

#### REGGIO CALABRIA 19-22 ottobre 2016



L'efficacia terapeutica nella pratica clinica: aderenza fattore discriminante tra successo ed insuccesso

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# VI CONGRESSO A A II TO

# Argomenti in discussione

- Introduzione
- Aderenza: ruolo del paziente
- · Aderenza: ruolo della farmacologia

Aderenza: relazione medico-

paziente

#### Can Guideline-defined Asthma Control Be Achieved?

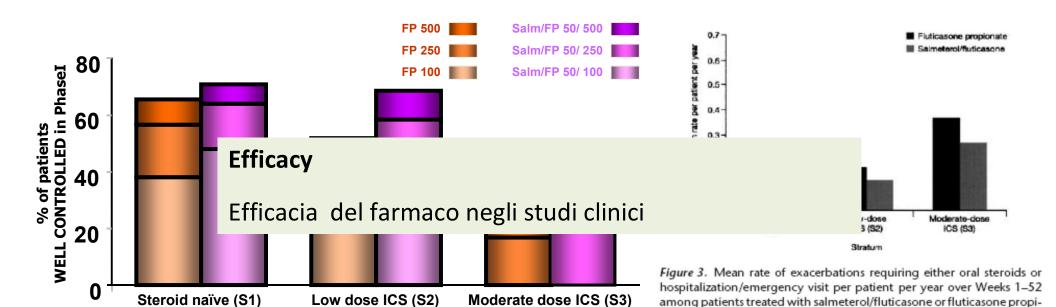
The Gaining Optimal Asthma Control Study

Eric D. Bateman, Homer A. Boushey, Jean Bousquet, William W. Busse, Tim J. H. Clark, Romain A. Pauwels, and Søren E. Pedersen for the GOAL Investigators Group

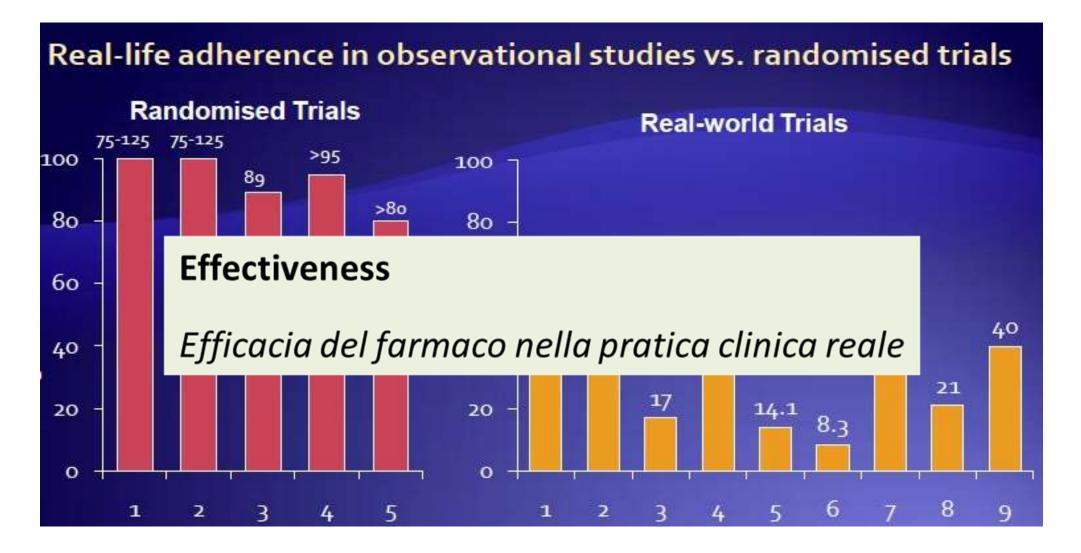
University of Cape Town, Cape Town, South Africa; University of California, San Francisco, San Francisco, California; Hôpital Arnaud De Villeneuve, Montpellier, France; University of Wisconsin Medical School, Madison, Wisconsin; Imperial College, London, United Kingdom; Ghent University Hospital, Ghent, Belgium; and University of Southern Denmark, Kolding Hospital, Kolding, Denmark

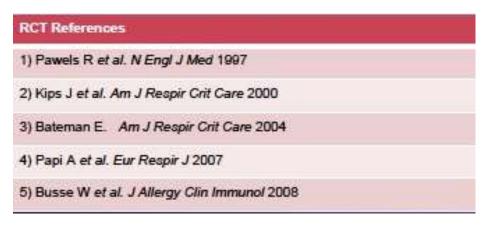
Am J Respir Crit Care Med Vol 170. pp 836-844, 2004

onate according to use of ICS in previous 6 months (S1–S3).  $p \le 0.009$  salmeterol/fluticasone versus fluticasone propionate, all strata.



In addition, the approach of aiming for total control and maintaining treatment resulted in the virtual elimination of exacerbations and near-normal quality of life in the majority of patients and brought substantial benefit even to those who failed to achieve this high level of control.





# Real-world References 1) Partridge Pulm Med 2006 2) De Marco et al. Int Arch Allergy Immunol 2005 3 and 4) Janson et al. Eur Respir J 2001 3=Italy 4=UK 5 and 6) Breekveldt-Postma et al. Pharmaco-epidemiol Drug Saf 2008 5=fixed combination 6=ICS 7) Stallberg et al. Resp Med 2003 8) Adams et al. J Allergy Clin Immunol 2002 9) Corrigan Prim Care Resp J 2011

#### Original article

Persistence with asthma treatment is low in Germany especially for controller medication – a population based study of 483 051 patients

#### Hasford et al.

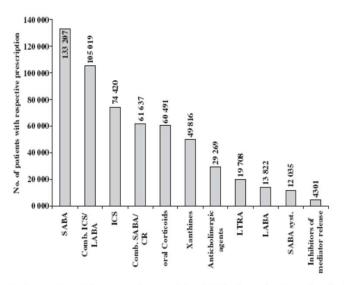


Figure 2. Number of asthma patients with corresponding prescription. SABA, short-acting  $\beta_2$ -agonists; Comb. SABA + CR, SABA + Cromoglycate; SABA sys, systemic SABA; ICS, inhaled corticosteroids; LABA, long acting  $\beta_2$ -agonists; Comb. ICS/LABA, ICS and LABA combined; LTRA, leukotriene receptor antagonists.

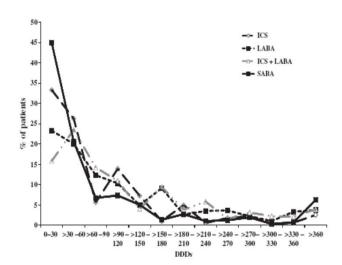
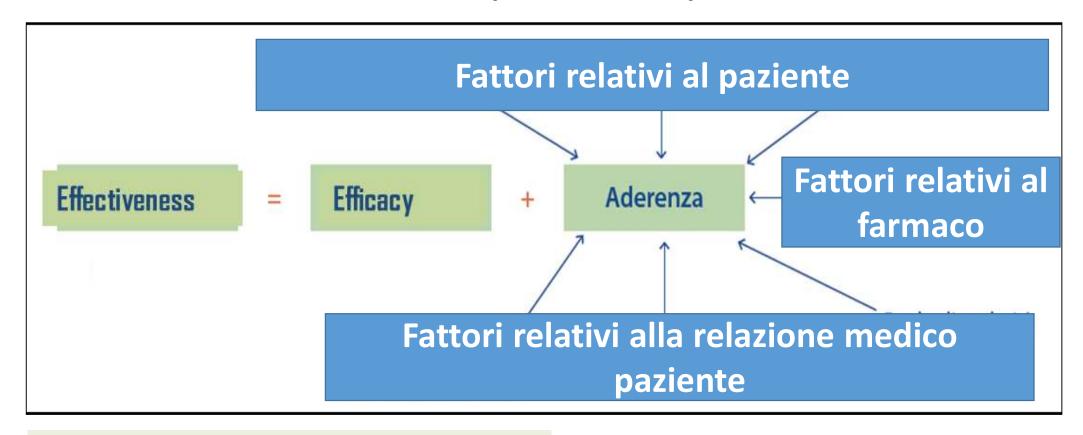


Figure 3. Proportion of patients receiving the indicated number of DDDs over the course of 1 year. ICS, inhaled corticosteroids; LABA, long acting  $\beta_2$ -agonists; SABA, short-acting  $\beta_2$ -agonists.

