

# Abstract

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Title of Doctoral Thesis: **The Importance of Self-Reported Medication Adherence in the Evaluation of the Effectiveness of Pharmacotherapy**

**Introduction and Objective:** Medication adherence (MA) is a highly variable factor affecting the response to the therapy. Especially in chronic disease, non-adherence presents a problem that may have health, social, and even economic consequences. Measuring MA is the most often performed by self-reported surveys which enables, among others, their simple application in research as well as in every day clinical practices. Self-reported MA monitoring may contribute to maximizing the effectiveness of pharmacotherapy and minimizing the risk of therapy failure, however, standardization of measuring process is needed. Moreover, some factors such as healthy adherer effect (HAE), which reflect patient health seeking behaviour but cannot be easily monitored, can favourably affect health outcomes. Acquired results may then be incorrectly attributed to drug therapy examined in the study. Hence, the main aims of this doctoral thesis were: **1)** to reviewed the literature assessing the HAE impact on MA and treatment outcomes; **2)** to verify the psychometric properties of the Czech version of Medication Adherence Report Scale (MARS-CZ) in patients chronically treated with statin and evaluate the relationship with low density lipoprotein cholesterol (LDL-c) goal achievement; **3)** to analyse self-reported MA and compliance to dosing regimen of oral bisphosphonates (BIS) by questionnaires specifically fitted to the therapy of osteoporosis.

**Methods:** **1)** Randomized controlled trials (RCT) and observational studies dealing with HAE were identified based on the systematic overview of literature from PubMed, EMBASE, and Cochrane Register of Controlled Trials. Included studies were further evaluated in respect of relationships between HAE, MA, and health outcomes. **2)** In the cross-sectional three-month prospective study outpatients chronically used statins. Anonymous structured interview was performed to determine among others self-reported MA by MARS-CZ. At the day of interview, patients' medication records were reviewed for disease and medication history and LDL-c examination. Based on these data, LDL-c goal achievement and cardiovascular risk (CV) level were assessed. Reliability and validity of MARS-CZ were tested as well as the relationship between self-reported adherence to statins, LDL-c goal achievement, and CV risk level. Statistical analysis was calculated using selected tests at the  $p < 0.05$

level of significance. **3)** The multicentre prospective survey was conducted in women  $\geq 55$  years old with the risk of osteoporosis fracture where MA was measured by Osteoporosis Specific Morisky Medication Adherence Scale (OS-MMAS). Compliance was determined by questions focused on five dosing instructions concerning the use of oral BIS. Finally, patients' attitudes to treatment were evaluated by Czech version of Beliefs about Medicines Questionnaire (BMQ-CZ).

**Results: 1)** Seven papers were identified (2 RCT and 5 cohort studies). Occurrence of HAE did not correlate with mortality while one RCT indicated the presence of HAE in relation to surrogate (bone mineral density). Observational studies were designed to assess drug class effect but HAE was not revealed. Factors associated with patient behaviour (e. g. smoking, regular preventive screening, vaccination) were not clearly associated with the occurrence of HAE. **2)** From 157 eligible patients 136 (86.6%) completed the interview (67 men, mean age 66.1 years and 69 women, 65.9 years). The mean score of MARS-CZ was 24.4 and showed positive skewing (high adherence by MARS-CZ was reported by 92.6% patients). Satisfactory internal consistency ( $\alpha=0.54$ ), strong test-retest reliability ( $r=0.83$ ,  $p<0.001$ ; ICC = 0.63, 95% CI: 0.35–0.81), and positive correlation with eight item Morisky Medication Adherence Scale ( $r=0.62$ ,  $p<0.001$ ) were indicated. MARS-CZ score correlated with LDL-c goal achievement and CV risk level ( $p<0.05$ ), i. e. all patients who did not achieve LDL-c goal reported low adherence to statins and 89% were in very high CV risk. **3)** From 363 patients responded to the survey (mean age 68.9 years) 36.6% used weekly and 63.4% monthly BIS. The mean score of OS-MMAS was 7.58. Adherence by OS-MMAS correlated only with BMQ-CZ necessity subscale ( $p<0.01$ ). Compliance to all five dosing instructions was reported by only 43.5% of patients. Lower compliance to instructions concerning fasting and staying upright after BIS administration was observed in patients used monthly BIS ( $p<0.001$ ).

**Conclusion: 1)** Only a few studies assessing HAE were found but did not provide any consistent conclusions. HAE impact was supposed particularly on treatment outcomes which may be easier affected by patient behaviour. One of the recommendations may be to include the detection of health seeking behaviour in designs of cohort studies. **2)** MARS-CZ was proved as a sufficiently acceptable self-reported MA measure. In outpatient settings, it could be helpful to reveal medication non-adherence in patients who did not achieve treatment goals and thereby, contributes to an enhancement of the care of chronically treated patients. **3)** Even though, the high MA by OS-MMAS, which was on the other hand associated with perceived necessity of the treatment, was reported, most of the patients did not follow dosing regimen correctly. Thus, the lower absorption or more adverse effects of BIS can be expected.