We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,300

Open access books available

172,000

International authors and editors

190M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Diagnosis of Chronic Obstructive Pulmonary Disease with Special Reference to Over- and Underdiagnosis Using Spirometry

Peter Montnemey and Sölve Elmståhl
Lund University
Sweden

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is increasingly recognized as a major public health problem. In the western world it is the 4th -5th most common cause of death and the only one that is rising among the top ten causes (Murray & Lopez, 1997). The disease is estimated to become the third leading cause of death worldwide by 2020 (Chapman et al., 2006). However, depending on the criteria used and the population studied, the estimated prevalence rates may vary. Historically, COPD has been defined symptomatically as chronic bronchitis, anatomically as emphysema. The current definition is physiologically based on airway obstruction as measured by a spirometer.

By searching PubMed for population based prevalence studies extending back to mid-1962 Halbert et al. identified 32 studies that had a satisfactory methodology to be included in the interpretation (Halbert et al., 2003). The methodology included spirometry with or without clinical examination, the presence of respiratory symptoms, self reported disease and expert opinion (WHO). In all, the prevalence rates of COPD were ranging from 2%-22% depending on the criteria used for definition. Eleven studies used spirometry either in combination with clinical examination or alone to estimate the prevalence rates of COPD. In the spirometry studies the prevalence rates of COPD also varied but most of them were between 4% and 10 %. Recently Chapman et al. (Chapman et al., 2006) and Mannino & Buist have reported that COPD affects 5-15% of all adults in industrialized countries (Mannino & Buist, 2007). A growing number of women are affected.

However, since COPD is such a common disease and new treatments have been introduced, it is important that it can be diagnosed accurately. According to the current definition of COPD, the diagnosis requires a spirometry examination.

2. History

The ancient Egyptians described a condition similar to asthma more than 3000 years ago. Hippocrates (460-370 BC) is supposed to be the first European to describe asthma. The knowledge concerning COPD and its manifestations emphysema, chronic bronchitis and asthmatic bronchitis goes back to Badham 1814 (Badham, 1814), who described the bronchiolitis and chronic cough and mucus hypersecretion that are the cardinal symptoms of COPD.

Emphysema and its symptoms has been described by Laënnec, the inventor of the stethoscope, in 1827. The CIBA Guest Symposium in 1959 (CIBA Guest Symposium, 1959) and the American Thoracic Society Committee on Diagnostic Standards in 1962 defined the components of COPD that are the foundation for the present definitions (Committee on Diagnostic Standards for Nontuberculous Respiratory Diseases, American Thoracic Society, 1962). William Briscoe is supposed to be the first person to use the term COPD in 1965 (Briscoe & Nash, 1965).

3. Definitions

There is a lack of a generally accepted definition of COPD. American Thoracic Society (ATS) and European Respiratory Society (ERS) define COPD as: “ A preventable and treatable disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking. Although COPD affects the lungs, it also produces significant systemic consequences.” (Celli & MacNee, 2004).

Global Initiative for Chronic Obstructive Lung Disease (Global Initiative for Chronic Obstructive Lung Disease GOLD, 2010) define COPD as: “A preventable and treatable disease with some significant extra-pulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases”.

A simple spirometric definition and classification of disease severity into four stages has been recommended by GOLD. The classification has recently been updated (GOLD, 2010). GOLD recommends that a post-bronchodilator Forced Expiratory Volume in one second (FEV1)/Forced Vital Capacity (FVC) < 0.7 confirms the diagnosis of COPD. FEV1 provides a way to stage the severity of the disease.

Stages of COPD according to GOLD
Stage I: Mild COPD Mild airflow limitation (FEV1/FVC<0.7; FEV1 ≥80% predicted) and sometimes, but not always, chronic cough and sputum production. At this stage, the individual may not be aware that his or her lung function is abnormal.
Stage II: Moderate COPD Worsening airflow limitation (FEV1/FVC < 0.7; 50%≤FEV1<80% predicted), with shortness of breath typically developing on exertion. This is the stage at which patients typically seek medical attention because of chronic respiratory symptoms or an exacerbation of their disease.
Stage II: Severe COPD Further worsening of airflow limitation (FEV1/FVC < 0.7; 30%≤FEV1<50% predicted), greater shortness of breath, reduced exercise capacity, and repeated exacerbations which have an impact on patients’ quality of life.
Stage IV: Very Severe COPD Severe airflow limitation (FEV1/FVC < 0.7; FEV1<30% predicted or FEV1<70% predicted plus chronic respiratory failure. Patients may have Very Severe (Stage IV) COPD even if the FEV1 is >30% predicted, whenever this complication is present. At this stage, quality of life is very appreciably impaired and exacerbations may be life-threatening.

However, the usage of a fixed Quotient FEV1/FVC to define pulmonary obstruction or COPD has been questioned. Considering that the FEV1/(F)VC ratio falls with age (Hedenstrom et al., 1985; Hedenstrom et al., 1986; Quanjer et al., 1993), the use of a fixed cut-off point for defining COPD overestimates the prevalence in the elderly and underestimates the prevalence in younger patients (Cerveri et al., 2008). The diagnosis and possible overestimation of COPD among elderly has previously been reported (Hansen et al., 2007; Lundbäck et al., 2003; Swanney et al., 2008; Vollmer et al., 2009).

While the current definitions of obstructive pulmonary disease are founded on spirometry measurements, the applied spirometric reference values and the applied guidelines are crucial. Several spirometric reference values are in use. In Europe the prediction equations by the European Coal and Steel Community (ECSC) are widely used for adults although the data were derived from lung function measurements over a long time period (1954-1980) and from different European countries. (Quanjer et al., 1993)

Globally several other spirometry reference values are in use or have been proposed, e.g. the prediction equations for Caucasian adult males and females derived from the Third US National Health and Nutrition Examination Survey (NHANES-III) (Hankinson et al., 1999) Brändli et al have published reference values of a Swiss population (Brädli et al., 1996; Brädli et al., 2000). In 2001 Langhammer et al. published forced spirometry reference values for Norwegian adults (Langhammar et al., 2001)

Recently Kuster et al published another set of reference equations for lung function of never smoking Swiss adults aged 18-80 years (Kuster et al., 2008). Falaschetti et al. have published reference values predicted for an English adult population using data from the 1995/1996 Health Survey for England (Falaschetti et al., 2004). Pistelli et al. have published spirometry reference equations from a general population sample aged 8-74 years in central Italy (P Pistelli et al., 2007). Recently reference equations have been published for Brazilian adults (Pereira et al., 2007), Polish adults (Ostrowoski et al., 2005), Chinese adults (Ip et al., 2006) and Kazakh adolescents (Facchini et al., 2007).

