

Studie POPE a její chystané pokračování

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POPE 2014-2016

- **Průřezová observační studie ambulantních pacientů**
- **Real-life study design**
- 10 zemí CEE
- Námět, sběr dat a analýza – IBA MU BRNO, CZ
- Finance Ludwig Boltzmann Institute Vienna a Boehringer Ingelheim RCV, AU
- www.copdplatform.com



Metodika POPE



Metodika POPE

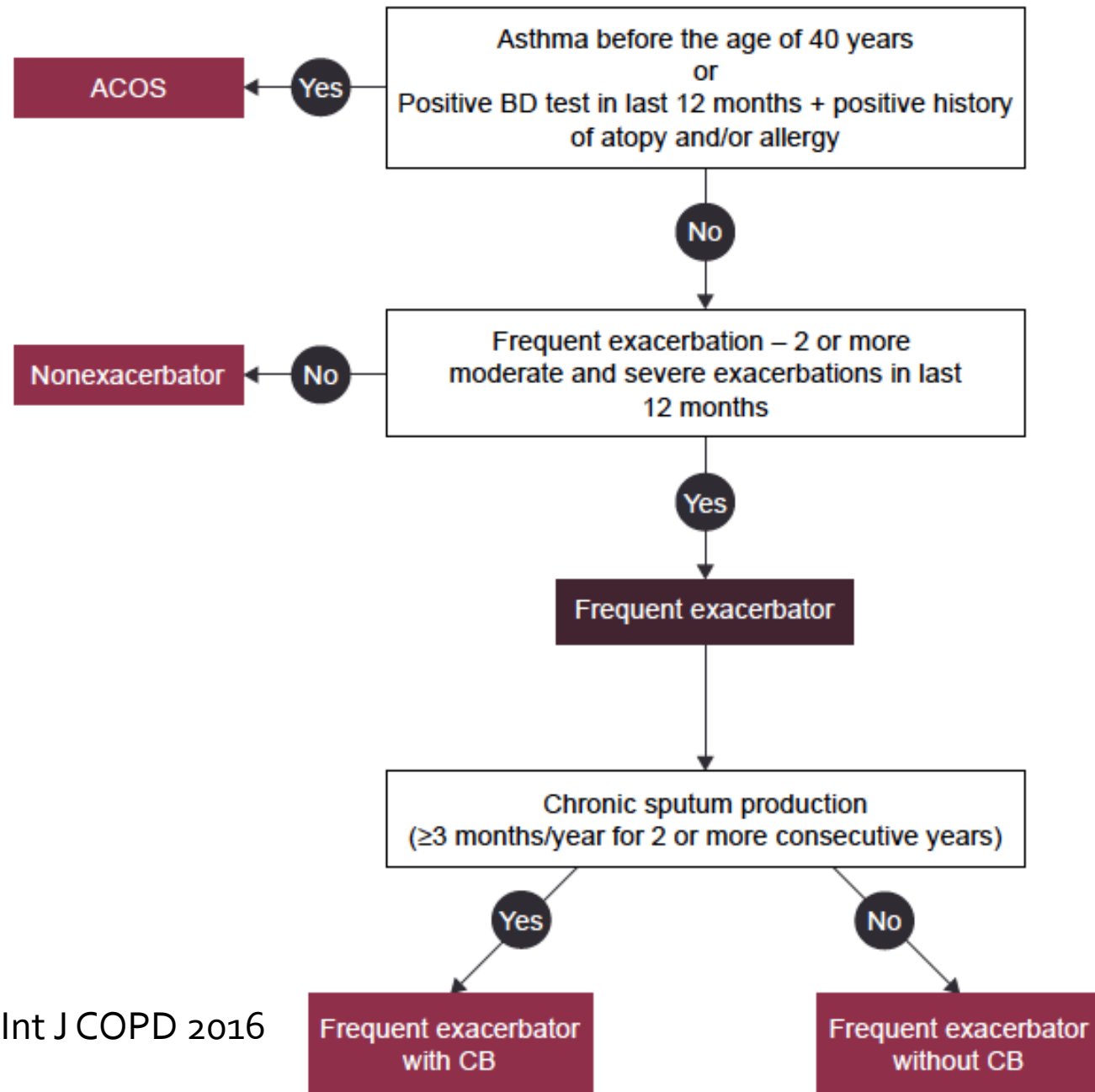
Form	Parameter
History	Demographic data Age of first diagnosis History of allergy/atopy COPD symptoms Smoking history Other than tobacco smoking risk factors ^a History of acute respiratory events Concomitant respiratory diseases Weight assessment Comorbidities – Charlson comorbidity index Comorbidities – others
Physical examination	BMI Heart and breath frequency Physical signs of COPD and heart failure sings