# Fattori determinanti dell'efficacia terapeutica nella pratica clinica (effectiveness)



#### **Efficacy**

Efficacia del farmaco negli studi clinici

#### **Effectiveness**

Efficacia del farmaco nella pratica clinica reale

Eichler HG NATURE REV DRUG DISCOVERY 2011

Ribeiro J et al Jornal de Pediatria 2006

# Argomenti in discussione

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- Aderenza: ruolo del paziente
- · Aderenza: ruolo della farmacologia

· Aderenza: relazione medico-paziente



# Circulation: Cardiovascular Quality and Outcomes



online 2015, 3/2

# Rischieresti la vita pur di evitare una pillola? <u>Prevenire le malattie cardiovascolari</u> <u>Sondaggio promosso dall'American Heart Association</u>

- L'8% dei partecipanti si è detto disposto a rinunciare a due anni di vita pur di evitare medicine da assumere giornalmente
- Il 13% dei soggetti interpellati ha dichiarato che pur di evitarle accetterebbe anche un minimo rischio di mortalità.
- Il 21% dei partecipanti inoltre pagherebbe più che volentieri 1000 dollari o anche di più se questo consentisse di evitare la pillola quotidiana.





#### Contents lists available at SciVerse ScienceDirect



#### Asthma medication adherence: the role of God and other health locus of control factors

Brian K. Ahmedani, PhD $^*$ ; Edward L. Peterson, PhD $^\dagger$ ; Karen E. Wells, MPH $^\dagger$ ; Cynthia S. Rand, PhD $^\dagger$ ; and L. Keoki Williams, MD, MPH $^{*,\S}$ 

#### ABSTRACT

Background: Medication adherence is an important determinant of disease outcomes, yet medication us on average tends to be low among patients with chronic conditions, including asthma. Although severa predictors of non-adherence have been assessed, more research is needed on patients' beliefs about God and how these relate to medication use.

Objective: To examine the relationship between perceptions about "God's" role in health and other locus of control factors with inhaled corticosteroid (ICS) adherence among asthma patients.

Methods: Participants were from a clinical trial to improve ICS adherence and were 5-56 years old, had a diagnosis of asthma, and were receiving ICS medication. Baseline adherence was estimated from electronic prescription and pharmacy fill records. Patients were considered to be adherent if ICS use was  $\geq$ 80% of prescribed. A baseline survey with the Multidimensional Health Locus of Control scale was used to assess five sources (God, doctors, other people, charge and internal).

Results: Medication adherence was low (36%). Patients' who had a stronger belief that God determined asthma control were less likely to be adherent (odds ratio [OR] 0.82, 95% confidence interval [CI] 0.70-0.96). This relationship was stronger among African American (OR 0.68, 95% CI 0.47-0.99) compared to white patients (OR 0.89, 95% CI 0.75-1.04), and among adults (OR 0.81, 95% CI 0.69-0.96) compared to children (OR 0.84, 95% CI 0.58-1.22).

**Conclusion:** Patients' belief in God's control of health appears to be a factor in asthma controller use, and therefore should be considered in physician-patient discussions concerning course of treatment.

Trial Registration: ClinicalTrials.gov: NCT00459368.

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Table 2
Predictors of inhaled corticosteroid adherence among individuals with asthma<sup>a</sup>

Predictor	Two-variable models <sup>b</sup>		Multivariable model <sup>c</sup>	
	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.45 (1.25-1.69)	.001	1.41 (1.23-1.63)	.001
Female sex <sup>d</sup>	0.90 (0.58-1.42)	.66	0.73 (0.47-1.23)	.19
African American racee	0.48 (0.33-0.70)	.001	0.51 (0.37-0.72)	.001
Medical history <sup>f</sup>	70 50		387/ 72	
ED visits for asthma	1.58 (0.96-2.60)	.07	2.21 (1.36-3.61)	.001
Oral corticosteroid medication fills	0.94 (0.81-1.08)	.38	0.89 (0.77-1.03)	.13
Health locus of control <sup>g</sup>				
God/higher power	0.74 (0.63-0.86)	.001	0.80 (0.67-0.94)	.008
Internal	1.07 (0.93-1.24)	.34	0.97 (0.84-1.12)	.66
Chance	0.89 (0.70-1.13)	.33	1.08 (0.79-1.48)	.61
Physicians	1.40 (1.12-1.75)	.003	1.34 (1.08-1.67)	.008
(Powerful others)				
Other people (powerful others)	0.97 (0.88-1.07)	.51	0.98 (0.89-1.09)	.75

Table 3

Predictors of inhaled corticosteroid adherence among individuals with asthma stratified by race<sup>a</sup>

Predictor	White individuals		African American individuals		
	OR (95% C) <sup>D</sup>	P value	OR (95% CI) <sup>b</sup>	P value	
Age	1.37 (1.19-1.59)	.001	1,60 (1,07-2,38)	.02	
Female sex <sup>c</sup>	0.82 (0.48-1.40)	.46	0.43 (0.16-1.13)	.09	
Medical history <sup>d</sup>				3000	
ED visits for asthma	0.97 (0.24-3.91)	.97	3.85 (2.05-7.24)	.001	
Oral corticosteroid medication fills	0.89 (0.75-1.0.)	.17	0.89 (0.68-1.16)	.40	
Health locus of control <sup>e</sup>				<b>4</b>	
God/higher power	0.89 (0.75-1.04)	.15	0.68 (0.47-0.99)	.04	
Internal	0.92 (0.78-1.08)	.31	1.21 (0.90-1.64)	.21	
Chance	1.12 (0.78-1.61)	.52	1.07 (0.69-1.65)	.76	
Physicians (powerful others)	1.44 (1.13-1.85)	.004	1.04 (0.70-1.53)	.86	
Other people (powerful others)	0.97 (0.85-1.09)	.58	0.93 (0.73-1.19)	.59	

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## I rischi percepiti della terapia

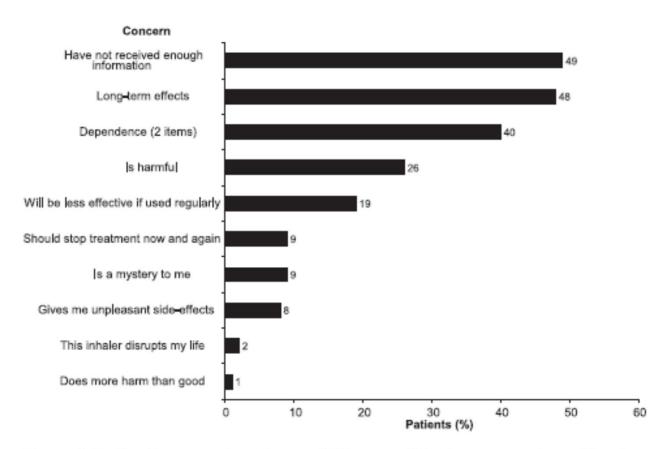
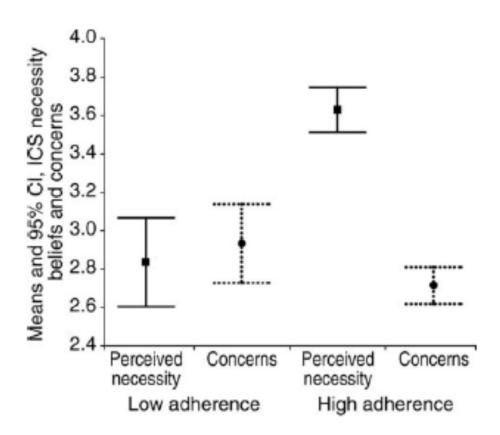


FIGURE 2. Profile of concerns about the use of ICS among 100 primary care patients with asthma (Horne and Weinman<sup>19</sup>).

The concerns about the adverse effects of ICS, is not necessarly related to actual experience, but rather to beliefs about the link between regular use and dependency or other perceived side effects.

Rob Home

Low rate of adherence are related to doubts about personal need for medication and concerns about potential adverse effects.



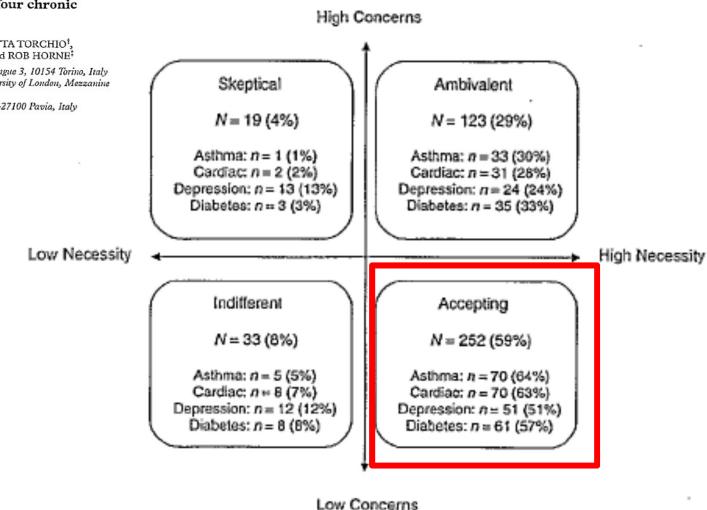
Patients with the greatest doubts about the need for ICS, coupled with the most concerns, had significantly higher rates of nonadherence, while the converse was also true.

