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Kooistra, Johan ; Metting, Esther; Dekhuijzen, Richard; Leendertse, Anne ; Hagedoorn, Paul; Janknegt, Robert

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## Rational Selection of Inhalation Devices in the Treatment of Asthma by Means of the System of Objectified Judgement Analysis

Johan Kooistra<sup>1</sup>, Esther Metting<sup>2</sup>, Richard Dekhuijzen<sup>3</sup>, Anne Leendertse<sup>4</sup>, Paul Hagedoorn<sup>5</sup> and Robert Janknegt<sup>6\*</sup>

<sup>1</sup>BENU Pharmacies, Maarssen, The Netherlands

<sup>2</sup>Epidemiologist/Behavioral Scientist, University Groningen, Faculty of Economics and Business and Medical Faculty, The Netherlands

<sup>3</sup>Pulmonologist, Radboud University Medical Center, Nijmegen, The Netherlands

<sup>4</sup>Clinical Pharmacist, Longfonds, Amersfoort, The Netherlands

<sup>5</sup>Sr. Technologist Inhalation, Department of Pharmaceutical Technology and Biopharmacy, University of Groningen, The Netherlands

<sup>6</sup>Hospital Pharmacist, Clinical Pharmacologist Sittard, The Netherlands

\*Corresponding Author: Robert Janknegt, Hospital Pharmacist, Clinical Pharmacologist Sittard, The Netherlands.

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### Abstract

**Objectives:** The large number of available medicines and devices makes it almost impossible to have sufficient knowledge of each individual medicine and device, especially for general practitioners. Reducing the number of medicines and devices, based on rational criteria, allows physicians and pharmacists to build experience with a more limited set of medicines and to standardise the inhalation instructions.

**Methods:** In this study inhalers are compared by means of the SOJA method. The following selection criteria were applied: uniformity in device, number of steps per inhalation, risk of errors, hygienic aspects, feedback mechanism, risk of inhalation with an empty inhaler.

**Results:** Substantial differences were seen in the overall scores, with the Turbuhaler device showing the highest score, followed by Nexthaler and Spiromax. Several devices require more or less identical techniques, such as Diskus and its "generics": Dry powder inhaler Glenmark or the Neutec have been scored separately, resulting in a much lower score than the Diskus, because only the LABA/ICS combination is available in these devices, without an option of rescue therapy in the same device.

**Conclusions:** A substantial reduction of inhalers, combined with optimal and standardised instructions should improve the care of asthma patients.

**Keywords:** Inhaled Corticosteroids; Short Acting Beta Sympathomimetics (SABA); Drug

### Introduction

Effective bronchodilatation and maintenance treatment with inhaled corticosteroids (ICS) are cornerstones of pharmacological treatment of asthma. The inhaled corticosteroids improve

symptom control and lung-function and decrease exacerbations and asthma related mortality with limited side-effects. Several different treatment options are available for inhalation, such as short acting beta sympathicomimetics (SABA) long acting

beta sympathicomimetics (LABA), short acting muscarine antagonists (SAMA), long acting muscarine antagonists (LAMA), inhaled corticosteroids (ICS), combinations of LABA and inhaled corticosteroids. The LABA/ICS combinations are first line treatment and recommended in the international and national asthma guidelines [1,2]. Each treatment option is used in different stages of asthma. Besides these pharmacological options, several inhalation devices, such as metered dose inhalers (MDIs), dry powder inhalers (DPIs) and soft mist inhalers are available.

The use of devices to inhale the medication is complicated and prone to errors. A bad inhaler technique leads to poor asthma control, poor adherence, increased risk of exacerbations and increased adverse effects [3,4]. Most patients (up to 70-80%) are unable to use their inhaler correctly and are, not always unaware of the problem. Also physicians are not always able to correctly demonstrate how to use the inhaler or unable to detect and correct the errors when their patient is inhaling their medication. The large number of available devices makes it difficult to have sufficient knowledge and experience of all details about the devices and medicine combination in general practice. Reducing the number of medicines and devices, based on rational criteria, allows physicians, nurses and pharmacists to build sufficient knowledge and experience with a more limited set of medicines and to standardize the inhalation instructions.

