**Additional file**

**Critical inhaler errors in asthma and COPD: A systematic review of impact on health outcomes
AUTHORS:**

Usmani, Omar Sharif1 <o.usmani@imperial.ac.uk>

Lavorini, Federico2 <federico.lavorini@unifi.it>

Marshall, Jonathan3 <jonathan.marshall@mundipharma.com>

Dunlop, William Christopher Nigel3 <will.dunlop@mundipharma.com>

Heron, Louise4 <louise.heron@adelphivalues.com>

Farrington, Emily4 <emily.farrington@adelphivalues.com>

Dekhuijzen, Richard5 <richard.dekhuijzen@radboudumc.nl>

**AFFILIATIONS:**

1. Imperial College London and Royal Brompton Hospital, London, SW3 6LY, UK

2. Department of Experimental and Clinical Medicine, Careggi University Hospital Florence Italy

3. Mundipharma International Ltd, Cambridge Science Park, Cambridge CB4 0AB, UK

4. Adelphi Values, Adelphi Mill, Macclesfield, Cheshire SK10 5JB, UK

5. Radboud University Medical Center, Nijmegen, Netherlands

Table S1: Search strategy for Search-1 and Search-2

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| **Search one (inhaler errors)** |
| “asthma” OR “chronic obstructive pulmonary disease” OR “COPD” [as multipurpose terms] |
| AND | "inhal$ technique" OR "inhal$ competence" OR "handling error$" OR "improper use" OR “critical error$” OR “misuse” OR “inhal$ mistake” OR “inhal$ mishandling” OR "incorrect inhaler use" OR "inhal$ ease of use" [as multipurpose terms] |
| AND | ”inhal$” or “autohaler” or “device$” or “metered dose inhal$” or “dry powder inhal$” or “breath-activated inhal$” or “spacer device” |
| **Search two (economic evaluations and health utility data)** |
| “asthma” OR “chronic obstructive pulmonary disease” OR “COPD” [in abstract AND title] |
| AND | \*"cost"/ OR \*"cost benefit analysis"/ OR \*"cost control"/ OR \*"cost effectiveness analysis"/ OR \*"cost minimi$ation analysis"/ OR \*"cost of illness"/ OR \*"cost utility analysis"/ OR \*economic evaluation/ OR \*economics/ OR economics/ OR "Costs and Cost Analysis"/ OR "cost allocation"/ OR "cost control"/ OR "cost savings"/ [as MeSH Major Topic]OR (standard gamble) OR (time trade off OR time tradeoff) OR (eq-5d or eq5d or euroquol\*) OR (hui1 or hui2 or hui3) OR (sf6d OR sf 6d OR short form 6d OR shortform 6d OR sf sixd OR sf six d) OR (QALY OR quality-adjusted life year) [as multipurpose terms] |

Note: In this analysis, the term ‘critical error’ refers to both critical errors and critical steps that, when performed incorrectly, constitute critical errors. The grey literature search scanned proceedings from conferences between 2013 and 2016, namely by the International Society for Pharmacoeconomics and Outcomes Research, Association for Respiratory Care, European Respiratory Society, American Thoracic Society, and Respiratory Drug Delivery.

