International conference on Occupational Health and Safety:
From policies to practice
Rīga, December 6-7, 2012

Retrospective Cohort Study of Industrial Workers: Contribution of Smoking and Occupational Factors to COPD Development

Nailya N. Mazitova, MD, PhD

Kazan State Medical University, Russian Federation

"Promotion of International Cooperation Activities of Rīga Stradiņš University in Science and Technologies", agreement No. 2010/0200/2DP/2.1.1.2.0/10/APIA/VIAA/006

Background

- Chronic obstructive pulmonary disease (COPD), one of the most prevalent health care problems in the world, constitutes a major cause of morbidity and mortality in developed and developing countries[1].
- The global economic burden of the disease is large and, according to the World Health Organization (WHO), is projected to rank fifth in burden of disease caused worldwide by year 2020[2].

[1] Decramer M, Sibille Y. Lancet 2011;377(9760): 104–6.

[2] WHO Statistical Information System (WHOSIS). 2008

Risk factors for COPD

Tobacco use remains the main risk factor for development of COPD.

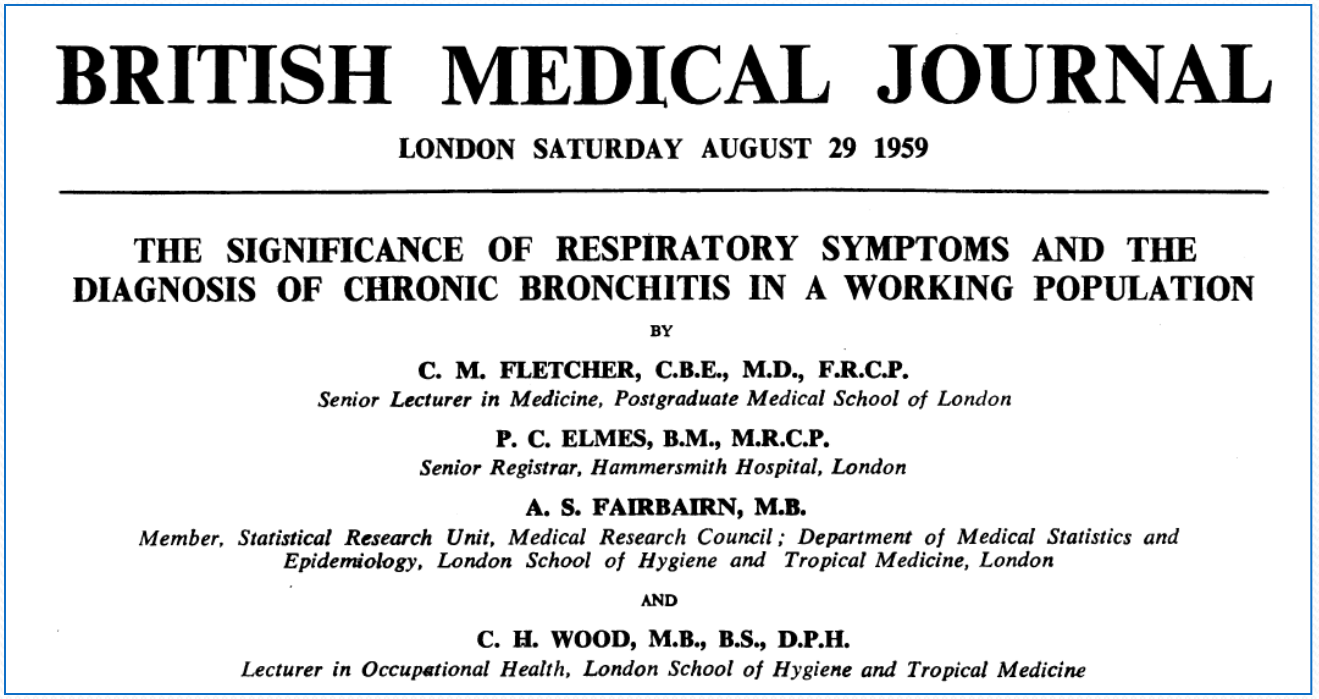
Lamprecht B, McBurnie MA, Vollmer WM, et al. Chest 2011;139(4):752–63.

Risk factors for COPD

Tobacco use remains the main risk factor for development of COPD; **nevertheless, this disease also develops in never smokers.**

Lamprecht B, McBurnie MA, Vollmer WM, et al. Chest 2011;139(4):752–63.

Historical retrospective



BRITISH MEDICAL JOURNAL

LONDON SATURDAY AUGUST 29 1959

THE SIGNIFICANCE OF RESPIRATORY SYMPTOMS AND THE DIAGNOSIS OF CHRONIC BRONCHITIS IN A WORKING POPULATION

BY

C. M. FLETCHER, C.B.E., M.D., F.R.C.P.
Senior Lecturer in Medicine, Postgraduate Medical School of London

P. C. ELMES, B.M., M.R.C.P.
Senior Registrar, Hammersmith Hospital, London

A. S. FAIRBAIRN, M.B.
Member, Statistical Research Unit, Medical Research Council; Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine, London

AND

C. H. WOOD, M.B., B.S., D.P.H.
Lecturer in Occupational Health, London School of Hygiene and Tropical Medicine

- Fletcher in 1959 stated that ”Men who work in dusty trades, especially coal miners, have a higher prevalence of symptoms of bronchitis and emphysema…”

Historical retrospective

1960 – 1985:

Tobacco smoke

No interest for w

Chronic airflow limit
in dusty occupatio

MR Becklake

Chest 1985;88;608-6

Ame

Ame
Cont

THIS OFFICIAL STATEMENT

Occupational Chronic Obstructive Pulmonary Disease
An Update

Enrique Diaz-Guzman, MD[a], Shambhu Aryal, MD[a],
David M. Mannino, MD[a,b,*]

KEYWORDS

• COPD • Chronic bronchitis • Emphysema • Occupation

KEY POINTS

- Chronic obstructive pulmonary disease (COPD) represents a major cause of morbidity and mortality in industrialized and nonindustrialized countries.
- Occupational risk factors represent an important and preventable cause of COPD.
- The most common occupationally related factors include exposure to organic dusts, metallic fumes, and a variety of other mineral gases and/or vapors.
- This article summarizes the literature on the subject and provides an update of the most recent advances in the field.

