NICE National Institute for Health and Care Excellence

NICE advice

The Airsonett temperature-controlled laminar airflow device for persistent allergic asthma

Medtech innovation briefing
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Summary

Effectiveness	Adverse events and safety
• Two randomised controlled trials (n=312, n=22) showed statistically significant improvement in asthma-related quality of life in people with severe persistent allergic asthma when Airsonett was compared with a placebo device. • There was no statistically significant difference in asthma medication usage or exacerbation rates, which were secondary outcome measures in 1 randomised controlled trial.	• The device is non-invasive and non-pharmaceutical. • No treatment-related adverse events were identified.
Cost and resource use	**Technical factors**
• The Airsonett device would be added to existing treatment and the average cost of long-term treatment is £5.72 per day. The estimated cost of an add-on therapy currently used in NHS practice, omalizumab, is £23 per day.	• The device is used in the home to deliver cooled and filtered laminar airflow around the user's breathing zone (their nose and mouth). It is powered by domestic mains electricity. • The manufacturer provides both maintenance and consumables for the device.

Introduction

In the UK, approximately 1 in 12 of the population (4.3 million adults and 1.1 million children) currently receive treatment for asthma, at an annual cost to the NHS of about £1 billion. Asthma prevalence has remained steady since the late 1990s, with an estimated 320,000 new diagnoses each year, and 1167 asthma-related deaths recorded in 2011. Asthma UK estimates that 75% of hospital admissions for asthma are avoidable, and that 90% of deaths from asthma are preventable. About 5% of people with asthma are unable to

control their asthma with high levels of medication. People in this group may have difficulty breathing almost all of the time, as well as frequent serious and life-threatening exacerbations that need hospital treatment. The management of asthma is well described in established national guidelines, based on a step-wise approach to treatment.

Technology overview

This briefing describes the regulated use of the technology for the indication specified, in the setting described, and with any other specific equipment referred to. It is the responsibility of healthcare professionals to check the regulatory status of any intended use of the technology in other indications and settings.

About the technology

CE marking

The Airsonett device is a class I medical device for which the manufacturer, Airsonett AB, received a CE mark in June 2010.

Description

The Airsonett device is a temperature-controlled laminar airflow device intended to be used as an add-on to standard treatment for people whose asthma is affected by exposure to airborne allergens, particularly those with severe persistent allergic asthma. It was previously marketed under the name Protexo, and may also be referred to as Airsonett Airshower. All of these names refer to the same model of the device.

The device consists of a base unit containing an air intake, filter and cooler, neck pipes, and an air supply nozzle. The base unit stands next to the patient's bed and the air supply nozzle is positioned above their head.

The device is principally designed to operate by the bedside while the patient sleeps. The device draws air from the room through a filter that captures allergens and other particles. This filtered air is then cooled to 0.5–0.8ºC below the ambient room temperature, before being slowly expelled from the air supply nozzle. This cooler air is more dense than the ambient room air and so it descends into the patient's breathing zone. The device provides

cooled, filtered air around the patient's face through the night, breaking the natural body convection without creating draught or dehydration. The manufacturer describes this as the key feature that differentiates the Airsonett device from other devices designed to supply filtered air to the breathing zone.

Intended use

The device is designed to reduce the level of allergens inhaled during the night. It does this by providing a temperature-controlled laminar flow of filtered air, thereby alleviating the symptoms of allergy-induced diseases.

Setting and intended user

The Airsonett is primarily intended for home use by people with poorly controlled persistent allergic asthma despite high-intensity treatment. Such patients are typically described as having reached Step 4 of the Global Initiative for Asthma (GINA) and the British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) guidelines. This is defined as having poor control of asthma symptoms despite treatment with moderate doses of inhaled steroid and add-on therapies. These patients can be further defined as having an Asthma Control Test (ACT) score of less than 18. The ACT provides an indication of how well a person's asthma has been controlled over the previous 4 weeks; scores range from 1 to 25, with any score below 20 indicating poor symptom control. Such patients are likely to be under the care of a hospital-based respiratory physician as well as receiving regular primary care management. The device may also be considered for people with less severe conditions such as rhinitis and eczema, although these uses are outside the scope of this briefing.

Current NHS options

The Airsonett device is intended to be used for people who are at Step 4 or above of the BTS/SIGN stepwise treatment approach. The 2012 BTS/SIGN guidelines recommend that add-on therapies can be considered for people who have reached Step 5, which means that continuous or frequent use of oral steroids is often necessary to control asthma symptoms.

Current add-on treatment options for severe allergic asthma as recommended in the NHS are daily corticosteroid tablets and omalizumab. Other available options include bronchial themoplasty and immunosuppressants such as methotrexate and ciclosporin.

Omalizumab for treating severe persistent allergic asthma (NICE technology appraisal guidance 278) recommends omalizumab as an optional add-on to standard therapy in people aged 6 years and older who need continuous or frequent treatment with oral corticosteroids.

Bronchial thermoplasty uses short pulses of radiofrequency energy to reduce the amount muscle in the airway. Bronchial thermoplasty for severe asthma (NICE interventional procedure guidance 419) states that the procedure shows some improvement in symptoms of severe asthma, including expiratory flow rate, beta-2 antagonist use, and number of exacerbations and hospital admissions. There is also evidence of improvement in quality of life. The guidance goes on to state that although the evidence on short- and medium-term safety are adequate, more evidence is needed on longer-term safety. Therefore, bronchial thermoplasty should be used only with special arrangements for clinical governance, consent and audit or research, and patients should be chosen by a respiratory team with special expertise in managing severe asthma.