A model for drug decision making for formulary purposes is described and tested, the System of Objectified Judgement Analysis (SOJA) [5]. In this SOJA method, selection criteria for a given group of drugs are prospectively defined and the extent to which each drug fulfils the requirements for each criterion is determined. In this article we adjust and apply the SOJA method for on a limited set of inhalers to be used in general practice.

**Methods**

**SOJA methodology**

The methodology was described extensively previously [6]. The present article is an adaptation of this score for the treatment of asthma instead of COPD. The criteria were further discussed within the authors of this article; researchers, pharmacists, medical doctors and a patient representative.

The analysis to compare DPIs, soft mist inhalers and MDIs in the treatment of asthma was performed by the authors. The properties of all inhalers are compared to the hypothetical 'ideal' device from

that group, which is assigned the full relative weight for each criterion. This device will be available in all treatment options of asthma, very easy to use, no errors possible, easy to clean, provides optimal feedback that the drug was correctly inhaled and is not associated with the risk of using an empty inhaler. Within the SOJA-method, 1000 points are divided over the criteria that are considered to be relevant in the treatment of asthma. In the interactive program, the users are free to assign their own relative weight to each criterion using any scale they wishes. The program then computes the ranking scores for the different inhalers.

The following devices were included in the analysis: Autohaler, Axahaler, Breezhaler, Cyclohaler, Diskus/Accuhaler, dry powder inhaler Glenmark, Easyhaler, Ellipta, Elpenhaler, Fospiro, MDIs, Neutec Airmaster, Nexthaler, Novolizer, Redihaler, Respimat, Spiromax and Turbuhaler. Some devices, which are not approved for the treatment of asthma, were excluded: Genuair, Handihaler, Neumohaler and Zonda.

**Selection criteria**

Criterion	Relative weight
Uniformity in device	250
Numbers of steps per inhalation	225
Risk of (critical) errors	225
Hygienic aspects	20
Feedback mechanism	180
Risk of inhalation with an empty inhaler	100
Total score	1000

**Table 1:** Selection criteria with relative weight score.

The identified criteria were linked to its use are: uniformity in device and number of steps per inhalation. Adherence is a serious problem in the treatment of asthma and also linked to the use of the inhaler and these criteria. Other factors relate to risk of errors: critical errors, feedback mechanism, and risk of inhalation with an empty inhaler (see table 1).

**1 Uniformity of device**

It is an advantage when patients can make use of the same type of inhaler during all steps in the treatment of asthma. This will reduce the number of errors, improves the inhaler technique and improve adherence. This will also allow the patient to use the same type of inhaler when medicines are added or changed during the

course of the disease. The scoring of the weighting was based on discussions within the working party.

Some devices are approved as MART (Maintenance And Reliever Therapy). This is a combination of the fast acting formoterol (LABA) with an ICS, which is recommended in the guidelines to improve adherence to ICS and to reduce morbidity and mortality.

This combination is also considered to be an advantage concerning uniformity of device. This was scored separately.

The sub criteria for this selection criterion were based on the 2020 version of the GINA guideline and the Dutch nation asthma guideline [1,2].

The scoring is described in table 2.

Treatment option	Score in percent
SABA as reliever therapy	SABA 5%
ICS as maintenance therapy, in combination with SABA as reliever therapy in same device	ICS in one strength only 15% ICS in more strengths 20%
LABA/ICS combination as maintenance therapy, in combination with SABA as reliever therapy in same device	LABA/ICS in one strength only 15% LABA/ICS in more strengths 20%
Formoterol/ICS combination as MART therapy	Approved as maintenance and reliever therapy combination (MART therapy) 45%
LAMA in combination with ICS/LABA and SABA in same device	Fixed combination = 10% Separate LAMA available in same device as LABA/ICS combination 5%

Table 2: Uniformity per device, methodology.

