COPD 비약물치료

국민건강보험 일산병원 호흡기내과 정은기

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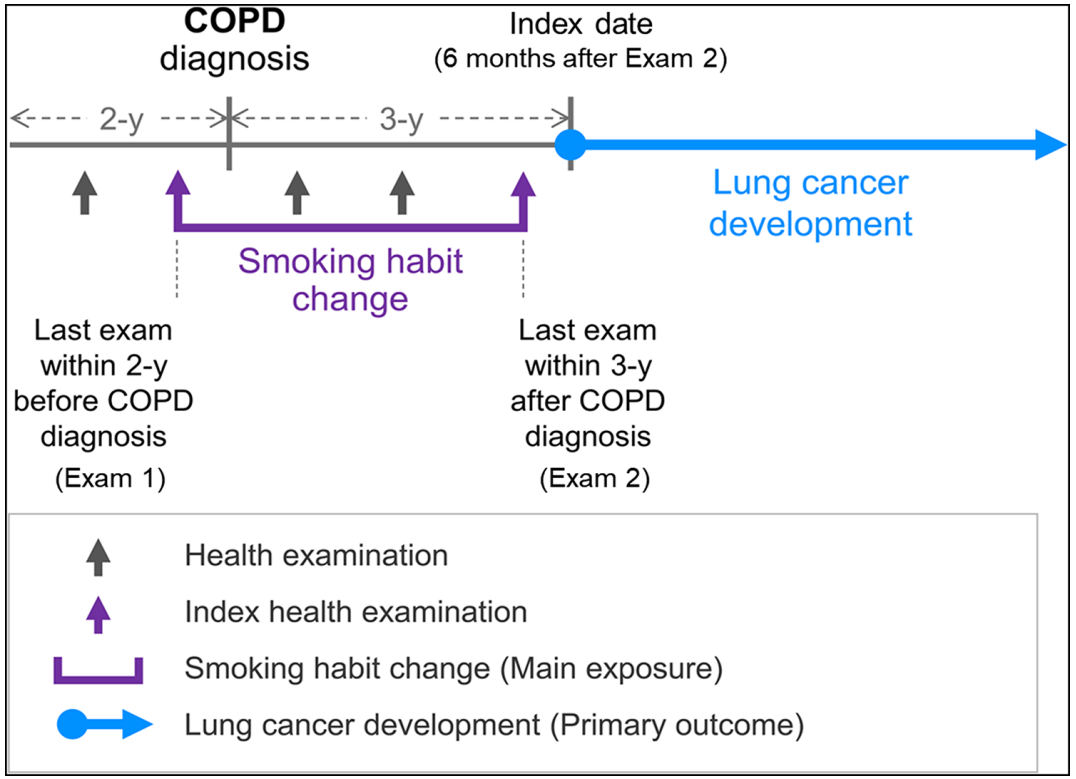
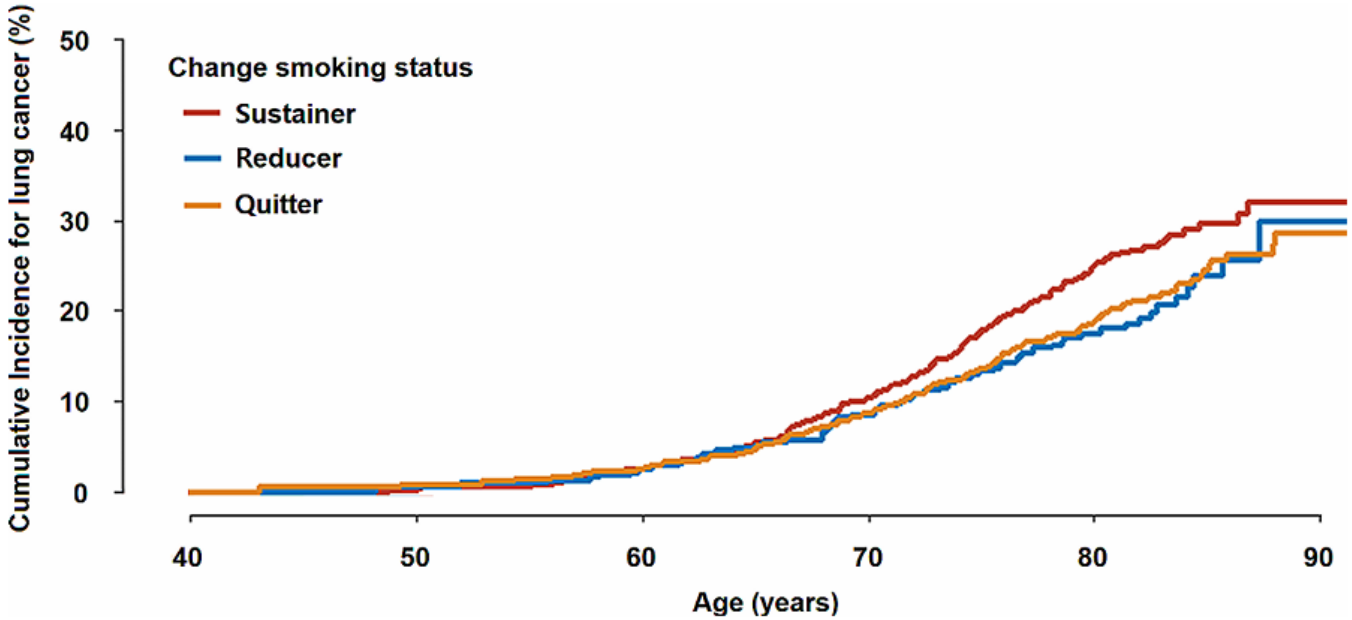
Smoking cessation

Impact of smoking reduction on lung cancer risk in patients with COPD who smoked fewer than 30 pack-years: a nationwide population-based cohort study

Sun Hye Shin[1†], Taeyun Kim[1†], Hyunsoo Kim[2], Juhee Cho[2,3], Danbee Kang[2*] and Hye Yun Park[1*]

- Korean National Health Insurance System database
- Patients with COPD aged ≥ 40 years (2014.01.01–2019.12.31)
- 16832 patients
- Sustainer, Reducer, quitter





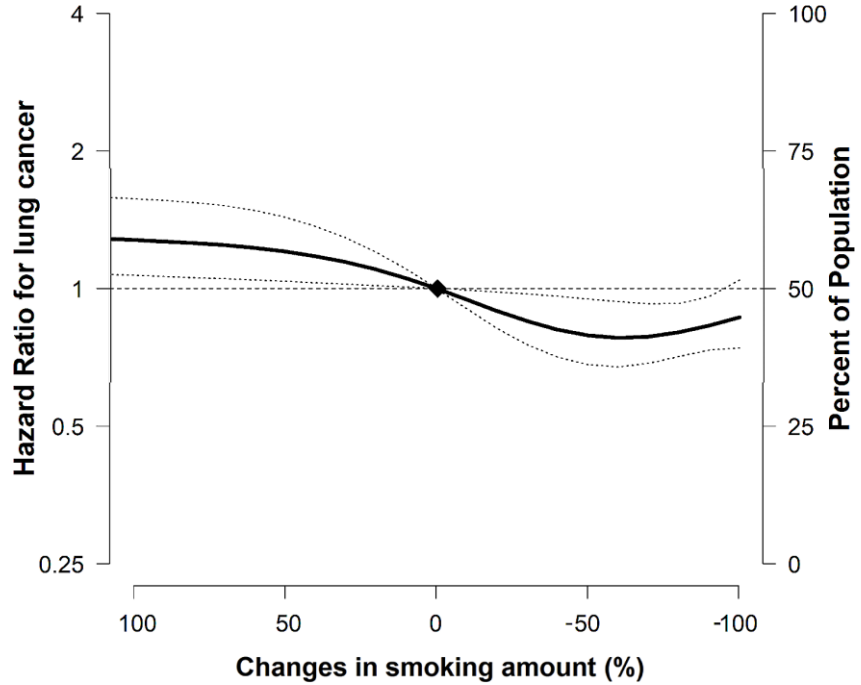


Fig. 2 Kaplan Meier curve for incidence of lung cancer. Age as time scale

Table 2 Hazard ratio (HR) with 95% confidence interval (CI) for incident lung cancer associated with change of smoking status

	No of cases	100-person year	Adjusted HR (95% CI)	Adjusted subHR* (95% CI)
Sustainer	225	0.75	*Reference*	*Reference*
Reducer	68	0.61	**0.74 (0.56, 0.98)**	**0.74 (0.57, 0.97)**
20–50% reducer	39	0.67	0.84 (0.60, 1.18)	0.83 (0.59, 1.17)
Over 50% reducer	29	0.55	**0.64 (0.64, 0.95)**	**0.64 (0.43, 0.95)**
Quitter	176	0.73	**0.78 (0.64, 0.96)**	**0.78 (0.64, 0.95)**

Adjusted for age, sex, BMI, residential area, income, regular physical activity, pack-years (Exam 1), ICS within 1 year of Exam 2, severe exacerbation within 1 year of Exam 2, and comorbidities within 1 year of Exam 2.

* Sub-distribution hazard ratios (subHRs) for lung cancer were modelled with mortality as a competing risk.

BMI, body mass index; COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroids

Pulmonary rehabilitation

Original research

Do pulmonary rehabilitation programmes improve outcomes in patients with COPD posthospital discharge for exacerbation: a systematic review and meta-analysis

Alex R Jenkins [1], Chris Burtin,[2,3] Pat G Camp,[4,5] Peter Lindenauer,[6] Brian Carlin,[7] Jennifer A Alison,[8,9] Carolyn Rochester,[10,11] Anne E Holland[12,13,14]

- The aim of this review was to examine the efficacy of pulmonary rehabilitation programmes **initiated within 3 weeks of hospital discharge** following an exacerbation of COPD.

- 17 studies, 1724 patients. randomized controlled trials

- **Primary outcome: hospital re-admissions**
- Secondary outcome: functional exercise capacity (6MWT, ISWT, ESWT), health-related quality of life (SGRQ, CRQ, CAT, EQ-5D-5L), dyspnoea (dyspnoea domain of CRQ, mMRC), mortality and adverse events.

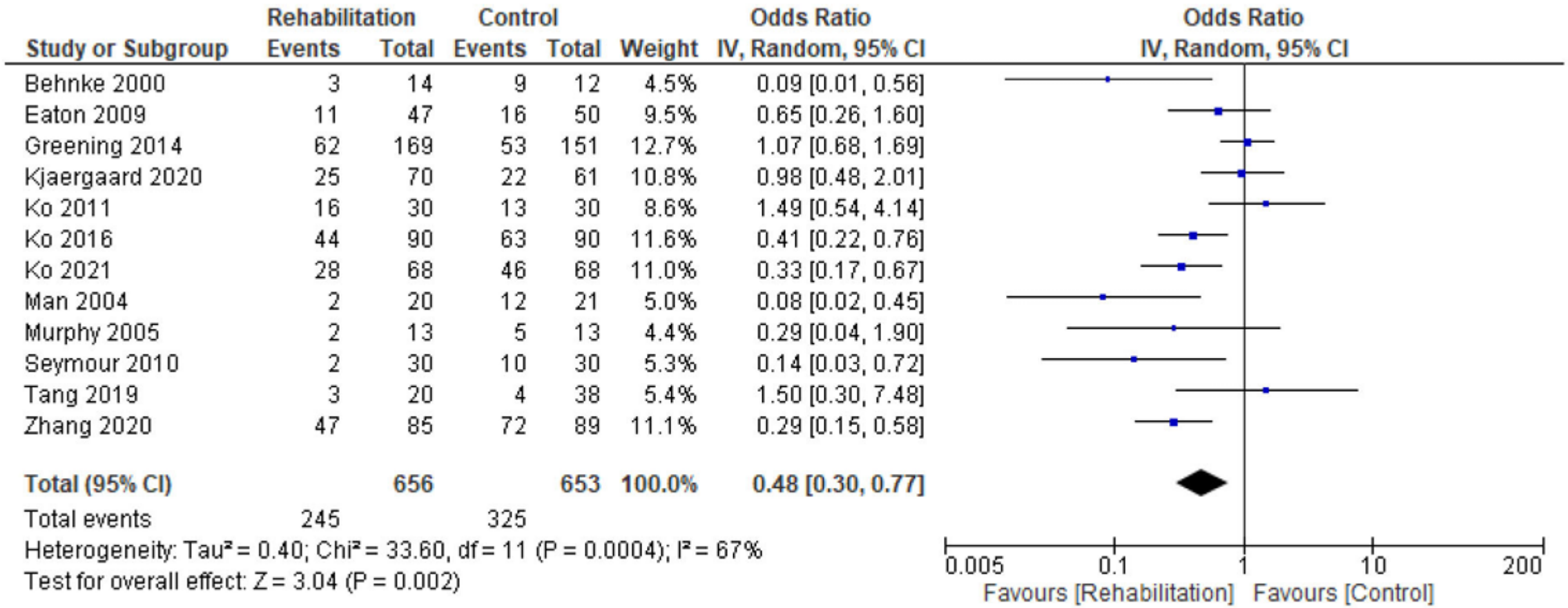


Figure 2 Trial-level data, effect estimates and forest plot of comparison for the odds of hospital re-admission (up to 12 months) following posthospital discharge pulmonary rehabilitation.

