COPD year in review 2018

강원대병원 내과 김우진

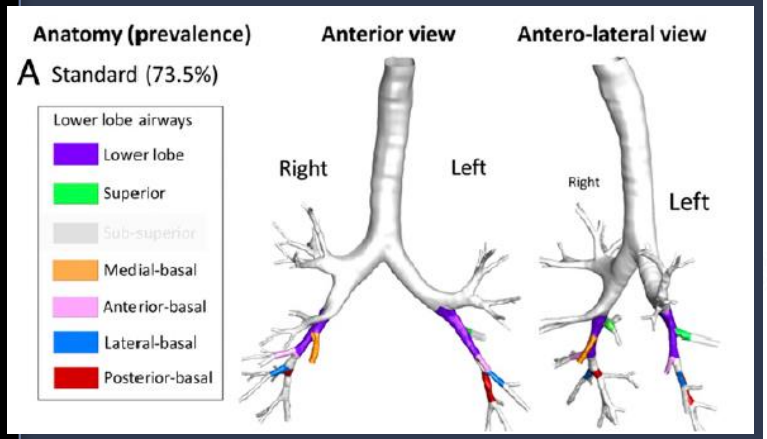
COPD 2018

- Biomarker/Risk factor
  - Branch variation (PNAS)
  - Airway Fractal Dimension (JCI)
  - Eosinophil (JACI)
  - PRISM (AJRCCM)
- Drug Treatment
  - IMPACT (NEJM)
  - TRIBUTE (Lancet)
  - SUNSET (AJRCCM)
  - Theophylline (JAMA)
- Self-management
  - Transition and long-term self-management (JAMA)

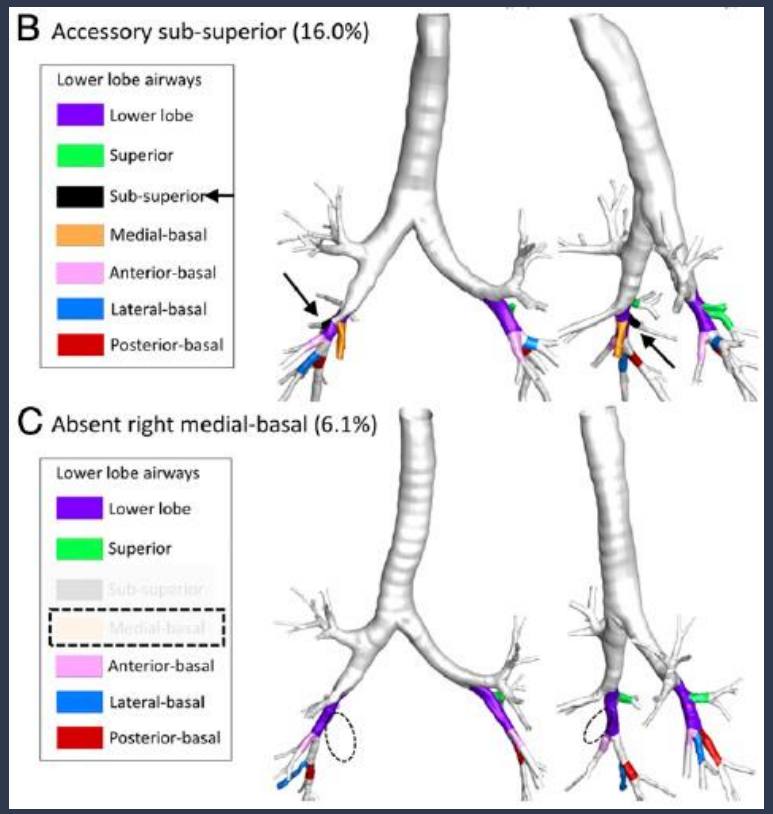
- Biomarker / Risk factor
  - Branch variation (PNAS)
  - Airway Fractal Dimension (JCI)
  - Eosinophil (JACI)
  - PRISM (AJRCCM)

Human airway branch variation and chronic obstructive pulmonary disease

Benjamin M. Smith[a,b,1], Hussein Traboulsi[b], John H. M. Austin[c], Ani Manichaikul[d], Eric A. Hoffman[e,f,g], Eugene R. Bleecker[h], Wellington V. Cardoso[a], Christopher Cooper[i], David J. Couper[j], Stephen M. Dashnaw[c], Jia Guo[k], MeiLan K. Han[l], Nadia N. Hansel[m], Emlyn W. Hughes[n], David R. Jacobs Jr.[o], Richard E. Kanner[p], Joel D. Kaufman[q], Eric Kleerup[i], Ching-Long Lin[r], Kiang Liu[s], Christian M. Lo Cascio[a], Fernando J. Martinez[t], Jennifer N. Nguyen[d], Martin R. Prince[c], Stephen Rennard[u], Stephen S. Rich[d], Leora Simon[b], Yanping Sun[a], Karol E. Watson[i], Prescott G. Woodruff[v], Carolyn J. Baglole[b], and R. Graham Barr[a,w], for the MESA Lung and SPIROMICS investigators



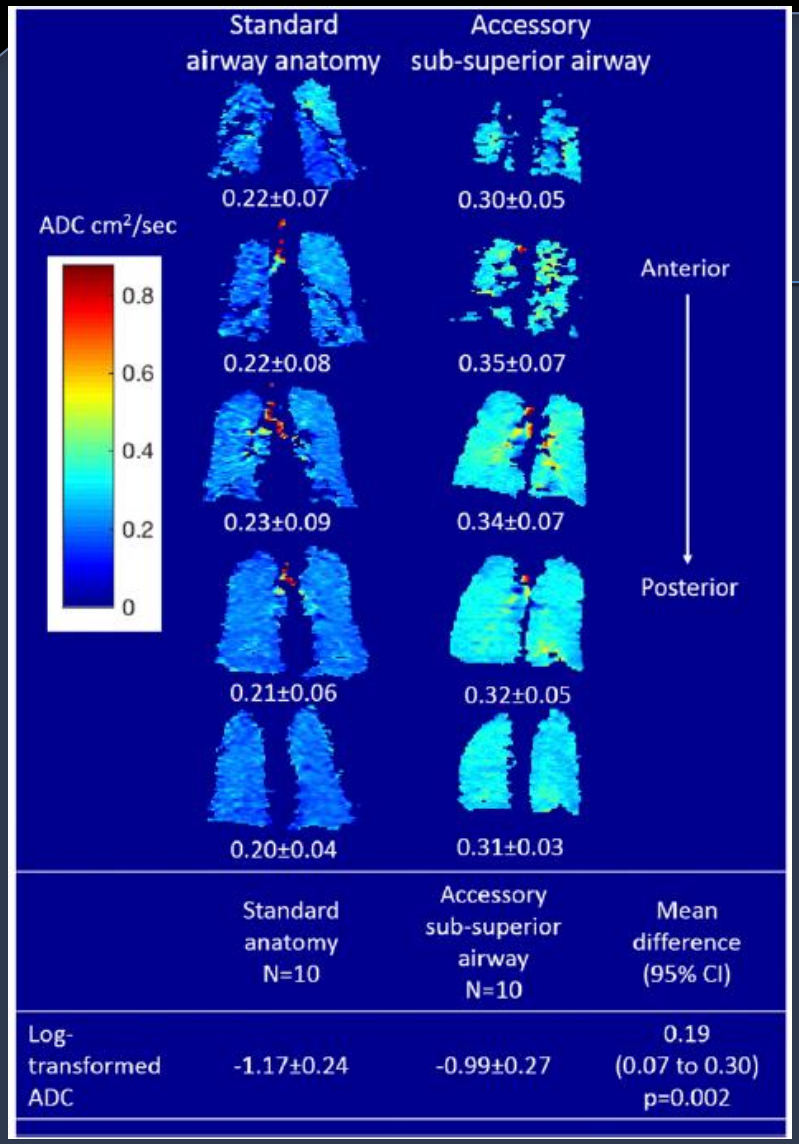
MESA n=3169, >5% variant



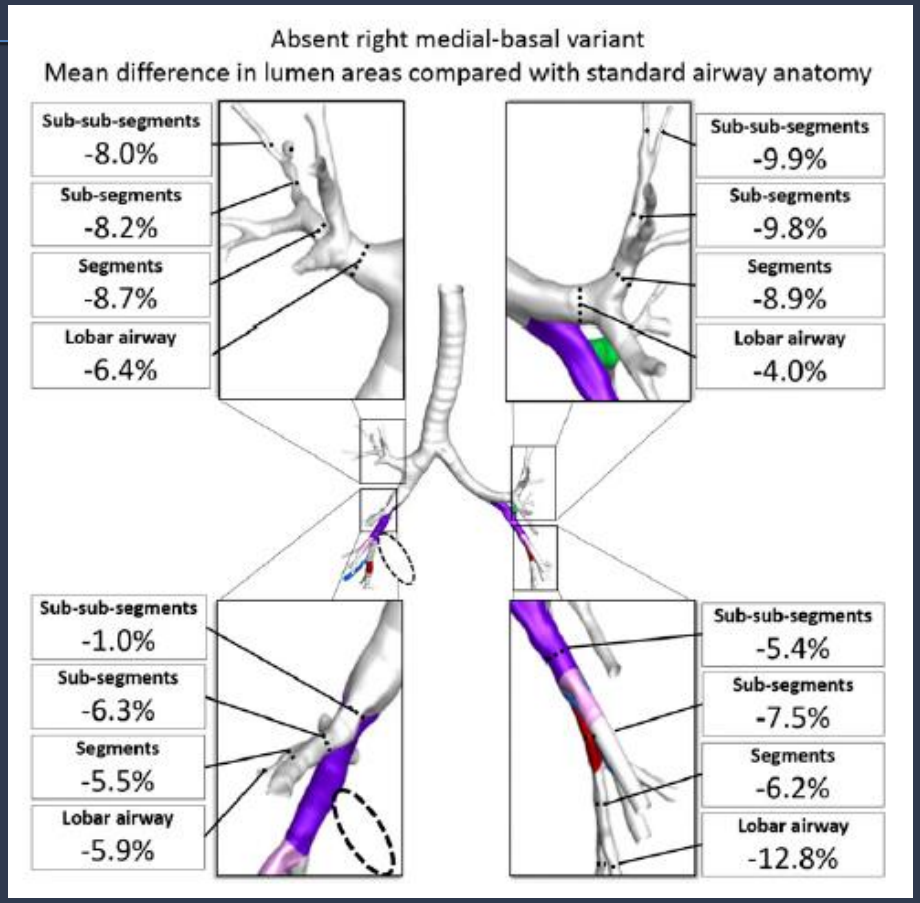
1.40 OR of COPD
p <0.001

1.55 OR of COPD
p =0.004

PNAS 2018;115:E974



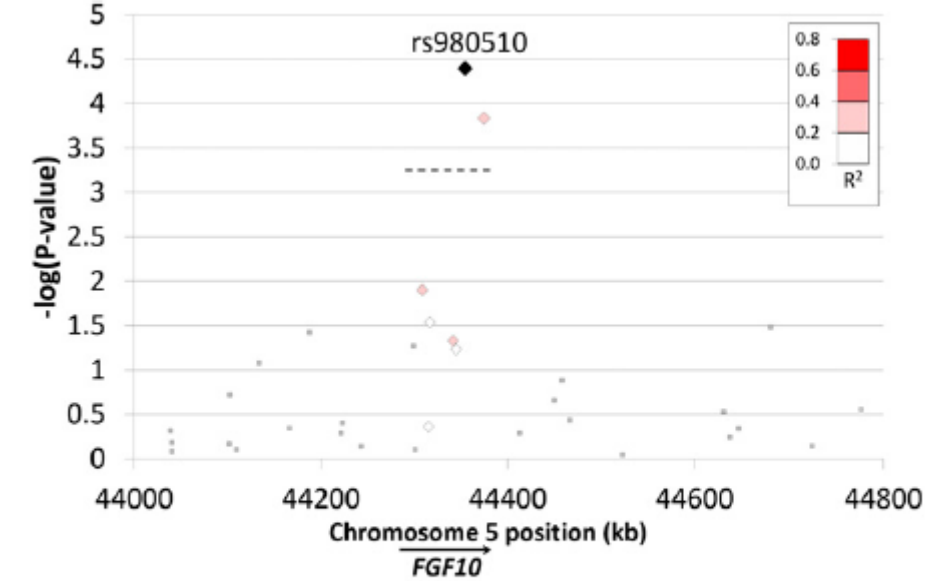
	Standard anatomy N=10	Accessory sub-superior airway N=10	Mean difference (95% CI)
Log-transformed ADC	-1.17±0.24	-0.99±0.27	0.19 (0.07 to 0.30) p=0.002



Percentage of emphysema-like lung
Chronic bronchitis or Dyspnea
Airway segment length