Pulmonary function tests, laboratory

Postbronchodilator spirometry values
Body plethysmography (TLC and RV)^b
TL_{CO} and K_{CO}^b
Bronchodilator test^b
Bronchial challenge test^b
FeNO^b
HRCT of thorax^b
Echocardiography^b
Blood/sputum eosinophil assessment^b
6-minute walk test^b
Total serum IgE measurement^b
ABG^b
HCT^b
CAT (total score and all 8 items separately)
mMRC
COPD pharmacological and nonpharmacological treatment
Other respiratory treatment
LTOT
Surgery and BVR
Vaccination
Nonrespiratory concomitant treatment

Questionnaires

Treatment

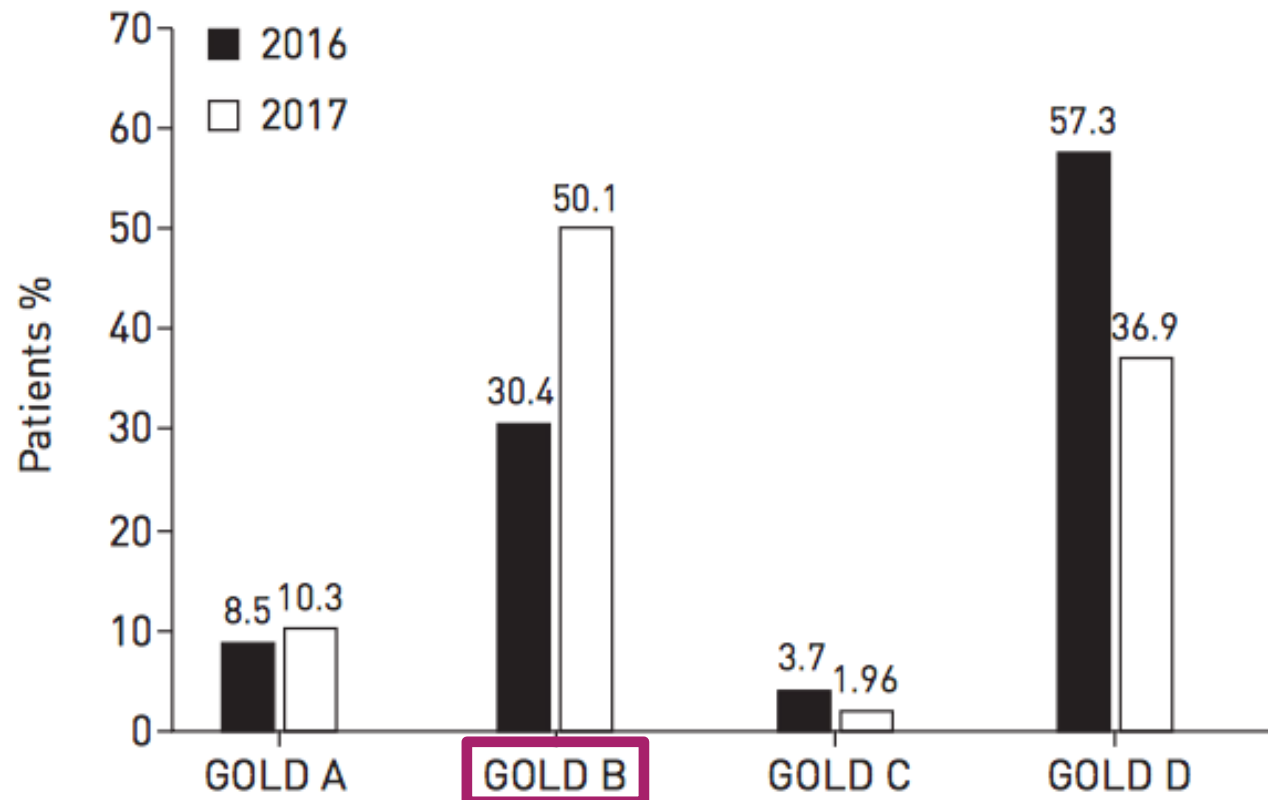


Zbozinkova et al Int J COPD 2016

Výsledky POPE

GOLD 2017 on the way to a phenotypic approach? Analysis from the Phenotypes of COPD in Central and Eastern Europe (POPE) Cohort

Výsledky POPE



Výsledky POPE

Phenotypes of COPD patients with a smoking history in Central and Eastern Europe: the POPE Study

