Prévention des Exacerbations de BPCO
Quoi de neuf en 2012 ?

Mercredi, 12 septembre 2012

Dr Etienne Perrin
Pneumologue FMH
Groupe Médical du Petit-Lancy

Dr Pierre-Olivier Bridevaux, PD
Service de Pneumologie
Hôpitaux Universitaires de Genève

HUG Hôpitaux Universitaires de Genève

e.perrin@bluewin.ch
pierre-olivier.bridevaux@hcuge.ch

UNIVERSITÉ DE GENÈVE

Conflits d'intérêt

Dr Pierre-Olivier Bridevaux, PD
Emoluments pour présentations (Novartis, Boeringher, GSK, Astra)
Conseils (Boeringher, Takeda)

Dr Etienne Perrin
Emoluments pour présentations (Novartis,
Boeringher, Astra)

Plan

BPCO en 2012

- Une maladie trop négligée
- Classification de la BPCO en 2012

Exacerbations de BPCO

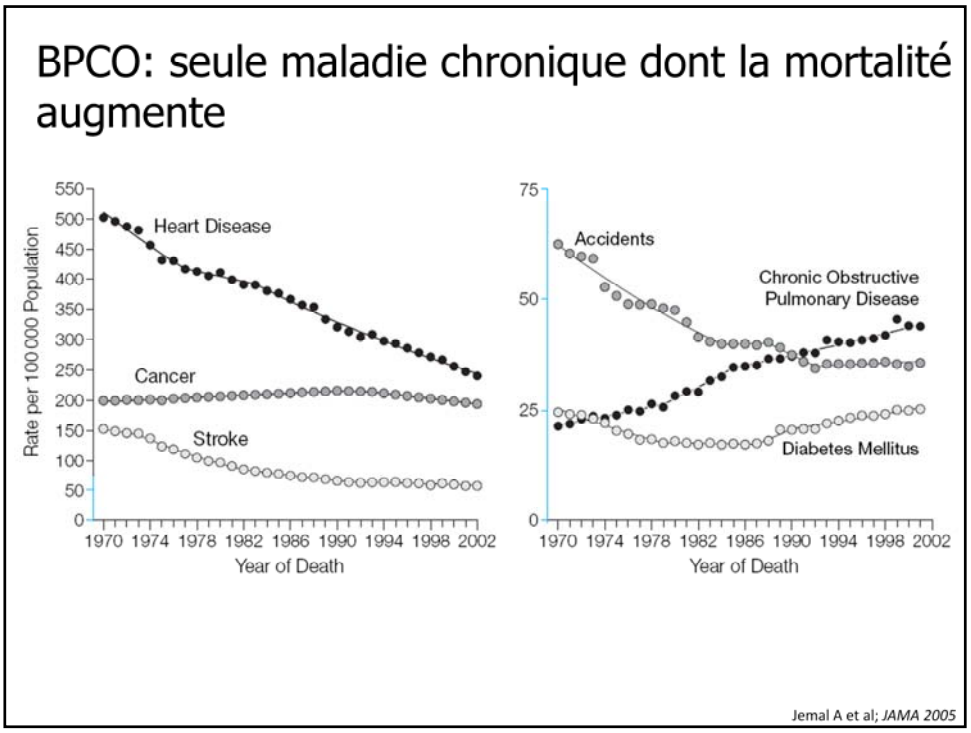
- Mise en perspective

Caractérisation des exacerbations de BPCO

- Existe-t-il des patients à risque accru d'exacerbation?

Vignette clinique

- Azithromycine
- Tiotropium vs salméterol
- Inhibiteurs de la PDE4
- Réhabilitation ambulatoire



Sur un plan de santé publique, la BPCO constitue un défi majeur, parce que parrmi les maladie chronique, la BPCO est la seul dont la mortalité augmente. Ainsi en 1970 aux USA , sur 100’000 personnes 500 mourait cahque années de maladie cardqiue et 150 d’attaque céréebrale. En 2002, ces nombre sont réduti à 250 et et 25 par année respectivement alors que les décès spécificquement causé par la BPCO sont passée de 25 par année en 1970 à 50/année en 2002.

Classification “classique” de la BPCO

	VEMS/CVF après salbutamol	VEMS après salbutamol (% prédit)
Stade 1: léger	<0.7	VEMS≥80%
Stade 2: Moyen	<0.7	50% VEMS <80%
Stade 3: Sévère	<0.7	30% VEMS <50%
Stade 4: Très sévère	<0.7	VEMS<30%

VEMS: Volume expiré maximal en 1 sec; CVF: capacité vitale forcée

The GOLD initiative
http://goldcopd.org

L’atteinte focntionnelle permet de classer la BPCO en 4 stade de léger à très sévère, deterrminé par le VEMS. Ainsi le stade 1 se définit par un VEMS à 80% ou plus de la valeur prdite pour lâge la taille et le sexe

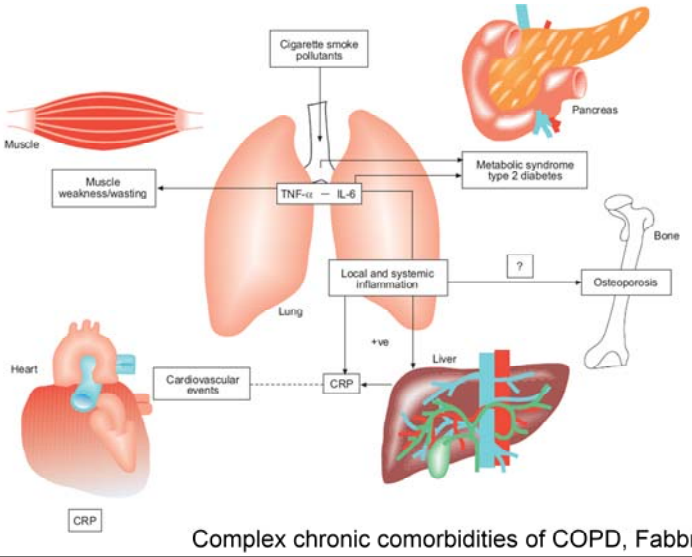
BPCO stade 2-4 en Suisse

	Hommes	Femmes
Adultes de 30 à 73 ans	6.1% [5.3 7.1]	4.0 % [3.3 4.7]
Age 30-39	3.2 % [2.0 5.0]	1.9 % [0.9 3.4]
Age 40-49	3.2 % [3.0 6.0]	4.0 % [2.9 5.6]
Age 50-59	6.1 % [4.7 7.9]	4.7 % [3.5 6.2]
Age 60-69	8.9 % [7.0 11.4]	5.0 % [3.6 6.9]
Age 70+	15.0 % [9.9 22.1]	2.4 % [0.8 6.1]

HUG Hôpitaux Universitaires de Genève

Prevalence of Airflow Obstruction in Smokers and Never Smokers in Switzerland
Bridevaux et al Eur Resp J 2010

Comorbidités de la BPCO



Complex chronic comorbidities of COPD, Fabbri ERJ 2007

Comorbidités de la BPCO

	Sujets adultes sains N=3342	BPCO 2-4 N=307	P
Diabète	2.1%	5.2%	<0.001
Hypertension	12.8%	20.2%	<0.001
Cardiopathie ischémique	4.6 %	8.5%	<0.001

HUG Hôpitaux Universitaires de Genève

Prevalence of Airflow Obstruction in Smokers and Never Smokers in Switzerland
Bridevaux et al Eur Resp J 2010

Management de la BPCO
Nouveautés 2012!

Dimensions	Outils
Fonction pulmonaire	Spirométrie
Fréquence des exacerbations	Anamnèse
Intensité des symptômes	Score CAT ou MMRC

Role of clinical questionnaires in optimizing everyday care of chronic obstructive pulmonary disease, Jones et al; Int J of COPD 2011

CAT™
COPD Assessment Test

BACK PRINT

Nom:

Date:

CAT™
COPD Assessment Test

Quel est l'état de votre BPCO ? Répondez au questionnaire CAT (COPD Assessment Test pour évaluer votre BPCO

