;5(2):020415. 3. Spencer S and Jones PW. Thorax. 2003;58(7):589-593. 4. Halpin D, et al. J R Soc Med. 2015;8(12):1-8. 5. Suissa S, et al. Thorax. 2012;67(11):957-963. 6. Bundesamt für Gesundheit. Available from https://www.bag.admin.ch/ (letzter Zugriff: Juli 2024). 7. Baty F, et al. PLoS One. 2013;8:e63285. 8. Vicedo-Cabrera AM, et al. Swiss Med Wkly. 2016;146:w14361.

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Prävalenz und Mortalität der COPD

Prävalenz
- 10–15 % der Erwachsenen
- steiler Anstieg ab dem 40. Lebensjahr
- höher bei Rauchern

Mortalität
- 1990: weltweit an 6. Stelle der zum Tode führenden Erkrankungen
- COPD im Jahr 2020 dritthäufigste zum Tode führende Erkrankung

Weltweite Rangliste der zum Tode führenden „Erkrankungen /Ursachen"

Erkrankungen 1990	Erkrankungen 2020
1. Ischämische Herzerkrankung	1. Ischämische Herzerkrankung
2. Schlaganfall	2. Schlaganfall
3. Pneumonie	3. COPD
4. Diarrhoe	4. Pneumonie
5. Perinatale Mortalität	5. Lungenkarzinom
6. COPD	6. Verkehrsunfall

1. Nationale Versorgungsleitlinie COPD, www.copd-versorgungsleitlinie.de, Version 1.7, 2010
2. Halbert et al. Global burden of COPD: systematic review and meta-analysis. Eur Respir J 2006;28:523-32.
3. Murray et Lopez. Global mortality, disability, and the contribution of risk factors: global burden of disease study. Lancet 1997;349:1436-42.

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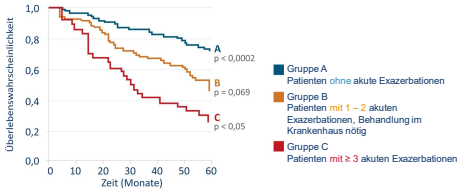
Exazerbationen



Soler-Cataluña et al. Thorax 2005;60:925-31

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Die COPD-Definition ist sehr heterogen[1]

Die Chronisch obstruktive Lungenerkrankung ist eine heterogene Erkrankung, die durch chronische respiratorische Symptome **(Atemnot, Husten, Auswurf und Exazerbationen)** charakterisiert ist, durch Anomalien in den **Atemwegen (Bronchitis, Bronchiolitis)** und/oder Alveolen **(Lungenemphysem)** gekennzeichnet ist und eine persistierende, oft progrediente Atemwegsobstruktion hervorruft.

COPD = Chronisch-obstruktive Lungenerkrankung.
1. GOLD Report 2024. Available from www.goldcopd.org. (letzter Zugriff: Juli 2024).

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Ätiologische Einteilung der COPD[1]

Classification	Description
Genetically determined COPD (COPD-G)	Alpha-1 antitrypsin deficiency (AATD) Other genetic variants with smaller effects acting in combination
COPD due to abnormal lung development (COPD-D)	Early life events, including premature birth and low birthweight, among others
Environmental COPD	
Cigarette smoking COPD (COPD-C)	• Exposure to tobacco smoke, including in utero or via passive smoking • Vaping or e-cigarette use • Cannabis
Biomass and pollution exposure COPD (COPD-P)	Exposure to household pollution, ambient air pollution, wildfire smoke, occupational hazards
COPD due to infections (COPD-I)	Childhood infections, tuberculosis-associated COPD, HIV-associated COPD
COPD & asthma (COPD-A)	Particularly childhood asthma
COPD of unknown cause (COPD-U)	

AATD = Alpha-1-Antitrypsin-Mangel. COPD = Chronisch-obstruktive Lungenerkrankung; HIV = Humanes Immundefizienz-Virus.
1. GOLD Report 2024. Available from www.goldcopd.org. (letzter Zugriff: Juli 2024).

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COPD wirkt sich auf das tägliche Leben der Patienten aus

Patienten sind durch zwei klinische Hauptmerkmale der COPD belastet:

Dyspnoe
(chronische Dyspnoe)

Hauptsymptom der COPD, gekennzeichnet durch:[1]
- Kurzatmigkeit[1]
- Müdigkeit[1]
- Eingeschränkte Aktivität[1]
- Negative Auswirkungen auf die psychische Gesundheit[2]

Dyspnoe ist ein Hauptrisikofaktor für Exazerbationen[3]

Exazerbationen

Eine Exazerbation ist der wichtigste Prädiktor für eine weitere Exazerbation[4,5]
Exazerbationen können die Dyspnoe verschlimmern[6]

COPD = Chronisch-obstruktive Lungenerkrankung.
1. Kessler R, *et al. Eur Respir J.* 2011;37(2):264-272. 2. Giacomini M, *et al. Ont Health Technol Assess Ser.* 2012;12(13):1-147. 3. Punekar YS, *et al. Pulm Ther.* 2016;2:59-72. 4. Suissa S, *et al. Thorax.* 2012;67(11):957-963. 5. Hurst JR, *et al. N Engl J Med.* 2010;363(12):1128-1138. 6. Bourbeau J, *et al. Eur Respir J.* 2007;30(5):907-913.

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Obstruktive Ventilationsstörungen

- Erst einmal die Diagnose stellen

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Unterschiede COPD-Asthma

Diagnose	Charakteristika
COPD	• Anhaltende Atemwegsobstruktion • Auftreten ab der Mitte des Lebens • Symptome langsam progredient • Vorgeschichte von Tabakrauchen oder Exposition gegenüber anderen Staub- und Rauchgasen • Allergien haben keinen Einfluss
Asthma	• Frühes erstes Auftreten (oft in der Kindheit) • Tägliche Schwankungen der Symptomintensität • Verschlechterung der Symptome in der Nacht / am frühen Morgen • Allergien spielen oft eine Rolle • Vorgeschichte von Asthma in der Familie

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Definitionen

COPD

- *Vermeidbare und behandelbare chronische progressive Erkrankung*
- *persistierende respiratorische Symptomen*
  - Dyspnoe, Husten und/oder Sputum
- *Atemflusslimitation (LUFU)*
  - bedingt durch Abnormitäten der Atemwege und/oder Lungen, meist herbeigeführt durch Inhalation von schädliche Partikel oder Gase.

