Remote Patient Monitoring and Digital Health for Patients with Difficult-to-Control Asthma

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Disclosures

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Learning Objectives

- Define Difficult-to-Control vs Severe Asthma
- Understand the impact of Inhaled Corticosteroid (ICS) Adherence
- Understand the impact of Inhaler Technique
- Describe the Potential Role of Digital Inhaler Systems as a Diagnostic Tool and Therapeutic Intervention

Difficult-to-Control vs Severe Asthma

Difficult-to-treat asthma[144] is asthma that is uncontrolled despite prescribing of medium or high dose inhaled corticosteroids (ICS) with a second controller (usually LABA) or with maintenance OCS, or that requires high dose treatment to maintain good symptom control and reduce the risk of exacerbations. It does not mean a 'difficult patient'. In many cases, asthma may appear to be difficult-to-treat because of modifiable factors such as incorrect inhaler technique, poor adherence, smoking or comorbidities, or because the diagnosis is incorrect.

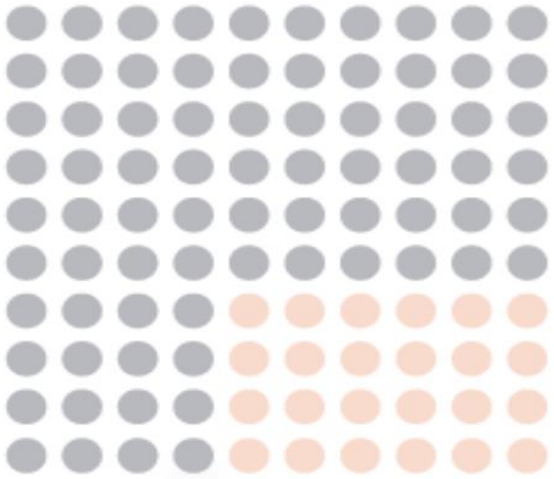
Severe asthma[144] is a subset of difficult-to-treat asthma (Box 3-15). It means asthma that is uncontrolled despite adherence with maximal optimized high dose ICS-LABA treatment and management of contributory factors, or that worsens when high dose treatment is decreased.[144] At present, therefore, 'severe asthma' is a retrospective label. It is sometimes called 'severe refractory asthma'[144] since it is defined by being relatively refractory to high dose inhaled therapy. However, with the advent of biologic therapies, the word 'refractory' is no longer appropriate.

Asthma is not classified as severe if it markedly improves when contributory factors such as inhaler technique and adherence are addressed.[144]

Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2021. https://ginasthma.org/

Difficult-to-Control vs Severe Asthma

Box 3-15. What proportion of adults have difficult-to-treat or severe asthma?



24%

High intensity treatment
= high dose ICS-LABA or medium dose ICS-LABA + OCS)

17%

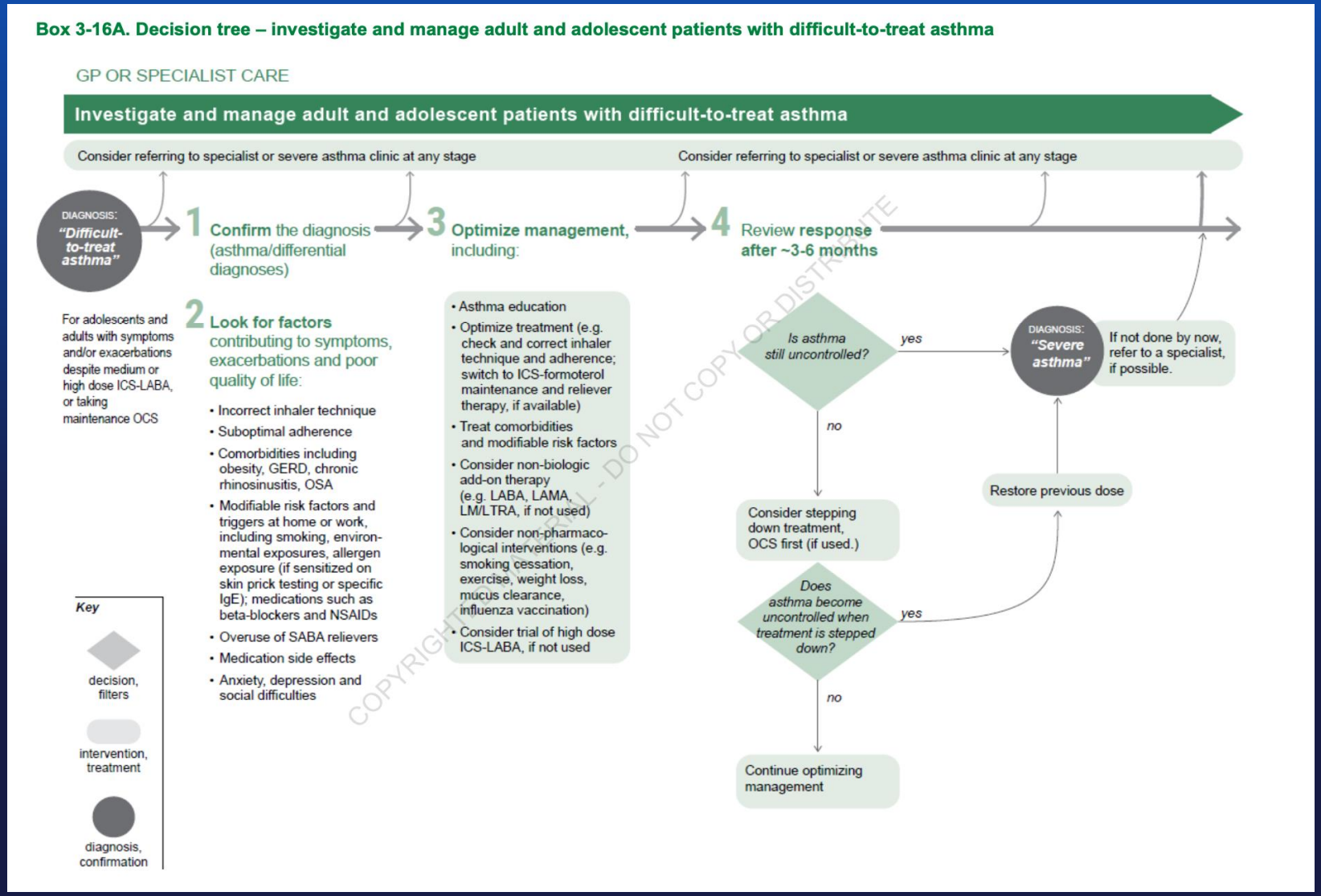
difficult-to-treat asthma
= high intensity treatment + poor symptom control

3.7%

severe asthma
= high intensity treatment + poor symptom control + good adherence and inhaler technique

Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2021. https://ginasthma.org/

Difficult-to-Control vs Severe Asthma



Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2021. https://ginasthma.org/

Definition of Adherence

[T]he extent to which a person's behavior, taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider

Chakrabarti S. What's in a name? Compliance, adherence and concordance in chronic psychiatric disorders. World J Psychiatry. 2014 June 22;4(2)30-36. Doi: 10.5498/wjp.v4.i2.30.

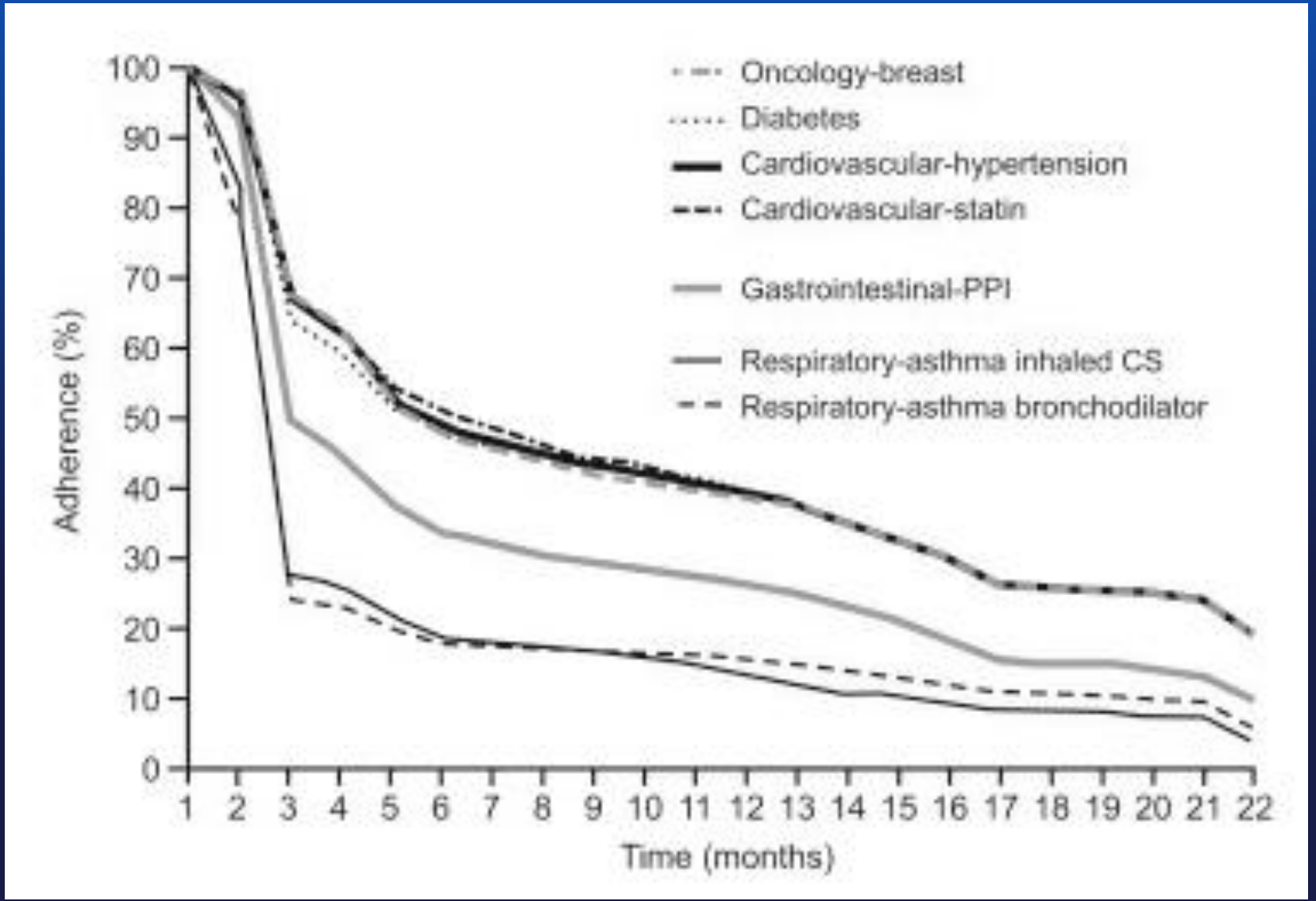
Types of Non-Adherence

- Intentional: lack of confidence that treatment works, denial of diagnosis, concerns about side effects, beliefs that treatment can be stopped because symptoms have improved, and cost.

- Unintentional: poor inhaler technique (even though patient thinks that they are using it correctly), lack of understanding as to when to use the inhaler, forgetfulness, and cannot keep a routine.

Dekhuijzen, R, Lavorini, F, Usmani, O, van Boven, J. Journal of Allergy and Clinical Immunology: In Practice, 2018-05-01 , Volume 6, Issue 3, Pages 785-793.

Adherence Across Chronic Diseases



Smith IJ, Bell J, Bowman N, Everard M, Stein S, Weers JG. Inhaler devices: What remains to be done? J Aerosol Med Pulm Derug Deliv 2010;23(Suppl 2);S25-37.