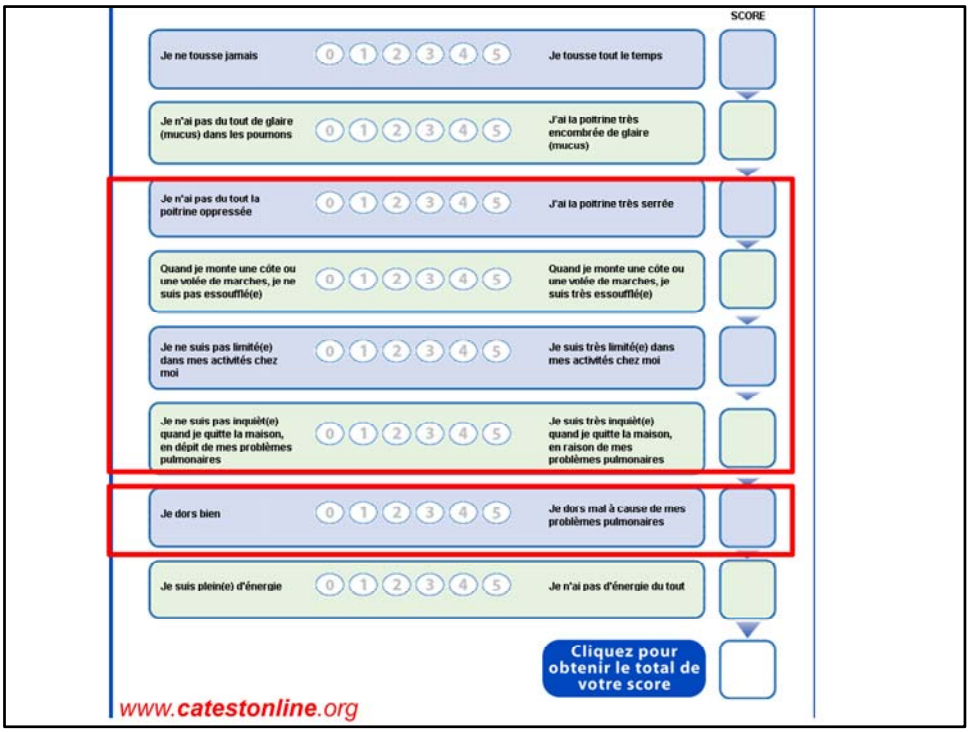
Ce questionnaire vous aidera, ainsi que votre médecin, à mesurer l'impact de la BPCO sur votre bien-être et votre santé au quotidien. Vous pourrez, ainsi que votre médecin, utiliser les réponses et les scores du questionnaire pour mieux soin de votre BPCO et tirer le plus grand bénéfice de votre traitement.

Si vous souhaitez remplir le questionnaire à la main sur papier, veuillez cliquer ici, puis imprimer le questionnaire.
Si vous remplissez le questionnaire en ligne, pour chaque question ci-dessous, cliquez à l'aide de votre souris pour cocher la case (X) qui correspond le mieux à votre état actuel.

Exemple: Je suis très heureux (heureuse) 0 X 2 3 4 5 Je suis très triste

www.catestonline.org

SCORE



								SCORE
Je ne tousse jamais	0	1	2	3	4	5	Je tousse tout le temps	
Je n'ai pas du tout de glaire (mucus) dans les poumons	0	1	2	3	4	5	J'ai la poitrine très encombrée de glaire (mucus)	
Je n'ai pas du tout la poitrine oppressée	0	1	2	3	4	5	J'ai la poitrine très serrée	
Quand je monte une côte ou une volée de marches, je ne suis pas essoufflé(e)	0	1	2	3	4	5	Quand je monte une côte ou une volée de marches, je suis très essoufflé(e)	
Je ne suis pas limité(e) dans mes activités chez moi	0	1	2	3	4	5	Je suis très limité(e) dans mes activités chez moi	
Je ne suis pas inquiète(e) quand je quitte la maison, en dépit de mes problèmes pulmonaires	0	1	2	3	4	5	Je suis très inquiète(e) quand je quitte la maison, en raison de mes problèmes pulmonaires	
Je dors bien	0	1	2	3	4	5	Je dors mal à cause de mes problèmes pulmonaires	
Je suis plein(e) d'énergie	0	1	2	3	4	5	Je n'ai pas d'énergie du tout	

Cliquez pour obtenir le total de votre score

www.catestonline.org

Echelle de dyspnée du Medical Research Council (mMRC)

Stade 0 : gène uniquement pour un effort intense

Stade 1: Essoufflé pour une marche rapide à plat ou une légère côte

Stade 2: marche plus lentement que des personnes du même âge ou doit faire des pauses à cause de sa dyspnée

Stade 3: Doit s'arrêter pour reprendre son souffle après une marche d'une centaine de mètres ou après quelques minutes

Stade 4: Est trop essoufflé pour sortir de chez lui ou est essoufflé en s'habillant ou se déshabillant

Exacerbation de BPCO, définition

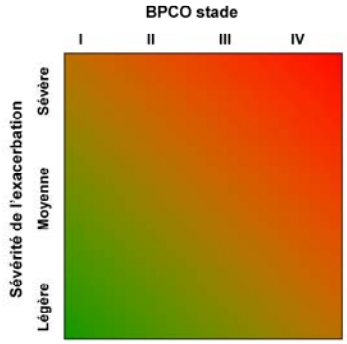
- Augmentation des symptômes respiratoires au-delà des variations quotidiennes
  - ↑toux en fréquence et sévérité
  - ↑expectorations en volume ou changement d'aspect
  - ↑dyspnée
- Radiographie inchangée
- Infections: 2/3 des cas (virale dans 50% des cas)

The GOLD initiative http://goldcopd.org
Upper-Respiratory Viral Infection, Biomarkers, and COPD Exacerbations, *Kherad, Kaiser, Bridevaux, Janssens, Rutschmann et al, Chest 2010*

INTRODUCTION — The Global Initiative for Chronic Obstructive Lung Disease (GOLD), a report produced by the National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO), defines an exacerbation of chronic obstructive pulmonary disease (COPD) as an acute increase in symptoms beyond normal day-to-day variation [1]. This generally includes an acute increase in one or more of the following cardinal symptoms:
Cough increases in frequency and severity
Sputum production increases in volume and/or changes character
Dyspnea increases

Exacerbations de BPCO, Pronostic

Mortality rate %					
In-hospital	3 months	6 months	1 yr	2 yrs	5 yrs
6.7 (5.7–7.7)	18 (14–22)	26 (20–32)	33 (25–40)	43 (37–50)	51 (38–63)



Case fatality of COPD exacerbations: a meta-analysis and statistical modelling approach M. Hoogendoorn, ERJ 2011

INTRODUCTION — The Global Initiative for Chronic Obstructive Lung Disease (GOLD), a report produced by the National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO), defines an exacerbation of chronic obstructive pulmonary disease (COPD) as an acute increase in symptoms beyond normal day-to-day variation [1]. This generally includes an acute increase in one or more of the following cardinal symptoms:
Cough increases in frequency and severity
Sputum production increases in volume and/or changes character
Dyspnea increases

Characterisation of COPD heterogeneity in the ECLIPSE cohort

Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) : 46 centres,12 pays

Sujets: - 2164 BPCO GOLD II-IV
- 337 témoins fumeurs
- 245 témoins non fumeurs

Evaluation à 3 mois, puis aux 6 mois pendant 3 ans:

Paramètres cliniques, BODE, St-George, MMRC, état nutritionnel, spirométrie, test de marche 6 min, degré d'emphysème au CT. Fréquence des exacerbations

A Agusti , P Calverley, B Celli, H Coxson, L Edwards, D Lomas, W MacNee, B Miller, S Rennard, E Silverman, R Tal-Singer, E Wouters, J Yates, J Vestbo Resp Res 2010

RESPIRATORY RESEARCH

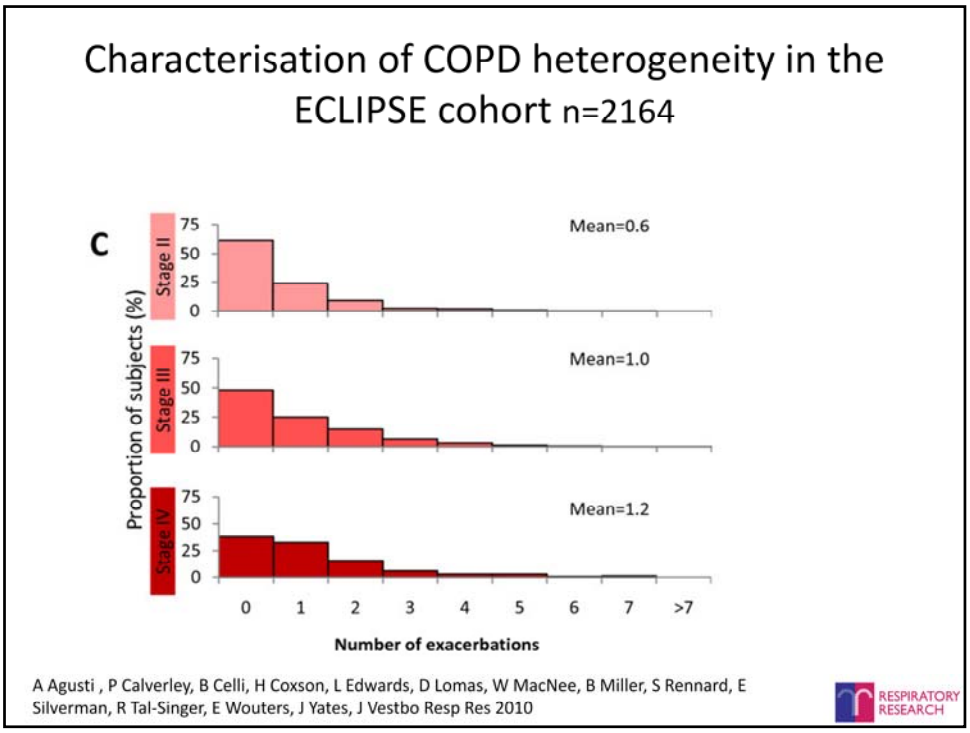
Background: Chronic obstructive pulmonary disease (COPD) is a complex condition with pulmonary and extrapulmonary manifestations. This study describes the heterogeneity of COPD in a large and well characterised and controlled COPD cohort (ECLIPSE).
Methods: We studied 2164 clinically stable COPD patients, 337 smokers with normal lung function and 245 never smokers. In these individuals, we measured clinical parameters, nutritional status, spirometry, exercise tolerance, and amount of emphysema by computed tomography.
Results: COPD patients were slightly older than controls and had more pack years of smoking than smokers with normal lung function. Co-morbidities were more prevalent in COPD patients than in controls, and occurred to the same extent irrespective of the GOLD stage. The severity of airflow limitation in COPD patients was poorly related to the degree of breathlessness, health status, presence of co-morbidity, exercise capacity and number of exacerbations reported in the year before the study. The distribution of these variables within each GOLD stage was wide. Even in subjects with severe airflow obstruction, a substantial proportion did not report symptoms, exacerbations or exercise limitation. The amount of emphysema increased with GOLD severity. The prevalence of bronchiectasis was low (4%) but also increased with GOLD stage. Some gender differences were also identified.
Conclusions: The clinical manifestations of COPD are highly variable and the degree of airflow limitation does not capture the heterogeneity of the disease.