Occupation in chronic obstructive pulmonary disease and chronic bronchitis: an update

P. D. Blanc,* K. Torén†

* Division of Occupational and Environmental Medicine, University of California San Francisco, San Francisco, California, USA; † Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital, Göteborg, Sweden

Is there the evidence?

- An impressive body of the literature accumulated over the past two decades demonstrates the relation between specific occupational exposures and the development of COPD.

Eisner MD et al. AJRCCM. 2010 Sep 1; 182(5):693-718.

What are the difficulties?

- The importance of occupational exposure remains still underappreciated, especially in developing countries[1].
- Despite COPD being a preventable and treatable disease, studies have shown that as many as 75 percent of those affected remain undiagnosed[2].

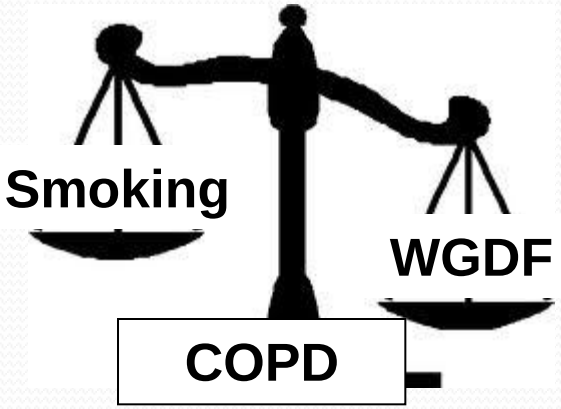
[1] Mazitova NN, et al. Arh Hig Rada Toksikol. 2012 Sep 25;63(3):345-56

[2] Rudolf M. Chest 2000;117(suppl): 29S-32S

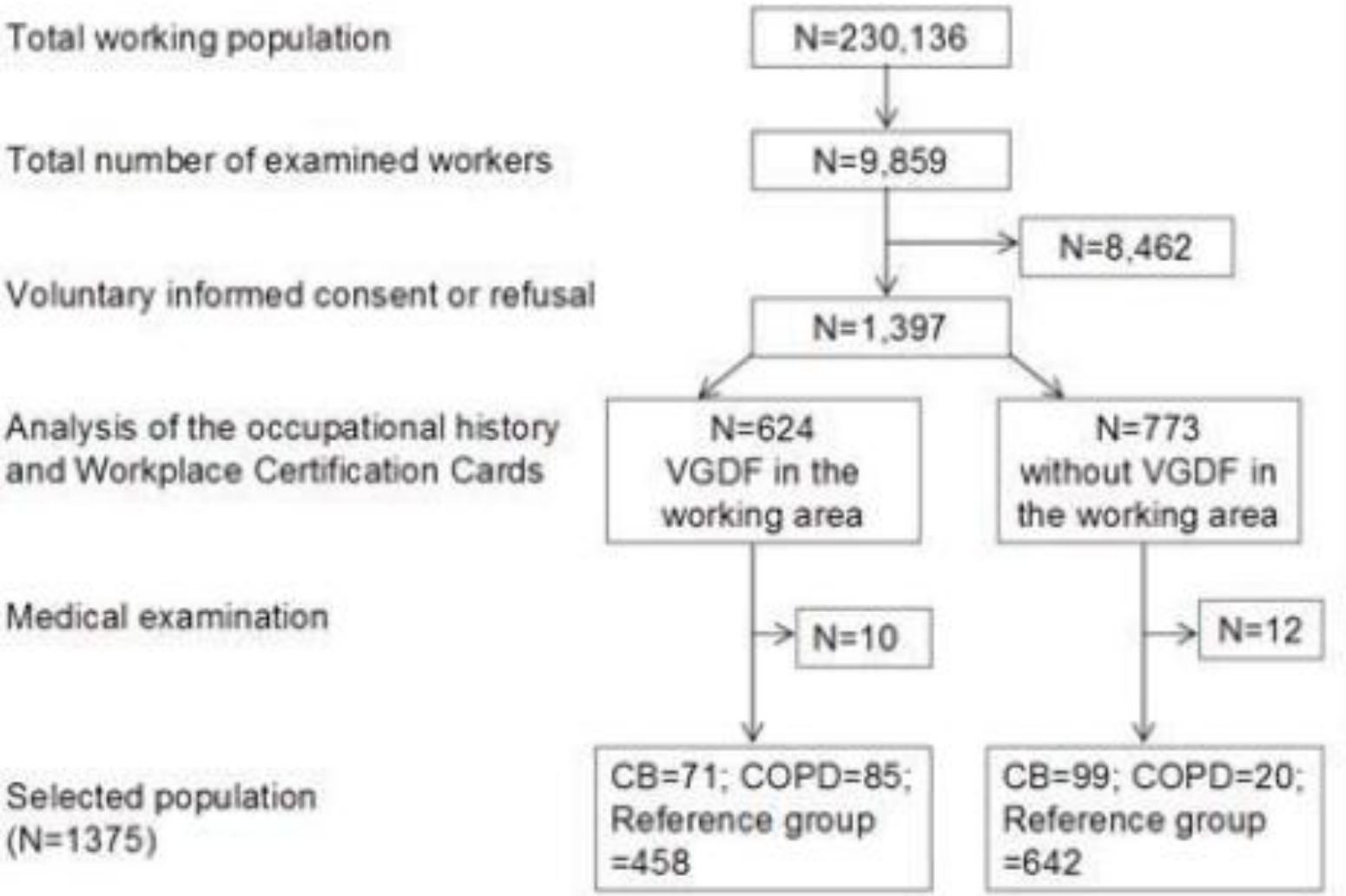
Aims and objectives

- To ascertain the prevalence of COPD among industrial workers in the Russian Federation
- To establish the relative contributions of smoking and occupational factors (vapors, gases, dusts, fumes - VGDF)

To justify the incluson of COPD in the National List of occupational diseases



Data sources



Inclusion & exclusion criteria

Inclusion criteria:

- Voluntary informed consent.
- Occupational exposure with VGDF for at least 5 years.

