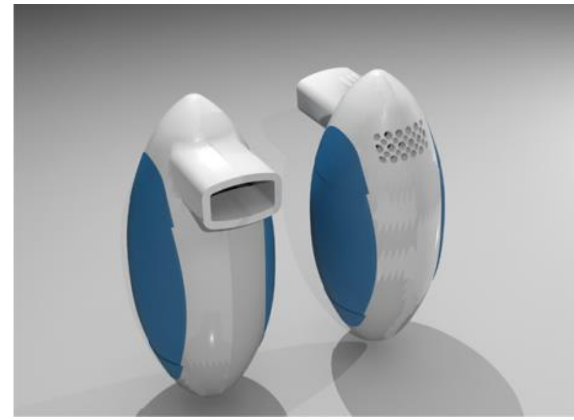
University Hospital Southampton NHS
NHS Foundation Trust

Wessex Asthma Network

Portsmouth Hospitals NHS
NHS Trust

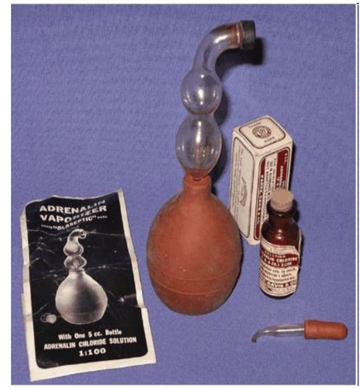
Smart-Inhalers

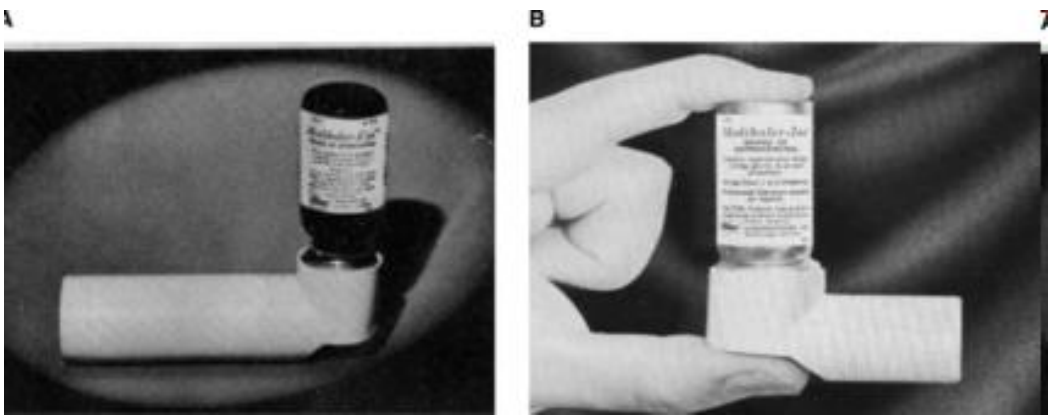
Dr Paddy Dennison



The first inhalers…

- Metered dose inhaler (MDI) - 1956, Charles Thiel, Riker laboratories
- “Why can’t you make my asthma medicine like my mother’s hairspray”



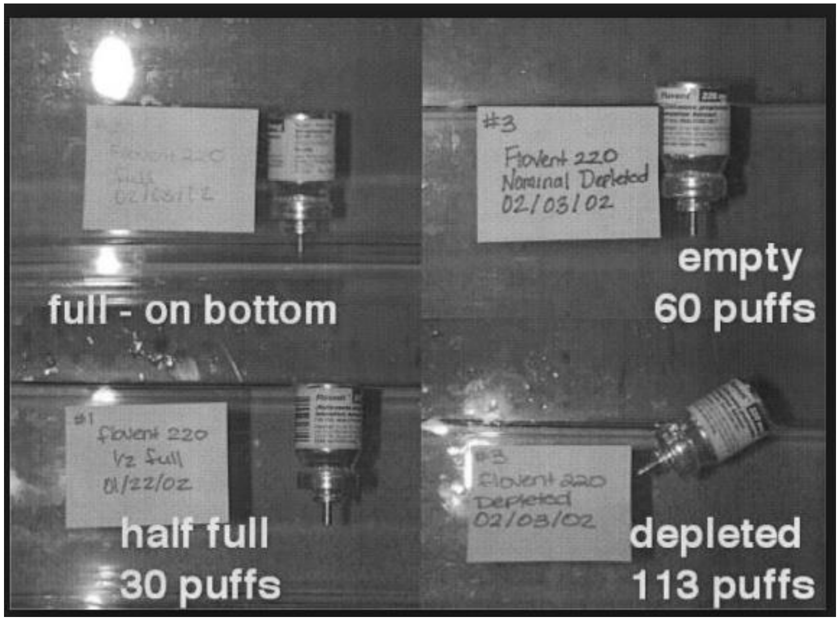


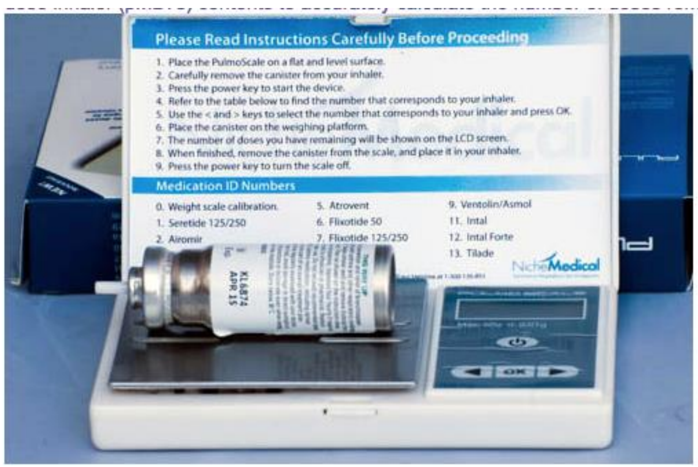
My daughter..