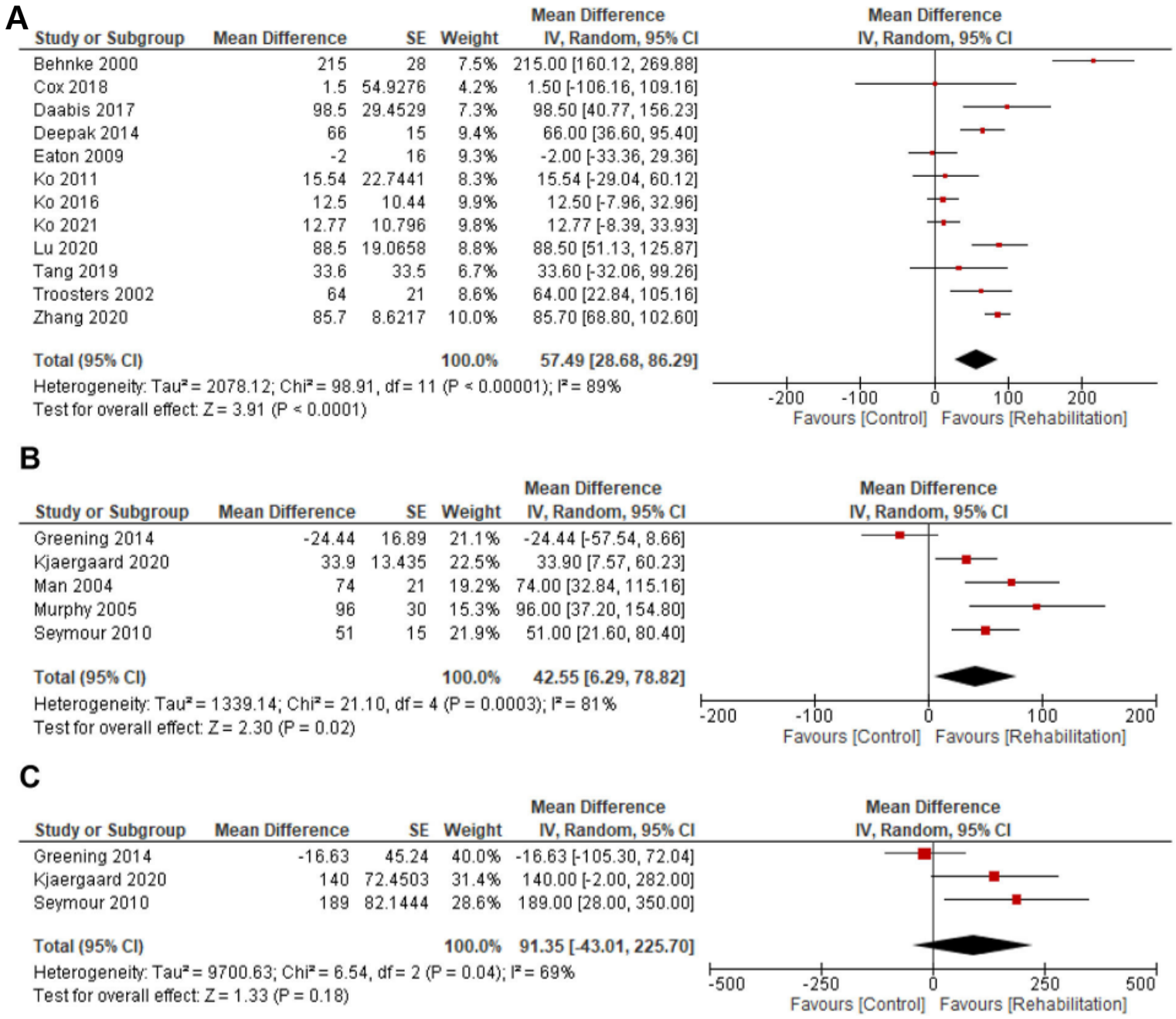


Figure 3 Trial-level data, effect estimates and forest plot of comparison for change in (A) 6 min walk test (6MWT), (B) Incremental shuttle walk test (ISWT) and (C) endurance shuttle walk test (ESWT) following posthospital discharge pulmonary rehabilitation.

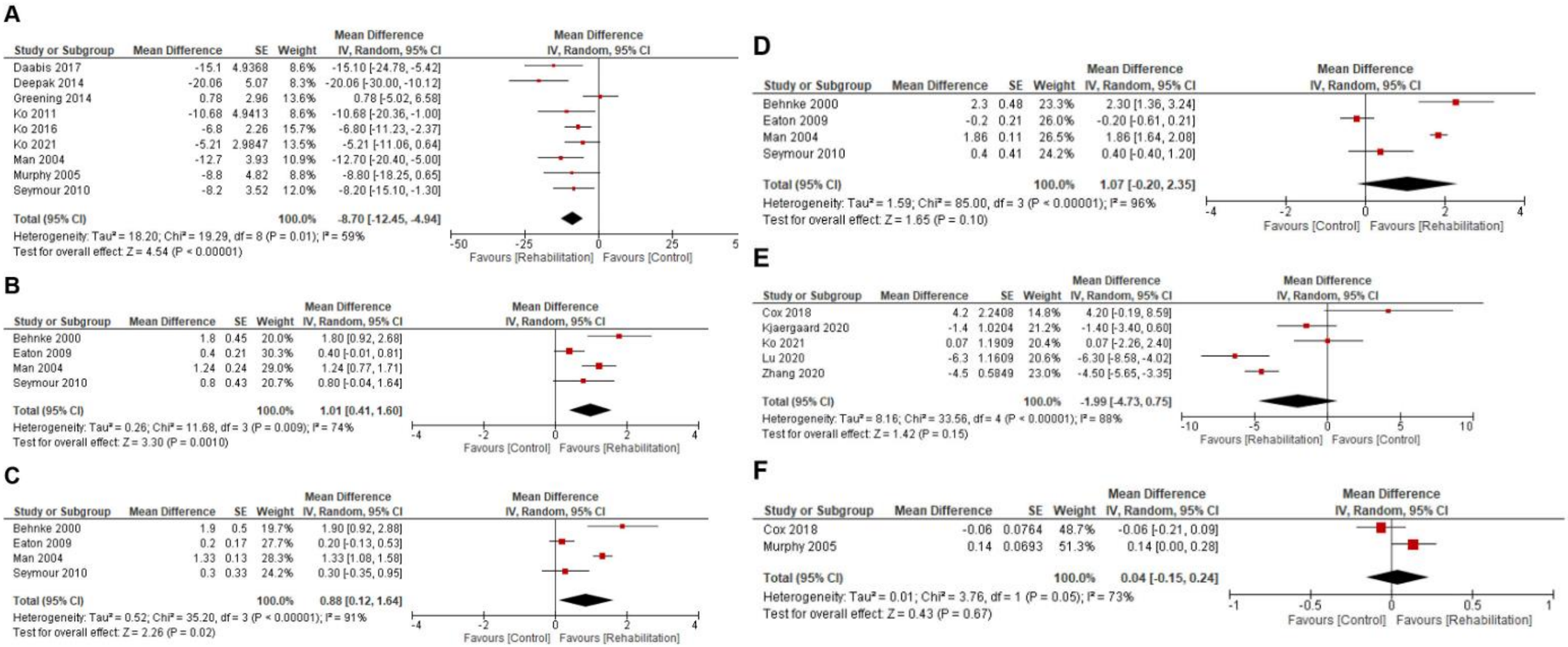


Figure 4 Trial-level data, effect estimates and forest plot of comparison for change in (A) St. George's Respiratory Questionnaire (SGRQ)-Total, (B) Chronic Respiratory Disease Questionnaire (CRQ)-emotion, (C) CRQ-fatigue, (D) CRQ-mastery, (E) chronic obstructive pulmonary disease (COPD) Assessment Test (CAT), and (F) EuroQol-5 Dimension-5 Level (EQ-5D-5L) following posthospital discharge pulmonary rehabilitation.

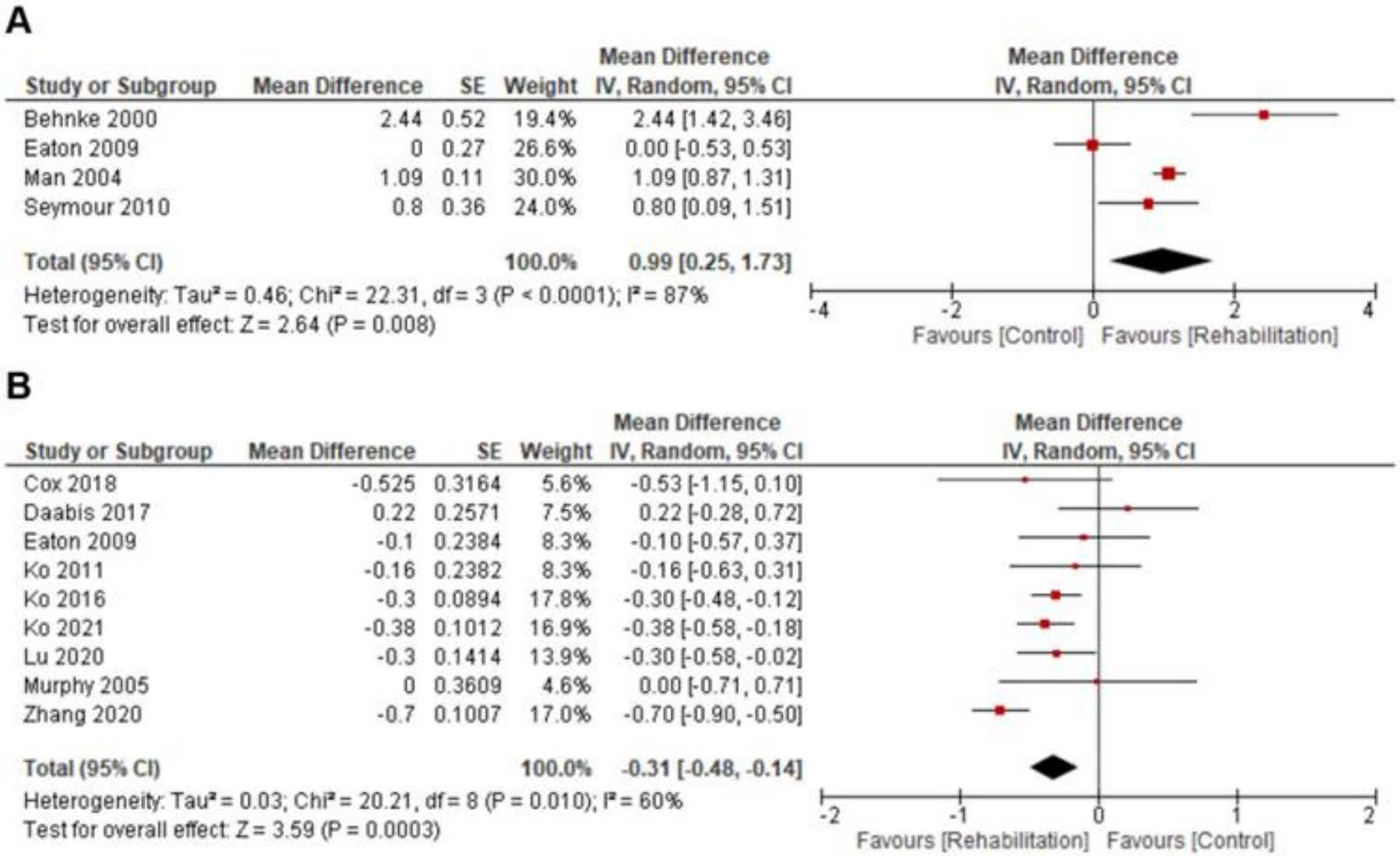


Figure 5 Trial-level data, effect estimates and forest plot of comparison for change in (A) Chronic Respiratory Disease Questionnaire (CRQ)-dyspnoea score and (B) Modified Medical Research Council (mMRC) score following posthospital discharge pulmonary rehabilitation.

