



Smartinhaler for asthma

Medtech innovation briefing Published: 11 January 2017

www.nice.org.uk/guidance/mib90

Summary

- The **technology** described in this briefing is Smartinhaler. It is a technology that monitors the activation of a person's asthma inhaler. This information is uploaded to a mobile or cloud-based application.
- The **innovative aspect** is that this has the potential to allow real-time monitoring of adherence to asthma treatments. This information can be used to give reminders and share data between patients and clinicians.
- The intended **place in therapy** would be for people with asthma in the community setting, together with personalised asthma plans and regular clinical review.
- The key points from the evidence summarised in this briefing are from 5 randomised controlled trials from the UK, Australia and New Zealand, including a total of 589 people with asthma (adults and children) using Smartinhaler in a community setting. The authors conclude that Smartinhaler devices were more effective than standard care in improving adherence to asthma medication. Two of the studies showed significant improvement in some clinical outcomes.

- **Key uncertainties** are that some of the available studies were either not designed to, or were not adequately powered to, show whether improved adherence is associated with significantly improved outcomes.
- The **cost** of Smartinhaler devices is £100 per unit (exclusive of VAT), plus £14.17 per month for each healthcare professional to access cloud-based data.
- The **resource impact** would be greater than standard care, because of the cost of the device and software access, unless reductions in GP and hospital visits were realised.

The technology

The Smartinhaler technology platform consists of a group of sensor devices and software. The sensors are contained in a small plastic case that clips around an asthma inhaler to detect and record inhaler activation. Audiovisual alerts on the sensor device remind patients if any medication is missed, and data on inhaler use can be shared with clinicians via the software.

There are 3 device groups, SmartTurbo2, SmartTouch and SmartTouch AV. Each group accommodates different types of inhaler, and has slightly different functionality:

- The SmartTurbo2 fits to the base of Turbohaler tubular inhalers.
- The SmartTouch and SmartTouch AV clip around angled "press and breathe" type inhalers.
- The SmartTouch AV has the additional feature of a small touch screen on the device itself. This allows reminders to be set and data to be reviewed directly on the device.

The Smartinhaler can also be used when a metered dose inhaler is combined with a spacer. Not all inhalers are compatible with the Smartinhaler.

Devices are available with non-rechargeable lithium coin cell batteries, or lithium polymer batteries that can be recharged using a USB connection. The expected service life for rechargeable devices is 2 years, and 1 year for non-rechargeable versions. For both types, low battery warnings are shown on the device.

All of the Smartinhaler devices record the date and time of inhaler activation. The devices do not record the quantity of medication inhaled by the patient, or how much medication is

left in the canister. It also cannot record whether a good inhalation technique was used.

The software packages in the Smartinhaler technology platform are:

- SmartinhalerLive, a cloud-based application that stores the uploaded data on inhaler activation. It is available for a monthly fee, and allows data to be shared by the inhaler user to their family and clinical teams, according to the permissions set. Data is uploaded using the Smartinhaler app or the Smartinhaler Connection Centre.
- Smartinhaler app, which is available for iPad, iPhone and Android smartphones and tablets. This allows the user to set the reminders on their device and to review their own data for the last 7 or 28 days. It also uploads the data from the device to the SmartinhalerLive website via a USB or Bluetooth connection.
- Smartinhaler Connection Centre, a desktop application that is used to upload data from the device to the SmartinhalerLive website via a USB connection on a computer.

The innovation

The innovative feature is the sensor to detect inhaler activation, and the communication of this information to the Smartinhaler app and SmartinhalerLive software. The technology sends reminders of missed medication doses to the patient, and potentially allows adherence to medication to be tracked and shared with clinical teams. This may help the patient to adhere to their medication schedule, and aid the clinical team in understanding patient adherence.

Current NHS pathway

NICE's <u>quality standard</u> on asthma states that people who are diagnosed with asthma should have a personalised action plan, and this should be reviewed at least once per year. The review should include medication, inhalation techniques and adherence (<u>Royal College of Physicians 2015</u>, <u>Asthma UK 2016</u>).