Treatment with immunosupressants can decrease long-term steroid tablet requirements, but these drugs have significant adverse effects. As most immunosuppressants act non-selectively, a common treatment effect is immunodeficiency, which results in increased susceptibility to infections.

NICE is aware of the following devices that appear to fulfil a similar function to the Airsonett:

- PureZone Personal Air Filtration System (PureZone Technologies).
- PureNight Pure Air System (Halo).

NICE has not investigated the regulatory status of these devices; it is the responsibility of healthcare professionals to check this status for any intended use.

Costs and use of the technology

The rental cost of Airsonett to the NHS is £174 (excluding VAT) per month, equivalent to £5.72 per night, on a managed service basis that includes replacement filters every 6 months. Replacement, repairs and technical support are included in the rental charge.

In cases of misuse or damage that necessitates repairs and replacements, the following

charges (excluding VAT) apply:

- Filter: £500.
- Refurbishment followed by self-installation: £250.
- Refurbishment on site by Airsonett: £500.
- Refurbishment at Airsonett facility: £1100.

The Airsonett device has an anticipated lifespan of 5 years when used every night for 8 to 10 hours. The cost of omalizumab ranges from £1665 per patient per year (75 mg dose every 4 weeks) to £26,640 per patient per year (600 mg dose – the recommended maximum dose in the summary of product characteristics – every 2 weeks), indicating a comparable daily cost per patient of £4.56 on the lower dose and £72.99 on the maximum dose. As part of the evidence preparation for Omalizumab for treating severe persistent allergic asthma (NICE technology appraisal guidance 278), a systematic review and economic evaluation by Norman et al. (2013) estimated the average daily cost per patient to be £23, based on the distribution of doses taken by people in the included trials. This included administration and monitoring costs.

Likely place in therapy

The technology is intended to be used as a long-term add-on therapy for children and adults with severe persistent allergic asthma whose disease, despite high-intensity pharmacotherapy, remains poorly controlled. This includes people who have reached BTS/SIGN Step 4 or above who would otherwise be considered for long-term oral steroids, omalizumab or bronchial thermoplasty.

Specialist commentator comments

One specialist commentator noted that the Airsonett device may be useful for patients whose immunoglobulin E concentration is too high for treatment with omalizumab. It is cheaper and less potentially harmful than omalizumab, although the evidence on effectiveness is limited.

One commentator suggested that dust mite pillow covers should be used with the Airsonett device, because they would reduce the inhalation of allergenic particles from pillows. However, these covers were not used in any of the clinical trials, so there is no

measure of their potential benefit.

One commentator noted that a number of people with severe asthma experience multisystem allergic disease, in particular eczema and allergic rhinitis. When used to treat these patients, temperature-controlled laminar airflow such as that provided by the Airsonett device shows multiple benefits. These include a reduction in topical treatment need, improvement in quality of life and reduction in healthcare resource use. However, this view was not supported by another commentator, who noted that there was no objective evidence to support the use of the Airsonett device in multisystem allergic disease.

Specialist commentators made generally positive comments about their experience of using the Airsonett device. They did, however, report difficulties in obtaining funding because the evidence on efficacy is limited, and severe asthma is not part of the NHS specialist commissioning arrangements.

Equality considerations

NICE is committed to promoting equality and eliminating unlawful discrimination. We aim to comply fully with all legal obligations to:

- promote race and disability equality and equality of opportunity between men and women, and
- eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief, in the way we produce our guidance. (NB these are protected characteristics under the Equality Act (2010)).

Some people with asthma are considered to have a disability according to the Equality Act (2010).

Evidence review

Clinical and technical evidence

Two relevant randomised controlled trials using the Airsonett device (tables 1–4) and 4

relevant abstracts of conference proceedings (table 5) were identified. Airsonett AB also provided data from 2 small case-series reports, which were described in an Airsonett AB press release in June 2014.

Published trials

In the trial by Boyle et al. (2012), 312 adults and children with persistent atopic asthma were randomised to receive either temperature-controlled laminar airflow (TLA) treatment using the Airsonett device or placebo (a TLA device without a filter or cooled airflow) for 1 year. The primary outcome was improved quality of life, measured as the proportion of patients with an improved score on the Asthma Quality of Life Questionnaire (AQLQ). In patients aged 12 years and over a short version of the AQLQ, the mini-AQLQ instrument, was used to determine 4 subscale scores: symptoms, emotions, activities and environment. For children aged under 12 years a child-specific version, the Paediatric Asthma Quality of Life Questionnaire (P-AQLQ), was used to assess outcomes using 3 subscale scores: symptoms, emotions and activities.

After 1 year of active treatment, the active and placebo groups showed no statistically significant difference in standard asthma medication use and asthma exacerbations.

Of those patients who had at least 1 day of treatment with the Airsonett device, there was a significantly greater proportion with an improved quality of life – measured as an increase in AQLQ score of at least 0.5 points – compared with the placebo group (odds ratio [OR] 1.92, 95% confidence interval [CI] 1.09 to 3.38; p=0.02). Statistically significant improvements using this measure were also reported in the following patient subgroups:

- those aged under 12 years (OR 5.57, 95% CI 1.13 to 27.48; p=0.02)
- those with high-intensity treatment (GINA 4) at baseline (OR 2.42, 95% CI 1.05 to 5.60; p=0.04)
- those with poor symptom control (ACT<18) at baseline (OR 3.45, 95% CI 1.66 to 7.2; p<0.001)
- those with both GINA 4 and ACT<18 at baseline (OR 4.47, 95% CI 1.48 to 15.19; p=0.009).

The difference did not reach statistical significance in the subgroup of patients aged 12 years and over, the group on which the study was powered.