- “Why can’t you make an inhaler like an Ipad”

Inhalers have got better

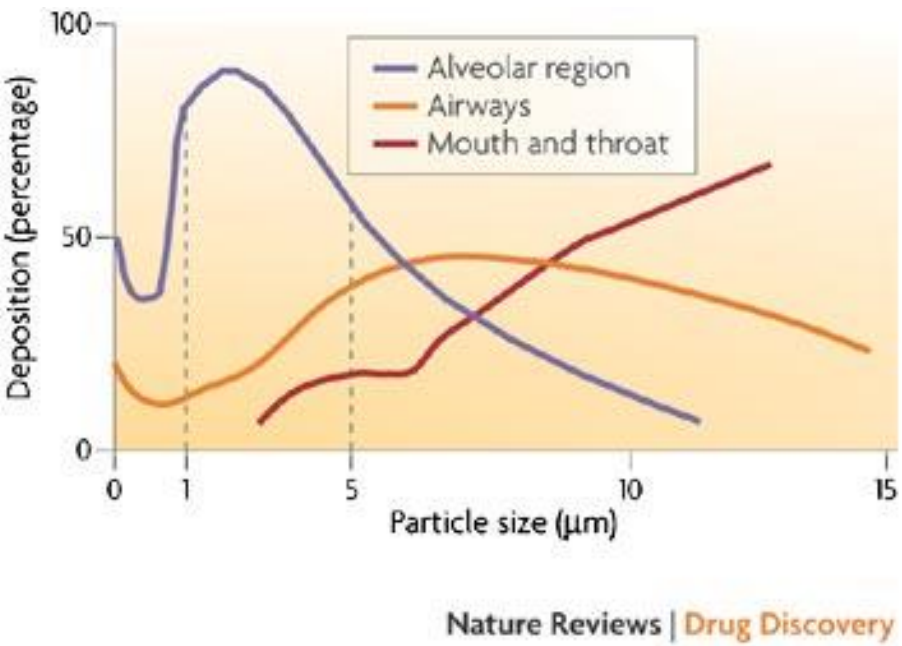
- Dose counters

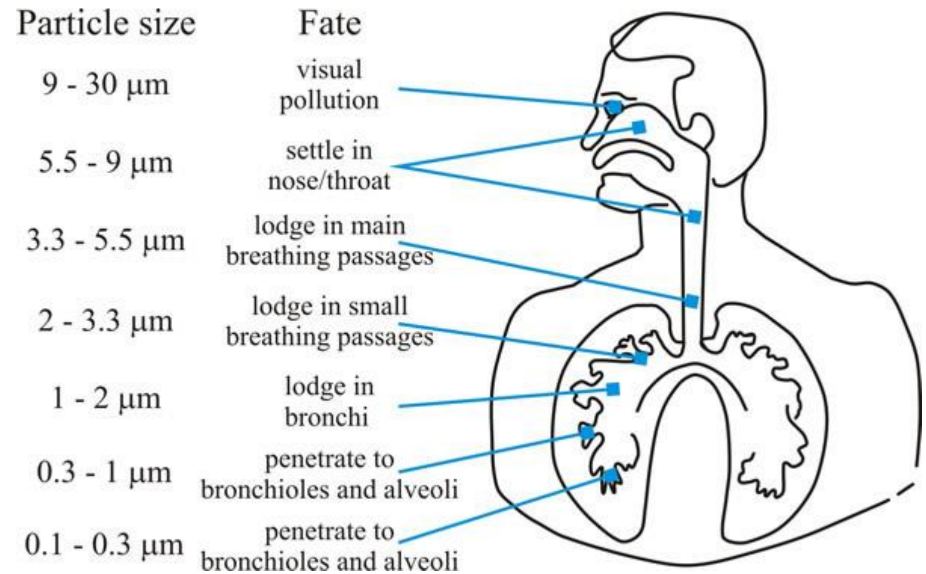




Lung deposition

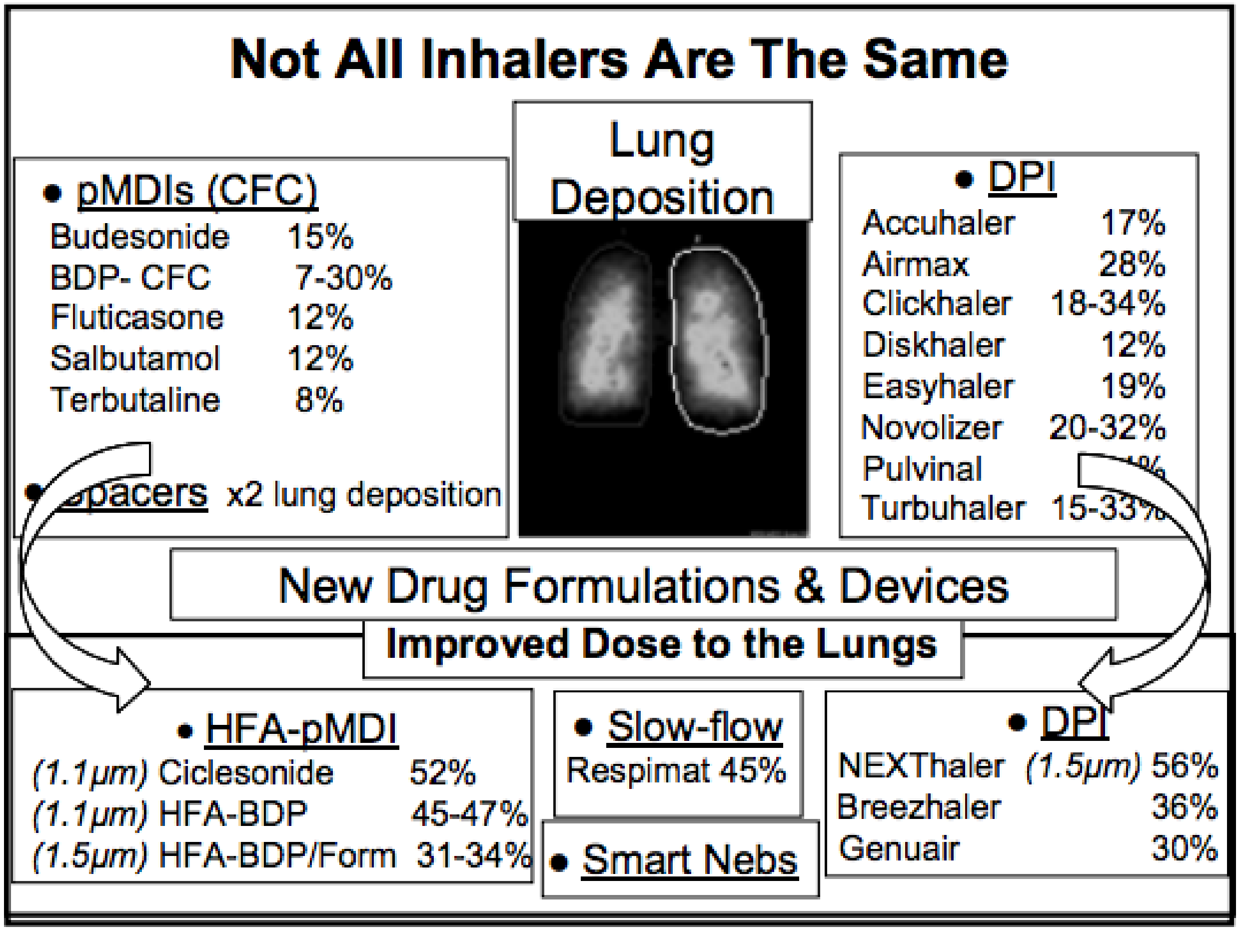
- Particle size





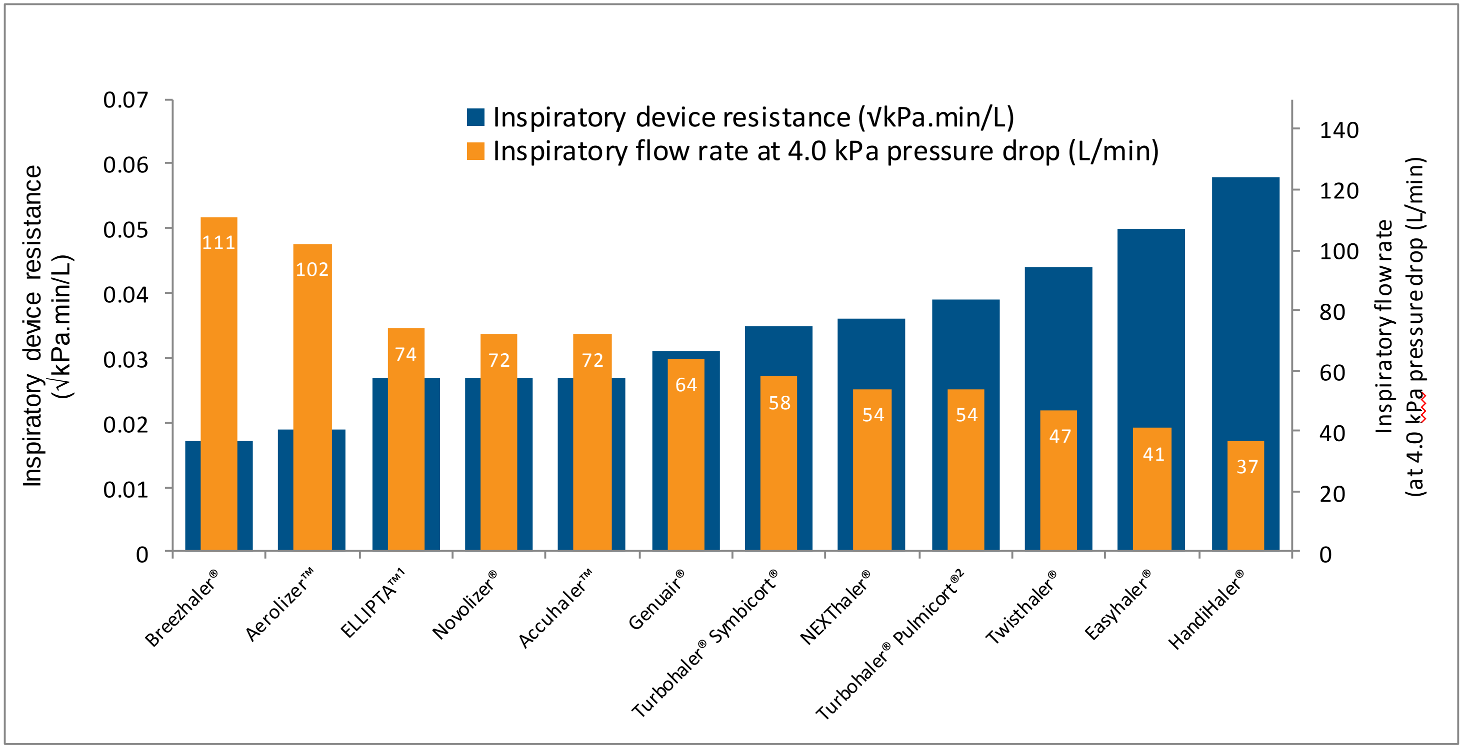
