BMJ Open

Development and internal validation of prognostic models to predict negative health outcomes in older patients with multimorbidity and polypharmacy in general practice

Beate S Müller ,[1] Lorenz Uhlmann,[2] Peter Ihle,[3] Christian Stock,[2] Fiona von Buedingen,[1] Martin Beyer,[1] Ferdinand M Gerlach,[1] Rafael Perera,[4] Jose Maria Valderas,[5] Paul Glasziou,[6] Marjan van den Akker,[1,7] Christiane Muth [1]

To cite: Müller BS, Uhlmann L, Ihle P, *et al*. Development and internal validation of prognostic models to predict negative health outcomes in older patients with multimorbidity and polypharmacy in general practice. *BMJ Open* 2020;**10**:e039747. doi:10.1136/bmjopen-2020-039747

► Prepublication history and additional material for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2020-039747).

Received 24 April 2020
Revised 26 August 2020
Accepted 02 October 2020

Check for updates

© Author(s) (or their employer(s)) 2020. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to
Dr Beate S Müller;
b.mueller@allgemeinmedizin.uni-frankfurt.de

ABSTRACT

Background Polypharmacy interventions are resource-intensive and should be targeted to those at risk of negative health outcomes. Our aim was to develop and internally validate prognostic models to predict health-related quality of life (HRQoL) and the combined outcome of falls, hospitalisation, institutionalisation and nursing care needs, in older patients with multimorbidity and polypharmacy in general practices.

Methods *Design*: two independent data sets, one comprising health insurance claims data (n=592 456), the other data from the PRIoritising MUltimedication in Multimorbidity (PRIMUM) cluster randomised controlled trial (n=502). *Population*: ≥60 years, ≥5 drugs, ≥3 chronic diseases, excluding dementia. *Outcomes*: combined outcome of falls, hospitalisation, institutionalisation and nursing care needs (after 6, 9 and 24 months) (claims data); and HRQoL (after 6 and 9 months) (trial data). *Predictor variables in both data sets*: age, sex, morbidity-related variables (disease count), medication-related variables (European Union-Potentially Inappropriate Medication list (EU-PIM list)) and health service utilisation. *Predictor variables exclusively in trial data*: additional socio-demographics, morbidity-related variables (Cumulative Illness Rating Scale, depression), Medication Appropriateness Index (MAI), lifestyle, functional status and HRQoL (EuroQol EQ-5D-3L). *Analysis*: mixed regression models, combined with stepwise variable selection, 10-fold cross validation and sensitivity analyses.

Results Most important predictors of EQ-5D-3L at 6 months in best model (Nagelkerke's R^2 0.507) were depressive symptoms (−2.73 (95% CI: −3.56 to −1.91)), MAI (−0.39 (95% CI: −0.7 to −0.08)), baseline EQ-5D-3L (0.55 (95% CI: 0.47 to 0.64)). Models based on claims data and those predicting long-term outcomes based on both data sets produced low R^2 values. In claims data-based model with highest explanatory power (R^2=0.16), previous falls/fall-related injuries, previous hospitalisations, age, number of involved physicians and disease count were most important predictor variables.

Conclusions Best trial data-based model predicted HRQoL after 6 months well and included parameters of well-being not found in claims. Performance of claims data-based models and models predicting long-term outcomes was relatively weak. For generalisability, future studies should refit models by considering parameters representing well-being and functional status.

Strengths and limitations of this study

- We developed our predictive models using two completely different data sets—claims data and data primarily collected in a cluster-randomised trial.
- The claims data contained a large number of cases, enabling our models to include many possible predictors without any convergence issues.
- The trial data provided a rich set of potential predictor variables of high data quality and included data on patient-reported outcome measures, such as well-being and functional status.
- Both data sets have their own methodological limitations, such as imprecise claims data (collected for reimbursement purposes) and the trial's small sample size.
- The nature of the data meant neither data set could be used to validate a predictive model based on the other.

BACKGROUND

Currently, up to 80% of primary care consultations involve patients with multiple chronic conditions (multimorbidity).[1] A multiplicity of disorders in patients is associated with polypharmacy. Both multimorbidity and polypharmacy are recognised as a major challenge facing healthcare systems.[2–5] Polypharmacy can increase the risk of mortality, hospitalisation[6 7] and falls and fall-related injuries with resulting disability and loss of autonomy.[8 9] It can also reduce cognitive and

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

physical function, as well as health-related quality of life (HRQoL).[2 10]

The *number of drugs* increases the *probability* of adverse drug reactions, but the relationship is inconsistent, suggesting that the number of medications alone may not adequately indicate the quality of an individual's medication regimen.[11 12] The kind of drugs prescribed plays an important role in the type of reaction, with certain medication classes, such as benzodiazepines, demonstrating a significant association with falls, and medications with anti-cholinergic properties being associated with impaired cognitive and physical function in elderly individuals.[13 14] At a physician level, the cause of these negative health outcomes of polypharmacy may be inappropriate prescribing, including undertreatment.[15–18] At a patient level, a high number of drugs and the complexity of a drug regimen is often associated with poor adherence,[19] which may be exacerbated by the presence of depression and/or cognitive impairment.[20] Moreover, polypharmacy may also result in an accumulation of potentially inappropriate medications (PIMs).

Several complex interventions have been developed to optimise (inappropriate) polypharmacy. However, despite their evidence-based rationale, they have led to inconsistent improvements in process parameters of care and failed to impact patient-relevant outcomes.[21 22] One possible reason for this is that the included populations are too heterogeneous in terms of their baseline risk and potentially achievable intervention effects. For example, the majority of the study population included in the PRIMUM (PRIoritising MUltimedication in Multimorbidity) trial showed very good quality of life and functional status at baseline, even though participants had at least three chronic conditions affecting more than two organ systems, five or more chronic drug prescriptions and were 60 years of age or older. The authors therefore concluded that there was not enough room for improvement.[23] This highlights current difficulties in defining inclusion criteria in polypharmacy trials in such a way that selected populations have a considerable baseline risk and can be expected to benefit from the intervention. Moreover, as polypharmacy interventions tend to address inappropriate prescribing, healthcare coordination, and so on, they are generally complex.[21 22] As the complex interventions are also resource-intensive, it would be preferable for a stratified approach to address patients that are at high risk of negative health outcomes and most likely to benefit from them.[24]

The course of multimorbidity (and associated polypharmacy) has been characterised by a decline in well-being (eg, functional decline or worsening of quality of life due to inappropriate prescriptions and/or deterioration in one or more chronic diseases), interrupted by adverse events (eg, exacerbations of chronic diseases or adverse drug reactions).[25 26] In order to identify a population at high risk, it is therefore necessary to predict a wide array of possible negative health outcomes. Several prognostic models have predicted single outcomes, mainly mortality or unplanned hospital (re-)admission and to a lesser extent a future decline in quality of life, but no studies have investigated the risk for the above-mentioned combined endpoints, or involved polypharmacy-related predictors.[27]

The aim of this exploratory study was to develop and internally validate prognostic models to predict the risk of adverse events or a decline in well-being in general practice patients with multimorbidity and polypharmacy, and to operationalise these negative health outcomes in terms of hospitalisation, falls, level of required nursing care, institutionalisation and HRQoL. The models were based on morbidity and medication-related variables, as well as socio-demographic characteristics and parameters of healthcare utilisation.

METHODS

We developed and internally validated prognostic models to identify key health problems linked with multimorbidity and associated polypharmacy (decline in well-being and adverse events: figure 1). (1) Based on claims data, we predicted the combined endpoint of hospitalisation, falls/fall-related injuries, need for nursing care, deterioration in the required level of care (nursing level) or institutionalisation, after 6, 9 and 24 months. (2) We predicted HRQoL after 6 and 9 months based on data from a cluster-randomised trial.[23]

Design and setting/study samples

Two data sets were used in modelling:

Claims data obtained from the *Techniker Krankenkasse* (TK) statutory health insurance company between January 2012 and December 2014. TK is the largest statutory health insurer in Germany and provided health insurance to 8.1 million persons in 2012.[28] In accordance with Social Code book V, all statutory health insurance companies in Germany collect basic data on socio-demographics, details of pharmacological and non-pharmacological prescriptions and information on other health services utilisation and data on morbidity.

Trial data from the cluster-randomised PRIMUM trial[23] conducted in general practices in Hesse, Germany, from August 2010 to February 2012.

Population

Claims-based models: We aimed to use the same inclusion criteria for both data sets as far as possible. We therefore included health insurance claims data of older patients (≥60 years) with multimorbidity (at least three documented chronic diseases, from a list of 46 diagnoses and conditions, from 01 January 2012 to 31 December 2012)[29] and polypharmacy (at least five documented and concurrent prescriptions from 01 July 2012 to 31 December 2012). Included patients had to have been continuously insured by TK from 01 January 2012 to 31 December 2014 (except in case of death at any time after 31 December 2012) and had to have contacted a primary care provider

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

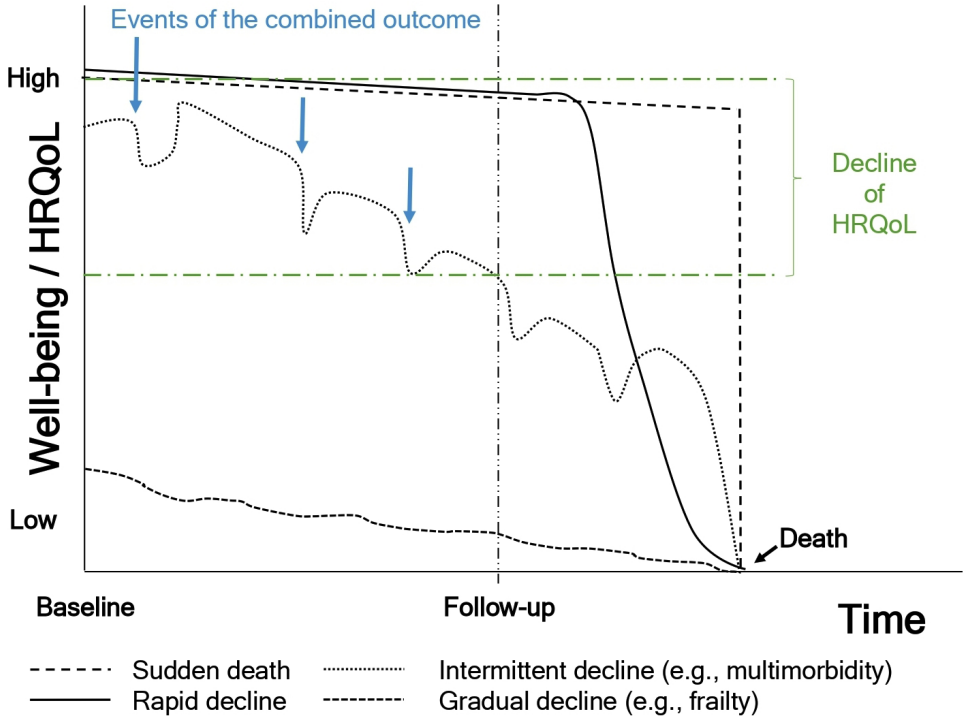


Figure 1 Predicted outcomes with regard to general trajectories of well-being and quality of life over time. HRQoL, health-related quality of life.

at least once in 2012. Patients were excluded if they were diagnosed with dementia (International Classification of Diseases, 10th Edition (ICD-10): F00-03, F05.1, G30-31, R54) or under guardianship from 01 January 2012 to 31 December 2012.

Trial data-based models: We included data from patients that participated in the cluster-randomised PRIMUM trial (n=502, intervention group: n=252, control group n=250).[23] Patients with multimorbidity and polypharmacy were included in the study if they were at least 60 years old, had at least three chronic diseases from two or more chapters of ICD-10 and at least five prescriptions. Patients were excluded if they were cognitively impaired (defined as a score lower or equal to 26 on the Mini-Mental Status Exam[30]), had an alcohol or drug addiction or were not able to participate in telephone interviews, fill in questionnaires or express their own free will. Four out of the 502 patients (0.79%) died during the 9-month follow-up period.

Outcomes

Models based on claims data: We predicted the combined endpoint of hospitalisation, falls/fall-related injuries or institutionalisation in a long-term care facility, or if the need for nursing care was recognised, or the level of care ('Pflegestufe') had worsened at 6-month, 9-month, 24-month follow-up. We treated the parameters of health service use (hospitalisation, level of nursing care and institutionalisation) as surrogate parameters for a decline in functional status and well-being, as details of these are not included in German claims data. Outcomes were operationalised as follows:

- Hospitalisation: We included all-cause hospitalisations, as our data did not permit us to differentiate between unplanned and elective hospitalisations.
- Falls and fall-related injuries: We included all fractures and injuries coded in ICD-10 chapters 'S' and 'T'. We excluded ICD codes for severe body injuries such as S31 ('open wound of abdomen, lower back and pelvis'), which we assessed as related to severe bodily impact, rather than drug-related falls (see online supplemental additional file 1 for all excluded ICD codes). We also excluded osteoporosis-related fractures (ICD-10 M80).
- Institutionalisation was defined as the admission of a patient to a long-term care facility for at least 28 days (in Germany, this is the maximum length of time considered as 'short-term care' in such facilities).
- Level of (nursing) care ('Pflegestufe') referred to dependency on care. In the period under review, the German nursing care insurance system recognised four levels of care ('1' – lowest level to '3' – highest level, and 'H', which was mainly used for people with mental illnesses who are in need for support). The onset of care and any increase in care level were taken into consideration.

Models based on trial data: We predicted HRQoL 6 and 9 months after baseline. HRQoL was measured using the EQ-5D-3L index score.[31–33] The EQ-5D-3L index score is a weighted summary score of five different dimensions of health (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each dimension has three levels. The index score is calculated based on time

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

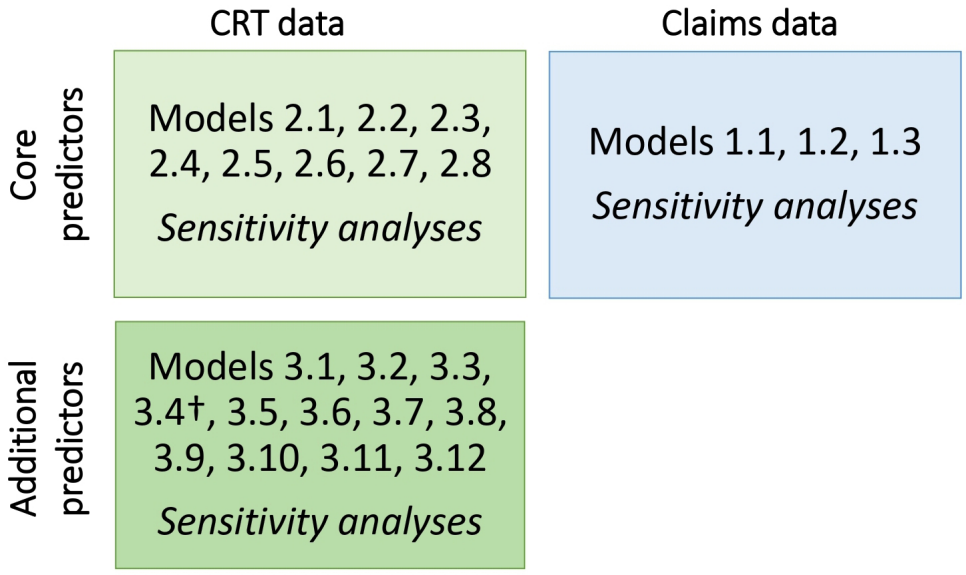


Figure 2 Models and sensitivity analyses with regard to data source and predictor set. CRT, cluster-randomised controlled trial; †Best Model.

trade-off (TTO) norm values and ranges from 0 to 1, with '0' signifying death and '1' in full health. Patients who died during follow-up were assigned the value '0'.

Potential predictors

The potential predictors that were initially used in the two modelling approaches were available in both claims and trial data *('core predictors'*, see figure 2*):* To compare the two models, we first used these 'core predictors' (all variables were continuous variables, if not stated otherwise).

- Socio-demographics: Age (in years), sex (male/female, binary)
- Morbidity-related (excluding dementia): Number of chronic diseases (based on a modified list of 46 diagnoses and conditions),[29] Charlson comorbidity index,[34] number of specific chronic conditions according to Diederichs' list[35] consisting of 17 chronic diseases identified in a systematic review of existing comorbidity indices. As dementia was excluded, the final list contained 16 diagnoses. (All instruments including ICD-10 codes are provided in online supplemental additional file 2)
- Medication: Number of prescriptions (defined as Anatomical Therapeutic Chemical (ATC) agents using fifth-level coding, ATC version 2011 to 2014), excluding drugs for topical applications and drug groups that were irrelevant to our research question, for example, contrast agents (ATC V-08, three-digit level).
- Potentially inappropriate medication: We constructed two patient co-variables: (1) exposure to any PIM (yes/no) and (2) number of PIMs between 01 July 2012 and 31 December 2012 (*claims-based models*) and at baseline (*trial data-based models*). We used the following two lists to identify PIMs:
  - *Modified EU-PIM list*[36]: The list of PIMs for the elderly contains 282 chemical substances or drug classes divided into 34 therapeutic groups.
  - *Modified PRISCUS list*[37]: The German list of PIMs for the elderly includes 83 chemical substances from a total of 18 drug classes.

