Observance et bonne utilisation des dispositifs d'inhalation

Université Paris Cité

Nicolas Roche
Pneumologie
Hôpital Cochin

Principes de base de l'inhalothérapie

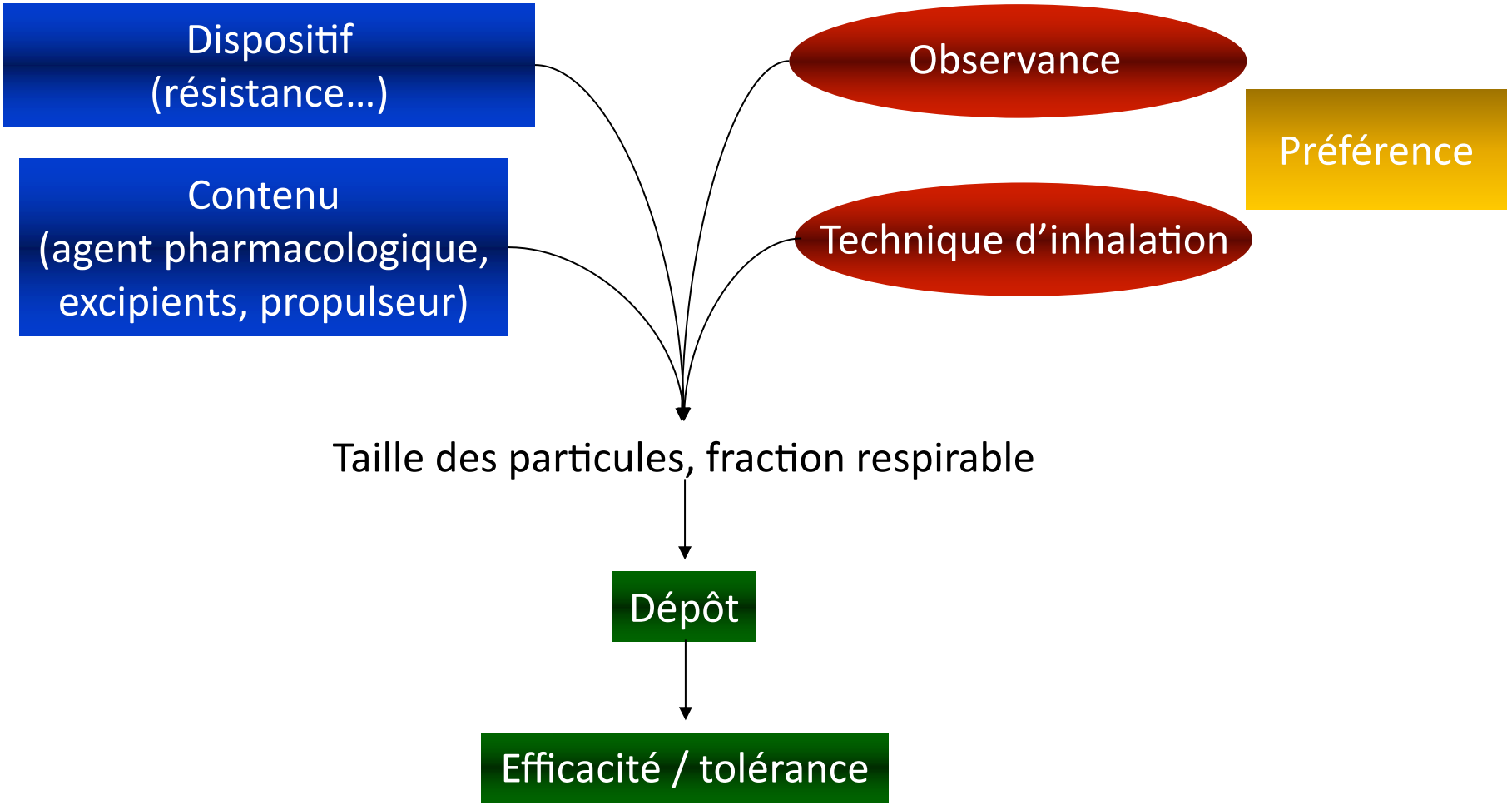


Schéma personnel

Principes de base de l'inhalothérapie

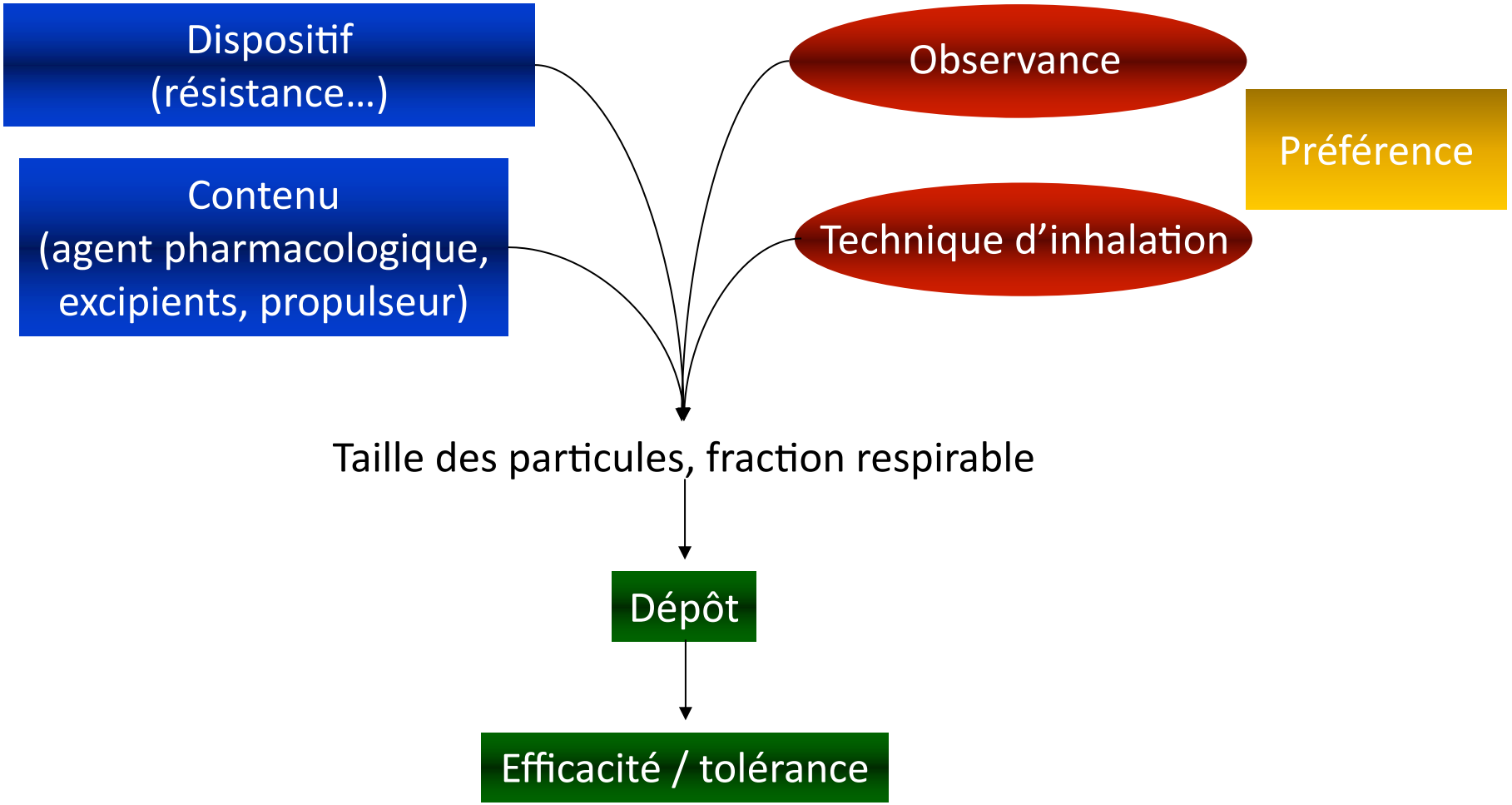
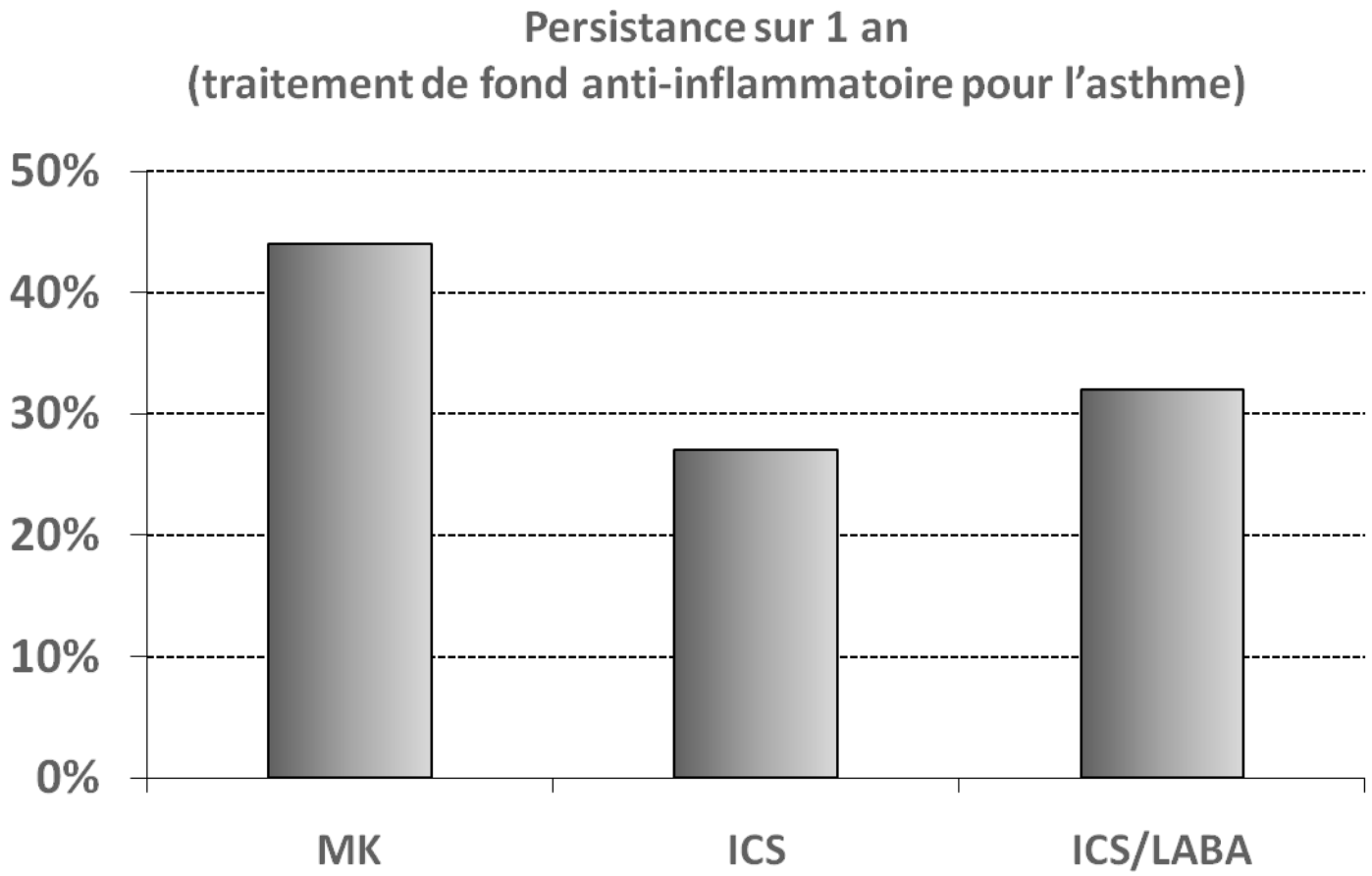


Schéma personnel

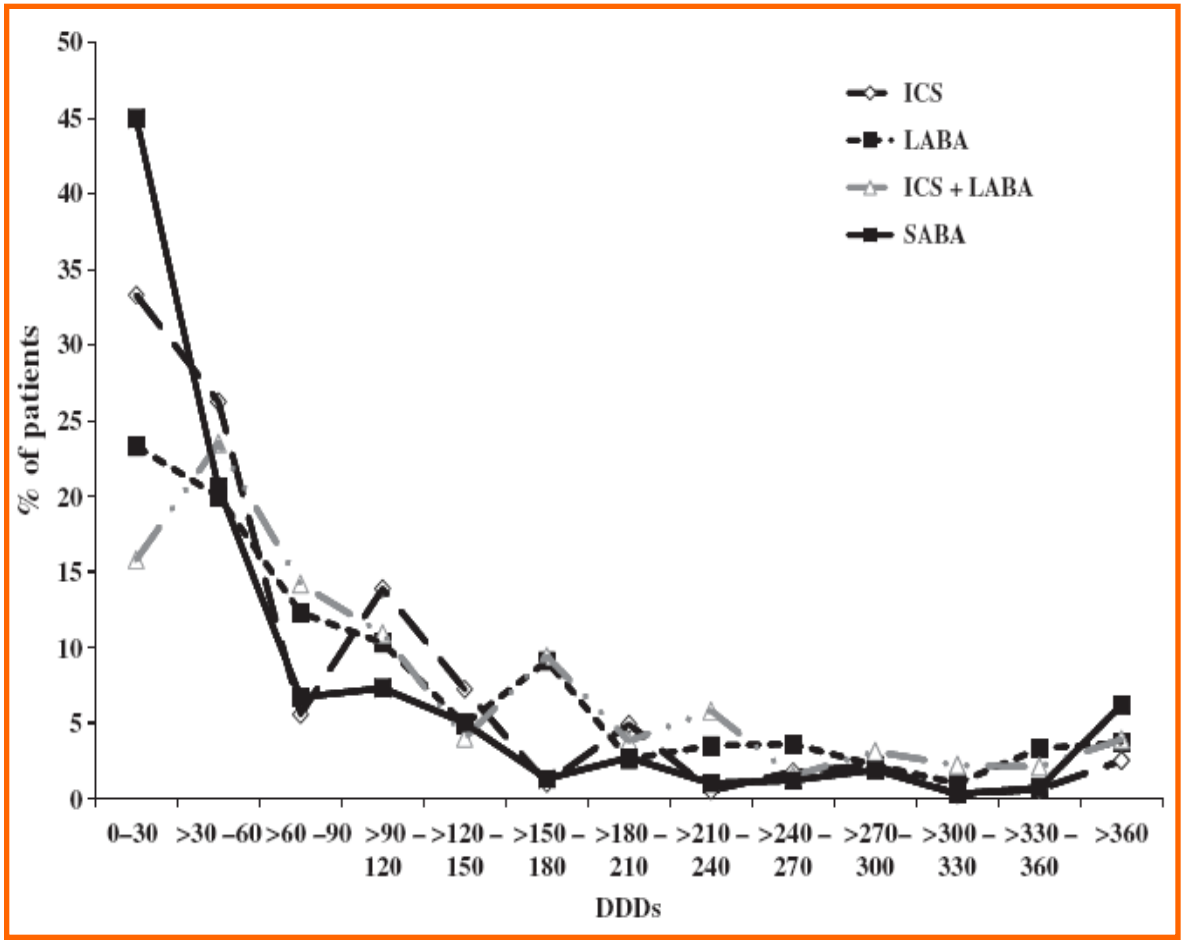
L'observance dans l'asthme en vie réelle

Assurance Maladie 2003-2005 ; n=12,502, suivi : 17 mois



Latry P et al - Clin Ther. 2008
Adherence to anti-inflammatory treatment for asthma in clinical practice in France.

Cela peut même être pire!

