2015 천식연구회 COPD 연구회
공동 심포지엄

Tx in Airway Disease: Improving Inhaler Adherence in Patients with Airway Disease

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Adherence: Quote

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.

Osterberg et al, NEJM 2005

Adherence: 불편한 진실

Do good adherers had lower mortality?

- Compliant phenotype -

	Medication group	Placebo group
5yr mortality	20%	21%
5yr mortality by Patterns of Adherence (good adherens defined as those taking at least 80% of prescribed med)	Good adherers: 15% Poor adherers: 25%	Good adherers: 15% Poor adherers: 28%

SPECIAL ARTICLE ARCHIVE

Influence of Adherence to Treatment and Response of Cholesterol on Mortality in the Coronary Drug Project

The Coronary Drug Project Research Group

N Engl J Med 1980; 303:1038-1041 | October 30, 1980 | DOI: 10.1056/NEJM198010303031804

Terminology: ISPOR/WHO

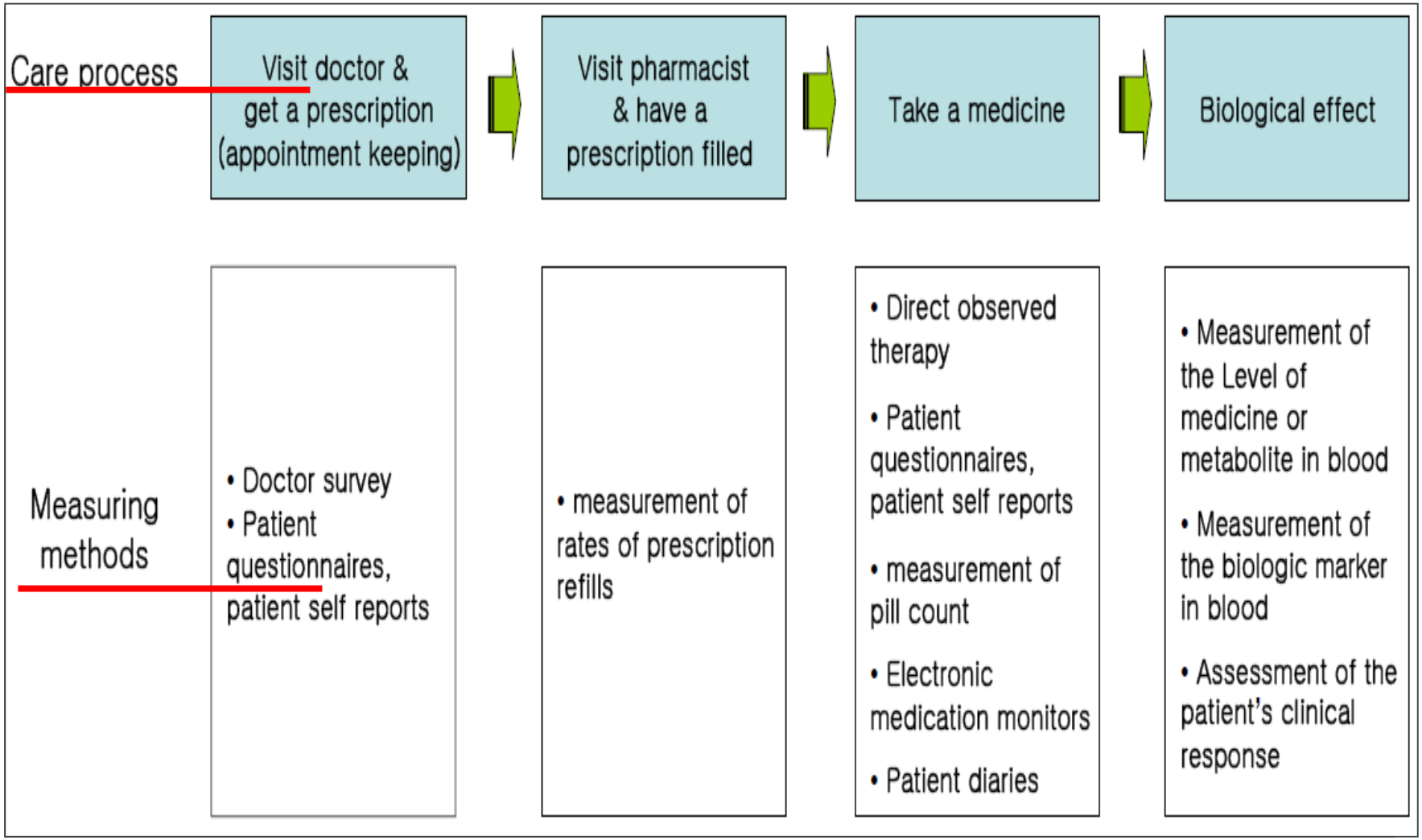
- **Compliance** (Cramer et al., 2008)
  - "act of conforming to the recommendations made by the provider with respect of timing, dosage and frequency of medication taking"
  - MPR (medication possession ratio)

Drugs	Months (1 month = 30 days)												Supply (days)	MPR
A	x	x	x	x	x	x				x	x	x	9x30=270	270/360=0.75
B		x	x	x	x		x	x	x	x			8x30=240	240/360=0.66
C			x		x		x	x		x	x	x	7x30=210	210/360=0.58

- **Adherence** : preferred term (WHO, 2003)
  - "the extent to which a person's behavior corresponds with agreed recommendations from a health-care provider"
  - emphasize the patient is free to decide to doctor's recommendations

