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RĪGAS STRADIŅA
UNIVERSITĀTE

Dins Šmits

**TREATMENT ADHERENCE
OF ASTHMA PATIENTS
IN LATVIA AND FACTORS
RELATED TO ADHERENCE**

Summary of the Doctoral Thesis
for obtaining the degree of a Doctor of Medicine

Specialty – Medicine
Subspecialty – Public Health

Riga, 2018



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ABBREVIATIONS

| | |
|------|---|
| ACT | Asthma Control Test |
| BMQ | Beliefs about Medicines Questionnaire |
| CI | Confidence interval |
| GP | General practitioner |
| IPQ | Brief Illness Perception Questionnaire |
| MARS | Medication Adherence Report Scale |
| MMAS | Morisky Medication Adherence Scale |
| NHS | National Health Service |
| OR | <i>Odds ratio</i> |
| SPSS | Statistical Package for the Social Sciences |

INTRODUCTION

The problem of nonadherence to the therapy is one of the main reasons of insufficient asthma control. Evaluating the beliefs about asthma medication, cognitive and emotional perceptions may help to identify patients with poor adherence to treatment in clinical practice in order to provide additional attention to increase the likelihood of taking his asthma medication regularly.

Objective

The general objective of this study was to find out whether beliefs about asthma medication, cognitive and emotional factors are associated with asthma treatment and control in a sample of Latvian asthma patients in 2015. In addition, we wanted to assess whether the most commonly used questionnaires assessing treatment adherence can predict asthma control and treatment adherence.

Methods

The study population of this cross-sectional patient survey consisted of asthma patients (n=352) attending outpatient pulmonologist consultations in Riga, Latvia during September 2013 to December 2015. Beliefs about asthma medicine, cognitive and emotional factors related to asthma were determined in a cross-sectional, self-administered survey of patients attending outpatient pulmonologist practices in Riga, Latvia. Good asthma control was assessed using the Asthma control test (ACT), a validated five-item scale that reliably assesses asthma control over a recall period of four weeks. The validated Beliefs about Medicines Questionnaire (BMQ) and the Brief Illness Perception Questionnaire (brief IPQ) were used. Adherence to asthma medication was

assessed using the Morisky Medication Adherence Scale (MMAS) and two different versions of the Medication Adherence Reporting Scale (MARS). Logistic regression models were used predict poor adherence to asthma treatment.

Results

Patients who felt they had a good control of their asthma (OR 0.70; 95% CI 0.61–0.79) or were confident that their asthma medication improves illness (OR 0.84; 95% CI 0.74–0.95) had a reduced risk of poor asthma control. The more symptoms (OR 1.63; 95% CI 1.44–1.84) the asthma patients perceived or the more their illness affects their life, the higher the probability of poor asthma control (OR 1.47; 95% CI 1.31–1.65). Several questions about necessity or concerns related to pharmaceutical treatment were able to predict poor adherence according to the Morisky scale. If the patient felt that without the asthma medication his life would be impossible, his risk to have poor treatment adherence was 46% reduced (OR 0.54; 95% Confidence interval (CI) 0.33–0.89). Furthermore, asthma patients who were convinced that their health depends on asthma treatment were less likely to have poor treatment adherence (OR 0.56; 95% CI 0.32–0.97). In case the patient was concerned by the need to constantly use asthma medication or sometimes concerned by long term effects of asthma medication the odds of poor treatment adherence were 1.96 (95% CI 1.19–3.24) and 2.43 (95% CI 1.45–4.08), respectively.

Conclusions

Medication beliefs, particularly concerns and necessity of asthma treatment were associated with poor treatment adherence when assessed with the Morisky or 5-item MARS scale. We recommend to use either the MMAS or the 5-item MARS scale in Latvian asthma patients to identify patients with poor treatment adherence. Existing questionnaires assessing beliefs of medication necessity, cognitive or emotional illness perception may be used to identify patients with poor asthma control, in order to help them to identify problems of poor control and offering better treatment solutions. Thus, it may be worthwhile to assess routinely the concerns and necessity of asthma medication in patients within the Latvian health-care system to improve treatment adherence in that vulnerable population group to improve treatment outcomes.

1. IMPORTANCE OF THE PROBLEM

It has been estimated that approximately 300 million people are suffering from asthma worldwide. This number is foreseen to increase by an additional 100 million in the next ten years resulting in 400 million people living with asthma by the end of 2025. The estimated prevalence of people living with asthma ranges from 1% to 21% in adults and with up to 20% of children aged 6–7 years experiencing severe wheezing episodes within a year.

The problem of nonadherence to the therapy is a one of the main reasons of insufficient asthma control. Therefore, one of the main challenges in asthma control is adherence to pharmaceutical treatment. Generally, poor adherence is common across many chronic diseases such as asthma. Studies assessing treatment plans in asthma patients have revealed that adherence to medication range between 30 to 70%. There is common agreement that low treatment adherence explains in great parts the observed insufficient disease control in asthma patients in both Europe and worldwide as adequate asthma control requires the use of regular asthma medication. The principal goal of asthma treatment is to achieve adequate asthma control in order to prevent disease progression and functional limitations that a patient experiences due to his disease. In addition, good asthma control has been shown to improve quality of life in both children and adult patients.

Adherence is the extent to which a person's behavior – taking medication, physical activity, following a diet, visits to health professionals corresponds with agreed recommendations from a health care provider.

The overall adherence process consists of prescribing the right treatment, filling prescription in the pharmacy, taking the medication following the prescription and continuing the treatment for its whole duration.

