



Review on Inhaler Market in India for Chronic Diseases

Swapnil Zarkar¹ and Dr. S. C. Atram²

Student, Vidyabharti College of Pharmacy, Amravati, Maharashtra, India¹

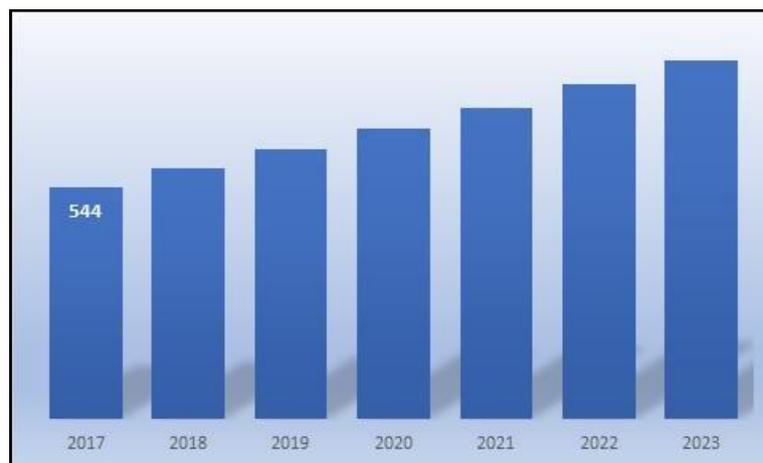
Assistant Professor, Department of Chemistry, Vidyabharti College of Pharmacy, Amravati, Maharashtra, India²

Abstract: Asthma is one of the most common chronic non-Communicable diseases in children and adults. Asthma is a disorder characterized by chronic airway inflammation, airway hypersensitivity to a variety of stimuli, and airway obstruction. It is at least partially reversible, either spontaneously or with treatment. An Inhaler is a device that gets medicine directly into a person's lungs. The medicine is a mist or spray that the person breathes in. Unlike a pill or liquid that is swallowed, an inhaler gets medicine right to the lungs. This helps people with asthma because the medicine works quickly to open up narrowed airways. The inhaler market in India is divided into four categories: device, type, application, and end-user. Metered dose inhaler, dry powdered inhaler, and nebulizer are the three device segments that make up the market. The goal of this report is to take a survey about the Inhaler market growth by years and years. Inhalers are developed and sold on a large scale from past few years the inhaler market has booked a profit of 500 million average profit.

Keywords: Bronchodilator, Oropharyngeal, Catastrophic, Nebulizers, Plethora

I. INTRODUCTION

During the forecast period, the Indian inhaler market is expected to develop at a significant rate of 7.4 percent. Large population base sensitive to asthma and COPD, expanding awareness about treatment for asthma and COPD, and considerable presence of market participants in the country are all aspects that contribute to the market's growth. The inhaler market in India is divided into four categories: device, type, application, and end-user. Metered dose inhaler, dry powdered inhaler, and nebulizer are the three device segments that make up the market. Due to its ease of use, the dry powder inhaler is expected to hold the biggest market share in the Indian inhaler industry. [1]



INDIA INHALER MARKET SIZE, 2017-2023 (\$ MILLION)

Figure 1: India inhaler market size, 2017 - 2023



Inhalers are classified as preventive, reliever, or long-acting bronchodilators. Furthermore, the market has been divided into asthma and COPD disorders based on application. In addition, homecare, hospitals, and clinics have been examined based on the end-user. India is the world's second most populous country and the world's fifth terms of GDP. India's GDP in 2022 was \$3.8 trillion, according to the International Monetary Fund. After China and Japan, it is Asia-third-largest Pacific's economy. In 2021, the country's population was 1.4 billion, with only approximately 6% of the population aged 65 and under, and roughly 9% of the population aged 0-4 years. [1]

India is expected to surpass China and become the world's most populous country in 2021 or 2022. Smoking, exposure to biomass-fuel smoke, and widespread "mosquito coil" insect repellent burning are all contributing to the high prevalence of respiratory or lung disorders in the country. Asthma affects over 15-20 million individuals in the country. According to the World Health Organization, lung disorders account for 11% of all deaths in the country. There are approximately 140 fatalities per 100,000 persons [2]

