The Influence of Smoking Status on Exhaled Breath Profiles in Asthma and COPD Patients

Stefania Principe [1,2], Job J.M.H. van Bragt [1], Cristina Longo [1], Rianne de Vries [1,3], Peter J. Sterk [1], Nicola Scichilone [2], Susanne J.H. Vijverberg [1], Anke H. Maitland-van der Zee [1,*]

[1]   Department of Respiratory Medicine, Amsterdam UMC, University of Amsterdam, 1105 AZ Amsterdam, The Netherlands

[2]   Dipartimento Universitario di Promozione della Salute, Materno Infantile, University of Palermo, Medicina Interna e Specialistica di Eccellenza "G. D'Alessandro"(PROMISE) c/o Pneumologia; AOUP "Policlinico Paolo Giaccone", 90127 Palermo, Italy

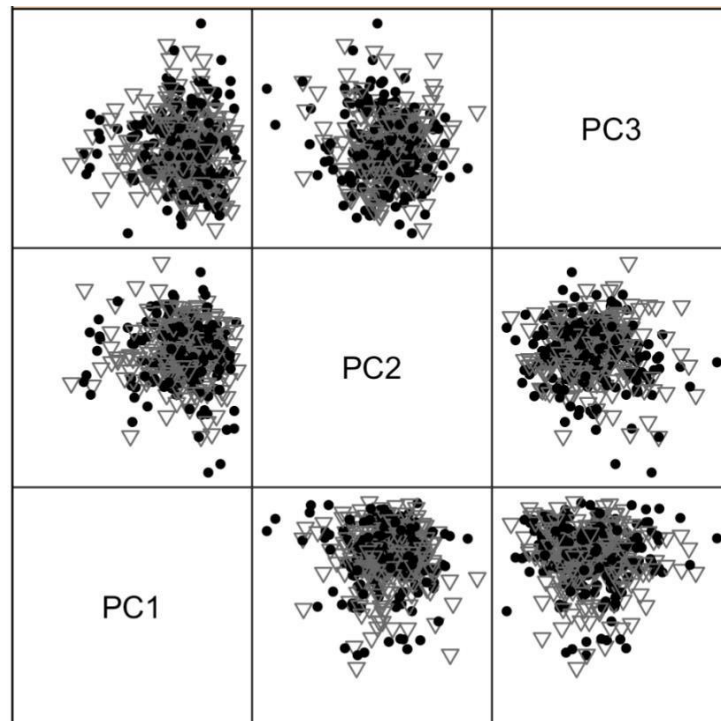[3]   Breathomix b.v., Leiden, 2333, Zuid Holland, The Netherlands