Cramer et al, 2008

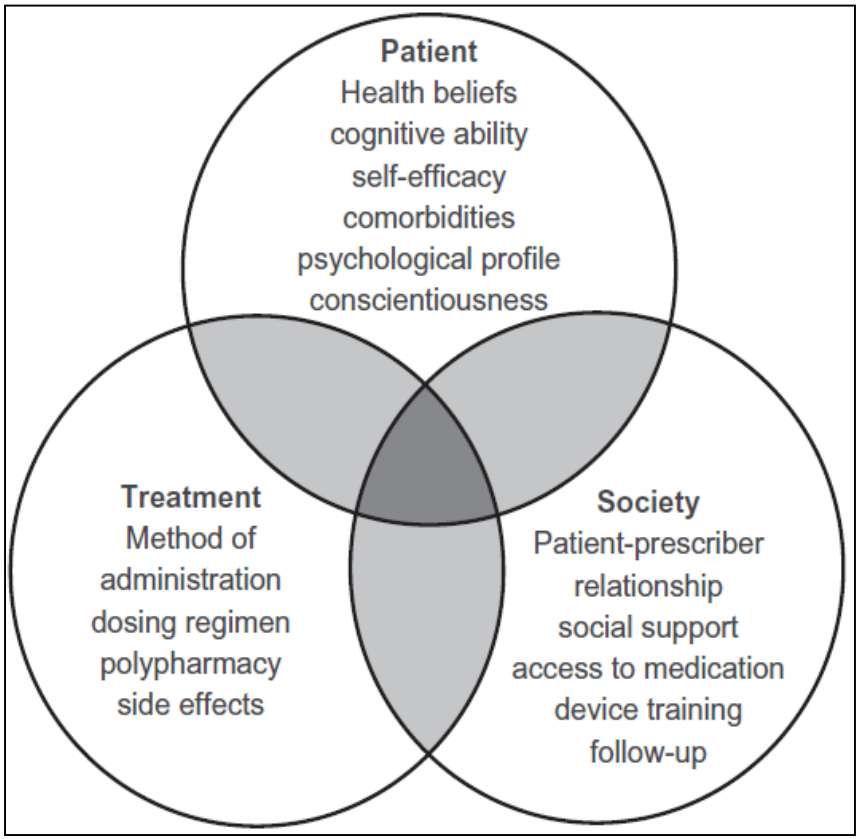
Methods of measuring adherence

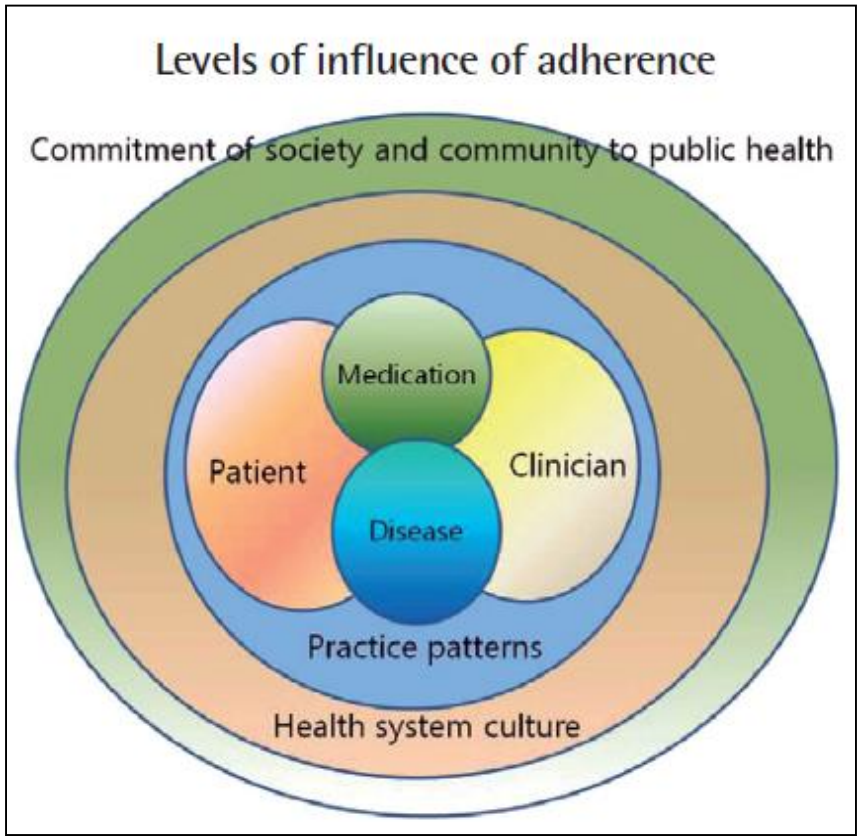


Adherence in asthma Tx

- Facts & multifactorial barriers -

- Adherence to asthma Tx is low: about 50% (chest 2014)
  - mean adherence rate to ICS in SR : 22~63% (Resp Care 2014)
  - older asthmatics (≥ 60 yrs) adherence rate to controller: 38.2% (chest 2014)
- Nonadherence causes severe exacerbation (JACI 2011, ERJ 2014)





Bourbeau J et al, Thorax 2008

MANIFESTO on Adherence in asthma

- **Barriers related to the patient**
- *presence of comorbid physical disorders*
- *cognitive difficulties*
- *psychiatric comorbidities*
- *age-related (children, adolescents and elderly have an increased risk of non-adherence)*
- *inadequate knowledge*
- *low expectations*
- *poor social and family support*
- *inadequate ability to coping with the disease*
- **Barriers related to the disease**
- *chronicity*
- *symptom stability*
- *absence of symptoms*
- **Barriers related to the treatment**
- *multiple daily doses*
- *presence of side effects*
- *complexity of the therapeutic regimes*
- *high lack of ease of use*
- *costs*
- **Barriers related to the doctor-patient relationship**
- *poor communication due to a poor relationship*
- *inappropriate doctor or patient behaviour*

Barriers of poor adherence in asthma

- 낮은 순응도의 원인과 확인법 -

낮은 순응도 관련 인자	낮은 순응도를 확인하는 방법
약물 관련 인자 • 흡입기 사용의 어려움(관절염 등) • 번거로운 처방(1일 4회 사용 등) • 여러 개의 다른 흡입기 **의도하지 않은 인자** • 이해 부족 • 잊어버림 • 매일 규칙적인 처방이 없음 • 비용 **의도적인 인자** • 치료가 필요 없다는 인식 • 천식과 천식치료에 대한 부정과 분노 • 부적절한 기대 • 부작용에 대한 걱정 • 의사에 대한 불만족 • 천식에 대한 수치심 • 문화적 종교적 원인 • 비용	**공감하는 질문을 한다.** • 순응도가 완벽할 수 없음을 알려주고 비판하지 않고 편안하게 토론을 할 수 있도록 한다. - '많은 환자들이 처방받은 대로 흡입기를 사용하지 않습니다. 지난 4주 동안 일주일에 며칠 흡입기를 사용했습니까? 전혀 사용하지 않으셨는지 아니면 하루, 이틀, 사흘……' – '아침에 사용하는 것과 저녁에 사용하는 것 중 언제가 흡입기 사용하는 것을 기억하기 쉽습니까?' **약제 사용을 확인** • 마지막 조절제 처방 날짜 확인 • 날짜와 흡입기의 남은 용량 확인 • 처방과 조제빈도의 모니터링을 전산화