Measured as an increase in AQLQ score of at least 1 point, the improvement seen in patients having TLA compared with placebo was significant only in those patients with ACT<18 (OR 2.78, 95% CI 1.36 to 5.67; p=0.005) and those with both GINA 4 and ACT<18 (OR 8.81, 95% CI 2.14 to 36.32; p=0.003).

There was a statistically significant improvement in fractional exhaled nitric oxide in patients receiving TLA compared with those receiving placebo, particularly in the subgroup with abnormally high levels (>45 ppb) at baseline. No treatment-related adverse events were observed.

In the Pedroletti et al. (2009) crossover trial, 22 patients were randomised to receive either the active Airsonett device or placebo Airsonett (with the filtration system treatment disabled) for 10 weeks, followed by a 2-week wash-out phase in which the patients did not use the device. Following this wash-out period, patients were switched to the opposite treatment group for another 10 weeks. The primary outcome measure was mean change in quality of life, measured as mini-AQLQ score. Bronchial inflammation (exhaled nitric oxide) and lung function (spirometry) were also measured.

Treatment with the active Airsonett device resulted in an improved mini-AQLQ score that was significant compared with placebo (difference in mean score change 0.54; p<0.05, n=20). Significantly lower values of fractional exhaled nitric oxide were also detected during the active treatment period (mean −6.95 ppb; p<0.05, n=22). No statistically significant changes in spirometry tests (forced expiratory volume in 1 second and peak expiratory flow) were observed.

Table 1 Summary of the Boyle et al. (2012) randomised controlled trial

Study component	Description
Objectives/ hypotheses	To determine whether environmental control using the Airsonett device could improve the quality of life of patients with persistent atopic asthma.
Study design	Phase III, multicentre, randomised, placebo-controlled, parallel-group trial. Follow-up assessment at 1, 3, 6, 9 and 12 months of the treatment.
Setting	19 European asthma clinics.

Inclusion/ exclusion criteria	Inclusion criteria were: a physician's diagnosis of asthma ≥1 year prior to study; age 7–70 years; AQLQ (mini-AQLQ for aged ≥12 years and PAQLQ for aged <12 years) score ≤5.5 at inclusion; allergic sensitisation to a pet allergen (cat or dog) or house dust mite demonstrated by specific IgE level ≥0.70 kU/litre or positive skin prick test (weal diameter ≥histamine control); daily inhaled corticosteroid ≥200 micrograms/day budesonide/ beclomethasone or ≥100 micrograms/day fluticasone for last 6 months; and features of partly controlled asthma according to GINA 2006. Exclusion criteria were: current active or passive cigarette smoke exposure; inclusion in another allergen avoidance programme or drug trial; treatment with allergen immunotherapy or omalizumab in previous 2 years (1 year for children); inhaled corticosteroid dose >1200 micrograms/day budesonide/beclomethasone or >1000 micrograms/day fluticasone. A history of frequent severe asthma exacerbations was not an inclusion criterion for the study.
Primary outcomes	Quality of life assessed with the mini-AQLQ (or with the PAQLQ in children ≤11 years). A change of 0.5 is considered clinically significant, and the primary outcome analysed was the proportion of patients with a significant increase in mini-AQLQ or PAQLQ score ('responders') after 1 year of treatment.
Statistical methods	The intention-to-treat population in this study was defined as all patients who had ≥1 day of device treatment following randomisation. Last observation carried forward was used for missing data. Per protocol analyses excluded patients with major protocol violations or documented treatment compliance <80%. The host country, patient gender, years since asthma diagnosis, GINA treatment step and AQLQ at baseline were adjusted. ANCOVA analyses were used for continuous data and logistic regression for binary data. The sample size was calculated based on a minimum difference of 20% between treatment groups in the proportion of responders (increase in AQLQ ≥0.5 points over the 12-month intervention), and a responder rate of 20% in the placebo group. Subgroup analyses were undertaken by age and asthma treatment intensity at baseline.
Participants	312 patients aged 7–70 years with inadequately controlled persistent atopic asthma who met the inclusion criteria.

Results	In all patients who had at least 1 day of treatment with the device, there was a significantly higher proportion with an improved quality of life (measured as an increase of ≥0.5 points in AQLQ score) after 1 year of active Airsonett treatment compared with placebo (OR 1.92, 95% CI 1.09 to 3.38; p=0.02). There was a similarly significant difference in the following patient groups: those aged <12 years (OR 5.57, 95% CI 1.13 to 27.48; p=0.02); those with high treatment intensity (GINA 4) at baseline (OR 2.42, 95% CI 1.05 to 5.60; p=0.04); those with poor symptom control (ACT <18) at baseline (OR 3.45, 95% CI 1.66 to 7.2; p<0.001); and those with both GINA 4 and ACT<18 at baseline (OR 4.47, 95% CI 1.48 to 15.19; p=0.009). The difference was not significant in patients aged ≥12 years on which the study was powered. When measured as an increase of ≥1 point in AQLQ score, the improvement with the active Airsonett device compared with placebo was only significant in those with ACT<18 (OR 2.78, 95% CI 1.36 to 5.67; p=0.005) and those with both ACT<18 and GINA 4 (OR 8.81, 95% CI 2.14 to 36.32; p=0.003). No statistically significant difference was demonstrated between active and placebo groups in standard asthma medication use and asthma exacerbation. No treatment-related adverse events were observed.
Conclusions	The Airsonett device may be an effective treatment option for patients with inadequately controlled persistent allergic asthma to improve quality of life and airway inflammation.
Abbreviations: ACT, Asthma Control Test; AQLQ, Asthma Quality of Life Questionnaire; ANCOVA, analysis of covariance; CI, confidence interval; GINA, Global Initiative for Asthma; FENO, fractional exhaled nitric oxide; IgE, immunoglobulin E; kU/L, kilo-units of antibody per litre; OR, odds ratio; PAQLQ, paediatric asthma quality of life questionnaire; SE, standard error; SD, standard deviation.	