Figure S1. Scatter plot matrices, that shows the correlation between each Principal Components (PCs) in a population of ever or non-smokers in the overall dataset (n = 896): dotplots are representing never smokers and triangles ever smokers.
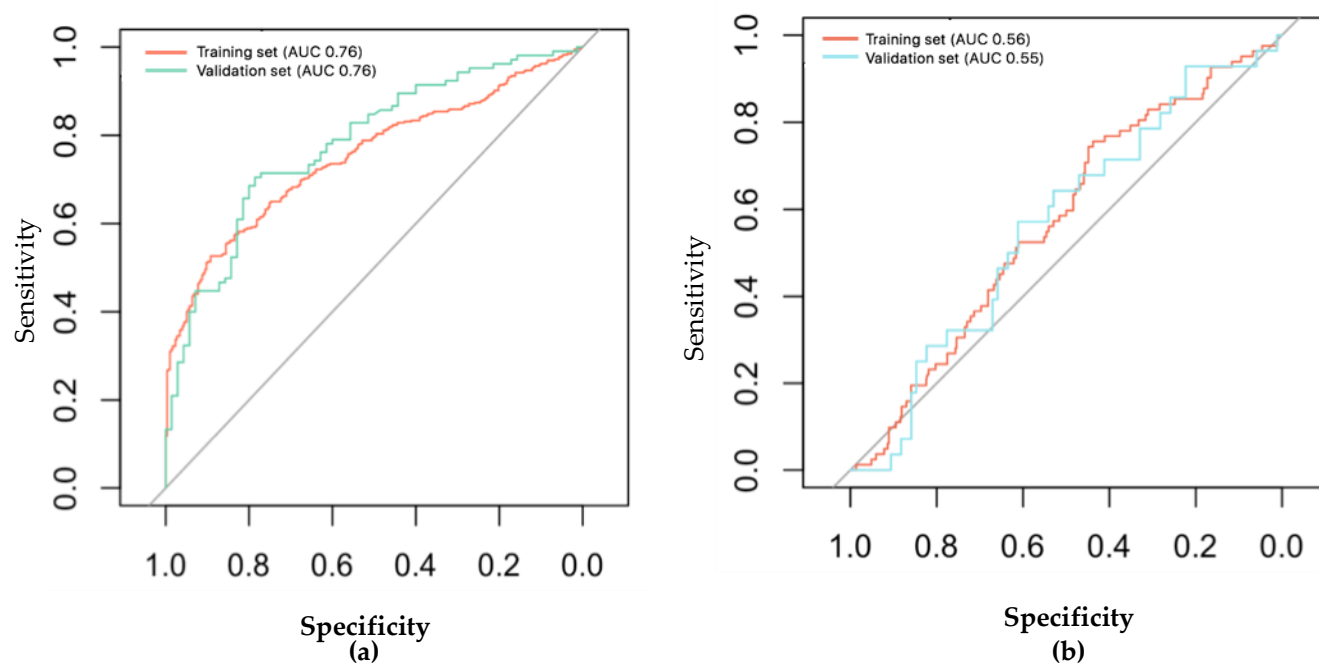
Figure S2. ROC analyses showing the accuracy of the linear discriminant model based on principal component reduction in the training set and the independent validation set according to pack/years (less than 5 pack/years, more than 5 pack/years) for (a) asthma and COPD group: (Control: < 5 pack/years; Case: > 5 pack/years): Training set: Case = 397; Control = 297; 95% CI: 0.72–0.78; AUC: 0.76. Validation set: Case = 105; Control = 72; 95% CI: 0.71–0.84; AUC: 0.76, and (b) for healthy control group (Control: < 5 pack/years; Case: > 5 pack/years): Training set: AUC: 0.56 (95% CI: 0.50–0.61); Validation set: AUC: 0.55 (95%CI: 0.58–0.74).
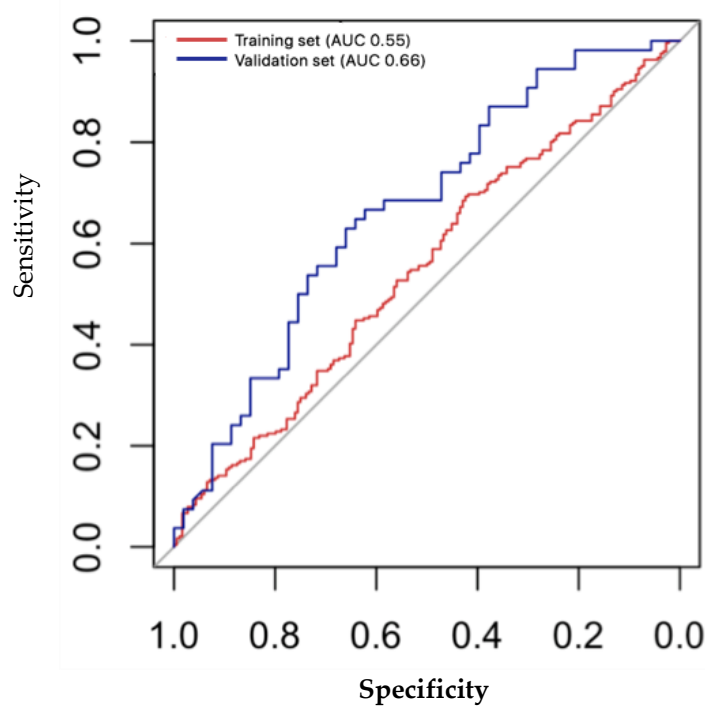
Figure S3. ROC-curve, which shows the accuracy of the linear discriminant model based on principal component reduction in the asthmatic population(training and validation set), to distinguish ever (n = 237) and never smokers (n = 295). Training set Case = 184; Control = 241: AUC: 0.55; 95% CI: 0.49–0.60; Validation set Case = 53; Control = 54: AUC 0.66; 95% CI 0.56–0.77.

