OBJECTIVES: The objective of our study was to compare the clinical outcomes of an adherence naïve framework versus a dynamic adherence framework using the case of statins for primary prevention of cardiovascular disease versus no statin use.

METHODS: Statin adherence was categorized as PDC ≥ .80, 20%<PDC<.80 and PDC < .20 based on a longitudinal epidemiological cohort study of US medical and pharmacy claims. Yearly adherence transitions were incorporated into a Markov simulation model using TreeAge software. Tracker variables were used to store adherence transitions which were then used to adjust probabilities of cardiovascular events (MI, stroke, acute angina) over the patient’s lifetime. Statin effectiveness was adjusted when 0% and 100% of trial-based risk reduction. 10,000 microsimulations were used to estimate incremental effectiveness as CV events avoided and quality-adjusted life-years (QALYs).

RESULTS: In the 10,000-patient statin user cohort simulated by the adherence-naïve model, it was estimated that statin use resulted in 1,162 CV events avoided and 0.39 QALYs gained over a lifetime horizon. The dynamic adherence model estimated that 42% of patients exhibited highest adherence, 40% exhibited intermediate adherence and 18% exhibited low adherence. This model simulated that overall, statin use resulted in 366 events avoided and 0.18 QALYs gained.

CONCLUSIONS: A Markov microsimulation used to simulate changes in patients’ medication adherence over time reveals differential risk reduction and effectiveness in terms of CV events and QALYs gained. The framework presented here is useful for comparing drugs in which optimal effectiveness and costs may be similar, but differential adherence may affect outcomes.

BACKGROUND
Adherence to medications for the prevention of asymptomatic chronic diseases in real-world practice settings is known to be suboptimal. Real-world patients do not exhibit the level of medication adherence seen in clinical trials. Hence, the effectiveness of medications in routine practice may differ. It is important to understand the manifestations of suboptimal medication adherence in a population to assess the potential of adherence-improving interventions and the real-world value of medications. Simulation models are useful for assessing the comparative effectiveness of drugs. A model that incorporates realistic, dynamic adherence may better represent a drug’s effectiveness in the real-world and allow comparison between drugs where adherence varies.

Two challenges exist in incorporating adherence patterns into a simulation model: conceptual and technical.
1. Translate evidence about adherence and outcomes to model parameter estimation.
2. Overcome ‘memoryless’ features of Markov model to allow patients’ history to influence future state transitions.

This study addresses both challenges using a model of statins for the primary prevention of cardiovascular disease.

Conceptual Framework

CONCEPTUAL ADDITION OF ADHERENCE TO A MARKOV MODEL
In the adherence-naïve model, medication adherence and associated effectiveness assumed to be trial level and static. The adherence-naïve model was modified to a dynamic adherence model in which medication adherence was dynamic and linked to changes in outcomes. In order to convert the adherence-naïve model to the dynamic adherence model, a number of structural changes were made to allow the conceptual addition of adherence to an existing CEA model through adherence levels and transition probabilities.

Re-conceptualize adherence as a categorical measure
Adherence was conceptualized as ‘levels’, to be more easily represented by a state-transition model.

OBJECTIVES:

METHODS: A previously published adherence-naïve model (Slejko, et al. CMRO, 2010) was used to simulate the statin primary prevention strategy in U.S. adult population; statin vs. no statin for CV event risk reduction. A Markov decision-analytic model using one-year cycles (lifetime horizon) was constructed in TreeAge Pro. Effectiveness was measured as quality-adjusted-life-years (QALYs). A 3% discount rate was used for QALYs.

Tracker variables allowed adherence to be stored from year to year creating a Markov microsimulation model. 10,000 Markov microsimulations were performed.

Year 1: All patients at highest adherence level.
Year 2: Patients face a probability of remaining adherent or transitioning to a lower level of adherence. Risk of CV event adjusted by adherence level.
Year 3+: Future probability of adherence and risk of CV events depends on previous adherence.

RESULTS: In the 10,000-patient statin user cohort simulated by the dynamic adherence model estimated, 42% of patients exhibited highest adherence, 40% exhibited intermediate adherence and 18% exhibited low adherence in Year 2.

DISCUSSION

In this example, incorporating real-world adherence evidence into a model reveals value differences in the statin strategy, overall. The Markov microsimulation approach allows the illustration of value differences by subgroup, an advantage over average patient cohorts. This model framework may be used to assess the value of adherence-improving interventions, or compare drug treatments with varying adherence. This approach may be particularly useful to assess the new class of oral anticoagulants, where adherence among the various agents may differ, and be compared to traditional strategies that incorporate closer patient monitoring.

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