#### SHORT REPORT

The utility of the Necessity-Concerns Framework in explaining treatment non-adherence in four chronic illness groups in Italy

GIUSEPPE TIBALDI<sup>†</sup>, JANE CLATWORTHY<sup>‡</sup>, ELISABETTA TORCHIO<sup>‡</sup>, PIERGIORGIO ARGENTERO<sup>§</sup>, CARMINE MUNIZZA<sup>†</sup> and ROB HORNE<sup>‡</sup>

Received 16 January 2009, Accepted 20 January 2009



with Cronbach's alphas of 0.78 (Necessity subscale) and 0.72 (Concerns subscale). Participants were divided into four attitudinal groups based on their responses to the BMQ: 59% Accepting (high Necessity, low Concerns), 29% ambivalent (high Necessity, high Concerns), 8% Indifferent (low Necessity, low Concerns) and 4% Skeptical (low Necessity, high Concerns). Those in the Accepting group reported the highest adherence to medication and those in the Skeptical group the lowest (p<0.01).

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Department of Psychology, University of Pavia, Piazza Botta 6, I-27100 Pavia, Italy

# Argomenti in discussione

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 Aderenza: relazione medicopaziente

## **Adherence to Asthma Treatment**

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2008; 17: 411-422

Published online 21 January 2008 in Wiley InterScience (www.interscience.wiley.com) DOI: 10.1002/pds.1552

#### ORIGINAL REPORT

# Treatment with inhaled corticosteroids in asthma is too often discontinued<sup>†</sup>

Nancy S. Breekveldt-Postma PhD<sup>1</sup>, Jeroen Koerselman MD, PhD<sup>1</sup>, Joëlle A. Erkens PhD<sup>1</sup>, Thys van der Molen MD, PhD<sup>2</sup>, Jan-Willem J. Lammers MD, PhD<sup>3</sup> and Ron M. C. Herings PhD<sup>1,4\*</sup> for the CAMERA Study Group<sup>‡</sup>

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<sup>&</sup>lt;sup>4</sup>Department of Health Policy & Management, Erasmus Medical Center, Rotterdam, The Netherlands

# CHEST

Official publication of the American College of Chest Physicians



#### Compliance, Adherence, and Concordance\*

Rob Horne

Chest 2006;130;65S-72S DOI 10.1378/chest.130.1\_suppl.65S

THE REPORT OF THE PROPERTY OF THE PROPERTY OF

#### Patient Beliefs

The necessity/concerns framework was perceived to be useful in understanding why many patients decide not to use ICS as prescribed (Fig 5). The panel agreed that because ICS do not immediately relieve symptoms, patients believed that they were ineffective and, therefore, unnecessary. The panel

# Does use of a corticosteroid/long-acting beta-agonist combination inhaler increase adherence to inhaled corticosteroids?

	ICS/LABA	ICS
N	25	57
Median age (IQR)	40 (36 to 42)	33 (26 to 40)
Gender, % female	62.5	63.8
Inhalers		
Seretide	21	
Symbicort	4	
Beclomethasone		51
Fluticasone		5
Budesonide		1
Adherence % (IQR)	72.2 (54.8 to 98.6)	40.5 27.4 to 82.2
Median SABA use (IQR)	3 (2 to 7)	4 (2 to 6)

Foden et al, 2008

ICS/LABA = Inhaled corticosteroid/long-acting beta-agonist combined inhaler; ICS = Inhaled corticosteroid inhaler; IQR = Interquartile range; SABA = Short-acting beta-agonist inhaler



#### **ORIGINAL RESEARCH**

#### Primary Adherence to Controller Medications for Asthma Is Poor

Ann Chen Wu<sup>1,2,3</sup>, Melissa G. Butler<sup>4</sup>, Lingling Li<sup>1</sup>, Vicki Fung<sup>5</sup>, Elyse O. Kharbanda<sup>6</sup>, Emma K. Larkin<sup>7</sup>, William M. Vollmer<sup>8</sup>, Irina Miroshnik<sup>1</sup>, Robert L. Davis<sup>9</sup>, Tracy A. Lieu<sup>1,2,3,10</sup>, and Stephen B. Soumerai<sup>1</sup>

<sup>1</sup>Center for Child Health Care Studies, Department of Population Medicine, Harvard Pilgrim Health Care Institute and Harvard Medical School; <sup>2</sup>Division of General Pediatrics, Department of Pediatrics, Children's Hospital, and <sup>3</sup>Harvard Medical School, Boston, Massachusetts; <sup>4</sup>Center for Health Research—Southeast, Kaiser Permanente Georgia, Atlanta, Georgia; <sup>5</sup>Mongan Institute for Health Policy, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts; <sup>6</sup>HealthPartners Institute for Education and Research, Minneapolis, Minnesota; <sup>7</sup>Vanderbilt University School of Medicine, Nashville, Tennessee; <sup>8</sup>Center for Health Research—Northwest, Kaiser Permanente, Portland, Oregon; <sup>9</sup>Center for Biomedical Informatics, University of Tennessee Health Sciences Center, Memphis, Tennessee; and <sup>10</sup>Division of Research, Kaiser Permanente Northern California, Oakland, California

We found that 14–20% of subjects who were prescribed controller medicines for the first time did not fill their prescriptions. The mean proportion of days covered was 19% for ICS, 30% for LTRA, and 25% for ICS/LABA over 12 months.

Table 3. Odds of medication adherence outcomes by asthma controller medication class

	0	R (CI)
	LTRA vs. ICS	ICS/LABA vs. ICS
Primary adherence Early-stage persistence Adjusted PDC ≥ 75%	0.82 (0.74-0.92) 1.82 (1.64-2.04) 6.21 (5.41-7.19)	0.88 (0.80-0.97) 0.96 (0.88-1.04) 2.13 (1.82-2.48)

Definition of abbreviations: CI = confidence interval; ICS = inhaled corticosteroid; ICS/LABA = inhaled corticosteroid/long-acting β-agonist; LTRA = leukotriene antagonist; OR = odds ratio; PDC = proportion of days covered.

#### REVIEW ARTICLE

### Adherence to Medication

Lars Osterberg, M.D., and Terrence Blaschke, M.D.

Drugs don't work in patients who don't take them.

— C. Everett Koop

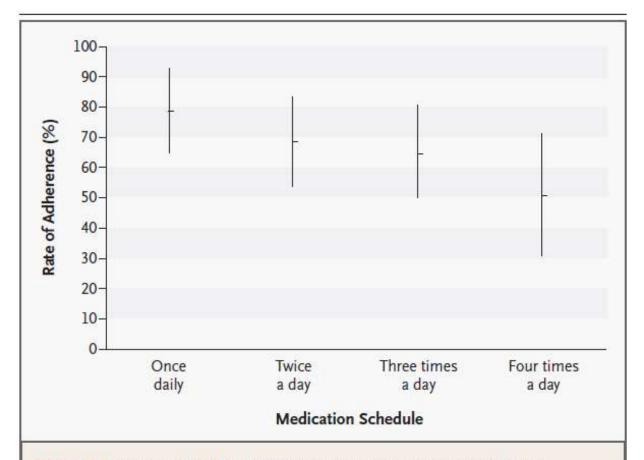


Figure 1. Adherence to Medication According to Frequency of Doses.