Due to the extremely small proportion of non-smokers in the COPD group (number of ever-smokers = 356; never smokers = 8), we did not perform the same analysis in the COPD group of patients, considering that the accuracy of the model would not have been a good performance measure in this case.
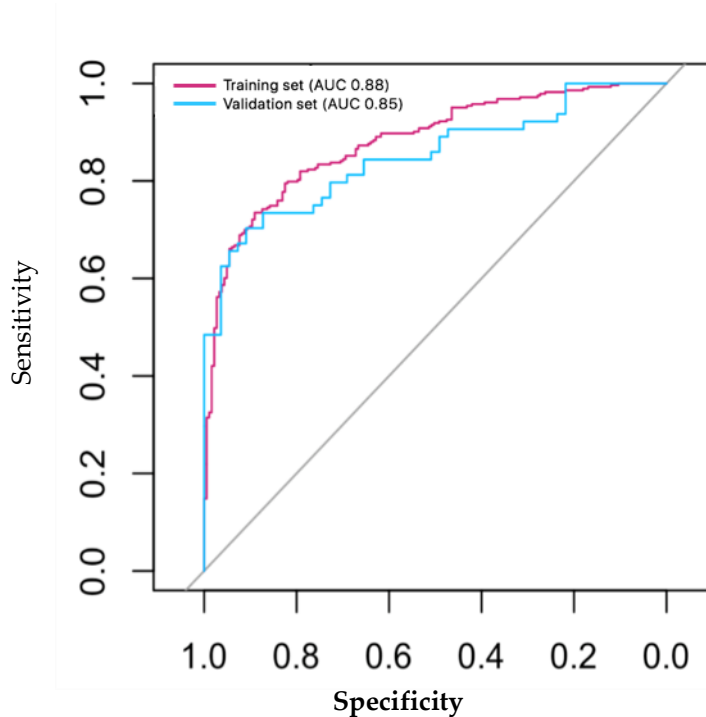

Figure S4. ROC-curve, which shows the accuracy of the linear discriminant model based on principal component reduction in the ever smokers population (train and validation set), to distinguish asthma (n = 237) and COPD (n = 356) patients. Training set Case = 182; Control = 292: AUC: 0.88; 95% CI: 0.85–0.91; Validation set Case = 55; Control = 64: AUC: 0.85; 95% CI: 0.78–0.92. .

Table S1. Demographics of asthma patients stratified by smoking status. Data are expressed in number of patients, mean ± standard deviation or median and range for non-normal distributions.

Asthma patients	Ever-smokers (n = 237)	Never Smokers (n = 295)	*p*-value
Age (mean (SD))	56.22 (12.47)	47.91 (17.94)	<0.001
BMI (mean (SD))	28.92 (5.82)	26.88 (6.27)	0.002
Gender = M/F (%)	108/129 (45.6/54.4)	109/186 (36.9/63.1)	0.074
Allergy = Y/N (%)	121/59 (51.0/24.9)	207/88 (70.2/29.8)	0.803
FEV1 (mean (SD)) (l)	2.60 (0.80)	2.65 (0.92)	0.194
FEV1/VC (mean (SD)) (%)	66 (13)	70 (14)	0.007
Pack/year (median [IQR])	12.00 [4.50, 21.00]	0.00 [0.00, 0.00]	<0.001
ACQ (median [IQR])	1.57 [0.71, 2.29]	1.43 [0.71, 2.29]	0.037
ICS = N/Y (%)	31/206 (13.1/87)	46/249 (15.6/84.4)	0.034
Oral corticosteroids (%)			0.020

Yes, now	5 (2.1)	5 (1.7)	
Yes, before	34 (14.3)	32 (10.8)	
No	198 (83.5)	258 (87.5)	

Table S2. Demographics of COPD patients stratified by smoking status. Data are expressed in number of patients, mean ± standard deviation or median and range for non-normal distributions.

COPD patients	Ever Smokers (n = 356)	Never Smokers (n = 8)	*p*-value
Age (mean (SD))	67.78 (8.93)	66.88 (10.51)	<0.001
BMI (mean (SD))	27.79 (5.74)	26.15 (5.84)	0.011
Gender = M/F (%)	175/181 (49.1/50.8)	4/4 (50.0/50.0)	0.508
FEV1 (mean (SD)) (l)	1.60 (0.67)	1.72 (0.85)	0.603
FEV1/VC (mean (SD)) (%)	60.97 (17.11)	71.88 (21.01)	0.161
Pack/year (median [IQR])	38.00 [20.25, 50.00]	0.00 [0.00, 0.00]	<0.001
CCQ (median [IQR])	2.00 [1.20, 2.80]	2.90 [1.68, 3.30]	0.231
ICS = No/Yes (%)	139/217 (39.0/60.9)	1/7 (12.5/87.5)	0.336
Oral corticosteroids (%)			0.830
Yes, now	9 (2.5)	0 (0.0)	
Yes, before	27 (7.6)	0 (0.0)	
No	320 (89.8)	8 (100.0)	