PNAS 2018;115:E974

Candidate genes association analysis of airway branch variants



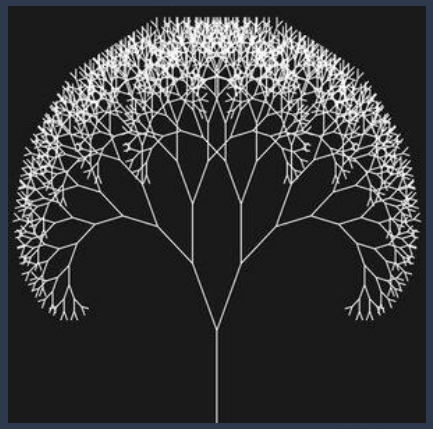
SNP	Minor Allele	Freq. in cases N=172	Freq. in controls N=2,425	Pooled odds ratio	I^2	Odds ratio by race-ethnicity				P value
						White	Black	Hispanic	Asian	
rs980510	T	0.564	0.447	1.63	0	1.75	1.27	1.67	1.69	3.95×10^{-5}
rs10512844	A	0.411	0.308	1.58	0	1.71	1.44	1.47	1.63	1.43×10^{-4}

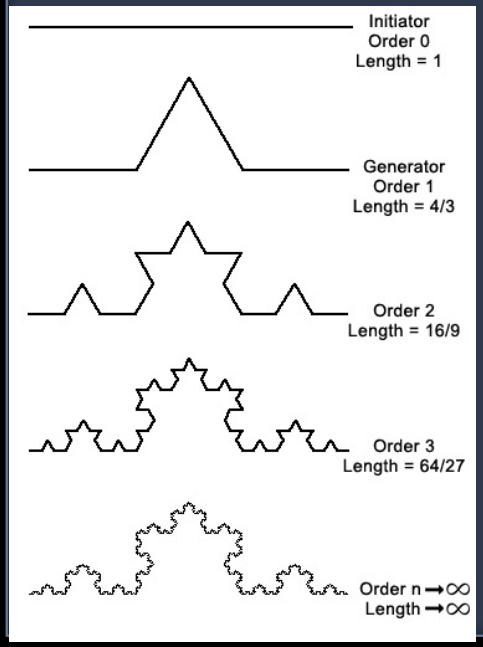
11 candidate genes 109 SNPs

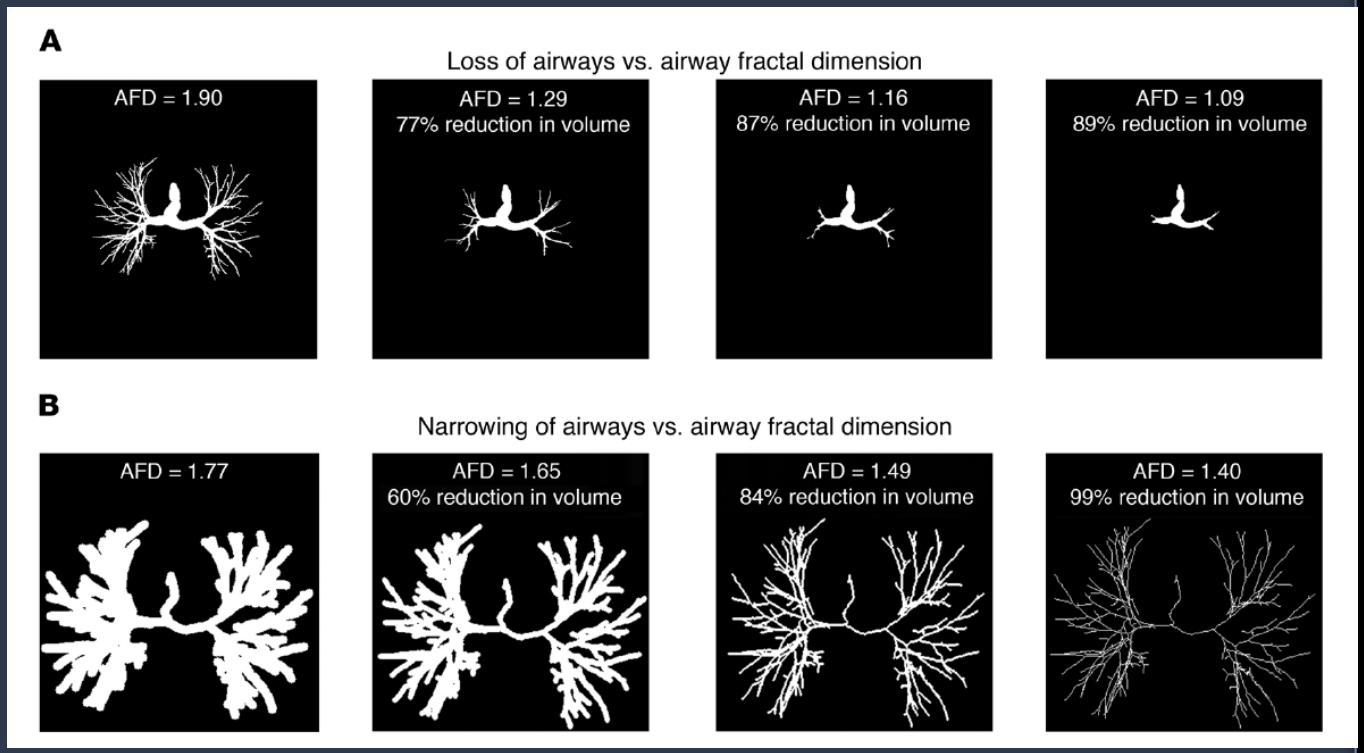
PNAS 2018;115:E974

Airway fractal dimension predicts respiratory morbidity and mortality in COPD

Sandeep Bodduluri,[1,2,3] Abhilash S. Kizhakke Puliyakote,[4] Sarah E. Gerard,[5] Joseph M. Reinhardt,[5] Eric A. Hoffman,[5,6] John D. Newell Jr.,[5,6] Hrudaya P. Nath,[2,7] MeiLan K. Han,[8] George R. Washko,[9] Raúl San José Estépar,[10] Mark T. Dransfield,[1,2,3] Surya P. Bhatt,[1,2,3] and COPDGene Investigators[11]







Increased turbulence, airflow obstruction, impaired airflow distribution

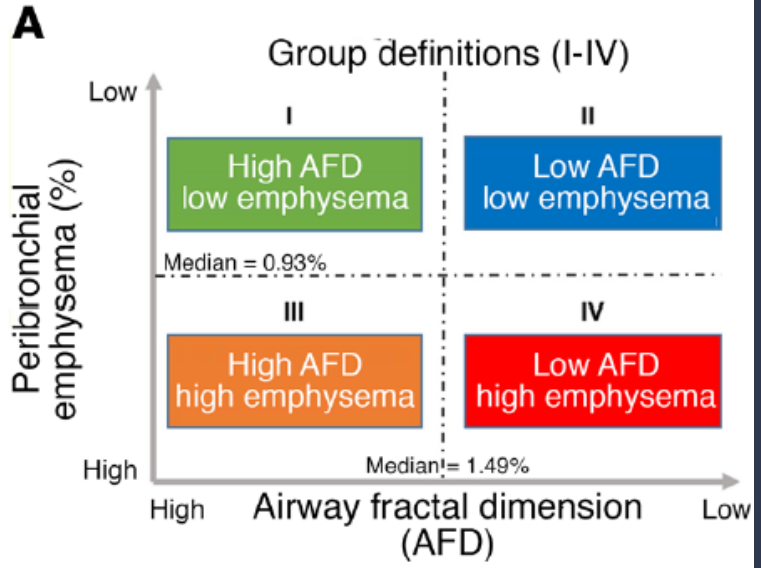
JCI 2018;128:5374

Association with lung function, exercise capacity, SGRQ, and change in FEV1

	Pi10		Airway fractal dimension (AFD)			
			Unadjusted for Pi10		Adjusted for Pi10	
	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*
FEV_1, liters[A]	−0.69 (−0.83, −0.55)	<0.001	1.14 (0.98, 1.29)	<0.001	1.17 (1.02, 1.33)	<0.001
FEV_1/FVC[A]	0.03 (0.01, 0.05)	<0.001	0.11 (0.10, 0.13)	<0.001	0.11 (0.10, 0.13)	<0.001
Six-minute walk distance, feet[B]	−254.94 (−360.07, −149.82)	<0.001	400.95 (277.64, 524.27)	<0.001	425.60 (301.54, 549.66)	<0.001
SGRQ[B]	13.12 (7.61, 18.63)	<0.001	−14.07 (−20.57, −7.58)	<0.001	−14.53 (−21.05, −8.01)	<0.001
Change in FEV_1 after 5-year follow-up[C]	4.71 (−17.43, 26.87)	0.676	−37.85 (−62.94, −12.77)	<0.001	−38.81 (−64.30, −13.31)	0.002

JCI 2018;128:5374

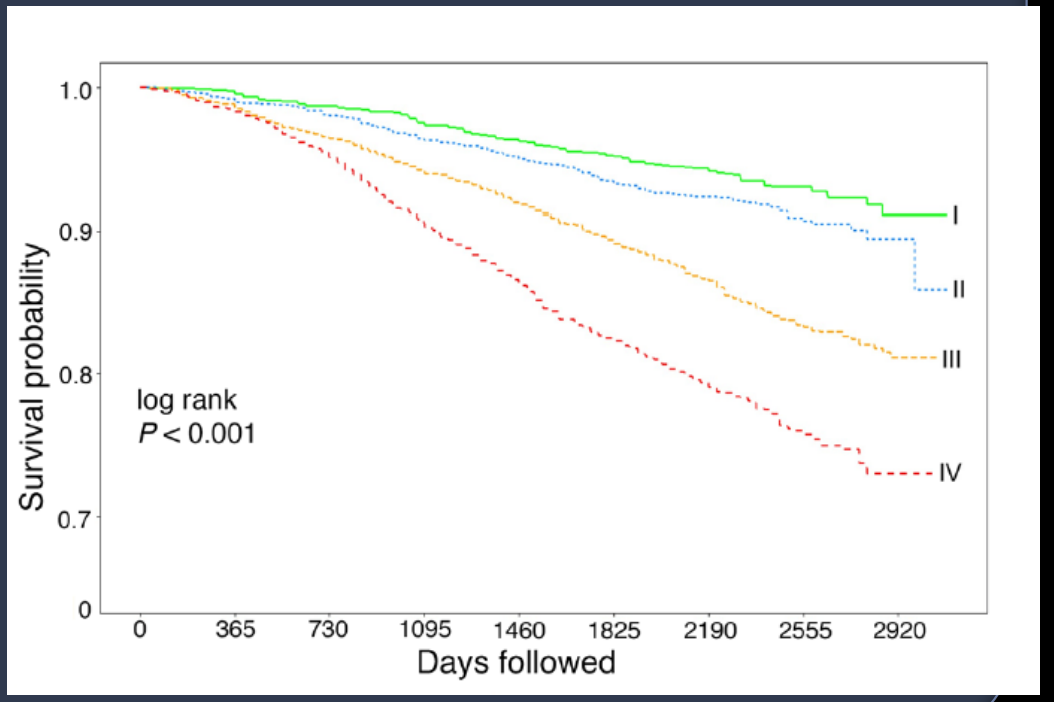
AFD, emphysema and survival



B

COPD severity distribution per group

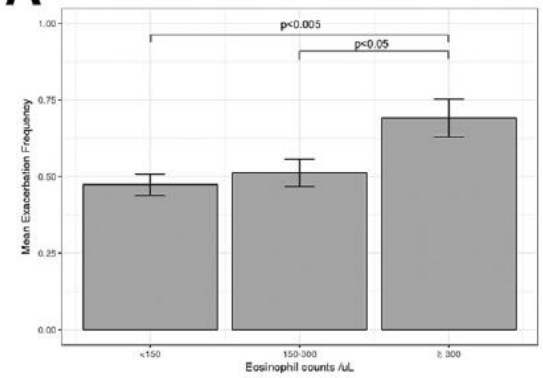
	GOLD 0	GOLD 1	GOLD 2	GOLD 3	GOLD 4
I	1457	134	175	21	5
II	999	137	435	146	20
III	796	245	459	273	130
IV	247	135	509	506	325



JCI 2018;128:5374

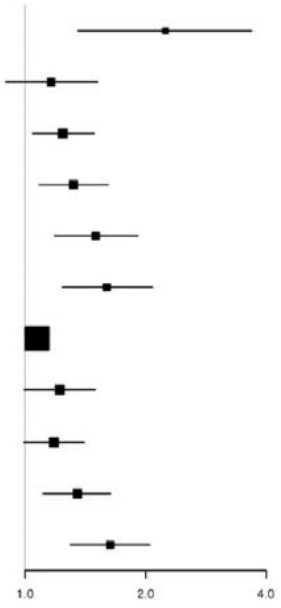
Blood eosinophil count thresholds and exacerbations in patients with chronic obstructive pulmonary disease

Jeong H. Yun, MD, MPH,[a,b,c] Andrew Lamb, MS,[a] Robert Chase, MS,[a] Dave Singh, MD,[d] Margaret M. Parker, PhD,[a,c] Aabida Saferali, PhD,[a,c] Jørgen Vestbo, DMSc,[d,e] Ruth Tal-Singer, PhD,[f] Peter J. Castaldi, MD,[a,c] Edwin K. Silverman, MD, PhD,[a,b,c] and Craig P. Hersh, MD, MPH,[a,b,c] for the COPDGene and ECLIPSE Investigators