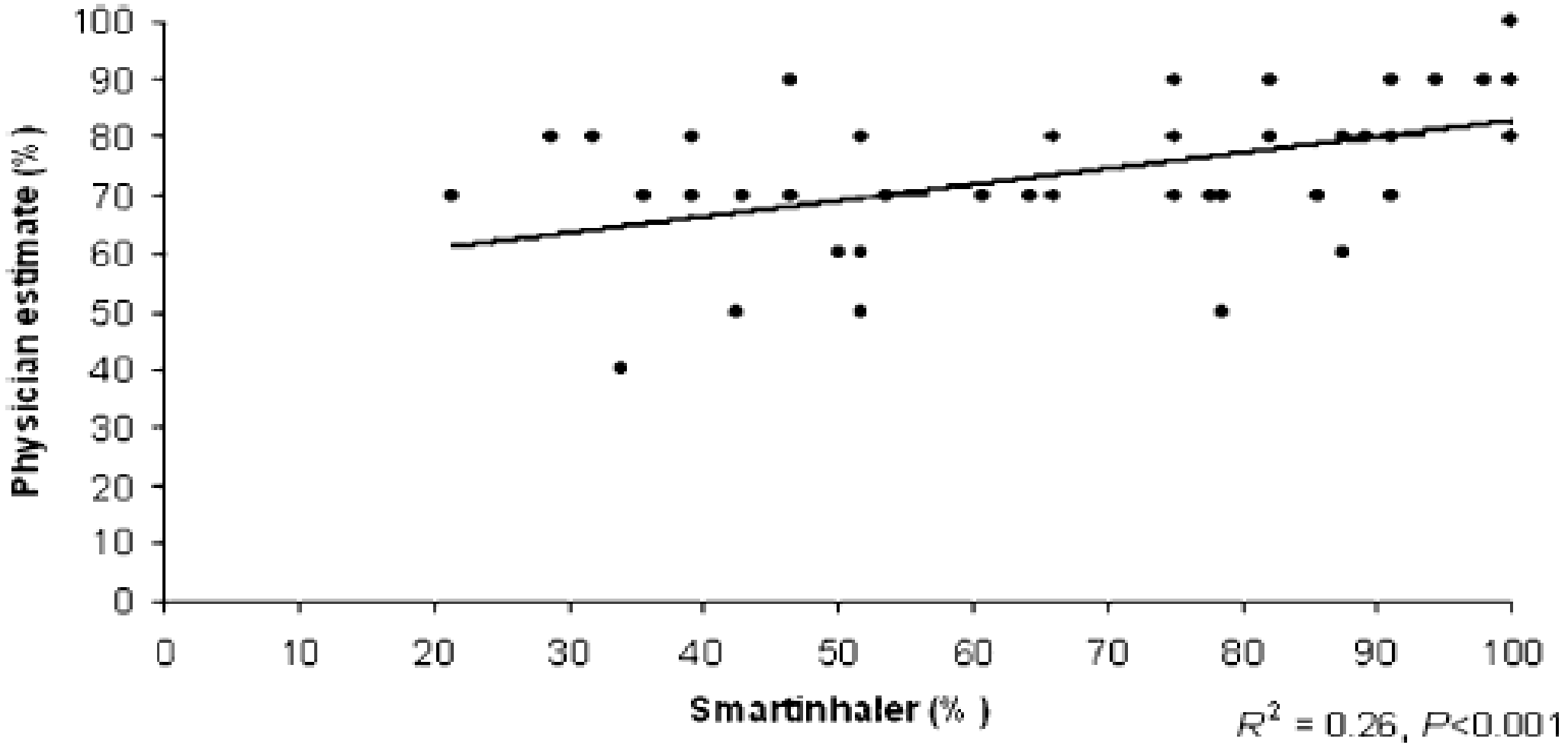
Clinically Significant Adherence

Although incremental improvements in inhaled corticosteroid adherence may be associated with a decreased risk of exacerbations, this relationship is nonlinear and that an adherence threshold of 75% of the prescribed dose is required to significantly reduce exacerbations.[1]

A study analyzing prescription refill data in patients with difficult-to-control asthma determined good adherence to be ≥ 80%.

1. Williams LK, Peterson EL, Wells K, Ahmedani BK, Kumar R, Burchard EG, et al. Quantifying the proportion of severe asthma exacerbations attributable to inhaled corticosteroid nonadherence. J Allergy Clin Immunol 2011;128;1185-91.e2.
2. Murphy AC, Proeschal A, Brightling CE, Wardlaw AJ, Pavord I, Bradding P, et al. The relationship between clinical outcomes and medication adherence in difficult-to-control asthma. Thorax 2012:67;751-3.

HCP Judgement of Patient Adherence is Inaccurate



Burgess SW, Sly PD, Morawska A, Devadason SG. Assessing adherence and factors associated with adherence in young children with asthma. Respirology 2008:13:559-63.0

Patient Self-Reported Adherence is Unreliable

Original Article

The Impact of Peer Support and mp3 Messaging on Adherence to Inhaled Corticosteroids in Minority Adolescents with Asthma: A Randomized, Controlled Trial

Giselle Mosnaim, MD, MS[a], Hong Li, PhD[a], Molly Martin, MD, MAPP[a], DeJuran Richardson, PhD[a,b], Paula Jo Belice, MS[a], Elizabeth Avery, MSPH[a], Norman Ryan, MD[c], Bruce Bender, PhD[d], and Lynda Powell, PhD[a] *Chicago, Ill; and Denver, Colo*

What is already known about this topic? A lack of adherence to inhaled corticosteroids is a significant risk factor for poor asthma outcomes among low-income African American and Hispanic adolescents with persistent asthma.

What does this article add to our knowledge? Face-to-face coping peer support and mp3-delivered peer asthma messages do not appear to influence adherence to inhaled corticosteroids among inner-city minority adolescents with persistent asthma.

How does this study impact current management guidelines? Asthma guidelines recommend monitoring patient adherence to his or her pharmacotherapeutic regimen at each visit. Reliance on self-report of adherence to inhaled corticosteroid medications among urban minority adolescents may give clinicians inadequate information to adjust their treatment regimens.

Mosnaim G, Li H, Martin M, Richardson D, Belice PJ, Avery E, Ryan N, Bender B, Powell L. The impact of peer support and mp3 messaging on adherence to inhaled corticosteroids in minority adolescents with asthma: a randomized, controlled trial. J Allergy Clin Immunol Pract. 2013 Sep-Oct;1(5):485-93.

Patient Self-Reported Adherence is Unreliable

Table III

Objectively Measured and Self-Reported Adherence to Inhaled Corticosteroids

This table shows differences in objectively measured versus self-reported adherence at week 5 and week 10 of the active treatment phase for treatment and attention control groups. Only participants whose self-reported data was available for the same two weeks as their objectively measured data were included.

	Week 5					Week 10				
	Objectively Measured		Self-Reported			Objectively Measured		Self-Reported		
Group	N	Median (Q1, Q3)	N	Median (Q1, Q3)	*P* value	N	Median (Q1, Q3)	N	Median (Q1, Q3)	*P* value
Treatment	19	16.1 (3.6, 23.2)	23	50.0 (30.4, 82.1)	0.0007	18	6.3 (1.8, 14.3)	21	50.0 (35.7, 78.6)	<.0001
Control	17	16.1 (14.3, 19.6)	20	63.4 (49.1, 79.5)	<.0001	21	14.3 (5.4, 21.4)	22	61.6 (48.2, 82.1)	<.0001
Total	36	16.1 (7.1, 22.3)	43	57.1 (41.1, 82.1)	<.0001	39	7.1 (1.8, 21.4)	43	57.1 (39.3, 78.6)	<.0001

Mosnaim G, Li H, Martin M, Richardson D, Belice PJ, Avery E, Ryan N, Bender B, Powell L. The impact of peer support and mp3 messaging on adherence to inhaled corticosteroids in minority adolescents with asthma: a randomized, controlled trial. J Allergy Clin Immunol Pract. 2013 Sep-Oct;1(5):485-93.

Patient Self-Reported Adherence is Unreliable

Participant self-report was significantly greater than objectively measured ICS adherence (97% vs 75%, p = 0.002)

Mosnaim GS, Stempel DA, Gonzalez C, Adams B, BenIsrael-Olive N, Gondalia R, Kaye L, Shalowitz M, Szefler S. Electronic Medication Monitoring versus Self-Reported Use of Inhaled Corticosteroids and Short-Acting Beta-Agonists in Uncontrolled Asthma. J Asthma 2021 Nov 2:1-4.

Which of the following is NOT one of the most common (white) lies people tell?

- I'm almost there
- It must have gone to my spam folder
- I'm good
- I have 11 goldfish and love to wash dishes

https://www.redbookmag.com/life/g27077358/lies-everyone-teslide=15tolls/?

Measuring ICS Medication Adherence

Prescription refill data may not indicate ingestion and are vulnerable to recording bias due to the use of multiple pharmacies or stockpiling[1]

The ideal measure of adherence should be objective, accurate and unobtrusive to minimize impact on patient behavior, and allow reliable data collection in real world settings[2]

Electronic medication monitors are the criterion standard among adherence measurement methods for inhaler treatments[1]

1: Hai Yan Chan, A, Harrison, J, Black,P, Mitchell, E, Foster, J. Using Electronic Monitoring Devices to Measure Inhaler Adherence: A Practical Guide for Clinicians. J Allergy Clin Immunol Pract 2015;3:335-49
2: Denhaerynck K, Schafer-Keller P, Young J, Steiger J, Bock A, De Geest S. Examining assumptions regarding valid electronic monitoring of medication therapy; development of a validation framework and its application on a European sample of kidney transplant patients. BMC Med Res Methodol 2008;8:5.

The Importance of Inhaler Technique

Original Article

Inhaler Errors in the CRITIKAL Study: Type, Frequency, and Association with Asthma Outcomes

David B. Price, FRCGP[a,b], Miguel Román-Rodríguez, MD[c], R. Brett McQueen, PhD[d], Sinthia Bosnic-Anticevich, BPharm (Hons), PhD[e,f], Victoria Carter, BSc[g], Kevin Gruffydd-Jones, BM BCh, FRCGP[h], John Haughney, FRCPE, FRCGP[a], Svein Henrichsen, MD[i], Catherine Hutton, BA[b], Antonio Infantino, MD[j], Federico Lavorini, MD, PhD[k], Lisa M. Law, MSc[b], Karin Lisspers, MD, PhD[l], Alberto Papi, MD[m], Dermot Ryan, MD[g,n], Björn Ställberg, MD, PhD[l], Thys van der Molen, MD, PhD[o], and Henry Chrystyn, Phd, FRPHarmS[b,p] *Aberdeen, Cambridge, Box, Edinburgh, and Plymouth, United Kingdom; Singapore, Singapore; Palma de Mallorca, Spain; Aurora, Colo; Sydney, Australia; Oslo, Norway; Bari, Florence, and Ferrara, Italy; Uppsala, Sweden; and Groningen, The Netherlands*

What is already known about this topic? The literature highlights the problem of poor inhaler technique, but to date no study has identified inhaler errors associated with poor outcomes.

How does this article add to our knowledge? Specific inhaler errors, while using either a Diskus or Turbohaler dry-powder inhaler or a metered-dose inhaler, have been identified by their frequency and their adverse impact on asthma outcomes.

How does this study impact current management guidelines? This study provides information on the key errors made when using inhalers. These errors may be targeted in asthma management, to improve inhaler training and potentially improve patient outcomes.

Price DB, Roman-Rodriguez M, McQueen RB, Bosnic-Anticevich S, Carter V, Gruffydd-Jones K, Haughney J, Henrichsen S, Hutton C, Infantino A, Lavorini F, Law LM et al. Inhaler Errors in the CRITIKAL Study: Type, Frequency and Association with Asthma Outcomes. J Allergy Clin Immunol Pract. 2017 Jul-Aug;5(4);1071-1081.e9

Has Patient Inhaler Technique Improved Over Time?

Sanchis, J, Gich I. Pederson S. Systematic review of errors in inhaler use: Has patient technique improved over time? Chest 2016;150;394-406.

Which of the following statements about inhaler technique is correct?

Of asthma patients under specialist care, inhaler technique is checked in 80%[1]

In a recent meta-analysis, only 15.5% of HCPs demonstrated proficiency in use of MDIs and DPIs[2]

Actual adherence is adherence based on time of medication use[3]

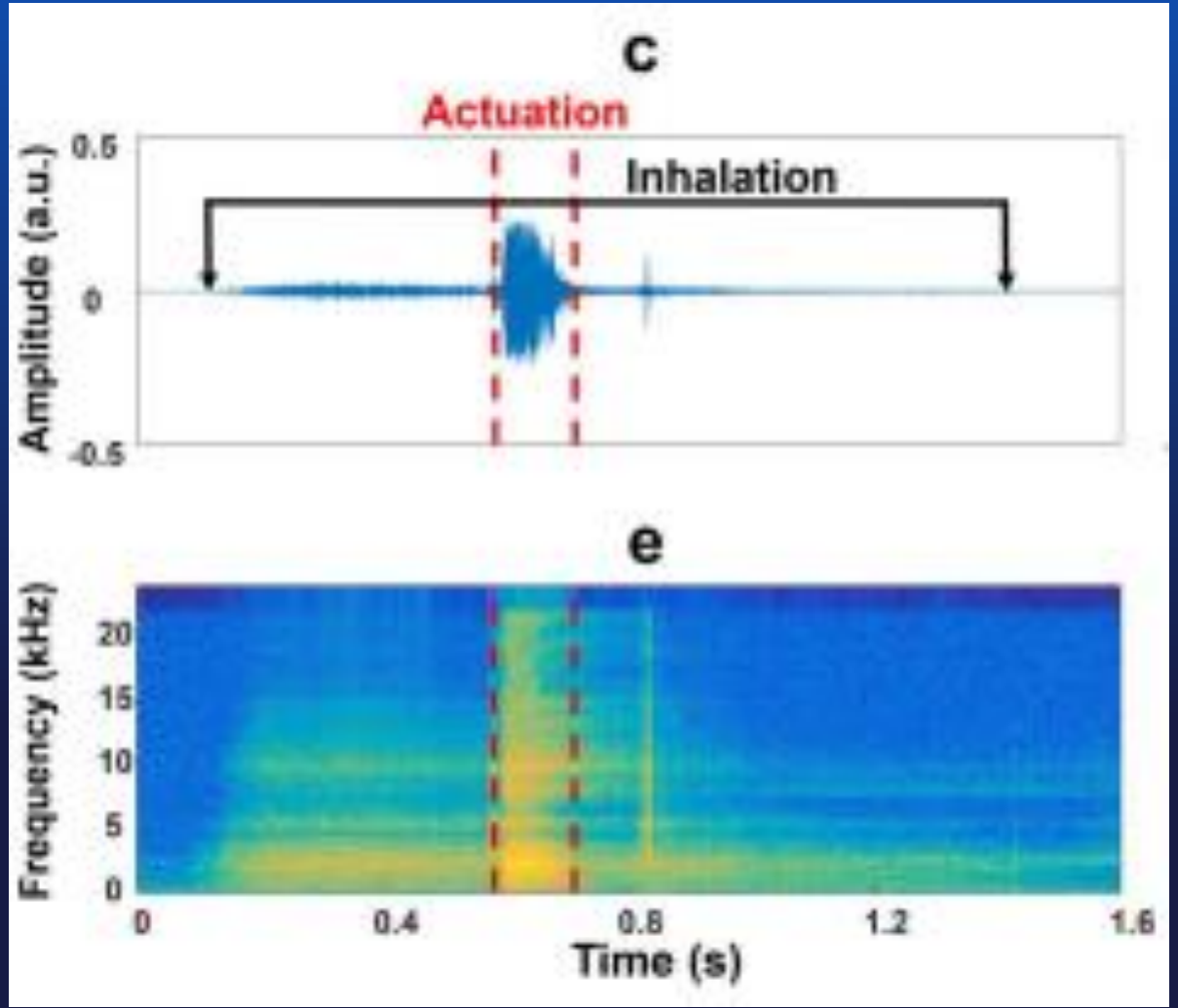
Attempted adherence is adherence based on proper use of the inhaler[3]

1: von Bulow A, Backer V, Bodtger U, Soes-Petersen NU, Assing KD, Skjold et. al. The level of diagnostic assessment in severe asthma: a nationwide real-life study. Respir Med 2017:124:21-9

2: Plaza V, Giner J, Rodrigo GJ, Dolovich MB, Sanchis J, Errors in the use of inhalers by health care professionals: a systematic review. J Allergy Clin Immunol Pract 2018;6:987-95.