People with asthma may be treated in primary or secondary care. Medication is generally prescribed in the form of preventer (corticosteroid) and reliever (bronchodilator) inhalers, although not all patients will need both of these. Some people have these combined into a single inhaler, known as maintenance and reliever therapy.

Preventer inhalers are taken regularly, even when feeling well. Non-adherence to preventer medication is associated with increased risk of poor asthma control.

Reliever inhalers are taken only when needed. Overuse of short-acting bronchodilators is a key indicator of poor asthma control and of higher risk of exacerbation and death (Royal College of Physicians, 2015). People experiencing a severe asthma attack may need emergency medical care; 185 people are admitted to hospital and 3 people die from an asthma attack in the UK each day, often before emergency medical care can be given (NHS Choices, Asthma UK).

It can be difficult for patients to accurately estimate the medication taken, and adherence is likely to be over-reported to clinicians (Morton 2014, BTS/SIGN 2016). Accurate information on adherence may help to identify if it is a factor in asthma control. Current guidance (BTS/SIGN 2016) mentions the use of prescription records and self-reporting to assess adherence. The use of electronic monitoring systems is described as a gold standard for research, but not normally available for clinical use.

NICE is aware of the following CE-marked devices that appear to fulfil a similar function as Smartinhaler:

- HeroTracker, Cohero Health
- CareTRx, Teva Pharmaceuticals
- Propeller System, Propeller Health

Population, setting and intended user

Smartinhalers are intended to be used by people with asthma in any setting including at home and in the community, as part of their normal routine. They may be used to monitor medication use for respiratory diseases including asthma. Smartinhalers can be used by adults and children.

Smartinhaler devices are available for preventer, reliever and maintenance and reliever therapy inhalers. Some training will be needed to familiarise patients and clinicians with the device and associated software. This may include fitting the device correctly and checking inhaler technique. Patients will need to be advised of what data is captured and how they are able to view it.

Smartinhaler does not monitor the inhalation technique when it is activated. Therefore patient education is important to ensure that the correct inhalation technique is used.

Costs

The Smartinhaler device attaches to a compatible inhaler. The 3 different types of Smartinhaler (SmartTouch, SmartTouch AV and SmartTurbo2) each cost £100. Prices may vary for high-volume purchasers. The cost of the inhaler is not included.

To collect and interpret the data from the Smartinhaler device, the cloud-based SmartinhalerLive software is needed. Access to this service costs £14.17 per month for each healthcare professional logging into the system. The manufacturer has stated that this cost would be subject to negotiation depending on the volume uptake. There is no additional cost to the patient to access their data via an app on a smartphone or tablet.

The device can be removed and attached to a new inhaler when the inhaler needs replacing. Non-rechargeable devices will operate for at least 1 year and rechargeable devices have an expected service life of 2 years.

Costs of standard care

Standard care for monitoring asthma medication use consists of the development of a personalised asthma plan and scheduled review. This would still be needed if Smartinhaler devices were used, and so Smartinhaler would be an additional cost to standard care.

Resource consequences

The manufacturer advises that the Smartinhaler is currently in use in the NHS both as part of the patient pathway and as a measurement tool in clinical trials.

Use of Smartinhaler could potentially lead to a change in the approach to reviewing personal action plans for asthma, with data used to identify people who need more frequent review, or who do not need to be seen in person for an annual review.

Currently, the use of Smartinhaler devices and software would be an additional cost to standard care. It could serve to improve interactions between people with asthma and their clinicians, and improve adherence to asthma therapy. This in turn could improve asthma symptoms, meaning fewer days missed from school, work or normal activities, and reduce the need for additional interventions or emergency admissions. The evidence for these possible resource consequences is limited at the present time.

Although the data recorded by Smartinhaler can be uploaded using a computer, in order to use the full functionality of some Smartinhaler devices, the user would need a smartphone. Clinicians will need to have enough time to review the data collected and give feedback on adherence.

Regulatory information

Smartinhaler devices and software were CE marked as class 1 devices between 2014 and 2016.