Exclusion criteria:

- Refusal to participate in the study,
- The presence of any other respiratory disease except of CB and/or COPD.

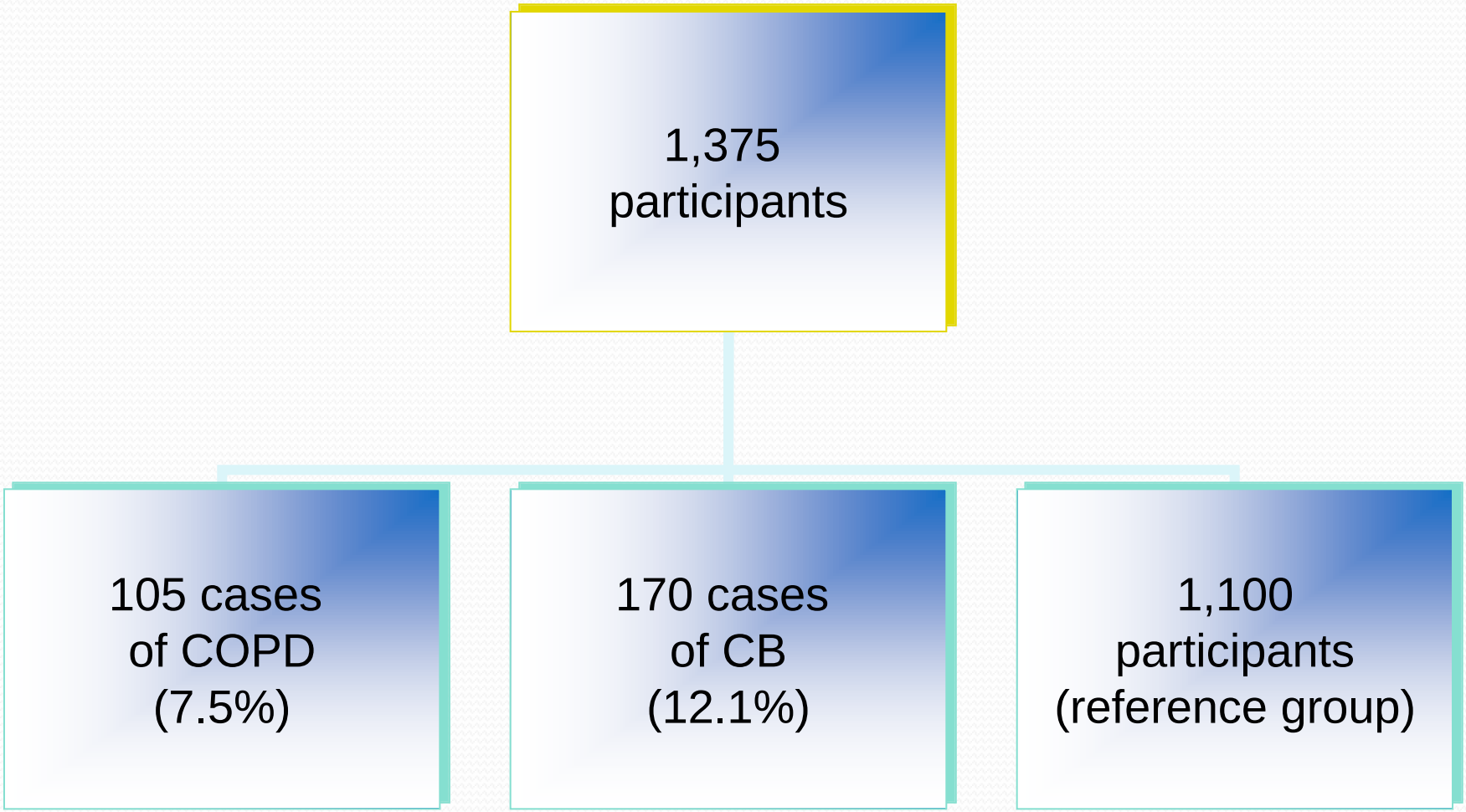
22 people were excluded from the analysis: 4 with newly diagnosed pneumoconiosis (4 / 1,397 cases, 0.3%) and 18 with asthma (18 / 1,397 cases, 1.3%).

Thus, we analyzed the survey results among 1,375 people.