### Number of steps per inhalation

The lower the number of steps per inhalation, the lower the risk of errors, the easier to use the device for the patient and more likely to adhere to the dosing regimen, and the more straightforward the instruction and easier to provide inhaler technique in a consult.

The device with the smallest number of steps was awarded 100%, whereas the device with the largest number of steps did not score. The scores for the other devices was obtained by linear interpolation.

### Risk of (critical) errors

Factors were considered as critical if there is a substantial risk of significant decrease of drug delivery with incorrect use. With an insufficient dose the clinical effect will be reduced and the goals of therapy will not be met. The methodology of scoring was extensively discussed in the Working Party. The estimation of the risk of incorrect use was based on both clinical studies [7,8] as well as observations during training and education of patients by authors JK and EM.

The scoring is described in table 3.

	Incidence	Risk	Deduction critical	Deduction non critical
Estimated error rate	<2%	Very low	2%	1%
	>2-5%	Low	3%	1%
	>5- <15%	Moderate	10%	2%
	15% -35%	High	25%	3%
	>35%	Very high	35%	5%

Table 3: Risk of critical errors, methodology.

### Hygienic aspects

Re-use of a device or space chamber could result in poor hygienic conditions. Also it is important that a re-usable device is easy to clean. Cleaning can prevent bacterial colonization in the device and ensure the quality and performance of the device [9].

### Feedback mechanism

Feedback mechanisms give information to the patient whether or not the device has produced a dose or if the patient did administer the prescribed amount of doses. This feedback information to the

use of the device may improve correct use and adherence to secure the outcome of the therapy [10].

This was scored as follows:

- 1 type of feedback: 60%
- 2 types of feedback: 90%
- 3 or more types of feedback: 100%.

	Score
Single dose device	100%
Dose counter and blockade after last dose	100%
Extra-large dose counter	90%
Dose-counter or dose-indicator	80%
No dose counter or dose-indicator	0%

Table 4: Scoring of risk empty inhaler.

**Risk of inhalation with an empty inhaler**

There is a risk that a patient keeps using an empty inhaler with no drug delivery and therefore no clinical effect.

For users of single dose devices it is obvious that these are empty and the risk of inhalation with an empty inhaler is low.

A counter is a useful tool in reducing the risk of inhalation with an empty inhaler, but it does not provide a guarantee. When the inhaler blocks, this makes it impossible to continue use of the inhaler.

**Results**

**Uniformity of device**

The score is presented in table 5.

**Number of steps per inhalation**

There are huge differences in the number of actions needed to inhale. The Ellipta inhaler showed the smallest number of steps and scored 100%. Various devices needed 14 steps per inhalation and one device even 15 steps. See table 6.

	SABA	ICS + SABA as needed	Combination of ICS/LABA + SABA as needed	LABA/ICS MART	Registered combination of ICS/LABA/LAMA	Total score
Weight	5	20	20	45	10	100
Autohaler	5	20	0	0	0	25
Axahaler	0	0	0	0	0	0
Breezhaler	0	0	0	0	10	10
Cyclohaler	5	20	0	0	0	25
Diskus	5	20	25	0	0	50
Dry powder inhaler Glenmark	0	0	0	0	0	0
Easyhaler	0	0	0	45	0	45
Ellipta	0	0	0	0	0	0
Elpenhaler	0	0	0	0	0	0
Forspiro	0	0	0	0	0	0
MDI	5	20	20	45	10	100
Neutec	0	0	0	0	0	0
Nexthaler	0	0	0	45	0	45
Novolizer	5	20	0	0	0	25
Redihaler	5	20	0	0	0	25
Respimat	0	0	0	0	0	0
Spiromax	0	0	0	45	0	45
Turbuhaler	5	20	20	45	0	90

Table 5: Uniformity per device, results.