A search of the Medicines and Healthcare Products Regulatory Agency website revealed that no manufacturer Field Safety Notices or Medical Device Alerts have been issued for this technology.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

Smartinhaler devices are intended to improve the quality of life for people with asthma. Severe asthma which has a substantial and long-term adverse effect on a person's ability to carry out normal day-to-day activities is considered a disability. Adherence may be a bigger issue for children and adolescents. Disability and age are protected characteristics under the Equality Act 2010.

Clinical and technical evidence

A literature search was done for this briefing in accordance with the published process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting medtech@nice.org.uk.

Published evidence

Five randomised controlled studies (RCTs) are summarised in this briefing, including 589 patients. One study was done in the UK, 2 in Australia and 2 in New Zealand.

All 5 RCTs reported that people in the intervention group, which used Smartinhaler reminders (and clinician feedback in some trials), had higher adherence to medication than those in the comparator group. Most trials found that both the intervention and control groups had improved clinical outcomes compared to baseline.

The differences in clinical outcomes between the intervention and comparator groups varied between the studies. Two studies found that the intervention arm showed significant improvement for some clinical outcomes (<u>Chan et al. 2015</u>, <u>Morton et al. 2016</u>). Chan (2015) recruited patients from the emergency department and they may have had poorer baseline adherence to medication than people in the other studies. Three studies found that there were no significant differences in any clinical outcomes.

An additional study considered the acceptability of Smartinhaler to 7 young people aged between 11 and 16 (Howard et al. 2017). Those surveyed felt that the ability to share information with healthcare professional was very useful, but were worried about how the device looked, and whether it would attract additional attention.

Also, 5 studies were identified that looked at the accuracy and reliability of the Smartinhaler device. Benchtop testing on small numbers of earlier device versions was reported by <u>Burgess et al. (2006)</u> and <u>Foster et al. (2011)</u>. Foster et al. (2011) also reported a 7 day field test with patients. Pilcher et al. (2015, 2016) reported that in bench testing, accurate recording occurred in 2,796 of 2,800 actuations (99.9%) for the SmartTurbo and 2,558 of 2,560 actuations (99.9%) for the SmartTouch. <u>Patel et al. (2013)</u> reported the reliability of Smartinhaler devices used as monitoring tools during a 24 week trial with

303 patients. Complete data was available from 2,498 of 2,642 dispensed monitors (94.5%) and 2,498 of 2,549 returned monitors (98.0%).

<u>Table 1</u> summarises the RCTs and their strengths and limitations.

Strengths and limitations of the evidence

Five good-quality RCTs were reported in full, and one of these was based in the UK NHS. The total patient group included a wide age range of adults and children.

Four of the 5 studies were sufficiently powered to investigate adherence, but may have been underpowered to detect a statistically significant difference in clinical outcomes between the intervention and the control. The study duration may also have been too short to show clinical outcomes.

Adherence reporting is based on a count of the number of activations of the inhaler. Some trials used checks to discount rapid sequences of activation indicating "dumping" medication prior to a review. There is no method to confirm that every activation resulted in delivery of medication to the person with asthma.

The different levels of medication being prescribed to people within a study and comparing the studies may have confused the results relating to clinical outcomes. Some authors noted that if prescription doses are very high, then people may be having the optimum level of medication even if they do not adhere to the prescription.

Reviews in the clinical trials were more frequent than in normal UK practice, and this may have influenced adherence levels.

Table 1 Summary of evidence

Study size,	Intervention	Outcomes	Strengths and limitations
design and	and		
location	comparator(s)		

Burgess et al. 2010 26 children with asthma which was not well controlled despite preventative medicine, 6 to 14 years inclusive RCT Single centre, Australia	Adherence feedback from Smartinhaler data at review (n=14). No feedback at review (n=12). All patients had a personalised plan, preventative medication and a Smartinhaler monitoring device. Monthly review for 6 months.	Adherence was 21.1% higher in the intervention group (average over 4 months). Asthma control measures improved for both groups, but there was no significant difference between groups.	Strengths: No conflicts of interest. Limitations: Results not fully reported with confidence intervals. Small sample size. Funding: not stated. The authors report no conflicts of interest.
---	--	---	--

Chan et al. 2015 220 children (6-15 years) attending the emergency department with asthma exacerbation. and were on, or needed, twice daily treatment with corticosteroids **RCT** Single centre New Zealand

All patients had preventer and reliever medication that incorporated a Smartinhaler. Followed up every 2 months for 6 months. Intervention group had audiovisual reminders enabled. Control group had audiovisual reminders disabled.