호흡기학회 천식진료지침 2014

ICS adherence & asthma exacerbation

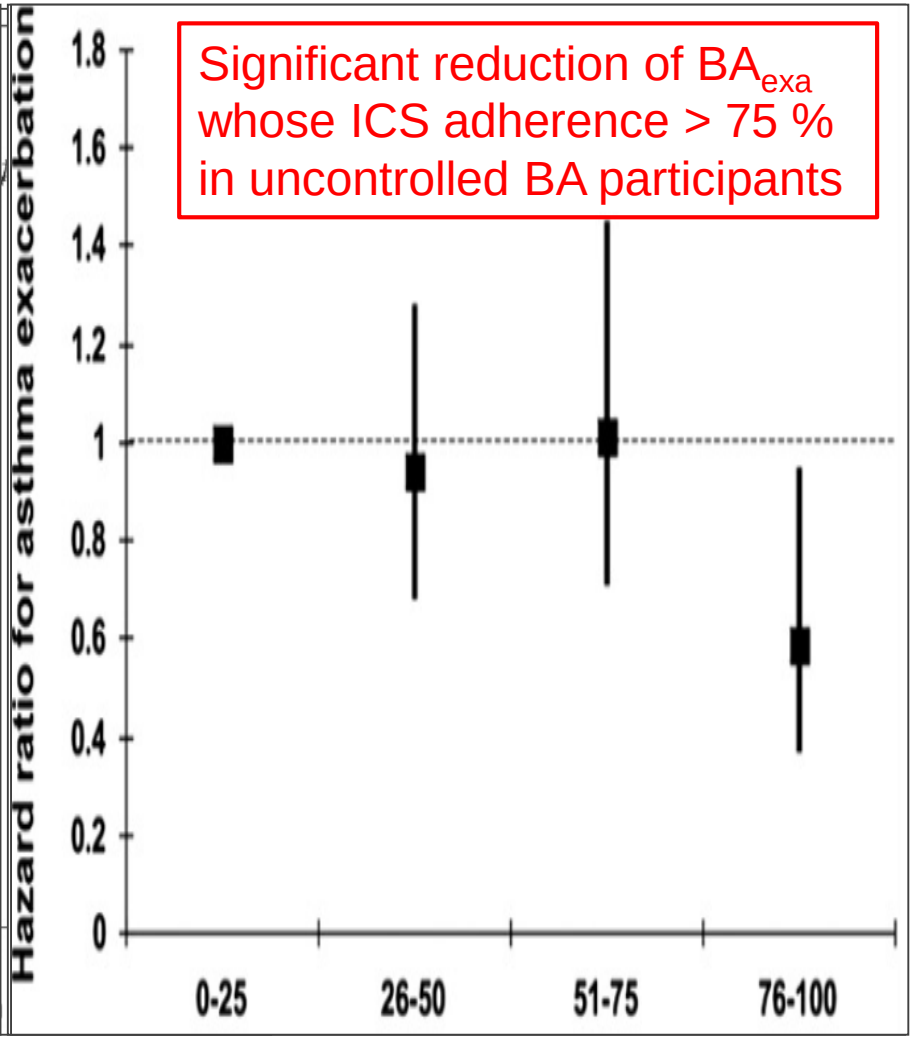
- SAPPHIRE study -

Outcome	Adherence to ICSs† HR (95% CI)	P value	aHR (95% CI)‡	P value
Primary outcome				
Combined asthma exacerbations*	1.12 (1.04-1.20)	.002	0.89 (0.81-0.97)	.009
Secondary outcomes				
Oral corticosteroid use	1.12 (1.03-1.22)	.006	0.90 (0.80-1.00)	.043
Asthma-related ED visit	1.06 (0.92-1.22)	.428	0.87 (0.73-1.03)	.114
Asthma-related hospitalization	1.37 (1.03-1.81)	.029	0.99 (0.65-1.51)	.971

aHR, Adjusted HR.

*An asthma exacerbation was considered to be an event requiring the initiation of oral corticosteroids, an asthma-related ED visit, or an asthma-related hospitalization. These events combined comprised the primary study outcome.

†HRs for adherence represent the estimated effect for a 25% improvement in ICS adherence.



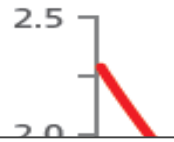
Significant reduction of BA_{exa} whose ICS adherence > 75 % in uncontrolled BA participants

Williams LK et al. JACI 2011

ICS adherence & asthma mortality

- Impact of ICS adherence on prevention of asthma death -

- To investigate whether ICS can prevent death from asthma
- Nested case–control study in subjects who died of asthma were matched with controls within the Saskatchewan Health cohort bet 1975-1991 (5-44 yrs,n=30,569)



- Rate of death decreased by 21%/ every additional ICS/yr (RR_a 0.79)
- More than 4 canister decreased

TABLE 3. CRUDE AND ADJUSTED RATE RATIOS FOR DEATH FROM ASTHMA IN RELATION TO DISCONTINUATION OF INHALED CORTICOSTEROID USE.*

CORTICOSTEROID USE	CASE PATIENTS (N=66)	CONTROLS (N=2681)	CRUDE RATE RATIO	ADJUSTED RATE RATIO (95% CI)†
Uninterrupted (%)	4.6	7.9	1.0	1.0 (reference group)
Discontinued (%)				
1–3 mo before index date	19.7	9.0	3.9	4.6 (1.1–19.1)
4–6 mo before index date	4.6	6.3	1.3	1.8 (0.3–10.9)
7–9 mo before index date	4.6	5.3	1.7	1.6 (0.3–9.4)

Suissa S et al., NEJM 2000

Strategies to improve adherence in asthma

- Intervention of therapy- related factor: simplifying regimen -

Real-world effects of once vs greater daily inhaled corticosteroid dosing on medication adherence

Karen E. Wells, MPH [*]; Edward L. Peterson, PhD [*]; Brian K. Ahmedani, PhD [†]; and L. Keoki Williams, MD, MPH [†,‡]

[*] *Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan*
[†] *Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, Michigan*
[‡] *Department of Internal Medicine, Henry Ford Health System, Detroit, Michigan*

	Change in level of adherence (95% CI)[c]	*P* value	Change in level of adherence (95% CI)[d]	*P* value	OR (95% CI)[c]	*P* value	Adjusted OR (95% CI)[d]	*P* value
Once daily ICS use[e]	19.3 (19.8 to 23.7)	.001	19.6 (15.3 to 23.9)	.001	3.28 (2.41 to 4.48)	.001	3.51 (2.53 to 4.85)	.001
Age (per 10-year interval)			4.0 (2.9 to 5.0)	.001			1.23 (1.13 to 1.35)	.001
Female			−3.6 (−6.9 to −0.2)	.036			0.84 (0.63 to 1.13)	.25
Race/ethnicity (referent: white)								
African American			−6.9 (−10.4 to −3.5)	.001			0.61 (0.44 to 0.84)	.002
Other			0.1 (−5.9 to 6.1)	.98			1.15 (0.72 to 1.85)	.55
Asthma severity (referent: low/low-moderate)			4.5 (0.7 to 8.4)	.02			1.46 (1.06 to 2.01)	.02
Taking additional asthma controller medication			5.6 (0.9 to 10.2)	.02			1.51 (1.05 to 2.17)	.02

Wells KE et al. Ann Allergy Asthma Immunol 2013

Strategies to improve adherence in asthma

- 자기관리 : 효과적인 흡입기 사용 전략 -

표 7-3. 흡입기를 효과적으로 사용하는지를 확인하는 전략

선택

- 선택 가능한 약제, 기구, 환자의 능력, 가격을 고려하여 환자에게 가장 적당한 흡입기를 고른다.
- 여러 개를 선택할 수 있으면 환자가 참여하여 정하도록 한다.
- 정량흡입기(MDI)인 경우 약제 도달을 향상시키고 흡입스테로이드의 부작용(쉰 목소리, 구강 캔디다증)을 줄이기 위해 흡입보조기를 사용할 수 있다.
- 흡입기 사용을 제한하는 관절염 등의 신체적인 장애가 없는지 확인한다.
- 혼란을 피하기 위하여 여러 종류의 다른 흡입기를 사용하지 않는다.

검토

- 기회가 있을 때마다 흡입기 사용법을 재확인한다.
- 환자에게 흡입기를 사용하는 것을 보여달라고 한다.
- 흡입기별 점검표를 이용하여 잘못된 점을 확인한다.

수정

- 모형을 이용하여 환자에게 흡입기를 제대로 사용하는 방법을 보여준다.
- 문제 있는 단계를 중심으로 사용방법을 2~3번 다시 확인한다[11].
- 반복훈련에도 흡입기를 제대로 사용하지 못할 때만 다른 기구 사용을 고려한다.
- 흡입기 사용법을 자주 재검토한다. 처음 교육 후에 문제점이 4~6주 안에 주로 나타난다[12].