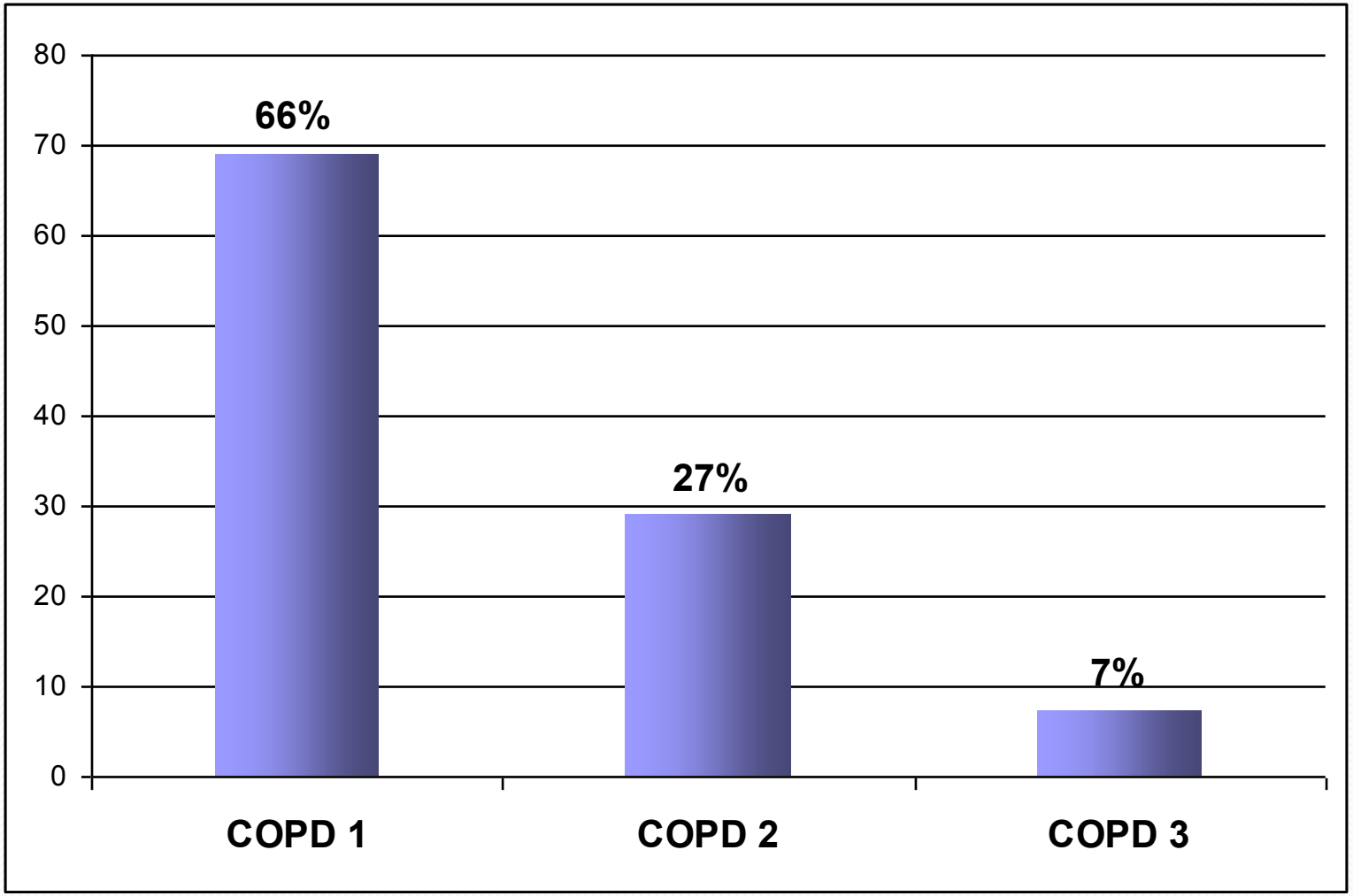
Methods

- Collecting data of 5 cross-sectional survey (2007-2010).
- Pre-interview: modified European Society of Coal and Steel Community questionnaire.
- Evaluation of the clinical symptoms: Paggiaro scale.
- Degree of tobacco addict: Fagerström test.
- Lung function exam: baseline spirometry at the worksite.
- Lung function exam plus for those with airflow limitation (FEV1/FVC <0.70): post-bronchodilator test.
- Data analysis: the Statistical system R, version 2.11.1.

Results


1,375 participants
105 cases of COPD (7.5%)
170 cases of CB (12.1%)
1,100 participants (reference group)

COPD stages



General characteristics of the studied cohort

	COPD (n=105)	CB (n=170)	Reference group (n=1100)
Age, M (SD)	51.7 (8.4)**	49.5 (8.1)	47.5 (9.9)
Women, n (%)	3 (2.9)***	46 (26.7)**	447 (40.56)
Education level, n (%):			
Secondary	99 (94.3)*	152 (89.4)	930 (84.5)
Higher	6 (5.7)**	18 (10.6)*	170 (15.5)
Income level, n (%):			
Low	16 (15.2)**	13 (7.6)	60 (5.5)
Middle	83 (79.0)	103 (60.6)*	910 (82.7)
High	6 (5.7)*	54 (31.8)*	130 (11.8)
Smoking status, n (%):			
Never smokers	20 (19.1) **	43 (25.3)**	713 (64.8)
Smokers	75 (71.4) **	113 (66.5)**	292 (26.5)
Former smokers	10 (9.5)	14 (8.2)	95 (8.6)
Smoking index, pack-years, n (%):			
Less than 20	55 (33.3) **	60 (35.3) **	231 (21.0)
20 or more	50 (47.6) **	67 (39.4) *	156 (14.2)
Occupational exposures:			
VGDF in working area, n (%)	85 (80.9) **	71 (41.8)	458 (41.6)
VGDF levels, n (%):			
Low (less than OEL – 3.0 OEL)	18 (17.1) **	36 (21.2)	325 (29.5)
Middle (3.1 OEL – 6 OEL)	46 (43.8) **	35 (20.6) **	106 (9.6)
High (more than 6.0 OEL)	21 (20.0) **	0	27 (2.5)

* $p<0.01$, ** - $p<0.05$, *** - $p<0.001$

Hypothesis:

1) COPD can be developed with the influence of dust only, regardless of smoking;
2) There is a "dose-effect relationship" between the levels of VGDF and COPD development;
3) Degrees of smoking and VGDF influence on the development of COPD are similar.