Characterisation of COPD heterogeneity in the ECLIPSE cohort n=2164

	GOLD II			GOLD III			GOLD IV		
	Females (n = 380)	Males (n = 574)	p value	Females (n = 293)	Males (n = 618)	p value	Females (n = 77)	Males (n = 219)	p value
Current smokers (%)	40	36	0.300	37	38	0.695	27	28	0.922
BMI (kg/m^2)	27.2 ± 6.4	27.5 ± 5.2	0.066	25.6 ± 6.0	26.4 ± 5.2	0.008	23.4 ± 6.4	25.5 ± 5.3	0.001
SGRQ-C (total)	43.8 ± 20.2	41.6 ± 20.9	0.193	55.4 ± 18.0	53.4 ± 18.5	0.215	61.3 ± 15.6	61.8 ± 16.1	0.885
Number of exacerbations[a]	0.8 ± 1.2	0.5 ± 0.9	< 0.001	1.2 ± 1.4	0.9 ± 1.3	0.005	1.5 ± 1.6	1.1 ± 1.4	0.044
Heart trouble (%)	19	30	< 0.001	17	30	< 0.001	22	27	0.343
Heart attack (%)	5	13	< 0.001	6	10	0.033	1	10	0.011

A Agusti , P Calverley, B Celli, H Coxson, L Edwards, D Lomas, W MacNee, B Miller, S Rennard, E Silverman, R Tal-Singer, E Wouters, J Yates, J Vestbo Resp Res 2010

RESPIRATORY RESEARCH



Background: Chronic obstructive pulmonary disease (COPD) is a complex condition with pulmonary and extrapulmonary manifestations. This study describes the heterogeneity of COPD in a large and well characterised and controlled COPD cohort (ECLIPSE).
Methods: We studied 2164 clinically stable COPD patients, 337 smokers with normal lung function and 245 never smokers. In these individuals, we measured clinical parameters, nutritional status, spirometry, exercise tolerance, and amount of emphysema by computed tomography.
Results: COPD patients were slightly older than controls and had more pack years of smoking than smokers with normal lung function. Co-morbidities were more prevalent in COPD patients than in controls, and occurred to the same extent irrespective of the GOLD stage. The severity of airflow limitation in COPD patients was poorly related to the degree of breathlessness, health status, presence of co-morbidity, exercise capacity and number of exacerbations reported in the year before the study. The distribution of these variables within each GOLD stage was wide. Even in subjects with severe airflow obstruction, a substantial proportion did not report symptoms, exacerbations or exercise limitation. The amount of emphysema increased with GOLD severity. The prevalence of bronchiectasis was low (4%) but also increased with GOLD stage. Some gender differences were also identified.
Conclusions: The clinical manifestations of COPD are highly variable and the degree of airflow limitation does not capture the heterogeneity of the disease.

Facteurs de risque des exacerbations de BPCO dans ECLIPSE n=2164

Analyse multivariée

Women (N = 376)		
Exacerbation during previous year — yes vs. no	8.89 (4.32–18.29)	<0.001
History of asthma — yes vs. no	3.38 (1.62–7.05)	<0.001
Fibrinogen — per increase of 1 SD on log scale	1.95 (1.28–2.97)	<0.002
Men (N = 569)		
Exacerbation during previous yr — yes vs. no	7.38 (4.44–12.27)	<0.001
FEV_1 — per 100-ml decrease*	1.20 (1.11–1.31)	<0.001
Chronic wheezing — yes vs. no	2.56 (1.55–4.23)	<0.001

J Hurst et al NEJM 2010 The NEW ENGLAND JOURNAL of MEDICINE

Caractérisation des exacerbations de BPCO en 2012

Fréquence : Entre 0.6/an (GOLD 2) et 1.2/an (GOLD 4)

Facteur de risque dominant: Une précédente exacerbation

Comment réduire la fréquence des exacerbations?

HUG Hôpitaux Universitaires de Genève

Objectives To compare standard high flow oxygen treatment with titrated oxygen treatment for patients with an acute exacerbation of chronic obstructive pulmonary disease in the prehospital setting.
Design Cluster randomised controlled parallel group trial.
Setting Ambulance service in Hobart, Tasmania, Australia.
Participants 405 patients with a presumed acute exacerbation of chronic obstructive pulmonary disease who were treated by paramedics, transported, and admitted to the Royal Hobart Hospital during the trial period; 214 had a diagnosis of chronic obstructive pulmonary disease confirmed by lung function tests in the previous five years.
Interventions High flow oxygen treatment compared with titrated oxygen treatment in the prehospital (ambulance/ paramedic) setting.
Main outcome measure Prehospital or in-hospital mortality.
Results In an intention to treat analysis, the risk of death was significantly lower in the titrated oxygen arm compared with the high flow oxygen arm for all patients (high flow oxygen n=226; titrated oxygen n=179) and for the subgroup of patients with confirmed chronic obstructive pulmonary disease (high flow n=117; titrated n=97). Overall mortality was 9% (21 deaths) in the high flow oxygen arm compared with 4% (7 deaths) in the titrated oxygen arm; mortality in the subgroup with confirmed chronic obstructive pulmonary disease was9% (11 deaths) in the high flow arm compared with 2% (2 deaths) in the titrated oxygen arm. Titrated oxygen treatment reduced mortality compared with high flow oxygen by 58% for all patients (relative risk 0.42, 95% confidence interval 0.20 to 0.89; P=0.02) and by 78% for the patients with confirmed chronic obstructive pulmonary disease (0.22, 0.05 to 0.91; P=0.04). Patients with chronic obstructive pulmonary disease who received titrated oxygen according to the protocol were significantly less likely to have respiratory acidosis (mean difference in pH 0.12 (SE 0.05); P=0.01; n=28) or hypercapnia (mean difference in arterial carbon dioxide pressure −33.6 (16.3) mm Hg; P=0.02; n=29) than were patients who received high flow oxygen.
Conclusions Titrated oxygen treatment significantly reduced mortality, hypercapnia, and respiratory acidosis compared with high flow oxygen in acute exacerbations of chronic obstructive pulmonary disease. These results provide strong evidence to recommend the routine use of titrated oxygen treatment in patients with breathlessness and a history or clinical likelihood of chronic obstructive pulmonary disease in the prehospital setting.
Trial registration Australian New Zealand Clinical Trials Register ACTRN12609000236291.

Mr B.

AP: 66 ans, employé de banque retraité, vit seul, ancien fumeur, en surpoids (BMI 27 kg/m2), Infarctus myocardique (2010), HTA traitée. deux exacerbations de BPCO traitées en ambulatoire en mai 2010 et novembre 2011.

Spirométrie c/o pneumologue de ville en janvier 2012: VEMS/CVF 0.68, VEMS 65%: BPCO GOLD II

A pris 6 mois de tiotropium (LAMA) (Spiriva®) puis arrêt spontané. Prend irrégulièrement du salméterol/fluticasone) (LABA/CSI)

AA: Depuis 3 jours, dyspnée +++ (marche à domicile quasi impossible), toux, expectorations jaunes
Status: Expirium prolongé, satu AA 84%, TA 175/100, FC 100
Radiographie thoracique: pas de foyer.

Diag: Exacerbation de BPCO.