확인

- 의사는 본인이 처방하는 각각의 흡입기를 제대로 시연할 수 있어야 한다.
- 약사와 간호사도 최대한 효과적인 흡입기 사용법을 교육할 수 있다[13,14].

호흡기학회 천식진료지침 2014

Strategies to improve adherence in asthma

- Intervention of patient- related factor: Age/forgetting -

	Total, %	Good ICS Adherence		*p*
		Yes	No	
Keep medication in a usual location	44.2	50.0	40.4	0.10
Bedside or elsewhere in bedroom	20.1	23.3	18.2	0.28
Bathroom	9.2	16.4	4.6	< 0.001
Purse or bag	4.9	1.7	5.7	0.10
Kitchen	3.9	4.3	4.0	0.91
Other locations	8.5	7.8	9.1	0.68
Integrate as part of a routine	32.6	50.0	22.2	< 0.001
Morning routine	12.5	25.0	5.1	< 0.001
Evening routine	8.2	12.9	6.1	0.04
Take at a specific time of day	21.7	29.3	16.7	0.008
Taken with other chronic medications	13.4	16.4	11.6	0.23
Use only when needed	13.4	0.0	21.2	< 0.001
Other reminders	11.9	9.48	14.1	0.23
Person to person reminder	1.2	0.0	2.0	0.12
Written note reminder	1.5	2.6	1.0	0.28
Alarm reminder	0.6	0.0	1.0	0.28
No specific strategy employed	4.3	5.2	4.0	0.64
Did not provide an answer	9.8	9.5	9.1	0.91

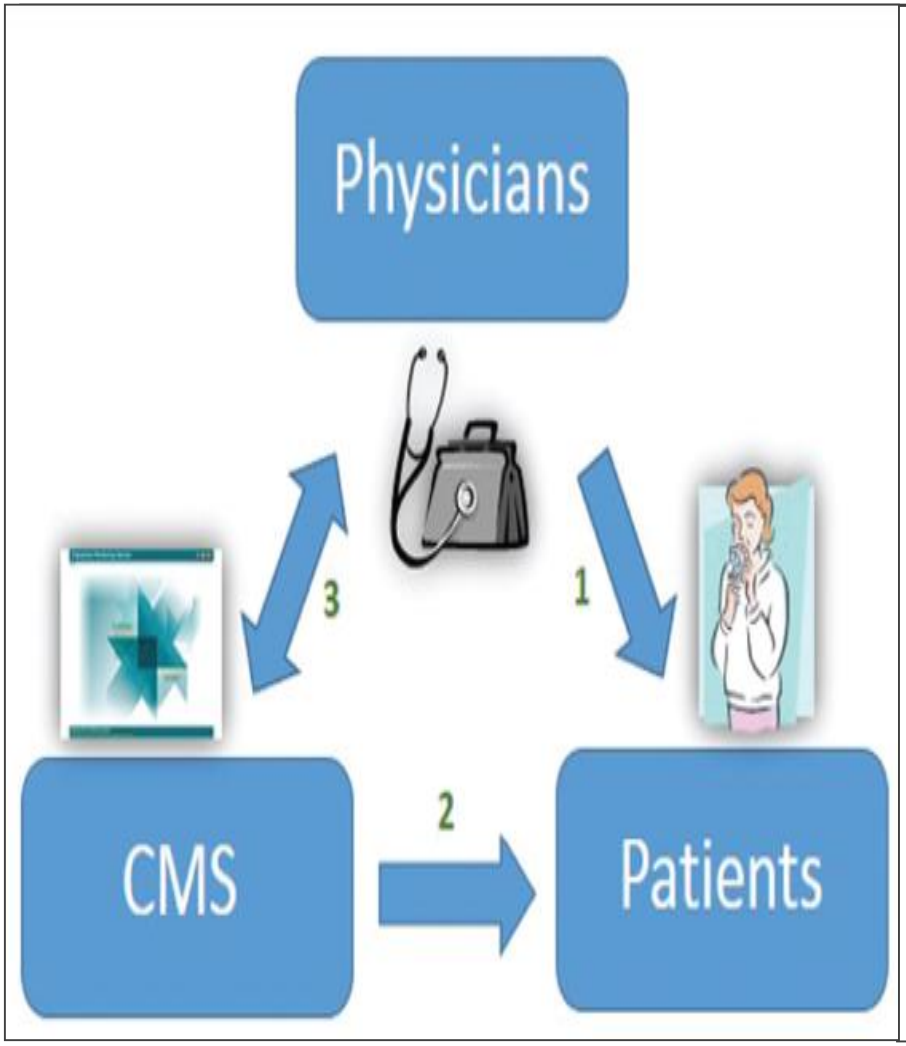
OR 3.05 (95% CI, 1.03-9.02)

OR 3.77 (95% CI, 1.62-8.77)

Brooks et al., J Gen Intern Med 2014

Strategies to improve adherence in asthma

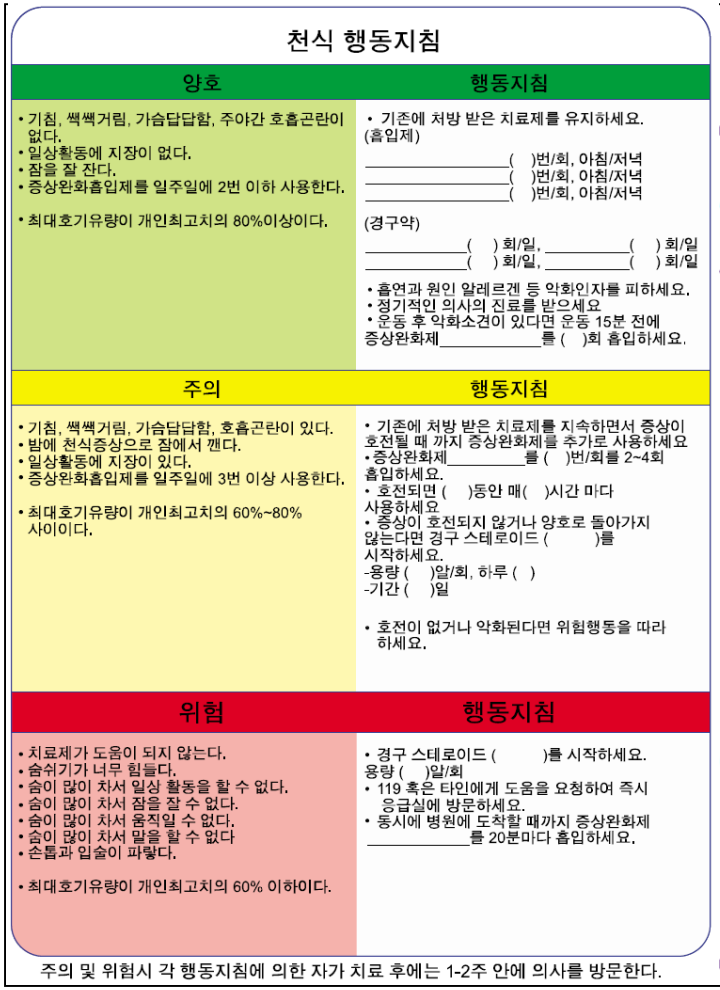
- Intervention of patient- related factor: need new technology ? -



