Andreas Daniel Meid
Dr. sc. hum.

Medication underuse in older outpatients: a pharmacoepidemiological approach towards an optimized pharmacotherapy using explicit prescribing criteria

Fach/Einrichtung: Klinische Pharmakologie
Doktorvater: Prof. Dr. med. Walter Emil Haefeli

Zusammenfassung:

Medication underuse is the most prominent form of inappropriate prescribing in older people. Despite the prevalence and expected worse outcomes, underuse of beneficial medications was rarely investigated in its nature, extent, consequences, and strategies for improvement. This thesis determined the extent of medication underuse detected with explicit prescribing criteria in German aging outpatients, explored associated factors, and investigated patient-relevant consequences. In this framework, interventional programs targeting medication underuse were summarized according to their ability to improve medication quality. With regard to (clinical) effectiveness and feasibility, the potential benefit for health care systems was modeled to emphasize the impact of medication underuse and support programs for its improvement.

The first project focused on cardiovascular disease as a leading cause of death in older people, where the impact of being exposed or not exposed to preventive cardiovascular medicines is accordingly high. Data from the prospective population-based ESTHER study were used to assess the prevalence, determinants, and outcomes of medication underuse based on a set of explicit cardiovascular START criteria. The findings revealed that underuse was present in more than two thirds of included participants (mean age 71.1 ± 6.1 years) and was significantly associated with frailty (odds ratio: 2.11 [95% confidence interval: 1.24; 3.63]), body mass index (1.03 [1.01; 1.07] per kg/m^2), and inversely with the number of prescribed drugs (0.84 [0.79-0.88] per drug). This information was used for adjustment in a follow-up evaluation (mean follow-up time 2.24 years) on cardiovascular and competing outcomes: Interestingly, no association of medication underuse with cardiovascular events was found (fatal and non-fatal). However, a significant association of medication underuse with competing deaths from non-cardiovascular causes (2.52 [1.01; 6.30]) may suggest that cardiovascular drugs were withheld because of serious co-morbidity or that concurrent illness can preclude benefit from cardiovascular prevention. In the latter case, adapted prescribing criteria should be developed and evaluated in those patients.

The second project investigated the factors promoting underuse in long-term medical care and the impact of withholding indicated medications on QoL. Based on the sequential follow-up

assessments of the ESTHER cohort, medication underuse was determined by START-2 criteria and its prevalence was constantly high. In contrast, several health conditions changed significantly within participants. Following variable selection accounting for subject-specific heterogeneity over time, multivariate results revealed that more drugs (OR = 0.83 [0.78; 0.87] per drug), and better cognitive status (OR = 0.93 [0.87; 0.99] per point on the MMSE scale) were preventive factors, while worse self-reported health status (OR = 1.33 [1.05; 1.67] per point on an 5-point scale) and increasing frequency of GP consultations (OR = 1.07 [1.00; 1.15] per visit within the preceding three months) were positively associated with medication underuse. An increase in omitted medications over time was associated with QoL as determined on the EuroQuol EQ-Vas and EQ-5D scales.

The third project was a multivariate meta-analysis and meta-regression of controlled trials assessing the impact of pharmaceutical care interventions (e.g., medication review) on medication underuse in older patients (≥65 years). The included interventions were associated with significant reductions in the mean number of omitted drugs per patient (pooled estimate: -0.44 [-0.61; -0.26]) and the proportion of patients with ≥1 omitted drug (pooled OR = 0.29 [0.13; 0.63]). The only significant influential factor for improving success was the utilization of explicit screening instruments when conducting a medication review (P = 0.033), which strengthens recommendation for their use in clinical practice.

The fourth project integrated findings from previous projects into the competing risk framework, where the growing risk for competing deaths gradually limits the success of preventive medicines with advancing age. In a modeling study starting with different ages of appropriate treatment initiation, the population's life course was obtained from life tables and combined with age-specific effect estimates from the first project. For different starting ages, the population proportions of the distinct states of the framework were calculated for each year of chronological age in subgroups of appropriate treatment and underuse. These proportions were used over a follow-up period to estimate measures of treatment effectiveness and risks of underuse. Results indicated that despite increasing relative effectiveness with advancing age, benefits measured by patient-relevant endpoints (LYG or gained QALYs) markedly dropped after the starting age of 75 years. However, even at an initiation age of 85 years, QALYs gained exceeded 1 year, which is quite remarkable. Future research should therefore confirm the findings of this thesis in controlled intervention studies and focus on the implementation of programs to reduce medication underuse.