

DETERMINANTS OF ASTHMA INHALER USE IN ADULTS: SYSTEMATIC REVIEW OF OBSERVATIONAL STUDIES

SUPPLEMENTARY MATERIAL 1: STUDY PROTOCOL

FIRST PROTOCOL

OBJECTIVE

To identify studies that report determinants of adherence to medication use

SEARCH - performed 6 June 2012 and updated 26 June 2014

Search Syntax: Asthma AND (adherence OR persistence OR compliance OR concordance) AND (determin* OR caus* OR influenc* OR barrier* OR factor OR factors OR reason OR reasons OR facilitat*) in All text

Databases: EMBASE & Medline (via Ovid) + PsychInfo & PsychArticles (via EBSCO)

Detailed search syntax:

For EBSCO:

TX Asthma AND (adherence OR persistence OR compliance OR concordance) AND (determin* OR caus* OR influenc* OR barrier* OR factor OR factors OR reason OR reasons OR facilitat*)

[http://search.ebscohost.com/login.aspx?direct=true&db=pdh&db=psyh&bquery=TX+\(Asthma+AND+\(adherence+OR+persistence+OR+compliance+OR+concordance\)+AND+\(determin*+OR+caus*+OR+influenc*+OR+barrier*+OR+factor+OR+factors+OR+reason+OR+reasons+OR+facilitat*\)\)&cli0=PY&clv0=199001-000001&cli1=RV&clv1=Y&dli0=DX1&dlv0=Y&dld0=psyh&type=1&site=ehost-live](http://search.ebscohost.com/login.aspx?direct=true&db=pdh&db=psyh&bquery=TX+(Asthma+AND+(adherence+OR+persistence+OR+compliance+OR+concordance)+AND+(determin*+OR+caus*+OR+influenc*+OR+barrier*+OR+factor+OR+factors+OR+reason+OR+reasons+OR+facilitat*))&cli0=PY&clv0=199001-000001&cli1=RV&clv1=Y&dli0=DX1&dlv0=Y&dld0=psyh&type=1&site=ehost-live)

Database	Limiters Applied
PsycARTICLES	Year of Publication from: 1990-; Scholarly (Peer Reviewed) Journals
PsycINFO	Year of Publication from: 1990-; Scholarly (Peer Reviewed) Journals; Exclude Dissertations

Results = 567

For Ovid:

(Asthma and (adherence or persistence or compliance or concordance) and (determin* or caus* or influenc* or barrier* or factor or factors or reason or reasons or facilitat*)).tw. = 4051

Limit to humans = 3611

Limit to 1990 – current = 3414

Deduplicated = 1975

Deduplicated ebSCO + ovid = 2324

2014 update:

EBSCO: 83; Ovid: 580; Deduplicated: 618; New: 554

CODING STUDY RELEVANCE FOR REVIEW OBJECTIVE

This first step aims to identify empirical studies that assess determinants of medication adherence in asthma. Theoretical and methodological articles and reviews are coded separately for general orientation.

Coding procedure:

1. In Endnote: use custom columns to define the following fields:

Edit → preferences → display fields

Column 1 – author

Column 2 – year

Column 3 – title

Column 4 – custom 1 - relevance

Column 5 – custom 2 - methodology

Column 6 – custom 3 - age

Column 7 – custom 4 - language & country

Column 8 – custom 5 - medication

2. For each paper, first code the relevance based on info from title and abstract (preview):

Go to quick edit → custom 1 and code:

1. **relevant** – empirical study on determinants of asthma medication use (observational studies)
2. irrelevant – empirical study on determinants of other adherence behaviours (inhaler technique, monitoring, trigger management, exacerbation management)
3. irrelevant – review on determinants of asthma medication use & other asthma care behaviours
4. irrelevant – adherence intervention or asthma management interventions targeting other outcomes
5. irrelevant – adherence measurement study
6. irrelevant – study on longitudinal relationship adherence (time1) and treatment outcomes (time2) (note: if relationship is cross-sectional or outcomes precede adherence, study qualifies as relevant!)
7. **relevant** – adherence and asthma care (observational studies examining the role of health care professionals' behaviours in patients' adherence to asthma treatment)
8. irrelevant – effectiveness/safety of an asthma-related treatment (drug treatments)
9. irrelevant – studies unrelated to asthma
10. irrelevant – measurement of burden of asthma
11. irrelevant – general guidelines for asthma
12. irrelevant – asthma-related questionnaire evaluation/development (include diagnostic tests as well)
13. irrelevant – use of treatments in clinical practice or physicians adherence to guidelines
14. irrelevant – other studies on asthma (descriptives, risk factors, ...)