Foster JM et al. J Asthma 2012/ JACI 2014

Strategies to improve adherence in asthma

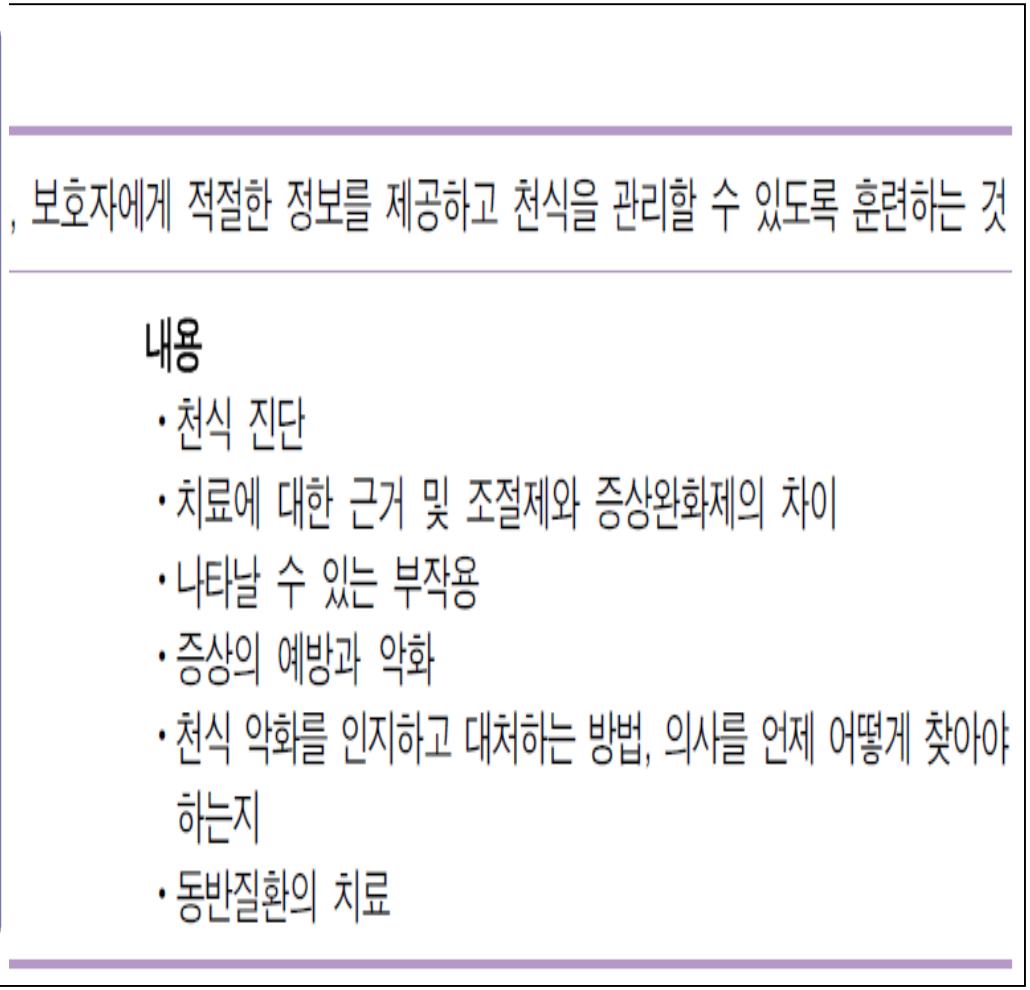
– 의사 환자 관계형성: 천식정보제공 교육, 행동지침 -



천식 행동지침

양호	행동지침
• 기침, 쌕쌕거림, 가슴답답함, 주아간 호흡곤란이 없다. • 일상활동에 지장이 없다. • 잠을 잘 잔다. • 증상완화흡입제를 일주일에 2번 이하 사용한다. • 최대호기유량이 개인최고치의 80%이상이다.	• 기존에 처방 받은 치료제를 유지하세요. (흡입제) _____( )번/회, 아침/저녁 _____( )번/회, 아침/저녁 _____( )번/회, 아침/저녁 (경구약) _____( ) 회/일, _____( ) 회/일 _____( ) 회/일, _____( ) 회/일 • 흡연과 원인 알레르겐 등 악화인자를 피하세요. • 정기적인 의사의 진료를 받으세요 • 운동 후 악화소견이 있다면 운동 15분 전에 증상완화제_____를 ( )회 흡입하세요.
주의	**행동지침**
• 기침, 쌕쌕거림, 가슴답답함, 호흡곤란이 있다. • 밤에 천식증상으로 잠에서 깬다. • 일상활동에 지장이 있다. • 증상완화흡입제를 일주일에 3번 이상 사용한다. • 최대호기유량이 개인최고치의 60%~80% 사이이다.	• 기존에 처방 받은 치료제를 지속하면서 증상이 호전될 때 까지 증상완화제를 추가로 사용하세요 • 증상완화제_____를 ( )번/회를 2~4회 흡입하세요. • 호전되면 ( )동안 매( )시간 마다 사용하세요 • 증상이 호전되지 않거나 양호로 돌아가지 않는다면 경구 스테로이드 ( )를 시작하세요. -용량 ( )알/회, 하루 ( ) -기간 ( )일 • 호전이 없거나 악화된다면 위험행동을 따라 하세요.
위험	**행동지침**
• 치료제가 도움이 되지 않는다. • 숨쉬기가 너무 힘들다. • 숨이 많이 차서 일상 활동을 할 수 없다. • 숨이 많이 차서 잠을 잘 수 없다. • 숨이 많이 차서 움직일 수 없다. • 숨이 많이 차서 말을 할 수 없다 • 손톱과 입술이 파랗다. • 최대호기유량이 개인최고치의 60% 이하이다.	• 경구 스테로이드 ( )를 시작하세요. 용량 ( )알/회 • 119 혹은 타인에게 도움을 요청하여 즉시 응급실에 방문하세요. • 동시에 병원에 도착할 때까지 증상완화제 _____를 20분마다 흡입하세요.

주의 및 위험시 각 행동지침에 의한 자가 치료 후에는 1-2주 안에 의사를 방문한다.



