SUPPLEMENTARY MATERIAL

Supplementary material 1

Appendix 1. Search strategies for QUESTION 1 and QUESTION 2.

RESEARCH QUESTION 1: What is the impact of pMDIs on the carbon footprint?

- (pMDI OR DPI) AND (climate change OR carbon footprint OR greenhouse gas OR CO2)
- inhalers AND asthma AND (climate change OR carbon footprint OR greenhouse gas OR CO2)

RESEARCH QUESTION 2: What is the possible impact of changing the treatment of patients with asthma from pMDIs to DPIs?

- (pMDI impact OR DPI impact) AND (asthma treatment OR asthma therapy OR asthma outcomes OR asthma QoL OR asthma patients OR asthma quality of life) AND switch
- ("Dry Powder Inhalers [Mesh]) AND "Metered Dose Inhalers"[Mesh] AND (impact OR switch OR asthma OR quality of life)
- pMDI AND asthma AND patient AND (profile OR characteristics OR preferences)

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Supplementary material 2

Appendix 2. Selection criteria for questions QUESTION 1 and QUESTION 2.

Clinical question	Inclusion criteria	Exclusion criteria
QUESTION 1: What is the impact of pMDIs on the carbon footprint?	• Original manuscripts, reviews and editorials • Studies evaluating the impact on the carbon footprint of inhalers for the treatment of asthma that use HFC-based propellants • Studies providing data from carbon footprint measurements of pMDIs or DPIs • Comparative studies, as long as calculations (kg, tons or gigatons) of CO_2, or other CO_2-equivalent emissions, and/or percentages of total emissions are available. • Publications with data related to emissions of the entire life cycle (only data about emissions generated by use and disposal) • Studies published within the last 11 years (2010-2021) • Publications in English or Spanish.	• Studies evaluating costs and the impact of inhalers for the treatment of asthma without data about emissions of CO_2 or CO_2-equivalent emissions and/or percentages of total emissions. • Studies about HFC uses other than health. • Studies based on HFC for health use but not focusing on the use of inhalers for the treatment of respiratory diseases (healing/cooling sprays, etc.). • Studies focusing on pathologies other than asthma.
QUESTION 2: What is the possible impact of changing the treatment of patients with asthma from pMDIs to DPIs?	• Original manuscripts. • Studies assessing the clinical implications of switching from pMDIs to DPIs: lack of asthma control, poor adherence, reduced pharmacological effect or reduction in quality of life. • Studies assessing the impact on drug absorption and the evaluation of patient profile according to their characteristics, needs or	• Reviews and editorials. • Studies not evaluating the clinical implications of a change from pMDIs to DPIs, the impact on drug absorption and the evaluation of patient profile according to their characteristics, needs or preferences when deciding the most convenient type of inhalation device. • Studies focusing on pathologies other than asthma.

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	preferences when deciding the most convenient type of inhalation device. • Studies published in the last 11 years (2010-2021) • Publications in English or Spanish.	

HFC, hydrofluorocarbons; DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers

Supplementary material 3

List of excluded publications after full-text reading (QUESTION 1).

Citation	Reason for exclusion
QUESTION 1: What is the impact of pMDIs on the carbon footprint?	
Płusa T, Badowska-Kozakiewicz AM. Carbon footprint of inhalers in COPD therapy in 2018 and 2019 in Poland in response to the Kigali amendment. Pol Merkur Lekarski. 2020 Dec 22;48(288):391-393. PMID: 33387424.	Focused on COPD
Starup-Hansen J, Dunne H, Sadler J, Jones A, Okorie M. Climate change in healthcare: Exploring the potential role of inhaler prescribing. Pharmacol Res Perspect. 2020 Dec;8(6):e00675. doi: 10.1002/prp2.675. PMID: 33124196; PMCID: PMC7596665.	No direct data on pMDI/DPI emissions
Beeh K, van Zyl-Smit R, Mezzi K, et al. Emergency room visits and rescue medication use in patients with asthma in the IRIDIUM study and their impact on carbon footprint. Thorax 2021;76:A6-A7.	No direct data on pMDI/DPI emissions; No original article/review
Hunt F, Wilkinson A. Carbon footprint analysis of the salford lung study (asthma): A SusQI analysis. Thorax 2021;76:A190.	No direct data on pMDI/DPI emissions; No original article/review
QUESTION 2: What is the possible impact of changing the treatment of patients with asthma from pMDI to DPI?	
A Cumulative Dose Study to Evaluate the Safety and Efficacy of Albuterol in a Dry Powder Inhaler and an HFA MDI (Hydrofluoroalkane Metered Dose Inhaler) https://clinicaltrials.gov/ct2/show/NCT01056159	Clinical trial information (design)
Bernstein DI, Murphy KR, Nolte H. Non-inferiority efficacy comparison of mometasone furoate/formoterol versus fluticasone propionate/salmeterol combination therapies in subjects with persistent asthma. Allergy, asthma and clinical immunology 2010; Conference: Canadian Society of Allergy and Clinical Immunology Annual Scientific Meeting 2010 Victoria, BC Canada. Conference Start: 20101103 Conference End: 20101106. Conference Publication: (6(Suppl 2): 12 [P33].	Conference abstract
Albuterol DPI (A006) Clinical Study-B2: efficacy, Dose-Ranging and Initial Safety Evaluation. xhttps://clinicaltrials.gov/ct2/show/NCT01189396	Clinical trial information (design)
Santos Dde O, Martins MC, Cipriano SL, Pinto RM, Cukier A, Stelmach R. Pharmaceutical care for patients with persistent asthma: assessment of treatment compliance and use of inhaled medications. J Bras Pneumol. 2010 Jan-Feb;36(1):14-22. English, Portuguese. doi: 10.1590/s1806-37132010000100005. PMID: 20209303.	Educational programme impact
Bernstein DI, Hébert J, Cheema A, Murphy KR, Chérrez-Ojeda I, Matiz-Bueno CE, Kuo WL, Nolte H. Efficacy and onset of action of mometasone furoate/formoterol and fluticasone propionate/salmeterol combination treatment in subjects with persistent asthma. Allergy Asthma Clin Immunol. 2011 Dec 7;7(1):21.	No DPI vs pMDI comparison studies