Median adherence was significantly greater in the group using Smartinhalers (84% vs 30%). There was no significant difference in the number of days absent from school for any reason, or because of asthma. There was a

There was a significant improvement in the group using Smartinhalers for the Childhood Asthma Control Test Score and % with 1 or more parental reported exacerbations.

Control group adherence was lower than in other studies; this may be because recruitment in the emergency department may have biased selection towards participants with poorly controlled asthma.

This may explain why differences between groups for clinical outcomes were observed in this study.

Funding: Smartinhalers provided by manufacturer (then called Nexus 6). Investigators provided feedback to the manufacturer about device functions, but the manufacturer had no involvement in any part of the study. Authors declared no competing interests.

Charles et al. 2007

110 participants

(12 to 65 years)

with diagnosis of asthma RCT Single centre, New Zealand All patients
were
prescribed 250
micrograms
fluticasone
propionate
twice daily via a
Smartinhaler.
Follow-up was
for 24 weeks
after a 2-week
run-in period.

Clinics were at 0, 6, 12, 18, and 24 weeks.

Intervention group had audiovisual reminders enabled.

Control group had audiovisual reminders disabled.

Adherence levels were significantly higher in the intervention group.

The percentage of medication taken during the final 12 weeks was: intervention mean 88% (standard deviation [SD] 16), control 66% (SD 27).

There were no significant differences in clinical outcomes between the 2 groups.

The 24-week time period was designed to allow participants to revert to normal practice over the duration of the study. Participants were not aware that adherence was the primary outcome.

The dose of fluticasone propionate was 500 micrograms per day for all patients to achieve maximum benefit.

Authors state that 80 to 90% of benefit can be obtained at a dose of 200 micrograms per day, which would be achieved at even 50% adherence to 500 micrograms per day. This could explain the lack of difference in lung function or quality of life between the 2 groups.

Funding: supported by a grant from GlaxoSmithKline, UK.
Authors declare no competing interests.

Foster et al. 2014

143 patients (14 to 65 years) with suboptimal asthma control, and prescribed twice daily combined corticosteroid and long-acting b2-agonist medication for 1 month or more Pragmatic cluster 2×2 factorial parallel-group. **RCT** 43 GPs. Australia

2010-13

or control

GPs randomised

to intervention

Inhaler
reminders and
feedback (IRF):
twice daily
Smartinhaler
reminders for
missed doses,
graphs
available to GPs
and patients.
Adherence
discussed at
GP follow-up.
Personalised

Personalised adherence discussion (PAD):

Discussion with GP about barriers to adherence, and patient set goals.

Usual care
(UC): GP
training,
asthma plan,
inhaler
education and
follow up
appointment.
Each branch
provided
separately plus
one with PAD
plus IRF.

All patients had

There was a statistically significant improvement in adherence between the groups with audiovisual reminders and feedback and the groups without.

There were no statistically significant differences between groups for other outcomes.

In general,
patients had a
significant
improvement in
clinical outcomes
between baseline
measurements
and the study
period.

Strengths: Pragmatic design in primary care setting.

Study data collected directly by study staff.

Limitations:

Several GPs were lost to the study meaning fewer patients were recruited than the planned 220 for the sample size calculation for asthma control. Sample sizes were not calculated for other outcomes.

Baseline fluticasone prescriptions were high (718 micrograms/day) compared to a suggested maximum efficiency at 500 micrograms/day. Authors suggest that a slight increase in adherence for all groups may have led to improved clinical outcomes, with higher adherence rates unable to produce further improvement.

Funding: National Health and Medical Research Council of Australia with support for equipment purchase (but not Smartinhaler) from manufacturers. Conflicts of interest are declared and are stated in the paper.

SmartTrack
devices, but
only the IRF
group (patients
and GPs) were
made aware of
the
functionality
during trial.
Data was
collected by
telephone at 0,
2, 4 and 6
months.