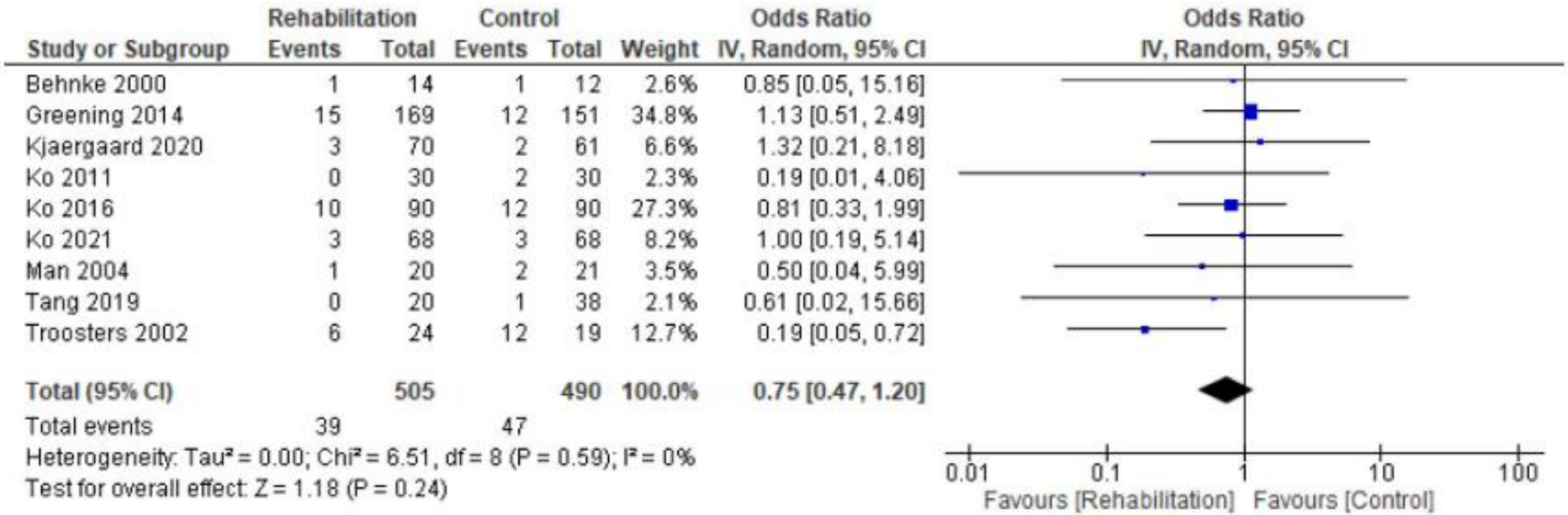


Figure 6 Trial-level data, effect estimates and forest plot of comparison for the odds of mortality following posthospital discharge pulmonary rehabilitation.

Pulmonary Rehabilitation Is Associated With Decreased Exacerbation and Mortality in Patients With COPD

A Nationwide Korean Study

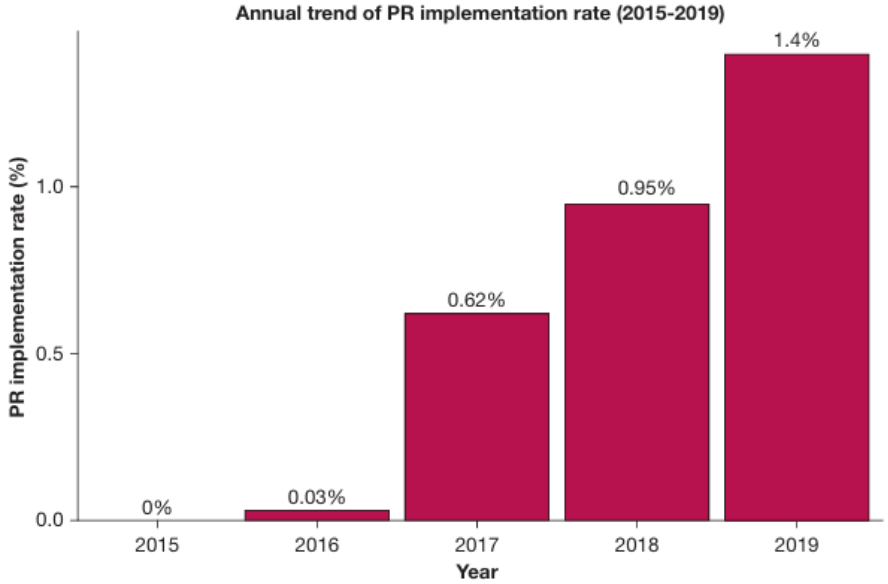
*Joon Young Choi, MD, PhD; Ki Uk Kim, MD, PhD; Deog Kyeom Kim, MD, PhD; Yu-Il Kim, MD, PhD; Tae-Hyung Kim, MD, PhD; Won-Yeon Lee, MD, PhD; Seong Ju Park, MD, PhD; Yong Bum Park, MD, PhD; Jin Woo Song, MD, PhD; Kyeong-Cheol Shin, MD, PhD; Soo-Jung Um, MD, PhD; Kwang Ha Yoo, MD, PhD; Hyoung Kyu Yoon, MD, PhD; Chang Youl Lee, MD, PhD; Ho Sung Lee, MD; Ah Young Leem, MD, PhD; Won-Il Choi, MD, PhD; Seong Yong Lim, MD, PhD; and Chin Kook Rhee, MD, PhD; on behalf of the Korean Pulmonary Rehabilitation Study Group**

- Does PR implementation improve outcomes in patients with COPD in terms of **direct cost, exacerbation, and mortality**?
- Korean Health Insurance Review and Assessment service database (2015–2019)
- PR: 6360 patients (1.43%), non-PR: 436498 patients.

TABLE 1] General Characteristics of Study Participants

Characteristic	PR Group (n = 6,360; 1.43%)	Non-PR Group (n= 436,498; 98.56%)	*P* Value
Mean age, y	70.94 ± 9.04	70.61 ± 10.56	.004
Sex, male	5,082 (79.9)	296,862 (68.0)	< .001
Insurance type			
NHI	5,472 (86.0)	371,693 (85.2)	.049
Medical aid	888 (14.0)	64,805 (14.8)	
mCCI	2.03 ± 1.98	2.42 ± 2.14	< .001
Moderate-to-severe AE in previous year	0.73 ± 2.15	0.32 ± 1.81	< .001
Severe AE in previous year	0.56 ± 1.38	0.14 ± 0.62	< .001
COPD medication during 1 y			
LAMA	708 (11.1)	69,564 (15.9)	< .001
LABA + LAMA	2,855 (44.9)	89,601 (20.5)	< .001
ICS + LABA	1,397 (22.0)	122,851 (28.1)	< .001
ICS + LABA + LAMA	1,778 (28.0)	50,904 (11.7)	< .001
Death, 2016-2019	627 (9.9)	47,559 (10.9)	.008

Data are presented as No. (%), mean ± SD, or as otherwise indicated. AE = acute exacerbation; ICS = inhaled corticosteroids; LABA = long-acting beta-2 agonist; LAMA = long-acting muscarinic antagonist; mCCI = modified Charlson Comorbidity Index; NHI = National Health Insurance; PR = pulmonary rehabilitation.



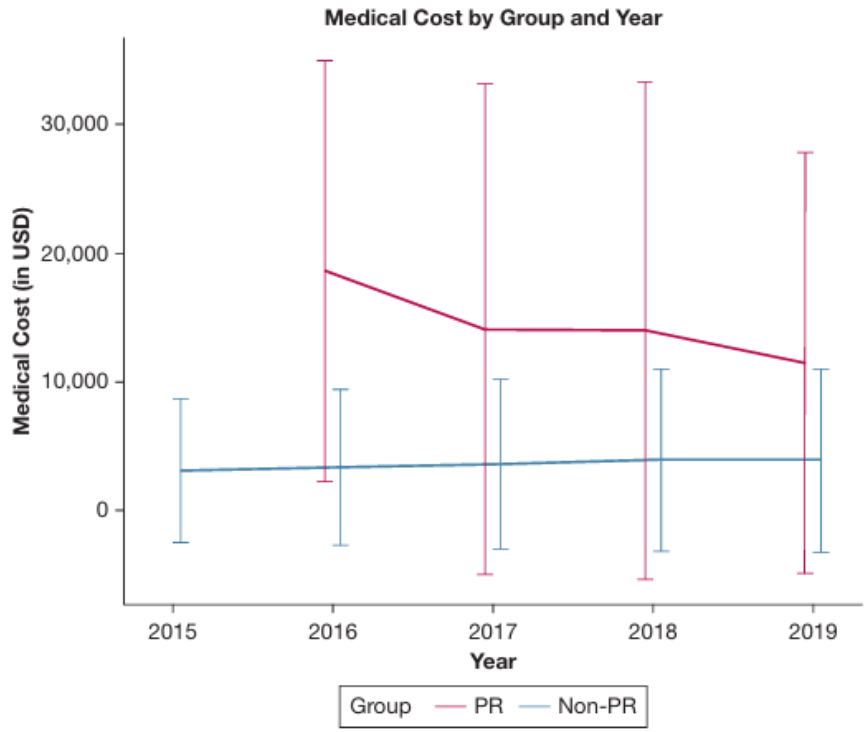


TABLE 2] Effect of PR in COPD Exacerbation

Exacerbation Severity	No. (%) of Patients With Events (n = 6,360)		Crude OR (95% CI)	Adjusted OR (95% CI)
	Pre-PR	Post-PR		
Moderate-to-severe AE	1,759 (27.7)	543 (8.5)	0.218 (0.198-0.240)	0.585 (0.539-0.635)
Severe AE	1,635 (25.7)	496 (7.8)	0.213 (0.193-0.236)	0.550 (0.502-0.602)
Exacerbation Severity	Mean No. of Events/Year ± SD (n = 6,360)		Crude IRR (95% CI)	Adjusted IRR (95% CI)
	Pre-PR	Post-PR		
Moderate-to-severe AE	0.733 ± 2.151	0.220 ± 1.209	0.921 (0.917-0.925)	0.973 (0.965-0.980)
Severe AE	0.560 ± 1.382	0.171 ± 0.847	0.850 (0.840-0.860)	0.999 (0.983-1.017)

Covariates included the following: age, sex, type of insurance, mCCI, and previous moderate-to-severe exacerbation. AE = acute exacerbation; IRR = incidence rate ratio; mCCI = modified Charlson Comorbidity Index; PR = pulmonary rehabilitation.

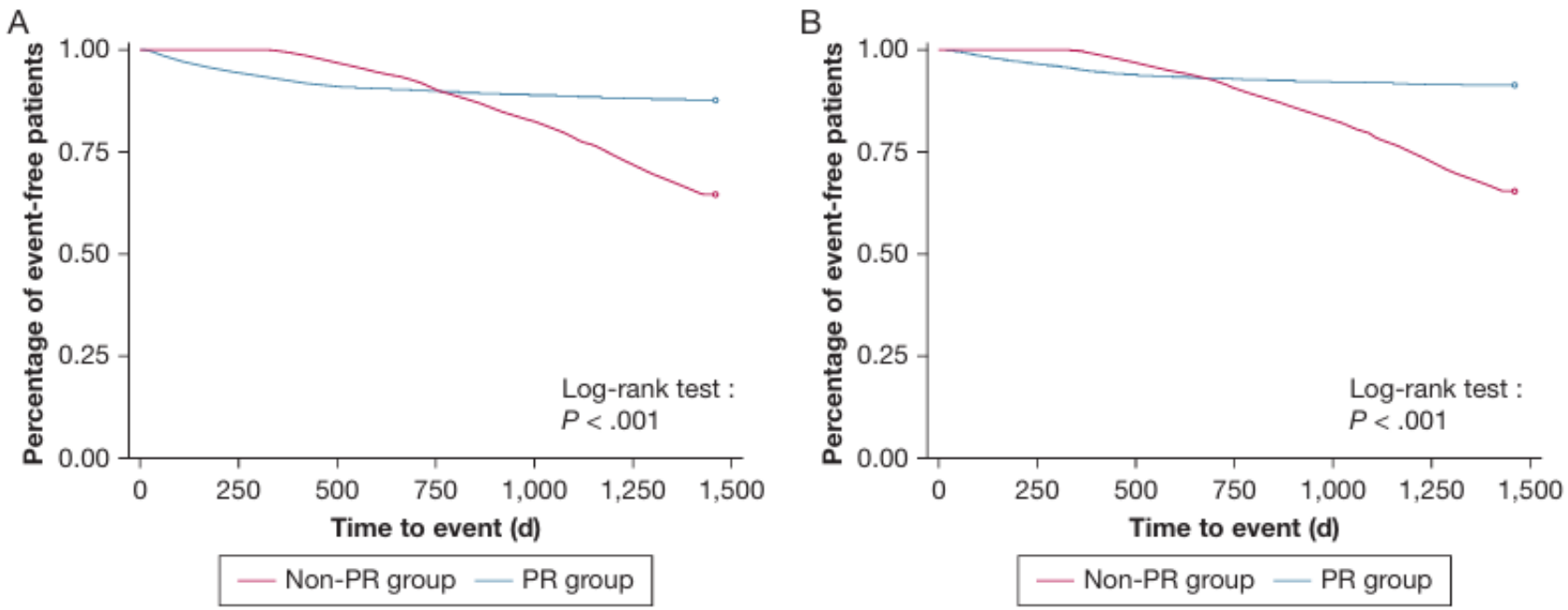


Figure 3 – *A, B, Time to first exacerbation: (A) moderate-to-severe exacerbation and (B) severe exacerbation.*

TABLE 3] Differences of Mortality Between the PR and Non-PR Groups

Variables	Hazard Ratio	95% CI	*P* Value
Age categories, y			
40-49	1 (reference)	…	…
50-59	0.925	(0.846-1.011)	.085
60-69	1.166	(1.073-1.266)	< .001
≥ 70	3.075	(2.839-3.331)	< .001
Sex, male	1.568	(1.535-1.602)	< .001
Type of insurance			
NHI	1 (reference)	…	…
Medical aid	1.096	(1.070-1.122)	< .001
mCCI	1.151	(1.146-1.155)	< .001
Previous exacerbation	2.210	(2.165-2.255)	< .001
PR (vs non-PR)	0.671	(0.620-0.727)	< .001

mCCI = modified Charlson Comorbidity Index; NHI = National Health Insurance; PR = pulmonary rehabilitation.