Patton and Byron *Nature Reviews Drug Discovery* **6**, 67–74

Lung deposition



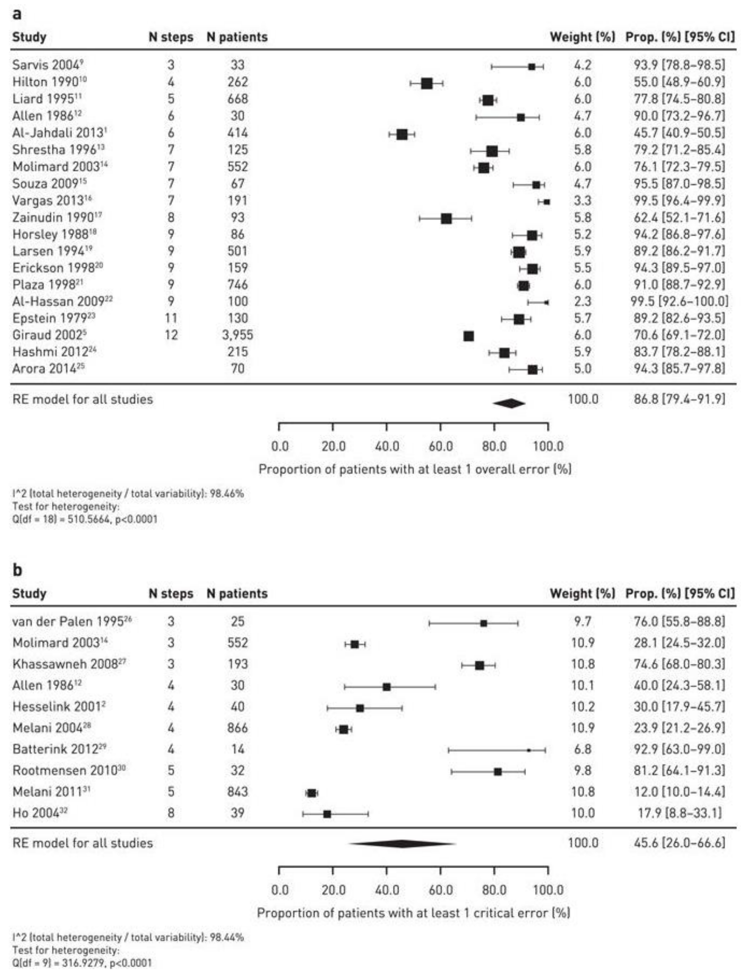
Usmani - ERJ workshop

Lower resistance/better flow



1. Krüger et al. (2014) *Eur Res J* vol. 44 no. Suppl 58

Inhalers have got easier??



