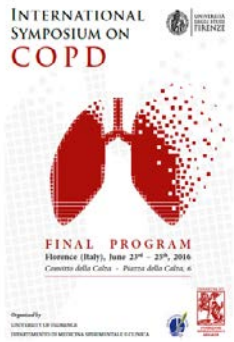
International Symposium on COPD

Florence (Italy), June 23-25, 2016

Highlights

Introduction



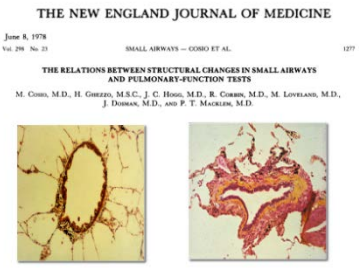
Prof. Pistolesi, the Chairman of the Symposium, opened the congress highlighting the scientific level of the faculty composed by some of the highest experts in COPD coming from all over the world. More than 300 people attended the event and among them, were physicians, experts in COPD and students. During the Symposium, some of the most interesting and updated topics in the field of COPD have been discussed and it was a very important opportunity to improve personal knowledge and professional skills.

To follow the presentations of this congress, click on this link: http://www.fondazione-menarini.it/Archivio-Eventi/2016/International-Symposium-on-COPD/Materiale-Multimediale … and, after having logged in, enter in the multimedia area.

Pathogenesis of COPD: a Dr. Hogg affair!
Introduced by Prof. Cosio

Centre for Heart Lung Innovation group photo, 2014

Prof. Cosio, introduced the opening lecture of Prof. Hogg (Vancouver, CND) on Pathogenesis of COPD, pointing out the history of this topic starting from the beginning of the studies performed by, then, Dr. Hogg, and the first publication in 1968 in the New England Journal of Medicine. A very exciting story that covers more than 70 years of discoveries that are linked to educational choices. The speaker emphasised the fact that many researchers have grown under the teaching of Dr. Hogg and that only in these last five years the "J. Hogg Centre" trained more than 590 young researchers from 31 countries.


THE NEW ENGLAND JOURNAL OF MEDICINE

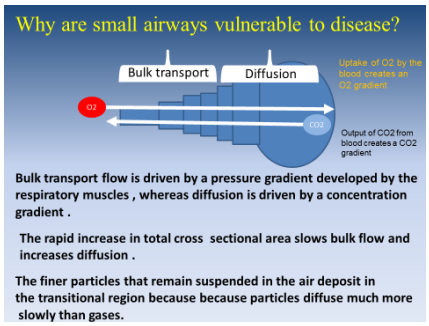
June 8, 1978

THE RELATIONS BETWEEN STRUCTURAL CHANGES IN SMALL AIRWAYS AND PULMONARY-FUNCTION TESTS

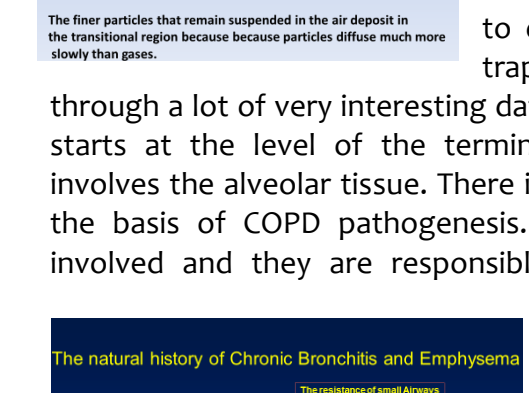
- **What is the main discovery performed by Dr. Hogg and published in 1968?**
- **What about the pulmonary tests and their publications in 1978?**
- **How many papers has Dr. Hogg published in 2015?**
- **How many young researchers have been trained in the last 5 years by the group of Prof. Hogg?**

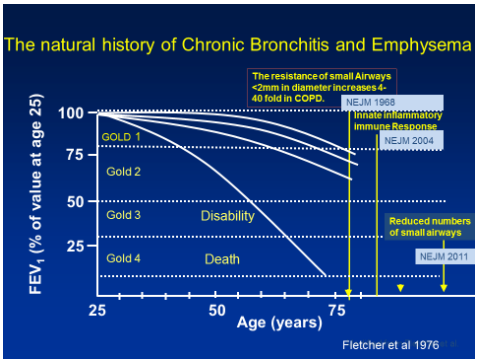
To reply to these and other questions just click on this link: http://www.fondazione-menarini.it/Archivio-Eventi/2016/International-Symposium-on-COPD/Materiale-Multimediale … and, after having logged in, enter the multimedia area.

Pathogenesis of COPD



Prof. Hogg addressed this very important topic pointing out the impact that the disease causes worldwide. In his speech, the speaker explained the deep mechanisms that lead to the elevation of resistances at the small airway level, the first step of the COPD pathogenesis. Prof. Hogg also presented the diagnostic technique applied in COPD to determine when people start to lose their terminal airways and to determine where the gas is trapped. The speaker, passing through a lot of very interesting data, demonstrated how COPD starts at the level of the terminal bronchioles and it then involves the alveolar tissue. There is a genetic predisposition at the basis of COPD pathogenesis. More than 100 genes are involved and they are responsible for a very high reactive response to air pollution and other similar factors. This event results first in an inflammation of the bronchioles and finally in an emphysema in the alveolar tissue. Prof. Hogg concluded his speech by underling that the knowledge of the pathogenesis of Chronic Bronchitis and Emphysema started in 1968 observing that the resistance of small airways < 2 mm in diameter increases 4-40 fold in COPD. This was nearly completed in 2011 observing how in COPD patients there is a significant reduced number of small airways.



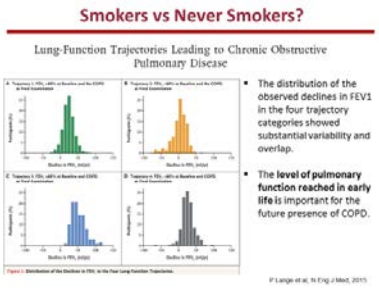


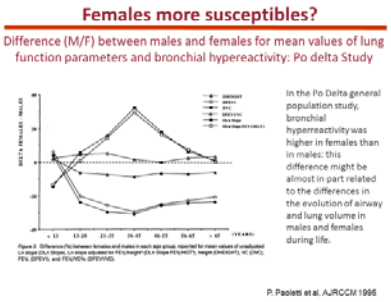
- **Why are small airways vulnerable to disease?**
- **What does it take to increase peripheral airway resistance 40 fold in COPD?**
- **What is the adaptive immune response in COPD?**
- **Why is microCT important in the diagnosis of COPD?**
- **What do the data of the population based study of 9 Canadian cities tell us on COPD distribution?**
- **Why is important to connect micro CT to histology?**
- **What is the main airways remodelling in COPD?**

To reply to these and other questions just click on this link: http://www.fondazione-menarini.it/Archivio-Eventi/2016/International-Symposium-on-COPD/Materiale-Multimediale … and, after having logged in, enter in the multimedia area.

Smokers and non-smokers, among males and females

Prof. Carrozzi from Pisa (I) presented very interesting data regarding this topic. The global prevalence of COPD is attested at 11.4% and in 2012, the World Health Assembly (WHA) endorsed reduction of premature death from COPD by 25% by the years 2025. With this data, the speaker started her presentation identifying other main risk factors for COPD in addition to smoking, such as air pollution and occupational exposure. She stressed the point that risk factors exposures may differ between gender and countries. Concerning gender, Prof. Carrozzi, pointed out the difference of prevalence of COPD between males and females, which are linked to smoking habits, raising in females and tending to decline in males.



