Background
Adherence and health-related quality of life (HRQoL) are two important indicators in determining success of drug treatments. Although medication adherence and HRQoL have been studied intensively, less is known about the association of these factors: how adherence affects HRQoL and what impact of HRQoL has on medication adherence.

Aim
This research aims to undertake a systematic review of the published literature on the relationship of medication adherence and HRQoL in patients with chronic obstructive pulmonary disease (COPD). To our knowledge, no comprehensive review has been published in this topic so far.

Methods
Publications were searched by computerized databases on medication adherence and HRQoL. The search terms were: “(compliance) OR "adherence" OR "persistence" OR "non-compliance" OR "non-adherence" OR "non- persistence" OR "noncompliance" OR "nonadherence" OR "treatment acceptance" OR "pharmaco-" OR "conformance") AND "quality of life" AND ("chronic obstructive pulmonary disease" OR "COPD"). The search was updated until June 2013.

Results
Our search resulted in 245 hits. Screening of titles and abstracts identified 21 potentially eligible articles. After review of relevant full texts, finally eight studies were included in our systematic review. Results of the selection process are presented in Figure 1.

Study characteristics
Five studies were prospective cohort studies, two were cross-sectional studies and one randomized clinical trial was included. The earliest study dated from 1995 and the most recent was published in 2013. Studies originated from Canada, The Netherlands, Japan, the United Kingdom and the United States (one multinational study was also included). Population size varied between 44 and 5,993 individuals, with mean age of 58 to 76 years (Table 1).

Measurement of quality of life
Questionnaires measuring HRQoL differed between studies. In most studies, disease specific instrument was used; only two studies measured generic HRQoL. The disease specific St. George’s Respiratory Questionnaire (SGRQ) was the most common used quality of life instrument (Table 1).

Association between medication adherence and quality of life
Most of the studies evaluated the correlation between adherence and quality of life (n=5) or the effect of adherence on quality of life (n=3); only one study explored the impact of quality of life on adherence. Results of the included studies are inconsistent (Table 1).

Evidence suggests that relationship between medication adherence and HRQoL is dual. Non-adherence does not have a clear negative impact on HRQoL. Adherence to medication may affect HRQoL due to more factors, e.g. effectiveness/efficacy and side effects of the medication, daily life limitation and social stigmatization caused by the therapy. Effect of non-adherence on HRQoL can be derived from the resultant of these factors. Nevertheless, HRQoL may also influence patients’ drug use; poor or good HRQoL may trigger non-adherence.

Conclusion
Association between medication adherence and HRQoL is multi-factorial. Results from previous studies are limited. Relationship between adherence and HRQoL may differ depend on the duration of the previous therapy (as therapy in newly diagnosed COPD patients may improve HRQoL more than in patients treated previously for longer durations), on the effectiveness/efficacy of the therapy, on the study design (cross-sectional versus longitudinal follow-up study) and on the used patient reported outcome instruments as well. Further scientific evaluations are needed to better understand the dynamics between these factors. Such information would be critically important and needs to be considered when integrating medication adherence into health-economics evaluations.