Table 2 Summary of the Boyle et al. (2012) randomised controlled trial

	TLA	Placebo	Analysis
Randomised	n=207	n=105	

Primary outcome			
Proportion of patients with an increase of ≥0.5 points in AQLQ score after 1 year of treatment			
• Intention to treat [a]	76% (143/189)	61% (56/92)	Difference=14.8% 95% CI 3.1 to 26.5 OR=1.92 95% CI 1.09 to 3.38 p=0.02
• Per protocol [b]	77% (106/136)	61% (40/61)	Difference=16.6% 95% CI 3 to 30 OR=2.22 95% CI 1.11 to 4.40 p=0.02
• <12 years (P-AQLQ)	80% (37/46)	64% (14/22)	Difference=16.8% 95% CI 8% to 38% OR=5.57 95% CI 1.13 to 27.48 p=0.02
• ≥12 years(mini-AQLQ) [c]	74% (106/134)	60% (42/70)	Difference=14.1% 95% CI 0.6 to 27.7 OR=1.89 95% CI 0.98 to 3.65 p=0.059

• GINA 4 group	77% (63/82)	62% (29/47)	Difference=15.1% 95% CI 2% to 31% OR=2.42 95% CI 1.05 to 5.60 p=0.04
• Poorly controlled	74% (93/125)	52% (30/58)	Difference=22.7% 95% CI 8% to 38% OR=3.45 95% CI 1.66 to 7.2 p<0.001
• GINA 4 poorly controlled	75% (43/57)	50% (15/30)	Difference=25.4% 95% CI 4% to 47% OR=4.74 95% CI 1.48 to 15.19 p=0.009
Proportion of patients with an increase of ≥1 point in AQLQ score after 1 year of treatment			
• Intention to treat [a]	63% (119/189)	51% (47/92)	Difference=14.8% 95% CI 3 to 26 OR=1.58 95% CI 0.93 to 2.65 p=0.09
• Per protocol [b]	65% (89/136)	50% (33/66)	Difference=15.4% 95% CI 1% to 30% OR=1.85 95% CI 0.97 to 3.53 p=0.06

• <12 years (PAQLQ)	72% (33/64)	50% (11/22)	Difference=21.7% 95% CI −3% to 46% OR=4.40 95% CI 0.99 to 19.57 p=0.05
• ≥12 years (mini-AQLQ)	60% (86/143)	51% (36/70)	Difference=8.7% 95% CI −5 to 23 OR=1.37 95% CI 0.74 to 2.52 p=0.31
• GINA 4 group	62% (51/82)	51% (24/47)	Difference=15.1% 95% CI 2% to 31% OR=1.96 95% CI 0.87 to 4.40 p=0.10
• Poorly controlled at baseline (ACT<18) (n=184)	62% (77/125)	41% (24/58)	Difference=20.2% 95% CI 5% to 35% OR=2.78 95% CI 1.36 to 5.67 p=0.005
• GINA 4 poorly controlled (n=87)	65% (37/57)	37% (11/30)	Difference=28.2% 95% CI 7% to 49% OR=8.81 95% CI 2.14 to 36.32 p=0.003

Selected secondary outcomes			
Change from baseline in AQLQ score after 3 months of treatment [d]			
• All patients (ITT analysis)	n=189	n=92	Difference=0.09 p=0.44
• ACT<18 (ITT analysis)	n=125	n=58	Difference=0.21 p=0.12
• GINA 3 and 4, ACT<18	n=103	n=50	Difference=0.84 p=0.01
• GINA 4, ACT<18	n=57	n=30	Difference=0.64 p=0.01
Change from baseline in AQLQ score after 12 months of treatment			
• All patients (ITT analysis)	n=189	n=92	Difference=0.21 p=0.12
• ACT<18 (ITT analysis)	n=125	n=58	Difference=0.52 p=0.005
• GINA 3 and 4, ACT<18	n=103	n=50	Difference=0.88 p=0.001
• GINA 4, ACT<18	n=57	n=30	Difference=0.79 p=0.002
Changes in the symptom domain of AQLQ score			
• Intention to treat [a]	1.3 (1.23)	0.99 (1.38)	Difference=0.31 95% CI 0.01 to 0.61 p=0.04
• Per protocol [b]	1.34 (1.14)	0.96 (1.34)	Difference=0.36 95% CI 0.01 to 0.71 p=0.04

• <12 years (P-AQLQ)	1.46 (1.36)	0.93 (1.49)	Difference=0.38 95% CI −0.34 to 1.10 p=0.29
• ≥12 years (mini-AQLQ)	1.27 (1.18)	1.01 (1.36)	Difference=0.28 95% CI −0.62 to 0.05 p=0.10
• GINA 4 group	1.45 (1.14)	1.00 (1.44)	Difference=0.47 95% CI 0.03 to 0.9 p=0.04
• ACT<18	1.41 (1.24)	0.95 (1.60)	Difference=0.58 95% CI 0.17 to 0.98 p=0.006
• GINA 4 and ACT<18 at baseline	1.45 (1.15)	0.86 (1.70)	Difference=0.70 95% CI 0.13 to 1.26 p=0.02
Use of standard pharmaceutical treatment			
• Use of ICS during TLA treatment [e]	Baseline: 0.72 (0.46); 3–12 months: 0.74 (0.53)	Baseline: 0.77 (0.47); 3–12 months: 0.77 (0.49)	Difference=0.03 (0.04) p=0.38