According to this, India is expected to contribute for between 1.6 and 2 million deaths in 2020. Inhalable medications are projected to be in great demand in the country due to the high frequency of respiratory disorders. When it comes to analyzing the Indian market capacity for inhalers, there is a lot of room for growth for individual companies. Due to abundant environmental and socio-cultural opportunities, the realm continues to expand rapidly. According to a Vision gain analysis, the global respiratory and inhaler industry is expected to reach US\$38 billion by 2023. Furthermore, respiratory-related illnesses such as asthma have seen a significant increase in recent years. Environmental pollution, industrialization, smoking, and other factors are all to blame. As a result, the need for breathing equipment has expanded in lockstep to fulfil the demand. [2]

Large population base sensitive to asthma and COPD, expanding awareness about treatment for asthma and COPD, and considerable presence of market participants in the country are all aspects that contribute to the market's growth. The inhaler market in India is divided into four categories: device, type, application, and end-user. Metered dose inhaler, dry powdered inhaler, and nebulizer are the three device segments that make up the market. Due to its ease of use, the dry powder inhaler is expected to hold the biggest market share in the Indian inhaler industry. Inhalers are classified as preventive, reliever, or long-acting bronchodilators. Furthermore, the market has been divided into asthma and COPD disorders based on application. In addition, homecare, hospitals, and clinics have been examined based on the end-user. [3]

II. INHALATION DEVICES IN CHRONIC DISEASES

For the treatment of asthma and COPD, a number of alternative medicine and inhaler combinations are available, improving the chances of finding an appropriate solution for each particular patient. The way medication is dispensed, whether the treatment is passively generated (e.g., using propellant, mechanical, or compressed air), aspects of the drug formulation (e.g., solution, dry powder, or mist), whether the inhaler contains a single-dose or multi-dose medication, and whether the device is disposable or refillable are all factors to consider. Each inhaler device has its own design, allowing patients to customize their choices to match their specific needs. [4]

2.1 Nebulizers

One of the oldest types of devices is the nebulizer. In general, they are utilized in the emergency room to treat acute patients or in chronic disease care for children or elderly patients who are unable to use an inhaler with a spacer or who have coordination issues. Nebulizers are simple to operate once they're up and running, and they provide a quick option to administer a larger dose of medicine to the airways if necessary. Because nebulizers eliminate the requirement for patient coordination between inhalation and actuation, they are especially beneficial to people who have cognitive, neuromuscular, or respiratory problems. 26–28 Because of physical or cognitive limitations, more than half of patients who use nebulizers instead of other devices do so.

Most nebulizer systems, on the other hand, are bulky and uncomfortable, necessitate regular maintenance, extend drug delivery from seconds to 10–20 minutes, and necessitate complete cleaning to sanitize the device on a regular basis. In



the acute care of disease, nebulizers were found to yield similar results to pMDIs with a spacer; however, when compared to DPIs, nebulizers may be useful in COPD patients with a suboptimal inspiratory flow.[4]



Figure 2: Nebulizer

III. PRESSURIZED METERED-DOSE INHALERS

The pMDIs is a widely used device, thanks to the large range of medications that may be delivered via this type of inhaler as well as the affordable cost. The move from chlorofluorocarbon (CFC) pMDIs, which are nearly obsolete, to primarily hydrofluoroalkane (HFA) pMDIs has occurred in recent years. The long-acting 2-agonist formoterol, the corticosteroids Ciclesonide (CIC), beclomethasone dipropionate (BDP), and flunisolide, and a medication combination of BDP/formoterol in a single inhaler are all available HFA solutions. Extra-fine particles (.2 m mass median aerodynamic diameter) in BDP and CIC formulations have been linked to lower oropharyngeal deposition and increased lung deposition. Extra-fine inhaled corticosteroids (ICS) have a considerably higher chance of establishing asthma control than fine particle ICSs, with lower exacerbation at significantly minimum doses. The pMDI was first introduced in 1956 to provide a delivery system for inhaled bronchodilators with a multi-dose capability and reproducible dosing characteristics. pMDIs contain propellants, which are currently being changed from chlorofluorocarbons (CFCs) to hydrofluoroalkanes (HFAs) because the former damage the ozone layer in the stratosphere.