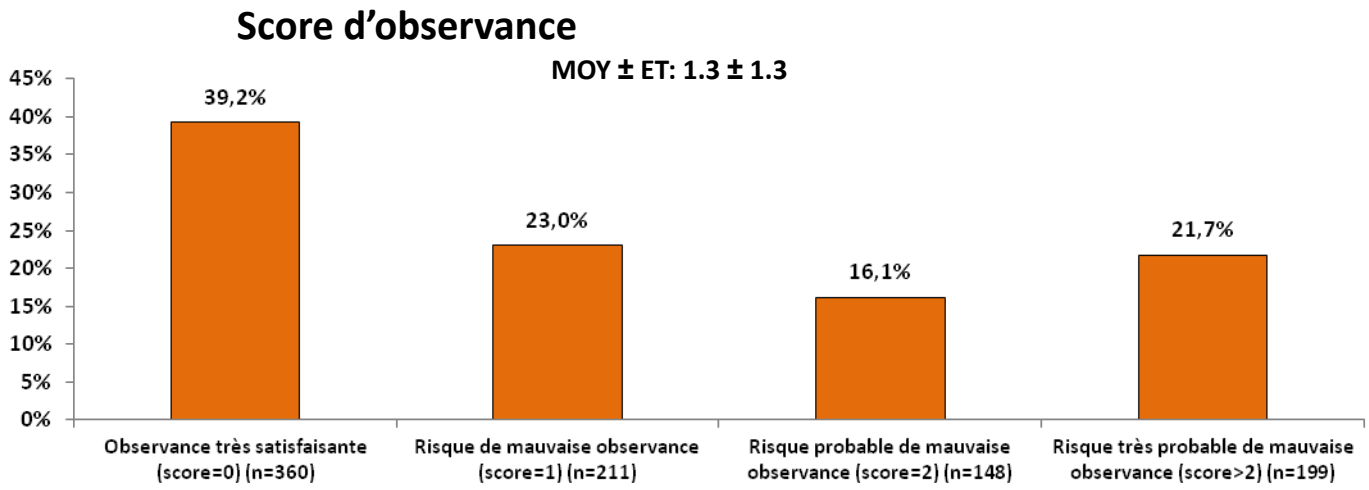


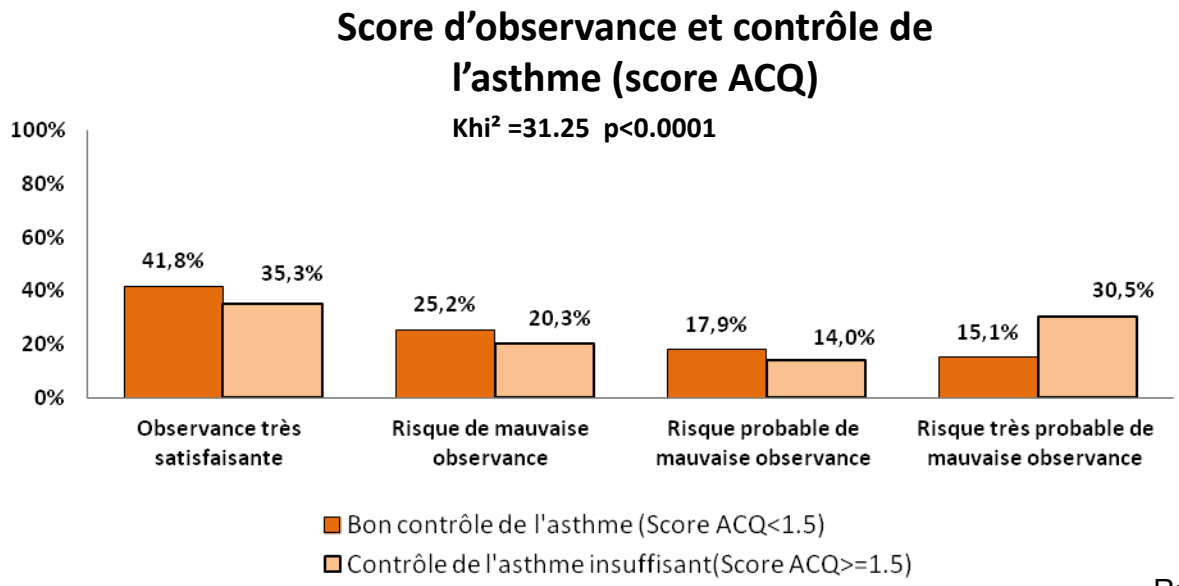
Allemagne
483 051 patients
Durée : 365 jours

Nombre de doses journalières dispensées sur 365 jours

Hasford J, Uricher J, Tauscher M, Bramlage P, Virchow JC. Allergy 2009; Aug 27

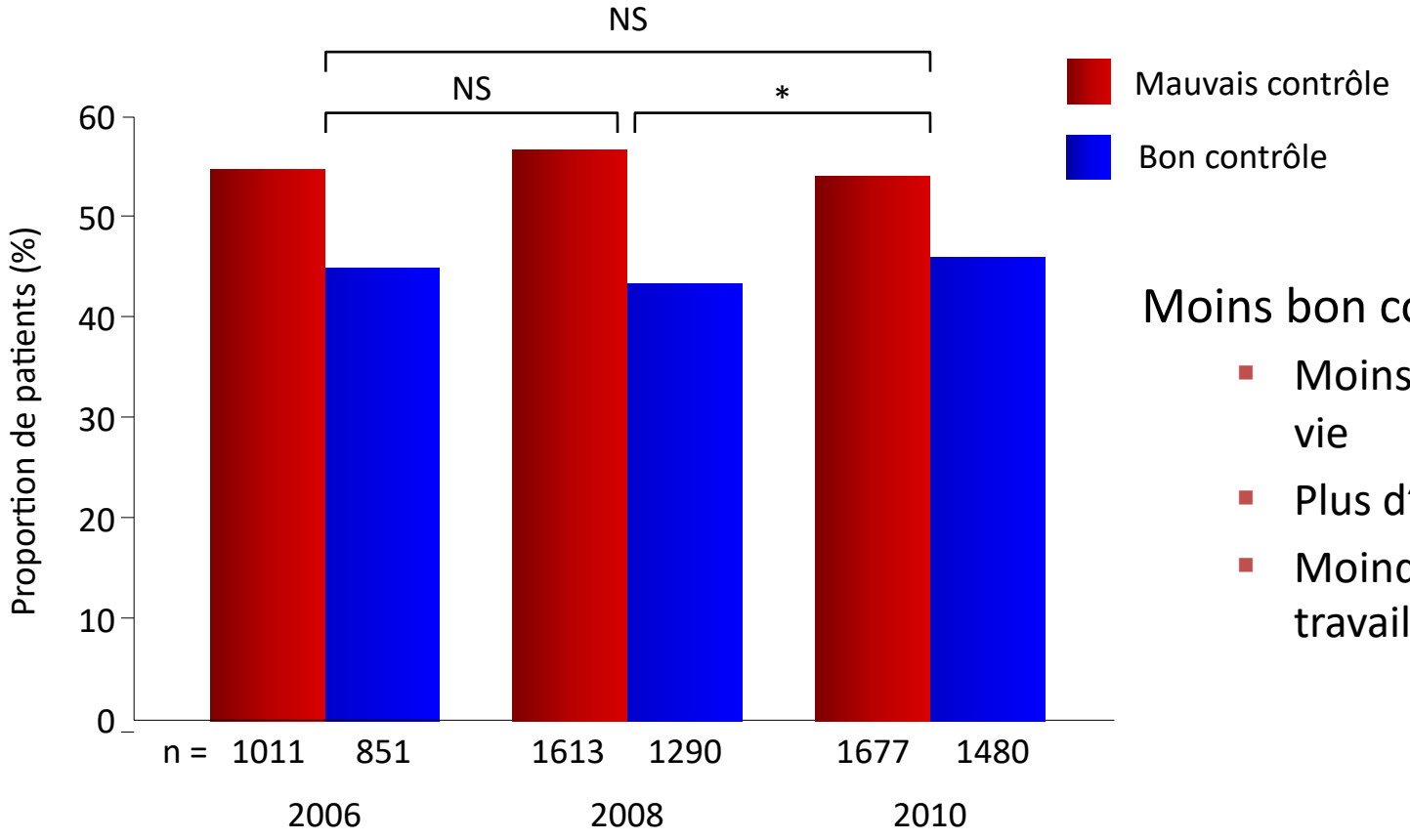
Observance et contrôle N=975





Raherison, en soumission

Le contrôle de l'asthme en vie réelle



Moins bon contrôle = :

- Moins bonne qualité de vie
- Plus d'exacerbations
- Moindre productivité au travail

*p = 0.035; NS: non-significant
Data from patients from five European countries. Asthma control was defined using the Asthma Control Test.
Adapted from Demoly P *et al*. *Eur Respir Rev* 2012;21:66–74

Un peu plus tard…

REALISE study (N=8,000)

45.1%
of patients had GINA-defined uncontrolled asthma (n=3,611)

83.7%
of these patients perceived their asthma as controlled (n=3,023)

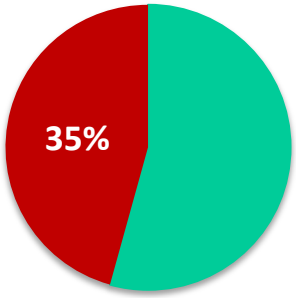
69.9%
of these patients perceived their asthma as not serious (n=2,523)

Price D, et al. NPJ Prim Care Respir Med. 2014

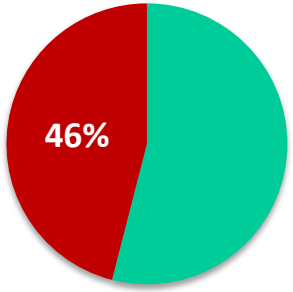
Très récemment (UK)

Proportion of patients with uncontrolled asthma despite receiving medium or high-dose LABA/ICS

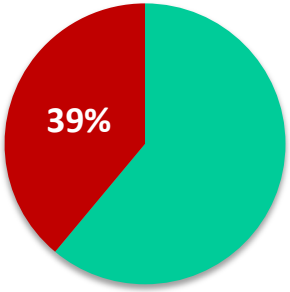
Medium-dose LABA/ICS (n=29,229)



High-dose LABA/ICS (n=16,575)

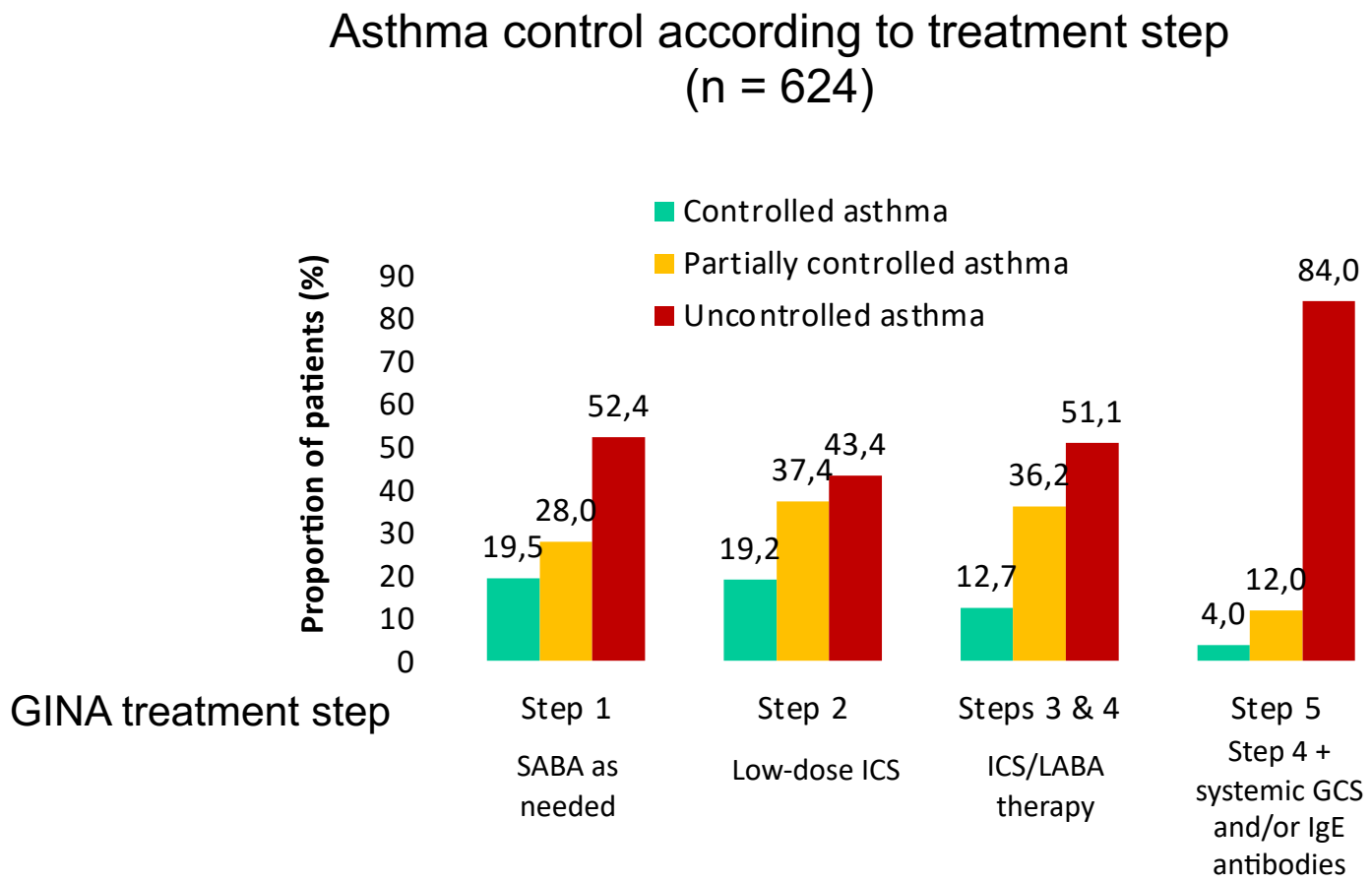


All patients (on medium- or high-dose LABA/ICS) (n=45,804)



Buhl R, et al. Resp Med 2020

MAGIC



Olaguibel JM, et al. Respir Res 2012

Pourquoi ? Les leçons de la « vraie vie »

- Mauvaise appréciation du contrôle
- Adaptation des traitements inadéquate

- Expositions environnementales
- Tabagisme

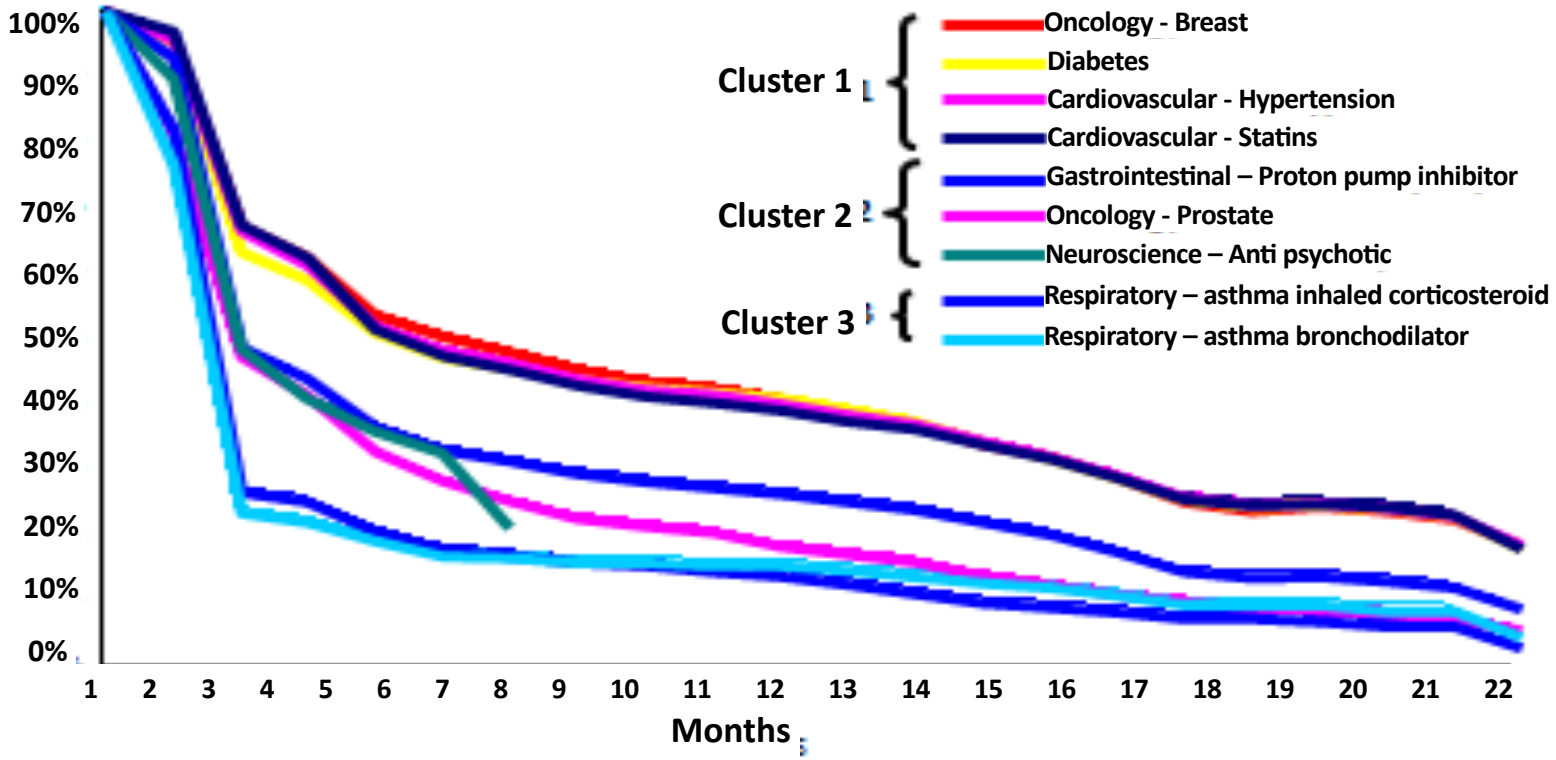
- Rhinite,
- RGO
- Surpoids

- Mauvaise utilisation
- Inobservance

- … (insuffisance cardiaque, BPCO, ABPA, Churg & Strauss…)