Vertical lines represent 1 SD on either side of the mean rate of adherence (horizontal bars). Data are from Claxton et al.<sup>7</sup>

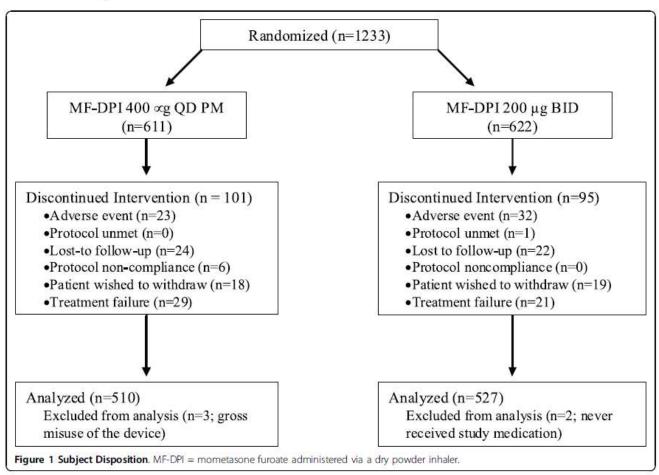


#### **RESEARCH ARTICLE**

**Open Access** 

Improved adherence with once-daily versus twice-daily dosing of mometasone furoate administered via a dry powder inhaler: a randomized open-label study

David Price1\*, Anne Robertson2, Kevin Bullen3, Cyntl



**Results:** 1233 patients were randomized. The mean adherence rates, as measured by the automatic dose counter, were significantly better (P < 0.001) with MF-DPI 400 µg once-daily in the evening (93.3%) than with MF-DPI 200 µg twice-daily (89.5%). Mean adherence rates based on self-reports were also significantly better (P < 0.001) with MF-DPI 400 µg QD PM (97.2%) than with MF-DPI 200 µg twice-daily (95.3%). Adherence rates were lower in adolescents (12-17 years old). Health-related quality of life improved by 20% in patients using MF-DPI once-daily in the evening and by 14% in patients using MF-DPI twice-daily. Very few (<8%) patients missed work/school.

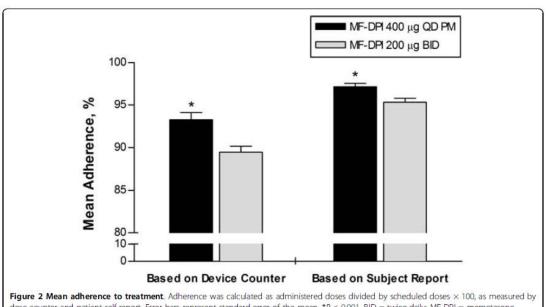


Figure 2 Mean adherence to treatment. Adherence was calculated as administered doses divided by scheduled doses  $\times$  100, as measured by dose counter and patient self-report. Error bars represent standard error of the mean. \*P < 0.001. BID = twice-daily; MF-DPI = mometasone furoate administered via a dry powder inhaler; QD = once-daily.

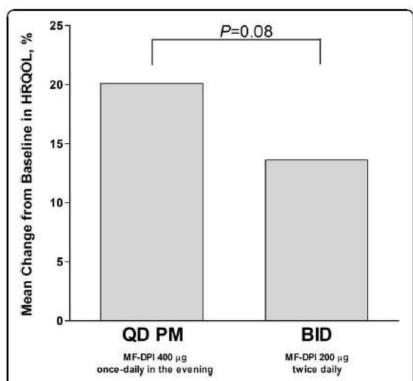
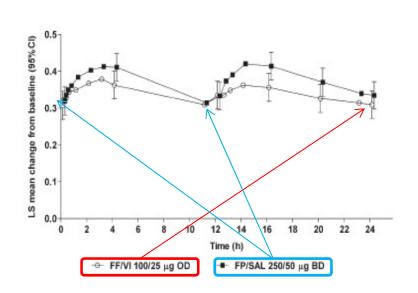


Figure 4 Mean percent change in HRQOL. Changes from baseline in HRQOL were measured by ITG-ASF scores in subjects ≥16 years of age. HRQOL = health-related quality of life; ITG-ASF = Integrated Therapeutics Group-Asthma Short Form; MF-DPI = mometasone furoate administered via a dry powder inhaler; QD = once-daily.

Efficacy and Safety of Fluticasone
Furoate/Vilanterol Compared With
Fluticasone Propionate/Salmeterol
Combination in Adult and Adolescent
Patients With Persistent Asthma
A Randomized Trial



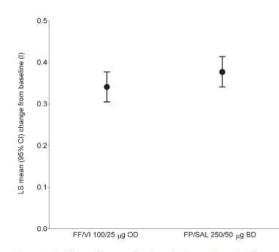


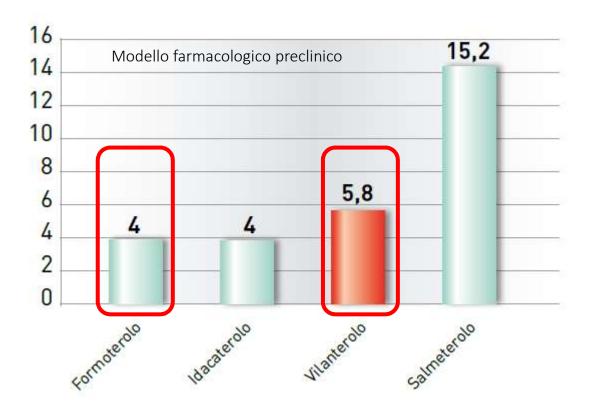
FIGURE 2. Adjusted means for 0- to 24-h serial weighted mean FEV<sub>1</sub> at week 24 (intention-to-treat population). LS = least squares. See Figure 1 legend for expansion of other abbreviations.

In a randomized, double-blind, double-dummy, parallel group study, **806** patients received FF/VI (100/25, n = 403) once daily in the evening delivered through ELLIPTA dry powder inhaler, or FP/SAL (250/50, n = 403) bid through DISKUS.

The efficacy of once-daily FF/VI was <u>similar</u> to bid FP/SAL in improving lung function in patients with persistent asthma. No safety issues were identified.

In Vitro Pharmacological Characterization of Vilanterol, a Novel Long-Acting  $\beta_2$ -Adrenoceptor Agonist with 24-Hour Duration of Action

#### VILANTEROLO: RAPIDA BRONCODILATAZIONE

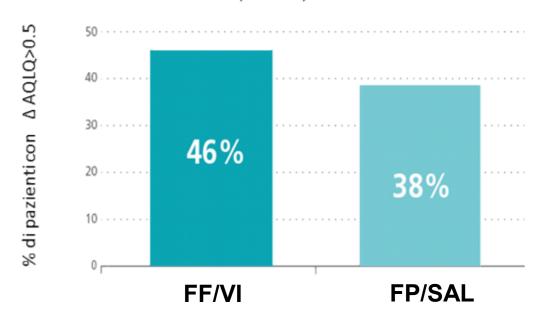


Incremento del FEV1 dopo **5 minuti** dall'inalazione



# Effetto sulla qualità della vita

OR 1.50; 95% CI, 1.06-2.13



FF/VI ha avuto miglioramento clinicamente rilevante nella QoL in una percentuale maggiore di pz rispetto a FP/SALM (analisi post-hoc).



ORIGINAL RESEARCH

Historical cohort study examining comparative effectiveness of albuterol inhalers with and without integrated dose counter for patients with asthma or chronic obstructive pulmonary disease

This article was published in the following Dove Press journal: Journal of Asthma and Allergy 20 August 2016 Number of times this article has been viewed

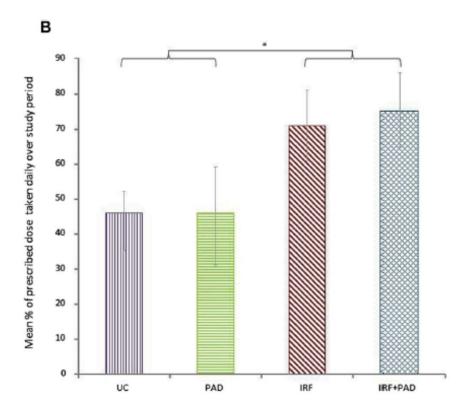
Results: A total of 93,980 patients were studied, including 67,251 (72%) in the dose counter cohort and 26,729 (28%) in the non-dose-counter cohort. The cohorts were broadly similar at baseline (55,069 [59%] female patients; median age, 37 years). The incidence rate of respiratory-related ED visits during the outcome year was 45% lower in the dose counter cohort than in the non-dose-counter cohort (adjusted rate ratio: 0.55; 95% confidence interval: 0.47–0.64). Exacerbation rates and short-acting β-agonist use were similar between cohorts.

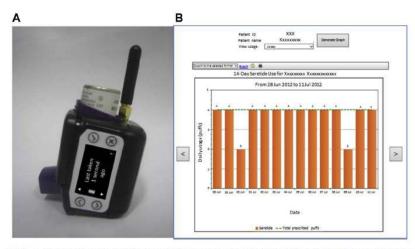
#### Conclusion

We found that the integration of dose counters into rescue inhaler devices is associated with decreased ED visit frequency. The presence of integrated dose counters on rescue inhalers can help patients avoid using an empty or near-empty inhaler during exacerbations, thereby ensuring available medication for relief of their symptoms. The integration of dose counters on rescue MDIs could represent a simple and effective tool to improve clinical outcomes during exacerbations, with a potential for cost savings to health care systems.

