

Airsonett® AIR4 Temperature controlled Laminar Airflow (TLA) treatment for patients (adults and children ≥ 6 years) with severe persistent allergic asthma

The following information is intended for UK professionals with a responsibility for financial and service planning, to support local commissioning and planning of asthma services.



Overview	PICO Availability	Technology	Clinical Programme	Randomised Controlled Studies	Observational study	Health Economy	Short Facts References
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Brand Name	Airsonett® AIR4
Mechanism of action	Airsonett uses the novel Temperature controlled Laminar Airflow (TLA) technology to protect the patient from the exposure to allergens and other airborne particulates that occur in bed at night while a sleep.
Licensed Intended Use	Alleviation of symptoms of allergy induced diseases such as allergic asthma. Airsonett AIR4 provides a reduction of airborne allergen exposure by means of Temperature controlled Laminar Airflow (TLA). The device is intended for home use.
Classification	Airsonett AIR4 is a CE-marked Class I device according to Medical Device Directive 93/42/EEC.
Anticipated Place in Therapy (BTS/SIGN guidelines)	<p>Eligible patients are either</p> <ul style="list-style-type: none"> at step 4 or 5 and remain uncontrolled despite high dose inhaled corticosteroid (ICS) plus additional maintenance treatment. <p>The current treatment options for these patients are limited to;</p> <ul style="list-style-type: none"> treatments with significantly less beneficial side effect profile (e.g. oral corticosteroids and immunosuppressants); and/or treatments associated with a high costs (e.g. omalizumab, mepolizumab). <p>Airsonett AIR4 is a non-pharmacological treatment option that comes without the risks of pharmacological side effects or interactions with standard asthma medications.</p>
Clinical Outcomes ¹⁻⁴	<p>The Airsonett TLA device has in clinical trials been shown to reduce airway inflammation and asthma symptoms as well as improving asthma related quality of life when used in addition to regular pharmacotherapy in children and adults with persistent allergic asthma.</p> <p>Patients uncontrolled on BTS step 4 treatment were shown to benefit the most. This patient population also experienced less asthma exacerbations and related health-care utilization.</p>
Estimated number of patients with severe persistent allergic asthma	A small proportion of patients, estimated at less than 5% of all asthmatics, have severe difficult to control asthma. ⁵ The proportion of severe asthmatics that are allergic has been reported to be about 60%. ⁶
Dosage and Administration	Airsonett is installed next to the bed and is easy to use. Airsonett is to be used every night in combination with prescribed medication. The device comes with a timer functionality that will turn on/off the device every night.
Duration of treatment	Airsonett is intended for long-term treatment. The need for continued therapy is to be assessed on a 6 month basis as determined by physician assessment of the patient's level of control.
Independent Expert Reviews	<p>The National Institute for Health and Care Excellence (NICE). The Airsonett temperature-controlled laminar airflow device for persistent allergic asthma. NICE Medtech Innovation Briefing 8, 2014⁷</p> <p>Healthcare Improvement Scotland. Airsonett: Innovative Medical Technology Overview: 003/2015⁸</p> <p>Warner JO. Use of temperature-controlled laminar airflow in the management of atopic asthma: clinical evidence and experience. Ther Adv Respir Dis 2017;11:181-188³</p>

P	Patient Population	=	Patients with persistent allergic asthma that are either at BTS/SIGN step 4 and remain uncontrolled despite high dose inhaled corticosteroid (ICS) plus additional maintenance treatment, or at step 5.
I	Intervention	=	Nocturnal allergen exposure reduction with TLA technology
C	Comparator	=	Standard of care
O	Outcome	=	Reduction in airway inflammation, improvement in asthma control and asthma related quality of life

Severe allergic asthma is recognised as an area of high unmet need. These patients are at high risk of exacerbations, suffer from daily symptoms and an impaired quality of life.