Several factors influence treatment adherence. Some of these factors are related to complexity of the therapy, fear of side effects of drugs, method of taking the drug, dosage regimen, adverse events, knowledge about the essence of the disease and its complications, illness perception and social support. Especially, medical beliefs, cognitive and emotional perceptions have shown to be related to medical adherence. Furthermore, individual asthma management might be improved by a better understanding of the types of beliefs or illness related perceptions that are associated with low adherence to preventer medication. Preventive medication is medicines that treat the underlying pathogenetic mechanism of asthma – chronic inflammation. For adult patients controller medicines most often used are inhaled corticosteroids in monotherapy or in combination with long acting beta 2 mimetic agents. Patient’s opinion about treatment is influenced by the fact that preventer medication does not provide any immediate clinical effect that a patient would feel. Evaluating the beliefs about asthma medication, cognitive and emotional perceptions may help to identify patients with poor adherence to treatment in clinical practice in order to provide additional attention in order increase the likelihood to take his asthma medication regularly.

One of the key roles of the healthcare professional is to adjust asthma treatment to reach and maintain optimal control. Generally, good control may also depend on several other factors such as individual’s understanding of his disease, the necessity or concerns of the current treatment. However, there is limited evidence about associations between medication beliefs, illness perception and asthma control. The few studies that have assessed one of the above mentioned indicators were mainly conducted to test associations with treatment compliance related to specific medication such as corticosteroids but not with the control of the disease in general.

As it is not easy to test clinically for adherence, several questionnaires have been developed to assess adherence to medication. These questionnaires are widely used in many countries.

Limited information is available about treatment adherence and control of asthma patients in the Baltic countries such as Latvia. Furthermore, comparing how well medical beliefs, cognitive, emotional perceptions predict treatment adherence in the currently available adherence scores, may give valuable insight in the questionnaire-of-choice for the Latvian asthma population in order to be implemented in clinical practice throughout the country.

2. OBJECTIVE OF THE WORK

2.1 Study aim

The aim of this study is to assess level of adherence and its association with disease control in asthma patients in Latvia and patient factors associated with adherence to asthma treatment and control.

2.2 Tasks of research

- I. To investigate whether sociodemographic and socio-economic factors (age, sex, education level and income) are associated with asthma control and asthma treatment adherence.
- II. To investigate whether patients' beliefs about specific necessity and concerns about medicines are associated with asthma control.
- III. To investigate whether patients' beliefs about specific necessity and concerns about medicines are associated with treatment adherence to asthma medication.
- IV. To study whether beliefs about asthma medication, cognitive and emotional factors are associated with asthma control.
- V. To study whether beliefs about asthma medication, cognitive and emotional factors are associated with treatment adherence to asthma medication.
- VI. To test the association between adherence to asthma medication and asthma control.

2.3 Hypothesis of the study

There is an association between beliefs about asthma medication, cognitive and emotional factors, illness perception, sociodemographic and socio-economic factors, adherence to medication and asthma control in Latvian asthma patients. Study concept is shown in Figure 1.

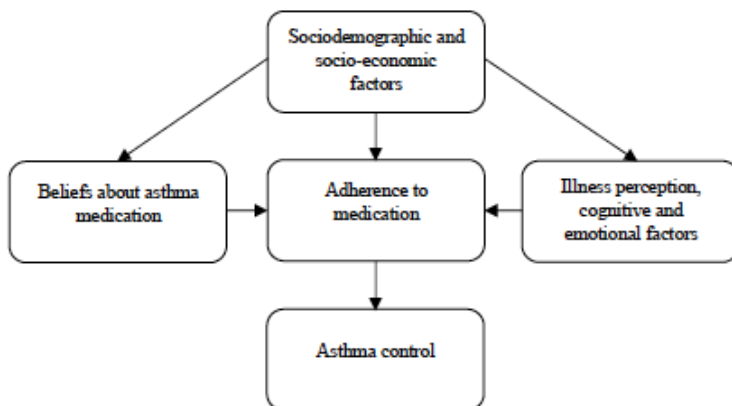


Figure 2.1. **Study concept**

3. MATERIAL AND METHODS

3.1 Structure of the study

3.1.1 Design and study participants

The study population of this cross-sectional patient survey consisted of asthma patients attending outpatient pulmonologist consultations in Latvia during September 2013 to December 2015. Patients who had been prescribed controller medication – inhaled corticosteroids in monotherapy or in combination therapy for at least 12 months were included in the study. Patients who were not prescribed to constantly use a controller medication – inhaled corticosteroids in monotherapy or in combination therapy for at least 12 months or patients who were prescribed to use controller medication intermittently, as well as children below age of 15 were excluded. Latvian patients according to Latvian regulations (regulation of the Cabinet of Ministers No. 1529) receive their initial disease diagnosis and treatment initiation in a pulmonologist practice. They get there in larger part by a referral by a general practitioner (GP) or by direct patient contact. The majority of GPs refer their asthma patients to a specialist at least once a year for control. The role of GPs within the Latvian health care system is mainly to ensure that a patient follows the treatment regime set forth by the specialist. Only patients referred by a GP to a NHS registered practice can get their medication reimbursed by NHS. Asthma patients receive their medication within the reimbursement system and only very few patients would be treated outside the reimbursement system. In a first step, a list of all pulmonologists from the database of the National Health Service (NHS) of the medical doctors that have contractual rights to prescribe reimbursed medicines was acquired. Then, pulmonologists in 15 medical centers and hospitals in Riga and Latvia were invited to join the study and all of these practices agreed to participate (convenience sample). Pulmonologists of these practices were advised to invite

their patients to join the survey. A total of 66 pulmonologists out of total of 129 pulmonologists that work within a contract with NHS were working in these medical centers. We assumed these 15 practices to be representative of all pulmonologist practices in Latvia.

3.1.2 Sample size calculations

The sample size was calculated to detect a prevalence of poor asthma control of 50% with a margin of error of 5%, and a power of 95%. As no information was available about the prevalence of poor asthma control in Latvia, we set poor asthma control to 50% to guarantee a big enough sample size to test our study question as a prevalence close to 50% require by definition a bigger sample size. The total sample size needed and respectively studied was 352 people. Only patients that have been using asthma medication for at least one year were included in this study.