# Inhaler reminders improve adherence with controller treatment in primary care patients with asthma

Juliet M. Foster, PhD,<sup>a</sup> Tim Usherwood, BSc, MD, BS,<sup>b</sup> Lorraine Smith, PhD,<sup>c</sup> Susan M. Sawyer, MBBS, MD,<sup>d,e,f</sup> Wei Xuan, MSc, MAppStat, PhD,<sup>g</sup> Cynthia S. Rand, PhD,<sup>h</sup> and Helen K. Reddel, MBBS, PhD<sup>a</sup> Sydney and Melbourne, Australia, and Baltimore, Md





RG 1. A, SmartTrack device installed on a fluticasone propionate/salmeterol inhaler. B, Example adherence feedback for IRF groups. The device electronically recorded the date/time of every actuation. The screen display (time since last dose taken) was seen only by patients in IRF groups. Feedback could be viewed by the IRF patient and his or her GP on a secure Web site. The graph showed the number of inhalations prescribed (dotted line) and the number of inhalations the patient took each day over a 14-day period. Patients and their GPs could access this graph on a password-protected Web site and a copy was e-mailed to them every 30 days.

Conclusions: Inhaler reminders offer an effective strategy for improving adherence in primary care compared with a behavioral intervention or usual care, although this may not be reflected in differences in day-to-day asthma control. (J Allergy Clin Immunol 2014:



## Treatment adherence in asthmatic patients: The last frontier?

Eric D. Bateman, MD, FRCP Cape Town, South Africa

Methods for ensuring adherence recommended in management guidelines focus mainly on improving the skills of health professionals to communicate and motivate patients, and some include aids to assist and encourage patients to take their medications. However, effecting behavior change, first among physicians and then in their patients, is difficult and time-consuming, and in general, published methods for achieving this are complex and impractical in the primary care setting because of time and other constraints.

## Treatment adherence in asthmatic patients: The last frontier?

Eric D. Bateman, MD, FRCP Cape Town, South Africa

than those who received usual care. Thus the primary message of the study is that patient-friendly technology is superior to a behavioral approach in improving adherence. However, the

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- · Aderenza: ruolo della farmacologia

 Aderenza: relazione medicopaziente





#### ORIGINAL RESEARCH

#### Adherence to Long-Acting Inhaled Therapies among Patients with Chronic Obstructive Pulmonary Disease (COPD)

Laura M. Cecere<sup>1,2</sup>, Christopher G. Slatore<sup>3,4</sup>, Jane E. Uman<sup>1</sup>, Laura E. Evans<sup>5</sup>, Edmunds M. Udris<sup>1</sup>, Chris L. Bryson<sup>1,6</sup>, and David H. Au<sup>1,2</sup>

self-management. Conclusions: Adherence to long-acting inhaled medications among patients with COPD is poor, and determinants of adherence likely differ by medication class. Patient perception of clinician expertise in lung disease was the factor most highly associated with adherence to long-acting therapies.

Table 3. Associations of patient perceptions with adherence status

	Long-Acting Beta Agonists		Inhaled Corticosteroids	
	Odds Ratio (95%CI)	P-value	Odds Ratio (95%CI)	P-value
Self-Efficacy*				
Confidence in self-management of breathing problems				
Never-some of the time	1.00	Referent <sup>†</sup>	1.00	Referent <sup>†</sup>
A good bit-most of the time	3.57 (1.09, 11.71)	0.036	0.69 (0.23, 2.07)	0.508
All of the time	5.92 (1.86, 18.85)	0.003	1.58 (0.47, 5.28)	0.461
Confidence in Provider*				
Perception of provider skill/knowledge				
Not at all-somewhat knowledgeable	1.00	Referent <sup>‡</sup>	1.00	Referent <sup>‡</sup>
Quite knowledgeable	4.21 (1.27, 13.93)	0.019	3.03 (0.67, 13.61)	0.149
Very knowledgeable	15.28 (4.25, 54.97)	< 0.001	2.62 (0.58, 11.94)	0.213
Expert	21.70 (6.79, 69.37)	< 0.001	7.93 (1.71, 36.67)	0.008

Odds of adherence to each medication estimated using multiple logistic regression clustered by clinician and using robust standard errors. \*Adjusted for Age, Education, Marital Status, Race, Income, SIC score. FEV<sub>1</sub>% predicted, and complexity of medication regimen; Values in bold indicate p-value < 0.05. †p-value for grouped linear trend = 0.003 for LABA and 0.240 for ICS; ‡ p-value for grouped linear trend = < 0.001 for LABA and 0.007 for ICS.



respiratoryMEDICINE

SHORT COMMUNICATION

Factors affecting adherence to asthma treatment in an international cohort of young and middle-aged adults

Angelo G. Corsico<sup>a,\*</sup>, Lucia Cazzoletti<sup>b</sup>, Roberto de Marco<sup>b</sup>, Christer Janson<sup>c</sup>, Deborah Jarvis<sup>d</sup>, Maria C. Zoia<sup>a</sup>, Massimiliano Bugiani<sup>e</sup>, Simone Accordini<sup>b</sup>, Simona Villani<sup>f</sup>, Alessandra Marinoni<sup>f</sup>, David Gislason<sup>g</sup>, Amund Gulsvik<sup>h</sup>, Isabelle Pin<sup>i</sup>, Paul Vermeire<sup>j</sup>, Isa Cerveri<sup>a</sup>

#### **Evidenze Ottenute**

- La non aderenza al trattamento è la principale ragione dello scarso controllo dell'asma
- Il controllo regolare presso il proprio medico curante è risultato il più forte predittore di miglioramento dell'aderenza (OR 3.32; 95% CI: 1.08–10.17).

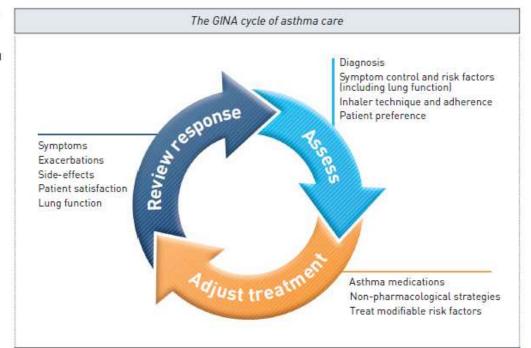


# A summary of the new GINA strategy: a roadmap to asthma control

Helen K. Reddel<sup>1</sup>, Eric D. Bateman<sup>2</sup>, Allan Becker<sup>3</sup>, Louis-Philippe Boulet<sup>4</sup>, Alvaro A. Cruz<sup>5</sup>, Jeffrey M. Drazen<sup>6</sup>, Tari Haahtela<sup>7</sup>, Suzanne S. Hurd<sup>8</sup>, Hiromasa Inoue<sup>9</sup>, Johan C. de Jongste<sup>10</sup>, Robert F. Lemanske Jr<sup>11</sup>, Mark L. Levy<sup>12</sup>, Paul M. O'Byrne<sup>13</sup>, Pierluigi Paggiaro<sup>14</sup>, Soren E. Pedersen<sup>1</sup> Emilio Pizzichini<sup>16</sup>, Manuel Soto-Quiroz<sup>17</sup>, Stanley J. Szefler<sup>18</sup>, Gary W.K. Wong<sup>19</sup> and J. Mark FitzGerald<sup>20</sup>







Good communication is essential - establish a partnership with the patient

· Consider health literacy, personal goals and fears, and cultural issues

#### Treatment choices

- Population-level decisions: efficacy, effectiveness, safety, cost, regulations
- Patient-level decisions for tailoring treatment: also discuss patient characteristics (phenotype) that
  predict response or risk; patient preference; practical issues inhaler technique, adherence, and
  cost; treat modifiable risk factors; use non-pharmacological strategies where appropriate

#### Stepwise medication adjustment

- Consider stepping up if uncontrolled symptoms, exacerbations or risks, but check diagnosis, inhaler technique, adherence and modifiable risk factors first
- Consider stepping down if symptoms controlled for 3 months and low risk for exacerbations.
   For adults, ceasing ICS is not advised.