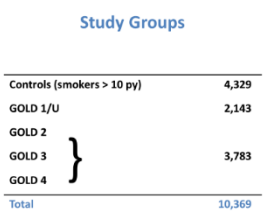


In the second part of her speech, the speaker presented data on clinical studies that deeply analyse the relationship between smoking habits and COPD. She also discussed the point about the difference between never smokers and ever smokers in COPD prevalence and finally described the difference in gender between males and females in terms of susceptibility in developing COPD.

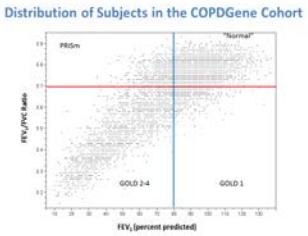
- **Are studies on the relationship between smoking and COPD still relevant?**
- **Is there a difference between COPD in never smokers and COPD in ever smokers?**
- **Are women more susceptible to COPD than men?**
- **What is the relationship between COPD and lung cancer?**
- **What is the mortality rate for males and females with COPD in the US?**
- **What is the prevalence of COPD in males and females in Po Delta Italian study?**
- **What is the difference in prevalence and incidence of COPD between smokers and non-smokers?**

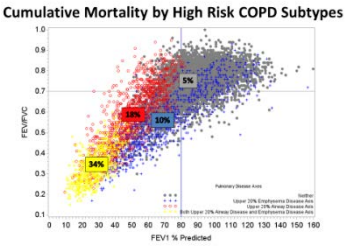
To reply to these and other questions, just click on this link: http://www.fondazione-menarini.it/Archivio-Eventi/2016/International-Symposium-on-COPD/Materiale-Multimediale … and, after having logged in, enter in the multimedia area.

The COPDGene study



Prof. Crapo from Denver (USA) addressed this topic presenting new data generated by his team of researchers. The COPDGene study is a trial running on more than 10.000 patients with COPD at different levels of severity. The speaker talked about the population enrolled in this cohort study pointing out the differences concerning age, sex, smoking habits and the evaluation to be performed from phenotyping to follow up, imaging and genetics. In this study the COPD subtypes are well defined by applying CT, clinical settings, biomarkers and genetics. Prof. Crapo presented data of early diagnosis of COPD and pointed out the principal components analysis to define high-risk subtypes of COPD. By applying this methodology, it was possible to define the study population, which is divided into two subpopulations: the so-called airway disease axis and the emphysema disease axis. The speaker presented data on mortality, dyspnoea, six-minute walk distance, SGRQ, exacerbations and cardiovascular disease in these two high risk COPD subtypes populations.

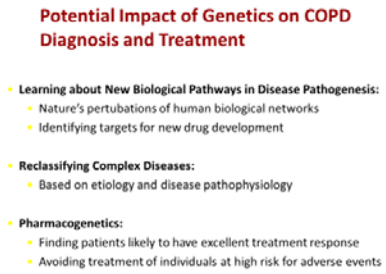




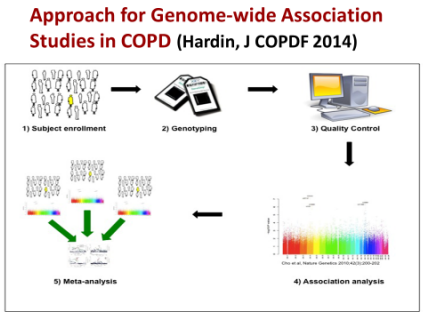
- **What are the principal components analysis performed in the COPDGene study?**
- **What are the COPD subtypes identified in the study population?**
- **What are the methods used for the cohort evaluation in the COPDGene study?**
- **What is the COPD distribution by age in the COPDGene study?**
- **Are smokers without obstruction really normal?**
- **What is the global mortality rate in the two subtypes COPD populations?**

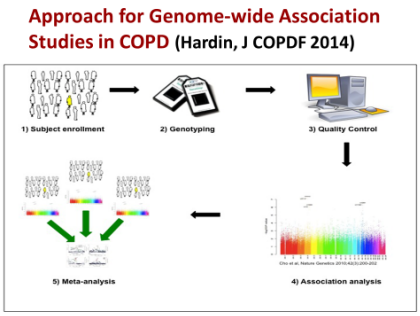
To reply to these and other questions, just click on this link: http://www.fondazione-menarini.it/Archivio-Eventi/2016/International-Symposium-on-COPD/Materiale-Multimediale … and, after having logged in, enter in the multimedia area.

Novel findings in genetics



Prof. Silverman from Boston (USA) talked about this very important topic and its impact on present-day medicine. The speaker started his speech pointing out the evidence of genetic determinants in COPD patients and explaining what the potential impact of genetics on COPD diagnosis and treatment is about. In recent years, the methods used to discover complex genetic disease has also changed, starting from linkage analysis to systems genetics/networks. The speaker went further on to explain these methodologies in order to define the state of the art of genetics applied to COPD research. Among the current approaches to find COPD susceptibility genes, Prof. Silverman presented genome-wide association studies that have the potentiality to discover new genes. Starting from this point, the speaker went on to explain the next steps represented by strategies of genes localization and genes functional validation based on cell and animal models. In the last part of his presentation Prof. Silverman presented data produced by applying these methodologies and in conclusion pointed out COPD as a model of complex disease.





- **What are the main reasons of COPD as a model of complex disease?**
- **What are the main strategies to be applied for the process of gene localization?**
- **What are the current approachs to find COPD susceptibility genes?**
- **What are the main steps in the approach for genome-wide association studies?**
- **What are the main steps passing through the discovery in complex disease genetics?**
- **What are the main evidences for genetics determinants in COPD?**

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Genotypes and phenotypes

Dr. Castaldi from Boston (USA) went deep into this topic with his talk. He started by explaining that COPD is a heterogeneous disease and it encompasses multiple disease processes. The speaker presented data related to COPD subtypes and to COPD axes applying a clustering method to identify novel COPD features and feature combinations that can describe distinct subset of COPD patients. In his presentation, Prof. Castaldi stated that clustering is a useful exploratory technique for identifying COPD-related features and subgroups for further investigation. The limit of this type of analysis has quite a low level of reproducibility. To better describe COPD phenotypic data, it is preferable to use continuous representations such as Principal components (disease axes) more respectable for the nature of COPD. The speaker concluded his talk underlying that the categorization in subtypes is necessary from a clinical point of view, but is also necessary to pay close attention to data structures, for an appropriate use of continuous versus categorical representations.

- **Why take a data-driven approach to COPD subtyping?**
- **Is COPD a pathology composed by different subtypes or is it a continuum of different clinical features?**
- **What is the definition of COPD subtypes?**
- **What is the definition of disease axes?**
- **How is COPD an heterogeneous disease?**

To reply to these and other questions, just click on this link:
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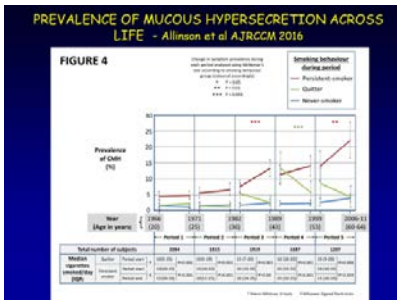
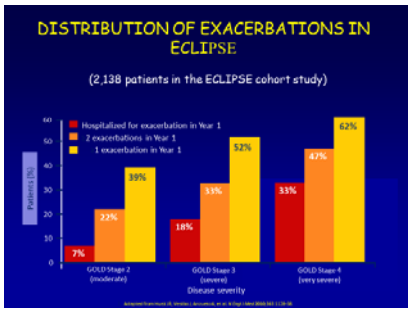
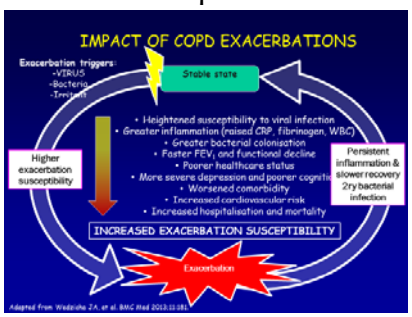
Is the frequent exacerbator a true phenotype?