According to the Asthma UK 'Living on a Knife Edge' report:⁹

- 2.1 million adults and 500,000 children in the UK experience severe asthma symptoms. Of these, up to half a million live with frequent, severe asthma symptoms despite taking high doses of medication.
- One in five are seriously concerned that the next asthma attack will kill them.
- Difficult to control asthma costs the NHS around £680 million a year.
- There are more than 71,000 hospital admissions for asthma every year in the UK costing the NHS more than £45.8 million a year.
- It is estimated that 80% of expenditure on asthma goes on the 20% of people whose asthma is more severe.

The current treatment options available for patients with severe persistent asthma uncontrolled with high dose inhaled corticosteroids in combination with other controller therapies are limited to:

- Treatments with significantly less beneficial side effect profile (e.g. oral corticosteroids and immunosuppressants); and/or;
- Treatments associated with a high costs (e.g. omalizumab, mepolizumab).

Airsonett AIR4 is a non-pharmacological treatment option that comes without the risks of pharmacological side effects or interactions with standard asthma medications.

Budget and Service Impact

Airsonett AIR4 should be prescribed by specialists with no additional testing required.

Treatment will be in patients own home. Airsonett offer to arrange the delivery and set up of the device according to the operating manual in the patients' homes and to train patients on its use. Airsonett do not anticipate that additional NHS staff and resource use will be required with the use of the device.

The current annual rental cost of the Airsonett AIR4 in the UK is £2,088, including filter replacements. Additional costs may be incurred if damage occurs due to misuse. A recent cost-efficacy analysis has shown that the £2,088 annual cost of Airsonett AIR4 is offset by economic savings in medical costs of £1,535, resulting in a net cost to the NHS of £553 per patient per annum (pp/pa). The incremental cost-effectiveness ratio (ICER) is £8,998, less than half of the £20,000/QALY threshold considered as the acceptable cost-effectiveness benchmark used by NICE.¹⁰

Nocturnal allergen exposure in the breathing zone may lead to allergic asthma reactions.

Asthma patients are particularly vulnerable during the night. While sleeping in the bed, the airways are close to pillows, mattresses and duvets that can be significant reservoirs of allergens such as house dust mite, dog and cat allergens that can cause worsening asthma symptoms.¹¹ In addition, the level of airborne house dust mite (HDM) allergens during sleep have been reported to be about 10-fold higher in the breathing zone than those during usual domestic life in the living room of the same houses.¹²

While sleeping in the bed, the nocturnal exposure to allergens and other airborne particles is increased by the body convection flow.¹³ The body convection flow is a persistent convection current established by the temperature difference between the warm air surrounding a human body and the ambient room temperature (Figure 1). These convection currents appear particularly prominent above the head, where they concentrate allergens from the bedding area to the breathing zone.



Figure1: The body convection flow

Airsonett AIR4 removes airborne particles and allergens from the breathing zone

The air from the room enters the Airsonett AIR4 device and passes a filter that captures allergens and other airborne particles. The filtered air is cooled to slightly below the ambient room temperature (at the level of the breathing zone) and is supplied with a very low velocity from the air supply nozzle. Since the filtered air is slightly cooler, and therefore heavier than the surrounding air, the filtered air will descend slowly from the air supply nozzle in a laminar manner enveloping the breathing zone (Figure 2a and b). This Temperature controlled Laminar Airflow (TLA) counteracts the allergen and particle rich body convection flow, minimising the level of inhalant particles and allergens in the patient's breathing zone all through the night (removes $\geq 99.5\%$ of particles $\varnothing \geq 0.5\mu\text{m}$).^{13,14}



Figure 2a: Breathing Zone



Figure 2b: TLA-generated laminar air flow enveloping the breathing zone

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Research hypothesis

The evaluation of the clinical performance of the Airsonett TLA device was based on the hypothesis that the highly significant reduction of airborne particles and allergens achieved by the Airsonett TLA device in the breathing zone during sleep, would further reduce allergic asthma reactions such as airway inflammation and asthma symptoms and thus improve health-related quality of life (QoL) when used in addition to conventional anti-inflammatory pharmacotherapy, in patients suffering from perennial allergic asthma.

