# Respiratory Medicine 141 (2018) 180-189



Contents lists available at ScienceDirect

# Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed



# Treatment perceptions in patients with asthma: Synthesis of factors influencing adherence



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# ARTICLE INFO

# Keywords: Asthma Perceptions Adherence Interventions Behavioural change

#### ABSTRACT

Background: Non-adherence to asthma treatment is a contributing factor for poorly controlled asthma. Aim: The aim of this systematic review is to explore patients' perceptions of their inhaled asthma treatment, and how these relate to adherence, using both qualitative and quantitative data.

*Methods:* Pre-determined search terms and inclusion criteria were used to search electronic databases (The Cochrane Library, MEDLINE, EMBASE and PsycINFO). Two researchers screened titles and abstracts using the Rayyan web app and data were extracted in relation to psychological components (beliefs about, and attitudes towards, medicines) and adherence.

Results: Of 1638 papers, 36 met the inclusion criteria. Key themes were: Perceived need for treatment - all 12 studies using the BMQ to measure patients' perceived need for treatment found that patients' beliefs about their necessity for treatment were associated with adherence-; Concerns about treatment - immediate and long-term side effects (58%), worries about safety (19%), and potential addiction to asthma medication (31%)-; and Perceived social stigma - 22% of studies reported that embarrassment contributed to poor adherence.

Conclusions: Acknowledging and addressing patient treatment beliefs and perceptual barriers to adherence is integral to designing adherence interventions for asthma patients. Further research is needed to better our understanding of the relationship between treatment perceptions and adherence.

## 1. Introduction

Asthma is a chronic respiratory disease experienced by over 334 million people worldwide [1]. Despite its high prevalence, asthma remains under-diagnosed and under-treated [2,3] contributing to a large global burden of disease. In the EU, at least 50% (7 million people) of patients with asthma from five European countries do not have their asthma well-controlled [4].

Effective pharmacological therapies exist, of which inhaled corticosteroids (ICS) are the mainstay of treatment [5] preventing asthma symptoms, exacerbations and hospitalisations. Despite the effectiveness of current asthma treatments, non-adherence to ICS remains a significant problem [6–8]. Although an 80% adherence rate with ICS has been suggested as the minimum acceptable level of adherence for achieving good asthma control [9], reported ICS adherence rates range from 30 to 70% in the literature [10]. A recent longitudinal study of

middle-aged adults with asthma found that 74% (n = 351) used in-adequate preventer medication [11]. Similarly, in children, inhalers are largely underused; one study in 8–16 year olds found that inhalers were underused on 33% of days in a month [8]. In a review of 18 studies using objective adherence monitoring, half of the studies in children reported adherence rates of  $\leq\!50\%$  [12]. In adolescents, adherence rates can be even lower, with one study reporting adherence to be  $<\!30\%$  in 16–17 year olds [12], leading to higher exacerbation rates, hospitalisation and mortality compared to children [13].

Non-adherence to ICS is associated with poor asthma control, decline in lung function, increased exacerbations, decreased quality of life, higher rates of health service utilisation, absenteeism from work or school, and has been reported to account for up to 80% of asthmarelated mortality [14–18]. In addition, suboptimal adherence to ICS may lead to the prescription of higher doses of medication when non-adherence is misidentified as refractory asthma [19], leading to a

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higher risk of adverse effects and wasted medication.

Reasons for non-adherence to asthma medication are varied and complex, however a common factor underlying non-adherence relates to patient behaviour. Although the use of asthma medication typically follows an asthma action plan provided by health care professionals, day-to-day asthma medication is self-managed by the patient. As such, adequate asthma control depends on patients' behaviour towards their medication, which in turn determines the success of their asthma treatment.

These adherence behaviours are influenced by patients' perceptions of their condition [20]. For example, patients tend to believe their asthma is under control even when they have experienced frequent symptoms, have used their reliever inhaler regularly or have had an acute exacerbation within the last year [21–23]. A series of multinational surveys [24–27] to gain insights on the attitudes and perceptions of patients with asthma found that patients' perceptions of how efficiently they were controlling their asthma were inconsistent with objective criteria recognised by asthma control guidelines. For example, in Europe and Canada, 81% (n = 2003) of surveyed patients perceived their asthma as completely or well controlled but, according to the Global Initiative for Asthma (GINA) guidelines, only 18% of these patients would have been classified as having controlled asthma. This trend extends globally in Latin America [26], Asia-Pacific [24], US [27] and the UK [28].

Patients' beliefs about their treatment can also influence their behaviour. There are differences in onset of effect in the various types of asthma medication – ICS may take several weeks before producing maximum benefit; in contrast, short-acting beta agonists, or reliever inhalers, provide immediate symptom relief [29,30]. These differences can promote under-use of ICS and over-use of the reliever. Bender et al. [31] showed that the use of reliever medication is influenced by a lack of perceived need for preventer medication [31] and the belief that medicines should only be used in response to symptoms.

There have been multiple strategies studied to promote adherence to medication, for example, through education, improved communication with health care practitioners or digital interventions, but these interventions have had limited effectiveness [32]. Interventions which target patient perceptions and beliefs may be more effective. For example, studies have shown that modifying patient perceptual and practical barriers to their treatment [33], such as forgetting to take the medication, incorrect inhaler technique and fear of long-term effects or side-effects may be effective in improving intentional or unintentional non-adherence [34].

To ensure the effectiveness of adherence interventions, it is necessary to understand the psychology of asthma patients in relation to their perceptions of inhaled medication. This is key for identifying reasons why patients do not adhere to their recommended treatment as addressing perceptual barriers, through behavioural-targeted interventions, have been shown to be more effective for improving adherence than addressing non-perceptual barriers [35]. A recent review of determinants of inhaler adherence in adults based on observational data linked adherence to a strong perceived need for medication (necessity beliefs); no other determinants were found to be predictive [36]. There is no literature review to date assessing the perceptions of asthma patients in relation to their treatment, using both qualitative and quantitative studies. Understanding these perceptual processes will inform future interventions on how to influence behavioural change that benefits patients' health through adherence to treatment. This review explores patients' perceptions of inhaled treatment that contribute to non-adherence.