, 보호자에게 적절한 정보를 제공하고 천식을 관리할 수 있도록 훈련하는 것

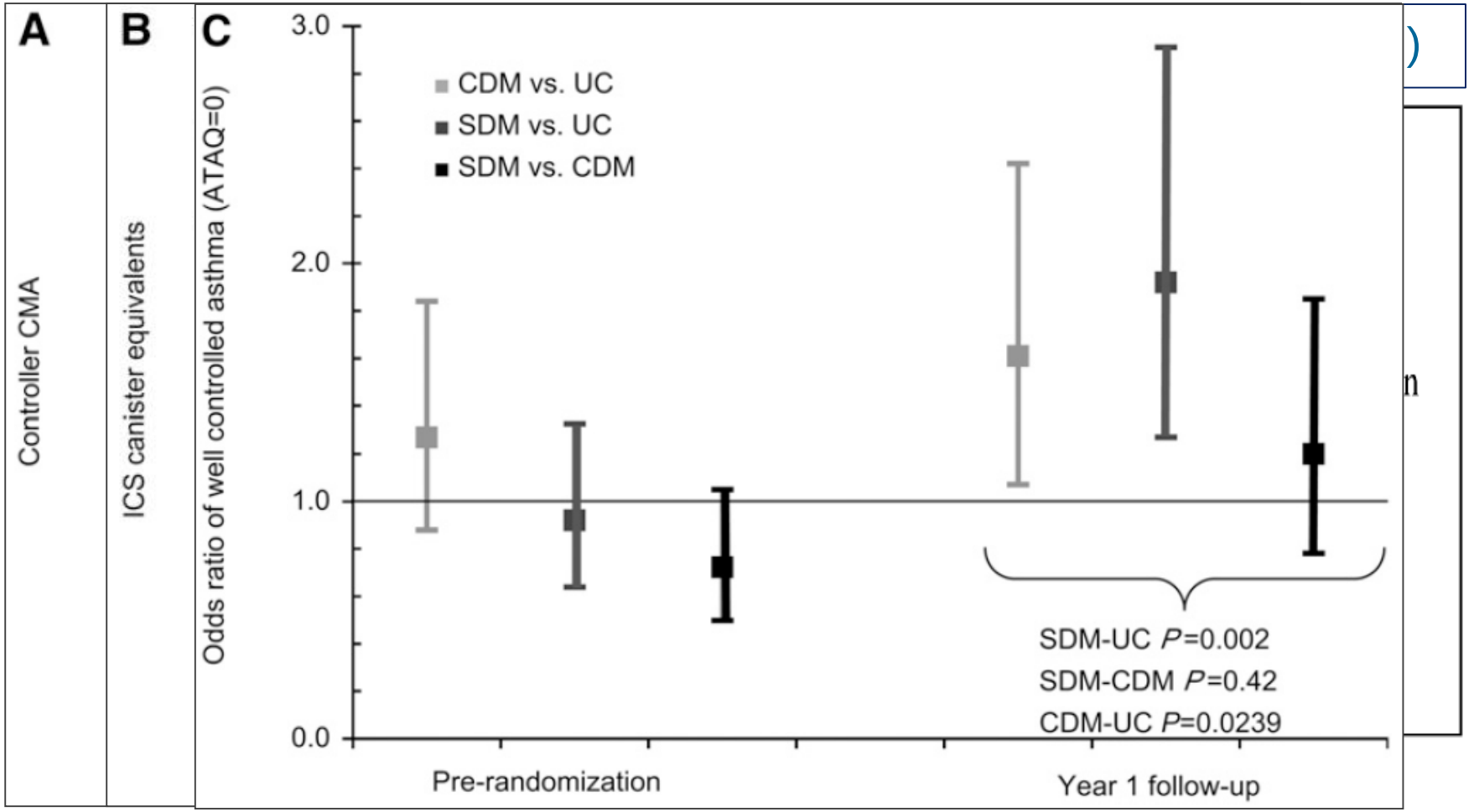
내용

- 천식 진단
- 치료에 대한 근거 및 조절제와 증상완화제의 차이
- 나타날 수 있는 부작용
- 증상의 예방과 악화
- 천식 악화를 인지하고 대처하는 방법, 의사를 언제 어떻게 찾아야 하는지
- 동반질환의 치료

호흡기학회 천식진료지침 2014

Strategies to improve adherence in asthma

- Patient- centered communication: shared decision making -



Wilson AR et al., AJRCCM 2010

Adherence in COPD Tx

- Facts & multifactorial barriers -

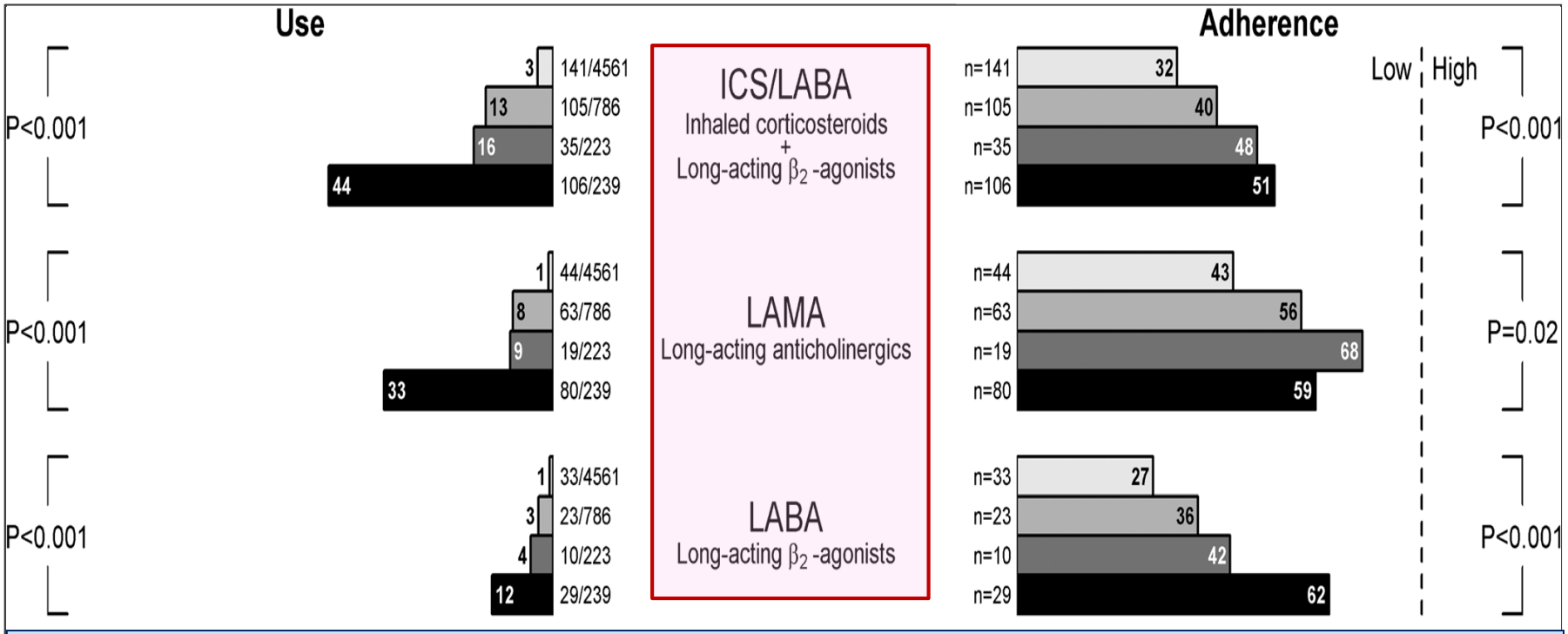
- Adherence rates approximately 50% (Bourbeau et al, Thorax 2008)
  - complex medication regimens and multiple comorbidities

COPD	Treatment
• Progressive nature of the disease ↓*	• Polypharmacy ↓
• Poor prognosis ↓	• Higher dosing frequency ↓
• Lack of clinical symptoms ↓	• Higher medication cost ↓
• Disease severity —	• Side effects ↓
• Lung function —	• Oral administration ↑
Patient	**Health-care provider–patient relationship**
• Gender -	• Higher quality of communication ↑
• Demographic factors: old age ↑	• Type of caregiver: specialist ↑
• Improved quality of life ↓	• Closer follow-up ↑
• Social support ↑	• Hospitalisation ↑
• Psychiatric co-morbidities ↓	

Adherence in COPD

- Low use & adherence in general population: Copenhagen study -

- Copenhagen General Population Study: GOLD grades identified in nationwide registry
- Use & adherence : ICS/LABA FDC, LABA, LAMA (n=5,812)