C

Eosinophil Cutoff	< n	≥ n	IRR	95% CI
cell/uL continuous	NA	1540	2.24	1.35-3.68
100 cells/uL	223	1330	1.16	0.90-1.52
200 cells/uL	814	739	1.24	1.04-1.48
300 cells/uL	1187	366	1.32	1.08-1.61
340 cells/uL	1350	203	1.5	1.18-1.91
400 cells/uL	1398	155	1.6	1.24-2.08
% continuous	NA	1540	1.07	1.02-1.11
2 %	408	1145	1.22	0.99-1.50
3 %	859	694	1.18	0.99-1.40
4 %	1166	387	1.35	1.11-1.63
5 %	1334	219	1.63	1.30-2.05



Max AUC

COPDGene study n=1,765 grade 2-4 COPD

JACI 2018;141:2037

Association with exacerbation risk

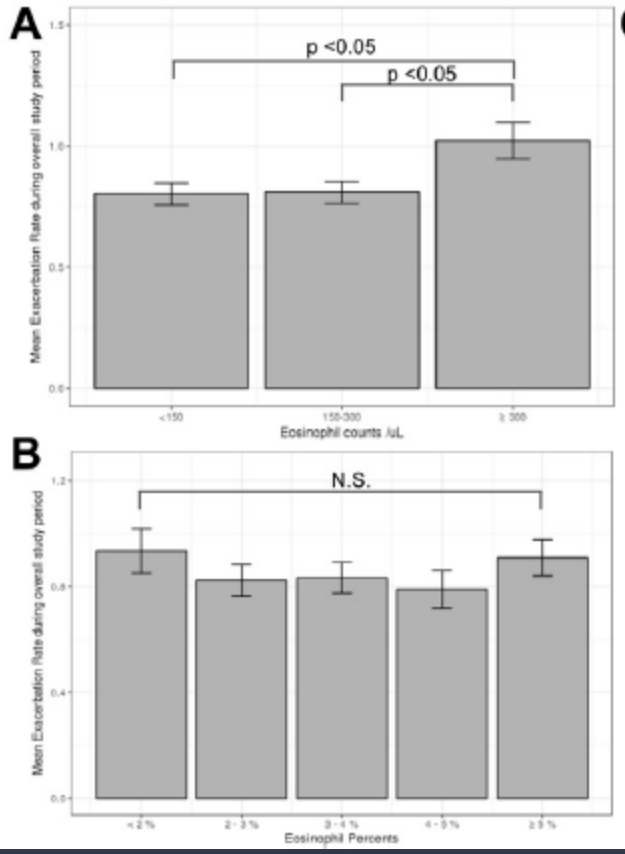
TABLE II. Multivariable models of blood eosinophil counts of 300 cells/μL or greater and exacerbation risk in the COPDGene study

	COPDGene: Year before visit 2 (cross-sectional)				COPDGene: Longitudinal follow-up	
	Exacerbation frequency* (n = 1,553)		Frequent exacerbation† (n = 1,281)		Exacerbation rate* (n = 1,113)	
Factors	**IRR* (95% CI)**	***P* value**	**OR† (95% CI)**	***P* value**	**IRR* (95% CI)**	***P* value**
Age	**0.98 (0.97-1.00)**	**.007**	**0.96 (0.94-0.99)**	**.003**	0.99 (0.97-1.01)	.48
Female sex	**1.43 (1.20-1.71)**	**<.001**	**1.83 (1.30-2.58)**	**<.001**	0.87 (0.65-1.15)	.31
Nonwhite race	**0.73 (0.57-0.92)**	**.008**	**0.63 (0.40-0.99)**	**.05**	**1.73 (1.19-2.55)**	**.005**
SGRQ total score‡	**1.02 (1.02-1.03)**	**<.001**	**1.04 (1.03-1.05)**	**<.001**	**1.02 (1.01-1.03)**	**<.001**
Postbronchodilator FEV_1 (% predicted)§	**0.98 (0.98-0.99)**	**<.001**	**0.97 (0.96-0.98)**	**<.001**	**0.99 (0.98-1.00)**	**.003**
GERD	**1.33 (1.11-1.59)**	**.002**	1.35 (0.95-1.91)	.09	1.08 (0.81-1.45)	.57
Current smoking	**0.71 (0.57-0.89)**	**.002**	**0.56 (0.37-0.84)**	**.006**	**0.63 (0.45-0.90)**	**.01**
Previous exacerbations	NA	NA	NA	NA	**2.51 (1.87-3.37)**	**<.001**
WBC count	1.00 (0.96-1.04)	.97	1.02 (0.94-1.10)	.66	1.03 (0.96-1.10)	.44
Eosinophil count ≥300 cells/μL	**1.32 (1.08-1.61)**	**.006**	**1.58 (1.07-2.30)**	**.019**	1.33 (0.92-1.95)	.13

COPDGene longitudinal follow-up stratified analysis						
	No exacerbations in the prior year (666 vs 98)		One exacerbation in the prior year (165 vs 28)		Two or more exacerbations in the prior year (125 vs 31)	
Noneosinophilic vs eosinophilic	**IRR (95% CI)**	***P* value**	**IRR (95% CI)**	***P* value**	**IRR (95% CI)**	***P* value**
Eosinophil count ≥300 cells/μL at phase 2 visit	1.12 (0.57-2.28)	.73	1.02 (0.48-2.20)	.97	**1.96 (1.21-3.21)**	**.008**

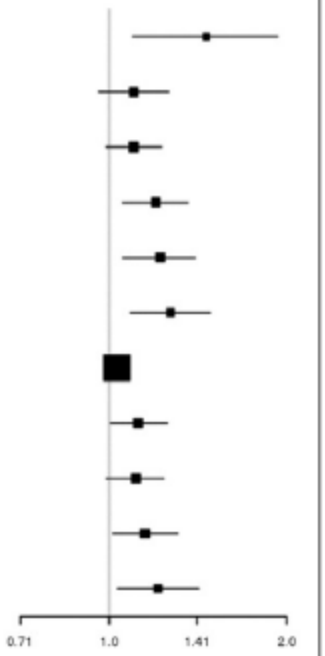
JACI 2018;141:2037

Validation with ECLIPSE study



C

Eosinophil Cutoff	< n	≥ n	IRR	95% CI
continuous cells/uL	NA	1895	1.46	1.09-1.93
100 cells/uL	368	1527	1.1	0.96-1.26
200 cells/uL	1032	863	1.1	0.99-1.23
300 cells/uL	1477	418	1.2	1.05-1.36
340 cells/uL	1584	311	1.22	1.06-1.40
400 cells/uL	1668	227	1.27	1.08-1.48
continuous %	NA	1895	1.03	1.01-1.06
2 %	720	1175	1.12	1.00-1.25
3 %	1178	717	1.11	0.99-1.24
4 %	1476	419	1.15	1.01-1.31
5 %	1660	235	1.21	1.03-1.42



n=1,895 grade 2-4 COPD

JACI 2018;141:2037

COPD with eo > 300 vs. ACO

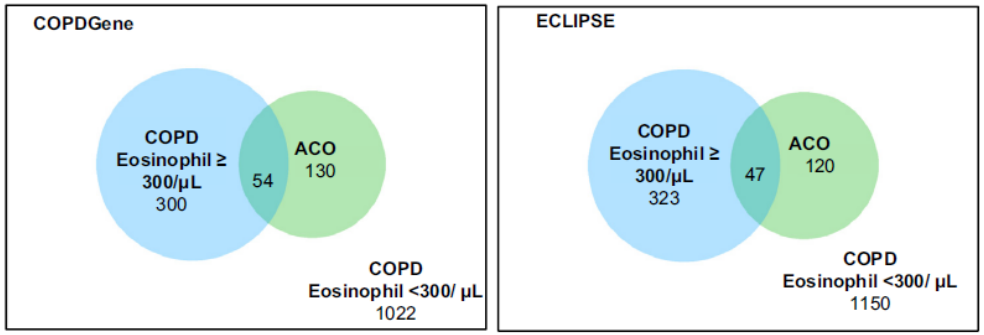


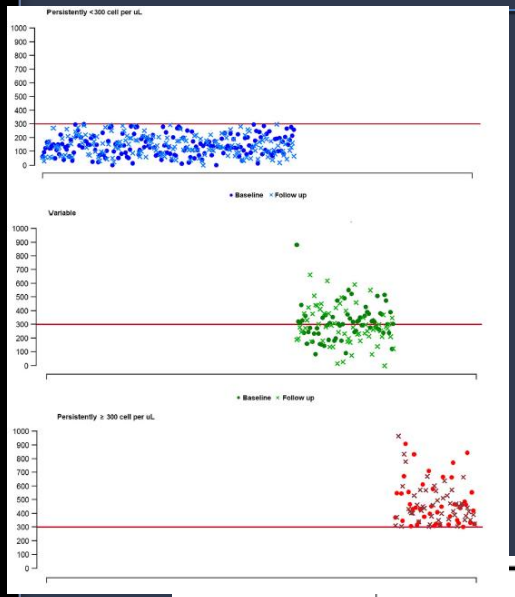
FIG 3. Venn diagrams of the number of subjects with ACO (defined by asthma diagnosis before the age of 40 years)[30] and patients with COPD with blood eosinophil counts of 300 cells/μL or greater in the COPDGene and ECLIPSE studies.

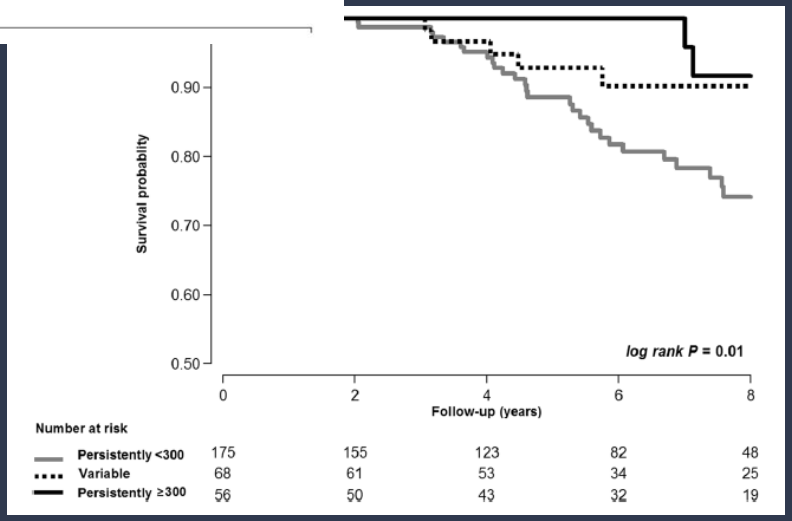
TABLE VI. ACO, which was defined by asthma diagnosis before age 40 years, and increased eosinophil counts (≥300 cells/μL) independently predict exacerbations

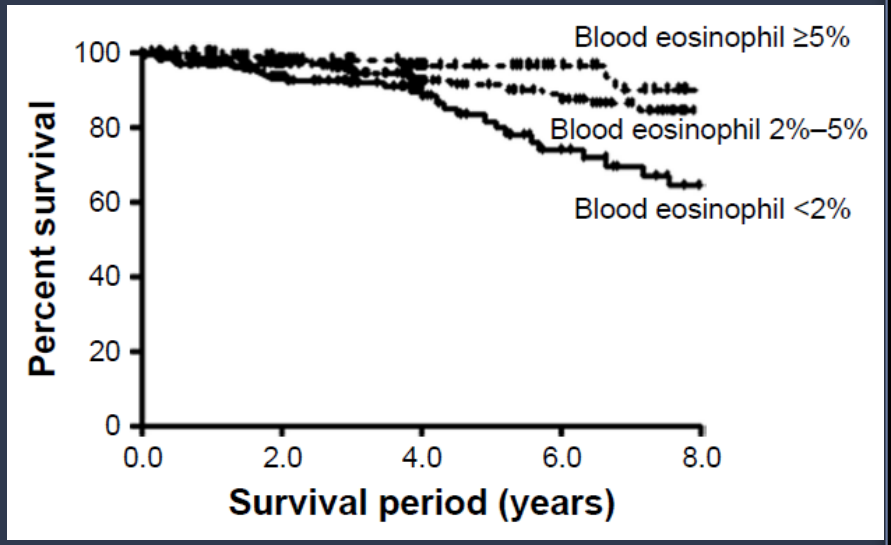
	COPDGene study		ECLIPSE study			
	Cross-sectional exacerbation frequency		Prospective exacerbation rate			
			1 y		Overall study period	
Factors	IRR (95% CI)	*P* value	IRR (95% CI)	*P* value	IRR (95% CI)	*P* value
Age	**0.99 (0.97-1.00)**	**.02**	**1.01 (1.00-1.02)**	**.006**	**1.01 (1.00-1.02)**	**.009**
Nonwhite race	**0.69 (0.54-0.88)**	**.003**	0.83 (0.54-1.25)	.37	0.69 (0.41-1.12)	.15
Female sex	**1.39 (1.16-1.66)**	**<.001**	**1.20 (1.06-1.36)**	**.004**	**1.29 (1.11-1.49)**	**<.001**
SGRQ score*	**1.02 (1.02 -1.03)**	**<.001**	**1.01 (1.01-1.01)**	**<.001**	**1.01 (1.01-1.01)**	**<.001**
Postbronchodilator FEV_1 (% predicted)†	**0.98 (0.98-0.99)**	**<.001**	**0.99 (0.98-0.99)**	**<.001**	**0.98 (0.98-0.99)**	**<.001**
GERD	**1.37 (1.14-1.64)**	**<.001**	**1.40 (1.23-1.59)**	**<.001**	**1.39 (1.20-1.61)**	**<.001**
Current smoking	**0.73 (0.58-0.90)**	**.004**	1.10 (0.97-1.25)	.12	**1.25 (1.08-1.44)**	**.003**
Previous exacerbations	**NA**	**NA**	**2.35 (2.08- 2.65)**	**<.001**	**2.77 (2.40-3.21)**	**<.001**
WBC count	1.01 (0.97-1.05)	.70	**1.03 (1.01-1.06)**	**.006**	**1.04 (1.01-1.07)**	**.004**
ACO	**1.33 (1.04-1.71)**	**.02**	**1.29 (1.08-1.54)**	**.005**	**1.33 (1.08-1.63)**	**.006**
Eosinophil count ≥300 cells/μL	**1.26 (1.03-1.54)**	**.02**	**1.21 (1.06-1.39)**	**.005**	**1.22 (1.04-1.42)**	**.01**