Digital therapeutics

Advancing Digital Solutions to Overcome Longstanding Barriers in Asthma and COPD Management

Sinthia Bosnic-Anticevich[1], Nawar Diar Bakerly[2], Henry Chrystyn[3], Mark Hew[4], Job van der Palen[5]

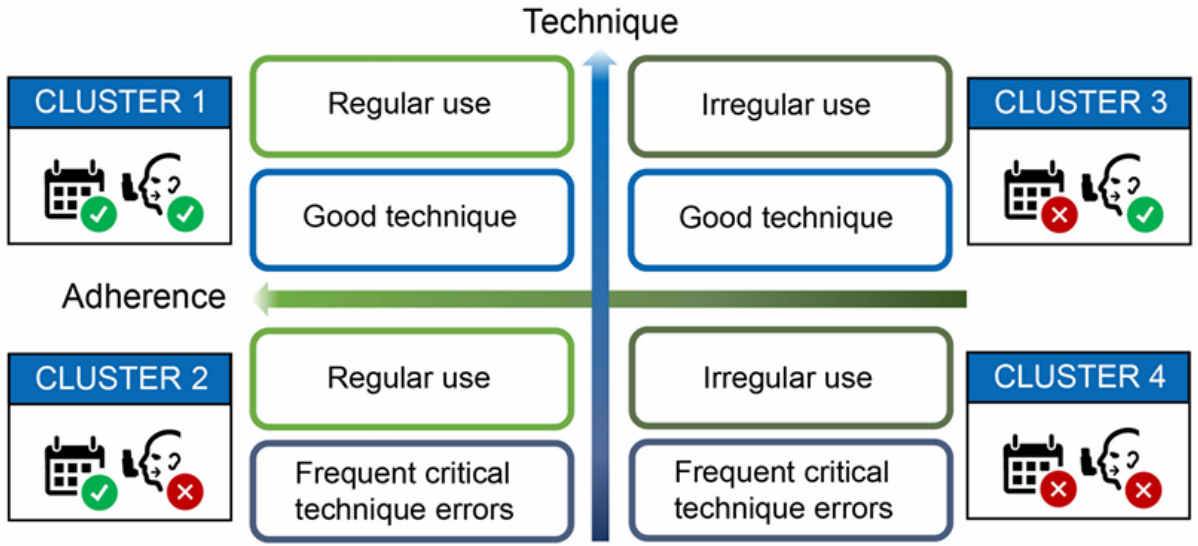
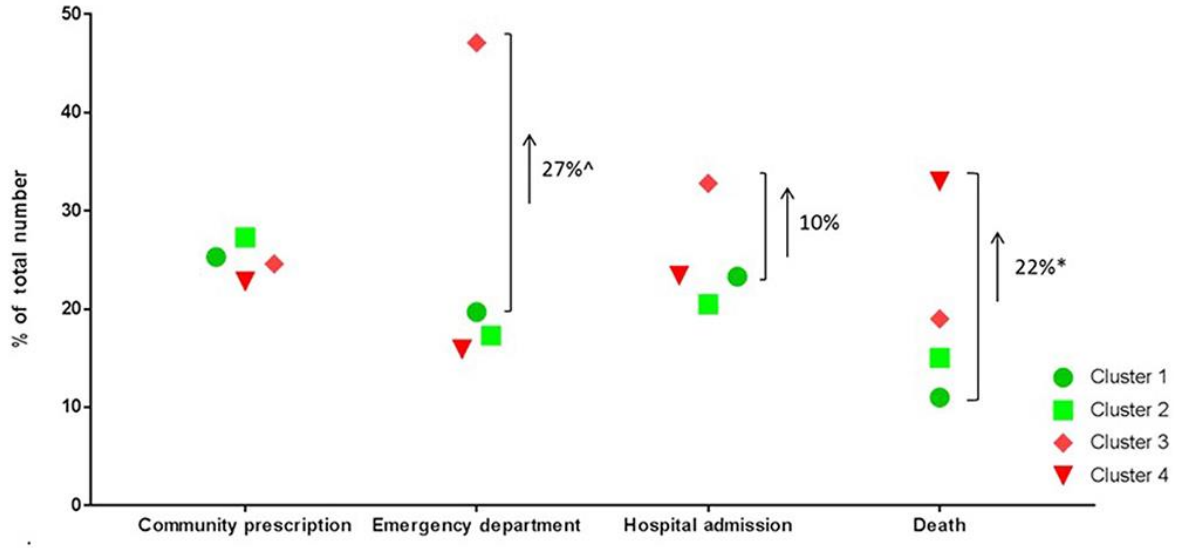


Figure 1 Four clusters of adherence behaviors as identified and reported by Cushen et al.[27]



Cluster 1: Regular use–Good technique
Cluster 2: Regular use–Frequent critical technique errors
Cluster 3: Irregular use–Good technique
Cluster 4: Irregular use–Frequent critical technique errors

Proportional contribution of each adherence cluster to all-cause clinical outcomes over the 12-month follow-up period (adjusted for the number of participants per cluster). Reported differences are the absolute differences in the proportion of events attributable to cluster 3 vs. cluster 1 for emergency department and hospital admission and cluster 4 vs. cluster 1 for death. ^ denotes $p = 0.05$, *$p < 0.05$

Table 2 Digital Inhaler Devices Currently Licensed for Use or Undergoing Clinical Trial Evaluation

Digital Device	Compatible Inhalers	Smartphone Application	Patient Reminder Available	Inhaler Technique Check	Measures Inspiratory Flow
Inhaler Compliance Assessment (INCA)™	Diskus®	x	x	✓	✓
Propeller Sensor	pMDI Diskus® Ellipta® Respimat® Breezhaler® Turbohaler® Easyhaler®	✓	✓	x	x
Hailie Sensor®	pMDI Diskus® Turbohaler® Handihaler®	✓	✓	✓	x
Turbu+™	Turbohaler®	✓	✓	x	x
CapMedic®	pMDI	✓	✓	✓	✓
Respiro®	pMDI Ellipta® Nexthaler® Spiromax®	✓	✓	✓	✓
Herotracker®	pMDI Diskus®	✓	✓	x	x
Digihaler®	Inbuilt Digihaler®	✓	✓	✓	✓

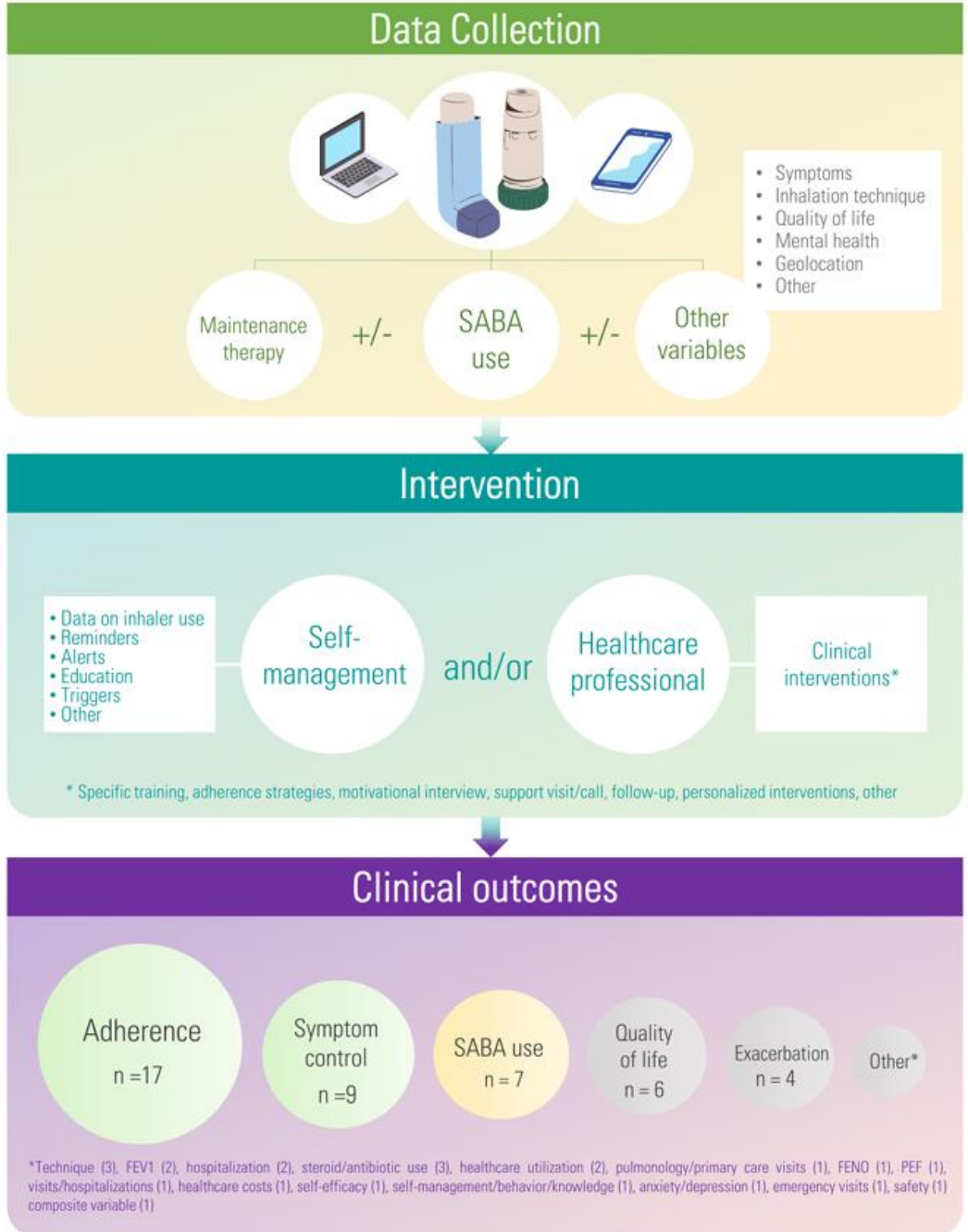
Notes: Reproduced with permission of the ERS 2022. Dhruve H & Jackson DJ. *European Respiratory Review*. 31 (164) 210271; DOI: 10.1183/16,000,617.0271–2021 Published 25 May 2022.[53]

Abbreviation: pMDI, pressurized metered-dose inhaler.

Systematic Review

Clinical Impact of Electronic Monitoring Devices of Inhalers in Adults with Asthma or COPD: A Systematic Review and Meta-Analysis

Noe Garin [1,2,3,*,†], Borja Zarate-Tamames [1,4,†], Laura Gras-Martin [1], Raimon Milà [2], Astrid Crespo-Lessmann [5], Elena Curto [5], Marta Hernandez [2], Conxita Mestres [2] and Vicente Plaza [5]



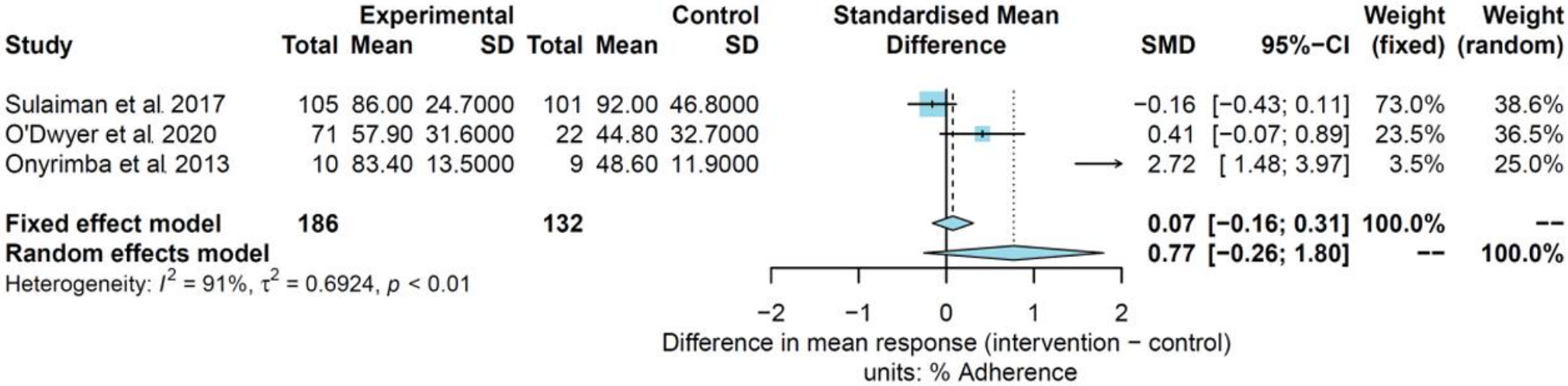


Figure 5. Adherence outcomes up to 3 months. References: [53,58,61].