3. Then code the next 5 custom fields only for relevant empirical studies.

custom 2 - methodology:

1. qualitative - interviews
2. qualitative - focus groups
3. quantitative - cross-sectional
4. quantitative - longitudinal

custom 3 - age – record age category (e.g. children/adults) or interval (years) as presented in the abstract/title

custom 4 - language & country – record language &/or country if info is presented in the abstract

custom 5 - medication – record medication type (e.g. inhaled corticosteroids, oral corticosteroids, bronchodilators, LABA, SABA) if info presented in the abstract/title

custom 6 – sample size – record sample size if info presented in the abstract/title

Examples:

Emtner, M., M. Finne, et al. (1998). "A 3-year follow-up of asthmatic patients participating in a 10-week rehabilitation program with emphasis on physical training."

Relevance: 4 (asthma management intervention)

Dykewicz, M. S. (2003). "7. Rhinitis and sinusitis."

Relevance: 9 (irrelevant – unrelated to asthma)

Lertchanaruengrith, P., P. Rattanasukol, et al. (2012). "The ability and predictive factors of preschool children to use swinghaler device."

Relevance: 2 (age as determinant of effective inhaler technique?)

Inter-rater agreement and reconciliation:

For 2 relevance categories (recoded 1 and 7 as relevant and the remaining codes as irrelevant): 304 were coded as categories 1 and 7, 144 represented agreements between the 2 coders, 160 were selected by only one of the coders (Cohen's Kappa = .60).

Reconciliation: a third coder reviewed the 160 disagreements

65 studies were selected as potentially relevant.

209 studies were included in further analyses, with the following characteristics:

Characteristics of selected articles:

Methods:	Cross-sectional: 218
	Longitudinal: 43
	Qualitative: 25
	No info: 13
Age group:	Children (<18): 103
	Adults (>18): 80
	Both: 37

	No info: 79
Country:	No info: 150
	US: 57
	Multiple countries; 9
	UK: 9
	Netherlands: 9
	(several other countries with less than 5 studies)
Medication:	Generic or unspecified: 160
	Inhaled (ICS, LABAs, SABAs): 112
	Other types (LTRA, OCS): 14
	Both inhaled and other types: 10

2014 update:

Ovid: of 554 studies, 144 were coded as relevant, 69 represented agreements between the 2 coders, 75 were selected by only one of the coders (update selection Cohen's Kappa = .56).

Reconciliation: a third coder reviewed the 75 disagreements, and selected 21 studies as potentially relevant.

90 additional studies were included in further analyses

Identification of previous systematic reviews relevant for the review objective:

Code 3 entries were examined to select articles that mention in the abstract at least a procedure for searching and selecting papers as part of the review process. The following information was extracted from the manuscripts:

- a. the objective (what adherence behaviour(s), if medication use - what type of medication, what age group, etc.)
- b. the eligibility criteria for the inclusion of papers
- c. the type of data they have extracted
- d. any conclusions relevant for the topic

Summary:

We identified only 2 reviews that focus on asthma adherence determinants and describe clear procedures for databases search, article selection, and data extraction. They both focus on ICS adherence, one in children (Drotar & Bonner, 2009), the other in adults (Charles, Ninot, & Sultan, 2011).

The first reviews both longitudinal and cross-sectional studies published before 2009 (PubMed, PsychInfo, CINAHL, EBSCO) on determinants of adherence to ICS in children with persistent asthma (up to 18 years). The authors exclude qualitative studies and studies without specific ICS adherence measurement (i.e. combined/generic measures of adherence behaviours). They identify 27 articles and report on sample size, design, race, age, determinants measurement, adherence measurement, and results. They classify the determinants into 5 domains: (1) family demographic characteristics and functioning; (2) parent characteristics; (3) child characteristics; (4) health care system and provider variables; and (5) child health outcomes. They provide methodological recommendations for future research (prospective design, hypothesis-driven, multivariate models, reliable and valid measures), and highlight gaps in the determinants literature (child behaviours and beliefs, extended family behaviours and beliefs, health care system & care process characteristics, peer influence).