Table S2: Critical errors cited in the literature, stratified by device type

| **Device type** | **Critical errors reported** | **Number of studies which categorize activity as critical errors**  |
| --- | --- | --- |
|  pMDI [[1-25](#_ENREF_1)] |  | n=25 |
| Did not activate device correctly | 1† |
| Did not actuate once at beginning of inhalation (did not coordinate) | 19 |
| Actuation after end or before start of inhalation | 9 |
| Actuation against teeth, lips or tongue | 3 |
| Inadequate lip closure | 4 |
| No (or short) breath holding after inhalation | 12 |
| Not breathing slowly and deeply | 20 |
| Not breathing out gently | 1 |
| Failure to remove cap | 17 |
| Inhalation through nose | 4 |
| Not inhaling through mouthpiece, and no seal | 3 |
| Place MDI in mouth or 1—2 inches away from mouth | 3 |
| No forceful inhalation | 1 |
| Inhaler upside down (did not keep upright) | 6 |
| Did not shake inhaler well | 15 |
| Stopping inhalation as device is fired | 3 |
| No inhalation | 2 |
| Did not wait for at least 30 second before next actuationDid not keep head (mostly) upright | 41 |
| Did not replace cap | 1 |
| Did not rinse mouth after dosing | 1 |
| pMDI with spacer [[1](#_ENREF_1), [5](#_ENREF_5), [8](#_ENREF_8), [10-13](#_ENREF_10), [15](#_ENREF_15), [17](#_ENREF_17), [25](#_ENREF_25), [26](#_ENREF_26)] |  | n=11 |
| Did not activate device correctly | 1† |
| Did not shake device | 9 |
| Did not connect MDI to spacer | 4 |
| Did not place canister correctly in spacer | 3 |
| Removed spacer from mouth between breaths | 1 |
| Did not inhale at least three times, slowly | 5 |
| Actuate the device once (no more) | 7 |
| Did not remove cap | 5 |
| Did not hold inhaler upright | 1 |
| Did not form a seal over facemask with mouth | 5 |
| Did not take 5–6 deep breaths | 5 |
| Did not wait at least 30 seconds before next actuation | 2 |
| Did not coordinate activation and inhalation | 4 |
| Did not hold breath for at least 10 seconds | 3 |
| Did not remove spacer from mouth before exhalation | 2 |
| Did not remove inhaler from spacer | 1 |
| Did not replace cap after use | 2 |
| *Diskus*® DPI [[1-4](#_ENREF_1), [7](#_ENREF_7), [8](#_ENREF_8), [12](#_ENREF_12), [18](#_ENREF_18), [19](#_ENREF_19), [27-33](#_ENREF_27)] |  | n=16 |
| Blowing into device before inhalation | 2 |
| Failed to open the device | 10 |
| Failure of loading | 6 |
| Device not level | 6 |
| Failure of priming | 6 |
| Gradual increase in speed on inhalation | 1 |
| Did not push the lever back fully (until it clicks, to prime the device) | 10 |
| Sliding back the lever after inhalation has started | 1 |
| Dropped device or held it with the open mouthpiece facing downwards | 2 |
| Exhaling into mouthpiece of device after loading | 3 |
| Mouthpiece between teeth and lips | 2 |
| Did not hold breath for at least 3s | 4 |
| Not exhaling away from mouthpiece | 5 |
| Not inhaling through the mouthpiece (i.e. inhaling through lever grooves) | 5 |
| Not sealing lips round mouthpiece during inhalation | 3 |
| Lips surround the mouthpiece shallowly against teeth or tongue | 5 |
| Inhaling by nose | 2 |
| Not activating inhaler | 1 |
| Not inhaling forcefully or deeply enough | 14 |
| Did not wait sufficient time before second use | 1 |
| Did not close cap after use | 1 |
| Failure to detect when device is empty | 1 |
| *Turbuhaler*® DPI [[1-4](#_ENREF_1), [7](#_ENREF_7), [8](#_ENREF_8), [11](#_ENREF_11), [12](#_ENREF_12), [18](#_ENREF_18), [19](#_ENREF_19), [25-27](#_ENREF_25), [30](#_ENREF_30), [33](#_ENREF_33)] |  | n=15 |
| Blowing into device before inhalation | 1 |