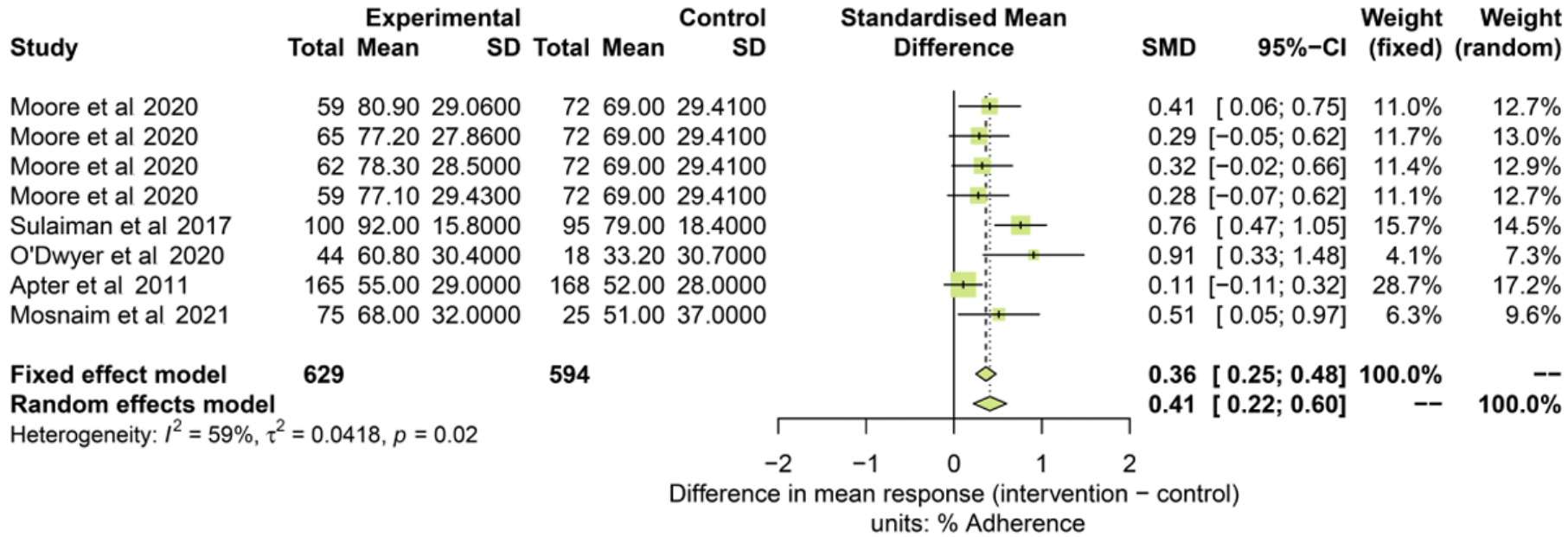


Figure 6. Adherence outcomes in studies 3 months or longer. References: [27,51–53,58].

Vaccination

Influenza Vaccine Effectiveness Pre-pandemic Among Adults Hospitalized With Congestive Heart Failure or Chronic Obstructive Pulmonary Disease and Older Adults

Ashley Tippett,[1] Gabby Ess,[1] Laila Hussaini,[1] Olivia Reese,[1] Luis Salazar,[1] Mary Kelly,[1] Meg Taylor,[1] Caroline Ciric,[1] Amy Keane,[1] Andrew Cheng,[2] Theda Gibson,[1] Wensheng Li,[1] Hui-Mien Hsiao,[1] Laurel Bristow,[2] Kieffer Hellmeister,[2] Zayna Al-Husein,[2] Robin Hubler,[3] Elizabeth Begier,[3] Qing Liu,[3] Bradford Gessner,[3] David L. Swerdlow,[3,a] Satoshi Kamidani,[1,4] Carol Kao,[1,4,b] Inci Yildirim,[5,6,7,8] Nadine Rouphael,[2] Christina A. Rostad,[1,4] and Evan J. Anderson[1,4,2,c]

- Prospective, case-control study, 2 US hospitals (2018.10-2020.03)
- aged ≥50 years + acute respiratory illnesses (56.7%)
  or aged ≥18 years + congestive heart failure (28.0%)
  or aged ≥18 years + COPD AE (15.3%)
- 1515 patients
  (Vaccinated: 701 patients, Unvaccinated: 814 patients)

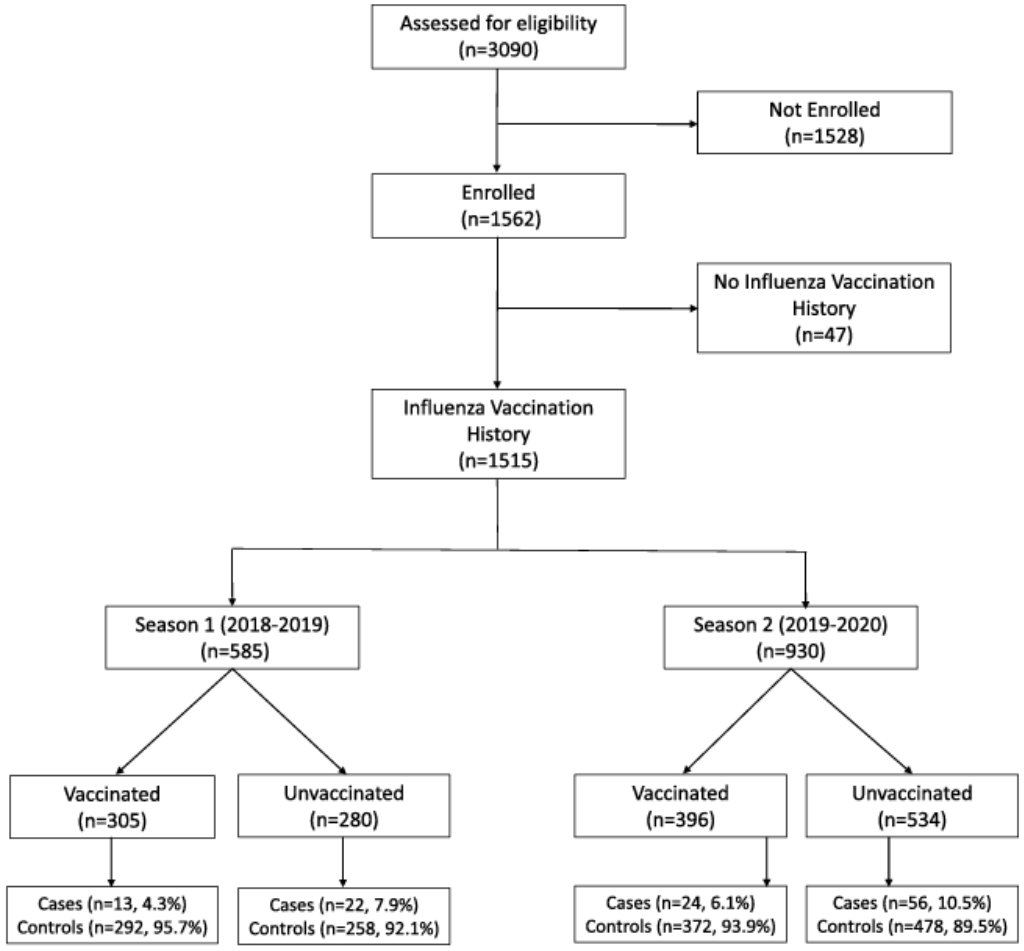


Table 2. Crude and Adjusted Influenza Vaccine Effectiveness Against Influenza-Related Hospitalizations by Season

	Crude VE	Crude 95% CI	Adj. VE[a]	Adj. 95% CI
Overall				
Season 1 and 2[b]	47.4	(21.2, 64.9)	63.1	(43.8, 75.8)
Season 1	47.8	(−5.8, 74.2)	50.5	(−2.5, 76.1)
Season 2	44.9	(9.5, 66.5)	68.0	(45.9, 81.1)
All ≥50 y				
Season 1 and 2	47.5	(20.7, 65.2)	61.7	(41.2, 75.1)
Season 1	41.8	(−20.3, 71.9)	47.3	(−11.6, 75.1)
Season 2	46.9	(11.9, 68.0)	67.9	(45.2, 81.2)
All ≥65 y				
Season 1 and 2	48.0	(5.6, 71.4)	65.5	(35.5, 81.5)
Season 1	31.5	(−142.5, 80.7)	26.71	(−176.1, 80.6)
Season 2	47.1	(−5.2, 73.5)	70.8	(38.8, 86.1)
CHF/COPD exacerbations				
All	69.7	(7.9, 90.1)	80.3	(36.3, 93.9)
≥50 y	66.7	(−3.3, 89.3)	79.0	(31.3, 93.6)
≥65 y	45.4	(−132.9, 87.2)	72.3	(−33.2, 94.2)
CHF/COPD history or exacerbation (≥50 y)	57.6	(27.8, 75.1)	68.2	(44.82, 81.7)
ARI				
All	43.0	(11.2, 63.5)	55.9	(29.9, 72.3)
≥65 y	48.1	(−.4, 73.2)	63.1	(25.3, 81.8)
ARI with CHF/COPD history	56.9	(19.5, 76.9)	63.2	(28.6, 81.0)
ARI without CHF/COPD history	24.2	(−43.0, 59.8)	48.2	(−2.7, 73.9)
HMPV				
Season 1 and 2	−75.1	(−394.5, 38.0)	−29.9	(−294.1, 57.2)
Season 1	−38.1	(−732.4, 77.1)	−53.9	(−1116.2, 80.5)
Season 2	−103.8	(−627.2, 42.9)	−36.1	(−441.6, 65.8)

Data are presented as percentages. Abbreviations: Adj., adjusted; ARI, acute respiratory illness; CHF, congestive heart failure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HMPV, human metapneumovirus; VE, vaccine effectiveness.

[a]Adjusted model included age, race/ethnicity, immunosuppression, month of admission, season.

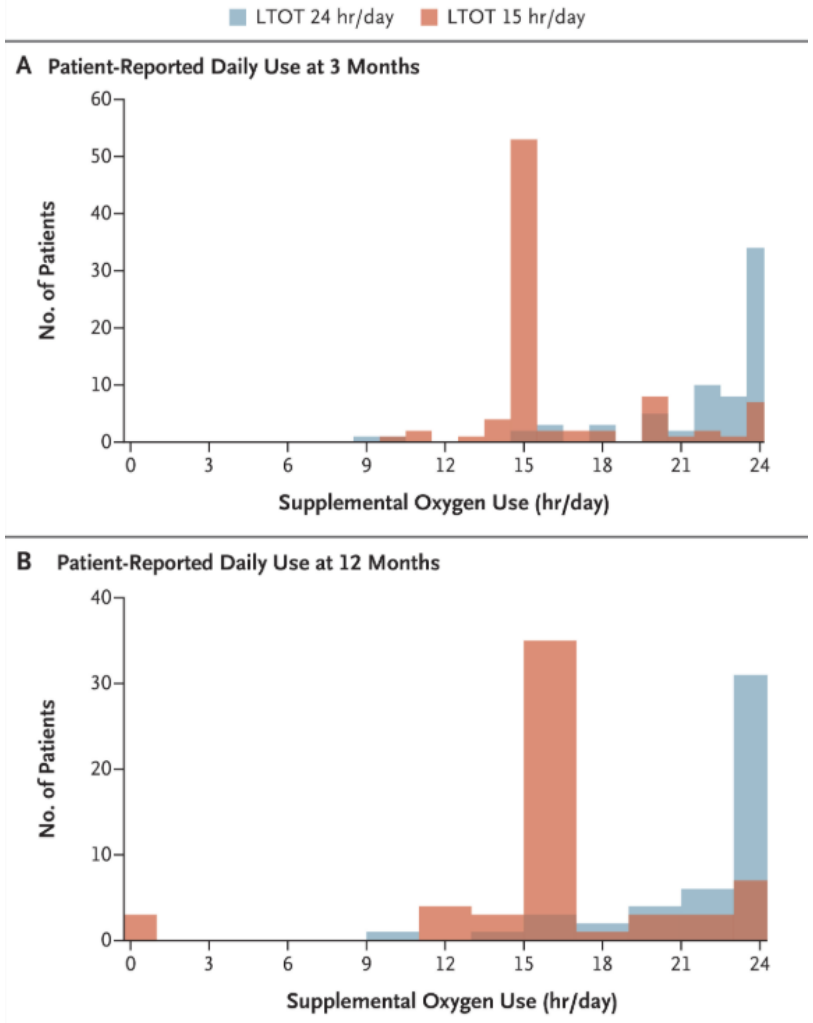
[b]Season 1 was 2018–2019; season 2 was 2019–2020.