JACI 2018;141:2037

Korean studies on eosinophil count







Emphysema severity

Shin, et al. Respir Res 2018;19:134

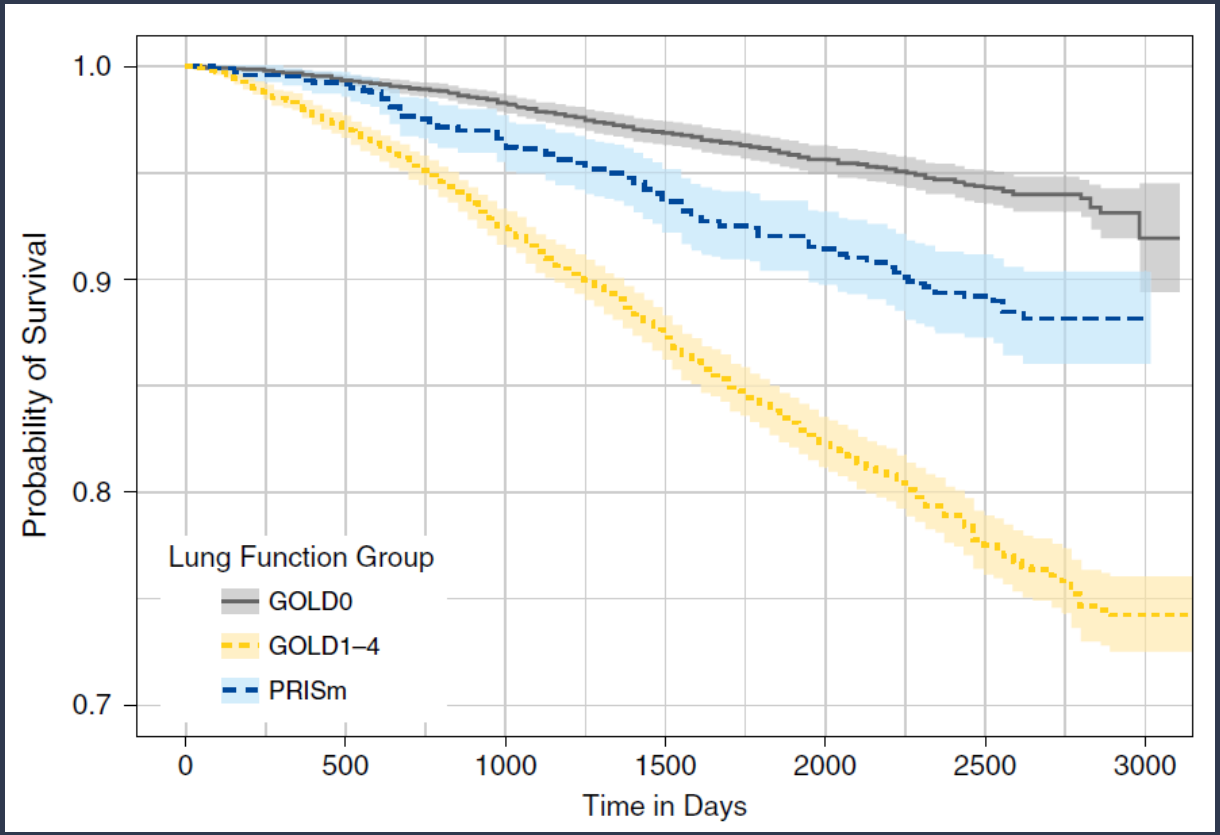
Oh, et al. IJCOPD 2018;13:3589

Longitudinal Phenotypes and Mortality in Preserved Ratio Impaired Spirometry in the COPDGene Study

Emily S. Wan[1,2], Spyridon Fortis[3], Elizabeth A. Regan[4], John Hokanson[5], MeiLan K. Han[6], Richard Casaburi[7], Barry J. Make[4], James D. Crapo[4], Dawn L. DeMeo[1], and Edwin K. Silverman[1]; for the COPDGene Investigators

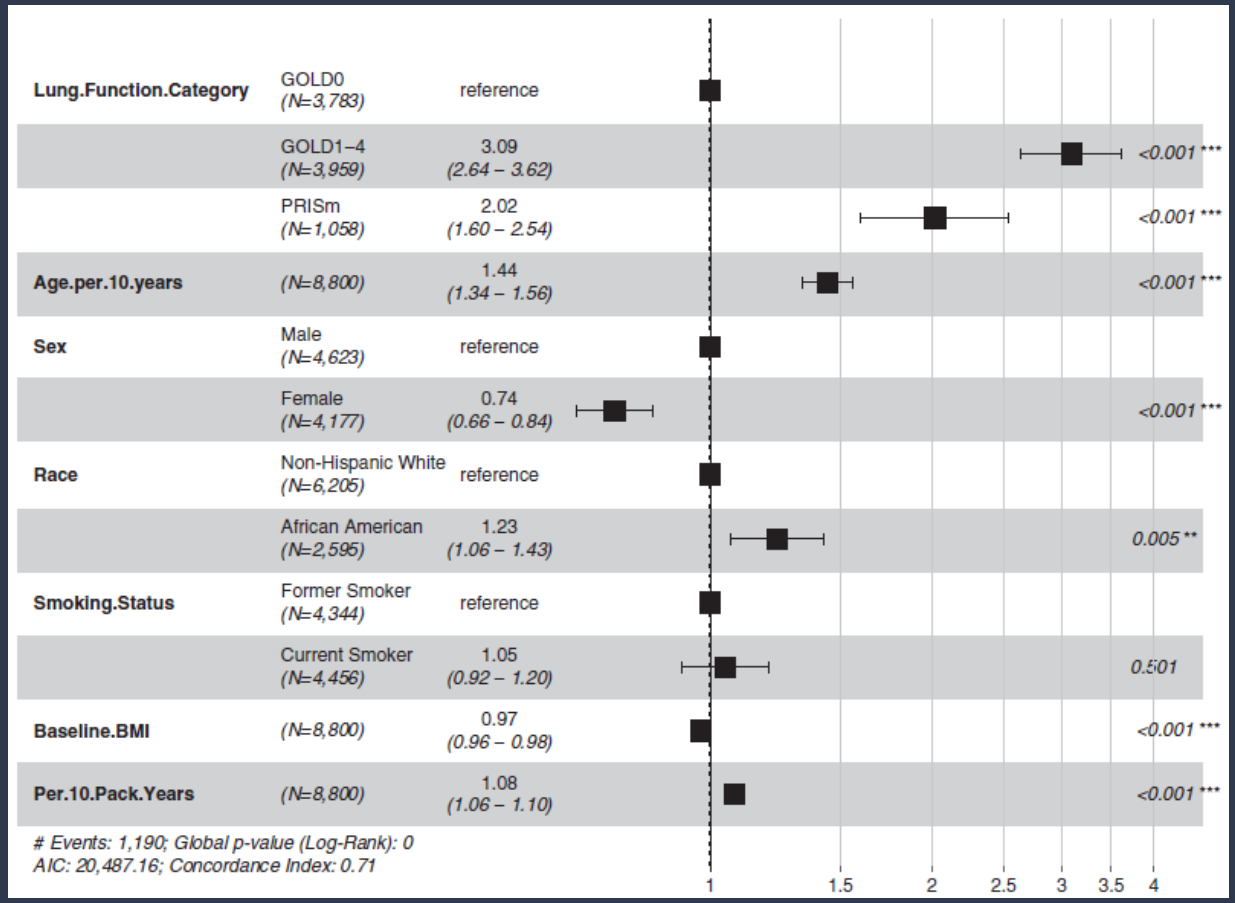
- $FEV_1/FVC > 0.7$ and $FEV_1 < 80\%$

3,783
3,959
1,058



AJRCCM 2018;198:1397

Hazard ratio for mortality



AJRCCM 2018;198:1397

Longitudinal change

A

Phase 1*	Phase 2*	N	%
PRISm	GOLD 0	152	22.2%
	COPD (GOLD 1–4)	172	25.1%
	PRISm	360	52.6%

*Among participants with lung function data at both Phase 1 and Phase 2

B

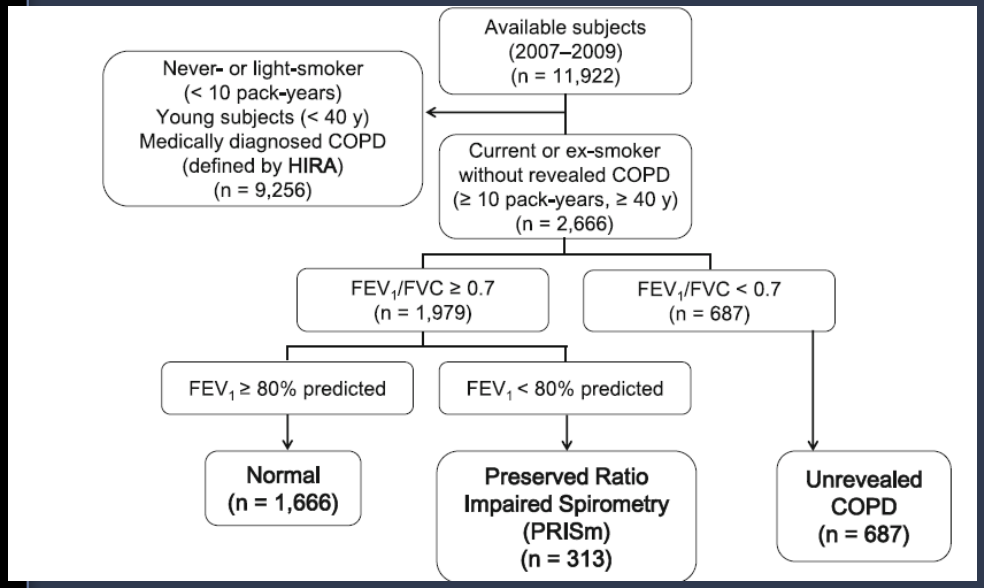
Phase 1*	N	%	Phase 2*
PRISm	360	51.9%	PRISm
GOLD 0	223	32.1%	
COPD (GOLD 1–4)	111	16%	

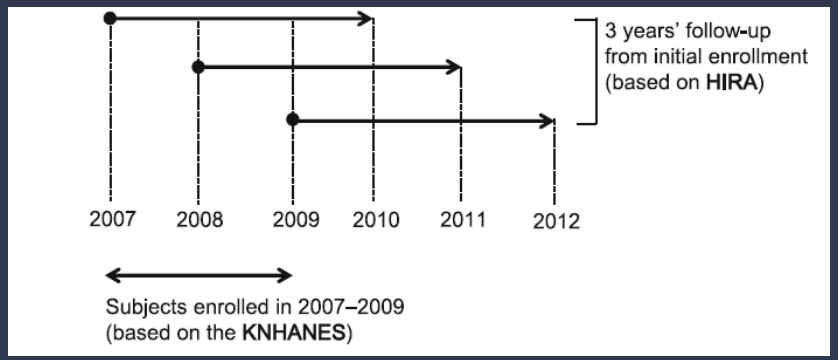
Reduction in BMI

Baseline TLC% and gas trapping

AJRCCM 2018;198:1397

Korean study on PRISm





	Normal	PRISm	Unrevealed COPD
COPD incidence (/1000PY)	4.4	17.0	45.1
OPD visit, *n* (%)	51 (3.1)	22 (7.0)	131 (19.1)
No. of OPD visit	0.10 ± 0.91	0.48 ± 2.96	1.86 ± 6.37
Hospitalization, *n* (%)	79 (4.7)	29 (9.3)	83 (12.1)
ER visit, n (%)	23 (1.4)	12 (3.8)	36 (5.2)
ICU admission, n (%)	12 (0.7)	6 (1.9)	19 (2.8)