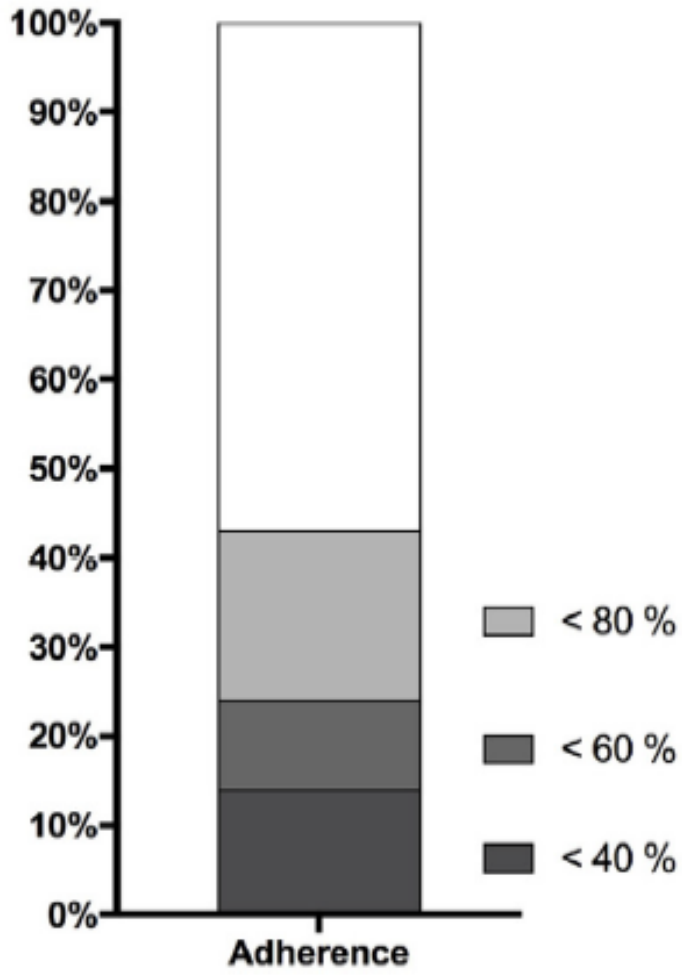
Cazzoletti L *et al. J Allergy Clin Immunol* 2007;120:1360–7; Haughney J *et al*. *Respir Med* 2008;102:1681–93

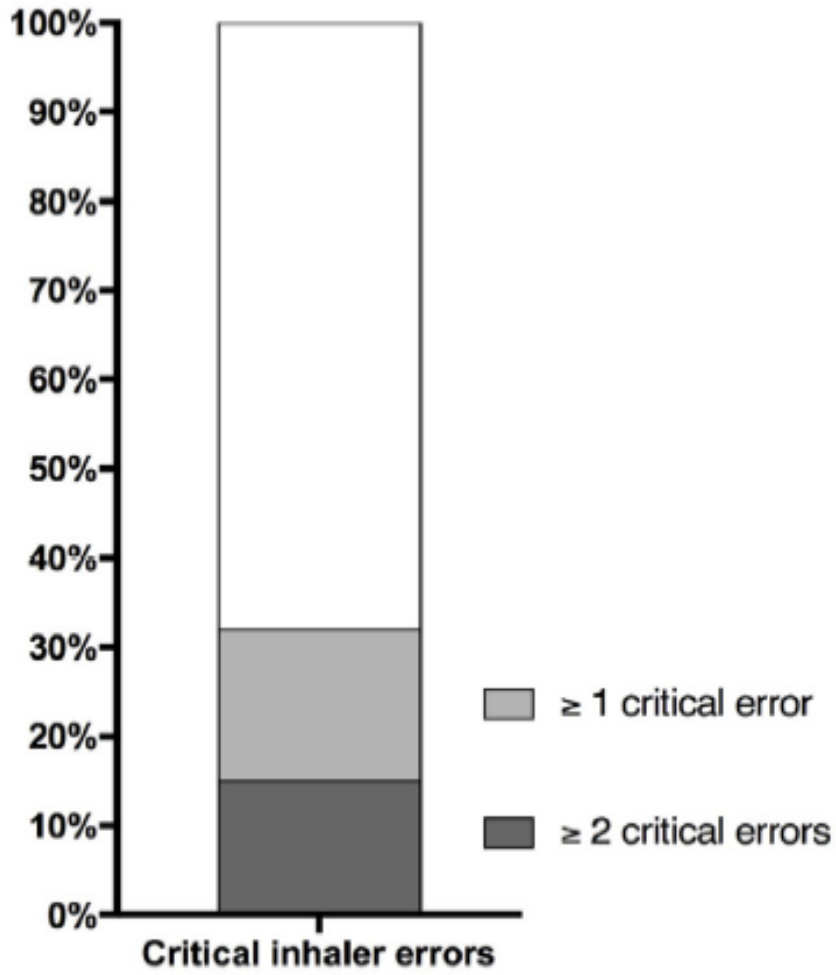
Adherence and persistence



Smith et al. 2010 J Aerosol Med: S25.

Asthme difficile





Von Bullow et al., Respir Med 2018

PRINCIPAUX FACTEURS ASSOCIÉS À L'OBSERVANCE

Asthme & Allergies ASSOCIATION

le cnam

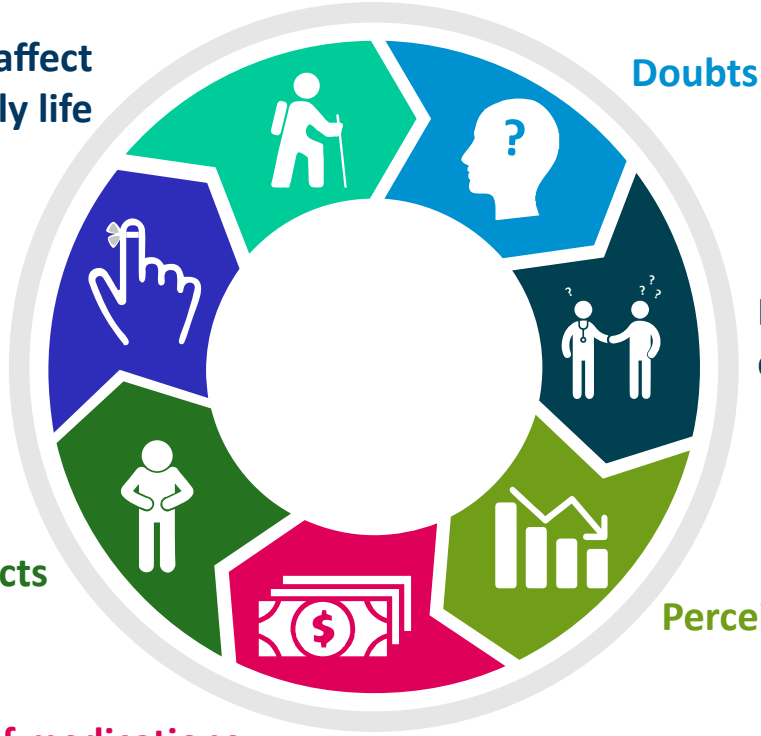
- Niveau socio économique
- Représentation de la santé
- Connaissance du traitement
- Effets secondaires
- Présentation du médicament
- Professionnels de santé

CRESIF, Colloque 2001
Test persona

Cousson-Gélie F, Rev Mal Respir 1998

Raherison, CPLF 2013

Les perceptions des patients



Amin, S et al. Patient Prefer Adherence 2020

Principes de base de l'inhalothérapie

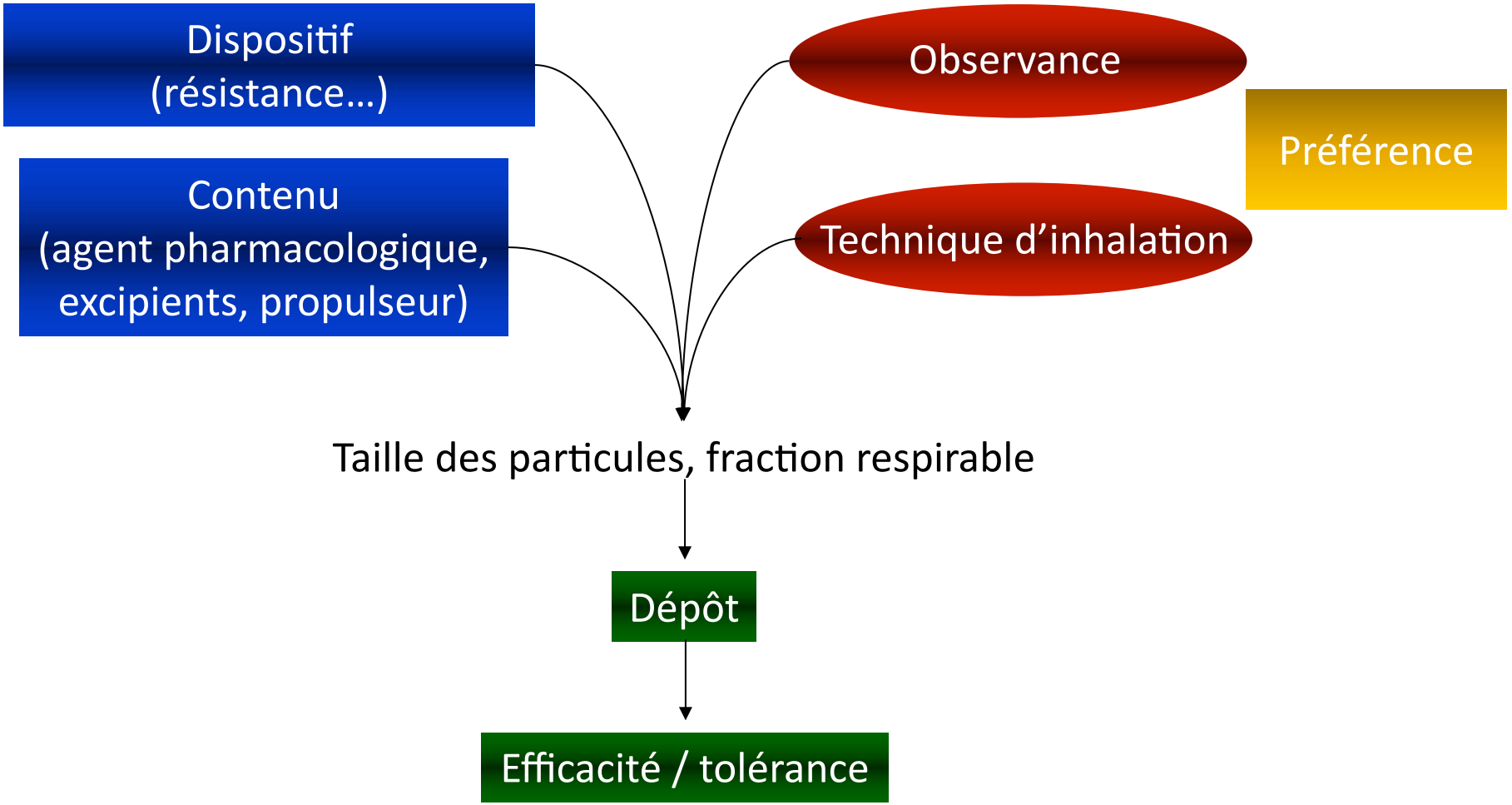


Schéma personnel

Les dispositifs sont tous différents

Les patients sont tous différents

Chaque dispositif a ses avantages et ses inconvénients

Device	Advantages	Disadvantages
pMDI	• Portable and compact • Multi-dose device • Quick to use • Relatively cheap • Cannot contaminate contents • Available for most inhaled medications	• Contains propellants • Not breath actuated • Many patients cannot use it correctly (*e.g.* coordination difficulties) • Cold Freon effect • High oropharyngeal deposition
pMDI+spacer	• Easier to coordinate inhaler actuation with inspiration than pMDI alone • Large drug doses delivered more conveniently than pMDI alone • Less oropharyngeal deposition • Higher lung deposition than a pMDI	• Bulkier and less portable than pMDI alone • Plastic spacers may acquire static charge • Additional cost to pMDIs
BA-MDI	• Portable and compact • Multi-dose device • Quick to use • Breath-actuated (no coordination needed) • Cannot contaminate contents	• Contains propellants • "Cold Freon'' effect • Require moderate inspiratory flow to be triggered • More bulky and noisy than pMDI
DPI	• Portable and compact • Quick to use • Breath actuated (no coordination needed) • Usually higher lung deposition than a pMDI • Does not contain propellants	• Require high inspiratory flow to be triggered • May not be appropriate for emergency situations • Many patients cannot use them correctly (*e.g.* capsule handling problems for elderly) • Most types are moisture sensitive
SMI (Respimat)	• Portable and compact • Multi-dose device • Probably easier to use correctly than pMDI • High lung deposition • Does not contain propellants	• Not breath actuated • Not currently available in most countries • Relatively expensive

Lavorini F et al. Breathe 2008

PRIMORDIAL

https://splf.fr/videos-zephir/

TRELEGY® ELLIPTA®

Fluticasone + Uméclidinium + Vilantérol

TRIMBOW®

Béclométasone + Formotérol + Glycopyrronium

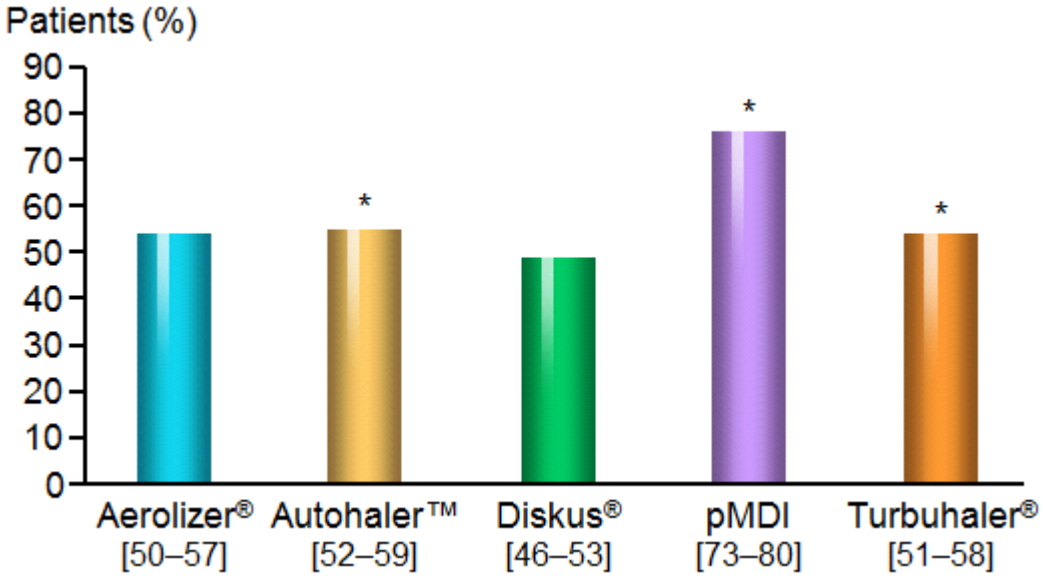
ULTIBRO® BREEZHALER®

Indacatérol + Glycopyrronium bromure

Comment inhaler ?