3.2 Structure of the study

A self-administered questionnaire was used to assess socio-demographic and economic factors such as age, education, income and sex. For education, there were four groups – basic education, secondary education, vocational education and higher education (includes bachelor, master and doctoral degrees). For net personal income, there were four groups – less than 300 EUR per month, between 300 and 550 EUR per month, between 550 and 750 EUR per month and more than 750 EUR per month. The majority (33.8%) of the patients had higher education and were earning at least 300 euros per month. Two out of three patients (63.3%) were using corticosteroids in monotherapy and one third (33.3%) a combination therapy consisting of corticosteroids and a beta 2 mimetic

drug. Age, income and education were statistically significantly differently distributed between men and women. Beliefs about medication were measured using Beliefs About Medication Questionnaire, BMQ. Treatment adherence was measured using Morisky Medication Adherence Scale, MMAS and two versions of Medication Adherence Reporting Scale, MARS. Beliefs about disease, cognitive and emotional factors were measured by The Brief Illness Perception Questionnaire, B-IPQ and Disease perception questionnaire. Level of disease control was determined using Asthma Control Test, ACT.

Table 3.1

Baseline characteristics of the study sample

| | Men | Women | Total | |
|--|----------------|-----------------|----------------|----------------|
| | (n= 85) | (n= 264) | (n=352) | p-value |
| Age, mean (SD) | 53.7 (17.4) | 58.7 (16.6) | 57.5 (16.9) | 0.017 |
| Education, % | – | – | – | 0.006 |
| Basic | 3.5 | 7.5 | 6.5 | – |
| Secondary | 23.3 | 27.1 | 26.1 | – |
| Professional | 47.7 | 28.9 | 33.5 | – |
| Higher | 25.6 | 36.5 | 33.8 | – |
| Income, % | – | – | – | 0.005 |
| < 300 €/month | 16.7 | 25.3 | 23.2 | – |
| 300–550 €/month | 36.9 | 48.2 | 45.5 | – |
| 550–750 €/month | 28.6 | 18.3 | 20.8 | – |
| > 750 €/month | 17.9 | 8.2 | 10.6 | – |
| Asthma medication, % | – | – | – | – |
| Inhaled Corticosteroids | 62.8 | 63.4 | 63.3 | 1.00 |
| Inhaled Corticosteroids+beta 2 mimetic | 33.7 | 33.2 | 33.3 | 1.00 |
| Poor asthma control, % | 62.8 | 66 | 65.3 | 0.604 |
| Poor treatment adherence, % | – | – | – | – |
| Morisky scale | 72.1 | 69.4 | 70.1 | 0.686 |
| MARS (5-item) scale | 58.1 | 68.7 | 66.1 | 0.089 |
| MARS (10-item) scale | 75.6 | 69 | 70.6 | 0.278 |

3.2.1 Asthma control

Level of asthma control was assessed using the Asthma Control Test (ACT), a validated five-item scale that reliably assesses asthma control over a recall period of four weeks. The ACT consists of the following questions:

- “How much of the time did your asthma keep you from getting as much done at work, school or at home?”
- “How often have you had shortness of breath?”
- “How often did your asthma symptoms wake you up at night or earlier than usual in the morning?”
- “How often have you used your rescue inhaler or nebulizer medication?” and
- “How would you rate your asthma control?”

Each item was scaled from 1 to 5, and by summing the response values a scale score was calculated ranging from poor (5) to total (25) control. Weight of all questions in ACT questionnaire is regarded as equal. ACT scores have shown to be well correlated with baseline per cent predicted forced expiratory volume. A score of 19 points and less were regarded as inadequate asthma control but 20 and more points were regarded as good disease control.

3.2.2 Assessment of adherence

World Health Organization in 2003 defined adherence to treatment as the extent to which a person’s behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider.

Adherence to asthma medication was assessed using the Morisky Medication Adherence Scale (MMAS) and two different versions of the Medication Adherence Reporting Scale (MARS). The MMAS is a self-report

tool, it was used to assess asthma medication adherence. The MMAS is an eight-item questionnaire that measures medication compliance on a scale of 0–11, with lower scores indicating better adherence. The total MMAS score was obtained by summing ratings for all scale items. Seven items were answered by either yes (score = 1) or no (score = 0) responses, and one item was assessed using 5 point Likert-type responses ranging from “usually” to “all the time” (usually = 0; all the time = 4). The MMAS has been used across many chronic diseases, including asthma, as a self-reported measure of adherence to medications and has demonstrated to be reliable and a valid tool for estimating compliance. The long version of the MARS is a validated 10-item questionnaire that has shown to have good internal, construct, and criterion validity, including correlations with objective measures of adherence (electronic monitoring and pharmacy dispensing data). The MARS contains items that measure intentional (“I avoid using it if I can”) and unintentional (“I forget to use it”) nonadherence and these questions are phrased such that nonadherence is considered common to minimize social desirability bias. Medication use is rated on a 5-point Likert scale. The short version of the MARS is a five-item self-report scale for assessment of adherent behavior that includes assessment of unintentional non-adherent behavior (“I forgot to take them”, item 1) and intentional non-adherent behavior:

- “I alter the dose”, item 2.
- “I stop taking them for a while”, item 3.
- “I decide to miss out a dose”, item 4.
- “I take less than instructed”, item 5.

Each item was answered using a five-graded response scale, ranging from very often (1) to never (5). Low scores indicate low levels of adherent behavior. During analysis the 5-item and 10-item versions were analyzed separately to detect data consistency of results.

3.2.3 Medication beliefs

Medication beliefs were assessed using the five items of greatest relevance to asthma medication adapted from the Beliefs about Medication Questionnaire (BMQ), a validated tool across many disease conditions. The specific–necessity scale contains 5 items that assess patients’ beliefs about specific necessity to take prescribed chronic medications. All three questions assessing patients’ beliefs about specific necessity to take prescribed chronic medications or concerns were selected from the original BMQ. All belief items had Likert scale responses.