| Did not lift off the cover | 3 |
| Did not remove cap from inhaler | 2 |
| Did not exhale away from mouthpiece | 3 |
| Failure of loading | 3 |
| Failure of priming | 5 |
| Did not hold the device upright (while priming) | 13 |
| Turn upright without occluding air vents | 6 |
| Not keeping the inhaler no more than 45 degrees from the vertical axis during loading | 5 |
| Did not rotate the grip fully (i.e. until a click was heard) | 3 |
| Did not rotate grip anti-clockwise and then back until a click is heard | 8 |
| Exhaling into mouthpiece of device after loading | 4 |
| Did not exhale to residual volume  | 1 |
| Did not inhale through mouthpiece | 3 |
| Inhaling through nose | 6 |
| Not sealing lips round mouthpiece during inhalation | 7 |
| Not inhaling forcefully or deeply enough | 15 |
| Did not hold breath | 2 |
| Did not wait adequate time before second use/ did not complete steps a second time when extra dose required | 2 |
| Did not close cap/cover after use | 2 |
| Did not check dose counter and expiry date | 1 |
| *Genuair*® DPI[[34](#_ENREF_34), [35](#_ENREF_35)] |  | n=2 |
| Blows into inhaler when the dose is loaded | 1 |
| Button pressed whilst inhaling | 1 |
| Control window not green before inhalation | 2 |
| Did not exhale before introducing mouthpiece into mouth | 1 |
| Did not inhale sufficiently through the inhaler (control window does not change from green to red) | 1 |
| Does not hold the inhaler upright with green button facing upwards for priming (45 degree tolerance), as part of dose preparation | 1 |
| Exhaled into inhaler when dose is loaded | 1 |
| Inhalation immediately stopped upon hearing the click | 1 |
| Inhaler is put down with the control window showing green | 2 |
| Inhaler not held horizontally with green button facing upwards for priming the dose (45 degree tolerance) | 1 |
| Inhaler shaken with mouthpiece facing the ground after priming the dose | 1 |
| Mouth cap not removed before use | 2 |
| Mouthpiece facing downwards after preparation of dose | 1 |
| Shakes the inhaler with the mouthpiece facing the ground after priming, as part of dose preparation | 1 |
| Unable to open pouch with scissors | 1 |
| *Aerolizer*® DPI [[2-4](#_ENREF_2), [7](#_ENREF_7), [13](#_ENREF_13), [18](#_ENREF_18), [27](#_ENREF_27)] |  | n=7 |
| Blowing in the device before inhalation | 1 |
| Did not open the dust cap and mouthpiece | 2 |
| Did not insert a capsule  | 1 |
| Did not insert a capsule in the well and close | 2 |
| Failure of loading | 2 |
| Did not place the capsule in the appropriate chamber | 1 |
| Failure of priming | 2 |
| Did not close the mouthpiece so a click was heard | 1 |
| Did not pierce capsule | 2 |
| Did not press buttons to pierce the capsule and then release them | 2 |
| Did not press the lateral buttons of the inhaler | 1 |
| Exhaling into mouthpiece of device after loading | 2 |
| Did not exhale to FRC before inhalation | 1 |
| Not sealing lips round mouthpiece during inhalation | 4 |
| Did not keep device horizontal  | 1 |
| Did not inhale through the mouthpiece | 2 |
| Inhaling by nose | 3 |
| Did not breathe in rapidly and deeply | 3 |
| Slow and not forceful inhalation | 3 |
| Did not exhale away from mouthpiece | 2 |
| *Handihaler*® DPI [[3](#_ENREF_3), [4](#_ENREF_4), [12](#_ENREF_12), [15](#_ENREF_15), [18](#_ENREF_18), [25-28](#_ENREF_25)] |  | n=9 |
| Did not open device correctly prior to priming | 3 |
| Did not place a capsule in the chamber | 4 |
| Failure of loading | 1 |
| Put a damaged capsule in the chamber | 1 |
| Did not close the mouthpiece until it clicks | 3 |