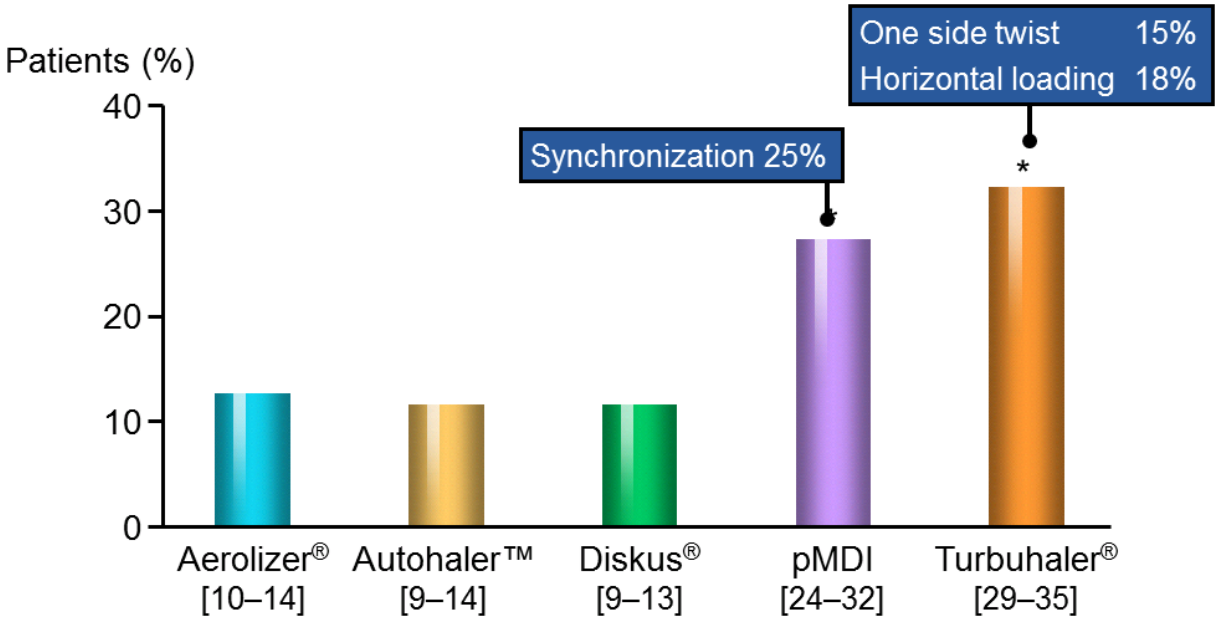
Vite, fort, à fond

Lentement, profondément, coordonné



Erreurs / Erreurs critiques

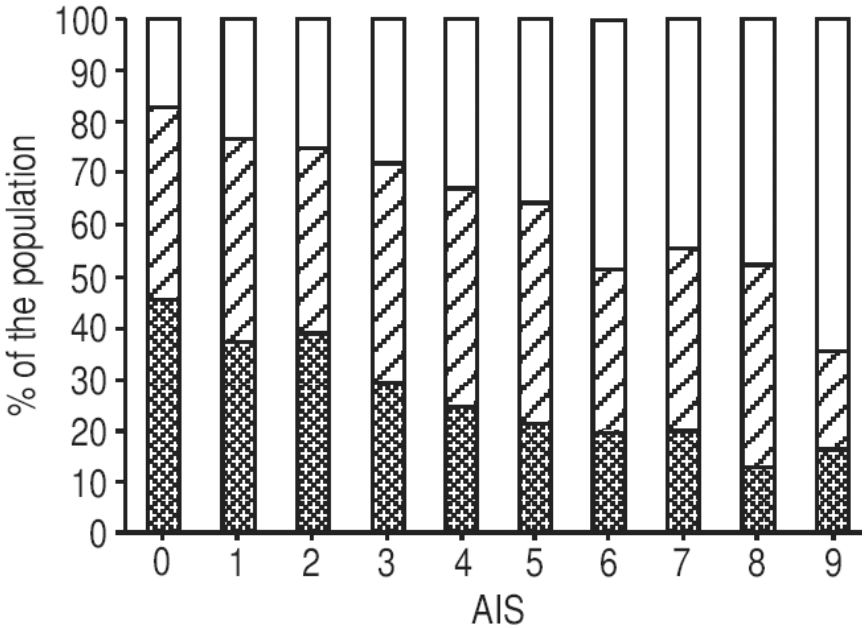
Molimard J Aerosol Med 2003



Et cela stagne !

Sanchis Chest 2016

Contrôle à long terme et technique d'utilisation

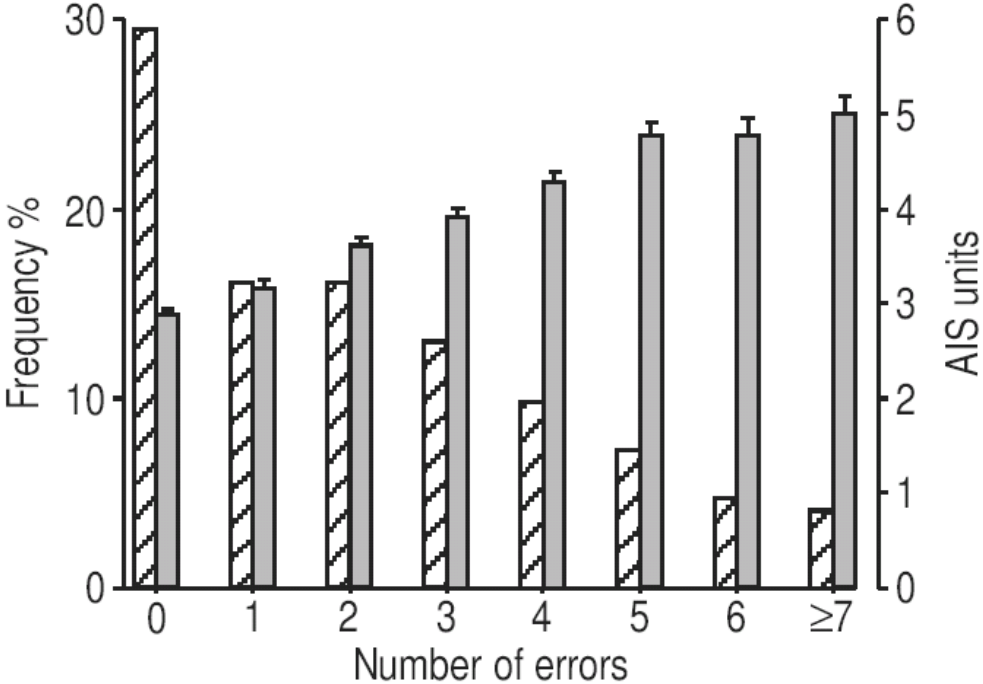


Mauvais coordinateurs
33%

71%

Mauvais utilisateurs
bon coordinateurs

Bons coordinateurs



3955 asthmatiques sous CSI / ADP

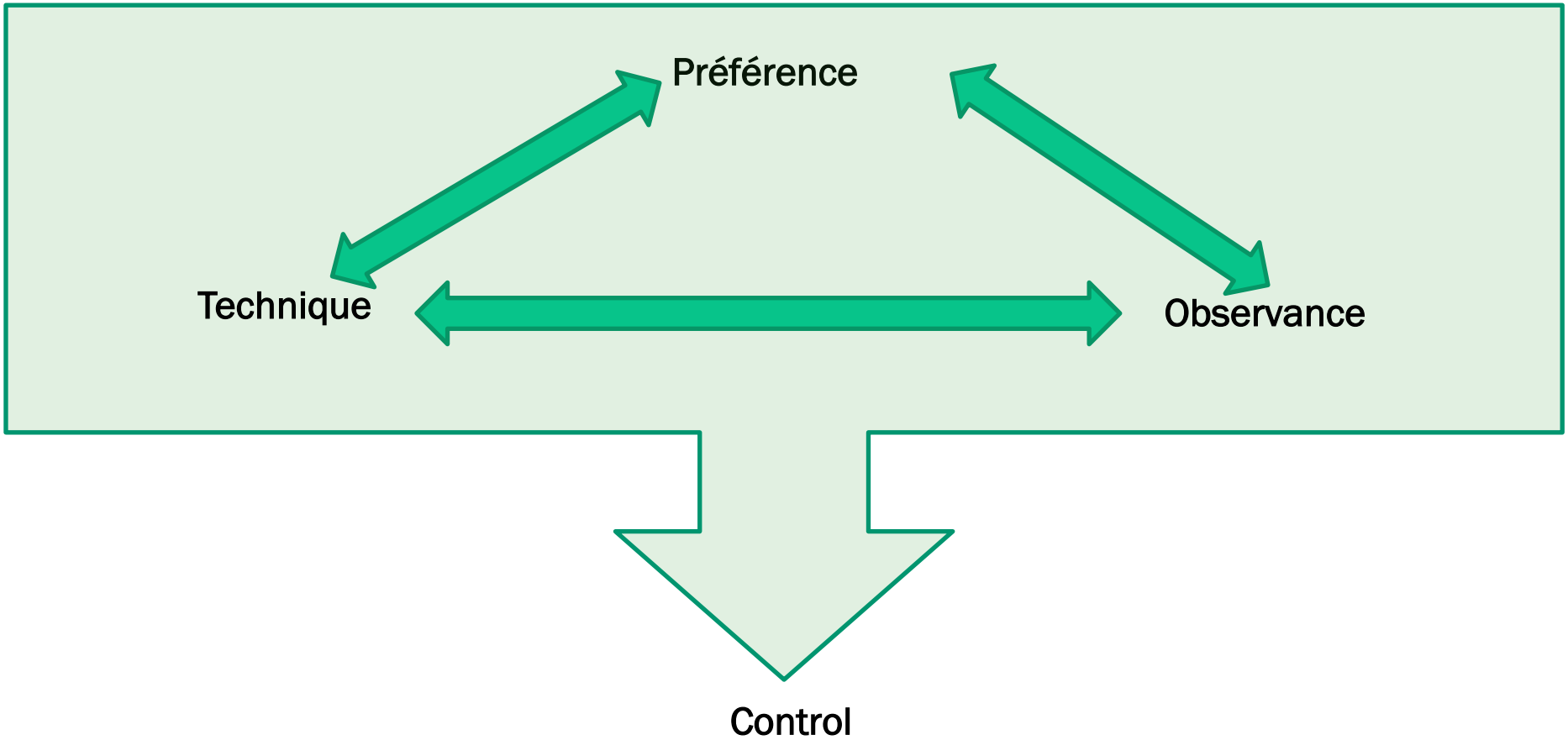
Giraud & Roche ERJ 2002

Technique, observance et contrôle (ADP)

Risque de mauvais contrôle (n = 727)	*p*	Odds ratio	95% CI
Tabagisme	**0.026**	**1.53**	**1.05–2.22**
Fumeur(vs non-fumeur)			
Technique d'inhalation	**0.0008**	**1.89**	**1.31–2.75**
Non-optimale (vs optimale)[a]			
Adhérence	**0.002**	**1.68**	**1.21–2.33**
Mauvaise ou très mauvaise (vs modérée ou bonne)			

Adapted from Giraud V *et al. Resp Med* 2011;105:1815–22

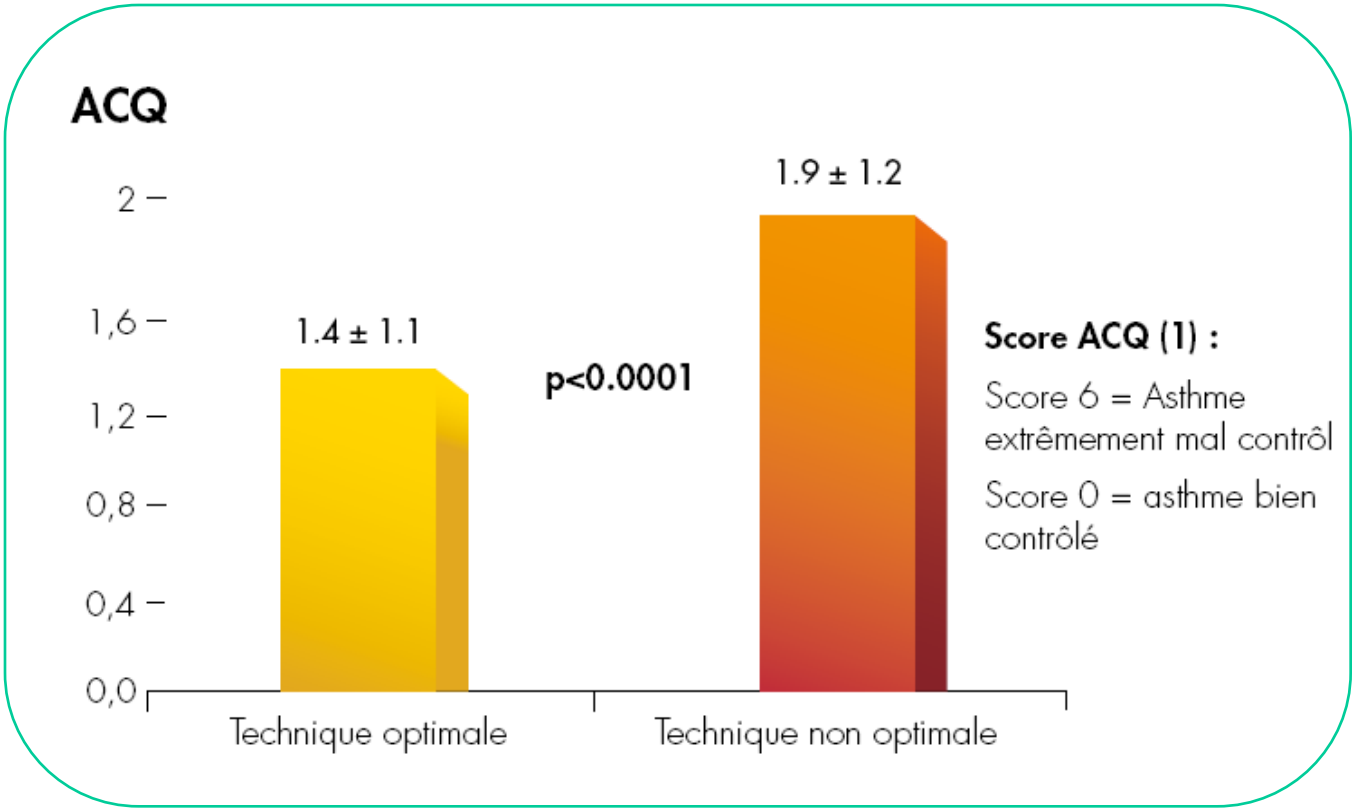
Tout est lié



Haughney J *et al. Respir Med* 2010;104:1237–45

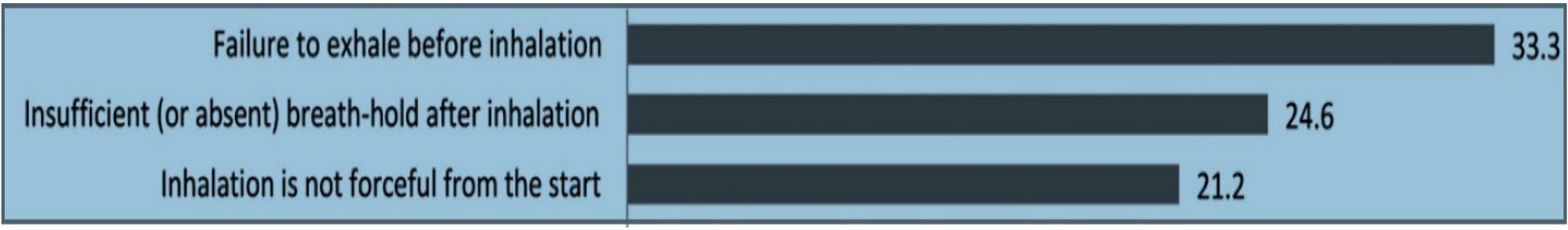
Item code: MINT/FLU-14020c
Date of preparation: XXXX 2014

Impact de la technique d'inhalation sur le contrôle de l'asthme (ADP)



Et avec un dispositif à poudre?