For ethnic populations of north-western Europe (Iceland, Norway, Denmark, Finland and Sweden), the almost 40-year-old Swedish reference material of Berglund et al has been used. The subjects were not randomly selected and included smokers as well as occupational exposures to dust. (Berglund et al., 1963).

In 1985 and 1986 Hedenström et al have published spirometric reference equations for Swedish females and males, which are widely used in Sweden. A total of 186 females, 100 never smokers and 86 smokers, and 270 males, 124 never smokers and 146 smokers respectively were investigated. The subjects were aged 20-70 years and divided in five age decades. Only subjectively healthy subjects with normal chest radiograms and who had had no significant occupational exposure to noxious dusts or fumes were included (Hedenstrom et al., 1985; Hedenstrom et al., 1986).

4. Risk factors

4.1 Smoking

Smoking is the major cause of COPD (Anto et al., 2001), and 85-90% of all patients with COPD are current or ex-smokers. In the literature it has been proposed that approximately

20% of smokers develop a clinically significant COPD (American Thoracic Society 1995; Fletcher et al., 1976; Rijcken et al., 1998). Lundbäck et al. have reported that as much as 50% of smokers who continue to smoke develop COPD (Lundbäck et al., 2003). Their results were based on the British Thoracic Society criteria (British Thoracic Society [BTS], 1997) and the GOLD criteria (GOLD, 2001) by the using the Swedish reference values published by Berglund et al. in 1963 (Berglund et al., 1963). Rennard et al. have also proposed that far more than 15% of smokers get COPD: in fact, most develop some amount of pulmonary impairment. (Rennard & Vestbo, 2006).

4.2 Occupational and environmental exposure

Other factors are thought to modulate the risk of developing COPD. Occupational exposure to dust and fumes are important risk factors (Trupin et al., 2003). Bakke et al. have examined a Norwegian general population aged 18-73 years. The authors concluded that exposure to specific agents and work processes may be independent risk factors for COPD when adjusted for gender, age and smoking. (Bakke et al., 1991). Urban air pollution may affect lung function. In a cross sectional study by Lindgren et al., living within 100 m of a road with >10 cars per minute was associated with prevalence of COPD diagnosis (OR = 1.64, 95%CI=1.11- 2.40) as well as chronic bronchitis symptoms as increased cough and sputum production compared with having no heavy road within this distance (Lindgren et al., 2009). Exposure to biomass fuels is also an important risk factor (Perez-Padilla, 1996; Varkey, 2004). It can be supposed that genetic and environmental factors interact to cause COPD. α_1 - antitrypsin deficiency has been recognized as one major genetic factor (Laurell & Eriksson, 1963).

4.3 Nasal features

In addition, a recent epidemiological study suggests that certain nasal features may be associated with COPD (Hurst, 2010; Montnemery et al., 2008).

4.4 Socio-economic status

Several previous studies have shown a relation between COPD and socioeconomic status as well as a recent study by Kanervisto et al. (Kanervisto, 2011) that measured low socioeconomic status by educational and income levels as risk factors using age, gender, smoking and body mass index as possible confounders.

4.5 Alcohol

Alcohol intake has been proposed to be a risk factor, but the results are inconsistent. Garshick et al. found that lifetime alcohol consumption was a predictor of lower levels of FEV1 in a model that included age and pack years (Garshick et al., 1989). Lange et al. found that consumption of 350 g of alcohol per week had an effect on FEV1 comparable to the effect of 15 g tobacco per day (Lange et al., 1988). Schunemann et al. did not find any correlation between total alcohol intake and lung function when adjusting for smoking, education and nutritional factors but a positive effect for wine intake, especially white wine (Schunemann et al., 2002). Tabak et al. found a beneficial effect of low alcohol consumption (1-30 g per day). The FEV1 was higher and the prevalence of COPD symptoms lower than in non-drinkers (Tabak et al., 2001).

4.6 Co-morbidity

Some data suggest that co-morbidity of coronary heart disease (CHD), chronic congestive heart failure (CHF) and COPD are common. van Manen et al. found that comorbidity was more common among COPD patients seventy three percent and sixty three percent respectively (van Manen et al., 2001). Comorbidity and COPD has also been emphasized by Siebeling et al. (Siebeling et al., 2011).

Left ventricular dysfunction has been found in 32% of patients with COPD (Render et al., 1995). In a prospective cohort study including >60 years old patients with echocardiographically confirmed CHF (n=201) and clinical spirometry confirmed COPD (n=218), the prevalence of airway obstruction among CHF patients was 37.3% and the prevalence of ventricular dysfunction among COPD patients was 17 %. (Macchia et al., 2011).

4.7 Gender

The role of gender is unclear. Previous studies have shown a greater prevalence in men related to a more frequent smoking compared to females. (Foreman et al., 2011; Silverman et al., 2000). Results from the worldwide BOLD study indicate that not only smoking is a risk factor for COPD but also female gender (Buist et al., 2007). There might be a higher susceptibility for tobacco-induced COPD among different population groups.

Recently Kikpatrick and Dransfield have suggested that women and African-Americans are particularly susceptible to tobacco smoke. (Kikpatrick & Dransfield, 2009). The underlying physiological mechanisms for females to be at an increased risk have been considered to involve either hormonal homeostasis or structural development of lungs. The racial disparities in a higher susceptibility for COPD among African Americans have also been emphasized by Garcia-Aymerich (Garcia-Aymerich, 2011).

5. Normal ageing of the lung

Maximal lung function is reached at approximately the age of 20 years for females and 20 years for males. Thereafter, ageing is associated with a decrease of lung function. The most important physiologic lung changes with normal ageing are characterized by significant reduction in the elastic recoil of the lung, greater chest wall rigidity, and loss of respiratory muscle strength. (Knudson et al., 1977; Turner et al., 1968). However, in contrast to COPD, the morphologic changes consist of alveolar enlargement but without destructive wall changes of the alveoli (Fukuchi, 2009). As a result of the ageing process residual volume increases (air trapping) by approximately 50% between 20 and 70 years of age (Janssens et al., 1999). These changes are responsible for the lowered FEV1/FVC quotient observed in the elderly (Hedenstrom et al., 1985; Hedenstrom et al., 1986; Quanjer et al., 1993). Thus, there is a risk of an over diagnosis of COPD when the disease is defined by a fixed ratio of FEV1/FVC (Swanney et al., 2008).