| Failure of priming | 2 |
| Did not pierce the capsule by pressing the blue button | 2 |
| Did not hold device upright as part of priming | 2 |
| Did not release the blue button before inhaling | 1 |
| Not releasing the pressed piercing button throughout inhalation | 1 |
| Shook the device with the mouthpiece facing the ground after priming | 2 |
| Did not exhale to FRC before placing mouthpiece in mouth | 2 |
| Exhaling into mouthpiece of device after loading | 1 |
| Not sealing lips around mouthpiece during inhalation | 5 |
| Inhaling by nose | 2 |
| Slow and not forceful inhalation | 6 |
| Did not hold breath for 10s | 3 |
| Did not remove inhaler from mouth whilst holding breath and exhale away from mouthpiece | 2 |
| Did not repeat inhalation step after first inhalation to ensure capsule is emptied | 2 |
| Does not make capsule rattle before putting the device down | 2 |
| Did not open lid and mouthpiece | 2 |
| Did not hold inhaler upright and press blue button fully | 1 |
| Blows into inhaler when the dose is loaded | 1 |
| Does not expire inhaled drug | 1 |
| *Diskhaler*® DPI [[1](#_ENREF_1), [8](#_ENREF_8)] |  | n=2 |
| Did not keep the device flat | 1 |
| Did not correctly load the device; lid was not raised | 1 |
| Did not inhale forcefully and deeply | 2 |
| Did not open and close device | 1 |
| *Elpenhaler*® [[28](#_ENREF_28), [32](#_ENREF_32)] |  | n=2 |
| Not closing mouthpiece correctly | 2 |
| Exhaling in mouthpiece | 2 |
| Not gently pulling off the protruding end of the[[1](#_ENREF_1)] strip | 2 |
| Mouthpiece not between teeth and lips | 2 |
| Not opening protective cap | 2 |
| Not placing blister strip correctly on supporting surface | 2 |
| Not pushing back mouthpiece to reveal supporting surface | 2 |
| Not taking blister strip from storage compartment | 2 |
| Did not Inhale | 2 |
| *Cyclohaler*® DPI [[1](#_ENREF_1), [8](#_ENREF_8)] |  | n=2 |
| Did not keep device upright during perforation | 1 |
| Did not correctly load the device by pressing the blue buttons once | 1 |
| Not inhaling forcefully and deeply | 2 |
| Not opening device in vertically position with body below | 1 |
| Not placing capsule in the device | 1 |
| Not pushing the buttons once | 1 |
| Not turning back mouthpiece | 1 |
| *Rotahaler*® [[8](#_ENREF_8), [23](#_ENREF_23)] |  | n=2 |
| Not correctly loading device for inhalation; not rotating the base | 2 |
| Not holding DPI in correct position; not keeping upright during perforation | 2 |
| Not Inhaling forcefully and deeply | 2 |
| *Breezhaler*® DPI [[34](#_ENREF_34)] |  | n=1 |
| Air entry blocked by finger whilst inhaling | 1 |
| Buttons not released during inhalation | 1 |
| Buttons on both sides not pressed simultaneously (capsule not pierced completely) | 1 |
| Buttons to pierce capsule pressed more than once | 1 |
| Capsule does not spin around in the chamber when inhaling due to possible problem with either the inhaler or the capsule | 1 |
| Capsule not removed after inhalation | 1 |
| Capsule placed directly into mouthpiece instead of into capsule chamber | 1 |
| Capsule swallowed instead of inhaling via inhaler | 1 |
| Damaged or contaminated capsule placed into capsule chamber | 1 |
| Did not exhale before introducing mouthpiece into mouth | 1 |
| Exhaled into inhaler (mouthpiece) when capsule is already placed into the chamber and mouthpiece is in patient's mouth | 1 |
| Inhalation not repeated due to powder residue in the capsule and capsule immediately removed without checking for existence of powder residue | 1 |