N=623 Au moins une erreur « sérieuse » : 55%



	Reference category	Category	Odds ratio (95% CI)
Sex	Male	Female	1.51 (1.08–2.10)
BMI	Underweight/Normal weight	Overweight	1.18 (0.80–1.74)
		Obese	1.75 (1.17–2.63)
Inhaler review	Yes	No	1.45 (1.04–2.02)
ATAQ	Good control/Partial control	Poor control	1.57 (1.04–2.36)
Inpatient admission or ED attendance	0	≥1	2.07 (1.26–3.40)

Westerik J Asthma 2016

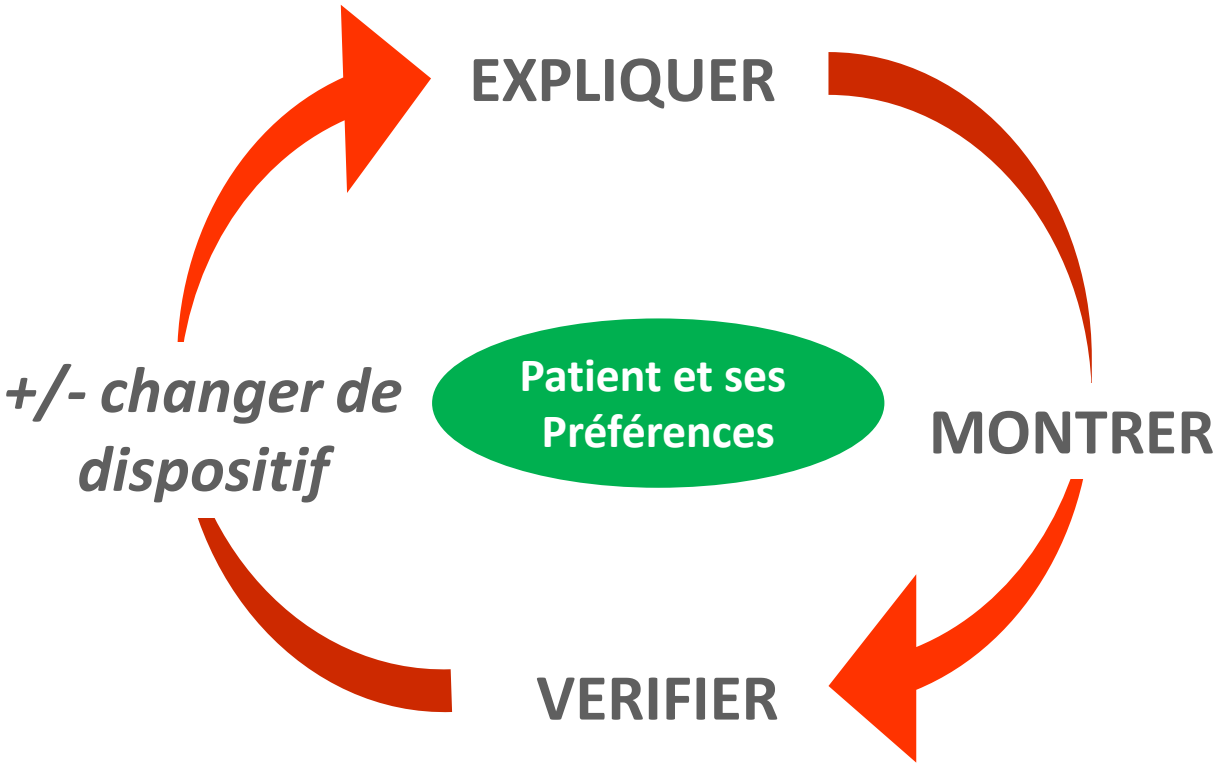
Tous types de dispositifs

Characteristic	COPD		Asthma		OR±SE; p level[a b]
At least a critical inhaler error	No	Yes	No	Yes	
Hospital admissions, %					
Never	62	55	86	76	1.47±0.17; p=0.001
1	23	26	9	13	
2–3	11	16	3	9	
>3	4	3	2	2	
Emergency department visits, %					
Never	71	64	81	69	1.62±0.20; p=0.0006
1	22	24	11	16	
2–3	4	10	3	10	
>3	3	2	4	5	
Antimicrobic courses, %					
Never	30	20	41	34	1.50±0.15; p=0.00004
1	29	31	30	25	
2–3	26	33	18	17	
>3	15	15	11	14	
Corticosteroid courses, %					
Never	37	29	35	27	1.54±0.16; p=0.00003
1	22	19	30	35	
2–3	30	26	22	19	
>3	11	26	13	19	

n=1664; BPCO/Asthme: 52/48%

Melani et al. Respir Med 2011;101:1462–1469

L'éducation peut-elle corriger ?



Aucun dispositif ne dispense d'une éducation appropriée

Education

- Ecoles de l'asthme
- Micro-objectifs
- Accompagnement

Cibles de l'éducation du patient asthmatique : connaissances

- La maladie : mécanismes, évolution
- Les facteurs déclenchants / aggravants
- Les symptômes
- Les signes de gravité
- Les moyens de prévention
- Les traitements (fond, crise)

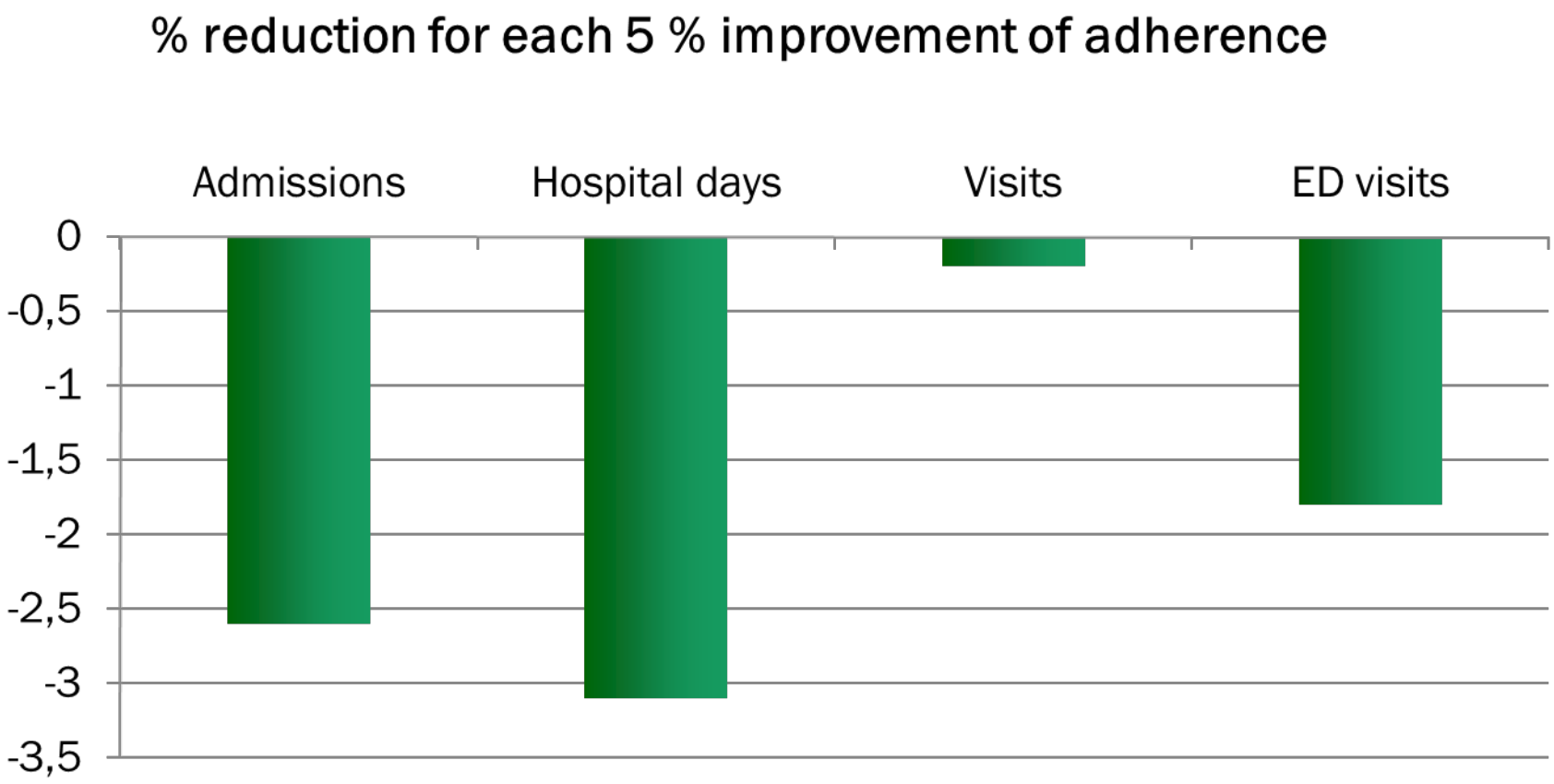
ANAES. Rapport. Education thérapeutique du patient asthmatique adulte et adolescent, Juin 2001

Cibles de l'éducation du patient asthmatique : compétences +++

- Contrôle de l'environnement
  - Allergènes
  - Tabagisme passif et actif
  - Autres aérocontaminants
- Observance
- Technique d'inhalation
- Gestion des exacerbations
  - Reconnaissance
  - Appréciation de la sévérité
  - Traitement
  - Contact avec les professionnels de santé (quel recours, quel délai?)

ANAES. Rapport. Education thérapeutique du patient asthmatique adulte et adolescent, Juin 2001

L'éducation pour améliorer l'observance

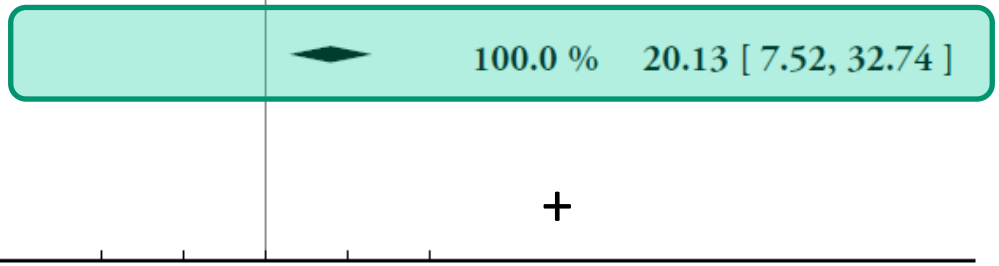


Database, 55 076 patients

Toy, Respir Med 2010

Effet de l'éducation sur l'observance mesurée (asthme)

Study or subgroup	Education N	Education Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Complex							
Foster 2014 (1)	21	46 (30.7561)	41	46 (31.6818)		15.7 %	0.0 [-16.34, 16.34]
Foster 2014 (2)	32	76 (30.5099)	35	71 (29.1111)		16.7 %	5.00 [-9.31, 19.31]
NCT00115323	25	64.5 (17.2)	25	49.1 (16.8)		19.1 %	15.40 [5.98, 24.82]
NCT00166582 (3)	16	81 (24.9)	16	37 (32.3)		13.9 %	44.00 [24.02, 63.98]
Onyirimba 2003	10	75 (18.9737)	9	28 (18)		15.6 %	47.00 [30.37, 63.63]
Subtotal (95% CI)	**104**		**126**			**80.9 %**	**21.55 [4.71, 38.39]**
Heterogeneity: Tau² = 306.52; Chi² = 26.29, df = 4 (P = 0.00003); I² =85%							
Test for overall effect: Z = 2.51 (P = 0.012)							
2 Simple education							
Bender 2010	25	64.5 (17.2)	25	49.1 (16.8)		19.1 %	15.40 [5.98, 24.82]
Subtotal (95% CI)	**25**		**25**			**19.1 %**	**15.40 [5.98, 24.82]**
Heterogeneity: not applicable							
Test for overall effect: Z = 3.20 (P = 0.0014)							
Total (95% CI)	**129**		**151**			**100.0 %**	**20.13 [7.52, 32.74]**
Heterogeneity: Tau² = 194.03; Chi² = 26.56, df = 5 (P = 0.00007); I² =81%							
Test for overall effect: Z = 3.13 (P = 0.0018)							
Test for subgroup differences: Chi² = 0.39, df = 1 (P = 0.53), I² =0.0%							



-50 -25 0 25 50

Favours control Favours education

Normansell Cochrane 2017

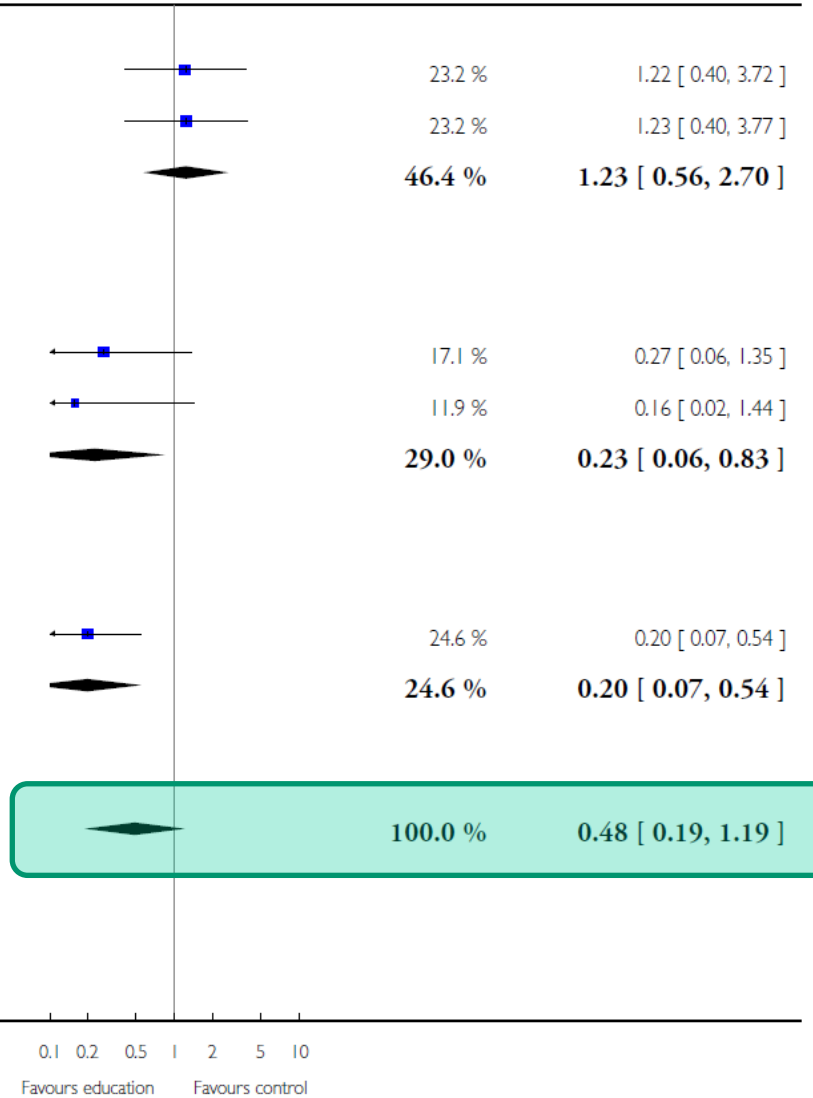
Effet de l'éducation sur les exacerbations d'asthme traitées par corticostéroïdes oraux

Study or subgroup	Education n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Foster 2014 (1)	5/35	2/29		12.0 %	2.25 [0.40, 12.57]
Foster 2014 (2)	11/23	8/44		26.6 %	4.13 [1.34, 12.65]
Gallefoss 1999	9/30	9/38		28.3 %	1.38 [0.47, 4.07]
Mehuys 2008	10/80	8/70		33.1 %	1.11 [0.41, 2.98]
Total (95% CI)	**168**	**181**		**100.0 %**	**1.82 [0.99, 3.36]**

Normansell Cochrane 2017

Effet de l'éducation sur les recours aux soins non programmés (asthme)

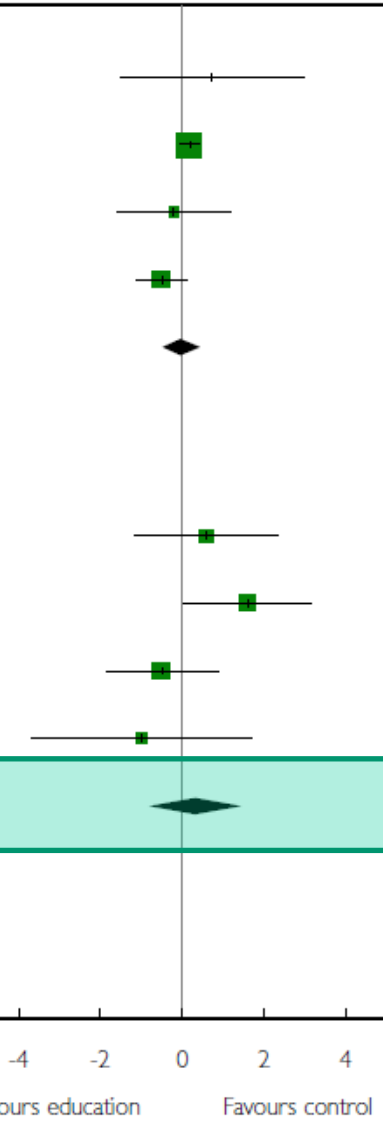
Study or subgroup	Education n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 Hospital					
NCT00233181 (1)	12/83	5/41		23.2 %	1.22 [0.40, 3.72]
NCT00233181 (2)	12/84	5/42		23.2 %	1.23 [0.40, 3.77]
Subtotal (95% CI)	**167**	**83**		**46.4 %**	**1.23 [0.56, 2.70]**
Total events: 24 (Education), 10 (Control)					
Heterogeneity: Tau² = 0.0; Chi² = 0.00, df = 1 (P = 0.99); I² =0.0%					
Test for overall effect: Z = 0.50 (P = 0.61)					
2 ED					
ADERE PEDIATRIC 1 (3)	2/108	7/109		17.1 %	0.27 [0.06, 1.35]
Mehuys 2008 (4)	1/80	5/70		11.9 %	0.16 [0.02, 1.44]
Subtotal (95% CI)	**188**	**179**		**29.0 %**	**0.23 [0.06, 0.83]**
Total events: 3 (Education), 12 (Control)					
Heterogeneity: Tau² = 0.0; Chi² = 0.14, df = 1 (P = 0.71); I² =0.0%					
Test for overall effect: Z = 2.24 (P = 0.025)					
3 GP					
Gallefoss 1999 (5)	9/32	26/39		24.6 %	0.20 [0.07, 0.54]
Subtotal (95% CI)	**32**	**39**		**24.6 %**	**0.20 [0.07, 0.54]**
Total events: 9 (Education), 26 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.14 (P = 0.0017)					
Total (95% CI)	**387**	**301**		**100.0 %**	**0.48 [0.19, 1.19]**
Total events: 36 (Education), 48 (Control)					
Heterogeneity: Tau² = 0.62; Chi² = 9.76, df = 4 (P = 0.04); I² =59%					
Test for overall effect: Z = 1.58 (P = 0.11)					
Test for subgroup differences: Chi² = 9.61, df = 2 (P = 0.01), I² =79%					