Device	Empty capsule	Rattling of the capsule	Empty strip	Click	Visual	Counter	Taste (lactose)	Spray	Total feedback mechanisms	Score	Lactose (mg)
Autohaler				1					1	60%	
Axahaler	1	1					1		3	100%	24.4
Breezhaler	1	1					1		3	100%	23.6
Cyclohaler	1	1					1		3	100%	25
Diskus						1	1		2	90%	12.5
Dry powder inhaler Glenmark						1	1		2	90%	13
Easyhaler						1	1		2	90%	3.8
Ellipta						1	1		2	90%	25
Elpenhaler			1				1		2	90%	24.6
Fospiro			1			1	1		3	100%	11.95
MDI solution						1		1	2	90%	
Neutec						1	1		2	90%	13
Nexthaler				1		1	1		3	100%	9.9
Novolizer				1	1	1	1		4	100%	10.7
Redihaler									0	0%	
Respimat				1		1			2	90%	
Spiromax						1	1		2	90%	5/10
Turbuhaler						1			1	60%	0.73

**Table 6:** Feedback mechanisms, results.

Note: Not every MDI device has a counter and a spray is not a guarantee that it contains medication. The MDI is used as a comparator with other devices and available with counter.

A specification of the steps per inhalation is provided in supplement S1.

Action	Aerolizer	Autohaler	Axahaler	Breezhaler	Cyclohaler	Diskus Accuhaler + Glenmark	Easyhaler
Number of actions	14	5	14	14	14	5	7
Fill with a dose unit, prepare for use							
Remove/open cover	1	1	1	1	1	1	1
Shake		1					1
Place spacer							
Slide backwards						1	
Hold inhaler vertical							
Press button							1
Release button							1

Hold inhaler vertical							1
Hold inhaler horizontal						1	
Turn to load dosage							
Push lever upwards		1					
Close lever							
Release cover							
Open mouthpiece/ inhaler	1		1	1	1		
Open blister	1		1	1	1		
Remove capsule out of blister	1		1	1	1		
Place capsule in device	1		1	1	1		
Place strip in device							
Close mouthpiece	1		1	1	1		
Hold inhaler vertical	1		1	1	1		
Push button to perforate capsule	1		1	1	1		
Release button	1		1	1	1		
Remove strip							
Inhale	1	1	1	1	1	1	1
Remove spacer							
Turn for second dose							
Shake for second dose							
Place inhaler for second dose							
Push for second dose							
Inhale							
Remove spacer after second inhalation							
Open mouthpiece	1		1	1	1		
Remove capsule/ strip	1		1	1	1		
Close mouthpiece	1		1	1	1		
Place cover	1	1	1	1	1	1	1
Remove strips							
Number of inhalations	1		1	1	1		
<b>Action</b>	<b>Ellipta</b>	<b>Elpenhaler</b>	<b>Fospiro</b>	<b>MDI</b>	<b>Nexthaler</b>	<b>Novolizer</b>	
Number of actions	3	13	6	12	4	7	
Fill with a dose unit, prepare for use						1	
Remove/open cover	1	1	1	1	1	1	
Shake				1			
Place spacer				1			
Slide backwards							
Hold inhaler vertical							

Press button				1		1	
Release button						1	
Hold inhaler vertical							
Hold inhaler horizontal						1	
Turn to load dosage							
Push lever upwards			1				
Close lever			1				
Release cover							
Open mouthpiece/ inhaler		1					
Open blister		1					
Remove capsule out of blister		1					
Place capsule in device							
Place strip in device		1					
Close mouthpiece		1					
Hold inhaler vertical							
Push button to perforate capsule							
Release button		1					
Remove strip		1					
Inhale	1	1	1	1	1	1	
Remove spacer				1			
Turn for second dose							
Shake for second dose				1			
Place spacer for second dose				1			
Push for second dose				1			
Inhale				1			
Remove spacer after second inhalation				1			
Open mouthpiece		1					
Remove capsule/ strip		1					
Close mouthpiece		1					
Place cover	1	1	1	1	1	1	
Remove strips			1				
Number of inhalations	1	1	1	2	1	1	

**Supplement 1:** Specification of number of steps per inhalation.



Table number of steps per inhalation scoring.