HUG *spitalisé.*

Objectives To compare standard high flow oxygen treatment with titrated oxygen treatment for patients with an acute exacerbation of chronic obstructive pulmonary disease in the prehospital setting.
Design Cluster randomised controlled parallel group trial.
Setting Ambulance service in Hobart, Tasmania, Australia.
Participants 405 patients with a presumed acute exacerbation of chronic obstructive pulmonary disease who were treated by paramedics, transported, and admitted to the Royal Hobart Hospital during the trial period; 214 had a diagnosis of chronic obstructive pulmonary disease confirmed by lung function tests in the previous five years.
Interventions High flow oxygen treatment compared with titrated oxygen treatment in the prehospital (ambulance/paramedic) setting.
Main outcome measure Prehospital or in-hospital mortality.
Results In an intention to treat analysis, the risk of death was significantly lower in the titrated oxygen arm compared with the high flow oxygen arm for all patients (high flow oxygen n=226; titrated oxygen n=179) and for the subgroup of patients with confirmed chronic obstructive pulmonary disease (high flow n=117; titrated n=97). Overall mortality was 9% (21 deaths) in the high flow oxygen arm compared with 4% (7 deaths) in the titrated oxygen arm; mortality in the subgroup with confirmed chronic obstructive pulmonary disease was9% (11 deaths) in the high flow arm compared with 2% (2 deaths) in the titrated oxygen arm. Titrated oxygen treatment reduced mortality compared with high flow oxygen by 58% for all patients (relative risk 0.42, 95% confidence interval 0.20 to 0.89; P=0.02) and by 78% for the patients with confirmed chronic obstructive pulmonary disease (0.22, 0.05 to 0.91; P=0.04). Patients with chronic obstructive pulmonary disease who received titrated oxygen according to the protocol were significantly less likely to have respiratory acidosis (mean difference in pH 0.12 (SE 0.05); P=0.01; n=28) or hypercapnia (mean difference in arterial carbon dioxide pressure −33.6 (16.3) mm Hg; P=0.02; n=29) than were patients who received high flow oxygen.
Conclusions Titrated oxygen treatment significantly reduced mortality, hypercapnia, and respiratory acidosis compared with high flow oxygen in acute exacerbations of chronic obstructive pulmonary disease. These results provide strong evidence to recommend the routine use of titrated oxygen treatment in patients with breathlessness and a history or clinical likelihood of chronic obstructive pulmonary disease in the prehospital setting.
Trial registration Australian New Zealand Clinical Trials Register ACTRN12609000236291.

Mr B. exacerbation sévère de BPCO

Le médecin hospitalier vous appelle: le patient va mieux avec une oxygénothérapie, des BD et une ventilation non-invasive transitoire.

Il a reçu des corticoïdes systémiques et une antibiothérapie.

Son retour à domicile est prévu le lendemain.

TTT à la sortie: tiotropium (LAMA) + formoterol/budesonide (LABA+CSI)

Sept jours plus tard, 1ère visite ambulatoire: Mr B a perdu 4 kg, de l'autonomie, le moral… Il ne veut plus revivre cette expérience.

HUG Hôpitaux Universitaires de Genève

Objectives To compare standard high flow oxygen treatment with titrated oxygen treatment for patients with an acute exacerbation of chronic obstructive pulmonary disease in the prehospital setting.
Design Cluster randomised controlled parallel group trial.
Setting Ambulance service in Hobart, Tasmania, Australia.
Participants 405 patients with a presumed acute exacerbation of chronic obstructive pulmonary disease who were treated by paramedics, transported, and admitted to the Royal Hobart Hospital during the trial period; 214 had a diagnosis of chronic obstructive pulmonary disease confirmed by lung function tests in the previous five years.
Interventions High flow oxygen treatment compared with titrated oxygen treatment in the prehospital (ambulance/paramedic) setting.
Main outcome measure Prehospital or in-hospital mortality.
Results In an intention to treat analysis, the risk of death was significantly lower in the titrated oxygen arm compared with the high flow oxygen arm for all patients (high flow oxygen n=226; titrated oxygen n=179) and for the subgroup of patients with confirmed chronic obstructive pulmonary disease (high flow n=117; titrated n=97). Overall mortality was 9% (21 deaths) in the high flow oxygen arm compared with 4% (7 deaths) in the titrated oxygen arm; mortality in the subgroup with confirmed chronic obstructive pulmonary disease was9% (11 deaths) in the high flow arm compared with 2% (2 deaths) in the titrated oxygen arm. Titrated oxygen treatment reduced mortality compared with high flow oxygen by 58% for all patients (relative risk 0.42, 95% confidence interval 0.20 to 0.89; P=0.02) and by 78% for the patients with confirmed chronic obstructive pulmonary disease (0.22, 0.05 to 0.91; P=0.04). Patients with chronic obstructive pulmonary disease who received titrated oxygen according to the protocol were significantly less likely to have respiratory acidosis (mean difference in pH 0.12 (SE 0.05); P=0.01; n=28) or hypercapnia (mean difference in arterial carbon dioxide pressure −33.6 (16.3) mm Hg; P=0.02; n=29) than were patients who received high flow oxygen.
Conclusions Titrated oxygen treatment significantly reduced mortality, hypercapnia, and respiratory acidosis compared with high flow oxygen in acute exacerbations of chronic obstructive pulmonary disease. These results provide strong evidence to recommend the routine use of titrated oxygen treatment in patients with breathlessness and a history or clinical likelihood of chronic obstructive pulmonary disease in the prehospital setting.
Trial registration Australian New Zealand Clinical Trials Register ACTRN12609000236291.

Mr B.
Prévention d'une nouvelle exacerbation

Les options en 2012:

A) Inhibiteur de la PDE4 (roflumilast, Daxas®) au long cours?

B) Azithromycine au long cours?

C) Tiotropium au long cours?

D) Réhabilitation ambulatoire?

E) Réhabilitation hospitalière?

HUG Hôpitaux Universitaires de Genève

Objectives To compare standard high flow oxygen treatment with titrated oxygen treatment for patients with an acute exacerbation of chronic obstructive pulmonary disease in the prehospital setting.
Design Cluster randomised controlled parallel group trial.
Setting Ambulance service in Hobart, Tasmania, Australia.
Participants 405 patients with a presumed acute exacerbation of chronic obstructive pulmonary disease who were treated by paramedics, transported, and admitted to the Royal Hobart Hospital during the trial period; 214 had a diagnosis of chronic obstructive pulmonary disease confirmed by lung function tests in the previous five years.
Interventions High flow oxygen treatment compared with titrated oxygen treatment in the prehospital (ambulance/ paramedic) setting.
Main outcome measure Prehospital or in-hospital mortality.
Results In an intention to treat analysis, the risk of death was significantly lower in the titrated oxygen arm compared with the high flow oxygen arm for all patients (high flow oxygen n=226; titrated oxygen n=179) and for the subgroup of patients with confirmed chronic obstructive pulmonary disease (high flow n=117; titrated n=97). Overall mortality was 9% (21 deaths) in the high flow oxygen arm compared with 4% (7 deaths) in the titrated oxygen arm; mortality in the subgroup with confirmed chronic obstructive pulmonary disease was9% (11 deaths) in the high flow arm compared with 2% (2 deaths) in the titrated oxygen arm. Titrated oxygen treatment reduced mortality compared with high flow oxygen by 58% for all patients (relative risk 0.42, 95% confidence interval 0.20 to 0.89; P=0.02) and by 78% for the patients with confirmed chronic obstructive pulmonary disease (0.22, 0.05 to 0.91; P=0.04). Patients with chronic obstructive pulmonary disease who received titrated oxygen according to the protocol were significantly less likely to have respiratory acidosis (mean difference in pH 0.12 (SE 0.05); P=0.01; n=28) or hypercapnia (mean difference in arterial carbon dioxide pressure −33.6 (16.3) mm Hg; P=0.02; n=29) than were patients who received high flow oxygen.
Conclusions Titrated oxygen treatment significantly reduced mortality, hypercapnia, and respiratory acidosis compared with high flow oxygen in acute exacerbations of chronic obstructive pulmonary disease. These results provide strong evidence to recommend the routine use of titrated oxygen treatment in patients with breathlessness and a history or clinical likelihood of chronic obstructive pulmonary disease in the prehospital setting.
Trial registration Australian New Zealand Clinical Trials Register ACTRN12609000236291.

Phosphodiesterase 4 inhibitors for COPD

23 RCT (roflumilast n=9211 patients, cilomilast n= 6457)

Effet anti-inflammatoire avec effet bronchodilatateur marginal

VEMS: + 45 ml (39-52 ml)
CVF: + 82 ml (66-99 ml)

Exacerbations: OR = 0,78 (0,72-0,85)

Effets secondaires:
- Perte de poids OR = 4,62 (roflumilast)
- Vomissements OR = 4,01
- Diarrhées OR = 2,81

caveat: effet non démontré sur exacerbation sévère (nécessitant une hospitalisation)

J Chong et al

Twenty-three separate RCTs studying roflumilast (nine trials, 9211 patients) or cilomilast (fourteen trials, 6457 patients) met the inclusion criteria. None of the trials exceeded a year in duration.
Treatment with a PDE_4 inhibitor was associated with a significant improvement in FEV_1over the trial period compared with placebo (MD 45.59 mL; 95% confidence interval (CI) 39.15 to 52.03), regardless of COPD severity or concomitant COPD treatment. There were some small improvements in quality of life (St George's Respiratory Questionnaire MD -1.04; 95% CI -1.66 to -0.41) and COPD-related symptoms, but no change in exercise tolerance. Treatment with a PDE_4 inhibitor was associated with a reduced likelihood of COPD exacerbation (OR 0.78; 95% CI 0.72 to 0.85). More participants in the treatment groups experienced non-serious adverse events compared with controls, particularly gastrointestinal symptoms and headache. Roflumilast was associated with weight loss during the trial period.

Authors' conclusions

In people with COPD, PDE_4 inhibitors offered benefit over placebo in improving lung function and reducing likelihood of exacerbations, however, they had little impact on quality of life or symptoms. Gastrointestinal adverse effects and weight loss were common. The optimum place of PDE_4 inhibitors in COPD management remains to be defined. Longer-term trials are needed to determine whether or not PDE_4 inhibitors modify FEV_1 decline, healthcare utilisation or mortality in COPD.