The latter focuses only on studies that examine the relationship between patient illness and treatment perceptions and adherence to ICS in adults with asthma. The authors review the literature following (Horne & Weinman, 1999) article on the extended self-regulatory model in asthma, up to 2009 (Pubmed, PsycInfo, Scopus; English and French). They identify 28 articles and report the type of representation (asthma or treatment or both), the language & location, design (qualitative/quantitative, cross-sectional/longitudinal), sample (N, age, gender distribution, duration of asthma), measure of adherence (qre ad-hoc, validated qre), measurement of illness perceptions (IPQ, BMQ, ad-hoc qre, interview). They provide summary data on treatment and illness perceptions associated with adherence: illness identity, perceived control, perceptions of illness timeline, causality, and consequences, and perceptions of treatment necessity and concerns (e.g. fear of side-effects, perception of low efficacy, belief that the prescribed dose is too high, fear of dependency). They also include a methodological discussion on the assessment of adherence and illness/treatment beliefs, the strength and causal direction of the relationship between beliefs and adherence.

In conclusion, there are only two systematic literature reviews that focus specifically on determinants of asthma treatment adherence (ICS); the rest of the reviews do not provide a comprehensive examination of adherence as a main topic of investigation. Thus, there is sufficient scope for new systematic reviews on asthma adherence determinants.

However, given that first review focused on studies up to 2009 and the quality of the review is good, ***a new systematic review on asthma adherence in children is less of a priority.***

By contrast, there is a ***clear need for a systematic review on treatment adherence in adults with asthma***, as the latter study only focuses on the self-regulatory model, and we have found no review that would include a ***broader range of determinants at both patient and health care professional level, and develop a logic model of adherence determinants.*** As there are numerous studies on asthma adherence determinants in adults, the review will have to be

restricted on type of medication (focus only on ICS and LABA use), and/or methodology (focus on quantitative studies, or perhaps only on longitudinal studies).

SECOND PROTOCOL

OBJECTIVE

Based on the results of the first protocol, we decided to focus on quantitative observational studies that examine determinants of adherence to inhaled medication in adults with asthma.

STUDY CHARACTERISTICS CHECK

2 coders confirmed & completed information on the study characteristics based on full manuscripts. The disagreements were discussed between the 2 coders and reconciled by discussion.

Methods:	Qualitative interviews
	Qualitative focus groups
	Cross-sectional
	Longitudinal
Age group:	Children (<18)
	Adults (>18)
	Both (range from < 18 to > 18)
Country:	Write the country name
Medication:	Inhaled (e.g. ICS, LABAs, SABAs)
	Other types (LTRA, OCS)
	Both (inhaled and other types)
	Not specified

INCLUSION CRITERIA

Based on the study characteristics extracted, one coder applied the inclusion criteria to the selected papers.

- Peer-reviewed article in English

- Empirical observational study (exclude conference abstracts, opinion papers, reviews)
- Age >18 (include studies with age range up to 19-20 years, and from <18 to >18)
- Medication adherence as outcome or mediator
- One or more predictors of medication adherence
- Medication type: inhaled (e.g. described as ICS, LABA, SABA, 'inhaled medication', 'inhaled controllers') (exclude studies that do not specify the type of medication addressed in adherence measurement or use generic measures for adherence, i.e. not specific to inhalers)
- Asthma (irrespective of severity) (if study addresses asthma as only one of several chronic conditions, include only if it analyses the asthma sample separately)
- Quantitative methodology (cross-sectional, longitudinal)
- Developed countries (based on UN Human Development Index, very high and high; http://www.undp.org/content/dam/undp/library/corporate/HDR/2011%20Global%20HDR/English/HDR_2011_EN_Tables.pdf)

DATA EXTRACTION

Two coders perform data extraction independently. To clarify the data extraction categories and procedure, the coders discuss several articles that are not part of the review before starting the coding procedure. The 2 codes for the selected papers are compared and disagreements discussed.