3 steps	Ellipta	100%
4 steps	Nexthaler, Redihaler, Spiromax	91%
5 steps	Autohaler, Diskus, Glenmark, Neutec, Turbuhaler	82%
6 steps	Forspiro	73%
7 steps	Easyhaler, Novolizer	64%
9 steps	Respimat	48%
12 steps	MDI	19%
13 steps	Elpenhaler	10%
14 steps	Aerolizer, Axahaler, Breezhaler, Cyclohaler	0%

**Table A**

**Risk of (critical) errors**

The error rate cannot be specified directly from a large scale comparative study including all available devices.

Several studies identifying the (critical) error rate of the available devices were taken into consideration [7,8].

A specification of the potential critical errors is provided in Supplement S2.

- 95%: Ellipta, Nexthaler, Spiromax
- 93%: Novolizer,
- 91%: Diskus, Glenmark, Forspiro, Neutec, Turbuhaler
- 95%: Redihaler
- 79%: Aerolizer, Axahaler, Breezhaler, Cyclohaler
- 75%: Autohaler
- 60%: Respimat
- 58%: Easyhaler
- 43%: Elpenhaler
- 19%: MDI.

Results					
Aerolizer, Axahaler, Breezhaler					
Deduction	Capsule inhalers	Aerolizer	Axahaler	Breezhaler	Critical error
1	Damage capsule when opening blister	Low	Low	Low	No
1	Wet hands when manipulating capsules	Low	Low	Low	No
2	Capsule at the wrong position	Very low	Very low	Very low	Yes
3	Inhaler vertical, no perforation of capsule	Low	Low	Low	Low
2	No perforation of capsule	Very low	Very low	Very low	Yes
3	Failure to release after perforation	Low	Low	Low	Yes
1	Too frequent perforation	Low	Low	Low	No
3	Shake after ready for use	Low	Low	Low	Yes
3	Change capsules	Very low	Very low	Very low	Yes
2	Swallow capsules instead of inhalation	Very low	Very low	Very low	Yes
	Deduction	21	21	21	
	Score	79%	79%	79%	
Cyclohaler, Handihaler, Zonda					
Deduction	Capsule inhalers	Cyclohaler	Handihaler	Zonda	Critical error
1	Damage capsule when opening blister	Low	Low	Low	No

1	Wet hands when manipulating capsules	Low	Low	Low	No
2	Capsule at the wrong position	Very low	Impossible	Very low	Yes
3	Inhaler vertical, no perforation of capsule	Low	Low	Low	Yes
2	No perforation of capsule	Very low	Very low	Very low	Yes
3	Failure to release after perforation	Low	Low	Low	Yes
1	Too frequent perforation	Low	Low	Low	No
3	Shake after ready for use	Low	Low	Low	Yes
3	Change capsules	Very low	Very low	Very low	Yes
2	Swallow capsules instead of inhalation	Very low	Very low	Very low	Yes
	deduction	21	19	20	
	Score	79%	81%	80%	
<b>Autohaler, Easyhaler</b>					
Autohaler	Incidence	Risk	Deduction	Score	
Failure to shake suspension	Moderate	Critical	10		
Insufficient shaking before use	Very high	Non critical	5		
Stop inhalation at click	Moderate	Critical	10		
			25	75%	
Easyhaler	Incidence	Risk	Deduction	Score	
failure to shake before use	Very low	Critical	35		
Not vertical	Very low	Critical?	2		
Press to click	Very low	Critical	2		
Shake after ready for use	Low	Critical	3		
			42	58%	
<b>Diskus, Diskus like inhaler Glenmark, Ellipta, Neutec</b>					
Diskus, Diskus like inhaler Glenmark, Neutec	Incidence	Risk	Deduction	Score	
Not horizontal after ready for use	Very high	Non critical	5		