  We excluded from the lists PIMs that referred to specific doses, treatment duration and disease severity, as valid information on these could not be obtained from the claims data. (All instruments including ATC codes are provided in online supplemental additional file 3)
- Anticholinergic drug burden: Scores were calculated based on all prescribed drugs with anticholinergic properties per patient. Despite substantial differences between existing scales, associations with adverse clinical outcomes, such as hospital admissions, fall-related hospitalisations, length of stays in hospital, and general practitioner (GP) visits, have been found for all of them.[38] As the evidence does not support the preferred use of any particular scale, we tested the following (all instruments including ATC codes are provided in online supplemental additional file 3):
  - *Anticholinergic Drug Scale (ADS)*[39] : The ADS weights anticholinergic properties per drug from '0' – no anticholinergic activity, '1' – mild, '2' – moderate and '3' – strong anticholinergic activity. The overall anticholinergic burden per patient was calculated as a sum score for the entire medication regimen.
  - *Modified Anticholinergic Drug Burden Index (DBI)*[13] : The DBI comprises drugs with sedative effects (which form the sedative burden (B_S)), and drugs with anticholinergic or both sedative and anticholinergic effects (which form the anticholinergic burden (B_{AC})). As claims data do not provide

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

dosages, the cumulative number of sedative and anticholinergic drugs was calculated (modified DBI score).

- Healthcare utilisation: For each patient, we obtained information on all-cause hospitalisations (yes/no), falls and fall-related injuries (yes/no) and the number of physicians involved in ambulatory healthcare, between 01 January 2012 and 31 December 2012 for models based on *claims data*, and in the 6 months previous to baseline for models based on *trial data*.

Additional potential predictor variables were used exclusively to re-fit models based on trial data, as they were only available in these data (*'additional predictors'*, see figure 2; all variables were continuous variables unless stated otherwise):

1. Socio-demographics: Education (CASMIN[40]) and number of persons living in the household.
2. Lifestyle: Alcohol consumption (audit-C, categorical variables on number of drinking occasions and amount of alcohol consumed),[41] smoking status (smoker/non-smoker, binary) and body mass index.
3. Inappropriateness of medication: MAI consists of 10 items (indication, effectiveness, correctness of dosage, correctness of direction, practicality of direction, drug–drug interactions, drug–disease interactions, unnecessary drug duplications, correctness of treatment duration and costs).[42] The MAI item on cost was omitted because variable discount contracts between pharmaceutical companies and statutory health insurers preclude cost comparisons in Germany. The medication reviews were conducted by a trained clinical pharmacologist (SH), who rated nine items for each prescription. Values ranged from '0' (appropriate) to '2' (inappropriate) whereby '1' represented a middle rating of uncertain appropriateness. The assigned values were summed to give an MAI score between 0 and 18 for each prescription and across the entire medication regimen of the patient.[23]
4. Morbidity-related: Severity of multimorbidity, as measured using the CIRS (the CIRS differentiates between 14 organ systems, which are assessed on a 5-point Likert scale according to severity of impairment, with the ratings ranging from no impairment to extreme impairment),[43] with scores calculated as the total sum score, the number of affected organ systems and the HRQoL-CI (HRQoL-CI consists of a mental and a physical subscale, whereby the presence of certain diseases are assigned weights from '1' to '3', see online supplemental additional file 2).[44]
5. Depressive symptoms, as measured using the GDS with 15 items.[45]
6. HRQoL at baseline, as measured using the EQ-5D-3L index score.[31–33]

Missing values and imputation

There were no missing values in the claims data, so no imputation was carried out in models that were based on them. In models based on trial data, imputation of missing values in predictors and outcomes was conducted using multiple imputation via chained equations.[46 47] We used a fully conditional specification approach by setting up an appropriate conditional density for each variable. In the imputation process, we included all variables that were used in each model. We imputed m=50 data sets and combined the results using 'Rubin's rules'.[46]

Statistical analyses

In both models, we first investigated the core predictors that were available in both data sets, including socio-demographics, morbidity-related and medication-related variables and variables for healthcare utilisation. We then refitted the trial data-based models using the additional predictors that were exclusively available for trial data, such as variables for lifestyle and well-being (figure 2).

Models based on claims data: In order to develop a prediction model for the binary combined outcome (containing all-cause hospitalisation, falls/fall-related injuries, institutionalisation or level of (nursing) care required) at 6-month, 9-month and 24-month follow-up, we performed multiple logistic regression analyses with the occurrence of at least one of the components at 6-month, 9-month and 24-month follow-up as the dependent variable. As patients were not always assigned a single general practice,[48] we did not perform cluster analysis on the claims data.

Models based on trial data: In order to develop a prediction model for the continuous outcome HRQoL at 6-month and 9-month follow-up, we performed multiple linear regression analyses using the EQ-5D-3L index score at 6-month and 9-month follow-up as the dependent variable. The cluster structure of the data was taken into account by including a random intercept to produce a mixed regression model. We assumed a compound symmetry structure when estimating the covariance matrix.

Univariate analyses in both claims and trial data: Prior to conducting regression analyses, we performed univariate analyses to identify any associations between our potential predictors (at baseline) and the outcomes (at 6-month, 9-month and 24-month follow-up).

Regression analyses and variable selection: To find out which predictor variables influence the outcome variables, we used a stepwise variable selection procedure (combining forward and backward steps). We started with the full model and all potential predictor variables. After this, we used a selection procedure based on p values.[49] In the backward selection step, we deleted the variable with the highest p value from the model if its p value was greater than 0.157. In the forward selection step, the variable with the lowest p value was included in the model if its p value was less than 0.156. As long as each covariate had only one df, the use of these boundaries led to the same results as variable selection using the Akaike Information Criterion.[50] The resulting models are presented by providing the estimated regression coefficients (models based on trial data) or ORs (models based on claims) with 95% CIs and corresponding p values. As we expected

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

the large sample size of claims-based models to result in low p values, we calculated additional z values and continuous net reclassification indices to gain information on the predictive power of each variable.[51] Multi-collinearity was assessed using the variance inflation factor (VIF).[52] In the models based on trial data, we did not account for the clustering structure when we calculated the VIF.

Performance of the models

We calculated R^2 for linear models based on trial data (according to Nakagawa and Schielzeth[53]), and Nagelkerke's R^2 for logistic models (according to Steyerberg and Nagelkerke[54 55]) based on claims data. Furthermore, in order to assess performance more realistically and to internally validate the models, we used the AUC (area under the receiver operator curve, equivalent to the concordance index) to validate the logistic regression model based on claims data, and R^2 to validate the linear regression model based on randomised controlled trial data, in combination with 10-fold cross-validation.[56] R^2 and Nagelkerke's R^2 are measures of the overall model's ability to assess explained variance. The AUC provides a measure of the model's discriminatory ability to distinguish patients at risk from those that are not.

Sensitivity analyses

Using sensitivity analysis, we applied two further modelling approaches (at first separately and then in combination): (1) modelling without multiple imputation and (2) modelling without variable selection.

Software: We made use of different statistical packages to analyse the data in R.[47 57–63]

We used TRIPOD reporting guidelines (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) in the preparation of this manuscript.[64]

Patient and public involvement statement

Neither patients nor the public were involved in this study.

RESULTS

Participants

Claims data

The total sample of those ≥60 years that were continuously insured by TK from 01 January 2012 to 31 December 2014, and had at least one primary care contact during 2012, amounted to 1 377 917 persons. Overall, 592 456 patients met the pre-specified criteria and were included in the analyses (see study flow-chart, online supplemental additional file 4).

Trial data

Of the 505 patients that participated in the PRIMUM trial, all but 3 were 60 years or older. The final analyses therefore included 502 patients.

Key characteristics of study participants are shown in table 1.

Univariate analyses

In the claims data, univariate analyses revealed significant associations between the combined outcome and the following predictors: Age, sex, disease count, Charlson Comorbidity Index, EU-PIMs, ADS, DBI, previous hospitalisations, previous falls and number of physicians involved in the patient's care at all follow-ups (after 6, 9 and 24 months) (online supplemental additional file 5). In the trial data, HRQoL was significantly correlated with the shared predictor variables disease count, number of chronic prescriptions, previous falls and sex and the additional predictors depression and HRQoL at baseline (online supplemental additional file 6).

Prognostic models

Claims data

The model predicting the combined endpoint at 6 months had the highest C-statistic (AUC with 10-fold cross validation: 0.71, see table 2), but a low explanation of variance (Nagelkerke's R^2 without cross validation: 0.16). Variables in the model with the highest predictive power were previous falls/fall-related injuries and previous hospitalisations, as well as age, number of involved physicians, and number of chronic diseases ('disease count') (table 3). The models predicting the combined outcome at 9 and 24 months had AUCs calculated with 10-fold cross validation of 0.68 (R^2 without cross validation: 0.15) and 0.69 (R^2 without cross validation: 0.13) respectively. The VIF (to assess any multi-collinearity) showed moderate values (maximum 7.5).

Trial data

All results presented in this section are based on the modelling approach and involve multiple imputation of missing values and the variable selection procedure. Models predicting the HRQoL endpoint at 6 months that were based on core predictors available in both claims and trial data showed low predictive accuracy (R^2 with 10-fold cross validation: 0.111) (table 3, model 2.4). HRQoL at 6 months was best predicted when additional predictors that were exclusively available in the trial data were also included (R^2 with 10-fold cross validation: 0.507). The variables with the highest predictive power were depressive symptoms (GDS) and EQ-5D-3L Index Score (Baseline). MAI was also predictive (table 3, model 3.4). The VIF showed small values (maximum 2.2).

Comparison of model quality and sensitivity analyses

The shorter the time span of the prediction, the better the explained variance and hence, the performance of the model. However, model performance remained fair to poor when it only included predictor variables that were available for both claims and trial data. Sensitivity analyses confirmed these results (table 2).

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

Table 1 Characteristics of study participants

Characteristic	Claims data* n=592 456	CRT data* n=502
Data collection period	January 2012 to December 2014†	August 2010 to February 2012
Study design	Cohort study	Cluster-randomised controlled trial
Setting	Claims data from the TK health insurance fund. TK serves about 10 million people in Germany	72 general practices in Hesse, Germany
Inclusion criteria	≥60 years ≥3 chronic diseases ≥5 prescriptions ≥1 GP visit Continuously insured (except in case of death in follow-up period)	≥60 years ≥3 chronic diseases ≥5 prescriptions ≥1 GP visit
Exclusion criteria	Person under legal guardianship Diagnosed dementia	Person under legal guardianship Cognitive dysfunction including dementia (MMSE ≤26)
Outcomes to be predicted	Combined‡ binary outcome after 6-month, 9-month, 24 month follow-up	HRQoL (continuous outcome) after 6-month and 9-month follow-up
Potential predictors in both samples at baseline¶		
Age (years)	71.3 (7.06)	72.2 (6.86)
Male sex (n, %)	319 453 (54)	240 (48)
Morbidity		
Disease count	9.7 (3.75)	9.6 (3.25)
No. of specific chronic diseases (Diederichs)	4.3 (1.97)	4.1 (1.60)
CCI	3.0 (2.54)	2.6 (1.92)
HRQoL-CI, mental	2.8 (2.12)	2.1 (1.81)
HRQoL-CI, physical	8.0 (3.57)	7.6 (3.12)
Medication		
No. of drugs	8.6 (3.80)	8.1 (2.57)
No. of PIM (EU-PIM)	1.1 (1.15)	0.9 (0.96)
ACh burden (ADS)	1.0 (1.45)	0.8 (1.21)
Modified Drug Burden Index	0.8 (1.03)	0.5 (0.77)
No. of involved physicians	9.95 (5.26)	2.6 (1.77)
Previous hospitalisation:		
Patients that have undergone hospital treatment (n, %)	194 984 (33)	81 (16)§
No. of hospitalisations	1.67 (1.25)	1.5 (0.86)§
No. of days in hospital	14.5 (18.20)	17 (12.66)§
Patients with previous falls/fall-related injuries (n, %)	163 387 (28)	83 (17)§
Patients requiring nursing care		
Any nursing level (n, %)	28 310 (5)	–
Nursing level 1 (n, %)	19 030 (3)	–
Nursing level 2 (n, %)	7968 (1)	–
Nursing level 3 (n, %)	1273 (0.2)	–
Nursing level H (n, %)	39 (0.007)	–
Additional predictor variables in CRT data at baseline¶		
Socio-demographics		

Continued

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

Table 1 Continued

Characteristic	Claims data* n=592 456	CRT data* n=502
Educational level (CASMIN)	–	1.4 (0.66)
No. of persons living in household	–	1.8 (0.70)
Lifestyle		
Alcohol intake (AUDIT C)	–	1.9 (1.96) (mv: 39)
Smoker (n, %)	–	46 (10) (mv: 25)
Body mass index	–	30.1 (6.58)
Morbidity		
CIRS sum score		7.7 (4.56)
CIRS, no. of organ systems		4.5 (2.35)
Depressive Symptoms (GDS)		2.4 (2.29) (mv: 8)
Medication		
MAI	–	4.7 (5.56)
HRQoL		
EQ-5D-3L Index Score	–	74.3 (23.72) (mv: 24)

*Values are arithmetic means and SD unless otherwise indicated.
†The anamnestic period for baseline data ran from 01 January 2012 to 31 December 2012, except for medication data, for which it ran from 01 July 2012 to 31 December 2012. The follow-up period started on 01 January 2013.
‡Combined outcome included hospitalisation, fall/fall-related injuries, institutionalisation and care level.
§6 months before study entry.
¶Number of patients with missing values (mv) is zero unless indicated in square parentheses.
ACh burden, anticholinergic drug burden; ADS, Anticholinergic Drug Scale; AUDIT, Alcohol Use Disorders Identification Test (WHO); CASMIN, Comparative Analysis of Social Mobility in Industrial Nations; CCI, Charlson Comorbidity Index; CIRS, Cumulative Illness Rating Scale; CRT, cluster-randomised controlled trial; GDS, Geriatric Depression Scale; GP, general practitioner; HRQoL, health-related quality of life; HRQoL-CI, HRQoL comorbidity index; MAI, Medication Appropriateness Index; MMSE, Mini-Mental Status Exam; PIM, potentially inappropriate medication; TK, *Techniker Krankenkasse*.

DISCUSSION

Main results

Our best overall prognostic model predicted HRQoL after 6 months in older general practice patients with multimorbidity and polypharmacy. It performed well, was based on trial data and explained more than half of the variance. The most important predictors were depressive symptoms, the initial level of HRQoL and MAI—all of which were only available as 'additional predictors' in trial data. Prognostic models in trial data, which were exclusively developed from 'core predictors' (available in both data sets) performed worse, as well as claims based models and models based on both data sets that had longer forecast periods (9 months or more). In both trial data-based and claims-based models, outcome components at baseline had a relatively high impact (ie, HRQoL at baseline in the trial data-based model and previous hospitalisation and previous falls/fall-related injuries in claims-based models). Although this is unsurprising and is often the case in prognostic models,[65] it nonetheless seems reasonable to retain the variables in the model. Furthermore, we identified further predictors, such as depressive symptoms and medication appropriateness, which had a relatively high predictive power.