http://www.goldcopd.org

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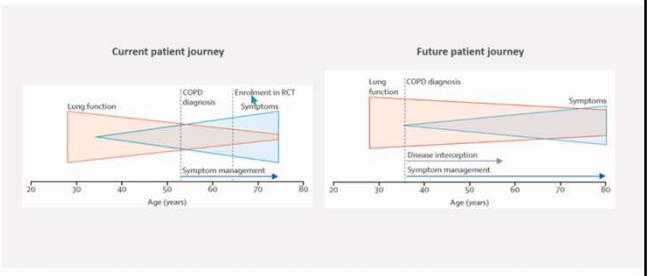
Zeitpunkt der COPD-Diagnose und die Folgen
Aktuell vs. Zukunft



Stolz D, et al. Lancet 2022;400:921–972

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Original Article

Early Diagnosis and Treatment of COPD and Asthma — A Randomized, Controlled Trial

Shawn D. Aaron, M.D., Katherine L. Vandemheen, M.Sc.N., G. Alex Whitmore, Ph.D., Celine Bergeron, M.D., Louis-Philippe Boulet, M.D., Andréanne Côté, M.D., R. Andrew McIvor, M.D., Erika Penz, M.D., Stephen K. Field, M.D., Catherine Lemière, M.D., Irvin Mayers, M.D., Mohit Bhutani, M.D., Tanweer Azher, M.D., M. Diane Lougheed, M.D., Samir Gupta, M.D., Nicole Ezer, M.D., Christopher J. Licskai, M.D., Paul Hernandez, M.D., Martha Ainslie, M.D., Gonzalo G. Alvarez, M.D., Sunita Mulpuru, M.D., for the UCAP Investigators

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- Case finding for symptomatic adults with undiagnosed asthma or COPD was coupled with a randomized trial to compare pulmonologist-directed and usual care.
- Pulmonologist-directed care led to less health care utilization.

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Respiratory Treatments Received during the 12-Month Trial Period.

Table 2. Respiratory Treatments Received during the 12-Month Trial Period.*

Treatment†	Intervention (N = 253)	Usual Care (N = 255)
	number of participants (percent)	
No respiratory treatments during the entire trial period	19 (7.5)	92 (36.1)
SABA only	15 (5.9)	35 (13.7)
LAMA	32 (12.6)	27 (10.6)
LABA	0	11 (4.3)
ICS	56 (22.1)	32 (12.5)
LTRA	1 (0.4)	2 (0.8)
LAMA + LABA	34 (13.4)	6 (2.4)
LABA + ICS	101 (39.9)	53 (20.8)
LAMA + LABA + ICS	29 (11.5)	9 (3.5)
Supplemental oxygen at home	3 (1.2)	1 (0.4)
Short-course systemic glucocorticoid	13 (5.1)	7 (2.7)

* Totals can exceed 100% because some participants had their medications changed during the 12-month trial period. ICS denotes inhaled glucocorticoid, LABA long-acting beta-agonist, LAMA long-acting muscarinic antagonist, LTRA leukotriene-receptor antagonist, and SABA short-acting beta-agonist.
† Most participants who received a LAMA, a LABA, an ICS, or an LTRA also received an as-needed prescription for a SABA.

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Secondary Outcomes.

Table 3. Secondary Outcomes.

Outcome	Intervention	Usual Care	Mean Difference (95% CI)*
SGRQ total score†			
At baseline	39.0	38.1	
At 12 mo	28.8	31.5	
Change over 12 mo — points	−10.2	−6.8	−3.5 (−6.8 to −0.9)
CAT total score‡			
At baseline	17.5	17.5	
At 12 mo	13.7	14.9	
Change over 12 mo — points	−3.8	−2.6	−1.3 (−2.4 to −0.1)
Prebronchodilator FEV$_1$§			
At baseline — % of predicted normal value	76.1	78.9	
At 12 mo — % of predicted normal value	80.8	80.4	
Change over 12 mo — percentage points	4.7	1.5	3.2 (1.3 to 4.9)
SF-36 total score¶			
At baseline	61.9	64.2	
At 12 mo	66.3	66.7	
Change over 12 mo — points	4.4	2.5	1.9 (−0.4 to 4.2)

*The mean between-group difference is the value in the intervention group minus the value in the usual-care group. The 95% confidence intervals have not been adjusted for multiplicity and should not be used to infer definitive treatment effects.
†Total scores on the SGRQ range from 0 to 100. Negative changes indicate improvements in disease-specific quality of life; the minimal clinically important change within individuals over time is −4 points. Baseline and 12-month data on the SGRQ total score were available for 236 participants in the intervention group and for 228 participants in the usual-care group.
‡Total scores on the CAT range from 0 to 40. Negative changes indicate reductions in symptom burden and its effect on daily activities and health status; the minimal clinically important change within individuals over time is −2 points. Baseline and 12-month data on the CAT total score were available for 241 participants in the intervention group and for 228 participants in the usual-care group.
§Baseline and 12-month data or the percentage of the predicted normal prebronchodilator FEV$_1$ were available for 223 participants in the intervention group and for 198 participants in the usual-care group.
¶Total scores on the SF-36 range from 0 to 100. Positive changes in the SF-36 indicate improvements in general quality of life; the minimal clinically important change established for this questionnaire is 5. Baseline and 12-month data on the SF-36 total score were available for 241 participants in the intervention group and for 228 participants in the usual-care group.

Aaron SD et al. N Engl J Med2024;390:2061-2073

The NEW ENGLAND JOURNAL of MEDICINE

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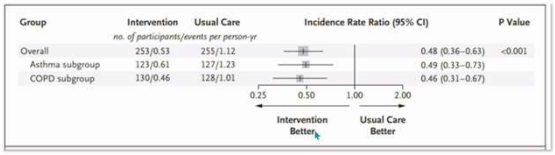
Aaron SD et al. N Engl J Med2024;390:2061-2073

Frühe Diagnose und Behandlung von nichtdiagnosizierten Fällen mit Asthma und COPD

Primärer Endpunkt – Ereignisse mit Anwendung von Gesundheitsleistungen für eine respiratorische Erkrankung über ein Jahr

Group	Intervention	Usual Care	Incidence Rate Ratio (95% CI)	P Value
	no. of participants/events per person-yr			
Overall	253/0.53	255/1.12	0.48 (0.36–0.63)	<0.001
Asthma subgroup	123/0.61	127/1.23	0.49 (0.33–0.73)	
COPD subgroup	130/0.46	128/1.01	0.46 (0.31–0.67)	