Prof. Wedzicha from London (UK) spoke about this very current topic in our times. The speaker started her presentation pointing out the factors predicting frequent exacerbations among COPD subjects as daily cough, sputum and a poor quality of life. In addition, persistent-smokers have a higher prevalence of exacerbations in comparison to non-smokers or never smokers. The presence of exacerbations is related to some signs of inflammation, like cytokine level in sputum, plasma fibrinogen levels and aortic pulse wave velocity changes depending on the presence of airway infection. From a social point of view, patients with frequent exacerbations have a characteristic profile: they spend more time at home and have a daily step count significantly lesser than patients with infrequent exacerbation. In the second part of her speech, Prof. Wedzicha presented data from clinical studies on patients with COPD to better define the phenotype profile of these patients. She explained the effect of inflammation and the effect of pharmacological treatment on patients with COPD exposed to exacerbation. In conclusion, Prof. Wedzicha pointed out the phenotype model for patients defined as frequent exacerbators.





- **What are the factors predicting frequent exacerbators?**
- **What are the differences in exacerbation's prevalence in COPD' patients with and without chronic cough and sputum?**
- **What is the relationship between FEV_1 and exacerbation frequency?**
- **What are the main powerful predictors of exacerbation?**
- **What is the effect of the pharmacological treatment on exacerbation?**

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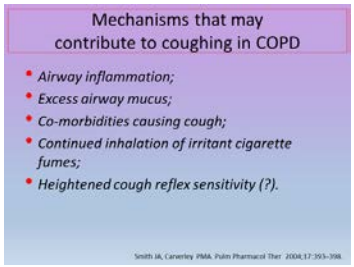
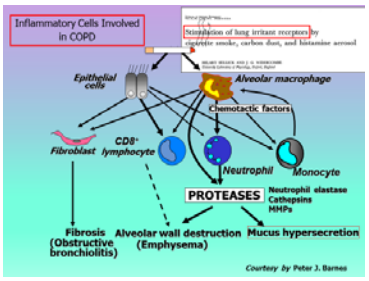
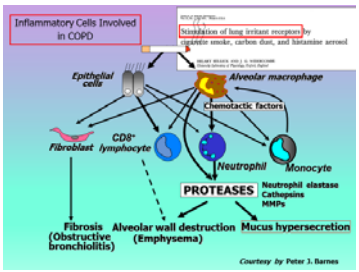
Cough



Prof. Fontana from Florence (I) in his talk went deeper into the topic by underling that in the COPD definition, there is a main lack: no reference to cough. Cough is intrinsically linked with COPD and the speaker presented data confirming this link. The presence of cough in COPD patients is predictive for higher risk for COPD exacerbation and death. Prof. Fontana pointed out all the main mechanisms leading to coughing in COPD: airway inflammation, excess airway mucus, comorbidities causing cough, cigarette smoking, heightened cough reflex sensitivity. In the last part of his presentation the speaker spoke about diagnosis and treatment of cough in patients with COPD, underlining that there are only to methods for measuring cough severity: subject reporting and cough counting. Also from a treatment point of view there are little data on medicines applicable for cough therapy and the most of them are clearly unsatisfactory in alleviating cough symptoms in COPD patients. There is also a lack in guidelines for optimal treatment of cough. Prof. Fontana concluded his presentation pointing out that Regulatory Authorities should promote simple and reliable means to objectively assess cough in the clinical setting.





- **What are the main mechanisms that may contribute to coughing in COPD?**
- **What is the role of airway inflammation in pathogenesis of cough in COPD patients?**
- **What is the effect of the treatment on cough in COPD patients?**
- **Why is cough important in COPD pathophysiology and evolution?**

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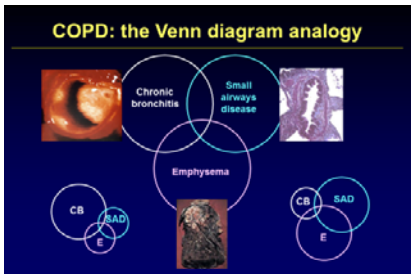
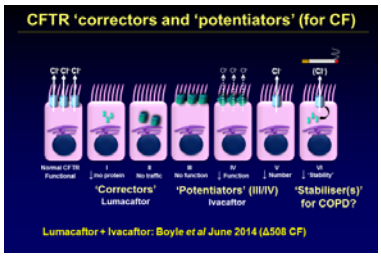
Mucous production



Prof. Duncan from London (GB) spoke about mucus production in COPD patients, starting from the description of a particular phenotype, the so called mucus hypersecretory, typical in patients with chronic bronchitis. From a treatment point of view there are a lot of possibilities in these patients and the speaker presented them by starting with the description of the interactions between EGF receptors and their blockers. In his speech Prof. Duncan presented data on Mans, a MARCKS related peptide, a new drug that in a mouse model of asthma has demonstrated to block mucus hypersecretion. Another very interesting option is represented by the so called "hydrators" that means synthetize drugs that are able to rehydrate the mucus present in the bronchia.



- **What is the relationship between chronic bronchitis, emphysema and small airways disease?**
- **What is the Clinical impact of airway mucus hypersecretion in COPD patients?**
- **What are the possibilities on Drug 'treatment' of airway mucus hypersecretion in COPD patients?**
- **What is the mechanism of action of the (GF-R blockers?**
- **What about MANS MARCKS related peptide?**

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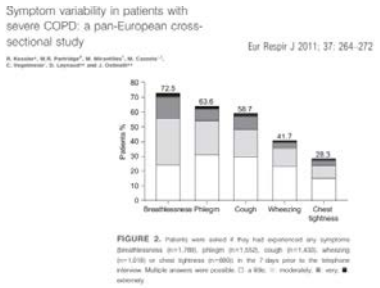
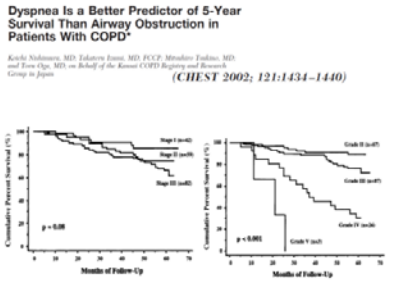
Dyspnea


Symptom variability in patients with severe COPD: a pan-European cross-sectional study

Eur Respir J 2011; 37: 264–272

FIGURE 2. Patients were asked if they had experienced any symptoms (breathlessness (n=1,788), phlegm (n=1,552), cough (n=1,435), wheezing (n=1,618) or chest tightness (n=880)) in the 7 days prior to the telephone interview. Multiple answers were possible. □ a little; ■ moderately; ■ very; ■ severely.

Prof. Torchio from Turin (I) spoke about dyspnea pointing out its clinical impact, diagnosis, treatment and rehabilitation procedures. From a psychopathological point of view there are some neurobiological models which are able to understand dyspnea and the speaker described the effect of dynamic hyperinflation during exercise, affecting some physiological mechanisms leading to dyspnea in COPD. Pointing at the methods for measuring the level of dyspnea, Prof. Torchio explained that the current instruments used for diagnosis are basically the same proposed in 1992 by the American Thoracic Society (ATS). They are composed by 0-10 category-ratio scale, visual analogical scale and other similar tests. Prof. Torchio also spoke about the relationship between COPD and obesity, stressing the point that "the most consistent finding in obesity is the shifting of the vital capacity and tidal breathing to lower lung volumes and in the COPD population, the apparent ability to breathe at these lung volumes without greater flow limitation". In the second part of his speech the speaker presented data on pharmacological intervention for the treatment of dyspnea and on rehabilitation strategies.