Comparison with the literature

The presented results are consistent with results from other studies. The AUC values in our claims-based models (AUC 0.68 to 0.71) are comparable to those of 23 prognostic models for Case Finding conducted in elderly patients in primary care. These models predicted (re) hospitalisation, functional impairment, institutionalisation and death.[65] The quality of models with a low risk of bias was AUC 0.60 to 0.78, but no explanation of variance was provided. The best model for predicting death within 4 years (AUC: 0.82) included 12 predictors comprising age, sex, body mass index, chronic diseases, smoking status and functional parameters.[65] Models that included additional trial data (eg, clinical data) predicted endpoints better than models based only on claims data.[65–67] In many models described in other studies, healthcare utilisation parameters, and especially previous hospitalisations, were predictive of (re)hospitalisations, emergency admissions and functional impairment.[66 68 69] The predictive power of sex is inconsistent: in 18/27 risk models, sex was included in the final model;[66] in 7/23 risk models, male sex was predictive,[65] while a further 25 studies found sex to have no influence.[68 69] Model quality also improved in studies that included multimorbidity and polypharmacy parameters.[66 68 70] However, the parameters and instruments used

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

Table 2 Comparison of models

	Models based on claims data: core predictors	AUC*	R^2	
1.1	Combined outcome after 6 months	0.71 (0.70)	0.16 (0.16)	
1.2	Combined outcome after 9 months	0.69 (0.69)	0.15 (0.14)	
1.3	Combined outcome after 24 months	0.68 (0.68)	0.13 (0.12)	
	Models based on CRT data: core predictors*	AIC	R^2	$R^{2\ (10x)}$
	EQ-5D-3L after 6 months			
2.1	No imputation, no variable selection	4138.86 (4069.41)	0.155 (0.159)	0.112 (0.103)
2.2	No imputation, with variable selection	4138.81 (4068.69)	0.150 (0.155)	0.129 (0.122)
2.3	With imputation, no variable selection	4582.30 (4507.71)	0.159 (0.163)	0.094 (0.108)
2.4	With imputation, with variable selection	4583.15 (4507.47)	0.919 (0.925)	0.111 (0.128)
	EQ-5D-3L after 9 months			
2.5	No imputation, no variable selection	3917.75 (3917.75)	0.150 (0.150)	0.030 (0.030)
2.6	No imputation, with variable selection	3921.95 (3921.95)	0.146 (0.146)	0.053 (0.053)
2.7	With imputation, no variable selection	4540.58 (4505.52)	0.156 (0.152)	0.090 (0.093)
2.8	With imputation, with variable selection	4546.42 (4511.10)	0.221 (0.218)	0.107 (0.106)
	Models based on CRT data: core predictors and additional predictors*			
	EQ-5D, after 6 months			
3.1	No imputation, no variable selection	3205.13 (3205.13)	0.034 (0.034)	0.442 (0.442)
3.2	With imputation, no variable selection	4308.94 (4308.94)	0.538 (0.538)	0.481 (0.481)
3.3	No imputation, with variable selection	3197.37 (3197.37)	0.526 (0.526)	0.483 (0.483)
3.4	With imputation, with variable selection†	4307.47 (4307.47)	0.677 (0.677)	0.507 (0.507)
	Models with 'fixed variables'			
3.5	No imputation, no variable selection	3208.58 (3208.58)	0.514 (0.514)	0.468 (0.468)
3.6	With imputation, with variable selection	4308.90 (4308.90)	0.665 (0.665)	0.499 (0.499)
	EQ-5D, after 9 months			
3.7	No imputation, no variable selection	3061.06 (3113.53)	0.042 (0.028)	0.411 (0.409)
3.8	With imputation, no variable selection	4307.28 (4361.36)	0.498 (0.477)	0.433 (0.404)
3.9	No imputation, with variable selection	3062.03 (3108.61)	0.490 (0.485)	0.448 (0.443)
3.10	With imputation, with variable selection	4309.88 (4360.32)	0.453 (0.346)	0.455 (0.431)
	Models with fixed variables			
3.11	No imputation, no variable selection	3064.76 (3113.08)	0.490 (0.485)	0.439 (0.434)
3.12	With imputation, with variable selection	4310.92 (4363.62)	0.113 (0.071)	0.447 (0.423)

(sensitivity analyses)
*Models based on randomised controlled trial data: fixed effects.
†Best overall model.
AIC, Akaike Information Criterion; AUC, area under the curve after 10-fold cross validation; R^2, Nagelkerke's R^2; $R^{2\ (10x)}$, Nagelkerke's R^2 with 10-fold cross validation.

in modelling (eg, CIRS, Charlson Comorbidity Index and disease count, as reported here) varied considerably among studies. They were neither consistently predictive, nor were certain parameters or instruments better than others.[66 69 70]

Most published models were developed to predict the risk of hospitalisation.[66 68–74] Other models predicted functional outcomes,[70] while four models predicted adverse drug reactions.[74] So far, little is known about the predictive power of polypharmacy parameters and the appropriateness of prescriptions, especially the MAI has never been used in prognostic models. Furthermore, no models have yet been developed to predict HRQoL in patients with multimorbidity and polypharmacy in general practice.[27 70]

Strengths and limitations

One strength of our study is that we could use two data sources with differing advantages in our exploratory analysis: claims data contained a large number of cases, and

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

Table 3 Best performing models per data set and set of predictors

Best model based on claims data: core predictors (model 1.1)	OR	(95% CI)	P value	z-value	NRI
Age (years)	1.02	(1.02 to 1.02)	<0.001	45.4	0.11
Sex (female)	0.99	(0.97 to 1.00)	0.025	−2.2	−0.03
Disease count	1.02	(1.02 to 1.03)	<0.001	19.2	0.05
CCI	1.03	(1.03 to 1.04)	<0.001	22.7	0.02
No. of specific chronic diseases (Diederichs)	1.01	(1.00 to 1.01)	<0.001	3.9	0.01
No. of PIM (EU-PIM)	1.03	(1.02 to 1.03)	<0.001	8.9	0.02
ACh burden (ADS)	1.04	(1.03 to 1.05)	<0.001	14.9	0.04
Modified Drug Burden Index	1.08	(1.07 to 1.08)	<0.001	20.1	0.08
Previous hospitalisations	1.67	(1.65 to 1.70)	<0.001	82.3	0.34
Previous falls/fall-related injuries	3.29	(3.25 to 3.34)	<0.001	188.6	0.55
No. of involved physicians	1.02	(1.02 to 1.02)	<0.001	29.0	0.08
Best model based on CRT data: core predictors (model 2.4)	Coefficient	(95% CI)	P value		
Intercept	101.18	(93.11 to 109.25)	<0.001		
Sex (female)	−11.26	(−15.59 to −6.94)	<0.001		
No. of specific chronic diseases (Diederichs)	−2.18	(−3.64 to −0.73)	0.004		
No. of drugs	−1.28	(−2.23 to −0.32)	0.010		
Modified Drug Burden Index	−5.19	(−8.26 to −2.12)	0.001		
Previous falls	−6.11	(−12.07 to −0.15)	0.045		
Best model based on CRT data: core predictors and additional predictors (model 3.4, best overall model)	Coefficient	(95% CI)	P value		
Intercept	51.74	(38.91 to 64.57)	<0.001		
Sex (female)	−3.61	(−6.96 to −0.27)	0.036		
No. of specific chronic diseases (Diederichs)	−1.03	(−2.08 to 0.01)	0.055		
No. of involved physicians	0.80	(−0.13 to 1.74)	0.093		
Body mass index	−0.28	(−0.53 to −0.03)	0.031		
Medication Appropriateness Index	−0.39	(−0.70 to −0.08)	0.015		
Depressive symptoms (GDS)	−2.73	(−3.56 to −1.91)	<0.001		
EQ-5D Index Score (baseline)	0.55	(0.47 to 0.64)	<0.001		

ACh burden, anticholinergic drug burden; ADS, Anticholinergic Drug Scale; CCI, Charlson Comorbidity Index; GDS, Geriatric Depression Scale; NRI, continuous net reclassification index; PIM, potentially inappropriate medication.

trial data provided additional high-quality patient data including functional status and HRQoL. Both data sets also have their limitations, since claims are documented for billing purposes and are therefore imprecise, whereas our trial data set consisted of only a limited number of observations. Thus, each data set allows its own endpoints to be modelled. Risk modelling is especially complex in multimorbid patients with polypharmacy, as predictor variables in this patient collective are often associated with one another (eg, diagnoses and prescriptions). In addition, comparable risk situations can lead to different endpoints, as risk often depends on context. For example, a drug-induced fall may have no health-related consequences or may lead to impairment and institutionalisation.

Further to these key limitations, our results need careful interpretation for several reasons: First, the combined endpoint in the claims-based models yielded a high event rate, which may have resulted in overoptimistic results in our logistic regression. However, other approaches would not have resolved this problem to suit our purposes either. Additionally, we still have enough cases in both categories of the dependent variable to conduct a valid model estimation. Nonetheless, the low performance of the claims model may have been because predictors acted in different ways on the different elements of the combined outcome, thus resulting in greater heterogeneity.[75] Second, the small sample size of the trial population may have led to some overfitting of the model. At the same time, the VIF (to assess any

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

multi-collinearity) showed only up to moderate values. The application of shrinkage methods would have been a possible alternative to address this limitation.[76] However, there is an ongoing debate whether it solves such problems, and a recent study has suggested that although shrinkage can result in improved calibration, it may not be superior in terms of reducing overfitting.[77] Furthermore, shrinkage models lead to biassed estimates of the regression coefficients, thus making results more difficult to interpret. Third, in our modelling approach we tested disease-based indicators such as the Charlson Comorbidity Index and CIRS that were developed and validated for other purposes. However, we chose indicators that showed a strong association with negative health outcomes.[35]

Relevance for primary care and research implications

As the models derived in our study have not been externally validated and our methods have some limitations, we do not claim to have developed comprehensive prognostic models to identify older general practice patients with multimorbidity and polypharmacy at risk of negative health outcomes. For this reason, we plan to conduct an individual patient data-based meta-analysis to further develop and externally validate the models presented here (PROSPERO ID: CRD42018088129).

It is, however, very likely that baseline components of our predicted endpoints are important predictors, especially considering these results are unsurprising and entirely plausible. A decline in HRQoL, a previous hospitalisation and a previous falls/fall-related injury can therefore be seen as a warning parameter ('red flag') that may help general practitioners in recognising older patients with multimorbidity and polypharmacy at high risk of adverse health outcomes. These patients are therefore more likely to benefit from an intervention than others with low or no risk.[24] Hence, researchers evaluating polypharmacy interventions, such as medication reviews, may like to consider our models when deciding on selection and inclusion criteria for a study population.

CONCLUSIONS

This study provides prognostic models to identify older general practice patients with multimorbidity and polypharmacy at high risk of deterioration in HRQoL, hospitalisation, falls/fall-related injuries, institutionalisation and a need of nursing care. Outcome components, such as previous falls, hospital stays, reduced HRQoL and depression, were important predictors of these negative health outcomes in our models. They can be seen as warning signs of future worsening and an indication that these patients are likely to benefit from interventions to optimise their medication. Future studies should externally validate the models and evaluate the effectiveness of polypharmacy interventions in high-risk patients.

Ethics approval and consent to participate

Claims may be analysed by statutory health insurance companies in accordance with § 284 of Social Code Book V. For the research questions of this project, claims data were analysed by Cologne University, Goethe-University Frankfurt and Heidelberg University collaboratively with TK. When claims are anonymously analysed in accordance with Good Practice in Claims Data Analysis,[78] no further ethics vote is required. Regarding our trial data, the ethics commission of the medical faculty of the Johann Wolfgang Goethe University, Frankfurt/Main approved the PRIMUM trial (resolution number E 46/10, file number 123/10, date: 20 May 2010) and all of the participants gave their written informed consent before taking part.

Author affiliations
[1]Institute of General Practice, Goethe University Frankfurt, Frankfurt am Main, Hessen, Germany
[2]Institute of Medical Biometry and Informatics, University of Heidelberg, Heidelberg, Baden-Württemberg, Germany
[3]PMV Research Group, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Nordrhein-Westfalen, Germany
[4]Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK
[5]APEx Collaboration for Academic Primary Care, University of Exeter Medical School, Exeter, UK
[6]Centre for Research in Evidence-Based Practice, Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Queensland, Australia
[7]Department of Family Medicine, School CAPHRI, Maastricht University, Maastricht, Limburg, The Netherlands

Twitter Rafael Perera @rafaoxford

Acknowledgements The authors would like to thank Phillip Elliott for the language review of the paper.

Contributors MB, FMG and CM designed the study. PI, LU and CS analysed the data. BSM, LU, PI, CS, FvB, MB, FMG, RP, JMV, PG, MvdA and CM contributed to the interpretation of the data. CM and BM drafted the manuscript and all authors revised it and subsequent versions of the manuscript critically for important intellectual content. All authors approved the version to be submitted for publication. LU, CS and CM had full access to all data and are responsible for the integrity and the accuracy of the data analysis.

Funding This study was supported by the German Statutory Healthcare Insurance Company *Techniker Krankenkasse*.

Competing interests FMG, BSM, MB and CM received grants from the German Statutory Healthcare Insurance Company *Techniker Krankenkasse* during the course of the study. CS has been employed by Boehringer Ingelheim GmbH & Co KG since October 2019.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement The data sets generated and analysed in the current study are not publicly available, as further analyses are ongoing.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iDs
Beate S Müller http://orcid.org/0000-0002-6745-1047
Christiane Muth http://orcid.org/0000-0001-8987-182X

REFERENCES

1 Salisbury C, Johnson L, Purdy S, *et al*. Epidemiology and impact of multimorbidity in primary care: a retrospective cohort study. *Br J Gen Pract* 2011;61:e12–21.
2 Moßhammer D, Haumann H, Mörike K, *et al*. Polypharmacy-an upward trend with unpredictable effects. *Dtsch Arztebl Int* 2016;113:627–33.
3 Muth C, Blom JW, Smith SM, *et al*. Evidence supporting the best clinical management of patients with multimorbidity and polypharmacy: a systematic guideline review and expert consensus. *J Intern Med* 2019;285:272–88.
4 Palmer K, Marengoni A, Forjaz MJ, *et al*. Multimorbidity care model: recommendations from the consensus meeting of the joint action on chronic diseases and promoting healthy ageing across the life cycle (JA-CHRODIS). *Health Policy* 2018;122:4–11.
5 Nobili A, Marengoni A, Tettamanti M, *et al*. Association between clusters of diseases and polypharmacy in hospitalized elderly patients: results from the REPOSI study. *Eur J Intern Med* 2011;22:597–602.
6 Oscanoa TJ, Lizaraso F, Carvajal A. Hospital admissions due to adverse drug reactions in the elderly. A meta-analysis. *Eur J Clin Pharmacol* 2017;73:759–70.
7 Angamo MT, Chalmers L, Curtain CM, *et al*. Adverse-Drug-Reaction-Related hospitalisations in developed and developing countries: a review of prevalence and contributing factors. *Drug Saf* 2016;39:847–57.
8 Deandrea S, Lucenteforte E, Bravi F, *et al*. Risk factors for falls in community-dwelling older people: a systematic review and meta-analysis. *Epidemiology* 2010;21:658–68.
9 Heinrich S, Rapp K, Rissmann U, *et al*. Cost of falls in old age: a systematic review. *Osteoporos Int* 2010;21:891–902.
10 Fried TR, O'Leary J, Towle V, *et al*. Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. *J Am Geriatr Soc* 2014;62:2261–72.
11 Payne RA, Abel GA, Avery AJ, *et al*. Is polypharmacy always hazardous? A retrospective cohort analysis using linked electronic health records from primary and secondary care. *Br J Clin Pharmacol* 2014;77:1073–82.
12 Gnjidic D, Hilmer SN, Blyth FM, *et al*. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. *J Clin Epidemiol* 2012;65:989–95.
13 Hilmer SN, Mager DE, Simonsick EM, *et al*. A drug burden index to define the functional burden of medications in older people. *Arch Intern Med* 2007;167:781–7.
14 Salahudeen MS, Duffull SB, Nishtala PS. Anticholinergic burden quantified by anticholinergic risk scales and adverse outcomes in older people: a systematic review. *BMC Geriatr* 2015;15:31.
15 Gurwitz JH, Field TS, Harrold LR, *et al*. Incidence and preventability of adverse drug events among older persons in the ambulatory setting. *JAMA* 2003;289:1107–16.
16 Kuijpers MAJ, van Marum RJ, Egberts ACG, *et al*. Relationship between polypharmacy and underprescribing. *Br J Clin Pharmacol* 2008;65:130–3.
17 Steinman MA, Landefeld CS, Rosenthal GE, *et al*. Polypharmacy and prescribing quality in older people. *J Am Geriatr Soc* 2006;54:1516–23.
18 Meid AD, Quinzler R, Freigofas J, *et al*. Medication underuse in aging outpatients with cardiovascular disease: prevalence, determinants, and outcomes in a prospective cohort study. *PLoS One* 2015;10:e0136339.
19 Müller BS, Uhl MC, Sophia NT, *et al*. Patienten MIT Multimedikation: Ambulante Herausforderungen und Lösungswege: Eine qualitative studie. *Zeitschrift für Allgemeinmedizin* 2018;94:396–400.
20 Horne R, Weinman J, Barber N, *et al*. *Concordance, adherence and compliance in medicine taking: Report for the National Co-ordinating Centre for NHS Service Delivery and Organisation R & D (NCCSDO*, 2005.
21 Rankin A, Cadogan CA, Patterson SM, *et al*. Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database Syst Rev* 2018;9:CD008165.
22 Johansson T, Abuzahra ME, Keller S, *et al*. Impact of strategies to reduce polypharmacy on clinically relevant endpoints: a systematic review and meta-analysis. *Br J Clin Pharmacol* 2016;82:532–48.
23 Muth C, Uhlmann L, Haefeli WE, *et al*. Effectiveness of a complex intervention on prioritising Multimedication in multimorbidity (primum) in primary care: results of a pragmatic cluster randomised controlled trial. *BMJ Open* 2018;8:e017740.
24 Glasziou PP, Irwig LM. An evidence based approach to individualising treatment. *BMJ* 1995;311:1356–9.
25 Murray SA, Kendall M, Mitchell G, *et al*. Palliative care from diagnosis to death. *BMJ* 2017;356:j878.
26 Lynn J. Living long in fragile health: the new demographics shape end of life care. *Hastings Cent Rep* 2005;Spec No:s14–18.
27 National Institute for Health and Care Excellence. *Multimorbidity: clinical assessment and management*. 56. NICE guideline NG, 2016.
28 Bundesministerium für Gesundheit. Km 6-Statistik, 2013. Available: https://www.bundesgesundheitsministerium.de/themen/krankenversicherung/zahlen-und-fakten-zur-krankenversicherung/mitglieder-und-versicherte.html [Accessed 23 Apr 2020].
29 Schäfer I, von Leitner E-C, Schön G, *et al*. Multimorbidity patterns in the elderly: a new approach of disease clustering identifies complex interrelations between chronic conditions. *PLoS One* 2010;5:e15941.
30 Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–98.
31 Graf J-M, Claes C, Greiner W, *et al*. Die Deutsche version des EuroQol-Fragebogens. *J Public Health* 1998;6:3–20.
32 Agborsangaya CB, Lahtinen M, Cooke T, *et al*. Comparing the EQ-5D 3L and 5L: measurement properties and association with chronic conditions and multimorbidity in the general population. *Health Qual Life Outcomes* 2014;12:74.
33 EuroQol Group. EuroQol--a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16:199–208.
34 Charlson ME, Pompei P, Ales KL, *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
35 Diederichs C, Berger K, Bartels DB. The measurement of multiple chronic diseases--a systematic review on existing multimorbidity indices. *J Gerontol A Biol Sci Med Sci* 2011;66:301–11.
36 Renom-Guiteras A, Meyer G, Thürmann PA. The EU(7)-PIM list: a list of potentially inappropriate medications for older people consented by experts from seven European countries. *Eur J Clin Pharmacol* 2015;71:861–75.
37 Holt S, Schmiedl S, Thürmann PA. Potentially Inappropiate medications in the elderly: the PRISCUS list. *Dtsch Arztebl* 2010;107:31–2.
38 Salahudeen MS, Hilmer SN, Nishtala PS. Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people. *J Am Geriatr Soc* 2015;63:85–90.
39 Carnahan RM, Lund BC, Perry PJ, *et al*. The anticholinergic drug scale as a measure of drug-related anticholinergic burden: associations with serum anticholinergic activity. *J Clin Pharmacol* 2006;46:1481–6.
40 Brauns H, Steinmann S. *Educational reform in France, West-Germany, the United Kingdom and Hungary.: updating the CASMIN educational classification. ZUMA-Nachrichten*, 1999: 7–44. www.gesis.org/fileadmin/upload/forschung/publikationen/zeitschriften/zuma_nachrichten/zn_44.pdf
41 Saunders JB, Aasland OG, Babor TF, *et al*. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. *Addiction* 1993;88:791–804.
42 Hanlon JT, Schmader KE, Samsa GP, *et al*. A method for assessing drug therapy appropriateness. *J Clin Epidemiol* 1992;45:1045–51.
43 Hudon C, Fortin M, Soubhi H. Abbreviated guidelines for scoring the cumulative illness rating scale (CIRS) in family practice. *J Clin Epidemiol* 2007;60:212.e1–212.e4.
44 Mukherjee B, Ou H-T, Wang F, *et al*. A new comorbidity index: the health-related quality of life comorbidity index. *J Clin Epidemiol* 2011;64:309–19.
45 Yesavage JA, Brink TL, Rose TL, *et al*. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res* 1982;17:37–49.
46 Rubin DB. *Multiple imputation for nonresponse in surveys*. Hoboken, N.J: Wiley-Interscience, 2004.
47 Buuren Svan, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in *R*. *J Stat Softw* 2011;45.
48 Grandt D, Lappe V, Schubert I. *Barmer Arzneimittel report 2018*. Wuppertal, 2018.
49 Wood AM, White IR, Royston P. How should variable selection be performed with multiply imputed data? *Stat Med* 2008;27:3227–46.

