BLUE, BROWN AND NOW GREEN

The 'NHS long-term plan' has called for a shift towards inhalers with a lower carbon footprint.

DAWN CONNELLY

Innovation in inhaler design

1778: The word 'inhaler' is first coined by English physician and astronomer John Mudge, who modified a pewter tankard to create a portable device to treat catarrhous cough.

1956: The first convenient, portable, user-friendly inhalation systems — metered-dose inhalers (MDIs) — are launched by Riker Laboratories (now 3M), delivering epinephrine, isoprenaline and octyl nitrate.

1967: The Spinhaler (sodium cromoglycate; Fisons), the first dry powder inhaler (DPI) with hard gelatin capsule technology, is launched, allowing a high dose of the drug to be delivered.

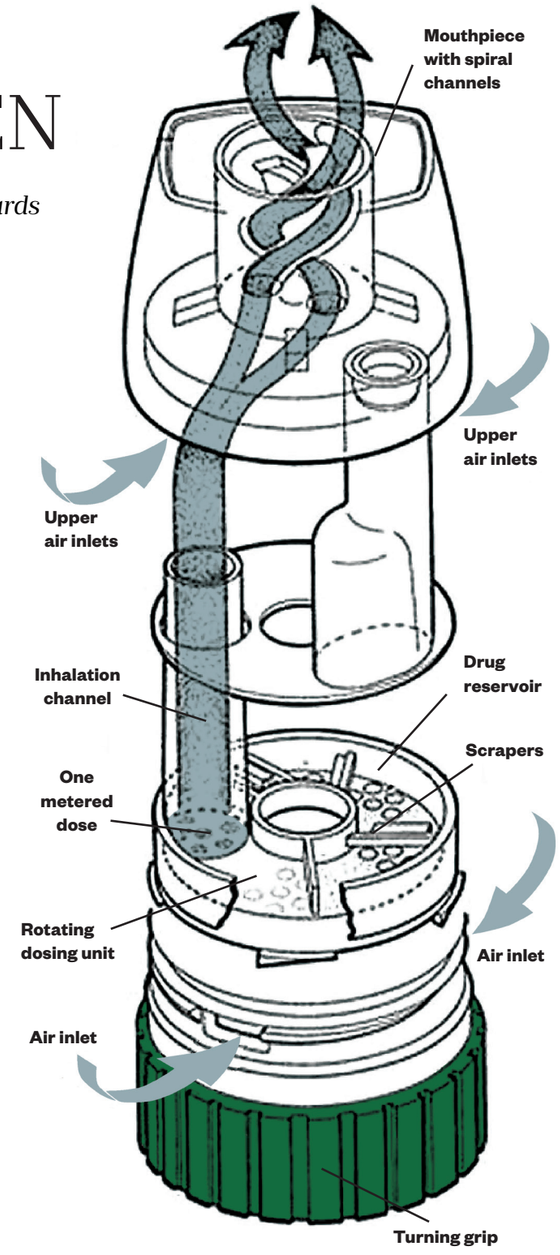
1969: Allen & Hanburys (now GSK) markets the first salbutamol MDI (Ventolin); it launches the first beclomethasone dipropionate MDI (Becotide) in 1972.

1970: The Autohaler, the first breath-actuated MDI, is launched by Riker as the Duohaler (isoprenaline and phenylephrine).

1976: The first valved spacer (Nebuhaler, AstraZeneca) — a large, pear-shaped device which reduces the need to coordinate actuation and breathing, and increases drug deposition in the lungs — is patented. The Allen & Hanburys Volumatic spacer device is launched in 1989.

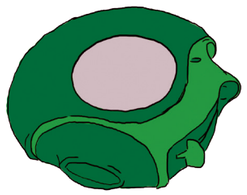
1987: The Montreal Protocol calls for elimination of chlorofluorocarbon (CFC) propellants, stimulating innovation within the inhaler industry. Turbohaler (terbutaline; AstraZeneca), the first reservoir multi-dose dry powder inhaler (DPI) is launched, which uses a carrier-free formulation, giving better lung deposition and simplifying dose loading.

1988: Allen & Hanburys introduces the Diskhaler, the first multi-unit dose DPI, which has sealed units to maintain dose uniformity, protect from humidity and reduce the effect of inhalation flow-dependent dose emission.



Turbohaler (terbutaline; AstraZeneca), reservoir multi-dose dry powder inhaler

1995: The first CFC-free hydrofluoroalkane (HFA) MDI to reach the market is Airomir (salbutamol suspension in HFA-134a, 3M). QVAR (beclomethasone, 3M), the first HFA inhaled corticosteroid (ICS), follows in 1998; it offers better lung deposition by using smaller drug particles, allowing the dose to be halved.

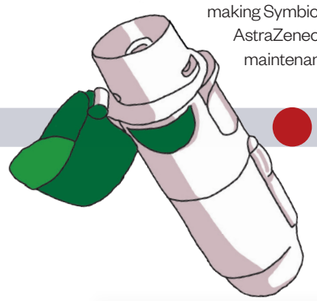


1999: The first ICS/long-acting beta-agonist (LABA) combination DPI inhaler Seretide Accuhaler (fluticasone propionate/salmeterol; Allen & Hanburys) is launched (pictured, left), simplifying treatment regimens. A Seretide MDI is launched in 2000.

2004: The first MDI with a built-in dose counter (Seretide Evohaler; Allen & Hanburys) is launched.

2006: Chiesi launches an HFA ICS equivalent to CFC ICS inhalers (Clenil Modulite), allowing a straight switch and prompting a phasing out of CFC ICS inhalers.