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doi: 10.1186/1710-1492-7-21. PMID: 22152089; PMCID: PMC3298511.	
Direkwatanachai C, Teeratakulpisarn J, Suntornlohanakul S, Trakultivakorn M, Ngamphaiboon J, Wongpitoon N, Vangveeravong M. Comparison of salbutamol efficacy in children--via the metered-dose inhaler (MDI) with Volumatic spacer and via the dry powder inhaler, Easyhaler, with the nebulizer--in mild to moderate asthma exacerbation: a multicenter, randomized study. Asian Pac J Allergy Immunol. 2011 Mar;29(1):25-33. PMID: 21560485.	Comparison of efficacy of 2 products in independent samples.
Lo Valvo L, Leonardi S, Marseglia GL, Miraglia Del Giudice M, Salpietro C, Ciprandi G, La Rosa M. Inhalation therapy in asthmatic and not asthmatic children. Int J Immunopathol Pharmacol. 2011 Oct;24(4 Suppl):61-7. doi: 10.1177/03946320110240S412. PMID: 22032789.	Review article
Randall Brown, MD; Lanny Rosenwasser, MD; Tom Uryniak, MS; Ubaldo Martin, MD; James Zangrilli, MD. Response to Budesonide/Formoterol Pressurized Metered-Dose Inhaler (BUD/FM pMDI) by Asthma Severity in 2 Populations. Chest. 2011;140(4_MeetingAbstracts):238A. doi:10.1378/chest.1118291	Conference abstract
Spector SL, Rosenwasser LJ, Uryniak T, Aggarwal A, Martin UJ. Relationship between study withdrawal and baseline characteristics in african-american patients with moderate to severe asthma. Annals of allergy, asthma and immunology. 2011; 107(5 SUPPL. 1): A36-A37.	Conference abstract
Albuterol DPI (A006) Clinical Study-B2: efficacy, Dose-Ranging and Initial Safety Evaluation. https://clinicaltrials.gov/ct2/show/NCT01581177	Clinical trial information (design)
Donald P. Tashkin, Bradley E. Chipps. Effect of fixed airflow obstruction on response to budesonide/formoterol pressurized metered-dose inhaler treatment in African-American adolescents and adults with moderate to severe asthma. American Journal of Respiratory and Critical Care Medicine 2012;185:A4234	Conference abstract
Fernández Tena A, Casan Clarà P. Deposition of inhaled particles in the lungs. Arch Bronconeumol. 2012 Jul;48(7):240-6. English, Spanish. doi: 10.1016/j.arbres.2012.02.003. Epub 2012 Mar 30. PMID: 22464044.	Review article
Francesco Sergio, Catherine Francisco, Annamaria Muraro, Frank Kanniess. Beclometasone/formoterol administered via extrafine dry powder inhaler in controlled asthmatic patients: Comparison with pMDI and beclometasone monotherapy. European Respiratory Journal Sep 2012, 40 (Suppl 56) P179	Conference abstract
Laszlo Kadar. Comparison of bronchodilator effect of salbutamol delivered via MDI + spacer and DPI in children with asthma. European Respiratory Journal Sep 2012, 40 (Suppl 56) P4572	Conference abstract
McCabe JC, Koppenhagen F, Blair J, Zeng XM. ProAir(®) HFA delivers warmer, lower-impact, longer-duration plumes containing higher fine particle dose than Ventolin(®) HFA. J Aerosol Med Pulm Drug Deliv. 2012 Apr;25(2):104-9. doi: 10.1089/jamp.2011.0891. Epub 2011 Dec 22. PMID: 22191397.	No DPI vs pMDI comparison studies
Murphy KR, Uryniak T, Martin U, Zangrilli J. Effect of budesonide/formoterol pressurized metered-dose inhaler on predefined asthma events in 4 different patient populations with	No DPI vs pMDI comparison studies

asthma. American journal of respiratory and critical care medicine 2011; 183(1 MeetingAbstracts):	
Behera RK, Behera D. A study to evaluate patient acceptance of dry powder inhaler versus pressurized metered dose inhaler in inhaler naive asthma patients of lower educational qualification. Indian journal of pharmacology 2013; 45(null): S271-S272.	Conference abstract
Berger WE, Gillen M, Eckerwall G, Uryniak T, Trudo FJ, Lampl KL. Bronchodilator effect of single-dose formoterol administered by pressurized metered-dose inhaler in children with asthma aged 6 to <12 years receiving budesonide. Allergy Asthma Proc. 2014 Mar-Apr;35(2):134-40. doi: 10.2500/aap.2014.35.3746. PMID: 24717790.	Dose-finding (dose-response) study.
Chipps BE, Tashkin DP, Uryniak T, Trudo F. Responder analysis evaluating the effect of budesonide/formoterol pressurized metered-dose inhaler in patients with mild to moderate asthma with versus without fixed airflow obstruction. American journal of respiratory and critical care medicine 2013; 187	Conference abstract
Dunlop, W., Heron, L., Fox, G. et al. Budget Impact Analysis of a Fixed-Dose Combination of Fluticasone Propionate and Formoterol Fumarate (FP/FORM) in a Pressurized Metered-Dose Inhaler (pMDI) for Asthma. Adv Ther 30, 933–944 (2013). https://doi.org/10.1007/s12325-013-0062-z	No DPI vs pMDI comparison studies
Effects of Particle Size in Small Airways Dysfunction. https://clinicaltrials.gov/ct2/show/NCT01892787	Clinical trial information (design)
Hojo, M; Hirashima, J; Sato, N; Iikura, M; Sugiyama, H. A clinical analysis to compare the anti-inflammatory effect on peripheral airway by salmeterol/fluticasone combination inhaler between DPI and PMDI products. Respirology (2013) 18 (Suppl. 4), 1–81	Conference abstract
Sanchis J, Corrigan C, Levy ML, Viejo JL; ADMIT Group. Inhaler devices - from theory to practice. Respir Med. 2013 Apr;107(4):495-502. doi: 10.1016/j.rmed.2012.12.007. Epub 2013 Jan 3. PMID: 23290591.	Review article
Svedsater H, Dale P, Garrill K, Walker R, Woepse MW. Qualitative assessment of attributes and ease of use of the ELLIPTA™ dry powder inhaler for delivery of maintenance therapy for asthma and COPD. BMC Pulm Med. 2013 Dec 7;13:72. doi: 10.1186/1471-2466-13-72. PMID: 24314123; PMCID: PMC4029771.	Qualitative research on usage preferences (Attribute) for Ellipta™
Berger WE, Bensch GW, Weinstein SF, Skoner DP, Prenner BM, Shekar T, Nolte H, Teper AA. Bronchodilation with mometasone furoate/formoterol fumarate administered by metered-dose inhaler with and without a spacer in children with persistent asthma. Pediatr Pulmonol. 2014 May;49(5):441-50. doi: 10.1002/ppul.22850. Epub 2013 Sep 9. PMID: 24019197.	No DPI vs pMDI comparison studies
Chipps BE, Tashkin D, DePietro M, Trudo F. Effect of fixed airflow obstruction status on peak expiratory flow and rescue medication use in response to budesonide/formoterol treatment in patients with moderate to severe asthma. Annals of allergy, asthma and immunology. 2014; 113(5 SUPPL. 1): A38-A39.	Conference abstract
ELLIPTATM„¢ vs. MDI Inhaler Preference Study, in Adult Subjects with Asthma. https://clinicaltrials.gov/ct2/show/NCT02135718	Clinical trial information (design)