Meta-analysis of the overall error rate frequency (**a**) and critical error rate frequency (**b**) for MDIs in prospective/cross-sectional studies

Chrystyn et al, NPJ Prim Care Resp Med 2017; 27:22

Systematic Review of Errors in Inhaler Use

Has Patient Technique Improved Over Time?

Joaquin Sanchis, MD, PhD; Ignasi Gich, MD, PhD; and Soren Pedersen, MD, PhD, Dr Med Sci; on behalf of the Aerosol Drug Management Improvement Team (ADMIT)

BACKGROUND: Problems with the use of inhalers by patients were noted shortly after the launch of the metered-dose inhaler (MDI) and persist today. We aimed to assess the most common errors in inhaler use over the past 40 years in patients treated with MDIs or dry powder inhalers (DPIs).

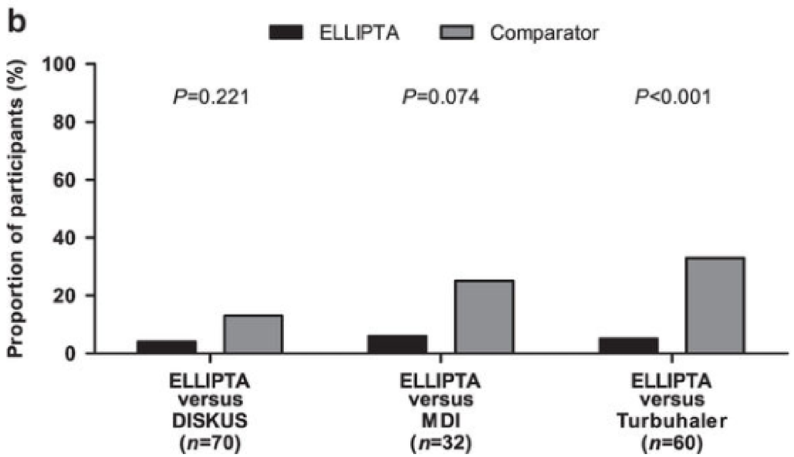
METHODS: A systematic search for articles reporting direct observation of inhaler technique by trained personnel covered the period from 1975 to 2014. Outcomes were the nature and frequencies of the three most common errors; the percentage of patients demonstrating correct, acceptable, or poor technique; and variations in these outcomes over these 40 years and when partitioned into years 1 to 20 and years 21 to 40. Analyses were conducted in accordance with recommendations from Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Strengthening the Reporting of Observational Studies in Epidemiology.

RESULTS: Data were extracted from 144 articles reporting on a total number of 54,354 subjects performing 59,584 observed tests of technique. The most frequent MDI errors were in coordination (45%; 95% CI, 41%-49%), speed and/or depth of inspiration (44%; 40%-47%), and no postinhalation breath-hold (46%; 42%-49%). Frequent DPI errors were incorrect preparation in 29% (26%-33%), no full expiration before inhalation in 46% (42%-50%), and no postinhalation breath-hold in 37% (33%-40%). The overall prevalence of correct technique was 31% (28%-35%); of acceptable, 41% (36%-47%); and of poor, 31% (27%-36%). There were no significant differences between the first and second 20-year periods of scrutiny.

CONCLUSIONS: Incorrect inhaler technique is unacceptably frequent and has not improved over the past 40 years, pointing to an urgent need for new approaches to education and drug delivery.

CHEST 2016; 150(2):394-406

Surely newer inhalers do better?



Percentage of patients with at least one critical error after reading the patient information leaflet in each substudy. (**a**) COPD patients and (**b**) asthma patients.

Table 3

Number of inhaler technique errors at Visit 2, by error category[a] (ITT population; *N*=123)

Error category	*Genuair*	*Breezhaler*
Critical errors prior to inhalation	0	0
Critical errors preparing for inhalation	2	3
Critical errors during inhalation	5	10
Critical errors after inhalation	NA	3
Non-critical errors	14	4

Van der Palen et al, 2016 NPJ Prim Care Resp 26

Pascual et al, NPJ Prim Care Respir Med. 2015; 25:

A study of 2,935 patients found that device handling errors were common[1]

- 212 GPs and 50 pulmonologists assessed the handling on 3,993 devices for continuous treatment of COPD on 2,395 patients[1]
  - Physicians observed patients taking a puff of their usual medication using their usual device and usual inhalation technique, with particular attention on dose preparation and delivery
  - Physicians did not give patients any instructions before the test

	Breezhaler®	Diskus®	Handihaler®	pMDI	Respimat®	Turbuhaler®	Total#
Devices n	876	452	598	422	625	420	3393
No error	36.5 (33.3–39.7)	29.2 (25.0–33.4)	10.7 (8.2–13.5)	16.4 (12.8–19.9)	23.0 (19.7–26.3)	30.5 (26.1–34.9)	25.3 (23.6–26.7)
Device-independent errors	53.5 (50.2–56.8)	50.9 (46.3–55.5)	54.8 (50.9–58.8)	53.8 (49.0–58.5)	56.8 (52.9–60.7)	51.9 (47.1–56.7)	53.8 (52.2–55.5)
Device-dependent errors	15.4 (13.0–17.8)	29.2 (25.0–33.4)	75.3 (71.8–78.7)	70.1 (65.8–74.5)	50.6 (46.6–54.5)	32.1 (27.7–36.6)	43.1 (41.5–44.8)
At least one critical error	15.4 (13.0–17.8)	21.2 (17.5–25.0)	29.3 (25.6–32.9)	43.8 (39.1–48.6)	46.9 (43.0–50.8)	32.1 (27.7–36.6)	30.0 (28.5–31.6)

- Handling errors were observed in over 50% of cases, regardless of device used
- Critical errors were more frequent with non-breath-actuated devices (pMDI and Respimat®), mainly due to poor hand–lung synchronisation.