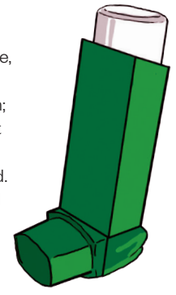
2007: Boehringer Ingelheim launches its Respimat (tiotropium) soft mist inhaler (SMI) (pictured, below)— the first compact aqueous delivery system. Symbicort SMART regimen is approved, making Symbicort (formoterol/budesonide; AstraZeneca) the first inhaler licensed for maintenance and reliever therapy.



2014: The first once-daily ICS/LABA DPI Relvar Ellipta (fluticasone furoate/vilanterol; GSK) is launched, followed by Anoro Ellipta, a once-daily LABA/long-acting muscarinic-antagonist (LAMA) (indacaterol/glycopyrronium; GSK). Chiesi launches Fostair NEXThaler (formoterol/beclometasone), the first DPI delivering extra-fine drug particles for better lung deposition.

2016: The Kigali amendment to the Montreal Protocol is agreed, which aims to achieve over 80% reduction in HFA consumption by 2047.

2017: Trimbow (beclometasone, formoterol and glycopyrronium; Chiesi), the first triple-therapy MDI is launched. Once-daily DPI Trelegy Ellipta (fluticasone, furoate, vilanterol and umeclidinium; GSK) is launched later the same year.



2019: In England, the NHS long-term plan calls for a shift from MDIs to lower carbon inhalers. Chiesi announces plans to develop an inhaler with a new propellant — HFA-152a — by 2025, which has a 90% lower carbon footprint. AstraZeneca announces similar plans in 2020. Boehringer Ingleheim launches the reusable Respimat SMI, estimated to reduce CO_2 emissions by 71%, compared with the single-use device.

What are the main differences between inhalers?

In adults, there is no difference in clinical effectiveness between a metered-dose inhaler (MDI) with a spacer and a dry powder inhaler (DPI) or soft-mist inhaler (SMI). The most important factor in choosing a device is whether the patient can use it effectively and is happy to do so, followed by cost and environmental impact.

Aerosols

Metered-dose inhalers

Design: Pressurised canister containing drug, propellants, surfactants, preservatives, and flavouring agents, released through a metering valve and stem when actuated. Can also be breath-actuated.
Technique: Slow, steady inhalation.
Advantages: Portable and compact; quick to use; over 100 doses; no contamination of contents; high-dose reproducibility; relatively cheap.
Disadvantages: Contain propellants; coordination of breathing and actuation needed (if not a breath-actuated device); low lung deposition (10–20%); upper limit to unit dose content; number of remaining doses is difficult to determine; potential for abuse; not all medicines available.
CO_2 equivalent: High (approximately 10–25kg per inhaler [e.g. generic salbutamol, Salamol, AirSalb, Clenil, QVAR, generic beclomethasone, Seretide Evohaler, Fostair, Sirdupla, AirFluSal, Serevent Evohaler and generic salmeterol]) to very high (approximately 25kg per inhaler or more [e.g. Ventolin Evohaler, Flutiform and Symbicort]).

Soft-mist inhalers

Design: An extremely fine nozzle atomises the drug solution using mechanical energy imparted by a spring, producing a fine, slow-moving mist.
Technique: Slow, steady inhalation.
Advantages: Propellant not required; compact and portable; multi-dose device; high lung deposition (>50%).
Disadvantages: Only two medicines available; some coordination of actuation and breathing required; some patients may find loading difficult.
CO_2 equivalent: Low (approximately 1kg per inhaler).

Dry powder inhalers

Design: Inhalation creates turbulent pressure that deaggregates the drug from the excipient in the dry powder formulation. The clinically effective inspiratory flow rate (IFR) for all DPIs is 30–90L/min, but the IFR for optimal delivery varies depending on the device's resistance.
Technique: Quick, deep inhalation.
Advantages: Coordination between actuation and breathing is not required; propellant not required; small and portable; quick to use; higher lung deposition than MDIs (15–40%); dose counters in most newer designs.
Disadvantages: May require moderate to high inspiratory flow; some units are single dose; can result in high pharyngeal deposition; not all medicines available.
CO2 equivalent: Low (approximately 1kg per inhaler).

Reducing the environmental impact

Clinicians can help to reduce the environmental impact of inhalers (and improve asthma management) by optimising inhaler technique, ensuring adherence with preventer medicines and reducing as required short-acting beta agonists. The following measures can also reduce the environmental impact:

Offer propellant free alternatives where clinically appropriate — up to 36kg	Change to lower carbon propellant (e.g. HFA-227ea to HFA-134a inhaler) — 20kg
Change from large volume to small volume reliever — 18kg	Return used inhalers to pharmacy for disposal — up to 17kg
Recycle used metered-dose inhalers — up to 18kg	If the inhaler has no dose counter, monitor the inhaled doses — 4kg

Potential CO_2 equivalent saving per inhaler (kg)

SOURCES: SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK/BRITISH THORACIC SOCIETY, GREEN INHALER, NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE, DRUG TARIFF, NHS BUSINESS SERVICES AUTHORITY, *BMJ OPEN. MULTIDISCIPLINARY RESPIRATORY MEDICINE*. **EDITORIAL ADVISERS:** ANNA MURPHY, CONSULTANT RESPIRATORY PHARMACIST AT UNIVERSITY HOSPITALS OF LEICESTER NHS TRUST; TOBY CAPSTICK, CONSULTANT PHARMACIST, RESPIRATORY MEDICINE, LEEDS TEACHING HOSPITALS NHS TRUST AND CHAIR OF THE UKCPA RESPIRATORY GROUP. **ILLUSTRATIONS:** COURTESY OF ASTRAZENECA; JAVIER TRIGO; MCLEAN