Age and wheezing predictors for COPD diagnosis

Park, et al. Respir Res 2018;19:185

- Drug treatment
  - IMPACT (NEJM)
  - TRIBUTE (Lancet)
  - SUNSET (AJRCCM)
  - TWICS (JAMA)
- Self-management

Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD

David A. Lipson, M.D., Frank Barnhart, D.V.M., Noushin Brealey, M.D., Jean Brooks, M.Sc., Gerard J. Criner, M.D., Nicola C. Day, Ph.D., Mark T. Dransfield, M.D., David M.G. Halpin, M.D., MeiLan K. Han, M.D., C. Elaine Jones, Ph.D., Sally Kilbride, M.Sc., Peter Lange, M.D., David A. Lomas, M.D., Ph.D., Fernando J. Martinez, M.D., Dave Singh, M.D., Maggie Tabberer, M.Sc., Robert A. Wise, M.D., and Steven J. Pascoe, M.B., B.S., for the IMPACT Investigators

FEV1 < 50% and ≥1 mod or severe exacerbation

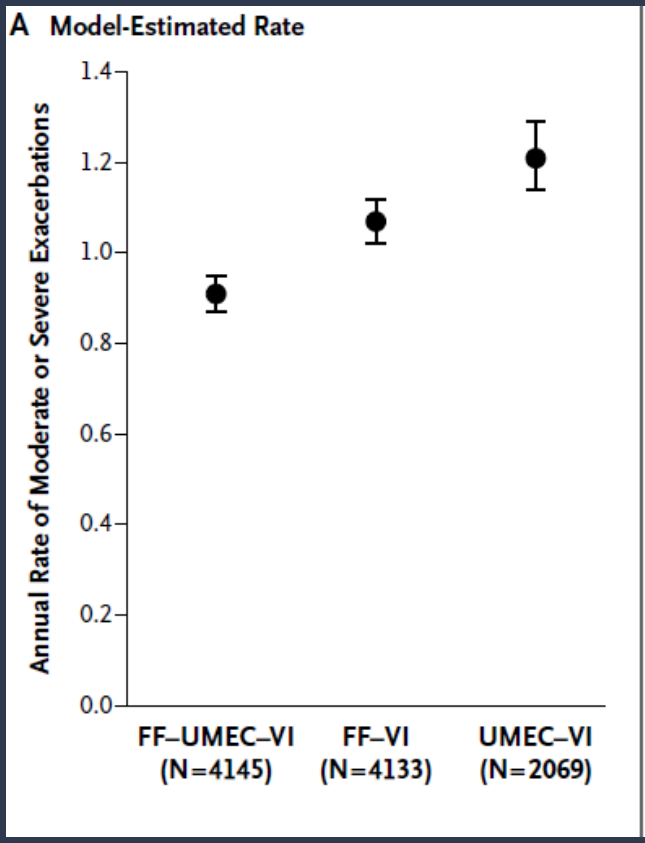
FEV1 50-80% and ≥ 2 mod or ≥1 severe exacerbation

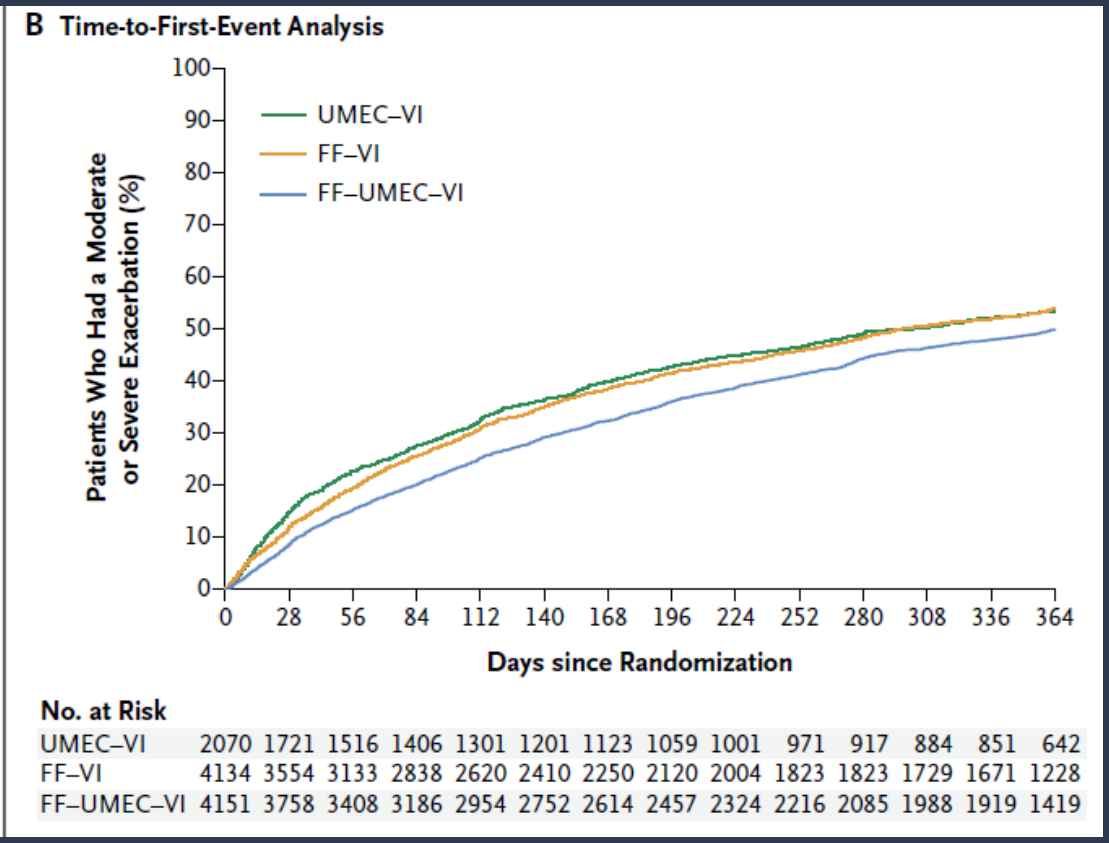
Table 1. Baseline Characteristics of the Patients (Intention-to-Treat Population).*

Characteristic	Triple Therapy (N=4151)	Fluticasone Furoate–Vilanterol (N=4134)	Umeclidinium–Vilanterol (N=2070)	Total (N=10,355)
Age — yr	65.3±8.2	65.3±8.3	65.2±8.3	65.3±8.3
Female sex — no. (%)	1385 (33)	1386 (34)	714 (34)	3485 (34)
Body-mass index†	26.6	26.7	26.6	26.6
Former smokers — no. (%)‡	2715 (65)	2711 (66)	1342 (65)	6768 (65)
Moderate or severe COPD exacerbations in the previous yr — no. (%)				
0	2 (<1)	5 (<1)	2 (<1)	9 (<1)
1	1853 (45)	1907 (46)	931 (45)	4691 (45)
2	1829 (44)	1768 (43)	890 (43)	4487 (43)
≥3	467 (11)	454 (11)	247 (12)	1168 (11)
≥2 Moderate COPD exacerbations in the previous yr — no. (%)	1967 (47)	1921 (46)	989 (48)	4877 (47)
≥1 Severe COPD exacerbation in the previous yr — no. (%)	1087 (26)	1069 (26)	515 (25)	2671 (26)
≥2 Severe COPD exacerbations in the previous yr — no. (%)	147 (4)	148 (4)	76 (4)	371 (4)
Postbronchodilator FEV_1 — % of predicted normal value	45.7±15.0	45.5±14.8	45.4±14.7	45.5±14.8
Mean score on the COPD Assessment Test at screening§	20.1±6.1	20.1±6.1	20.2±6.2	20.1±6.1

NEJM 2018;378:1671

Moderate of severe COPD exacerbations





0.91 1.07 1.21

NEJM 2018;378:1671

Table 2. Trough FEV_1 and St. George's Respiratory Questionnaire (SGRQ) Total Score (Intention-to-Treat Population).*

Outcome	Triple Therapy (N=4151)	Fluticasone Furoate–Vilanterol (N=4134)	Umeclidinium–Vilanterol (N=2070)
Trough FEV_1			
No. of patients evaluated	3366	3060	1490
Mean at wk 52 (95% CI) — ml	1274 (1265 to 1282)	1177 (1168 to 1185)	1220 (1208 to 1232)
Mean change from baseline (95% CI) — ml	94 (86 to 102)	−3 (−12 to 6)	40 (28 to 52)
Difference between triple therapy and dual-therapy comparator (95% CI) — ml	—	97 (85 to 109)†	54 (39 to 69)†
SGRQ total score‡			
No. of patients evaluated	3318	3026	1470
Mean at wk 52 (95% CI)	45.0 (44.5 to 45.4)	46.8 (46.3 to 47.2)	46.8 (46.1 to 47.4)
Mean change from baseline (95% CI)	−5.5 (−5.9 to −5.0)	−3.7 (−4.2 to −3.2)	−3.7 (−4.4 to −3.0)
Difference between triple therapy and dual-therapy comparator (95% CI)	—	−1.8 (−2.4 to −1.1)†	−1.8 (−2.6 to −1.0)†

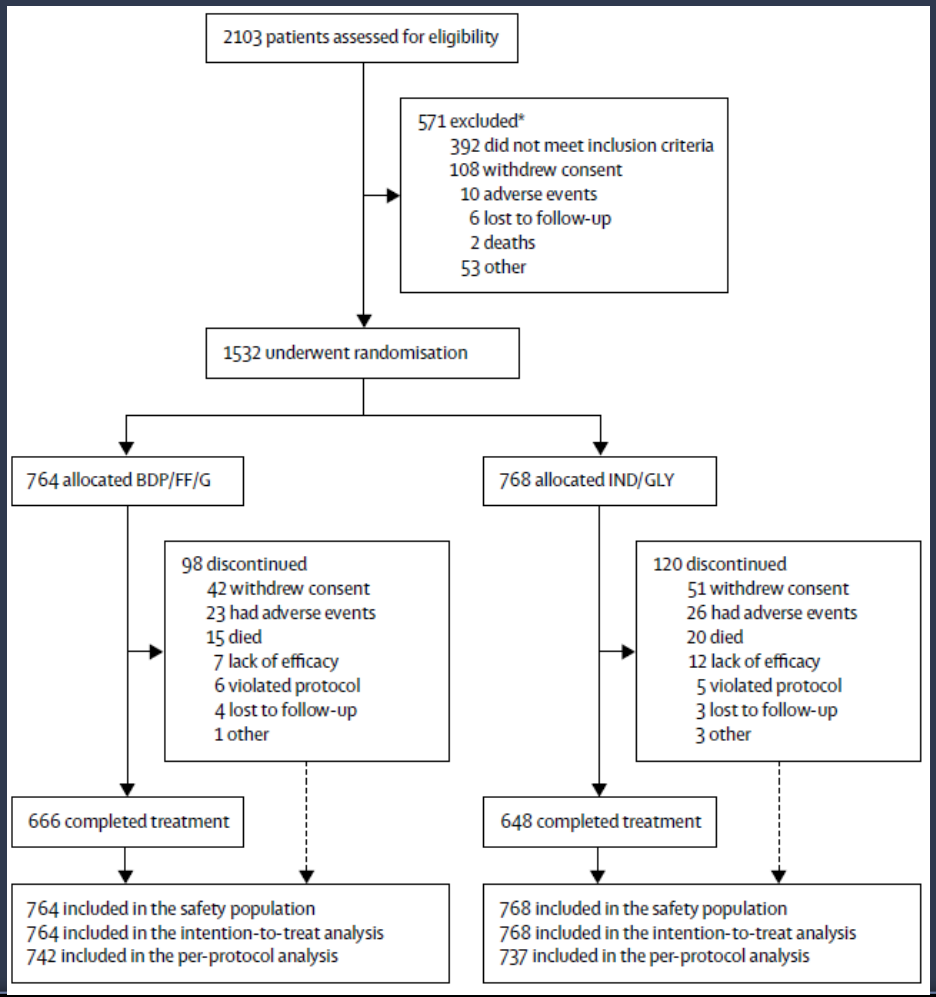
Table 3. Adverse Events of Special Interest in the Intention-to-Treat Population.*