3: Sulaiman I, Scheult J, Sadsivuni N, MacHale E, Killane I, Giannoustos S, et al. The impact of common inhaler errors on drug delivery: investigating critical errors with a dry powder inhaler. J Aerosol Med Pulm Drug Deliv 2017;30:247-55.

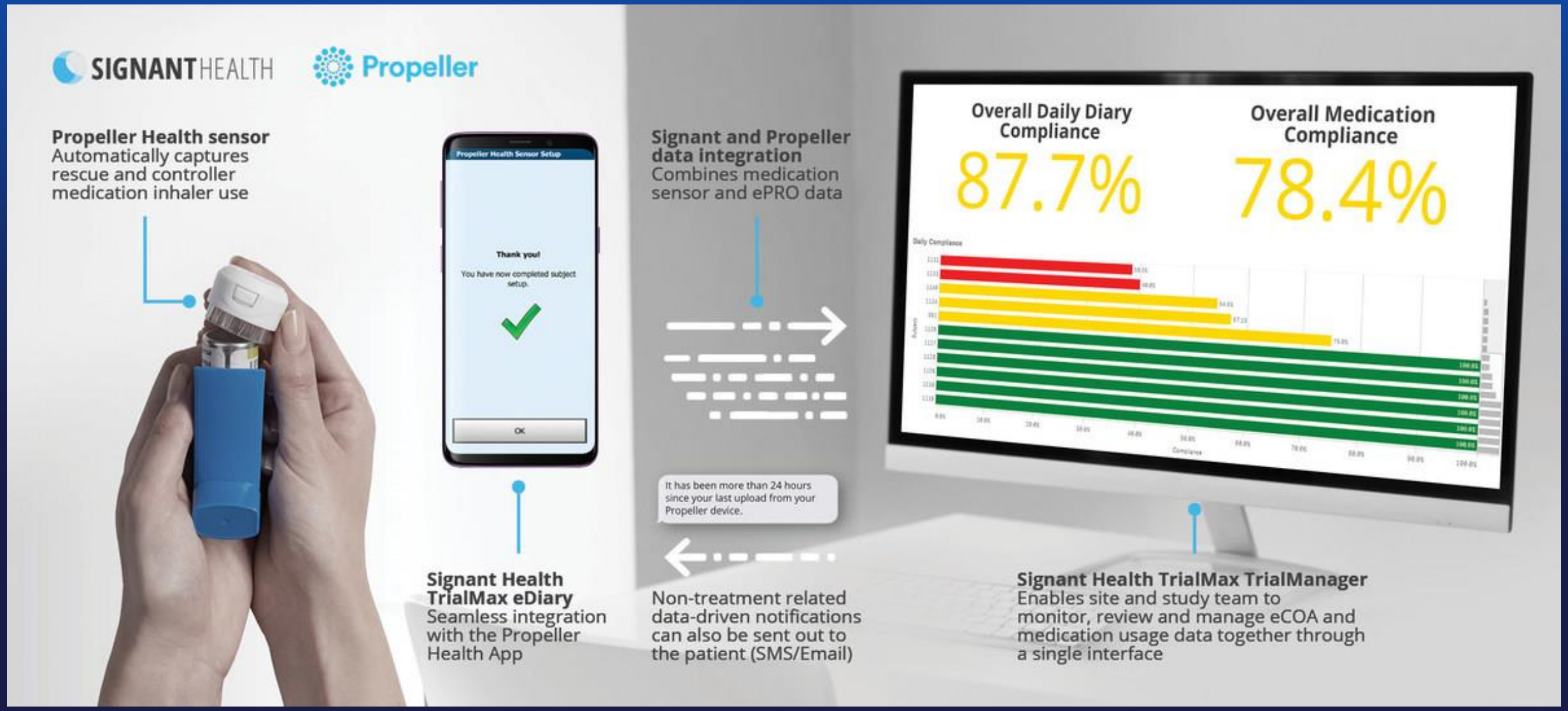
The INCA Device



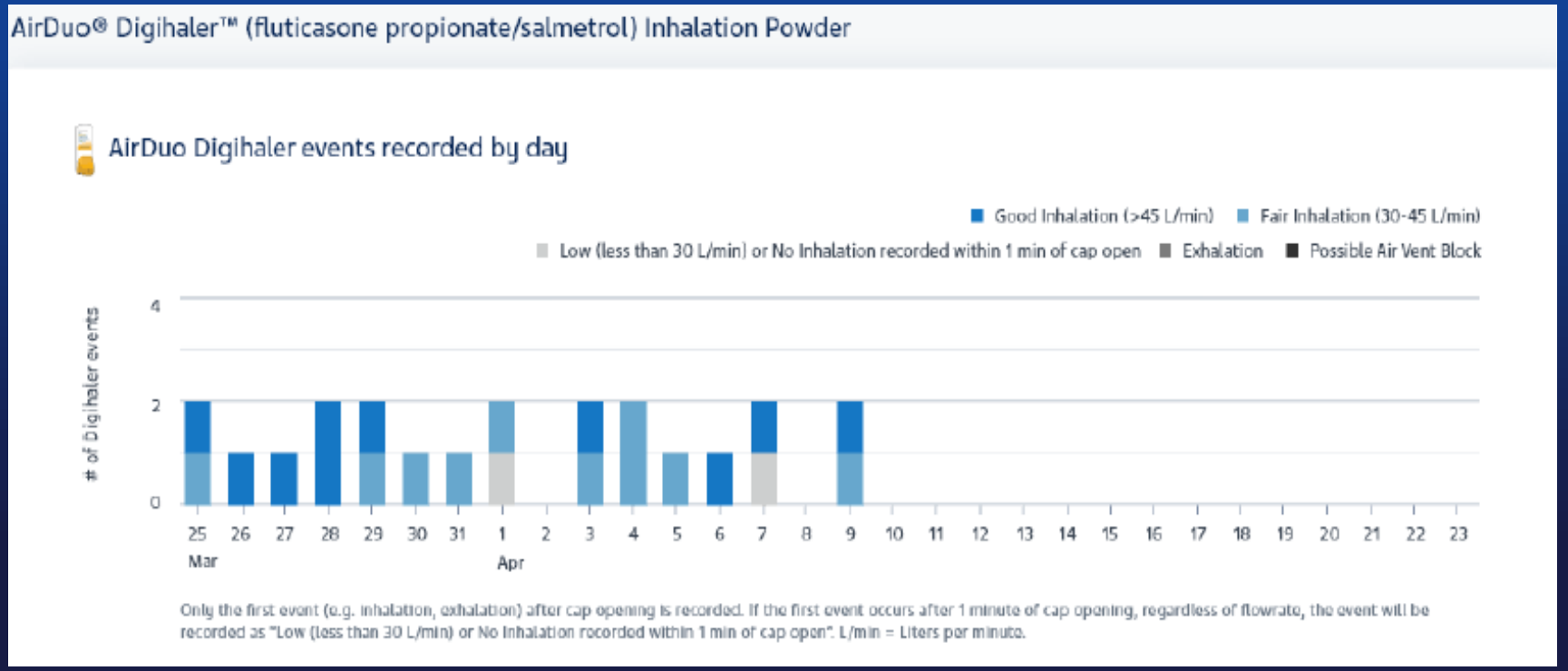
Martin S Holmes 1, Jansen N Seheult, Colm Geraghty, Shona D'Arcy, Ultan O'Brien, Gloria Crispino O'Connell, Richard W Costello, Richard B Reilly. Physiol Meas. 2013 Aug;34(8):903-14.

Terence E. Taylor1,2, Yaniv Zigel1,3, Clarice Egan4, Fintan Hughes1, Richard W. Costello4 & Richard B. Reilly 1,2. Objective Assessment of Patient Inhaler User Technique Using an Audio-Based Classification Approach. Sci Rep 8, 2164 (2018).

The Propeller Health Platform



The Digihaler Platform



https://www.ux-designawards.com/en/gewinner/digihaler-system

https://www.digihaler.com/globalassets/css-official/digihaler-dashboard-reference-guide.pdf

Original Article

Digital Health Technology in Asthma: A Comprehensive Scoping Review

Giselle Mosnaim, MD, MS[a], Guilherme Safioti, MD[b], Randall Brown, MD, MPH[c], Michael DePietro, MD[c], Stanley J. Szefler, MD[d], David M. Lang, MD[e], Jay M. Portnoy, MD[f], Don A. Bukstein, MD[g], Leonard B. Bacharier, MD[h], and Rajan K. Merchant, MD, FACAAI[i] *Evanston, Ill; West Chester, Pa; Aurora and Cleveland, Colo; Kansas City, Mo; Greenfield, Wis; Nashville, Tenn; Woodland, Calif; and Amsterdam, The Netherlands*

What is already known about this topic? Digital technology provides an opportunity to improve and individualize asthma self-management significantly across a variety of intervention types; however, the impact of different digital intervention characteristics has yet to be assessed.

What does this article add to our knowledge? Significant heterogeneity exists in study designs, patient populations, and outcomes measurement for digital interventions; more alignment is needed to measure impacts accurately on different dimensions of care and to guide future successful interventions.

How does this study impact current management guidelines? This scoping review does not directly affect current guidelines for asthma self-management, but it is hoped that it will inform the design of future digital intervention studies.

Mosnaim G, Safioti G, Brown R, DePietro M, Szefler SJ, Lang DM, Portnoy JM, Bukstein DA, Bacharier LB, Merchant RK. Digital Health Technology in Asthma: A Comprehensive Scoping Review. J Allergy Clin Immunol Pract. 2021;9(6):2377-2398.

TABLE I. Classification of different intervention types

Intervention category	Intervention types
Generalized studies (not patient-specific or bidirectional): content given *to* patient	• Automated/speech recognition and SMS dose and pharmacy-refill reminders • Noninteractive education or motivational coaching by telephone, text, e-mail and other digital means (eg, simple access to static content)
Patient-specific, noninteractive studies (unidirectional): data collected *from* or sent *to* patient	• Decision support tool for randomized controlled trial enrollment • Device monitoring: noninhaler digital parameter tracking (eg, lung function) not resulting in immediate or ongoing asthma management feedback to patient (ie, data collection to inform health care professional at next visit) • Individualized static education and/or motivation • Digital questionnaires (by SMS/Web/phone) including ecological momentary association for data collection only (ie, not informing therapy) • Inhaler only: data collected on device from digital inhalers or adherence monitors but not fed back to patient for self-management • Inhaler platform: data collected from digital inhalers and a Web or app platform but not fed back to patient for self-management • Platform only: online digital chat platform (by Web or mobile app) providing nonindividualized education
Patient-specific interactive studies including telehealth and video counseling: bidirectional interaction	• Interactive education or motivational coaching • Device monitoring: noninhaler digital parameter tracking (eg, lung function, inhaler technique) with feedback to patient (usually by smartphone app) • Digital inhalers with electronic adherence monitors and individualized patient feedback • Digital inhaler studies with accompanying individualized asthma management Web or app platform • Interactive asthma management platforms that support self-management by collecting symptoms or Asthma Control Test/other data and give responses to guide patient's asthma treatment • Telemedicine interventions by phone, video, or SMS

Mosnaim G, Safioti G, Brown R, DePietro M, Szefler SJ, Lang DM, Portnoy JM, Bukstein DA, Bacharier LB, Merchant RK. Digital Health Technology in Asthma: A Comprehensive Scoping Review. J Allergy Clin Immunol Pract. 2021;9(6):2377-2398.