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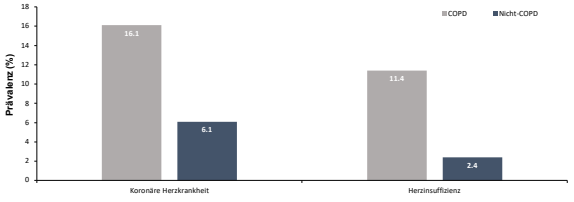
Im Vergleich zu Patienten ohne COPD besteht bei COPD-Patienten ein erhöhtes Risiko für Herz-Kreislauf-Erkrankungen …[1–5]

Prävalenz **verschiedener kardiovaskulärer Erkrankungen** in **COPD-** (n = 958) **und Nicht-COPD-Populationen** (n = 17.384)*†



*Daten aus der Gruppe der Erwachsenen der nationalen Gesundheitsbefragung von 2002 (2002 National Health Interview Survey). †P < 0.0001 für alle Variablen (Wald chi-squared test)
1. Gurkendall SM, et al. Ann Epidemiol 2006;16:63–70. 2. Mölleneva H, et al. Chest 2013;144:1163–1178. 3. Finkelstein J, et al. Int J Chron Obstruct Pulmon Dis 2009;4:337–349. 4. Chen W, et al. Lancet Respir Med 2015;3:631–639. 5. Williams MC, et al. Thorax 2014;69:718–723

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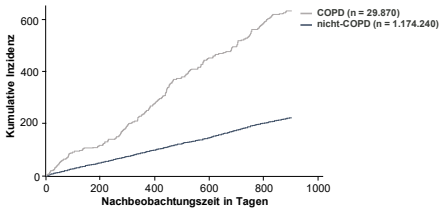
… oder für zukünftige kardiovaskuläre Vorfälle einschliesslich von Myokardinfarkten[1,2]

Kumulative Inzidenz eines **erstmaligen akuten Myokardinfarkts bei COPD** im Vergleich zu **Nicht-COPD-Populationen**[2*]



Reproduziert von Thorax, Feary JR et al. 65, 956–962, 2010 mit Erlaubnis der BMJ Publishing Group Ltd
*Es wurden die Daten aller Patienten analysiert, die am 25. Februar 2005 noch lebten und an THIN teilnahmen (n = 1.204.110), mit einem Median von 895 Tagen.
MI, Myokardinfarkt; THIN, The Health Improvement Network
1. Gurkendall SM, et al. Ann Epidemiol 2006;16:63–70. 2. Feary JR, et al. Thorax 2010;65:956–962

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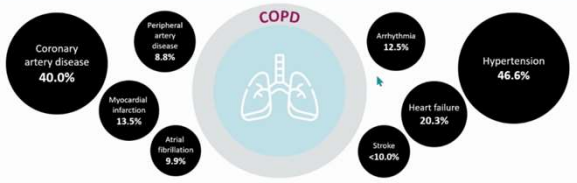
COPD und kardiovaskuläre Erkrankungen

Different **pathophysiological mechanisms** and triggering factors link the two disorders and contribute to the increased CV risk in patients with COPD

Prevalence of CVD in patients with COPD



Rogliani P, et al. Expert Rev Respir Med 2021;15:59–70

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CF Vogelmeier et al. Elucidating the risk of cardiopulmonary consequences of an exacerbation of COPD: results of the EXACOS-CV study in Germany. BMJ Open Respir Res. 2024;11:e002153

EL Graul et al. Factors associated with non-fatal heart failure and atrial fibrillation or flutter within the first 30 days post COPD exacerbation: a nested case-control study. BMC Pulm Med. 2024;24:221

- COPD-Exazerbationen - Risiko für Entwicklung von schweren kardiovaskulären Ereignissen
- Risiko nach stationären Aufenthalten wegen einer COPD-Exazerbation massiv erhöht
- Patienten, die im Nachgang einer COPD-Exazerbation ein Herzversagen und/oder Vorhofflimmern/Vorhofflattern entwickeln
- in der Vorgeschichte und/oder bezüglich der vorhandenen Medikamente deutliche Anhaltspunkte für Risiko

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GOLD 2023 bekräftigt die Bedeutung der Prävention vorzeitiger Sterblichkeit durch die Pharmakotherapie[1]

Eine **Dreifach-Therapie** ist die **einzige Pharmakotherapie**, bei der es Hinweise gibt, dass sie die **Mortalität** in COPD-Patienten **reduziert**[1]

Therapie	RCT*	Behandlungseffekt auf die Mortalität	Patienten-Charakteristika
Pharmakotherapie			
LABA + LAMA + ICS	Ja	Vergleich der relativen Risiko-Reduktion von Dreifach- und Zweifach-LABD: **IMPACT:** HR 0,72 (95 % KI 0,53–0,99)[2] **ETHOS:** HR 0,51 (95 % KI 0,33–0,80)[3]	Symptomatische Patienten mit regelmässigen und/oder schweren Exazerbationen in der Vergangenheit

Nicht-pharmakologische Optionen, die die Mortalität reduzieren beinhalten Rauchstopp, Lungen-Rehabilitation, langfristige Sauerstoff-Therapie, nicht-invasive Überdruckbeatmung sowie operative Verringerung des Lungenvolumens

GOLD 2023, Seite 68, Tabelle 3.6

*RCT mit einer vordefinierten Analyse des Mortalitätsergebnisses (primär oder sekundär)

ETHOS, Efficacy and Safety of Triple Therapy in Obstructive Lung Disease; HR, Hazard Ratio; LABD, langfristig wirksame Bronchodilatator-Therapie; RCT, randomisiert-kontrollierte Studie

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for prevention, diagnosis and management of COPD. 2023.; 2. Lipson DA, et al. N Engl J Med 2018;378:1671-1680. 3. Rabe KF, et al. N Engl J Med 2020;383:35–48.

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COPD: medikamentöse Therapie

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Biologica bei COPD??

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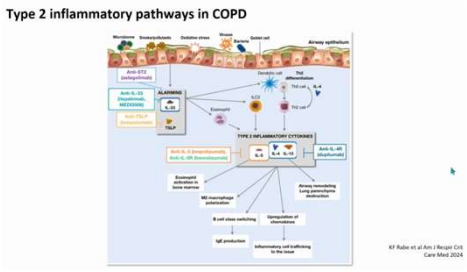
Biologica bei COPD??