6. Pathology and pathogenesis of COPD

6.1 Pathology

The chronic airflow limitation characteristic of COPD is caused by inflammatory processes of the airways and lung tissue as a result of exposure to inhaled irritants. The airflow

limitation is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema). The relative contributions vary from person to person. The inflammation causes structural changes and narrowing of the small airways and airway remodeling. Destruction of the lung parenchyma leads to loss of alveolar attachments to the small airways and decreases lung elastic recoil. These changes diminish the ability of the airways to remain open during expiration. (GOLD, 2010 ; Snider, 2000). The inflammation also leads to excess mucus production due to hypertrophy of the goblet cells and mucous glands of the airways. There is also a reduction of mucociliary clearance.

6.2 Pathogenesis

There are two major views of the pathogenesis of COPD.

6.2.1 The British hypothesis

The British hypothesis says that recurrent bronchial infections are the reason that some smokers develop airway obstruction. COPD (Anthonisen, 2004). The British hypothesis emphasizes that repeated chest infections and air pollution contribute to the development of the disease (Anthonisen, 2004).

6.2.2 The Dutch hypothesis

The Dutch hypothesis suggests that allergy and airway hyperresponsiveness interacting with genetic and environmental factors are important in the development both of asthma and COPD. (Dirjke et al., 2004; Vestbo & Prescott, 1998).

British hypothesis emphasizes exogenous factors but the Dutch hypothesis emphasizes endogenous factors. Both hypotheses are probably correct. Both bronchial hyperreactivity and recurrent pulmonary infections interacting with exposure to air irritants such as cigarette smoke or air pollution contribute to the development of and COPD and chronic bronchitis (Petty, 2006)

7. The natural history of COPD

The natural history of COPD begins with cellular and biochemical changes in the small airways and alveoli due to a chronic inflammation caused by the long term inhalation of noxious gases and particles such as cigarette smoke. COPD is characterized by a reduced FEV1 and an accelerated decline of FEV1 compared to healthy subjects. The airflow limitation measured by reduced FEV1 progresses over a long time, most often over several decades without any symptoms (Huib et al., 1997). In non-smokers without respiratory disease, FEV1 declines by 20-30 ml per year beginning at an age of about 35 years (Burrows et al., 1983; Huib et al., 1997). The rate of decline in smokers is steeper and the heavier the smoking, the steeper the rate of decline (Anthonisen et al., 1994; George, 1999). This indicates some dose – response relationship in the deterioration. In addition there are individuals who are unusually susceptible to the effects of tobacco smoke and in whom FEV1 declines at even at greater rates. Burrows et al. have described that a low FEV1/FVC ratio on entry of a spirometric study was associated with a high rate of decline in FEV1 at least among male smokers. This phenomena is called the horse racing effect (Burrows et al., 1987).

7.1 Smoking cessation

Almost every study on the effect of smoking cessation has shown that it has clinical and physiological benefits. Indeed it is the only measure that so far has been proven to stop the decline of FEV1. In 1961 Fletcher and Peto started to investigate 792 working males aged 30 to 59 with spirometry, of whom 103 were non-smokers (Fletcher & Peto, 1977).

All the men were seen regularly over the next eight years. The decline of FEV1 in ex-smokers was slower than that in smokers, 37 and 62 mL/year respectively. After, smoking cessation the abnormal rate in FEV1 decline in ex-smokers gradually becomes similar to that found in non-smokers (Fletcher & Peto, 1977).

Their findings of reduced decline of FEV1 after quitting smoking have been confirmed by several other investigators as reviewed by Willemse et al. and Lee & Fry (Lee and Frey, 2010; Willemse et al., 2004). After having reviewed 47 studies, Lee and Fry concluded that never smokers had a decline of FEV1 10.8 mL/year less than continuing smokers and for quitters 8.5 mL/year less. Some but not all studies showed that the annual decline of FEV1 was greater in those with reduced lung function, particularly in those who continued smoking.

8. Spirometry

Hutchinson invented the spirometer in 1846.

The diagnosis of COPD is confirmed by spirometry, a test that measures the forced expiratory volume in one second (FEV1), which is the greatest volume of air that can be breathed out in the first second of a large breath. Spirometry also measures the forced vital capacity (FVC), which is the greatest volume of air that can be breathed out in a whole large breath. Normally at least 70% of the FVC comes out in the first second (FEV1/FVC ratio >0.7). Spirometric diagnosis and severity classification of COPD are based on post bronchodilator values after the administration of an adequate dose of an inhaled bronchodilator. (e.g. 400 µg salbutamol or 1000 µg terbutalin). Most investigators perform the spirometry according to the ATS guidelines (American Thoracic Society, 1995).

Fig. 1 shows a normal spirogram of a 57 years old female. The FVC and FEV1 values are normal. The FEV1/FVC ratio is normal. There was no increase of the lung volumes after a bronchodilator (400 µg salbutamol) was given.

Fig. 2. shows an abnormal spirogram (COPD) of a 62 years old female with a life long smoking history with about 44 pack years. One pack year is defined as 20 cigarettes a day for one year.

9. Over and under-diagnosis of COPD

COPD is one of the leading causes of morbidity and mortality among the adult population worldwide (GOLD, 2010). However, differences in the definition of COPD make it difficult to quantify the morbidity. Spirometry is the golden standard for diagnosing COPD but there are also different recommendations in the guidelines concerning how to perform spirometry (Nathell et al., 2007). Most guidelines define airway obstruction by a FEV1/FVC ratio less than 0.7. It is well known that the FEV1/FVC ratio declines with

Fig. 1. Normal spirogram. Female 57 years old, height 162 cm. Predicted values according to Hedenström et al., 1985.

Fig. 2. Severe COPD according to the GOLD criteria. Female 62 years old, height 175 cm. Predicted values according to Hedenström et al., 1985.

Normal spirogram Fig.1.

	Pre-bronchodilator values (grey line)	Post-bronchodilator values (green line)	Percent (%) of predicted values. Post bronchodilator	Predicted values
FVC	3.4	3.4	97%	3.5
FEV1	2.8	2.8	104%	2.7
FEV1/FVC	0.82	0.82	106%	0.77

Abnormal spirogram (COPD) Fig.2.

	Pre-bronchodilator values (grey line)	Post-bronchodilator values (green Line)	Percent (%) of predicted values. Post bronchodilator	Predicted values
FVC	2.3	2.5	61%	4.1
FEV1	0.8	0.9	31%	2.9
FEV1/FVC	0.35	0.36	51%	0.71

increasing age, even in healthy non-smokers (Falaschetti et al., 2004; Quanjer et al., 1993; Stanojevic et al., 2010). Thus, there is a risk of an over-diagnosis of COPD in the elderly patient but a risk of under-diagnosis in younger individuals when the disease is defined by a fixed ratio of FEV1/FVC (Swanney et al., 2008). By using four prediction equations derived from large European studies, Schermer et al. have illustrated the decline of the FEV1/FVC ratio by age (Schermer et al., 2007) They concluded that the fixed 0.70 ratio leads to false negative results in younger adults and to false positive test results in older adults. Using the large NHANES III database (Hankinson et al., 1999) it has been demonstrated that above the age of 50 years, about 50% of subjects regarded to be obstructive were false positives (Schermer et al., 2007).