# 2. Methods

# 2.1. Literature search

Searches were conducted using CENTRAL (The Cochrane Library),

Table 1

Search terms. Terms within columns were combined using the Boolean 'OR' operator, terms between columns were then combined with 'AND' – i.e. papers were retrieved if the title/abstract/keywords contained at least one term from each column.

| SABA                        | Adhere <sup>a</sup>  | Asthma <sup>a</sup> (explode)   |
|-----------------------------|--|---|
| LABA                        | Nonadhere <sup>a</sup>   |   |
| ICS                         | Non-adherea  |   |
| Inhaler                     | Persist <sup>a</sup>   |   |
| Combination                 | Complian <sup>a</sup>  |   |
| Steroid                     | Noncomplian <sup>a</sup>   |   |
| Corticosteroid              | Non-complian <sup>a</sup>  |   |
| fluticasone <sup>a</sup>    | Concord <sup>a</sup>   |   |
| budesonide <sup>a</sup>     | Engagement   |   |
| beclomethasone <sup>a</sup> |  |   |
| ciclesonide <sup>a</sup>    |  |   |
| flunisolide <sup>a</sup>    |  |   |
| mometasone <sup>a</sup>     |  |   |
| Triamcinolone <sup>a</sup>  |  |   |
|                             | LABA ICS Inhaler Combination Steroid Corticosteroid fluticasone <sup>a</sup> budesonide <sup>a</sup> beclomethasone <sup>a</sup> ciclesonide <sup>a</sup> flunisolide <sup>a</sup> mometasone <sup>a</sup> | LABA Nonadhere <sup>a</sup> ICS Non-adhere <sup>a</sup> Inhaler Persist <sup>a</sup> Combination Complian <sup>a</sup> Steroid Noncomplian <sup>a</sup> Corticosteroid Non-complian <sup>a</sup> fluticasone <sup>a</sup> Concord <sup>a</sup> budesonide <sup>a</sup> Engagement beclomethasone <sup>a</sup> ciclesonide <sup>a</sup> flunisolide <sup>a</sup> mometasone <sup>a</sup> |

<sup>&</sup>lt;sup>a</sup> Denotes truncation.

MEDLINE, EMBASE and PsycINFO. Pre-determined search terms and keywords were used to identify relevant studies (Table 1). Reference lists within these initial studies were hand searched and additional relevant studies were identified. Searches were completed on the 16th August 2017. This systematic review was conducted in accordance with the PRISMA statement [37].

# 2.2. Selection of papers

The Rayyan Web app [38] was used to independently screen titles, abstracts and keywords of all identified studies for possible inclusion. Two researchers (HL/EW) independently screened and coded each study as 'include' (eligible or potentially eligible/unclear) or 'exclude' with 100% overlap. Full texts of relevant studies were then retrieved, examined and independently screened for inclusion by two researchers (HL/EW). Disagreements between reviewers were resolved by discussion. Reference lists within these papers were again hand searched for any further relevant titles and subjected to the same process as above. Final papers were selected according to the inclusion/exclusion criteria in Table 2. The selection process of papers for the review is summarised in Fig. 1.

# 2.3. Data extraction and synthesis

Data were extracted by two independent researchers (HL and EW) with 100% overlap. Data extraction included: study aim, study design (quantitative/qualitative), mean age of sample population, percentage females, age group of population (adult, children, adolescent), number of participants, type of asthma treatment, and adherence rates (where reported). Narrative synthesis was used to describe the psychological components (e.g. beliefs about medicines) and outcomes (e.g. adherence, engagement), and how they were measured.

Table 2
Inclusion/exclusion criteria.

| Inclusion Criteria              | Exclusion Criteria                          |
|---------------------------------|---|
| Article in English              | Conference abstract                         |
| Patients with asthma at any age | Full-text not available                     |
| Empirical study <sup>a</sup>    | Pregnant women                              |
| Reports on perceptions          | Focus of study not on patients <sup>b</sup> |
| Reports on treatment            |   |

<sup>&</sup>lt;sup>a</sup> Pilot, feasibility, evaluative, quantitative or qualitative – data on adherence to prescribed medicines.

b e.g. on clinician/physician views.

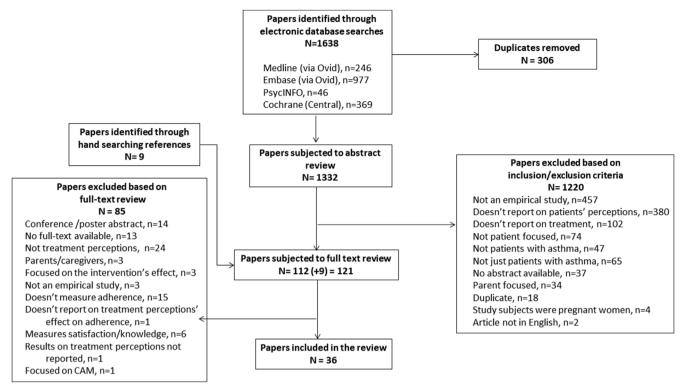


Fig. 1. Flow diagram of the selection of studies included in the systematic search.

#### 3. Results

#### 3.1. Studies included

From 1638 articles originally identified, 306 duplicates were removed, leaving 1332 abstracts for review; of these, 1220 were excluded based on pre-determined inclusion/exclusion criteria (Table 2). 112 papers, and an additional nine (retrieved through scanning relevant reference lists) were subjected to a full-text review; 36 studies met the inclusion criteria and were included in this review (Fig. 1).

# 3.2. Study characteristics

Table 3 summarises the characteristics of the 36 studies, 81% of these reported quantitative data [33,39–66] and 19% reported qualitative data [13,67–72].

# 3.3. Participants

26 (72%) of the included studies had adult participants ( $\geq$ 20 years old) [33,39–42,44–47,49,50,52,54–59,61–64,66,68–70] and 6 (17%) adolescents (between 12 and 20 years) [13,51,65,67,71,72]. The age threshold for adult and adolescent participants within this review was guided by the age categories used in a study by Wamboldt et al. [72] who categorised patients between 12 and 20 years old as adolescents. Finally, four studies (11%) included both adults and adolescents [43,48,53,60]. There were no studies in children below 12 years of age.