Figure 3: Pressurized metered dose

The pMDI produces a rapid-moving plume of aerosol, the duration of which is typically 0.1–0.4 s. The velocity of the aerosol plume may be 8 ms^{-1} at a distance of 10 cm from the actuator, and is even higher at distances closer to the nozzle. The plume often feels cold on the back of the throat as the propellants evaporate. [5-6]



Pneumonia, acute COPD exacerbations, and respiratory events were reduced in patients who switched to extra-fine particle ICS formulations. Inhaling too quickly (rather than slowly and deeply), failing to tilt the head to the proper posture, failing to empty the lungs before inhalation, and failing to hold breath after inhalation are all common user problems with pMDIs. Patients can't always identify how many doses are remaining since, despite FDA advice from 2003, pMDI devices without a dose counter are still on the market. In a survey of patient satisfaction with their pMDIs, 52 percent said they were "very unsure" of how much medication was left, and 10% said they were "slightly unsure." While the inclusion of dose counters to many devices has remedied this problem, the patient must be aware of the necessity to maintain track of remaining medical.[6]

IV. DRY POWDER INHALER



Figure 4: Dry powder inhaler

DPIs were introduced into clinical practice as a more user-friendly alternative to the CFC- and HFA-powered pMDIs. Breath-activated DPIs are designed to solve problems with inhaler actuation and inspiration coordination. There are three primary systems: capsule-based pre-metered single-dose devices; multi-unit dose inhalers (preloaded with a blister foil by the manufacturer); and multiple-dose inhalers having an in-built mechanism that meters out a single dose from a reservoir of powder with each actuation. Each dose must be primed and loaded correctly in order to use a DPI effectively. The user's inspiratory flow provides the energy for DPIs to empty the drug system, and the failure to generate a forceful inspiratory flow via a device is the most common catastrophic mishandling error with DPIs, occurring in 26%–38% of cases. [7-8] DPIs were first introduced in 1970, and the earliest models were single-dose devices containing the powder formulation in a gelatin capsule, which the patient loaded into the device prior to use. Since the late 1980s, multi-dose devices have been available, giving the same degree of convenience as a pMDI. The first of these was the Turbuhaler (AstraZeneca, Lund, Sweden). By early 2005, at least 17 DPIs were marketed in different countries, consisting of both single-dose multi-dose models. Most multi-dose DPIs hold the powder in a reservoir, from which individual doses are metered. However, in one study, COPD patients with a mean forced expiratory volume in one second (FEV₁) of 0.7 L could generate peak inhaled flow rates of 28–78 L¹ min⁻¹ via the Turbuhaler DPI. Failure to hold the device in the correct position when loading the dose, failing to tilt the head in the correct position, insufficient inspiratory effort, and failure to empty the lungs before inhalation are all common DPI problems. Many patients with asthma and COPD are increasingly realizing that producing the necessary ideal inspiratory flow rates for DPIs is challenging, ineffective drug delivery and therapeutic benefit. Heat and moisture are also harmful to DPIs, so great care must be given to avoid dampness. As a result, its use in hot and humid climate zones is restricted, and special care must be made to maintain the gadget properly. [11]

V. SOFT MIST INHALERS

The SMI is an alternative to pMDIs and DPIs, with the goal of improving drug delivery to the lungs in order to benefit the patient and improve adherence. The inhaler, which is currently the only commercially available SMI for asthma and



COPD, was created with the goal of delivering optimal drug administration to the lungs without the need of propellants, as well as reducing the requirement for patient coordination and inspiratory effort. Individual doses are given via a specially developed nozzle system as a slow-moving aerosol cloud, and because the gadget is driven by the energy of a compressed spring inside the inhaler, it does not require propellants. Furthermore, because the SMI is made from a solution rather than a powder, it is moisture resistant, making it suited for humid locations. [12-13]