Data are presented as % (95% CI), unless otherwise indicated
pMDI, pressurised metered-dose inhaler
#total number of evaluated devices

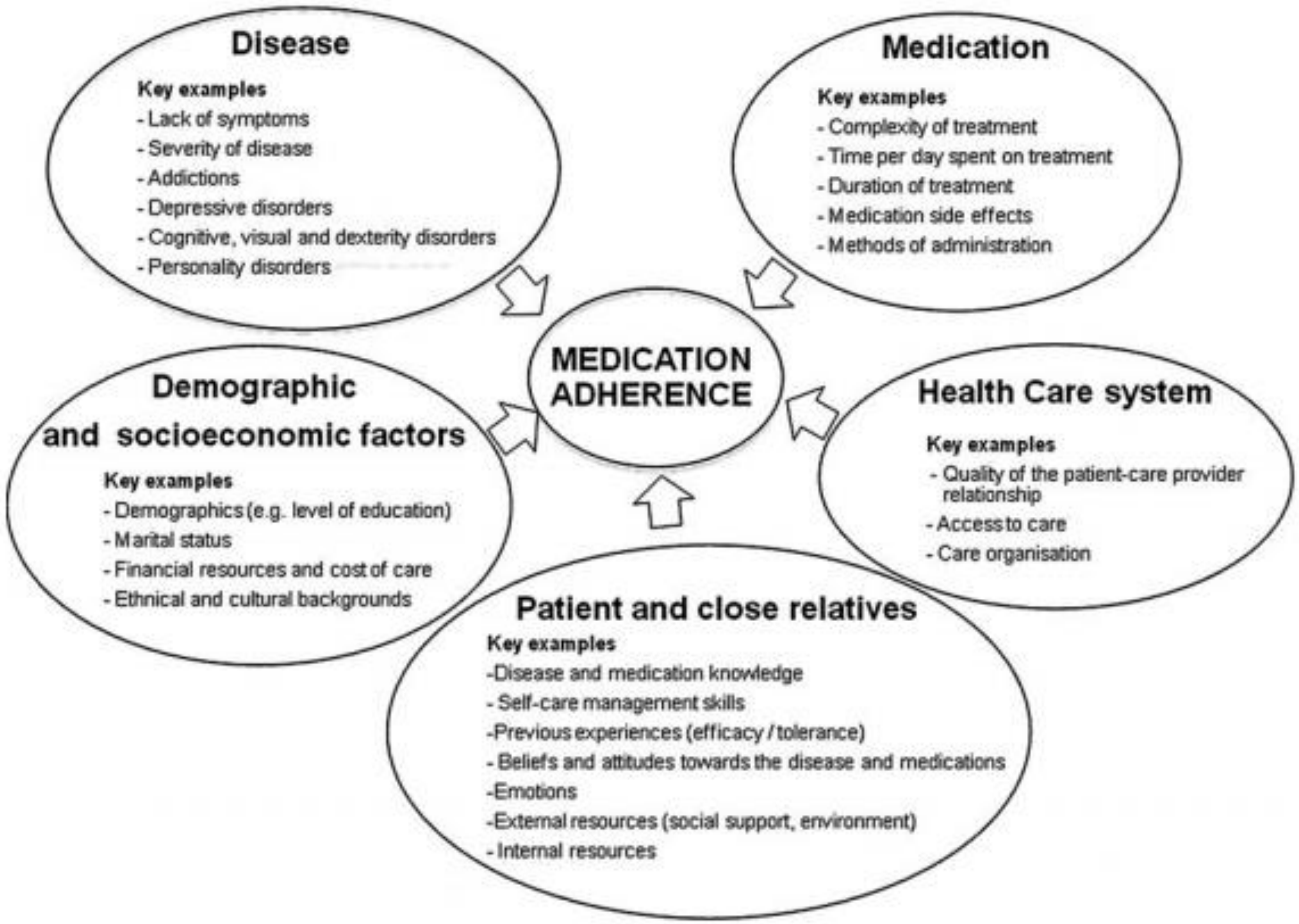
1. Molimard M et al. (2017); *Eur Resp J.* 49:1601794

Do inhalers need to get smarter?

- What is the problem we are trying to solve?
  - Adherence?
    - But this is complex

Do inhalers need to get smarter?

- What is the problem we are trying to solve?
  - Adherence?
    - But this is complex
  - Technique?
  - Proving patients are taking their treatment?
    - Trials
    - Advanced treatments
    - Recompense (USA)
  - Identifying high risk patients/high SABA use?



Lehman et al, [Int J Clin Pharm.] 2014 Feb;36

Asthma UK February 2017

MY AIR COACH
PREDICTIVE SELF-MANAGEMENT OF ASTHMA

“myAirCoach project aims to support asthma patients to control their disease through mHealth. New monitoring approaches, combined with the development of novel sensors will form a system that will address the needs of patients on a daily basis.”

EU funded 3 year project

What is there out there?

“Smartinhaler” = Sellotape

Propeller (Propeller Health)

CareTRx (Teva)

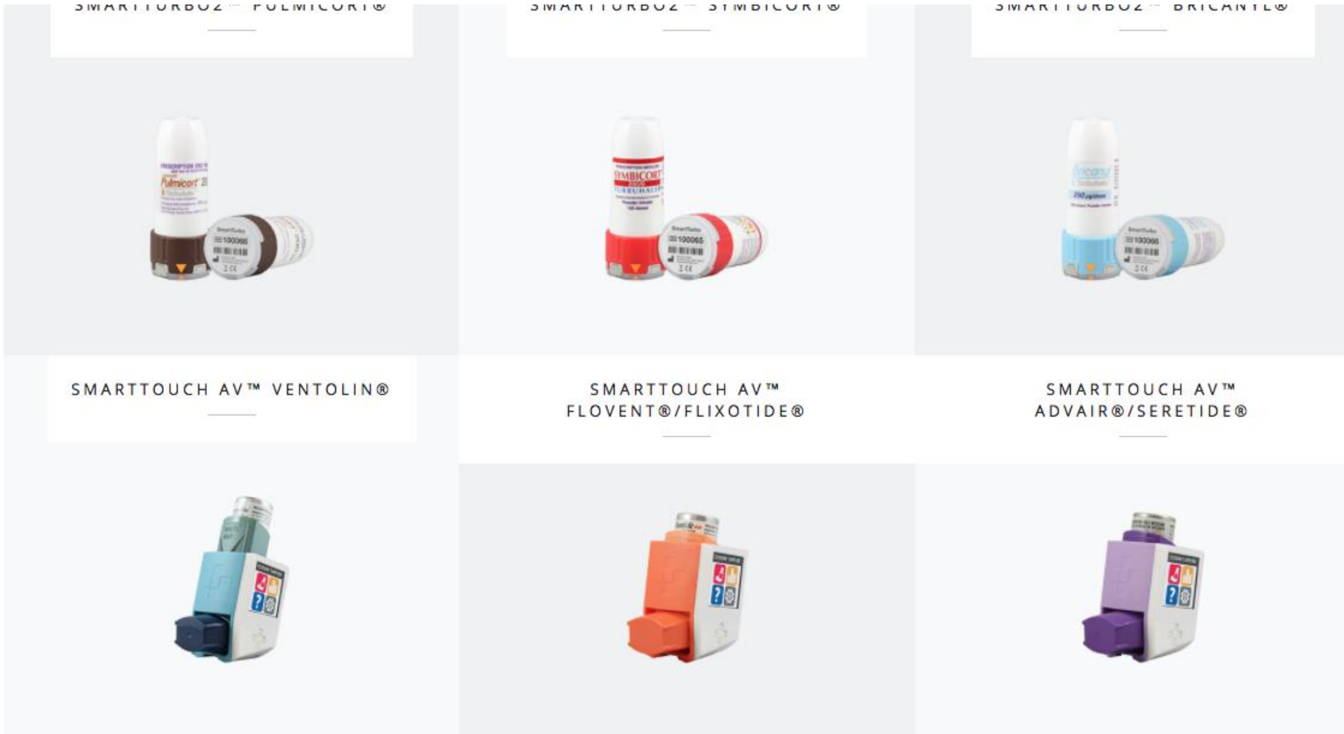
HeroTracker (Cohero Health)

HEROTRACKERS

HeroTrackers record your inhaler usage.