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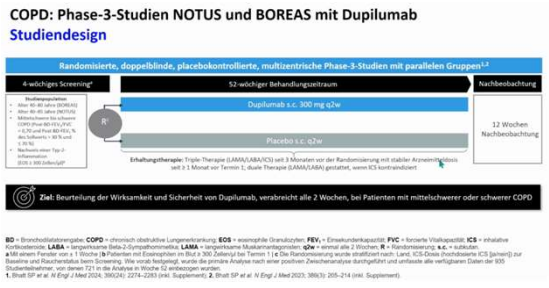

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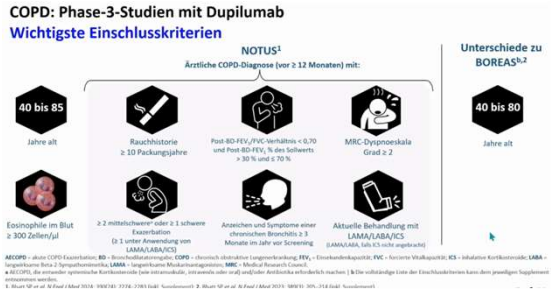

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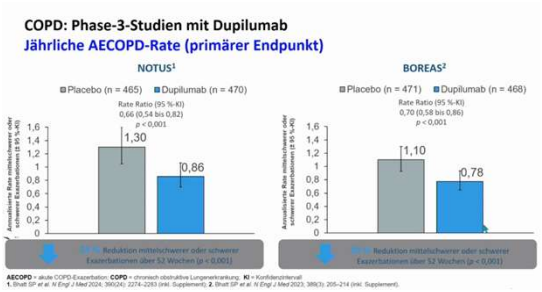

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SP Bhatt et al. Dupilumab for COPD with Blood Eosinophil Evidence of Type 2 Inflammation. N Engl J Med. 2024;390:2274-2283

- Zwei positive Studien für die Anwendung von Dupilumab bei ausgewählten Patienten
- Ergebnisse (sehr) ähnlich
- Konsistente Daten für alle Endpunkte

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COPD – nicht medikamentöse Therapie

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COPD – nicht medikamentöse Therapie

- Langzeit-O2-Therapie
- Nicht-invasive Beatmung
  - Vs nasale Highflow-O2-Therapie (NHFC)
- Ambulante/stationäre pulmonale Rehabilitation
- Oszillierende PEP Devices
- Schulungen (Besser leben mit COPD)
- LVRS/E, LTPx
- Palliativmedizin
- ……

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Oszillatorische positive exspiratorische Druck Therapie bei COPD Patienten mit Sekret

SM Alghamdi et al Thorax. 2023;78:136-143

Stabile COPD + Sputum täglich bzw. die meisten Tage (n=122)

Acapella© Device (OPEP) — 3x täglich

Usual care (UC)

- Primärer Outcome Parameter – Husten bezogene Lebensqualität: Leicester Cough Questionnaire (LCQ)
- Sekundärer Outcome Parameter – Fatigue (Functional Assessment of Chronic Illness Therapy, FACIT score), generic quality of life (EuroQol-5 Dimensions, EQ-5D)

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Wie werden **Exazerbationen definiert?**

GOLD-Leitlinie 2020:[1]

„Eine COPD-Exazerbation ist definiert als akute Verschlimmerung der respiratorischen Symptome, die zu einer zusätzlichen Therapie führt."

Definition nach dem **Rome-Proposal**:*[2]

...ein Ereignis, das durch Dyspnoe und/oder Husten und Auswurf gekennzeichnet ist, die sich über einen Zeitraum von ≤14 Tage verschlechtern, das von Tachypnoe und/oder Tachykardie begleitet sein kann und oft mit einer erhöhten lokalen und systemischen Entzündung einhergeht, die durch eine Atemwegsinfektion, Luftverschmutzung oder eine andere Beeinträchtigung der Atemwege verursacht wird."

**Adaptiert von GOLD 2024*[3]

COPD = Chronisch-obstruktive Lungenerkrankung. GOLD = Global Initiative for Chronic Obstructive Lung Disease.
1. GOLD 2020 Pocket Guide. Available from www.goldcopd.org. (letzter Zugriff: Juli 2024). 2. Celli BR, et al. Am J Respir Crit Care Med. 2021;204(11):1251-1258. 3. GOLD Report 2024. Available from www.goldcopd.org. (letzter Zugriff: Juli 2024).

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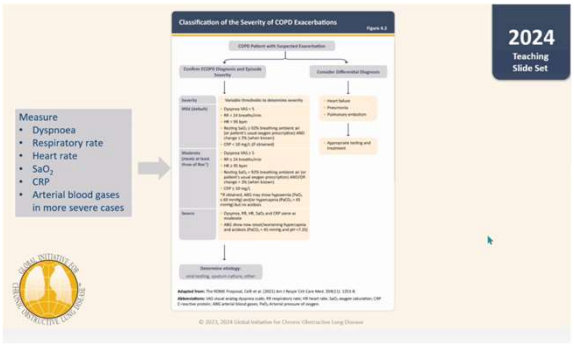

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J Zheng et al. Validation of the Rome Severity Classification of Chronic Obstructive Pulmonary Disease Exacerbation: A Multicenter Cohort Study. Int J Chron Obstruct Pulmon Dis. 2024;19:193-204

- Guter Vorhersagewert bzgl. Aufnahme auf Intensivstation und Notwendigkeit für Beatmung
- Cave: keine prospektive Studie

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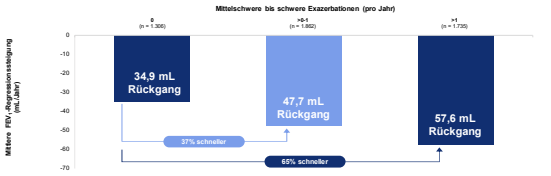
Selbst eine einzige Exazerbation kann **langfristige Folgen** haben[1]

Das Auftreten von mehr als einer Exazerbation führt zu einer 65% schnelleren Verschlechterung der Lungenfunktion im Vergleich zur Situation ohne Exazerbation*

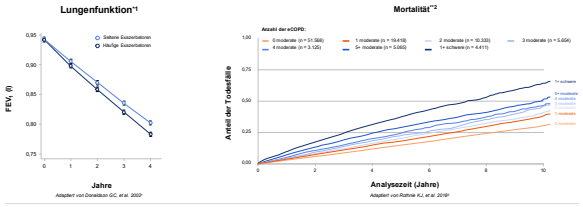


Adaptiert von Celli BR, et al. 2008[1]