Normansell Cochrane 2017

Effet de l'éducation sur le contrôle de l'asthme

Study or subgroup	Education N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 ACQ							
Bender 2010	25	-1.12 (3.9)	25	-1.84 (4.14)		4.0 %	0.72 [-1.51, 2.95]
NCT00115323	165	1.5 (1.2)	168	1.3 (1.1)		56.2 %	0.20 [-0.05, 0.45]
NCT01064869	7	2.9 (1.4)	11	3.1 (1.6)		9.2 %	-0.20 [-1.60, 1.20]
NCT01132430	26	1.7 (1.2379)	28	2.2 (1.0316)		30.6 %	-0.50 [-1.11, 0.11]
Subtotal (95% CI)	**223**		**232**			**100.0 %**	**-0.03 [-0.49, 0.43]**
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 4.81$, df = 3 (P = 0.19); $I^2 = 38\%$							
Test for overall effect: Z = 0.13 (P = 0.90)							
2 ACT							
Foster 2014 (1)	21	-18 (3.2953)	41	-18.6 (3.485)		24.8 %	0.60 [-1.17, 2.37]
Foster 2014 (2)	32	-18.3 (3.3284)	35	-19.9 (3.2022)		28.5 %	1.60 [0.03, 3.17]
Mehuys 2008	80	-20.2 (3.5)	70	-19.7 (4.8)		33.0 %	-0.50 [-1.86, 0.86]
NCT01132430	26	-19 (4.9516)	28	-18 (5.1578)		13.7 %	-1.00 [-3.70, 1.70]
Subtotal (95% CI)	**159**		**174**			**100.0 %**	**0.30 [-0.82, 1.43]**
Heterogeneity: $Tau^2 = 0.52$; $Chi^2 = 4.97$, df = 3 (P = 0.17); $I^2 = 40\%$							
Test for overall effect: Z = 0.53 (P = 0.60)							
Test for subgroup differences: $Chi^2 = 0.29$, df = 1 (P = 0.59), $I^2 = 0.0\%$							



Normansell Cochrane 2017

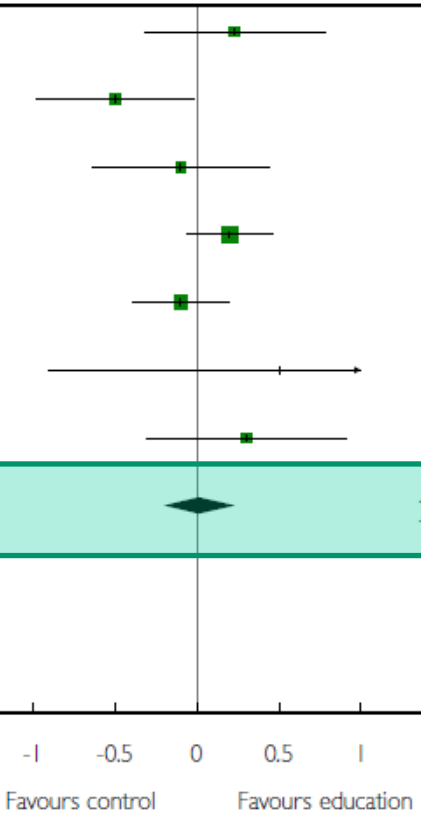
Effet de l'éducation sur la qualité de vie (asthme)

Study or subgroup	Education N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Bender 2010	25	-0.15 (0.92)	25	-0.38 (1.06)		11.3 %	0.23 [-0.32, 0.78]
Foster 2014 (1)	21	4.9 (0.8787)	41	5.4 (0.9505)		13.9 %	-0.50 [-0.98, -0.02]
Foster 2014 (2)	32	5.4 (1.1095)	35	5.5 (1.1644)		11.4 %	-0.10 [-0.64, 0.44]
Mehuys 2008	80	6 (0.7)	70	5.8 (0.9)		27.0 %	0.20 [-0.06, 0.46]
NCT00115323	165	4.7 (1.3)	168	4.8 (1.4)		24.6 %	-0.10 [-0.39, 0.19]
NCT01064869	7	4.3 (1.4)	11	3.8 (1.6)		2.2 %	0.50 [-0.90, 1.90]
NCT01132430	26	5 (1.2379)	28	4.7 (1.0316)		9.6 %	0.30 [-0.31, 0.91]
Total (95% CI)	**356**		**378**			**100.0 %**	**0.01 [-0.20, 0.23]**

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 9.09$, df = 6 (P = 0.17); $I^2 = 34\%$

Test for overall effect: Z = 0.13 (P = 0.90)

Test for subgroup differences: Not applicable

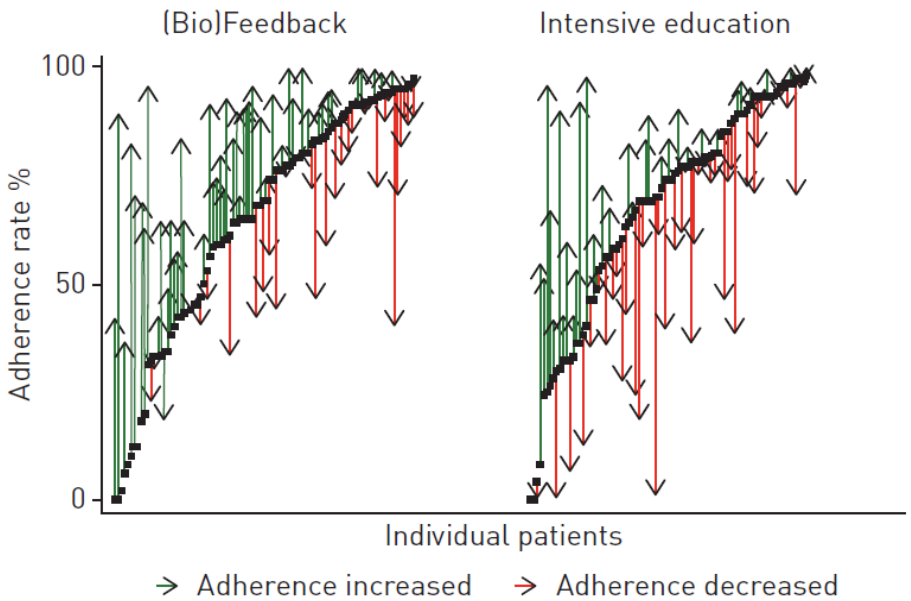


Normansell Cochrane 2017

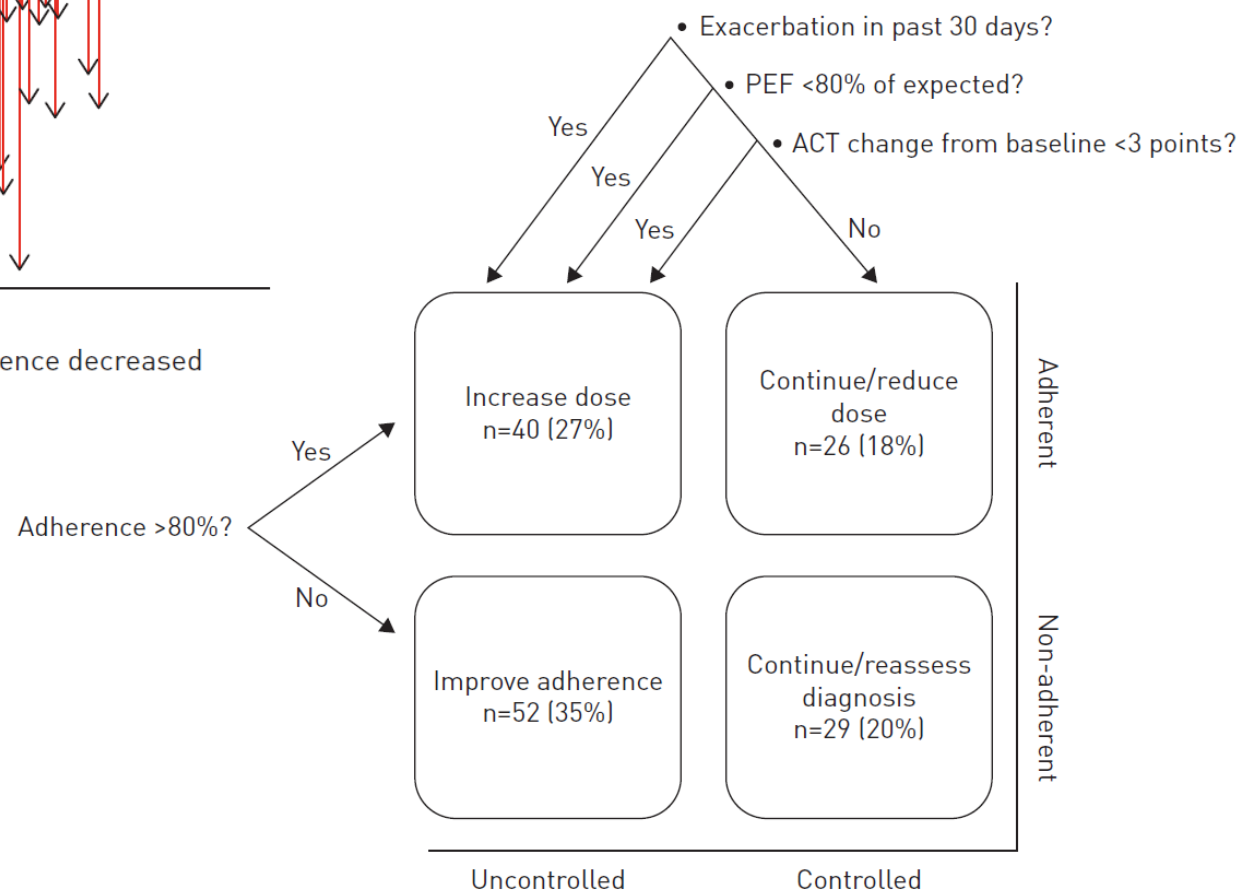
L'avenir : les « bidules » intelligents et connectés ?

Smart Asthma report, Asthma UK 2017

Asthme sévère non contrôlé: feedback vs éducation



3 mois

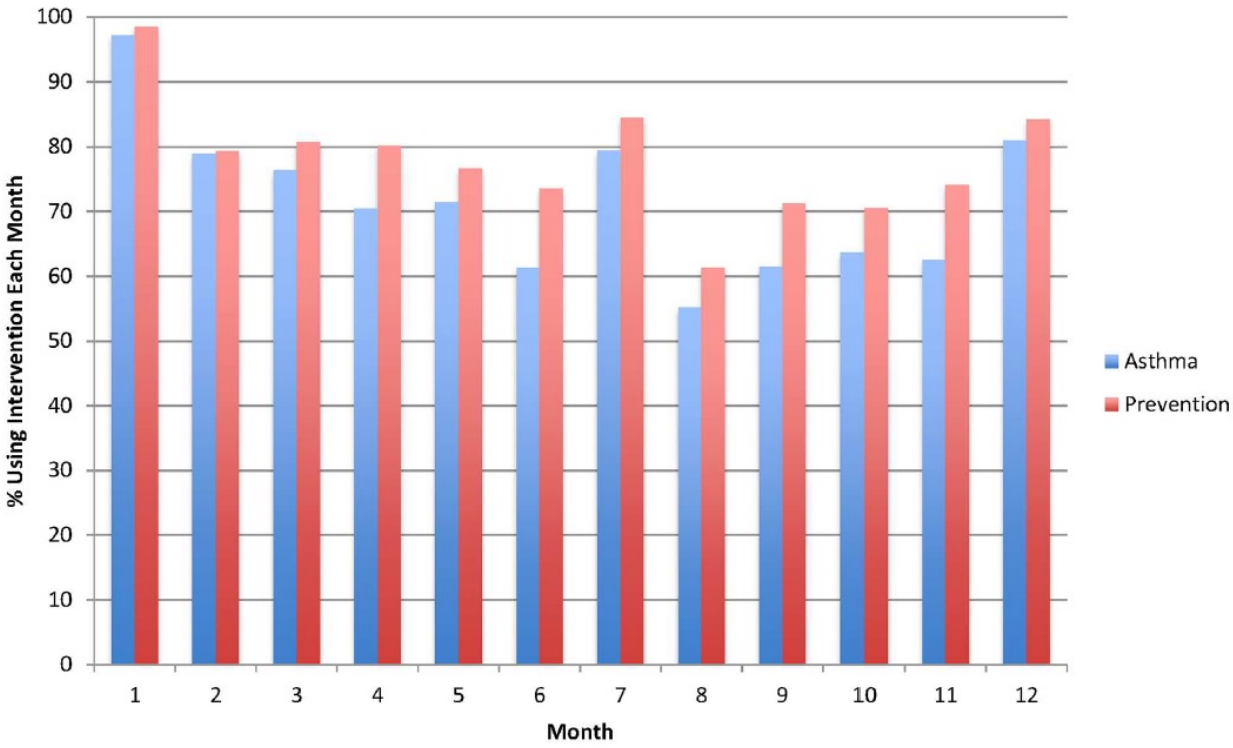


Sulaiman ERJ 2018

Pense-bêtes

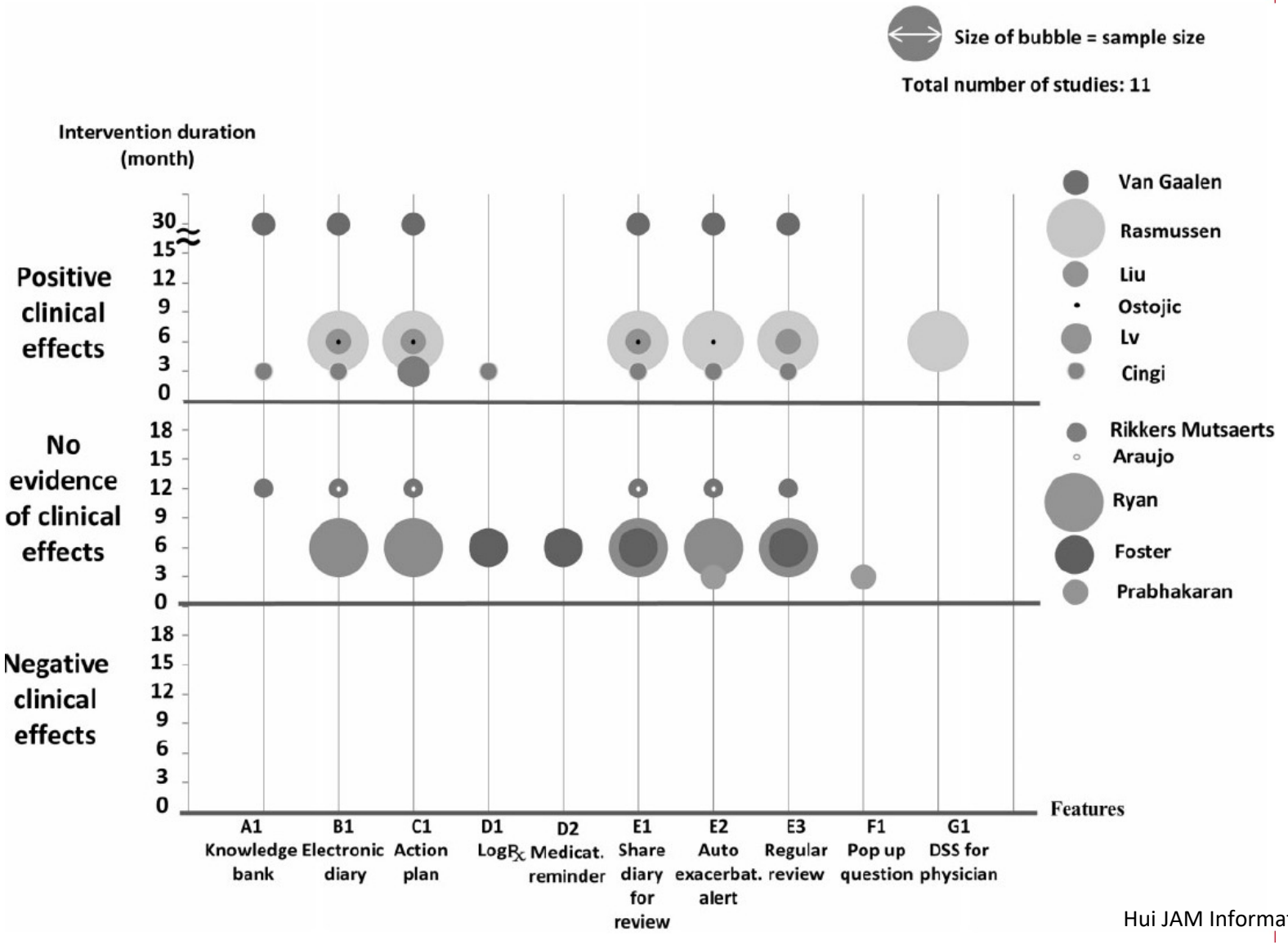
- Contrôle
- Exacerbations
- Plan d'action
- Disponibilité des traitements
- Facteurs aggravants
- Consultation spécialisée
- Technique d'inhalation