Bluetooth enabled medication inhaler sensors designed for both control and rescue medications fit most MDI and Diskus inhalers and automatically track when you use each of your respiratory medications.

SmartInhaler (Adherium)

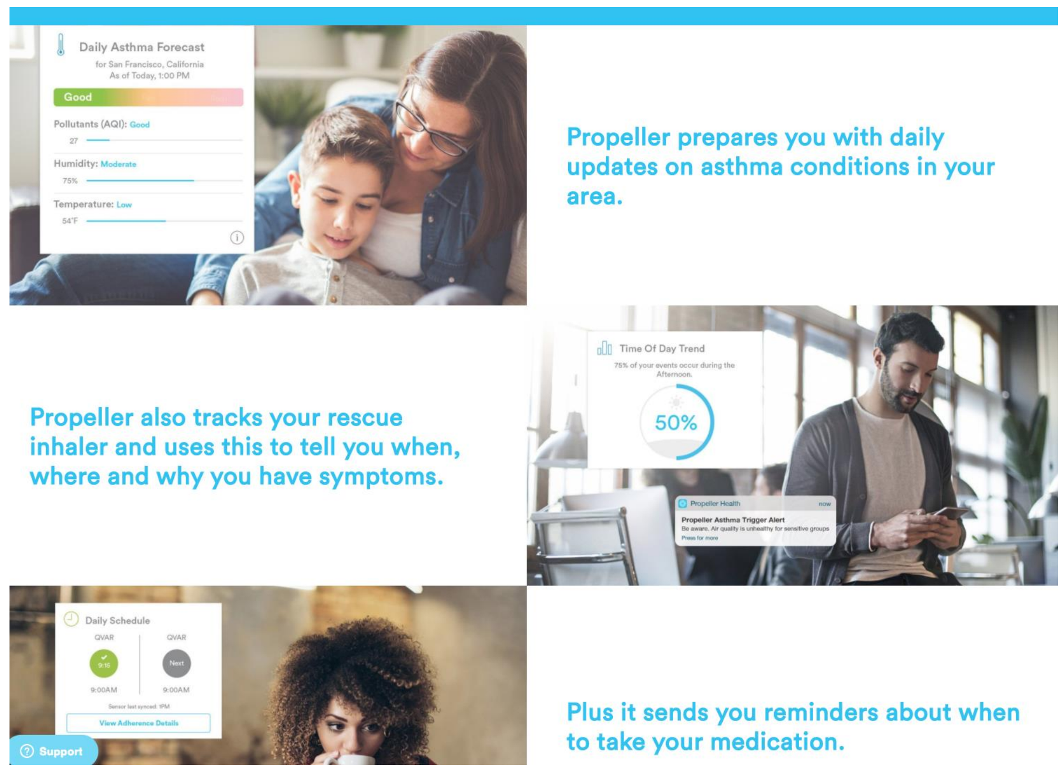


Some general points

- Currently marketed in USA, available online
- Tech companies partnering with Pharma
  - E.g. Smartinhaler with AstraZeneca, Propeller with GSK, etc
- Clip-on devices (next generation integrated)
  - "Most people with asthma (over 70%) have shown that they are happy to carry an additional device with them were it designed to monitor their inhaler usage" (myAirCoach public deliverable 2015).
- Bluetooth/GPS
- Combination of sensors e.g. microphone, infrared and accelerometer to detect device actuation.

Some general points

- Come with software
- Data sharing potentially with patient, clinician (and company)



Next generation devices

- Integrated within inhaler (Qualcomm/Novartis)
- Data on technique (using acoustic information)
  - Trials in progress

Potential downsides

- Adherence is complex
- How long will the effect last/‘the Fitbit effect’
- ‘Level of interactivity with a given digital technology’
- Need smartphone/bluetooth
- Multiple devices/apps (for pt and clinician)
- Multiple alerts
- Who’s responsible/ Big brother
- Regular fees
- Training/Resources (for patient and clinician)
- Not all devices for all inhalers ?change needed to get the device you wanted

NICE National Institute for Health and Care Excellence

NICE advice

Smartinhaler for asthma

Medtech innovation briefing

Published: 11 January 2017

nice.org.uk/guidance/mib90

- Different devices, £100 each (not including medication)
- £14.71 per month subscription for a healthcare professional logging on to system (free for the patient
- Device moved between inhalers but lifespan 1-2 years