3.2.4 Illness perception

The Brief Illness Perception Questionnaire (brief IPQ) was used to obtain information on illness perception of the study participants. The Brief IPQ consists of nine items and a causal question.

All of the items except the causal question are rated using a 0 to 10 response scale.

Five of the items assess cognitive illness representations:

- consequences (item 1),
- timeline (item 2),
- personal control (item 3),
- treatment control (item 4),
- and identity (item 5).

Two of the items assess emotional representations:

- concern (item 6) and
- emotions (item 8).

One item assesses illness comprehensibility (item 7). Assessment of the causal representation is by an open-ended response, which asks patients to list the three most important causal factors in their illness (item 9). IPQ was used as a continuous variable. For every unit increase in IPQ, the odds of the outcome event (i.e., MMAS, MARS) increased by the odds. For instance, for one unit increase in IPQ for “How much does your illness affect your life” the probability of poor asthma control increased by 47% (or 1.47-fold).

3.3 Ethical considerations

Methods and patient consent form were approved in writing by the P. Stradins Clinical University Hospital Development Society Ethics committee for clinical research (original name in Latvian: P. Stradiņa Klīniskās universitātes slimnīcas Attīstības biedrības klīniskās izpētes ētikas komiteja). A written consent was obtained from all participants involved in the study.

3.4 Statistical analysis

The Statistical Package for the Social Sciences (SPSS) IBM 21.0 was used to analyse the data. Means, standard deviations, and frequencies are presented to describe the characteristics of the study sample.

ACT test interpretation:

- A cut-off point of ≤ 19 was defined to indicate poorly controlled asthma,
- and scores of 20 points or more corresponded to well-controlled asthma.

A cutoff point of > 6 (MARS-5), > 14 (MARS-10), > 1 (MMAS) was used to define poor medical adherence. These cut-off points were chosen according to the ones proposed in previous studies.

The answers of the BMQ were dichotomized into:

- (i) “I agree/I completely agree” and
- (ii) “Not sure/I disagree/I completely disagree” similar to the methods of previous study to ease clinical application.

The logistic regression analyses were first conducted for each variable alone. In the multivariate logistic analysis the outcome variable was controlled for age, income and educational level. The odds ratio (OR) and respective 95% confidence interval (CI) are presented for all models. The OR presented in the tables are for the “I agree/I completely agree” categories with the “Not sure/I disagree/I completely disagree” category as reference group. The validity of each logistic regression model was assessed by the Hosmer-Lemeshow test.

4. RESULTS

4.1 Sociodemographic and socio-economic factors in regard poor asthma control and poor treatment adherence

None of the sociodemographic or socio-economic factors were predictors of poor treatment adherence according to the Morisky or the MARS 10-item scale (Table 4.1, 4.2 and 4.3). Further adjustment did not change the findings of the unadjusted model. The problem in clinical practice is poor adherence and therefore analysis has focused on factors associated with poor adherence.

Table 4.1

Associations of socio-demographic and socio-economic factors with poor treatment adherence in asthma patients using the Morisky scale

| | Morisky scale | | OR | (95% CI) |
|--|-----------------|-----------------------|------|-------------|
| | Unadjusted | Adjusted ³ | | |
| | OR ¹ | (95% CI) ² | OR | (95% CI) |
| Age | 1 | (0.98–1.01) | 1 | (0.98–1.01) |
| Female sex | 0.88 | (0.51–1.50) | 0.86 | (0.48–1.54) |
| Education | – | – | – | – |
| Basic or secondary | 1 | Ref ⁴ | 1 | Ref |
| Professional | 1.43 | (0.82–2.51) | 1.55 | (0.86–2.78) |
| Higher | 1.45 | (0.83–2.53) | 1.72 | (0.92–3.22) |
| Income | – | – | – | – |
| < 300 €/month | 1 | Ref | 1 | Ref |
| 300–550 €/month | 0.83 | (0.45–1.52) | 0.74 | (0.40–1.38) |
| 550–750 €/month | 0.67 | (0.33–1.34) | 0.51 | (0.24–1.09) |
| > 750 €/month | 1.27 | (0.50–3.22) | 0.92 | (0.33–2.54) |
| Asthma medication | – | – | – | – |
| Inhaled Corticosteroids | 1.34 | (0.83–2.16) | 0.82 | (0.49–1.36) |
| Inhaled Corticosteroids+beta 2 mimetic | 1.04 | (0.64–1.69) | 0.85 | (0.51–1.41) |

¹Odds ratio; ²Confidence interval; ³adjusted for age, sex, education and income;

⁴Reference group

Table 4.2

Associations of socio-demographic and socio-economic factors with poor treatment adherence in asthma patients using the MARS 5-item scale

| | MARS (5-item) | | | | |
|-------------------------------|-----------------|-----------------------|-----------------------|-------------|------|
| | Unadjusted | | Adjusted ³ | | OR |
| | OR ¹ | (95% CI) ² | OR | (95% CI) | |
| Age | 0.98 | (0.97–1.00) | 0.98 | (0.96–0.99) | 1 |
| Female sex | 1.58 | (0.96–2.60) | 1.87 | (1.07–3.27) | 0.72 |
| Education | – | – | – | – | – |
| Basic or secondary | 1 | Ref ⁴ | 1 | Ref | 1 |
| Professional | 1.79 | (1.03–3.11) | 1.91 | (1.05–3.45) | 1.23 |
| Higher | 1.27 | (0.75–2.16) | 1.25 | (0.68–2.29) | 0.97 |
| Income | – | – | – | – | – |
| < 300 €/month | 1 | Ref | 1 | Ref | 1 |
| 300–550 €/month | 0.86 | (0.48–1.55) | 0.89 | (0.48–1.65) | 0.86 |
| 550–750 €/month | 0.8 | (0.41–1.59) | 0.66 | (0.31–1.43) | 0.62 |
| > 750 €/month | 0.87 | (0.38–2.03) | 0.75 | (0.29–1.93) | 0.77 |
| Asthma medication | – | – | – | – | – |
| Corticosteroids | 0.57 | (0.35–0.91) | 0.56 | (0.33–0.93) | 0.69 |
| Corticosteroids+beta2 mimetic | 1.93 | (1.18–3.16) | 2.04 | (1.19–3.49) | 1.18 |