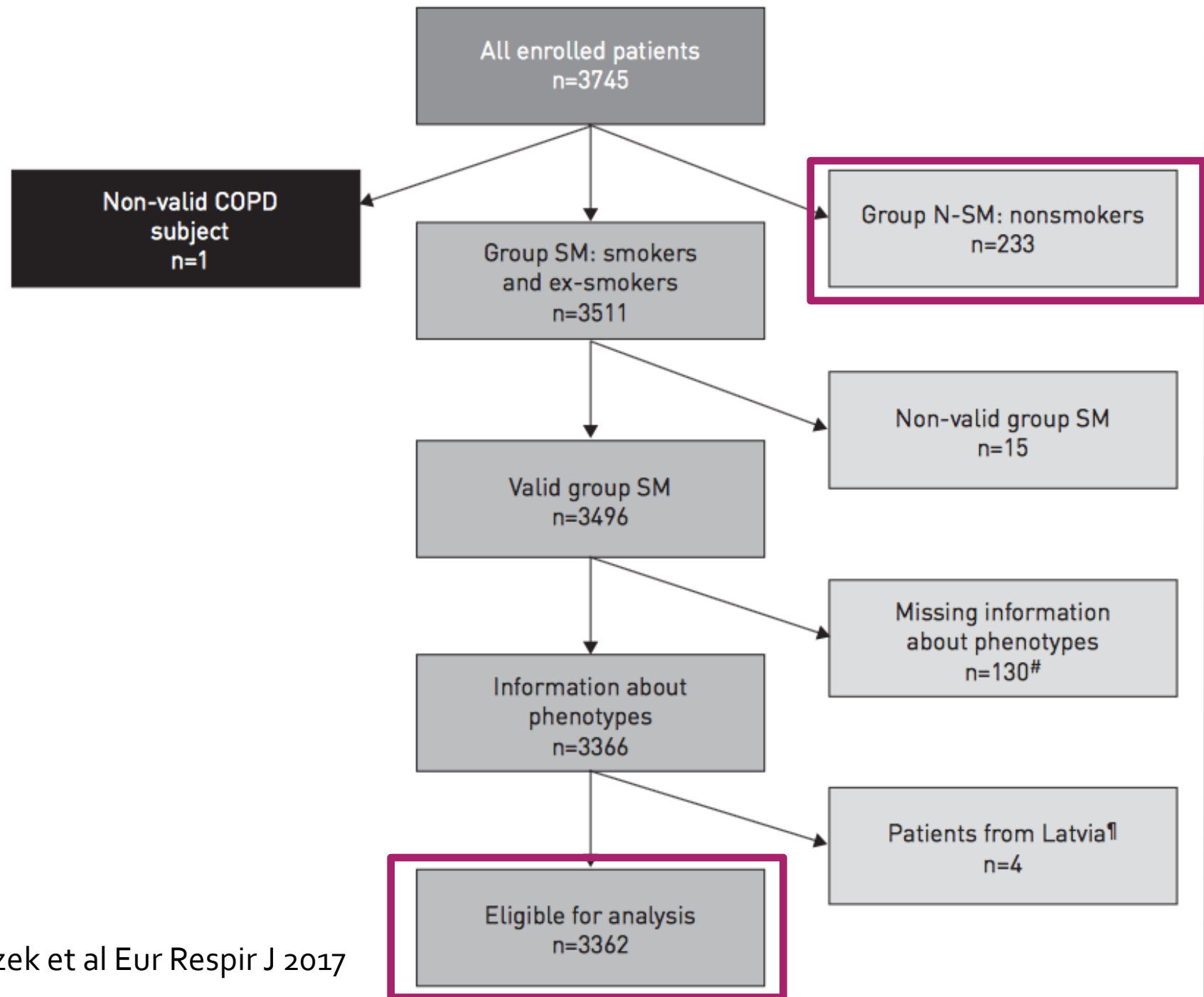
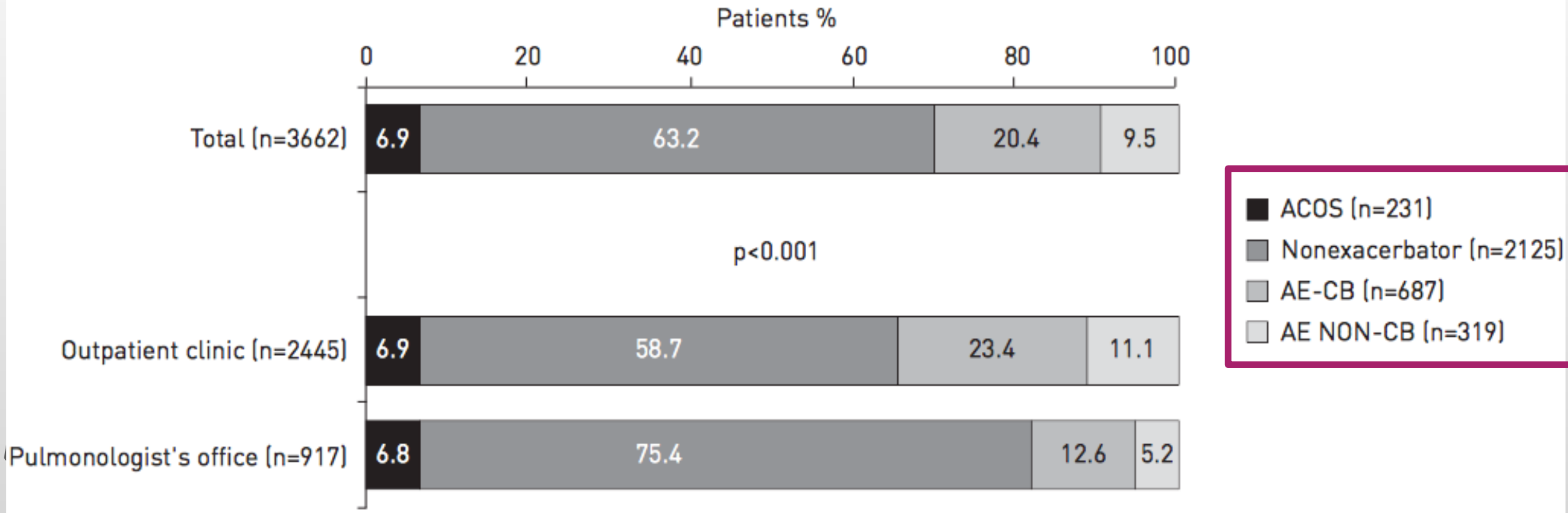