Written asthma action plan for all patients





#### Original article

Unmet needs in asthma: Global Asthma Physician and Patient

(GAPP) Survey: global adult findings

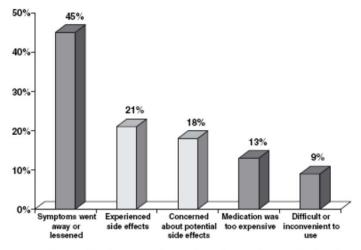
#### G. W. Canonica<sup>1</sup>, C. E. Baena-Cagnani<sup>2</sup>, M. S. Blaiss<sup>3</sup>, R. Dahl<sup>4</sup>, M. A. Kaliner<sup>5</sup>, E. J. Valovirta<sup>6</sup> (The GAPP Survey Working Group)

<sup>1</sup>Department of Internal Medicine, University of Genova Pad., Genova, Italy; <sup>2</sup>Catholic University of Córdoba, Córdoba, Argentina; <sup>3</sup>University of Tennessee Health Science Center, Memphis, TN, USA; <sup>4</sup>Department of Respiratory Diseases, Aarhus University Hospital, Aarhus, Denmark; <sup>5</sup>Institute for Asthma and Allergy, Chevy Chase, MD, USA; <sup>6</sup>Turku Allergy Center, Turku, Finland

#### Levels of asthma education

When questioned on perceptions of asthma education, 87% of physicians and 64% of patients said that up to half of the office visit was devoted to educational issues, such as correct inhaler technique, monitoring peak expiratory flow and developing an individual management plan. On average, patients reported that only 25% of office visit time was devoted to asthma education, and 23% of patients estimated that no time was spent discussing techniques for successful asthma management. Patients who categorize their asthma as Awareness and impact of side effects

Most patients (>70%) reported that they 'never' or 'rarely' had discussions with their physician about medication side effects, while most physicians (>60%) reported that they 'sometimes' or 'always' discussed side effects with patients. The majority of patients and physicians reported that they initiated discussions about side effects (60% vs 76%).



rom one asthma medication to another or discontinue asthma medication due to various reasons. Question: the asthma, have you ever switched from one asthma medication to another or discontinued an asthma ie: Currently or has ever used asthma medication (patients).







### Inhaler mishandling remains common in real life and is associated with reduced disease control

Andrea S. Melani <sup>a,\*</sup>, Marco Bonavia <sup>b</sup>, Vincenzo Cilenti <sup>c</sup>, Cristina Cinti <sup>d</sup>, Marco Lodi <sup>e</sup>, Paola Martucci <sup>f</sup>, Maria Serra <sup>g</sup>, Nicola Scichilone <sup>h</sup>, Piersante Sestini <sup>i</sup>, Maria Aliani <sup>j</sup>, Margherita Neri <sup>k</sup>, on behalf of the Gruppo Educazionale Associazione Italiana Pneumologi Ospedalieri (AIPO)<sup>1</sup>

We have a total of 2288 records of inhaler technique. Critical mistakes were widely distributed among users of all the inhalers, ranging from 12% for MDIs, 35% for Diskus® and HandiHaler® and 44% for Turbuhaler®. Independently of the inhaler, we found the strongest association between inhaler misuse and older age (p=0.008), lower schooling (p=0.001) and lack of instruction received for inhaler technique by health caregivers (p<0.001). Inhaler misuse was associated with increased risk of hospitalization (p=0.001), emergency room visits (p<0.001), courses of oral steroids (p<0.001) and antimicrobials (p<0.001) and poor disease control evaluated as an ACT score for the asthmatics (p<0.0001) and the whole population (p<0.0001).

We conclude that inhaler mishandling continues to be common in experienced outpatients referring to chest clinics and associated with increased unscheduled health-care resource use and poor clinical control. Instruction by health caregivers is the only modifiable factor useful for reducing inhaler mishandling

# Improved asthma outcomes with a simple inhaler technique intervention by community pharmacists

Iman A. Basheti, BPharm Sci<sup>a</sup>
Helen K. Reddel, MBBS, PhD, FRACP<sup>b</sup>
Carol L. Armour, BPharm(Hons), PhD<sup>a</sup>
Sinthia Z. Bosnic-Anticevich, BPharm(Hons), PhD<sup>a</sup>

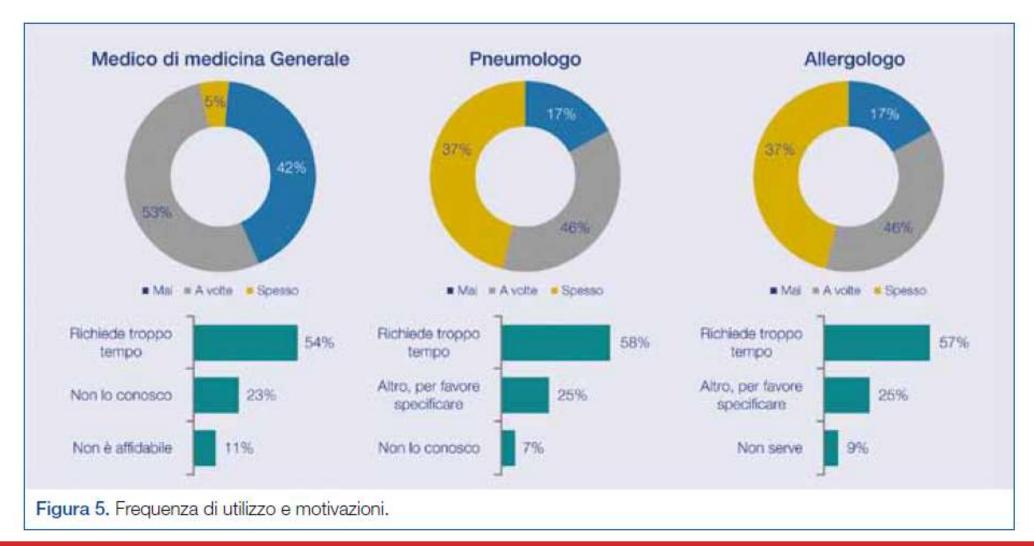


In summary, this study demonstrated that a simple educational intervention taking only 2.5 minutes and targeting inhaler technique was feasible for delivery by community pharmacists and resulted in improved clinical and humanistic outcomes for patients with asthma. Active patients had significantly better inhaler technique, reduced peak expiratory flow variability, and improved AQOL and PC of asthma than control patients. For patients in the active group, inhaler technique, although maintained during monthly retraining, tended to decline over the final 3 months during which no further education was delivered. This was associated with a decrease in some asthma outcomes.

These observations confirm that rechecking and reeducating patients about inhaler technique needs to be a regular and ongoing process. Community pharmacists are well placed to do this because they can engage the patient every time an inhaler is dispensed. This study thus highlights the critical role of face-to-face pharmacistpatient interactions about inhaled medications. Improved inhaler technique will have an effect on asthma control and health care use.



Medico di medicina generale e specialisti: opinioni a confronto su identificazione, diagnosi e monitoraggio del paziente asmatico in Italia



#### Long-Term Inhaled Corticosteroid Adherence in Asthma Patients with Short-Term Adherence

Laurent Laforest, MD, PhD<sup>a,b</sup>, Manon Belhassen, MSc<sup>a,b</sup>, Gilles Devouassoux, MD, PhD<sup>c</sup>, Alain Didier, MD, PhD<sup>d</sup>, Marine Ginoux, MSc<sup>b</sup>, and Eric Van Ganse, MD, PhD<sup>a,b,c</sup> Lyon and Toulouse, France

In summary, in patients with asthma identified at selection by regular ICS use, this regularity did not last over the following months, with less than 25% of patients continuously using ICS over 12 months. Adherence increased with asthma severity, lower control, and continuity of care. A better understanding of the determinants of this discontinuous use of controller therapy is needed, along with identification of specific patient or health care professional profiles.