Dyspnea Is a Better Predictor of 5-Year Survival Than Airway Obstruction in Patients With COPD*

(CHEST 2002; 121:1434–1440)

Pharmacological management of breathlessness in COPD: recent advances and hopes for the future

EXPERT REVIEW OF RESPIRATORY MEDICINE, 2016 VOL. 10, NO. 7, 823–834

Table 1. Oral morphine-based approaches for dyspnea palliation in COPD patients.

Drug Presentation	Initial dose	Frequency
Immediate release [119]	0.5–1 mg	Increased to 1–2.5-mg q4 h while awake by end of week 1
Immediate release [120]	1 mg	Week 1: 1-mg daily Week 2: 1-mg twice daily Thereafter increase by 1 mg/week until the lowest effective dose is found
Short acting [118]	5–10 mg	q3–4 h
Short acting [117]	2.5–5 mg 2.5 mg for breakthrough	q4 h q2 h
Sustained release [116]	20 mg	Daily

- **What is the definition of dyspnea?**
- **What is the clinical impact of dyspnea?**
- **What are the neurobiologicals models usefull for understanding dyspnea?**
- **What are the main drugs applied in the treatment of dyspnea?**
- **What are the best topics related to rehabilitation procedures?**

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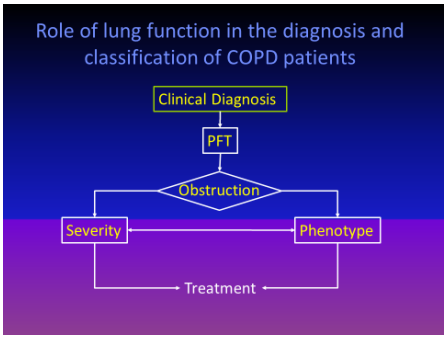
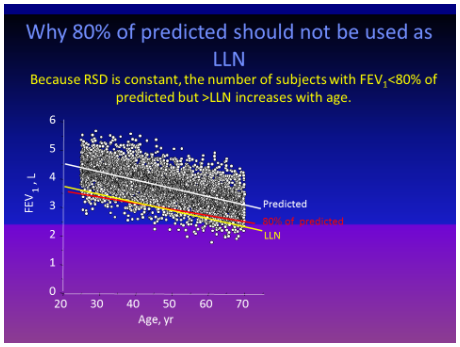
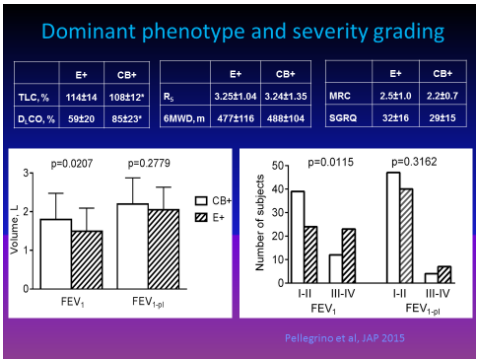
Diagnosis and classification: which recommendations?



Prof. Brusasco from Genoa (I) spoke about COPD diagnosis and classification pointing out the role of lung function in the diagnosis and classification of COPD patients. The GOLD criteria, widely used in the diagnosis of irreversible airway obstruction, in some studies has been suspected to overestimate this phenomenon with the risk of applying an inappropriate medical therapy to patients. Also the spirometric definitions of COPD can lose patients with discordant airways obstruction and also age can contribute to produce biases in the definition of airflow obstruction. The speaker pointed out that lung function abnormalities must be defined based on suitable predicting equations, not by arbitrary criteria and that in order to perform a correct diagnosis, measurement of lung volumes and DlCO are often necessary. In order to perform a correct phenotyping of COPD patients, based on the experience of the speaker, it is necessary to perform comprehensive pulmonary functions tests, together with chest X ray and collecting patients' clinical data. Prof. Brunasco at the conclusion of his speech stated that the severity of the disease from a classification point of view is often affected by the choice of indices and the disease phenotypes.





- **Why 80% of predicted should not be used as LLN?**
- **What are the proposed definitions of obstructive abnormality?**
- **What is the role of lung function in the diagnosis and classification of COPD patients?**
- **What is the effect of obesity on spirometry?**

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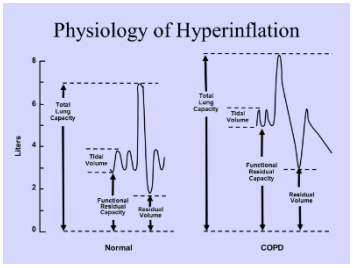
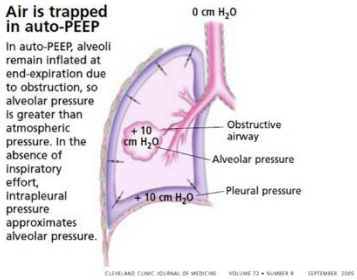
Lung hyperinflation and symptoms: road map



Prof. Rossi from Verona (I) presented some very interesting data on lung pathophysiology, more in particular on lung hyperventilation starting from its definition and etiology characterized by short expiratory time, increased airflow resistance, decreased lung recoil pressure and expiratory flow limitation. The presence of lung hyperventilation is responsible for increased ventilator load, decrease in inspiratory muscle pressure generating capacity and cardiovascular adverse events. The raising of positive end-expiratory pressure is responsible for a phenomenon similar to an "airbag effect" as pointed out by the speaker.



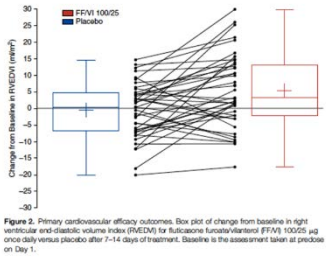


Figure 2. Primary cardiovascular efficacy outcomes. Box plot of change from baseline in right ventricular end-diastolic volume index (RVEDVI) for fluticasone furoate/vilanterol (FF/VI) 100/25 µg once daily versus placebo after 7–14 days of treatment. Baseline is the assessment taken at predose on Day 1.

These pathophysiologic mechanisms lead to cardiovascular abnormalities that are often present in these type of patients. In the last part of his talk the speaker spoke about the treatment to be applied in these patients, pointing out that Bronchodilators are useful in facilitating the external breathing. External PEEP are to be applied with the intent to decrease ventilator workload and venous return to the right ventricle.

- **What are the consequences of lung hyperventilation?**
- **Why does auto PEEP increase the work of breathing?**
- **What are the causes of dynamic hyperventilation?**
- **What is the physiology of hyperventilation?**

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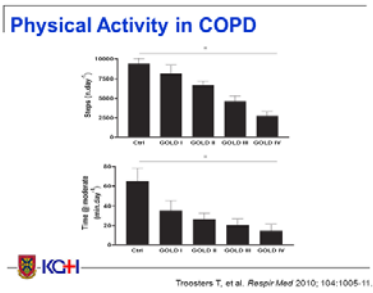
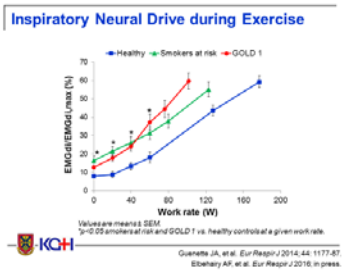
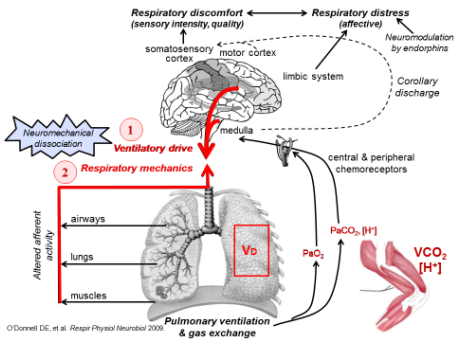
What spirometry doesn't tell you in mild COPD?