*Post-hoc-Analyse der 3-jährigen randomisierten TORCH-Studie bei Patienten mit mittelschwerer bis schwerer COPD (n = 6.112). TORCH hat für den primären Endpunkt der Differenz der Gesamtmortalität nach drei Jahren im Vergleich zu Fluticasonpropionat und Salmeterol vs. Placebo keine statistische Signifikanz erreicht. Die dargestellten Daten vergleichen Patienten mit <0-1 mittelschweren/schweren Exazerbation pro Jahr vs. 0 Exazerbationen pro Jahr.[1]
COPD = Chronisch-obstruktive Lungenerkrankung; FEV1 = Forciertes Exspirationsvolumen in 1 Sekunde; n = Anzahl der Patienten.
1. Celli BR, et al. Am J Respir Crit Care Med. 2008;178(4):332-338.*

37

Lungenfunktionsverschlechterung und erhöhte Sterblichkeitsrate als Folge häufiger COPD Exazerbationen

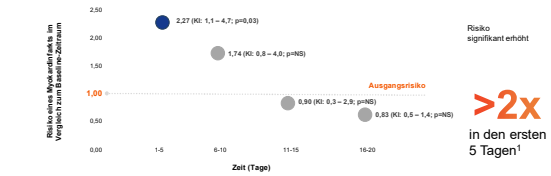


Adaptiert von Donaldson GC, et al. 2002[1]
Adaptiert von Rothnie KJ, et al. 2018[2]

*In dieser Studie wurde prospektiv über einen Zeitraum von vier Jahren an einer Kohorte von 109 Patientinnen und Patienten mit moderater bis schwerer COPD der Zusammenhang zwischen Lungenfunktionsverschlechterung und Exazerbationshäufigkeit untersucht. Zur Feststellung der Exazerbationen wurden täglich Daten zur Lungenfunktion sowie zu den Symptomen erhoben.
**Populationsbasierte Studie an 99.074 Patientinnen und Patienten mit COPD aus dem UK Clinical Practice Research Datalink vom 1. Januar 2004 bis zum 31. März 2015; die Zeit bis zum Tod wurde mithilfe eines Proportional-Hazard-Models nach Cox geschätzt.
COPD = Chronisch-obstruktive Lungenerkrankung; eCOPD = COPD-Exazerbation; FEV1 = Forciertes Exspirationsvolumen in 1 Sekunde; n = Anzahl der Patienten.
1. Donaldson GC, et al. Thorax. 2002;57(10):847-852. 2. Rothnie KJ, et al. Am J Respir Crit Care Med. 2018;198(4):464-471.*

38

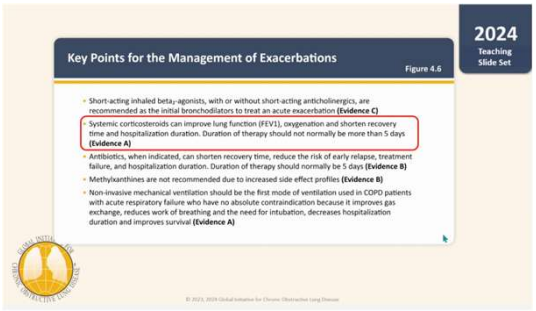
Das **Risiko eines Herzinfarkts verdoppelt sich** in den ersten Tagen nach einer Exazerbation*[1]



Adaptiert von Donaldson GC, et al. 2010[1]

*Analyse der Daten von 25.857 Patienten mit COPD, die in die Datenbank des Health Improvement Network in Grossbritannien eingegeben wurden. Exazerbationen wurden anhand Verwendung einer im Gesundheitswesen gebräuchlichen Definition der Verordnung oraler Kortikosteroide in einer Dosierung von > 20 mg/Tag und/oder ausgewählter oraler Antibiotika definiert (health-care use definition). In dem 5-Tageszeitraum nach der Exazerbation bestand ein 2,27-fach (95%-KI: 1,1; 4,7; p = 0,03) erhöhtes Herzinfarktrisiko.[1]
*Exazerbation, die eine Behandlung, einschl mit oralen Steroiden als auch einem ausgewählten oralen Antibiotikum erforderlich machte.[1]
COPD = Chronisch-obstruktive Lungenerkrankung; KI = Konfidenzintervall.
1. Donaldson GC, et al. Chest. 2010;137(5):1091-1097.*

39



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Take-Home Message

COPD ist eine häufige, klinisch relevante und kostenintensive Erkrankung

Exazerbationen spielen eine entscheidende Rolle im Verlauf der Erkrankung

Symptombehandlung und Risikoreduktion beeinflussen die Mortalität[6]

Ziele in der Therapie sind
a. Symptomatik verbessern
b. Exazerbationen verhindern
c. Überleben verlängern (ev. ICS, LTOT > LVRS > Transplantation)

ICS in Erwägung ziehen bei
a. Erhöhte Bluteosinophilenzahl
b. Gehäufte Exazerbationen (≥ 1 moderate Exazerbation)[#]

Nicht vergessen: nicht-medikamentöse Therapie und Therapieadhärenz im Auge behalten

#trotz einer angemessenen langwirksamen Bronchodilatator-Inhalationstherapie.
COPD = Chronisch-obstruktive Lungenerkrankung; ICS = Inhalatives Kortikosteroid; LTOT = Langzeit-Sauerstofftherapie; LVRS = Chirurgischen Lungenvolumenreduktion; PRISm = Preserved ratio impaired spirometry

1. Adeloye D, et al. J Glob Health. 2015;5(2):020415. 2. Bely F, et al. PLoS One. 2013;8:e63285. 3. Vinolo-Cabrera AM, et al. Swiss Med Wkly. 2016;146:w14381. 4. Villegas CG, et al. Health Econ Rev. 2021;11(1):31. 5. Hurst JR, et al. N Engl J Med. 2010;363(12):1128-1138. 6. GOLD Report 2024. Available from www.goldcopd.org. (letzter Zugriff: Juli 2024). 7. Sandozi A, et al. Multidiscipln Resp Med. 2014;9:60.