TABLE 1 Demographic data

Subjects	3362
Age at inclusion into POPE study years	66.0±8.8
Age at diagnosis years	58.4±9.0
Female	1010 (30.0)
Smoking exposure	
Ex-smoker	2147 (63.9)
Current smoker	1215 (36.1)
Duration of school education[#] years	11.3±2.8
Urban residence	2421 (73.1)
Rural residence	848 (25.6)
BMI^{††} kg·m⁻²	27.2±5.7
CAT	17.4±7.8
mMRC	2.0±1.0
FEV₁ L	1.4±0.6
FEV₁^{††} % pred	52.8±18.5
FVC L	2.8±0.9
FVC⁺ % pred	80.0±20.4
FEV₁/FVC	0.5±0.1
Moderate AEs[§] events·year⁻¹	0.9±1.3
Severe AEs^f events·year⁻¹	0.3±0.7
Total AEs events·year⁻¹	1.2±1.6
Charlson comorbidity index^{##}	
1	1684 (50.1)
2	805 (24.0)
3	458 (13.6)
≥4	414 (12.3)

TABLE 2 Characteristics of patients with chronic obstructive pulmonary disease (COPD) according to phenotypes

	Subjects	NON-AE (a)	AE NON-CB (b)	AE-CB (c)	ACOS (d)	p-value
Subjects		2125	319	687	231	
Female[#]		625 (29.4) ^d	87 (27.3) ^d	193 (28.1) ^d	105 (45.5) ^{a,b,c}	<0.001
Age at diagnosis[¶] years		59.3±9.0 ^{b,c,d}	57.7±8.9 ^{a,d}	57.7±8.4 ^{a,d}	53.6±8.6 ^{a,b,c}	<0.001
Age at inclusion[¶] years		66.3±8.7 ^d	65.9±8.8 ^d	66.6±8.3 ^d	62.3±10.2 ^{a,b,c}	<0.001
BMI[¶] kg·m⁻²	3360	27.4±5.7 ^c	26.6±5.3 ^d	26.5±5.6 ^{a,d}	28.3±6.0 ^{b,c}	<0.001
FEV₁[¶] % pred	3360	56.0±18.3 ^{b,c}	44.4±16.5 ^{a,d}	45.7±16.9 ^{a,d}	55.9±18.8 ^{b,c}	<0.001
FVC[¶] % pred	3359	82.0±20.0 ^{b,c}	74.5±20.5 ^{a,d}	75.3±20.6 ^{a,d}	83.3±20.3 ^{b,c}	<0.001