Celli et al. have also used the NHANES III database to evaluate the impact of different definitions of airway disease by different criteria: 1) self-reported disease, 2) the GOLD criteria $FEV_1/FVC < 0.7$ and $FEV_1 < 80\%$ predicted, 3) $FEV_1/FVC < LLN$, $FEV_1/FVC < 88\%$ predicted in males and $< 89\%$ predicted in females and $FEV_1/FVC < 0.7$. They concluded that prevalence rates can vary by $> 200\%$ depending on which definition was used (Celli et al., 2003). Vollmer et al. have analyzed data from the large international Burden of Obstructive Lung Disease (BOLD) study including data from 10,001 individuals aged ≥ 40 years recruited from 14 sites (Vollmer et al., 2009). They concluded that using $FEV_1/FVC < LLN$ criterion instead of the fixed FEV_1/FVC criterion should minimize known age biases and better reflect clinically significant irreversible airflow limitation (Vollmer et al., 2009). Miller et al. determined the discrepancy rates in pulmonary function test interpretation between the GOLD guidelines of $FEV_1/FVC < 0.7$ for detecting airway obstruction and an FEV_1 of 80% predicted for detecting and classifying the severity of COPD (Miller et al., 2011). They investigated 11,413 patients with pre bronchodilator lung function tests and concluded that using 80% predicted and fixed thresholds can lead to substantial misclassification of disease that affects $> 20\%$ of patients compared to using LLN in diagnosing pulmonary obstruction. Shirtcliffe et al. investigated 749 people by post bronchodilator spirometric tests (Shirtcliffe et al., 2007). For adults ≥ 40 years, 14.2% were obstructive according to the GOLD definition and 9.0% according to obstruction defined using LLN.

In an editorial published in the European Respiratory Journal in 2007, Mannino argued for the fixed FEV1/FVC quotient to define pulmonary obstruction in favor of simplicity and that it is more sensitive to identify patients at risk of death and COPD related hospitalization (Mannino et al., 2003).

The latter position was also argued by Firdaus et al (Firdaus et al., 2011). However, the prediction of death and hospitalization has nothing to do with defining the diagnosis of the disease (Pellegrino et al. 2008). Spirometry software and hardware have changed and there is no longer a need for manual calculations of predicted spirometric values.

In a recent Swedish study, a random sample of 518 men and women in nine age cohorts 60, 66, 72, 78, 81, 84, 87, 90 and 93 years were drawn from the municipality registers and were investigated with spirometry using different guidelines and reference values (Szanto, et al., 2010). In the whole population, the prevalence of airway obstruction was 22.5% using FEV1/(F)VC <0.7 and 10.1% using the FEV1/(F)VC<expected for age and gender to define obstruction by using the Swedish spirometric reference values by Hedenström et al. Smoking habits had a great impact on the prevalence figures. Among current smokers the prevalence of pulmonary obstruction was 41.7%, among ex-smokers 22.7% and 15.5% among never-smokers using FEV1/(F)VC <0.7 to define obstruction. The corresponding figures using FEV1/(F)VC<expected for age and gender to define obstruction were 25.0%, 9.7% and 4.9% respectively. Using the FEV1/(F)VC<expected for age and gender definition yielded lower prevalence rates in all age groups and in both genders. The highest prevalence, 76.9%, was seen among current male smokers in the age cohort 72-81 years when airway obstruction was defined as FEV1/(F)VC <0.7. Using the FEV1/(F)VC< expected for age and gender definition yielded a prevalence of 46.2% in the same group. It is notable that 23.9% of never-smokers in the age cohort 84-93 years were classified as obstructive using FEV1/(F)VC <0.7 to define obstruction but 10.1% using the age and gender adjusted ratio (Table1).

Age cohorts Gender	60-94			60-71			72-82			83-94		
	All (n=565)	M (n=223)	F (n=342)	All (n=200)	M (n=90)	F (n=110)	All (n=208)	M (n=83)	F (n=125)	All (n=157)	M (n=50)	F (n=107)
Current-smokers												
FEV1/(F)VC<0.7	41.7	50.0	35.7	35.2	33.3	36.7	57.7	76.9	38.5	37.5	66.7	30.8
FEV1/(F)VC<LLN	25.0	30.0	21.4	22.2	20.8	23.3	34.6	46.2	23.1	18.8	33.3	15.4
Ex-smokers												
FEV1/(F)VC<0.7	22.7	19.8	27.0	14.9	7.3	24.2	25.3	27.7	21.9	34.4	26.1	55.6
FEV1/(F)VC<LLN	9.7	9.0	10.8	9.5	2.4	18.2	8.9	12.8	3.1	12.5	13.0	11.1
Never-smokers												
FEV1/(F)VC<0.7	15.5	18.1	14.6	6.9	8.0	6.4	12.6	13.0	12.5	23.9	33.3	21.2
FEV1/(F)VC<LLN	4.9	6.9	4.2	1.4	0	2.1	1.9	0	2.5	10.1	20.8	7.1

Table 1. Variation in prevalence of airway obstruction defined FEV1/(F)VC<0.7 and Lower Limit of Normal (FEV1/(F)VC<expected for age and gender) in the study population (n=565) related to smoking habits. Hedenstrom et al. normal spirometric values. No smoking data in 9 subjects. M= males, F= females. Figures in percent.

In an open letter by Philip Quanjer, Paul Enright, Martin Miller, Janet Stocks, Gregg Ruppel, Maureen Swanney, Robert Crapo, Ole Pedersen, Emanuel Falaschetti, Jan Schouten and Robert Jensen to the members of the GOLD committee, the group appealed to change the method by which mild airway obstruction is defined by the GOLD guidelines in order to abandon the fixed ratio in favor of the lower limit of normal (Quanjer et al., 2010).

10. Conclusions

A diagnosis of COPD should be considered in any smoker, especially in smokers who have breathing symptoms characterized by dyspnea, chronic cough or sputum production and who are aged 40 years or more. For the diagnosis and assessment of COPD, spirometry is the golden standard.

However, the diagnosis of pulmonary obstruction depends very much on the criteria used for definition of airway obstruction and on which spirometric normal values are applied. Normal values derived from the population investigated should be used.