The hypothesis: the COPD & CB can be the result of VGDF exposure

	VGDF (+)	VGDF (-)
COPD	85	20
Healthy workers	457	642

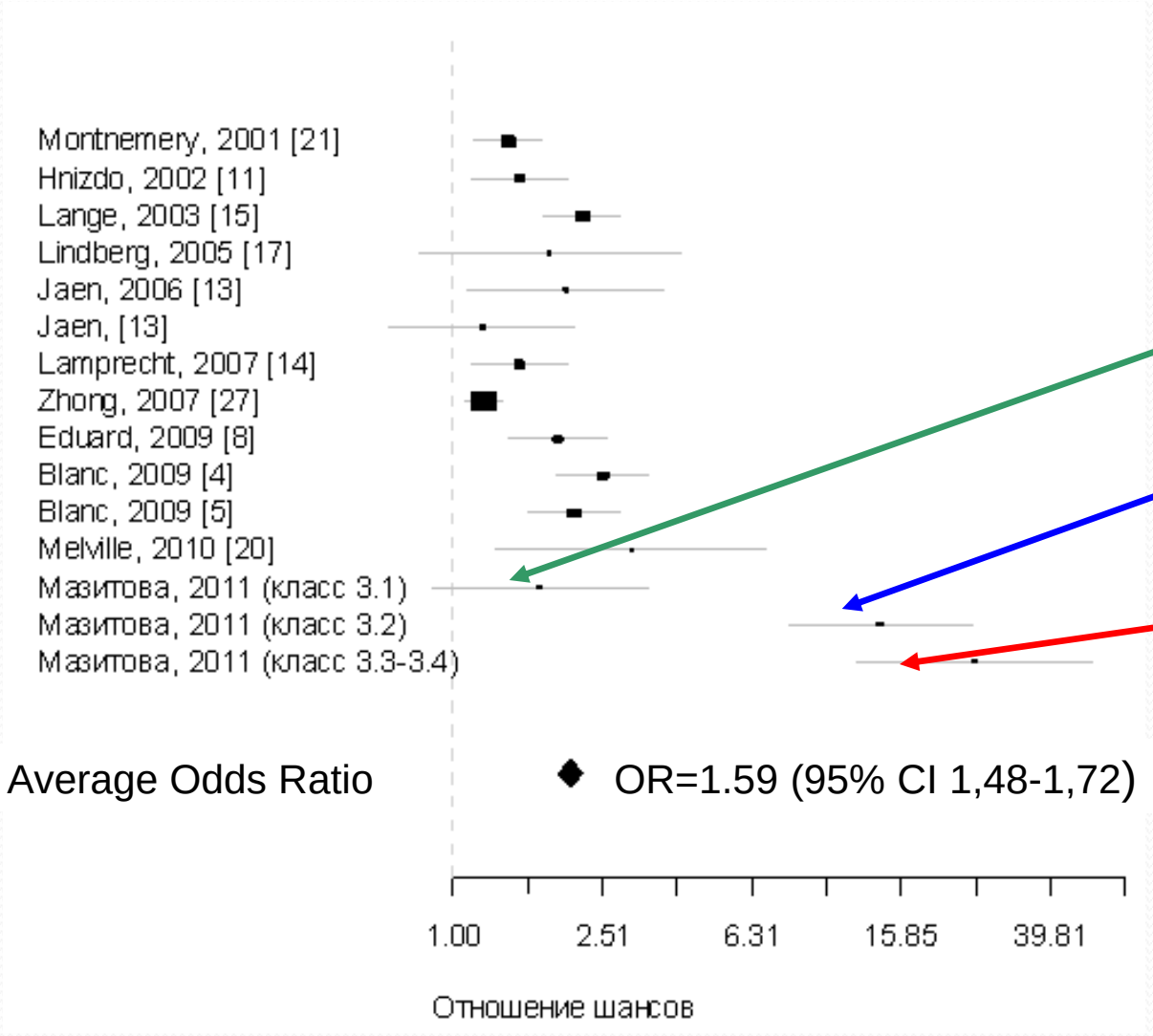
	VGDF (+)	VGDF (-)
CB	71	99
Healthy workers	457	642

	COPD	CB
Pexp	0.087	0.13
OR	**5.9** (95% CI 3.6-9.8)	**1.005** (95% CI 0.72-1.39)
RR	5.1	1.003
PAR	65.4	0.044
AR	0.87	0.003

The hypothesis: there is a dose-effect relationship between the levels of VGDF and COPD development

	OR (95% CI)	PAR, %	p-value
Contact with VGDF, in average	5.9 (3.6-9.8)	65.3	0.0001
Low levels of VGDF (less than OEL – 3.0 OEL)	1.7 (0.9-3.4)	20.0	0.07
Middle levels of VGDF (3.1 OEL – 6 OEL)	13.9 (7.9-24.5)	62.7	<0.0001
High levels of VGDF (more than 6.0 OEL)	24.9 (12.1-51.5)	47.6	<0.0001

The contribution of occupational factors in COPD development



Levels of WGDF:

Low

(1.7; 95%CI 0.9-3.4)

Middle

13.9; 95%CI 7.9-24.5)

High

(24.9; 95%CI 12.1-51.5)

Degrees of smoking and VGDF influence on the development of COPD

	OR (95% CI)	PAR, %	p-value
Non-smoking dusty trade's workers	**22.2 (4.9-100.5)**	**6.4**	**<0.0001**
Smoking dusty trade's workers (risk due to occupational exposures)	**3.4 (1.8-6.5)**	**9.8**	**0.0001**
Smoking dusty trade's workers (overall risk from occupational and non-occupational exposures)	82.7 (19.9-342.3)	18.9	<0.0001
Smokers who do not have any VGDF in the working area	34.68 (7.9-151.5)	9.8	<0.0001