# 3.4. Location

The included studies covered 18 different countries: 11 studies took place in the USA [39,44,54,56,59,63,66,68,70–72], five in the UK [13,33,42,43,67], four in The Netherlands [41,51,55,62], three in Sweden [40,47,64], three in Australia [48,49,73] and one each in Nigeria [46], Saudi Arabia [50], Taiwan [52], France [53], Latvia [58], Iran [60], Denmark [61]. Chiu et al. [45] did not specify in which six

Asian countries they conducted their study and two studies [65,69] did not state the country.

# 3.5. Prescribed medication

16 (44%) of the studies reported on patients using preventer asthma medications [33,39,41,44,50–52,54–56,62,66,68,70–72], seven (19%) on a combination of preventer and reliever therapies [13,42,45,47,48,67,69]; eight (22%) on different treatments for different groups within the studies (monotherapy and combination therapies) [49,53,57–59,61,63,64]. In five (14%) of the studies, no type of medication was stated [40,43,46,60,65].

# 3.6. Psychological component

All studies investigated patients' treatment perceptions. Studies used either validated questionnaires or designed study-specific questions, with some studies using more than one questionnaire. Twenty-four of the studies (67%) [13,39,41,42,44–46,48–50,52–54,56,57,60,61,65,67–72] used specifically designed study-specific questions to explore patients' perceptions of treatment including beliefs, behaviours and attitudes toward medications. The validated Beliefs about Medicines Questionnaire (BMQ), which measures patient treatment beliefs, was used in 12 (33%) studies [33,40,43,47,51,55,58,59,62–64,66], whilst five (14%) used the validated Illness Perceptions Questionnaire [33,43,58,59,66] which elicits patient beliefs about their illness.

# 3.7. Adherence rates and adherence measures

Studies reported on adherence either descriptively as qualitative data or quantitatively as a summary score, or percentage adherence to inhaled asthma medication. Seven (19%) studies did not provide adherence data quantitatively, whilst 6 (17%) studies reported adherence data as a score or by categorisation of different types of adherence behaviour, rather than an overall percentage. Of the 23 (64%) studies that reported an overall percentage adherence, pooled mean  $\pm$  SD

Study characteristics. BMQ: Beliefs about Medicines Questionnaire; EM: Electronic Monitor; IPQ: Illness Perceptions Questionnaire; MARS: Medication Adherence Report Scale; MMAS: Morisky Medication Adherence Scale; NS: not stated; SR: self-report. Treatment type: both: all population on preventer and reliever; mixed: monotherapy or combination for different groups within the study. Table 3