Figure 5: Soft Mist Inhaler

The development of soft mist inhalers (SMIs) has opened up new opportunities for inhaled drug delivery. SMIs use liquid formulations similar to those in nebulizers, but are generally multi-dose devices that have the potential to compete with pMDIs and DPIs in the portable inhaler market. While a number of SMIs are known to be in development, the only device currently marketed is Respimat1 Soft Mist Inhaler (Boehringer Ingelheim GmbH & Co. KG, Ingelheim, Germany). This device contains sufficient doses of a bronchodilator formulation for 1 month's dosing, stored in a fluid reservoir. Respimat1 Soft Mist Inhaler is powered by the energy of a compressed spring inside the inhaler; no propellants are required. [12-13]

However, scintigraphy studies have shown that lung deposition is several times higher than that from a CFC-based pMDI, and clinical trials have confirmed that drugs delivered by the Respimat1 Soft Mist Inhaler are effective in correspondingly smaller doses in COPD patients. Dry powder inhalers (DPIs), metered dose inhalers (MDIs), and soft mist inhalers are all part of the inhalers category (SMIs). Compressor nebulizers, ultrasonic nebulizers, and mesh nebulizers are all included in the nebulizers category. Inhalers also accounted for the highest share of the COPD and asthma devices market in 2019, owing to factors such as inhalation being the quickest and most effective means of delivering medications to the respiratory system during COPD and asthma treatment. [14]

VI. ROTAHALER DEVICE

Rotahaler Device is an inhaler used to deliver dry powder medications for treating lung-related ailments. Features of Rotahaler Device: Simple to use: Requires a Rotacap, a capsule containing the drug powder, to be fitted into the capsule chamber, and inhalation of the drug using the mouthpiece twice. Breath-actuated: The device automatically releases the medication when the user inhales. Consistent and accurate dosage: The Rotahaler inhalation device is pre-metered and provides a single, fixed dose of medication through each capsule that is discarded after each use. Portable: Being small and handy, this COPD device can be easily carried around for use anywhere as required. [15]

Rotacaps are capsules which contain a medicine called salbutamol sulphate. This medicine belongs to a group of medicines called beta-2 adrenoceptor agonists. The medicine is a very fine powder mixed with lactose (which contains milk protein). Each capsule contains the equivalent of 200 micrograms of salbutamol. Rotacaps are used in a plastic



device called a Rotahaler. When used in your Rotahaler, your Rotacaps provide a measured amount of medicine for you to breathe into your lungs. Your Rotacaps help you to breathe more easily. When you are having difficulty breathing, or your chest is tight, or when you are wheezing, Rotacaps open up the breathing tubes in your lungs to help with breathing. Because the medicine in your Rotacaps gives fast relief from your chest symptoms, it is often called a 'reliever'. Some people start wheezing or their chest starts to feel tight when they exercise. This is called exercise-induced asthma. [16]

If you have exercise-induced asthma, your doctor may tell you to inhale one or two Rotacaps before you exercise. This can help prevent the symptoms of exercise-induced asthma. This medicine is only one part of a plan to help you manage your asthma or other chest condition. You should discuss this plan with your doctor. Ask your doctor to check your treatment regularly. The medicine in Rotacaps is not addictive.

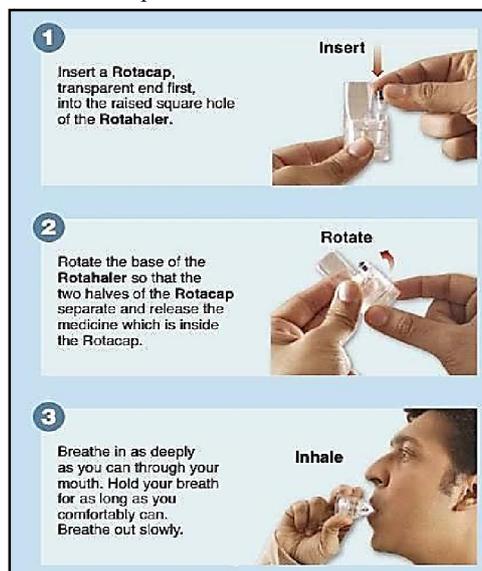


Figure 6: Step to Fill Rotahaler

How much to take -The pharmacist's label will usually tell you how many capsules to use and how often to use your Rotacaps with the Rotahaler. If you are not sure, ask your doctor or pharmacist. Adults: one or two Rotacaps (200-400 micrograms) inhaled via Rotahaler 3 or 4 times daily. The maximum dose is 12 Rotacaps in a 24-hour period. children (to 12 years): one Rotacap (200 micrograms) inhaled via Rotahaler 3 or 4 times daily. The maximum dose is 6 Rotacaps in a 24-hour period. [17-20]