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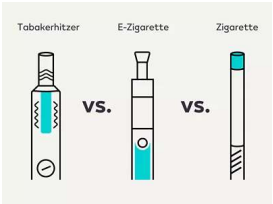

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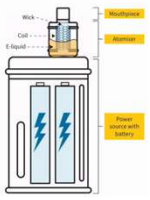
COPD

• E-Zigaretten



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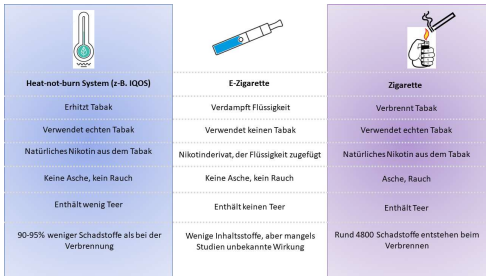

Heat-not-burn System (z-B. IQOS)	E-Zigarette	Zigarette
Erhitzt Tabak	Verdampft Flüssigkeit	Verbrennt Tabak
Verwendet echten Tabak	Verwendet keinen Tabak	Verwendet echten Tabak
Natürliches Nikotin aus dem Tabak	Nikotinderivat, der Flüssigkeit zugefügt	Natürliches Nikotin aus dem Tabak
Keine Asche, kein Rauch	Keine Asche, kein Rauch	Asche, Rauch
Enthält wenig Teer	Enthält keinen Teer	Enthält Teer
90-95% weniger Schadstoffe als bei der Verbrennung	Wenige Inhaltsstoffe, aber mangels Studien unbekannte Wirkung	Rund 4800 Schadstoffe entstehen beim Verbrennen

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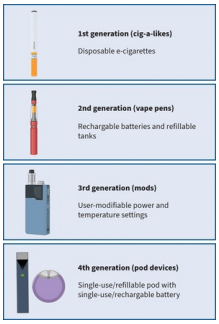

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A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy N Engl J Med 2019; 380:629-637

Table 2. Abstinence Rates at Different Time Points and Smoking Reduction at 52 Weeks.^

Outcome	E-Cigarettes (N = 438)	Nicotine Replacement (N = 446)	Primary Analysis: Relative Risk (95% CI)†	Sensitivity Analysis: Adjusted Relative Risk (95% CI)
Primary outcome: abstinence at 52 wk — no. (%)	79 (18.0)	44 (9.9)	1.83 (1.30–2.58)	1.75 (1.24–2.46)‡
Secondary outcomes				
Abstinence between wk 26 and wk 52 — no. (%)	93 (21.2)	53 (11.9)	1.79 (1.32–2.44)	1.82 (1.34–2.47)§
Abstinence at 4 wk after target quit date — no. (%)	192 (43.8)	134 (30.0)	1.45 (1.22–1.74)	1.43 (1.20–1.71)¶
Abstinence at 26 wk after target quit date — no. (%)	155 (35.4)	112 (25.1)	1.40 (1.14–1.72)	1.36 (1.15–1.67)‡
Carbon monoxide–validated reduction in smoking of ≥50% in participants without abstinence between wk 26 and wk 52 — no./total no. (%)	44/345 (12.8)	29/393 (7.4)	1.75 (1.12–2.72)	1.73 (1.11–2.69)‖

^ Abstinence at 52 weeks was defined as a self-report of smoking no more than five cigarettes from 2 weeks after the target quit date, validated biochemically by an expired carbon monoxide level of less than 8 ppm at 52 weeks. Abstinence between week 26 and week 52 was defined as a self-report of smoking no more than five cigarettes between week 26 and week 52, plus an expired carbon monoxide level of less than 8 ppm at 52 weeks. Abstinence at 4 weeks was defined as a self-report of no smoking from 2 weeks after the target quit date, plus an expired carbon monoxide level of less than 8 ppm at 4 weeks. Abstinence at 26 weeks was defined as a self-report of smoking no more than five cigarettes from 2 weeks after the target quit date to 26 weeks; there was no validation by expired carbon monoxide level.
† The analysis was adjusted for trial center only.
‡ The analysis was adjusted for trial center, marital status, age at smoking initiation, and score on the Fagerström Test for Cigarette Dependence.
§ The analysis was adjusted for trial center, age, score on the Fagerström Test for Cigarette Dependence, and age at smoking initiation.
¶ The analysis was adjusted for trial center, education level, partner who smokes (yes or no), and score on the Fagerström Test for Cigarette Dependence.
‖ The analysis was adjusted for trial center, sex, age, and partner who smokes (yes or no).

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Vaping helps adults quit smoking better than traditional methods, says Cochrane *BMJ* 2022;379:o2782

- University of Oxford
  - 78 studies, including 40 randomised controlled trials, which involved 22 052 adults
  - who smoked to assess the
  - effectiveness, tolerability, and safety of e-cigarettes to help quitting
  - They found that quit rates among adults using nicotine e-cigarettes were higher than those receiving nicotine replacement therapy (risk ratio 1.63, 95% confidence interval 1.30 to 2.04; I^2=10%; six studies, 2378 participants)
  - This could translate to an additional 4 quitters per 100 (95% CI 2 to 6
- Although their findings show that e-cigarettes are an effective way to help adults stop smoking, the researchers said that e-cigarettes were not risk-free and should not be used by those who do not smoke, especially young

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Prospective study of e-cigarette use and respiratory symptoms in adolescents and young adults 2023 Aug

15:thoraxjnl-2022-218670

- **Rationale:** Electronic cigarette (e-cigarette) aerosol contains volatile aldehydes, including flavourings and oxidant metals with known pulmonary toxicity
- **Conclusions:** E-cigarette use in young adults was associated with respiratory symptoms, independent of combustible cannabis and cigarette exposures

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Original Article

Electronic Nicotine-Delivery Systems for Smoking Cessation

Reto Auer, M.D., Anna Schoeni, Ph.D., Jean-Paul Humair, M.D., M.P.H., Isabelle Jacot-Sadowski, M.D., Ivan Berlin, M.D., Ph.D., Mirah J. Stuber, M.D., Moa Lina Haller, M.D., Rodrigo Casagrande Tango, M.D., M.P.H., Anja Frei, Ph.D., Alexandra Strassmann, Ph.D., Philip Bruggmann, M.D., Florent Baty, Ph.D., Martin Brutsche, M.D., Ph.D., Kali Tal, Ph.D., Stéphanie Baggio, Ph.D., Julian Jakob, M.D., Nicolas Sambiagio, Ph.D., Nancy B. Hopf, Ph.D., Martin Feller, M.D., Nicolas Rodondi, M.D., and Aurélie Berthet, Ph.D.

N Engl J Med
Volume 390(7):601-610
February 15, 2024

The NEW ENGLAND JOURNAL of MEDICINE

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Original Article

Electronic Nicotine-Delivery Systems for Smoking Cessation

- Untersucht wurde
  - Wirksamkeit, Sicherheit und Toxikologie von E-Dampfern im Rahmen einer umfassenden Rauchstoppberatung

  verglichen mit

  - einer ebenso umfassenden Rauchstoppberatung ohne E-Dampfer.
  - Zur Rauchstoppberatung in beiden Gruppen gehörten
    - diverse therapeutische Angebote sowie Empfehlungen zu Arzneimitteln und Nikotinersatzprodukten

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- In this randomized trial, the addition of electronic cigarettes to standard smoking-cessation counseling resulted in greater abstinence from smoking at 6 months but also greater nicotine use.