|  | Author, Year                   | Country                      | Study design   | Mean age (or<br>range)                             | % female | % female Population | No. of<br>subjects | Treatment type | Measure of<br>treatment<br>perceptions   | Adherence measures                        | Adherence rates  |
|--|--------------------------------|------------------------------|--|--|----------|---------------------|--------------------|----------------|--|---|--|
| UK, Clasgow   Indepth interviews   15.6   29.1%   Adults   394   Percented   Survey specific   St Philadelphia   Cross-sectional startery   Medlan 198. 56   75%   Adults   64   NS   BMO, Proc. precific   St Philadelphia   Cross-sectional state   23.65 (5D 13.85)   50%   Mixed   64   NS   BMO, Proc. precipiton reall   Melbourne, Potal questionanie   23.65 (5D 13.85)   50%   Adults   876   Maded   Cabura precipit   St Proc. precipion reall   Melbourne, Potal questionanie   23.85 (5D 13.81)   61%   Adults   246   Procenter   SMO, Proc. precipion reall   Melbourne, Potal questionanie   47.55 (5D 12.78)   62.6%   Mixed   160   New realer   SMO, Proc. precipion reall   Melbourne, Potal questionanie   47.55 (5D 12.78)   62.6%   Mixed   160   NS   Smoky specific   SMO, Proc. precipion reall   Mixed   44   Mixed   M   | Bosley, 1995<br>[42]           | London, UK                   | Prospective study                                    | Compliant 47 (SD 16); Non-compliant 43 (SD 15)     | 61%      | Adults              | 72                 | Both           | Study specific<br>questions              | ЕМ  | 49% compliant (p = 0.05)   |
| UK, Glasgow         In-depth interviews         15.6         59.1%         Adoltoserul         49         Beth         Study specified spruds operations of the specified  | Chambers, 1999<br>[44]         | USA,<br>Philadelphia         | Cross-sectional survey                               | Median age 36                                      | 75%      | Adults              | 394                | Preventer      | Survey specific                          | SR  | (n = 386) 38% compliant  |
| UK   Oucestionnaire   39.63 (SD 13.83)   50%   Mixed   64 NS   BMO; IPQ   Description refill Ambleume, and a survey specific of 33, C2 33, G3 (SD 13.83)   61%   Adults   876   Mixed   Subty-specific   61 ari, SR   Adults   62%   Mixed   Cross-sectional design   61 33, C2 33, G3 (SD 13.83)   61%   Adults   62%   Preventer   BMO; IPQ   MASS   MASS   Cohort study   67 (SD 12.78)   63.6%   Adults   65%   Preventer   Subty-specific   SR   Adults   65%   Adults   65%   Mixed   Subty-specific   SR   Adults   65%   Adults   65%   Adults   65%   Mixed   Consistence   Consisten   | Buston, 2000<br>[67]           | UK, Glasgow                  | In-depth interviews                                  | 15.6   | 59.1%    | Adolescent          | 49                 | Both           | Study specific<br>questions              | Study specific questions, SR              | 4/45 (9%) compliant  |
| Methourne,   Method   Methourne,   Method   Methourne,   Method   Methourne,   Method   Metho   | Byer, 2000 [43]                | UK                           | Questionnaire  | 39.63 (SD 13.83)                                   | 20%      | Mixed               | 64                 | NS             | вмо; гро                                 | Prescription refill                       | No quantitative adherence data reported  |
| Taiwan   Stross-sectional design   23   SD 18.1)   S1%   Adults   S4%   Preventer   Gudy specific   SIM AGAS   | Reid, 2000 [73]                | Melbourne,                   | Postal questionnaire                                 | G1 33; G2 33; G3                                   | 61%      | Adults              | 876                | Mixed          | Study specific                           | SR  | 41% compliant  |
| 1   124   124   124   124   124   125      | Horne, 2002                    | Austrana<br>UK               | survey<br>Cross-sectional design                     | 35<br>49.3 (SD 18.1)                               | 61%      | Adults              | 100                | Preventer      | questions<br>BMQ; IPQ                    | MARS                                      | 14% compliant  |
| 1.18A,   | Kuo, 2002 [52]                 | Taiwan                       | Face-to-face interviews                              | NS   | NS       | Adults              | 246                | Preventer      | Study specific<br>questions              | SR  | (n = 189) 53.4% compliant  |
| Principy Annia   | Apter, 2003 [39]               | USA,                         | Cohort study   | 47 (SD 15)   | 72%      | Adults              | 82                 | Preventer      | Study specific                           | ЕМ  | Mean adherence: 68% ± 42%. Mean truncated  |
| Denmark   Questionnaire   47.67 (SD 12.78)   65.6%   Mixed   160   NS   Study specific SR  | George, 2003                   | Pennsylvania<br>USA,         | Focus groups   | 53   | %08      | Adults              | 15                 | Preventer      | questions<br>Study specific              | EM  | Adherence: $60\% \pm 30\%$ . No quantitative adherence data reported   |
| Denmark Questionnaire Range 18-45 62% Adults 509 Mixed Study specific SR Adults 10 Borb Study specific Br Adults 10 Borb Study Study specific Br Adults 10 Borb Study    | [70]<br>Tavasoli, 2006<br>[60] | Pennsylvania<br>Tehran, Iran | Questionnaire  | 47.67 (SD 12.78)                                   | 65.6%    | Mixed               | 160                | NS             | questions<br>Study specific<br>questions | SR  | Mean compliance score: 2.56 $\pm$ 1.06. Frequency of compliance based on their scores: score 0, 4 (2.5%);  |
| Denmark Questionnaire Range 18-45 62% Adults 509 Mixed Study specific SR questions   Study specific SR questions   Study specific SR dutis   Study specific   Study specific SR dutis   Study specific      |                                |                              |  |  |          |                     |                    |                |  |   | score 1, 27 (16.9%); score 2, 35 (21.9%); score 3, 62 (38.8%); score 4, 32 (20%)   |
| NS   Nospective study   47.2 (SD 17.9)   63.5%   Adults   334   Preventer   Study specific   SR  | Ulrik, 2006 [61]               | Denmark                      | Questionnaire  | Range 18-45  | 62%      | Adults              | 209                | Mixed          | Study specific<br>questions              | SR  | 66% reported taking controller therapy as prescribed. Of those prescribed ICS, 30% reported not taking ICS regularly (within the past week)  |
| NS   Unstructured   44   70%   Adults   10   Both   Adults   Study specific SR   | Al-Jahdali, 2007               | Riyadh                       | Prospective study                                    | 47.2 (SD 17.9)                                     | 63.5%    | Adults              | 334                | Preventer      | Study specific                           | SR  | (n = 208) 62% compliant  |
| Australia Population-based 40.7 61% Adults 101 Mixed Study specific SR arrayey questions survey questions sectional study analysis and study specific study specific study specific study specific cohort Caucasian 45.0 (SD 70% Adults 86 Preventer Study specific EM adults and study at 13.5); Minorities Adults 13.5); Minorities Adults 13.5); Minorities Survey Adults 13.6) Mixed BMQ Prescription data cleetronic)  France Cross-ectional S1.8 (SD 19.6) 5.9% Mixed 2.04 Mixed Study specific SR questions are cleetronic)   | Samble, 2007<br>[69]           | NS                           | Unstructured   | 44   | %02      | Adults              | 10                 | Both           | Study specific                           | SR  | No quantitative adherence data reported  |
| USA, NYC Qualitative analysis 43 87% Adults 52 Preventer Study specific consessectional study)  USA, Baltimore, Prospective cohort study study and study study at 42.0 (SD 8.4)    Author Survey   Author S   | Heiner, 2007<br>[49]           | Australia                    | Population-based survey                              | 40.7   | 61%      | Adults              | 101                | Mixed          | Study specific<br>questions              | SR  | No quantitative adherence data reported  |
| USA, Baltimore, Prospective cohort Caucasian 45.0 (SD 70% Adults 86 Preventer Study 13.5); Minorities 42.0 (SD 8.4)  Rayland study 13.5); Minorities 42.0 (SD 8.4)  3] Michigan Survey 43.1 (SD 10.4) 71% Adults 1006 Mixed BMQ [electronic) (electronic) (e | Zhoi, 2008 [68]                | USA, NYC                     | Qualitative analysis (part of cross-sectional study) | 43   | 87%      | Adults              | 52                 | Preventer      | Study specific<br>questions              | MMAS (0–4) higher score = worse adherence | ± SD); 1.6 ±   |
| Michigan Survey 43.1 (SD 10.4) 71% Adults 1006 Mixed BMQ Prescription data (electronic)  France Cross-sectional Sudy Specific SR adults observational study specific SR adults observational study   | .e, 2008 [54]                  | USA, Baltimore,<br>Maryland  | Prospective cohort study                             | Caucasian 45.0 (SD 13.5); Minorities 42.0 (SD 8.4) | 70%      | Adults              | 98                 | Preventer      | Study specific<br>questions              | ЕМ  | Average daily adherence over 1-month: $34\% \pm 24\%$ .  |
| France Cross-sectional 53.8 (SD 19.6) 59% Mixed 204 Mixed Study specific SR questions  | Wells, 2008 [63]               | Michigan                     | Survey   | 43.1 (SD 10.4)                                     | 71%      | Adults              | 1006               | Mixed          | ВМО                                      | Prescription data (electronic)            | ICS adherence (%). Respondents 36.6 $\pm$ 34.4; Nonrespondents 25.0 $\pm$ 28.6 (p = 0.00)  |
|  | [53]                           | France                       | Cross-sectional observational study                  | 53.8 (SD 19.6)                                     | 20%      | Mixed               | 204                | Mixed          | Study specific questions                 | . XS                                      | Data reported as % of different types of adherence behaviours (no overall rates given): Accidental interruption of ICS - Never/scarcely: 74.6%, Sometimes/often/very often 25.4%; Interruption of ICS when feeling better 68.4%, 31.6%; Interntional interruption of ICS when feeling worse 94.6%; 5.4%; Less frequent use of ICS when feeling better 68.7%; 31.3%; More frequent use of ICS in case of premonitory signs of asthma attack 78.8%; 21.2%; Intentional change in the dosing of ICS (overall) 18.3% |