Event	Triple Therapy (N=4151)		Fluticasone Furoate–Vilanterol (N=4134)		Umeclidinium–Vilanterol (N=2070)	
	No. of Patients (%)	Rate per 1000 Patient-Yr (No. of Events)	No. of Patients (%)	Rate per 1000 Patient-Yr (No. of Events)	No. of Patients (%)	Rate per 1000 Patient-Yr (No. of Events)
Anticholinergic syndrome	184 (4)	60.8 (226)	140 (3)	47.1 (163)	70 (3)	47.7 (81)
Asthma or bronchospasm	27 (<1)	7.5 (28)	34 (<1)	10.1 (35)	16 (<1)	9.4 (16)
Cardiovascular effects	450 (11)	167.2 (621)	430 (10)	157.0 (543)	224 (11)	166.6 (283)
Cardiac arrhythmia	153 (4)	50.9 (189)	161 (4)	51.5 (178)	81 (4)	51.2 (87)
Cardiac failure	138 (3)	42.5 (158)	126 (3)	42.8 (148)	68 (3)	44.8 (76)
CNS hemorrhages and cerebrovascular conditions	41 (<1)	12.1 (45)	28 (<1)	9.3 (32)	11 (<1)	6.5 (11)
Hypertension	113 (3)	35.5 (132)	115 (3)	35.0 (121)	54 (3)	34.2 (58)
Ischemic heart disease	80 (2)	26.1 (97)	57 (1)	18.5 (64)	47 (2)	30.6 (52)
Lower respiratory tract infection, excluding pneumonia	200 (5)	63.0 (234)	199 (5)	69.7 (241)	108 (5)	76.0 (129)
Pneumonia	317 (8)	95.8 (356)	292 (7)	96.6 (334)	97 (5)	61.2 (104)
Urinary retention	8 (<1)	2.7 (10)	12 (<1)	3.5 (12)	9 (<1)	5.3 (9)

NEJM 2018;378:1671

Extrafine inhaled triple therapy versus dual bronchodilator therapy in chronic obstructive pulmonary disease (TRIBUTE): a double-blind, parallel group, randomised controlled trial

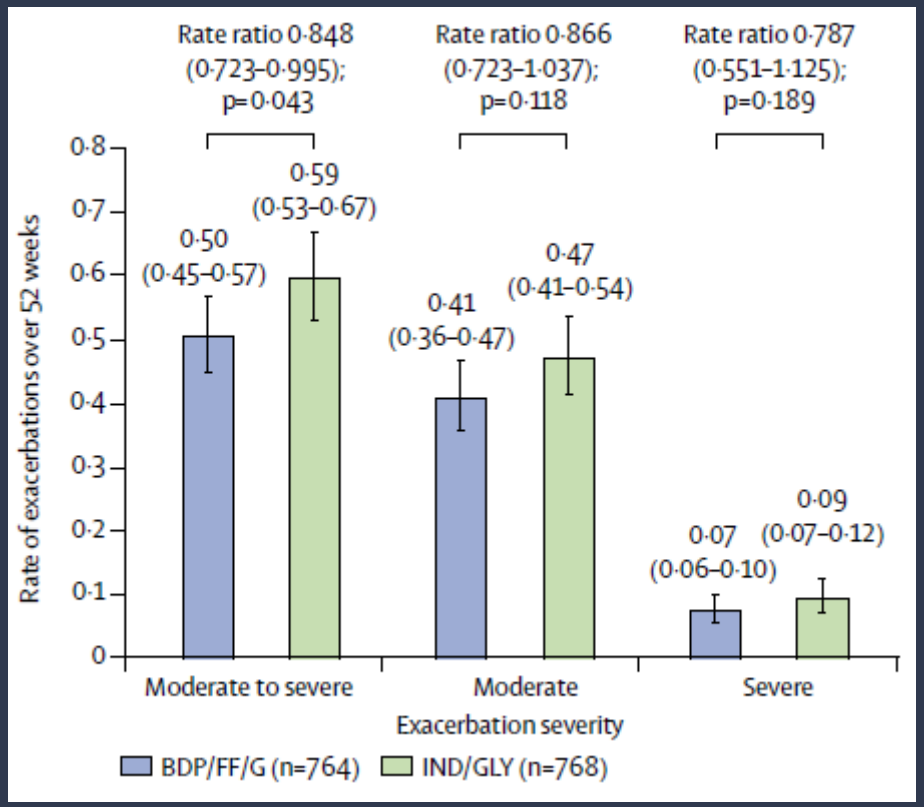
Alberto Papi, Jørgen Vestbo, Leonardo Fabbri, Massimo Corradi, Hélène Prunier, Géraldine Cohuet, Alessandro Guasconi, Isabella Montagna, Stefano Vezzoli, Stefano Petruzzelli, Mario Scuri, Nicolas Roche, Dave Singh**

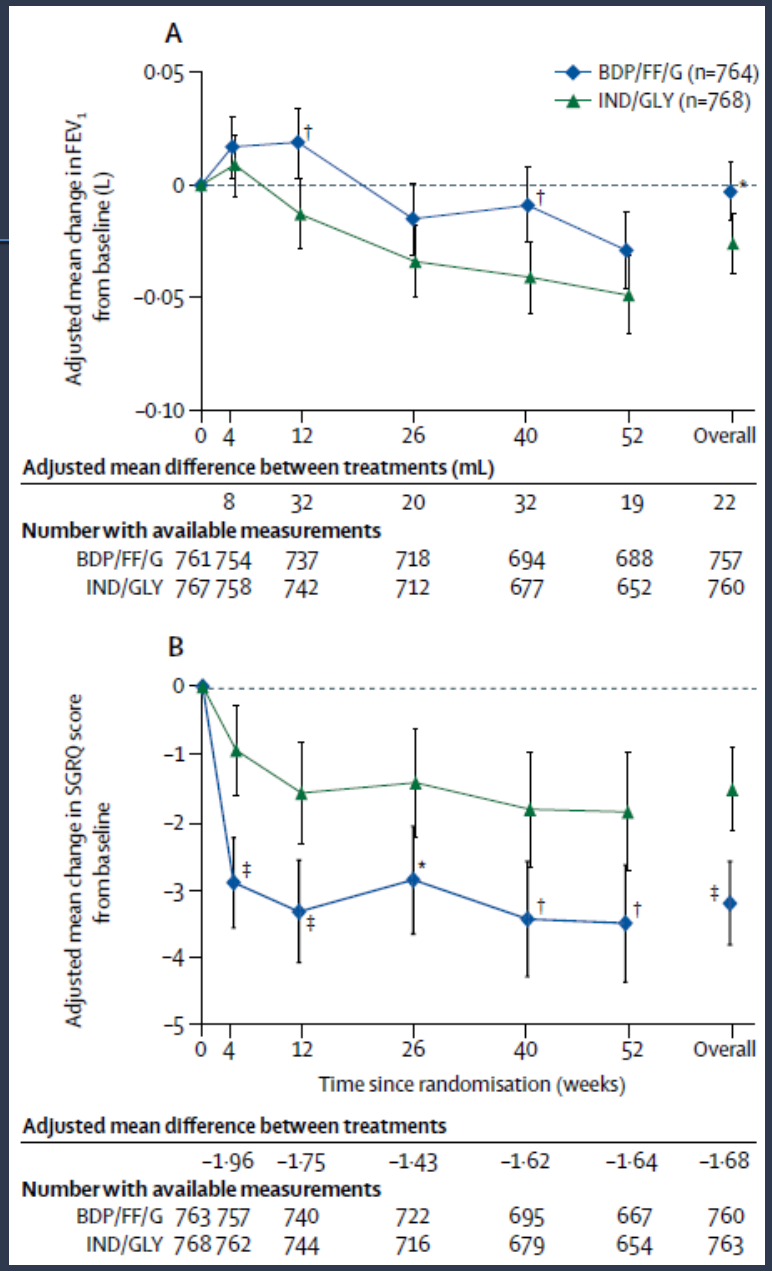


FEV1 < 50%

≥ 1 mod or severe exacerbation

Lancet 2018;391:1076



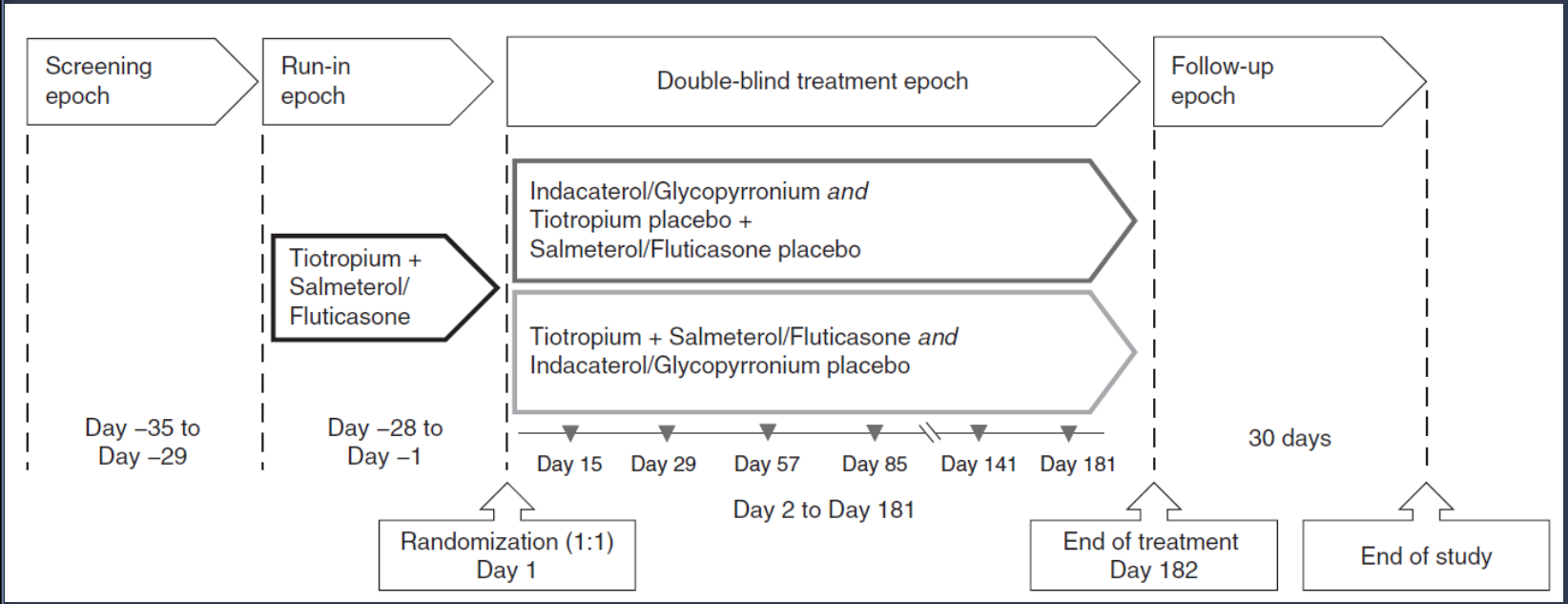


Lancet 2018;391:1076

Long-Term Triple Therapy De-escalation to Indacaterol/ Glycopyrronium in Patients with Chronic Obstructive Pulmonary Disease (SUNSET): A Randomized, Double-Blind, Triple-Dummy Clinical Trial

Kenneth R. Chapman[1*], John R. Hurst[2*], Stefan-Marian Frent[3‡], Michael Larbig[4], Robert Fogel[5], Tadhg Guerin[6], Donald Banerji[5], Francesco Patalano[4], Pankaj Goyal[4], Pascal Pfister[4], Konstantinos Kostikas[4], and Jadwiga A. Wedzicha[7]