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RESEARCH SUMMARY

Electronic Nicotine-Delivery Systems for Smoking Cessation

Auer R et al. DOI: 10.1056/NEJMoa2308815

CLINICAL PROBLEM

Some tobacco smokers use electronic nicotine-delivery systems, or e-cigarettes, as a smoking-cessation aid. Evidence regarding the efficacy and safety of these systems is needed.

CLINICAL TRIAL

Design: An open-label, multicenter, randomized, controlled trial in Switzerland assessed the efficacy and safety of e-cigarettes added to standard-of-care smoking-cessation counseling in adult tobacco smokers who wanted to quit smoking.

Intervention: 1246 adult volunteers who had smoked at least five cigarettes per day for ≥12 months and who wanted to quit smoking within 3 months were assigned to either an intervention group that received free e-cigarettes (e-cigarette starter kits and e-liquids for up to 6 months) plus standard-of-care smoking-cessation counseling or a control group that received standard-of-care counseling and a voucher that they could use for any purpose, including nicotine-replacement therapy. The primary outcome was biochemically validated, continuous abstinence from tobacco smoking at 6 months.

RESULTS

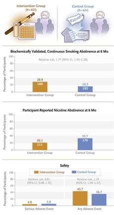
Efficacy: Among evaluable participants, the proportion with continuous smoking abstinence at 6 months was higher in the intervention group than in the control group. The proportion who reported nicotine abstinence at 6 months, a secondary outcome, was lower in the intervention group, however.

Safety: The incidence of serious adverse events was similar in the two groups, whereas the incidence of any adverse event was higher in the intervention group.

LIMITATIONS AND REMAINING QUESTIONS

- Participants were aware of their group assignments.
- Participants in the intervention group received free e-cigarettes and e-liquids, whereas those in the control group received a voucher that they could use for any purpose, including nicotine-replacement therapy.
- Whether the intervention will have sustained benefits is unknown; ongoing follow-up will collect data at 12, 24, and 60 months.

Links: Full Article | NEJM Quick Take | Editorial



CONCLUSIONS

The addition of e-cigarettes to standard smoking-cessation counseling resulted in greater abstinence from tobacco use among smokers than smoking-cessation counseling alone.

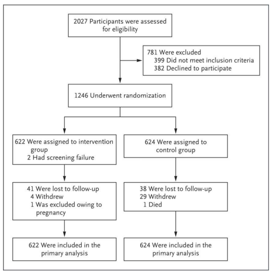


Table 1. Characteristics of the Participants at Baseline.*

Characteristic	Control Group (N=624)	Intervention Group (N=622)	Total (N=1246)
Median age (IQR) — yr	39 (30–52)	37 (28–51)	38 (29–51)
Female gender identity — no. (%)	295 (47.3)	290 (46.6)	585 (47.0)
Employed — no. (%)	465 (74.5)	438 (70.4)	903 (72.5)
Highest educational level — no. (%)			
Obligatory school, some obligatory school, or no formal schooling†	45 (7.2)	50 (8.0)	95 (7.6)
Secondary education	277 (44.4)	291 (46.8)	568 (45.6)
Tertiary education	302 (48.4)	281 (45.2)	583 (46.8)
Median age at which smoking was started (IQR) — yr‡	16 (15–19)	16 (15–18)	16 (15–19)
Median no. of cigarettes per day (IQR)	15 (10–20)	15 (10–20)	15 (10–20)
At least one previous attempt to quit smoking — no. (%)‡	530 (84.9)	531 (85.4)	1061 (85.2)
Fagerström Test for Nicotine Dependence score‡§	4.4±2.3	4.3±2.3	4.3±2.3
Median expired CO level (IQR) — ppm¶	20 (12–29)	20 (13–29)	20 (12–29)

* Plus–minus values are means ±SD. CO denotes carbon monoxide, and IQR interquartile range.
† Obligatory school (i.e. compulsory school) lasts between 9 and 11 years in Switzerland, depending on local laws.
‡ Data are missing for 2 participants, 1 in each group.
§ The Fagerström Test for Nicotine Dependence consists of 6 questions that evaluate the quantity of cigarette consumption, the compulsion to use, and dependence; scores range from 0 to 10, with higher scores indicating greater dependence.[21]
¶ Data are missing for 18 participants, 11 in the intervention group and 7 in the control group.

Table 2. Primary and Secondary Outcomes.

Outcome	Control Group N=624	Intervention Group N=622	Difference, Intervention vs. Control (95% CI)*	Crude Relative Risk (95% CI)†	Adjusted Relative Risk (95% CI)‡
	number (percent)		*percentage points*		
Primary outcome: continuous abstinence from smoking at 6 months§	102 (16.3)	180 (28.9)	12.6 (8.0–17.2)	1.77 (1.43–2.20)	1.71 (1.39–2.12)
Secondary outcomes¶					
Continuous abstinence, without biochemical validation	146 (23.4)	237 (38.1)	14.7 (9.6–19.8)	1.63 (1.37–1.94)	1.57 (1.32–1.85)
Sustained abstinence allowing a 2-week grace period, with biochemical validation	110 (17.6)	191 (30.7)	13.1 (8.4–17.8)	1.74 (1.42–2.14)	1.70 (1.39–2.08)
Sustained abstinence allowing up to 5 cigarettes, with biochemical validation	109 (17.5)	219 (35.2)	17.7 (12.9–22.5)	2.02 (1.65–2.46)	1.96 (1.61–2.38)
Abstinence within previous 7 days, with biochemical validation	133 (21.3)	245 (39.4)	18.1 (13.1–23.1)	1.85 (1.54–2.21)	1.74 (1.47–2.07)
Abstinence within previous 7 days, without biochemical validation	200 (32.1)	332 (53.4)	21.3 (16.0–26.7)	1.67 (1.45–1.91)	1.56 (1.37–1.77)

* The absolute difference between the groups was calculated with 95% Newcombe-hybrid-score confidence intervals.
† Relative risk was calculated with 95% Koopman confidence intervals.
‡ The adjusted relative risk was a sensitivity analysis, which was performed with the use of a multivariable adjusted model with stabilized inverse probability of censoring weights, adjusted for trial site, age, identified gender, employment status, education, age that the participant started smoking, the number of cigarettes smoked per day, previous quit attempts, and Fagerström score.
§ The primary outcome, continuous abstinence from smoking at 6 months, was defined as a participant-reported abstinence from the target quit date to the 6-month follow-up visit, validated biochemically by a urinary anabasine level of less than 3 ng per milliliter and, if not available, by an expired CO level of 9 ppm or less. P<0.001 for the chi-square test between the control and intervention groups. The percentage meeting the primary outcome was 16.3% (95% CI, 13.6 to 19.4) in the control group and 28.9% (95% CI, 25.5 to 32.6) in the intervention group (Wilson confidence intervals[22]).
¶ The widths of the confidence intervals for the secondary outcomes have not been adjusted for multiplicity and may not be used in place of hypothesis testing.