(continued on next page)

Table 3 (continued)

| es Adherence rates                     | Mean score of self-reported adherence assessed by MARS: 19.4 ( $\pm$ 4.4). Mean adherence calculated by pharmacy dispensing records: 73.4% ( $\pm$ 38.6%) ( $n=222$ ) | Median adherence of 43% (range, 4%–89%)                     | 4.3 at baseline and at 1 and 3 months                                  | 72% used PAM as prescribed      | No quantitative adherence data reported | inhaled controller adherence (%) > 75% of prescribed doses taken – participants 36.0; decliners 25.7; unreachable 18.2 35–75% of prescribed doses taken - 32.0; 42.9; 40.9 < 35% of prescribed doses taken 32.0; 31.4; 40.9 | Probabilities of adherence reported but not measured sneetifically | (r = 85) mean EM adherence = 75% $\pm$ 25; mean SR adherence = 85% $\pm$ 26%. | No quantitative adherence data reported | 18.7% reported that they were 100% compliant and 13.3% were > 80% compliant. 5.7% of physicians reported their patients were 100% compliant and 17.1% were > 80% compliant | 43% compliant           | Mean MMAS score was 5.5 $\pm$ 2.0; 53% were adherent | Self-report: 24.4% adherent; pharmacy refill data: $57.7\%$ adherent ( $P < 0.001$ ) | Mean adherence 68%       | Mean ICS = $20.3 \pm 4.2$ (range 7.0–25.0) and 40.9% of patients were defined as adherent using a cut-off point of 23 | 55% non-adherent                | No quantitative adherence data reported | Prevalence of poor treatment adherence ranged<br>between 58 and 76% in men and 69% in women |
|--|---|---|--|---------------------------------|---|---|--|---|---|--|-------------------------|--|--|--------------------------|---|---------------------------------|---|---|
| Adherence measures                     | MARS  | ЕМ  | MARS<br>(range 1–5. Higher<br>values indicate better<br>adherence).    | MARS                            | MARS                                    | ЕМ  | Prescription refill  | EM; MMAS  | MARS                                    | SR   | MARS                    | MMAS-8   | SR   | Prescription refill data | MARS  | MMAS                            | NS                                      | MARS; MMAS  |
| Measure of<br>treatment<br>perceptions | ВМQ   | Study specific<br>questions                                 | Study specific<br>questions  | Study specific questions        | BMQ-Specific                            | Study specific<br>questions   | Study specific   | Study specific<br>questions   | ВМО                                     | Study specific<br>questions  | Brief-IPQ; BMQ          | Study specific<br>questions                          | ВМО  | ВМО                      | ВМО   | вмо; про                        | Study specific questions                | BMQ; IPQ  |
| Treatment type                         | Preventer   | Preventer   | Preventer  | Preventer                       | Both                                    | Preventer   | NS   | Both  | NS                                      | NS   | Mixed                   | Both   | Preventer  | Mixed                    | Preventer   | Preventer                       | Both                                    | Mixed   |
| No. of<br>subjects                     | 233   | 40  | 261  | 139                             | 35                                      | 26  | 47   | 66  | 516                                     | 150  | 242                     | 1054   | 93   | 165                      | 182   | 392                             | 54                                      | 352   |
| Population                             | Adults  | Adolescent  | Adults   | Adults                          | Adults                                  | Adolescent  | Adolescent   | Mixed   | Adults                                  | Adults   | Adults                  | Adults   | Adults   | Adults                   | Adolescent  | Adults                          | Adolescent                              | Adults  |
| % female Population                    | 67%   | 48%   | 82%  | 70.5%                           | 71.4%                                   | 35%   | 25%  | 28%   | , %09                                   | , %89  | 83.9%                   | 61.8%  | 59.1%  | , %99                    | . 26%   | 61%                             | 48.1%                                   | 75  |
| Mean age (or<br>range)                 | 36.2 (SD 6.3)   | 16  | 48 (SD 13)   | 31.5 (SD 5.6)                   | 52.8 (SD 14.7)                          | At focus group 15.3 (SD1.9); At 1st study visit 10 (SD1.9)  | NS   | 47.6 (15.8)   | 47.36 (15.6)                            | 39 (SD 16)   | 67.4 (SD 6.8)           | 53.0 (SD 14.4)                                       |  | 49.65 (SD 15.64)         | 15 (SD 2)   | 48.71                           | Range 13-59                             | 57.5 (SD 16.9)  |
| Study design                           | Cross-sectional study   | Observational cohort study (Mixed-method exploratory study) | Data from multi-site,<br>prospective,<br>observational cohort<br>study | Cross-sectional mail out survey | Survey                                  | Focus groups  | Online survey  | Prospective cross-<br>sectional observational<br>study                        | Population-based study                  | Cross-sectional  | Observational study     | Cross-sectional observational study                  | Questionnaire  | Population-based study   | Survey  | A cross-sectional online survey | Qualitative analysis                    | Gross-sectional survey  |
| Country                                | Netherlands   | USA,<br>Philadelphia  | USA, East<br>Harlem, NY  | The Netherlands                 | Sweden                                  | USA, Denver   | USA  | Sydney,<br>Australia  | Sweden                                  | Nigeria  | USA, NYC and<br>Chicago | Asia   | Utrecht,<br>Netherlands  | West Sweden              | Netherlands   | USA                             | UK                                      | Latvia  |
| Author, Year                           | Menckeberg,<br>2008 [55]  | Naimi, 2009<br>[71]   | Ponieman, 2009<br>[56]   | Bolman, 2011<br>[41]            | Emilsson, 2011<br>[47]                  | Wamboldt, 2011<br>[72]  | Brandt, 2012<br>[65]   | Foster, 2012<br>[48]  | Axelsson, 2013<br>[40]                  | Desalu, 2013<br>[46]   | Sofianou, 2013<br>[59]  | Chiu, 2014 [45]                                      | van Steenis,<br>2014 [62]  | Axelsson, 2015<br>[64]   | Koster, 2015<br>[51]  | Unni, 2016 [66]                 | De Simoni, 2017<br>[13]                 | Smits, 2017 [58]  |