Degrees of smoking and VGDF influence on the development of COPD

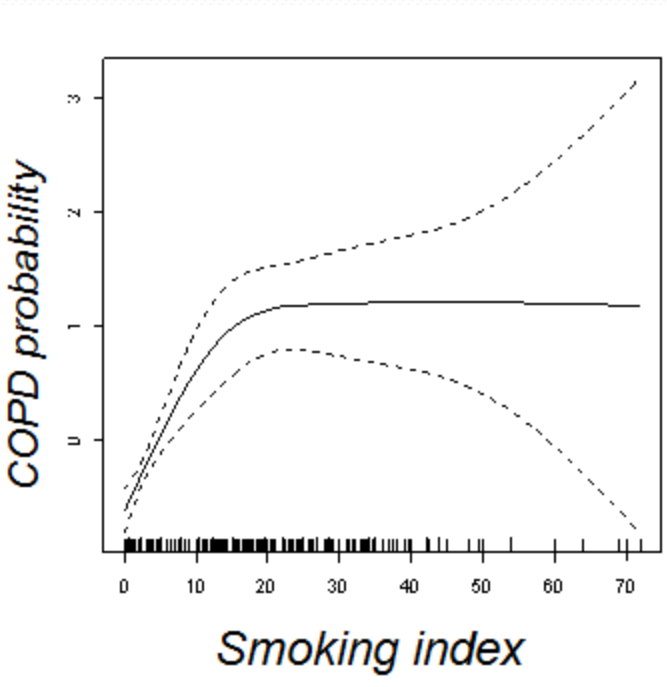
	OR (95% CI)	PAR, %	p-value
Non-smoking dusty trade's workers	**22.2 (4.9-100.5)**	**6.4**	**<0.0001**
Smoking dusty trade's workers (risk due to occupational exposures)	3.4 (1.8-6.5)	9.8	0.0001
Smoking dusty trade's workers (overall risk from occupational and non-occupational exposures)	**82.7 (19.9-342.3)**	**18.9**	**<0.0001**
Smokers who do not have any VGDF in the working area	34.68 (7.9-151.5)	9.8	<0.0001

Degrees of smoking and VGDF influence on the development of COPD

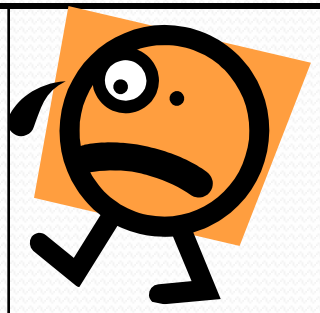
	OR (95% CI)	PAR, %	p-value
Non-smoking dusty trade's workers	**22.2 (4.9-100.5)**	**6.4**	**<0.0001**
Smoking dusty trade's workers (risk due to occupational exposures)	3.4 (1.8-6.5)	9.8	0.0001
Smoking dusty trade's workers (overall risk from occupational and non-occupational exposures)	82.7 (19.9-342.3)	18.9	<0.0001
Smokers who do not have any VGDF in the working area	**34.68 (7.9-151.5)**	**9.8**	**<0.0001**

The significance of predictors in the model of COPD development

Predictors	Initial values of smoking index		Transformed values of smoking index	
	χ^2	p-value	χ^2	p-value
Type of VGDF	**64.5**	<0.0001	0.9	0.6288
Level of VGDF	**63.3**	<0.0001	**70.8**	<0.0001
Smoking index	**43.2**	<0.0001	**43.5**	<0.0001
Age	5.7	<0.0200	5.9	<0.0140
Heating microclimate	5.2	<0.0230	5.3	<0.0220



Predictive logistic regression models

	 Healthy workers	 CB patients	 COPD patients
1.general three level GLM	+	+	+
2.two level GLM	+	+	
3.two level GLM	+		+
4.two level GLM	+	+	
5.two level GLM		+	+
6.two level GLM	+		+
7.general three level POLR	+	+	+

Levels of statistical significance of predictors in models

Predictors	Generalized Linear Models						Proportional Odds Logistic Regression
	1	2	3	4	5	6	
Age	<0,001	<0,001	0,001	0,001		0,01	<0,001
Gender		0,01	<0,001	<0,001	<0,001	0,001	
Level of VGDF	<0,001	<0,001	<0,001	<0,001	<0,001	<0,001	<0,001
Type of VGDF				0,01			
Level of irritants	<0,001	<0,001	<0,001		<0,001	<0,001	<0,001
Physical stress							0,001
Heating microclimate	<0,001					<0,001	
Smoking status						0,01	
Smoking index	<0,001	<0,001		<0,001		0,01	0,01
Length of smoking	<0,001						<0,001

The values of linear coefficients of the predictors in models

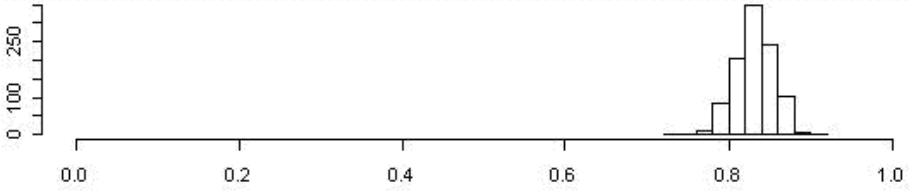
Predictors	Generalized Linear Model						Proportional Odds Logistic Regression
	1	2	3	4	5	6	
Age	0,034	0,036	0,040	0,033		0,035	0,032
Gender (male)		-0,516	-2,350	-1,265	-2,164	-2,221	
Low levels of VGDF							
Middle levels of VGDF			0,731				-0,264
High levels of VGDF	2,115	2,040	2,362	2,034	1,076	0,358	1,682
Silica dust	**2,746**	**1,916**	**3,993**			**0,739**	**2,313**
Other kinds of dust							
Dust & irritants				-1,038			
Levels of irritants	1,040	0,631	1,753		1,550	0,522	0,802
Physical stress							
Heating mycroclimat							0,875
Former smokers	0,775						
Smokers	0,844		0,721				1,095
Smoking index	**1,410**	**1,358**	**1,402**	**1,505**		**0,483**	**1,580**
Length of smoking						0,014	
Duration of smoking cessation	0,029	0,038		0,046			0,028

