A 3-month period of electronic monitoring can provide important information to the healthcare team to assess adherence and improve asthma control

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To the Editor:

Poor adherence to inhaled corticosteroids (ICS) results in poor asthma control, asthma attacks and increased healthcare costs [1, 2]. Measuring adherence using electronic monitoring devices is more accurate than self-report, prescription refill data or canister weight [3–5].

Asthma attacks, hospital admissions and asthma morbidity are reduced in patients with improved adherence after a period of electronic monitoring [6, 7]. However, most children have suboptimal adherence despite being electronically monitored [8]. In our previous observational study we electronically monitored adherence in asthmatic children over 3 months and checked their asthma control variables before and after monitoring. Those with good adherence (⩾80%) during a period of electronic monitoring had improved lung function, inflammatory markers and quality of life after monitoring. We also identified four groups of children defined by asthma control and adherence and described management strategies for each group. For example, those with good adherence and ongoing poor control should be considered for a step-up in therapy, such as the addition of a biologic [8].

In this proof-of-concept study we compared adherence and asthma control over two monitoring periods in two groups of children: 1) those given feedback on their adherence after the first monitoring period; and 2) those who had two monitoring periods without any intervention. We hypothesised that improvements in asthma control achieved by electronic monitoring would be sustained over a second monitoring period; and that in those whose adherence was poor, adherence would improve between the first and second monitoring period after feedback. This is a small cohort but the largest time series to our knowledge comparing electronically monitored adherence in children with asthma over two monitoring periods.

60 children aged 5–17 years, with asthma diagnosed on conventional criteria as previously described [9] were prospectively recruited from the outpatient department of the Royal Brompton Hospital (London, UK). 35 children had taken part in our previous study [8] and were recruited for a second period of electronically monitoring adherence. They received feedback on adherence and measures of asthma control following the first period of monitoring. The median time between the two monitoring periods was 3.9 (interquartile range 2.3–5.7) months.

25 patients were newly recruited for two consecutive periods of electronic monitoring without any such feedback after the first period. They had no time interval between the first and the second monitoring period. At recruitment, after the first monitoring period (follow-up 1 visit) and after the second monitoring period (follow-up 2 visit) assessments were carried out in both study groups.

10 (17%) patients were excluded due to technical problems because we were unable to download the Smartinhaler data. 15 (28%) patients dropped out during the course of the study (lost Smartinhaler: n=7; did not return to clinic: n=7; withdrew: n=1). There were no significant differences in age, sex, asthma severity, treatment and comorbidities between the protocol population and those lost to follow-up (data not shown).

Shareable abstract (@ERSpublications)
In children with difficult asthma, a single period of electronic monitoring can help to assess a patient's adherence and the possible impact of improved adherence on asthma control
https://bit.ly/3c3Gj6n

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Duration of follow-up was variable because research appointments were combined with routine clinic appointments (which, to minimise hospital visits, are scheduled quarterly according to the family's availability).

The study was approved by the Regional Ethical Committee (NRES Committee London-Westminster, registered with ClinicalTrials.gov (NCT02252289)). All carers gave written informed consent and the children gave age-appropriate consent.

The following assessments of asthma control were carried out at recruitment, at follow-up 1 and follow-up 2 visit: the Asthma Control Test (ACT) [10] for children aged ⩾12 years and the Childhood Asthma Control Test for children <12 years [11], spirometry, bronchodilator reversibility testing, exhaled nitric oxide (F_{eNO}) and the mini Paediatric Asthma Quality of Life Questionnaire (mPAQLQ) [12]. Asthma attacks in the 3 months prior to the baseline visit and during the monitoring period were recorded from interviews and hospital records [8]. If not already known, atopy was assessed at baseline either by skin prick test or specific immunoglobulin E [8]. Daily adherence was measured for two monitoring periods using an electronic monitoring device (Smartinhaler; Adherium, New Zealand) that recorded actuation but not inhalation flow. Families were aware that monitoring was taking place. Suboptimal adherence to ICS was defined as <80% [8, 13].