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**Table 4**Themes relating to perceptions of treatment, description and examples.

| Theme                                   | Description and example  |  |  |  |  |  |  |
|---|--|--|--|--|--|--|--|
| Perceived need for treatment (necessity | Perceptions that regular inhaler treatment is necessary and effective were linked with higher adherence:   |  |  |  |  |  |  |
| beliefs)                                | " after I was in the hospital three times, I took it [ICS], just about every day!" [72]  |  |  |  |  |  |  |
|   | Conversely, beliefs that regular preventive therapy is unnecessary or ineffective were related to poor adherence:  |  |  |  |  |  |  |
|   | "If I need it [ICS], I'll take it I don't need it every day" [70]  |  |  |  |  |  |  |
|   | "It is 'bad' to take regular treatment for breathing" [73]   |  |  |  |  |  |  |
|   | "When I take my medicine, sometimes I still get sick. When I don't take my medicine, I don't get sick. I really don't see where it comes i<br>handy" [71]  |  |  |  |  |  |  |
|   | An adolescent stated that "she did not really need them and that she had been 'over-diagnosed with asthma'." [13]  |  |  |  |  |  |  |
| Concerns about treatment                | Fear and worries about short- and long-term side effects of treatment, including safety of the medication and addiction to it, were related to poorer adherence:   |  |  |  |  |  |  |
|   | " side effects are always on my mind." [69]  |  |  |  |  |  |  |
|   | "I don't really think I need it and if I was to continue using it I feel I'd get hooked on it." [71].  |  |  |  |  |  |  |
|   | "I just don't like too much of that being in my system" [70]   |  |  |  |  |  |  |
|   | "I had to take steroids, which has made me gain weight " [68]  |  |  |  |  |  |  |
| Social stigma                           | Attraction of unwanted attention due to the negative social perception of asthma and asthma medication, leading to embarrassment, reluctance to take medication and consequently poor adherence:   |  |  |  |  |  |  |
|   | " when I first told my friends in middle school that I had asthma, they thought it was a disease that they could catch from me. And the was something I went through trying to get them to believe that they're not going to get asthma from me. It's not something that I can pas on to people." [72] |  |  |  |  |  |  |
|   | Father said to son: "just tough it out, you'll be fine." [72]  |  |  |  |  |  |  |
|   | "I wouldn't take them in work; I'd wait till I'm on my own." [69]  |  |  |  |  |  |  |
| Denial of asthma                        | Denial of asthma diagnosis or the seriousness of having asthma, with adolescents holding the belief they will 'outgrow' their asthma at some point:  |  |  |  |  |  |  |
|   | "I don't think I have asthma, not real asthma." [72]   |  |  |  |  |  |  |
|   | "It's like, trying to escape from it [] maybe if I don't have to take the medicine it'll go away." [72]  |  |  |  |  |  |  |
|   | "I went through the stage of 'I haven't got asthma, that's it'." [67]  |  |  |  |  |  |  |
| Need for attention                      | Deliberate non-adherence to allow the use of poorly controlled asthma as a means of attracting attention from others:  |  |  |  |  |  |  |
|   | [from parent about their son, their son may be] "using his asthma as a form of attention seeking both at home and at school, as he migl<br>have been doing it as a cry for help for some reason." [13]   |  |  |  |  |  |  |

adherence across these studies was 48  $\pm$  18%.

In terms of adherence measures, four studies used more than one type of adherence measure [43,48,58,66]. Self-report was the most frequently used measure (75%): nine (25%) of the studies used The Medication Adherence Report Scale [33,40,41,47,51,55,56,58,59]; five (14%) The Morisky Medication Adherence Scale [45,48,58,66,68], and 14 (39%) designed study specific questions [43,44,46,49,50,52,53,57,60–62,65,67,69].

# 3.8. Themes relating to perceptions of treatment

The insights gathered from both the quantitative and qualitative studies fall into five main themes relating to patients' psychology behind their medication-taking behaviour: perceived need for treatment (necessity beliefs), concerns about treatment, social stigma, denial of asthma, and need for attention (Table 4). The latter three of these themes were found to be more prominent within the adolescent age group.

# 3.9. Perceived need for treatment

Perceived need for treatment was a theme which was noted in many studies to be a key driver of regular medication-taking. Conversely, the most important reasons for not taking asthma medications as prescribed (feeling well without treatment, irregular need, trying without medicines, denying asthma) could be categorised as doubts about the need

for treatment [40]. These necessity beliefs may arise following a negative health event, which the patient may attribute to their prior non-adherence with medication, thus acting as an impetus for behaviour change [67,72]. Smits [58] and Axelsson [64] similarly found that patients who were convinced of the necessity of their asthma treatment for their health were more likely to adhere to treatment both at present and in the future.

On the other hand, all of the 12 studies [33,40,43,47,51,55, 58,59,62–64,66] measuring patients' perceptions of their personal need for asthma treatment using the BMQ found that patients' beliefs about their necessity for treatment were associated with adherence, with stronger beliefs leading to higher adherence rates.