CAT⁺		15.8±7.3 ^{b,c,d}	18.2±7.4 ^{a,c}	22.2±7.5 ^{a,b,d}	17.8±7.8 ^{a,c}	<0.001
mMRC⁺		1.8±1.0 ^{b,c}	2.2±1.0 ^{a,c}	2.5±0.9 ^{a,b,d}	2.0±1.1 ^c	<0.001
Atopy[#]		129 (6.1) ^d	21 (6.6) ^d	49 (7.1) ^d	161 (69.7) ^{a,b,c}	<0.001
Asthma[#]					173 (74.9)	
Moderate AEs^{¶,§} events·year⁻¹		0.3±0.5 ^{b,c,d}	1.9±1.3 ^{a,d}	2.1±1.6 ^{a,d}	1.3±1.5 ^{a,b,c}	<0.001
Severe AEs^{¶,f} events·year⁻¹		0.1±0.3 ^{b,c,d}	0.8±0.9 ^{a,d}	0.9±1.0 ^{a,d}	0.3±0.7 ^{a,b,c}	<0.001
Total AEs[¶] events·year⁻¹		0.4±0.5 ^{b,c,d}	2.8±1.5 ^{a,c,d}	3.0±1.8 ^{a,b,d}	1.6±1.8 ^{a,b,c}	<0.001
Positive bronchodilator test	2524	284 (18.5) ^{b,c,d}	27 (11.2) ^{a,d}	66 (11.8) ^{a,d}	92 (50.3) ^{a,b,c}	<0.001
Charlson index[#]	3361					
1		1095 (51.6) ^c	177 (55.5) ^c	297 (43.2) ^{a,b}	115 (49.8)	<0.001
2		508 (23.9)	74 (23.2)	163 (23.7)	60 (26.0)	0.884
3		290 (13.7) ^{b,c}	25 (7.8) ^{a,c}	118 (17.2) ^{a,b,d}	25 (10.8) ^c	<0.001
≥4		231 (10.9) ^c	43 (13.5)	109 (15.9) ^a	31 (13.4)	0.006



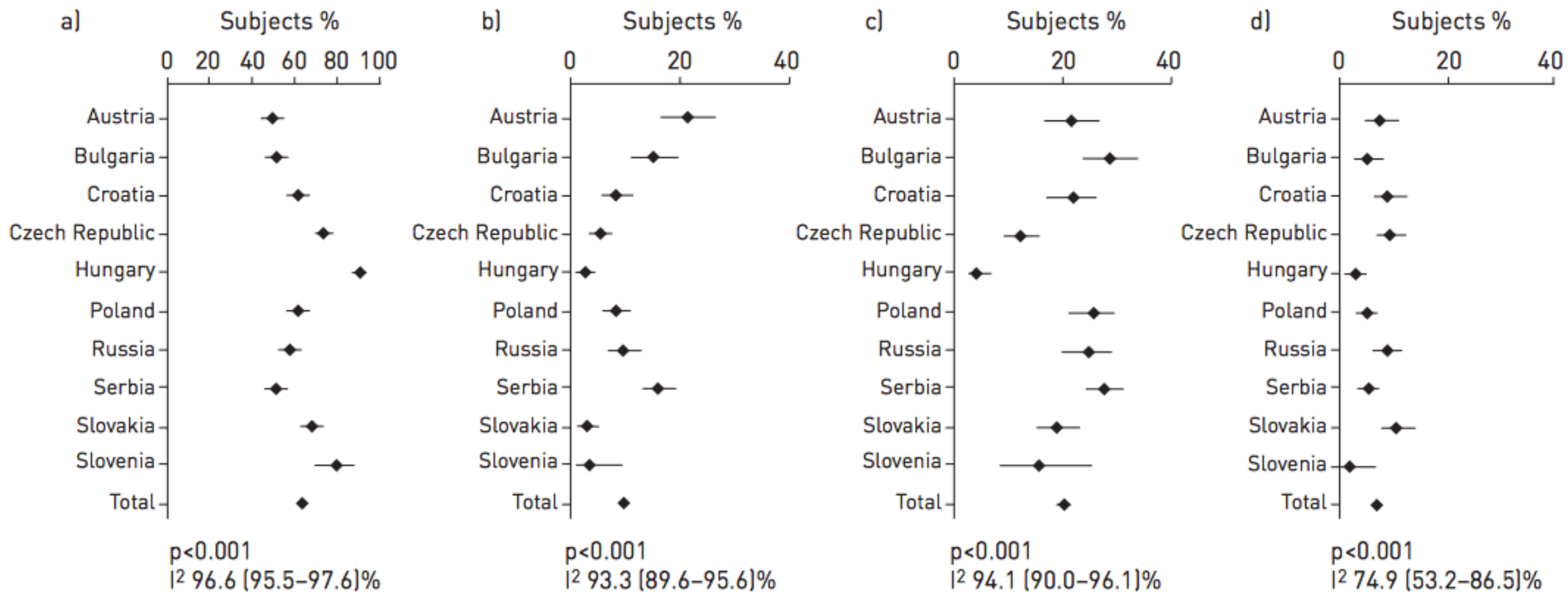


FIGURE 3 Country-specific heterogeneity distribution of chronic obstructive pulmonary disease [COPD] phenotypes. Data are presented as % [95% CI]. a) Nonexacerbators; b) frequent exacerbators without chronic bronchitis; c) frequent exacerbators with chronic bronchitis; d) asthma-COPD overlap syndrome.