Pool PLOS One 2017



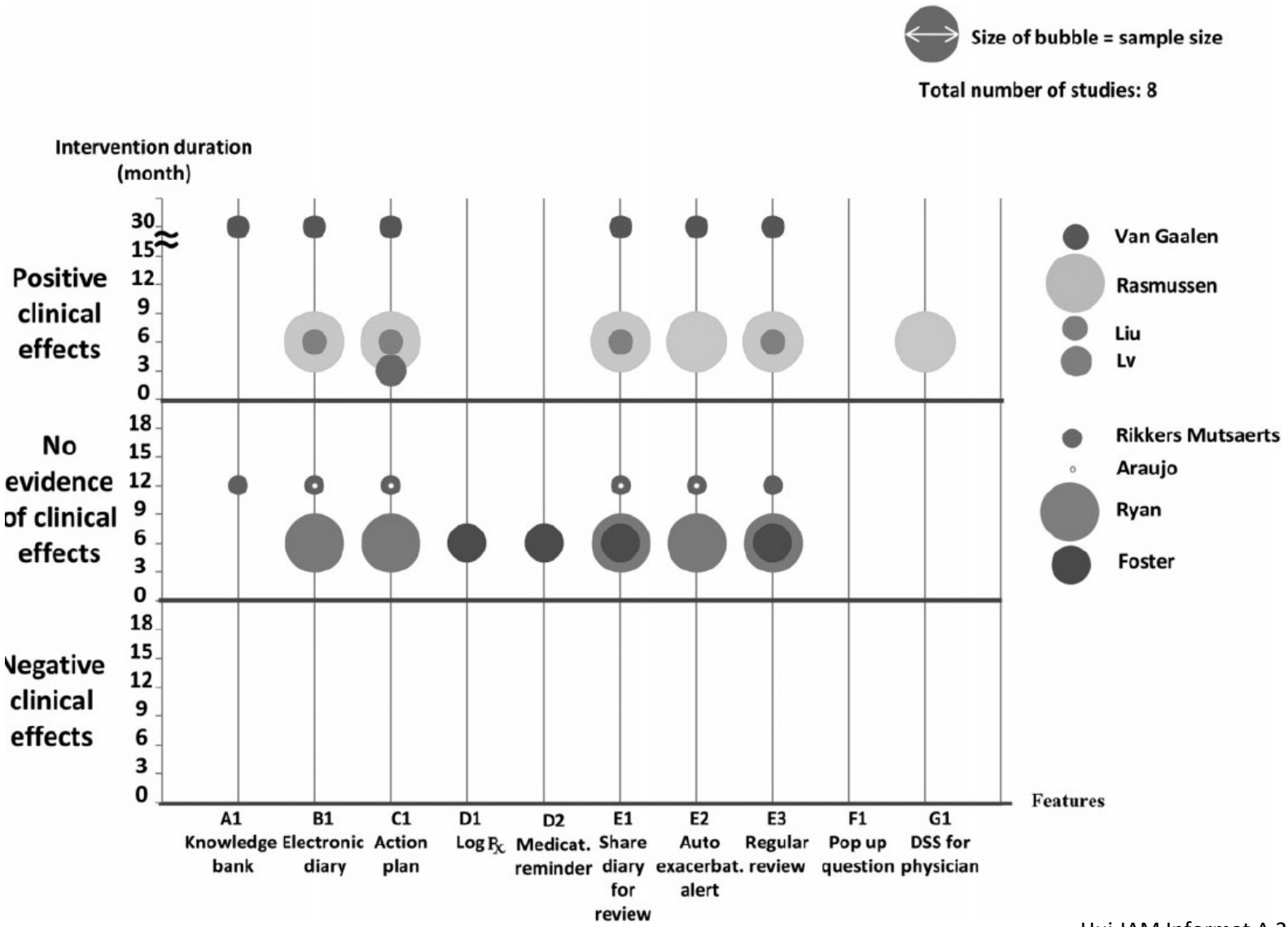
Outcome †	Intervention (N = 157)*			Control (N = 168)*			P-value
	Baseline	12 Months	Change from Baseline	Baseline	12 Months	Change from Baseline	
Asthma Control Test (ACT)							
Asthma Control Test (ACT) Score	17.7 (16.7, 18.6)	19.9 (18.9, 20.9)	2.3 (1.6, 2.9)	17.9 (17.0, 18.8)	19.1 (18.2, 20.0)	1.2 (0.6, 1.8)	0.02

Applis et contrôle



Hui JAM Informat A 2017

Applis et qualité de vie



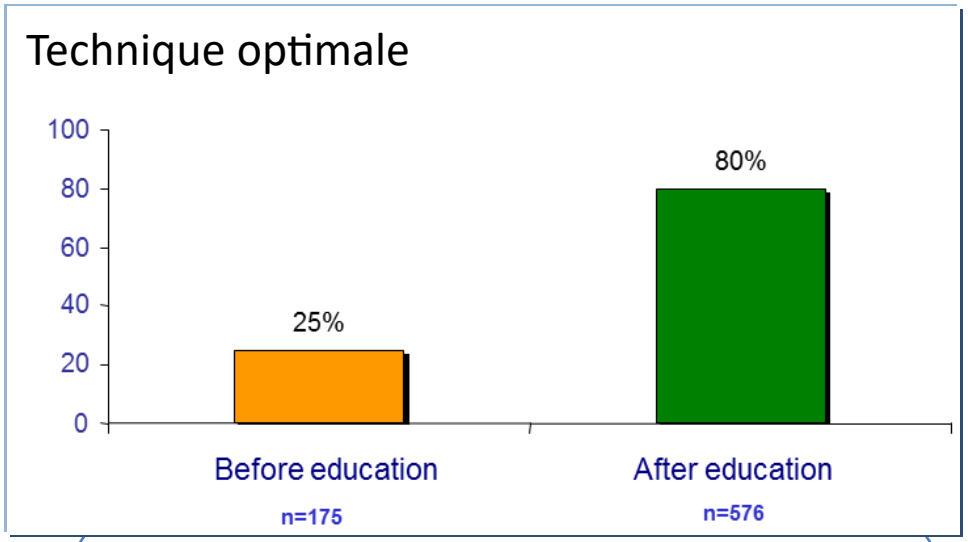
Sur la technique d'inhalation…

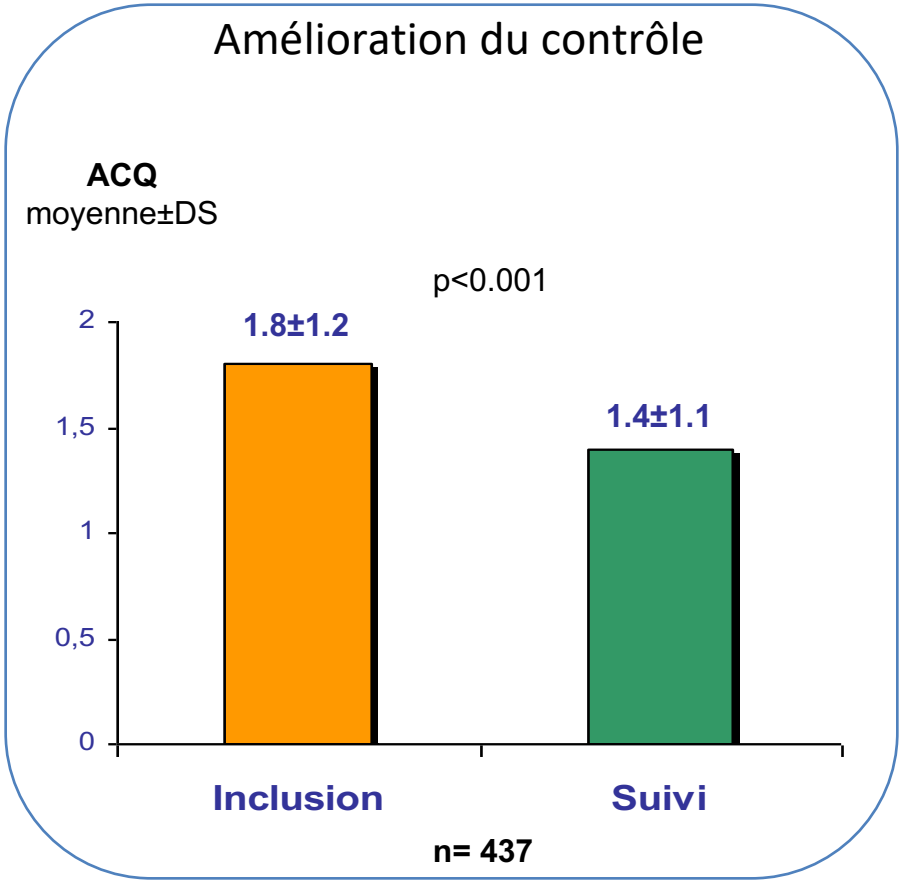
		OR	*95% CI*
Age (years)	<60	1.00	
	≥60	1.40	0.67–2.94
Educational level[a]	low	2.01	0.67–4.61
	middle	1.84	0.73–4.61
	high	1.00	
FEV_1/VC[b]	<0.6	1.15	0.55–2.41
	≥0.6	1.00	
Received inhalation instruction[c]	yes	1.00	
	no	2.22	1.02–4.80
Device	single	1.00	
	multiple	2.23	1.07–5.02

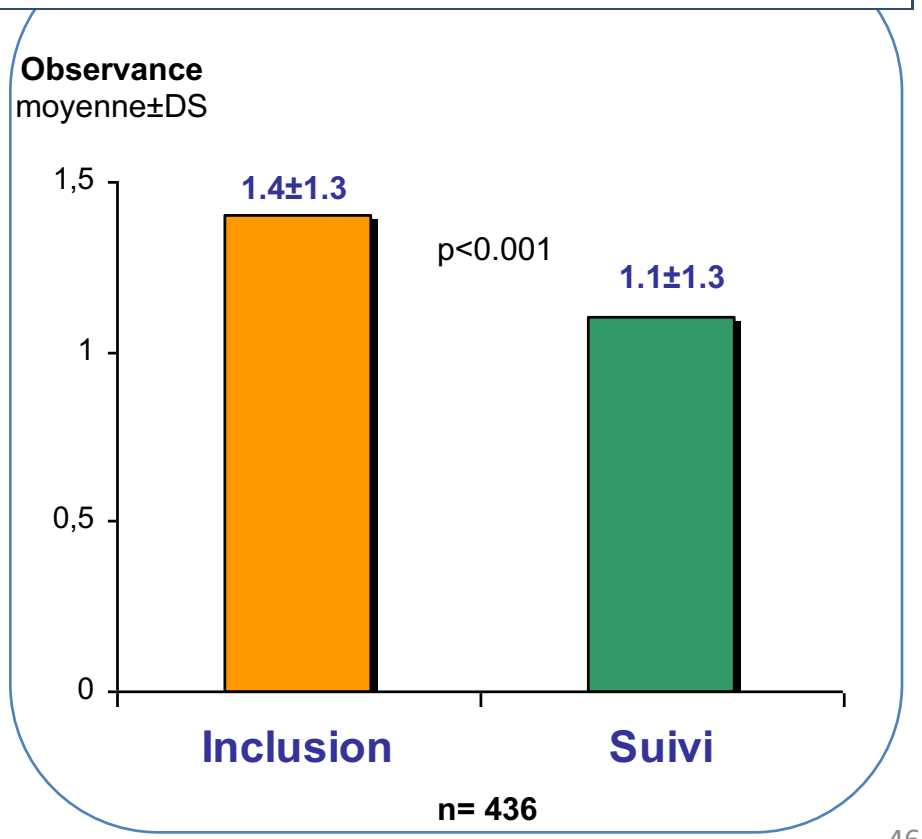
Rootmensen, JAMPDD 2010 ; n=156

Education courte

- n=727, éducation courte (moyenne 6 min) à la technique d'inhalation



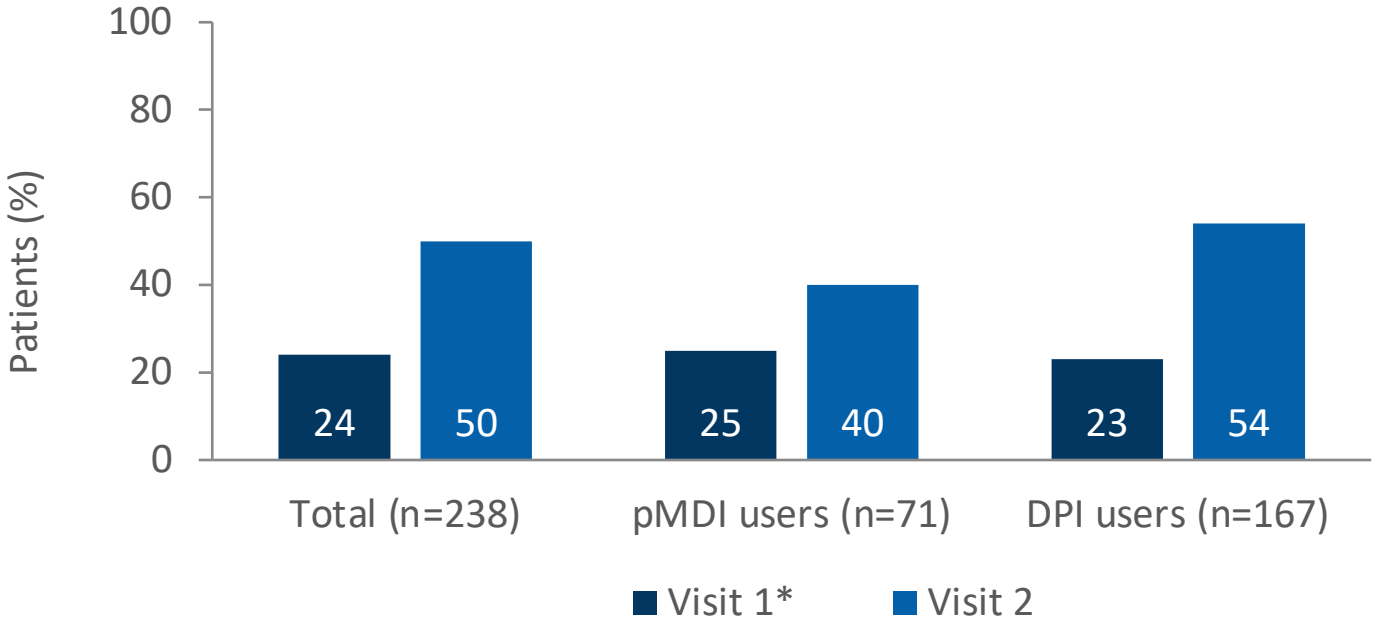




Giraud, Allaert & Roche, Respir Med 2011

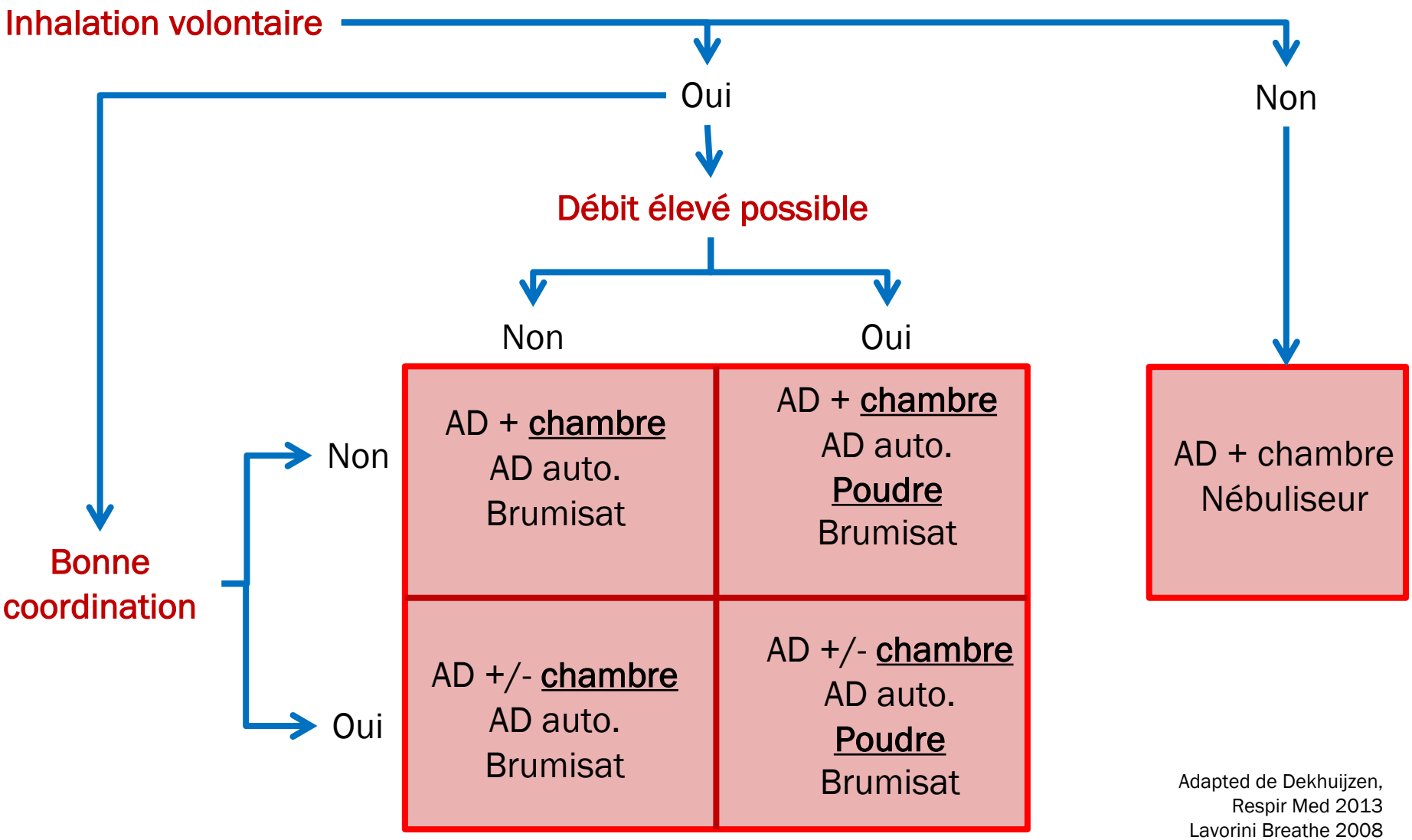
L'education ne suffit pas toujours

Patients with correct inhaler technique prior to and one month after training



Azzi E, et al. NPJ Prim Care Respir Med 2017;27:29.