Two validated instruments were chosen to demonstrate the effectiveness of adding the Airsonett TLA device to regular conventional pharmacotherapy on allergic asthma reactions:

- **The mini-Asthma Quality of life Questionnaire (mini-AQLQ)** was chosen to measure improved QoL and alleviation of asthma symptoms as perceived by the patient
- **Fractional Nitric Oxide concentration in exhaled breath (FENO; NIOX MINO™)** was chosen to acquire an objective measure of the effect on airway inflammation

Clinical Trials

22 week Pilot Study:	Pedroletti C et al. Clinical effects of purified air administered to the breathing zone in allergic asthma: A double-blind randomized cross-over trial. Respir Med 2009;103:1313-9 ClinicalTrials.gov: NCT00987064
1 year Pivotal Study	Boyle RJ et al. Nocturnal temperature controlled laminar airflow for treating atopic asthma: a randomized controlled trial. Thorax 2012;67:215-221 ClinicalTrials.gov: NCT00986323
1 year Observational Study	Schauer U et al. Improved asthma control in patients with severe persistent allergic asthma after 12 months of nightly temperature-controlled laminar airflow (TLA): An observational study with retrospective comparisons. Eur Clin Respir J 2015; 2: 28531

Summary of the Clinical Study Outcomes

The clinical studies confirmed the pre-specified hypothesis that using Airsonett TLA treatment to minimise nocturnal exposure to allergens and other airborne irritants can reduce airway inflammation and asthma symptoms as well as improving asthma related quality of life when used in addition to regular pharmacotherapy in children and adults with persistent allergic asthma.

Patients uncontrolled on BTS step 4 treatment were shown to benefit the most. This patient population also experienced less asthma exacerbations and required less healthcare resources.

As a non-invasive, non-pharmacological treatment the Airsonett TLA device has an inherent beneficial safety profile. The adverse events reported were very similar between the Airsonett TLA device group and the placebo group. No device related serious adverse events have been