Azithromycin for prevention of exacerbations of COPD

Etude randomisée contrôlée multicentrique (17 centres), durée 1 an

1142 patients >40 ans avec BPCO, VEMS < 80% et

- Oxygène au long cours, ou
- CS systémiques année précédente, ou
- Admission aux Urgences ou hospitalisation année précédente

Randomisation: AZM 250 mg/j ou placebo

Exacerbation:

Apparition ou augmentation de plus d'un symptôme (toux, expectoration, sifflements, dyspnée, serrement thoracique) ≥3 jours et ATB ou CS systémique

R Albert et al NEJM 2011 The NEW ENGLAND JOURNAL of MEDICINE

Acute exacerbations adversely affect patients with chronic obstructive pulmonary disease (COPD). Macrolide antibiotics benefit patients with a variety of inflammatory airway diseases.

Methods

We performed a randomized trial to determine whether azithromycin decreased the frequency of exacerbations in participants with COPD who had an increased risk of exacerbations but no hearing impairment, resting tachycardia, or apparent risk of prolongation of the corrected QT interval.

Results

A total of 1577 subjects were screened; 1142 (72%) were randomly assigned to receive azithromycin, at a dose of 250 mg daily (570 participants), or placebo (572 participants) for 1 year in addition to their usual care. The rate of 1-year follow-up was 89% in the azithromycin group and 90% in the placebo group. The median time to the first exacerbation was 266 days (95% confidence interval [CI], 227 to 313) among participants receiving azithromycin, as compared with 174 days (95% CI, 143 to 215) among participants receiving placebo (P<0.001). The frequency of exacerbations was 1.48 exacerbations per patient-year in the azithromycin group, as compared with 1.83 per patient-year in the placebo group (P = 0.01), and the hazard ratio for having an acute exacerbation of COPD per patient-year in the azithromycin group was 0.73 (95% CI, 0.63 to 0.84; P<0.001). The scores on the St. George's Respiratory Questionnaire (on a scale of 0 to 100, with lower scores indicating better functioning) improved more in the azithromycin group than in the placebo group (a mean [±SD] decrease of 2.8±12.8 vs. 0.6±11.4, P = 0.004); the percentage of participants with more than the minimal clinically important difference of −4 units was 43% in the azithromycin group, as compared with 36% in the placebo group (P = 0.03). Hearing decrements were more common in the azithromycin group than in the placebo group (25% vs. 20%, P = 0.04).

Conclusions

Among selected subjects with COPD, azithromycin taken daily for 1 year, when added to usual treatment, decreased the frequency of exacerbations and improved quality of life but caused hearing decrements in a small percentage of subjects. Although this intervention could change microbial resistance patterns, the effect of this change is not known. (Funded by the National Institutes of Health; ClinicalTrials.gov number, NCT00325897.)

Azithromycin for prevention of exacerbations of COPD

Table 1

	AZM n=558	Placebo n=559
VEMS post bd	39 %	40 %
GOLD II	26 %	26 %
GOLD III	40 %	40 %
GOLD IV	34 %	33 %
LABA et/ou LAMA	86 %	88 %
ICS	76 %	79 %

R Albert et al NEJM 2011 The NEW ENGLAND JOURNAL of MEDICINE

Acute exacerbations adversely affect patients with chronic obstructive pulmonary disease (COPD). Macrolide antibiotics benefit patients with a variety of inflammatory airway diseases.

Methods

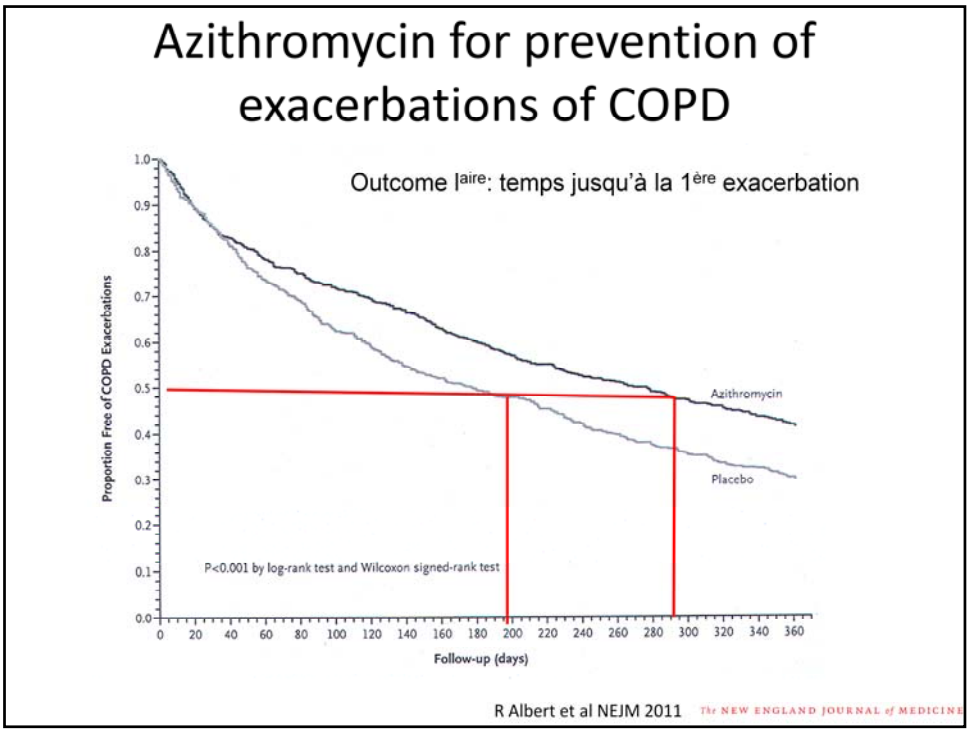
We performed a randomized trial to determine whether azithromycin decreased the frequency of exacerbations in participants with COPD who had an increased risk of exacerbations but no hearing impairment, resting tachycardia, or apparent risk of prolongation of the corrected QT interval.

Results

A total of 1577 subjects were screened; 1142 (72%) were randomly assigned to receive azithromycin, at a dose of 250 mg daily (570 participants), or placebo (572 participants) for 1 year in addition to their usual care. The rate of 1-year follow-up was 89% in the azithromycin group and 90% in the placebo group. The median time to the first exacerbation was 266 days (95% confidence interval [CI], 227 to 313) among participants receiving azithromycin, as compared with 174 days (95% CI, 143 to 215) among participants receiving placebo (P<0.001). The frequency of exacerbations was 1.48 exacerbations per patient-year in the azithromycin group, as compared with 1.83 per patient-year in the placebo group (P = 0.01), and the hazard ratio for having an acute exacerbation of COPD per patient-year in the azithromycin group was 0.73 (95% CI, 0.63 to 0.84; P<0.001). The scores on the St. George's Respiratory Questionnaire (on a scale of 0 to 100, with lower scores indicating better functioning) improved more in the azithromycin group than in the placebo group (a mean [±SD] decrease of 2.8±12.8 vs. 0.6±11.4, P = 0.004); the percentage of participants with more than the minimal clinically important difference of −4 units was 43% in the azithromycin group, as compared with 36% in the placebo group (P = 0.03). Hearing decrements were more common in the azithromycin group than in the placebo group (25% vs. 20%, P = 0.04).

Conclusions

Among selected subjects with COPD, azithromycin taken daily for 1 year, when added to usual treatment, decreased the frequency of exacerbations and improved quality of life but caused hearing decrements in a small percentage of subjects. Although this intervention could change microbial resistance patterns, the effect of this change is not known. (Funded by the National Institutes of Health; ClinicalTrials.gov number, NCT00325897.)



Background
Acute exacerbations adversely affect patients with chronic obstructive pulmonary disease (COPD). Macrolide antibiotics benefit patients with a variety of inflammatory airway diseases.
Methods
We performed a randomized trial to determine whether azithromycin decreased the frequency of exacerbations in participants with COPD who had an increased risk of exacerbations but no hearing impairment, resting tachycardia, or apparent risk of prolongation of the corrected QT interval.
Results
A total of 1577 subjects were screened; 1142 (72%) were randomly assigned to receive azithromycin, at a dose of 250 mg daily (570 participants), or placebo (572 participants) for 1 year in addition to their usual care. The rate of 1-year follow-up was 89% in the azithromycin group and 90% in the placebo group. The median time to the first exacerbation was 266 days (95% confidence interval [CI], 227 to 313) among participants receiving azithromycin, as compared with 174 days (95% CI, 143 to 215) among participants receiving placebo (P<0.001). The frequency of exacerbations was 1.48 exacerbations per patient-year in the azithromycin group, as compared with 1.83 per patient-year in the placebo group (P = 0.01), and the hazard ratio for having an acute exacerbation of COPD per patient-year in the azithromycin group was 0.73 (95% CI, 0.63 to 0.84; P<0.001). The scores on the St. George's Respiratory Questionnaire (on a scale of 0 to 100, with lower scores indicating better functioning) improved more in the azithromycin group than in the placebo group (a mean [±SD] decrease of 2.8±12.8 vs. 0.6±11.4, P = 0.004); the percentage of participants with more than the minimal clinically important difference of −4 units was 43% in the azithromycin group, as compared with 36% in the placebo group (P = 0.03). Hearing decrements were more common in the azithromycin group than in the placebo group (25% vs. 20%, P = 0.04).
Conclusions
Among selected subjects with COPD, azithromycin taken daily for 1 year, when added to usual treatment, decreased the frequency of exacerbations and improved quality of life but caused hearing decrements in a small percentage of subjects. Although this intervention could change microbial resistance patterns, the effect of this change is not known. (Funded by the National Institutes of Health; ClinicalTrials.gov number, NCT00325897.)

