



RESEARCH NOTE

# Achieving good adherence to inhaled corticosteroids after weighing canisters of asthmatic children [version 1; referees: 2 approved, 1 approved with reservations]

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**v1** First published: 14 Mar 2017, 6:266 (doi: [10.12688/f1000research.10710.1](https://doi.org/10.12688/f1000research.10710.1))  
 Latest published: 14 Mar 2017, 6:266 (doi: [10.12688/f1000research.10710.1](https://doi.org/10.12688/f1000research.10710.1))

**Abstract**

**Background:** The metered-dose inhalers (MDIs) currently available for inhaled corticosteroid delivery do not offer an integrated dose counter; therefore, it is difficult to evaluate adherence of patients. The present authors developed a linear regression equation using canister weight to calculate the number of doses actuated from the MDIs. This study aimed to assess medical adherence after the integration of regular weighing of the canisters into the routine service. **Methods:** A cohort study was carried out between May 2013 and April 2014. Children aged less than 8 years with a diagnosis of asthma were recruited. The duration of adherence assessment was 24 weeks. Participants had a regular schedule every 8 weeks to obtain a new FLIXOTIDE® 125 inhaler. Parents were asked to collect the discarded MDI canisters, which were then weighed by a laboratory scale. The weight of each canister was replaced in the regression equation to calculate the number of doses actuated from the MDIs. **Results:** A total of 52 asthmatic children participated in the study. The median age was 52.7 months. At the end of 24 weeks, 44, 33, and 23 discarded MDI canisters were collected from visits 1, 2, and 3, respectively. The median percentages of adherence were 96.8%, 96.3%, and 96.3%, respectively. In 11 discarded canisters (11%), the remaining medication was more than 30% of the labeled doses. Approximately 90% of the participants had no asthma exacerbation during 24-week study period. **Conclusion:** High adherence rates were achieved after integration of canister weighing into the asthma care service.

**Open Peer Review**

Referee Status:

	Invited Referees		
	1	2	3
<b>version 1</b>			
published 14 Mar 2017	report	report	report

- 1 **Wiparat Manuyakorn** , Mahidol University, Thailand
- 2 **Bee Wah Lee**, National University of Singapore, Singapore
- 3 **Orathai Piboonpocanun**, Mahidol University, Thailand

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Comments (0)

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**Competing interests:** No competing interests were disclosed.

**How to cite this article:** Chuenjit W, Engchuan V, Yuenyongviwat A and Sangsupawanich P. **Achieving good adherence to inhaled corticosteroids after weighing canisters of asthmatic children [version 1; referees: 2 approved, 1 approved with reservations]** *F1000Research* 2017, 6:266 (doi: [10.12688/f1000research.10710.1](https://doi.org/10.12688/f1000research.10710.1))

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**Grant information:** The study was funded by Faculty of Medicine, Prince of Songkla University (55-021-01-1-2). *The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.*

**First published:** 14 Mar 2017, 6:266 (doi: [10.12688/f1000research.10710.1](https://doi.org/10.12688/f1000research.10710.1))

## Introduction

Inhaled corticosteroids (ICSs) are the standard treatment for asthmatic children. Non-adherence with prescribed ICS treatment clearly causes uncontrolled asthma<sup>1</sup>. Feedback from parents is the traditional approach to assess the adherence to the treatment regimen; however, there is an overestimation by the patients of the remaining amount of medication<sup>2</sup>. Even though integration of a dose counter into the inhaler device improves the tracking adherence to prescribed medication<sup>3</sup>, the metered-dose inhalers (MDIs) currently available for ICS delivery do not offer integrated dose counters.

Weighing of the MDI canisters may be an alternative method to assess a patient's medication adherence. The present authors previously developed a linear regression equation using canister weight to calculate the number of doses actuated from the MDIs<sup>4</sup>. Weighing of the canisters was implemented into our asthma care system in March 2013. This study was designed to assess a patient's medication adherence after the integration of regular weighing of the canisters into the routine service.