• Use of short-acting beta-2 agonist [e]	Baseline: 0.20 (0.40); 3–12 months: 0.19 (0.25)	Baseline: 0.22 (0.39); 3–12 months: 0.22 (0.41)	Difference=0.02 (0.02) p=0.39
• Use of long-acting beta-2 agonist [e]	Baseline: 0.51 (0.51); 3–12 months: 0.52 (0.48)	Baseline: 0.53 (0.48); 3–12 months: 0.55 (0.47)	Difference=−0.01 (0.03) p=0.77
• Leukotriene receptor antagonist [e]	Baseline: 0.29 (0.46); 3–12 months: 0.31 (0.53)	Baseline: 0.24 (0.41); 3–12 months: 0.28 (0.43)	Difference=−0.00 (0.02) p=0.88
• ≥3 of systemic corticosteroids for ≥1 occasion during the whole study period	13.2% (25/189)	12.9% (12/93)	p=0.94
• Mean (SD) number of systemic corticosteroid courses administered per patient	0.17 (0.53)	0.24 (0.83)	p=0.50
Asthma exacerbations (mean)	0.17	0.24	p=0.50
• for those with ACT<18 at baseline	0.18	0.34	p=0.28

• for those with GINA 4 treatment intensity at baseline	0.24	0.4	p=0.23
• for those with GINA 4 and ACT<18 at baseline	0.23	0.57	p=0.07
Changes in FENO from baseline	−4.88 95% CI −9.3 to −0.4	2.82 95% CI −3.5 to 9.2	Difference=−7.13 95% CI −13.6 to −0.7 p=0.03
• for those with high FENO (>45 ppb) at baseline	−27.3 95% CI −37.6 to −17.0	−2.53 95% CI −24.0 to 18.9	Difference=−29.7 95% CI −47.2 to −12.2 p=0.001
Safety	n=189	n=93	Not applicable
Patients reporting serious adverse events (none treatment-related)	17% (32/189)	15% (14/93)	Reported as no significant difference
Upper respiratory tract infection [f]	61.9% (117/189)	66.7% (62/93)	Not reported
Upper respiratory tract symptoms [f]	28.6% (54/189)	23.7% (22/93)	Not reported
General symptoms [f]	22.8% (43/189)	20.4% (19/93)	Not reported

Abbreviations: ACT, Asthma Control Test; AQLQ, Asthma Quality of Life Questionnaire; CI, confidence interval; GINA, Global Initiative for Asthma; FENO, fractional exhaled nitric oxide; ICS, inhaled corticosteroid; ITT, intention to treat; n, number of patients; p, p value; PAQLQ, Paediatric Asthma Quality of Life Questionnaire; RR, relative risk; SE, standard error; SD, standard deviation; TLA, temperature-controlled laminar airflow.

[a] ITT in this study was defined as the analysis that consists of all randomised patients who have had at least 1 treatment day with the intervention.

[b] Per protocol analysis: consists of all randomised patients who have used the intervention minimum 80% of the 1-year study period, as recorded on a data chip in the machine and 80% of the last 3 weeks prior to visit month 3 and 12.

[c] The study was powered on the patients aged ≥12 years for the analysis of treatment response rate.

[d] Data from the manufacturer's report.

[e] All medication does are expressed as mean (SD) proportion of the 'defined daily dose'; difference = mean (SE) of [(active during 3–12 months) – (active at baseline)] – [(placebo during 3–12 months) – (placebo at baseline)].

[f] Adverse events affecting ≥5% of patients on ≥1 occasion.

Table 3 Summary of the Pedroletti et al. (2009) randomised controlled trial

	Description
Objectives/ hypotheses	To examine the treatment with the Airsonett device in teenagers and young adults with mild to moderate allergic asthma during night sleep. The researchers hypothesised that the decreased allergen exposure during the night would have an effect on bronchial inflammation and quality of life.

Study design	Randomised, 2-centre, double-blind, placebo-controlled crossover trial. (No details on the randomisation and blinding methods were reported). A total of 22 patients entered the trial to receive either active or placebo treatment for 10 weeks (number of patients randomised to each group was not reported), followed by a 2-week washout phase in which the patients did not use the device. Following the washout period patients were switched to the other treatment group for another 10 weeks. Clinical assessments including FENO, spirometry, physical examination and urine sample were conducted at baseline (week 0) and the end of the study (week 22). FENO and spirometry assessments were conducted at visit weeks 5, 10, 12 and 17 during the study.
Setting	Sweden. The device was placed in the patients' bedroom and used during night-time sleep.
Inclusion/ exclusion criteria	Inclusion criteria: perennial allergic asthmatic adolescents and young adults, 12–33 years of age, taking a daily maintenance dose of at least ≥400 mg/day of budesonide or 200 mg/day of fluticasone and short-acting beta 2-agonist treatment on less than 4 days per week. Asthma diagnosis was confirmed by lung function testing and/or bronchial provocation test (metacholine or cold dry air). Exclusion criteria: current active or passive cigarette smoke exposure; inclusion in another allergen avoidance programme or drug trial; treatment with allergen immunotherapy or omalizumab in previous 2 years (1 year for children); inhaled corticosteroid dose >1200 mg/day budesonide/beclomethasone or >1000 mg/day fluticasone; a history of frequent severe asthma exacerbations.
Primary outcomes	The change in quality of life between active versus placebo treatment assessed on the mini-AQLQ. The change in quality of life as the difference in the mini-AQLQ summary score was defined as from start to end (10 weeks) of each study period. Mini-AQLQ scores range from 0 to 7, where 7 is no symptoms. A change of 0.5 was considered clinically significant.