¹Odds ratio; ²Confidence interval; ³adjusted for age, sex, education and income;

⁴Reference group

Table 4.3

Associations of socio-demographic and socio-economic factors with poor treatment adherence in asthma patients using the MARS 10-item scale

| | MARS (10-item) | | | |
|--------------------------------|-----------------|-----------------------|-----------------------|-------------|
| | Unadjusted | | Adjusted ³ | |
| | OR ¹ | (95% CI) ² | OR | (95% CI) |
| Age | 1 | (0.99–1.02) | 1 | (0.98–1.01) |
| Female sex | 0.72 | (0.41–1.26) | 0.65 | (0.35–1.18) |
| Education | – | – | – | – |
| Basic or secondary | 1 | Ref ⁴ | 1 | Ref |
| Professional | 1.23 | (0.69–2.17) | 1.15 | (0.63–2.08) |
| Higher | 0.97 | (0.56–1.69) | 1.16 | (0.62–2.17) |
| Income | | | | |
| < 300 €/month | 1 | Ref | 1 | Ref |
| 300–550 €/month | 0.86 | (0.46–1.58) | 0.81 | (0.43–1.53) |
| 550–750 €/month | 0.62 | (0.31–1.26) | 0.54 | (0.25–1.17) |
| > 750 €/month | 0.77 | (0.32–1.84) | 0.64 | (0.25–1.69) |
| Asthma medication | | | | |
| Corticosteroids | 0.69 | (0.42–1.12) | 0.72 | (0.43–1.21) |
| Corticosteroids+beta 2 mimetic | 1.18 | (0.72–1.93) | 1.11 | (0.66–1.86) |

¹Odds ratio; ²Confidence interval; ³adjusted for age, sex, education and income;

⁴Reference group

A higher level of education seemed to increase the odds to have poor treatment adherence, but the association was not statistically significant. However, when the MARS 5-item scale was used, increasing age (OR 0.98 (95% confidence interval (CI) 0.97–1.00) and monotherapy with corticosteroids (OR 0.57; 95% CI 0.35–0.91) reduced the odds of poor treatment adherence. Moreover, professional education level (OR 1.79; 95% CI 1.03–3.11) or the combined use of corticosteroids and beta 2 mimetics (OR 1.93; 95% CI 1.18–3.16) increased the odds of poor treatment adherence.

Table 4.4

Odds ratio of socio-demographic and economic factors in regard poor treatment adherence

| | Morisky scale | |
|--|-----------------|------------------------|
| | Univariate | |
| | OR ^a | (95% CI ^b) |
| Age | 1 | (0.98–1.01) |
| Female sex | 0.88 | (0.51–1.50) |
| Education | – | – |
| Basic or secondary | 1 | Ref |
| Professional | 1.43 | (0.82–2.51) |
| Higher | 1.45 | (0.83–2.53) |
| Income | – | – |
| < 300 €/month | 1 | Ref |
| 300–550 €/month | 0.83 | (0.45–1.52) |
| 550–750 €/month | 0.67 | (0.33–1.34) |
| > 750 €/month | 1.27 | (0.50–3.22) |
| Asthma medication | – | – |
| Inhaled Corticosteroids | 1.34 | (0.83–2.16) |
| Inhaled Corticosteroids+beta 2 mimetic | 1.04 | (0.64–1.69) |

^aOdds ratio; ^bConfidence interval

Table 4.5 shows the associations of different asthma medication adherence scores with poor asthma control in the study sample. None of the three adherence scores was able to predict poor disease control in Latvian asthma patients.

Associations of different asthma medication adherence¹ scores with poor asthma control²

| | Univariate | | Multivariate ⁵ | |
|----------------|-----------------|------------------------|---------------------------|-------------|
| | OR ³ | (95% CI ⁴) | OR | (95% CI) |
| Men | – | – | – | – |
| MARS (5-item) | 0.39 | (0.15–1.00) | 0.36 | (0.12–1.09) |
| MARS (10-item) | 1.05 | (0.38–2.90) | 1.41 | (0.43–4.65) |
| Morisky | 1.02 | (0.38–2.69) | 1.48 | (0.49–4.50) |
| Women | – | – | – | – |
| MARS (5-item) | 1.04 | (0.60–1.79) | 1.2 | (0.67–2.17) |
| MARS (10-item) | 1.68 | (0.98–2.87) | 1.61 | (0.91–2.86) |
| Morisky | 1.09 | (0.63–1.89) | 0.94 | (0.52–1.70) |
| All | – | – | – | – |
| MARS (5-item) | 0.81 | (0.51–1.30) | 0.87 | (0.52–1.44) |
| MARS (10-item) | 1.5 | (0.93–2.40) | 1.43 | (0.87–2.36) |
| Morisky | 1.07 | (0.67–1.72) | 0.99 | (0.60–1.66) |

¹> 6 (MARS-5), >14 (MARS-10), >1 (MMAS) was used to define poor medical adherence; ≤19 for the ACT was defined to indicate poorly controlled asthma;

³Odds ratio; ⁴Confidence interval; ⁵adjusted for age, education and income

4.2 Patients' beliefs about specific necessity and concerns about medicines in regard poor asthma control

Table 4.6 shows the results of the logistic regression analysis of the different beliefs about medicines in regard of poor asthma control. Agreement on necessity of asthma medication was statistically significantly related to an increase in the odds of poor asthma control. The increase in risk of poor asthma control was almost three-fold in patients who were convinced that their life fully depends on their medication (OR 2.89; 95% CI 1.78–4.71). In addition, beliefs such as “without asthma medication life would be impossible” (OR 2.69; 95% CI 1.56–4.12) or “without asthma medication the patient would be very ill” (OR 2.69; 95% CI 1.66–4.38) were significantly related to poor asthma control after adjustment for age, education and income. Finally, if the patient was concerned by the need to use his asthma medication constantly, the probability

of poor asthma control doubled (OR 1.94; 95% CI 1.19–3.17) compared to those without concerns. Neither were concerns regarding long-term use nor understanding of ones asthma medication statistically significantly related with poor asthma control.