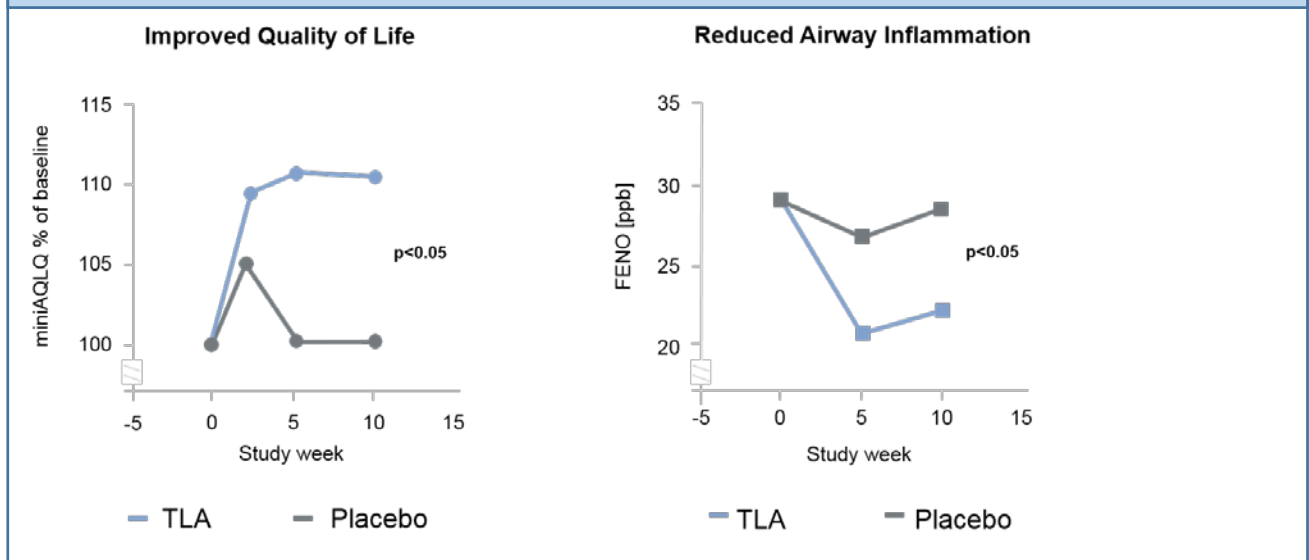
22-week Pilot Study¹

Objective:	To demonstrate the efficacy of TLA treatment when used in addition to regular pharmacotherapy to reduce allergic reactions in a population of subjects with mild to moderate persistent allergic asthma.
Design:	Randomized, controlled, double blind, cross-over study in 22 patients with mild to moderate persistent allergic asthma who received 10 + 10 weeks treatment with the Airsonett TLA device and placebo device (with 2 weeks wash-out period).
Patient Population:	<p><i>Key inclusion criteria</i></p> <ul style="list-style-type: none"> • Patients 12-33 years with diagnosed asthma. • Perennial allergy demonstrated by a positive skin prick test to at least one of the following allergens; cat, dog, house dust mites and/or mold. • Daily medication with inhaled corticosteroid equivalent to $\geq 400\mu\text{g/day}$ of inhaled budesonide. <p><i>Key exclusion criteria</i></p> <ul style="list-style-type: none"> • Current smoker. • Participation in another allergen avoidance program or in a drug trial.
Primary Endpoint:	Difference in quality of life between active versus placebo treatment as assessed by change in miniAQLQ score over 10 weeks
Key Secondary Endpoints:	Difference in airway inflammation between active versus placebo treatment as assessed by change in FENO over 10 weeks

Clinical Outcomes

The mean improvement in overall miniAQLQ score in the group treated with the Airsonett TLA device was significantly greater than in the placebo group (mean difference = 0.54; SEM ± 0.28 , $p < 0.05$) after 10 week treatment. FENO was significantly reduced by 6.4 ppb (SEM ± 2.50 , $p < 0.05$) after 10 week Airsonett TLA treatment as compared with placebo.

Nocturnal TLA treatment provided a statistically and clinically significant improvement asthma related quality of life (AQLQ) and significant reduction in airway inflammation (FENO)¹



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1-year Pivotal Study²

Objective:	To demonstrate the effectiveness and safety of the Airsonett TLA device when used in addition to regular pharmacotherapy to reduce allergic reactions in a population of subjects with poorly controlled persistent allergic asthma over 12 months.
Design:	312 patients with moderate to severe poorly controlled persistent allergic asthma were enrolled in this randomized (2:1 ratio), double-blind, placebo-controlled, parallel-group study conducted in 19 European asthma clinics in 6 countries over 12 months.
Patient Population:	<p><i>Key inclusion criteria</i></p> <ul style="list-style-type: none"> • Patients (7-70 years) with diagnosed asthma • Allergy to cat, dog and/or house dust mite demonstrated by specific IgE level ≥ 0.70 kU/L or positive skin prick test • Daily maintenance dose of at least ICS $\geq 200\mu\text{g/day}$ of budesonide or $\geq 100\mu\text{g/day}$ of fluticasone since at least 6 months • Partly uncontrolled asthma according to GINA 2006 • mini-AQLQ/PAQLQ score of ≤ 5.5 <p><i>Key Exclusion Criteria</i></p> <ul style="list-style-type: none"> • Current smoker (Non-smoker is defined as abstinent since >1 year). Children: Parents' indoor smoking. • ICS $\geq 1200\mu\text{g/day}$ of budesonide or $1000\mu\text{g/day}$ of fluticasone
Primary Endpoint:	Difference between TLA treatment and placebo in the proportion of patients with an increase of ≥ 0.5 points* in the miniAQLQ score and the corresponding paediatric PAQLQ score ("responders") after one year of treatment
Key Secondary Endpoints:	Change in FENO, asthma symptoms and quality of sleep, and exacerbation rates.