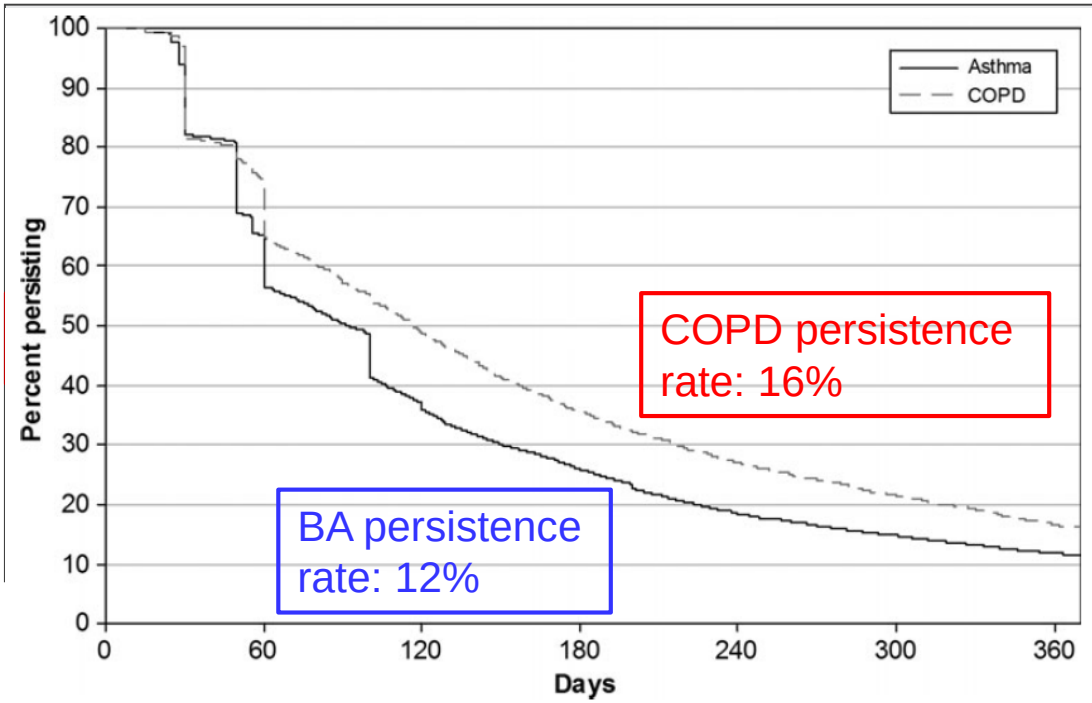
- Use of and adherence to maintenance medication for COPD in the general population was associated with the severity of COPD as defined by GOLD
- Even in severe and very severe COPD, use and adherence was low

Vestbo et al., JGIM 2014

Adherence in COPD

- Low adherence & persistence in UK -

- Retrospective UK 44 GP prescribing database cohort bet 2008-2009
- Adherence & persistence: ICS, LABA, FDC, LAMA, TP (n=10,521 BA, n= 2801 COPD)



	TP*		LAMA
COPD	Asthma	COPD	COPD
833 (39.6)	56 (26.7)	43 (16.4)	768 (30.3)
909 (43.2)	102 (48.6)	155 (58.9)	1324 (52.2)
363 (17.2)	52 (24.7)	65 (24.7)	444 (17.5)

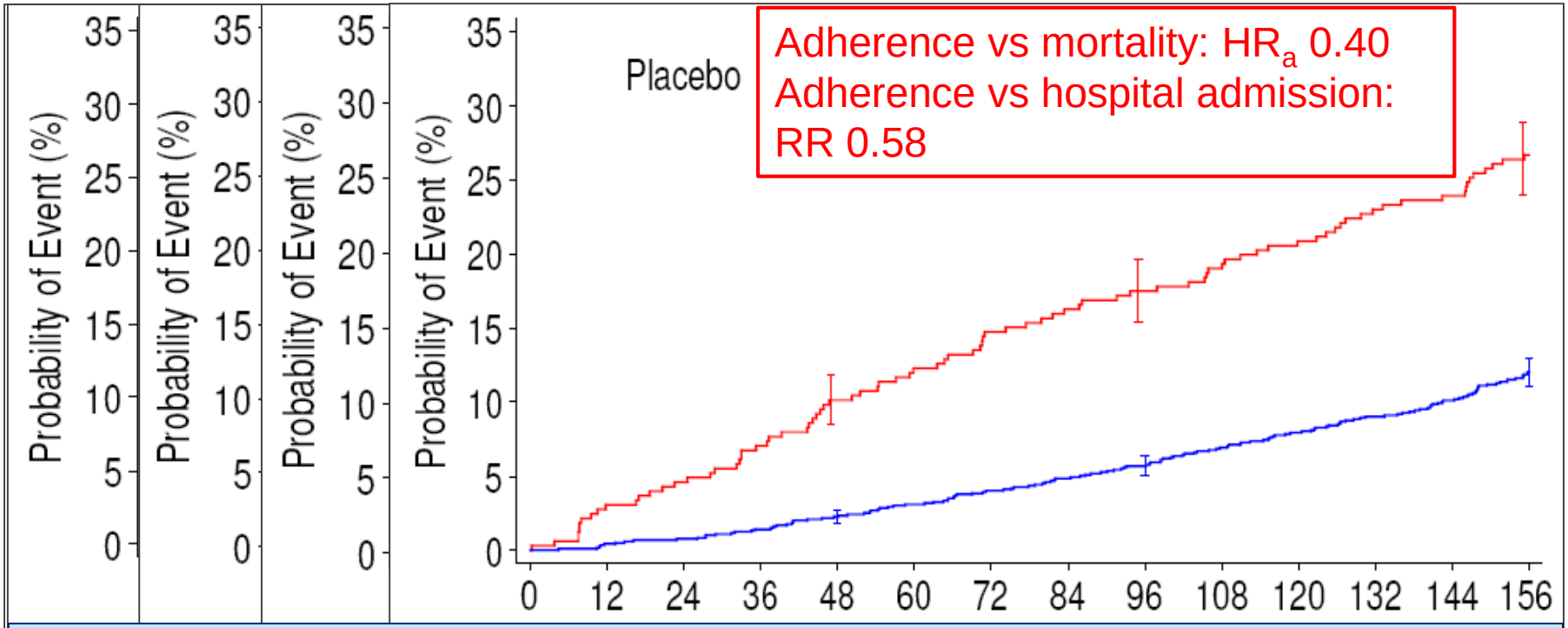
- Adherence in BA/COPD is low, but higher in COPD compared with patients with asthma.
- Less than 20% of patients in this UK cohort remained persistent with Tx at 1 year

Cowey JR et al., IJCP 2014

Adherence & COPD outcome

- Impact of adherence on COPD outcome -

- To investigate impact of adherence on COPD mortality, and morbidity
- Adherence from TORCH study : SFC bid vs FP vs SAL vs PBO (n=6112)
- All-cause mortality and exacerbations leading to hospital admission were 1° 2° end points



- Adherence and improved mortality & admission was independent of study Tx
- " Healthy adherer effect " adherence as a surrogate marker for overall healthy behavior