Doubts about the necessity of medications were also linked to a perceived lack of effectiveness of ICS, therefore justifying poor adherence. Participants in 7 (19%) of the studies [45,48,58,61,67,68,71] expressed concern about the effectiveness of their asthma medicines. These concerns related to factors such as symptoms still being experienced regardless of preventers being taken [71] and medicines not being effective when they were most needed [68].

The perceived severity of asthma also determined adherence behaviour. Patients who perceived their condition to be chronic and carrying severe consequences were more likely to believe in a need for their asthma treatment [33]. Conversely, 14 (39%) of the studies reported that patients felt they only needed to take their medication when experiencing symptoms [44,48–51,55,56,59–61,67,70,71,73] and patients considered reducing their medicines when they were

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asymptomatic ('no symptoms, no asthma belief') [59,68] or believed their asthma was not serious [31].

#### 3.10. Concerns about treatment

The most common concerns reported regarding medication adherence were: immediate and long-term side effects (58%) [13,33,39,42,44,45,48–52,55,56,58,59,61,68–71], worries about safety (19%) [39,45,46,48–50,54] and the belief that people can become addicted to, or dependent on, asthma medication (31%) [39,42, 48–50,56,61,65,68,70,71]. One study reported that general concerns regarding ICS/LABA therapy were more predictive of patients' poor adherence than specific side effects [48]. Similarly, patients' perceived concerns about side effects were more important factors influencing adherence than the actual experience of side effects (31% vs 14% of studies, respectively).

Other concerns included: dislike of the medicine [31,39,54], the belief that ICS were unnatural products that should be avoided [70], being tired of taking the medicine [40], concerns about being prescribed too many medicines [71], inconvenience of obtaining a new inhaler [45], financial concerns relating to the costs of medication [45], the belief that herbal medicines are safer than inhalers [45], the belief that respiratory drugs are unhealthy [53] and, among adolescents, the taste of their inhaler [71].

Some studies found that treatment concerns were often 'masked' behind 'forgetfulness'. Forgetfulness was a justification that was commonly made for poor adherence [13,71], however, upon further examination, negative medication beliefs were often stated to be the driver of forgetting. One study reported that busy lives coupled with negative perceptions of medication and inhaler taking were key reasons for 'forgetfulness' [13], demonstrating that 'forgetfulness' can be driven by other perceptual barriers to adherence.

# 3.11. The relationship between necessity beliefs and concerns

From the 36 studies, 15 of the studies [13,33,40,43,47,48,51,55,56,58,59,62–64,66] reported on a relationship between perceived need for treatment (necessity) with the concerns patients have about taking medicines. This was primarily established using the BMQ.

Using the BMQ, Menckeberg et al. [55] found evidence of four attitudinal types in asthma patients as defined by their necessity and concern profiles. Patients were categorised as either accepting of their medication (high necessity, low concerns), indifferent (low necessity, low concerns), ambivalent (high necessity, high concerns) or sceptical (low necessity, high concerns). Adherence to ICS (objectively assessed using pharmacy records) was highest in the accepting and ambivalent sub-groups, and equally low in both the sceptical and indifferent subgroups. The findings reveal the importance of strong necessity beliefs in adherence to ICS, but also showed a correlation between concerns and self-reported adherence [55]. Van Steenis et al. [62] also categorised patients based on the same four attitudinal beliefs, however this study only found a positive association between necessities and self-reported adherence, and no significant association with concerns.

Unni et al. [66] clustered patients into 1 of 5 clusters based on their medication beliefs and illness perceptions. These were: rationally accepting (high necessity, low concerns), illness stimulated accepting (high necessity, low concerns), indifferent (low necessity, low concerns), ambivalent (high necessity, high concerns), and sceptical (low necessity, high concerns). In accordance with Menckeberg's [55] findings, researchers in this study found that self-reported adherence was highest in the accepting clusters, and lowest in the ambivalent and sceptical clusters. Of note, was the difference between the 2 accepting clusters; the rationally accepting cluster of patients had low threatening illness perceptions, whereas the illness stimulated cluster had high threatening illness perceptions [66].

#### 3.12. Social stigma

Another theme related to asthma attracting unwanted attention in the form of social stigma related to having an illness, with 8 (22%) of the studies reporting on embarrassment as a reason contributing to poor adherence [13,42,45,65,67,69,71,72]. In one study, the social comparisons with their healthy peers around the illness led to feelings of embarrassment about their asthma and described how a parent promoted the belief that 'real men' don't take medications, unless one is 'sick' [72]. In a study by Chiu et al. [45] embarrassment related to the use of medication; patients who reported low adherence were more likely to feel uneasy using their inhaler in public places.

# 3.13. Denial of asthma

In the study by Wamboldt et al. [72], which examined the beliefs, feelings and behaviours of 26 adolescents (aged 12–20 years) in relation to inhaled asthma medication, several core beliefs related to illness denial and poor adherence were highlighted. For instance, participants held the belief that asthma may not be 'real' or 'serious', with more serious asthma warranting better adherence. Additionally, some participants in this study purposefully did not take their medication as a means for testing whether they had 'out-grown' their asthma. In accordance with the debate around whether 'out-growing' asthma was possible, others responded to this 'out-growing' belief by being adherent to their medication, as they believed that regular medication would facilitate the process by which one 'out-grows' their asthma and would aid them to get better and stronger.

# 3.14. Need for attention

Interestingly, asthma and non-adherence with treatment were highlighted as being a purposeful behaviour in one study [13], a behaviour used by adolescents as leverage to attract attention from parents and school teachers. The study suggested that teenagers purposefully did not take their medication, so they could use poorly controlled asthma as a bid for attention when stressful things were going on in their lives. This claim was furthered by observations from parents who stated that their children often used asthma as a form of attention seeking both at home and at school.