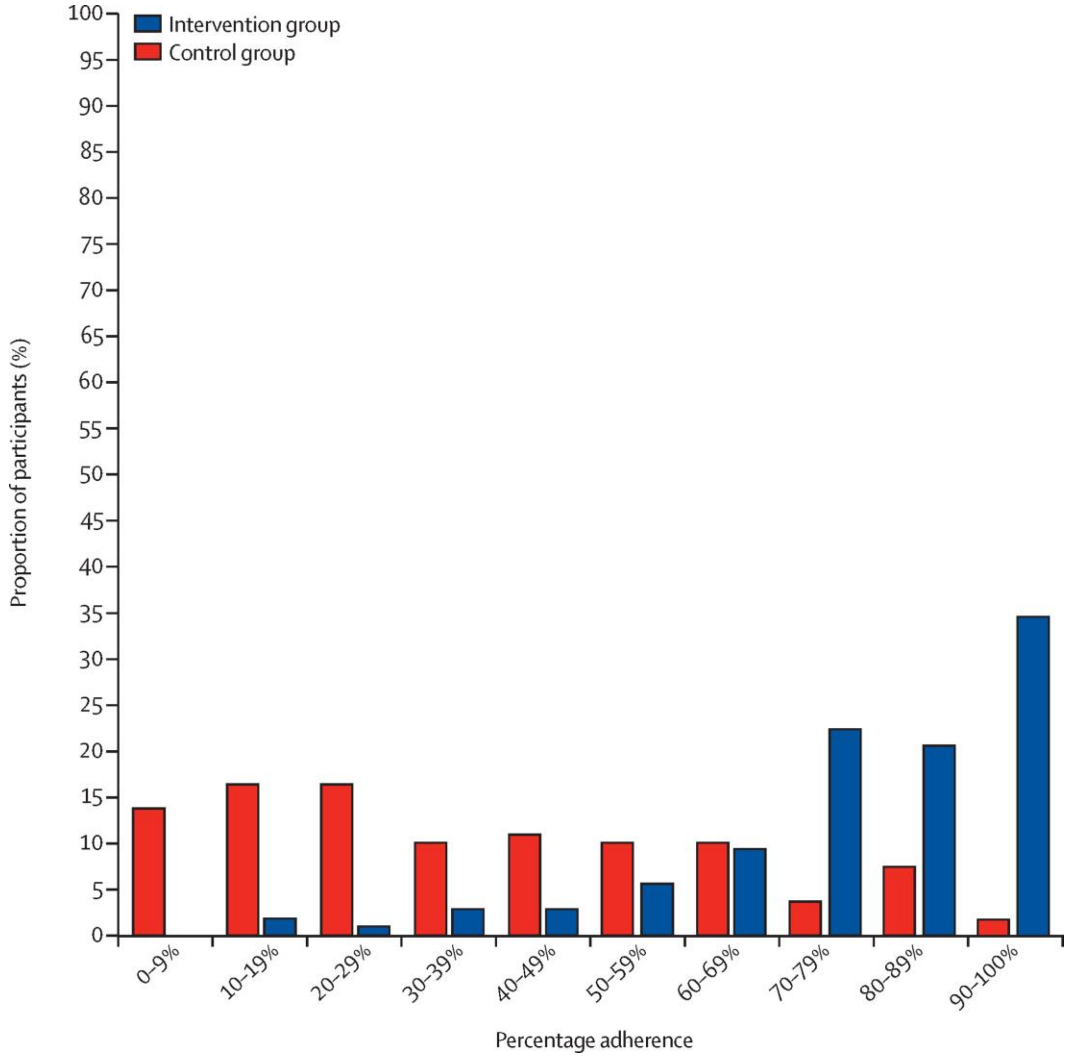
NICE assessment of Smartinhaler

- 5 RCT’s, 589 patients, adults and children, different countries.
- Devices generally accurate/reliable
- Adherence generally increased
- Differing effects on clinical outcomes e.g. control/exacerbations
  - May depend on population studied/baseline level of control
- Is it cost-effective

THE REAL WORLD

1st example

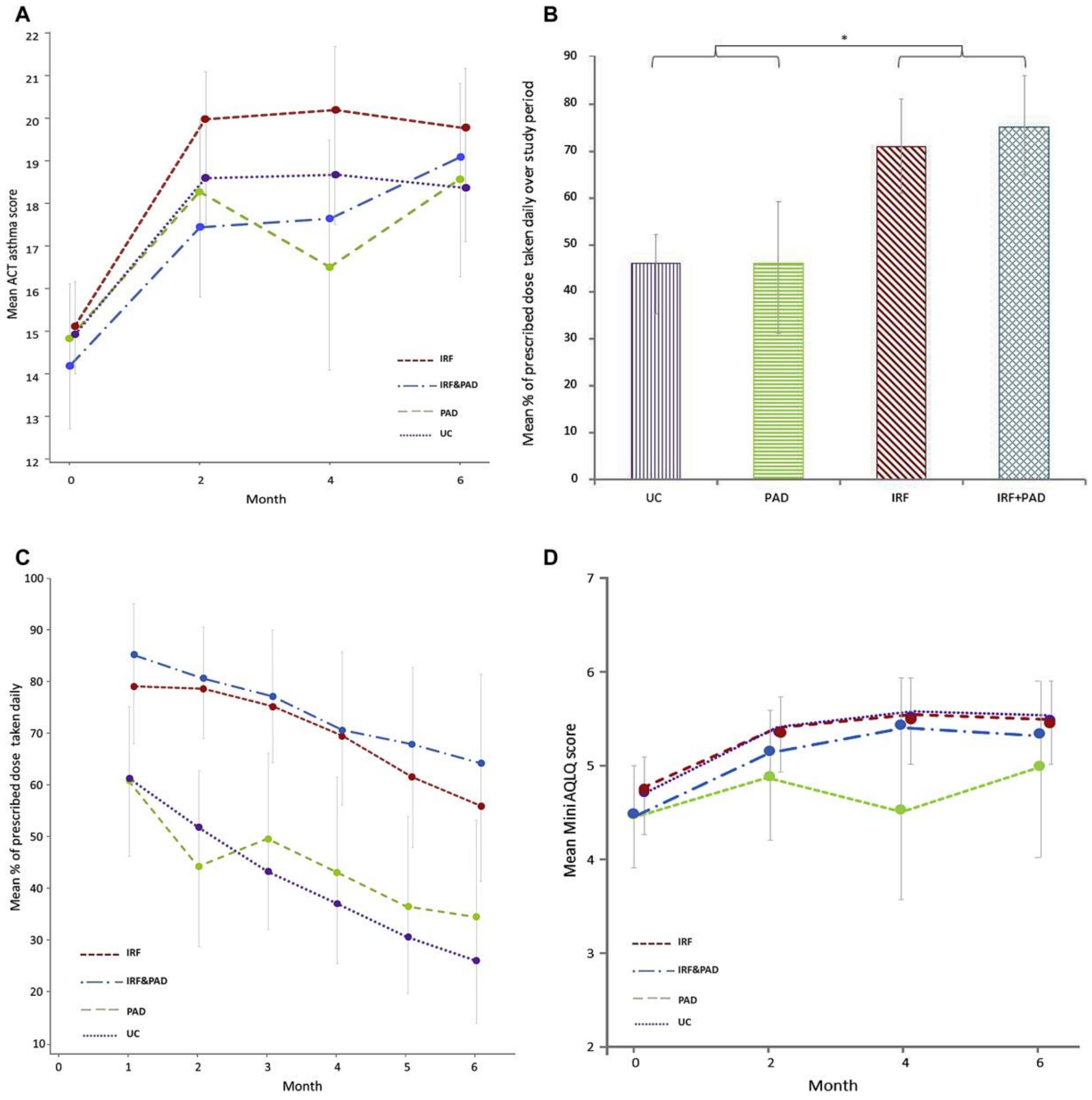
- Chan et al, Lancet Resp Med 2015
  - 220 children (6-15 years) attending ED with exacerbation (New Zealand)
  - Smartinhaler AV device attached to preventer inhalers but with reminders turned on/off.
  - All switched to fluticasone/Seretide
  - 2 monthly follow-up for 6 months
  - Mean adherence 84% in intervention group, 30% in control group
  - No difference in absenteeism
  - Better ACT scores, Less SABA usage
  - Less exacerbations reported (but only first 2 months, small numbers)