| Inhalation not sufficiently strong to hear the buzzing indicating that the capsule is spinning around the chamber | 1 |
| Inhaler not held upright after capsule was pierced | 1 |
| Inhaler not held with buttons facing left and right | 1 |
| Inhaler shaken after capsule has been pierced | 1 |
| Mouthpiece facing downwards after preparation of dose | 1 |
| Mouthpiece not closed correctly before piercing the capsule | 1 |
| Second capsule exposed to light in the process of opening first capsule and exposed capsule not discarded | 1 |
| Unable to open mouthpiece | 1 |
| Unable to pull cap off | 1 |
| Unable to remove capsule from the blister | 1 |
| *Easi-Breathe*® breath actuated pMDI [[9](#_ENREF_9)] |  | n=1 |
| Not breathing in slowly and deeply | 1 |
| Not breathing out gently | 1 |
| Not holding inhaler upright | 1 |
| Inhaling through the nose | 1 |
| No inhalation | 1 |
| Put lever down before inhalation | 1 |
| Not putting mouthpiece in mouth and closing lips | 1 |
| Not raising the level to the vertical position | 1 |
| Not removing/ opening cap | 1 |
| Stop breathing at actuation | 1 |
| *Autohaler*® breath-actuated [[5](#_ENREF_5), [9](#_ENREF_9)] |  | n=2 |
| Not breathing in slowly and deeply | 1 |
| Not breathing out gently | 1 |
| Not holding inhaler upright | 1 |
| Inhaling through the nose | 1 |
| No inhalationNot pushing up top lever | 1 |
| Put lever down before inhalation | 1 |
| Not putting mouthpiece in mouth and closing lips | 1 |
| Not raising the lever to the vertical positionNot removing cap | 12 |
| Stop breathing at actuation | 1 |
| *Accuhaler*® [[11](#_ENREF_11), [15](#_ENREF_15), [25](#_ENREF_25), [26](#_ENREF_26)] |  | n=4 |
| Failed to identify if the product was within the expiration date | 1 |
| Not holding Accuhaler horizontally | 2 |
| Not pushing the lever away from the mouthpiece until you hear the ‘click’ | 5 |
| Did not breathe out to residual volume before inhalation | 1 |
| Did not create an adequate seal with lips around mouthpiece | 2 |
| Did not hold breath for correct length of time | 3 |
| Did not breathe out away from inhaler | 4 |
| Not Inhaling forcefully and deeply | 4 |
| *Revolizer*® DPI [[36](#_ENREF_36)] |  | n=1 |
| Did not hold the breath after inhalation | 1 |
| Inhalation was slow | 1 |
| *Pulvinal*® DPI [[13](#_ENREF_13)] |  | n=1 |
| Not rotating the inhaler body counter-clockwise | 1 |
| Not rotating the inhaler body clockwise until it clicks | 1 |
| Not inhaling quickly and deeply | 1 |
| *Fostex*® DPI [[22](#_ENREF_22)] |  | n=1 |
| Protective cap not removed | 1 |
| Mouthpiece not placed between lips | 1 |
| Did not inhale slowly while actuating the device | 1 |
| *Pulmojet*® DPI [[33](#_ENREF_33)] |  | n=1 |
| Did not remove cap | 1 |
| Placed fingers or mouth completely over holes in the device body | 1 |
| Fails to put in mouth and seal lips around mouthpiece | 1 |
| Inhalation is not fast enough to hear soft plop | 1 |
| Cap is not securely screwed down and no click is heard | 1 |
| Fails to inhale through mouthpiece | 1 |
| Critical errors listed are inclusive of stated critical errors and steps which, if not completed, were classed as critical errors. As wordings / terminology of the same critical errors differed between studies (n=299 critical errors in total), the table presents a consolidated list per device type.‘n’ refers to the total amount of studies reporting critical errors for corresponding device.\*: did not differentiate between the two devices.†: this error was defined as not fulfilling the technical specifications of the device as recommended by the device manufacturer. |