Miller D, Wayne D, Ferro T, Taveras H, Iverson H. Cumulative dose comparison of the efficacy and safety of albuterol-multidose dry powder inhaler and albuterol-hydrofluoroalkane metered dose inhaler in adults with asthma. Annals of allergy, asthma and immunology. 2014; 113(5 SUPPL. 1): A46.	Conference abstract
Nilsson E, Chawes BL, Bønnelykke K, Vindfeld S, Moore AC, Bisgaard H. Effect of delivery device on systemic exposure to inhaled fluticasone propionate in children with asthma. Br J Clin Pharmacol. 2014 Aug;78(2):435-7. doi: 10.1111/bcp.12340. PMID: 24527946; PMCID: PMC4137838.	Letter to the editor
Tashkin DP, Chipps BE, Uryniak T, Trudo F. Responder analysis evaluating the effect of budesonide/formoterol pressurized metered-dose inhaler (BUD/FM pMDI) in patients with moderate to severe asthma with versus without fixed airflow obstruction (FAO). Allergy and asthma proceedings 2014; 35(1): 85-86.	Conference abstract
Aydemir Y. Assessment of the factors affecting the failure to use inhaler devices before and after training. Respir Med. 2015 Apr;109(4):451-8. doi: 10.1016/j.rmed.2015.02.011. Epub 2015 Mar 4. PMID: 25771037.	Data for pMDI and DPI before a training plan
Bulac S, Cimrin A, Ellidokuz H. The effect of beclometasone dipropionate/formoterol extra-fine fixed combination on the peripheral airway inflammation in controlled asthma. J Aerosol Med Pulm Drug Deliv. 2015 Apr;28(2):82-7. doi: 10.1089/jamp.2013.1062. Epub 2014 Jul 22. PMID: 25050594.	No DPI vs pMDI comparison studies
Ekberg-Jansson A, Svenningsson I, Rågdell P, Stratelis G, Telg G, Thuresson M, Nilsson F. Budesonide inhaler device switch patterns in an asthma population in Swedish clinical practice (ASSURE). Int J Clin Pract. 2015 Oct;69(10):1171-8. doi: 10.1111/ijcp.12685. Epub 2015 Aug 3. PMID: 26234385.	pMDI to DPI switch
Kirsten AM, Watz H, Brindicci C, Piccinno A, Magnussen H. Effects of beclomethason/formoterol and budesonide/formoterol fixed combinations on lung function and airway inflammation in patients with mild to moderate asthma--an exploratory study. Pulm Pharmacol Ther. 2015 Apr;31:79-84. doi: 10.1016/j.pupt.2014.08.007. Epub 2014 Sep 4. PMID: 25194884.	No DPI vs pMDI comparison studies
Murphy KR, Dhand R, Trudo F, Uryniak T, Aggarwal A, Eckerwall G. Therapeutic equivalence of budesonide/formoterol delivered via breath-actuated inhaler vs pMDI. Respir Med. 2015 Feb;109(2):170-9. doi: 10.1016/j.rmed.2014.12.009. Epub 2015 Jan 3. PMID: 25596138.	Comparative pMDI vs BAI comparison studies
Scichilone N, Benfante A, Bocchino M, Braido F, Paggiaro P, Papi A, Santus P, Sanduzzi A. Which factors affect the choice of the inhaler in chronic obstructive respiratory diseases? Pulm Pharmacol Ther. 2015 Apr;31:63-7. doi: 10.1016/j.pupt.2015.02.006. Epub 2015 Feb 24. PMID: 25724817.	Review article
Zambelli-Simões L, Martins MC, Possari JC, et al. Validation of scores of use of inhalation devices: valoration of errors. J Bras Pneumol. 2015;41(4):313-322. doi:10.1590/S1806-37132015000004435	Study for the validation of a scale
A Single Dose PD & PK Study With Two Formulations of Abediterol in Patients With Asthma. https://clinicaltrials.gov/ct2/show/NCT02777827	Clinical trial information (design)

Basheti I. Inpatients with asthma: effect of education on inhaler technique and asthma control test. International journal of pharmacy practice. Conference: 19th international social pharmacy workshop. United Kingdom. Conference start: 20160719. Conference end: 20160722 2016; 24(null): 5.	Conference abstract
Clarenbach CF, Nicod LP, Kohler M. Real-world asthma management with inhaler devices in Switzerland-results of the asthma survey. J Thorac Dis. 2016;8(11):3096-3104. doi:10.21037/jtd.2016.11.95	Comparison according to different languages in Switzerland
Crisafulli E, Zanini A, Pisi G, Pignatti P, Poli G, Scuri M, Chetta A. Inhaled beclometasone dipropionate/formoterol fumarate extrafine fixed combination for the treatment of asthma. Expert Rev Respir Med. 2016;10(5):481-90. doi: 10.1586/17476348.2016.1161508. Epub 2016 Mar 16. PMID: 26938578.	Review article
David Bell, Lucielle Mansfield, Mark Lomax. Fluticasone propionate/formoterol breath-triggered inhaler: Ease-of-use and patient preference. European Respiratory Journal Sep 2016, 48 (suppl 60) PA4109; DOI: 10.1183/13993003.congress-2016.PA4109	Conference abstract
Miller DS, Yiu G, Hellriegel ET, Steinfeld J. Dose-ranging study of salmeterol using a novel fluticasone propionate/salmeterol multidose dry powder inhaler in patients with persistent asthma. Allergy Asthma Proc. 2016 Jul;37(4):291-301. doi: 10.2500/aap.2016.37.3963. Epub 2016 May 27. PMID: 27216137.	No DPI vs pMDI comparison studies
Nelson HS. Inhalation devices, delivery systems, and patient technique. Ann Allergy Asthma Immunol. 2016 Dec;117(6):606-612. doi: 10.1016/j.anai.2016.05.006. PMID: 27979017.	Review article
Niran J. Amar, Tulin Shekar, Tracey Varnell, Anish Mehta, George Philip. Mometasone Furoate/Formoterol Reduces Asthma Deteriorations and Improves Lung Function. J Allergy Clin Immunol, 2016.	Conference abstract
Phase IV Study in Asthma Subjects for Dry Powder Inhaler (DPI) Versus (vs) Metered Dose Inhaler (MDI) Correct Use. https://clinicaltrials.gov/ct2/show/NCT02794480	Clinical trial information (design)
Roche N, Dekhuijzen PN. The Evolution of Pressurized Metered-Dose Inhalers from Early to Modern Devices. J Aerosol Med Pulm Drug Deliv. 2016 Aug;29(4):311-27. doi: 10.1089/jamp.2015.1232. Epub 2016 Jan 29. PMID: 26824873.	Review article
Sanchis J, Gich I, Pedersen S; Aerosol Drug Management Improvement Team (ADMIT). Systematic Review of Errors in Inhaler Use: Has Patient Technique Improved Over Time? Chest. 2016 Aug;150(2):394-406. doi: 10.1016/j.chest.2016.03.041. Epub 2016 Apr 7. PMID: 27060726.	Review article
Tashkin DP, Moore GE, Trudo F, DePietro M, Chipps BE. Assessment of Consistency of Fixed Airflow Obstruction Status during Budesonide/Formoterol Treatment and Its Effects on Treatment Outcomes in Patients with Asthma. J Allergy Clin Immunol Pract. 2016 Jul-Aug;4(4):705-12. doi: 10.1016/j.jaip.2016.02.014. Epub 2016 Mar 30. PMID: 27039236.	No DPI vs pMDI comparison studies
Lavorini F, Pedersen S, Usmani OS; Aerosol Drug Management Improvement Team (ADMIT). Dilemmas, Confusion, and Misconceptions Related to Small Airways Directed Therapy. Chest.	Review article