Prof. O'Donnell from Kingston (CDN) spoke about spirometry and its meaning in the clinical field starting from the demonstration of the utility in studying COPD also when it is present in mild condition. In patients with mild COPD the resistance to exercise is significantly reduced in comparison to normal controls. The speaker spoke also about the investigative tools to be applied for these examinations. In these patients is present an increased inspiratory neural drive to the diaphragm drived by increased VCO_2, increased acidosis and increased respiratory muscle loading and weakening. In the second part of his talk the speaker spoke about the mechanisms leading to respiratory abnormalities in mild COPD patients, at the conclusion of this presentation prof. O'Donnell stressed the importance to perform additional tests for a better knowledge in phenotyping these patients.





- **Why is important to perform a more specific characterization of smokers in the early phase of the disease?**
- **What are the main measurements of pulmonary gas exchange?**
- **What are the main investigative tools used in the diagnosis of patients with mild COPD?**
- **What are the main characteristics of COPD grade 1B from a clinical point of view?**
- **Why is it necessary to study mild COPD?**

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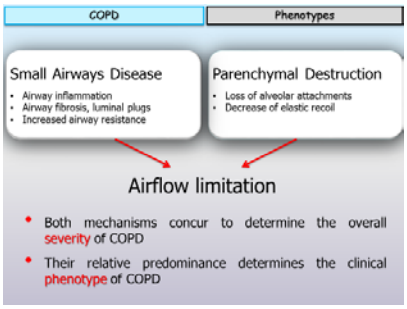
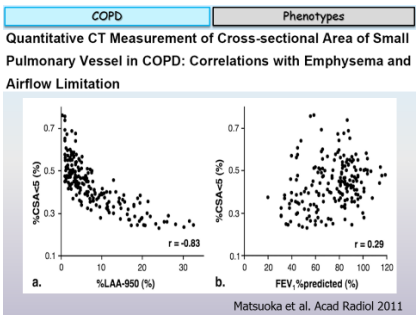
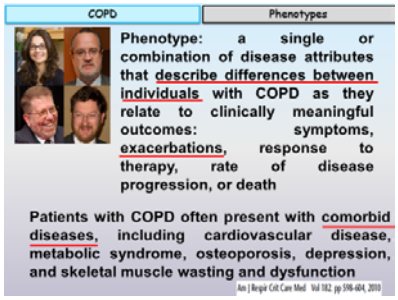
Lung function and clinical phenotypes



Prof. Camiciottoli from Florence (I) presented data on lung function taking in account for the different phenotypes from a clinical point of view. The speaker started her talk speaking about the definition of phenotype and pointing at the huge number of publications registered in PubMed from 2005 till now. The main part of her presentation passed through a deep comparison between clinical findings and phenotype's models giving the opportunity for a better definition of phenotype as a "single or combination of diseases' attributes that describe differences between individuals with COPD, as they relate to clinically meaningful outcomes, also influenced by the presence of comorbidities like cardiovascular diseases, metabolic syndrome, osteoporosis and others". The speaker concluded her presentation pointing out that the clinical phenotypes are not related to frequency of exacerbation or severity of the disease, rather, they are associated to specific panels of comorbidities.





- **What is the relationship between COPD and comorbidities?**
- **What is the definition of phenotype stressed by the speaker?**
- **What is the relationship between small airways disease, parenchymal destruction and phenotype?**
- **How many publications on COPD phenotypes have been registered in PubMed from 2006 to 2016?**

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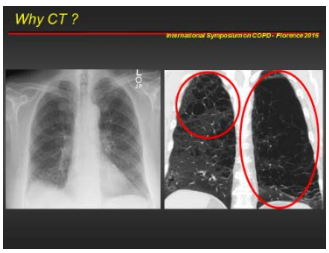
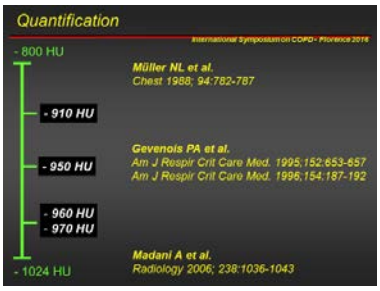
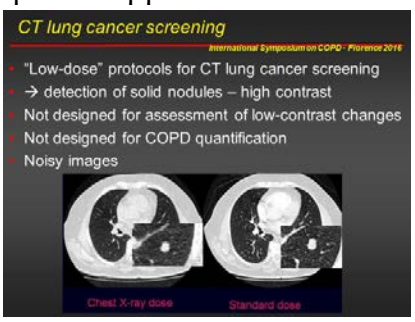
CT and parenchymal destruction



Prof. Bankier from Boston (USA) spoke about Computed Tomography and its application in the diagnosis of lung's parenchimal damages and more in particular on emphysema. The CT-definable subtypes of chronic obstructive pulmonary disease are composed by emphysema itself, airways diseases and the so called "associated features" like large airways disease, bronchiectasis, pulmonary arterial enlargement and interstitial lung abnormality. The speaker in his presentation pointed out the emphysema and the methods used for quantifying the parenchymal damage, its diagnosis with or without CT and the directions for future research. CT is an ideal technique for imaging studies in emphysema better than conventional radiograph and also MRI for quite opposite reasons. Prof. Bankier highlighted the recommended CT parameters for emphysema diagnosis, stressing the effect of iterative reconstruction on computer tomography in the assessment of emphysema, air trapping and airways dimensions. The speaker concluded his presentation highlighting these necessities: perform a better quantification from an objective point of view, implement standardized examination protocols and dose-reduction algorithms and, finally, perform validation against pathology.





- **What is the relationship between CT emphysema and lung cancer?**
- **What are the main iterative reconstructions referred by the speaker?**
- **How do we assess emphysema?**
- **What are the main differences between panlobular emphysema and centrelobular emphysema at the CT scan?**
- **What are the main limits of conventional radiograph and MRI in diagnosis of emphysema?**

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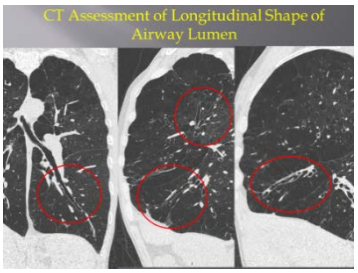
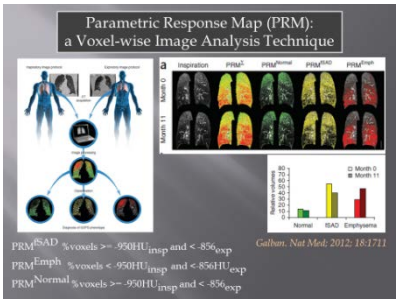
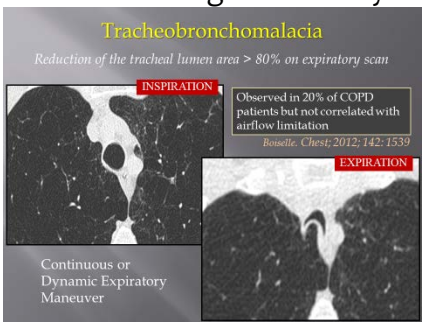
CT and conductive airways pathology



Prof. Grenier from Paris (F) presented data on conductive airways pathology and its diagnosis by computed tomography scan. More in particular the speaker spoke about CT technique applied to the diagnosis of small airway disease, characterized by inflammatory pictures and obstructive alterations as bronchiolitis and gas trapping. Than he spoke about other pathologies like bronchial wall thickening, bronchiectasis and bronchi abnormalities at the central and trachea level. Pof. Greier after presenting the principal CT technique applicable in these pathologies, pointed out that using CT in both visual and quantitative assessment of structural changes in airways of COPD patients, may contribute to get better phenotyping. The speaker concluded his presentation speaking about reproducibility of measurements between multiple CT acquisitions. He also pointed out that this technique has to be well standardized for detecting any modification and its significance, in gas trapping extent or airways dimensions during follow-up.