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

50 Sauerbrei W. The use of resampling methods to simplify regression models in medical statistics. *J R Statist Soc C* 1999;48:313–29.
51 Kerr KF, Wang Z, Janes H, *et al*. Net reclassification indices for evaluating risk prediction instruments: a critical review. *Epidemiology* 2014;25:114–21.
52 James G, Witten D, Hastie T, *et al*. *An introduction to statistical learning: with applications in R*. 8th edn. New York,Heidelberg, Dordrecht, London: Springer, 2017.
53 Nakagawa S, Schielzeth H, O'Hara RB. A general and simple method for obtaining R^2 from generalized linear mixed-effects models. *Methods Ecol Evol* 2013;4:133–42.
54 Steyerberg EW, Vickers AJ, Cook NR, *et al*. Assessing the performance of prediction models: a framework for traditional and novel measures. *Epidemiology* 2010;21:128–38.
55 Nagelkerke NJD. A note on a general definition of the coefficient of determination. *Biometrika* 1991;78:691–2.
56 Hastie T, Tibshirani R, Friedman JH. *The elements of statistical learning: data mining, inference, and prediction*. 12th edn. New York: Springer, 2017.
57 R Core Team. *R: a language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing, 2016.
58 Pinhero J, Bates D, DebRoy S. *nlme: linear and nonlinear mixed effects models. R package*. version 3, 2016: 1–128.
59 Kundu S, Aulchenko YS, Janssens A, *et al*. *PredictABEL: assessment of risk prediction models. R package version*. version 1.2-2, 2014: 2.
60 Lumley T. *mitools: tools for multiple imputation of missing data. R package*. version 2.3, 2014.
61 Nakazawa M. *fmsb: functions for medical statistics book with some demographic data. R package*. version 0.5.2, 2015.
62 Dahl DB. *xtable: export tables to latex or HTML. R package*. version 1.8-2, 2016.
63 Xie Y. *knitr: a general-purpose package for dynamic report generation in R. R package*. version 1.13, 2016.
64 Collins GS, Reitsma JB, Altman DG, *et al*. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. *Ann Intern Med* 2015;162:55–63.
65 O'Caoimh R, Cornally N, Weathers E, *et al*. Risk prediction in the community: a systematic review of case-finding instruments that predict adverse healthcare outcomes in community-dwelling older adults. *Maturitas* 2015;82:3–21.
66 Wallace E, Stuart E, Vaughan N, *et al*. Risk prediction models to predict emergency hospital admission in community-dwelling adults: a systematic review. *Med Care* 2014;52:751–65.
67 Coleman EA, Min S-joon, Chomiak A, *et al*. Posthospital care transitions: patterns, complications, and risk identification. *Health Serv Res* 2004;39:1449–66.
68 Campbell SE, Seymour DG, Primrose WR, *et al*. A systematic literature review of factors affecting outcome in older medical patients admitted to hospital. *Age Ageing* 2004;33:110–5.
69 García-Pérez L, Linertová R, Lorenzo-Riera A, *et al*. Risk factors for hospital readmissions in elderly patients: a systematic review. *QJM* 2011;104:639–51.
70 Alonso-Morán E, Nuño-Solinis R, Onder G, *et al*. Multimorbidity in risk stratification tools to predict negative outcomes in adult population. *Eur J Intern Med* 2015;26:182–9.
71 Wallace E, Hinchey T, Dimitrov BD, *et al*. A systematic review of the probability of repeated admission score in community-dwelling adults. *J Am Geriatr Soc* 2013;61:357–64.
72 Kansagara D, Englander H, Salanitro A, *et al*. Risk prediction models for hospital readmission: a systematic review. *JAMA* 2011;306:1688–98.
73 Vest JR, Gamm LD, Oxford BA, *et al*. Determinants of preventable readmissions in the United States: a systematic review. *Implement Sci* 2010;5:88.
74 Stevenson JM, Williams JL, Burnham TG, *et al*. Predicting adverse drug reactions in older adults; a systematic review of the risk prediction models. *Clin Interv Aging* 2014;9:1581–93.
75 Glynn RJ, Rosner B. Methods to evaluate risks for composite end points and their individual components. *J Clin Epidemiol* 2004;57:113–22.
76 Steyerberg EW, Eijkemans MJ, Harrell FE, *et al*. Prognostic modeling with logistic regression analysis: in search of a sensible strategy in small data sets. *Med Decis Making* 2001;21:45–56.
77 van Calster B, van Smeden M, de CB, *et al*. Regression shrinkage methods for clinical prediction models do not guarantee improved performance: simulation study. *Stat Methods Med Res* 2020:962280220921415.
78 Swart E, Gothe H, Geyer S, *et al*. Gute praxis Sekundärdatenanalyse (GPs): Leitlinien und Empfehlungen. *Gesundheitswesen* 2015;77:120–6.

BMJ Open: first published as 10.1136/bmjopen-2020-039747 on 22 October 2020. Downloaded from http://bmjopen.bmj.com/ on July 27, 2021 at StUB/Seb Frankfurt. Protected by copyright.

Additional file 1: Falls and fall-related injuries: list of excluded ICD-10-codes

Conditions	**ICD-10-Code** (ICD-10-GM Version 2014)
▪ Osteoporosis with pathological fracture	M80
▪ Open wound of neck	S11
▪ Dislocation, sprain and strain of joints and ligaments at neck level	S13
▪ Injury of nerves and spinal cord at neck level	S14
▪ Injury of blood vessels at neck level	S15
▪ Injury of muscle and tendon at neck level	S16
▪ Crushing injury of neck	S17
▪ Traumatic amputation at neck level	S18
▪ Other and unspecified injuries of neck	S19
▪ Injury of blood vessels of thorax	S25
▪ Injury of heart	S26
▪ Injury of other and unspecified intrathoracic organs	S27
▪ Crushing injury of thorax and traumatic amputation of part of thorax	S28
▪ Other and unspecified injuries of thorax	S29
▪ Open wound of abdomen, lower back and pelvis	S31
▪ Injury of blood vessels at abdomen, lower back and pelvis level	S35
▪ Injury of pancreas	S36.2
▪ Injury of stomach	S36.3

▪ Injury of small intestine	S36.4
▪ Injury of colon	S36.5
▪ Injury of rectum	S36.6
▪ Injury of multiple intra-abdominal organs	S36.7
▪ Injury of other intra-abdominal organs	S36.8
▪ Injury of ureter	S37.1
▪ Injury of bladder	S37.2
▪ Injury of urethra	S37.3
▪ Injury of ovary	S37.4
▪ Injury of fallopian tube	S37.5
▪ Injury of uterus	S37.6
▪ Injury of multiple pelvic organs	S37.7
▪ Injury of other pelvic organs	S37.8
▪ Crushing injury and traumatic amputation of part of abdomen, lower back and pelvis	S38
▪ Injury of intra-abdominal organ(s) with pelvic organ(s)	S39.6
▪ Other multiple injuries of abdomen, lower back and pelvis	S39.7
▪ Other specified injuries of abdomen, lower back and pelvis	S39.8
▪ Crushing injury of shoulder and upper arm	S47
▪ Traumatic amputation of shoulder and upper arm	S48
▪ Traumatic amputation of forearm	S58
▪ Traumatic amputation of wrist and hand	S68

▪ Traumatic amputation of hip and thigh	S78
▪ Traumatic amputation of lower leg	S88
▪ Traumatic amputation of ankle and foot	S98
▪ Crushing injuries involving multiple body regions	T04
▪ Traumatic amputations involving multiple body regions	T05
▪ Effects of foreign body entering through natural orifice	T15-19
▪ Burns and corrosions	T20-32
▪ Frostbite	T33-35
▪ Poisoning by specified narcotics and psychodysleptic agents (hallucinogenic drugs)	T40.0-T40.1, T40.3, T40.5-T40.9
▪ Toxic effects of substances chiefly nonmedicinal as to source	T51-65
▪ Other and unspecified effects of external causes	T66-77
▪ Complications of surgical and medical care, not elsewhere classified	T80-87
▪ Sequelae of injuries, of poisoning and of other consequences of external causes	T90-98

Potentially inappropriate drugs EU-PIM	**ATC-Code 2014**	**ATC-Code 2013**	**ATC-Code 2012**	**ATC-Code 2011**
Magnesium hydroxide 1	A02AA04	A02AA04	A02AA04	A02AA04
Aluminium-containing antacids 1	A02AB01	A02AB01	A02AB01	A02AB01
Aluminium-containing antacids 2	A02AB02	A02AB02	A02AB02	A02AB02
Aluminium-containing antacids 3	A02AB03	A02AB03	A02AB03	A02AB03
Aluminium-containing antacids 4	A02AB04	A02AB04	A02AB04	A02AB04
Aluminium-containing antacids 5	A02AB05	A02AB05	A02AB05	A02AB05
Aluminium-containing antacids 6	A02AB06	A02AB06	A02AB06	A02AB06
Aluminium-containing antacids 7	A02AB07	A02AB07	A02AB07	A02AB07
Aluminium-containing antacids 8	A02AB10	A02AB10	A02AB10	A02AB10
Aluminium-containing antacids 15	A02AD02	A02AD02	A02AD02	A02AD02
Aluminium-containing antacids 16	A02AD03	A02AD03	A02AD03	A02AD03
Aluminium-containing antacids 17	A02AD04	A02AD04	A02AD04	A02AD04
Aluminium-containing antacids 18	A02AD05	A02AD05	A02AD05	A02AD05
Aluminium-containing antacids 9	A02AD06	A02AD06	A02AD06	A02AD06
Aluminium-containing antacids 10 (Magnesium hydroxide 2)	A02AD10	A02AD10	A02AD10	A02AD10
Aluminium-containing antacids 11	A02AF01	A02AF01	A02AF01	A02AF01
Aluminium-containing antacids 12	A02AF03	A02AF03	A02AF03	A02AF03
Aluminium-containing antacids 13	A02AF04	A02AF04	A02AF04	A02AF04
Aluminium-containing antacids 14	A02AF05	A02AF05	A02AF05	A02AF05
Cimetidine 1	A02BA01	A02BA01	A02BA01	A02BA01
Ranitidine 1	A02BA02	A02BA02	A02BA02	A02BA02
Famotidine 1	A02BA03	A02BA03	A02BA03	A02BA03
Ranitidine 2	A02BA07	A02BA07	A02BA07	A02BA07
Cimetidine 2	A02BA51	A02BA51	A02BA51	A02BA51
Famotidine 2	A02BA53	A02BA53	A02BA53	A02BA53
Mebeverine	A03AA04	A03AA04	A03AA04	A03AA04
Trimebutine	A03AA05	A03AA05	A03AA05	A03AA05
Dihexyverine	A03AA08	A03AA08	A03AA08	A03AA08
Otilonium bromide 1	A03AB06	A03AB06	A03AB06	A03AB06
Tiemonium (iodide) 1	A03AB17	A03AB17	A03AB17	A03AB17
Trospium 2	A03AB20	A03AB20	A03AB20	A03AB20
Pinaverium	A03AX04	A03AX04	A03AX04	A03AX04
Belladonna alkaloids 2	A03BA01	A03BA01	A03BA01	A03BA01
Belladonna alkaloids 3 (Hyoscyamine 1)	A03BA03	A03BA03	A03BA03	A03BA03
Belladonna alkaloids 4	A03BA04	A03BA04	A03BA04	A03BA04
Belladonna alkaloids 5	A03BA20	A03BA20	A03BA20	A03BA20
Belladonna alkaloids 6	A03BB01	A03BB01	A03BB01	A03BB01
Belladonna alkaloids 7	A03BB02	A03BB02	A03BB02	A03BB02
Belladonna alkaloids 8	A03BB03	A03BB03	A03BB03	A03BB03
Belladonna alkaloids 9	A03BB04	A03BB04	A03BB04	A03BB04
Belladonna alkaloids 10	A03BB05	A03BB05	A03BB05	A03BB05
Clidinium	A03CA02	A03CA02	A03CA02	A03CA02
Otilonium bromide 2	A03CA04	A03CA04	A03CA04	A03CA04
Belladonna alkaloids 11	A03CB01	A03CB01	A03CB01	A03CB01
Belladonna alkaloids 12	A03CB02	A03CB02	A03CB02	A03CB02
Belladonna alkaloids 13	A03CB03	A03CB03	A03CB03	A03CB03
Belladonna alkaloids 14	A03CB04	A03CB04	A03CB04	A03CB04
Belladonna alkaloids 15 + Hyoscyamine 2	A03CB31	A03CB31	A03CB31	A03CB31
Belladonna alkaloids 16	A03CB37	A03CB37	A03CB37	A03CB37
Belladonna alkaloids 17	A03CB38	A03CB38	A03CB38	A03CB38
Pitofenone	A03DA02	A03DA02	A03DA02	A03DA02
Trospium 3	A03DA06	A03DA06	A03DA06	A03DA06
Tiemonium (iodide) 2	A03DA07	A03DA07	A03DA07	A03DA07
Belladonna alkaloids 18	A03DB04	A03DB04	A03DB04	A03DB04
Trospium 4	A03EA04	A03EA04	A03EA04	A03EA04