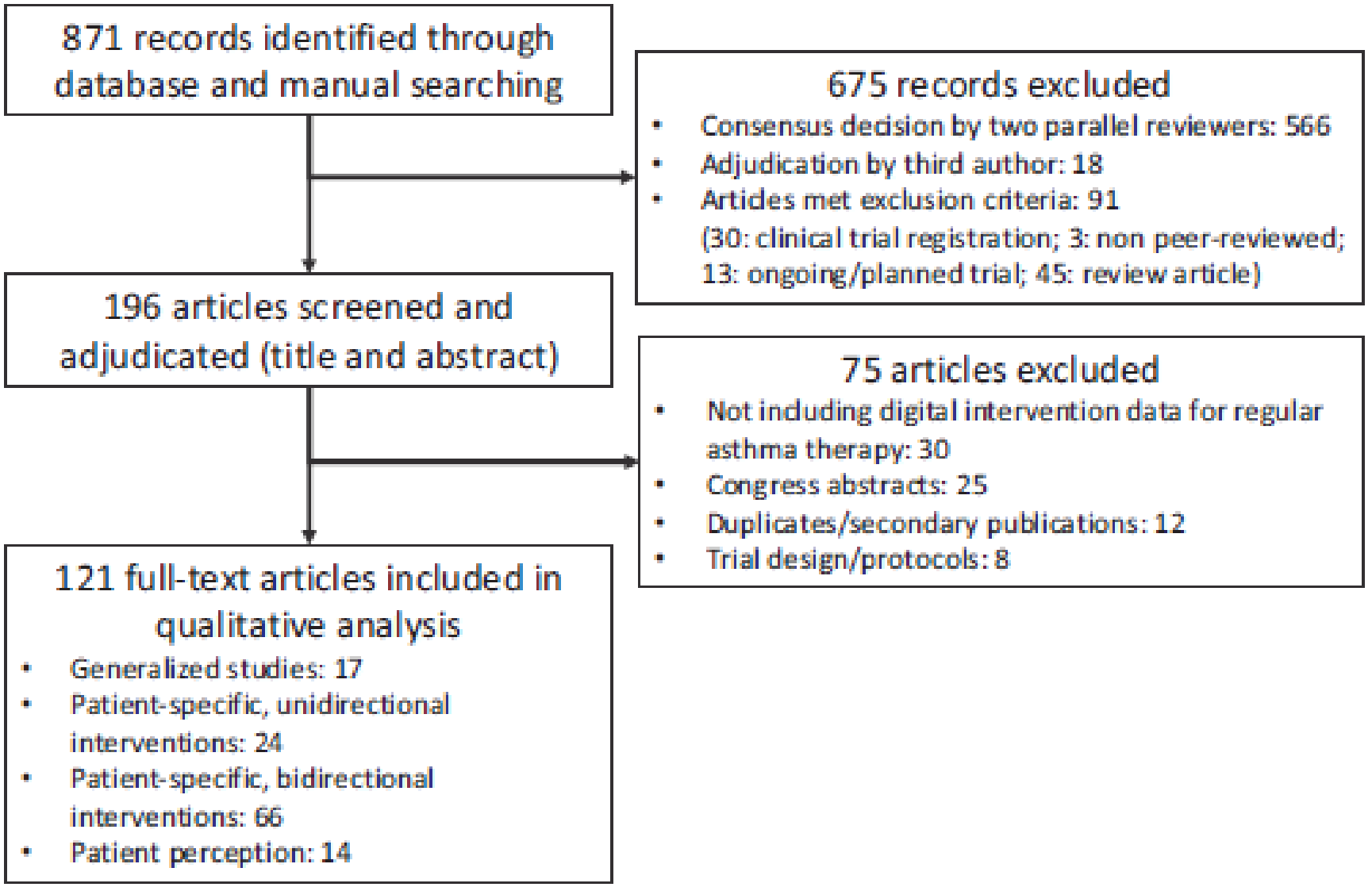


FIGURE 1. Articles selected for analysis.

Mosnaim G, Safioti G, Brown R, DePietro M, Szefler SJ, Lang DM, Portnoy JM, Bukstein DA, Bacharier LB, Merchant RK. Digital Health Technology in Asthma: A Comprehensive Scoping Review. J Allergy Clin Immunol Pract. 2021;9(6):2377-2398.

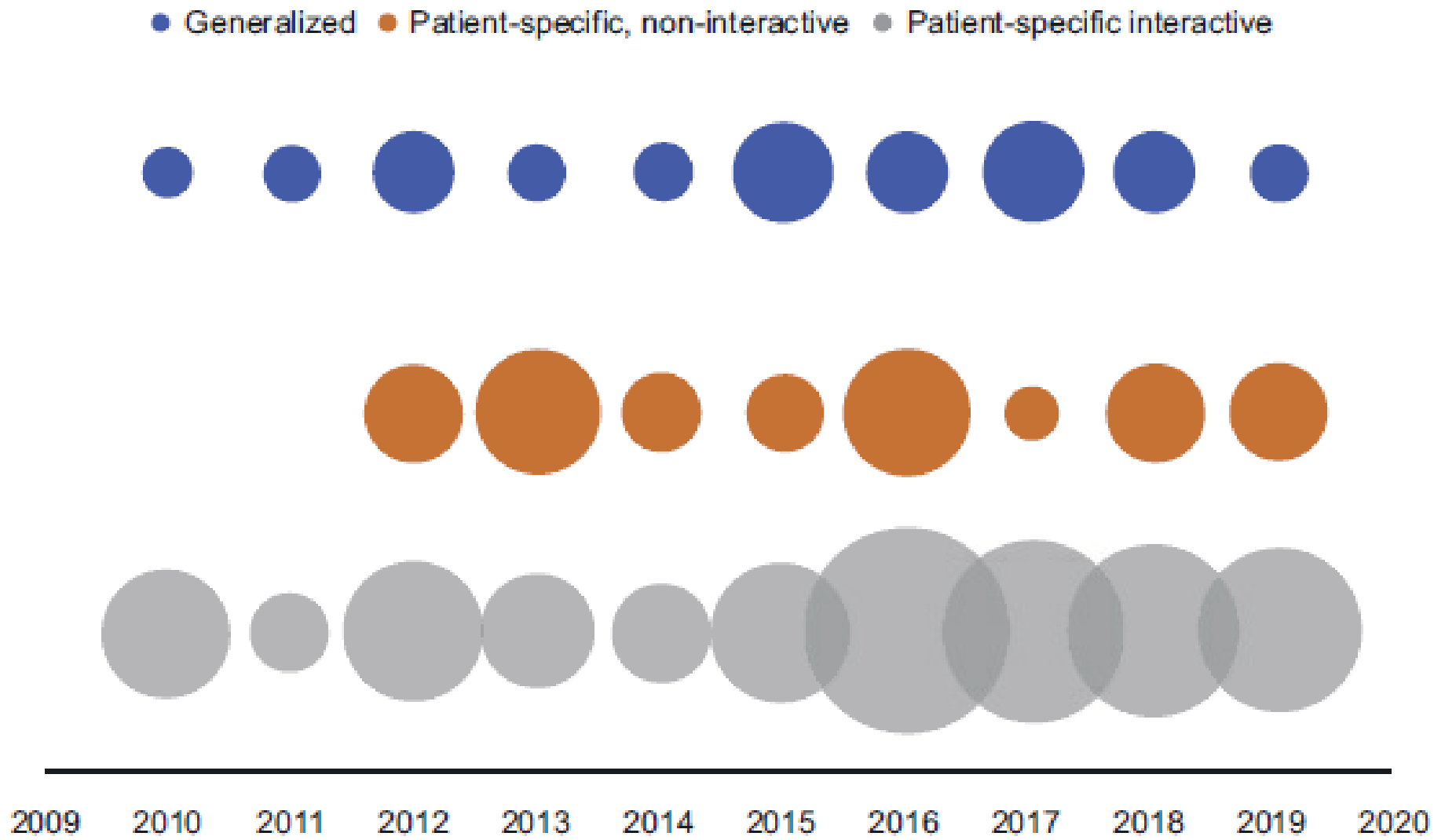


FIGURE 2. Bubble plot showing relative numbers of publications for different intervention categories by year.

Mosnaim G, Safioti G, Brown R, DePietro M, Szefler SJ, Lang DM, Portnoy JM, Bukstein DA, Bacharier LB, Merchant RK. Digital Health Technology in Asthma: A Comprehensive Scoping Review. J Allergy Clin Immunol Pract. 2021;9(6):2377-2398.

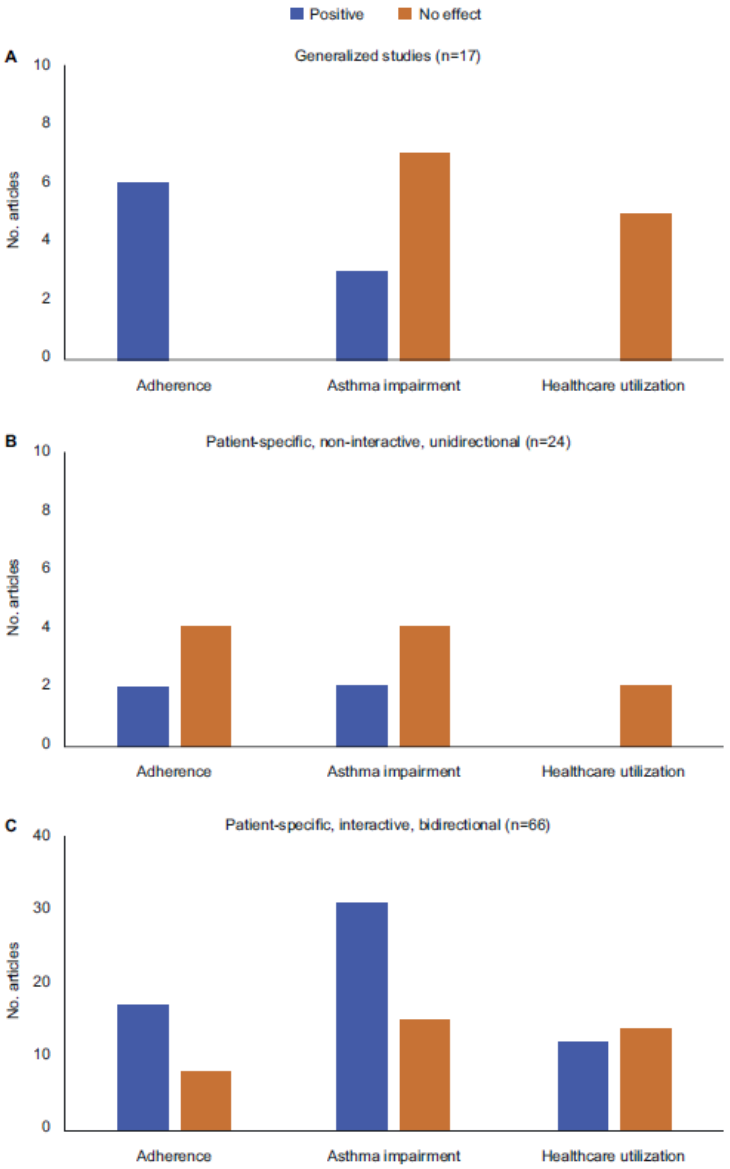


FIGURE 3. Balance of articles reporting positive effect versus no effect on adherence, asthma impairment, and health care use: A Generalized studies (n = 17). B Patient-specific, noninteractive, unidirectional interventions (n = 24). C Patient-specific interactive, bidirectional interventions (n = 66).

Mosnaim G, Safioti G, Brown R, DePietro M, Szefler SJ, Lang DM, Portnoy JM, Bukstein DA, Bacharier LB, Merchant RK. Digital Health Technology in Asthma: A Comprehensive Scoping Review. J Allergy Clin Immunol Pract. 2021;9(6):2377-2398.

Clinical Endpoints of Interest

- Increased SABA-free days
- Increased adherence (or less of a decline in adherence) to prescribed ICS
- Patient satisfaction
- Improved asthma control
- Improved lung function
- Improved biomarkers
- Reduced asthma-related healthcare utilization
- Appropriate use of biologics

Original Article

The Impact of Patient Self-Monitoring Via Electronic Medication Monitor and Mobile App Plus Remote Clinician Feedback on Adherence to Inhaled Corticosteroids: A Randomized Controlled Trial

Giselle S. Mosnaim, MD, MS[a], David A. Stempel, MD[b], Candy Gonzalez, BA[c], Brittany Adams, MS[c], Naomi BenIsrael-Olive, MSN, APRN[a], Rahul Gondalia, PhD, MPH[d], Leanne Kaye, PhD, MPH[d], Madeleine Shalowitz, MD, MS[c], and Stanley Szefler, MD[e] *Evanston, Ill; San Francisco, Calif; and Aurora, Colo*

What is already known about this topic? Poor adherence to inhaled corticosteroids and overreliance on short-acting beta$_2$-agonists are risk factors for uncontrolled asthma.

What does this article add to our knowledge? Compared with a control group, patient self-monitoring via electronic medication monitors and a smartphone application plus remote clinician feedback helped maintain baseline adherence to inhaled corticosteroids and decrease short-acting beta$_2$-agonist use.

How does this study impact current management guidelines? Although asthma guidelines endorse self-monitoring and feedback to increase or maintain adherence, most strategies are resource intensive. This intervention is delivered remotely via a digital platform and clinician phone calls, thereby increasing flexibility and reducing costs.

Mosnaim GS, Stempel DA, Gonzalez C, Adams B, BenIsrael-Olive N, Gondalia R, Kaye L, Shalowitz M, Szefler S. The Impact of Patient Self-Monitoring Via Electronic Medication Monitor and Mobile App Plus Remote Clinician Feedback on Adherence to Inhaled Corticosteroids: A Randomized Controlled Trial. J Allergy Clin Immunol Pract. 2020 Nov 16:S2213-2198(20)31220-4.