Table 3. Participant-Reported Use of Tobacco Cigarettes, E-cigarettes, and Nicotine-Replacement Therapy at 6 Months.*

Participant-Reported Use	Control Group N=504	Intervention Group N=552	Difference, Intervention vs. Control
	number (percent)		*percentage points*
No tobacco cigarettes: "tobacco abstainers"	194 (38.5)	329 (59.6)	21.1
No tobacco cigarettes, no e-cigarettes: "tobacco and e-cigarette abstainers"	179 (35.5)	62 (11.2)	−24.3
With nicotine-replacement therapy	14 (2.8)	1 (0.2)	−2.6
With smoking-cessation medication	1 (0.2)	0	−0.2
E-cigarettes and no tobacco cigarettes: "exclusive e-cigarette users"	15 (3.0)	267 (48.4)	45.5
E-cigarettes without nicotine	5 (1.0)	50 (9.1)	8.1
E-cigarettes with nicotine	10 (2.0)	217 (39.3)	37.3
E-cigarettes and nicotine-replacement therapy	0	1 (0.2)	0.2
E-cigarettes and smoking-cessation medication	0	0	0
No nicotine: "nicotine abstainers"†	170 (33.7)	111 (20.1)	−13.6
Tobacco cigarettes	310 (61.5)	223 (40.4)	−21.1
Tobacco cigarettes and no e-cigarettes: "exclusive smokers"	294 (58.3)	122 (22.1)	−36.2
Tobacco cigarettes and nicotine-replacement therapy	18 (3.6)	4 (0.7)	−2.9
Tobacco cigarettes and smoking-cessation medication	2 (0.4)	0	−0.4
E-cigarettes and tobacco cigarettes: "dual users"	16 (3.2)	101 (18.3)	15.1
Without nicotine in e-cigarettes	5 (1.0)	10 (1.8)	0.8
With nicotine in e-cigarettes	11 (2.2)	91 (16.5)	14.3
With nicotine-replacement therapy	1 (0.2)	4 (0.7)	0.5
With smoking-cessation medication	0	0	0

* Categories of exposure are based on participant-reported use of e-cigarettes and tobacco cigarettes in the 7 days before the 6-month follow-up visit, and use of nicotine-replacement therapy within the 24 hours before the visit. This table shows data for 1056 out of 1246 participants (84.7%) who provided reports of their use of tobacco cigarettes and e-cigarettes at the 6-month follow-up visit (504 of 624 participants in the control group [80.8%] and 552 of 622 participants in the intervention group [88.7%]) (Table S3). The percentages for each category of exposure were computed with the number of participants reporting their use as the denominator. Participants who reported use of e-cigarettes with missing information on nicotine concentration in the e-cigarettes (5 in the control group and 23 in the intervention group) were classified as having used e-cigarettes without nicotine.

† This category is defined as no participant-reported exposure to nicotine through tobacco cigarettes, e-cigarettes with nicotine, or nicotine-replacement therapy.

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- The addition of e-cigarettes to standard smoking-cessation counseling resulted in greater abstinence from tobacco use among smokers than smoking-cessation counseling alone.

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The paradox of the safer cigarette: understanding the pulmonary effects of electronic cigarettes

K. Allbright et al

European Respiratory Journal 2024; 63(6): 2301494;
DOI: https://doi.org/10.1183/13993003.01494-2023

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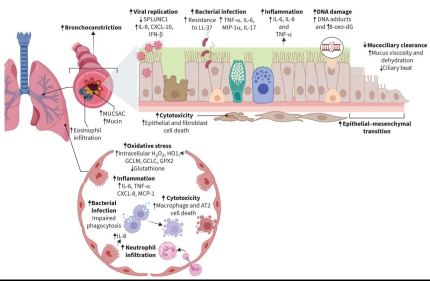

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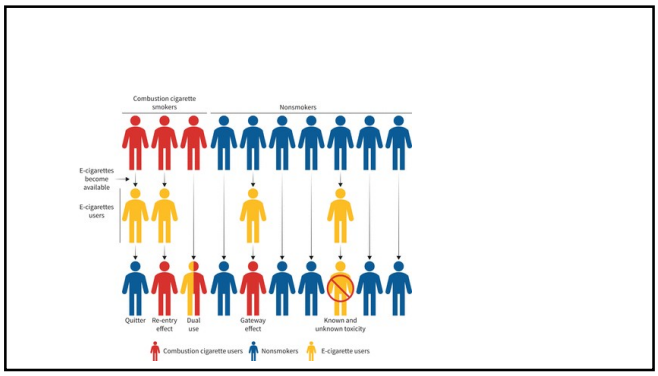

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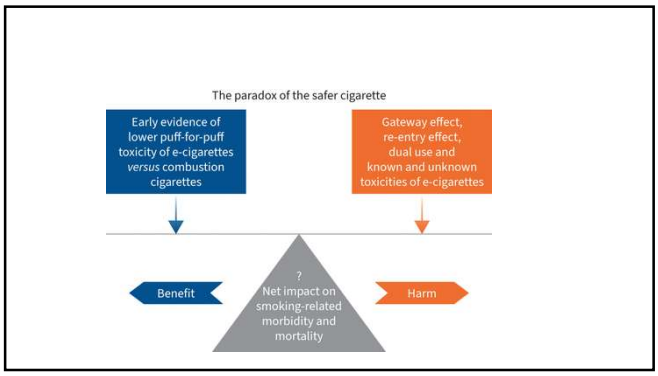

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Fazit für die Praxis

K Allbright et al. The paradox of the safer cigarette: understanding the pulmonary effects of electronic cigarettes. Eur Respir J. 2024;63:2301494

- E-Zigaretten keine sicherere Alternative zu üblichen Zigaretten

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