Metoclopramide 1	A03FA01	A03FA01	A03FA01	A03FA01
Alizapride	A03FA05	A03FA05	A03FA05	A03FA05
Metoclopramide 2	A03FA51	A03FA51	A03FA51	A03FA51
Dimenhydrinate 1	A04AB02	A04AB02	A04AB02	A04AB02
Meclozine 3	A04AB04	A04AB04	A04AB04	A04AB04
Diphenhydramine 3	A04AB05	A04AB05	A04AB05	A04AB05
Dimenhydrinate 2	A04AB52	A04AB52	A04AB52	A04AB52
Meclozine 4	A04AB54	A04AB54	A04AB54	A04AB54
Diphenhydramine 6	A04AB55	A04AB55	A04AB55	A04AB55
Doxylamine 4	A04AB56	A04AB56	A04AB56	A04AB56
Promethazine 3	A04AB58	A04AB58	A04AB58	A04AB58
Scopolamine 1 (=Hyoscin)	A04AD01	A04AD01	A04AD01	A04AD01
Metopimazine	A04AD05	A04AD05	A04AD05	A04AD05
Scopolamine 2 (=Hyoscin)	A04AD51	A04AD51	A04AD51	A04AD51
Viscous paraffin (=Liquid paraffin) 1	A06AA01	A06AA01	A06AA01	A06AA01
Docusate sodium (oral)	A06AA02	A06AA02	A06AA02	A06AA02
Viscous paraffin (=Liquid paraffin) 2	A06AA51	A06AA51	A06AA51	A06AA51
Castor oil (=Ricinus communis, =Neoloid)	A06AB05	A06AB05	A06AB05	A06AB05
Senna glycosides 1	A06AB06	A06AB06	A06AB06	A06AB06
Cascara sagrada 1	A06AB07	A06AB07	A06AB07	A06AB07
Sodium picosulfate 1	A06AB08	A06AB08	A06AB08	A06AB08
Aloe 1	A06AB13	A06AB13	A06AB13	A06AB13
Belladonna alkaloids 1	A06AB30	A06AB30	A06AB30	A06AB30
Senna glycosides 2	A06AB56	A06AB56	A06AB56	A06AB56
Cascara sagrada 2	A06AB57	A06AB57	A06AB57	A06AB57
Sodium picosulfate 2	A06AB58	A06AB58	A06AB58	A06AB58
Aloe 2	A06AB63	A06AB63	A06AB63	A06AB63
Prucalopride	A06AX05	A03AE04	A03AE04	A03AE04
Diphenoxylate-Atropin	A07DA01	A07DA01	A07DA01	A07DA01
Racecadotril	A07XA04	A07XA04	A07XA04	A07XA04
Norephedrine (=Phenylpropanolamine) 3	A08AA13	A08AA13	A08AA13	A08AA13
Norephedrine (=Phenylpropanolamine) 4	A08AA63	A08AA63	A08AA63	A08AA63
Glibenclamide 1	A10BB01	A10BB01	A10BB01	A10BB01
Chlorpropamide	A10BB02	A10BB02	A10BB02	A10BB02
Carbutamide	A10BB06	A10BB06	A10BB06	A10BB06
Glipizide	A10BB07	A10BB07	A10BB07	A10BB07
Glimepiride 1	A10BB12	A10BB12	A10BB12	A10BB12
Glimepiride 2	A10BD04	A10BD04	A10BD04	A10BD04
Pioglitazone 3	A10BD05	A10BD05	A10BD05	A10BD05
Glimepiride 3 + Pioglitazone 2	A10BD06	A10BD06	A10BD06	A10BD06
Sitagliptine 3	A10BD07	A10BD07	A10BD07	A10BD07
Vildagliptine 2	A10BD08	A10BD08	A10BD08	A10BD08
Pioglitazone 4	A10BD09	A10BD09	A10BD09	A10BD09
Pioglitazone 5	A10BD12	A10BD12	A10BD12	n/a
Sitagliptine 4	A10BD12	A10BD12	A10BD12	n/a
Glibenclamide 2	A10BD15	n/a	n/a	n/a
Acarbose	A10BF01	A10BF01	A10BF01	A10BF01
Pioglitazone 1	A10BG03	A10BG03	A10BG03	A10BG03
Sitagliptine 1	A10BH01	A10BH01	A10BH01	A10BH01
Vildagliptine 1	A10BH02	A10BH02	A10BH02	A10BH02
Sitagliptine 2	A10BH51	n/a	n/a	n/a
Cyproheptadine 2	A15AA01	A15AA01	A15AA01	A15AA01
Cyproheptadine 3	A15AA51	A15AA51	A15AA51	A15AA51
Acenocoumarol	B01AA07	B01AA07	B01AA07	B01AA07
Ticlopidine	B01AC05	B01AC05	B01AC05	B01AC05
Dipyridamole 1	B01AC07	B01AC07	B01AC07	B01AC07
Prasugrel	B01AC22	B01AC22	B01AC22	B01AC22
Dipyridamole 2	B01AC36	n/a	n/a	n/a

Dabigatran	B01AE07	B01AE07	B01AE07	B01AE07
Rivaroxaban	B01AF01	B01AF01	B01AX06	B01AX06
Apixaban	B01AF02	B01AF02	B01AX08	n/a
Acetyldigitoxin	C01AA01	C01AA01	C01AA01	C01AA01
Acetyldigoxin 1	C01AA02	C01AA02	C01AA02	C01AA02
Digitoxin 1	C01AA04	C01AA04	C01AA04	C01AA04
Digoxin 1	C01AA05	C01AA05	C01AA05	C01AA05
Metildigoxin 1	C01AA08	C01AA08	C01AA08	C01AA08
Acetyldigoxin 2	C01AA52	C01AA52	C01AA52	C01AA52
Digitoxin 2	C01AA54	C01AA54	C01AA54	C01AA54
Digoxin 2	C01AA55	C01AA55	C01AA55	C01AA55
Metildigoxin 2	C01AA58	C01AA58	C01AA58	C01AA58
Quinidine and combinations 1	C01BA01	C01BA01	C01BA01	C01BA01
Procainamide	C01BA02	C01BA02	C01BA02	C01BA02
Disopyramide	C01BA03	C01BA03	C01BA03	C01BA03
Quinidine and combinations 2	C01BA51	C01BA51	C01BA51	C01BA51
Quinidine and combinations 3	C01BA71	C01BA71	C01BA71	C01BA71
Propafenone	C01BC03	C01BC03	C01BC03	C01BC03
Flecainide	C01BC04	C01BC04	C01BC04	C01BC04
Amiodarone	C01BD01	C01BD01	C01BD01	C01BD01
Dronedarone	C01BD07	C01BD07	C01BD07	C01BD07
Dipyridamole 4	C01DX21	C01DX21	C01DX21	C01DX21
Dipyridamole 3	C01DX71	C01DX71	C01DX71	C01DX71
Indometacin 2	C01EB03	C01EB03	C01EB03	C01EB03
Trimetazidine	C01EB15	C01EB15	C01EB15	C01EB15
Ivabradine	C01EB17	C01EB17	C01EB17	C01EB17
Theophylline 2	C01EB22	C01EB22	C01EB22	C01EB22
Theophylline 3	C01EX66	C01EX66	C01EX66	C01EX66
Reserpine 1	C02AA02	C02AA02	C02AA02	C02AA02
Reserpine 2	C02AA52	C02AA52	C02AA52	C02AA52
Methyldopa 1	C02AB01	C02AB01	C02AB01	C02AB01
Methyldopa 2	C02AB02	C02AB02	C02AB02	C02AB02
Clonidine 1	C02AC01	C02AC01	C02AC01	C02AC01
Guanfacine	C02AC02	C02AC02	C02AC02	C02AC02
Moxonidine 1	C02AC05	C02AC05	C02AC05	C02AC05
Rilmenidine	C02AC06	C02AC06	C02AC06	C02AC06
Prazosin 1	C02CA01	C02CA01	C02CA01	C02CA01
Doxazosin 1	C02CA04	C02CA04	C02CA04	C02CA04
Urapidil	C02CA06	C02CA06	C02CA06	C02CA06
Terazosin 2	C02CA08	C02CA08	C02CA08	C02CA08
Guanethidine 1	C02CC02	C02CC02	C02CC02	C02CC02
Hydralazine 1	C02DB02	C02DB02	C02DB02	C02DB02
Reserpine 3	C02LA01	C02LA01	C02LA01	C02LA01
Reserpine 4	C02LA51	C02LA51	C02LA51	C02LA51
Reserpine 5	C02LA71	C02LA71	C02LA71	C02LA71
Methyldopa 3	C02LB01	C02LB01	C02LB01	C02LB01
Clonidine 2	C02LC01	C02LC01	C02LC01	C02LC01
Moxonidine 2	C02LC05	C02LC05	C02LC05	C02LC05
Clonidine 3	C02LC51	C02LC51	C02LC51	C02LC51
Prazosin 2	C02LE01	C02LE01	C02LE01	C02LE01
Guanethidine 2	C02LF01	C02LF01	C02LF01	C02LF01
Hydralazine 2	C02LG02	C02LG02	C02LG02	C02LG02
Niacin (=Nicotinic acid) 2	C04AC51	C04AC51	C04AC51	C04AC51
Pentoxifylline	C04AD03	C04AD03	C04AD03	C04AD03
Ergoloid mesylate (= dihydroergotoxine) 1	C04AE01	C04AE01	C04AE01	C04AE01
Nicergoline 1	C04AE02	C04AE02	C04AE02	C04AE02
Dihydroergocristine 1	C04AE04	C04AE04	C04AE04	C04AE04
Ergoloid mesylate (= dihydroergotoxine) 2	C04AE51	C04AE51	C04AE51	C04AE51

Dihydroergocristine 2	C04AE54	C04AE54	C04AE54	C04AE54
Cyclandelate (=Cyclospasmol) 1	C04AX01	C04AX01	C04AX01	C04AX01
Vincamine 1	C04AX07	C04AX07	C04AX07	C04AX07
Moxisylyte 1	C04AX10	C04AX10	C04AX10	C04AX10
Piribedil 2	C04AX13	C04AX13	C04AX13	C04AX13
Vinburnine	C04AX17	C04AX17	C04AX17	C04AX17
Buflomedil	C04AX20	C04AX20	C04AX20	C04AX20
Naftidrofuryl	C04AX21	C04AX21	C04AX21	C04AX21
Quinine and derivatives 5	C05AF01	C05AF01	C05AF01	C05AF01
Quinine and derivatives 6	C05AF51	C05AF51	C05AF51	C05AF51
Digitoxin 3	C05BZ05	C05BZ05	C05BZ05	C05BZ05
Escin (=Aescin) 3	C05BZ09	C05BZ09	C05BZ09	C05BZ09
Escin (=Aescin) 4	C05BZ59	C05BZ59	C05BZ59	C05BZ59
Hidrosmin	C05CA05	C05CA05	C05CA05	C05CA05
Escin (=Aescin) 1	C05CA07	C05CA07	C05CA07	C05CA07
Vincamine-Rutoside	C05CA51	C05CA51	C05CA51	C05CA51
Troxerutin-Vincamine	C05CA54	C05CA54	C05CA54	C05CA54
Escin (=Aescin) 2	C05CA57	C05CA57	C05CA57	C05CA57
Dihydroergotaminmesilat 1	C06AA02	C06AA02	C06AA02	C06AA02
Dihydroergotaminmesilat 2	C06AA50	C06AA50	C06AA50	C06AA50
Oxprenolol 1	C07AA02	C07AA02	C07AA02	C07AA02
Pindolol 1	C07AA03	C07AA03	C07AA03	C07AA03
Propranolol 1	C07AA05	C07AA05	C07AA05	C07AA05
Sotalol 1	C07AA07	C07AA07	C07AA07	C07AA07
Nadolol 1	C07AA12	C07AA12	C07AA12	C07AA12
Sotalol 2	C07AA57	C07AA57	C07AA57	C07AA57
Labetalol 1	C07AG01	C07AG01	C07AG01	C07AG01
Oxprenolol 2	C07BA02	C07BA02	C07BA02	C07BA02
Propranolol 5	C07BA05	C07BA05	C07BA05	C07BA05
Sotalol 3	C07BA07	C07BA07	C07BA07	C07BA07
Nadolol 2	C07BA12	C07BA12	C07BA12	C07BA12
Labetalol 3	C07BG01	C07BG01	C07BG01	C07BG01
Oxprenolol 3	C07CA02	C07CA02	C07CA02	C07CA02
Pindolol 2	C07CA03	C07CA03	C07CA03	C07CA03
Propranolol 4	C07CA05	C07CA05	C07CA05	C07CA05
Labetalol 2	C07CG01	C07CG01	C07CG01	C07CG01
Propranolol 2	C07DA05	C07DA05	C07DA05	C07DA05
Pindolol 3	C07EA03	C07EA03	C07EA03	C07EA03
Propranolol 6	C07EA05	C07EA05	C07EA05	C07EA05
Oxprenolol 4	C07FA02	C07FA02	C07FA02	C07FA02
Propranolol 3	C07FA05	C07FA05	C07FA05	C07FA05
Nifedipine 4	C07FB22	C07FB22	C07FB22	C07FB22
Nifedipine 5	C07FB23	C07FB23	C07FB23	C07FB23
Nicardipine	C08CA04	C08CA04	C08CA04	C08CA04
Nifedipine 1	C08CA05	C08CA05	C08CA05	C08CA05
Nifedipine 2	C08CA55	C08CA55	C08CA55	C08CA55
Verapamil 1	C08DA01	C08DA01	C08DA01	C08DA01
Verapamil 5	C08DA51	C08DA51	C08DA51	C08DA51
Verapamil 2	C08DA81	C08DA81	C08DA81	C08DA81
Diltiazem	C08DB01	C08DB01	C08DB01	C08DB01
Nifedipine 3	C08GA01	C08GA01	C08GA01	C08GA01
Verapamil 3	C08GA02	C08GA02	C08GA02	C08GA02
Verapamil 4	C09BB10	C09BB10	C09BB10	C09BB10
Niacin (=Nicotinic acid) 1	C10AD02	C10AD02	C10AD02	C10AD02
Niacin (=Nicotinic acid) 3	C10AD52	C10AD52	C10AD52	C10AD52
Niacin (=Nicotinic acid) 4	C10BA01	C10BA01	C10BA01	C10BA01
Niacin (=Nicotinic acid) 5	C10BB01	C10BB01	C10BB01	C10BB01
Dimetindene 2	D04AA13	D04AA13	D04AA13	D04AA13