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2017 Jun;151(6):1345-1355. doi: 10.1016/j.chest.2016.07.035. Epub 2016 Aug 11. PMID: 27522955.	
Mahon J, Fitzgerald A, Glanville J, Dekhuijzen R, Glatte J, Glanemann S, Torvinen S. Misuse and/or treatment delivery failure of inhalers among patients with asthma or COPD: A review and recommendations for the conduct of future research. Respir Med. 2017 Aug;129:98-116. doi: 10.1016/j.rmed.2017.05.004. Epub 2017 May 15. PMID: 28732842.	Review article
Melin J, Prothon S, Kloft C, Cleton A, Amilon C, Jorup C, Bäckman P, Olsson B, Hamrén UW. Pharmacokinetics of the Inhaled Selective Glucocorticoid Receptor Modulator AZD5423 Following Inhalation Using Different Devices. AAPS J. 2017 May;19(3):865-874. doi: 10.1208/s12248-016-0042-8. Epub 2017 Mar 9. PMID: 28281196.	No DPI vs pMDI comparison studies
Rogliani P, Calzetta L, Coppola A, Cavalli F, Ora J, Puxeddu E, Matera MG, Cazzola M. Optimizing drug delivery in COPD: The role of inhaler devices. Respir Med. 2017 Mar;124:6-14. doi: 10.1016/j.rmed.2017.01.006. Epub 2017 Jan 24. PMID: 28284323.	Review article
Singh D, Ciurlia G, Piccinno A, Muraro A, Bocchi M, Scuri M. Acute cardiovascular safety of two formulations of beclometasone dipropionate/formoterol fumarate in COPD patients: A single-dose, randomised, placebo-controlled crossover study. Pulm Pharmacol Ther. 2017 Feb;42:43-51. doi: 10.1016/j.pupt.2016.12.004. Epub 2017 Jan 5. PMID: 28065679.	Focused on COPD
Stein SW, Thiel CG. The History of Therapeutic Aerosols: A Chronological Review. J Aerosol Med Pulm Drug Deliv. 2017 Feb;30(1):20-41. doi: 10.1089/jamp.2016.1297. Epub 2016 Oct 17. PMID: 27748638; PMCID: PMC5278812.	Review article
Yingxue Chen, Susanne Prothon, Ulf Eriksson, Henrik Forsman, Hong-lin Su, Mary Brown, Ajay Aggarwal, Helen Jackson. Pharmacokinetics (PK) of a single dose AZD7594 administered intravenously (IV), orally, and inhaled via two dry powder inhalers (DPI) and a pressurized metered-dose inhaler (pMDI). European Respiratory Journal Sep 2017, 50 (suppl 61) PA531; DOI: 10.1183/1393003.congress-2017.PA531	Conference abstract
Engelkes M, van Blijderveen JC, Overbeek JA, Kuiper J, Herings RCM, Sturkenboom MCJM, de Jongste JC, Verhamme KMC, Janssens HM. Brand and generic use of inhalation medication and frequency of switching in children and adults: A population-based cohort study. J Asthma. 2018 Oct;55(10):1086-1094. doi: 10.1080/02770903.2017.1396468. Epub 2017 Nov 29. PMID: 29185812.	Estimate of the prevalence of switching from branded to generic drugs
Gillen M, Forte P, Svensson JO, Lamarca R, Burke J, Rask K, Larsdotter Nilsson U, Eckerwall G. Effect of a spacer on total systemic and lung bioavailability in healthy volunteers and in vitro performance of the Symbicort® (budesonide/formoterol) pressurized metered dose inhaler. Pulm Pharmacol Ther. 2018 Oct;52:7-17. doi: 10.1016/j.pupt.2018.08.001. Epub 2018 Aug 2. PMID: 30077809.	Bioavailability study of Symbicort pMDI with or without a spacer chamber
Plaza V, Giner J, Rodrigo GJ, Dolovich MB, Sanchis J. Errors in the Use of Inhalers by Health Care Professionals: A Systematic Review. J Allergy Clin Immunol Pract. 2018 May-Jun;6(3):987-995. doi: 10.1016/j.jaip.2017.12.032. Epub 2018 Jan 31. PMID: 29355645.	Review article

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Pohlmann G, Hohlfeld JM, Haidl P, Pankalla J, Cloes RM. Assessment of the Power Required for Optimal Use of Current Inhalation Devices. J Aerosol Med Pulm Drug Deliv. 2018 Dec;31(6):339-346. doi: 10.1089/jamp.2017.1376. Epub 2018 May 23. PMID: 29791260.	Evaluation of performance requirements of standard inhalation devices
Wang GD, Macaulay R. Right to breathe, right to choose?. Value in health. Volume 21, Supplement 3, S415, October 01, 2018	Conference abstract
Axelsson I, Naumburg E, Prietsch SO, Zhang L. Inhaled corticosteroids in children with persistent asthma: effects of different drugs and delivery devices on growth. Cochrane Database Syst Rev. 2019 Jun 10;6(6):CD010126. doi: 10.1002/14651858.CD010126.pub2. PMID: 31194879; PMCID: PMC6564081.	Review article
David Bernstein, Kevin Murphy, and Hendrik Nolte. Efficacy Comparison of Mometasone Furoate/Formoterol Versus Fluticasone Propionate/Salmeterol Combination Therapies in Subjects With Persistent Asthma: Noninferiority and Onset-of- Action Findings. WAO Journal, 2012.	Conference abstract
Fuglø-Mortensen R, Lange P, Mortensen J. [Inhalers and inhalation techniques in the treatment of asthma and chronic obstructive pulmonary disease]. Ugeskr Laeger. 2019 Aug 12;181(33):V07180510. Danish. PMID: 31495355.	Article in Danish
Gogtay J, Laouar L, Gaur V. Preference of diagnostic tools, medications, and devices for asthma management: A survey of doctors in Algeria. Perspect Clin Res. 2019 Apr-Jun;10(2):67-72. doi: 10.4103/picr.PICR_63_18. PMID: 31008072; PMCID: PMC6463497.	Descriptive study of asthma management in Algeria and physician opinion
Hedieh Amin Moghadassi, Atefeh Fakharian, Alireza Eslaminejad, Masoumeh Mehdipour, Saranaz Azari-Marhabi. Oral manifestations in asthmatic patients using metered dose inhaler and dry powder inhaler. European Respiratory Journal Sep 2019, 54 (suppl 63) PA4005; DOI: 10.1183/13993003.congress-2019.PA4005	Conference abstract
Hiroyuki Ohbayashi, Takamitsu Asano, Sahori Kudo, Mitsue Ariga. A randomized cross-over study of user satisfaction with inhalant devices in asthma patients. European Respiratory Journal Sep 2019, 54 (suppl 63) PA4004; DOI: 10.1183/13993003.congress-2019.PA4004	Conference abstract
Kerwin EM, Preece A, Brintziki D, Collison KA, Sharma R. ELLIPTA Dry Powder Versus Metered-Dose Inhalers in an Optimized Clinical Trial Setting. J Allergy Clin Immunol Pract. 2019 Jul-Aug;7(6):1843-1849. doi: 10.1016/j.jaip.2019.02.023. Epub 2019 Mar 2. PMID: 30836228.	Focused on inhaler technique in trial settings. No DPI vs pMDI comparison studies
Munteanu LA, Fildan AP, Tudorache E, Fira-Mladinescu O, Frandes M, Timar B, Oancea C, Tofolean DE. Inhaler technique errors in Romanian patients with asthma - a multicenter study. Patient Prefer Adherence. 2019 Aug 19;13:1401-1414. doi: 10.2147/PPA.S209717. PMID: 31695337; PMCID: PMC6707372.	pMDI vs SMI comparison studies
Omar Usmani, Nicolas Roche, Jonathan Marshall, Helen Danagher & David Price (2019) An innovative corticosteroid/long-acting β2-agonist breath-triggered inhaler: facilitating lung delivery of fluticasone propionate/formoterol fumarate for the treatment of	Review article