Study characteristics (fill in the columns using the descriptions in the article manuscript)

- o Study objectives
- o country
- o setting (e.g. primary care, A&E, hospital)
- o population (sample size, age range, gender, asthma severity)
- o type of inhaled medication studied (ICS, LABA, etc)

Quality of methodology - criteria based on STROBE guidelines (see coding sheet)

1. Strobe 6 – Participants selection
2. Strobe 7 - Definition of variables
3. Strobe 8 - Sources of data and measurement
4. Strobe 9 - Addressing potential sources of bias
5. Strobe 10 - Study size justification
6. Strobe 11-12 – Data analysis

Measurement & results (see data_extraction.xls)

- Definition of adherence
- Assessment of adherence (e.g. validated scale - specify -, other self-report measure, prescription vs refill records, canister weighting, electronic monitoring, other – specify -)
- Adherence determinants examined (examples in the table below)
- Measurement of determinant variables (validated scale, self-report question, etc.)
- Univariate analyses – tests, results & significance
- Multivariate analyses – tests, results & significance

WHO Categorization:

Dimension	subdimensions	examples
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Social and economic factors	Family support	Financial support, emotional support, irregular supervision, child self-responsibility
Social and economic factors	Family/caregivers factors	Disorganized biologic families, family in conflict, low parental education level, family illness beliefs, number of people in household, number of adults involved in supervision
Social and economic factors	Social support	SS, low acculturation, low social functioning,
Social and economic factors	Social stigma	High stigma, no/low disclosure
Social and economic factors	Costs of treatment	Co-payment, price of medication
Social and economic factors	Prescription coverage	Health insurance
Social and economic factors	Socio-economic status	Low income, low SES, financial constraints
Social and economic factors	Employment status	Unemployment, ES
Social and economic factors	Community-related factors	Index crime rate in area of residence
Social and economic factors	Area of residence	Rural/urban; geographical location
Health care team and system-related factors	Barriers to healthcare	access to health care facilities, distance from clinic, language barriers,
Health care team and system-related factors	Medication supply	Unavailability of medication
Health care team and system-related factors	Type of health care professional	Prescription by a generalist
Health care team and system-related factors	Education provision	Clarity of information, guidelines adherence by clinicians
Health care team and system-related factors	HCP-patient communication and relationship	Quality, duration, frequency of interactions, P-P communication, patient satisfaction with care, patient involvement in decision-making, doctor empathy
Health care team and system-related factors	Follow-up	Discharge planning, follow-up planning
Condition-related factors	Presence of symptoms	Nighttime symptoms, morbidity index
Condition-related factors	Asthma severity	

Condition-related factors	Asthma exacerbations	
Condition-related factors	Health-related Quality of Life	
Condition-related factors	Clinical improvement	
Condition-related factors	Duration	
Therapy-related factors	Adverse effects	
Therapy-related factors	Patient-friendliness	Complexity, dosing frequency, number of medications, instability of regimen,
Therapy-related factors	Drug effectiveness	
Therapy-related factors	Duration	
Therapy-related factors	Type of medication	
Therapy-related factors	Self-management	
Patient-related factors	Age	
Patient-related factors	Gender	
Patient-related factors	Marital status	
Patient-related factors	Education	
Patient-related factors	Ethnicity	
Patient-related factors	Housing	
Patient-related factors	Cognitive function	
Patient-related factors	Knowledge of asthma	
Patient-related factors	Knowledge of medication	
Patient-related factors	Attitude	
Patient-related factors	General health beliefs	
Patient-related factors	Illness beliefs	
Patient-related factors	Treatment beliefs - positive	
Patient-related factors	Treatment beliefs - negative	
Patient-related factors	Self-efficacy/skills	
Patient-related factors	Forgetfulness/reminders	
Patient-related factors	Psychological profile	Personality factors, locus of control

Patient-related factors	Comorbidity	
Patient-related factors	Patient history	
Patient-related factors	Smoking status	
Patient-related factors	Symptom perception	
Patient-related factors	General health status	