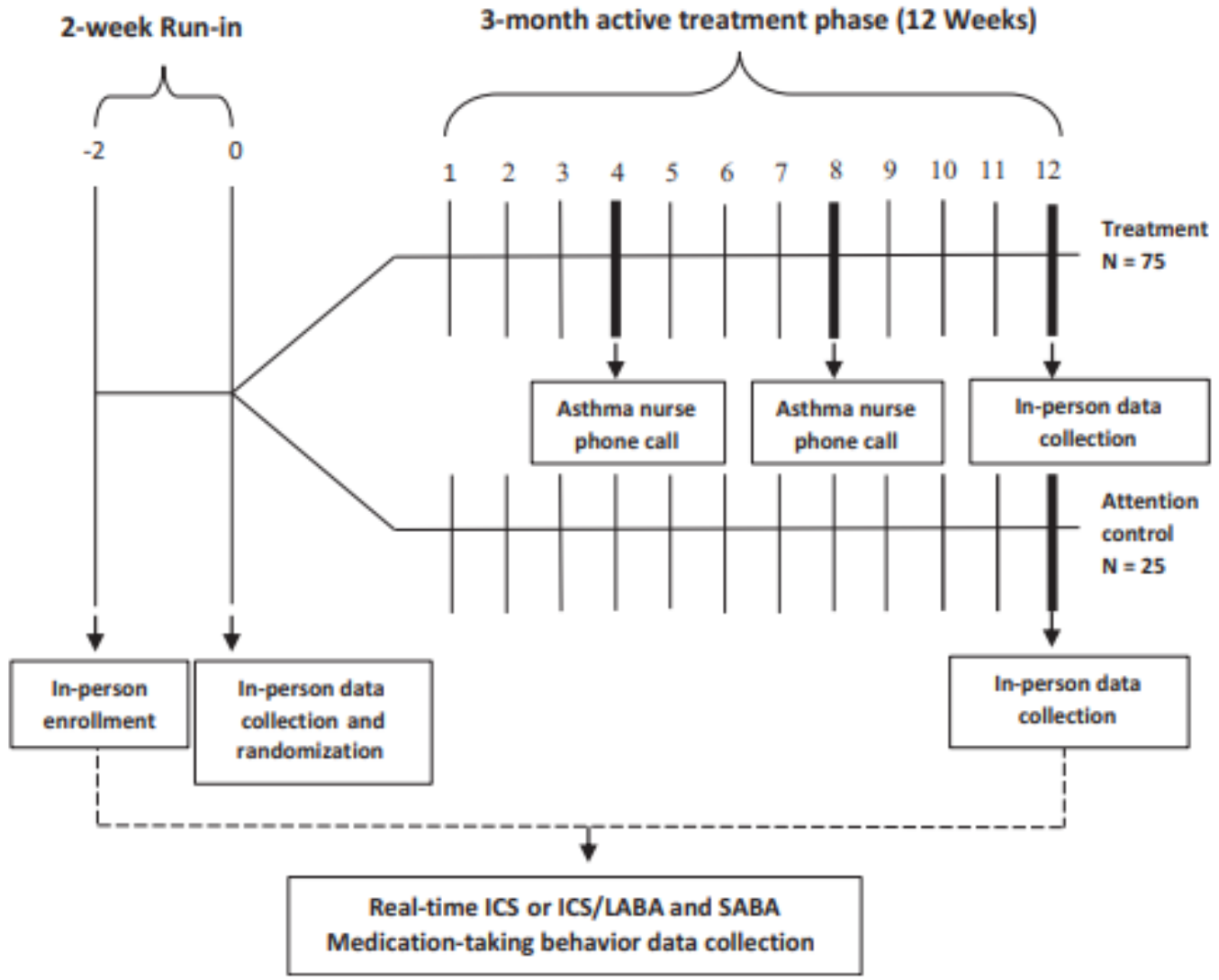


FIGURE 2. The study timeline illustrates the run-in and active treatment phases. Data collection occurred in real time throughout the study using the Propeller Health medication sensor, mobile phone app, and health care professional dashboard. In-person data collection occurred at the 0-week and 3-month study visits. *LABA*, Long-acting beta-adrenoceptor agonist.

Mosnaim GS, Stempel DA, Gonzalez C, Adams B, BenIsrael-Olive N, Gondalia R, Kaye L, Shalowitz M, Szefler S. The Impact of Patient Self-Monitoring Via Electronic Medication Monitor and Mobile App Plus Remote Clinician Feedback on Adherence to Inhaled Corticosteroids: A Randomized Controlled Trial. J Allergy Clin Immunol Pract. 2020 Nov 16:S2213-2198(20)31220-4.

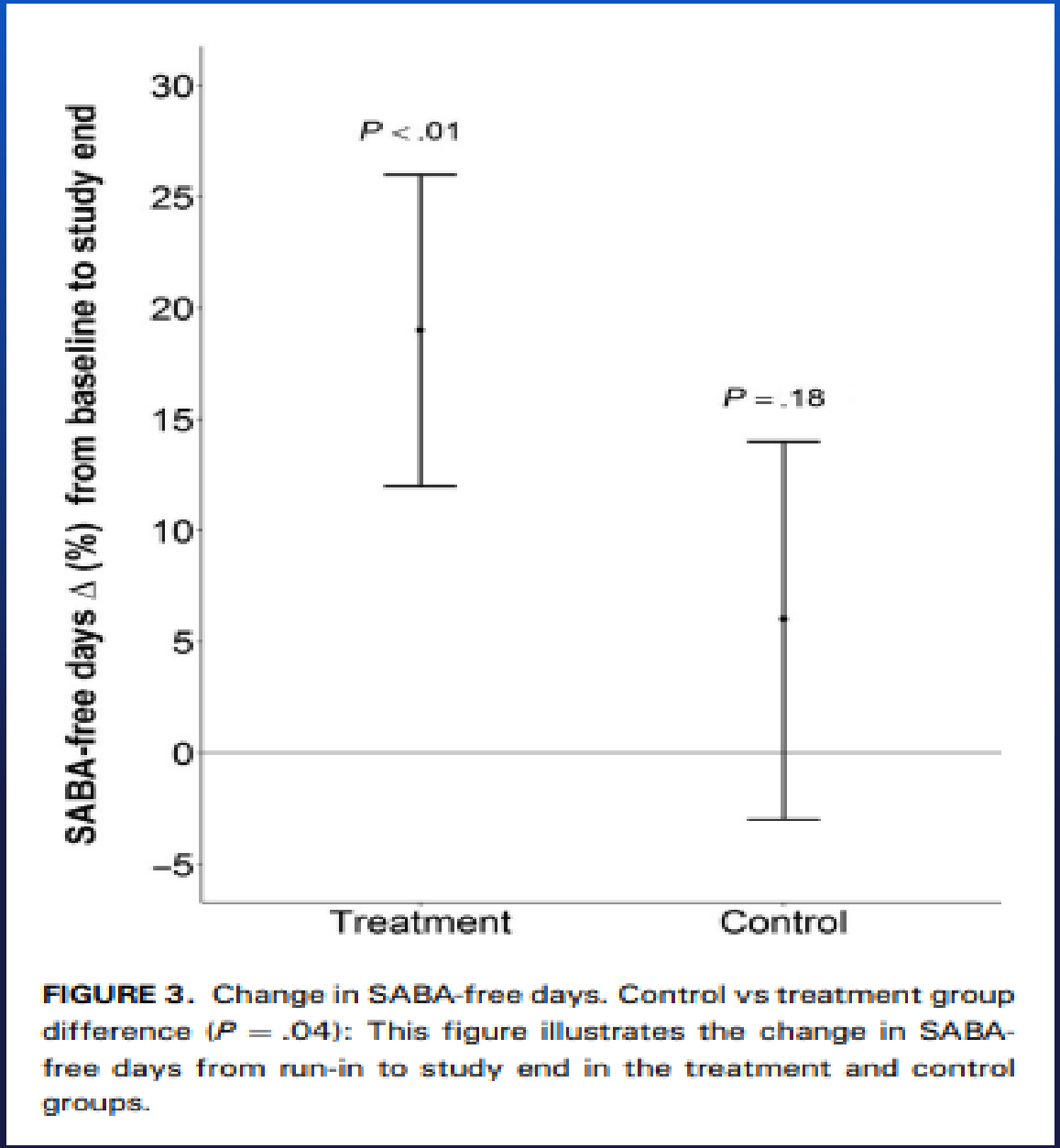


FIGURE 3. Change in SABA-free days. Control vs treatment group difference ($P = .04$): This figure illustrates the change in SABA-free days from run-in to study end in the treatment and control groups.

Mosnaim GS, Stempel DA, Gonzalez C, Adams B, BenIsrael-Olive N, Gondalia R, Kaye L, Shalowitz M, Szefler S. The Impact of Patient Self-Monitoring Via Electronic Medication Monitor and Mobile App Plus Remote Clinician Feedback on Adherence to Inhaled Corticosteroids: A Randomized Controlled Trial. J Allergy Clin Immunol Pract. 2020 Nov 16:S2213-2198(20)31220-4.

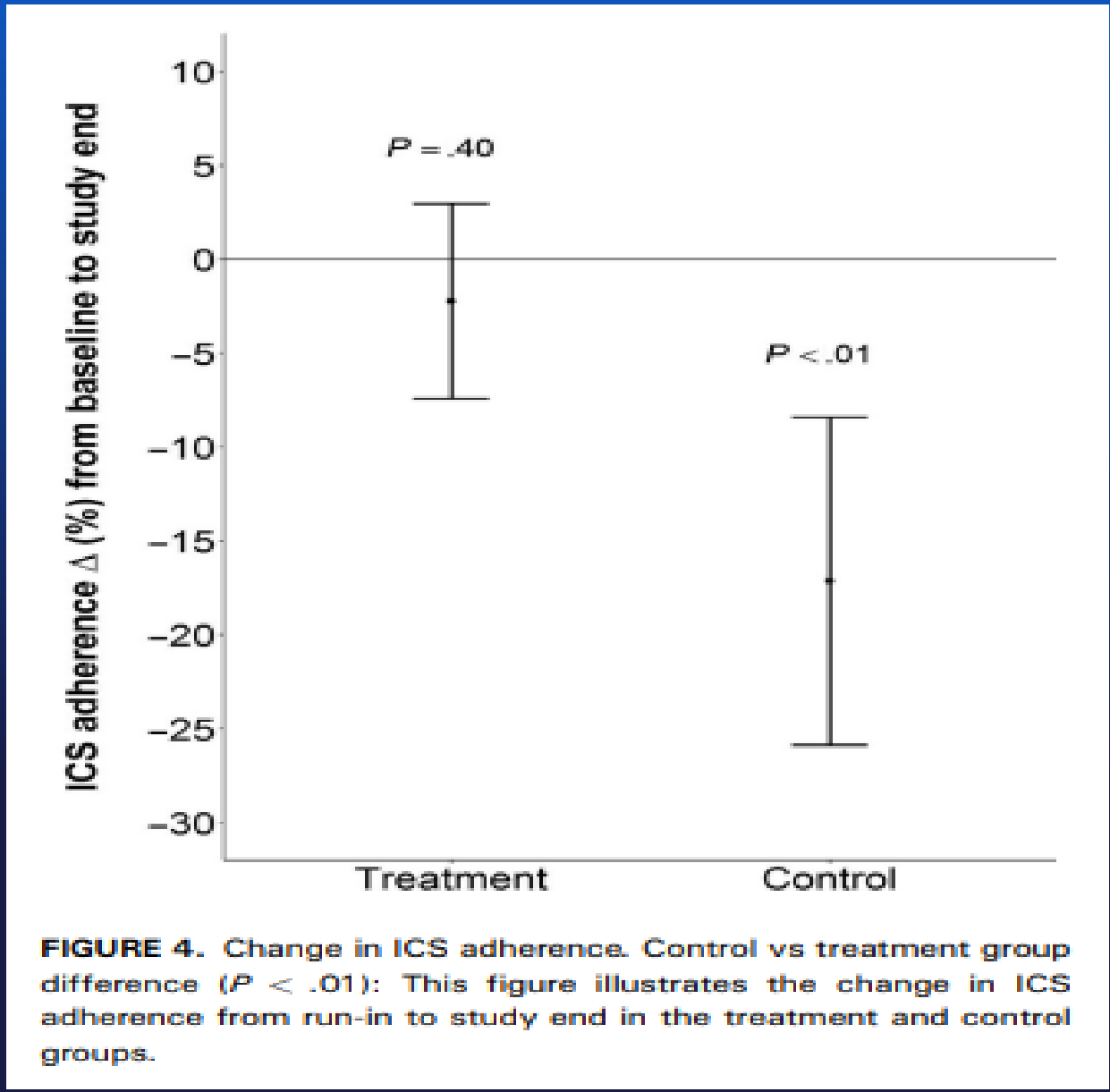


FIGURE 4. Change in ICS adherence. Control vs treatment group difference ($P < .01$): This figure illustrates the change in ICS adherence from run-in to study end in the treatment and control groups.

Mosnaim GS, Stempel DA, Gonzalez C, Adams B, BenIsrael-Olive N, Gondalia R, Kaye L, Shalowitz M, Szefler S. The Impact of Patient Self-Monitoring Via Electronic Medication Monitor and Mobile App Plus Remote Clinician Feedback on Adherence to Inhaled Corticosteroids: A Randomized Controlled Trial. J Allergy Clin Immunol Pract. 2020 Nov 16:S2213-2198(20)31220-4.

Original Article

Effectiveness of a Digital Inhaler System for Patients With Asthma: A 12-Week, Open-Label, Randomized Study (CONNECT1)

Flavia C.L. Hoyte, MD[a], Giselle S. Mosnaim, MD, MS[b], Linda Rogers, MD[c], Guilherme Safioti, MD[d], Randall Brown, MD, MPH[e], Thomas Li, PhD[e], Michael DePietro, MD[e,*], Michael Reich, MS[f], Tanisha D. Hill, MPH[e], and Michael E. Wechsler, MMS[a] *Denver and Aurora, Colo; Evanston, Ill; New York, NY; Amsterdam, The Netherlands; Parsippany, NJ; and Tel Aviv, Israel*

Hoyte F, Mosnaim GS, Rogers L, Safioti G, Brown R, Li T, Depietro M, Reich M, Hill T, Wechsler M. Effectiveness of a digital inhaler system for patients with asthma: a 12-week, open-label, randomized study (CONNECT1). J Allergy Clin Immunol Pract. 2022 Oct:10(10):2579-87.