asthma, Expert Opinion on Drug Delivery, 16:12, 1367-1380, DOI: 10.1080/17425247.2019.1689957	
Karle E, Patel TP, Zweig J, Krvavac A. Understanding the Knowledge Gap and Assessing Comfort Level among Healthcare Professionals Who Provide Inhaler Education. COPD. 2020 Apr;17(2):197-204. doi: 10.1080/15412555.2020.1746251. Epub 2020 Apr 1. PMID: 32237908.	Addressing collateral issues concerning prescribers' and non-prescribers' knowledge of inhalation techniques.
Lavorini F, Bianco A, Blasi F, Braido F, Corsico AG, Di Marco F, Gentile A, Paggiaro PL, Pegoraro V, Pelaia G, Rogliani P, Santus P, Scichilone N, Soldi A, Canonica GW. What drives inhaler prescription for asthma patients? Results from a real-life retrospective analysis. Respir Med. 2020 May;166:105937. doi: 10.1016/j.rmed.2020.105937. Epub 2020 Mar 20. PMID: 32250870.	Drivers of physician's choice in selecting therapy
Maciej Kupczyk, Pawel Majak, Piotr Kuna, Beata Asankowicz-Bargiel, Eliza Baranska, Rafal Dobek, Slawomir Garbicz, Joanna Jerzynska, Anna Latos, Wojciech Machowiak, Bernadetta Majorek-Olechowska, Anna Olech-Cudzik, Iwona Poziomkowska-Gesicka, Miroslawa Rulewicz-Warniello, Anna Swiderska, Michal Tarnowski, Przemyslaw Kopyto. Efficacy and safety of new formulation of fluticasone propionate/salmeterol delivered via a HFA pMDI inhaler in patients with asthma. European Respiratory Journal Sep 2020, 56 (suppl 64) 3182; DOI: 10.1183/13993003.congress-2020.3182	Conference abstract
Ocakli B, Ozmen I, Tuncay EA, Gungor S, Ozalp A, Yasin Y, Adiguzel N, Gungor G, Karakurt Z. Influence of Gender on Inhaler Technique. Respir Care. 2020 Oct;65(10):1470-1477. doi: 10.4187/respcare.06917. Epub 2020 Jan 28. PMID: 31992675.	Comparison by gender
Price R, Shur J, Ganley W, Farias G, Fotaki N, Conti DS, Delvadia R, Absar M, Saluja B, Lee S. Development of an Aerosol Dose Collection Apparatus for In Vitro Dissolution Measurements of Orally Inhaled Drug Products. AAPS J. 2020 Feb 13;22(2):47. doi: 10.1208/s12248-020-0422-y. PMID: 32060670; PMCID: PMC7021740.	In vitro data
Pritchard JN. The Climate is Changing for Metered-Dose Inhalers and Action is Needed. Drug Des Devel Ther. 2020;14:3043-3055. Published 2020 Jul 29. doi:10.2147/DDDT.S262141	Review article
Starup-Hansen J, Dunne H, Sadler J, Jones A, Okorie M. Climate change in healthcare: Exploring the potential role of inhaler prescribing. Pharmacol Res Perspect. 2020 Dec;8(6):e00675. doi: 10.1002/prp2.675. PMID: 33124196; PMCID: PMC7596665.	Review article
Attar-Zadeh D, Lewis H, Orlovic M. Health-care Resource Requirements and Potential Financial Consequences of an Environmentally Driven Switch in Respiratory Inhaler Use in England. J Health Econ Outcomes Res. 2021 Sep 23;8(2):46-54. doi: 10.36469/001c.26113. PMID: 34616856; PMCID: PMC8460426.	Only cost evaluation
Barbara SA, Kritikos V, Price DB, Bosnic-Anticevich S. Identifying patients at risk of poor asthma outcomes associated with making inhaler technique errors. J Asthma. 2021 Jul;58(7):967-978. doi: 10.1080/02770903.2020.1742353. Epub 2020 Mar 31. PMID: 32162572.	No DPI vs pMDI comparison studies

Budesonide/Formoterol TurbuhalerÂ® Versus Terbutaline Nebulization as Reliever Therapy in Children With Moderate Asthma Exacerbation. https://clinicaltrials.gov/ct2/show/NCT04705727	Clinical trial information (design)
Haughney J, Lee AJ, McKnight E, Pertsovskaya I, O'Driscoll M, Usmani OS. Peak Inspiratory Flow Measured at Different Inhaler Resistances in Patients with Asthma. J Allergy Clin Immunol Pract. 2021 Feb;9(2):890-896. doi: 10.1016/j.jaip.2020.09.026. Epub 2020 Oct 1. PMID: 33011302.	No DPI vs pMDI comparison studies
Płusa T, Badowska-Kozakiewicz A. Can we minimize carbon footprint by using "greener" inhalers and improve clinical outcome at the same time in asthma therapy? Pol Merkur Lekarski. 2021 Aug 16;49(292):252-254. PMID: 34464363.	No clinical data
Pohunek P, Varoli G, Reznichenko Y, Mokia-Serbina S, Brzostek J, Kostromina V, Kaladze M, Muraro A, Carzana E, Armani S, Kaczmarek J. Bronchodilating effects of a new beclometasone dipropionate plus formoterol fumarate formulation via pressurized metered-dose inhaler in asthmatic children: a double-blind, randomized, cross-over clinical study. Eur J Pediatr. 2021 May;180(5):1467-1475. doi: 10.1007/s00431-020-03888-x. Epub 2021 Jan 6. PMID: 33404895.	No DPI vs pMDI comparison studies

Supplementary material 4

Summary of full-text articles reporting CO_2 footprint due to inhalers used for the treatment of asthma.

Publication	Study type	Carbon footprint (Kg CO_2-eq/year/pack)				MMAT appraisal
		DPIs	pMDIs	SMI	Total	
Wilkinson AJK, et al. (2020)[85]	Qualitative	0.74	23.38	0.35	13.56	100
Pritchard JN. (2020)[48]	Qualitative					100
Lavorini F, et al. (2021)[5]	Qualitative	0.58	23.00		11.79	100
Murayama N, et al. (2018)[86]	Quantitative descriptive					60
Ortsäter G, et al. (2019)[53]	Quantitative non-randomized			0.62	0.62	60
Wilkinson AJK, et al. (2019)[56]	Quantitative descriptive	2.27	20.50		16.45	60
Hänsel M, et al. (2019)[87]	Quantitative descriptive		15.54	0.78	8.16	60
Janson C, et al. (2020)[88]	Quantitative descriptive	0.83	22.33		10.04	60
Panigone S, et al. (2020)[41]	Quantitative descriptive	0.92	14.57		10.67	60
Plusa T, et al. (2021)[89]	Quantitative descriptive					60
Emeryk AW, et al. (2021)[40]	Quantitative descriptive	0.86	11.39		8.29	60

DPIs, dry-powder inhalers; MMAT, Mixed Methods Evaluation Tool; SMI, Soft Mist Inhaler pMDIs, pressurised metered-dose inhalers

Supplementary material 5

Summary of full-text articles reporting clinical outcomes of patients with asthma treated with either pMDIs or DPIs.