Table 4.6

Odds ratio of patients’ beliefs about specific necessity and concerns about medicines in regard poor asthma control

| | Univariate | | Multivariate ³ | |
|---|-----------------|-----------------------|---------------------------|-------------|
| | OR ¹ | (95% CI) ² | OR | (95% CI) |
| Necessity | – | – | – | – |
| My health is fully dependent on the asthma medication | 2.85 | (1.80–4.50) | 2.89 | (1.78–4.71) |
| Without asthma medication my life would be impossible | 2.51 | (1.60–3.93) | 2.53 | (1.56–4.12) |
| Without my asthma medication I would be very ill | 2.75 | (1.75–4.33) | 2.69 | (1.66–4.38) |
| My future health depends on my asthma medication | 1.63 | (1.02–2.60) | 1.54 | (0.94–2.54) |
| Controlling my asthma medication prevents health deterioration | 1.00 | (0.57–1.76) | 0.91 | (0.49–1.68) |
| Concerns | – | – | – | – |
| I am concerned by the need to constantly use my asthma medication | 1.90 | (1.20–3.01) | 1.94 | (1.19–3.17) |
| I am sometimes concerned by long term effects of my asthma medication | 1.45 | (0.92–2.27) | 1.33 | (0.82–2.15) |
| My asthma medication is incomprehensible to me | 1.00 | (0.58–1.72) | 0.82 | (0.45–1.47) |

¹Odds ratio; ²Confidence interval; ³adjusted for age, education and income

4.3 The association between cognitive and emotional illness questionnaire and poor asthma control

Several cognitive and emotional illness indicators predicted poor asthma control in the study patients regardless of controlling for other covariates (Table 4.7). The more the asthma patients perceived that their illness affect their

life, the higher the probability of poor asthma control (OR 1.47; 95% CI 1.31–1.65). On one hand, estimated duration, concern and emotional affection of asthma increased the odds of poor asthma control. On the other, a better self-perception of asthma control (OR 0.7; 95% CI 0.61–0.79) or considering that the current treatment is helpful (OR 0.84; 95% CI 0.74–0.95) were related to improved asthma control. Understanding their illness did not affect asthma control in the study population.

Table 4.7

Odds ratio of each of the eight items of the cognitive and emotional illness questionnaire in regard probability of poor asthma control

| | Univariate | | Multivariate ³ | |
|---|-----------------|-----------------------|---------------------------|-------------|
| | OR ¹ | (95% CI) ² | OR | (95% CI) |
| How much does your illness affect your life? | 1.46 | (1.32–1.62) | 1.47 | (1.31–1.65) |
| How long do you think your illness will continue? | 1.14 | (1.05–1.25) | 1.16 | (1.05–1.27) |
| How much control do you feel you have over your illness? | 0.69 | (0.62–0.78) | 0.70 | (0.61–0.79) |
| How much do you think your treatment can help your illness? | 0.84 | (0.75–0.95) | 0.84 | (0.74–0.95) |
| How much do you experience symptoms from your illness? | 1.65 | (1.47–1.85) | 1.63 | (1.44–1.84) |
| How concerned are you about your illness? | 1.24 | (1.15–1.34) | 1.23 | (1.14–1.34) |
| How well do you feel you understand your illness? | 1.00 | (0.92–1.08) | 1.00 | (0.92–1.09) |
| How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?) | 1.34 | (1.24–1.45) | 1.36 | (1.25–1.48) |

¹Odds ratio; ²Confidence interval; ³adjusted for age, education and income

4.4 Association of cognitive and emotional illness indicators and poor treatment adherence

The associations of cognitive and emotional illness indicators and poor treatment adherence measured using three different scores in asthma patients in Latvia are presented in Table 4.8, 4.9 and 4.10. None of the eight items of the brief IPQ was a statistically significant predictor of poor treatment adherence in any of the three adherence scores. Adjustment for age, education or income did not alter the results.

Table 4.8

Associations of cognitive and emotional illness indicators and poor treatment adherence in asthma patients in Latvia using the Morisky scale

| | Morisky scale | | | |
|---|-----------------|-----------------------|-----------------------|-------------|
| | Unadjusted | | Adjusted ³ | |
| | OR ¹ | (95% CI) ² | OR | (95% CI) |
| How much does your illness affect your life? | 0.98 | (0.90–1.07) | 0.99 | (0.89–1.08) |
| How long do you think your illness will continue? | 0.96 | (0.87–1.06) | 0.97 | (0.88–1.07) |
| How much control do you feel you have over your illness? | 0.94 | (0.85–1.04) | 0.95 | (0.85–1.06) |
| How much do you think your treatment can help your illness? | 0.99 | (0.89–1.10) | 1 | (0.89–1.12) |
| How much do you experience symptoms from your illness? | 1.04 | (0.95–1.13) | 1.03 | (0.94–1.13) |
| How concerned are you about your illness? | 1.02 | (0.95–1.10) | 1.03 | (0.96–1.11) |
| How well do you feel you understand your illness? | 1.05 | (0.97–1.14) | 1.05 | (0.96–1.14) |
| How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?) | 1.03 | (0.97–1.11) | 1.05 | (0.98–1.13) |