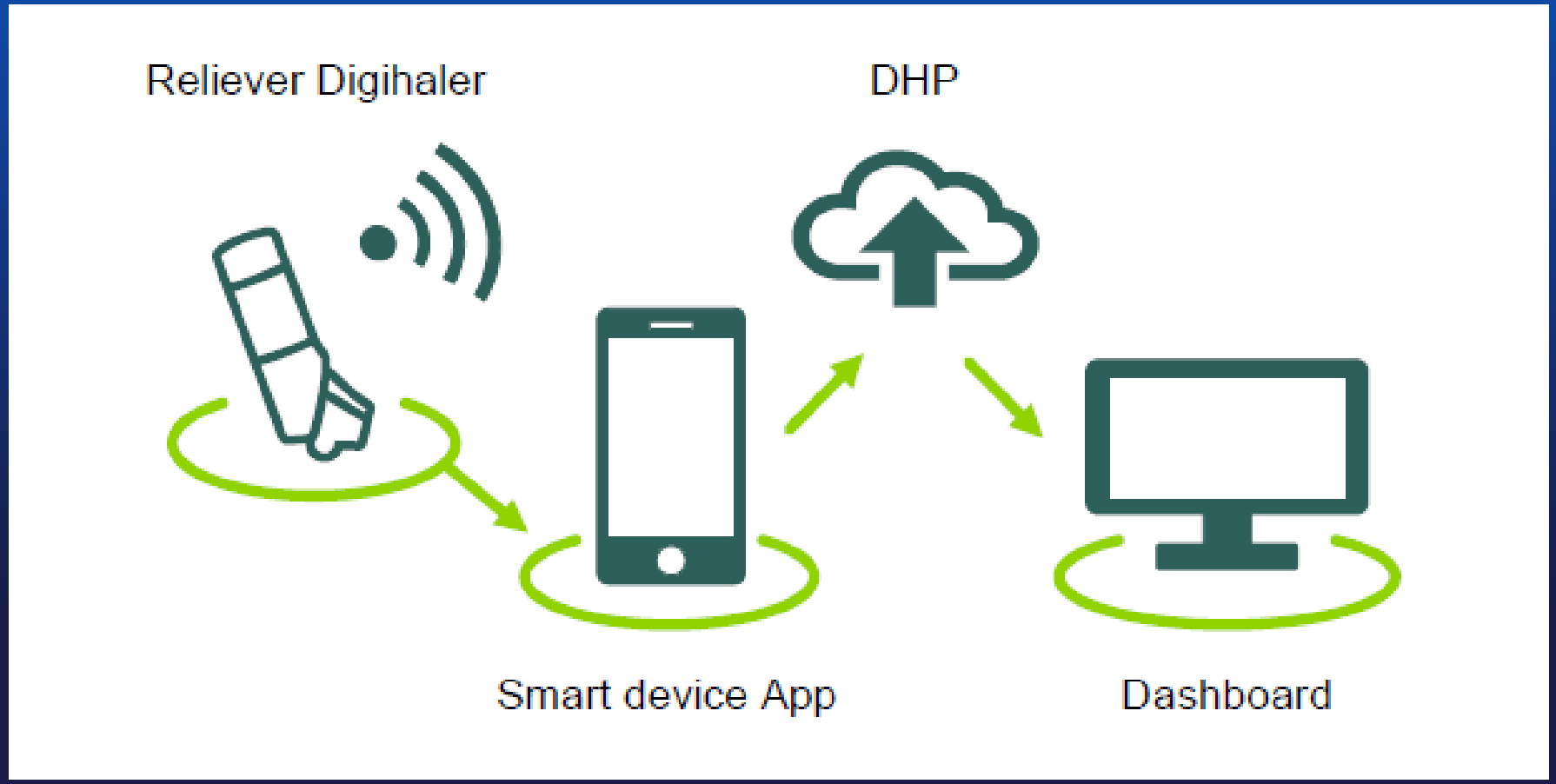


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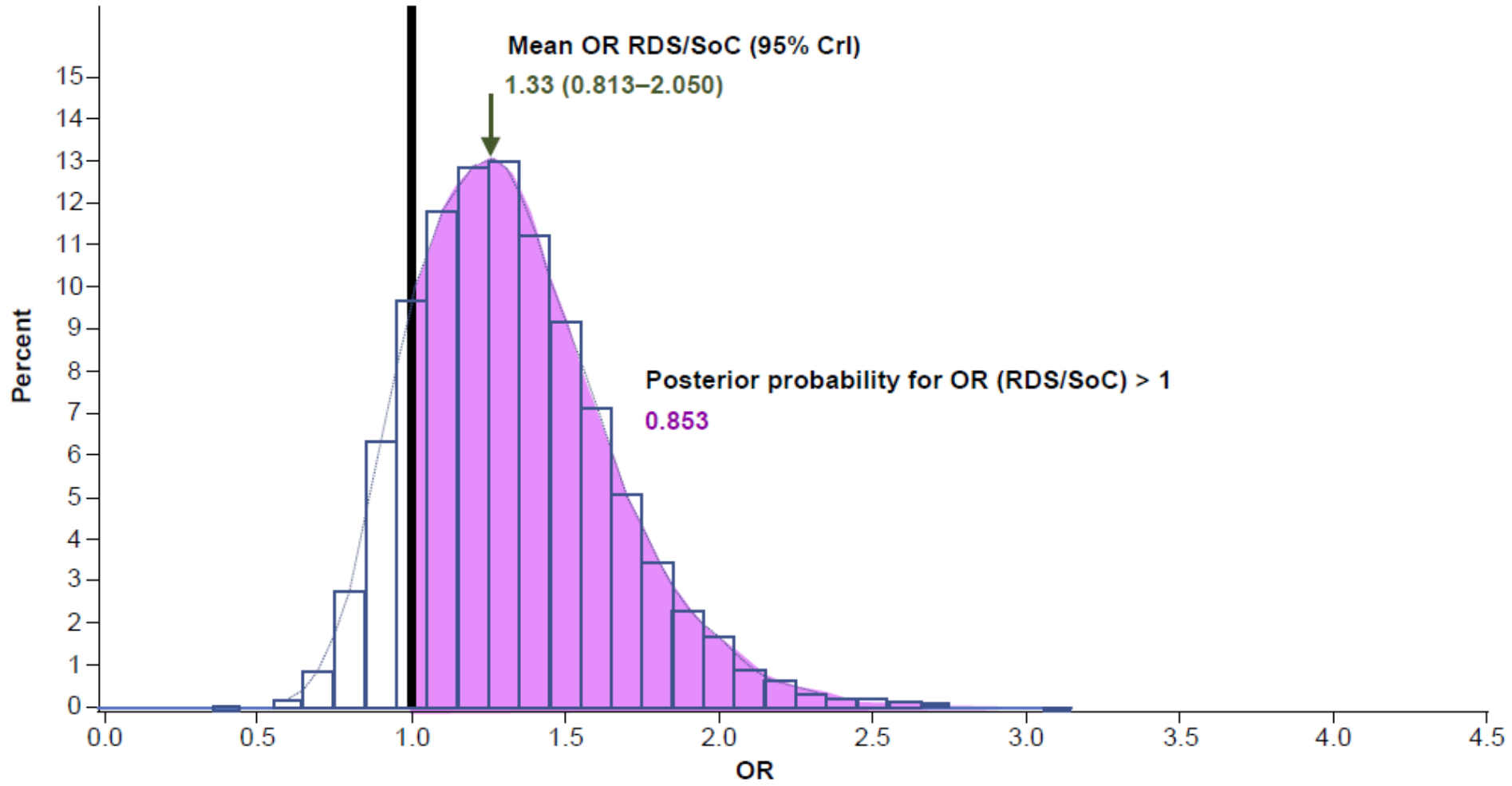
TABLE I. Participant demographics*

Demographic	RDS	SoC	Total
Age, y	n = 167	n = 166	n = 333
Mean (range)	43.9 (13–78)	43.6 (13–77)	43.7 (13–78)
<18, n (%)	13 (7.8)	10 (6.0)	23 (6.9)
≥18, n (%)	154 (92.2)	156 (94.0)	310 (93.1)
Sex, n (%)	n = 167	n = 166	n = 333
Female	120 (72)	110 (66)	230 (69)
Race, n (%)	n = 167	n = 166	n = 333
White	116 (69)	124 (75)	240 (72)
Black or African American	43 (26)	30 (18)	73 (22)
Asian	2 (1)	4 (2)	6 (2)
American Indian or Alaskan Native	0 (0)	0 (0)	0 (0)
Native Hawaiian or other Pacific Islander	0 (0)	1 (<1)	1 (<1)
Not reported	5 (3)	6 (4)	11 (3)
Other	1 (<1)	1 (<1)	2 (<1)
Weight, kg	n = 155	n = 156	n = 311
Mean (SD)	85.8 (23.2)	87.2 (24.1)	86.5 (23.6)
Height, cm	n = 155	n = 156	n = 311
Mean (SD)	165.7 (10.1)	166.8 (9.3)	166.3 (9.7)
BMI, kg/m^2	n = 155	n = 156	n = 311
Mean (SD)	31.1 (7.7)	31.4 (8.1)	31.2 (7.9)
ACT score	n = 150	n = 163	n = 313
Mean (SD)	14.1 (3.2)	14.5 (2.9)	-

BMI, Body mass index; *ITT*, intention-to-treat.
*Participant demographics are shown for ITT population, other than ACT score data, which are for the mITT population

Hoyte F, Mosnaim GS, Rogers L, Safioti G, Brown R, Li T, Depietro M, Reich M, Hill T, Wechsler M. Effectiveness of a digital inhaler system for patients with asthma: a 12-week, open-label, randomized study (CONNECT1). J Allergy Clin Immunol Pract. 2022 Oct:10(10):2579-87.



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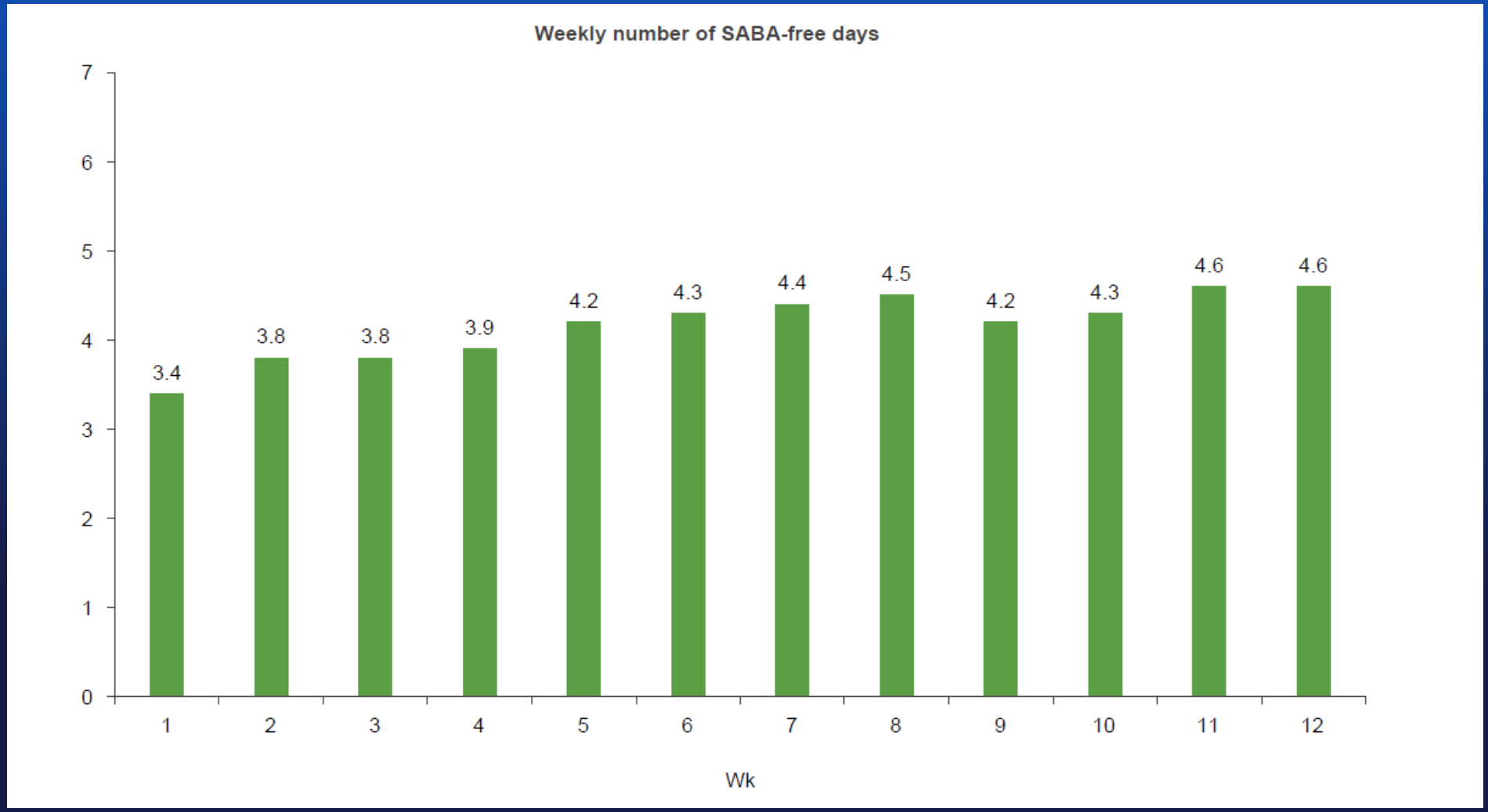