The values of predictive capacity of regression models

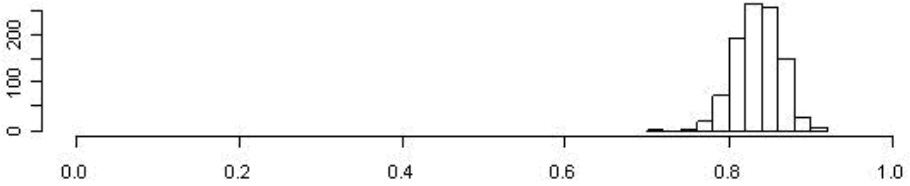
	Generalized Linear Models						Proportional Odds Logistic Regression Model
	1	2	3	4	5	6	
Cross-validation: overall average result	0,793	0,752	**0,834**	0,613	0,752	**0,846**	**0,840**
Cross-validation: Sensitivity	0,768	0,753	0,778	**0,813**	0,755	**0,835**	-
Cross-validation: Specificity	0,797	0,751	**0,838**	0,582	0,751	**0,847**	-
ROC-analysis: area under curve	-	**0,828**	**0,912**	**0,815**	**0,866**	**0,931**	-

Results of model verification (1)

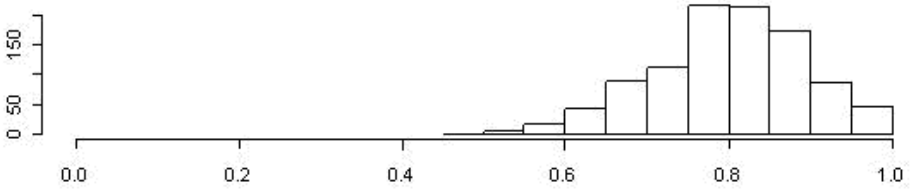
1) Cross-validation



The proportion of correctly predicted outcomes

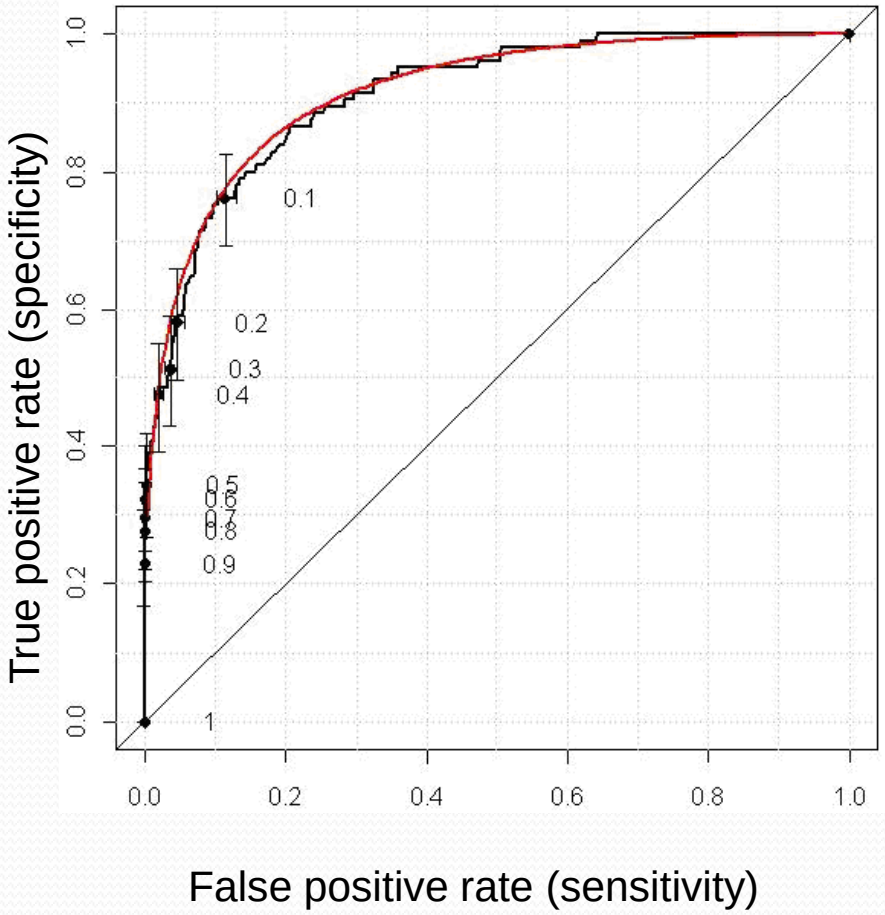


Sensitivity



Specificity

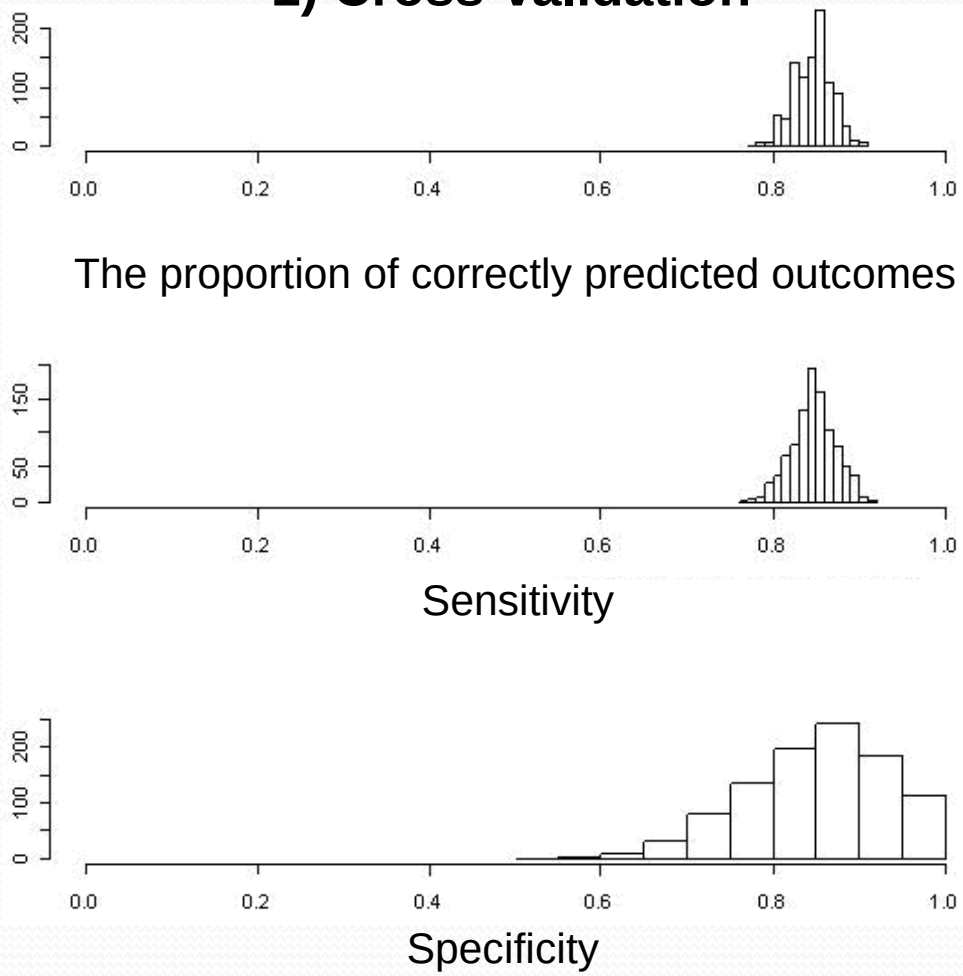
2) ROC-analysis



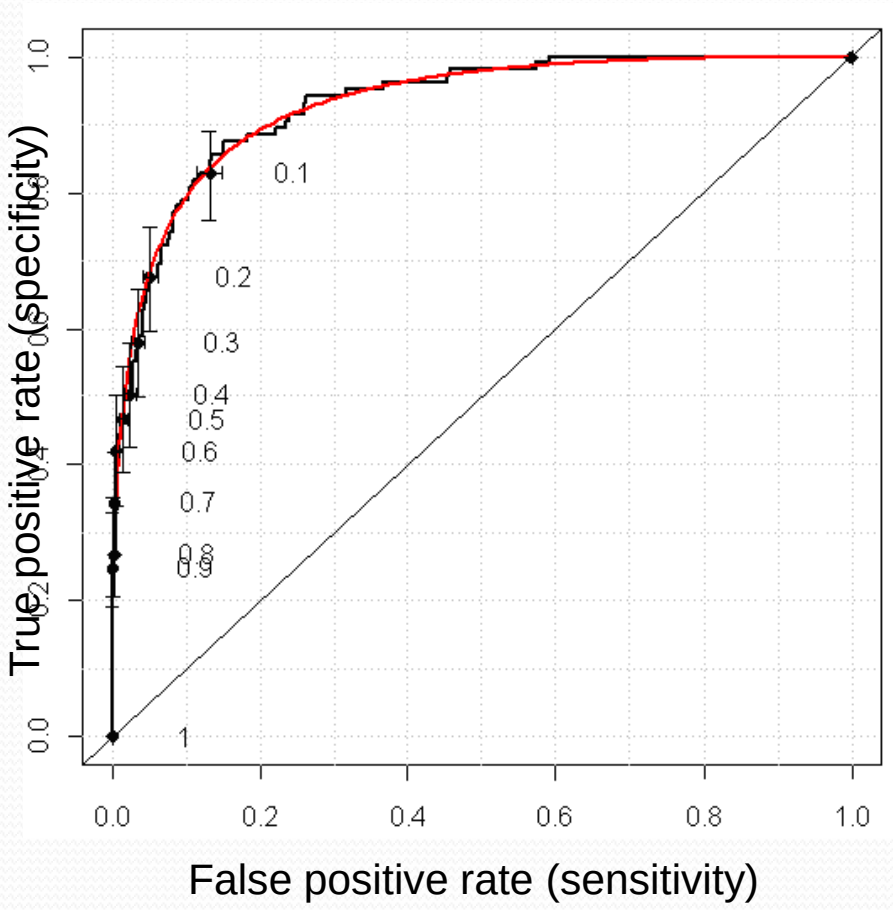
GLM-model “0 – healthy workers;1 – COPD patients”

Results of model verification (2)

1) Cross-validation



2) ROC-analysis



GLM-model “0 – healthy workers and CB patients; 1 – COPD patients”

Conclusions

1) COPD can be developed with the influence of dust only, regardless of smoking;

2) There is a "dose-effect relationship" between the levels of VGDF and COPD development;

3) Degrees of smoking and VGDF influence on the development of COPD are similar.

- The differentiation between the various effects of different kinds of inhaled noxious particles and gases seems to be complex.
- Therefore, a comprehensive assessment of its contribution is of special interest for occupational medicine specialists.
- Future investigations of occupational COPD seem to be important for the development of prevention strategies.

Thank you for the attention!

nailya.mazitova@gmail.com