Publication	Study type	Devices	MMAT appraisal
Rootmensen GN, et al. (2010)[90]	Quantitative randomised controlled	Diskus® Turbuhaler® Diskhaler™ pMDI with spacer pMDI	100
Price D, et al. (2011)[64]	Quantitative non-randomised	pMDI vs DPI, all brands	100
Price D, et al. (2011)[65]	Quantitative non-randomised	pMDI vs DPI, all brands	100
Spector SL, et al. (2012)[68]	Quantitative randomised controlled	pMDI, all BUD/FM DPI, all BUD	100
Kanniess F, et al. (2015)[62]	Quantitative randomised controlled	Foster ® Clenil®Pulvinal® Nexthaler ®	100
Darbà J, et al. (2016)[83]	Quantitative non-randomised	Accuhaler® Turbuhaler® NEXThaler® pMDI, all brands	100
Kerwin EM, et al. (2016)[75]	Quantitative randomised controlled	pMDI vs DPI, all brands	100
Melani AS, et al. (2017)[82]	Quantitative non-randomised	Diskus® vs pMDI, all brands HandiHaler vs pMDI, all brands Aerlolizer vs pMDI, all brands Turbuhaler® vs pMDI, all brands	100
Kerwin E, et al. (2018)[76]	Quantitative randomised controlled	pMDI vs DPI, all brands	100
Rhee CK, et al. (2019)[72]	Quantitative non-randomised	pMDI vs DPI, all brands	100
Berger WE, et al. (2010)[44]	Quantitative randomised controlled	pMDI vs DPI, all brands	80
Müller V, et al. (2011)[71]	Quantitative non-randomised	pMDI vs DPI, all brands	80
Basheti IA, et al. (2016)[46]	Quantitative non-randomised	Turbuhaler® Accuhaler® pMDI, all brands	80
Qaqundah PY, et al. (2016)[77]	Quantitative randomised controlled	Albuterol 90 µg DPI vs albuterol 90 µg pMDI Albuterol 180 µg DPI vs albuterol 180 µg pMDI	80
Sicras A, et al. (2017)[66]	Quantitative non-randomised	pMDI vs DPI, all brands	80
Castel-Branco MM, et al. (2017)[81]	Quantitative non-randomised	pMDI vs DPI, all brands	80

Aggarwal AN, et al. (2018)[45]	Quantitative non-randomised	pMDI vs DPI, all brands	80
Pessôa CLC, et al. (2019)[80]	Quantitative non-randomised	Aerolizer® Aerocaps Diskus® pMDI, all brands	80
Park HS, et al. (2019)[73]	Quantitative non-randomised	pMDI vs DPI, all brands	80
Can C, et al. (2020)[78]	Quantitative non-randomised	pMDI, all brands vs Turbuhaler® pMDI, all brands vs capsules-based DPI, all brands	80
Woo S-D, et al. (2020)[70]	Quantitative randomised controlled	pMDI vs DPI, all brands	80
Bickel S, et al. (2021)[74]	Quantitative non-randomised	pMDI vs DPI, all brands	80
Kupczyk M, et al. (2021)[63]	Quantitative randomised controlled	pMDI vs DPI, all brands	80
O'Connor RD, et al. (2010)[47]	Quantitative randomised controlled	adjustable-dose pMDI, all brands	60
Gillespie M, et al. (2015)[84]	Quantitative randomised controlled	mDPI Diskus® pMDI, all brands	60
van der Palen J, et al. (2016)[79]	Quantitative randomised controlled	Ellipta™ pMDI, all brands	60
Srichana T, et al. (2016)[69]	Quantitative randomised controlled	Pulmicort® Turbohaler®Aeronide®	60
Hojo M, et al. (2016)[61]	Quantitative randomised controlled	SFC DPI, SFC pMDI, all brands	60
Singh D, et al. (2019)[67]	Quantitative randomised controlled	Foster® NEXThaler®	60
Khaled S, et al. (2014)[91]	Quantitative randomised controlled	pMDI with spacer, all brands DPI, all brands	40
Ratnayake A, et al. (2016)[92]	Quantitative randomised controlled	Albuterol DPI vs albuterol pMDI	40
Ramadan WH, et al. (2017)[93]	Quantitative non-randomised	pMDI vs DPI, all brands	40
Amar NJ, et al. (2017)[94]	Quantitative randomised controlled	pMDI vs DPI, all brands	40
Ohbayashi H, et al. (2021)[95]	Quantitative randomised controlled	pMDI FFC vs VFC DPI Ellipta™	40
Muraki M, et al. (2017)[96]	Quantitative randomised controlled	Adoair® 250 Diskus® Adoair® 125 Aerosol	20

BUD, budesonide; DPIs, dry-powder inhalers; FM,formoterol; FFC, formoterol/fluticasone combination; MMAT, Mixed Methods Evaluation Tool; pMDIs, pressurised metered-dose inhalers; SFC, salmeterol-fluticasone; VFC: vilanterol/fluticasone combination

Supplementary material 6

Efficacy outcomes according to the type of inhaler in all publications.

Publication	Favouring DPIs	Favouring pMDIs	Undetermined	Not significant	Total
Aggarwal AN, et al. (2018)[45]		**3**		**3**	**6**
Asthma control		1			1
Lung function		2		3	5
Amar NJ, et al. (2017)[94]				**1**	**1**
Lung function				1	1
Basheti IA, et al. (2016)[46]				**2**	**2**
Asthma control				2	2
Berger WE, et al. (2010)[44]		**6**			**6**
Asthma control		2			2
Lung function		4			4
Bickel S, et al. (2021)[74]		**1**		**1**	**2**
Lung function		1		1	2
Hojo M, et al. (2016)[61]		**5**	**1**	**29**	**35**
Asthma control			1		1
Lung function		5		29	34
Kanniess F, et al. (2015)[62]		**5**	**1**	**5**	**11**
Asthma control		4		3	7
Lung function		1	1	2	4
Kerwin EM, et al. (2016)[75]				**10**	**10**
Lung function				10	10
Kerwin E, et al. (2018)[76]	**4**	**7**		**13**	**24**
Lung function	4	7		13	24
Khaled S, et al. (2014)[91]			**2**	**1**	**3**
Asthma control			2		2
Lung function				1	1
Kupczyk M, et al. (2021)[63]			**1**	**4**	**5**
Asthma control			1		1
Lung function				4	4
Müller V, et al. (2011)[71]		**5**			**5**
Asthma control		5			5
Muraki M, et al. (2017)[96]				**10**	**10**
Asthma control				1	1
Lung function				9	9
O'Connor RD, et al. (2010)[47]				**1**	**1**
Asthma control				1	1
Ohbayashi H, et al. (2021)[95]		**3**		**5**	**8**
Asthma control				1	1
Lung function		3		4	7

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Park HS, et al. (2019)[73]		**7**	**8**	**6**	**21**
Asthma control		7	8	6	21
Price D, et al. (2011)[64]	**1**		**1**	**3**	**5**
Asthma control	1		1	3	5
Price D, et al. (2011)[65]		**2**		**1**	**3**
Asthma control		2		1	3
Qaqundah PY, et al. (2016)[77]			**2**	**8**	**10**
Duration of response			**1**	**1**	**2**
Lung function				7	7
Time to response			1		1
Ramadan WH, et al. (2017)[93]		**1**			**1**
Asthma control		1			1
Rhee CK, et al. (2019)[72]		**5**		**2**	**7**
Asthma control		5		2	7
Sicras A, et al. (2017)[66]		**4**		**5**	**9**
Asthma control		4		4	8
Lung function				1	1
Singh D, et al. (2019)[67]				**1**	**1**
Asthma control				1	1
Lung function					
Spector SL, et al. (2012)[68]		**2**	**6**	**4**	**12**
Asthma control			6	2	8
Lung function		2		2	4
Srichana T, et al. (2016)[69]				**6**	**6**
Asthma control				2	2
Lung function				4	4
Woo S-D, et al. (2020)[70]				**9**	**9**
Asthma control				4	4
Lung function				5	5
Total	**5**	**56**	**22**	**130**	**213**

DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers

Supplementary material 7

Quality of life outcomes according to the type of inhaler in all publications.