- **What the main pictures in inspiration and expiration CT in COPD?**
- **What are the main airways disease in COPD patients?**
- **What are the main morphometric analysis of airways in multislice CT?**

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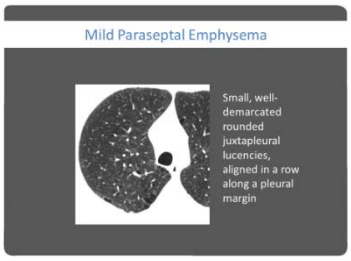
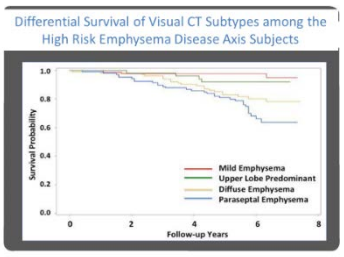
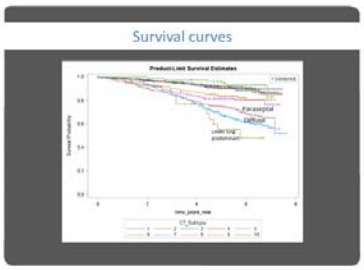
CT subtypes of COPD



Prof. Lynch from Denver (USA) spoke about computed tomography and its subtypes, by presenting data produced by his team of researchers. The speaker started his presentation pointing out the visual classification of CT subtypes of COPD and the relationship between CT subtypes and physiology, disease's progression and outcome. From a survival point of view, the worst outcome between mild emphysema, upper lobe predominant diffuse emphysema and paraseptal emphysema is represented by paraseptal emphysema. The survival's probability is equal to the half of mild emphysema. The speaker concluded his presentation pointing out that CT-based subtypes of COPD differ in demographics, comorbidities and mortality.





- **What are the main differences in demographics among the CT subtypes of COPD?**
- **What are the main differences in physiology and morbidity?**
- **What are the main differences in comorbidities?**
- **What are the main differences in mortality?**

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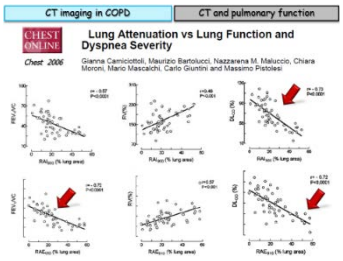
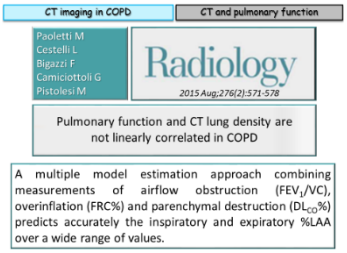
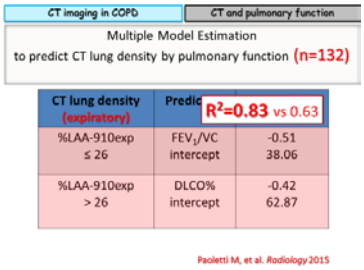
CT vs lung function



Prof. Bigazzi from Florence (I) spoke about this topic: the comparison between computed tomography clinical features and lung function detected with the most common respiratory tests. The aim of the speaker was to provide evidence that lung function changes measured by PFT could be used to predict lung structural changes measured by CT in COPD patients. In order to reach this aim, the speaker presented updated data on the relationship between quantitative CT and lung function in COPD, then in the second part of his speech, Prof. Bigazzi presented data produced by her team of researchers, on the prediction of CT lung changes by pulmonary function testing in clinical practice. In conclusion, Prof. Bigazzi pointed out that pulmonary function and CT lung attenuation show a weak linear relationship in COPD and that a multiple model approach combining functional parameters of airflow obstruction, overinflation and parenchymal destruction can more accurately predict CT lung attenuation.





- **What is the level of prediction of small airways dimensions using compute tomography?**
- **What is the relationship between airways dimension and emphysema in smokers?**
- **What is the relationship between lung attenuation and lung function related to dyspnoea severity?**
- **What is the model presented by the speaker for the quantification of emphysema?**

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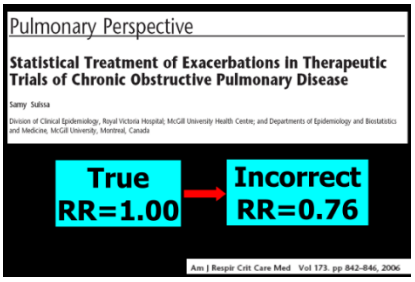
Messages from pharmacological trials



Prof. Suissa from Montreal (CDN) presented data taken from the most important clinical trials performed in this field, trying to find out the main messages for the optimal treatment of lung diseases. More in particular the speaker talked about the early RCTs conducted on inhaled corticosteroid therapy and performed in the 1990s, stressing the point of the lack of reliability for the presence of some discrepancies in their publications. Than the speaker analysed the so called "mega trials" conducted in the 2000s, with an improving in methodology but also linked to conclusions very far from real life and real patients. The observational studies performed in the same years, were conducted in a real world setting but the most of them presented some biases in the cohort population leading to the so called "immortal time bias". The new controlled randomized trials, started in the late 2000s have been designed on the basis of biased observational trials. Prof. Suissa pointed out in his conclusion at the need to design new RCTs with more accurate interpretations and targeting specific patients group based on biomarkers similarity, co-morbidity and others.

- **What are the main biases in the design of the observational studies runned in the 2000s?**
- **How to perform new studies based on "precision" medicine in COPD patients?**
- **How to design new studies in patients with exacerbations?**
- **What does "immortal time bias" mean?**

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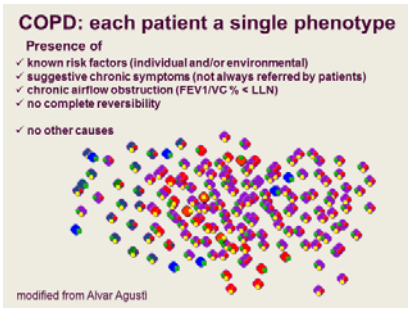
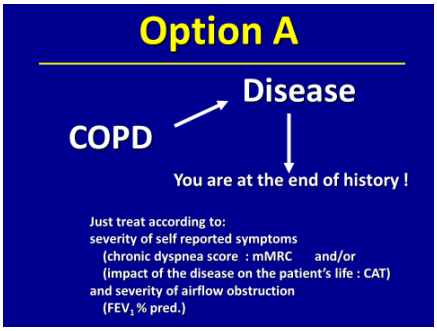
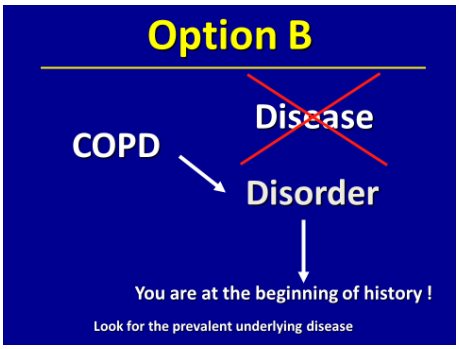
Personalized therapy



Prof. Tantucci from Brescia (I) spoken about this very current topic: the personalized therapy. The speaker presented two options: A and B, based on the decision taken by the physician and related to the interpretation of COPD as disease or disorder. In the first case the story is finished before starting, the only option is represented by treat the patient based on the state of the disease. In the second case, the story is at the beginning, for the necessity to go deep into the knowledge of this disorder starting from the prevalent underling diseases. In his talk Prof. Tantucci presented also clinical cases of patients, all suffering from COPD, but with different basal clinical conditions. The speaker aimed to compare their clinical settings to the data taken by RCTs on COPD and its co-morbidities and complications. Prof. Tantucci finally, presented data about the pharmacological therapy of COPD, with particular attention to inhaled corticosteroids, LAMA and LABA drugs, suggesting that it is time to change the baseline pharmacological management of the disease.





