Pharmacological treatment plays an essential role in controlling chronic conditions such as hypercholesterolemia; however, patients' adherence to long-term therapies for chronic diseases is crucial to achieve optimal health outcomes (1). Further than medication adherence, pharmacological care is affected by the prescribing inappropriateness and adverse drug reactions (ADRs) (2). ADRs can lead to a perceived lack of therapy effectiveness and subsequent suboptimal adherence. Conversely, poor adherence to chronic disease medications may potentially lead to adverse drug events (ADEs), suggesting a bidirectional causal link between non-adherence to prescribed drug therapy and ADEs/ADRs occurrence (6). In the last decade, the use of statins showed a positive trend in Italy, consistently with the recent revisions of the statin reimbursement criteria (NOTA 13) by the Italian Medicines Agency (Agenzia Italiana del Farmaco) (3). Nevertheless, recent real practice analyses documented suboptimal rates of adherence to statin therapy in different Italian outpatient settings (4;5), resulting in poor low-density lipoprotein cholesterol (LDL-C) control, increased risk for cardiovascular events and increasing healthcare costs.

For this reason, we explored the association between serum level of the enzyme creatine phosphokinase (CPK), the number of its measurements and adherence to statin therapy in a large Italian cohort of dyslipidemic patients, with the ultimate aim to evaluate the impact of statin-induced, muscle-related ADRs on patients' therapy adherence, and how this relationship may compromise the efficacy of physicians' prescribing choices and health outcomes in clinical practice. A retrospective cohort study was performed using data from databases of 4 Local Health Units (LHUs) located in Emilia-Romagna, Toscana and Umbria regions, with an overall population of about 1.1 millions of inhabitants. All subjects aged ≥ 18 years with a first prescription for statins in the period between January 1, 2007 and June 30, 2008 were included. All statin prescriptions over a 12 months follow-up period were analyzed to assess treatment adherence. Baseline and follow-up LDL-C levels were considered. All CPK measurements in the follow-up period were analyzed. A total of 71855 patients (51% men, average age 68.6 ± 10.6 years) were included. Among them, 31544 (43.9%) were monitored for LDL-C at least one time during the follow-up period: only 37.4% of these patients achieved LDL-C target. 23.6% of patients underwent at least one serum CPK measurement: out of range values were identified in 37.8% of them. However, they were not switched to other statin drug and/or dosage. Depending on the increase of CPK measurements, patients with steadily normal values of CPK showed a better medication-taking behavior compared to patients whose CPK values were out of normal range. Furthermore, a greater percentage of switching to other statin drug and/or dosage was observed in patients with out of range CPK levels compared to those with normal serum CPK levels.

Our findings indicate that physiological serum CPK levels were associated with greater adherence to statin therapy, supporting a causal link between non-adherence behavior and muscle-related ADRs occurrence. Since statin benefits are associated with their chronic use, physicians should be aware about the relevance of monitoring their patients for this harmful link to prevent unsuitable therapeutic decisions, further decreasing adherence, and achieve long-term health outcomes.

2) Bustacchini et al. (2009). Drugs Aging 26 Suppl 1, 75-87.