Bien choisir le dispositif



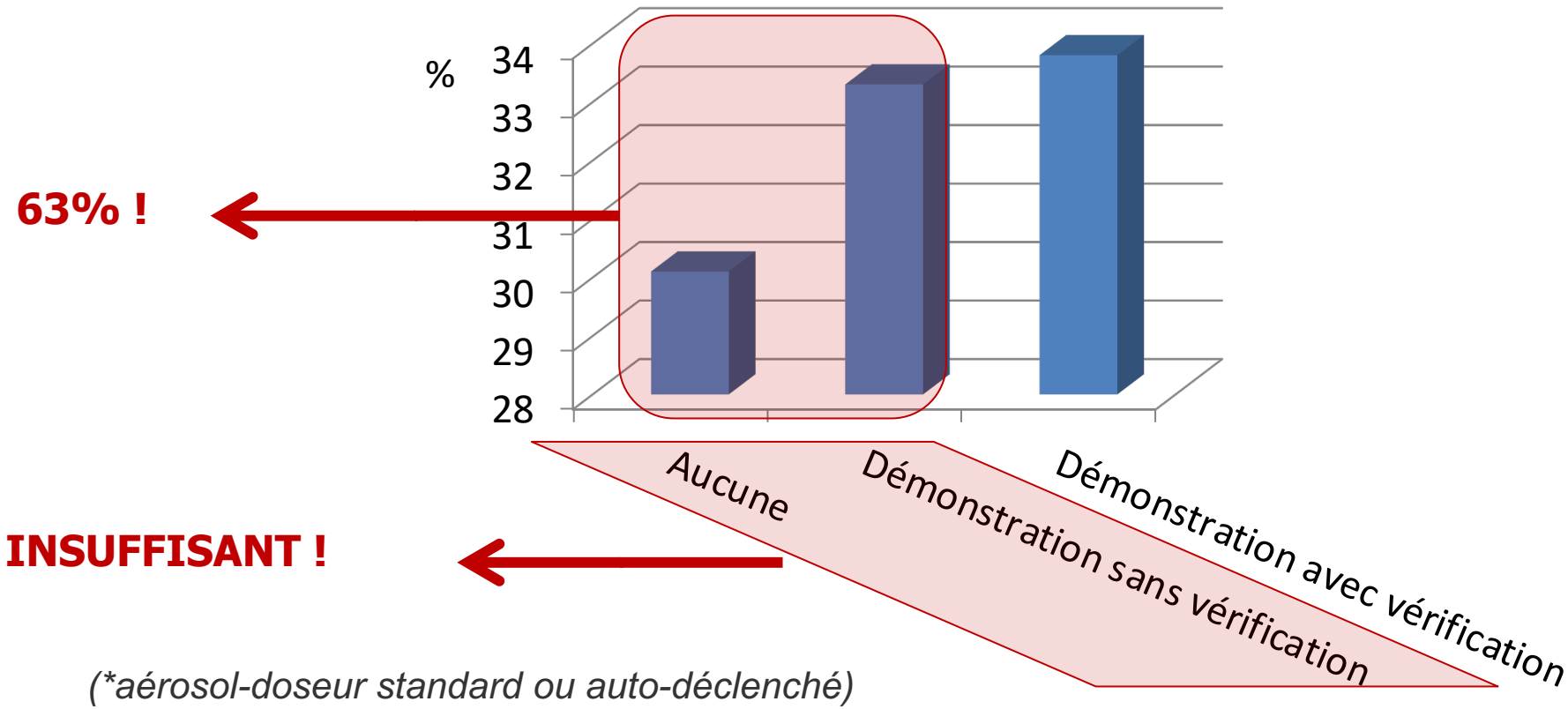
Adapted de Dekhuijzen, Respir Med 2013
Lavorini Breathe 2008

Freins

- Manque de conscience du problème
- Manque de temps
- Nombre croissant de dispositifs
  - Chacun ayant ses spécificités
- Imagination débordante des patients

Pratique de l'éducation en vie réelle

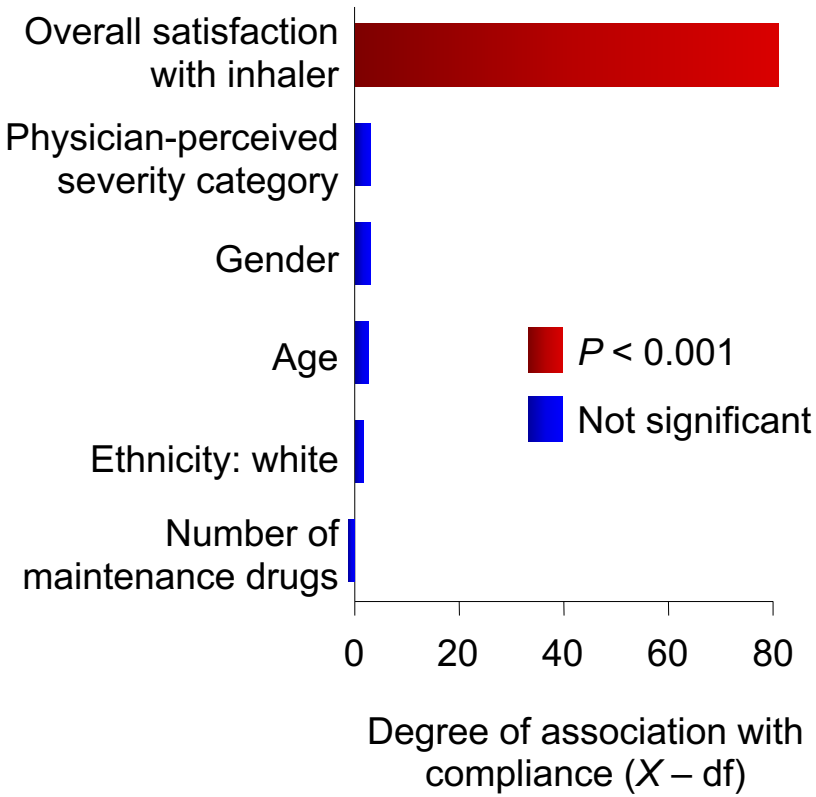
- Proportion de patients ayant reçu une éducation
- Parmi 727 patients venant en pharmacie avec une prescription de traitement inhalé*

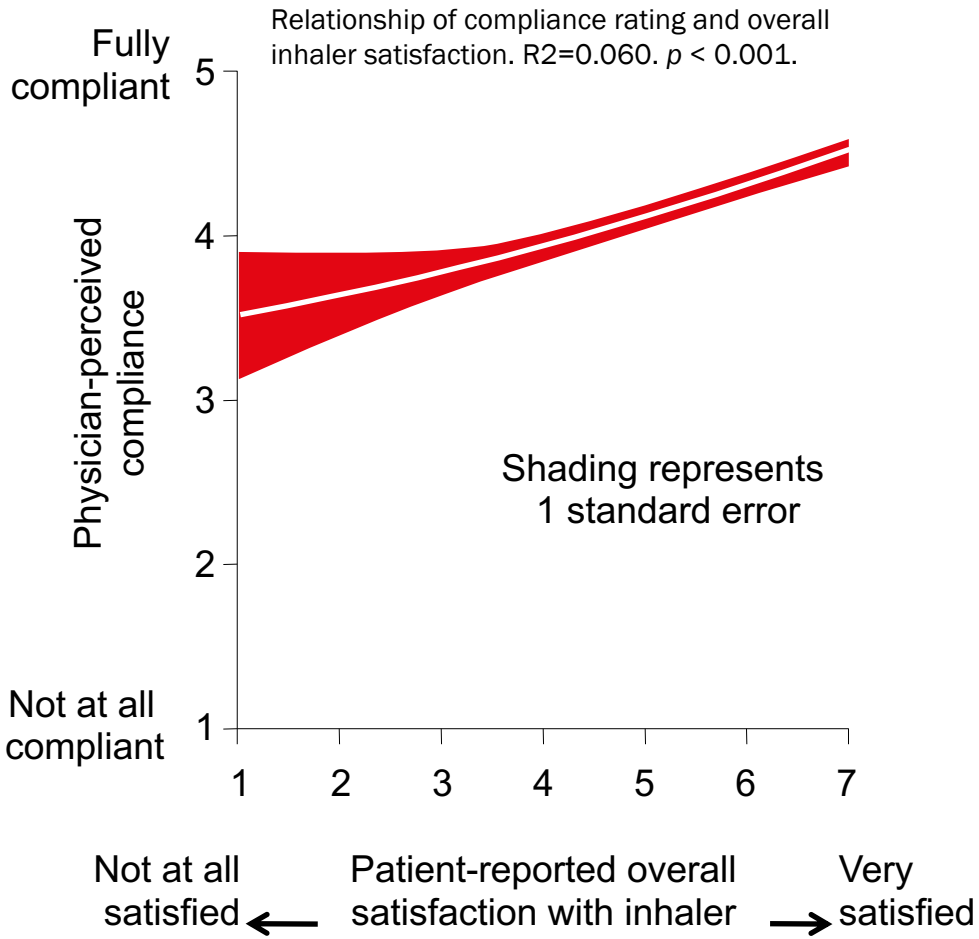


(*aérosol-doseur standard ou auto-déclenché)

Giraud, Allaert & Roche, Respir Med 2011

Satisfaction → adhérence

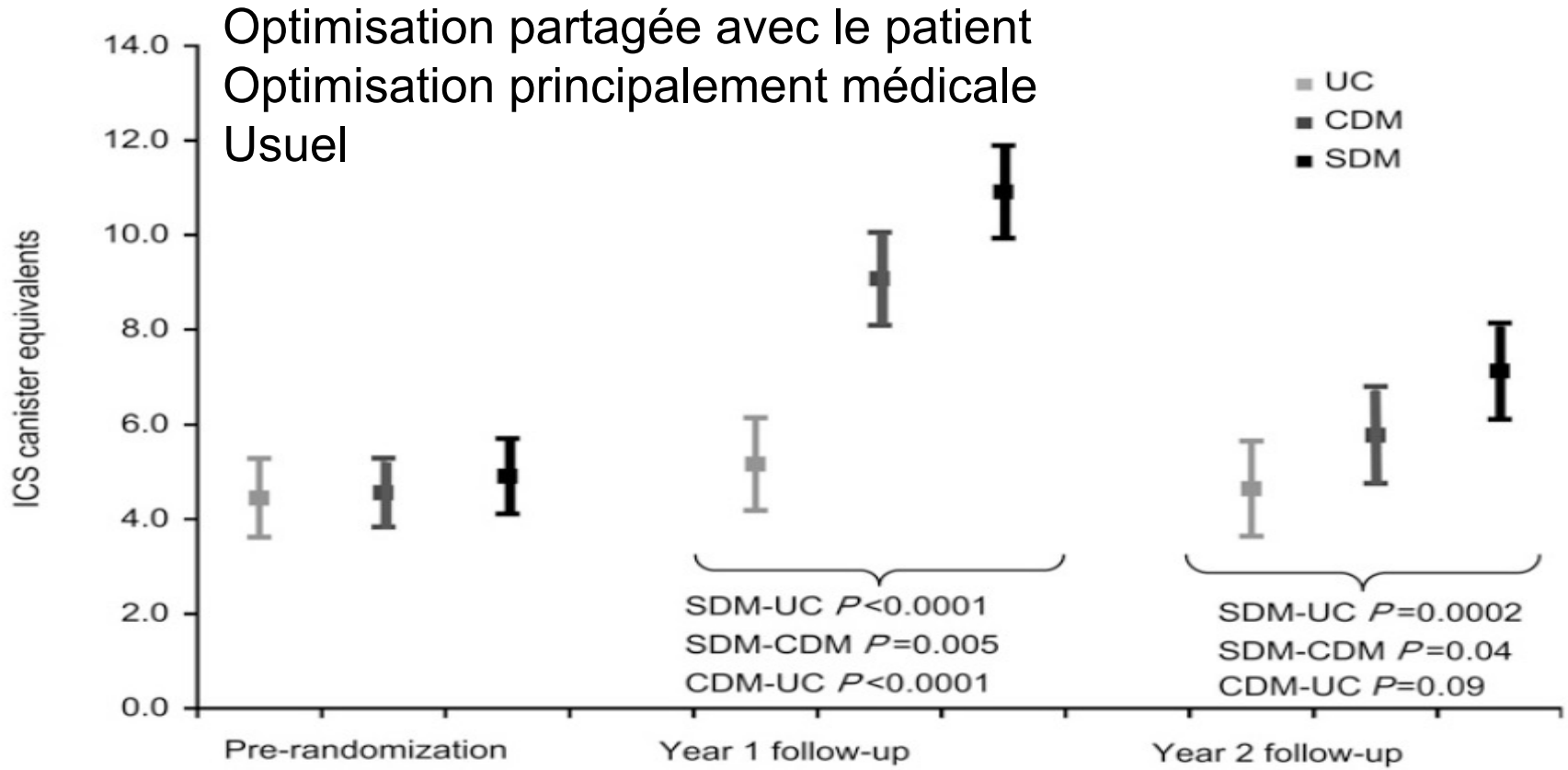




Small M et al. Adv Ther 2011;28:202–12

Participation → meilleure observance

- Observance de la corticothérapie inhalée (n=612, randomisé)



Am J Respir Crit Care Med Vol 181. pp 566–577, 2010

Les senseurs connectés

	Pharma company	Digital partner	Device platform	Sensor name
Add-on inhaler sensors • Can be added to an existing drug-device combination • Reusable and detachable • Do not require any modification of existing design	NOVARTIS	Propeller	Breezhaler	Breezhaler sensor
	gsk		Ellipta	Ellipta add-on
	Boehringer Ingelheim		Respimat	Respimat add-on
	Chiesi		Modulite	Modulite add-on
	AstraZeneca	adherium	pMDI Turbuhaler	SmartTouch SmartTurbo
	teva	GECKO HEALTH INNOVATIONS	pMDI	CareTrx
	Chiesi	amiko	NEXThaler	Respiro
Integrated sensors • Sensor is built into an existing design • Disposable with the product	teva	IBM	RespiClick	Digihaler

Inhaler sensor

Smartphone app

Personalized profile

Messages

- La mauvaise utilisation est très fréquente
- De même que l'inobservance
- L'une et l'autres rendent compte de la grande majorité des non-contrôles
- Et la situation n'évolue pas depuis de très nombreuses années

- Les professionnels de santé, comme les patients, n'y prêtent pas suffisamment attention
- Pourtant l'éducation est efficace
- Les choix thérapeutiques doivent être partagés

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Date of preparation: XXXX 2014