VII. SMART INHALERS

The way medicine is being practiced has undergone dramatic changes with the development of novel technologies that help examine the health of the patient as a whole. This is particularly so with the Internet of Things (IoT). Now that the internet has become a standard component of daily life, whether at home, the workplace or school, connectivity is the watchword for all kinds of technological processes. Such connectivity was earlier achieved by wireless (wi-fi) or Bluetooth networks, but now artificial intelligence (AI) is giving rise to new-generation medical devices that deliver smart care. [21-23]

The inhaler is part of this transformation, with smart inhalers having emerged on the scene. A smart inhaler is an inhaler that integrates connectivity with a mobile app, via Bluetooth, for instance. These devices are built with sensor technology that helps record data about the time and date of use, and the location of the patient at each use. The world's first smart inhaler to receive approval from the Food and Drug Administration (FDA) was Teva's ProAir Digi haler (albuterol sulphate), which has a use-tracking real-time sensor that syncs it to a mobile app. The sensors may be either an integral part of the inhaler itself or be external devices that are attached to the primary inhaler. Several devices now



being developed belong to the latter clip-on category, such as that from the United States-based company Propeller Health and New Zealand-based Adherium. These records can provide data that predicts asthma attacks, thus allowing the patient to forestall them.[23]



Figure 7: Smart Inhaler

Use of smart inhalers allows patients and their doctors to track their condition and monitor the efficacy of treatment in individual patients over time, without having to keep diaries or other written records. The time and location tracking may also help identify trigger factors, share the data instantly with the doctor, and accumulate data for research. Some advanced models even sense high levels of air pollutants or pollen to warn patients of possible exacerbations. Some tell if the patient has the right inhaler technique that delivers adequate amounts of the drug to the lungs and minimizes side effects. For instance, an Irish team developed an add-on that uses acoustic sensors to tell if the patient is using the inhaler correctly, concerning both the period of each inhalation or the technique. [23]

This prevents effective management and increases asthma severity, ultimately reflecting in inadequate cost management as well. Are smart inhalers really useful Digital therapeutics is the wave of the future, offering further personalization of chronic disease management as well as unprecedented follow-up of patient wellness and treatment compliance. Digital inhalers can enable asthma or COPD patients to gain more control over their disorder, identify triggers, connect and share information with their medical providers, and collect valuable research data. The technology is a useful tool for facilitating adherence to treatment schedules, dosage reminders, and tracking usage of the inhalers by setting relevant alerts or notifications. [24]

VIII. BREATH-ACTUATED METERED DOSE INHALER

A breath-actuated metered-dose inhaler (MDI) is a type of inhaler that delivers asthma medication directly to the lungs. With this type of MDI, it's your inhalation combined with a propellant that gets the medication where it needs to go rather than just a propellant, as is the case with a conventional MDI. When using a breath-actuated MDI, proper technique is important for making sure the entire dose of medicine reaches your lungs. Breath-actuated MDIs are sometimes simply called breath-actuated inhalers (BAIs), while conventional MDIs may be called pressurized MDIs (pMDIs). [25-28]

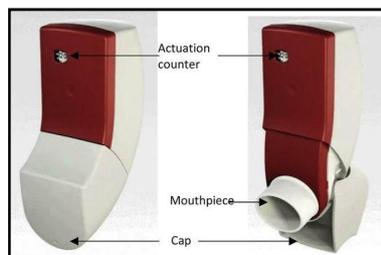


Figure 8: Breath-actuated metered-dose inhaler

Since poor coordination between firing and inhaling is usually considered to be the most significant problem patients have with pMDIs, the development of breath-actuated (BA) pMDIs is logical. Two such devices are



currently being marketed and several others are in development. With BA pMDIs, the patient’s inhalation through the device triggers a mechanism that fires the pMDI, so that firing and inhaling are automatically coordinated. These devices can achieve good lung deposition and clinical efficacy in patients unable to use a standard “press and breathe” pMDI correctly because of coordination difficulties. BA pMDIs do not solve cold Freon problems and would be unsuitable for a patient who has this kind of difficulty using pMDIs. However, errors when using BA pMDIs are less frequent than when using a standard pMDI. It is essential that the BA pMDI is correctly prepared (e.g., by raising the priming lever, removing the mouthpiece cover etc.); the inhalation must also be strong enough to trigger the firing mechanism.[28]