Clinical Outcomes:

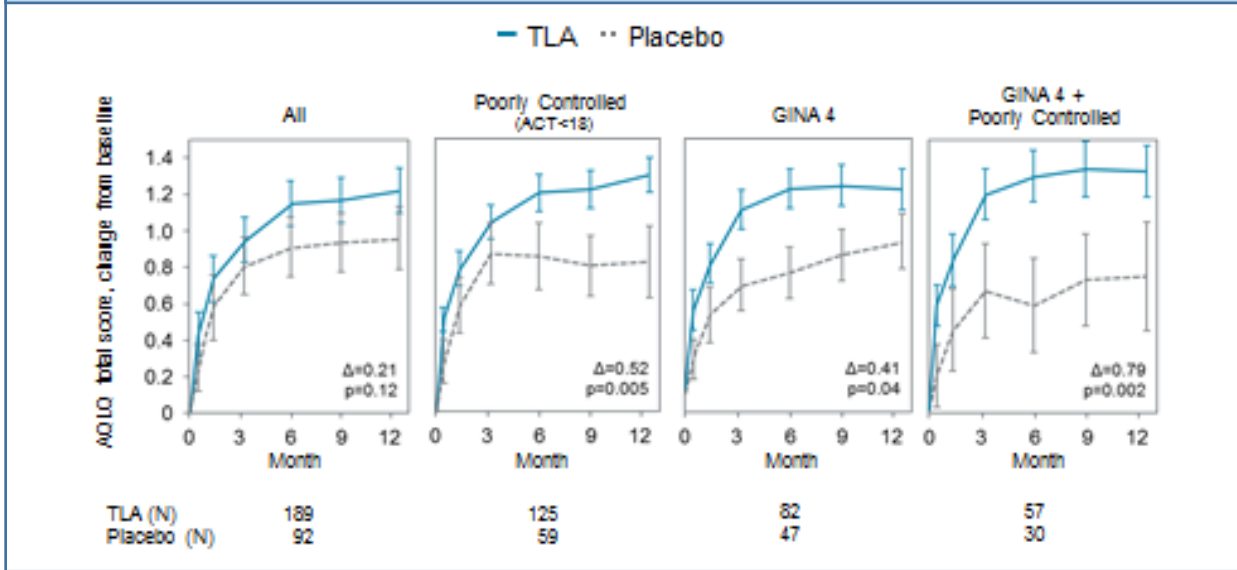
The primary efficacy analysis demonstrated a significant difference in AQLQ responder rate between active (143 of 189, 76%) and placebo (56 of 92, 61%) groups after 12 months - absolute difference 14.8% (OR: 1.99; 95% CI 3.1 to 26.5, $p=0.02$). This was also true for the pediatric subgroup (<12 years; absolute difference 16.8%; OR:7.63, $p=0.04$). The absolute differences in AQLQ responder rates corresponds to Numbers Needed to Treat (NNT; $1/\text{absolute difference in responder rates}$) values of 6.8 (ITT) and 6.0 (<12 years).

A pre-specified subgroup analysis based on asthma severity and asthma control showed that patients with more severe disease (based on high intensity treatment such as GINA step 4 at baseline) and uncontrolled asthma (based on an ACT < 18 at baseline) identifies the patients that will benefit the most (absolute difference TLA vs placebo 25.4%; OR=4.74; $p=0.009$). In this subgroup the NNT can be calculated to 3.9.