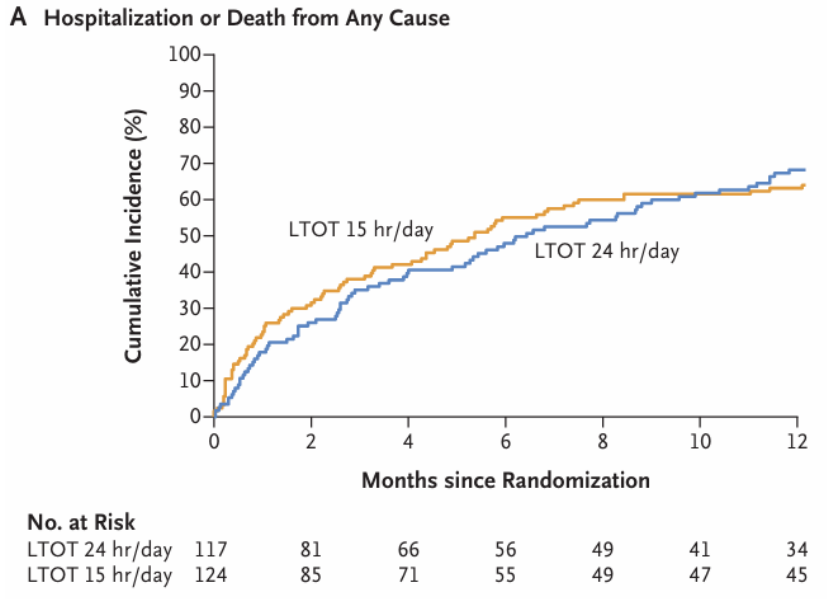
Long-term oxygen therapy

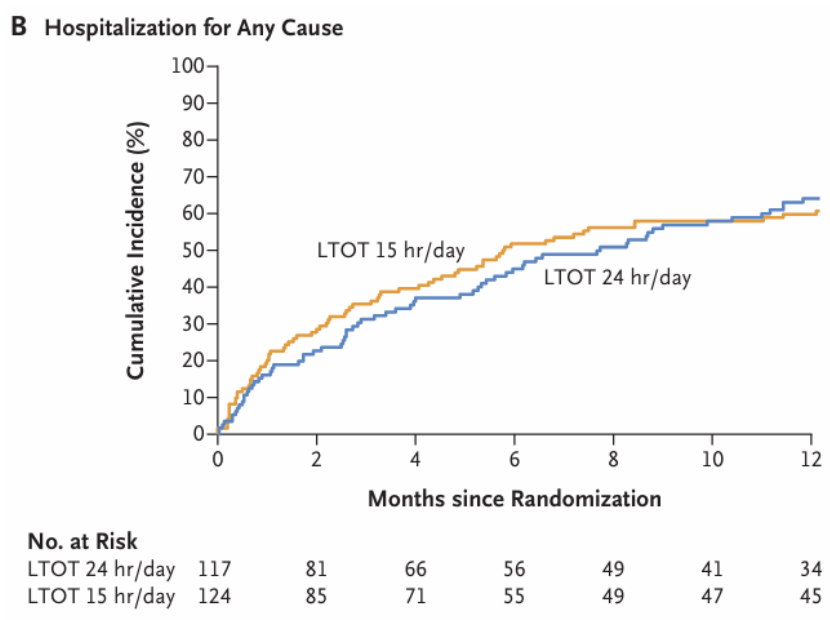
Long-Term Oxygen Therapy for 24 or 15 Hours per Day in Severe Hypoxemia

Magnus Ekström, M.D., Ph.D., Anders Andersson, M.D., Ph.D., Savvas Papadopoulos, M.D., Taivo Kipper, M.D., Bo Pedersen, M.D., Ozren Kricka, M.D., Pierre Sobrino, M.D., Michael Runold, M.D., Ph.D., Andreas Palm, M.D., Ph.D., Anders Blomberg, M.D., Ph.D., Ranjh Hamed, M.D., Eva Lindberg, M.D., Ph.D., Björn Sundberg, M.D., Nermin Hadziosmanovic, M.Sc., Filip Björklund, M.D., Christer Janson, M.D., Ph.D., Christine F. McDonald, M.D., Ph.D., David C. Currow, M.D., Ph.D., and Josefin Sundh, M.D., Ph.D., for the REDOX Collaborative Research Group*

- Multicenter, RCT, REDOX trial
- 241 patients (**LTOT 24hr/day**: 117 patients, **LTOT 15hr/day**: 124 patients) [2018.05.18-2022.04.04]
- Primary outcome: **hospitalization or death from any cause within 1 year**
- Chronic severe hypoxemia at rest (COPD 71%, pulmonary fibrosis 14%)


LTOT 24 hr/day
LTOT 15 hr/day
A Patient-Reported Daily Use at 3 Months
No. of Patients
Supplemental Oxygen Use (hr/day)
B Patient-Reported Daily Use at 12 Months
No. of Patients
Supplemental Oxygen Use (hr/day)


A Hospitalization or Death from Any Cause
Cumulative Incidence (%)
LTOT 15 hr/day
LTOT 24 hr/day
Months since Randomization
No. at Risk
LTOT 24 hr/day 117 81 66 56 49 41 34
LTOT 15 hr/day 124 85 71 55 49 47 45


B Hospitalization for Any Cause
Cumulative Incidence (%)
LTOT 15 hr/day
LTOT 24 hr/day
Months since Randomization
No. at Risk
LTOT 24 hr/day 117 81 66 56 49 41 34
LTOT 15 hr/day 124 85 71 55 49 47 45

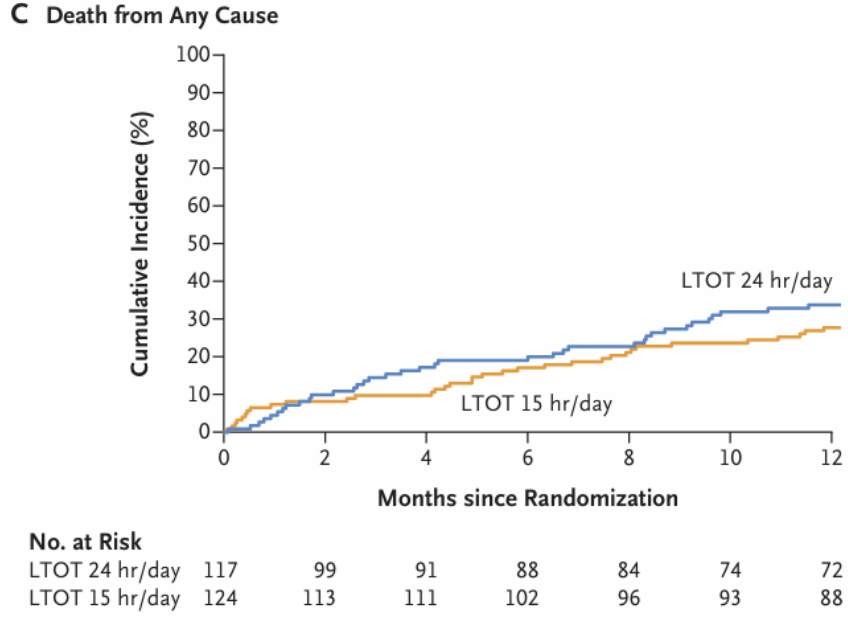

C Death from Any Cause
Cumulative Incidence (%)
LTOT 24 hr/day
LTOT 15 hr/day
Months since Randomization
No. at Risk
LTOT 24 hr/day 117 99 91 88 84 74 72
LTOT 15 hr/day 124 113 111 102 96 93 88

Table 2. Trial Outcomes at 12 Months in the Intention-to-Treat Population.*

Outcome	LTOT 24 Hr/Day (N=117)	LTOT 15 Hr/Day (N=124)	Estimated Effect (95% CI), 24 vs. 15 Hr/Day†
Primary outcome			
Hospitalization or death from any cause — no. (%)	75 (64.1)	79 (63.7)	0.99 (0.72 to 1.36)
Secondary outcomes			
Death from any cause — no. (%)	37 (31.6)	34 (27.4)	1.26 (0.79 to 2.01)
Hospitalization for any cause — no. (%)	67 (57.3)	71 (57.3)	1.00 (0.72 to 1.40)
MDP A1 scale score for overall unpleasantness‡			
No. of patients assessed	46	59	
Mean score	4.46±2.65	4.05±2.85	0.41 (–0.67 to 1.48)
Median score (IQR)	5.0 (2.0 to 6.0)	4.0 (2.0 to 7.0)	
FACIT scale score for fatigue§			
No. of patients assessed	37	55	
Mean score	22.51±11.23	22.20±9.78	0.31 (–4.07 to 4.70)
Median score (IQR)	22.0 (13.0 to 29.0)	23.0 (16.0 to 29.0)	
CAT score for health status¶			
No. of patients assessed	43	57	
Mean score	21.56±5.34	18.82±7.28	2.73 (0.12 to 5.35)
Median score (IQR)	21.0 (18.0 to 25.0)	19.0 (14.0 to 23.0)	
EQ-5D VAS score for perceived overall well-being‖			
No. of patients assessed	47	58	
Mean score	46.70±22.75	46.98±22.54	–0.28 (–9.09 to 8.53)
Median score (IQR)	50.0 (30.0 to 60.0)	45.0 (30.0 to 60.0)	
Preferred daily duration of therapy — no./total no. (%)			
15 hr/day	18/41 (43.9)	37/54 (68.5)	0.36 (0.15 to 0.84)
24 hr/day	23/41 (56.1)	17/54 (31.5)	—

Noninvasive positive pressure ventilation (NIPPV)

JAMA | Original Investigation

Effect of High-Intensity vs Low-Intensity Noninvasive Positive Pressure Ventilation on the Need for Endotracheal Intubation in Patients With an Acute Exacerbation of Chronic Obstructive Pulmonary Disease
The HAPPEN Randomized Clinical Trial

Zujin Luo, MD; Yichong Li, PhD; Wenjun Li, MD; Ying Li, MD; Qingrong Nie, MD; Yu Shi, PhD; Juan Wang, BSN; Qiuling Ji, MD; Xuefeng Han, MD; Sijie Liu, MD; Dongmei Li, MD; ShaSha Wang, MD; Zhijun Li, MD; Dong Jia, MD; Huiqing Ge, MD; Peifeng Xu, BSc; Zhijun Feng, MD; Fengjie Li, MD; Fucheng An, MD; Na Tai, MD; Lili Yue, MD; Hongwei Xie, MD; Xiuhong Jin, MD; Hongru Liu, MD; Qiang Dang, MD; Yongxiang Zhang, MD; Li Sun, MD; Jinxiang Wang, MD; He Huang, MD; Liang Chen, MD; Yingmin Ma, MD; Zhixin Cao, MD; Chen Wang, MD, PhD; for the HAPPEN Investigators

- To determine whether the use of **high-intensity NPPV vs low-intensity NPPV** reduces the need for **endotracheal intubation** in patients with an acute exacerbation of COPD and hypercapnia.

- RCT, 30 general respiratory non-intensive care unit wards of Chinese hospitals (2019.01.03-2022.01.31)
- $pCO_2 \geq 45$mmHg after receiving 6 hours of low-intensity NPPV
- 1:1 randomized, 147 patients (**High intensity, 10-15 mL/kg** of PBW), 153 (**Low-intensity, 6-10 mL/kg** of PBW)
- Primary outcome: the need for endotracheal intubation during hospitalization