## Methods

### Study design and subjects

A cohort study was carried out between May 2013 and April 2014. The inclusion criteria were children aged less than 8 years with a diagnosis of asthma who attended the Pediatric Allergy Clinic at Songklanagarind Hospital (Hat Yai, Songkhla, Thailand) and had exacerbation of asthma requiring hospitalization or an emergency department visit within the previous year. Patients who had a previous history of intubation or other chronic conditions were excluded.

The research protocol (REC 55-021-01-1-2) was approved by the Human Research Ethics Committee, Faculty of Medicine, Prince of Songkla University. Informed consent was obtained from the parents/guardians.

### Asthma management

Fluticasone propionate was selected as the ICS therapy for the study. A FLIXOTIDE® 125 Inhaler (GlaxoSmithKline) is a pressurized metered-dose inhaler, which delivers 125 microgram of fluticasone propionate per actuation. Each canister supplies 120 actuations. FLIXOTIDE® 125 Inhaler and BabyHALER® (GlaxoSmithKline), a device to help patients taking inhaled medicine, were prescribed to all participants. The dosage of fluticasone propionate was one actuation twice a day. The add-on asthma therapies were provided according to the GINA guideline<sup>5</sup>. Participants needed to participate in a regular schedule every 8 weeks to obtain a new FLIXOTIDE® 125 inhaler. For patients who did not achieve adequate control or maintain the adherence rate, the inhalation technique and medication doses were revised at the time they visited the clinic. Exacerbation was defined as asthma deterioration that required treatment with systemic corticosteroids or emergency department utilization or hospitalization.

## Adherence assessment

The duration of adherence assessment was 24 weeks. Each participant received three canisters of FLIXOTIDE® 125 Inhaler. Parents were asked to collect the discarded inhalers at the 8-week (visit 1), 16-week (visit 2), and 24-week (visit 3) after recruitment. The discarded MDI canisters were weighed by a laboratory scale (Sartorius Basic®). The weight of each canister was replaced in the regression equation to calculate the number of doses actuated from the MDIs. A regression equation for a fluticasone propionate MDI canister gives the number (n) of doses actuated from the MDIs:

$$n = 276.16 - (14.62 \times \text{canister weight}).^4$$

## Statistical analysis

All of the statistical analyses were conducted with R software (version 3.3.2) by the R Foundation for Statistical Computing. Adherence in each 8-week interval was calculated as the amount of medication actuated divided by the amount prescribed. Percentage of adherence was reported as median and range.

## Results

A total of 52 asthmatic children participated in the study. The characteristics of the participants are shown in Table 1. Half of the participants were male. The median age was 52.7 months (range, 18.3–91.7) and the age at the onset of asthma was 12 months (range, 1.0–48.0). Parents were the major caregivers. In total, 32% of the participants had other allergic co-morbidities. Most of participants had received ICS therapy for longer than 3 months. At the end of 24 weeks, 44, 33, and 23 (total 100) discarded MDI canisters were collected from visits 1, 2, and 3, respectively. The remaining median weights of the discarded canisters from visits 1, 2, and 3 were 11.172g, 11.229g, and 11.113 g, respectively, and the median percentages of adherence were 96.8%, 96.3%, and 96.3%, respectively. In 11 discarded canisters (11%), the remaining medication was more than 30% of the labeled doses. Approximately 90% of the participants had no asthma exacerbation during 24-week study period (Table 2).

### Dataset 1. Canister weight and percent of adherence

<http://dx.doi.org/10.5256/f1000research.10710.d150970>

Raw data of canister weight (original and discarded weight), results of the actuated dose equation and percent of adherence.

## Discussion

The present study demonstrated high adherence rates with low variations between the three visits. The percentage of discarded canisters, which had more than 30% of the labeled dosage of medication remaining, reduced from 22% in our previous cross-sectional study<sup>6</sup> to 11% in this study. Achieving good adherence in this cohort could be explained by the Hawthorn effect: the parents and participants knew that their adherence would be measured