TABLE 3 Prevalence of comorbidities in Central and Eastern European patients with chronic obstructive pulmonary disease (COPD) according to phenotype

	Phenotypes				p-value
	NON-AE (a)	AE NON-CB (b)	AE-CB (c)	ACOS (d)	
Subjects n	2125	319	687	231	
Cardiovascular disease [#]	1553 (73.1)	222 (69.6)	517 (75.3)	156 (67.5)	0.070
Myocardial infarction	186 (8.8)	26 (8.2)	67 (9.8)	12 (5.2)	0.186
Congestive heart failure	230 (10.8) ^{b,c}	53 (16.6) ^a	133 (19.4) ^{a,d}	27 (11.7) ^c	<0.001
Peripheral vascular disease	258 (12.1)	27 (8.5)	95 (13.8)	22 (9.5)	0.061
Cerebrovascular disease	192 (9.0)	24 (7.5)	78 (11.4)	25 (10.8)	0.158
Coronary artery disease	444 (20.9) ^c	82 (25.7)	179 (26.1) ^a	59 (25.5)	0.011
Hypertension	1367 (64.3)	192 (60.2)	451 (65.6)	138 (59.7)	0.193
Atrial fibrillation	169 (8.0)	25 (7.8)	62 (9.0)	15 (6.5)	0.655
Pulmonary embolism	46 (2.2)	10 (3.1)	10 (1.5)	3 (1.3)	0.301
Peptic ulcer disease	160 (7.5) ^c	22 (6.9) ^c	77 (11.2) ^{a,b}	25 (10.8)	0.010
Liver disease	84 (4.0)	12 (3.8)	38 (5.5)	13 (5.6)	0.227
Gastro-oesophageal reflux disease	212 (10.0) ^{b,d}	46 (14.4) ^a	79 (11.5) ^d	41 (17.7) ^{a,c}	0.001
Renal disease	50 (2.4) ^{b,c}	18 (5.6) ^a	34 (4.9) ^a	7 (3.0)	0.001
Solid tumour	109 (5.1) ^d	13 (4.1)	42 (6.1) ^d	4 (1.7) ^{a,c}	0.039
Diabetes mellitus	323 (15.2)	44 (13.8)	125 (18.2)	45 (19.5)	0.082
Hyperlipidaemia	541 (25.5) ^d	81 (25.4) ^d	192 (27.9) ^d	82 (35.5) ^{a,b,c}	0.010
Anaemia	50 (2.4) ^c	8 (2.5) ^c	41 (6.0) ^{a,b}	7 (3.0)	<0.001
Osteoporosis	164 (7.7) ^{b,c,d}	43 (13.5) ^a	80 (11.6) ^a	34 (14.7) ^a	<0.001
Depression	151 (7.1) ^{b,c,d}	37 (11.6) ^{a,c}	129 (18.8) ^{a,b,d}	27 (11.7) ^{a,c}	<0.001
Anxiety	158 (7.4) ^{b,c}	37 (11.6) ^a	99 (14.4) ^{a,d}	15 (6.5) ^c	<0.001
Insomnia	231 (10.9) ^c	30 (9.4) ^c	128 (18.6) ^{a,b}	32 (13.9)	<0.001

TABLE 4 Inhaler therapy in Central and Eastern European patients with chronic obstructive pulmonary disease (COPD) according to phenotype