IX. COPD AND ASTHMA DEVICES MARKET

By Product Type

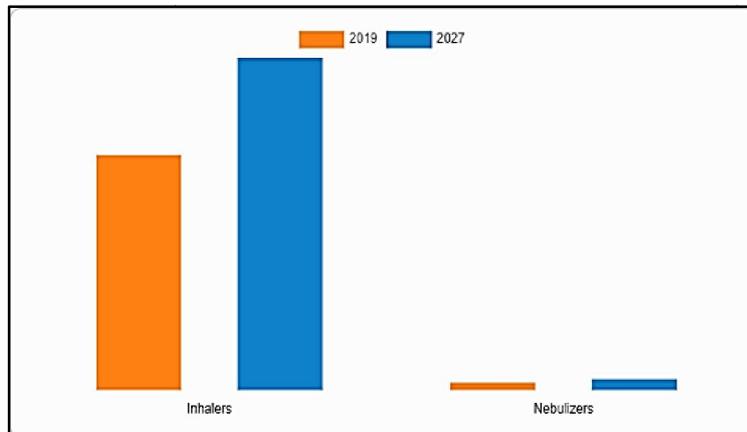


Figure 9: COPD and Asthma devices market (By product type)

The COPD and asthma devices market share held by retail pharmacies was the greatest in 2019 and is expected to grow at the quickest rate during the forecast period. Due to its wide chain of distribution network of pharmacy stores, the market is growing due to factors such as the fact that it is the oldest and most traditional medium for providing respiratory equipment to customers. [33-34]

By Distribution channel

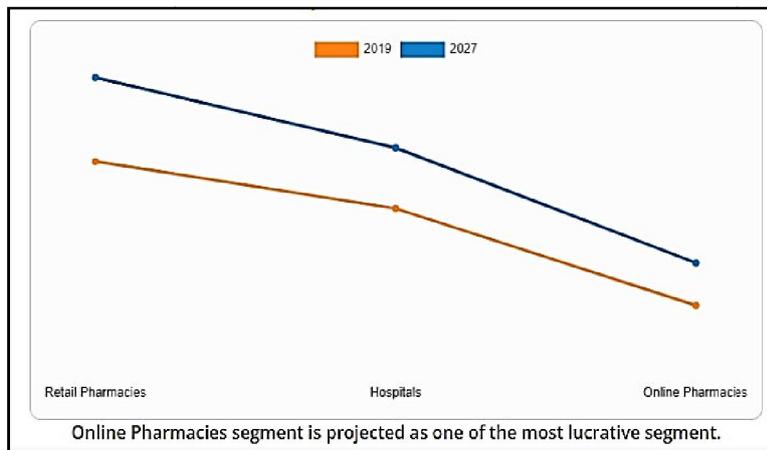


Figure 10: COPD and Asthma devices market (By distribution type)

The broad and early acceptance of inhalers and nebulizers, and the enormous pool of patients suffering from respiratory disorders, COPD and asthma devices market size is predicted to continue to grow in 2019. Furthermore, as healthcare



expenses rise, understanding of improved portable COPD and asthma devices grows, and disposable income rises, the Asia-Pacific region is expected to grow quickly. [34-36]