Vestbo et al., Thorax 2009

Strategies to improve adherence in COPD

- Intervention of therapy- related factor: simplifying regimen -

Treatment of COPD: Relationships between daily dosing frequency, adherence, resource use, and costs

Edmond L. Toy [a], Nicolas U. Beaulieu [b], Joshua M. McHale [b], Timothy R. Welland [a], Craig A. Plauschinat [c], Andrine Swensen [c], Mei Sheng Duh [b,*]

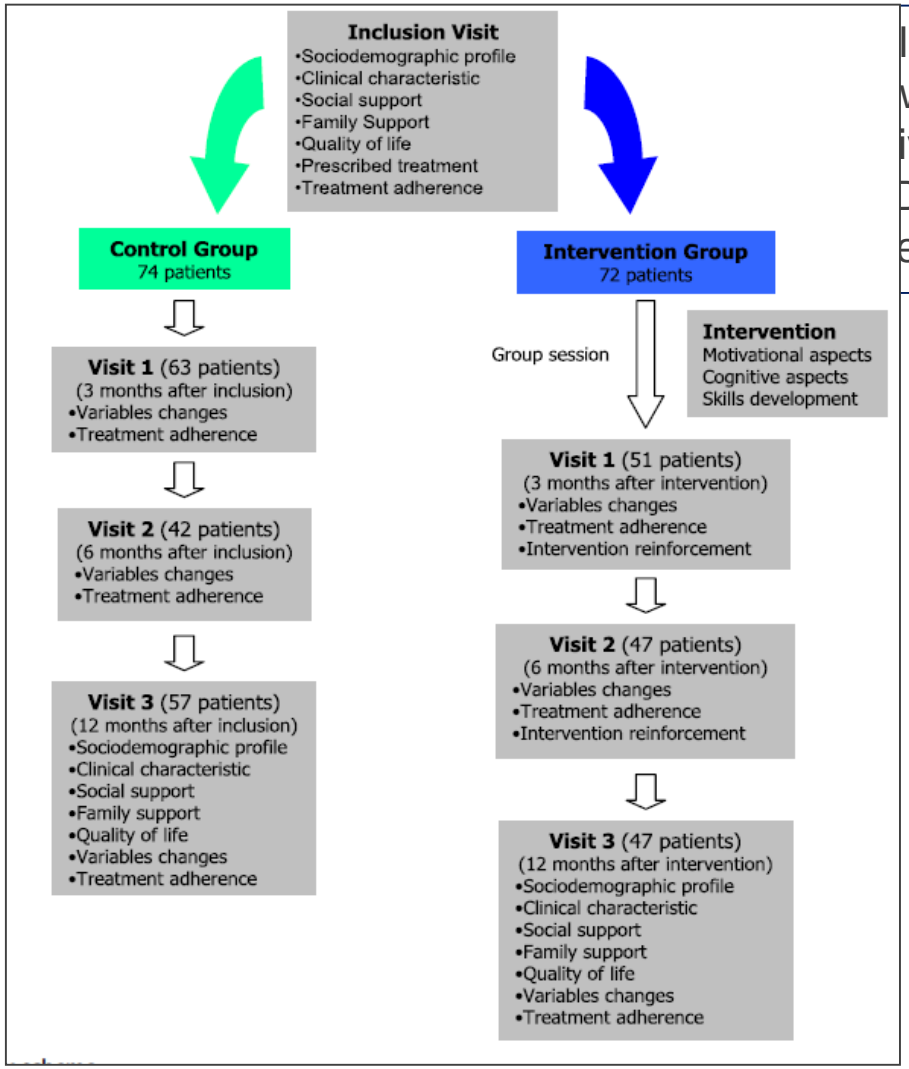
Table 4 The effect of increasing PDC on predicted 12 month mean healthcare resource use and cost based on 1000 COPD patients.

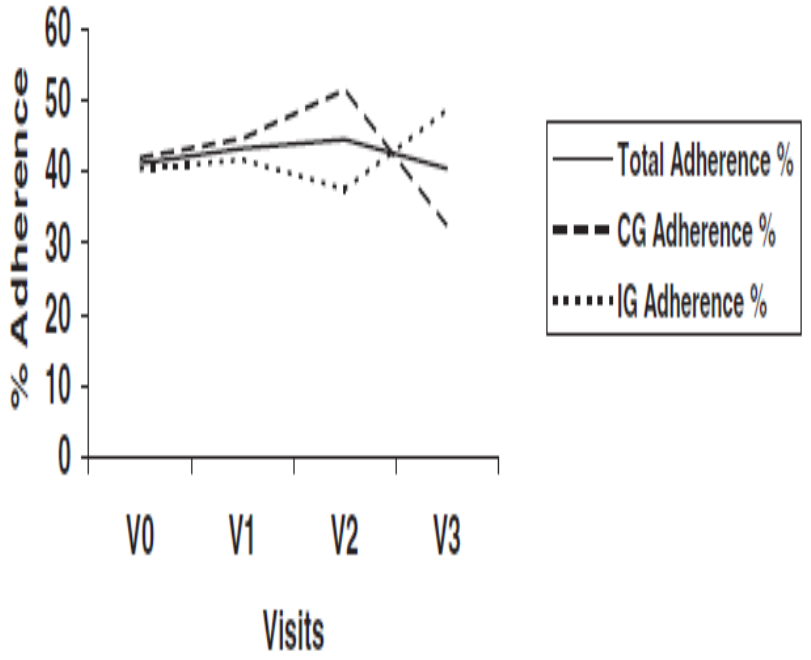
	Resource Use			Cost[a]		
Utilization	Baseline PDC	Baseline PDC + 5 Percentage Points	Difference (%)	Baseline PDC	Baseline PDC + 5 Percentage Points	Difference (%)
Hospital Visits	1275	1243	−33 (−2.6%)	$11,635,099	$11,338,501	-$296,598 (−2.6%)
Inpatient Days[b]	5906	5720	−186 (−3.1%)	–	–	–
Outpatient Visits	16,981	17,010	29 (−.2%)	$1,867,863	$1,871,082	$3219 (−.2%)
ER Visits	817	802	−15 (−1.8%)	$412,658	$405,248	-$7410 (−1.8%)

Toy EL et al. Resp Med 2011

Strategies to improve adherence in COPD

- *Multifactorial combined intervention* -





	Visit 0 (V0)	Visit 1 (V1)	Visit 2 (V2)	Visit 3 (V3)
Total Sample	41.1	43.2	44.5	40.4
Control Group (CG)	41.9	44.6	51.4	32.4
Intervention Group (IG)	40.3	41.7	37.5	48.6
p	0.843	0.721	0.092	0.046

Leiva-Fernandez et al. BMC Pulm Med 2014

Strategies for inhaler adherence enhancement

- *Combined actions for improving adherence to inhaled med* -

Therapy intervention

- simplifying regimen (once daily or FDC inhalers) or tailor to patient preference
- optimizing inhaler technique by repeated instruction
- understanding patient barrier to adherence (fear about S/E, Tx effect, cost)

Patient intervention

- reinforcement for patients' efforts to change health-related behaviors
- providing education resources & feedback
- teaching self-management skills
- treat comorbidities, especially depression and anxiety

Society/health system intervention

- establishing a partnership bet patient and health care provider
- Improving access to medication
- social support