Defining and diagnosing pulmonary obstruction using a fixed FEV1/(F)VC quotient <0.7 is simple to use in clinical practice but might result in an under-diagnosis in younger subjects and a substantial over-diagnosis in older subjects. Using an age-adjusted FEV1/(F)VC quotient to define pulmonary obstruction can be suggested to reduce the risk of over-diagnosis among elderly and under-diagnosis in younger subjects.

COPD is usually a progressive disease and lung-function can be expected to degrade over time. Therefore spirometry should be repeated over time, E.g. once a year.

Earlier diagnosis will allow earlier, and more aggressive efforts to make the patients quit smoking, the most important and effective therapy.

11. Appendix

11.1 Reference equations

The range of spirometric values obtained from a healthy population is assumed to represent normal. There are an overwhelming number of published reference equations.

11.2 Abbreviations

NA = Not Available

VC = Vital Capacity

FVC = Forced Vital Capacity

FEV1 = Forced Expiratory Volume in one second

FEV6 = Forced Expiratory Volume in six seconds

H = Height (cm or m)

A = Age (yrs)

pr = Predicted

LLN = Lower Limit of Normal (The lower fifth percentile of the reference population. Can be calculated by subtracting 1.64 times the standard deviation from the mean, i.e. the expected value (Firdaus et al., 2011).

11.3 Equations

Swedish participants. Between 7 to 70 years of age. Smokers and non smokers. (Berglund et al., 1963).

Male subjects:

$$\text{FVC Berglund} = (4.81 \times H) - (0.020 \times A) - 2.81$$

$$\text{FEV1 Berglund} = (3.44 \times H) - (0.033 \times A) - 1.00$$

Female subjects:

$$\text{FVC Berglund} = (4.04 \times H) - (0.022 \times A) - 2.35$$

$$\text{FEV1 Berglund} = (2.67 \times H) - (0.027 \times A) - 0.54$$

Swedish participants. Between 20 to 70 years of age. Smokers and non smokers. (Hedenström et al., 1985; Hedenström et al., 1986)

Male subjects:

$$\text{VC Hedenstrom} = (7.52 \times H) + (0.0471 \times A) - (0.000686 \times A^2) - 8.56$$

$$\text{FVC Hedenstrom} = (7.44 \times H) + (0.0467 \times A) - (0.000705 \times A^2) - 8.44$$

$$\text{FEV1 Hedenstrom} = (5.09 \times H) + (0.0145 \times A) - (0.000406 \times A^2) - 4.67$$

Female subjects:

$$\text{VC Hedenstrom} = (5.52 \times H) - (0.0119 \times A) - (0.000145 \times A^2) - 4.329$$

$$\text{FVC Hedenstrom} = (5.45 \times H) - (0.0143 \times A) - (0.000118 \times A^2) - 4.205$$

$$\text{FEV1 Hedenstrom} = (2.58 \times H) - (0.0281 \times A) + 0.13 \quad (A^2 \text{ this term is not included})$$

The European Community of Coal and Steel (ECCS) European Participants. Between 18 to 70 years of age. Smokers and non smokers. (Quanjer et al., 1993)

Male subjects:

VC ECCS NA

$$\text{FVC ECCS} = (5.76 \times H) - (0.0260 \times A) - 4.340$$

$$\text{FEV1 ECCS} = (4.30 \times H) - (0.0290 \times A) - 2.49$$

Female subjects:

NA NA

$$\text{FVC ECCS} = (4.43 \times H) - (0.0260 \times A) - 2.89$$

$$\text{FEV1 ECCS} = (3.95 \times H) - (0.0250 \times A) - 2.60$$

Lifelong asymptomatic non-smoking Caucasian US subjects as part of NHANS III. Between 20 to 80 years of age. (Hankinson et al., 1999).

Male subjects:

$$\text{FVC pr Hankinson} = (0.00018642 \times H^2) + (0.00064 \times A) - (0.000269 \times A^2) - 0.1933$$

$$\text{FVC}_{LLN} = (0.00015695 \times H^2) + (0.00064 \times A) - (0.000269 \times A^2) - 0.1933$$

$$\text{FEV1pr} = (0.00014098 \times H^2) - (0.01303 \times A) - (0.000172 \times A^2) + 0.5536$$

$$\text{FEV1}_{LLN} = (0.00011067 \times H^2) - (0.01303 \times A) - (0.000172 \times A^2) + 0.5536$$

$$\text{FEV6 pr} = (0.00018188 \times H^2) - (0.00842 \times A) - (0.000223 \times A^2) + 0.1102$$

$$FEV6_{LLN} = (0.00015323 \times H^2) - (0.00842 \times A) - (0.000223 \times A^2) + 0.1102$$

Female subjects:

$$FVC_{pr} = (0.00014815 \times H^2) + (0.01870 \times A) - (0.000382 \times A^2) - 0.3560$$

$$FVC_{LLN} = (0.00012198 \times H^2) + (0.01870 \times A) - (0.000382 \times A^2) - 0.3560$$

$$FEV1_{pr} = (0.00011496 \times H^2) - (0.00361 \times A) - (0.000194 \times A^2) + 0.4333$$

$$FEV1_{LLN} = (0.00009283 \times H^2) - (0.00361 \times A) - (0.000194 \times A^2) + 0.4333$$

$$FEV6_{pr} = (0.00014395 \times H^2) + (0.01317 \times A) - (0.000352 \times A^2) - 0.1373$$

$$FEV6_{LLN} = (0.00011827 \times H^2) + (0.01317 \times A) - (0.000352 \times A^2) - 0.1373$$

H=height in cm!

**Asymptomatic never smoking adults in Norway. Between 20 to 80 years of age.
(Langhammar et al., 2001)**

Male subjects:

$$FVC_{Langhammar} = e^{(-12.396 + 2.7333 \times \ln H - 0.0000592 \times AA)}$$

$$FEV1_{Langhammar} = e^{(-10.556 + 2.342 \times \ln H - 0.0000685 \times AA)}$$

Female subjects:

$$FVC_{Langhammar} = e^{(-9.851 + 2.189 \times \ln H - 0.000143 \times AA + 0.006439 \times A)}$$

$$FEV1_{Langhammar} = e^{(-9.091 + 2.004 \times \ln H - 0.000163 \times AA + 0.007237 \times A)}$$

H=height in cm!