Statistical analyses were performed using Stata® (release 15; STATA Cooperation, College Station, TX, USA). Data were tested for normality using visual inspection, histograms and Kolmogorov–Smirnov testing. Mann–Whitney U-test, Fisher's Exact, Wilcoxon signed rank, ANOVA or Kruskal Wallis were used with $p<0.05$ indicating statistical significance.

35 patients (21 male) with a mean±SD age of 11.9±3 years completed the two monitoring periods. Eight (23%) were severe therapy resistant asthmatics, 16 (46%) difficult asthmatics and 11 (31%) mild-to-moderate asthmatics. The majority (91%) were atopic. The median ICS dose was 800 (range 200–2400) $\mu g \cdot day^{-1}$ of budesonide or equivalent. Median duration of the first monitoring period was 84 (IQR 63–98) days, and the second monitoring period was 105 (IQR 70–161) days.

The median adherence level of the whole study population was not significantly different over the two monitoring periods (table 1). Most participants (30 (86%) out of 35) retained their adherence classification (good/suboptimal) at the end of each monitoring period, five participants had improved adherence in the second period and changed classification from suboptimal to good (three who received feedback and two who did not).

After the first monitoring period there were significant improvements in lung function, bronchodilator reversibility testing, inflammatory parameters and exacerbations which were sustained over the second monitoring period. There were further improvements in ACT, mPAQLQ and exacerbation rate (table 1). It is acknowledged that there were five missing data points for F_{eNO} at follow-up 2, which may have influenced our results. However, although there was a large decrease in F_{eNO} from baseline to follow-up 1, F_{eNO} then remained stable until follow-up 2, which means the missing data likely had no major impact on

TABLE 1 Change in asthma control parameters between baseline, follow-up 1 and follow-up 2

	Baseline (n=35)	Follow-up 1 (n=35)	Follow-up 2 (n=35)	p-value: comparison baseline *versus* follow-up 1	p-value: comparison follow-up 1 *versus* follow-up 2
FEV_1, % pred	82.2±21.8	92.5±16.1	95.8±16.2	<0.001	0.087
BDR, %	20.3±22.8[#]	8.7±10.4[#]	7.2±9.3[¶]	<0.001	0.445
F_{eNO}, ppb	55 (26–87)[¶]	21 (13–61)[¶]	22.5 (11–40)[+]	0.002	0.724
mPAQLQ	3.5 (3–4.7)	5.5 (4.3–6.4)	5.9 (4.3–6.8)[¶]	0.001	0.006
Exacerbations, n	2 (0–8)	1 (0–4)[#]	0 (0–4)	0.033	0.001
Adherence	Not assessed	78 (54–92)	83 (56–93)		0.302
ACT	12.6±6.1[#]	16.2±6.1[#]	19.1±5.8[¶]	0.001	0.005

Data are presented as mean±SD or median (interquartile range), unless otherwise stated. According to the data distribution, Wilcoxon signed rank or paired t-test were used. FEV_1: forced expiratory volume in 1 s; BDR: bronchodilator reversibility; F_{eNO}: exhaled nitric oxide fraction; mPAQLQ: median paediatric quality of life questionnaire score; ACT: Asthma Control Test. [#]: missing data for one child; [¶]: missing data for two children; [+]: missing data for five children.

our conclusions. Irrespective of whether feedback was given or not, both groups showed significant improvements in all shown asthma control parameters.

This study has demonstrated that a single period of monitoring of 2–3 months can help to classify a participant's adherence to ICS. This is important when deciding on appropriate management, particularly when a biologic is being considered. However, as noted elsewhere, even non-adherent children may merit treatment with a biologic to prevent an asthma death [14]. For those with poor adherence despite monitoring, an additional adherence intervention is needed [15]. Since adherence is a trait that can vary over time, if management becomes difficult (even in patients with previously documented good adherence) monitoring should be repeated.