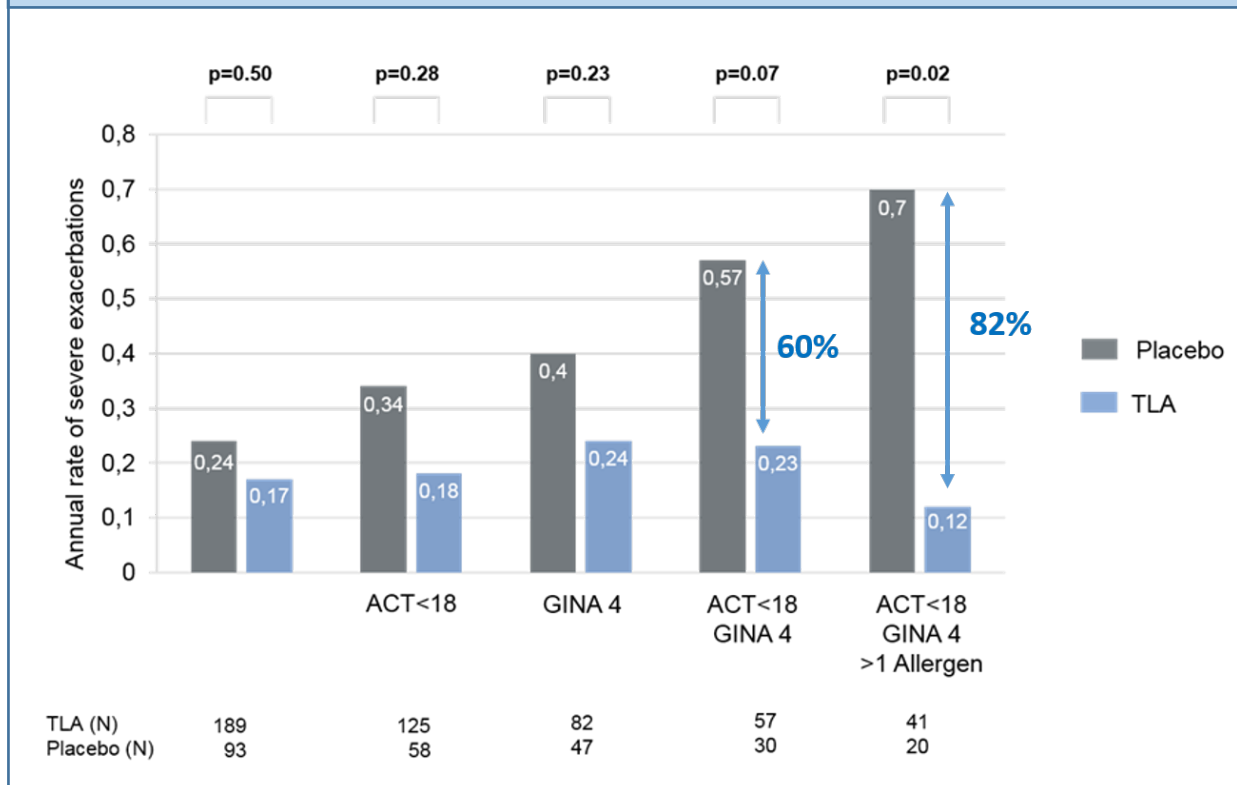
Although this study was not primarily designed to evaluate the effect of the Airsonett TLA device on asthma exacerbation rates, and in general the patients showed relatively low rates of severe asthma exacerbations (approx. 0.2 exacerbations/year). A subgroup analysis based on markers of increased exacerbation risk (such as ACT <18 and/or GINA 4 treatment intensity or ACT <18 and GINA 4 combined with sensitivity to multiple allergens at baseline) showed a clear trend towards a reduced exacerbation risk with TLA treatment vs. placebo in patients with increased exacerbation risk.³

* The minimal important difference of quality of life score per item has been defined to be 0.5 points for the overall asthma-specific quality of life score as well as for the individual domains.¹⁵

Patients with uncontrolled allergic asthma despite BTS step 4 treatment showed both a statistically significant and clinically meaningful improvement in Asthma related Quality of Life²



Post-hoc analysis showed a significant reduction of exacerbations in patients with uncontrolled allergic asthma despite BTS step 4 treatment sensitized to > 1 allergen³



Safety:

The adverse event reporting was very similar in the Airsonett TLA group and the placebo group. Serious adverse events occurred in 17% of the participants in the Airsonett TLA device group and 15% in the placebo group, none of which were considered treatment related.