12. References

- American Thoracic Society. Standardization of spirometry, 1994 update. *Am J Respir Crit Care Med*, 152, 1107-1136.
- American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. (1995) *Am J Respir Crit Care Med*, 152, 77s-120s.
- Anthonisen, N.R., Connett, J.E., Kiley, J.P., Altose, M.D. & Bailey, W.C. (1994) Effects of smoking intervention and the use of inhaled anticholinergic bronchodilator on the rate of decline of FEV1. The lung health study. *JAMA*, 272(19), 1497-14505.
- Anthonisen, N.R. (2005) The British hypothesis revisited. *Eur Respir J*, 23, 657-658.
- Antó, J.M., Vermeire, P., Vestbo, J., & Dunyer, J. (2001) Epidemiology of chronic obstructive pulmonary disease. *Eur Respir J*, 17(5), 982-984.
- Badham C, (1814) An essay on bronchitis: with a supplement containing remarks on simple pulmonary abscess. 2nd ed. London: J Callow
- Bakke, P.S., Baste, V., Hanao, R., & Gulsvik, A. (1991) Prevalence of obstructive lung disease in a general population: telation to occupational title and exposure to some airborne agents. *Thorax*, 46(12), 863-870.
- Berglund, E., Birath, G., Grimsby, G., Kjellmer, I., Sandqvist, L., & Söderholm, B. (1963) Spirometric studies in normal subjects. Forced expirograms in subjects between 7 and 70 years of age. *Acta Med Scand* 173, 185- 192.
- Briscoe W.A., Nash E.S. (1965) The slow space in chronic obstructive pulmonary disease *Ann NY Acad Sci*, 121, 706-722.

- Brändli, O., Schindler, C., Künzli, N., Keller, R., & Perruchoud, A.P. (1996) Lung function in healthy never smoking adults: reference values and lower limits of normal of a Swiss population. *Thorax*, 51(3), 277-283.
- Brändli, O., Schindler, C., Leuenberger, P.H., Baur, X., Degens, P., et al. (2000) Re-estimated equations for 5th percentiles of lung function variables. *Thorax*, 55(2), 173-174.
- Buist, A.S., McBurnie, M.A., Vollmer, W.M., Gillespie, S., Burney, P., et al. (2007) International variation in the prevalence of COPD (The Bold Study): a population-based prevalence study. *Lancet*, 370, 741-750.
- Burrows, B., Cline, M.G., Knudson, R.J., Taussig, L.M., & Lebowitz, M.D. (1983) A descriptive analysis of the growth and decline of the FVC and FEV1. *Chest*, 83(5), 717-724.
- Burrows, B., Knudson, R.J., Camilli, A.E., Lyle, S.K., & Lebowitz, M.D. (1986) The "Horse-Racing Effect" and predicting decline in forced expiratory volume in one second from screening spirometry. *Am Rev Respir Dis*, 135, 788-793.
- Celli, B.R., Halbert, R.J., Isonaka, S., & Schau, B. (2003) Population impact of different definitions of airway obstruction. *Eur Respir J*, 22, 268-273.
- Celli B.R. & MacNee W. (2004) Standards for diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J*, 23(6), 932-946.
- Cerveri, I., Corsico, A.G., Accordini, S., Ansaldo, E., Anto, J.M., et al. (2008) Underestimation of airflow obstruction among young adults using FEV1/FVC < 70% as a fixed cut-off: a longitudinal evaluation of clinical and functional outcomes. *Thorax*, 63(12), 1040-1045.
- Chapman, K.R., Mannino D.M., Soriano J.B., Vermeire P.A., et al. (2006) Series "The Global Burden of Chronic Obstructive Pulmonary Disease. *Eur Respir J*, 27, 188-207.
- Ciba Guest Symposium 1959. Terminology, definition, and classification of chronic pulmonary emphysema and related conditions. *Thorax*, 14, 286-299
- Committee on Diagnostic Standards for Nontuberculous Respiratory Diseases, American Thoracic Society. Definitions and classification of chronic bronchitis, asthma, and pulmonary emphysema. (1962) *Am Rev Respir Dis*, 85, 762-769
- Facchini, F., Flori, G., Bedogni, G., Galetti, L., Ismagulov, O., et al. (2007) Spirometric reference values for children and adolescents from Kazakhstan. *Ann hum Biol*, 34(5), 519-534.
- Falaschetti, E., Laiho, J., Primatesta, P., & Purdon, S. (2004) Prediction equations for normal and low lung function from the Health Survey for England. *Eur Respir J*, 23, 456-463.
- Firdaus, A.A., Hoesein, M., Zanen, & Lammers, J-W.J (2011) Lower limit of normal or FEV1/FVC < 0.70 in diagnosing COPD: An evidence-based review. *Respir Med*, 105, 907-915.
- Fletcher, C., Peto, R., Tinker, R., & Speitzer, F.E. (1976) The natural History of Chronic Bronchitis and Emphysema. Oxford University Press.
- Fletcher, C., & Peto, R. (1977) The natural history of chronic airflow obstruction. *Br Med J*, 1, 1645-1648.
- Foreman, M.G., Zhang, L., Murphy, J., Hansel, B., et al. (2011) Early-onset Chronic Obstructive Pulmonary Disease is associated with female sex, material factors and African American race in COPD Gene study. *Am J Respir Crit Care Med*, 184(4), 414-420.