Table 2. Primary and Secondary Outcomes

	Noninvasive positive pressure ventilation (NPPV)				Ratio measure (95% CI)[b]	
	High intensity (n = 147)	Low intensity (n = 153)	Unadjusted absolute difference (95% CI)[a]	*P* value	Unadjusted	Adjusted[c]
Primary outcome[d]						
Need for endotracheal intubation during hospitalization, No. (%)	7 (4.8)	21 (13.7)	−9.0 (−15.4 to −2.5)	.004[e]	0.35 (0.14 to 0.76)	0.30 (0.11 to 0.69)
Secondary outcomes[d]						
Endotracheal intubation during hospitalization, No. (%)	5 (3.4)	6 (3.9)	−0.5 (−4.8 to 3.7)	.81	0.87 (0.25 to 2.72)	0.88 (0.24 to 2.97)
Endotracheal intubation at 28 d, No. (%)						
Met prespecified criteria for the need for intubation	7 (4.8)	21 (13.7)	−9.0 (−15.4 to −2.5)	.008	0.35 (0.14 to 0.76)	0.30 (0.11 to 0.69)
Intubated	5 (3.4)	6 (3.9)	−0.5 (−4.8 to 3.7)	.81	0.87 (0.25 to 2.72)	0.88 (0.24 to 2.97)
Composite of endotracheal intubation or avoiding intubation, No. (%)[f]	5 (3.4)	17 (11.1)	−7.7 (−13.5 to −1.9)	.01	0.31 (0.10 to 0.76)	0.27 (0.08 to 0.69)
NPPV weaning success, No. (%)	97 (66.0)	104 (68.0)	−2.0 (−12.6 to 8.7)	.71	0.97 (0.80 to 1.12)	0.98 (0.81 to 1.13)
Mortality, No./total (%)						
During hospitalization	1/147 (1.0)	4/153 (2.6)	−1.9 (−6.0 to 1.4)[g]	.37[h]	0.26 (0.01 to 1.72)	0.25 (0.01 to 1.78)
At 28 d	2/147 (1.4)	3/153 (2.0)	−0.6 (−4.5 to 3.2)[g]	>.99[h]	0.69 (0.09 to 3.97)	0.81 (0.10 to 5.37)
At 90 d	6/146 (4.1)	6/152 (4.0)	0.2 (−4.3 to 4.6)	.94	1.04 (0.33 to 3.11)	1.00 (0.31 to 3.07)
ICU admission, No. (%)	4 (2.7)	5 (3.3)	−0.6 (−5.2 to 4.0)[g]	>.99[h]	0.83 (0.21 to 2.98)	0.81 (0.19 to 3.01)
Discharged alive from the hospital, No. (%)	143 (97.3)	144 (94.1)	3.2 (−1.4 to 7.7)	.18	1.03 (0.98 to 1.05)	1.03 (0.97 to 1.05)
Length of hospital stay, median (IQR), d						
Overall	10 (8 to 13)	10 (9 to 15)	0 (−1 to 1)[i]	.22	HR, 1.10 (0.88 to 1.38)	HR, 1.10 (0.88 to 1.38)
After randomization	9 (7 to 13)	10 (8 to 14)	−1 (−2 to 1)[i]	.09	HR, 1.08 (0.86 to 1.35)	HR, 1.08 (0.86 to 1.36)
Invasive ventilator-free days at 28 d, median (IQR), d	28 (28 to 28)	28 (28 to 28)	0	.79	NA[j]	NA[j]
ICU-free days at 28 d, median (IQR), d	28 (28 to 28)	28 (28 to 28)	0	.77	NA[j]	NA[j]
Hospital readmission at 90 d, No./total (%)	21/146 (14.4)	22/152 (14.5)	−0.1 (−8.1 to 7.9)	.98	0.99 (0.56 to 1.68)	0.93 (0.52 to 1.60)

Abbreviations: HR, hazard ratio; ICU, intensive care unit; NA, not applicable.

[a] Expressed as percentages unless otherwise indicated.

[b] Expressed as a rate ratio unless otherwise indicated.

[c] Adjusted for respiratory tract infection, days from exacerbation to randomization, pH level at randomization, and ratio of Pa_{O_2} to fraction of inspired oxygen (F_{IO_2}) at randomization.

[d] The outcome definitions appear in the eMethods in Supplement 3.

[e] This is a 1-sided *P* value. All other *P* values are 2-sided.

[f] In the high-intensity NPPV group, defined as the incidence of endotracheal intubation. In the low-intensity NPPV group, defined as the composite incidence of endotracheal intubation or avoiding intubation by crossover to high-intensity NPPV.

[g] Indicates a Clopper-Pearson 95% CI for the rate difference.

[h] The Fisher exact test was used to calculate the *P* value.

[i] The 95% CIs for the median time differences were estimated using resampling with 5000 bootstrap samples.

[j] The estimation was not applicable for the Cox regression model because the count of days was interrupted for invasive ventilator–free days and ICU-free days.

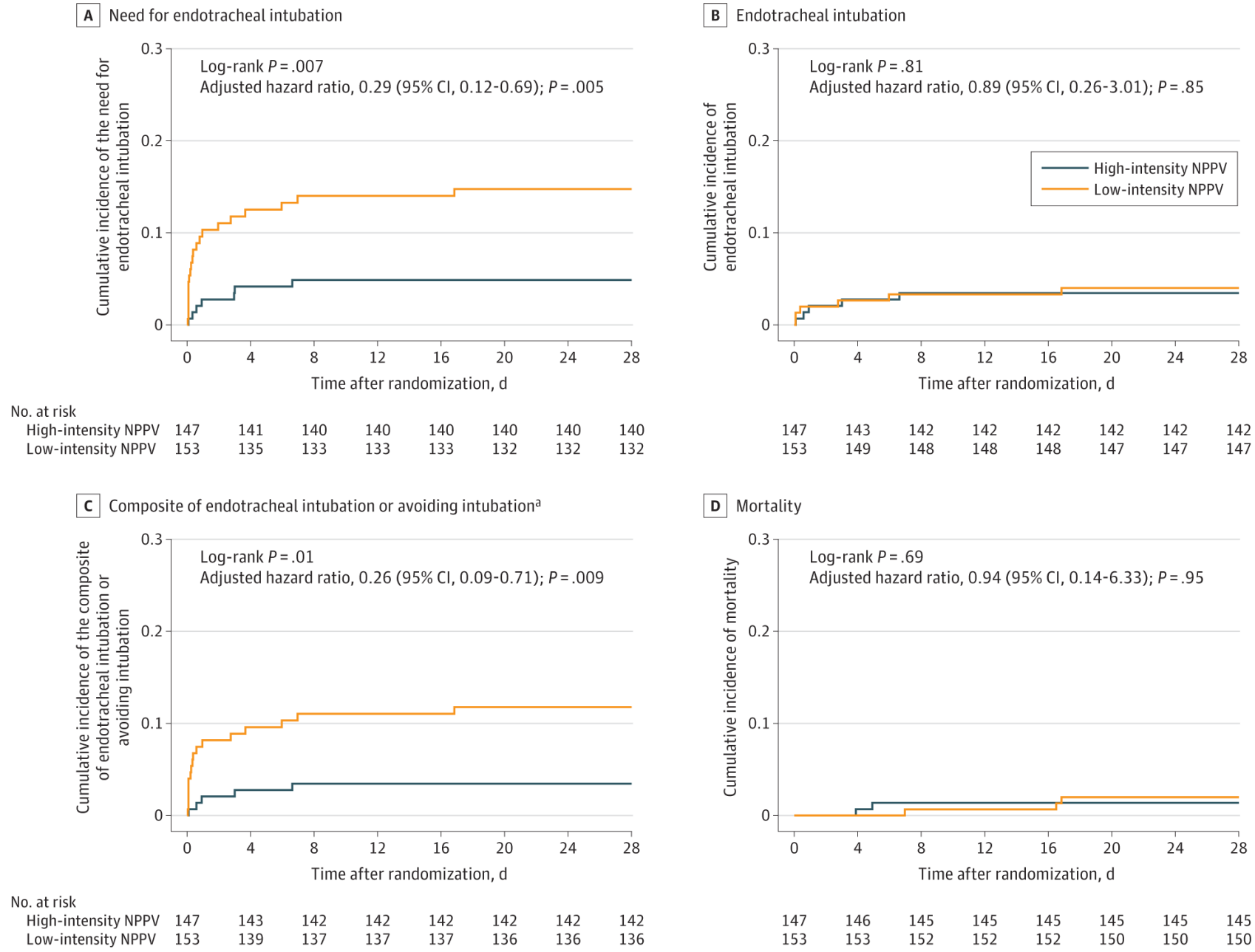

A Need for endotracheal intubation
Log-rank P = .007
Adjusted hazard ratio, 0.29 (95% CI, 0.12-0.69); P = .005
Cumulative incidence of the need for endotracheal intubation
0.3
0.2
0.1
0
0 4 8 12 16 20 24 28
Time after randomization, d
No. at risk
High-intensity NPPV 147 141 140 140 140 140 140 140
Low-intensity NPPV 153 135 133 133 133 132 132 132
B Endotracheal intubation
Log-rank P = .81
Adjusted hazard ratio, 0.89 (95% CI, 0.26-3.01); P = .85
Cumulative incidence of endotracheal intubation
High-intensity NPPV
Low-intensity NPPV
0.3
0.2
0.1
0
0 4 8 12 16 20 24 28
Time after randomization, d
147 143 142 142 142 142 142 142
153 149 148 148 148 147 147 147
C Composite of endotracheal intubation or avoiding intubation[a]
Log-rank P = .01
Adjusted hazard ratio, 0.26 (95% CI, 0.09-0.71); P = .009
Cumulative incidence of the composite of endotracheal intubation or avoiding intubation
0.3
0.2
0.1
0
0 4 8 12 16 20 24 28
Time after randomization, d
No. at risk
High-intensity NPPV 147 143 142 142 142 142 142 142
Low-intensity NPPV 153 139 137 137 137 136 136 136
D Mortality
Log-rank P = .69
Adjusted hazard ratio, 0.94 (95% CI, 0.14-6.33); P = .95
Cumulative incidence of mortality
0.3
0.2
0.1
0
0 4 8 12 16 20 24 28
Time after randomization, d
147 146 145 145 145 145 145 145
153 153 152 152 152 150 150 150

Table 3. Safety Outcomes and Serious Adverse Events

	Noninvasive positive pressure ventilation (NPPV), No. (%)	
	High intensity (n = 147)	Low intensity (n = 153)
Safety outcomes[a]		
Complications related to NPPV		
Abdominal distension	55 (37.4)	39 (25.5)
Nasal or oral dryness	44 (29.9)	46 (30.1)
Severe air leakage[b]	26 (17.7)	17 (11.1)
Severe intolerance to NPPV[c]	11 (7.5)	6 (3.9)
Inability to remove respiratory secretions	8 (5.4)	9 (5.9)
Nasal or facial skin necrosis	3 (2.0)	6 (3.9)
Claustrophobia	3 (2.1)	4 (2.6)
Intolerance to NPPV because of abdominal distension	5 (3.4)	1 (0.7)
Aspiration	1 (0.7)	1 (0.7)
Hypotension	2 (1.4)	0
Conjunctivitis	0	1 (0.7)
Serious adverse events		
Severe alkalosis	6 (4.1)	0
Gastrointestinal tract bleeding	0	3 (2.0)
Nosocomial pneumonia	0	2 (1.3)
Septic shock	1 (0.7)	1 (0.7)
Multiple organ failure	1 (0.7)	1 (0.7)
Cardiac arrest	0	2 (1.3)

[a] The outcome definitions appear in the eMethods in Supplement 3.

[b] Defined as an unintentional air leakage volume exceeding 25 L/min.

[c] Defined as a tolerance level of 0 or 1; 0 indicates very poor tolerance requiring immediate discontinuation of NPPV and 1 indicates poor tolerance, but did not require immediate discontinuation of NPPV.

ORIGINAL ARTICLE
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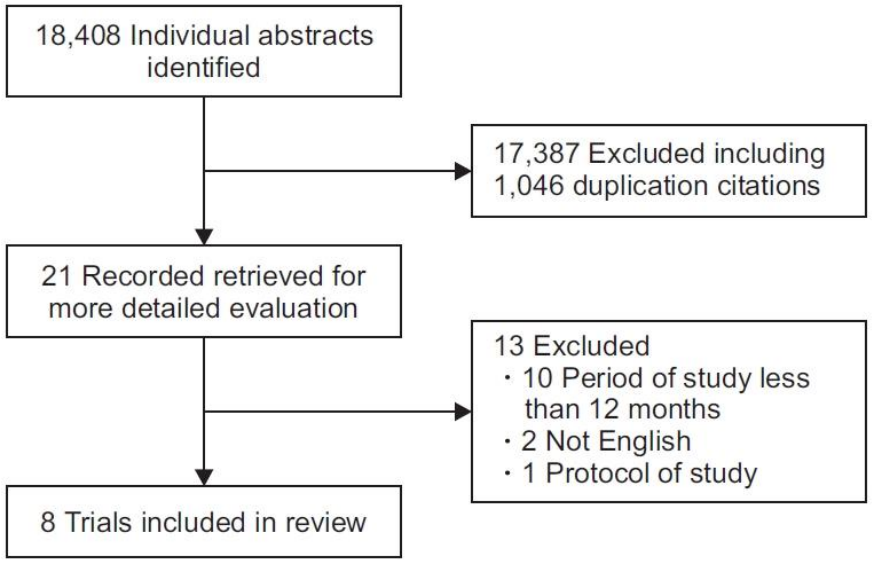
The Long-term Efficacy of Domiciliary Noninvasive Positive-Pressure Ventilation in Chronic Obstructive Pulmonary Disease: A Meta-Analysis of Randomized Controlled Trials

So Young Park, M.D., Ph.D.[1], Kwang Ha Yoo, M.D., Ph.D.[2], Yong Bum Park, M.D., Ph.D.[3], Chin Kook Rhee, M.D., Ph.D.[4], Jinkyeong Park, M.D., Ph.D.[5], Hye Yun Park, M.D., Ph.D.[6], Yong Il Hwang, M.D., Ph.D.[7], Dong Ah Park, Ph.D.[8] and Yun Su Sim, M.D.[9]



- To evaluate the effects of domiciliary NIPPV lasting **more than a year** on mortality rate, differences in QOL, admission rates, and treatment withdrawal of patients with COPD.