Azithromycin for prevention of exacerbations of COPD

Risque relatif: AZM vs placebo:

	HR (ajusté)	P
Exacerbations	0,73	<0,001
Consultations non prévues	0,85	0,02
Hospitalisations pour BPCO	0,82	NS
Hospitalisations (toutes)	0,94	NS
Intubations	0,79	NS

R Albert et al NEJM 2011 The NEW ENGLAND JOURNAL of MEDICINE

Background
Acute exacerbations adversely affect patients with chronic obstructive pulmonary disease (COPD). Macrolide antibiotics benefit patients with a variety of inflammatory airway diseases.
Methods
We performed a randomized trial to determine whether azithromycin decreased the frequency of exacerbations in participants with COPD who had an increased risk of exacerbations but no hearing impairment, resting tachycardia, or apparent risk of prolongation of the corrected QT interval.
Results
A total of 1577 subjects were screened; 1142 (72%) were randomly assigned to receive azithromycin, at a dose of 250 mg daily (570 participants), or placebo (572 participants) for 1 year in addition to their usual care. The rate of 1-year follow-up was 89% in the azithromycin group and 90% in the placebo group. The median time to the first exacerbation was 266 days (95% confidence interval [CI], 227 to 313) among participants receiving azithromycin, as compared with 174 days (95% CI, 143 to 215) among participants receiving placebo (P<0.001). The frequency of exacerbations was 1.48 exacerbations per patient-year in the azithromycin group, as compared with 1.83 per patient-year in the placebo group (P = 0.01), and the hazard ratio for having an acute exacerbation of COPD per patient-year in the azithromycin group was 0.73 (95% CI, 0.63 to 0.84; P<0.001). The scores on the St. George's Respiratory Questionnaire (on a scale of 0 to 100, with lower scores indicating better functioning) improved more in the azithromycin group than in the placebo group (a mean [±SD] decrease of 2.8±12.8 vs. 0.6±11.4, P = 0.004); the percentage of participants with more than the minimal clinically important difference of −4 units was 43% in the azithromycin group, as compared with 36% in the placebo group (P = 0.03). Hearing decrements were more common in the azithromycin group than in the placebo group (25% vs. 20%, P = 0.04).
Conclusions
Among selected subjects with COPD, azithromycin taken daily for 1 year, when added to usual treatment, decreased the frequency of exacerbations and improved quality of life but caused hearing decrements in a small percentage of subjects. Although this intervention could change microbial resistance patterns, the effect of this change is not known. (Funded by the National Institutes of Health; ClinicalTrials.gov number, NCT00325897.)

Azithromycin for prevention of exacerbations of COPD

	AZM	Placebo	P
Colonisation:			
Initiale	14 %	15 %	NS
dont macrolides R	52 %	57 %	NS
Ultérieure	12 %	31 %	<0,001
dont macrolides R	81 %	41 %	<0,001
Diminution de l'audition:	25%	20%	0.04

R Albert et al NEJM 2011 The NEW ENGLAND JOURNAL of MEDICINE

Background
Acute exacerbations adversely affect patients with chronic obstructive pulmonary disease (COPD). Macrolide antibiotics benefit patients with a variety of inflammatory airway diseases.
Methods
We performed a randomized trial to determine whether azithromycin decreased the frequency of exacerbations in participants with COPD who had an increased risk of exacerbations but no hearing impairment, resting tachycardia, or apparent risk of prolongation of the corrected QT interval.
Results
A total of 1577 subjects were screened; 1142 (72%) were randomly assigned to receive azithromycin, at a dose of 250 mg daily (570 participants), or placebo (572 participants) for 1 year in addition to their usual care. The rate of 1-year follow-up was 89% in the azithromycin group and 90% in the placebo group. The median time to the first exacerbation was 266 days (95% confidence interval [CI], 227 to 313) among participants receiving azithromycin, as compared with 174 days (95% CI, 143 to 215) among participants receiving placebo (P<0.001). The frequency of exacerbations was 1.48 exacerbations per patient-year in the azithromycin group, as compared with 1.83 per patient-year in the placebo group (P = 0.01), and the hazard ratio for having an acute exacerbation of COPD per patient-year in the azithromycin group was 0.73 (95% CI, 0.63 to 0.84; P<0.001). The scores on the St. George's Respiratory Questionnaire (on a scale of 0 to 100, with lower scores indicating better functioning) improved more in the azithromycin group than in the placebo group (a mean [±SD] decrease of 2.8±12.8 vs. 0.6±11.4, P = 0.004); the percentage of participants with more than the minimal clinically important difference of −4 units was 43% in the azithromycin group, as compared with 36% in the placebo group (P = 0.03). Hearing decrements were more common in the azithromycin group than in the placebo group (25% vs. 20%, P = 0.04).
Conclusions
Among selected subjects with COPD, azithromycin taken daily for 1 year, when added to usual treatment, decreased the frequency of exacerbations and improved quality of life but caused hearing decrements in a small percentage of subjects. Although this intervention could change microbial resistance patterns, the effect of this change is not known. (Funded by the National Institutes of Health; ClinicalTrials.gov number, NCT00325897.)

Tiotropium versus Salmeterol for the Prevention of Exacerbations of COPD

Etude randomisée contrôlée multicentrique (725 centres), durée 1 an

7376 patients >40 ans avec BPCO, VEMS ≤ 70% et ≥ 1 exacerbation/an

Randomisation:

- Tiotropium 18 µg/jour par Handihaler

  vs

- Salmeterol 2x50 µg/jour par aérosol-doseur

Traitement habituel sauf anticholinergiques et LABA

K Vogelmeier et al NEJM 2011 The NEW ENGLAND JOURNAL of MEDICINE

Treatment guidelines recommend the use of inhaled long-acting bronchodilators to alleviate symptoms and reduce the risk of exacerbations in patients with moderate-tovery-severe chronic obstructive pulmonary disease (COPD) but do not specify whether a long-acting anticholinergic drug or a β2-agonist is the preferred agent. We investigated whether the anticholinergic drug tiotropium is superior to the β2-agonist salmeterol in preventing exacerbations of COPD.

METHODS

In a 1-year, randomized, double-blind, double-dummy, parallel-group trial, we compared the effect of treatment with 18 µg of tiotropium once daily with that of 50 µg of salmeterol twice daily on the incidence of moderate or severe exacerbations in patients with moderate-to-very-severe COPD and a history of exacerbations in the preceding year.

RESULTS

A total of 7376 patients were randomly assigned to and treated with tiotropium (3707 patients) or salmeterol (3669 patients). Tiotropium, as compared with salmeterol, increased the time to the first exacerbation (187 days vs. 145 days), with a 17% reduction in risk (hazard ratio, 0.83; 95% confidence interval [CI], 0.77 to 0.90; P<0.001). Tiotropium also increased the time to the first severe exacerbation (hazard ratio, 0.72; 95% CI, 0.61 to 0.85; P<0.001), reduced the annual number of moderate or severe exacerbations (0.64 vs. 0.72; rate ratio, 0.89; 95% CI, 0.83 to 0.96; P = 0.002), and reduced the annual number of severe exacerbations (0.09 vs. 0.13; rate ratio, 0.73; 95% CI, 0.66 to 0.82; P<0.001). Overall, the incidence of serious adverse events and of adverse events leading to the discontinuation of treatment was similar in the two study groups. There were 64 deaths (1.7%) in the tiotropium group and 78 (2.1%) in the salmeterol group.

CONCLUSIONS

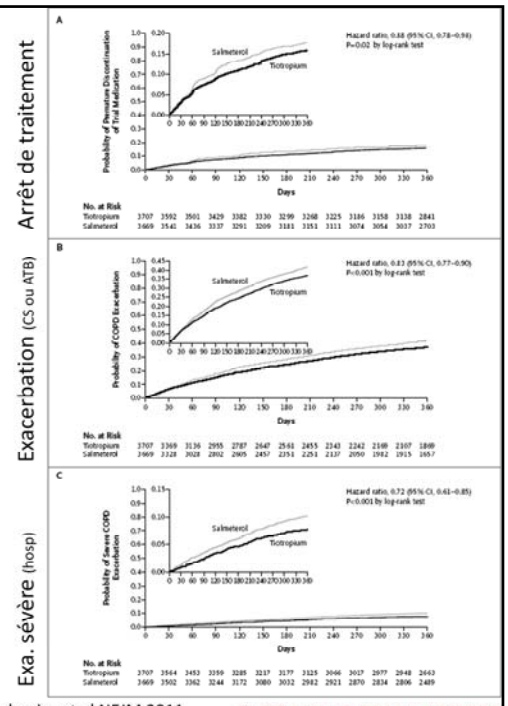
These results show that, in patients with moderate-to-very-severe COPD, tiotropium is more effective than salmeterol in preventing exacerbations. (Funded by Boehringer Ingelheim and Pfizer; ClinicalTrials.gov number, NCT00563381.)