1-year Observational Study⁴

Objective:	To demonstrate the effectiveness of the TLA device when used during real-life conditions in addition to regular pharmacotherapy to reduce exacerbations and improve asthma control in a population of subjects with severe persistent allergic asthma during 12 months.
Design:	Multicentre, pre- and post- retrospective observational study in patients with severe persistent allergic asthma who received add-on treatment with the TLA device for 12 consecutive months.
Patient Population:	<ul style="list-style-type: none"> • 30 patients with diagnosed severe persistent allergic asthma. • 7-80 years (mean age was 28, and 50% were <18 years at baseline). • History of at least one episode of severe exacerbation were included. All patients were treated with inhaled corticosteroids, ten patients (33%) were on regular treatment with oral corticosteroids (OCS) and 13 (43%) were treated with anti-IgE monoclonal antibodies at the beginning of the study
Primary Endpoint:	The primary objective of the study was to evaluate the intra-individual change in asthma control after 12 months of Airsonett TLA device use: <ul style="list-style-type: none"> • the number of exacerbations; • the need of asthma-related emergency care; • the need of asthma-related hospital admissions; • the need of asthma-related intensive care; • the use of OCS; and • changes in asthma control according to Asthma Control Test (ACT) scores.
Key Secondary Endpoints:	Lung function, medication use and ability to work (or go to school).

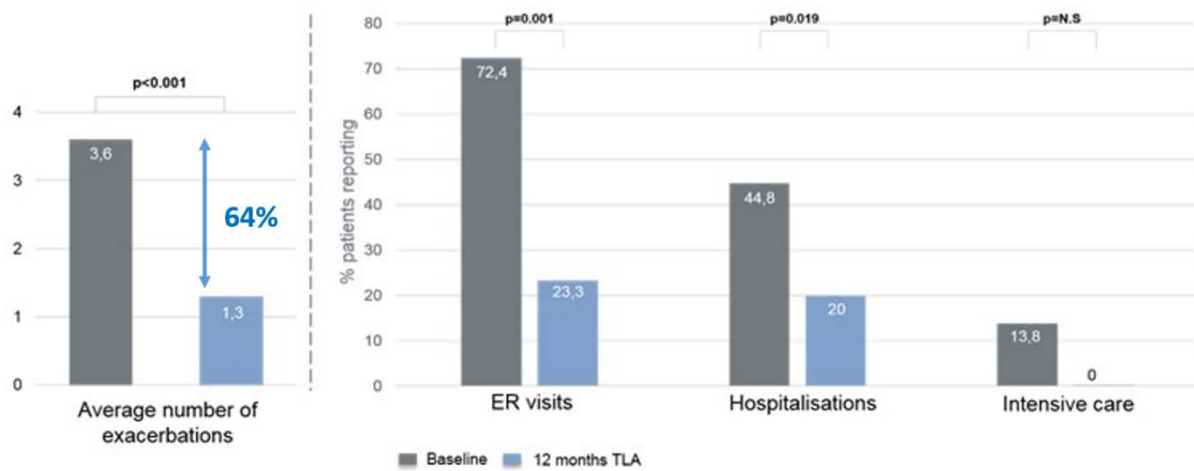
Clinical Outcomes:

30 patients completed measurements at baseline and 4 months and 27 patients the 12 months visit.