	Phenotypes				p-value
	NON-AE (a)	AE NON-CB (b)	AE-CB (c)	ACOS (d)	
Subjects n	2125	319	687	231	
Mono-LAMA	286 [13.5] ^{b,c,d}	23 [7.2] ^{a,d}	33 [4.8] ^a	7 [3.0] ^{a,b}	<0.001
Mono-LABA	214 [10.1] ^{b,c,d}	8 [2.5] ^a	17 [2.5] ^a	8 [3.5] ^a	<0.001
Mono-ICS	12 [0.6]	2 [0.6]	5 [0.7]	5 [2.2]	0.077
LAMA + LABA	376 [17.7] ^{b,c,d}	35 [11.0] ^a	74 [10.8] ^a	18 [7.8] ^a	<0.001
LAMA + ICS	11 [0.5]	4 [1.3]	6 [0.9]	2 [0.9]	0.291
LABA + ICS	296 [13.9] ^d	51 [16.0] ^d	113 [16.4] ^d	58 [25.1] ^{a,b,c}	<0.001
LAMA + LABA + ICS	782 [36.8] ^{b,c,d}	191 [59.9] ^a	417 [60.7] ^a	124 [53.7] ^a	<0.001
No maintenance inhaler therapy	147 [6.9] ^{b,c}	5 [1.6] ^a	22 [3.2] ^a	9 [3.9]	<0.001

Závěr POPE

- FENOTYPY SE DAJÍ APLIKOVAT NA POPULACI CHOPN pts CEE
- JSOU ODLIŠNÉ V RŮZNÝCH TYPECH PRAXÍ
- JSOU SPOJENY S FUNKCÍ PLIC, SYMPTOMY, KOMORBIDITAMI
- VEDOU K JINÉ LÉČBĚ
- *JAK JETO V ČASE ?*

Budoucnost POPE = POPE-UP

- POPE-UP A

jak fenotypy CHOPN ovlivňují naši **iniciální volbu udržovací terapie** a co se děje v čase pokud dojde ke změně projevů CHOPN ?

- POPE-UP B

jaké je riziko **nové exacerbace nebo smrti** poté co pacient prodělá první nemocniční exacerbaci ?

POPE – UP A

- Předpoklad 14 zemí
(nově MOLDAVSKO, LITVA, RUMUNSKO, ESTONSKO)
- Od 2018
- Prospektivní charakter (a 1 rok)
- Ambulance plicních lékařů CEE

POPE – UP A



POPE – UP A

Parameters	Baseline	Month 6	Year 1	Year 2	Year 3	Year 4	Year 5
Symptoms, lung function and other clinical data							
Demographic characteristics	x						
History of asthma/allergy/atopy	x						
Smoking and other COPD risk factors	x	x	x	x	x	x	x
COPD symptoms using CAT, mMRC, SGRQ	x	x	x	x	x	x	x
AE frequency/12months	x		x	x	x	x	x
<u>Charlson comorbidity index</u>	x	x	x	x	x	x	x
Physical exam	x	x	x	x	x	x	x
Spirometry (post BD)	x	x	x	x	x	x	x
<u>Bodyplethysomography</u>	Optional	Optional	Optional	Optional	Optional	Optional	Optional
Diffusion capacity	Optional	Optional	Optional	Optional	Optional	Optional	Optional
6-MWT or 1-STS	Optional	Optional	Optional	Optional	Optional	Optional	Optional
<u>Hemoglobin, Blood</u>	Optional						

POPE – UP A

Treatment							
Short acting inhaled BDs	x	x	x	x	x	x	x
Long acting inhaled BDs alone or in combinations		x	x	x	x	x	x
ICS/LABA		x	x	x	x	x	x
<u>Roflumilast</u>		x	x	x	x	x	x
Long term ATB		x	x	x	x	x	x
Theophylline		x	x	x	x	x	x
Oral steroid		x	x	x	x	x	x
Long term <u>mucoactive Rx</u>		x	x	x	x	x	x
Rehabilitation		x	x	x	x	x	x
LTOT		x	x	x	x	x	x
NIV		x	x	x	x	x	x
BLVR		x	x	x	x	x	x
LVRS		x	x	x	x	x	x
<u>LuTx</u>		x	x	x	x	x	x
Hospitalisation from any reason (number/12 months)			x	x	x	x	x
All cause death		x	x	x	x	x	x

POPE – UP B

- Předpoklad 14 zemí
(nově MOLDAVSKO, LITVA, RUMUNSKO, ESTONSKO)
- Od 2018
- Prospektivní charakter
- Nemocnice - plicní kliniky a oddělení zemí CEE