Tiotropium versus Salmeterol for the Prevention of Exacerbations of COPD

1ère exacerbation: RR 0.83
Exacerbation sévère: RR 0.72

Conclusion:
➢Comparé au salmeterol le tiotropium réduit la probabilité d'exacerbation de BPCO

CAVEAT: Différence explicable par mode d'application: poudre vs spray (MDI)?



K Vogelmeier et al NEJM 2011 The NEW ENGLAND JOURNAL of MEDICINE

BACKGROUND
Treatment guidelines recommend the use of inhaled long-acting bronchodilators to alleviate symptoms and reduce the risk of exacerbations in patients with moderate-tovery-severe chronic obstructive pulmonary disease (COPD) but do not specify whether a long-acting anticholinergic drug or a β2-agonist is the preferred agent. We investigated whether the anticholinergic drug tiotropium is superior to the β2-agonist salmeterol in preventing exacerbations of COPD.
METHODS
In a 1-year, randomized, double-blind, double-dummy, parallel-group trial, we compared the effect of treatment with 18 µg of tiotropium once daily with that of 50 µg of salmeterol twice daily on the incidence of moderate or severe exacerbations in patients with moderate-to-very-severe COPD and a history of exacerbations in the preceding year.
RESULTS
A total of 7376 patients were randomly assigned to and treated with tiotropium (3707 patients) or salmeterol (3669 patients). Tiotropium, as compared with salmeterol, increased the time to the first exacerbation (187 days vs. 145 days), with a 17% reduction in risk (hazard ratio, 0.83; 95% confidence interval [CI], 0.77 to 0.90; P<0.001). Tiotropium also increased the time to the first severe exacerbation (hazard ratio, 0.72; 95% CI, 0.61 to 0.85; P<0.001), reduced the annual number of moderate or severe exacerbations (0.64 vs. 0.72; rate ratio, 0.89; 95% CI, 0.83 to 0.96; P = 0.002), and reduced the annual number of severe exacerbations (0.09 vs. 0.13; rate ratio, 0.73; 95% CI, 0.66 to 0.82; P<0.001). Overall, the incidence of serious adverse events and of adverse events leading to the discontinuation of treatment was similar in the two study groups. There were 64 deaths (1.7%) in the tiotropium group and 78 (2.1%) in the salmeterol group.
CONCLUSIONS
These results show that, in patients with moderate-to-very-severe COPD, tiotropium is more effective than salmeterol in preventing exacerbations. (Funded by Boehringer Ingelheim and Pfizer; ClinicalTrials.gov number, NCT00563381.)

Outpatient pulmonary rehabilitation following acute exacerbations of COPD

61 patients au décours d'une exacerbation sévère (RCT)

Intervention: Réhabilitation ambulatoire (n=30)
[2x/sem pdt 8 sem + éducation thérapeutique]
vs UC (n=30)

Outcome: 1aire: Récidive d'exacerbations durant 3 mois
2aire:Force du quadriceps

J Seymour et al, 2010 THORAX

ABSTRACT
Background Exacerbations of chronic obstructive pulmonary disease (COPD) are characterised by increased dyspnoea, reduced quality of life and muscle weakness. Re-exacerbation and hospital admission are common. Pulmonary rehabilitation (PR) administered after hospital admission for an exacerbation can improve quality of life and exercise capacity.
Objective To determine whether outpatient postexacerbation PR (PEPR) could reduce subsequent hospital admission episodes.
Methods Patients admitted to hospital for an exacerbation of COPD were randomised to receive either usual follow-up care (UC) or PEPR after discharge. Hospital admission and emergency department attendances for COPD exacerbations were recorded over a 3-month period and analysed on an intention-to-treat basis. Secondary outcomes included exercise capacity and quadriceps strength.
Results 60 patients underwent concealed randomisation at the time of their hospital discharge (UC: n¼30, mean (SD) age 65 (10) years, forced expiratory volume in 1 s (FEV1) 52 (22)% predicted; PEPR: n¼30, 67(10) years, 52 (20)% predicted). The proportion of patients readmitted to hospital with an exacerbation was 33% in the UC group compared with 7% in those receiving

Outpatient pulmonary rehabilitation following acute exacerbations of COPD

Table 1 Baseline characteristics of patients with COPD

	UC (N=30)	PEPR (N=30)
Age (years)	65 (10)	67 (10)
Sex (M:F)	14:16	13:17
Recruitment site (1:2:3)	16:13:1	18:9:3
Median (IQR) admission length (days)	5 (4–8)	6 (4–8)
Median (IQR) no of admissions in previous year	1 (0–3)	1 (0–2)
Median (IQR) smoking pack-years	40 (23–57)	44 (30–61)
Smoking status (active:prior)	10:20	11:19
FEV_1 (l)	1.3 (0.6)	1.2 (0.4)
FEV_1 (%predicted)	52 (22)	52 (20)
Sao_2 (%)	95 (3)	94 (2)
MRC dyspnoea score (range 1–5)	3.2 (0.7)	3.6 (0.8)
BMI (kg/m^2)	28.7 (7.8)	29.1 (9.1)

J Seymour et al, 2010 THORAX

ABSTRACT

Background Exacerbations of chronic obstructive pulmonary disease (COPD) are characterised by increased dyspnoea, reduced quality of life and muscle weakness. Re-exacerbation and hospital admission are common. Pulmonary rehabilitation (PR) administered after hospital admission for an exacerbation can improve quality of life and exercise capacity.

Objective To determine whether outpatient postexacerbation PR (PEPR) could reduce subsequent hospital admission episodes.

Methods Patients admitted to hospital for an exacerbation of COPD were randomised to receive either usual follow-up care (UC) or PEPR after discharge. Hospital admission and emergency department attendances for COPD exacerbations were recorded over a 3-month period and analysed on an intention-to-treat basis. Secondary outcomes included exercise capacity and quadriceps strength.

Results 60 patients underwent concealed randomisation at the time of their hospital discharge (UC: n¼30, mean (SD) age 65 (10) years, forced expiratory volume in 1 s (FEV1) 52 (22)% predicted; PEPR: n¼30, 67(10) years, 52 (20)% predicted). The proportion of patients readmitted to hospital with an exacerbation was 33% in the UC group compared with 7% in those receiving

Outpatient pulmonary rehabilitation following acute exacerbations of COPD

Table 2 Healthcare utilisation in the UC and PEPR arms over 3 months

	Number (% subjects within group)		
	UC (N=30)	PEPR (N=30)	p Value
Hospital admission for exacerbation	10 (33%)	2 (7%)	0.02
Hospital or ED attendance for exacerbation	17 (57%)	8 (27%)	0.02

Table 3 Incremental and endurance walking capacity, fat-free mass, quadriceps strength and quality of life at baseline and 3 months

	UC (n=26)		PEPR (n=23)		PEPR vs UC
	Baseline	3 months	Baseline	3 months	Difference (95% CI), p value*
QMVC (kg)	25.6 (13.1)	24.4 (13.2)	22.3 (7.2)	26.2 (8.9)	5.1 (2.5 to 7.6), p<0.01
ISW (m)	165 (96)	183 (98)	147 (98)	216 (126)	51 (22 to 79), p<0.01
ESW (m)	224 (175)	224 (133)	214 (402)	402 (400)	189 (28 to 350), p=0.02

Quadriceps maximum volontary contraction
Incremental walking capacity
Endurance walking capacity

Conclusions:
1) diminution de 85% du risque d'exacerbation dans le groupe réhabilitation!
2) Effet médié par la force du quadriceps.

J Seymour et al, 2010 THORAX

ABSTRACT
Background Exacerbations of chronic obstructive pulmonary disease (COPD) are characterised by increased dyspnoea, reduced quality of life and muscle weakness. Re-exacerbation and hospital admission are common. Pulmonary rehabilitation (PR) administered after hospital admission for an exacerbation can improve quality of life and exercise capacity.
Objective To determine whether outpatient postexacerbation PR (PEPR) could reduce subsequent hospital admission episodes.
Methods Patients admitted to hospital for an exacerbation of COPD were randomised to receive either usual follow-up care (UC) or PEPR after discharge. Hospital admission and emergency department attendances for COPD exacerbations were recorded over a 3-month period and analysed on an intention-to-treat basis. Secondary outcomes included exercise capacity and quadriceps strength.
Results 60 patients underwent concealed randomisation at the time of their hospital discharge (UC: n¼30, mean (SD) age 65 (10) years, forced expiratory volume in 1 s (FEV1) 52 (22)% predicted; PEPR: n¼30, 67(10) years, 52 (20)% predicted). The proportion of patients readmitted to hospital with an exacerbation was 33% in the UC group compared with 7% in those receiving

BPCO Mise à jour 2010-2011
Conclusions I

Classification de la BPCO:
Spirométrie + **symptômes** + **fréquence des exacerbations**

Phénotype de la BPCO:
« Exacerbateur fréquent» mieux caractérisé. ECLIPSE.