less than 1 exacerbation in the previous year, more than 6 mo on triple therapy

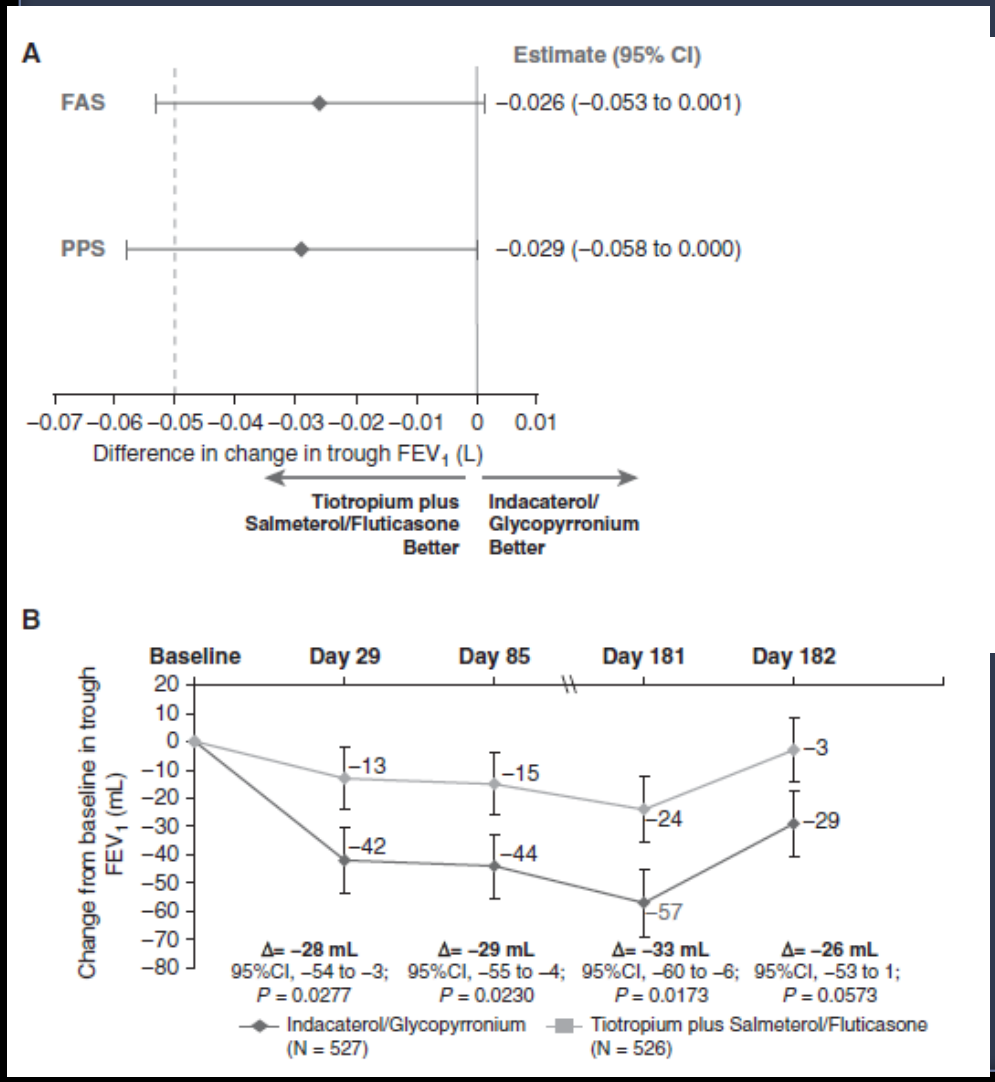


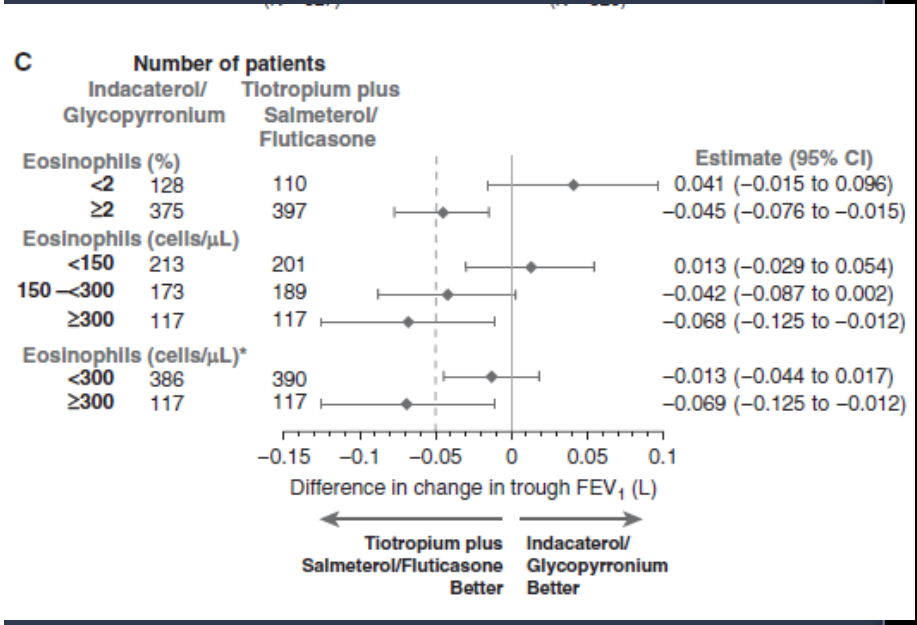
N=456

N=472

AJRCCM 2018;198:329

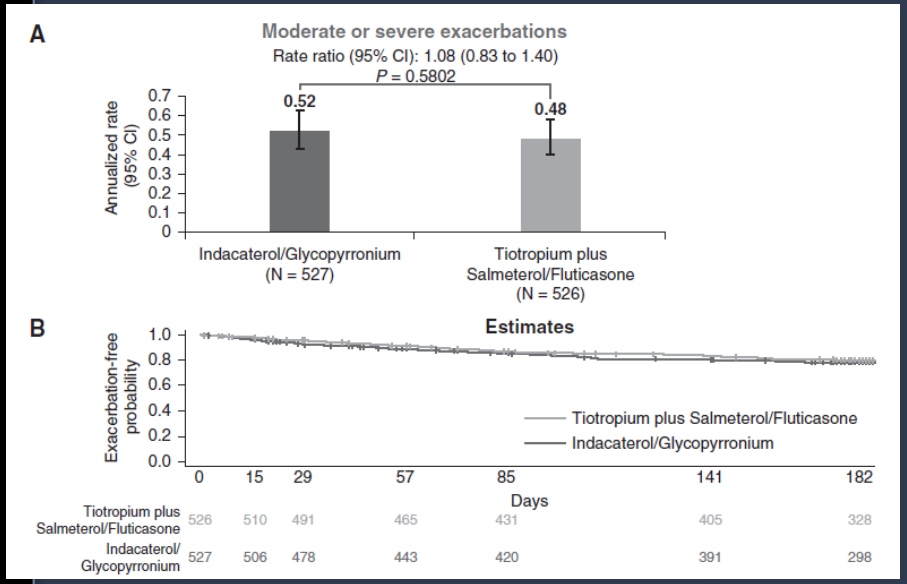
Non-inferiority on Trough FEV1

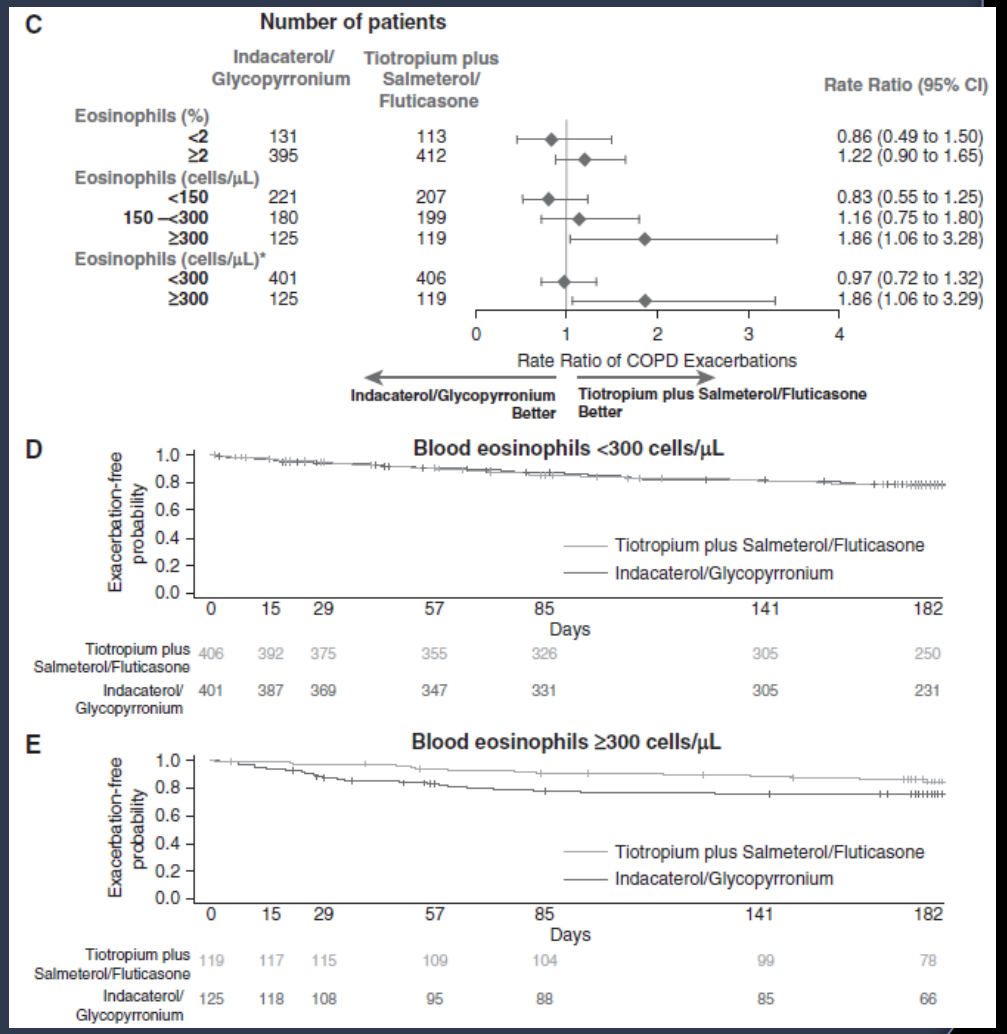




AJRCCM 2018;198:329

Exacerbations



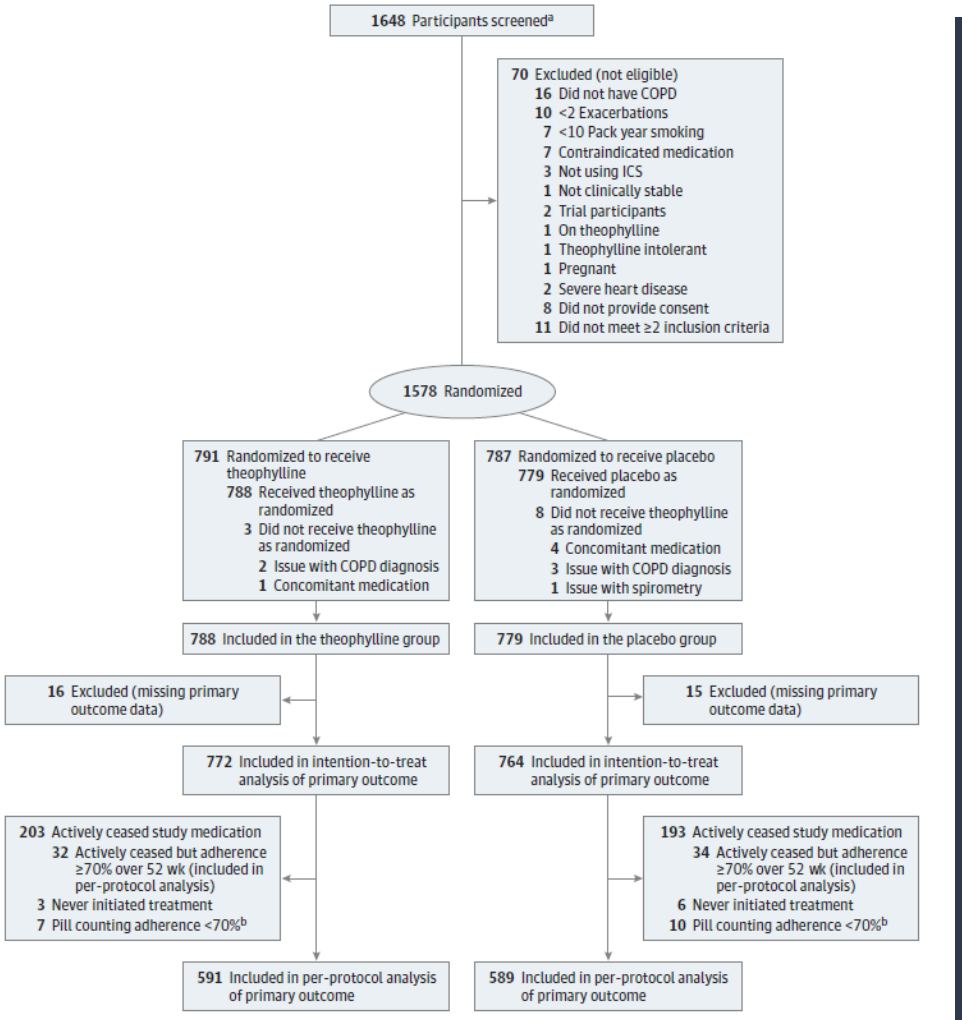


AJRCCM 2018;198:329

Effect of Theophylline as Adjunct to Inhaled Corticosteroids on Exacerbations in Patients With COPD

A Randomized Clinical Trial

Graham Devereux, PhD; Seonaidh Cotton, PhD; Shona Fielding, PhD; Nicola McMeekin, MSc; Peter J. Barnes, DSc; Andrew Briggs, PhD; Graham Burns, PhD; Rekha Chaudhuri, MD; Henry Chrystyn, PhD; Lisa Davies, FRCP; Anthony De Soyza, PhD; Simon Gompertz, MD; John Haughney, FRCGP; Karen Innes, MSc; Joanna Kaniewska, PhD; Amanda Lee, PhD; Alyn Morice, FRCP; John Norrie, MSc; Anita Sullivan, PhD; Andrew Wilson, PhD; David Price, FRCGP



