

Title: Is ‘cardiopulmonary’ the new ‘cardiometabolic’? Making a case for systems change in COPD

Authors: Nathaniel M Hawkins¹, Alan Kaplan², Dennis T Ko³, Erika Penz⁴, Mohit Bhutani⁵

Author affiliations:

¹Division of Cardiology, University of British Columbia, Vancouver, British Columbia, Canada

²Family Physician Airways Group of Canada, University of Toronto, Toronto, Ontario, Canada

³Division of Cardiology, Schulich Heart Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada

⁴Division of Respiriology, Critical Care and Sleep Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

⁵Department of Medicine, University of Alberta, Edmonton, Alberta, Canada

Corresponding author:

Nathaniel M. Hawkins, M.D., M.P.H.

Centre for Cardiovascular Innovation, University of British Columbia

2775 Laurel Street, 9th Floor Room 9123, Vancouver, British Columbia V5Z 1M9 Canada

Telephone: 604 875 5487

Fax: 604 875 5504

E-mail: nat.hawkins@ubc.ca

SUPPLEMENTARY MATERIAL

Table S1. Risk of MACE after moderate or severe exacerbations

Source	Design	Population	N	Time periods (days)	Endpoint	Results (HR unless otherwise state)
Løkke [1]	Retrospective cohort	COPD clinic Denmark + CVD	1,501	1-30	CV event (HF, MI, CVA)	Severe 6.4 Moderate 1.5
Dransfield [2]	Prospective Cohort	RCT IMPACT, <50 1m/s, 50-80 2m	10,355	During, 1-30, 31-90, 91-365	IHD, HF, arrhythmia, CVA	CVAESIs 41.3 vs 2.5 severe vs moderate
Wang [3]	Retrospective Case control	Taiwan admin data	Cases	90	MI, CVA, ICH	Severe exacerbation: MI OR 1.33, CVA 1.46,
Reilev [4]	Case-crossover	Denmark admin data	118,807 cases	42 weeks	MACE, MI, CVA, CV death	Moderate or severe exacerbation: MACE OR 3.70, MI 3.57, CVA 2.78, CV death 4.33, stronger elderly
Rothnie [5]	Self-control case series	UK CPRD	5,696	1-3, 4-7, 8-14, 15-28, 29-91	MI, ischemic CVA	Severe 91 days IRR MI 2.58, CVA 1.97 Moderate 91 days MI 1.58, CVA 1.45
Kunisaki [6]	Prospective Cohort	SUMMIT <70, CVD or CV risk	16,485	1-30, 31-90, 91-365, >365	MACE (CV death, MI, CVA, UA, TIA)	Moderate MACE 3.8 (d1-30) Severe MACE 9.9 (d1-30)
Goto [7]	Self-control case series	US administrative data	362,867	1-30, 31-365	MACE (MI, HF, AF, PE, CVA, ICH)	IRR 1.34 (d1-30), 1.20 (1 year) Separate outcomes CVA>MI
Portegies [8]	Prospective Cohort	Rotterdam	13,115		CVA	Any exacerbation not significant Severe 6.66
Halpin [9]	Prospective cohort	UPLIFT <70	5,992	1-3, 31-180	HF, AF, MI, CVA	30d HF 14.1, AF 17.1, MI 13.0, CVA 4.5 180d 10.7, 6.7, 3.2, 2.3
Donaldson [10]	Self-control case series	Health Improvement Net	25,857	1-5, 6-10, 11-15, 16-49	MI, CVA	1-5d MI 2.27, CVA 1.26

Abbreviations: AF = atrial fibrillation; COPD = chronic obstructive pulmonary disease; CPRD = Clinical Practice Research Datalink; CV = cardiovascular; CVA = cerebrovascular accident; CVAESI = cardiovascular adverse events of special interest; CVD = cardiovascular disease; HF = heart failure; HR = hazard ratio; ICH = ischemic heart disease; IRR = incidence rate ratio; MACE = major adverse cardiovascular event; MI = myocardial infarction; PE = pulmonary embolism; RCT = randomized controlled trial; UK = United Kingdom; US = United States.

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