Traitements non- pharmacologiques:

Azithromycine vs placebo: ↓exacerbation RR 0.73 (surtout exa peu sévère) *mais ↑résistance ATB et ↓ audition*

Tiotropium vs salméterol: tio supérieur avec ↓exacerbation RR 0.83. *Effet poudre vs spray?*

Roflumilast vs placebo: ↓exacerbation RR 0.83 sur exacerbation *mais nausée et perte de poids possible*

HUG Hôpitaux Universitaires de Genève

pierre-olivier.bridevaux@hcuge.ch

Objectives To compare standard high flow oxygen treatment with titrated oxygen treatment for patients with an acute exacerbation of chronic obstructive pulmonary disease in the prehospital setting.
Design Cluster randomised controlled parallel group trial.
Setting Ambulance service in Hobart, Tasmania, Australia.
Participants 405 patients with a presumed acute exacerbation of chronic obstructive pulmonary disease who were treated by paramedics, transported, and admitted to the Royal Hobart Hospital during the trial period; 214 had a diagnosis of chronic obstructive pulmonary disease confirmed by lung function tests in the previous five years.
Interventions High flow oxygen treatment compared with titrated oxygen treatment in the prehospital (ambulance/ paramedic) setting.
Main outcome measure Prehospital or in-hospital mortality.
Results In an intention to treat analysis, the risk of death was significantly lower in the titrated oxygen arm compared with the high flow oxygen arm for all patients (high flow oxygen n=226; titrated oxygen n=179) and for the subgroup of patients with confirmed chronic obstructive pulmonary disease (high flow n=117; titrated n=97). Overall mortality was 9% (21 deaths) in the high flow oxygen arm compared with 4% (7 deaths) in the titrated oxygen arm; mortality in the subgroup with confirmed chronic obstructive pulmonary disease was9% (11 deaths) in the high flow arm compared with 2% (2 deaths) in the titrated oxygen arm. Titrated oxygen treatment reduced mortality compared with high flow oxygen by 58% for all patients (relative risk 0.42, 95% confidence interval 0.20 to 0.89; P=0.02) and by 78% for the patients with confirmed chronic obstructive pulmonary disease (0.22, 0.05 to 0.91; P=0.04). Patients with chronic obstructive pulmonary disease who received titrated oxygen according to the protocol were significantly less likely to have respiratory acidosis (mean difference in pH 0.12 (SE 0.05); P=0.01; n=28) or hypercapnia (mean difference in arterial carbon dioxide pressure −33.6 (16.3) mm Hg; P=0.02; n=29) than were patients who received high flow oxygen.
Conclusions Titrated oxygen treatment significantly reduced mortality, hypercapnia, and respiratory acidosis compared with high flow oxygen in acute exacerbations of chronic obstructive pulmonary disease. These results provide strong evidence to recommend the routine use of titrated oxygen treatment in patients with breathlessness and a history or clinical likelihood of chronic obstructive pulmonary disease in the prehospital setting.
Trial registration Australian New Zealand Clinical Trials Register ACTRN12609000236291.

BPCO Mise à jour 2010-2011
Conclusions II

Traitements non-pharmacologiques:

Réhabilitation précoce après exacerbation: ↓récidive exacerbation OR 0.14! *Effet supérieur aux médicaments mais à confirmer sur une large échelle*

...

HUG Hôpitaux Universitaires de Genève

pierre-olivier.bridevaux@hcuge.ch

Objectives To compare standard high flow oxygen treatment with titrated oxygen treatment for patients with an acute exacerbation of chronic obstructive pulmonary disease in the prehospital setting.
Design Cluster randomised controlled parallel group trial.
Setting Ambulance service in Hobart, Tasmania, Australia.
Participants 405 patients with a presumed acute exacerbation of chronic obstructive pulmonary disease who were treated by paramedics, transported, and admitted to the Royal Hobart Hospital during the trial period; 214 had a diagnosis of chronic obstructive pulmonary disease confirmed by lung function tests in the previous five years.
Interventions High flow oxygen treatment compared with titrated oxygen treatment in the prehospital (ambulance/ paramedic) setting.
Main outcome measure Prehospital or in-hospital mortality.
Results In an intention to treat analysis, the risk of death was significantly lower in the titrated oxygen arm compared with the high flow oxygen arm for all patients (high flow oxygen n=226; titrated oxygen n=179) and for the subgroup of patients with confirmed chronic obstructive pulmonary disease (high flow n=117; titrated n=97). Overall mortality was 9% (21 deaths) in the high flow oxygen arm compared with 4% (7 deaths) in the titrated oxygen arm; mortality in the subgroup with confirmed chronic obstructive pulmonary disease was9% (11 deaths) in the high flow arm compared with 2% (2 deaths) in the titrated oxygen arm. Titrated oxygen treatment reduced mortality compared with high flow oxygen by 58% for all patients (relative risk 0.42, 95% confidence interval 0.20 to 0.89; P=0.02) and by 78% for the patients with confirmed chronic obstructive pulmonary disease (0.22, 0.05 to 0.91; P=0.04). Patients with chronic obstructive pulmonary disease who received titrated oxygen according to the protocol were significantly less likely to have respiratory acidosis (mean difference in pH 0.12 (SE 0.05); P=0.01; n=28) or hypercapnia (mean difference in arterial carbon dioxide pressure −33.6 (16.3) mm Hg; P=0.02; n=29) than were patients who received high flow oxygen.
Conclusions Titrated oxygen treatment significantly reduced mortality, hypercapnia, and respiratory acidosis compared with high flow oxygen in acute exacerbations of chronic obstructive pulmonary disease. These results provide strong evidence to recommend the routine use of titrated oxygen treatment in patients with breathlessness and a history or clinical likelihood of chronic obstructive pulmonary disease in the prehospital setting.
Trial registration Australian New Zealand Clinical Trials Register ACTRN12609000236291.

Mr B.
Prévention (personnalisée) des exacerbations

Thérapie	Diminution du risque d' exacerbation	Prix/mois	Commentaires
Roflumilast 500/j Daxas®	-17%	78 CHF	ES: nausée et perte de poids
Azithromycine 250/j	-27%	104 CHF	ES: audition, QT, **résistances**
Tiotropium (vs selmeterol)	-17%	66 CHF	Privilégier les BD en poudres
Rehabilitation ambulatoire*	-84%	200 à 640 CHF	A confirmer dans d'autres RCT

* 2 séances de ré-entraînement/sem: 25CHF/séance en groupe , 80CHF en individuel

HUG Hôpitaux Universitaires de Genève

Objectives To compare standard high flow oxygen treatment with titrated oxygen treatment for patients with an acute exacerbation of chronic obstructive pulmonary disease in the prehospital setting.
Design Cluster randomised controlled parallel group trial.
Setting Ambulance service in Hobart, Tasmania, Australia.
Participants 405 patients with a presumed acute exacerbation of chronic obstructive pulmonary disease who were treated by paramedics, transported, and admitted to the Royal Hobart Hospital during the trial period; 214 had a diagnosis of chronic obstructive pulmonary disease confirmed by lung function tests in the previous five years.
Interventions High flow oxygen treatment compared with titrated oxygen treatment in the prehospital (ambulance/ paramedic) setting.
Main outcome measure Prehospital or in-hospital mortality.
Results In an intention to treat analysis, the risk of death was significantly lower in the titrated oxygen arm compared with the high flow oxygen arm for all patients (high flow oxygen n=226; titrated oxygen n=179) and for the subgroup of patients with confirmed chronic obstructive pulmonary disease (high flow n=117; titrated n=97). Overall mortality was 9% (21 deaths) in the high flow oxygen arm compared with 4% (7 deaths) in the titrated oxygen arm; mortality in the subgroup with confirmed chronic obstructive pulmonary disease was9% (11 deaths) in the high flow arm compared with 2% (2 deaths) in the titrated oxygen arm. Titrated oxygen treatment reduced mortality compared with high flow oxygen by 58% for all patients (relative risk 0.42, 95% confidence interval 0.20 to 0.89; P=0.02) and by 78% for the patients with confirmed chronic obstructive pulmonary disease (0.22, 0.05 to 0.91; P=0.04). Patients with chronic obstructive pulmonary disease who received titrated oxygen according to the protocol were significantly less likely to have respiratory acidosis (mean difference in pH 0.12 (SE 0.05); P=0.01; n=28) or hypercapnia (mean difference in arterial carbon dioxide pressure −33.6 (16.3) mm Hg; P=0.02; n=29) than were patients who received high flow oxygen.
Conclusions Titrated oxygen treatment significantly reduced mortality, hypercapnia, and respiratory acidosis compared with high flow oxygen in acute exacerbations of chronic obstructive pulmonary disease. These results provide strong evidence to recommend the routine use of titrated oxygen treatment in patients with breathlessness and a history or clinical likelihood of chronic obstructive pulmonary disease in the prehospital setting.
Trial registration Australian New Zealand Clinical Trials Register ACTRN12609000236291.

Merci de votre attention

Etienne Perrin
Pierre-Olivier Bridevaux

HUG
Hôpitaux Universitaires de Genève