The Lancet Respiratory Medicine 2015 3,

2nd example

- Forster et al, JACI 2014 134
  - 143 patients (age 14-65)
  - Australian GPs in 4 practises, GP’s trained in delivering action plan, inhaler technique review and education
  - Patients randomised to above ‘usual care’ +/- ‘personalised adherence discussion’ +/- Smartinhaler (4 groups)
  - Data collected at 0,2,4 and 6 months
  - Adherence better with Smartinhaler (but drifted down over time)
  - No difference in clinical outcomes (as all groups did better)



Journal of Allergy and Clinical Immunology 2014 134,

3rd example

- Propeller Health sensor
- 2 x US ‘healthcare units’, asthma registry, invitation letter and doctor referral, age 5 upwards
- Sensor attached to SABA, intervention group and their doctors had access to data (to guide treatment decisions)
- Followed up for a year, 495 patients

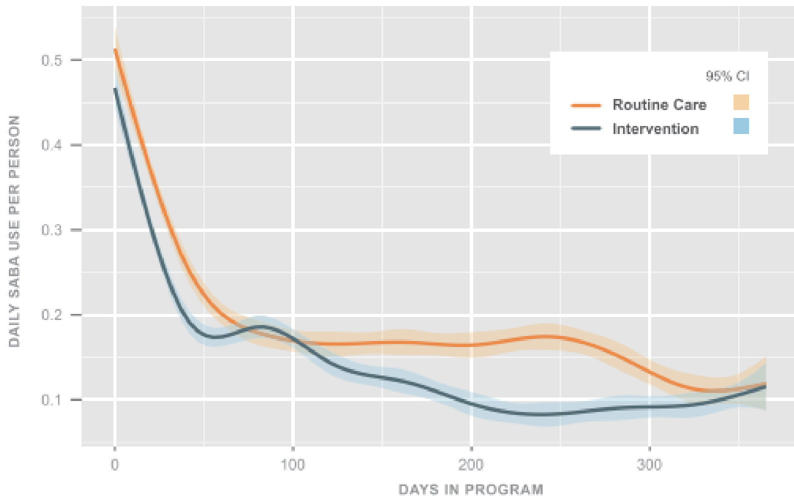


FIGURE 2. All participants: mean daily short-acting β-agonist (SABA) use per person.

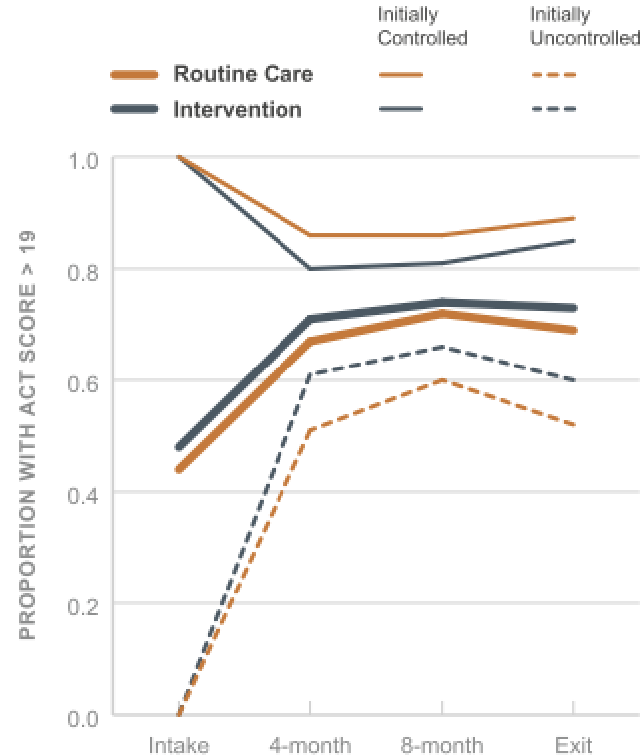


FIGURE 4. All participants: proportions with Asthma Control Test (ACT) score > 19.

TABLE VI. ACT scores

	Study arm	n	Mean ACT score, baseline period	Mean ACT score, study period	Change from baseline to study period	*P* value comparing changes in intervention vs routine care
Adults, initially uncontrolled	Routine care	113	14.2	18.8	+4.6	
	Intervention	106	13.8	20.0	+6.2	.009
Children, initially uncontrolled	Routine care	23	15.0	21.0	+6.0	
	Intervention	22	15.1	20.0	+4.9	.40
Adults, initially controlled	Routine care	87	22.2	21.9	−0.3	
	Intervention	93	22.1	22.2	+0.1	.45
Children, initially controlled	Routine care	22	23.3	22.7	−0.6	
	Intervention	25	21.6	21.4	−0.2	.71

ACT, Asthma Control Test.
Initial asthma control as determined by ACT.
Baseline period is visit 1 (enrollment). Study period is visits 2-4.

Cochrane review

- April 2017 "Interventions to improve adherence to inhaled steroids for asthma"
  - Effect of electronic trackers or reminders, 11 studies, follow-up ~30-50 weeks

Outcome	Anticipated absolute effect (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)
	Control Group	Treatment group			
% Adherence (measured objectively)	Mean adherence 53.3%	Mean adherence 19.9% higher in this group (14.5-25.3)		555 (6 RCTs)	Moderate
Exacerbations requiring OCS	218 per 1000	169 per 1000	OR 0.72 (0.37-1.39)	3063 (4 RCTs)	Very Low
ACQ	Mean score 0.89	Mean score 0.24 better in this group (0.29 worse - 0.78 better)		109 (2 RCT's)	Low
Emergency visit to healthcare	84 per 1000	95 per 1000	OR 1.14 (0.88-1.47)	2918 (2 RCT's)	Moderate
AQLQ	Mean score 5.15	Mean score 0.03 worse (0.13 better to 0.2 worse)		369 (4 RCT's)	Moderate

Summary

- Smartinhalers are coming/already here
- Likely to improve with time
- May bring problems as well as solve them
- Improve adherence, do they improve clinical outcomes?
- Who would/should get them
  - ?Adolescents/poorly controlled/ED attenders/proven non-adherers/mental health problems/cognitive defects/FeNO high patients/other
- Need to show they're cost-effective

A smart person knows what to say.

A wise person knows whether to say it or not.