- Fukuchi, Y. (2009) The aging lung and chronic obstructive pulmonary disease. *Proc Am Thorac Soc*, 6(7), 570-572.
- Garcia-Aymerich, J., (2011) Are we ready to say that sex and race are key risk factors for COPD. *Am J Respir Crit Care Med*, 184, 388-390.
- Garshick, E., Segal, M.R., Worobec, T.G., Salekin, CM., & Miller, M.J. (1989) Alcohol consumption and chronic obstructive pulmonary disease. *Am Rev Respir Dis*, 140, 373-378.
- George, R.B. (1999) Course and prognosis of chronic obstructive pulmonary disease. *Am J Med Sci*, 318(2), 103-106.
- Global Initiative for Chronic Obstructive Lung Disease [GOLD] Updated 2010 <http://www.goldcopd.org/guidelines-resources.html>
- Halbert R.J., Isonaka S., George D., Iqbal. (2003) Interpreting COPD Prevalence Estimates. What is the True Burden of the Disease? *Chest*, 123(5), 1684-1692
- Hankinson J.L., Odencrantz, J.R., & Feden, K.B. (1999) Spirometric reference values from a sample of the general U.S. population. *Am J Respir Crit Care Med*, 159(1), 179-187.
- Hansen, J.E., Sun, X.G., & Wasserman, K. (2007) Spirometric criteria for airways obstruction: Use percentage of FEV1/FVC ratio below the fifth percentile, not <70%. *Chest*, 131, 349-355.
- Hedenstrom, H., Malmberg, P., & Agarwal K. (1985) Reference values for lung function tests in females. Regression equations with smoking variables. *Bull Eur Physiopathol Respir*, 21, 551-557
- Hedenstrom, H., Malmberg, P., & Fridriksson, H.V. (1986) Reference values for pulmonary function tests in men. Regression equations which include tobacco smoking variable. *Uppsala J Med Sci*, 91, 299-310.
- Hurst, J.R. (2010) Upper airway.3: Sinonasal involvement in chronic obstructive pulmonary disease. *Thorax*, 65(1), 85-90.
- Ip, M.S., Ko, F.W., Lau, A.C., Tang, K.S. & Choo, K., et al. (2006) Updated spirometric reference values for adult Chinese in Hong Kong and implications on clinical utilization. *Chest*, 129(2), 384-392.
- Janssens, J.P., Pache, J.C., & Nicod, L.P. (1999) Physiological changes in respiratory function associated with ageing. *Eur Respir J*, 13, 197-205,
- Kanervisto, M., Vasankari, T., Laitinen, T., Heliövaara, M., Jousilathi, S., et al. (2011) Low socioeconomic status is associated with chronic obstructive diseases. *Respire Med*, 105(8), 1140-1146.
- Kerstjens, H.A.M., Rijcken, B., Schouten, J.P., & Postma, D.S. (1997) Decline of FEV1 by age and smoking status : facts, figures, and fallacies. *Thorax*, 52, 820-827.
- Kirkpatrick, P., & Dransfield, M.T. (2009) Racial and sex differences in chronic obstructive pulmonary disease susceptibility, diagnosis, and treatment. *Curr Opin Pulm Med*, 15(2), 100-104.
- Knudson, R.J., Clark, D.F., Kennedy, T.C., & Knudson, D.E. (1977) Effect of ageing alone on mechanical properties of the normal adult human lung. *J Appl Physiol*, 43, 1054-1062.
- Kuster, S.P., Kuster, D., Schindler, C., Rochat, M.K., Braun, J., et al. (2008) Reference equations for lung function screening of healthy never-smoking adults 18-80 years. *Eur Respir J*, 31, 860-868.

- Lange, P., Groth, S., Mortensen, J., Appleyard, M., Nyboe, J., et al. (1998) Pulmonary function is influenced by heavy alcohol consumption. *Am Rev Respir Dis*, 137, 1119-1123.
- Langhammer, A., Johnsen, R., Gulsvik, A., Holmen, T.R., & Bjermer, L. (2001) Forced spirometry reference values for Norwegian adults: the Bronchial Obstruction in Nord-Trøndelag Study. *Eur Respir J*, 18(5), 770-779.
- Laurell, C.B., Eriksson, S. (1963). The electrophoretic alpha 1-globulin pattern of serum in alpha 1-antitrypsin deficiency. *Scand J Clin Lab Invest*, 15 (2), 132-140.
- Lee, P.N., & Fry, J.S. (2010) Systematic review of the evidence relating FEV1 decline to giving up smoking. *BMC Med*, 8 (84).
- Lindgren, A., Stroh, E., Montnmery, P., Nihln, U., Jakobsson, K., & Axmon A. (2009) Traffic-related air pollution associated with the prevalence of asthma and COPD/chronic bronchitis. A cross-sectional study in Southern Sweden. *Int J Health Geogr*, 8:2.
- Lundbck, B., Lindberg, A., Lindstrm, M., Rnnmark, E., Jonsson, A.C. et al. (2003) Not 15 but 50% of smokers develop COPD? Report from the Obstructive Lung Disease in Northern Sweden Studies. *Respir Med*, 97(2), 115-122.
- Macchia, A., Moncalvo, J.J., Kleinert, M., Comignani, P.D., Gimeneo, G., et al. (2011) Unrecognized ventricular dysfunction in chronic obstructive pulmonary disease. *Eur Respir J* Jun 23. [Epub ahead of print]
- van Manen, J.G., Bindels, P.J., Jzermans, C.J., van der Zee, J.S., Bottema, B.J., et al. (2001) Prevalence of comorbidity in patients with a chronic airway obstruction and controls over the age of 40. *J Clin Epidemiol*, 54(3), 287-293.
- Mannino, D.M., Buist, A., Petty, T., Enright, P., & Redd, S. (2003) Lung function and mortality in the United States: data from the First National Health and Nutrition Examination Survey follow up study. *Thorax*, 58(5), 388-393.
- Mannino D.M., & Buist A.S. (2007) Global burden of COPD: risk factors, prevalence, and future trends. *Lancet*, 370(9589), 765-773.
- Mannino, D.M. (2007) Defining chronic obstructive pulmonary disease... and the elephant in the room. *Eur Respir J*, 30, 189-190.
- Miller, M.R., Quanjer, P.H., Swanney, M.P., Ruppel, G., & Enright, P.L. (2011) Interpreting lung function data using 80% predicted and fixed thresholds misclassifies more than 20% of patients. *Chest*, 139(1), 52-59.
- Murray, C.J., & Lopez A.D. (2007) Global mortality, disability, and the contribution of risk factors: Global Burden of Disease study. *Lancet*, 349(9063), 1436-1442
- Nathell, L., Nathell, M., Malmberg, & Larsson, K. (2007) COPD diagnosis related to different guidelines and spirometry techniques. *Respir Res*, 8(89)
- Nihln, U., Montnmery, P., Andersson, M., Persson, C.G., Nyberg, P., et al. (2008) Specific nasal symptoms and symptom-provoking factors may predict increased risk of developing COPD. *Clin Physiol Funct Imaging*, 28(4), 240-250.
- Ostrowski, S., Grzywa-Celinska, A., Mieczkowska, J., Rychlik, M., Lachowska-Kotowska, P., et al. (2005) Pulmonary function between 40 and 80 years of age. *J Physiol Pharmacol*, 56, Suppl 4, 137-133.
- Pellegrino, P., Brusasco, V., Viegi, R.O., Crapo, F., Burgos, F., et al. (2008) Definition of COPD: based on evidence or opinion? *Eur Respir J*, 31, 681-690.
- Pereira, C.A., Sato, T., & Rodrigues, S.C. (2007) New reference values for forced spirometry in white adults in Brazil. *J Bras Pneumol*, 33(4), 397-406.