TABLE III. Probability of achieving a CMA value of ≥80% over 12 mo postindex date, multivariate logistic regression

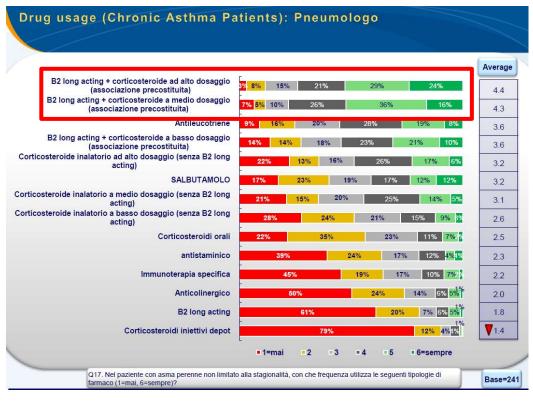
		N = 5044	-
Patient characteristics at baseline or during study period	OR		P
Age group			.0021
Adults (17-40 y)	1.00	_	
Teenagers (13-16 y)	1.28	1.01-1.61	
Children (6-12 years)	1.34	1.13-1.59	
Sex			.0555
Male	1.00	_	
Female	0.87	0.76-1.00	
ree-access-to-care status	0.07	0.70 1.00	.5065
No	1.00	_	15005
Yes	1.06	0.89-1.27	
Previous SABAs (12 mo before the index date)	1.00	0.07 1.27	<.0001
None	1.00	_	0.0001
1-4 refills	0.98	0.83-1.16	
≥5 refills	1.97	1.61-2.41	
	1.97	1.01-2.41	0.1148
systemic corticosteroids (12 mo before the index date)  None	1.00	_	0.1140
1-2 refills	0.87	0.75-1.01	
≥3 refills	1.03	0.84-1.26	1100
Rhinitis (12 mo before the index date)	2.22		.1179
No	1.00	_	
Yes	1.12	0.97-1.30	
Depression, anxiety (12 mo before the index date)			.1164
No	1.00	_	
Yes	1.24	0.95-1.63	
.TD status and/or hospitalization for asthma (12 mo before the index date)			.0073
No	1.00	_	
Yes	1.41	1.10-1.81	
No. of doses in the ICS device dispensed at the index date			<.0001
<100	1.00	_	
100-199	1.27	0.98-1.64	
200	3.30	2.33-4.67	
CS/LABA fixed-dose combination at the index date			.7054
No	1.00	_	
Yes	1.05	0.83-1.32	
nhaler device at the index date			.0453
Pressurized metered-dose inhaler	1.00	_	
Dry powder inhaler multidose Diskus	0.91	0.67-1.23	
Dry powder inhaler Turbuhaler	1.22	0.98-1.52	
Breath-actuated device	1.26	0.89-1.78	
Others	1.08	0.74-1.57	
speciality of initial prescriber (index date)			.0025
GP	1.00	_	
Private practice specialist	0.99	0.81-1.20	
Hospital physician	1.48	1.18-1.86	
Any switch of ICS during the study period	1.10	1.10 1.00	<.0001
No	1.00	_	3.0001
Yes	1.58	1.36-1.82	
23 different prescribers of respiratory drugs during the study period	1.56	1.,00-1.02	.0002
	1.00		.002
No V	1.00	1 10 1 71	
Yes	1.42	1.18-1.71	<.0001
requency of GP visits during the study period	2 AL 1		<.0001
0-2	1.00		
3-6	1.45	1.20-1.74	
>6 	1.79	1.47-2.19	
1 visit to a specialist* during the study period			.629
No	1.00	_	
Yes	1.04	0.89-1.22	

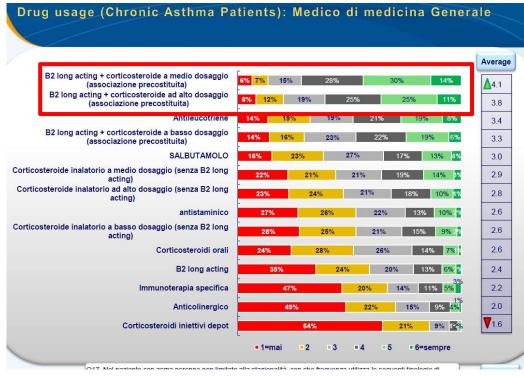
ABA, Long-acting beta agonist,

<sup>\*</sup>Respiratory physician, ear, nose, and throat specialist, pediatrician, hospital physician. The specialty was not documented in the database for hospital physicians.

M. Caminati<sup>1</sup>, M. S. Magnoni<sup>2</sup>, A. Rizzi<sup>2</sup>, F. Braido<sup>3</sup>, A. Foresi<sup>4</sup>, G. Bettoncelli<sup>5</sup>, A. Infantino<sup>6</sup>, C. D'Andria<sup>7</sup>, L. Antonicelli<sup>8</sup>, P. L. Paggiaro<sup>9</sup>, F. Falcone<sup>10</sup>, G. Senna<sup>1</sup>

## Asthma management among different specialists: results from a national Italian survey





RESEARCH Open Access



# Determinants and impact of suboptimal asthma control in Europe: The INTERNATIONAL CROSS-SECTIONAL AND LONG/TUDINAL ASSESSMENT ON ASTHMA CONTROL (LIAISON) study

Fulvio Braido<sup>1</sup>, Guy Brusselle<sup>2,3</sup>, Daniele Guastalla<sup>4</sup>, Eleonora Ingrassia<sup>4\*</sup>, Gabriele Nicolini<sup>4</sup>, David Price<sup>5</sup>, Nicolas Roche<sup>6</sup>, Joan B. Soriano<sup>7</sup>, Heinrich Worth<sup>8</sup> and on behalf of the LIAISON Study Group

**Results:** Overall, 8111 asthmatic patients were enrolled in 12 European countries. Asthma control was suboptimal in 56.5 % of patients and it was associated with poorer asthma-related QoL, higher risk of exacerbations and greater consumption of healthcare resources.

Variables associated with suboptimal control were age, gender, obesity, smoking and comorbidities. Major determinants of poor asthma control were seasonal worsening and persisting exposure to allergens/irritants/triggers, followed by treatment-related issues.

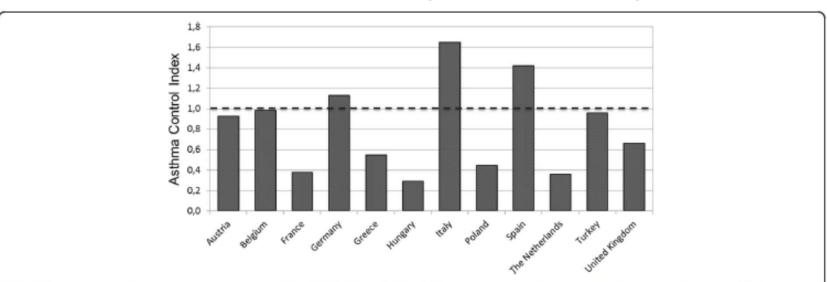
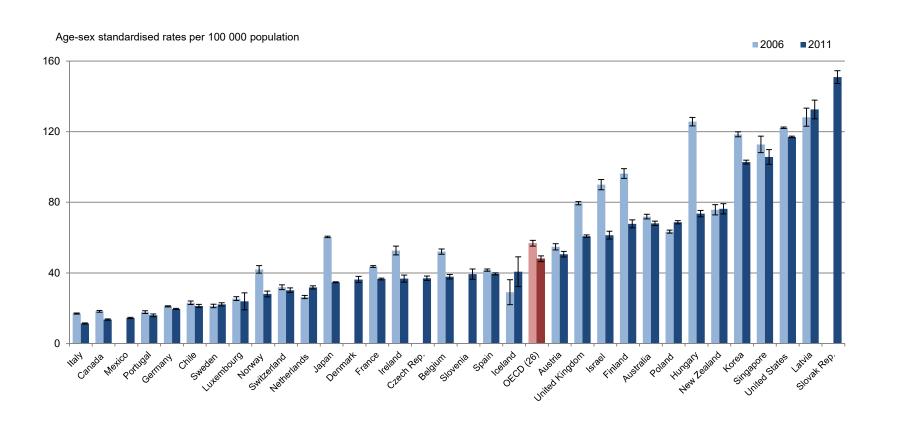


Fig. 1 Asthma Control Index among countries of the LIAISON study. The index was computed as the ratio of patients with controlled asthma (6-item ACQ < 0.75) to patients with not well-controlled asthma (6-item ACQ  $\le 0.75$ ). Asthma Control Index > 1: greater proportion of patients with controlled asthma. Asthma Control Index < 1: greater proportion of patients with not well-controlled asthma

# Asthma hospital admission in adults, 2006 and 2011 (or nearest year)



Note: 95% confidence intervals represented by H.

Source: OECD Health Statistics 2013, http://dx.doi.org/10.1787/health-data-en.