- 8 studies, randomized controlled trials

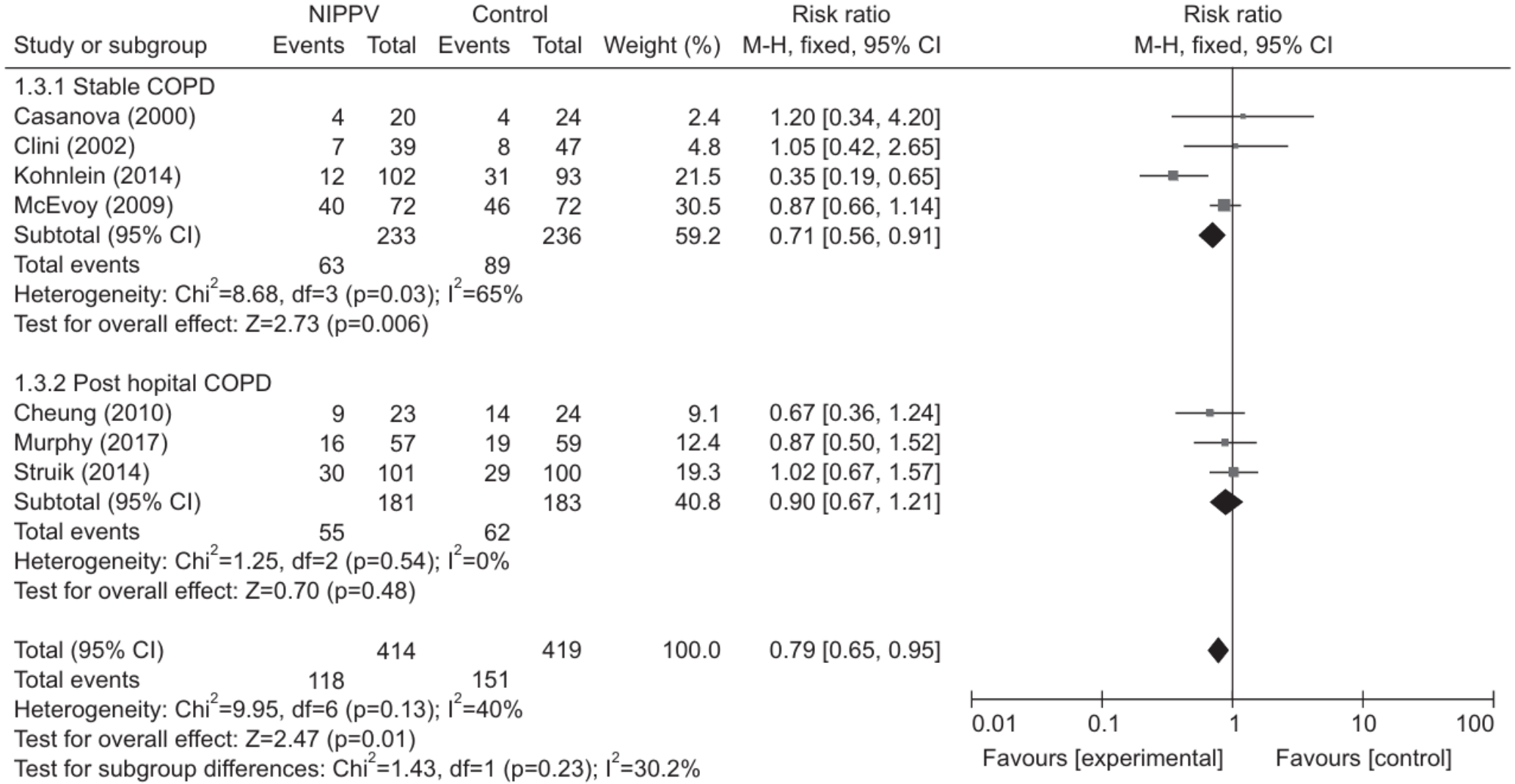


Figure 2. Forest plot describing the effect of noninvasive positive-pressure ventilation (NIPPV) on all-cause mortality, and the mortality rate according to the status of patients with chronic obstructive pulmonary disease (COPD)[7-9,11-14]. The vertical line depicts the equivalence in mortality rates between the two groups (NIPPV vs. control), and horizontal lines correspond to the 95% confidence intervals (CIs). The size of each square represents the proportion of information provided by each study.

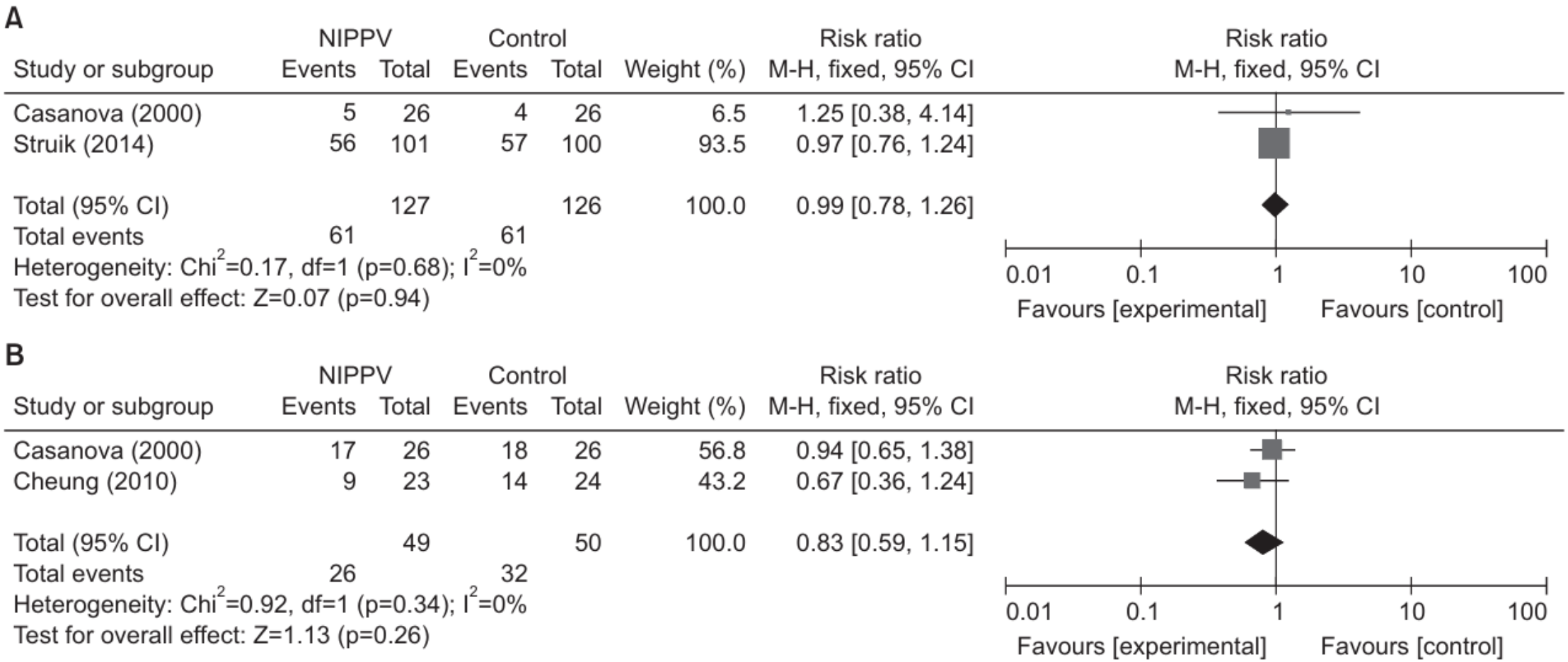


Figure 3. Forest plot depicting the effect of noninvasive positive-pressure ventilation (NIPPV) on admission (A) and acute exacerbation (B)[7,8,14]. The vertical line depicts the equivalence in mortality rates between the two groups (NIPPV vs. control), and the horizontal lines correspond to the 95% confidence intervals (CIs). The size of each square represents the proportion of information provided by each study.

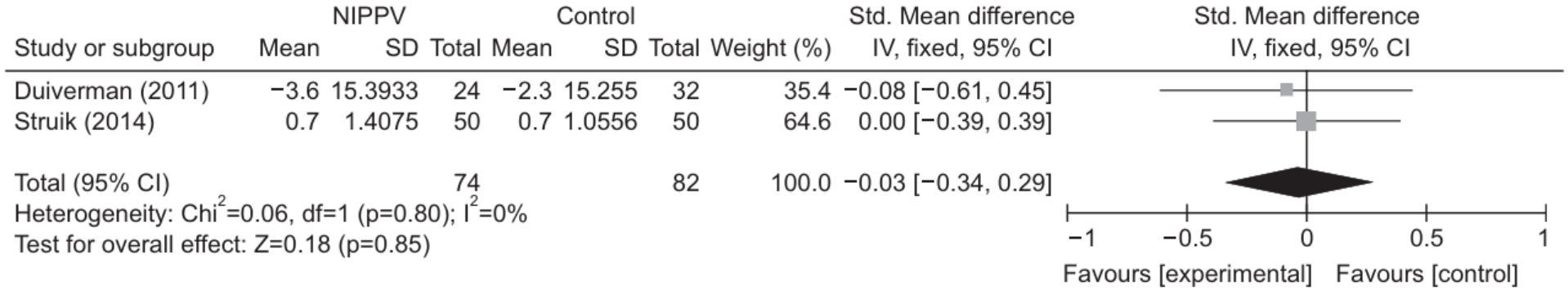


Figure 4. Forest plot depicting the effect of noninvasive positive-pressure ventilation (NIPPV) on the Chronic Respiratory Questionnaire[10,14]. The vertical line depicts the equivalence in mortality rates between the two groups (NIPPV vs. control), and the horizontal lines correspond to the 95% confidence intervals (CIs). The size of each square represents the proportion of information provided by each study. SD: standard deviation.

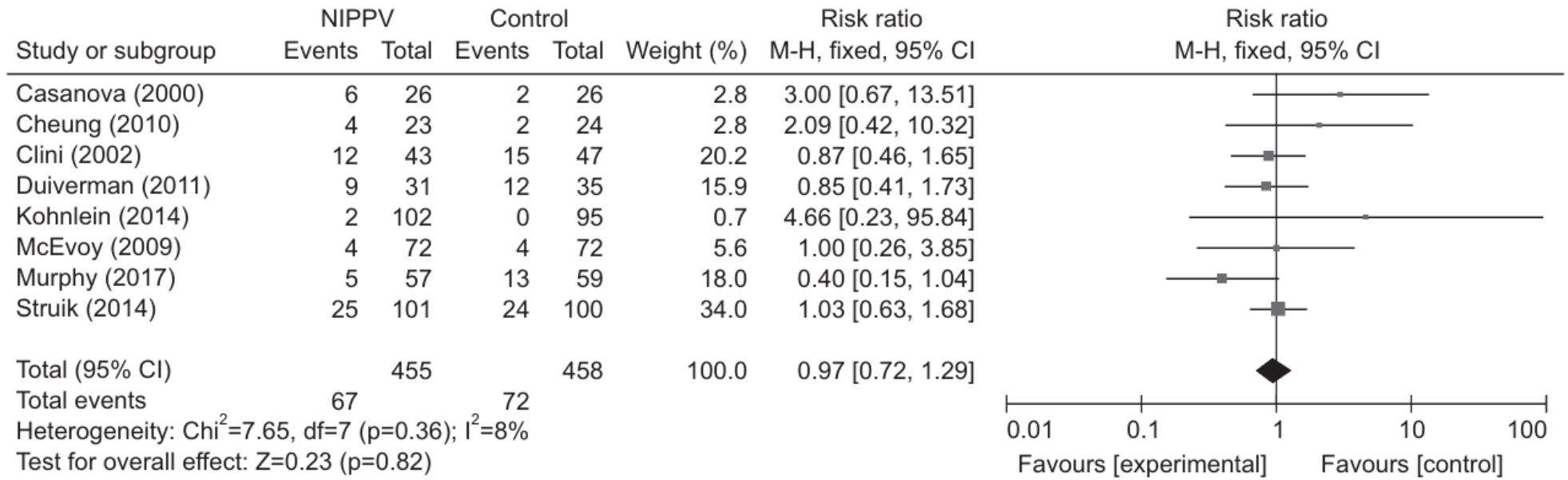


Figure 5. Forest plot depicting the effect of noninvasive positive-pressure ventilation (NIPPV) on withdrawal rates according to mean level of inspiratory positive airway pressure (IPAP) (≥20 cm H_2O)[7-14]. The vertical line depicts the equivalence in mortality rates between the two groups (NIPPV vs. control), and the horizontal lines correspond to the 95% confidence intervals (CIs). The size of each square represents the proportion of information provided by each study.

Summary

- **Smoking cessation:**

  Smoking reduction and cessation lower the risk of lung cancer

- **Pulmonary rehabilitation:**

  Pulmonary rehabilitation reduces COPD exacerbations and mortality, and improves exercise capacity and quality of life, but its implementation rate remains low

- **Digital therapeutics:**

  Adjunctive methods to improve patient adherence

Summary

- **Vaccination:**

  Influenza vaccination strategies are still effective in patients with COPD

- **Long-term oxygen therapy:**

  LTOT 15hr/day is not inferior to LTOT 24hr/day

- **Noninvasive positive pressure ventilation:**

  high-intensity NIPPV reduces the need for endotracheal intubation in patients with an acute exacerbation of COPD and hypercapnia