**Table 1. Demographic data of asthmatic children.**

Variable	Results (N=52)
Male, n (%)	29 (55.8)
Weight, kg, median (range)	18.2 (10.9–30.0)
Height, cm, median (range)	107.4 (84.6–127.5)
Age, months, median (range)	52.7 (18.3–91.7)
Age onset, months, median (range)	12 (1.0–48.0)
Allergic disease, n (%)	17 (32.7)
• Atopic dermatitis	3 (5.8)
• Allergic rhinitis	12 (23.1)
• Food allergy	5 (9.6)
Caregiver, n (%)	
• Parents	44 (84.6)
• Grandparents	7 (13.5)
Number of hospitalizations, times/person, median (range)	1 (1–5)
Number of exacerbations within previous year, times/person, median (range)	3 (1–9)
Duration from last exacerbation, months, median (range)	4 (3–11)
Duration of ICS therapy, n (%)	
• 0–3 months	15 (28.9)
• More than 3 months	37 (71.1)
Number of studied canisters, n (%)	
• Visit 1	44 (84.6)
• Visit 2	33 (63.4)
• Visit 3	23 (44.2)

**Table 2. Canister weight and percentage of adherence.**

Variables	Visit 1	Visit 2	Visit 3
Number of canisters	44	33	23
New canister weight, g, median (range)	18.838 (18.663–18.929)	18.819 (18.607–18.907)	18.812 (18.470–18.913)
Discard canister weight, g, median (range)	11.172 (7.889–16.042)	11.229 (7.825–17.146)	11.113 (9.400–16.020)
Actuated doses calculated from canister weight, median (range)	112.8 (41.6–160.8)	112.0 (25.5–161.8)	113.7 (42.0–138.7)
Percentage of adherence, median (range)	96.8% (33.0–143.6)	96.3% (20.2–126.4)	96.3% (36.8–118.7)
Number of participants with exacerbation	1	2	1

by weighing the canisters; therefore, the individuals modified or improved their adherence in response to the awareness of being observed.

Approximately 90% of the participants had no asthma exacerbation throughout the study period. In our previous study, only 59% of the patients had adequate control<sup>6</sup>. Patients had access to the same educational and medication intervention, but the adherence rates were significantly different. Previous studies verified that the adherence rates had an association between lower adherence rates and poor asthma control<sup>7,8</sup>.

Although weighing of canisters was less accurate than a dose counter for measuring adherence<sup>9</sup>, the present study demonstrated that a weight-remaining dose correlation could be used to determine the inhaler medication adherence in real life, and intensive monitoring of adherence was successful in achieving control.

In conclusion, our results demonstrated that high adherence rates were achieved after integration of canister weighing into the asthma care service. The present study highlighted the need to incorporate a method to monitor medical adherence in clinical practice, which may contribute to adequate asthma control.

## Data availability

**Dataset 1: Canister weight and percent of adherence.** Raw data of canister weight (original and discarded weight), results of the actuated dose equation and percent of adherence. doi, [10.5256/f1000research.10710.d150970](https://doi.org/10.5256/f1000research.10710.d150970)<sup>10</sup>

## Author contributions

All authors contributed to study design, interpretation of study findings, manuscript preparation, and approved the final manuscript. WC, VE and AY contributed to data acquisition and validation. PS was responsible for project management, data analysis and funding.

## Competing interests

No competing interests were disclosed.

## Grant information

The study was funded by Faculty of Medicine, Prince of Songkla University (55-021-01-1-2).