¹Odds ratio; ²Confidence interval; ³adjusted for age, education and income

Table 4.9

**Associations of cognitive and emotional illness indicators and poor
treatment adherence in asthma patients in Latvia using the
MARS 5-item scale**

| | MARS (5-item) | | | |
|---|-----------------------|-----------------------------|-----------------------------|-----------------|
| | Unadjusted | | Adjusted³ | |
| | OR¹ | (95% CI²) | OR | (95% CI) |
| How much does your illness affect your life? | 0.96 | (0.88–1.05) | 0.96 | (0.88–1.05) |
| How long do you think your illness will continue? | 0.96 | (0.87–1.05) | 0.98 | (0.89–1.08) |
| How much control do you feel you have over your illness? | 0.98 | (0.89–1.08) | 0.98 | (0.88–1.08) |
| How much do you think your treatment can help your illness? | 0.96 | (0.86–1.07) | 0.96 | (0.85–1.07) |
| How much do you experience symptoms from your illness? | 1.01 | (0.93–1.10) | 1.01 | (0.92–1.11) |
| How concerned are you about your illness? | 0.99 | (0.93–1.07) | 1.01 | (0.94–1.09) |
| How well do you feel you understand your illness? | 1.06 | (0.98–1.15) | 0.98 | (0.97–1.15) |
| How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?) | 1.03 | (0.96–1.10) | 1.03 | (0.96–1.11) |

¹Odds ratio; ²Confidence interval; ³adjusted for age, education and income

Table 4.10

Associations of cognitive and emotional illness indicators and poor treatment adherence in asthma patients in Latvia using the MARS 10-item scale

| | MARS (10-item) | | | |
|---|-----------------------|-----------------|-----------------|-----------------|
| | Unadjusted | | Adjusted | |
| | OR | (95% CI) | OR | (95% CI) |
| How much does your illness affect your life? | 0.96 | (0.88–1.05) | 0.96 | (0.88–1.05) |
| How long do you think your illness will continue? | 0.96 | (0.87–1.05) | 0.98 | (0.89–1.08) |
| How much control do you feel you have over your illness? | 0.98 | (0.89–1.08) | 0.98 | (0.88–1.08) |
| How much do you think your treatment can help your illness? | 0.96 | (0.86–1.07) | 0.96 | (0.85–1.07) |
| How much do you experience symptoms from your illness? | 1.01 | (0.93–1.10) | 1.01 | (0.92–1.11) |
| How concerned are you about your illness? | 0.99 | (0.93–1.07) | 1.01 | (0.94–1.09) |
| How well do you feel you understand your illness? | 1.06 | (0.98–1.15) | 1.05 | (0.97–1.15) |
| How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?) | 1.03 | (0.96–1.10) | 1.03 | (0.96–1.11) |

4.5 Association between medication beliefs and poor treatment adherence

Differences were found in regard associations between beliefs about medication and poor treatment adherence according to adherence scales (Table 4.11, 4.12 and 4.13). Whereas beliefs about medication were not associated with poor treatment adherence on the MARS 10-item scale, several questions about necessity or concerns related to pharmaceutical treatment were able to predict poor adherence according to the Morisky scale (Table 4.5). If the patient felt that without his asthma medication his/her life would be impossible, his risk to have poor treatment adherence was 46% reduced (OR 0.54; 95%

Confidence interval (CI) 0.33–0.89). Furthermore, asthma patients who were convinced that their health depends on the asthma treatment were less likely to have poor treatment adherence (OR 0.56; 95% CI 0.32–0.97). Each of the three concerns about medication questions was a statistically significant predictor of poor treatment adherence. In case the patient was concerned by the need to constantly use asthma medication or sometimes concerned by long-term effects of their asthma medication the odds of poor treatment adherence were 1.96 (95% CI 1.19–3.24) and 2.43 (95% CI 1.45–4.08), respectively. Furthermore, patients who felt that their asthma medication is incomprehensible to them had a two-fold increase in risk of poor treatment adherence. In regard MARS 5-item scale, only two variables were able to predict poor treatment adherence. The risk of poor adherence was 58% reduced (95% CI 0.24–0.74) if the patients felt that their future health depends on their asthma medication. In addition, concerns about long-term effects of asthma medication increased the risk of poor treatment adherence two-fold (95% CI 1.22–3.27).

Table 4.11

Associations between medications beliefs and poor treatment adherence measured in asthma patients in Latvia using the Morisky scale

| | Morisky scale | | | |
|---|-----------------|------------------------|-----------------------|-------------|
| | Unadjusted | | Adjusted ^c | |
| | OR ^a | (95% CI ^b) | OR | (95% CI) |
| Necessity | – | – | – | – |
| My health is fully dependent on the asthma medication | 0.67 | (0.41–1.10) | 0.67 | (0.40–1.12) |
| Without asthma medication my life would be impossible | 0.53 | (0.33–0.85) | 0.54 | (0.33–0.89) |
| Without my asthma medication I would be very ill | 0.59 | (0.36–0.96) | 0.61 | (0.36–1.02) |
| My future health depends on my asthma medication | 0.53 | (0.31–0.90) | 0.56 | (0.32–0.97) |

Table 4.11 continued

| | | | | |
|---|------|-------------|------|-------------|
| Controlling my asthma medication prevents health deterioration | 0.58 | (0.30–1.09) | 0.66 | (0.34–1.27) |
| Concerns | – | – | – | – |
| I am concerned by the need to constantly use my asthma medication | 2.03 | (1.24–3.30) | 1.96 | (1.19–3.24) |
| I am sometimes concerned by long term effects of my asthma medication | 2.3 | (0.27–0.71) | 2.43 | (1.45–4.08) |
| My asthma medication is incomprehensible to me | 2.01 | (1.06–3.78) | 1.97 | (1.02–3.80) |