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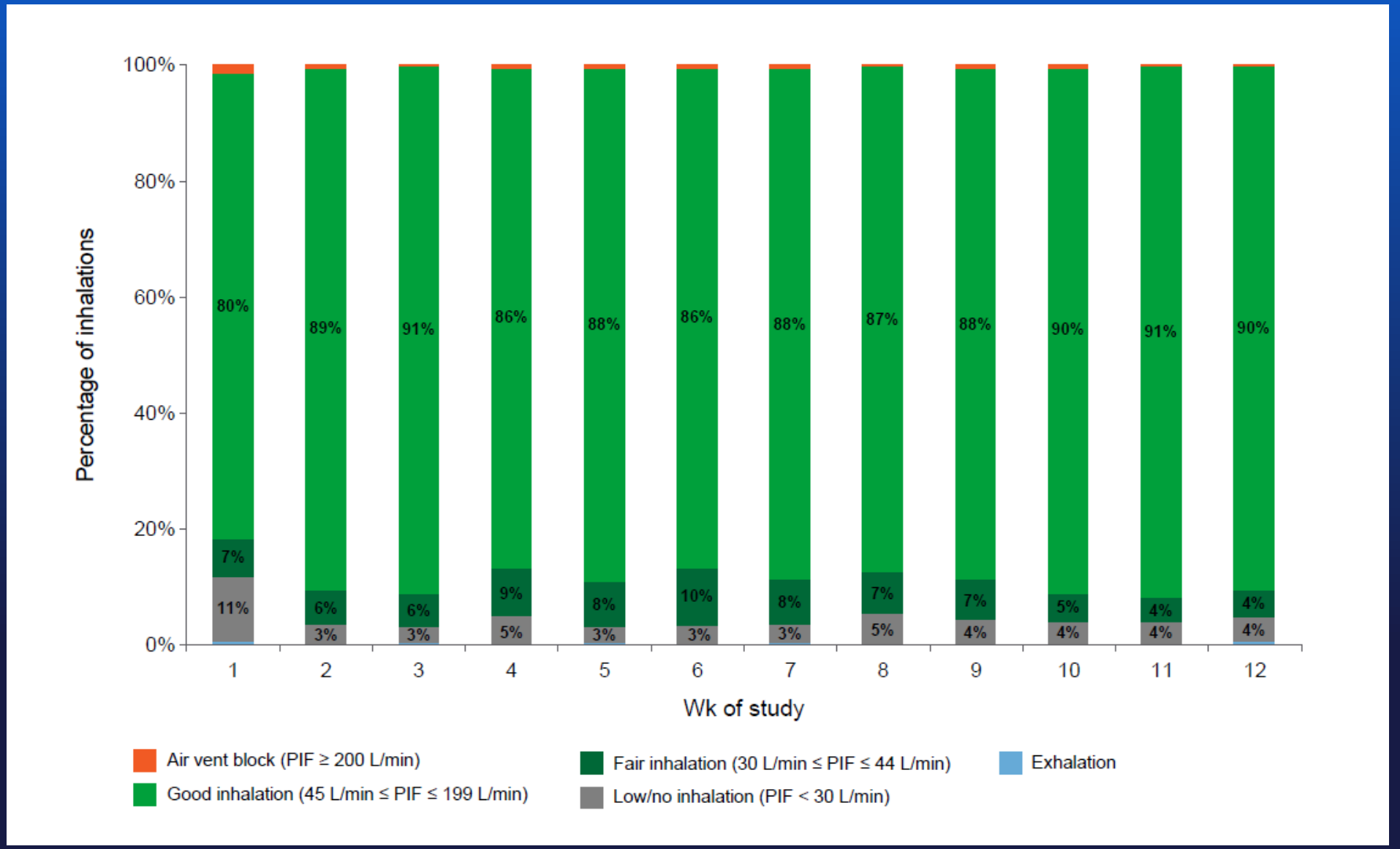

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Original Article

Clinical Outcomes in People with Difficult-to-Control Asthma Using Electronic Monitoring to Support Medication Adherence

Claire E. Boddy, BA(Hons), RGN[a], Shamsa Naveed, MD, PhD[a,b], Michelle Craner, RN[a], Anna C. Murphy, DPharm[a], Salman Siddiqui, MD, PhD[a,b], and Peter Bradding, DM[a,b] *Leicester, United Kingdom*

What is already known about this topic? Seven-day FeNO suppression testing with fluticasone+Inhaler Compliance Assessment (INCA) electronic monitoring added to usual therapy, coupled with home FeNO monitoring, identifies medication nonadherence in difficult-to-control asthma. Long-term clinical outcomes are not known.

What does this article add to our knowledge? A simplified approach where usual inhaled corticosteroid (ICS)/long-acting β_2-agonist (LABA) is replaced with fluticasone/salmeterol+INCA for 28 days with repeat assessments in clinic provides similar results to the 7-day test. Clinical outcomes improved for many previously nonadherent patients.

How does this study impact current management guidelines? Use of the 28-day fluticasone/salmeterol+INCA protocol as a pre-step/stratification tool for biological therapy in patients with a high baseline FeNO may reduce unnecessary biologic prescribing and oral corticosteroid exposure, whilst optimizing treatment with ICS/LABA therapy.

Boddy, C, Naveed, S, Craner, M, Murphy, A, Siddiqui, S, Bradding, P. Clinical Outcomes in People with Difficult-to-Control Asthma Using Electronic Monitoring to Support Medication Adherence. J Allergy Clin Immunol Pract 2021;9:1529-38

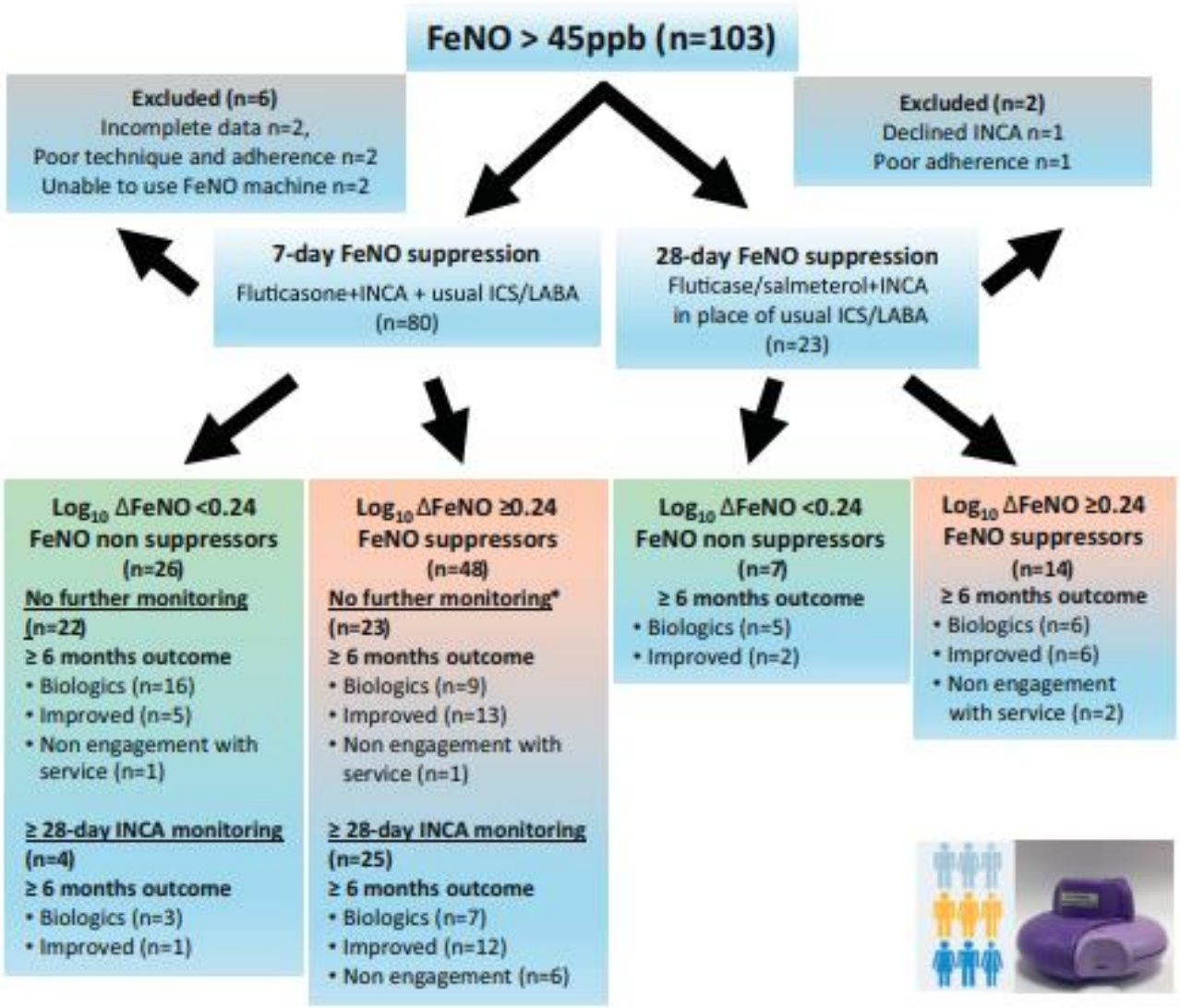

FIGURE 1. A summary of the patient assessments and outcomes. *Further 28-day monitoring was not undertaken in n = 23 7-day FeNO suppressors as we did not commence this for 12 months after starting 7-day FeNO suppression testing, and INCA supplies were limited for a period. *ICS*, Inhaled corticosteroid; *INCA*, Inhaler Compliance Assessment; *LABA*, long-acting β_2-agonist; *ppb*, parts per billion.

Boddy, C, Naveed, S, Craner, M, Murphy, A, Siddiqui, S, Bradding, P. Clinical Outcomes in People with Difficult-to-Control Asthma Using Electronic Monitoring to Support Medication Adherence. J Allergy Clin Immunol Pract 2021;9:1529-38

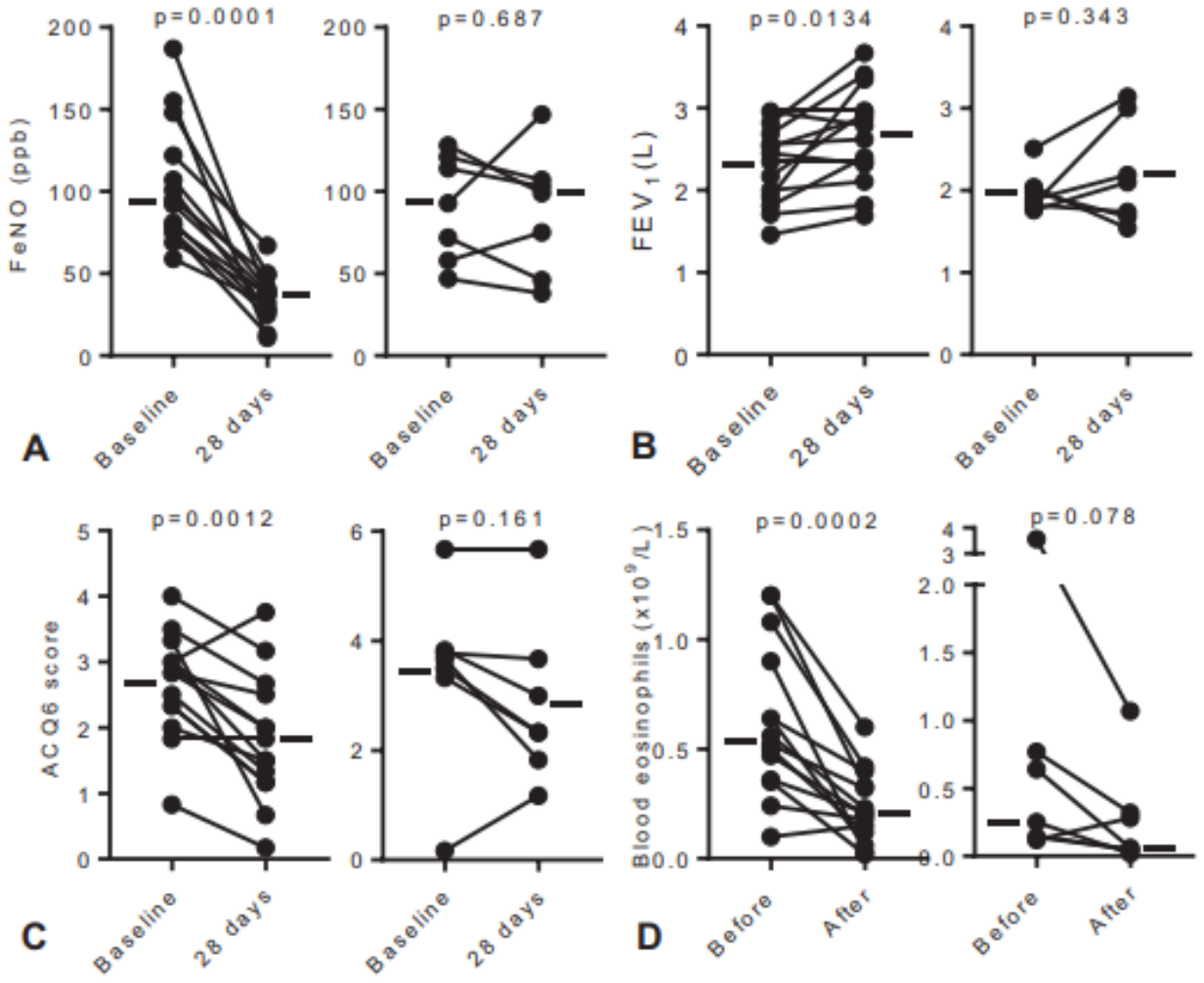

FIGURE 2. Clinical responses in FeNO-high patients with difficult-to-control asthma when usual ICS/LABA therapy is replaced with fluticasone/salmeterol+INCA electronic monitoring. **A,** FeNO. **B,** FEV_1. **C,** ACQ6. **D,** Blood eosinophils. FeNO suppressors are shown in the left panel of each figure, and FeNO nonsuppressors on the right panel of each figure. Horizontal bars represent medians (FeNO, blood eosinophils) or means (FEV_1, ACQ6). *ACQ*, Asthma Control Questionnaire; *FEV_1*, forced expiratory volume in 1 second; *ICS*, inhaled corticosteroid; *INCA*, Inhaler Compliance Assessment; *LABA*, long-acting β_2-agonist; *ppb*, parts per billion.