Table S3: Studies which report link between control and resource use, economic burden and worsened QoL

|  |  |
| --- | --- |
| **Reference** | **Key conclusions** |
| Demoly *et al.* [[37](#_ENREF_37)] | “at least well-controlled asthma” was associated with:* Improved SF-12 scores (physical components)
* significantly lower number of healthcare contacts in the previous 6 months
* significantly less impact on Work Productivity Loss and Activity Impairment
 |
| Doz *et al*. [[38](#_ENREF_38)] | EQ-5D scores were worse in patients with uncontrolled asthma and partially controlled asthma in comparison to those with controlled asthma (health utility score: 0.63–0.69, 0.78–0.82 and 0.88–0.89, respectively, p<0.0001)Average cost (euros/3-months/patient) were higher for uncontrolled asthma than controlled asthma:France (p<0.0001):* €85.4 well controlled
* €314.0 partially controlled
* €537.9 poorly controlled

Spain (p<0.0001):* €152.6 well controlled
* €241.2 partially controlled
* €556.8 poorly controlled
 |
| Szende *et al*. [[39](#_ENREF_39)] | QoL, as measured by the EQ-5D, SF-35 and SGRQ is worse in asthma patients with poor control in comparison to those with good control:EQ-5D (high score is better):* 0.93 good control
* 0.52 poor control

SF-36 (high score is better):* 48 physical, 55 mental good control
* 31 physical, 44 mental poor control

SGRQ (low score is better)* 21 good control
* 60 poor control
 |
| Vervloet *et al*. [[40](#_ENREF_40)]] | Mean per patient annual costs were higher for not-well controlled patients:* €232 (95%CI: €192–286) well controlled
* €512 (€404–660) poorly controlled
* €1,604 (€1,219–€2,084) not-well controlled
 |
| Williams *et al*.[[41](#_ENREF_41)] | Patients with controlled asthma reported (all p<0.001):* Better QoL (higher SF-8 physical and mental scores)
* fewer emergency room visits
* fewer hospitalization days and medical provider visits
* lower work productivity loss
* reduced activity impairment
 |