Statistical methods	The study hypothesis was tested by examining the difference in change in mini-AQLQ score, FENO and spirometry during active versus placebo treatment periods. All patients who completed measurements at both baseline and end point of each treatment period were analysed. Results were summarised by treatment periods as mean scores with confidence interval. Changes from baseline within each treatment period (active or placebo) were analysed using paired t-tests. An ANOVA model was used to compare the changes (measured as least square mean with confidence interval) between the 2 treatment periods. The country and baseline scores were varieties. It was calculated that a sample size of 20 would have a 62% power to detect a 30% improvement of mini-AQLQ for active treatment compared with placebo, with the error set at 0.05 and SD based on a previous pilot study.
Participants	28 children and young adults (aged 12 to 33 years) with mild to moderate allergic asthma who fulfilled the inclusion criteria.
Results	22 patients completed measurements at baseline and endpoint of both treatment periods. Active treatment resulted in an improved mini-AQLQ score that was statistically significant compared with placebo (mean score 0.54, $p<0.05$, n=20). An effect on bronchial inflammation was detected with significantly lower FENO values during the active treatment period (mean −6.95 ppb, $p<0.05$, n=22). Both effects were evident after 5 weeks. No statistically significant changes in lung function were observed.
Conclusions	Laminar airflow of purified air directed to the breathing zone during night sleep, as provided by the Airsonett device, may have a positive effect on bronchial inflammation in patients with perennial allergic asthma.
Abbreviations: ANOVA, analysis of variance; AQLQ, Asthma Quality of Life Questionnaire; CI, confidence interval; FENO, fractional exhaled nitric oxide; n, number of patients; SD, standard deviation.	

Table 4 Summary of the Pedroletti et al. (2009) randomised controlled trial

	Active TLA	Placebo	Analysis
Randomised	n=22	n=22	
Efficacy	n=22	n=22	

Primary outcome: mean mini-AQLQ score	Baseline: 5.36 95% CI 4.82 to 5.90 End: 5.92 95% CI 5.56 to 6.28	Baseline: 5.69 95% CI 5.23 to 6.14 End: 5.70 95% CI 5.19 to 6.22)	Difference in change, mean (SEM): 0.54 (0.28) p<0.05 (n=20)
Selected secondary outcomes			
FENO (ppb)	Baseline: 29.2 95% CI 18.9 to 39.5 End: 22.2 95% CI 14.8 to 29.7	Baseline: 29.0 95% CI 18.2 to 39.8 End: 28.5 95% CI 16.4 to 40.6	Difference in change, mean (SEM): -6.4 (2.5) p<0.05 (n=22)
Change in lung function: mean percentage difference in FEV_1	Not reported	Not reported	1.14% Not significant
Change in lung function: mean percentage difference in PEF	Not reported	Not reported	3.44% Not significant
Safety	Not reported	Not reported	Not reported
Patients reporting serious adverse events	Not reported	Not reported	Not reported
Abbreviations: AQLQ, Asthma Quality of Life Questionnaire; CI, confidence interval; FENO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; ITT, intention to treat; n, number of patients; PEF, peak expiratory flow rate; RR, relative risk; SEM, standard error of mean; TLA, temperature-controlled laminar airflow.			

Relevant abstracts

Table 5 summarises 4 abstracts reporting 3 relevant studies that were identified. Two of the studies were randomised controlled trials, and the other was a case-series study. All 4 abstracts contained very limited information on the study design and methods.

The randomised controlled trial reported by Vincenzo et al. (2009) had a total of 9 patients; 4 received treatment with the Airsonett device (called Protexo in the study) and the other 5 received control treatment. The study follow-up was 2 to 3 months. Asthma symptoms, fractional exhaled nitric oxide levels, eosinophil count in sputum and lung function were evaluated at baseline and follow-up. However, no statistical tests were reported on the differences between the comparison groups for these outcome measures.

Mohan et al. (2010) and Moffatt et al. (2011) reported results from the same randomised controlled trial (Boyle et al, 2012), each reporting different outcomes. This study enrolled 52 children aged 8 to 16 years with allergic asthma and rhinitis sensitised to a perennial allergen; 36 of the children received TLA and 16 received a placebo TLA for 1 year. The Mohan et al. abstract reported sleep quality (using the Paediatric Sleep Questionnaire) and sleep patterns (using wristwatch actigraphy), which both showed no statistically significant difference between the comparison groups. The Moffatt et al. abstract reported rhinitis-related quality of life and nasal airflow using the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). There was no statistically significant difference between the comparisons in the overall RQLQ score and nasal airflow, but a significant improvement was observed in the sleep domain (details of the individual items were not reported in the abstract) for the TLA group compared with the placebo group (mean difference 1.41, 95% CI 0.25 to 2.56; p=0.019).

The case series included 7 patients with allergic asthma. After 4 weeks of treatment with the Airsonett device, the mean (standard deviation) maximum change of the total sum of asthma quality of life score (measured on the mini-AQLQ) was 22.4% (9.1). There was no medication change during the study.