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Determinants and impact of suboptimal asthma control in Europe: The INTERNATIONAL CROSS-SECT/ONAL AND LONG/TUDINAL ASSESSMENT ON ASTHMA CONTROL (LIAISON) study

Fulvio Braido<sup>1</sup>, Guy Brusselle<sup>2,3</sup>, Daniele Guastalla<sup>4</sup>, Eleonora Ingrassia<sup>4\*</sup>, Gabriele Nicolini<sup>4</sup>, David Price<sup>5</sup>, Nicolas Roche<sup>6</sup>, Joan B. Soriano<sup>7</sup>, Heinrich Worth<sup>8</sup> and on behalf of the LIAISON Study Group

Treatment-related factors are crucial for the control of the disease, representing 60.0 % and 42.6 % of all reasons for poor control (as expressed by doctors and patients, respectively), as a whole. The risk of non-adherence was low in the overall study population as well as in uncontrolled subjects (16.3 %). Two times more physicians

No significant interaction was found between the asthma control level and the non-adherence categories (p = 0.398; Additional file 1: Table S3).

Table 4 Reasons for poor asthma control, according to patients' and doctors' perspective

Reasons for poor control <sup>a</sup> : $n = 4585$	Patients' perspective n (%)	Doctors' perspective n (%)	Kappa coefficient <sup>b</sup>
Seasonal worsening	1848 (40.3)	1756 (38.3)	0.72
Continued exposure to allergens/irritants/triggers	1148 (25.0)	1270 (27.7)	0.73
Comorbidities	769 (16.8)	1028 (22.4)	0.68
Poor adherence to therapy	507 (11.1)	965 (21.0)	0.47
nadequate therapy	571 (12.5)	868 (18.9)	0.56
Poor efficacy of therapy	675 (14.7)	622 (13.6)	0.53
Active smoking	339 (7.4)	462 (10.1)	0.81
Depression	388 (8.5)	453 (9.9)	0.67
Passive smoking	421 (9.2)	319 (7.0)	0.64
nadequate inhalation technique	104 (2.3)	195 (4.3)	0.39
Poor patient-physician communication	78 (1.7)	197 (4.3)	0.27
Poor tolerability of therapy	97 (2.1)	100 (2.2)	0.44
Co-administration of drugs	70 (1.5)	68 (1.5)	0.55
ncorrect diagnosis	57 (1.2)	40 (0.9)	0.30

N number of patients

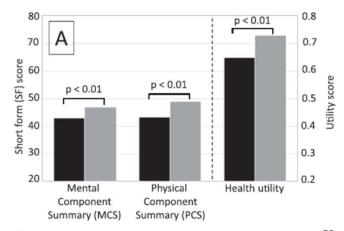
<sup>&</sup>lt;sup>a</sup>More than one reason could be indicated

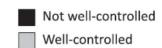
<sup>&</sup>lt;sup>b</sup>Kappa agreement interpretation: <0: poor, 0.01–0.20: slight, 0.21–0.40: fair, 0.41–0.60: moderate, 0.61–0.80: good, 0.81–1.00; very good

Asthma control in patients treated with inhaled corticosteroids and long-acting beta agonists: A population-based analysis in Germany

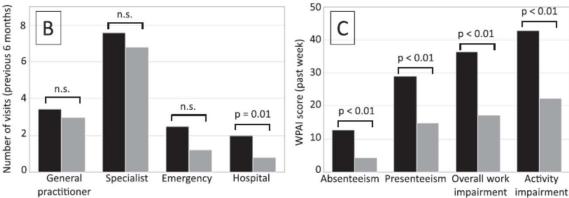
Anke Kondla b, Thomas Glaab b, Riccardo Pedersini c, d, Marek Lommatzsch a, \*

d RTI Health Solutions, Barcelona, Spain





Self-reported medication adherence did not differ significantly between groups: 55.4% of well-controlled patients and 60.4% of not well-controlled patients reported high levels of adherence as measured by MMAS-4 and -8. The result was confirmed by a logistic



However, it is noteworthy that patient attitudes toward their patient-physician relationship were the main differentiator between well-controlled and not well-controlled ICS-LABA treated patients (in contrast to the plethora of different patient character-

<sup>2</sup> University of Rostock, Department of Respiratory Medicine, Rostock, Germany

<sup>&</sup>lt;sup>b</sup> Boehringer Ingelheim Pharma GmbH & Co. KG, Medical Affairs Respiratory Medicine, Ingelheim, Germany

c Kantar Health, Epsom, Surrey, UK

## Argomenti in discussione

- Aderenza alla terapia :una interazione complessa
- Aderenza ruolo del paziente
- Aderenza ruolo del medico
- Aderenza ruolo della farmacologia
- Conclusioni

#### The NEW ENGLAND JOURNAL of MEDICINE

#### REVIEW ARTICLE

#### DRUG THERAPY

#### Adherence to Medication

Lars Osterberg, M.D., and Terrence Blaschke, M.D.

Drugs don't work in patients who don't take them.

— C. Everett Koop, M.D.

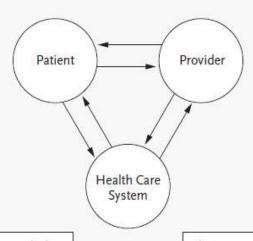
Poor provider-patient communication

the medication

Patient has a poor understanding of the disease Patient has a poor understanding of the benefits and

risks of treatment Patient has a poor understanding of the proper use of

Physician prescribes overly complex regimen



Patient's interaction with the health care system
Poor access or missed clinic appointments
Poor treatment by clinic staff
Poor access to medications
Switching to a different formulary
Inability of patient to access pharmacy
High medication costs

Physician's interaction with the health care system Poor knowledge of drug costs Poor knowledge of insurance coverage of different formularies Low level of job satisfaction

#### Figure 2. Barriers to Adherence.

The interactions among the patient, health care provider, and health care system depicted are those that can have a negative effect on the patient's ability to follow a medication regimen.



## Treatment adherence in asthmatic patients: The last frontier?

Eric D. Bateman, MD, FRCP Cape Town, South Africa

controlled. However, acceptance of this fact, and that poor adherence is endemic might be better than current practice, in which physicians, believing that the prescribed dose is being taken, are likely to overprescribe (increase the dose or add other medications), adding cost and potential for side effects, which introduce a further burden on the patient and erode adherence.



## Treatment adherence in asthmatic patients: The last frontier?

Eric D. Bateman, MD, FRCP Cape Town, South Africa

Thus the term "intentional nonadherence" should be reviewed and possibly be changed to "patient-adjusted maintenance therapy."

The implications of revised terminology for maintenance treatment is that rather than expecting patients to adapt to an unrealistic regimen, perhaps treatment strategies should be designed to better fit normal human behavior. This is not peculiar to asthma but is the basis for promoting once-daily or even intermittent treatment for avoiding use of more than 1 treatment and for the use of depot injections for certain conditions.



## Treatment adherence in asthmatic patients: The last frontier?

Eric D. Bateman, MD, FRCP Cape Town, South Africa

However, this study, together with other studies that have accurately measured inhaler use, has exposed deficiencies in our concepts of adherence and points to a need for a broader view than simply counting doses. Customized patient-friendly treatment that anticipates and accommodates usual behavior and addresses conscious and unconscious medication beliefs is more likely to achieve the desired goal of disease control. Arguably, this, rather than the development of new drugs, should be viewed as the "last frontier" of asthma management.



## Randomized controlled trial of adherence with single or combination inhaled corticosteroid/long-acting $\beta$ -agonist inhaler therapy in asthma

Kyle Perrin, MBChB, FRACP, a,b Mathew Williams, Dip Ex Sci, Meme Wijesinghe, BSc, MBBS, MRCP, a,b Kate James, MBChB, a,b Mark Weatherall, MBChB, FRACP, b,c and Richard Beasley, MBChB, DSca,b,c Wellington, New Zealand

Conclusion: In the setting of a randomized controlled trial, use of a combination ICS/LABA inhaler does not markedly increase adherence above that observed with separate inhaler use. LABA monotherapy was observed in a small proportion of patients prescribed ICS and LABA therapy via separate inhalers.

(J Allergy Clin Immunol 2010;126:505-10.)

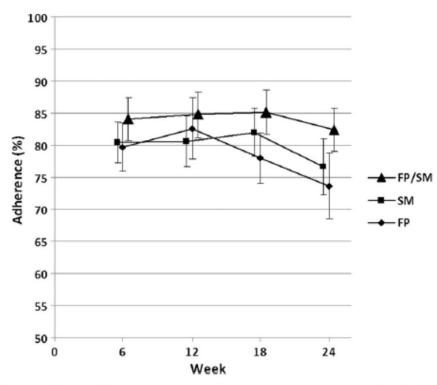


FIG 2. Adherence in the four 6-week periods of the study in the subjects prescribed FP/salmeterol (SM; ▲), SM (■), and FP (♦). The symbols show the mean and the error bars the SEM.