Morton et al. 2016

90 children
(6 to16 years)
with poorly
controlled
asthma (asthma
control
questionnaire
[ACQ] at least
1.5).

All taking regular inhaled steroids.

Open label RCT. 2 hospital clinics in UK. 2013–14. NCT02451709 All patients were reviewed in routine asthma clinics at 3, 6, 9 and 12 months.

Prior to randomisation all patients had a review of inhaler technique and an education session.

Intervention:
Smartinhaler
device with
reminders
activated. Data
reviewed and
adherence
discussed at
clinic visits.

Comparator:
Smartinhaler
device with
reminders
deactivated. No
review of data
until the end of
study.

Primary outcome was ACQ score at 3, 6, 9 and 12 months. This decreased in both groups, but there were no significant differences between the groups.

The intervention group experienced significantly fewer unplanned attendances at the GP or emergency department for asthma, and significantly fewer courses of oral steroids were needed.

FEV, days off school due to asthma and use of beta agonists were not significantly different between groups.

There was a high rate of lost or broken devices, particularly in the Strengths:

UK setting

Protocol based on routine clinical practice

12-month duration.

Limitations:

Non-blinded.

Funding: Not stated. No competing interests declared.

	intervention arm.	

Recent and ongoing studies

NCT02386722 Intervention to Improve Inhalative Adherence Cantonal Hospital, Baselland, Switzerland has a primary outcome date of March 2016, but the status is recruiting.

Specialist commentator comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Three out of 5 specialist commentators were familiar with this type of technology, with 1 out of 5 using a similar device regularly. None of the specialist commentators had used Smartinhalers.

Level of innovation

Three commentators said that Smartinhaler device was a novel concept, 2 felt that there was a limited level of innovation. It was noted that there are other similar devices, and that some emerging technologies can monitor the quality of inhaler usage, although these are not yet widely available and have less communication functionality. Several noted that the Smartinhaler is not compatible with all inhaler devices.

Potential patient impact

Commentators agreed that improving adherence in appropriate groups of patients was likely to lead to better control and reduced symptoms, and could potentially reduce the number of hospital visits and need for escalation of treatment. They also agreed that the existing evidence on Smartinahler user was not sufficient to show these outcomes at this point in time. One commentator felt the technology was not sufficiently advanced to result in fewer hospital visits or less invasive treatments.

Several commentators noted groups who may benefit in particular including adolescents, people who have repeated emergency attendance, people with poorly controlled asthma

and people with very busy lifestyles. Other groups mentioned were people under consideration for advanced therapies, people with high fractional exhaled nitric oxide levels, and people with cognitive defects or mental health disorders. Commentators noted that there was currently no evidence for benefit in any of these groups.

One commentator noted that some patients may find this 'supervision' of treatment invasive especially if this is then used to frame further adherence discussions, but another said that Smartinhalers may reinforce good adherence behaviour and self-management as well as supporting a move to managing people according to their need.

Limitations on impact are that non-adherence is only one of the factors to be considered when a patient's asthma is poorly controlled. The technology does not address other reasons for non-adherence, such as such as inhalers running out or prescription costs. It also does not address inhaler technique which can be a very important factor.

Potential system impact

The system would require some level of training for patients and staff, and patients would need to understand what data was collected and who would access it.

Some commentators noted that there would be a significant resource implication to using this technology, and that currently there was no evidence to show that there would be a reduction in the number of clinic visits needed.

It was noted that resource implications include purchasing the devices, accessing software, having IT systems in place, and clinician time to set up devices and review data. There is likely to be an additional cost to replace lost or broken devices.

One commentator noted that the cost to access the data may be particularly significant for GPs with low numbers of patients using the system.

One commentator felt that Smartinhaler might be used only for brief periods with patients to look at adherence prior to a medication review, because of device costs, and that this would diminish the potential benefits.

One commentator felt there may be an increase in reviews for patients in the short term, but that improved control would lead to fewer emergency visits and admissions to hospital over time.

General comments

Current care pathways rely on subjective measures of adherence and can be time consuming and inaccurate. Early identification of non-adherence may prevent unnecessary treatment escalation and allow discussion of barriers to adherence. One commentator noted that the trials had much higher frequency of review than normal clinical practice, which will also influence adherence.