POPE – UP B

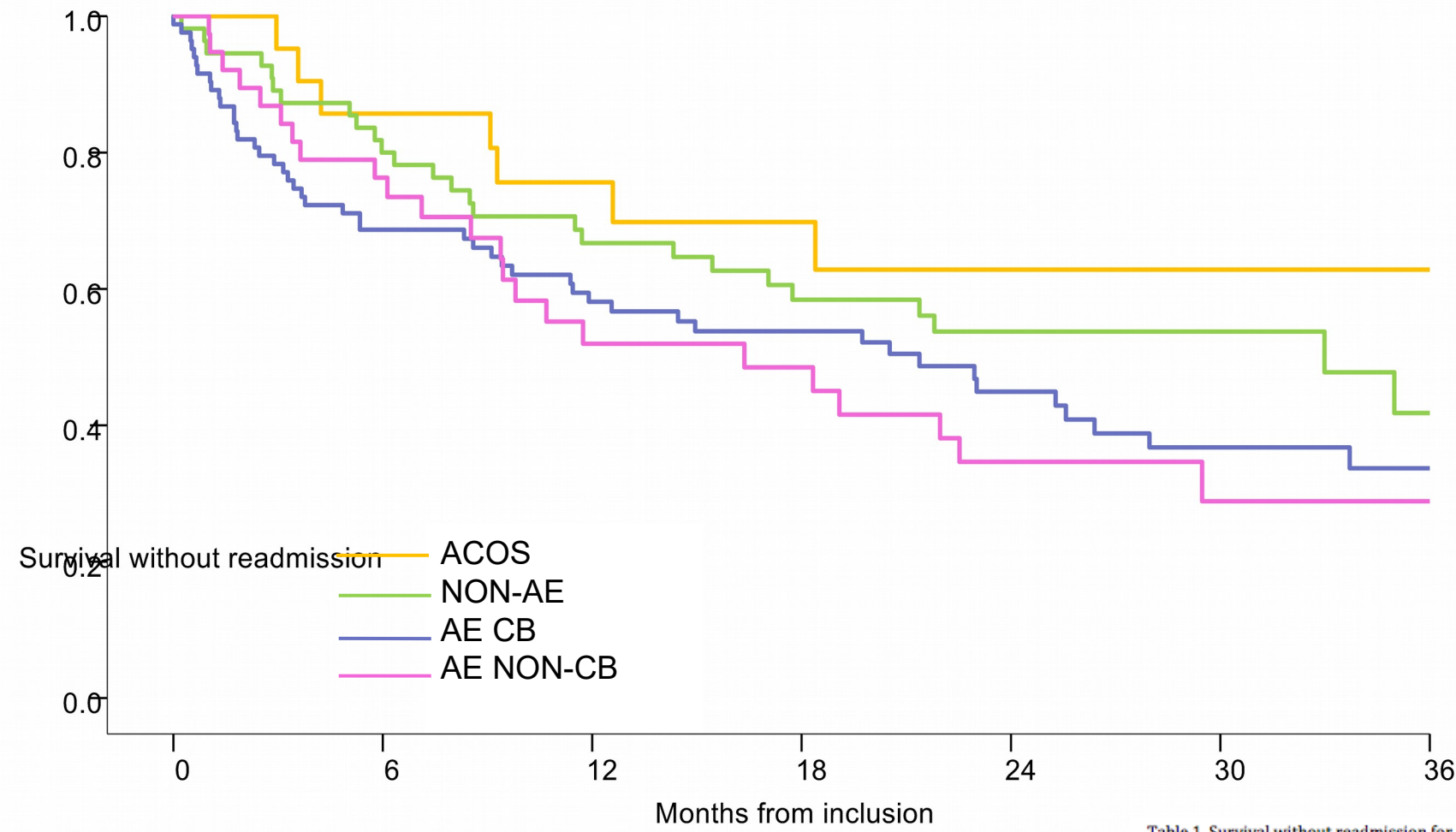


Table 1. Survival without readmission for exacerbations of COPD (Czech multicentre research database of COPD patients) – only for patients with at least one hospitalization for exacerbation in last year before inclusion to registry (N=203)

	N	Median of survival (95% CI)	3-year survival (95% CI)
ACOS	N=24	-	0.628 (0.404–0.853)
NON-AE	N=56	33 (17–49)	0.418 (0.237–0.599)
AE CB	N=84	21 (12–31)	0.337 (0.213–0.461)
AE NON-CB	N=39	16 (6–27)	0.289 (0.116–0.462)



POPE – UP B



- Jak daleko je od přijetí pro první těžkou AE ke smrti nebo novému přijetí?
- Pacienti s různými fenotypy mají různé riziko nového přijetí a/nebo smrti.
- Náběr 1 rok a poté další 2-3 roky trvání (od 2018 do 2022)

POPE plán pro rok 2018-2022-2024

- Cca 10 ambulantních specialistů
se zkušenostmi s **klinickými studii** na poli CHOPN
- Cca 10 nemocničních zařízení
se zavedenou **péčí o akutně** exacerbované pacienty

Financování nadcházejících projektů

- Ludwig Boltzmann Institute Vienna, AU
- GSK Global London, UK
- Boehringer Ingelheim, RVC, AU
- Chiessi a AstraZeneca (CEE)