X. CONCLUSION

A variety of inhaler devices are now available to deliver inhaled drugs to patients with Chronic diseases. The inhaled drug delivery field is a dynamic one, with many inhalers available already and new ones being introduced on a regular basis. The plethora of inhaler devices available, requiring different inhalation techniques for optimal drug delivery, may confuse patients and healthcare providers alike, a situation described as “device dementia”. That said, a number of actions or steps are common to all types of devices reviewed in this article. For healthcare professionals and patients, these are arguably the most important elements of inhaler technique for the purposes of teaching and learning how to use each device, as most patients are likely to try more than one type of inhaler device during their lifetime and mastering a new device will thus be made easier. The final step in the sequence for all devices is the breath-hold. Studies of pMDI use show that lung deposition is greater after holding the breath for 10 s than for 4 s, because the extra time allowed for sedimentation in the small airways of the lung increases the amount of inhaled drug that is deposited. Given that the particle size distribution of aerosols delivered by the other devices in this article is quite similar to that from pMDIs, breath-holding is likely to have equal value in patients who use them. There is no perfect inhaler, and each has advantages and disadvantages, but there is increasing recognition that a successful clinical outcome is determined as much by choice of an appropriate inhaler device as by the drugs that go in them. Drug delivery from all inhaler devices depends on how the patient prepares the device and then inhales from it. The relative difficulties in completing these two steps correctly can be shown on a scale, with pMDI being the easiest to prepare (and hardest to inhale from correctly) and nebulizers at the opposite end. The best device for chronic diseases patients is arguably one for which both these steps can be performed successfully without major challenges. There is evidence that a patient is most likely to use correctly an inhaler that he or she prefers, and each patient’s choice of device will be determined by individual perceptions of how its advantages and disadvantages balance out. This decision could be quite different to the judgement of a prescriber or a formulator, who may give more weight to technical points. Choice of an inhaler device should therefore take into account the likelihood that patients will be able to use a particular device correctly, cost-effectiveness, preference and likely compliance.

REFERENCES

- [1]. <https://www.techsciresearch.com/report/india-respiratory-inhalers-market/7468.html>
- [2]. <https://www.researchandmarkets.com/reports/5530729/india-respiratory-care-devices-market-by-product>
- [3]. Lewis A, Torvinen S, Dekhuijzen PN, et al. The economic burden of asthma and chronic obstructive pulmonary disease and the impact of poor inhalation technique with commonly prescribed dry powder inhalers in three European countries. *BMC Health Serv Res.* 2016; 16:251.
- [4]. Asthma UK. Asthma facts and statistics. Available from: <https://www.asthma.org.uk/about/media/facts-and-statistics/>. Accessed February 12, 2018.
- [5]. World Health Organization. Chronic respiratory diseases. Available from: <http://www.who.int/respiratory/en/>. Accessed October 26, 2017.
- [6]. Stein SW, Thiel CG. The history of therapeutic aerosols: a chronological review. *J Aerosol Med Plum Drug Deliv.* 2017;30(1):20–41.
- [7]. Newman SP, Weisz AW, Talaei N, Clarke SW. Improvement of drug delivery with a breath actuated pressurised aerosol for patients with poor inhaler technique. *Thorax* 1991; 46: 712–716.
- [8]. Molimard M, Raheison C, Lignot S, et al. Assessment of handling of inhaler devices in real life: an observational study in 3811 patients in primary care. *J Aerosol Med* 2003; 16: 249–254.