Publication	Favouring DPIs	Favouring pMDIs	Undetermined	Not significant	Total
Berger WE, et al. (2010)[44]		**2**			**2**
Activities of daily living,		1			1
PAQLQ		1			1
Muraki M, et al. (2017)[96]				**1**	**1**
AHQ-33-Japan				1	1
Total		**2**		**1**	**3**

AHQ, Asthma Health Questionnaire; DPIs, dry-powder inhalers; PAQLQ, Pediatric Asthma Quality of Life Questionnaire; pMDIs, pressurised metered-dose inhalers

Supplementary material 8

Handling outcomes according to the type of inhaler in all publications.

Publication	Favouring DPIs	Favouring pMDIs	Undetermined	Not significant	Total
Basheti IA, et al. (2016)[46]		**3**			**3**
Correct technique		2			2
Technique score		1			1
Can C, et al. (2020)[78]			**1**		**1**
Correct technique			1		1
Pessôa CLC, et al. (2019)[80]	**1**				**1**
Error rate	1				1
Castel-Branco MM, et al. (2017)[81]			**1**		**1**
Error rate			1		1
Rootmensen GN, et al. (2010)[68]			**1**		**1**
Error rate			1		1
Melani AS, et al. (2017)[82]	**1**				**1**
Time to correct use	1				1
Muraki M, et al. (2017)[96]	**1**		**1**	**2**	**4**
Correct technique			1		1
Easiness of use	1			2	3
Ohbayashi H, et al. (2021)[95]				**4**	**4**
Easiness of use				4	4
Ramadan WH, et al. (2017)[93]	**1**	**2**			**3**
Correct technique		1			1
Easiness of use	1	1			2
van der Palen J, et al. (2016)[79]	**1**			**4**	**5**
Critical errors				1	1
Easiness of use	1				1
Overall errors				1	1
Patient requiring instructions				1	1
Time to correct use				1	1
Woo S-D, et al. (2020)[70]				**1**	**1**
Correct technique				1	1
Total	**5**	**5**	**4**	**11**	**25**

DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers

Supplementary material 9

Adherence outcomes according to the type of inhaler in all publications.

Publication	Favouring DPIs	Favouring pMDIs	Undetermined	Not significant	Total
Aggarwal AN, et al. (2018)[45]		**1**			**1**
Adherence score		1			1
Darbà J, et al. (2016)[83]		**1**			**1**
Treatment persistence		1			1
Muraki M, et al. (2017)[96]				**1**	**1**
Adherence score				1	1
Price D, et al. (2011)[65]	**1**	**1**			**2**
Change in therapy		**1**			**1**
Treatment persistence	**1**				**1**
Rhee CK, et al. (2019)[72]				**1**	**1**
Treatment persistence				1	1
Sicras A, et al. (2017)[66]		**3**			**3**
Treatment persistence		3			3
Woo S-D, et al. (2020)[70]				**1**	**1**
Treatment persistence				1	1
Total	**1**	**6**		**3**	**10**

DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers

Supplementary material 10

Satisfaction outcomes according to the type of inhaler in all publications.

Publication	Favouring DPIs	Favouring pMDIs	Undetermined	Not significant	Total
Aggarwal AN, et al. (2018)[45]		**1**		**1**	**2**
TSQM score		1		1	2
Basheti IA, et al. (2016)[46]				**1**	**1**
CQ score				1	1
Muraki M, et al. (2017)[96]			**1**	**1**	**2**
Patient satisfaction questionnaire			1	1	2
O'Connor RD, et al. (2010)[47]		**1**		**1**	**2**
ATSM score		1		1	2
Ohbayashi H, et al. (2021)[95]		**1**		**1**	**2**
Patient satisfaction questionnaire		1		1	2
Ramadan WH, et al. (2017)[93]			**1**		**1**
Preference			1		1
Total	**0**	**3**	**2**	**5**	**10**

ATSM, Asthma Treatment Satisfaction; CQ, questionnaire for consumers; DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers; TSQM, Treatment Satisfaction Questionnaire for Medication

Supplementary material 11

Use of resources outcomes according to the type of inhaler in all publications.

Publication	Favouring DPIs	Favouring pMDIs	Undetermined	Not significant	Overall total
Berger WE, et al. (2010)[44]		**1**		**4**	**5**
Caregiver off work				1	1
Caregiver routine interrupted				1	1
Visits to emergency room		1			1
Phone calls to doctor				1	1
Unscheduled doctor visit				1	1
Sicras A, et al. (2017)[66]		**6**		**3**	**9**
Complementary tests		1			1
Days off work				1	1
Doctor in-hospital visit				1	1
Visits to emergency room		1			1
Hospital admissions				1	1
Hospitalisation days		1			1
Laboratory tests		1			1
Visits to family doctor		1			1
X-rays		1			1
Woo S-D, et al. (2020)[70]			**1**		**1**
Visits to emergency room			1		1
Overall total	**0**	**7**	**1**	**7**	**15**

DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers

Supplementary material 12

Safety outcomes according to the type of inhaler in all publications.

Publication	Favouring DPIs	Favouring pMDIs	Undetermined	Not significant	Total
Amar NJ, et al. (2017)[94]			**9**		**9**
Accidental overdose			1		1
Nasopharyngitis			1		1
Overall adverse events			4		4
Pharyngitis			1		1
Rhinitis			1		1
Upper respiratory tract infection			1		1
Berger WE, et al. (2010)[44]			**7**		**7**
Heart rate			1		1
Oral thrush			1		1
Overall adverse events			2		2
QT interval			1		1
Serum glucose			1		1
Serum potassium			1		1
Gillespie M, et al. (2015)[84]			**1**		**1**
Overall adverse events			1		1
Park HS, et al. (2019)[73]				**1**	**1**
Oral thrush				1	1
Kerwin E, et al. (2018)[76]			**4**		**4**
Overall adverse events			4		4
Khaled S, et al. (2014)[91]			**1**		**1**
Heart rate			1		1
Kupczyk M, et al. (2021)[63]				**8**	**8**
Cold				1	1
Dyspnoea				1	1
Electrocardiogram deviations				1	1
Headache				1	1
Heart rate				1	1
Hoarseness				1	1
Lab test abnormalities				1	1
Mild adverse events out of all adverse events				1	1
Muraki M, et al. (2017)[96]				**11**	**11**
Aftertaste				1	1
Cough after inhalation				1	1
Diastolic blood pressure				1	1
Discomfort in throat				1	1
Headache				1	1
Heart rate				1	1
Hoarseness				1	1
Palpitations				1	1
Systolic blood pressure				1	1

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Throat irritation				1	1
Tremor				1	1
Ramadan WH, et al. (2017)[93]		**1**			**1**
Oral thrush		1			1
Spector SL, et al. (2012)[68]			**1**		**1**
Overall adverse events			1		1
Woo S-D, et al. (2020)[70]			**1**	**8**	**9**
Bronchitis				1	1
Headache				1	1
Nasopharyngitis				1	1
Oral thrush				1	1
Overall adverse events				1	1
Rhinitis			1		1
Throat discomfort				1	1
Throat irritation				1	1
Voice change				1	1
Ratnayake A, et al. (2016)[92]				**1**	**1**
Pharmacodynamics. Increase in systolic blood pressure, diastolic blood pressure or heart rate				1	1
Total		**1**	**24**	**29**	**54**

DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers

Supplementary material 13

Efficacy outcomes according to the type of drug in all publications.

