prescribed medication regimens (2, 3). The consequences of medication non-adherence extend beyond individual patients and affect various participants, including healthcare providers, caregivers, and healthcare systems as a whole (1, 4). Research has revealed that nearly half of individuals who use chronic prescription medications exhibit some form of non-adherence, leading to poor health-related outcomes, increased disease progression, greater healthcare service utilization, escalating care costs, and elevated mortality rates (5, 6). In Europe, poor medication adherence is linked to approximately 200,000 premature deaths annually. The financial impact of non-adherence is significant, with the annual costs being estimated at EUR 125 billion in Europe and USD 105 billion in the United States due to preventable hospitalizations, emergency care, and outpatient visits (7). According to a systematic review of economic impact, the cost of non-adherence for various diseases ranged from $949 to $44,190 per patient per year (in 2015 US$) (8).

Patients with chronic conditions, such as hypertension, diabetes, asthma, and chronic obstructive pulmonary disease (COPD), face a heightened risk of non-adherence, with estimated rates of 50% for hypertension, 50–60% for asthma, and 70% for COPD (9). In general, around 4% of patients fail to start treatment, 30% show non-adherence by day 100, and 40% discontinue their medications within a year (10). In a recent cross-over study, Dietrich et al. highlighted the critical importance of medication adherence for stroke patients with atrial fibrillation, particularly in relation to direct oral anticoagulants (DOACs) to prevent thromboembolic events (11). The adherence rates to DOACs show significant variability, ranging from 38,0% to 99,7% (12). Often, suboptimal adherence is associated with patient perceptions of limited benefits and the challenges of adhering to the strict dosing schedule of DOACs, which is crucial due to their short half-lives of 8 to 17 hours (11). Kim et al. found in their study that the risk for cardiovascular events was lowest in patients who took at least 90% of their prescribed DOAC doses (13). This observation aligns with findings by Solla-Ruiz et al. who reported increased thromboembolic events in patients with less than 95% adherence to DOAC doses compared to those with perfect adherence (14). These findings stress the importance of optimizing DOAC adherence for effective treatment (11).

Tab. 1. *Various factors contributing to non-adherence*

Factor Category	Specific Factors	Impact on Non-Adherence
Patient Beliefs	Perception of medication necessity; concerns about side effects	Influential in shaping adherence behavior
Economic Factors	High medication costs; unemployment; poverty	Significant role in non-adherence, particularly in marginalized groups
Complexity of Regimens	Multiple medications; strict dosing schedules; long-term treatment	Increases the difficulty of adherence; prevalent in chronic diseases
Side Effects	Fear of adverse reactions; impact on quality of life	Leads to intentional non-adherence or discontinuation of therapy

Studies have shown that factors contributing to non-adherence are multifaceted and complex (15–17). Patient perceptions, beliefs, and attitudes toward medication, as well as concerns about side effects, are influential in shaping their adherence behavior (5). Moreover, economic factors, such as unemployment, poverty, and high medication costs, play a significant role in non-adherence (Table 1) (15, 17). These multifaceted factors underline the need for tailored measures and interventions to improve medication adherence and patient outcomes (15, 17–19).

Accurate assessment of medication adherence is essential for designing effective treatment plans and interventions (20, 21). Various methods are available to assess adherence, each with its advantages and limitations (22, 23). The choice of measurement method is crucial, as it can impact the accuracy of the results. For example, patient self-reports may lead to under-reporting or over-reporting, while electronic medication monitoring may not confirm actual consumption (24–26).

The aims of this review were to provide a comprehensive examination of medication adherence and to deepen our understanding of the underlying mechanisms of non-adherence, recognizing it as a significant issue in clinical practice. It acknowledges that medication adherence, while being of vital importance, is also a complex issue influenced by numerous factors (27–31). To address this complexity, a multi-approach strategy may be necessary to gain deeper insights into adherence behavior (32). Furthermore, collaboration among healthcare professionals, including physicians, nurses, and pharmacists, is essential for addressing non-adherence (33, 34). Standardized reporting forms, questionnaires, and improved care coordination can all simplify the evaluation of adherence and ultimately lead to better patient outcomes (35–38). In addressing medication non-adherence, a key challenge is the limited awareness among stakeholders, often resulting in its exclusion from national health policy agendas. This oversight contributes to inadequate monitoring and utilization of adherence metrics, ultimately limiting the enhancement of healthcare outcomes. Healthcare providers frequently underestimate the prevalence of non-adherence, and there is a notable lack of evidence-based, cost-effective strategies to improve adherence at a systemic level (7). In summary, medication adherence is a critical factor for therapeutic success, and this review explores its challenges.

History of medication adherence

The historical perspective on patient adherence in medicine traces its origins to ancient times, with Hippocrates being the first to have highlighted the challenges of relying on patient-reported medication use. This concern persisted through the centuries, notably with the discovery of tuberculosis as a contagious disease in 1882. Monitoring patient adherence, particularly among transient individuals and alcoholics, proved challenging. In the early 20th century, the convergence of urbanization, industrialization, and social disparities shaped views on non-adherence. Efforts to address this issue had been limited until World War II, when it gained renewed attention, particularly among tuberculous veterans. The introduction of antibiotics in the late 1940s offered hope for tuberculosis treatment, but patient non-adherence remained a frustration (39).