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Catch not backwards	Very low	Critical	2	
Open catch to click	Very low	Critical	2	
			9	91%
Ellipta	Incidence	Risk	Deduction	Score
Hold upside down after opening	Very low	Critical	2	
Failure to open catch until click	Very low	Critical	2	
Lips partly on opening	Low	Non critical	1	
			5	95%
<b>Elpenhaler, Forspiro</b>				
Elpenhaler	Incidence	Risk	Deduction	Score
failure to close mouth-piece	Moderate	Critical	10	
draw too firmly and loose powder	Moderate	Critical	10	
failure to draw strip	Moderate	Critical	10	
Shake after ready for use	Very low	Critical	2	
Failure to turn after strip	High	Critical	25	
			57	43%
Forspiro	Incidence	Risk	Deduction	Score
Handle not open	Low	Critical	3	
Handle not open enough	Very low	Critical	2	
Close handle until click	Very low	Critical	2	
Shake after ready for use	Very low	Critical	2	
			9	91%

<b>Genuair and Novolizer, Nexthaler</b>				
Genuair and Novolizer	Incidence	Risk	Deduction	Score
Not horizontal	Very low	Non critical	1	
Failure to release button	Very low	Critical	2	
Upside down after ready for use	Very low	Critical	2	
Stop inhaling after click	Very low	Critical	2	
			7	93%
Nexthaler	Incidence	Risk	Deduction	Score
Not vertical	Very low	Non critical	1	
No correct opening until click	Very low	Critical	2	
Shake after ready for use	Very low	Critical	2	
			5	95%
<b>Redihaler, Respimat</b>				
Redihaler	Incidence	Risk	Deduction	Score
Insufficient shaking before use	Very high	Non critical	5	
failure to shake before use	Moderate	Critical	10	
			15	85%
Respimat	Incidence	Risk	Deduction	Score
Mouth around air supply	Low	Critical	5	
Insufficient hand mouth coordination	High	Critical	25	

Fire too early	Moderate	Critical	10	
			40	60%
<b>Spiromax, Turbuhaler</b>				
Spiromax	Incidence	Risk	Deduction	Score
Not vertical	Very low	Non critical	1	
Open until click	Very low	Critical	2	
Shake after ready for use	Very low	Critical	2	
			5	95%
Turbuhaler	Incidence	Risk	Deduction	Score
Not vertical	Very high	Non critical	5	
Failure to turn until click	Very low	Critical	2	
Shake after ready for use	Very low	Critical	2	
			9	91%
<b>MDI suspension</b>				
MDI suspension	Incidence	Risk	Deduction	Score
Failure to shake	Fairly frequent	Critical	10	
Insufficient shaking	Very frequent	Non critical	5	
Failure to inhale within 5 seconds after shaking	Infrequent	Non critical	3	
Failure to use spacer	Frequent	Critical	25	
Two puffs at the same time in spacer	Low	Critical	3	
Bad/long time use of spacer	Very frequent	Critical	35	
			81	19%

**Supplement S2:** Specification of critical errors.

**Hygienic aspects**

Most devices scored 100%: change inhaler each time, and easy to clean.

This was the case for Autohaler, Axahaler, Breezhaler, Diskus, Dry powder inhaler Glenmark, Easyhaler, Ellipta, Fospiro, Neutec, Nexthaler, Redihaler, Spiromax and Turbuhaler.

Cyclohaler and Novolizer and Respimat have to be replaced actively and are relatively easy to clean and therefore score 50%.

Elpenhaler is difficult to clean, because the inhaler contains removable strips and therefore scores 50%.

MDI's have to be actively replaced and the spacer is difficult to clean and do not score.

**Feedback mechanisms**

The score is presented in table 6.

Device	Empty capsule	Rattling of the capsule	Empty strip	Click	Visual	Counter	Taste (lactose)	Spray	Total feedback mechanisms	Score	Lactose (mg)
Autohaler				1					1	60%	
Axahaler	1	1					1		3	100%	24.4
Breezhaler	1	1					1		3	100%	23.6
Cyclohaler	1	1					1		3	100%	25
Diskus						1	1		2	90%	12.5
Dry powder inhaler Glenmark						1	1		2	90%	13
Easyhaler						1	1		2	90%	3.8
Ellipta						1	1		2	90%	25
Elpenhaler			1				1		2	90%	24.6
Fospiro			1			1	1		3	100%	11.95
MDI solution						1		1	2	90%	
Neutec						1	1		2	90%	13
Nexthaler				1		1	1		3	100%	9.9
Novolizer				1	1	1	1		4	100%	10.7
Redihaler									0	0%	
Respimat				1		1			2	90%	
Spiromax						1	1		2	90%	5/10
Turbuhaler						1			1	60%	0.73

**Table 6:** Feedback mechanisms, results.

Note: Not every MDI device has a counter and a spray is not a guarantee that it contains medication. The MDI is used as a comparator with other devices and available with counter.