Boddy, C, Naveed, S, Craner, M, Murphy, A, Siddiqui, S, Bradding, P. Clinical Outcomes in People with Difficult-to-Control Asthma Using Electronic Monitoring to Support Medication Adherence. J Allergy Clin Immunol Pract 2021;9:1529-38

Editorial

The Adoption and Implementation of Digital Health Care in the Post–COVID-19 Era

Giselle S. Mosnaim, MD, MS[a], Hilary Stempel, MD, MPH[b], David Van Sickle, PhD[c], and David A. Stempel, MD[d] *Evanston, Ill; Denver, Colo; Madison, Wis; and San Francisco, Calif*

Mosnaim, G, Stempel, H, Van Sickle, D, Stempel, D. The Adoption and Implementation of Digital Health Care in the Post-COVID-19 Era. Journal of Allergy and Clinical Immunology: In Practice, 2020-09-01, Volume 8, Issue 8, Pages 2484-2486

Hogan, B. How Do You Eat An Elephant?: One Bite at a Time. New York, Aeon Publishing, 2004.

Clinical Management Review

Digital Inhalers and Remote Patient Monitoring for Asthma

Giselle S. Mosnaim, MD, MS[a,*], Justin Greiwe, MD[b,c,*], Sunit P. Jariwala, MD[d], Roy Pleasants, PharmD[e], and Rajan Merchant, MD[f] *Evanston, Ill; Cincinnati, Ohio; Bronx, NY; Raleigh, NC; and Woodland, Calif*

Mosnaim GS, Greiwe J, Jariwala SP, Pleasants R, Merchant R. Digital Inhalers and Remote Patient Monitoring for Asthma. J Allergy Clin Immunol Pract 2022 Oct:10(10):2525-33.

TABLE I. Medicare RTM codes

CPT# 98975	Initial Set-up & Patient Education on use of equipment, each 30 d	RTM (eg, respiratory system status, musculoskeletal system status, therapy adherence, therapy response); device(s) supply with scheduled (eg, daily) recording(s) and/or programmed alert(s) transmission to monitor respiratory system
CPT# 98976	Supply of Device for Monitoring Respiratory System, each 30 d	RTM (eg, respiratory system status, musculoskeletal system status, therapy adherence, therapy response); device(s) supply with scheduled (eg, daily) recording(s) and/or programmed alert(s) transmission to monitor respiratory system
CPT# 98977	Supply of Device for Monitoring Musculoskeletal System, each 30 d	RTM (eg, respiratory system status, musculoskeletal system status, therapy adherence, therapy response); device(s) supply with scheduled (eg, daily) recording(s) and/or programmed alert(s) transmission to monitor musculoskeletal system
CPT# 98980	Monitoring/Treatment Management Services, first 20 min	RTM treatment management services, physician/other qualified HCP time in a calendar month requiring at least 1 interactive communication with the patient/caregiver during the calendar month
CPT# 98981	Monitoring/Treatment Management Services, each additional 20 min	RTM treatment management services, physician/other qualified HCP time in a calendar month requiring at least 1 interactive communication with the patient/caregiver during the calendar month

CPT, Current Procedural Terminology.

Mosnaim GS, Greiwe J, Jariwala SP, Pleasants R, Merchant R. Digital Inhalers and Remote Patient Monitoring for Asthma. J Allergy Clin Immunol Pract 2022 Oct:10(10):2525-33.

US Centers for Medicare & Medicaid Services Requirements

Physiologic Remote Patient Monitoring Code		Remote Patient Monitoring Code (Remote Therapeutic Monitoring/Adherence)	
Device involves remote monitoring of physiologic parameters (e.g. respiratory flow rate)		Device involves remote monitoring of respiratory symptom status (e.g. therapy adherence, therapy response)	
Device must meet FDA's definition of a medical device		Device must meet FDA's definition of a medical device	
Device must transmit 16 days of data over a 30-day period (for CPT code 99454)		Device must transmit 16 days of data over a 30-day period (for CPT code 98976)	
Physiologic data is automatically transmitted from the device to the HCP		Non-physiologic data con be self-reported as well as digitally uploaded to the HCP	
Device and monitoring are medically necessary		Device and monitoring are medically necessary	
Data collected must be used to develop and manage a plan of treatment		Data collected must be used to develop and manage a plan of treatment	

Remote Therapeutic Monitoring/Remote Treatment Monitoring HCPCS codes	Clinician reimbursed for onboarding the patient to a program, device supply with ongoing non-physiological (including therapy/medication adherence or response) monitoring, patient monitoring treatment management services	*98975, 98976, 98977, 98980, 98981*
Remote Physiologic Monitoring/Remote Patient Monitoring CPT® codes	Clinician reimbursed for onboarding the patient to a program, device supply with ongoing physiological monitoring, patient monitoring treatment management services	*99453, 99454, 99457, 99458*, 99091 (unbundled in 2018)*
Chronic Care Management /Complex Chronic Care Management CPT®/HCPCS codes	Clinician provides care management services for two or more chronic conditions, psychosocial needs and activities of daily living	*99487, 99489*, 99490, G2058*, 99491*
Principal Care Management HCPCS codes	Similar to CCM codes, but clinician only oversees management for a single chronic condition (primary care or other practitioner)	*G2064, G2065*

Clinical Vignette

- Adult male referred to you for evaluation and treatment of uncontrolled asthma. History reveals 4 immediate care visits with accompanying courses of OCS over the past 12 months, despite being prescribed a high dose ICS/LABA DPI during this time. Recent labs reveal an absolute eosinophil count of 300. His ACT score is 17, and reveals albuterol use several times a day for day time symptoms and every night for nighttime awakenings. In-office spirometry demonstrates 15% (and greater than 200 ml) reversibility post bronchodilator, and in-office testing demonstrates a FE_{NO} level of > 50 ppb. When you inquire about ICS/LABA usage and inhaler technique, he reports he is taking the medications as prescribed and knows how to use them. Of the options below, what is the next best step in the management of this patient?

- **Add low dose daily oral corticosteroids**
- **Switch to an MDI ICS/LABA formulation**
- **Discuss the option of adding a biologic therapy**
- **Ask non-judgemental follow up questions about ICS/LABA use, review inhaler technique, and prescribe a digital inhaler system**

Discussion and Future Directions

Defining Difficult-to-Control vs Severe Asthma

Understand the impact of ICS Adherence

Understand the impact of Inhaler Technique

Describe the Potential Role of Digital Inhaler Systems as a Diagnostic Tool and Therapeutic Intervention

Thank you!

Email address: gmosnaim@gmail.com

Extra Slides – Not Needed

TABLE II. Change in SABA-free days and ICS-containing controller medication adherence from baseline to study end (last 14 d of the study or sync* if last sync occurs before the final visit)

SABA-free days and ICS-adherence	Baseline (prerandomization)	Study end (last 14 d of study or sync)	Δ (95% CI)†	*P* value†	Treatment vs control Δ (95% CI)†‡	Treatment vs control Δ *P* value†‡	N
SABA-free days (%), mean ± SD							
Control group	75 ± 32	81± 34	6 (−3 to 14	.18	13 (1 to 26)	.04	23§
Treatment group	58 ± 37	77 ± 30	19 (12 to 26)	<.01			68§
Daily ICS adherence (%), mean ± SD							
Control group	68 ± 30	51 ± 37	−17 (−26 to −8)	.01	15 (4 to 25)	<.01	23‖
Treatment group	70 ± 27	68 ± 32	−2 (−7 to 3)	.40			73‖

Δ, Change.

*Sync is defined as the successful communication between the Propeller electronic medication monitor and the paired smartphone app.

†Estimated using linear mixed models that accounted for repeated measures.

‡Δ (95% CI) and *P* value are for the interaction term between the intervention group and the study period.

§Sum of N does not equal 100 due to early withdrawal (n = 1), lacked a final study visit (n = 2), or first synced their inhaler sensor after baseline (n = 2) or did not have a sensor for their SABA inhaler (n = 4).

‖Sum of N does not equal 100 due to early withdrawal (n = 1), lacked a final study visit (n = 2), or first synced their inhaler sensor after baseline (n = 1).

Mosnaim GS, Stempel DA, Gonzalez C, Adams B, BenIsrael-Olive N, Gondalia R, Kaye L, Shalowitz M, Szefler S. The Impact of Patient Self-Monitoring Via Electronic Medication Monitor and Mobile App Plus Remote Clinician Feedback on Adherence to Inhaled Corticosteroids: A Randomized Controlled Trial. J Allergy Clin Immunol Pract. 2020 Nov 16:S2213-2198(20)31220-4.

For Illustrative Purposes Only for Eligible Patients

One-time initial set-up and patient education

RPM #99453

RTM #98975

$19.03-$19.38

Device supply and data transmitted from device (billable monthly)

RPM #99454

RTM #98976

$55.72

Clinical staff review (20min billable monthly)

RPM #99457

RTM #98980

$50.18

Clinical staff review (additional 20min billable monthly)

RPM #99458

RTM #98981

$40.84

Adherence "Usage" Remote Patient Monitoring Code 98976

US Centers for Medicare & Medicaid Services (CMS) RTM Requirements
Device involves remote monitoring of respiratory system status, therapy adherence, therapy response
Device must meet FDA's definition of a medical device
Device must record 16 days of data over a 30-day period (for CPT® codes 98976)
Non-physiologic data can be self-reported as well as digitally uploaded to the provider
Device and monitoring are medically necessary
Data collected must be used to develop and manage a plan of treatment

Physiologic Remote Patient Monitoring Code 99454

US Centers for Medicare & Medicaid Services (CMS) RPM Requirements
Device involves remote monitoring of physiologic parameters (e.g., respiratory flow rate)
Device must meet FDA's definition of a medical device
Device must transmit 16 days of data over a 30-day period (for CPT® code 99454)
Physiologic data is automatically transmitted from the device to the provider
Device and monitoring are medically necessary
Data collected must be used to develop and manage a plan of treatment

The Propeller Health Platform

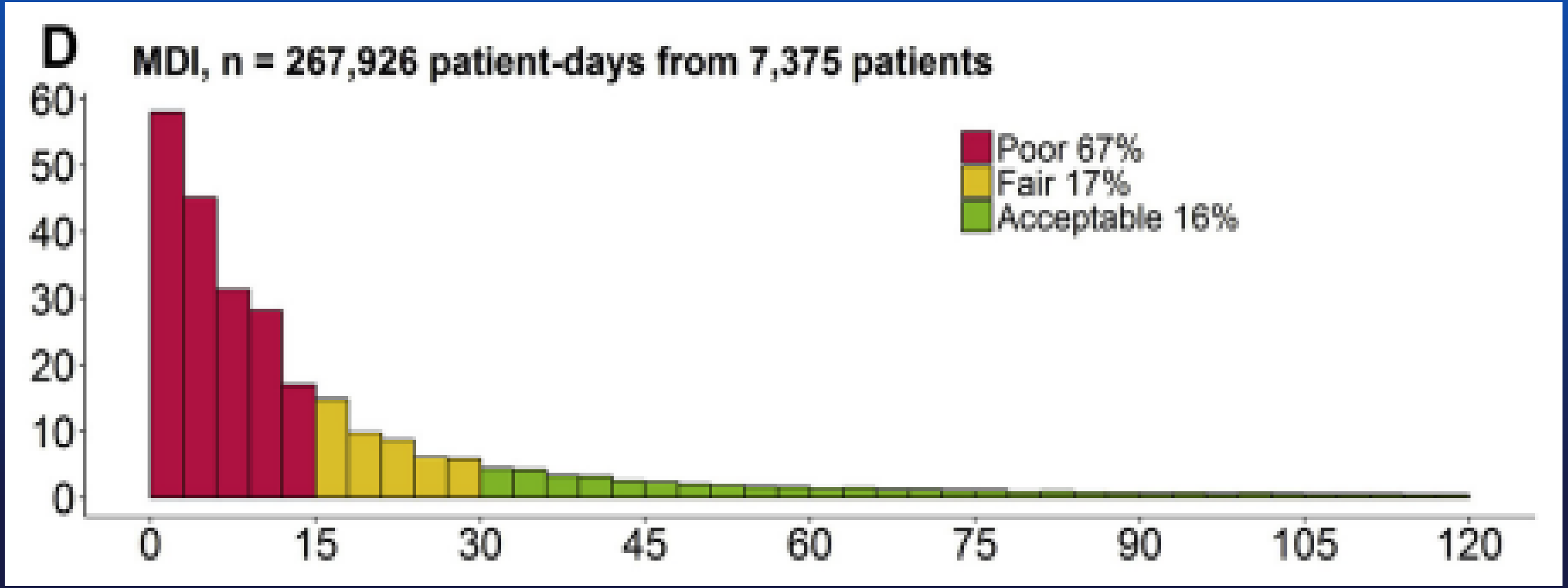

FIGURE 1. Distribution of interval between actuations measured over patient-days. *DPI*, Dry powdered inhaler; *MDI*, metered dose inhaler.

Anderson, W, Gondalia, R, Hoch, H, Kaye,L, Szefler, S.Stempel, D. Journal of Allergy and Clinical Immunology: In Practice, 2019-07-01 , Volume 7, Issue 6, Pages 2065-2067