- Pérez-Padilla, R., Regalado, J., Vedal, S., Paré, P. Chapela, R., et al. (1996) Exposure to biomass smoke and chronic airway disease in Mexican women. A case-control study. *Am J Respir Crit Care Med*, 154(3 Pt 1), 701-706.
- Petty,T.L. (2006) The history of COPD. *Int J Chron Obstruct Pulmon Dis*, 1(1), 3-14.
- Pistelli, F., Bottai, M., Carrozzi, L., Baldacci, S., Simoni, M., et al. (2007) Reference equations for spirometry from a general population in central Italy. *Respir Med*, 101(4), 814-824.
- Postma, D.S., & Boezen, H.M. (2004) Rationale for the Dutch hypothesis. Allergy and airway hyperresponsiveness as genetic factors and their interaction with environment in the development of asthma and COPD. *Chest*, 126(2 Suppl), 96S-104S.
- Quanjer, P.H., Tammeling, G.J., Cotes, J.E., Pedersen, O.F., Peslin, R., & Yernault,J.C. (1993) Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests. European Community for steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J*, 6(Suppl. 16) 5s-40s.
- Quanjer, P., Enright, P., Miller, M., Stocks., Ruppel, G., et al. (2010) Open letter to the members of the GOLD committee.
http://www.spirxpert.com/controversies/Open_Letter.pdf
- Render, M.L., Weinstein, A.S., & Blaustein, A.S. (1995) Left ventricular dysfunction in deteriorating patients with chronic obstructive pulmonary disease. *Chest*, 107, 162-168.
- Rennard, S.I., & Vestbo, J. (2006) COPD: the dangerous underestimate of 15%. *Lancet*, 367(9518), 1216-1219.
- Rijcken, B., & Britton, J. (1998) Epidemiology of chronic obstructive pulmonary disease. *Eur Respir Mon*, 7, 41-73.
- Schermer, T.R.J., & Quanjer, P.H. (2007) COPD screening in primary care: who is sick? *Prim Care Respi J*, 16(1), 49-52.
- Schuneman, H.J., Grant, B.J., Frudenheim, J.L., Muti, P., McCann, S.E., et al. (2002) Evidence for a positive association between pulmonary function and wine intake in a population-based study. *Sleep Breath*, 6, 161- 173.
- Shirtcliffe, P., Weatherall, M., Marsh, S., Travers, J., & Hansell, A. (2007) COPD prevalence in a random population survey: a matter of definition. *Eur Respir J*, 30(2), 232-239.
- Siebling, L., Puhan, M.A., Muggensturm, P., Zoller, M., & ter Riet, G. (2011) Characteristics of Dutch and Swiss primary care COPD patients – baseline data of the ICE COLD ERIC study. *Clinical Epidemiology*, 3, 273-283.
- Silverman, E.K., Weiss, S.T., Drazen, J.M., Chapman, H.A., Carey, V., et al. (2000) Gender-Related Differences in Severe, Early-onset Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med*, 162(6), 2152-2158.
- Snider, G.L. (2000) Clinical relevance summary: Collagene vs elastin in pathogenesis of emphysema; cellular origin of elastases; bronchiolitis vs emphysema as a cause of airflow obstruction. *Chest*, 117, 244S-246S.
- Stanojevic, S., Wade, A., & Stocks, J. (2010) Reference values for lung function: past present and future. *Eur Respir J*, 36, 12-19.
- Swanney,M.P., Ruppel,G., Enright,P.L., Pedersen, O.F., Crapo,R.O., et al. (2008) Using the lower limit of normal for the FEV1/FVC ratio reduces the misclassification of airways obstruction. *Thorax*, 63,1046-1051.

- Szanto, O., Montnemery., & Elmstahl., S. (2010) Prevalence of airway obstruction in the elderly: results from a cross-sectional spirometric study of nine age cohorts between the ages of 60 and 93 years. *Prim Care Respi J*, 19(3), 231-236.
- Tabak,C., Smit, H.A., Rasanen, L., Fidanza, F., Menotti, A., et al. (2001) Alcohol consumption in relation to 20-year COPD mortality and pulmonary function in middle-aged men from three European countries. *Epidemiology*, 12, 239-245.
- Trupin, L., Earnest, G., San Pedro, M., Balmes, J.R., & Eisner. (2003) The occupational burden of chronic obstructive pulmonary disease. *Eur Respir J*, 22(3), 462-469.
- Turner, J.M., Mead, J., & Wohl, M.E. (1968) Elasticity of human lungs in relation to age. *Appl Physiol*, 25, 664-671. Varkey, A.B. (2004) Chronic obstructive pulmonary disease in women: exploring gender differences. *Curr Opin Pulm Med*, 10(2), 98-103.
- Vestbo, J., & Prescott, E. (1998) Update on the “Dutch hypothesis” for chronic respiratory disease. *Thorax*, 53(Suppl 2), 15S-19S.
- Vollmer,W., Gislason,P., Burney,P., Enright,P., Gulsvik,A. et al. (2009) Comparison of spirometric criteria for the diagnosis of COPD: results from the BOLD study. *Eur Respir J*, 34,588-597.
- Willemse, B.W.M., Postma, D.S., Timens, W, & ten Hacken, N.H.T. (2004) The impact of smoking cessation on respiratory symptoms, lung function, airway hyperresponsiveness and inflammation. *Eur Respir J*, 23, 464- 476.

IntechOpen

Primary Care at a Glance - Hot Topics and New Insights

Edited by Dr. Oreste Capelli

ISBN 978-953-51-0539-8

Hard cover, 446 pages

Publisher InTech

Published online 27, April, 2012

Published in print edition April, 2012

"Both among scientists and clinical practitioners, some find it easier to rely upon trivial explanations, while others never stop looking for answers". With these surprising words, Augusto Murri, an Italian master in clinical medicine, reminds us that medical practice should be a continuous journey towards knowledge and the quality of care. The book brings together contributions by over 50 authors from many countries, all around the world, from Europe to Africa, from Asia to Australia, from North to South America. Different cultures are presented together, from those with advanced technologies to those of intangible spirituality, but they are all connected by five professional attributes, that in the 1978 the Institute of Medicine (IOM)¹ stated as essentials of practicing good Primary Care: accessibility, comprehensiveness, coordination, continuity and accountability. The content of the book is organized according to these 5 attributes, to give the reader an international overview of hot topics and new insights in Primary Care, all around the world.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Peter Montnemey and Sölve Elmståhl (2012). Diagnosis of Chronic Obstructive Pulmonary Disease with Special Reference to Over- and Underdiagnosis Using Spirometry, Primary Care at a Glance - Hot Topics and New Insights, Dr. Oreste Capelli (Ed.), ISBN: 978-953-51-0539-8, InTech, Available from: <http://www.intechopen.com/books/primary-care-at-a-glance-hot-topics-and-new-insights/diagnosis-of-chronic-obstructive-pulmonary-disease-with-special-reference-to-over-and-underdiagnosis>

INTECH
open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](https://creativecommons.org/licenses/by/3.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen