

# XXXIV

## Congreso Nacional de la Sociedad Española de Medicina Interna (SEMI)

XXIX Congreso de la  
Sociedad Andaluza de  
Medicina Interna (SADEMI)

**21-23**

Noviembre 2013

Palacio de Ferias y Congresos de Málaga  
**Málaga**



# **BRONCODILATACIÓN: PIEDRA ANGULAR EN EL TRATAMIENTO DE LA EPOC**

## **VARIABILIDAD DE SÍNTOMAS RESPIRATORIOS**

- Existencia, importancia y diagnóstico
- Implicaciones en el tratamiento broncodilatador

**Francisco López García**  
**Medicina Interna**  
**Hospital General Universitario de Elche, Alicante**

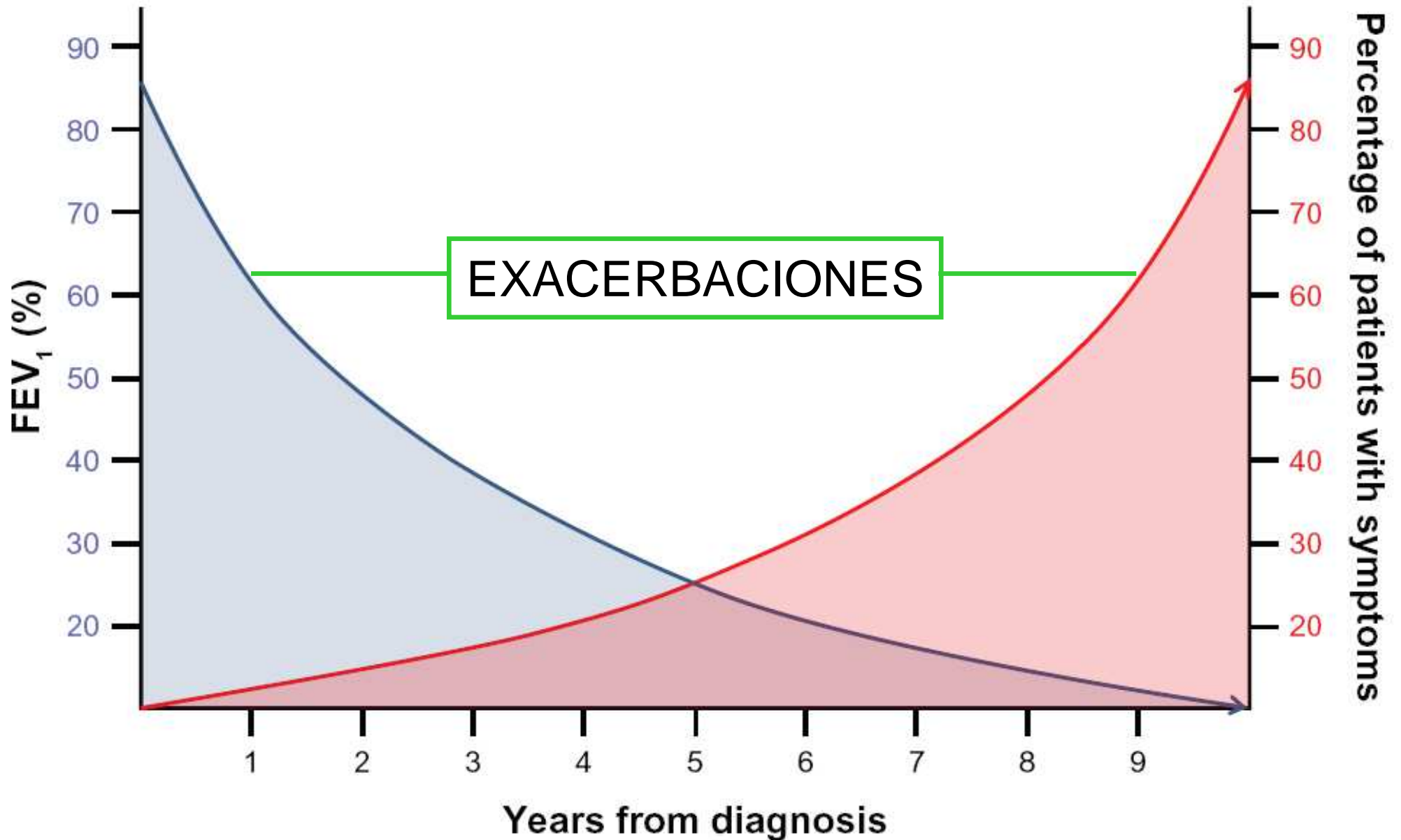


# DISCLOSURE INFORMATION

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Francisco López García has acted in consultant and has served information, scientific advice and participation in clinical studies or writing for publications for (in alphabetical order): Almirall, AstraZeneca, Boehringer Ingelheim, Esteve, Faes, Ferrer, GlaxoSmithKline, Menarini, MSD, Novartis, Pfizer and Takeda (Nycomed).

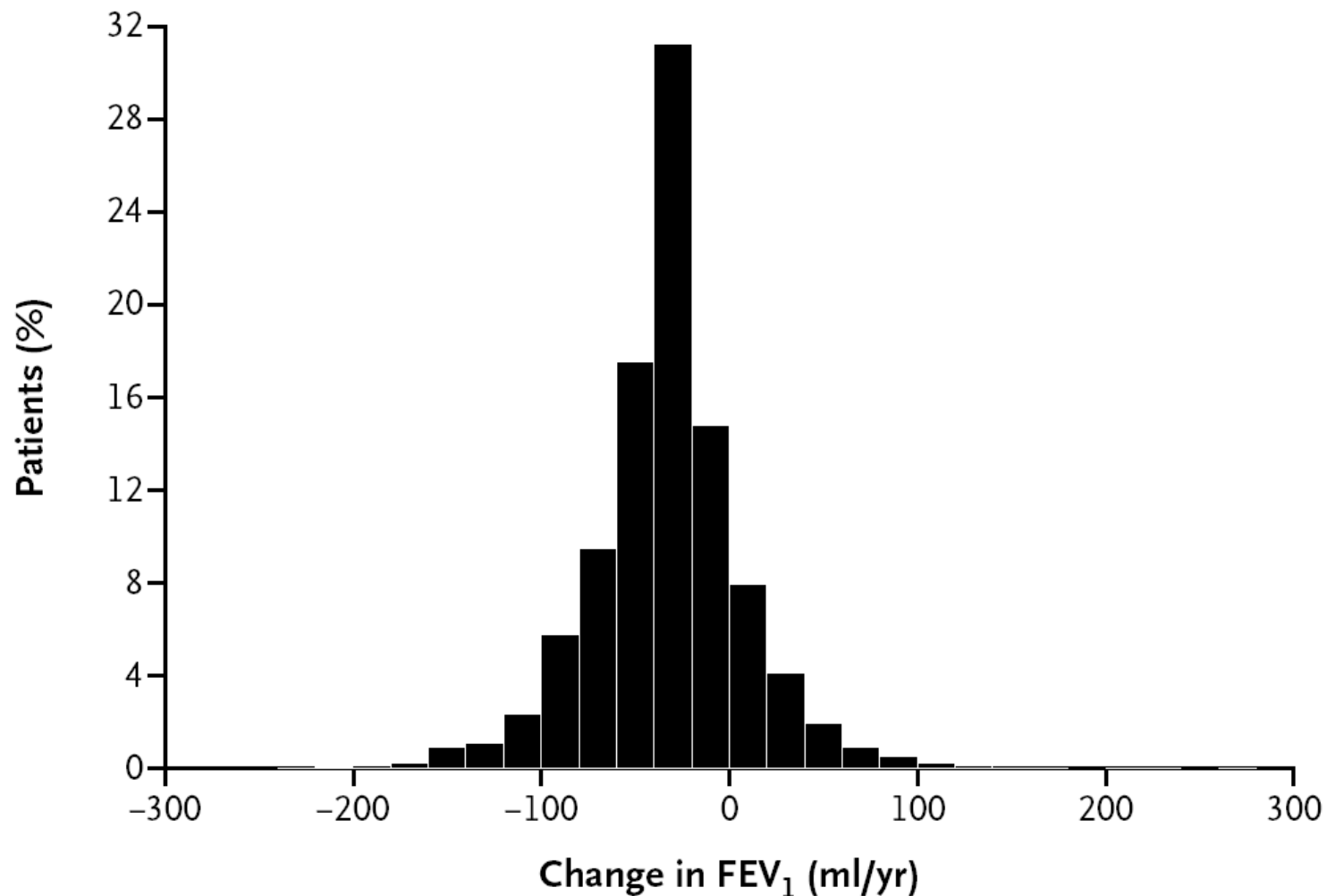
# DECLIVE DEL FEV1 Y SÍNTOMAS



# Changes in Forced Expiratory Volume in 1 Second over Time in COPD

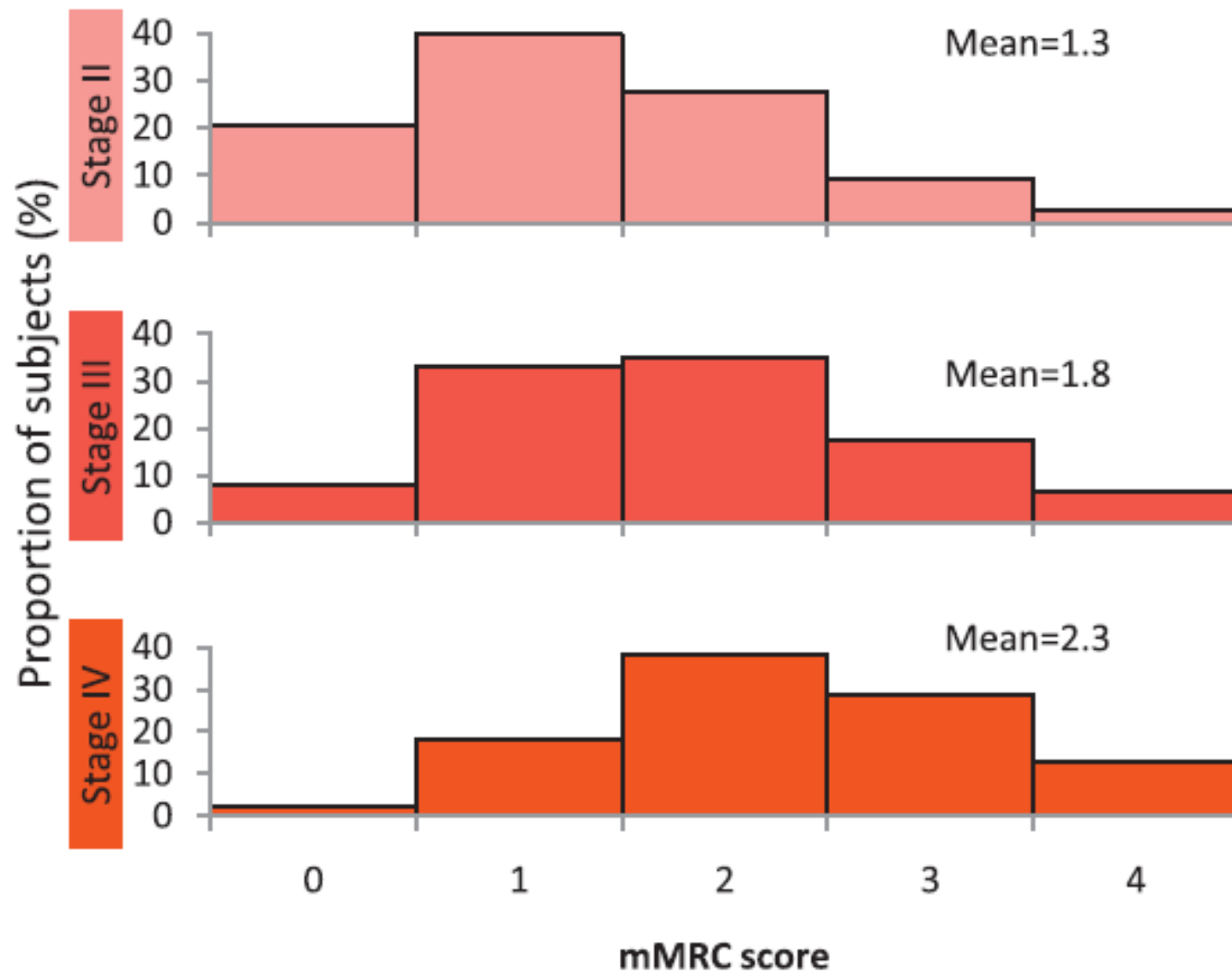
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The rate of change in FEV<sub>1</sub> among patients with COPD is highly variable.



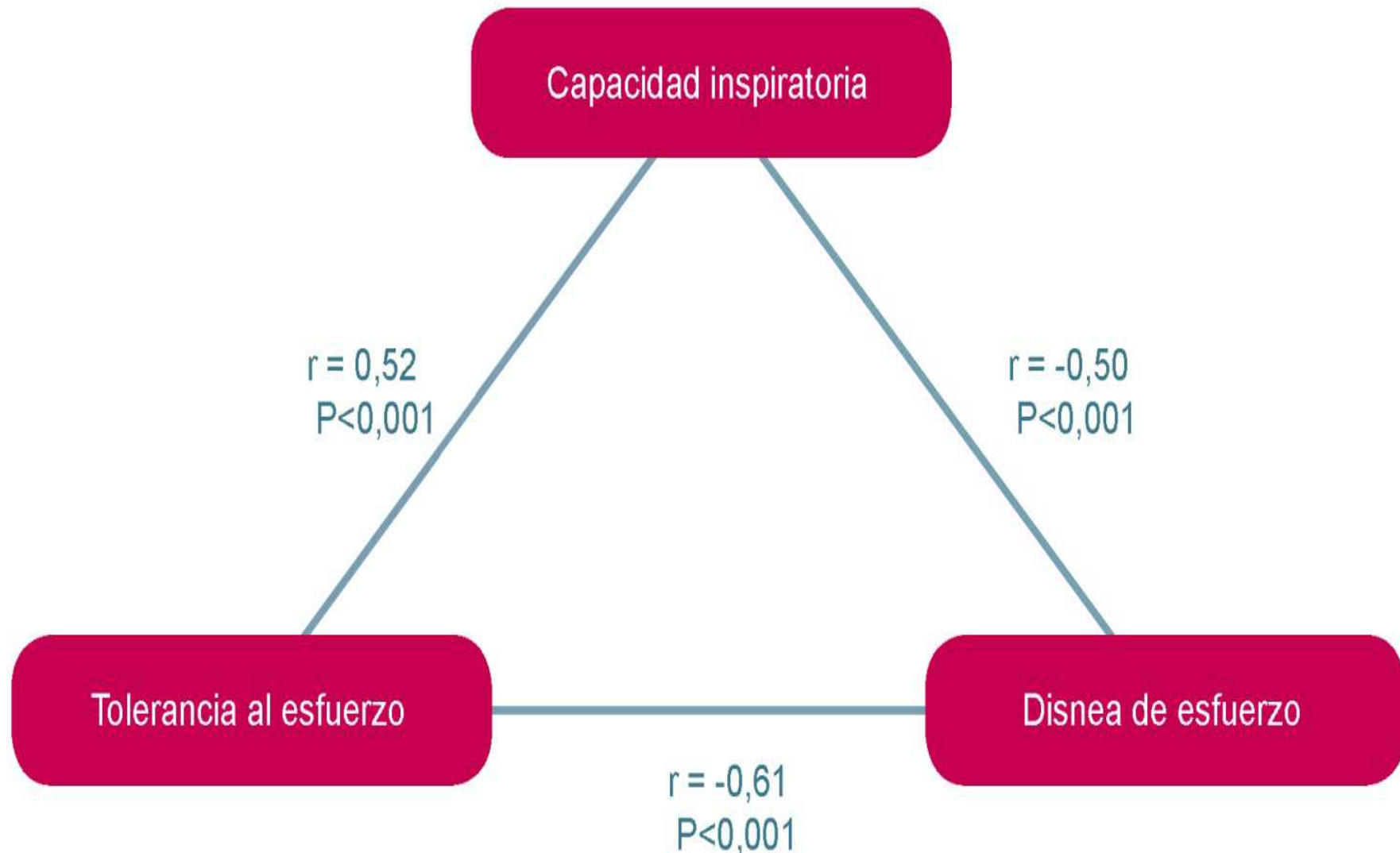
# Characterisation of COPD heterogeneity in the ECLIPSE cohort

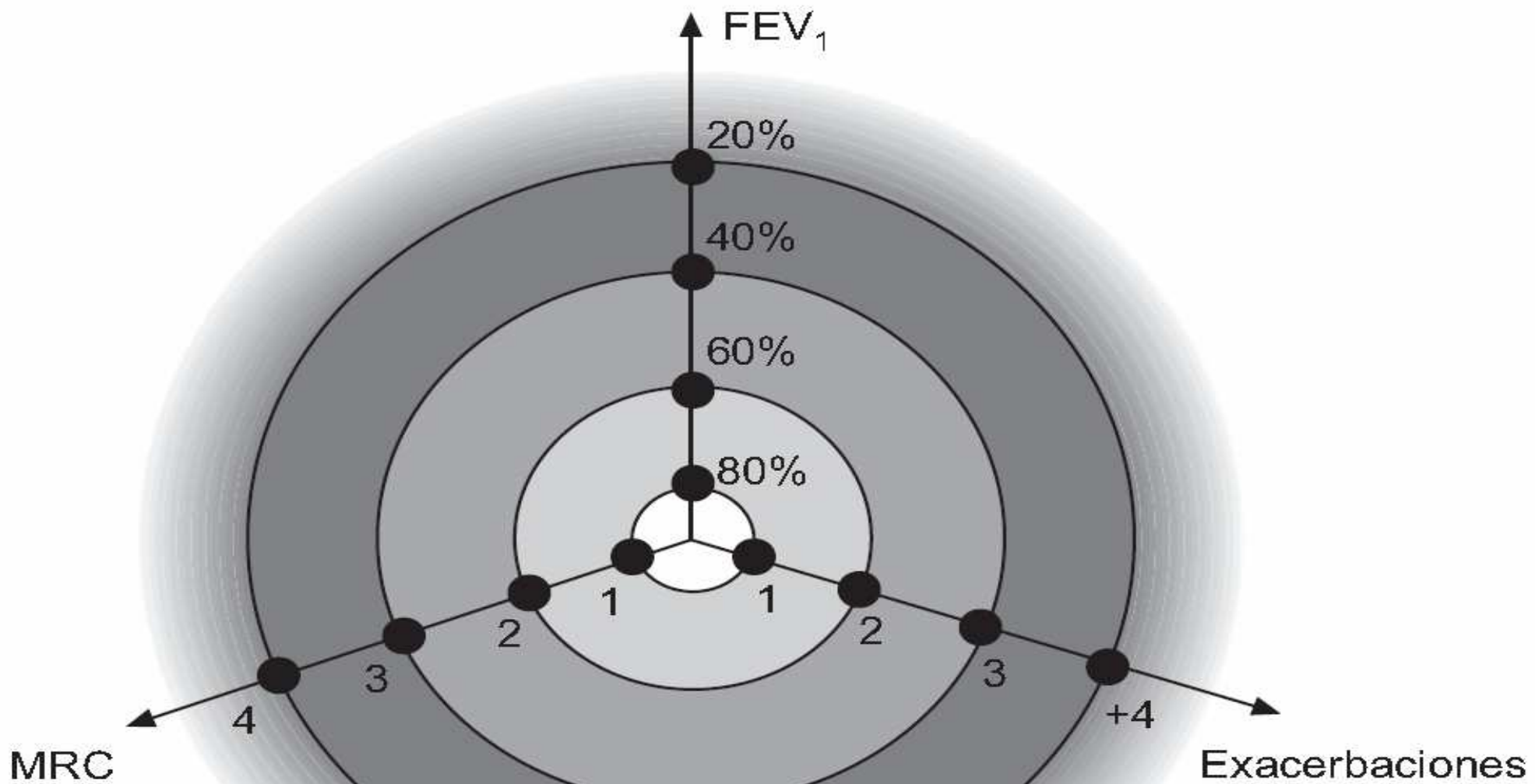
Agusti et al. *Respiratory Research* 2010, **11**:122





# DISNEA Y ATRAPAMIENTO AÉREO

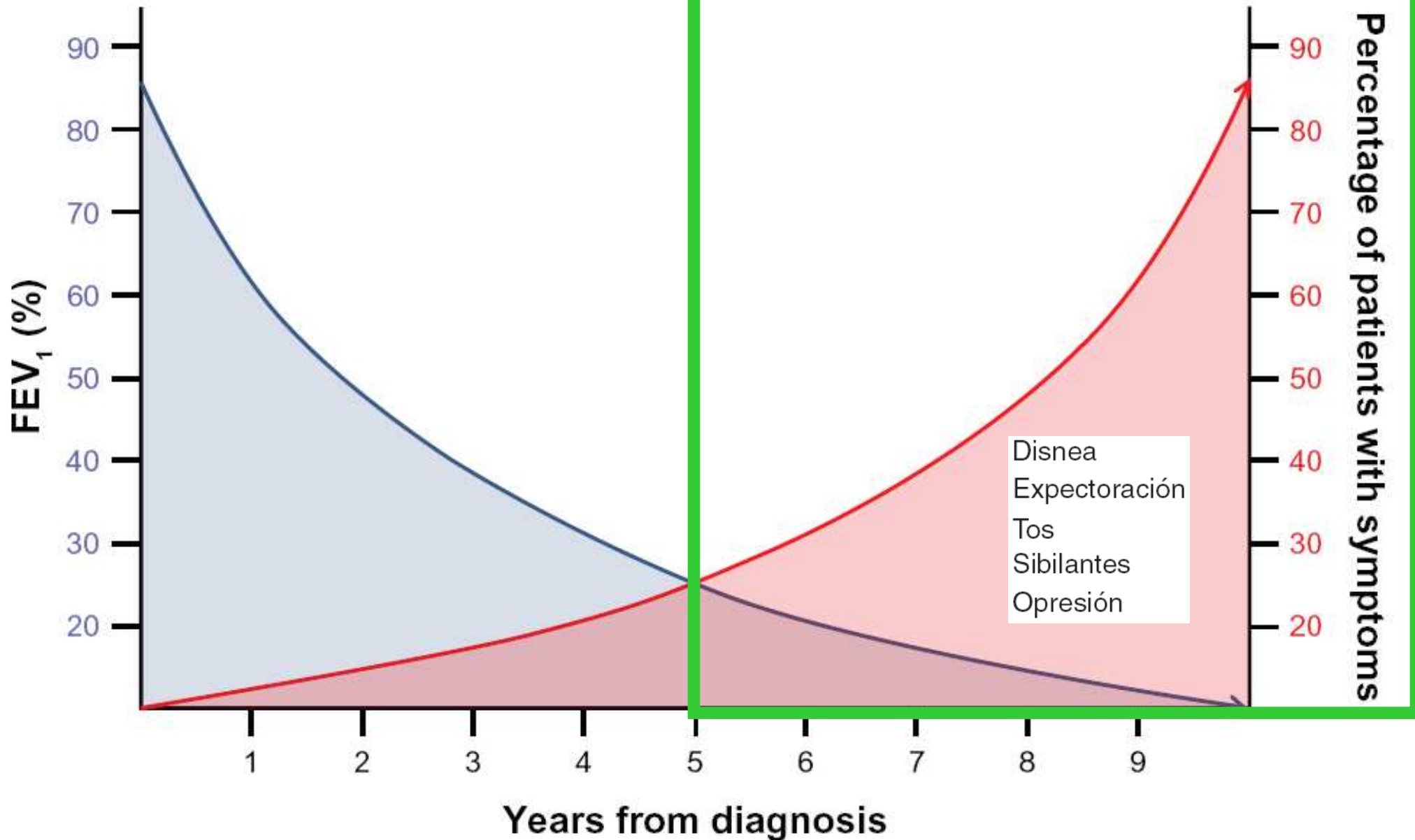




- |   |   |
|---|---|
|  ED de rescate |  2 BD de larga o 1 BD+CI |
|  1 BD de larga |  Tripleterapia           |

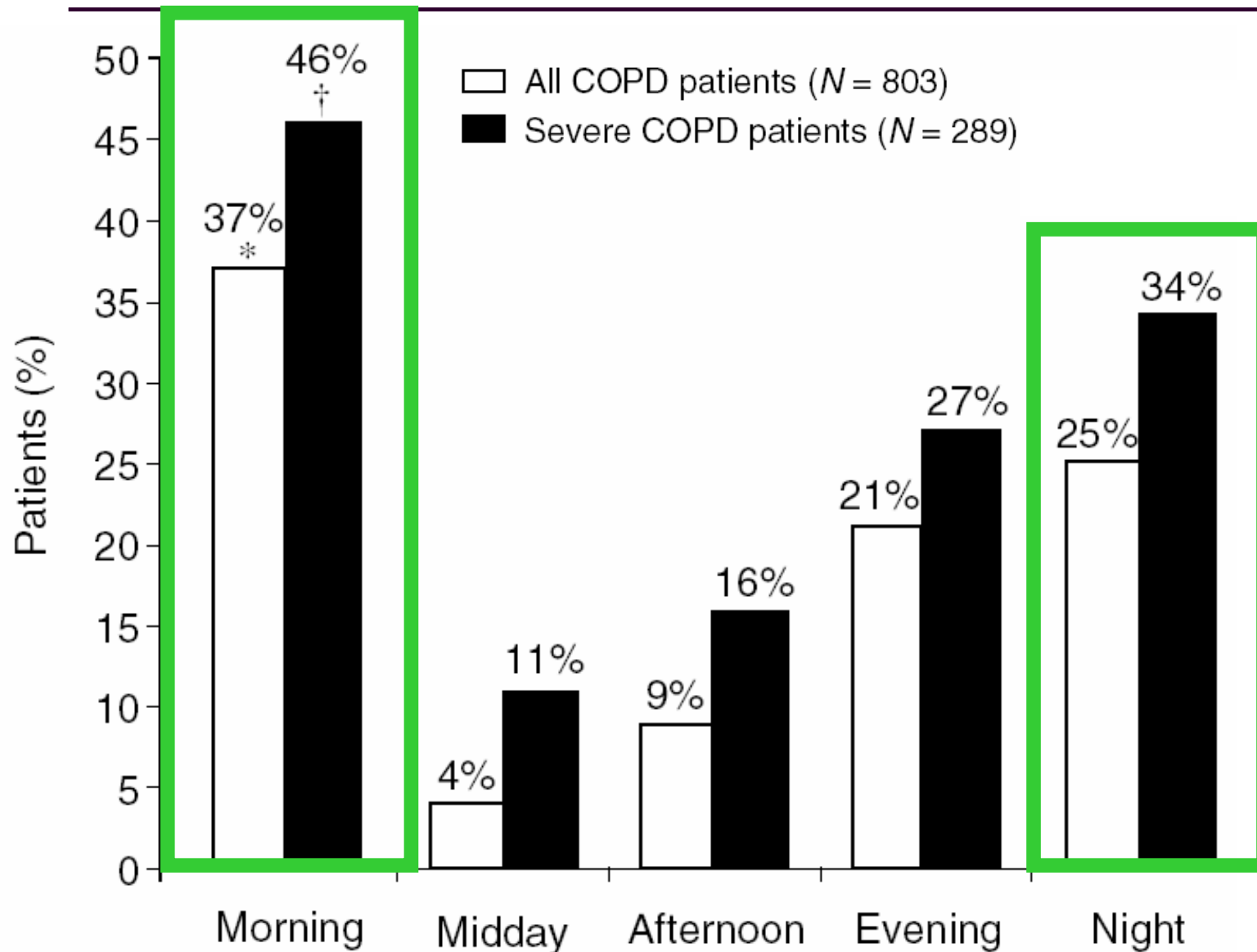


# Síntomas en EPOC: ¿ESTABLES?



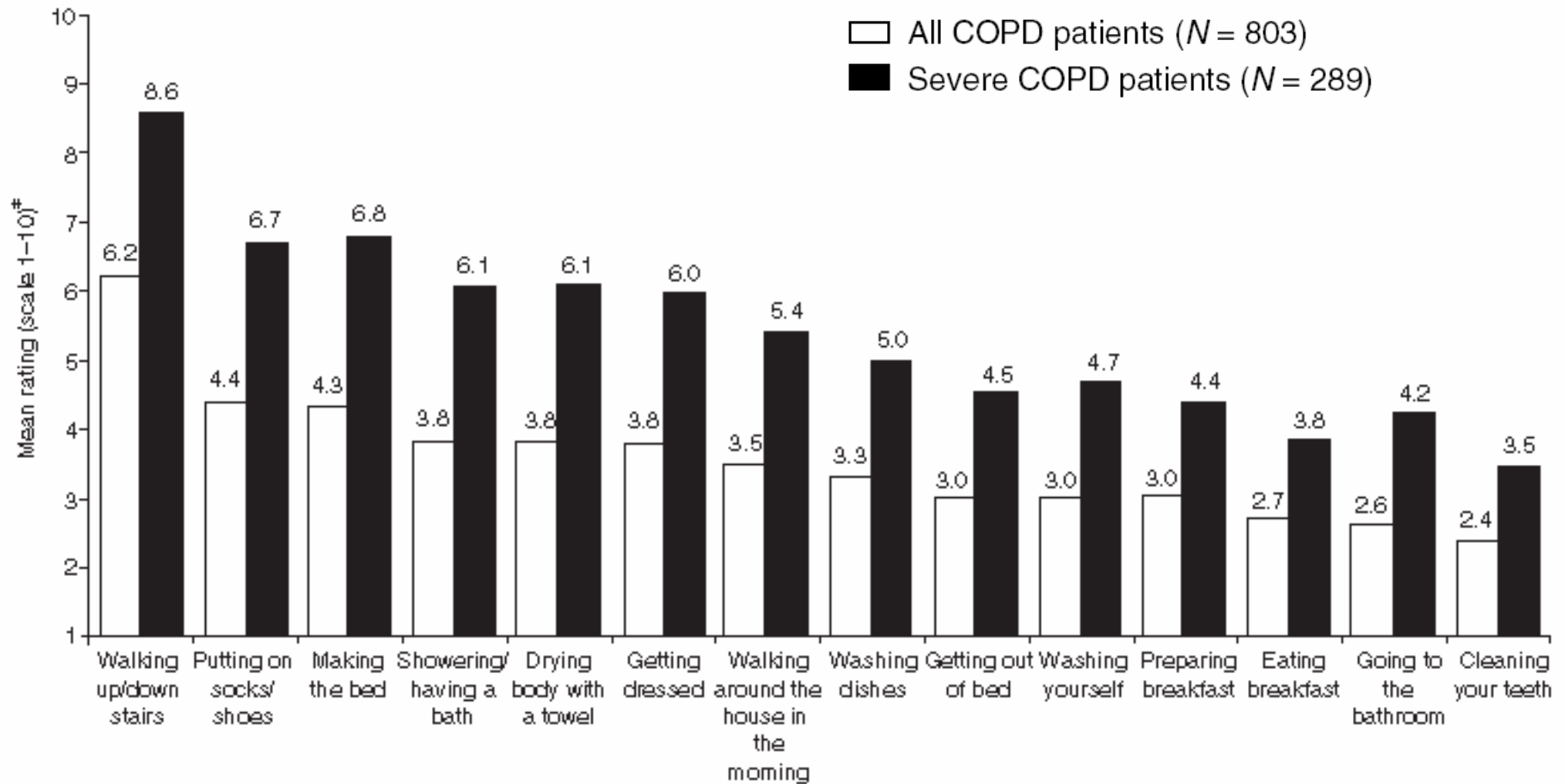
# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

## Estudio piloto



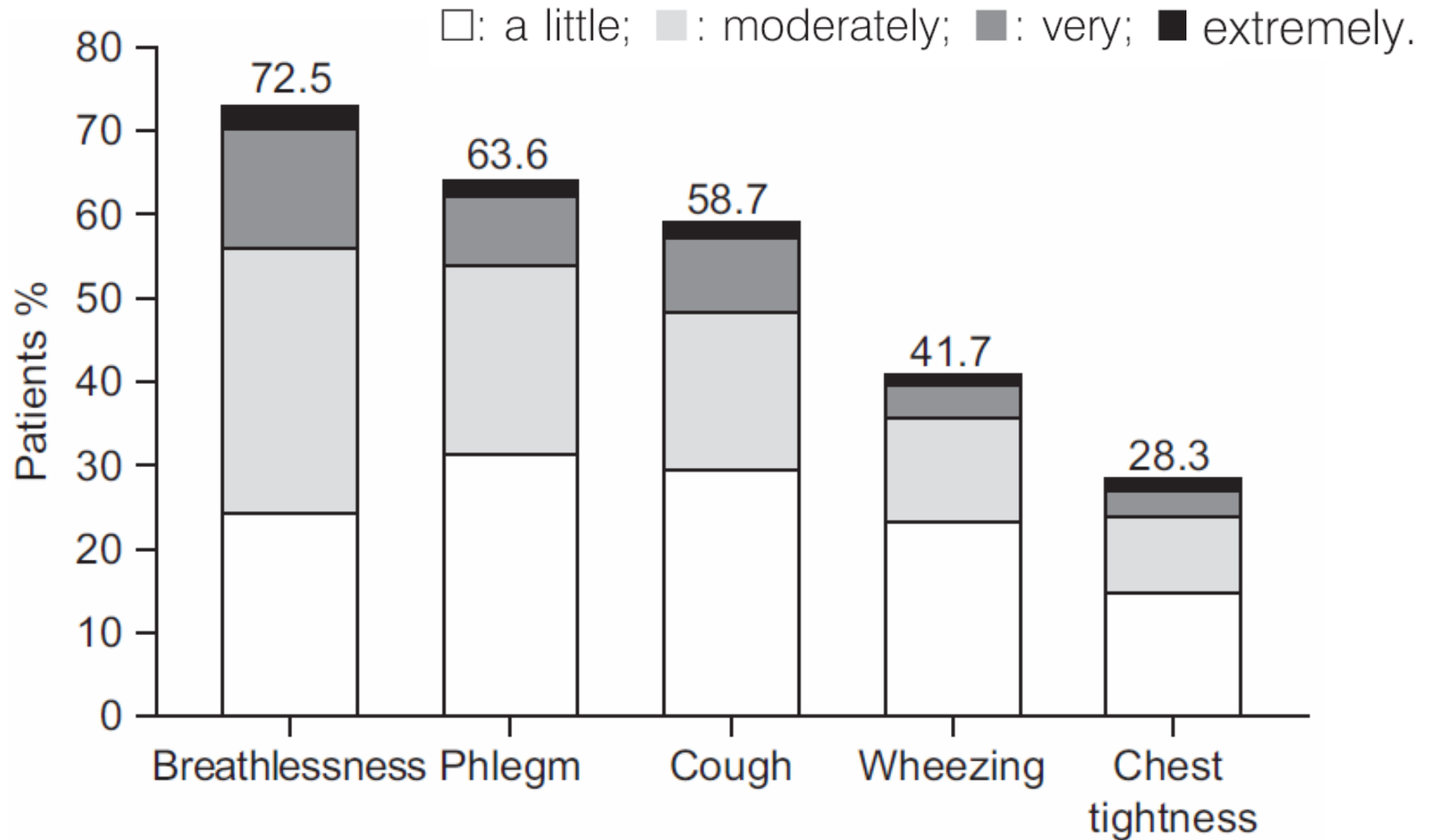
# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

## Estudio piloto



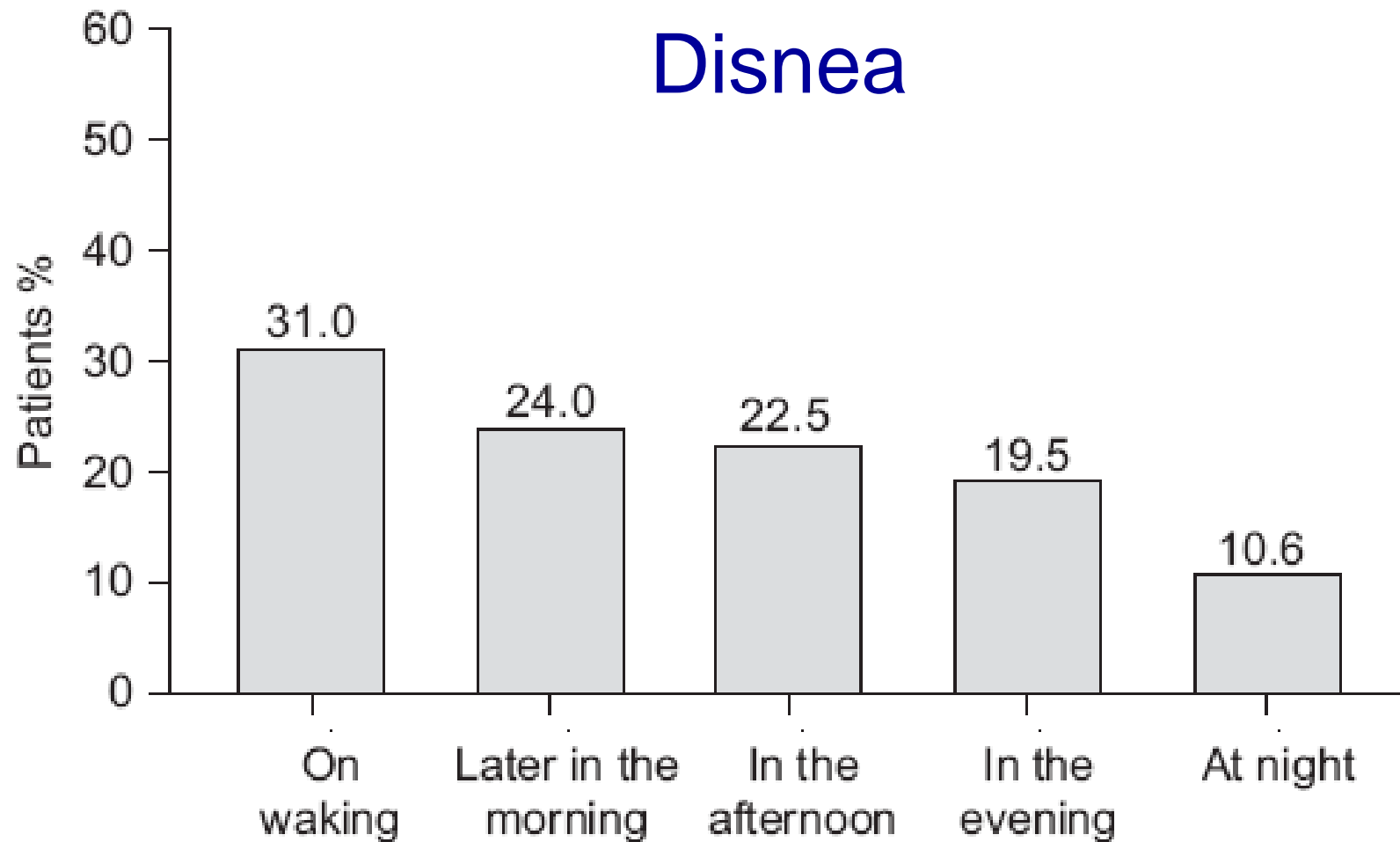
# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

## Estudio pan-Europeo



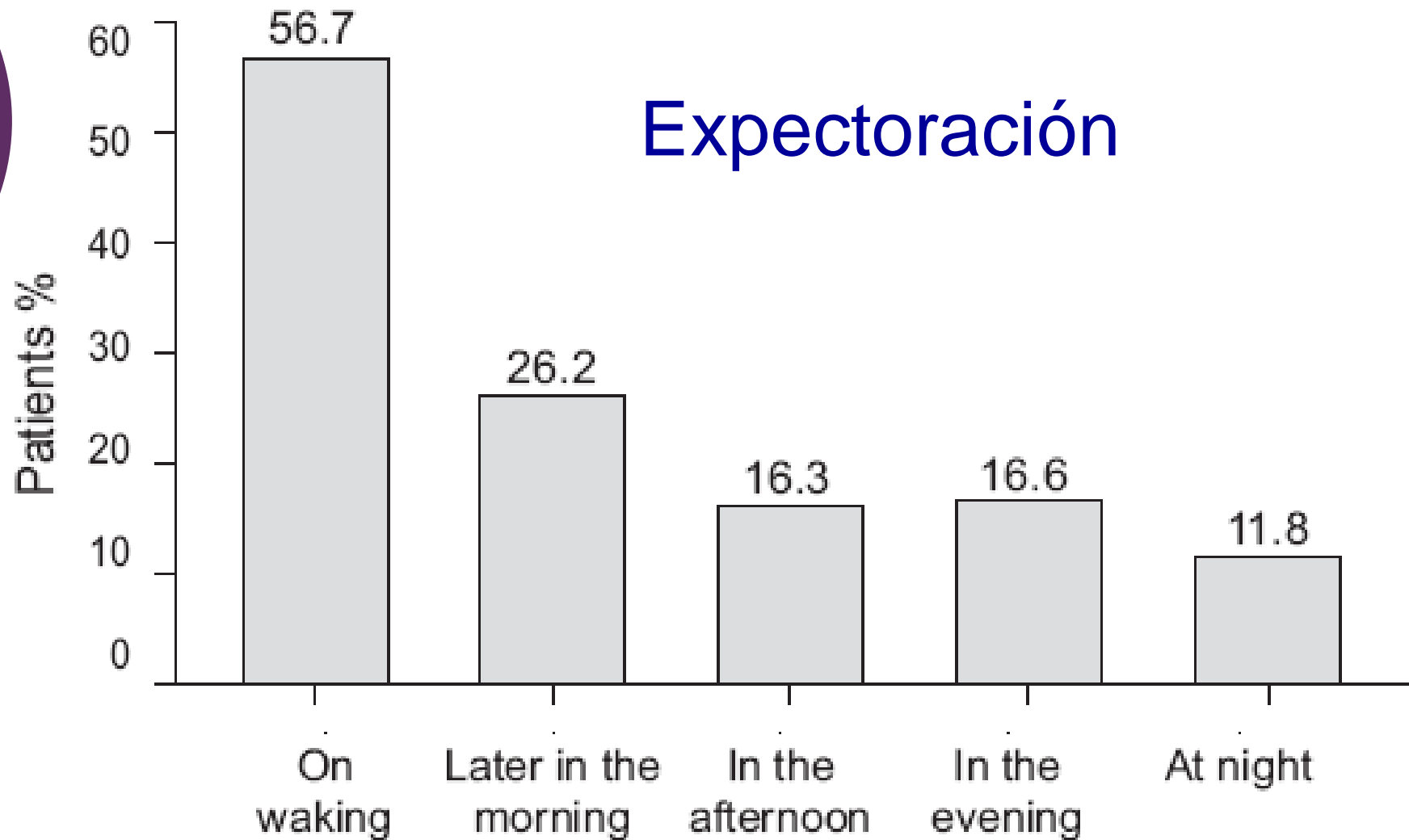
# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

## Estudio pan-Europeo



# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

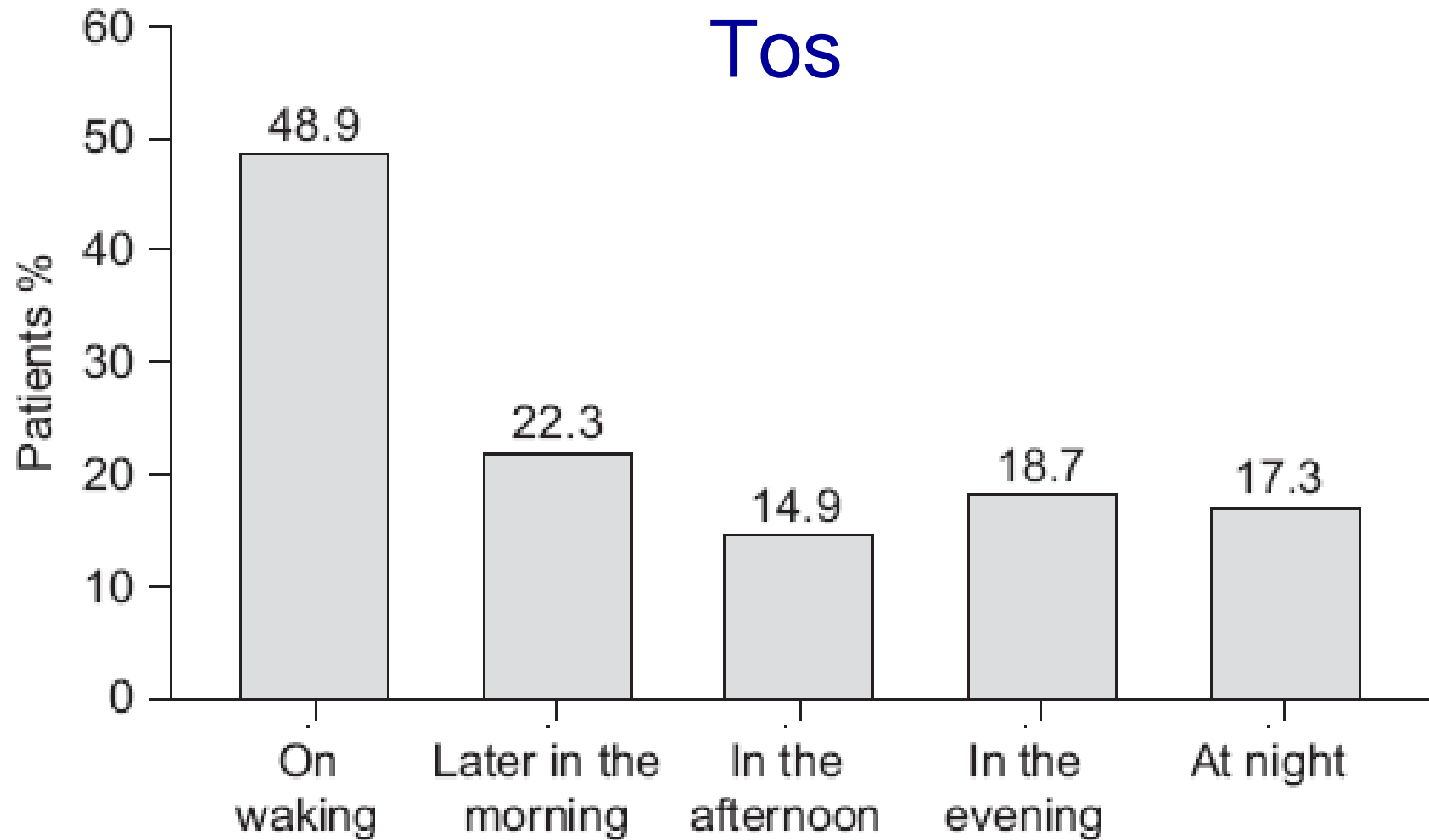
## Estudio pan-Europeo





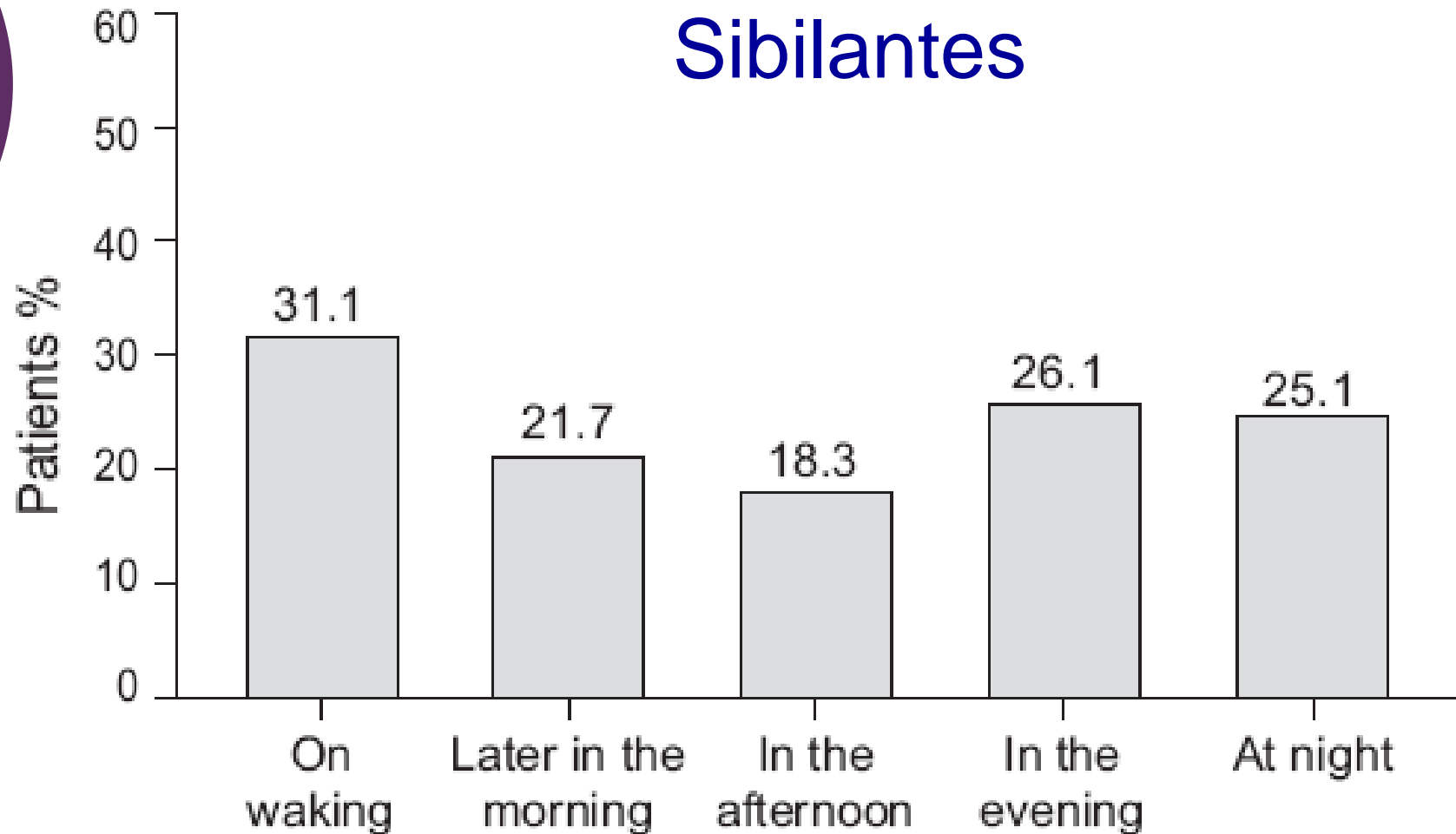
# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

## Estudio pan-Europeo



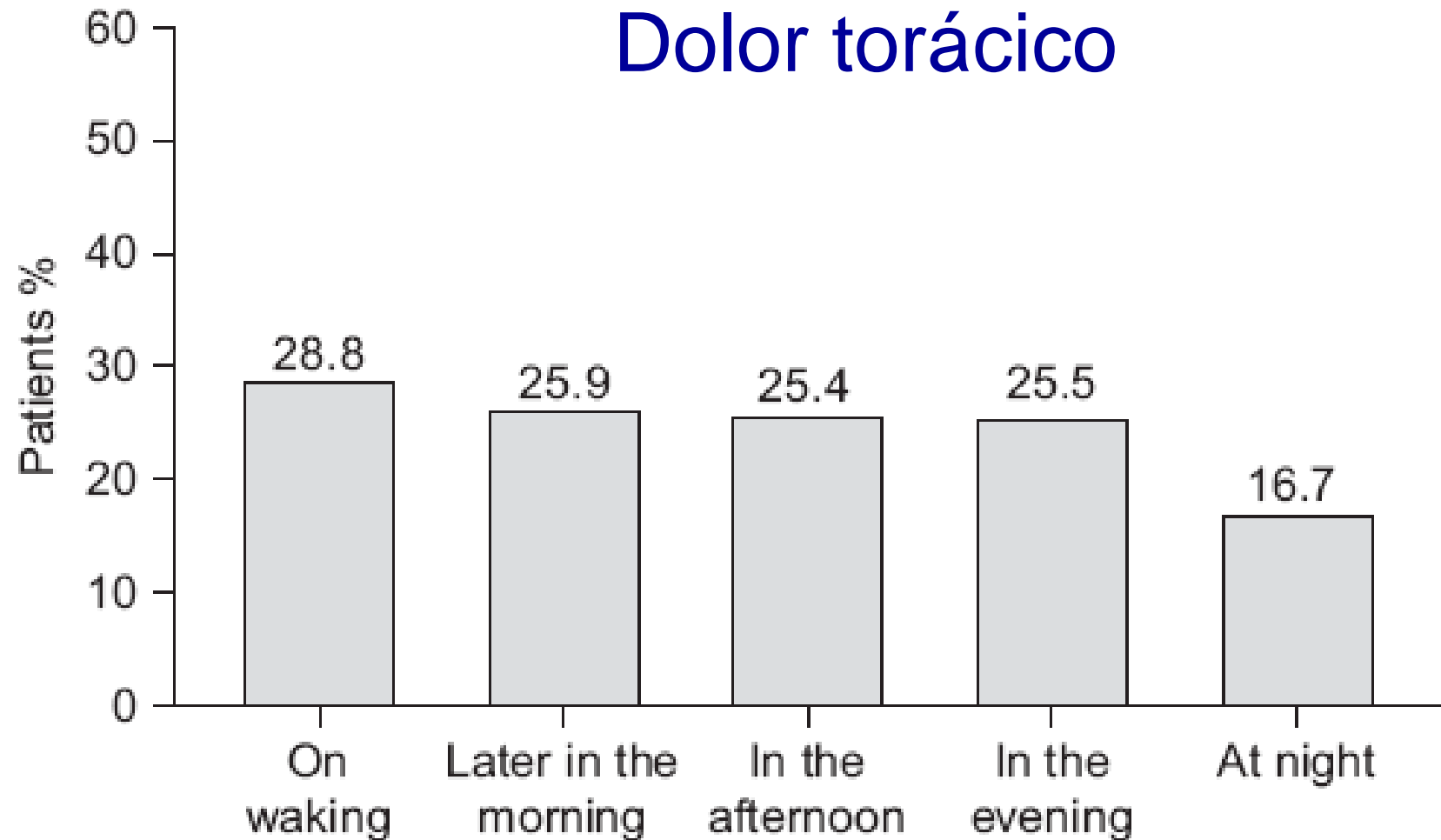
# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

## Estudio pan-Europeo



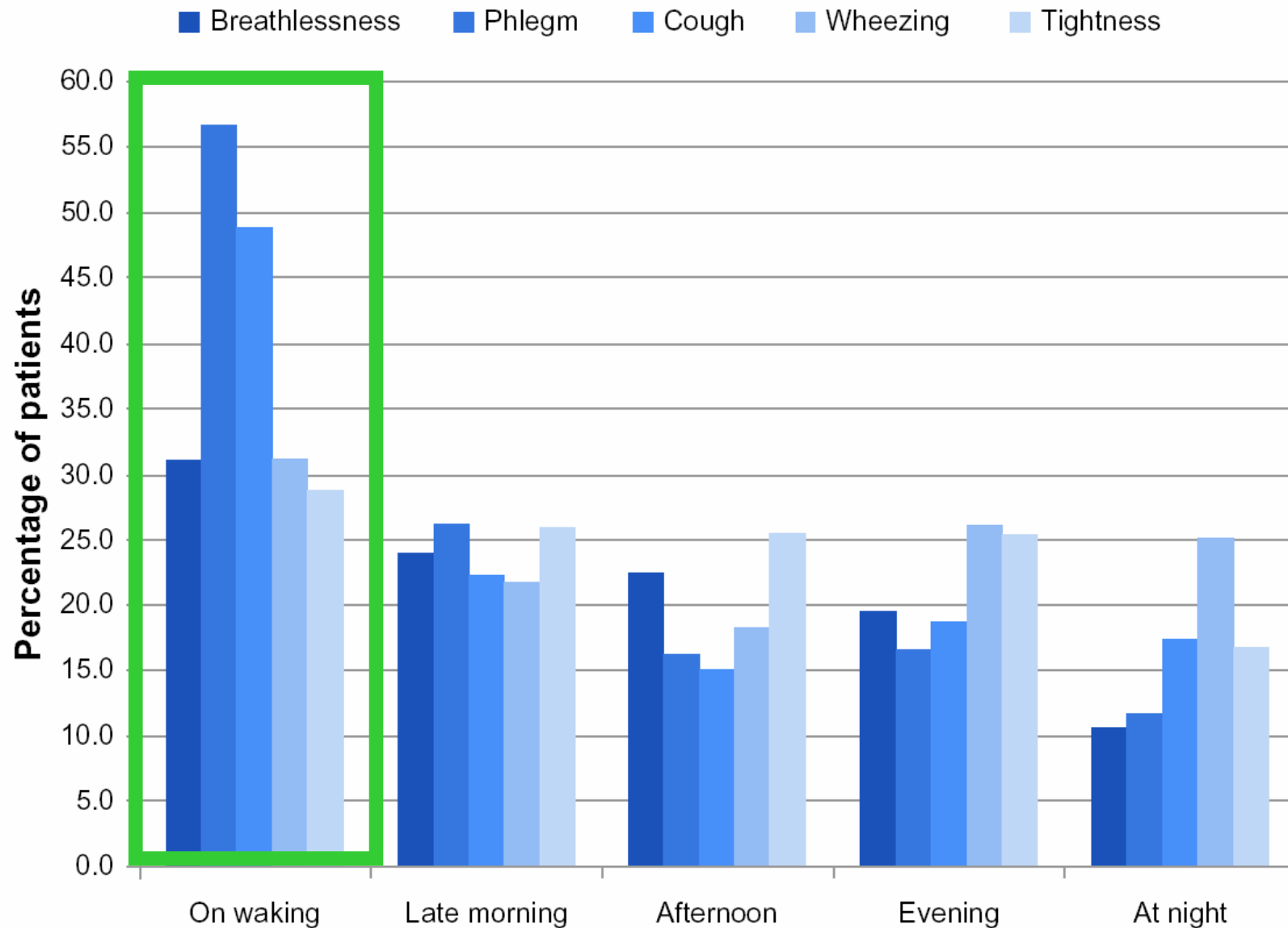
# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

## Estudio pan-Europeo



# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

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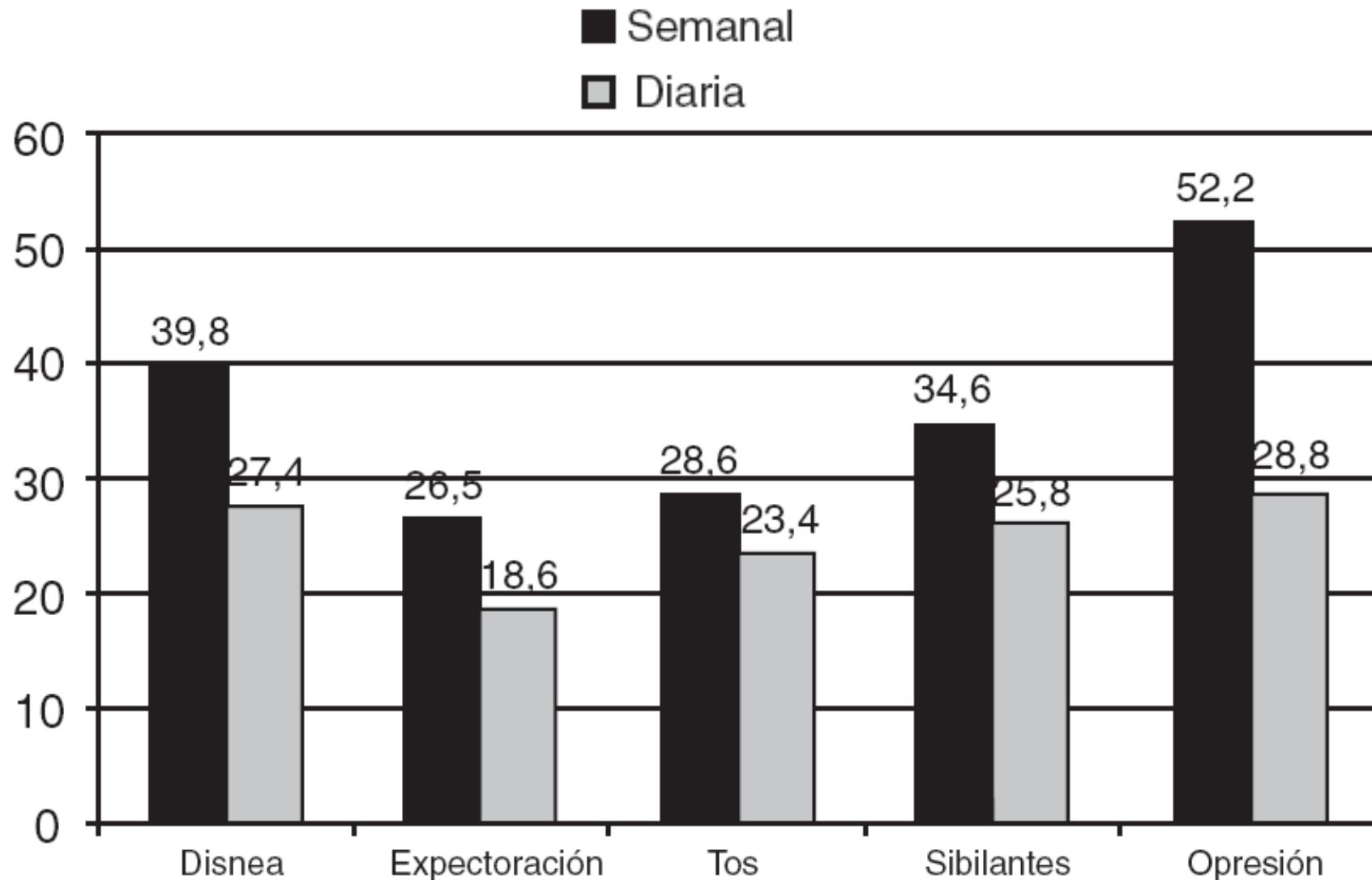
## Estudio pan-Europeo. Pacientes de España

Frecuencia de síntomas respiratorios en la población analizada

|                                      |             |
|--------------------------------------|-------------|
| No refieren síntomas                 | 75 (15,9%)  |
| → Algún síntoma                      | 396 (84,1%) |
| <i>Frecuencia de los síntomas</i>    |             |
| → Disnea                             | 226 (47,9%) |
| → Tos                                | 235 (49,8%) |
| Opresión torácica                    | 111 (23,5%) |
| → Expectoración                      | 264 (55,9%) |
| Sibilancias                          | 163 (34,5%) |
| <i>Número de síntomas declarados</i> |             |
| 0                                    | 75 (15,9%)  |
| 1                                    | 102 (21,6%) |
| 2                                    | 85 (18%)    |
| → 3                                  | 111 (23,5%) |
| 4                                    | 56 (11,9%)  |
| 5                                    | 30 (6,4%)   |

# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

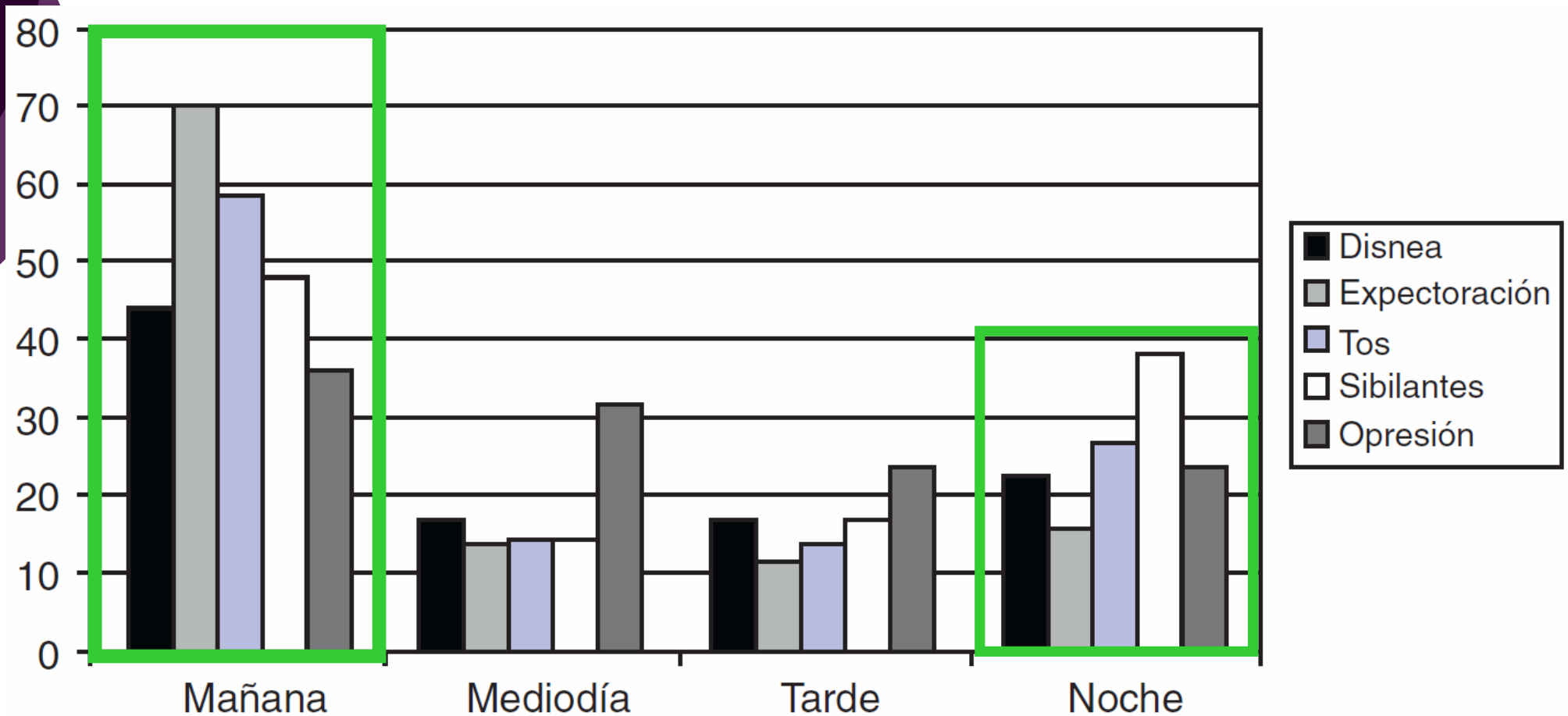
## Estudio pan-Europeo. Pacientes de España





# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

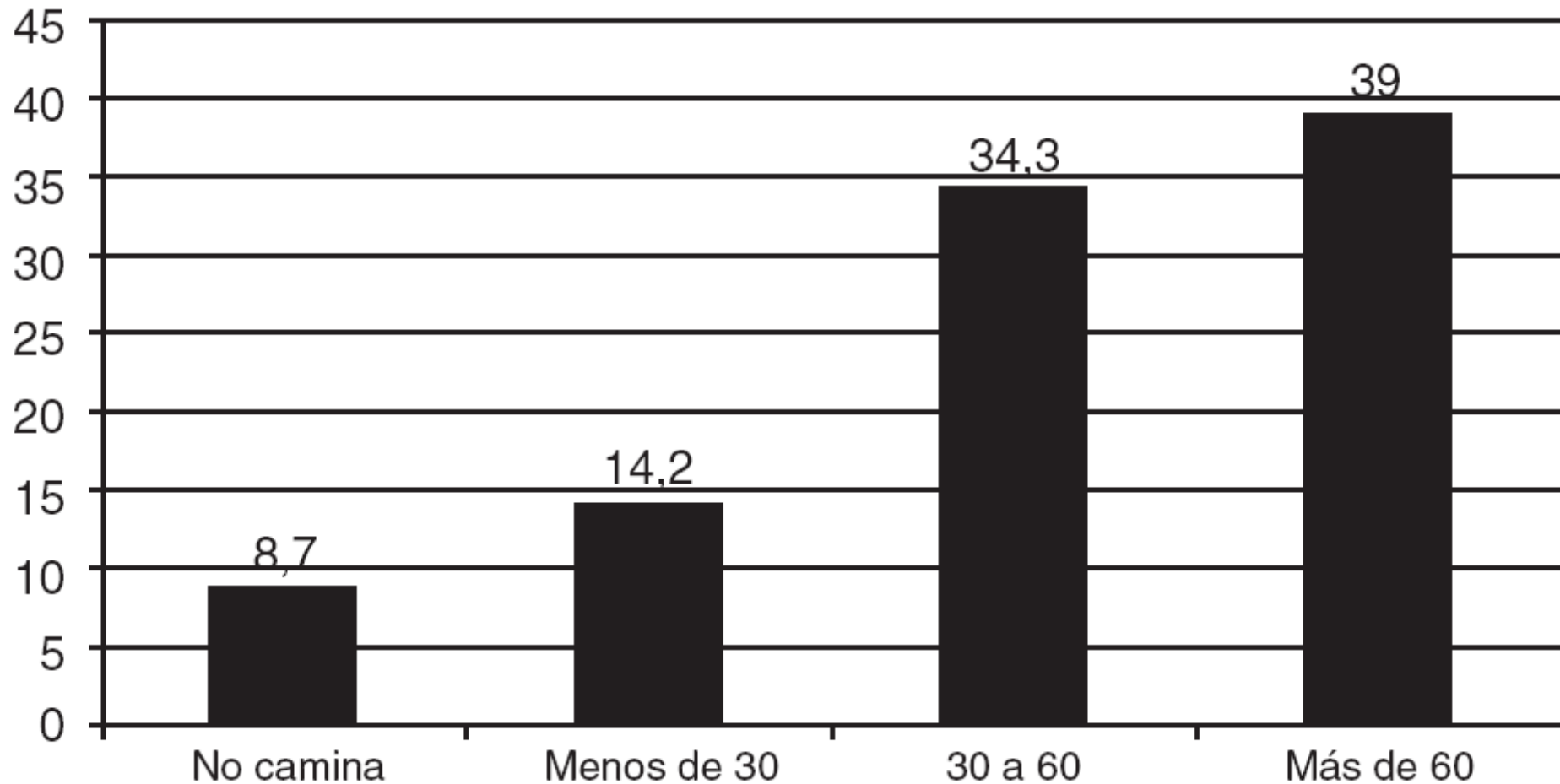
## Estudio pan-Europeo. Pacientes de España



# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

## Estudio pan-Europeo. Pacientes de España

% de pacientes según tiempo caminado en minutos

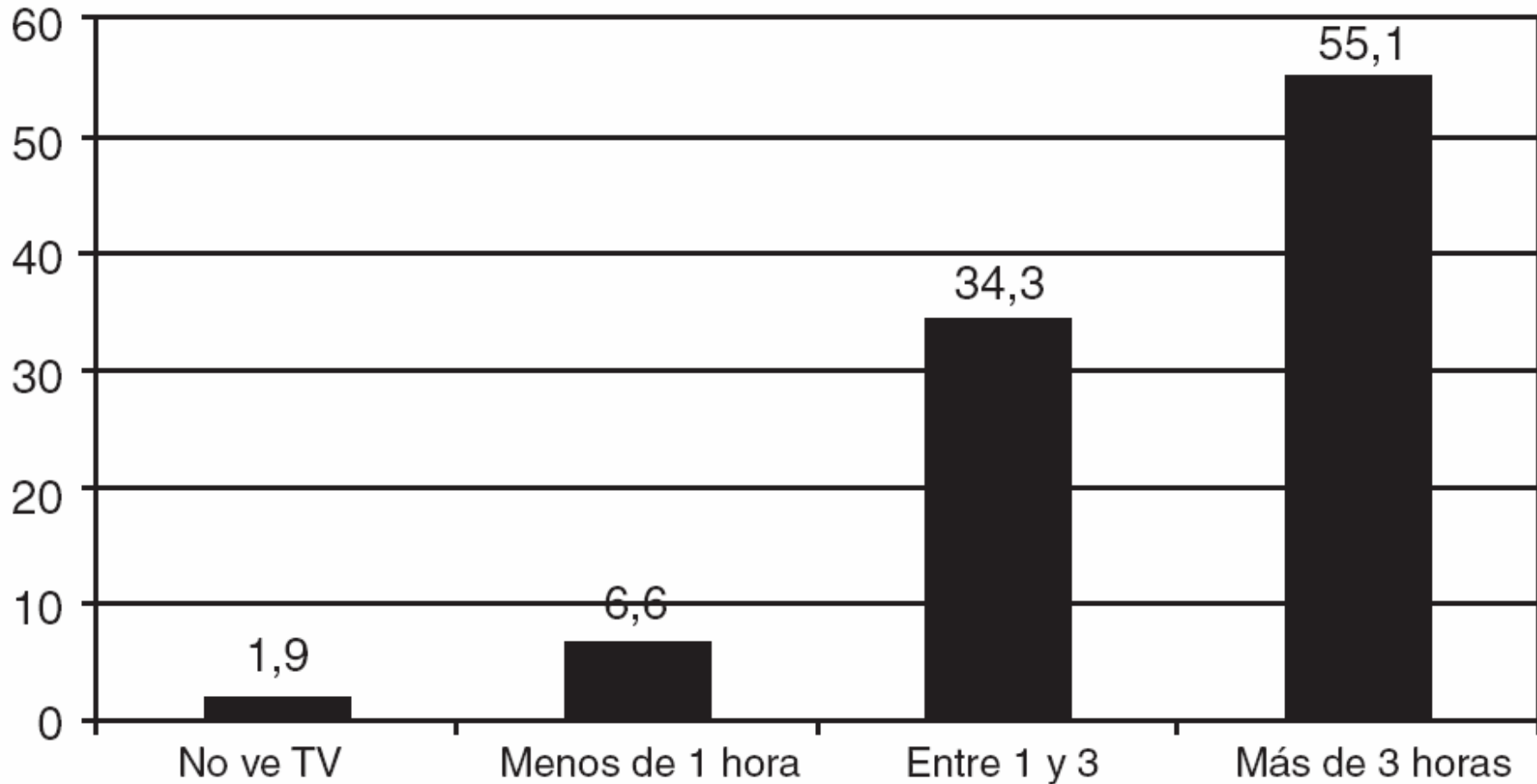


# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

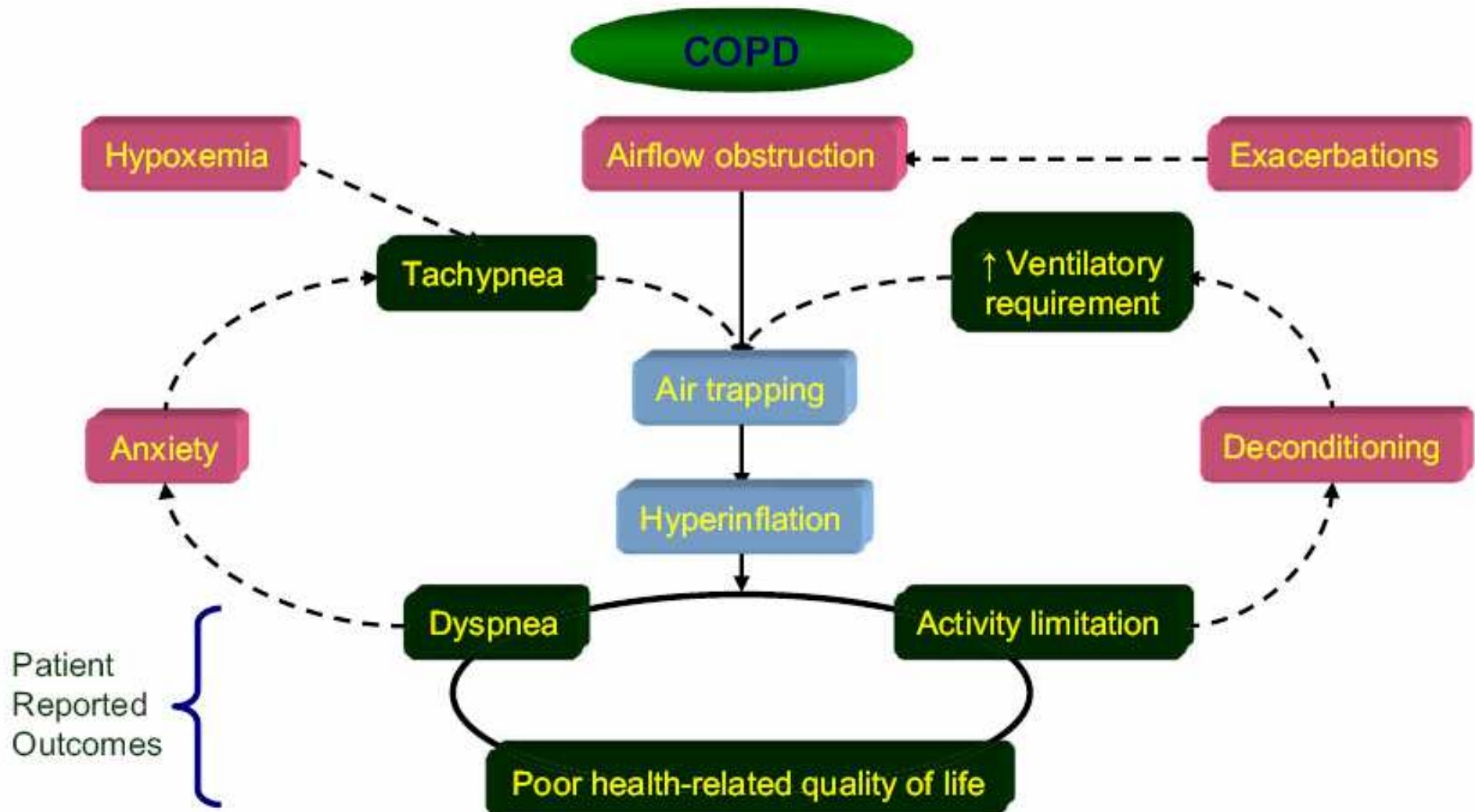
## Estudio pan-Europeo. Pacientes de España

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### Horas de TV vistas en la semana previa a la encuesta



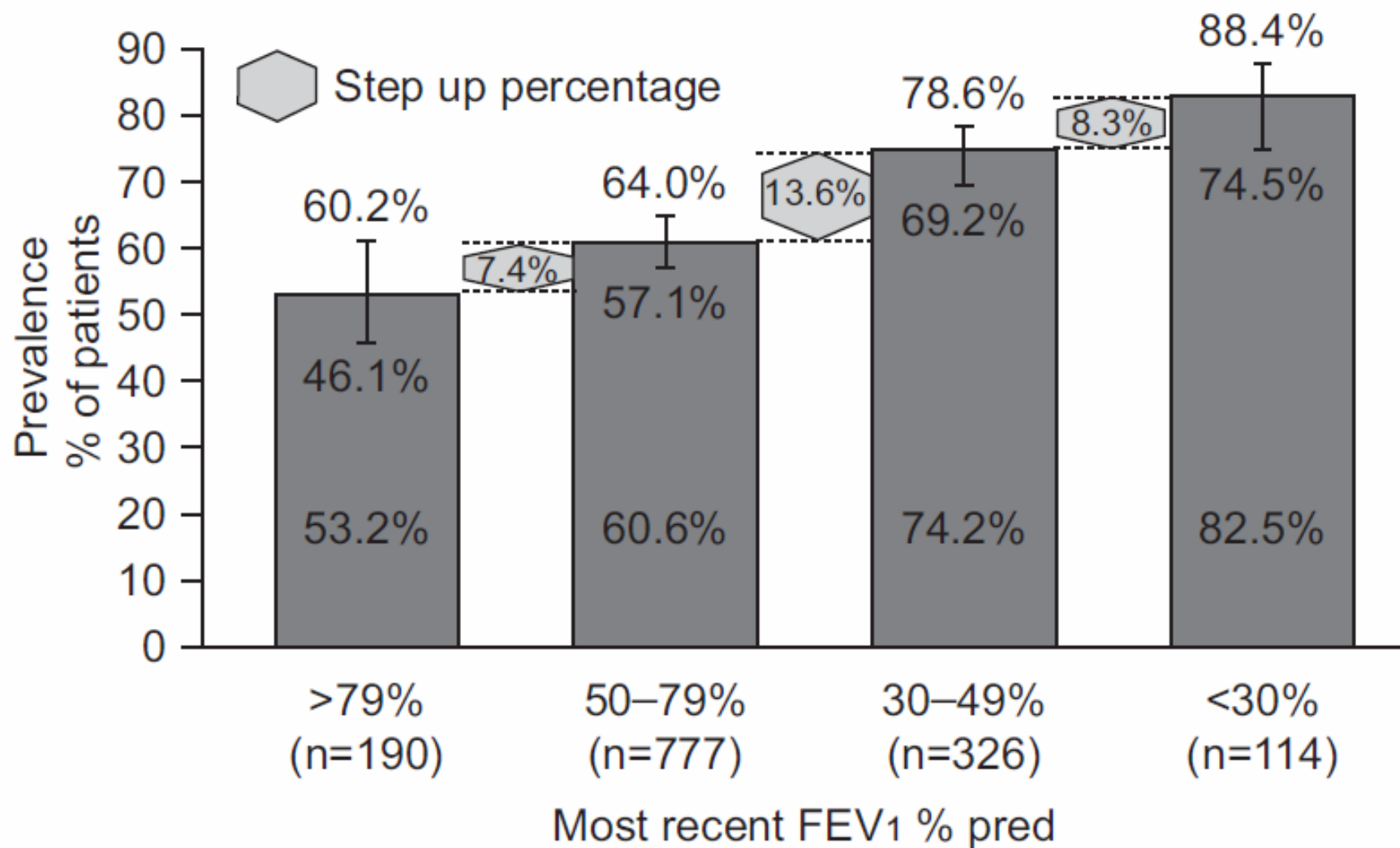
# CÍRCULO VICIOSO DE LA EPOC



# VARIABILIDAD DE SÍNTOMAS Y FEV1

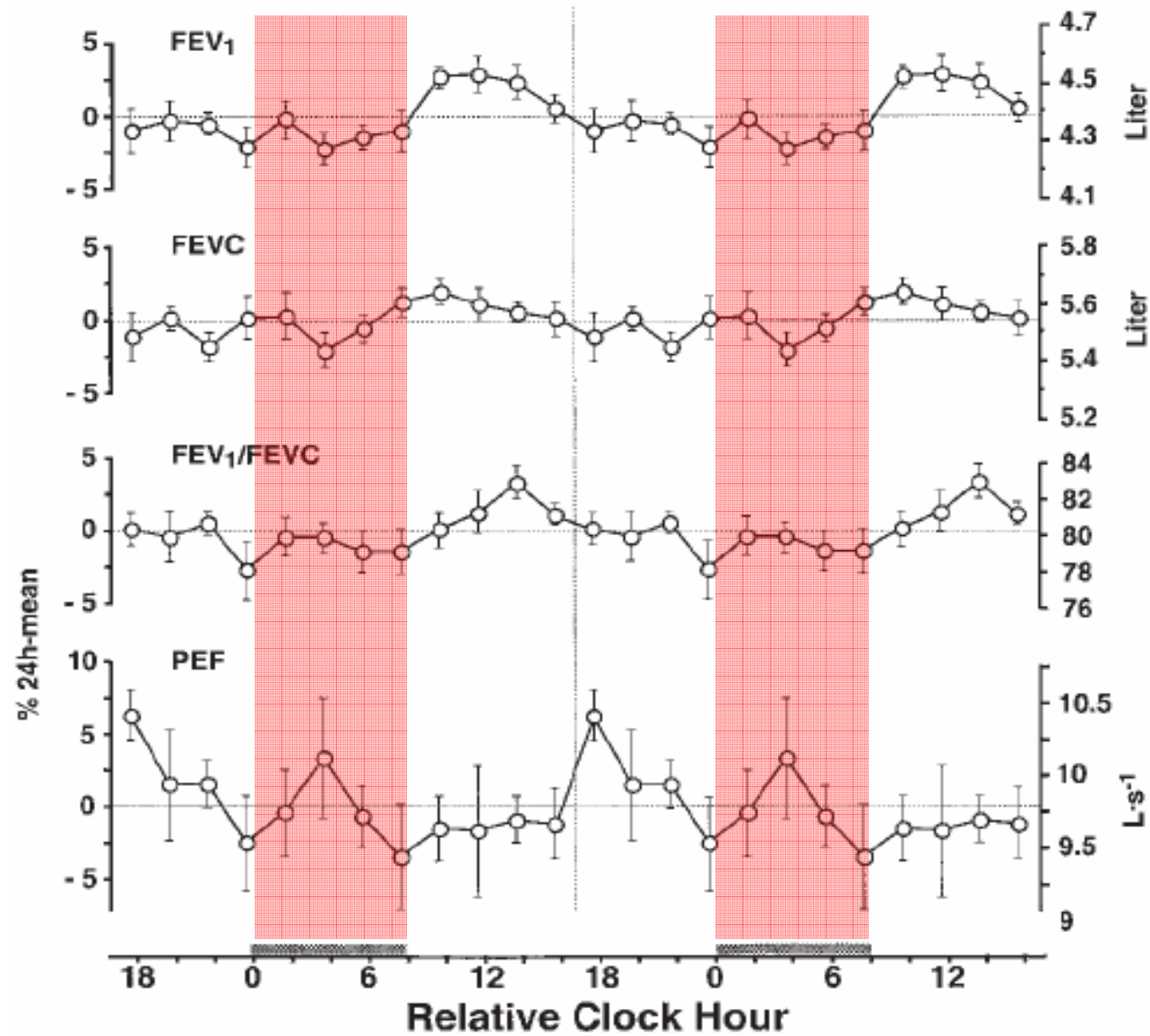
| Characteristic                                    | Study 1        |                | Study 2      |
|---|----------------|----------------|--------------|
|   | PBO + TIO      | BUD/Form + TIO | All          |
| <b>Subjects n</b>                                 | 331            | 329            | 442          |
| <b>Males</b>                                      | 245 (74)       | 251 (76)       | 316 (71)     |
| <b>Mean age yrs (range)</b>                       | 62.5 (41–82)   | 62.4 (40–85)   | 63.0 (40–86) |
| <b>Median time since diagnosis yrs (range)</b>    | 5.7 (0.2–52.6) | 5.7 (0.3–43.4) | 6.3 (0–52)   |
| <b>Previous smokers %</b>                         | 54             | 58             | 66           |
| <b>Median smoking history pack-yrs (IQR)</b>      | 38 (11)        | 36 (12)        | 40 (30)      |
| <b>Mean FEV<sub>1</sub> % pred normal (range)</b> | 37.7 (16–51)   | 38.1 (10–58)   | 36.1 (13–51) |
| <b>GOLD severity stage<sup>+</sup></b>            |                |                |              |
| II ≥50–<80%                                       | 70 (21)        | 90 (27)        | 98 (22)      |
| III ≥30–<50%                                      | 217 (66)       | 203 (62)       | 261 (59)     |
| IV <30%   | 42 (13)        | 33 (10)        | 82 (19)      |

# SÍNTOMAS NOCTURNOS Y FEV1

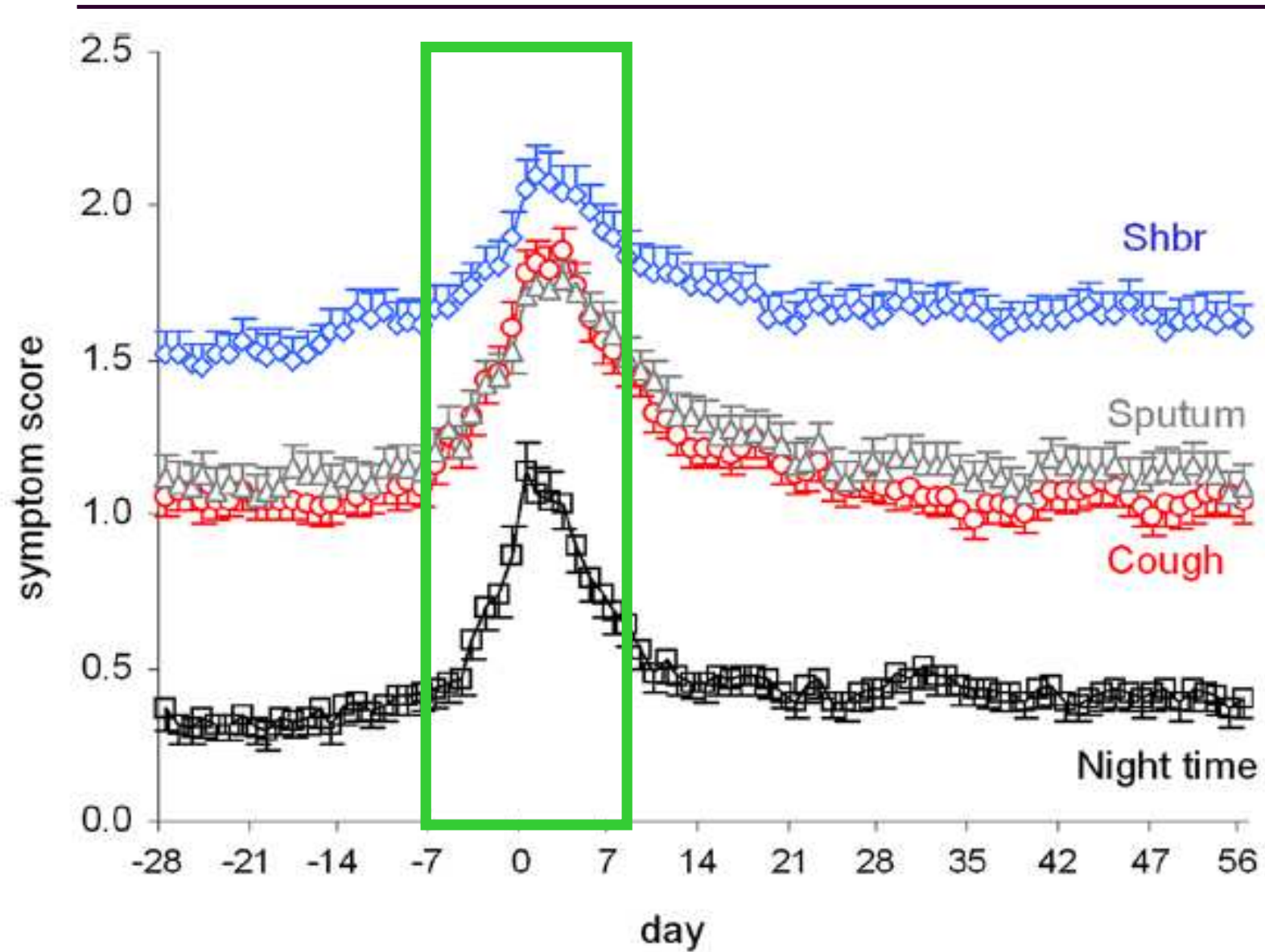




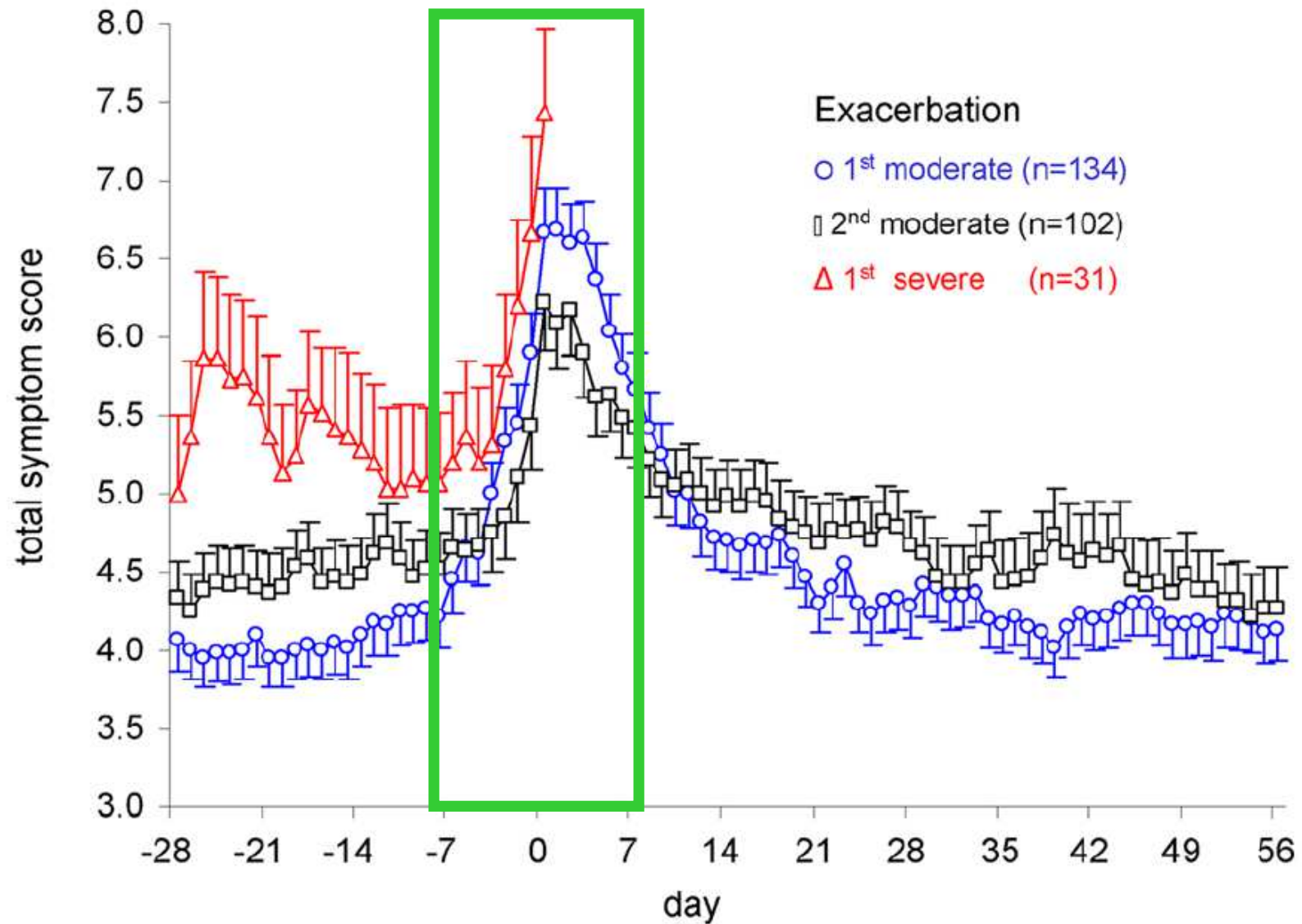
# FEV1 MÁS BAJO EN LA NOCHE



# VARIABILIDAD y EXACERBACIONES



# VARIABILIDAD y EXACERBACIONES



**TABLE 1**

Items included in the Capacity of Daily Living during the Morning (CDLM) questionnaire and the Global Chest Symptoms Questionnaire (GCSQ)

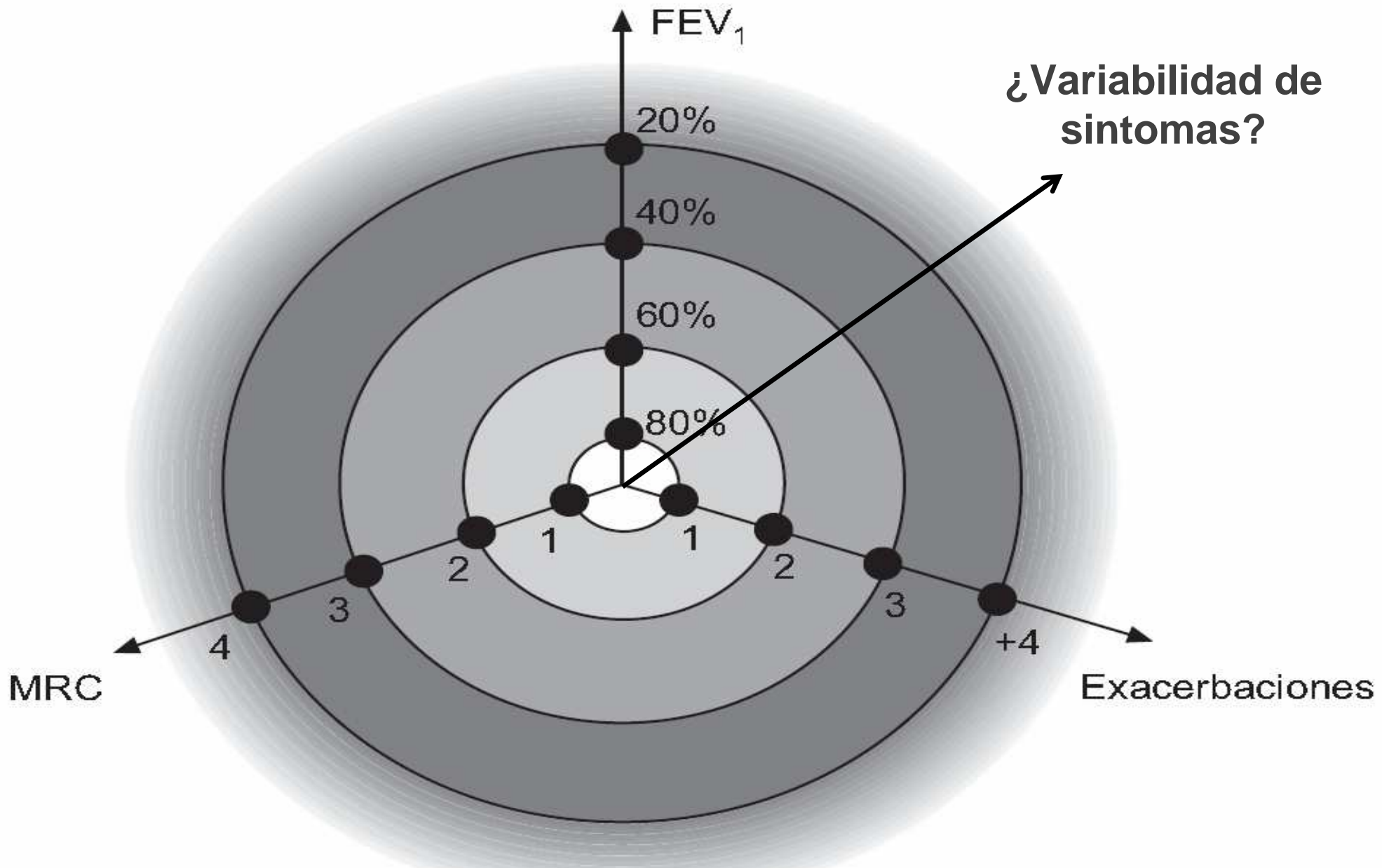
**Items****Response options****CDLM questionnaire**

- |  |      |
|--|------|
| 1) Did you wash yourself this morning other than your face <i>i.e.</i> body wash, shower or bathe? | a, c |
| 2) Did you dry yourself with a towel after washing this morning?                                   | a, c |
| 3) Did you get dressed this morning?   | b, c |
| 4) Did you eat breakfast this morning?   | b, c |
| 5) Did you walk around your home early this morning after taking your medicine?                    | b, c |
| 6) Did you walk around your home later this morning?   | b, c |

Response options were as follows. a: “Yes, I did it by myself”; “Yes, but I needed help”; “No, I was unable to”; “No, I did not for other reasons”. b: “Yes, I did”; “No, I was unable to”; “No, I did not for other reasons”. c: If answering “yes”, subjects were asked to answer the follow-up question “How difficult was it for you to perform the task?” by selecting from the following response options “Not at all”, “A little”, “Moderately”, “Very” or “Extremely”. d: “Not at all”, “A little”, “Moderately”, “Very”, “Extremely”.

### **CDLM questionnaire**

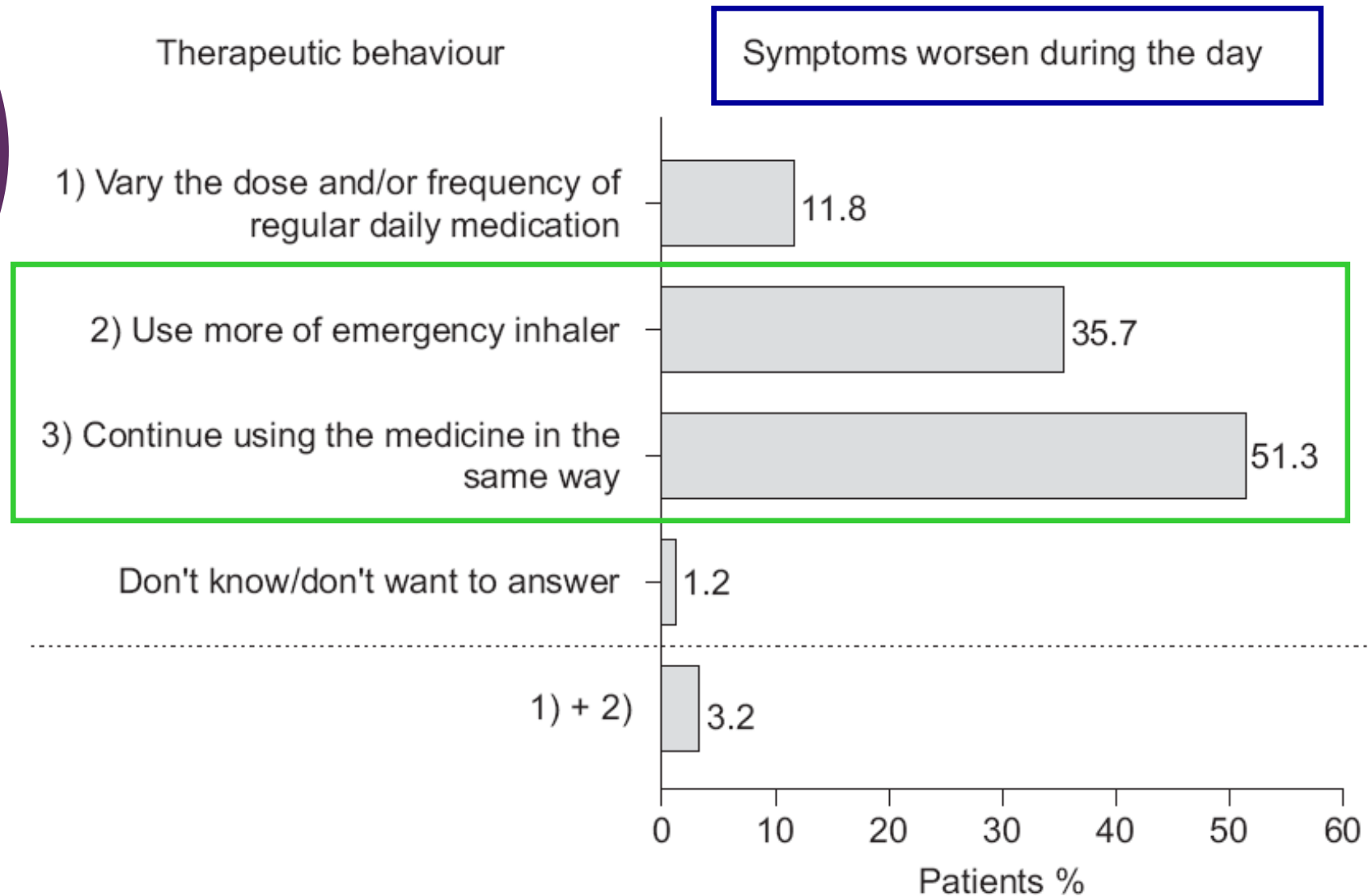
- |  |      |
|--|------|
| 1) Did you wash yourself this morning other than your face <i>i.e.</i> body wash, shower or bathe? | a, c |
| 2) Did you dry yourself with a towel after washing this morning?                                   | a, c |
| 3) Did you get dressed this morning?   | b, c |
| 4) Did you eat breakfast this morning?   | b, c |
| 5) Did you walk around your home early this morning after taking your medicine?                    | b, c |
| 6) Did you walk around your home later this morning?   | b, c |



- |   |   |
|---|---|
|  ED de rescate |  2 BD de larga o 1 BD+CI |
|  1 BD de larga |  Tripleterapia           |

# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

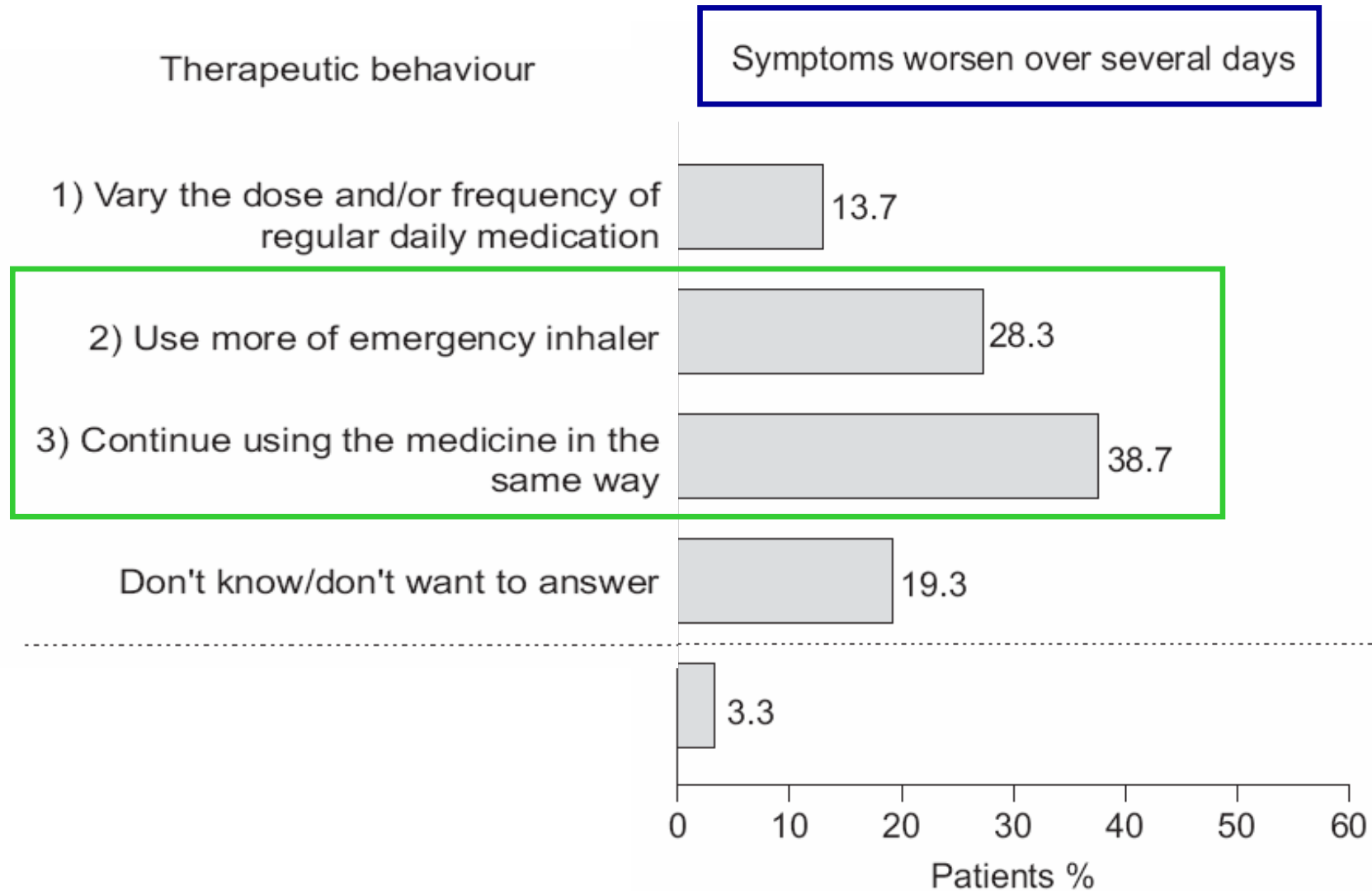
## Estudio pan-Europeo





# VARIABILIDAD SÍNTOMAS RESPIRATORIOS

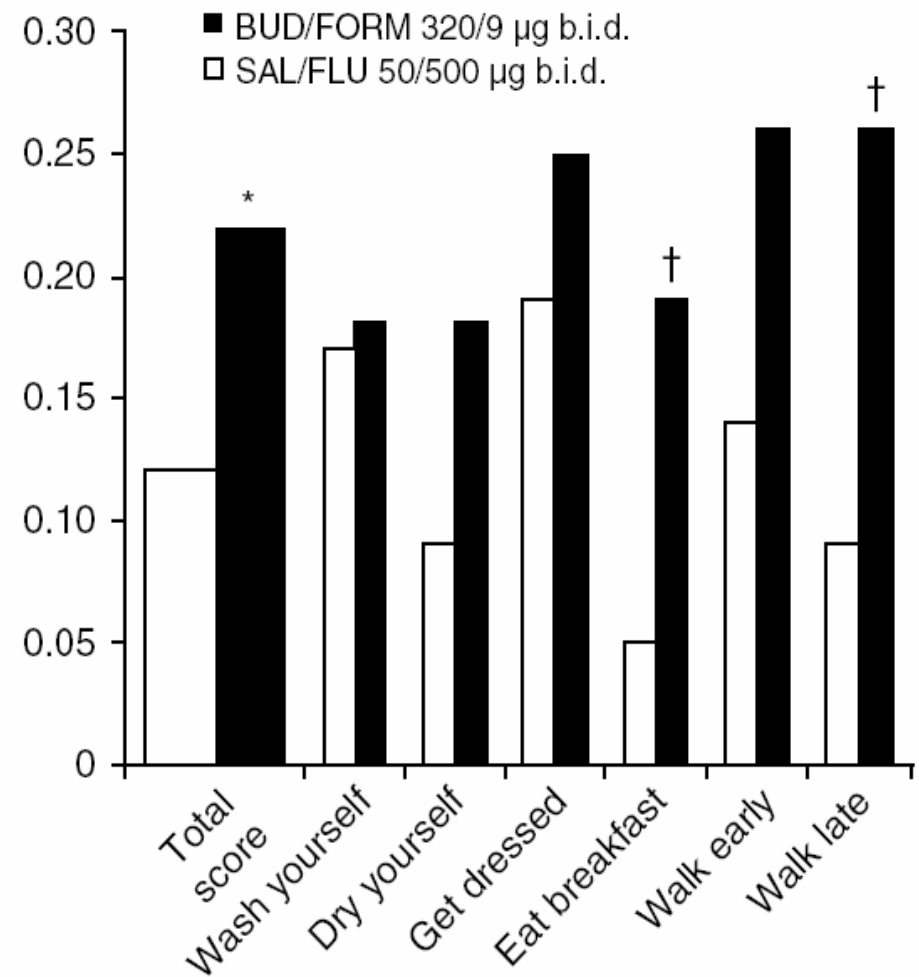
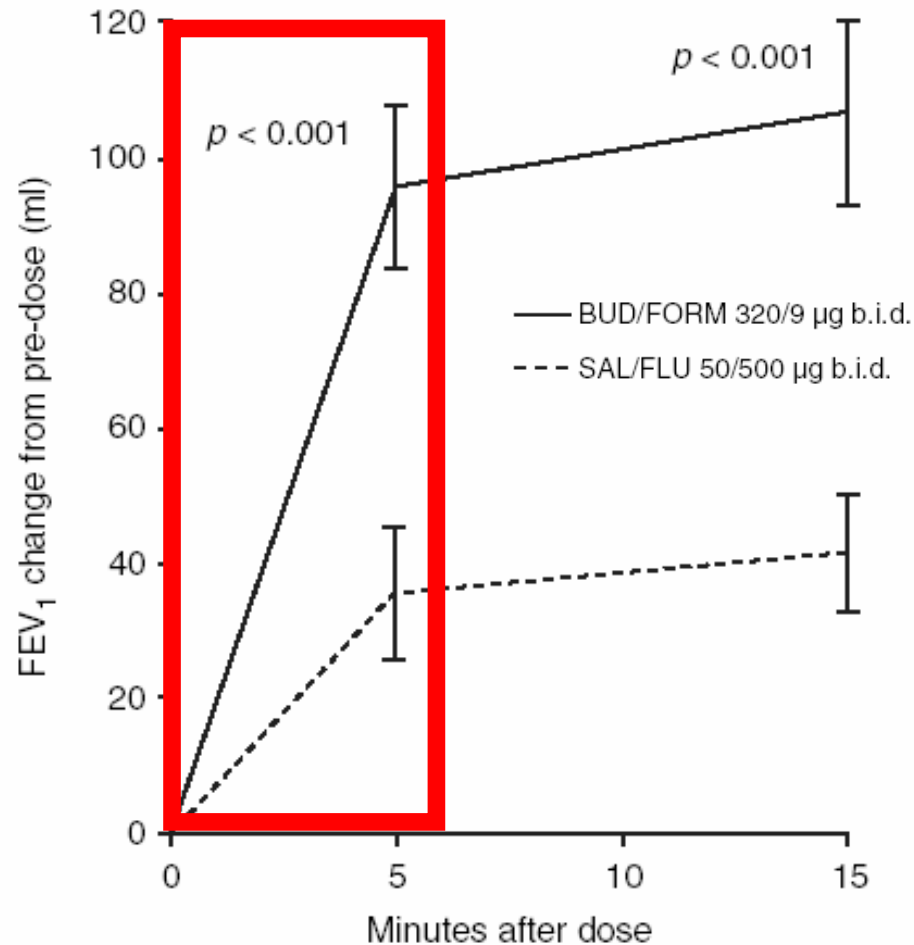
## Estudio pan-Europeo





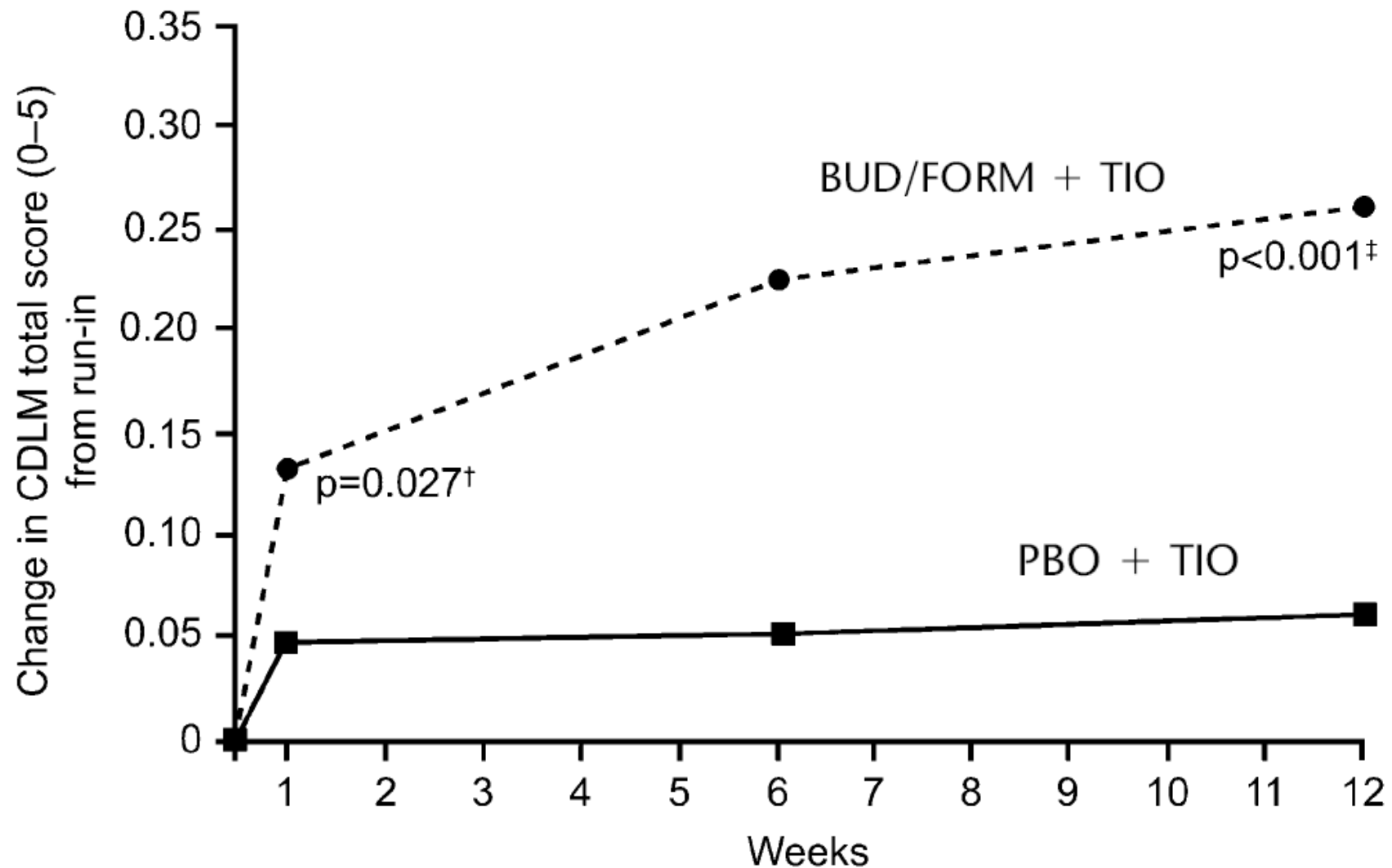
# TRATAMIENTO VARIABILIDAD

## Formoterol vs salmeterol

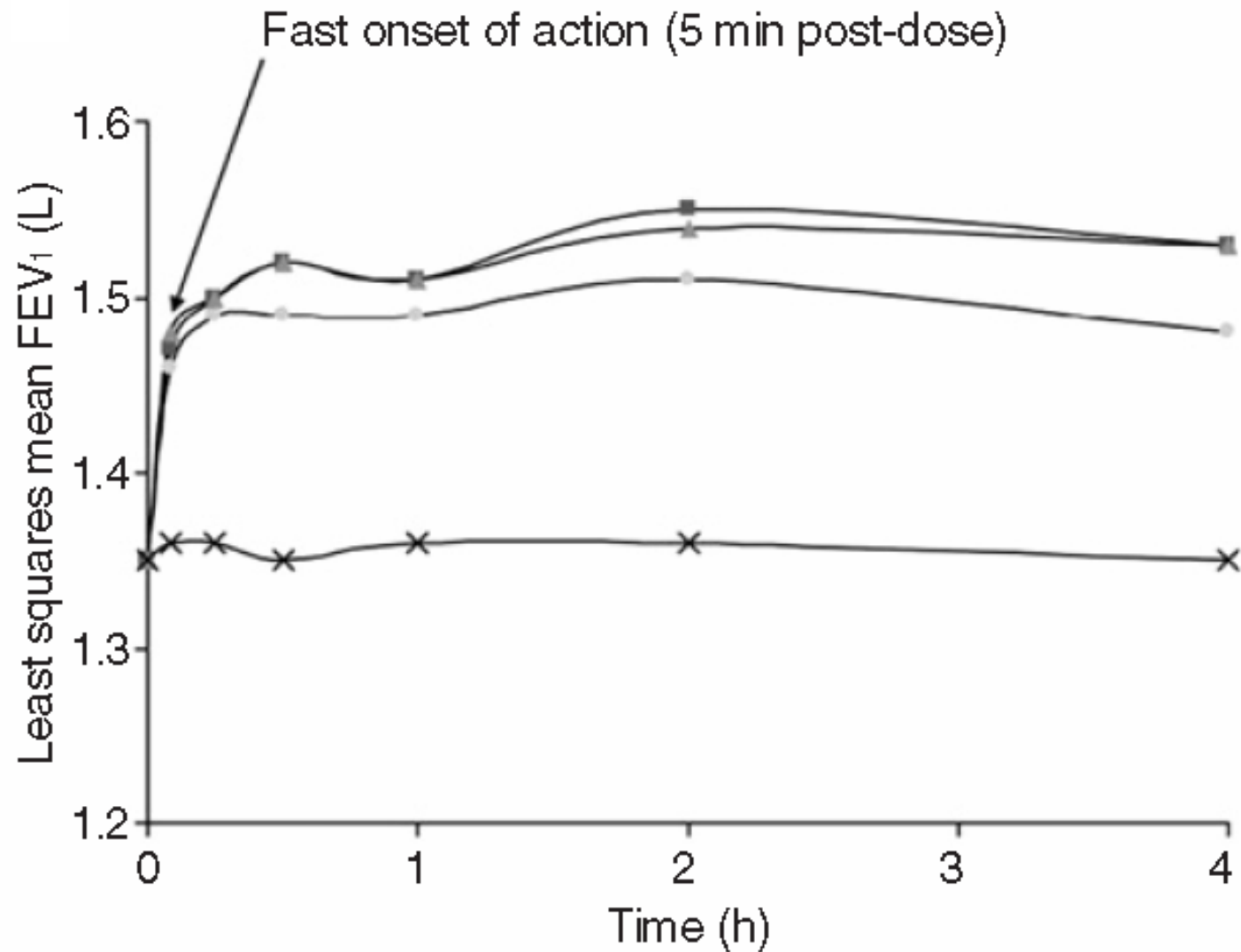


# TRATAMIENTO VARIABILIDAD

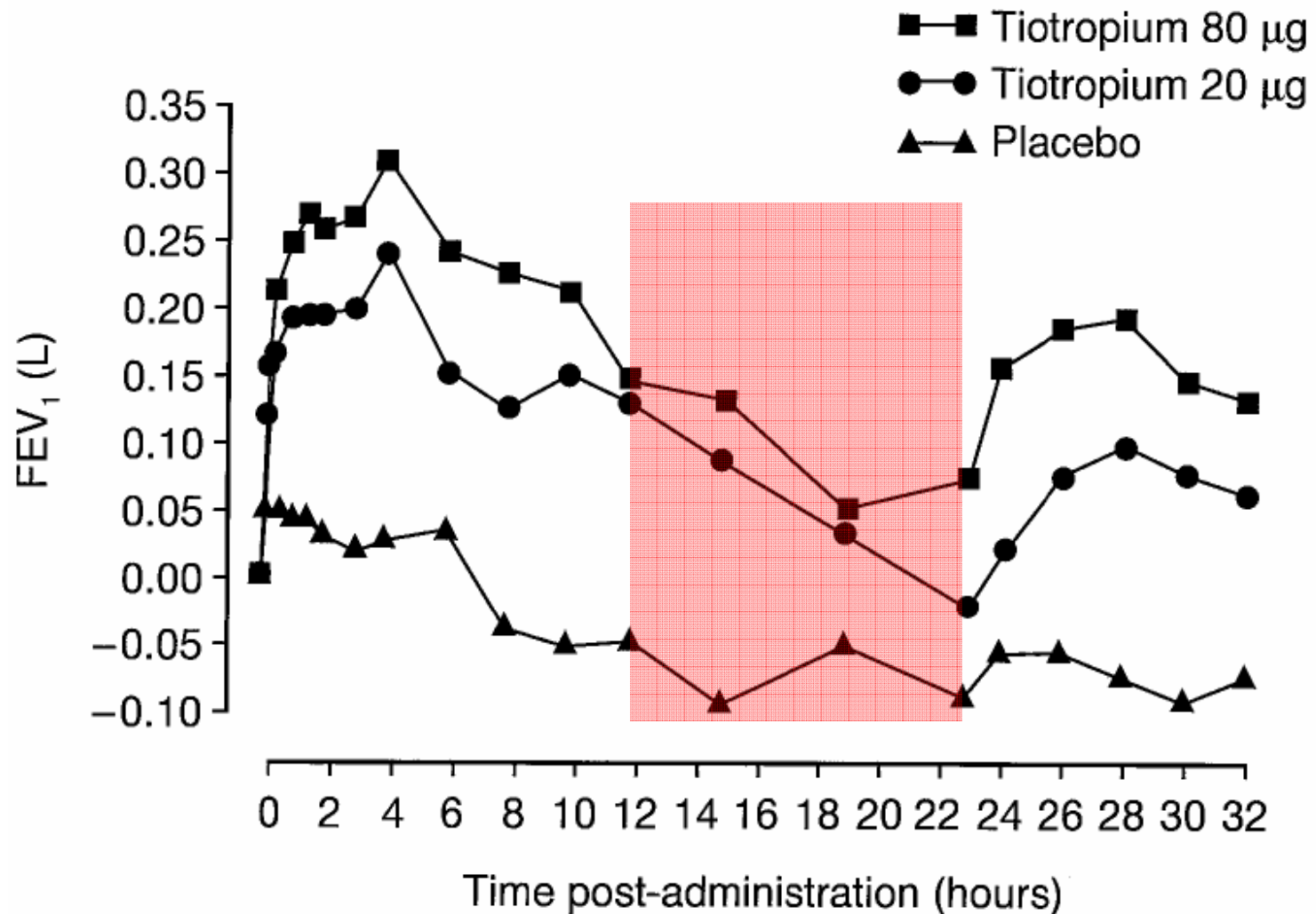
## Formoterol



# TRATAMIENTO VARIABILIDAD. Indacaterol



# TRATAMIENTO VARIABILIDAD. ¿Tiotropio?

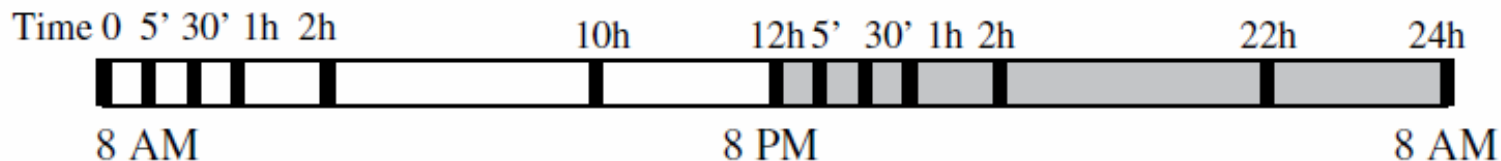


# TRATAMIENTO VARIABILIDAD. ¿Tiotropio?

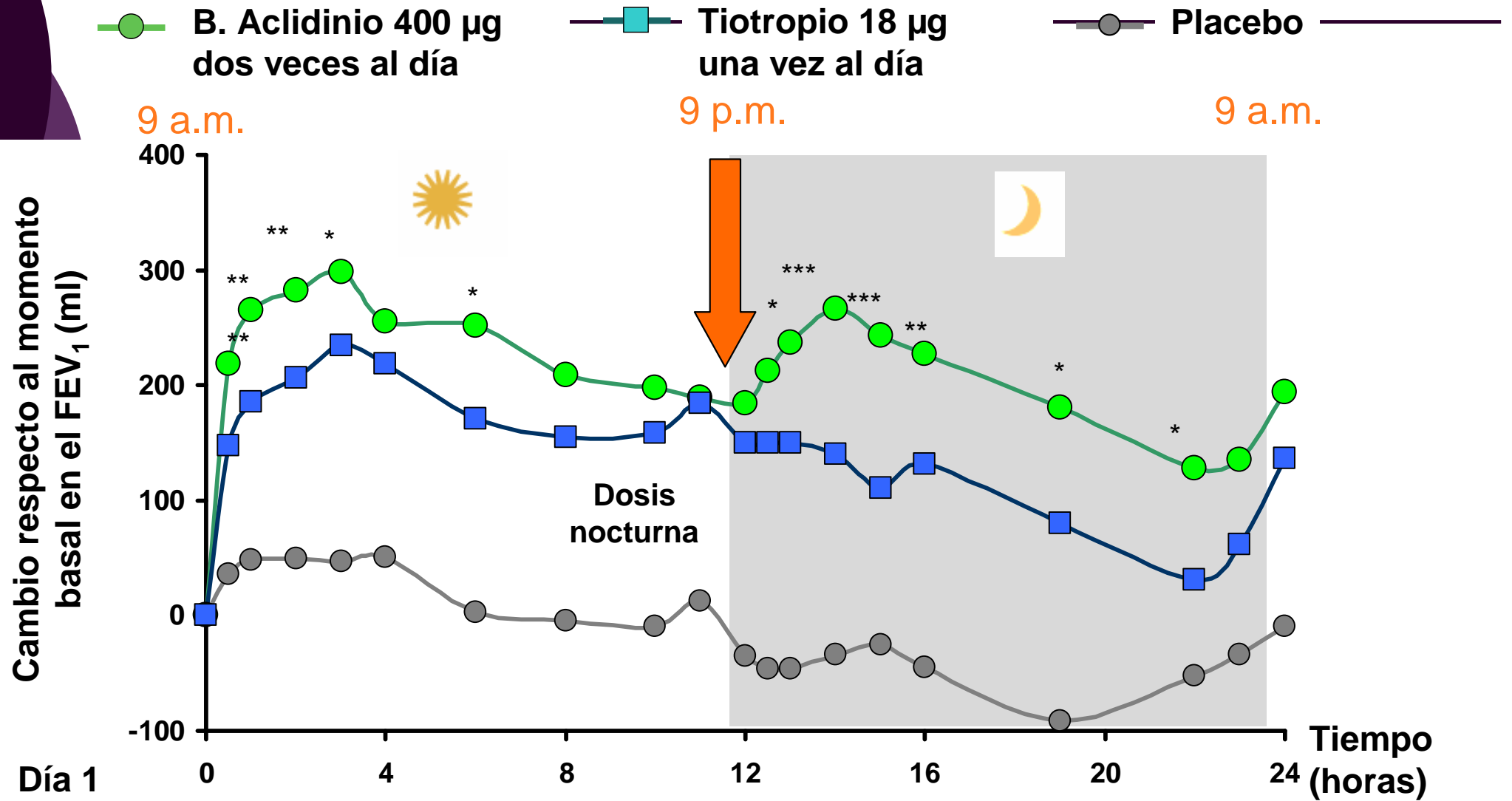


|                    |                                  |                                 |
|--------------------|----------------------------------|---------------------------------|
| <b>Treatment 1</b> | <b>TIO</b> Hand.+Placebo MDI     | Placebo MDI+Placebo Hand.       |
| <b>Treatment 2</b> | <b>TIO</b> Hand.+Placebo MDI     | <b>FOR</b> MDI+Placebo Hand.    |
| <b>Treatment 3</b> | <b>FOR</b> MDI+Placebo Hand.     | <b>FOR</b> MDI+Placebo Hand.    |
| <b>Treatment 4</b> | <b>TIO</b> Hand.+ <b>FOR</b> MDI | <b>FOR</b> MDI+Placebo Hand.    |
| <b>Treatment 5</b> | <b>FOR</b> MDI+Placebo Hand.     | <b>TIO</b> Hand+ <b>FOR</b> MDI |

## Spirometric Assessment (*DAY1 and DAY30*)



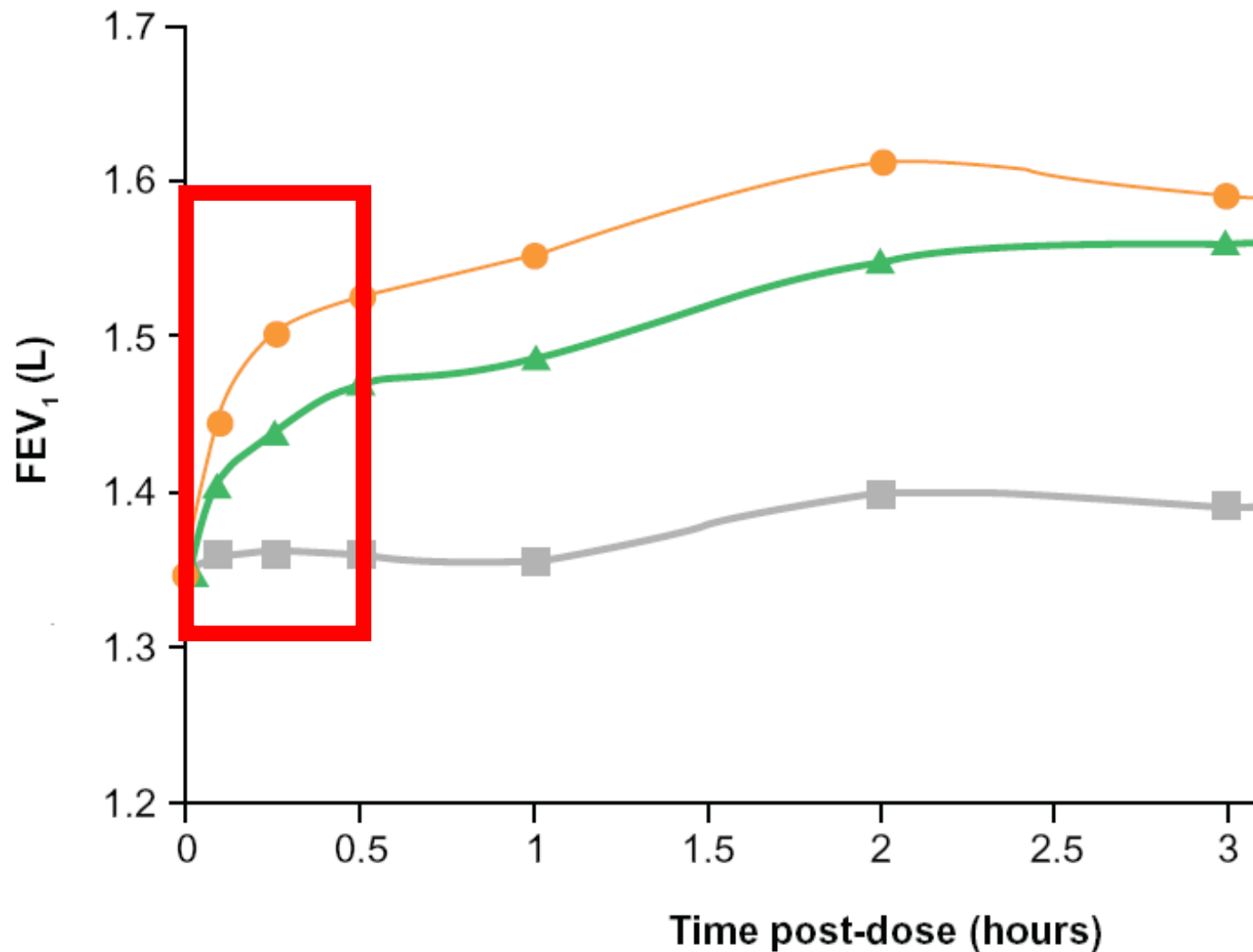
# ACLIDINIO. Efecto nocturno y matutino



\*p<0,05, \*\*p<0,01, \*\*\*p<0,001 acclidinio frente a tiotropio

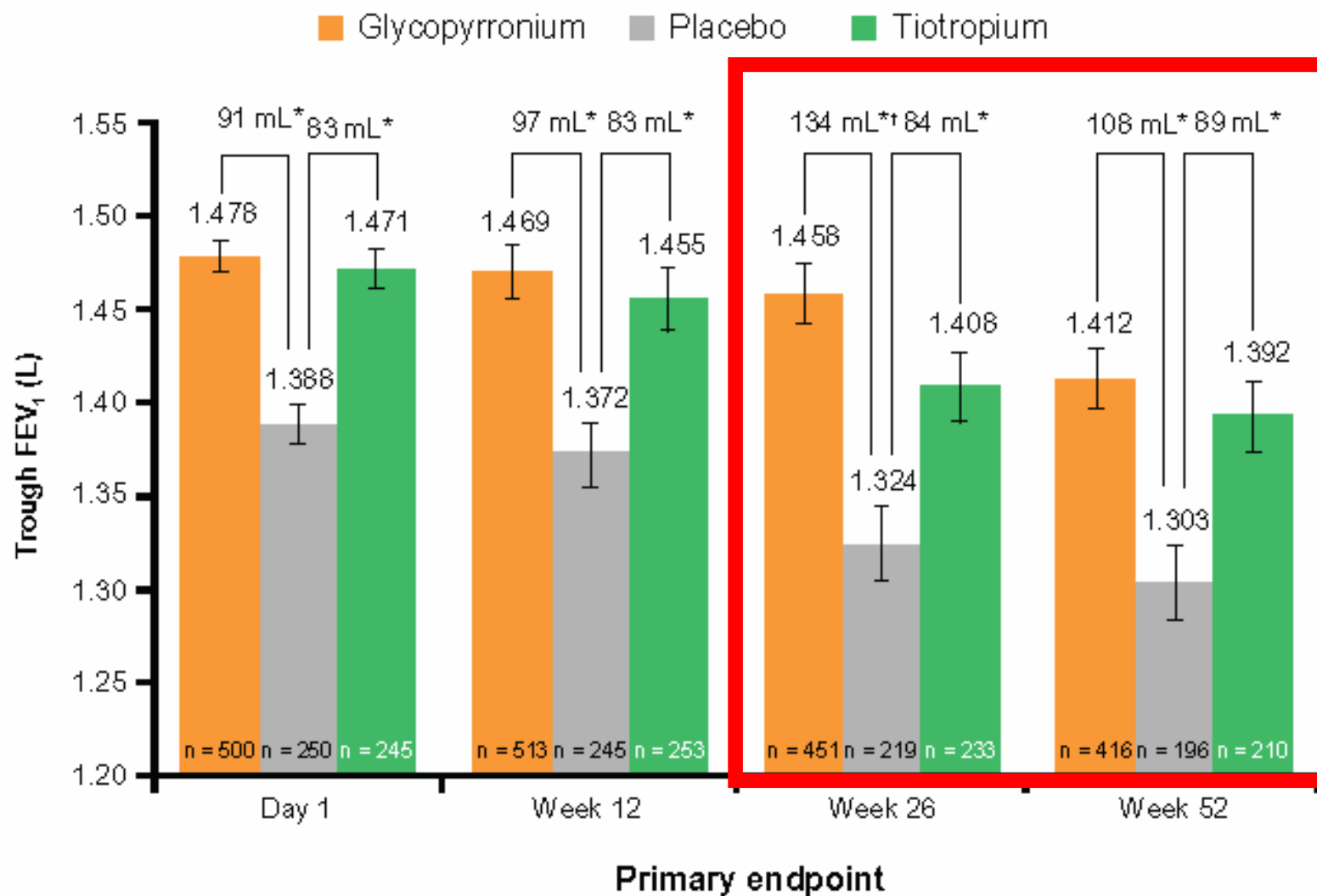
# TRATAMIENTO VARIABILIDAD. Glicopirronio

**GLOW 2**    ●—● Glycopyrronium    ■—■ Placebo    ▲—▲ Tiotropium



# TRATAMIENTO VARIABILIDAD. Glicopirronio

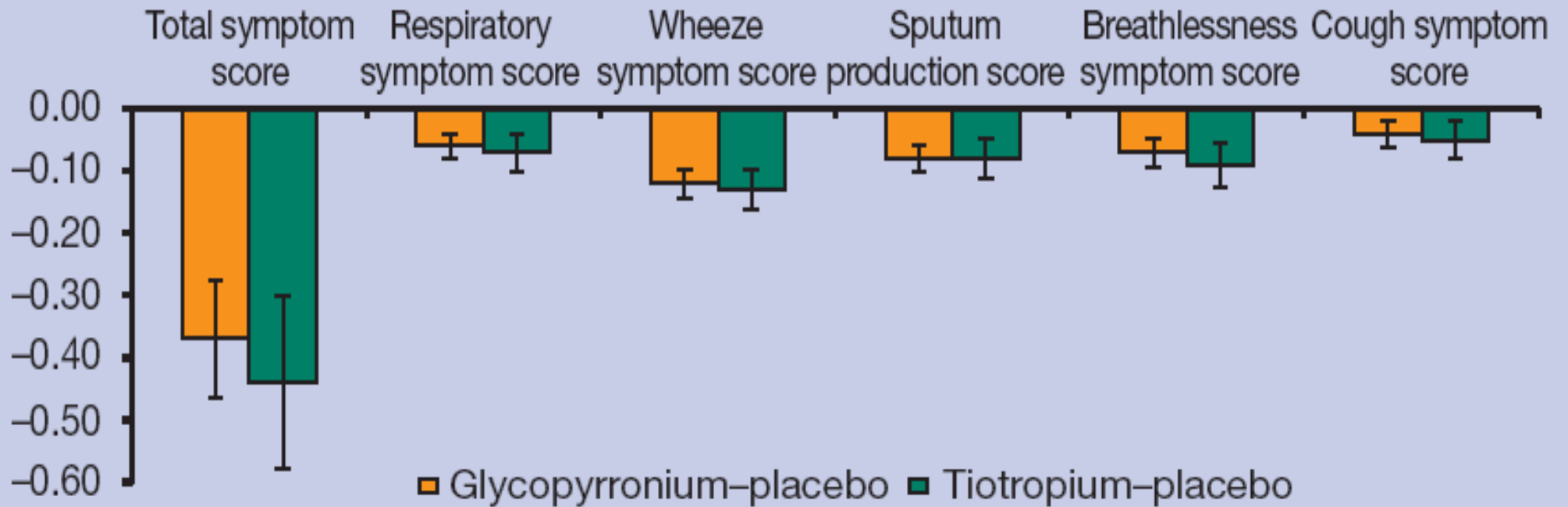
## GLOW 2





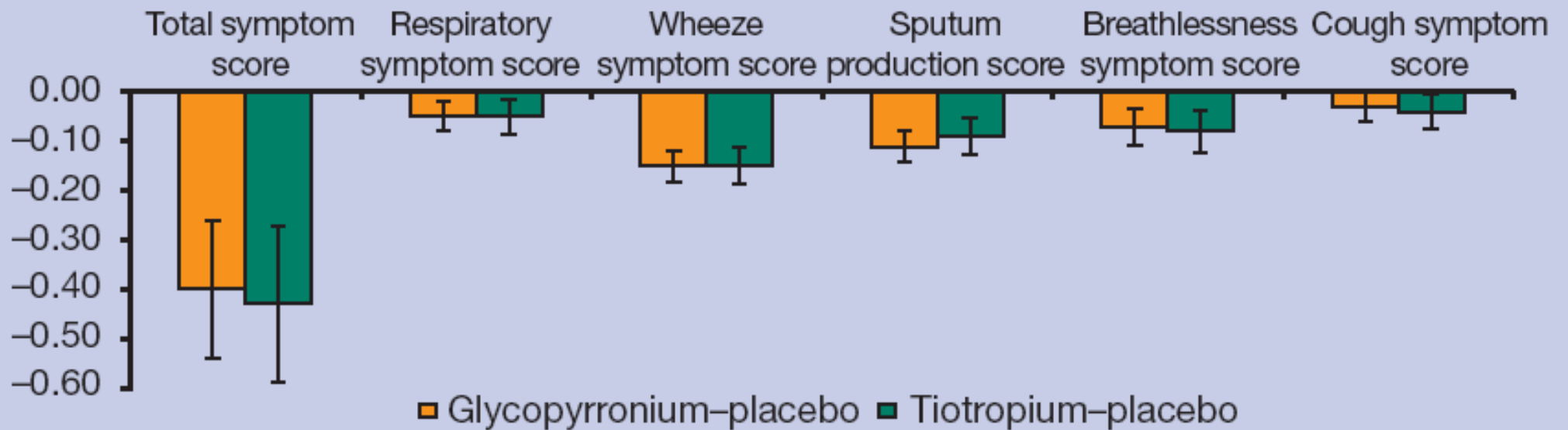
# Tratamiento de síntomas matutinos. Glicopirronio