Some patients have multiple inhalers stored in different locations.

Patient organisation comments

Asthma UK provided the following comments on Smartinhaler.

Digitally connected inhaler devices could allow healthcare professionals to provide useful feedback remotely based on the data received to help improve adherence or advice patients on whether they need to have their treatment or action plan reviewed. It is also important to also ensure that the quality of inhaler use is good.

Suboptimal or non-adherence to inhaled asthma medication is associated with poor symptom control, higher healthcare utilisation and healthcare costs, and reductions in health-related quality of life (<u>Mäkeläa et al. 2012</u>).

There is potential for better self-management from this technology and this may result in fewer GP appointments, accident and emergency department attendance and ultimately more targeted interventions identifying who is most at need of annual reviews. Digitally connected inhalers could be of benefit to all people with asthma, and not limited to people with severe asthma.

The data collected could help improve patient experience of the annual asthma review. People with asthma often do not find the annual review useful, and can find it difficult to recall all the occasions in a 12-month period when their asthma control fluctuated. Some estimates suggest that as many as two-thirds of people do not attend their annual asthma review (Gruffydd-Jones et al. 1999).

Medication monitoring could also aid patients in ensuring they are on the most appropriate treatment. Having reliable adherence data could help clinicians ensure those patients that

have severe asthma are referred to specialised services, having ruled out poor adherence to inhaled medication as a factor for their poor control.

Using a short-acting reliever inhaler more than 3 times a week is a strong warning sign of poor asthma control and a predictor of future asthma attacks. These patients are at increased risk of an asthma attack and should be invited in for a review with a GP or nurse, as highlighted in the Asthma UK report highlighting unsafe prescribing (Asthma UK; 2015).

Most people with asthma (over 70%) have shown that they are happy to carry an additional device with them were it designed to monitor their inhaler usage (<u>myAirCoach</u> public deliverable 1.2; 2015).

Unless the digitally connected inhaler device is available for all prescriptions there is a risk that people with asthma will not be able to use it, or need to change prescription to a different inhaler. People with asthma often dislike switching inhalers that they have become accustomed to, and this can negatively impact on care (Scichilone; 2015). Less than half of people with asthma surveyed stated they would be happy to change their inhaler in order to have access to a mobile health (mHEALTH) system (myAirCoach public deliverable 1.2; 2015).

The information obtained needs to interact with existing NHS systems in a standard manner. If patients need to change their treatment, and possibly the digital device, this should not impact on their ability to self-manage their asthma.

There is potential for a large amount of data to be sent to clinicians; this information must be used in effective ways that do not add significantly more to clinicians' time.

Clear guides and support for the devices should be available to patients.

Specialist commentators

The following clinicians contributed to this briefing:

• Dr Thomas Brown, Consultant Respiratory Physician, Portsmouth Hospitals NHS Trust, no conflicts of interest.

- Dr Paddy Dennison, Respiratory consultant physician, University Hospital Southampton NHS Foundation Trust. Paddy has had a consultancy fee from Novartis for attendance at acute asthma workshop. The department has received Novartis grants for improving non-acute services, and delivering biological. Wessex Asthma Network receives sponsorship from several drug companies.
- Dr Adel Mansur, Respiratory consultant physician, Birmingham Regional Severe Asthma Services, Birmingham Heartlands Hospital, no conflicts of interest.
- Miss Rachel Stead, Asthma Clinical Nurse Specialist, Royal Brompton and Harefield NHS Foundation Trust, no conflicts of interest.
- Dr Andrew Whittamore, GP, Portsmouth, and Clinical Lead at Asthma UK. Executive Committee member at Primary Care Respiratory Society UK (PCRS-UK). Andrew is chair of a session organised by Pfizer at the PCRS-UK annual conference (charity working to support respiratory healthcare professionals). Fees related to this role were paid to PCRS-UK.

Representatives from the following patient organisations contributed to this briefing:

Asthma UK

Development of this briefing

This briefing was developed for NICE by Cedar. The <u>interim process and methods</u> <u>statement</u> sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

ISBN: 978-1-4731-2261-1