Synergism between theophylline and corticosteroid in preclinical and small study

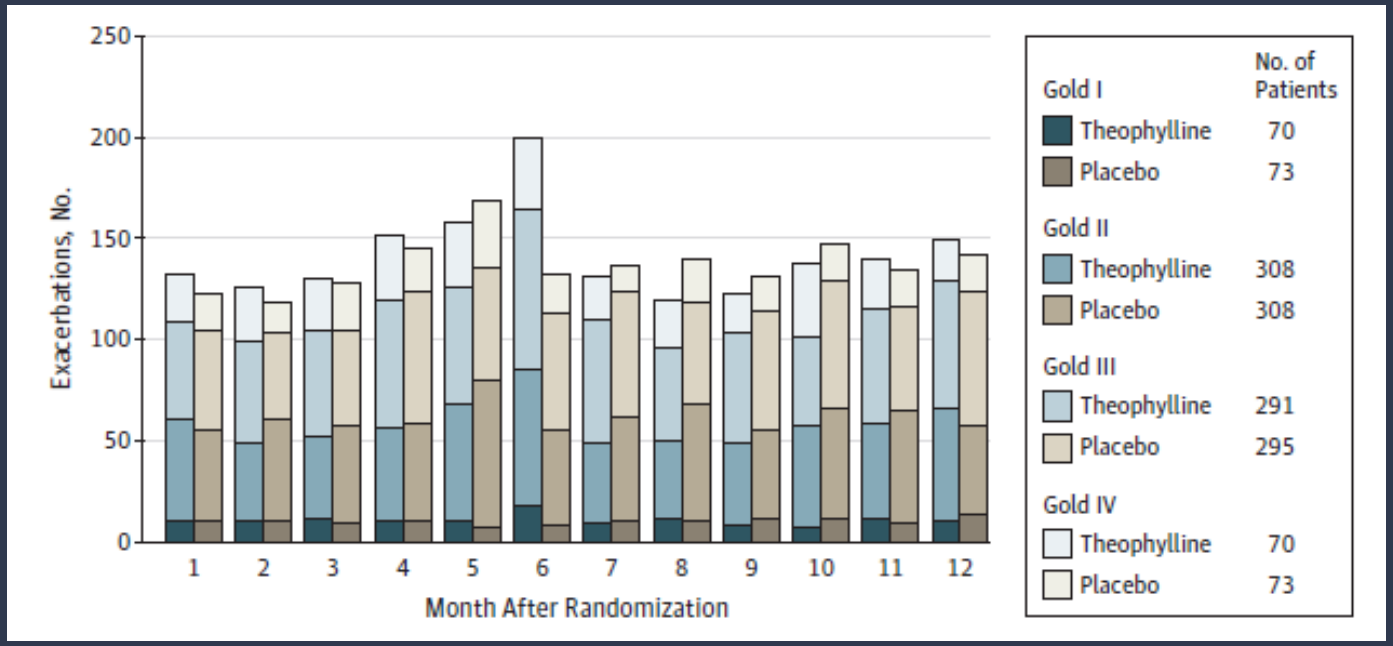
COPD using ICS and at least 2 exacerbations

Theophylline 200 mg qd
Or bid if smoker and >60kg

JAMA 2018;320:1548

Primary outcome

- Number of exacerbations
  - 2.24[2.10-2.38] vs. 2.23[2.09-2.37] placebo



JAMA 2018;320:1548

Secondary outcome

	Baseline to Week 52			
	Theophylline Group (n=772)	Placebo Group (n=764)	Value (95% CI)	*P* Value
COPD hospital admissions				
Total admissions, No.	134	185	Adusted IRR, 0.72 (0.55 to 0.94)[a]	.02
Mean (SD) per participant	0.17 (0.49)	0.24 (0.66)	Mean difference, −0.07 (−0.13 to −0.01)[b]	
Non-COPD hospital admissions				
Participants, No.	762	755		
Total admissions, No.	116	119	Adjusted IRR, 0.99 (0.71 to 1.38)[a]	
Mean (SD) per participant	0.15 (0.56)	0.16 (0.47)	Mean difference, −0.01 (−0.06 to 0.05)[b]	

JAMA 2018;320:1548

Effect of a Program Combining Transitional Care and Long-term Self-management Support on Outcomes of Hospitalized Patients With Chronic Obstructive Pulmonary Disease
A Randomized Clinical Trial

Hanan Aboumatar, MD, MPH; Mohammad Naqibuddin, MBBS, MPH; Suna Chung, MPH; Hina Chaudhry, MPH; Samuel W. Kim, BA; Jamia Saunders, MD, MS; Lee Bone, MPH; Ayse P. Gurses, MS, MPH, PhD; Amy Knowlton, ScD, MPH; Peter Pronovost, MD, PhD; Nirupama Putcha, MD, MHS; Cynthia Rand, PhD; Debra Roter, DrPH; Carol Sylvester, RN, MS; Carol Thompson, MS, MBA; Jennifer L. Wolff, PhD; Judith Hibbard, PhD, MPH, FCCM; Robert A. Wise, MD

- Intervention (BREATH program)
  - Transition support
  - Individualized COPD self-management
    - Medication correctly, recognize exacerbation signs and action plan
    - Practice breathing exercise, stop smoking
  - Access to community programs and treatment services

COPD nurses - during hospital and for 3 mo after discharge

JAMA 2018;320:2335

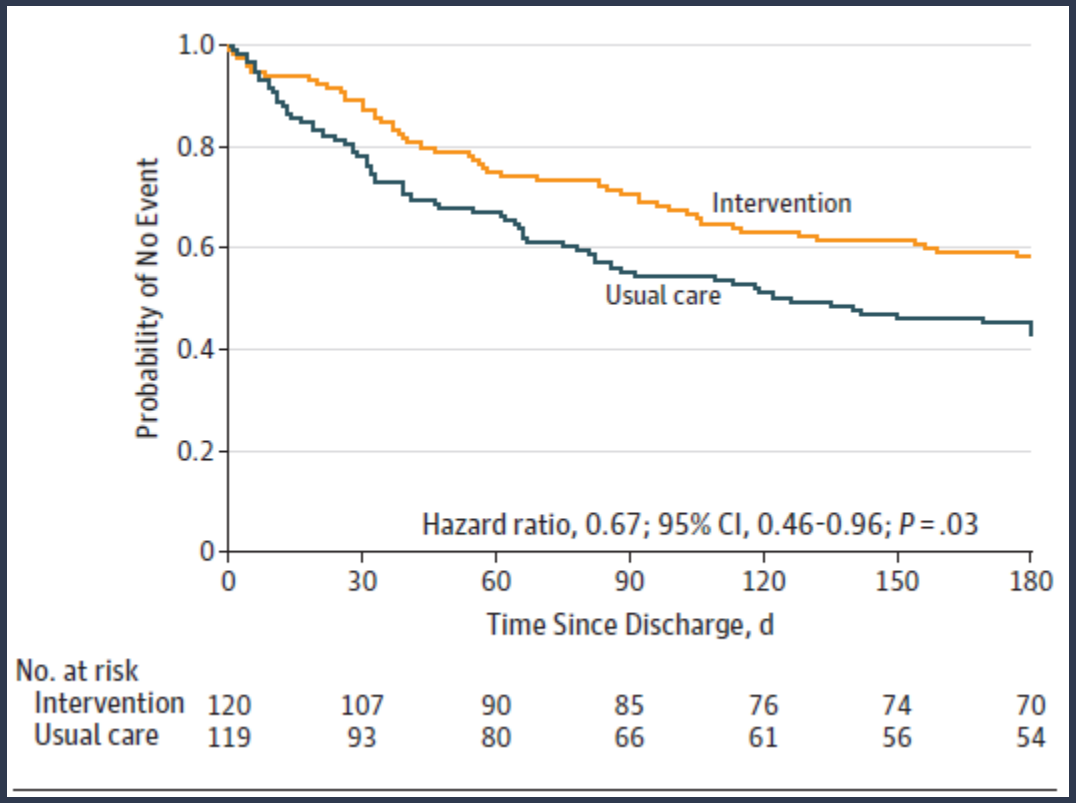
Primary outcomes

- COPD-related hospitalization or ED visits
  - Events per participant at 6 mo
  - 0.72[0.45-0.97] vs. 1.40[1.01-1.79] in usual care
- Health related QOL

Measure	Intervention			Usual Care				
	Mean (SD) Score		Change in Score, Mean (95% CI)	Mean (SD) Score		Change in Score, Mean (95% CI)	Adjusted Difference, Mean Change (95% CI)[b]	*P* Value[c]
	Baseline	At 6 mo		Baseline	At 6 mo			
Co-primary Outcome[d]								
Total score	64.0 (17.8)	62.5 (22.1)	−1.53 (−5.20 to 2.14)	62.8 (18.9)	68.3 (23.2)	5.44 (0.82 to 10.05)	−6.69 (−12.97 to −0.40)	.04
Post Hoc Outcomes[d]								
Symptom score	67.1 (20.4)	61.6 (23.9)	−5.54 (−10.59 to −0.49)	64.7 (22.1)	68.0 (24.2)	3.32 (−2.40 to 9.03)	−7.16 (−13.39 to −0.93)	.04
Activity score	83.0 (17.4)	79.2 (21.9)	−3.72 (−7.67 to 0.22)	80.3 (20.8)	82.1 (21.2)	1.82 (−2.64 to 6.28)	−4.57 (−11.67 to 2.53)	.13
Impact score	52.1 (21.5)	52.6 (26.2)	0.50 (−3.62 to 4.63)	52.1 (22.2)	60.3 (27.8)	8.23 (2.77 to 13.70)	−7.87 (−15.37 to −0.38)	.04

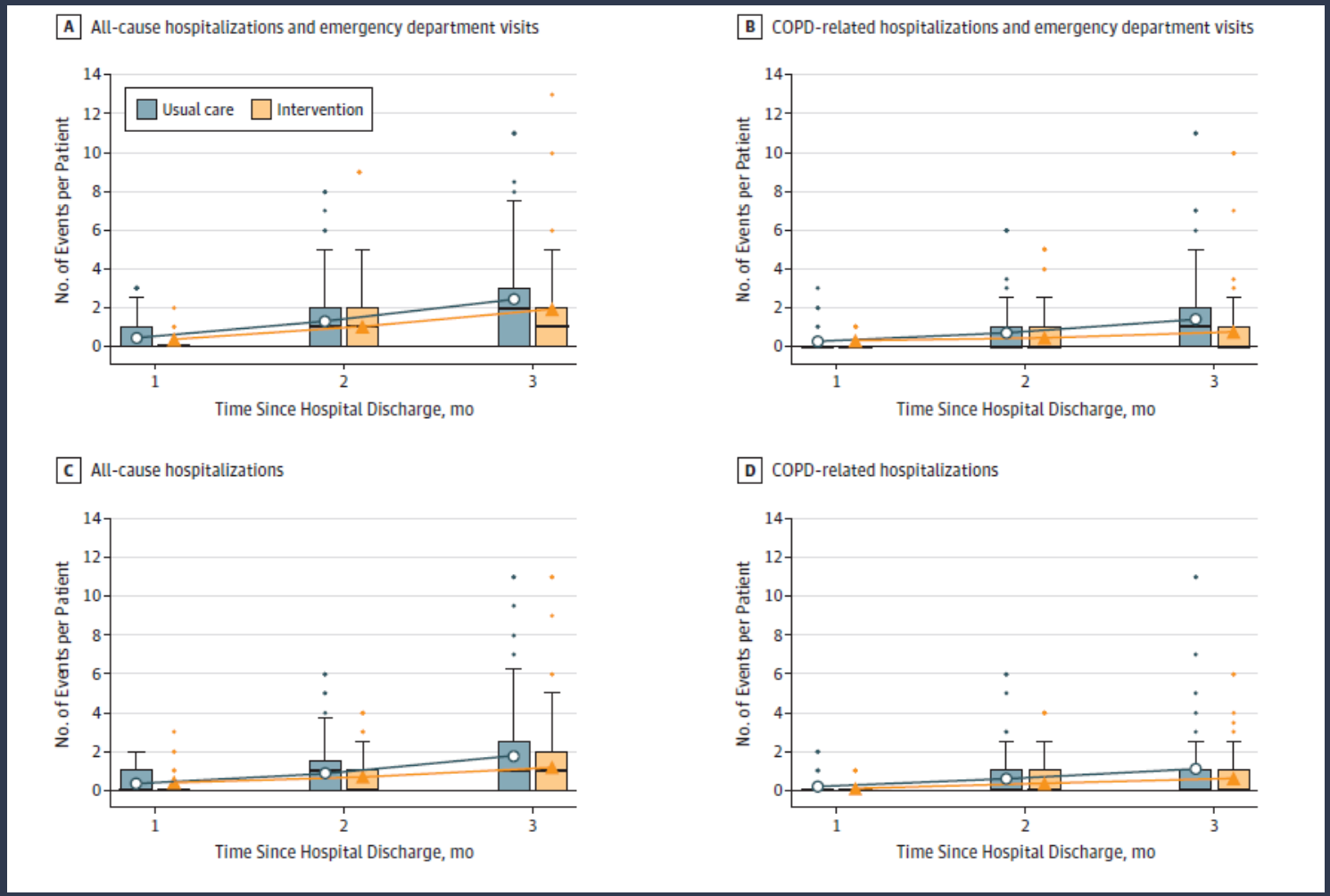
JAMA 2018;320:2335

Time to first COPD-related acute care event or death



JAMA 2018;320:2335

Cumulative number of events at 1,3,6 months after discharge



JAMA 2018;320:2335

Summary

- Biomarker
  - CT imaging – Risk factor
  - Blood eosinophil – predict exacerbations
- Drug treatment
  - Triple therapy – Indication and side effects
- Self-management
  - Rehabilitation, education, self-management