The clinical benefits of improved adherence seen after one period of electronic monitoring are maintained in the medium term over a second monitoring period of 3 months.

The number of dropouts in this study and those without usable data is noteworthy and reflects the reality of monitoring adherence in patients with difficult asthma. It is likely that many of these had suboptimal adherence that they did not want to disclose to the healthcare team or their caregivers and therefore decided to not return their Smartinhaler.

Future studies looking at a larger population are needed to evaluate whether adherence monitoring can improve the outcome of asthma patients in the long term. This is particularly important since Smartinhalers are expensive and not available in many centres. The data on asthma control and adherence obtained during a period of monitoring could also be used to tailor adherence interventions.

This study demonstrates that 3 months of electronic monitoring can give the healthcare team important information about a patient's adherence to help guide further management.

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References

1 Bender B, Milgrom H, Apter A. Adherence intervention research: what have we learned and what do we do next? *J Allergy Clin Immunol* 2003; 112: 489–494.

2 van Boven JFM, Lavorini F, Dekhuijzen PNR, *et al.* Urging Europe to put non-adherence to inhaled respiratory medication higher on the policy agenda: a report from the First European Congress on Adherence to Therapy. *Eur Respir J* 2017; 49: 1700076.

3 Bender B, Wamboldt FS, O'Connor SL, *et al.* Measurement of children's asthma medication adherence by self report, mother report, canister weight, and Doser CT. *Ann Allergy Asthma Immunol* 2000; 85: 416–421.

4 Patel M, Perrin K, Pritchard A, *et al.* Accuracy of patient self-report as a measure of inhaled asthma medication use. *Respirology* 2013; 18: 546–552.
5 Foster JM, Smith L, Usherwood T, *et al.* The reliability and patient acceptability of the SmartTrack device: a new electronic monitor and reminder device for metered dose inhalers. *J Asthma* 2012; 49: 657–662.
6 Morton RW, Elphick HE, Rigby AS, *et al.* STAAR: a randomised controlled trial of electronic adherence monitoring with reminder alarms and feedback to improve clinical outcomes for children with asthma. *Thorax* 2017; 72: 347–354.
7 Chan AH, Stewart AW, Harrison J, *et al.* The effect of an electronic monitoring device with audiovisual reminder function on adherence to inhaled corticosteroids and school attendance in children with asthma: a randomised controlled trial. *Lancet Respir Med* 2015; 3: 210–219.
8 Jochmann A, Artusio L, Jamalzadeh A, *et al.* Electronic monitoring of adherence to inhaled corticosteroids: an essential tool in identifying severe asthma in children. *Eur Respir J* 2017; 50: 1700910.
9 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2015. www.ginasthma.org
10 Nathan RA, Sorkness CA, Kosinski M, *et al.* Development of the asthma control test: a survey for assessing asthma control. *J Allergy Clin Immunol* 2004; 113: 59–65.
11 Liu AH, Zeiger R, Sorkness CA, *et al.* Development and cross-sectional validation of the Childhood Asthma Control Test. *J Allergy Clin Immunol* 2007; 119: 817–825.
12 Juniper EF, Guyatt GH, Feeny DH, *et al.* Measuring quality of life in children with asthma. *Qual Life Res* 1996; 5: 35–46.
13 Santos PM, D'Oliveira A, de Araújo Costa Beisl Noblat L, *et al.* Predictors of adherence to treatment in patients with severe asthma treated at a referral center in Bahia, Brazil. *J Bras Pneumol* 2008; 34: 995–1002.
14 Bush A, Saglani S, Fleming L. Severe asthma: looking beyond the amount of medication. *Lancet Respir Med* 2017; 5:844–846.
15 Pike KC, Levy ML, Moreiras J, *et al.* Managing problematic severe asthma: beyond the guidelines. *Arch Dis Child* 2018; 103: 392–397.