A device was scored for lactose content when this was 3 mg or more. It was shown that 80% of subjects were able to taste 3 mg of lactose [11].

**Risk of inhalation with an empty device**

All single dose devices are awarded 100%: Aerolizer, Axahaler, Breezhaler, Cyclohaler, and Elpenhaler.

A combination of counter and blockade is applicable to Respimat this device scores 100% as well.

A large counter is available for Ellipta: this device scores 90%.

The following devices have a counter and score 80%: Diskus, Dry powder inhaler Glenmark, Easyhaler, Forspiro, MDIs, Neutec, Nexthaler, Novolizer, Spiromax, and Turbuhaler.

No counter is applicable for Autohaler and Redihaler: these devices do not score.

Note: Not every MDI device has a counter and a spray is not a guarantee that it contains medication. We have given MDIs the “benefit of the doubt”.

The SOJA score is presented in table 7.

Device	Uniformity	Steps	Critical errors	Hygiene	Feed back	Risk of empty inhaler	Score
Weight	250	225	225	20	180	100	1000
Autohaler	63	185	168	20	108	0	544
Axahaler	0	0	178	20	180	100	478
Breezhaler	25	0	178	20	180	100	503
Cyclohaler	63	0	178	10	180	100	531
Diskus	125	185	205	20	162	80	777
Dry powder inhaler Glenmark	0	185	205	20	162	80	652
Easyhaler	113	144	131	20	162	80	650
Ellipta	0	225	214	20	162	80	701
Elpenhaler	0	23	97	10	162	100	392
Forspiro	0	165	205	20	180	80	650
MDI	250	43	83	0	162	80	618
Neutec	0	185	205	20	162	80	652
Nexthaler	113	205	214	20	180	80	812
Novolizer	63	144	209	10	180	80	686
Redihaler	63	205	191	20	0	0	479
Respimat	0	104	135	20	162	100	531
Spiromax	113	205	214	20	162	80	794
Turbuhaler	225	185	204	20	108	80	822

Table 7: SOJA score for inhalation devices in asthma treatment.

### Outcome

Substantial differences were seen in the overall scores, with the Turbuhaler device showing the highest score, followed by Nexthaler and Spiromax. Several devices require more or less identical techniques, such as Diskus and its “generics”: Dry powder inhaler Glenmark or the Neutec have been scored separately, resulting in a much lower score than the Diskus, because only the LABA/ICS combination is available in these devices, without an option of rescue therapy in the same device.

The score is quite different from the previously published score on devices in COPD [6], because of major differences in the availability of treatment options per device.

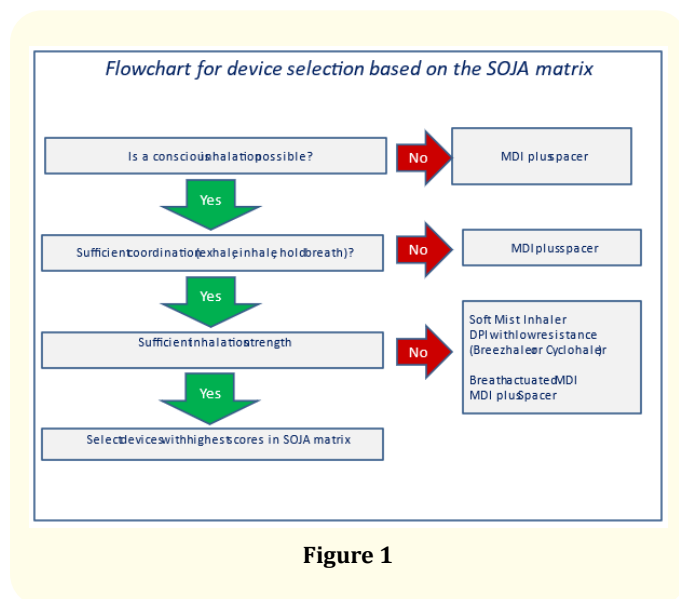
### Discussion

It was feasible to apply the SOJA method to rank the different inhaler devices in a transparent way and to make a well-considered selection of inhalation devices for a formulary in general practice.