Table 5 Summary of abstracts

Study	Study design	Population	Intervention	Outcome measure	Finding

Vincenzo et al. (2010)	RCT	9 children with moderate to severe dust mite allergic asthma who lived in a dust mite-free environment (Dolomites-Alps) for > 3 months	• Protexo [the Airsonett device] (n=4) • Control (n=5)	Asthma symptoms; FENO level, eosinophils count in sputum and lung function	FENO level • TLA: 27.3 ppb before and 18.3 ppb after • Control: 12.4 before and 19.5 after Sputum eosinophils • TLA: 1.7 before and 2.0 after • Control: 1.6 before and 7.0 after Lung function: • no difference observed
Mohan et al. (2011)	RCT	52 children aged 8–16 years with allergic asthma and rhinitis sensitised to a perennial allergen	• TLA (n=36) • Placebo (n=16)	Sleep quality assessed using the parent reported PSQ, the self-reported CSHQ and wristwatch actigraphy, after 1 year treatment.	TLA vs placebo: mean fall in PSQ 0.12 vs 0.12; p=0.96; mean fall in CSHQ 1.82 vs 2.81; p=0.57

Moffatt et al. (2011)	RCT	52 children aged 8–16 years with allergic asthma and mild to moderate rhinitis sensitised to a perennial allergen	• TLA (n=36) • Placebo (n=16)	Rhinitis related quality of life using the RQLQ and nasal airflow measured using PNIF meters after 1 year treatment.	RQLQ score: mean difference 0.17 points in favour of TLA, 95% CI −0.47 to 0.80; p=0.597. Improvement in the sleep domain of the RQLQ: mean difference 1.41 points in favour of TLA, 95% CI 0.25 to 2.56; p=0.019. Reduction in overnight nasal congestion measured as [evening PNIF − morning PNIF]: mean difference 22.6 l/min in favour of TLA, 95% CI −0.3 to 45.6; p=0.053
Svensson (2005)	Case series	7 adults patients with asthma and verified allergy for animal dander, dust mites and several other allergens	The Airsonett device	Quality of life measured with mini-AQLQ after 4 weeks' treatment	Mean (SD) maximum change of the total sum of mini-AQLQ: 22.4% (9.1). The medication was not changed during the study.

Abbreviations: CSHQ, Child's Sleep Habits Questionnaire; FENO, fractional exhaled nitric oxide; PSQ, Paediatric Sleep Questionnaire; PNIF, peak nasal inspiratory flow; RQLQ, Rhinoconjunctivitis Quality of Life Questionnaire; TLA, temperature-controlled laminar airflow; vs, versus.

Conference presentation

At the 2014 annual conference of the European Academy of Allergy and Clinical Immunology in Copenhagen, Airsonett AB presented medical records data for a prospective study comparing exacerbations and asthma control the year before and after introduction of the Airsonett device in 30 German children and adults with poorly controlled asthma. The data showed the following:

- reductions in the annual rate of exacerbations needing an increase in medication (3.57 before and 1.30 after, n=30; p=0.00013)
- the percentage of patients needing at least 1 emergency or unplanned clinic visit (76% before and 33% after, n=21; p=0.0126) or hospitalisation per year (32% before and 14% after, n=22; p=0.102)
- the percentage of patients showing symptoms of bronchial hyper-reactivity (70% before and 30% after, n=27; p=0.0045).

Asthma control was significantly improved by both doctors' evaluation (controlled 8% before and 35% after; partially controlled 38% before and 65% after; uncontrolled 54% before and 0% after; n=26 and p=0.0003) and patient (ACT) evaluation (14 before, 18.5 after; n=30 and p <0.0001).

The manufacturer also presented retrospective study data of 70 children and adults with poorly controlled asthma, comparing exacerbations the year before and after the introduction of the Airsonett device into Swedish healthcare. The results demonstrated significant reductions in the annual rate of patient emergency room visits (4.0 before and 0.7 after; p<0.0001), hospital admissions (0.8 before and 0.1 after; p=0.0004) and planned clinic visits (5.7 before and 1.7 after; p<0.0001).

Ongoing studies

Although 4 registered trials of the Airsonett device were identified, no associated

publications were identified, either in abstract or full text. Three of these trials are completed. The other is currently in progress and is due to end in November 2016. It is funded by the UK National Institute for Health Research and aims to determine whether nocturnal TLA treatment reduces the frequency of severe asthma exacerbations. Table 6 summarises these trials.

Table 6. Summary of registered trials

Trial ID	Status	Title	PICO	Study design	Publicati
ISRCTN46346208	Ongoing	Laminar Airflow in Severe Asthma for Exacerbation Reduction (LASER)	P: adults (aged 18–75) with severe, poorly controlled asthma. I: the Airsonett device C: placebo device O: clinically significant exacerbations over the 12-month period	Multicentre randomised double-blind placebo-controlled parallel group trial of 12 months duration with a 4-month internal pilot	Not applicabl
NCT00986934	Completed	Effect of Temperature Controlled Laminar Airflow on the Peripheral Bronchial Airway in Asthma	P: asthma patients aged 7–70 years I: the Airsonett device C: placebo device O: measurements of lung clearing index (weeks 0, 12 and 52)	Phase III, randomised, controlled, double-blind, parallel group trial with 52-week follow-up	Not identified

ISRCTN67027605	Completed	A Pilot Proposal to Determine the Effect of the Airsonett Airshower on Sleep Quality	P: patients aged 18–65 years with doctor-diagnosed allergic rhinitis I: 4 nights of study, 2 with placebo Airsonett device and 2 with active Airsonett device C: allerguard pillow protectors to be used on all 4 nights O: total nasal symptom score	Single-blind placebo-controlled trial	Not identified
NCT00986388	Completed	Effect of Temperature Controlled Laminar Airflow on Bronchial Inflammation in Asthma	P: patients with perennial allergic asthma, age 7–70 years I: the Airsonett device C: placebo device O: concentration of inflammatory cells and mediators in induced sputum (weeks 0, 4, 12 and 52)	Phase III, randomised, controlled, double-blind, parallel group trial, with 52-week follow-up	Not identified
Abbreviations: PICO, participants, intervention, control, outcome.					

Costs and resource consequences

The Airsonett device is intended as an add-on treatment for patients who experience

symptoms caused by exposure to airborne allergens. The most common of these is persistent allergic asthma, which at its most severe may be treated with omalizumab in accordance with NICE guidance. It is in this group of patients that the greatest potential cost and resource savings may be realised. The rental cost for the Airsonett device, including replacement filters and technical support, is £2088 per patient per year.