Bromocriptine 2	G02CB01	G02CB01	G02CB01	G02CB01
Cabergoline 2	G02CB03	G02CB03	G02CB03	G02CB03
Oestrogen (oral) 1	G03CA01	G03CA01	G03CA01	G03CA01
Oestrogen (oral) 2	G03CA03	G03CA03	G03CA03	G03CA03
Oestrogen (oral) 3	G03CA04	G03CA04	G03CA04	G03CA04
Oestrogen (oral) 4	G03CA06	G03CA06	G03CA06	G03CA06
Oestrogen (oral) 5	G03CA07	G03CA07	G03CA07	G03CA07
Oestrogen (oral) 6	G03CA09	G03CA09	G03CA09	G03CA09
Oestrogen (oral) 7	G03CA10	G03CA10	G03CA10	G03CA10
Oestrogen (oral) 8	G03CA53	G03CA53	G03CA53	G03CA53
Oestrogen (oral) 9	G03CA57	G03CA57	G03CA57	G03CA57
Oestrogen (oral) 10	G03CB01	G03CB01	G03CB01	G03CB01
Oestrogen (oral) 11	G03CB02	G03CB02	G03CB02	G03CB02
Oestrogen (oral) 12	G03CB03	G03CB03	G03CB03	G03CB03
Oestrogen (oral) 13	G03CB04	G03CB04	G03CB04	G03CB04
Oestrogen (oral) 14	G03CC02	G03CC02	G03CC02	G03CC02
Oestrogen (oral) 15	G03CC03	G03CC03	G03CC03	G03CC03
Oestrogen (oral) 16	G03CC04	G03CC04	G03CC04	G03CC04
Oestrogen (oral) 17	G03CC05	G03CC05	G03CC05	G03CC05
Oestrogen (oral) 18	G03CC06	G03CC06	G03CC06	G03CC06
Oestrogen (oral) 19	G03CC07	G03CC07	G03CC07	G03CC07
Oestrogen (oral) 20	G03CC08	G03CC08	G03CC08	G03CC08
Oestrogen (oral) 21	G03CX01	G03CX01	G03CX01	G03CX01
Flavoxat	G04BD02	G04BD02	G04BD02	G04BD02
Oxybutynine	G04BD04	G04BD04	G04BD04	G04BD04
Tolterodine	G04BD07	G04BD07	G04BD07	G04BD07
Solifenacin 1	G04BD08	G04BD08	G04BD08	G04BD08
Trospium 1	G04BD09	G04BD09	G04BD09	G04BD09
Darifenacin	G04BD10	G04BD10	G04BD10	G04BD10
Fesoterodin	G04BD11	G04BD11	G04BD11	G04BD11
Trospium 5	G04BD59	G04BD59	G04BD59	G04BD59
Moxisylyte 2	G04BE06	G04BE06	G04BE06	G04BE06
Magnesium hydroxide 3	G04BX01	G04BX01	G04BX01	G04BX01
Terazosin 1	G04CA03	G04CA03	G04CA03	G04CA03
Doxazosin 2	G04CA05	G04CA05	G04CA05	G04CA05
Solifenacin 2	G04CA53	n/a	n/a	n/a
Ofloxacin	J01MA01	J01MA01	J01MA01	J01MA01
Amantadine 2	J05AC04	J05AC04	J05AC04	J05AC04
Demecolcin	L01CC01	L01CC01	L01CC01	L01CC01
Celecoxib 2	L01XX33	L01XX33	L01XX33	L01XX33
Phenylbutazone 1	M01AA01	M01AA01	M01AA01	M01AA01
Phenylbutazone 2	M01AA51	M01AA51	M01AA51	M01AA51
Indometacin 1	M01AB01	M01AB01	M01AB01	M01AB01
Diclofenac 1	M01AB05	M01AB05	M01AB05	M01AB05
Acemetacin	M01AB11	M01AB11	M01AB11	M01AB11
Ketorolac	M01AB15	M01AB15	M01AB15	M01AB15
Aceclofenac 1	M01AB16	M01AB16	M01AB16	M01AB16
Indometacin 3	M01AB51	M01AB51	M01AB51	M01AB51
Diclofenac 2	M01AB55	M01AB55	M01AB55	M01AB55
Piroxicam 1	M01AC01	M01AC01	M01AC01	M01AC01
Lornoxicam	M01AC05	M01AC05	M01AC05	M01AC05
Meloxicam 1	M01AC06	M01AC06	M01AC06	M01AC06
Meloxicam 2	M01AC56	M01AC56	n/a	n/a
Ketoprofen 1	M01AE03	M01AE03	M01AE03	M01AE03
Flurbiprofen 1	M01AE09	M01AE09	M01AE09	M01AE09
Dexketoprofen	M01AE17	M01AE17	M01AE17	M01AE17
Ketoprofen 2	M01AE53	M01AE53	M01AE53	M01AE53
Mefenamic acid	M01AG01	M01AG01	M01AG01	M01AG01

Celecoxib 1	M01AH01	M01AH01	M01AH01	M01AH01
Etoricoxib	M01AH05	M01AH05	M01AH05	M01AH05
Nabumetone	M01AX01	M01AX01	M01AX01	M01AX01
Phenylbutazone 3	M01BA01	M01BA01	M01BA01	M01BA01
Phenylbutazone 5	M02AA01	M02AA01	M02AA01	M02AA01
Piroxicam 2	M02AA07	M02AA07	M02AA07	M02AA07
Ketoprofen 3	M02AA10	M02AA10	M02AA10	M02AA10
Diclofenac 3	M02AA15	M02AA15	M02AA15	M02AA15
Flurbiprofen 2	M02AA19	M02AA19	M02AA19	M02AA19
Indometacin 4	M02AA23	M02AA23	M02AA23	M02AA23
Aceclofenac 2	M02AA25	M02AA25	M02AA25	M02AA25
Indometacin 5	M02AA73	M02AA73	M02AA73	M02AA73
Niacin (=Nicotinic acid) 6	M02AD50	M02AD50	M02AD50	M02AD50
Carisoprodol 1	M03BA02	M03BA02	M03BA02	M03BA02
Methocarbamol 1	M03BA03	M03BA03	M03BA03	M03BA03
Carisoprodol 2	M03BA52	M03BA52	M03BA52	M03BA52
Methocarbamol 2	M03BA53	M03BA53	M03BA53	M03BA53
Meprobamate 4	M03BA57	M03BA57	M03BA57	M03BA57
Carisoprodol 3	M03BA72	M03BA72	M03BA72	M03BA72
Methocarbamol 3	M03BA73	M03BA73	M03BA73	M03BA73
Orphenadrine 1	M03BC01	M03BC01	M03BC01	M03BC01
Orphenadrine 2	M03BC51	M03BC51	M03BC51	M03BC51
Baclofen	M03BX01	M03BX01	M03BX01	M03BX01
Tizanidine	M03BX02	M03BX02	M03BX02	M03BX02
Tetrazepam	M03BX07	M03BX07	M03BX07	M03BX07
Cyclobenzaprine	M03BX08	M03BX08	M03BX08	M03BX08
Colchicin	M04AC01	M04AC01	M04AC01	M04AC01
Strontium ranelate	M05BX03	M05BX03	M05BX03	M05BX03
Quinine and derivatives 1	M09AA01	M09AA01	M09AA01	M09AA01
Quinine and derivatives 2	M09AA02	M09AA02	M09AA02	M09AA02
Quinine and derivatives 3	M09AA52	M09AA52	M09AA52	M09AA52
Quinine and derivatives 4	M09AA72	M09AA72	M09AA72	M09AA72
Diphenhydramine 4	N01BX06	N01BX06	N01BX06	N01BX06
Ethylmorphine 2	N02AA57	N02AA57	N02AA57	N02AA57
Diclofenac 4	N02AA65	N02AA65	N02AA65	N02AA65
Pethidine (=Meperidine) 1	N02AB02	N02AB02	N02AB02	N02AB02
Pethidine (=Meperidine) 2	N02AB52	N02AB52	N02AB52	N02AB52
Pethidine (=Meperidine) 3	N02AB72	N02AB72	N02AB72	N02AB72
Methadone 3 (Levomethadone)	N02AC06	N02AC06	N02AC06	N02AC06
Methadone 2	N02AC52	N02AC52	N02AC52	N02AC52
Pentazocine	N02AD01	N02AD01	N02AD01	N02AD01
Pethidine (=Meperidine) 4	N02AG03	N02AG03	N02AG03	N02AG03
Tramadol 1	N02AX02	N02AX02	N02AX02	N02AX02
Tramadol 2	N02AX52	N02AX52	N02AX52	N02AX52
Dihydroergotamine 1	N02CA01	N02CA01	N02CA01	N02CA01
Ergotamine 1	N02CA02	N02CA02	N02CA02	N02CA02
Dihydroergotamine 2	N02CA51	N02CA51	N02CA51	N02CA51
Ergotamine 2	N02CA52	N02CA52	N02CA52	N02CA52
Dihydroergotamine 3	N02CA71	N02CA71	N02CA71	N02CA71
Ergotamine 3	N02CA72	N02CA72	N02CA72	N02CA72
Triptanes / Selektive Serotonin-5HT1-Agonisten 1	N02CC01	N02CC01	N02CC01	N02CC01
Triptanes / Selektive Serotonin-5HT1-Agonisten 2	N02CC02	N02CC02	N02CC02	N02CC02
Triptanes / Selektive Serotonin-5HT1-Agonisten 3	N02CC03	N02CC03	N02CC03	N02CC03
Triptanes / Selektive Serotonin-5HT1-Agonisten 4	N02CC04	N02CC04	N02CC04	N02CC04
Triptanes / Selektive Serotonin-5HT1-Agonisten 5	N02CC05	N02CC05	N02CC05	N02CC05
Triptanes / Selektive Serotonin-5HT1-Agonisten 6	N02CC06	N02CC06	N02CC06	N02CC06
Triptanes / Selektive Serotonin-5HT1-Agonisten 7	N02CC07	N02CC07	N02CC07	N02CC07
Clonidine 4	N02CX02	N02CX02	N02CX02	N02CX02

Topiramate 2	N02CX12	N02CX12	N02CX12	N02CX12
Metoclopramide 3	N02CX59	N02CX59	N02CX59	N02CX59
Phenobarbital 1	N03AA02	N03AA02	N03AA02	N03AA02
Phenytoin 1	N03AB02	N03AB02	N03AB02	N03AB02
Phenytoin 3 (Fosphenytoin)	N03AB05	N03AB05	N03AB05	N03AB05
Phenytoin 2	N03AB52	N03AB52	N03AB52	N03AB52
Clonazepam	N03AE01	N03AE01	N03AE01	N03AE01
Midazolam 2	N03AE02	N03AE02	n/a	n/a
Carbamazepine	N03AF01	N03AF01	N03AF01	N03AF01
Topiramate 1	N03AX11	N03AX11	N03AX11	N03AX11
Trihexyphenidyl	N04AA01	N04AA01	N04AA01	N04AA01
Biperiden	N04AA02	N04AA02	N04AA02	N04AA02
Tropatepin	N04AA12	N04AA12	N04AA12	N04AA12
Orphenadrine 3	N04AB02	N04AB02	N04AB02	N04AB02
Benzatropine 1	N04AC01	N04AC01	N04AC01	N04AC01
Benzatropine 2 (Etybenzatropin)	N04AC30	N04AC30	N04AC30	N04AC30
Amantadine 1	N04BB01	N04BB01	N04BB01	N04BB01
Bromocriptine 1	N04BC01	N04BC01	N04BC01	N04BC01
Pergolide	N04BC02	N04BC02	N04BC02	N04BC02
Dihydroergocryptine	N04BC03	N04BC03	N04BC03	N04BC03
Ropinirole	N04BC04	N04BC04	N04BC04	N04BC04
Pramipexole	N04BC05	N04BC05	N04BC05	N04BC05
Cabergoline 1	N04BC06	N04BC06	N04BC06	N04BC06
Piribedil 1	N04BC08	N04BC08	N04BC08	N04BC08
Rotigotine	N04BC09	N04BC09	N04BC09	N04BC09
Selegiline	N04BD01	N04BD01	N04BD01	N04BD01
Chlorpromazine	N05AA01	N05AA01	N05AA01	N05AA01
Levomepromazine	N05AA02	N05AA02	N05AA02	N05AA02
Clorazepate-Acepromazine 1	N05AA04	N05AA04	N05AA04	N05AA04
Cyamemazine	N05AA06	N05AA06	N05AA06	N05AA06
Fluphenazine	N05AB02	N05AB02	N05AB02	N05AB02
Perphenazine	N05AB03	N05AB03	N05AB03	N05AB03
Prochlorperazine	N05AB04	N05AB04	N05AB04	N05AB04
Trifluoperazine	N05AB06	N05AB06	N05AB06	N05AB06
Propericiazine (=Periciazine)	N05AC01	N05AC01	N05AC01	N05AC01
Thioridazine	N05AC02	N05AC02	N05AC02	N05AC02
Pipotiazine	N05AC04	N05AC04	N05AC04	N05AC04
Droperidol	N05AD08	N05AD08	N05AD08	N05AD08
Sertindole	N05AE03	N05AE03	N05AE03	N05AE03
Ziprasidone	N05AE04	N05AE04	N05AE04	N05AE04
Flupentixole	N05AF01	N05AF01	N05AF01	N05AF01
Chlorprothixen	N05AF03	N05AF03	N05AF03	N05AF03
Zuclopenthixol	N05AF05	N05AF05	N05AF05	N05AF05
Pimozide	N05AG02	N05AG02	N05AG02	N05AG02
Clozapine	N05AH02	N05AH02	N05AH02	N05AH02
Lithium	N05AN01	N05AN01	N05AN01	N05AN01
Aripiprazole	N05AX12	N05AX12	N05AX12	N05AX12
Reserpine 6	N05AX15	N05AX15	N05AX15	N05AX15
Diazepam	N05BA01	N05BA01	N05BA01	N05BA01
Chlordiazepoxide	N05BA02	N05BA02	N05BA02	N05BA02
Medazepam	N05BA03	N05BA03	N05BA03	N05BA03
Clorazepate-Acepromazine 2 (Dipotassium clorazepate)	N05BA05	N05BA05	N05BA05	N05BA05
Bromazepam	N05BA08	N05BA08	N05BA08	N05BA08
Clobazam	N05BA09	N05BA09	N05BA09	N05BA09
Prazepam	N05BA11	N05BA11	N05BA11	N05BA11
Alprazolam	N05BA12	N05BA12	N05BA12	N05BA12
Halazepam	N05BA13	N05BA13	N05BA13	N05BA13

Nordazepam	N05BA16	N05BA16	N05BA16	N05BA16
(Ethyl-) Loflazepate	N05BA18	N05BA18	N05BA18	N05BA18
Hydroxyzine 1	N05BB01	N05BB01	N05BB01	N05BB01
Hydroxyzine 3	N05BB51	N05BB51	N05BB51	N05BB51
Meprobamate 1	N05BC01	N05BC01	N05BC01	N05BC01
Meprobamate 2	N05BC51	N05BC51	N05BC51	N05BC51
Phenobarbital 2	N05CA24	N05CA24	N05CA24	N05CA24
Chloralhydrate 1	N05CC01	N05CC01	N05CC01	N05CC01
Flurazepam	N05CD01	N05CD01	N05CD01	N05CD01
Nitrazepam	N05CD02	N05CD02	N05CD02	N05CD02
Flunitrazepam	N05CD03	N05CD03	N05CD03	N05CD03
Estazolam	N05CD04	N05CD04	N05CD04	N05CD04
Triazolam	N05CD05	N05CD05	N05CD05	N05CD05
Temazepam	N05CD07	N05CD07	N05CD07	N05CD07
Midazolam 1	N05CD08	N05CD08	N05CD08	N05CD08
Quazepam	N05CD10	N05CD10	N05CD10	N05CD10
Clomethiazole 1	N05CM02	N05CM02	N05CM02	N05CM02
Scopolamine 3 (=Hyoscin)	N05CM05	N05CM05	N05CM05	N05CM05
Propiomazine	N05CM06	N05CM06	N05CM06	N05CM06
Diphenhydramine 5	N05CM20	N05CM20	N05CM20	N05CM20
Doxylamine 3	N05CM21	N05CM21	N05CM21	N05CM21
Promethazine 4	N05CM22	N05CM22	N05CM22	N05CM22
Meprobamate 3	N05CX01	N05CX01	N05CX01	N05CX01
Clomethiazole 2	N05CX04	N05CX04	N05CX04	N05CX04
Diphenhydramine 2	N05CX07	N05CX07	N05CX07	N05CX07
Chloralhydrate 2	N05CX11	N05CX11	N05CX11	N05CX11
Promethazine 5	N05CX13	N05CX13	N05CX13	N05CX13
Desipramine	N06AA01	N06AA01	N06AA01	N06AA01
Imipramine 1	N06AA02	N06AA02	N06AA02	N06AA02
Imipramine 2	N06AA03	N06AA03	N06AA03	N06AA03
Clomipramine	N06AA04	N06AA04	N06AA04	N06AA04
Trimipramine	N06AA06	N06AA06	N06AA06	N06AA06
Amitriptyline 1	N06AA09	N06AA09	N06AA09	N06AA09
Nortriptyline 1	N06AA10	N06AA10	N06AA10	N06AA10
Doxepin	N06AA12	N06AA12	N06AA12	N06AA12
Dosulepin 1	N06AA16	N06AA16	N06AA16	N06AA16
Amoxapine	N06AA17	N06AA17	N06AA17	N06AA17
Maprotiline	N06AA21	N06AA21	N06AA21	N06AA21
Amitriptyline 3	N06AA25	N06AA25	N06AA25	N06AA25
Fluoxetine 1	N06AB03	N06AB03	N06AB03	N06AB03
Paroxetine	N06AB05	N06AB05	N06AB05	N06AB05
Fluvoxamine	N06AB08	N06AB08	N06AB08	N06AB08
Tranylcypromine 1	N06AF04	N06AF04	N06AF04	N06AF04
Bupropion 1	N06AX12	N06AX12	N06AX12	N06AX12
Venlafaxine 1	N06AX16	N06AX16	N06AX16	N06AX16
Reboxetine	N06AX18	N06AX18	N06AX18	N06AX18
Venlafaxine 2 (Desvenlafaxine)	N06AX23	N06AX23	N06AX23	N06AX23
Methylphenidat	N06BA04	N06BA04	N06BA04	N06BA04
Piracetam	N06BX03	N06BX03	N06BX03	N06BX03
Amitriptyline 2	N06CA01	N06CA01	N06CA01	N06CA01
Fluoxetine 2	N06CA03	n/a	n/a	n/a
Nortriptyline 2	N06CA06	N06CA06	N06CA06	N06CA06
Tranylcypromine 2	N06CA07	N06CA03	N06CA03	N06CA03
Dosulepin 2	N06CA10	N06CA10	N06CA10	N06CA10
Ginkgo biloba	N06DP01	N06DP01	N06DP01	N06DH01
Ergoloid mesylate (= dihydroergotoxine) 4	N06DX07	N06DX07	N06DX07	N06DX07
Vincamine 2	N06DX09	N06DX09	N06DX09	N06DX09
Nicergoline 2	N06DX13	N06DX13	N06DX13	N06DX13