- **What to do for dual bronchodilatation?**
- **Why to distinguish in COPD patients the underlying diseases?**
- **Why is important to identify the different phenotypes in COPD patients?**
- **How to establish the right baseline pharmacotherapy for a given COPD patient?**

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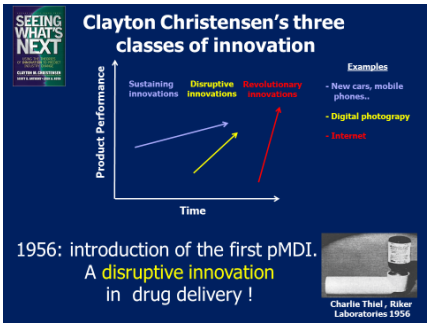
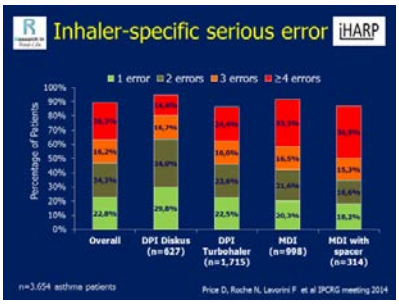
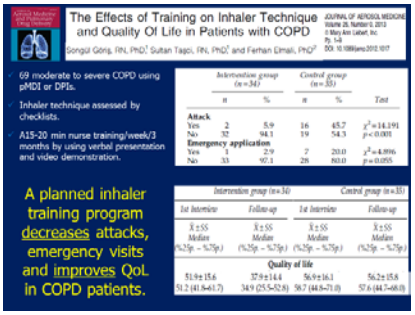
How to get into the target



Dr. Lavorini from Florence spoke about this topic: the optimal medical therapy and the target to be reached. The speaker divided his presentation into three parts: at the beginning an overview on the innovations of current aerosol delivery systems, then the problems linked to the uncorrected use of these inhalators by patients and finally the impact that this uncorrected use has on the asthma control and COPD outcomes. Dr. Lavorini highlighted that the innovations of the new inhalers have really improved their efficiency, but at the same time, the complexity of the instructions for their correct use remains a major problem, for the incorrect use of the inhalers reduces patient adherence and treatment efficacy. Only a few patients are able to correctly use these devices, more or less the 10% of the total population treated with the inhaled therapy, and this situation leads to poor disease outcomes and also contributes to increase the health care costs. Dr. Lavorini concluded his presentation stressing the importance to select the best available inhalers to meet each patient's need as the new road to be taken for solving this problem.





- **What are the consequences of a poor inhaler technique?**
- **What are the main errors in utilizing these devices?**
- **What are the main innovations of the inhalers of the present-days?**
- **What are the main differences between device' types in their use?**

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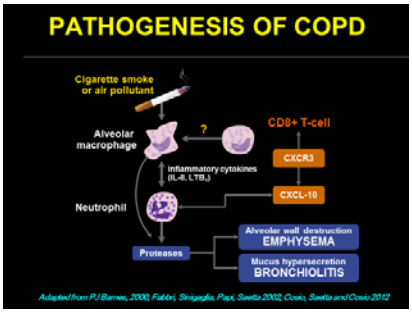
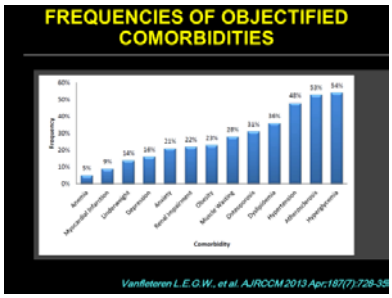
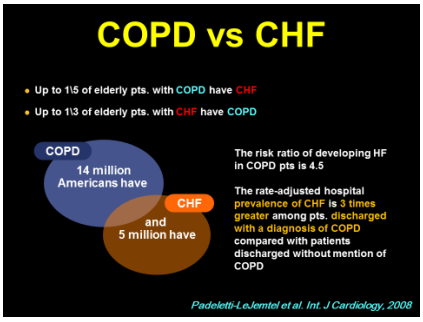
How to cope with comorbidities



Prof. Fabbri from Modena (I) spoke about the main comorbidities to be coped in patients with lung diseases, starting with the indication that COPD is the pulmonary component of a so called "multimorbidity syndrome" that involves more organs and systems like heart, kidney, muscles, liver and others. The speaker stressed the point that patients with COPD also have ischemic heart disease in a very high rate of cases and the presence of these two comorbidities significantly worsens the prognosis in terms of outcome. Prof. Fabbri highlighted that COPD per sè should be diagnosed only in smokers, with chronic respiratory symptoms and non-reversible airflow limitation. This disease takes part of a larger syndrome involving also heart, liver, kidney and muscles and is linked to the same risks factors like ageing, smoking, inactivity and others. The other point stressed by the speaker, concerned on exacerbations, their meaning and their treatment. Prof. Fabbri pointed out that COPD exacerbations should be addressed as exacerbations of respiratory symptoms in patients with COPD, and their treatment should always consider the complexity of the mechanisms underlying the worsening of the symptoms.





- **What is the incidence of CHF in patients with COPD?**
- **What are the leading causes of death in USA in patients with COPD?**
- **What are the main comorbidities in patients with COPD?**
- **What are the rate of COPD' patients with lung abnormalities and ischemic heart disease?**

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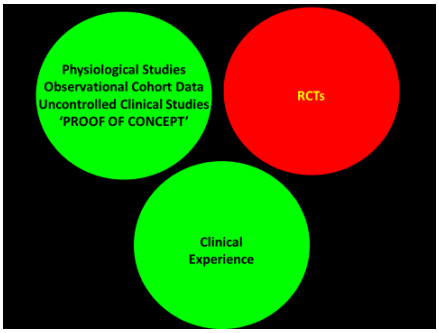
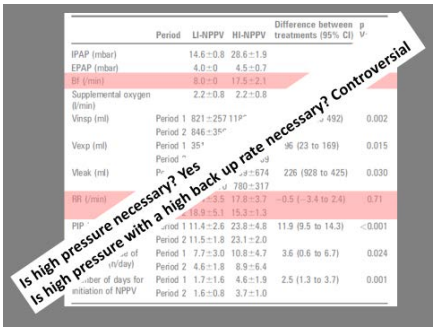
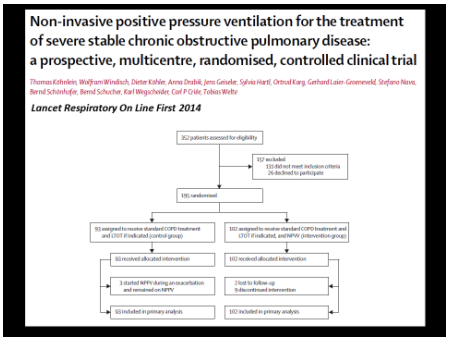
Domiciliary Non-invasive Ventilation



Prof. Hart from London (UK) spoken about ventilation, a main problem in patients with lung diseases. The speaker started his presentation, pointing out two questions: who, how and when do COPD patients benefit from HMV, and the second one: how do we evaluate benefit or lack of benefit from HMV. Starting from the analysis of physiological, observational, uncontrolled clinical studies, RCTs and the given clinical experience, the speaker went deep into the questions trying to correctly define the answers. The presentation analysed other problems like if it is better an high-intensity versus a low-intensity non-invasive ventilation in patients with stable hypercapnic COPD, or if it is better an high intensity than an high pressure ventilation. One more problem raised by the speaker was about the timing of starting a domiciliary non-invasive ventilation program in patients discharged after an adverse event linked to COPD, like hypercapnic respiratory failure. Prof. Hart concluded his speech, highlighting that, in order to correctly delivering this type of intervention, it is necessary to know the appropriate primary outcome, the appropriate target population and the potentiality of the intervention in term of clinical effectiveness.