# 4. Discussion

This review is the first to explore perceptions of patients with asthma and how these relate to adherence to inhaled treatment, using quantitative and qualitative data. Several key themes were identified which relate to patients' necessity and concerns, social stigma, denial of asthma, and need for attention. Of these themes, necessity beliefs and concerns about the medication were the predominant themes influencing adherence to asthma medication. These studies highlighted that the decision-making process undertaken by patients typically involves weighing up both their perceived need for their treatment (necessity beliefs), and their concerns about their medication. This is in line with previous research which demonstrates the importance of considering patients' treatment beliefs in adherence. A large meta-analytic review was conducted by Horne et al. [74], which examined the 'Necessity-Concerns Framework (NCF)', a framework describing the relationship between necessity and concerns in relation to adherence across a range of chronic diseases [75]. The review found that the odds of being adherent were 1.7 times higher in patients with strong necessity beliefs; patients with fewer concerns about treatment had twice the odds of being adherent.

The finding that fear of side effects was a more important factor influencing adherence than the actual experience of side effects coincides with findings reported by Cooper et al. [76]. The cross-sectional study found that, while concerns about adverse effects were associated

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with low adherence to asthma treatment, the actual experience of side effects was not. This indicates that concerns about *potential* side effects and worries about long-term effects of the medicine may be more important determinants of non-adherence than the experience of adverse effects. This has significant implications for practice and research, as self-report rating scales of side effects, which are often used in practice, may be measuring a different construct (perception) rather than being a measure of actual experienced side effects.

The results of this review echo the recommendations made by Di Matteo et al. [77] and O'Carroll et al. [78] who both concluded that interventions to improve adherence should target medication beliefs held by patients. Furthermore, Di Matteo et al. reported that interventions should include three key aspects: the provision of information and knowledge regarding how to adhere, encouragement of motivation to adhere and belief in treatment, and assistance in overcoming barriers that are present. In line with these conclusions, the current findings highlight the need for improved patient information which not only educates but targets patient perceptions of asthma and treatment, and a multi-faceted approach to combat the negative misconceptions and fears many patients hold with respect to medications.

Beyond treatment beliefs, this review also found that patients with asthma often experience negative social effects from their asthma, such as social stigma and embarrassment. The two other themes identified asthma denial and need for attention - may be related to this negative social impact as these behaviours may be used by patients as a coping mechanism to manage the negative emotions associated with the illness. Indeed, previous research has shown that emotion-focused coping strategies, such as denial, are more common in patients with poor adherence [79]. These concerns also seem particularly relevant for young patients with asthma. Consistent with the systematic review by Ahmad et al. [80] on adherence to asthma treatment among adolescents, our findings suggest that adolescents may have additional barriers to adherence and engagement, such as feeling embarrassed about their asthma, social stigma and dependence on their peer group; and addressing these barriers can be highly complex as these may be influenced by psychosocial factors [81]. These findings also suggest that treatment beliefs and concerns can differ with age. Young children depend on parental attitudes towards the treatment to adhere [8], whereas in adolescence, parental responsibility decreases and the child becomes more independent, with adherence becoming reliant on selfmanagement [14]. At this stage of life, as adolescents assume more responsibility for their asthma and treatment management, psychosocial influences from their peers may become more important - a factor which adherence interventions targeted for young people may need to address.

#### 4.1. Limitations

Although all studies included in this review investigated treatment perceptions and treatment adherence, not all studies explored the relationship between these components. The studies that did investigate this though showed a significant relationship, however the conclusions drawn may have limited validity due to the limited number of studies that explicitly explored this. Another limitation of the current review is the narrative approach taken to synthesising the findings; whilst this provides in-depth insights around patient perceptions, it prevents us from establishing direct causation with adherence. Due to the descriptive nature of the review, mechanisms and drivers of the relationships identified between patient perceptions and adherence are not explored. The review does, however, provide a platform for further research to build on.

Although there is a growing body of evidence suggesting that social backgrounds can have an impact on the beliefs and barriers experienced around treatment, our search did not yield any studies that focused on ethnic minorities and differences between populations. This may be in line with other studies which also show that sociodemographic factors

do not tend to relate to adherence consistently [82]. However, there is a possibility that the generalisability of our findings may be limited as no data were found around how perceptions may vary between and within different social groups (e.g. [83]). Methods of adherence reporting also varied between studies, which limited direct comparisons between studies. The average adherence of the studies which reported percentage adherence in our review was 48%, which reflects the typical rates reported in asthma adherence literature [84,85] (usually estimated to be  $\sim$ 50%). Whilst this supports the generalisability of our findings to most asthma populations, they may not be applicable to populations with very poor adherence.

Cultural differences may also impact on adherence, however the reporting of the data in the studies precluded analysis of the effect of culture on adherence. This is because cultural effects on treatment necessity beliefs and concerns are not directly linked to study country, as these can vary between countries, and between disparate cultural groups within a country [86,87]. For example, some minority groups distrust medication which translate to higher rates of non-adherence than their counterparts of a different cultural background but of the same nationality [88], while certain cultures may show lower adherence rates than others because patients have more difficulties in accessing healthcare services [87].

# 4.2. Implications of the findings

Overall, these findings underline the importance of considering patients' perceptions of treatment and its role in influencing adherence to inhaled asthma treatment. The results indicate that adherence to asthma medication may be increased by addressing doubts about the necessity for medicines, as well as concerns about adverse effects of inhaled medication for asthma. In addition, the studies included in the review showed that patients also experience other barriers to adherence to inhaled medicines, such as social stigma and embarrassment. These findings allow us to better understand the reasons why patients may not adhere to inhaled medication in asthma, the experiences they face, and how they may manage these experiences. Together, these findings provide rich information that can inform the design of adherence interventions and highlight the need for interventions to be tailored to a patients' specific perceptual barriers.

#### 5. Conclusion

This review is the first to explore how patient perceptions are associated with treatment adherence in asthma, using quantitative and qualitative data. The findings highlight the importance of addressing patient treatment beliefs when designing adherence interventions in asthma, as attempts to improve patient self-management will be ineffective if perceptual barriers to adherence such as concerns about the medication or doubts about the necessity for treatment exist. Future research should focus on further establishing the relationship between treatment perceptions and adherence behaviour by exploring interventions that address perceptual barriers to adherence to investigate how negative perceptions around treatment can be overcome to improve adherence.

# Acknowledgements

AstraZeneca commissioned and funded Spoonful of Sugar Ltd. to undertake this review. The funders have had no influence on the content of the review.

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