Type of drug	Favouring DPIs	Favouring pMDIs	Undetermined	Not significant	Total
Albuterol			**2**	**18**	**20**
Duration of response			1	1	2
Lung function				17	17
Time to response			1		1
Beclomethasone and Formoterol		**10**	**1**	**6**	**17**
Asthma control		9		4	13
Lung function		1	1	2	4
Budesonide				**6**	**6**
Asthma control				2	2
Lung function				4	4
Budesonide and Formoterol		**2**	**6**	**6**	**14**
Asthma control			6	4	10
Lung function		2		2	4
Fluticasone and Formoterol				**9**	**9**
Asthma control				4	4
Lung function				5	5
Glycopyrrolate		**6**		**6**	**12**
Lung function		6		6	12
Salmeterol	**4**	**1**		**7**	**12**
Lung function	4	1		7	12
Salmeterol and Fluticasone		**5**	**1**	**40**	**46**
Asthma control			1	2	3
Lung function		5		38	43
Umeclidinium, Vilanterol and Fluticasone		**3**		**5**	**8**
Asthma control				1	1
Lung function		3		4	7
Various				**1**	**1**
Asthma control				1	1
Not specified	**1**	**29**	**12**	**26**	**68**
Total	**5**	**56**	**22**	**130**	**213**

DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers

Supplementary material 14

Quality of life outcomes according to the type of drug in all publications.

Type of drug	Favouring DPIs	Favouring pMDIs	Undetermined	Not significant	Total
Salmeterol and Fluticasone				**1**	**1**
AHQ-33-Japan				1	1
Not specified		**2**			**2**
Limitation to daily activity		1			1
PAQLQ		1			1
Total	**0**	**2**	**0**	**1**	**3**

AHQ, Asthma Health Questionnaire; DPIs, dry-powder inhalers; PAQLQ, Pediatric Asthma Quality of Life Questionnaire; pMDIs, pressurised metered-dose inhalers

Supplementary material 15

Handling outcomes according to the type of drug in all publications.

Type of drug	Favouring DPIs	Favouring pMDIs	Undetermined	Not significant	Total
Budesonide and Formoterol		**3**			**3**
Correct technique		2			2
Technique score		1			1
Salmeterol and Fluticasone	**1**		**2**	**3**	**6**
Correct technique			1	1	2
Easiness of use	1			2	3
Error rate			1		1
Umeclidinium, Vilanterol and Fluticasone	**1**			**8**	**9**
Critical errors				1	1
Easiness of use	1			4	5
Overall errors				1	1
Patient requiring instructions				1	1
Time to correct use				1	1
Various	**1**				**1**
Time to correct use	1				1
Not specified	**2**	**2**	**2**		**6**
Correct technique		1	1		2
Easiness of use	1	1			2
Error rate	1		1		2
Total	**5**	**5**	**4**	**11**	**25**

DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers

Supplementary material 16

Adherence outcomes according to the type of drug in all publications.

Type of drug	Favouring DPIs	Favouring pMDIspMDIs	Undetermined	Not significant	Total
Formoterol and Fluticasone				**1**	**1**
Treatment persistence				1	1
Salmeterol and Fluticasone				**1**	**1**
Adherence score				1	1
Various		**1**			**1**
Treatment persistence		1			1
Not specified	**1**	**5**		**1**	**7**
Adherence score		1			1
Change in therapy		1			1
Treatment persistence	1	3		1	5
Total	**1**	**6**	**0**	**3**	**10**

DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers

Supplementary material 17

Satisfaction outcomes according to the type of drug in all publications.

Type of drug	Favouring DPIs	Favouring pMDIspMDIs	Undetermined	Not significant	Total
Budesonide and Formoterol		**1**		**2**	**3**
ATSM score		1		1	2
CQ score				1	1
Fluticasone and Formoterol					
Patients' satisfaction questionnaire					
Salmeterol and Fluticasone			**1**	**1**	**2**
ATSM score					
CQ score					
Patients' satisfaction questionnaire			1	1	2
Umeclidinium, Vilanterol and Fluticasone		**1**		**1**	**2**
Patients' satisfaction questionnaire		1		1	2
Various					
ATSM score					
CQ score					
Patients' satisfaction questionnaire					
Not specified		**1**	**1**	**1**	**3**
CQ score					
Preference			1		1
TSQM score		1		1	2
Total	**0**	**3**	**2**	**5**	**10**

ATSM, Asthma Treatment Satisfaction; CQ, questionnaire for consumers; DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers; TSQM, Treatment Satisfaction Questionnaire for Medication

Supplementary material 18

Safety outcomes according to the type of drug in all publications.

Type of drug	Favouring DPIs	Favouring pMDIs	Undetermined	Not significant	Total
Albuterol				**1**	**1**
Pharmacodynamics. Increase in SBP, DBP or heart rate				1	1
Budesonide and Formoterol			**1**		**1**
Overall adverse events			1		1
Fluticasone and Formoterol			**1**	**8**	**9**
Bronchitis				1	1
Headache				1	1
Nasopharyngitis				1	1
Oral thrush				1	1
Overall adverse events				1	1
Rhinitis			1		1
Throat discomfort				1	1
Throat irritation				1	1
Voice change				1	1
Glycopyrrolate			**4**		**4**
Overall adverse events			4		4
Inhaled corticosteroid//long-acting β2 agonist				**1**	**1**
Oral thrush				1	1
Salmeterol and Fluticasone				**11**	**11**
Aftertaste				1	1
Cough after inhalation				1	1
Diastolic BP				1	1
Discomfort in throat				1	1
Headache				1	1
Heart rate				1	1
Hoarseness				1	1
Palpitations				1	1
Systolic BP				1	1
Throat irritation				1	1
Tremor				1	1
Not specified		**1**	**18**	**8**	**27**
Accidental overdose			1		1
Cold				1	1
Dyspnea				1	1
ECG deviations				1	1
Headache				1	1
Heart rate			2	1	3
Hoarseness				1	1
Lab test abnormalities				1	1
Mild AE over all AE				1	1

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Nasopharyngitis			1		1
Oral thrush		1	1		2
Overall adverse events			7		7
Pharyngitis			1		1
QT interval			1		1
Rhinitis			1		1
Serum glucose			1		1
Serum potassium			1		1
Upper respiratory tract infection			1		1
Total	**0**	**1**	**24**	**29**	**54**

DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers

Supplementary material 19

Use of resources outcomes according to the type of drug in all publications.

Type of drug	Favouring DPIs	Favouring pMDIs	Undetermined	Not significant	Total
Fluticasone and Formoterol			**1**		**1**
ER visit			1		1
Salmeterol and Fluticasone					
ER visit					
Not specified		**7**		**7**	**14**
Caregiver off work				1	1
Caregiver routine interrupted				1	1
Complementary tests		1			1
Days off work				1	1
Doctor visit in hospital				1	1
ER visit		1			1
ER visits		1			1
Hospital admissions				1	1
Hospitalization days		1			1
Lab tests		1			1
Phone calls to doctor				1	1
Unscheduled doctor visit				1	1
Visits to family doctor		1			1
X-rays		1			1
Total	**0**	**7**	**1**	**7**	**15**

DPIs, dry-powder inhalers; pMDIs, pressurised metered-dose inhalers