- **Who is the ideal patient to be selected for HMV?**
- **What is the best mode of non-invasive ventilation?**
- **What is the best timing for the initation of the non-invasive ventilation? What are the best outcome measures?**

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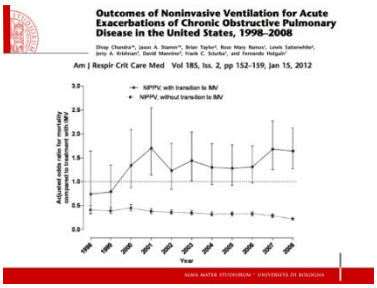
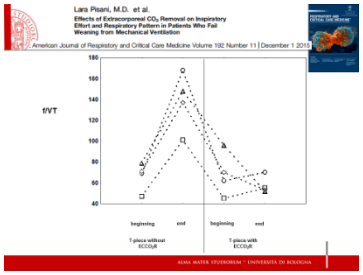
Extracorporeal CO_2 removal



Prof. Nava from Bologna (I) presented data about this topic, starting from a new physiological approach to the non-invasive ventilation in acute respiratory failure, based on the unloading of the muscle effort, in order to remove CO2, by decreasing VE. The speaker spoke about the main systems used for CO2 removal (ECCO2R), very different from extracorporeal membrane oxygenation devices (ECMO), and, in order to demonstrate the efficacy and safety of these non-invasive devices, presented data derived from a clinical trial conducted in his clinic. Prof. Nava concluded his speech, highlighting that ECCO2R may avoid endotracheal intubation (ETI) in those patients with COPD at risk of failure or failing NIV, and that this technique has shown to reduce the respiratory distress in the weaning process. Nevertheless, it is necessary to be cautious in using this technique outside a protected environment, the speaker pointed out.



- **What are the advantages of ECCO2R vs ECMO?**
- **What the Decap circuit is?**
- **What is the primary endpoint of the clinical study running in the clinical center of Prof. Nava?**
- **What are the criteria for being at risk of "NIV-failure"?**
- **What are the main study limitations?**

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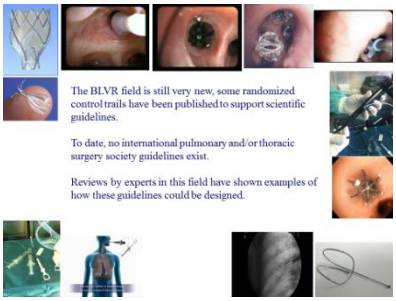
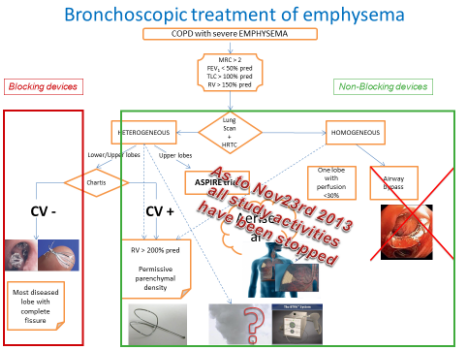
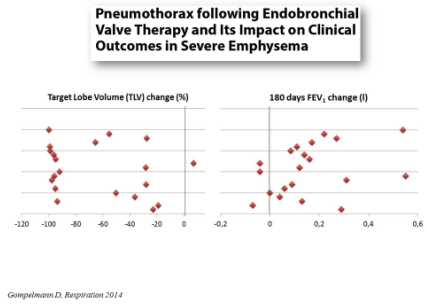
Bronchoscopic lung volume reduction



Prof. Bezzi from Florence (I) spoke about this topic, highlighting that it is possible to perform a lung volume reduction surgery without surgery! It is easy and available via bronchoscopy. In order to apply this new technique, it is necessary the support of a wide team of professionals of different specialities. The speaker spent all her presentation in explaining which patients are available for this new technique, what are the main techniques to be applied and the related complications. In order to avoid these complications is necessary a better patient selection and also a better post-treatment observation. Prof. Bezzi pointed out that prior to perform a BLVR technique should be mandatory inform the patient and also explain all the risks linked to this procedure, like pneumothorax. Then it is necessary keeping the patient in hospital for at least 48 hours after the volume reduction and in particular situations consider the possibility for valve removal or also valve replacement. In conclusion the speaker highlighted that it is better do not be afraid to fail than to be afraid for not try.





- **What are the main valve complications?**
- **What are the efficacy results of the VENT study?**
- **Who should perform the BLVR procedures?**
- **What are the main complications of the BLVR procedure?**

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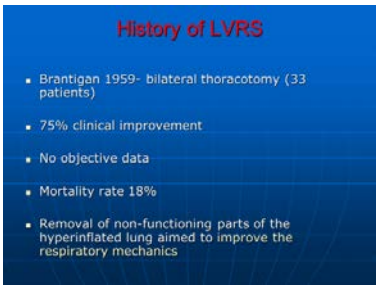
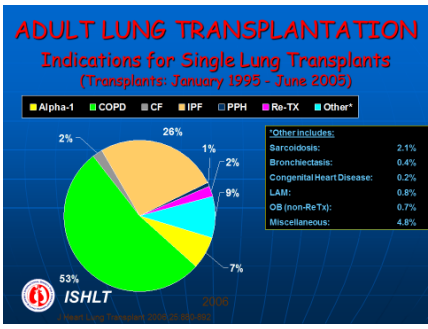
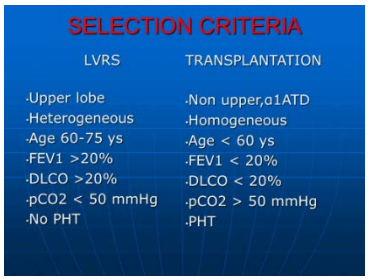
Surgery



Prof. Voltolini from Florence (I) spoke about the main surgical techniques applied in patients with lung diseases to be treated with surgery. More in particular the speaker presented two main techniques; the surgery for lung volume reduction in comparison with the lung transplantation in patients with emphysema. Prof. Voltolini starting from the history of these techniques, analysed the main topics, like benefits, complications and outcomes. In the second part of his presentation the speaker pointed out the possibility for combining these two techniques, starting from the concept of LVRS as a bridge to transplantation. In this view Prof. Voltolini spoke also about the applicability of this option, mainly linked to limitations in the therapeutic Prof. Voltolini concluded some quite different selection criteria. personalize any his speech, highlighting the necessity to characteristics of the intervention based on the main patients from a clinical point of view.





- **What is the reality of LVRS as a bridge of lung transplantation?**
- **What is the ideal patient for transplantation?**
- **What is the ideal patient for LVRS?**
- **What is the functional status of the adult lung recipients?**
- **What are the main limitations of lung transplantation?**

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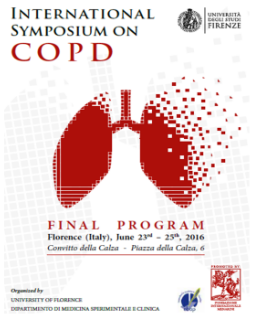

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