(b) 26 Weeks



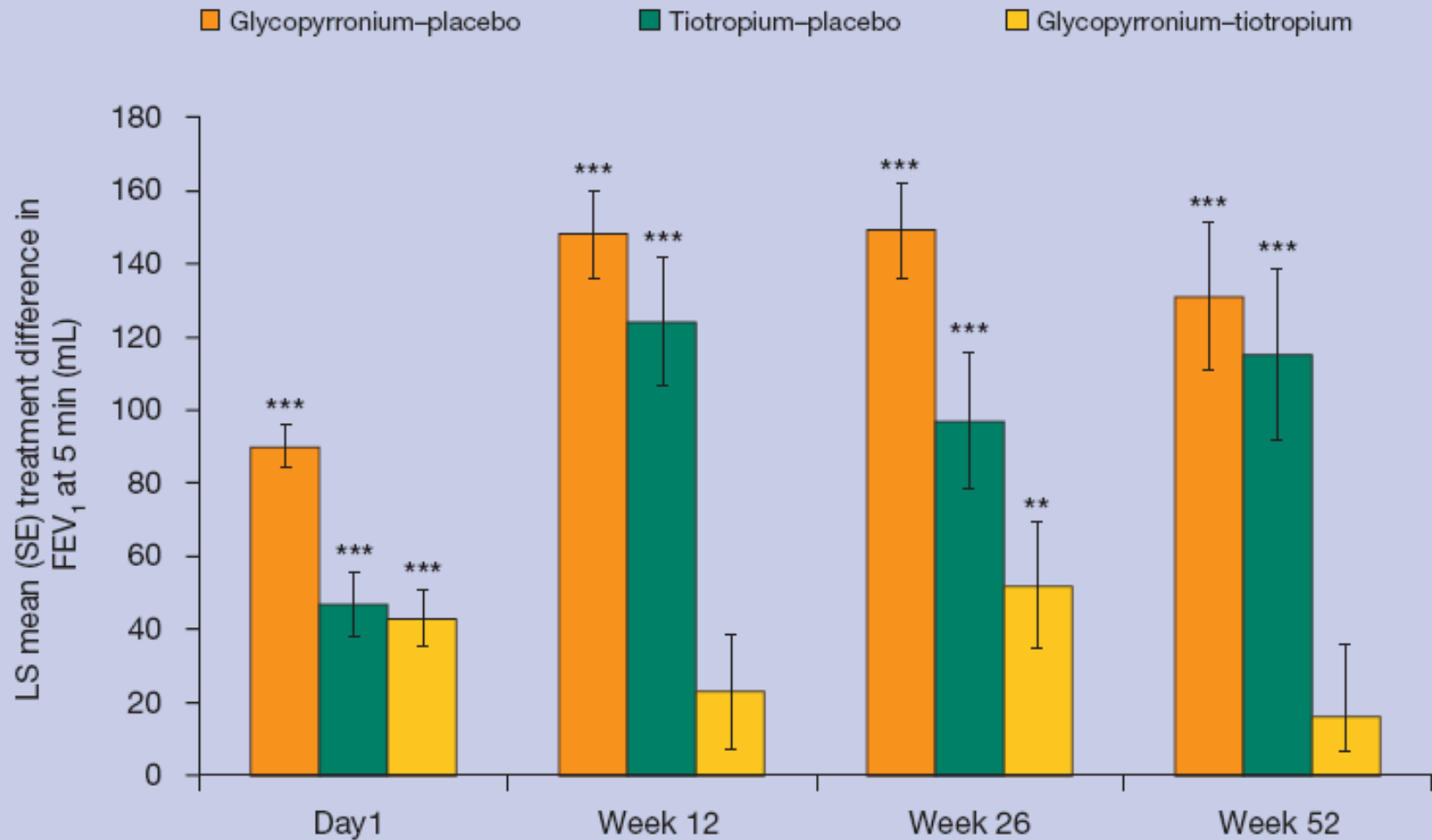
# Tratamiento de síntomas matutinos. Glicopirronio

(c) 52 Weeks



# Mejoría del FEV<sub>1</sub> en la mañana. Glicopirronio

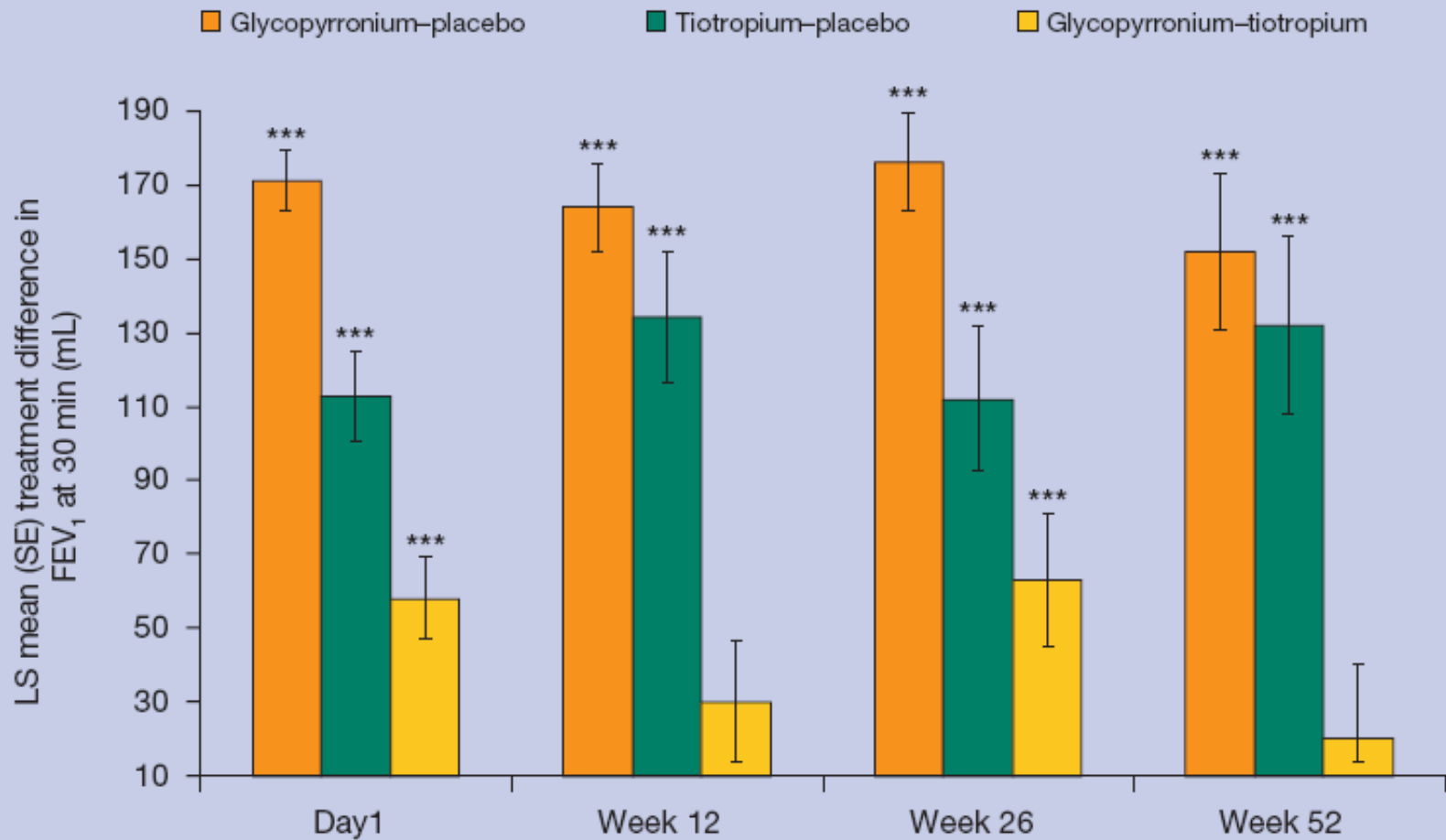
Figure 2. FEV<sub>1</sub> at 5 min (mL)



\*\*\*p<0.001, \*\*p<0.01; SE=standard error; Week 52 includes GLOW2 data only

# Mejoría del FEV<sub>1</sub> en la mañana. Glicopirronio

Figure 3. FEV<sub>1</sub> at 30 min (mL)

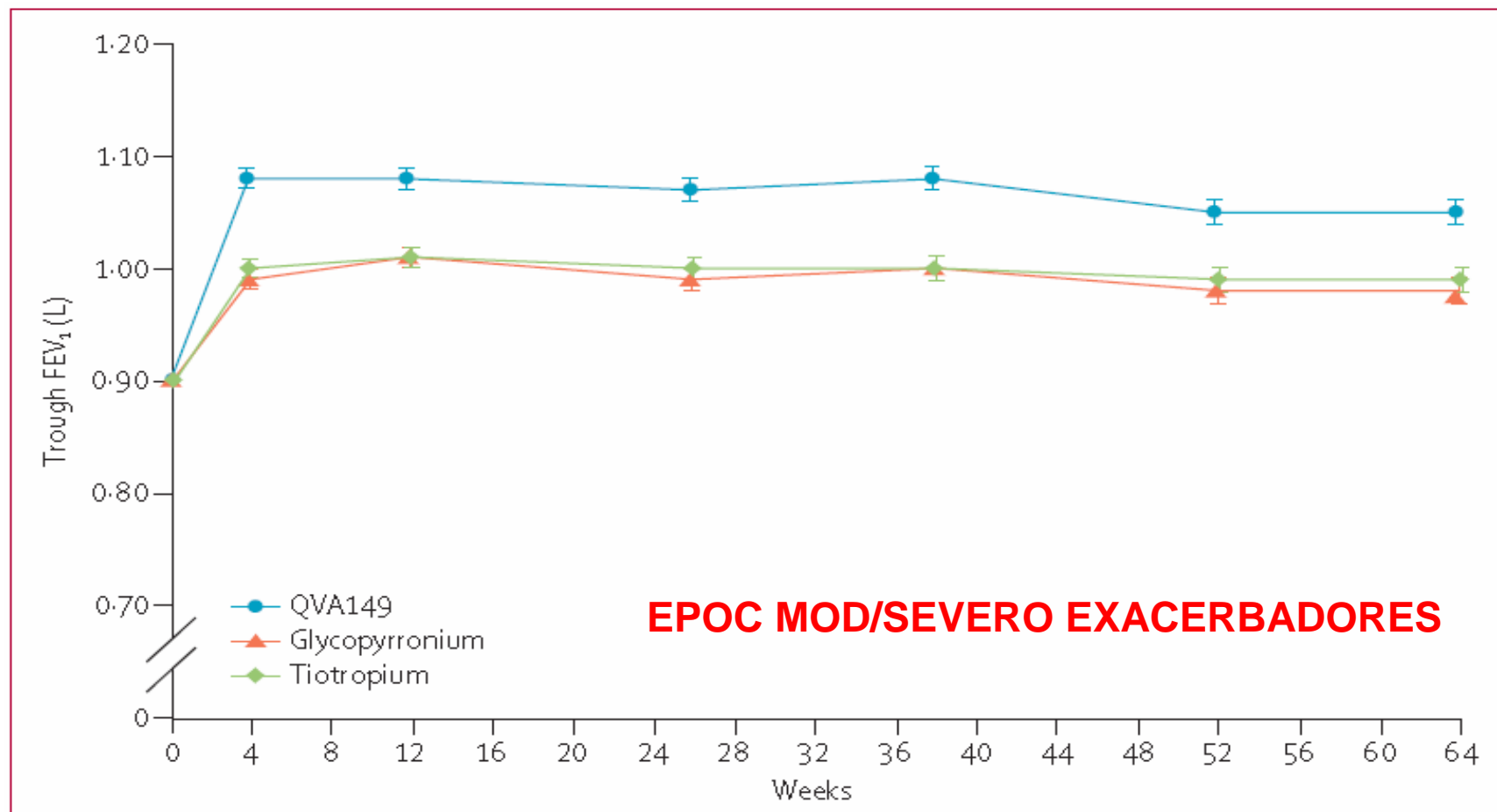


\*\*\*p<0.001; SE=standard error; Week 52 includes GLOW2 data only

# Analysis of chronic obstructive pulmonary disease exacerbations with the dual bronchodilator QVA149 compared with glycopyrronium and tiotropium (SPARK): a randomised, double-blind, parallel-group study

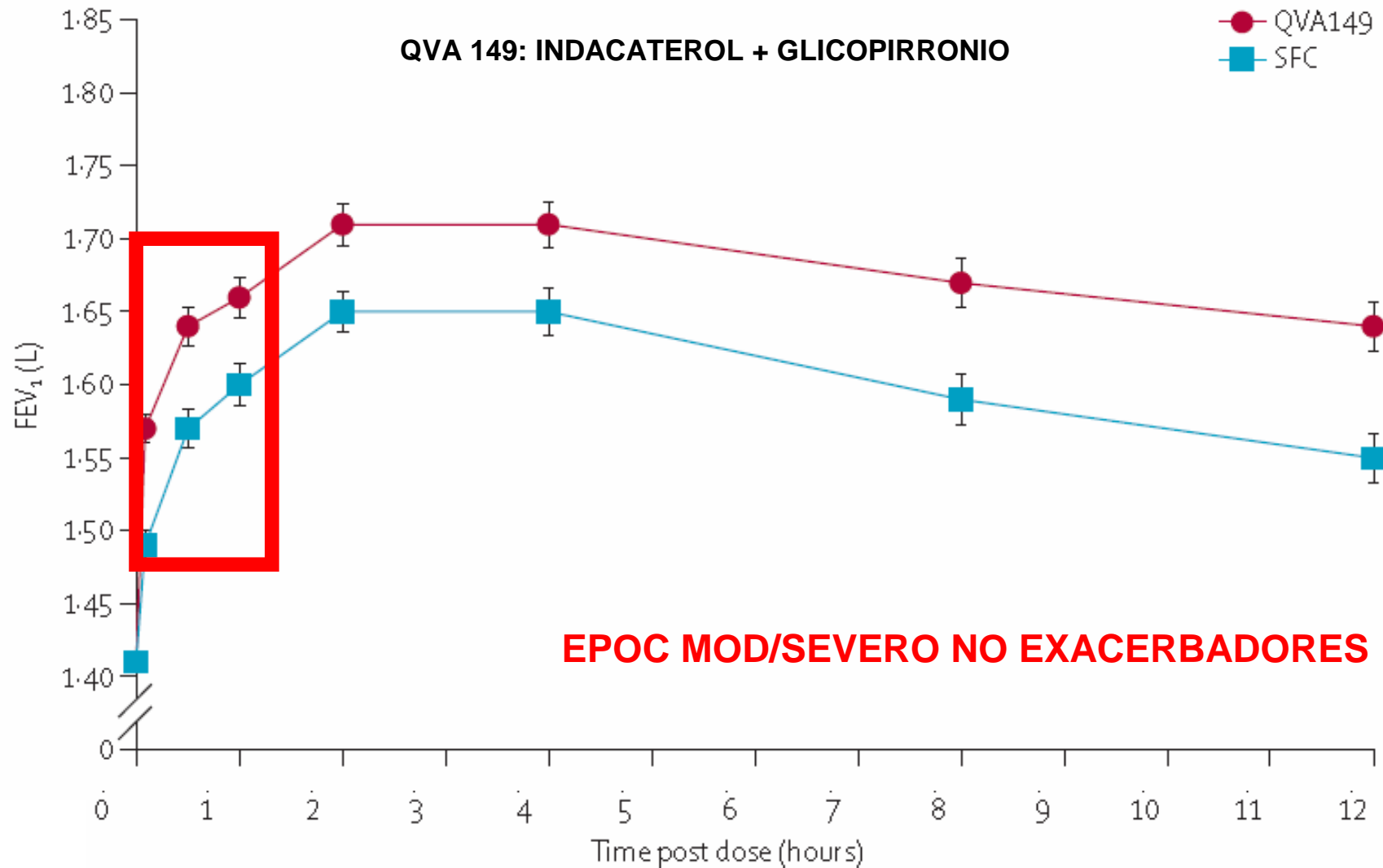
[www.thelancet.com/respiratory](http://www.thelancet.com/respiratory)

## QVA 149: INDACATEROL + GLICOPIRRONIO



# Efficacy and safety of once-daily QVA149 compared with twice-daily salmeterol-fluticasone in patients with chronic obstructive pulmonary disease (ILLUMINATE): a randomised double-blind, parallel group study

[www.thelancet.com/respiratory](http://www.thelancet.com/respiratory)



# LAMA, LABA, CI. Cronoterapia

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|               | LAMA                                      | LABA  | CORTICOIDES  |
|---------------|---|---|--|
| CADA 12 HORAS | Aclidinio<br>Darotropio                   | Salmeterol<br>Formoterol                              | Beclometasona<br>Budesonida<br>Fluticasona (prop)  |
| CADA 24 HORAS | Tiotropio<br>Glicopirronio<br>Umeclidinio | Indacaterol<br>Vilanterol<br>Olodaterol<br>Carmoterol | Ciclesonida<br>Mometasona<br>Fluticasona (furoato) |

**VARIABILIDAD DE SÍNTOMAS (matutinos y nocturnos)**

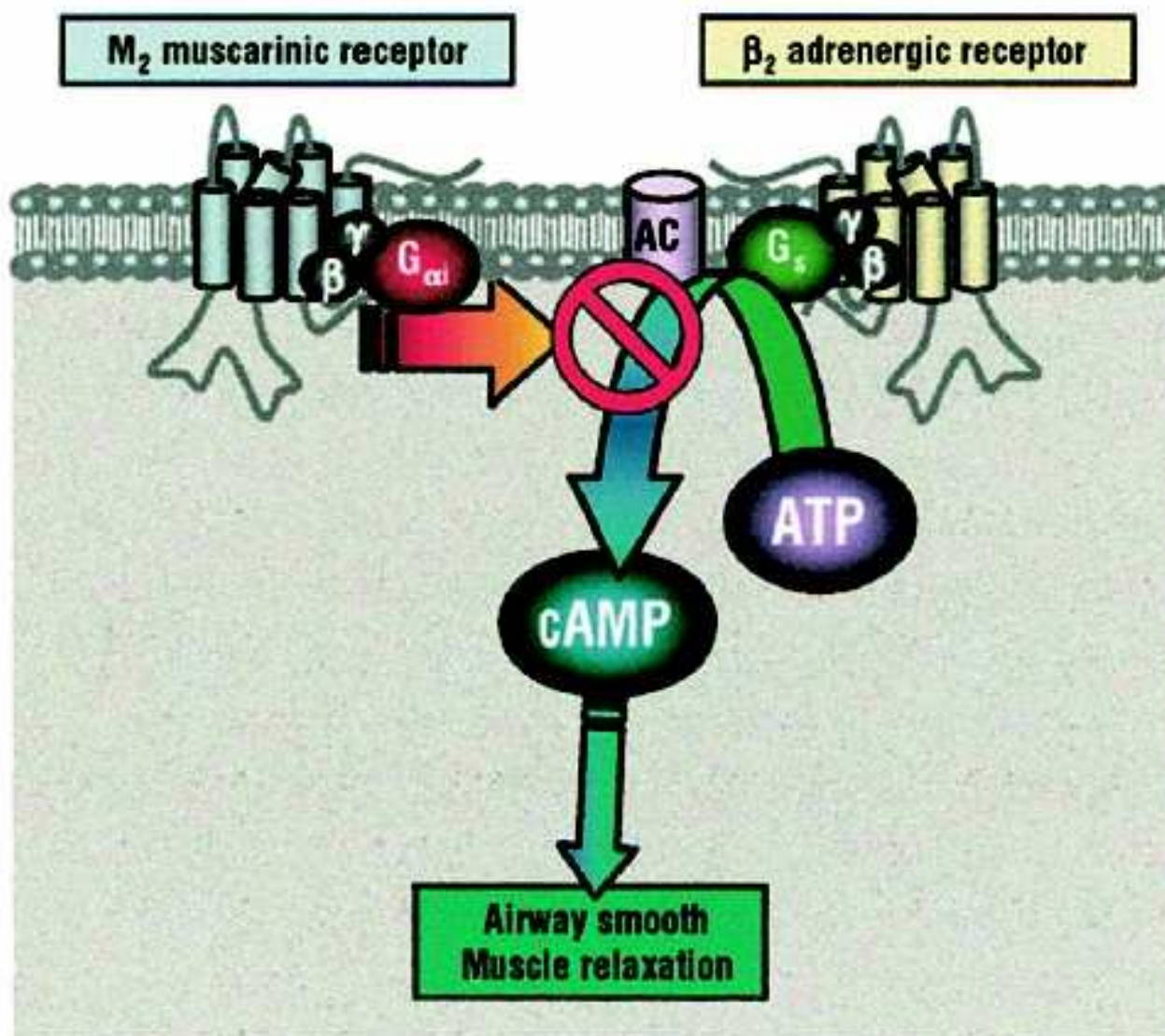
**INTERACCIÓN RECEPTORES M2-BETA2**

# Interacción $M_2$ - $\beta_2$ : bases para el tratamiento broncodilatador combinado

## $M_2$ - $\beta_2$ Interaction: A Basis for Combined Bronchodilator Treatment

José Luis López-Campos<sup>a,b</sup>

Arch Bronconeumol. 2013;**49**(7):279-281





# LAMA, LABA, CI. Cronoterapia

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|                                 | LAMA                                      | LABA  | CORTICOIDES  |
|---------------------------------|---|---|--|
| INTERACCIÓN RECEPTORES M2-BETA2 |   |   |  |
| CADA 12 HORAS                   | Aclidinio<br>Darotropio                   | Salmeterol<br>Formoterol                              | Beclometasona<br>Budesonida<br>Fluticasona (prop)  |
| CADA 24 HORAS                   | Tiotropio<br>Glicopirronio<br>Umeclidinio | Indacaterol<br>Vilanterol<br>Olodaterol<br>Carmoterol | Ciclesonida<br>Mometasona<br>Fluticasona (furoato) |

**VARIABILIDAD DE SÍNTOMAS (matutinos y nocturnos)**

# GRACIAS

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