Based on data from Novartis, the manufacturer of omalizumab, the costing statement produced by NICE to accompany Omalizumab for treating severe persistent allergic asthma (NICE technology appraisal guidance 278) estimated that approximately 1400 people in England aged 12 years and over are currently receiving treatment with omalizumab. Extending the guidance to include children aged 6 and over is expected to increase this number by 150. The cost of omalizumab ranges from £1665 per patient per year (75 mg dose every 4 weeks) to £26,640 per patient per year (600 mg dose – the recommended maximum dose in the summary of product characteristics – every 2 weeks), indicating a comparable daily cost per patient of £4.56 on the lower dose and £72.99 on the maximum dose. The costing statement estimates the average annual cost of treatment, including initial consultation, administration, and monitoring, as approximately £8400 per adult. This represents a potential annual cost saving of £6312 per patient, if the use of the Airsonett device were to eliminate the need for omalizumab. However, these costs are based on the list price of the drug, whereas the NICE guideline recommends usage 'only if the manufacturer makes omalizumab available with the discount agreed in the patient access scheme'. The actual available cost saving from omalizumab therefore depends on the level of this discount and any reduction in medication. Further cost and resource savings could be realised if the device were shown to reduce the number of severe asthma exacerbations that need medical attention.

There is currently no published evidence on how the use of the Airsonett device would affect NHS resources by either reducing omalizumab use or reducing asthma exacerbations. The study by Boyle et al. (2012) showed no statistically significant differences between active and placebo arms for either outcome. However, this study was designed to evaluate changes in quality of life, rather than medication levels or adverse events, and was powered accordingly. Data presented at the 2014 annual conference of the European Academy of Allergy and Clinical Immunology, describing the Airsonett AB-led prospective study, showed significant improvements in asthma symptoms, medication levels and emergency hospital admissions. This is has not yet been published in full in a peer-reviewed journal.

Strengths and limitations of the evidence

The Boyle et al. trial (2012) was a phase III, randomised, placebo-controlled trial. The study was powered for the primary outcome of the effect on quality of life, with patients, investigators and statisticians all blinded. Overall, the study was of reasonable methodological quality and reporting quality.

Pedroletti et al. (2009) was a crossover study with a very small sample size, and no details were reported on the methods of randomisation or blinding. Three other relevant randomised controlled trials and 1 case-series study were identified, available as abstracts. All had small sample sizes and provided insufficient information to assess their quality. There were also 4 registered trials which, despite being completed, had no associated publications. No studies have yet directly compared the Airsonett device with omalizumab.

Relevance to NICE guidance programmes

NICE has issued the following guidance which is relevant to this briefing:

- Omalizumab for the treatment of severe persistent allergic asthma (review of TA133 and TA201). NICE technology appraisal guidance 278 (2013)
- Bronchial thermoplasty for severe asthma. NICE interventional procedure guidance 419 (2012)

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Svensson P (2005) Influence of clean air directly in the breathing zone on allergy and asthma patients during night-time. The Journal of Allergy and Clinical Immunology, 115(2), 239

Vincenzo R, Silvia C, Ahmad K (2010) Temperature controlled Laminar Airflow controls inflammation during summer leave after long term high altitude stay in dust mite allergic asthmatic children. Allergy: European Journal of Allergy and Clinical Immunology. Conference: 29th Congress of the European Academy of Allergy and Clinical Immunology, EAACI London United Kingdom. Conference Publication: 65 (pp 170)

Search strategy and evidence selection

Search strategy

1. Databases were searched from inception to April 2014 using the following keywords: 'airsonett', 'protexo', 'temperature controlled laminar airflow', and 'TLA device'. The number of citations found is in brackets after each database.

Medline (via OVID) (2), Embase (via OVID) (12), MEDLINE(R) In-Process (via OVID) (2), CAB Abstracts (0), Web of Science Science Citation Index (1), Cochrane Library [Cochrane Reviews (2), Other Reviews (0), Trials (11), Methods Studies (0), Technology Assessments (0), Economic Evaluations (1), Cochrane Groups (0)].

These citations were sifted through to find any relevant material, using the inclusion

criteria below.

2. ClinicalTrials.gov, WHO ICTRP, and Current Controlled Trials were also searched for ongoing trials.

3. Information provided by the manufacturer in supporting this briefing was checked to identify any further information.

4. The manufacturer's website was thoroughly investigated.

Evidence selection

The inclusion criteria were as follows:

- Patients: adults or children with poorly controlled persistent allergic asthma.
- Intervention: the Airsonett device as an add-on to standard asthma treatment.
- Comparator: standard asthma treatment without Airsonett, or any other device that is intended to reduce allergen exposure in the same setting, used as an add-on to standard asthma treatment, or any other add-on treatments to reduce the allergic symptoms, such as omalizumab in patients aged 6 years or older.
- Outcomes: any relevant clinical outcomes and costs.
- Study design: for effectiveness – any comparative study; for other aspects of the device – any, including case reports.

About this briefing

Medtech innovation briefings summarise the published evidence and information available for individual medical technologies. The briefings provide information to aid local decision-making by clinicians, managers, and procurement professionals.

Medtech innovation briefings aim to present information and critically review the strengths and weaknesses of the relevant evidence, but contain no recommendations and **are not formal NICE guidance**.

Development of this briefing

This briefing was developed for NICE by Birmingham and Brunel Consortium. The Interim Process & Methods Statement sets out the process NICE uses to select topics, and how the briefings are developed, quality assured and approved for publication.

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