Treatment with the Airsonett TLA device significantly improved asthma control over 12 months as shown by:

- A significant reduction in mean annual exacerbation frequency from 3.6 (range 1-12) to 1.3 (range 0-5; $p < 0.001$).
- A reduction in the proportion of patients requiring asthma exacerbation related healthcare utilization as demonstrated by:
 - Emergency Room visits declined from 72 to 23% ($p = 0.001$);
 - Hospitalisations declined from 45 to 20% ($p < 0.05$); and
 - Intensive care unit treatment declined from 14% to 0% ($p > 0.05$; NS).
- Asthma Control Test (ACT) scores were significantly improved from 14.1 to 18.5 ($p < 0.0001$) with a clinically meaningful difference (≥ 3 points) compared with baseline.
- Lung function measured as Forced Expiratory Volume in 1 second (FEV_1) improved significantly from 1.9 to 2.3 L ($p < 0.01$).

Airsonett® AIR4 significantly reduced exacerbations and related healthcare utilization⁴



In addition the proportion of patients treated with oral steroids decreased during the study from 10 patients (33%) to 6 patients (22%) ($p>0.05$; NS). The proportion of patients reporting an asthma-related inability to work (or go to school) was lower but did not reach significance (43% vs 22%).

Health Economic Analysis of the 12 months observational study¹⁰

The objective of this analysis was to quantify the cost-effectiveness of Airsonett AIR4 as an add-on to standard asthma management drug therapy in the UK.

The incremental cost of TLA use was based on

- The 12 months observational clinical study monitoring the incidence of exacerbations and related healthcare utilisation¹⁶
- English health service costs
- The 12 months randomised double-blind placebo controlled clinical trial was used to derive the incremental QALY data from the pre-specified subgroup with an equivalent asthma condition (Patients with uncontrolled allergic asthma despite treatment with BTS Step 4 medication)⁴

Cost-effectiveness outcomes:¹⁰

- | | |
|--|--------------------|
| • Total savings = cost per episode × reduction in episodes | - £46,039 |
| • Savings per person = total savings/30 study participants | - £1,535 |
| • Incremental cost per person =
TLA (Airsonett) cost £2088 - savings per person £1535 | £553 |
| • Incremental cost-effective ratio (ICER) =
Incremental cost (£553)/incremental QALY gain (0.0615) | £8,998/QALY |

The sensitivity analysis performed, based on severity of condition, showed that **for certain high-risk individuals, with more severe and less well-controlled asthma, avoidance of two hospital admissions (via A&E or general admission), or one ICU admission per year, would result in treatment with Airsonett AIR4 being a cost saving to the NHS.**

Overview	PICO Availability	Technology	Clinical Programme	Randomised Controlled Studies	Observational study	Health Economy	Intended use References
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Intended use

Alleviation of symptoms of allergy induced diseases such as allergic asthma. Airsonett provides a reduction of airborne allergen exposure by means of Temperature controlled Laminar Airflow (TLA). The device is intended for home use.

Precaution

Airsonett is an additional treatment to regular pharmaceutical treatments. Airsonett is used for regular treatment, not fast relief or emergency treatment. This means you should use your Airsonett every night in combination with prescribed medication. Always consult your doctor before changing or reducing your medication. At any uncertainty, contact your doctor.

Pregnancy, breast-feeding and small children

Experience from using Airsonett during pregnancy, breast-feeding and in small children is limited. However, Airsonett does not supply any substances that can affect the pregnancy, breast-feeding or small children.

Usage

Airsonett is installed next to the bed and is easy to use. Effectiveness is dependent on following these Instructions for Use. Use your Airsonett every night in combination with prescribed medication. Sporadic use of Airsonett reduces the effectiveness.

Brief Facts

- Height: 119-139 cm (can be adjusted depending on type of bed)
- Base unit: Length: 54 cm Width: 34 cm
- Weight: 23 kg
- Energy consumption: Equivalent to a 60 W bulb



References

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Airsonett®

Breathe for a change

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