Cyclandelate (=Cyclospasmol) 2	N06DX14	N06DX14	N06DX14	N06DX14
Dihydroergocristine 3	N06DX19	N06DX19	N06DX19	N06DX19
Ergoloid mesylate (= dihydroergotoxine) 3	N06DX57	N06DX57	N06DX57	N06DX57
Bethanechol	N07AB02	N07AB02	N07AB02	N07AB02
Bupropion 2	N07BA02	N07BA02	N07BA02	N07BA02
Clonidine 5	N07BB06	N07BB06	N07BB06	N07BB06
Methadone 1	N07BC02	N07BC02	N07BC02	N07BC02
Dextrometorphan 2	N07XX59	n/a	n/a	n/a
Quinine and derivatives 7	P01BC01	P01BC01	P01BC01	P01BC01
Norephedrine (=Phenylpropanolamine) 1	R01BA01	R01BA01	R01BA01	R01BA01
Pseudoephedrine 1	R01BA02	R01BA02	R01BA02	R01BA02
Norephedrine (=Phenylpropanolamine) 2	R01BA51	R01BA51	R01BA51	R01BA51
Pseudoephedrine 2	R01BA52	R01BA52	R01BA52	R01BA52
Flurbiprofen 3	R02AX01	R02AX01	R02AX01	R02AX01
Terbutaline (oral) 2	R03AC03	R03AC03	R03AC03	R03AC03
Terbutaline (oral) 1	R03CC03	R03CC03	R03CC03	R03CC03
Terbutaline (oral) 3	R03CC53	R03CC53	R03CC53	R03CC53
Theophylline 1	R03DA04	R03DA04	R03DA04	R03DA04
Theophylline 4	R03DA54	R03DA54	R03DA54	R03DA54
Theophylline 5	R03DA74	R03DA74	R03DA74	R03DA74
Theophylline 6	R03DB04	R03DB04	R03DB04	R03DB04
Ethylmorphine 1	R05DA01	R05DA01	R05DA01	R05DA01
Dextrometorphan 1	R05DA09	R05DA09	R05DA09	R05DA09
Dextrometorphan 3	R05DA59	R05DA59	R05DA59	R05DA59
Phenylbutazone 4	R05XA10	R05XA10	R05XA10	R05XA10
Diphenhydramine 1	R06AA02	R06AA02	R06AA02	R06AA02
Clemastine 1	R06AA04	R06AA04	R06AA04	R06AA04
Carbinoxamine	R06AA08	R06AA08	R06AA08	R06AA08
Doxylamine 1	R06AA09	R06AA09	R06AA09	R06AA09
Diphenhydramine 7	R06AA52	R06AA52	R06AA52	R06AA52
Clemastine 2	R06AA54	R06AA54	R06AA54	R06AA54
Doxylamine 2	R06AA59	R06AA59	n/a	n/a
Brompheniramine 1	R06AB01	R06AB01	R06AB01	R06AB01
Dexchlorpheniramine 1	R06AB02	R06AB02	R06AB02	R06AB02
Dimetindene 1	R06AB03	R06AB03	R06AB03	R06AB03
Chlorpheniramine (=Chlorphenamine) 1	R06AB04	R06AB04	R06AB04	R06AB04
Pheniramine	R06AB05	R06AB05	R06AB05	R06AB05
Dexbrompheniramin 1	R06AB06	R06AB06	R06AB06	R06AB06
Brompheniramine 2	R06AB51	R06AB51	R06AB51	R06AB51
Dexchlorpheniramine 2	R06AB52	R06AB52	R06AB52	R06AB52
Chlorpheniramine (=Chlorphenamine) 2	R06AB54	R06AB54	R06AB54	R06AB54
Dexbrompheniramin 2	R06AB56	R06AB56	R06AB56	R06AB56
Tripelennamine	R06AC04	R06AC04	R06AC04	R06AC04
Alimemazine	R06AD01	R06AD01	R06AD01	R06AD01
Promethazine 1	R06AD02	R06AD02	R06AD02	R06AD02
Promethazine 8 (Hydroxyethylpromethazin 1)	R06AD05	R06AD05	R06AD05	R06AD05
Mequitazine	R06AD07	R06AD07	R06AD07	R06AD07
Oxomemazine	R06AD08	R06AD08	R06AD08	R06AD08
Promethazine 7 (Dioxopromethazin)	R06AD10	R06AD10	R06AD10	R06AD10
Promethazine 2	R06AD52	R06AD52	R06AD52	R06AD52
Promethazine 9 (Hydroxyethylpromethazin 2)	R06AD55	R06AD55	R06AD55	R06AD55
Buclizine 1	R06AE01	R06AE01	R06AE01	R06AE01
Cyclizine 1	R06AE03	R06AE03	R06AE03	R06AE03
Meclozine 1	R06AE05	R06AE05	R06AE05	R06AE05
Buclizine 2	R06AE51	R06AE51	R06AE51	R06AE51
Cyclizine 2	R06AE53	R06AE53	R06AE53	R06AE53
Meclozine 2	R06AE55	R06AE55	R06AE55	R06AE55
Cyproheptadine 1	R06AX02	R06AX02	R06AX02	R06AX02

Triprolidine 1	R06AX07	R06AX07	R06AX07	R06AX07
Terfenadine	R06AX12	R06AX12	R06AX12	R06AX12
Ebastine	R06AX22	R06AX22	R06AX22	R06AX22
Pimethixene	R06AX23	R06AX23	R06AX23	R06AX23
Hydroxyzine 2	R06AX32	R06AX32	R06AX32	R06AX32
Triprolidine 2	R06AX57	R06AX57	R06AX57	R06AX57
Promethazine 6	V03AB05	V03AB05	V03AB05	V03AB05

PRICSCUS List	ATC-Code 2014	ATC-Code 2013	ATC-Code 2012	ATC-Code 2011
Acemetacin	M01AB11	M01AB11	M01AB11	M01AB11
Acetyldigoxin 1	C01AA02	C01AA02	C01AA02	C01AA02
Acetyldigoxin 2	C01AA52	C01AA52	C01AA52	C01AA52
Alprazolam	N05BA12	N05BA12	N05BA12	N05BA12
Amitriptyline 1	N06AA09	N06AA09	N06AA09	N06AA09
Amitriptyline 2	N06CA01	N06CA01	N06CA01	N06CA01
Amitriptyline 3	N06AA25	N06AA25	N06AA25	N06AA25
Baclofen	M03BX01	M03BX01	M03BX01	M03BX01
Bromazepam	N05BA08	N05BA08	N05BA08	N05BA08
Chinidin = Quinidine 1	C01BA01	C01BA01	C01BA01	C01BA01
Chinidin = Quinidine 2	C01BA51	C01BA51	C01BA51	C01BA51
Chinidin = Quinidine 3	C01BA71	C01BA71	C01BA71	C01BA71
Chloralhydrat 1	N05CC01	N05CC01	N05CC01	N05CC01
Chloralhydrat 2	N05CX11	N05CX11	N05CX11	N05CX11
Chlordiazepoxid	N05BA02	N05BA02	N05BA02	N05BA02
Chlorpheniramine (=Chlorphenamine) 1	R06AB04	R06AB04	R06AB04	R06AB04
Chlorpheniramine (=Chlorphenamine) 2	R06AB54	R06AB54	R06AB54	R06AB54
Clemastin 1	R06AA04	R06AA04	R06AA04	R06AA04
Clemastin 2	R06AA54	R06AA54	R06AA54	R06AA54
Clobazam	N05BA09	N05BA09	N05BA09	N05BA09
Clomipramin	N06AA04	N06AA04	N06AA04	N06AA04
Clonidin 1	C02AC01	C02AC01	C02AC01	C02AC01
Clonidin 2	C02LC01	C02LC01	C02LC01	C02LC01
Clonidin 3	C02LC51	C02LC51	C02LC51	C02LC51
Clonidin 4	N02CX02	N02CX02	N02CX02	N02CX02
Clonidin 5	N07BB06	N07BB06	N07BB06	N07BB06
Clozapin	N05AH02	N05AH02	N05AH02	N05AH02
Diazepam	N05BA01	N05BA01	N05BA01	N05BA01
Dickflüssiges Paraffin 1	A06AA01	A06AA01	A06AA01	A06AA01
Dickflüssiges Paraffin 2	A06AA51	A06AA51	A06AA51	A06AA51
Digoxin 1	C01AA05	C01AA05	C01AA05	C01AA05
Digoxin 2	C01AA55	C01AA55	C01AA55	C01AA55
Dihydroergocryptinmesilat	N04BC03	N04BC03	N04BC03	N04BC03
Dihydroergotamin 1	N02CA01	N02CA01	N02CA01	N02CA01
Dihydroergotamin 2	N02CA51	N02CA51	N02CA51	N02CA51
Dihydroergotamin 3	N02CA71	N02CA71	N02CA71	N02CA71
Dihydroergotaminmesilat 1	C06AA02	C06AA02	C06AA02	C06AA02
Dihydroergotaminmesilat 2	C06AA50	C06AA50	C06AA50	C06AA50
Dihydroergotoxin 1	N06DX07	N06DX07	N06DX07	N06DX07
Dihydroergotoxin 2	N06DX57	N06DX57	N06DX57	N06DX57
Dikaliumclorazepat	N05BA05	N05BA05	N05BA05	N05BA05
Dimenhydrinate 1	A04AB02	A04AB02	A04AB02	A04AB02
Dimenhydrinate 2	A04AB52	A04AB52	A04AB52	A04AB52
Dimetindene 1	R06AB03	R06AB03	R06AB03	R06AB03
Dimetindene 2	D04AA13	D04AA13	D04AA13	D04AA13
Diphenhydramine 1	R06AA02	R06AA02	R06AA02	R06AA02
Diphenhydramine 2	N05CX07	N05CX07	N05CX07	N05CX07
Diphenhydramine 3	A04AB05	A04AB05	A04AB05	A04AB05

Diphenhydramine 4	N01BX06	N01BX06	N01BX06	N01BX06
Diphenhydramine 5	N05CM20	N05CM20	N05CM20	N05CM20
Diphenhydramine 6	A04AB55	A04AB55	A04AB55	A04AB55
Diphenhydramine 7	R06AA52	R06AA52	R06AA52	R06AA52
Doxazosin 1	C02CA04	C02CA04	C02CA04	C02CA04
Doxazosin 2	G04CA05	G04CA05	G04CA05	G04CA05
Doxepin	N06AA12	N06AA12	N06AA12	N06AA12
Doxylamine 1	R06AA09	R06AA09	R06AA09	R06AA09
Doxylamine 2	R06AA59	R06AA59	n/a	n/a
Doxylamine 3	N05CM21	N05CM21	N05CM21	N05CM21
Doxylamine 4	A04AB56	A04AB56	A04AB56	A04AB56
Ergotamine 1	N02CA02	N02CA02	N02CA02	N02CA02
Ergotamine 2	N02CA52	N02CA52	N02CA52	N02CA52
Ergotamine 3	N02CA72	N02CA72	N02CA72	N02CA72
Etoricoxib	M01AH05	M01AH05	M01AH05	M01AH05
Flecainid	C01BC04	C01BC04	C01BC04	C01BC04
Flunitrazepam	N05CD03	N05CD03	N05CD03	N05CD03
Fluoxetine 1	N06AB03	N06AB03	N06AB03	N06AB03
Fluoxetine 2	N06CA03	n/a	n/a	n/a
Fluphenazin	N05AB02	N05AB02	N05AB02	N05AB02
Flurazepam	N05CD01	N05CD01	N05CD01	N05CD01
Hydroxyzine 1	N05BB01	N05BB01	N05BB01	N05BB01
Hydroxyzine 2	R06AX32	R06AX32	R06AX32	R06AX32
Hydroxyzine 3	N05BB51	N05BB51	N05BB51	N05BB51
Imipramin	N06AA02	N06AA02	N06AA02	N06AA02
Imipraminoxid	N06AA03	N06AA03	N06AA03	N06AA03
Indometacin 1	M01AB01	M01AB01	M01AB01	M01AB01
Indometacin 2	C01EB03	C01EB03	C01EB03	C01EB03
Indometacin 3	M01AB51	M01AB51	M01AB51	M01AB51
Indometacin 4	M02AA23	M02AA23	M02AA23	M02AA23
Indometacin 5	M02AA73	M02AA73	M02AA73	M02AA73
Ketoprofen 1	M01AE03	M01AE03	M01AE03	M01AE03
Ketoprofen 2	M01AE53	M01AE53	M01AE53	M01AE53
Ketoprofen 3	M02AA10	M02AA10	M02AA10	M02AA10
Levomepromazin	N05AA02	N05AA02	N05AA02	N05AA02
Maprotilin	N06AA21	N06AA21	N06AA21	N06AA21
Medazepam	N05BA03	N05BA03	N05BA03	N05BA03
Meloxicam 1	M01AC06	M01AC06	M01AC06	M01AC06
Meloxicam 2	M01AC56	M01AC56	n/a	n/a
Methyldopa 1	C02AB01	C02AB01	C02AB01	C02AB01
Methyldopa 2	C02AB02	C02AB02	C02AB02	C02AB02
Methyldopa 3	C02LB01	C02LB01	C02LB01	C02LB01
Metildigoxin 1	C01AA08	C01AA08	C01AA08	C01AA08
Metildigoxin 2	C01AA58	C01AA58	C01AA58	C01AA58
Naftidrofuryl	C04AX21	C04AX21	C04AX21	C04AX21
Nicergoline 1	C04AE02	C04AE02	C04AE02	C04AE02
Nicergoline 2	N06DX13	N06DX13	N06DX13	N06DX13
Nifedipine 1	C08CA05	C08CA05	C08CA05	C08CA05
Nifedipine 2	C08CA55	C08CA55	C08CA55	C08CA55
Nifedipine 3	C08GA01	C08GA01	C08GA01	C08GA01

Nifedipine 4	C07FB22	C07FB22	C07FB22	C07FB22
Nifedipine 5	C07FB23	C07FB23	C07FB23	C07FB23
Nitrazepam	N05CD02	N05CD02	N05CD02	N05CD02
Nitrofurantoin 1	J01XE01	J01XE01	J01XE01	J01XE01
Nitrofurantoin 2	J01XE51	J01XE51	J01XE51	J01XE51
Oxybutynin	G04BD04	G04BD04	G04BD04	G04BD04
Pentoxifyllin	C04AD03	C04AD03	C04AD03	C04AD03
Perphenazin	N05AB03	N05AB03	N05AB03	N05AB03
Pethidine (=Meperidine) 1	N02AB02	N02AB02	N02AB02	N02AB02
Pethidine (=Meperidine) 2	N02AB52	N02AB52	N02AB52	N02AB52
Pethidine (=Meperidine) 3	N02AB72	N02AB72	N02AB72	N02AB72
Pethidine (=Meperidine) 4	N02AG03	N02AG03	N02AG03	N02AG03
Phenobarbital 1	N03AA02	N03AA02	N03AA02	N03AA02
Phenobarbital 2	N05CA24	N05CA24	N05CA24	N05CA24
Phenylbutazone 1	M01AA01	M01AA01	M01AA01	M01AA01
Phenylbutazone 2	M01AA51	M01AA51	M01AA51	M01AA51
Phenylbutazone 3	M01BA01	M01BA01	M01BA01	M01BA01
Phenylbutazone 4	R05XA10	R05XA10	R05XA10	R05XA10
Phenylbutazone 5	M02AA01	M02AA01	M02AA01	M02AA01
Piracetam	N06BX03	N06BX03	N06BX03	N06BX03
Piroxicam 1	M01AC01	M01AC01	M01AC01	M01AC01
Piroxicam 2	M02AA07	M02AA07	M02AA07	M02AA07
Prasugrel	B01AC22	B01AC22	B01AC22	B01AC22
Prazepam	N05BA11	N05BA11	N05BA11	N05BA11
Prazosin 1	C02CA01	C02CA01	C02CA01	C02CA01
Prazosin 2	C02LE01	C02LE01	C02LE01	C02LE01
Reserpine 1	C02AA02	C02AA02	C02AA02	C02AA02
Reserpine 2	C02AA52	C02AA52	C02AA52	C02AA52
Reserpine 3	C02LA01	C02LA01	C02LA01	C02LA01
Reserpine 4	C02LA51	C02LA51	C02LA51	C02LA51
Reserpine 5	C02LA71	C02LA71	C02LA71	C02LA71
Reserpine 6	N05AX15	N05AX15	N05AX15	N05AX15
Solifenacin 1	G04BD08	G04BD08	G04BD08	G04BD08
Solifenacin 2	G04CA53	n/a	n/a	n/a
Sotalol 1	C07AA07	C07AA07	C07AA07	C07AA07
Sotalol 2	C07AA57	C07AA57	C07AA57	C07AA57
Sotalol 3	C07BA07	C07BA07	C07BA07	C07BA07
Temazepam	N05CD07	N05CD07	N05CD07	N05CD07
Terazosin 1	G04CA03	G04CA03	G04CA03	G04CA03
Terazosin 2	C02CA08	C02CA08	C02CA08	C02CA08
Tetrazepam	M03BX07	M03BX07	M03BX07	M03BX07
Thioridazin	N05AC02	N05AC02	N05AC02	N05AC02
Ticlopidin	B01AC05	B01AC05	B01AC05	B01AC05
Tolterodin	G04BD07	G04BD07	G04BD07	G04BD07
Tranylcypromine 1	N06AF04	N06AF04	N06AF04	N06AF04
Tranylcypromine 2	N06CA07	N06CA03	N06CA03	N06CA03
Triazolam	N05CD05	N05CD05	N05CD05	N05CD05
Trimipramin	N06AA06	N06AA06	N06AA06	N06AA06
Verapamil in Kombination mit Chinidin	C08DA81	C08DA81	C08DA81	C08DA81