- [9]. Lenney J, Innes JA, Crompton GK. Inappropriate inhaler use: assessment of use and patient preference of seven inhalation devices. *Respir Med* 2000; 94: 496–500.
- [10]. Newman SP, Newhouse MT. Effect of add-on devices for aerosol drug delivery: deposition studies and clinical aspects. *J Aerosol Med* 1996; 9: 55–70.
- [11]. Asthma.org.uk. (2020). Smart inhalers. Retrieved on 12/28/2020 from: <https://www.asthma.org.uk/advice/inhalers-medicines-treatments/inhalers-and-spacers/smart-inhalers/>
- [12]. Mohammadi, D. (2017). Smart inhalers: will they help to improve asthma care? *The Pharmaceutical Journal*. Retrieved on 12/28/2020 from: <https://www.pharmaceutical-journal.com/news-and-analysis/features/smart-inhalers-will-they-help-to-improve-asthma-care/20202556.article>
- [13]. Blakey, J. D. et al. (2018). Digital technologies and adherence in respiratory diseases: the road ahead. *European respiratory journal*. <https://dx.doi.org/10.1183%2F13993003.01147-2018>. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6364097/>
- [14]. Van Boven, J. F. M. et al. (2018). Personalising adherence-enhancing interventions using a smart inhaler in patients with COPD: an exploratory cost-effectiveness analysis. *npj Primary care respiratory* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6021429/>
- [15]. <https://www.verywellhealth.com/breath-actuated-metered-dose-inhaler-201191>
- [16]. Kesten S, Zive K, Chapman KR. Pharmacist knowledge and ability to use inhaled medication delivery systems. *Chest* 1993; 104: 1737–1742.
- [17]. Crompton GK. Problems patients have using pressurized aerosol inhalers. *Eur J Respir Dis Suppl* 1982; 119: 101–104.
- [18]. Pedersen S, Ostergaard PA. Nasal inhalation as a cause of inefficient pulmonary aerosol inhalation technique in children. *Allergy* 1983; 38: 191–194.
- [19]. Lindgren S, Bake B, Larsson S. Clinical consequences of inadequate inhalation technique in asthma therapy. *Eur J Respir Dis* 1987; 70: 93–98.
- [20]. Giraud V, Roche N. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *Eur Respir J* 2002; 19: 246–251.
- [21]. Hochrainer D, Ho lz H. Comparison of the aerosol velocity and spray duration of Respimat1 Soft Mist™ inhaler and pressurised metered dose inhalers. *J Aerosol Med* 2005; 18: 273–282.
- [22]. O’Callaghan C, Wright P. The metered-dose inhaler. In: Bisgaard H, O’Callaghan C, Smaldone GC, eds. *Drug Delivery to the Lung*. New York, Marcel Dekker, 2002; pp. 337–370.
- [23]. Newman SP, Pavia D, Clarke SW. How should a pressurized beta-adrenergic bronchodilator be inhaled? *Eur J Respir Dis* 1981; 62: 3–21.
- [24]. Hindle M, Newton DA, Chrystyn H. Investigations of an optimal inhaler technique with the use of urinary salbutamol excretion as a measure of relative bioavailability to the lung. *Thorax* 1993; 48: 607–610.
- [25]. Connolly CK. Method of using pressurized aerosols. *BMJ* 1975; 3: 21.
- [26]. Epstein SW, Manning CP, Ashley MJ, Corey PN. Survey of the clinical use of pressurized aerosol inhalers. *Can Med Assoc J* 1979; 120: 813–816.
- [27]. Shim C, Williams MH Jr. The adequacy of inhalation of aerosol from canister nebulizers. *Am J Med* 1980; 69: 891–894.
- [28]. Kelling JS, Strohl KP, Smith RL, Altose MD. Physician knowledge in the use of canister nebulizers. *Chest* 1983; 83: 612–614.
- [29]. Dolovich MB, Ahrens RC, Hess DR, et al. Device selection and outcomes of aerosol therapy: Evidence-based guidelines: American College of Chest Physicians/American College of Asthma, Allergy, and Immunology. *Chest* 2005; 127: 335–371.
- [30]. Derom E, Thorsson L. Factors affecting the clinical outcome of aerosol therapy. In: Bisgaard H, O’Callaghan C, Smaldone GC, eds. *Drug Delivery to the Lung*. New York, Marcel Dekker, 2002; pp. 143–171.



- [31]. van der Palen J, Klein JJ, Kerkhoff AH, van Herwaarden CL, Seydel ER. Evaluation of the long-term effectiveness of three instruction modes for inhaling medicines. *Patient Educ Couns* 1997; 32: S87–S95.
- [32]. Brennan VK, Osman LM, Graham H, Critchlow A, Everard ML. True device compliance: the need to consider both competence and contrivance. *Respir Med* 2005; 99: 97–102.
- [33]. Thiel CG. From Susie’s question to CFC free: an inventor’s perspective on forty years of MDI development and regulation. In: Dalby RN, Byron PR, Farr SJ, eds. *Respiratory Drug Delivery V*. Buffalo Grove, Interpharm Press, 1996; pp. 115–123.
- [34]. McDonald KJ, Martin GP. Transition to CFC-free metered dose inhalers-into the new millennium. *Int J Pharm* 2000; 201: 89–107