**Strength and limitations of the methodology**

This has been described extensively in the article on devices in COPD [6].

The cost of the devices was not taken into account, because this varies with time and country and are often not public. Costs also vary for the same inhaler with different medicines. In practice, Costs are of course important and should be evaluated in the final selection process Exclusion of this criterion makes this comparison more sustainable and more internationally applicable. Patient-related factors should also be taken into consideration if a device is selected for an individual patient. This is expressed in figure 1.



**Figure 1**

The main outcome of this matrix may be that major steps can be made in reducing the number of different devices, thereby allowing standardized and optimal patient information, which can be the same provided by all caregivers.

The scoring of the MDIs in this article is only used for comparison with the DPIs. We made no distinction between the different MDIs to make the method more comprehensible. The results of the scoring for the MDI provides insight into the difference with the DPIs and emphasizes that combining a DPI and an MDI is not desired. We do realize that an MDI is an important treatment option in patient with asthma who suffer from dry powder induced cough or do have insufficient inhalation flow for a DPI. The scoring of the MDI will be elaborated in a future article with the use of the SOJA method for several MDIs combined with spacers.

**Conclusions**

Large differences are observed in the scores of the devices. It seems logical to limit the number of different devices that are used in the treatment of asthma through regional or local formulary decisions. This results in a smaller number of different devices used by individual patients, which will likely result in better treatment results through fewer inhalation errors. Also, reducing the number of different devices prescribed by physicians and dispensed by pharmacists will make it easier to standardize inhalation instructions, which may even further improve treatment outcomes.

**Bibliography**

1. "GINA guideline" (2021).
2. "NHG standaard astma bij volwassenen" (2021).
3. Usmani OS, *et al.* "Critical inhaler errors in asthma and COPD: a systematic review of impact on health outcomes". *Respiratory Research* 19.1 (2018): 10.
4. Kocks JWH, *et al.* "Systematic review of association between critical errors in inhalation and health outcomes in asthma and COPD". *npj Primary Care Respiratory Medicine* 28.1 (2018): 43.
5. Janknegt R and Steenhoek A. "The System of Objectified Judgement Analysis. A tool in rational drug selection for formulary purposes". *Drugs* 53 (1997): 550-562.
6. Janknegt R, *et al.* "Rational selection of inhalation devices in the treatment of chronic obstructive pulmonary disease by means of the System of Objectified Judgement Analysis (SOJA)". *European Journal of Hospital Pharmacy* (2020).
7. Van der Palen J, *et al.* "A randomised open-label cross-over study of inhaler errors, preference and time to achieve correct inhaler use in patients with COPD or asthma: comparison of ELLIPTA with other inhaler devices". *npj Primary Care Respiratory Medicine* 26 (2016): 16079.
8. Chrystyn H, *et al.* "Device errors in asthma and COPD: systematic literature review and meta-analysis". *npj Primary Care Respiratory Medicine* 27 (2017): 22.
9. Uematsu T, *et al.* "Evaluation of Hygiene in Dry Powder Steroid Drug Inhalers Used by Elderly Asthma Patients". *Yakugaku Zasshi* 140 (2020): 789-798.
10. Denyer J. "Adherence monitoring in drug delivery". *Expert Opinion on Drug Delivery* 7 (2010): 1127-1131.



11. Higham MA., *et al.* "Determination of the minimum dose of lactose drug carrier that can be sensed during inhalation". *British Journal of Clinical Pharmacology* 40 (1995): 281-282.

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