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| Table S4: Definitions of a critical error with a device |
| **Authors** | **Year** | **Definition of critical errors** |
| ***Publications stating that a critical error would certainly affect inhalation and drug delivery:*** |
| Basheti *et al.* [[30](#_ENREF_30)] | 2011 | “Essential step: if not performed correctly, little or no medication will reach the lungs” |
| Batterink *et al.* [[12](#_ENREF_12)] | 2012 | “Critical errors were defined as those resulting in little or no medication reaching the lungs.” |
| Deerojanawong *et al.* [[10](#_ENREF_10)] | 2009 | “The MDI checklist contained 10 steps; 7 of which were considered essential for adequate drug delivery.” |
| Van der Palen *et al.* [[28](#_ENREF_28)] | 2013 | “Critical errors were defined as those that will lead to an insufficient drug deposition in the lungs.” |
| Van der Palen *et al.* [[35](#_ENREF_35)] | 2013 | “… critical errors included those that impeded delivery of sufficient dose or drug deposition in the lungs.” |
| Voshaar *et al.* [[42](#_ENREF_42)] | 2014 | “A critical error was defined as any error that prevented a dose being delivered.” |
| Wieshammer*et al.* [[27](#_ENREF_27)] | 2008 | “… operating errors that make significant deposition of the medication to the lung impossible were defined *a priori* as ‘essential’.” |
| Capstick *et al.* [[43](#_ENREF_43)] | 2013 | “at least one critical error, significantly affecting lung deposition” |
| Nama *et al.* [[44](#_ENREF_44)] | 2014 | “critical errors that would result in inadequate amounts of drug reaching the lung“ |
| Pothirat *et al.* [[15](#_ENREF_15)] | 2016 | “…Essential steps required for adequate drug delivery” |
| Madkour *et al.* [[18](#_ENREF_18)] | 2015 | “Essential steps were defined as those considered necessary for optimal delivery of the active drug into the lungs” |
| Vanderman *et al.* [[14](#_ENREF_14)] | 2015 | “Errors that if made will significantly reduce or eliminate the delivery of medication to the lungs” |
| Chrystyn *et al.*[[33](#_ENREF_33)] | 2016 | “those that would definitely preclude adequate dose delivery to the lungs” |
| Ozturk *et al.* [[45](#_ENREF_45)] | 2015 | “…Causing insufficient drug inhalation…” |
| ***Publications stating that a critical error could affect inhalation and drug delivery:*** |
| Coelho *et al.* [[13](#_ENREF_13)] | 2011 | “… we identified the “key steps” in performing the inhalation maneuvers … the steps that, when incorrectly performed by users, can significantly affect total deposition of the dose in the lungs.” |
| Giraud *et al.* [[9](#_ENREF_9)] | 2011 | “… critical errors were defined, per Molimard *et al*., as errors that could substantially affect dose delivery to the lung.” |
| Hagmolen *et al.* [[8](#_ENREF_8)] | 2008 | “When errors are made regarding key actions, it is likely that no, or only an insignificant amount of medicine will be inhaled.” |
| Mehuys *et al.* [[5](#_ENREF_5)] | 2010 | “… crucial errors (i.e., errors probably leading to no drug deposition in the lungs)...” |
| Molimard *et al.* [[2](#_ENREF_2)] | 2008 | “A critical error is one that is likely to affect delivery of the full dose of the drug to the bronchi…” |
| Rajan *et al.* [[36](#_ENREF_36)] | 2014 | “The errors were classified as critical errors – those that can have a significant effect on the drug delivery to the lungs or non‑critical errors – those that do not affect dose delivery to the lungs.” |
| Rootmensen *et al.* [[1](#_ENREF_1)] | 2010 | “When one or more errors were made regarding these essential steps, we considered it unlikely that a significant amount of medicine would be inhaled.” |
| Schulte *et al.* [[46](#_ENREF_46)] | 2008 | “Handling errors that could result in a reduced or zero dose delivery were defined as critical handling errors.” |
| Molimard *et al.* [[47](#_ENREF_47)] | 2005 | “Inhalation errors were considered critical if they could have substantially affected drug delivery to the lung” |
| Van der Palen *et al.* [[48](#_ENREF_48)] | 2012 | “critical errors that may result in receiving no drug or a suboptimal dose” |
| Westerik *et al.* [[31](#_ENREF_31)] | 2016 | “Serious inhaler technique errors identified by the HCPs were defined as errors potentially limiting drug uptake to the lungs” |
| Thomas *et al.* [[49](#_ENREF_49)] | 2015 | “Errors likely to result in significantly reduced drug delivery” |
| Chrystyn *et al.* [[50](#_ENREF_50)] | 2015 | “those potentially affective dose delivery” |
| ***Publications stating that a critical error would make aerosol therapy useless:*** |
| Li *et al.* [[29](#_ENREF_29)] | 2014 | “The analysis focused on the critical errors that are likely to make aerosol therapy useless...” |
| Melani *et al.* [[3](#_ENREF_3)] | 2011 | “… critical errors, which are likely to make therapy with aerosols useless...” |
| Melani *et al.* [[4](#_ENREF_4)] | 2012 | “… critical errors, which are likely to make therapy aerosol useless.” |
| Capanoglu *et al.* [[19](#_ENREF_19)] | 2015 | “steps that are essential for correct use of inhaler medications”\* |
| ***Publication stating that a critical error would make aerosol therapy useless by affecting inhalation or drug delivery:*** |
| Pascual *et al.* [[34](#_ENREF_34)] | 2015 | “Critical errors were defined as those that compromised the potential benefit of the treatment, such as impeding drug deposition in the lungs or the delivery of an insufficient dose...” |
| Note: In this table the term “critical error” refers to both critical errors and critical steps that, when performed incorrectly, constitute critical errors. \*The definition provided by Capanoglu et al. is considered to infer that making an error in an “essential” step will mean that the inhaler is used incorrectly, and that the benefit of treatment is compromised. |

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