^aOdds ratio; ^bConfidence interval; ^cadjusted for age, education and income

Table 4.12

Associations between medications believes and poor treatment adherence measured in asthma patients in Latvia using the MARS 5-item scale

| | MARS (5-item) | | | |
|---|-----------------|------------------------|-----------------------|-------------|
| | Unadjusted | | Adjusted ^c | |
| | OR ^a | (95% CI ^b) | OR | (95% CI) |
| Necessity | | | | |
| My health is fully dependent on the asthma medication | 0.58 | (0.36–0.94) | 0.61 | (0.37–1.01) |
| Without asthma medication my life would be impossible | 0.64 | (0.41–1.01) | 0.62 | (0.38–1.01) |
| Without my asthma medication I would be very ill | 0.71 | (0.45–1.12) | 0.72 | (0.44–1.19) |
| My future health depends on my asthma medication | 0.42 | (0.25–0.70) | 0.42 | (0.24–0.74) |
| Controlling my asthma medication prevents health deterioration | 0.51 | (0.28–0.96) | 0.61 | (0.32–1.17) |
| Concerns | – | – | – | – |
| I am concerned by the need to constantly use my asthma medication | 1.69 | (1.07–2.68) | 1.59 | (0.98–2.57) |
| I am sometimes concerned by long term effects of my asthma medication | 1.89 | (1.19–3.01) | 2 | (1.22–3.27) |
| My asthma medication is incomprehensible to me | 1.03 | (0.60–1.79) | 1.27 | (0.70–2.29) |

^aOdds ratio; ^bConfidence interval; ^cadjusted for age, education and income

Associations between medications believes and poor treatment adherence measured in asthma patients in Latvia using the MARS 10-item scale

| | MARS (10-item) | | | |
|---|-----------------|------------------------|-----------------------|-------------|
| | Unadjusted | | Adjusted ^c | |
| | OR ^a | (95% CI ^b) | OR | (95% CI) |
| Necessity | – | – | – | – |
| My health is fully dependent on the asthma medication | 1.07 | (0.67–1.73) | 1.03 | (0.63–1.70) |
| Without asthma medication my life would be impossible | 0.99 | (0.62–1.55) | 0.92 | (0.56–1.50) |
| Without my asthma medication I would be very ill | 0.88 | (0.55–1.41) | 0.85 | (0.52–1.40) |
| My future health depends on my asthma medication | 0.64 | (0.38–1.07) | 0.58 | (0.34–1.01) |
| Controlling my asthma medication prevents health deterioration | 0.53 | (0.28–1.02) | 0.53 | (0.27–1.05) |
| Concerns | – | – | – | – |
| I am concerned by the need to constantly use my asthma medication | 1.36 | (0.84–2.18) | 1.33 | (0.82–2.16) |
| I am sometimes concerned by long term effects of my asthma medication | 1.44 | (0.89–2.31) | 1.48 | (0.90–2.42) |
| My asthma medication is incomprehensible to me | 0.86 | (0.49–1.50) | 0.81 | (0.45–1.46) |

^aOdds ratio; ^bConfidence interval; ^cadjusted for age, education and income

CONCLUSIONS

1. Sociodemographic and socio-economic factors (age, sex, education level and income) were not associated with asthma control and asthma treatment adherence.
2. Medication beliefs, particularly acceptance of necessity and concerns about constant use of asthma treatment were associated with increased risk of poor disease control.
3. Medication beliefs, particularly concerns and necessity of asthma treatment were associated with poor treatment adherence when assessed with the MMAS or 5-item MARS scale.
4. Several cognitive and emotional disease factors were associated with poor asthma control.
5. Beliefs about asthma medication, cognitive and emotional factors were not associated with treatment adherence to asthma medication.
6. None of the tested asthma treatment adherence scales were able to predict poor asthma control in Latvian patients.

According to our results we recommend to use either the MMAS or the 5-item MARS scale in Latvian asthma patients to identify patients with poor treatment adherence. Thus, it may be worthwhile to assess routinely the concerns and necessity of asthma medication in patients within the Latvian health-care system to improve treatment adherence in that vulnerable population group to improve treatment outcomes. We also recommend to develop and approve Latvian language terminology for treatment adherence.

PUBLICATIONS ON THE STUDY

1. **Smits, D.**, Brigis, G., Pavare, J., Maurina, B., Barengo, N.C. 2017. Factors related to poor asthma control in Latvian asthma patients between 2013 and 2015. *Scand J Prim Health Care*. 35(2), 186–191. doi: 10.1080/02813432.2017.1333302. Epub 2017 Jun 6.
2. **Smits, D.**, Brigis, G., Pavare, J., Maurina, B., Barengo, N.C. 2017. Factors related to good asthma control using different medical adherence scales in Latvian asthma patients: an observational study. *NPJ Prim Care Respir Med*. 27(1), 39. doi: 10.1038/s41533-017-0042-x.
3. **Šmits, D.**, Factors related to good asthma control in Latvian asthma patients in 2015. *6th International Interdisciplinary Scientific Conference Society. Health. Welfare: Living in the World of Diversity: Social Transformations. Innovations. Solutions* (Rīga, Nov. 23–25, 2016), Abs.
4. **Smits, D.** Factors related to good treatment adherence in asthma patients in Latvia in 2015. *9th European Public Health Conference 2016, Vienna, Austria*. Abs. ref.: S201600013.
5. **Šmits, D.** Bronhiālās astmas zāļu lietošanas līdzestība Latvijas pacientiem. *2013. gada Zinātniskās konferences tēzes* (Rīga, 2013.g. 21.–22.martā), 74.
6. **Šmits, D.** Bronhiālās astmas slimnieku uzskati par ārstēšanu un to saistība ar viņu slimības kontroles pakāpi. *2016. gada Zinātniskās konferences tēzes* (Rīga, 2016. g. 17.–18.martā), 79.