*The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.*

## References

1. Ismaila A, Corriveau D, Vaillancourt J, *et al.*: **Impact of adherence to treatment with fluticasone propionate/salmeterol in asthma patients.** *Curr Med Res Opin.* 2014; **30**(7): 1417–25.  
[PubMed Abstract](#) | [Publisher Full Text](#)
2. Holt S, Holt A, Weatherall M, *et al.*: **Metered dose inhalers: a need for dose counters.** *Respirology.* 2005; **10**(1): 105–6.  
[PubMed Abstract](#) | [Publisher Full Text](#)
3. Jentzsch NS, Camargos PA, Colosimo EA, *et al.*: **Monitoring adherence to beclomethasone in asthmatic children and adolescents through four different methods.** *Allergy.* 2009; **64**(10): 1458–62.  
[PubMed Abstract](#) | [Publisher Full Text](#)
4. Sahajarat T, Sangsupawanich P: **Relationship of canister weight to the amount of medication actuated from metered-dose inhalers.** *J Allergy Clin Immunol.* 2012; **129**(2 Supplement): AB41.  
[Publisher Full Text](#)
5. Global Initiative for Asthma: **Global Strategy for Asthma Management and Prevention.**  
[Reference Source](#)
6. Dampant W, Sangsupawanich P, Yuenyongviwat A: **Medication Remaining In Discarded Metered Dose Inhalers Of Asthmatic Children.** *J Allergy Clin Immunol.* 2014; **133**(2 Supplement): AB179.  
[Publisher Full Text](#)
7. Lasmar L, Camargos P, Champs NS, *et al.*: **Adherence rate to inhaled corticosteroids and their impact on asthma control.** *Allergy.* 2009; **64**(5): 784–9.  
[PubMed Abstract](#) | [Publisher Full Text](#)
8. Jentzsch NS, Camargos P, Sarinho ES, *et al.*: **Adherence rate to beclomethasone dipropionate and the level of asthma control.** *Respir Med.* 2012; **106**(3): 338–43.  
[PubMed Abstract](#) | [Publisher Full Text](#)
9. 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**(5): 416–21.  
[PubMed Abstract](#) | [Publisher Full Text](#)
10. Chuenjit W, Engchuan V, Yuenyongviwat A, *et al.*: **Dataset 1 in: Achieving good adherence to inhaled corticosteroids after weighing canisters of asthmatic children.** *F1000Research.* 2017.  
[Data Source](#)

# Open Peer Review

Current Referee Status:



Version 1

Referee Report 09 August 2017

doi:10.5256/f1000research.11547.r24513



**Orathai Piboonpocanun**

Division of Allergy and Immunology, Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

The authors tried to use canister weight to calculate the number of doses actuated from the MDIs and to assess medical adherence to MDIs.

There are some issues which need clarification

1. Please clarify why the numbers of collected MDI canisters were not the same in each visit.
2. Please mentioned about patients who had exacerbation. Were they the same patients? Were these patients nonadherence to medication or did they have any specific problem?

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Partly

**Are the conclusions drawn adequately supported by the results?**

Partly

**Competing Interests:** No competing interests were disclosed.

**I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

Referee Report 24 April 2017

doi:10.5256/f1000research.11547.r22150

**Bee Wah Lee**

Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore

This study evaluated adherence to ICS prophylaxis in asthmatic children by using weight of canister as a means to determine inhaler compliance, by calculating doses used by using a regression equation based on canister weight. The authors conclude that in the absence of an inbuilt dose counter, weighing the canister was a useful means of improving adherence to daily treatment with ICS.

**Detailed comments:**

1. There were 52 children participating in the study. However, with each follow up visit (n=3) the number of canisters measure reduced progressively (44, 33, 23). Was there loss to follow up or did these patients fail to return their canisters? Could these patients be used as their comparative group in terms of asthma control over the period of follow up?
2. For the subjects with the 11 canisters that had remaining medication, was their asthma control affected by non compliance?
3. It may be more appropriate to use the term 'used' rather than 'discarded' canisters.
4. Under the paragraph: adherence assessment. Some editing of sentences may improve readability: Parents were asked to 'return' the 'used inhalers at the 8 week.....

'The weight of the canister was replaced in the regression equation' to "The number of remaining doses of remaining doses was extrapolated by using the weight of the used MDI canisters into the regression equation as shown:.....

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Partly

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Partly

**Competing Interests:** No competing interests were disclosed.

**I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.**

Referee Report 21 April 2017

doi:10.5256/f1000research.11547.r21967



**Wiparat Manuyakorn** 

Division of Allergy, Immunology, and Rheumatology, Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

The article is well written. However, there is some minor comment.

1. The authors mentioned that "The metered-dose inhalers (MDIs) currently available for inhaled corticosteroid delivery do not offer an integrated dose counter". This statement was true at the time when this study was performed. But currently, there are some MDIs that have dose counter. So this statement needs some amendment.

2. Method: the authors mentioned that "Participants needed to participate in a regular schedule every 8 weeks to obtain a new FLIXOTIDE® 125 inhaler." And the duration of treatment was 24 weeks. So it means that each participant would receive 3 inhalers. A total of 52 children was participated. So I wonder why only 100 MDI canister was evaluated. It should be  $52 \times 3 = 156$ ?. This may need the clarification.

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**