Anticholinergic Drug Scale	**ATC-Code 2014**	**ATC-Code 2013**	**ATC-Code 2012**	**ATC-Code 2011**	**Score**
Dexamethasone 2	A01AC02	A01AC02	A01AC02	A01AC02	1
Hydrocortisone 2	A01AC03	A01AC03	A01AC03	A01AC03	1
Cimetidine	A02BA01	A02BA01	A02BA01	A02BA01	2
Ranitidine 1	A02BA02	A02BA02	A02BA02	A02BA02	2
Famotidine 1	A02BA03	A02BA03	A02BA03	A02BA03	1
Nizatidine	A02BA04	A02BA04	A02BA04	A02BA04	1
Ranitidine 2	A02BA07	A02BA07	A02BA07	A02BA07	2
Famotidine 2	A02BA53	A02BA53	A02BA53	A02BA53	1
Omeprazole	A02BC01	A02BC01	A02BC01	A02BC01	0
Pantoprazole	A02BC02	A02BC02	A02BC02	A02BC02	0
Lansoprazole	A02BC03	A02BC03	A02BC03	A02BC03	0
Rabeprazol	A02BC04	A02BC04	A02BC04	A02BC04	0
Dicyclomine (=Dicycloverin) 1	A03AA07	A03AA07	A03AA07	A03AA07	3
Propantheline 1	A03AB05	A03AB05	A03AB05	A03AB05	3
Atropine 1	A03BA01	A03BA01	A03BA01	A03BA01	3
Hyoscyamine 1	A03BA03	A03BA03	A03BA03	A03BA03	3
Propantheline 2	A03CA34	A03CA34	A03CA34	A03CA34	3
Hyoscyamine 2	A03CB31	A03CB31	A03CB31	A03CB31	3
Metoclopramide 1	A03FA01	A03FA01	A03FA01	A03FA01	0
Metoclopramide 2	A03FA51	A03FA51	A03FA51	A03FA51	0
Dimenhydrinate 1	A04AB02	A04AB02	A04AB02	A04AB02	3
Meclozine 3	A04AB04	A04AB04	A04AB04	A04AB04	3
Diphenhydramine 3	A04AB05	A04AB05	A04AB05	A04AB05	3
Dimenhydrinate 2	A04AB52	A04AB52	A04AB52	A04AB52	3
Meclozine 4	A04AB54	A04AB54	A04AB54	A04AB54	3
Diphenhydramine 6	A04AB55	A04AB55	A04AB55	A04AB55	3
Promethazine 3	A04AB58	A04AB58	A04AB58	A04AB58	3
Scopolamine 1 (=Hyoscin)	A04AD01	A04AD01	A04AD01	A04AD01	3
Scopolamine 2 (=Hyoscin)	A04AD51	A04AD51	A04AD51	A04AD51	3
Bisacodyl	A06AB02	A06AB02	A06AB02	A06AB02	0
Senna glycosides 1	A06AB06	A06AB06	A06AB06	A06AB06	0
Senna glycosides 2	A06AB56	A06AB56	A06AB56	A06AB56	0
Vancomycin 2	A07AA09	A07AA09	A07AA09	A07AA09	1
Diphenoxylate	A07DA01	A07DA01	A07DA01	A07DA01	0
Loperamide 1	A07DA03	A07DA03	A07DA03	A07DA03	1
Morphine 2	A07DA52	A07DA52	A07DA52	A07DA52	1
Loperamide 2	A07DA53	A07DA53	A07DA53	A07DA53	1
Insulin 1	A10AB01	A10AB01	A10AB01	A10AB01	0
Insulin 2	A10AB02	A10AB02	A10AB02	A10AB02	0
Insulin 3	A10AB03	A10AB03	A10AB03	A10AB03	0
Insulin 4	A10AB04	A10AB04	A10AB04	A10AB04	0
Insulin 5	A10AB05	A10AB05	A10AB05	A10AB05	0
Insulin 6	A10AB06	A10AB06	A10AB06	A10AB06	0
Insulin 7	A10AB30	A10AB30	A10AB30	A10AB30	0
Insulin 8	A10AC01	A10AC01	A10AC01	A10AC01	0
Insulin 9	A10AC02	A10AC02	A10AC02	A10AC02	0
Insulin 10	A10AC03	A10AC03	A10AC03	A10AC03	0

Insulin 11	A10AC04	A10AC04	A10AC04	A10AC04	0
Insulin 12	A10AC30	A10AC30	A10AC30	A10AC30	0
Insulin 13	A10AD01	A10AD01	A10AD01	A10AD01	0
Insulin 14	A10AD02	A10AD02	A10AD02	A10AD02	0
Insulin 15	A10AD03	A10AD03	A10AD03	A10AD03	0
Insulin 16	A10AD04	A10AD04	A10AD04	A10AD04	0
Insulin 17	A10AD05	A10AD05	A10AD05	A10AD05	0
Insulin 18	A10AD30	A10AD30	A10AD30	A10AD30	0
Insulin 19	A10AE01	A10AE01	A10AE01	A10AE01	0
Insulin 20	A10AE02	A10AE02	A10AE02	A10AE02	0
Insulin 21	A10AE03	A10AE03	A10AE03	A10AE03	0
Insulin 22	A10AE04	A10AE04	A10AE04	A10AE04	0
Insulin 23	A10AE05	A10AE05	A10AE05	A10AE05	0
Insulin 24	A10AE30	A10AE30	A10AE30	A10AE30	0
Insulin 25	A10AF01	A10AF01	A10AF01	A10AF01	0
Metformin	A10BA02	A10BA02	A10BA02	A10BA02	0
Glipizide	A10BB07	A10BB07	A10BB07	A10BB07	0
Pioglitazone 3	A10BD05	A10BD05	A10BD05	A10BD05	0
Pioglitazone 2	A10BD06	A10BD06	A10BD06	A10BD06	0
Pioglitazone 4	A10BD09	A10BD09	A10BD09	A10BD09	0
Pioglitazone 5	A10BD12	n/a	n/a	n/a	0
Rosiglitazone	A10BG02	A10BG02	A10BG02	A10BG02	0
Pioglitazone 1	A10BG03	A10BG03	A10BG03	A10BG03	0
Cyproheptadine 2	A15AA01	A15AA01	A15AA01	A15AA01	2
Cyproheptadine 3	A15AA51	A15AA51	A15AA51	A15AA51	2
Clopidogrel	B01AC04	B01AC04	B01AC04	B01AC04	0
Dipyridamole 1	B01AC07	B01AC07	B01AC07	B01AC07	1
Dipyridamole 2	B01AC36	n/a	n/a	n/a	1
Digitoxin 1	C01AA04	C01AA04	C01AA04	C01AA04	1
Digoxin 1	C01AA05	C01AA05	C01AA05	C01AA05	1
Digitoxin 2	C01AA54	C01AA54	C01AA54	C01AA54	1
Digoxin 2	C01AA55	C01AA55	C01AA55	C01AA55	1
Disopyramide	C01BA03	C01BA03	C01BA03	C01BA03	2
Nitroglycerin	C01DA02	C01DA02	C01DA02	C01DA02	0
Isosorbidedinitrate 1	C01DA08	C01DA08	C01DA08	C01DA08	1
Isosorbidemononitrate	C01DA14	C01DA14	C01DA14	C01DA14	1
Isosorbidedinitrate 2	C01DA58	C01DA58	C01DA58	C01DA58	1
Dipyridamole 4	C01DX21	C01DX21	C01DX21	C01DX21	1
Dipyridamole 3	C01DX71	C01DX71	C01DX71	C01DX71	1
Theophylline 2	C01EB22	C01EB22	C01EB22	C01EB22	1
Theophylline 3	C01EX66	C01EX66	C01EX66	C01EX66	1
Hydralazine 1	C02DB02	C02DB02	C02DB02	C02DB02	1
Hydralazine 2	C02LG02	C02LG02	C02LG02	C02LG02	1
Hydrochlorothiazide	C03AA03	C03AA03	C03AA03	C03AA03	0
Chlortalidone 1	C03BA04	C03BA04	C03BA04	C03BA04	1
Chlortalidone 2	C03BB04	C03BB04	C03BB04	C03BB04	1
Furosemide 1	C03CA01	C03CA01	C03CA01	C03CA01	1
Furosemide 2	C03CB01	C03CB01	C03CB01	C03CB01	1
Spironolactone	C03DA01	C03DA01	C03DA01	C03DA01	0
Triamterene 1	C03DB02	C03DB02	C03DB02	C03DB02	1

Chlortalidone 3	C03EA06	C03EA06	C03EA06	C03EA06	1
Triamterene 2	C03EA21	C03EA21	C03EA21	C03EA21	1
Furosemide 3	C03EB01	C03EB01	C03EB01	C03EB01	1
Furosemide 4 + Triamterene 3	C03EB21	C03EB21	C03EB21	C03EB21	1
Isosorbidedinitrate 3	C05AE02	C05AE02	C05AE02	C05AE02	1
Digitoxin 3	C05BZ05	C05BZ05	C05BZ05	C05BZ05	1
Propranolol 1	C07AA05	C07AA05	C07AA05	C07AA05	0
Timolol	C07AA06	C07AA06	C07AA06	C07AA06	0
Metoprolol 1	C07AB02	C07AB02	C07AB02	C07AB02	0
Atenolol 1	C07AB03	C07AB03	C07AB03	C07AB03	0
Atenolol 8 (Enantiomer S-Atenolol)	C07AB11	C07AB11	C07AB11	C07AB11	0
Metoprolol 2	C07AB52	C07AB52	C07AB52	C07AB52	0
Propranolol 5	C07BA05	C07BA05	C07BA05	C07BA05	0
Metoprolol 3	C07BB02	C07BB02	C07BB02	C07BB02	0
Atenolol 2	C07BB03	C07BB03	C07BB03	C07BB03	0
Metoprolol 4	C07BB52	C07BB52	C07BB52	C07BB52	0
Propranolol 4	C07CA05	C07CA05	C07CA05	C07CA05	0
Metoprolol 5	C07CB02	C07CB02	C07CB02	C07CB02	0
Atenolol 3	C07CB03	C07CB03	C07CB03	C07CB03	0
Atenolol 4	C07CB53	C07CB53	C07CB53	C07CB53	0
Propranolol 2	C07DA05	C07DA05	C07DA05	C07DA05	0
Atenolol 5	C07DB01	C07DB01	C07DB01	C07DB01	0
Propranolol 6	C07EA05	C07EA05	C07EA05	C07EA05	0
Propranolol 3	C07FA05	C07FA05	C07FA05	C07FA05	0
Metoprolol 6	C07FB02	C07FB02	C07FB02	C07FB02	0
Atenolol 7	C07FB03	C07FB03	C07FB03	C07FB03	0
Metoprolol 7	C07FB22	C07FB22	C07FB22	C07FB22	0
Atenolol 6	C07FB23	C07FB23	C07FB23	C07FB23	0
Metoprolol 8	C07FB24	C07FB24	C07FB24	C07FB24	0
Amlodipine	C08CA01	C08CA01	C08CA01	C08CA01	0
Verapamil 1	C08DA01	C08DA01	C08DA01	C08DA01	0
Verapamil 5	C08DA51	C08DA51	C08DA51	C08DA51	0
Verapamil 2	C08DA81	C08DA81	C08DA81	C08DA81	0
Diltiazem	C08DB01	C08DB01	C08DB01	C08DB01	1
Verapamil 3	C08GA02	C08GA02	C08GA02	C08GA02	0
Captopril 1	C09AA01	C09AA01	C09AA01	C09AA01	1
Enalapril	C09AA02	C09AA02	C09AA02	C09AA02	0
Lisinopril	C09AA03	C09AA03	C09AA03	C09AA03	0
Benazepril	C09AA07	C09AA07	C09AA07	C09AA07	0
Trandolapril	C09AA10	C09AA10	C09AA10	C09AA10	0
Captopril 2	C09BA01	C09BA01	C09BA01	C09BA01	1
Verapamil 4	C09BB10	C09BB10	C09BB10	C09BB10	0
Losartan	C09CA01	C09CA01	C09CA01	C09CA01	0
Simvastatin	C10AA01	C10AA01	C10AA01	C10AA01	0
Atorvastatin	C10AA05	C10AA05	C10AA05	C10AA05	0
Gemfibrozil	C10AB04	C10AB04	C10AB04	C10AB04	0
Bromocriptine 2	G02CB01	G02CB01	G02CB01	G02CB01	1
Flavoxate	G04BD02	G04BD02	G04BD02	G04BD02	3

Oxybutynin	G04BD04	G04BD04	G04BD04	G04BD04	3
Tolterodine	G04BD07	G04BD07	G04BD07	G04BD07	3
Darifenacin	G04BD10	G04BD10	G04BD10	G04BD10	3
Dicyclomine (=Dicycloverin) 2	G04BD13	G04BD13	G04BD13	G04BD13	3
Atropine 2	G04BD15	G04BD15	G04BD15	G04BD15	3
Dicyclomine (=Dicycloverin) 3	G04BD63	G04BD63	G04BD63	G04BD63	3
Atropine 3	G04BD65	G04BD65	G04BD65	G04BD65	3
Dexamethasone 1	H02AB02	H02AB02	H02AB02	H02AB02	1
Methylprednisolone 1	H02AB04	H02AB04	H02AB04	H02AB04	1
Prednisolone 1	H02AB06	H02AB06	H02AB06	H02AB06	1
Prednisolone 4 (Prednisone)	H02AB07	H02AB07	H02AB07	H02AB07	1
Triamcinolone 1	H02AB08	H02AB08	H02AB08	H02AB08	1
Hydrocortisone 1	H02AB09	H02AB09	H02AB09	H02AB09	1
Cortisone	H02AB10	H02AB10	H02AB10	H02AB10	1
Methylprednisolone 2	H02AB54	H02AB54	H02AB54	H02AB54	1
Prednisolone 2	H02AB56	H02AB56	H02AB56	H02AB56	1
Methylprednisolone 3	H02BX01	H02BX01	H02BX01	H02BX01	1
Dexamethasone 3	H02BX02	H02BX02	H02BX02	H02BX02	1
Prednisolone 3	H02BX06	H02BX06	H02BX06	H02BX06	1
Triamcinolone 2	H02BX08	H02BX08	H02BX08	H02BX08	1
Ampicillin 1	J01CA01	J01CA01	J01CA01	J01CA01	1
Ampicillin 5 (Prodrug Pivampicillin)	J01CA02	J01CA02	J01CA02	J01CA02	1
Amoxicillin	J01CA04	J01CA04	J01CA04	J01CA04	0
Ampicillin 6 (Prodrug	J01CA06	J01CA06	J01CA06	J01CA06	1
Piperacillin 1	J01CA12	J01CA12	J01CA12	J01CA12	1
Ampicillin 7 (Prodrug Metampicillin)	J01CA14	J01CA14	J01CA14	J01CA14	1
Ampicillin 8 (Prodrug Talampicillin)	J01CA15	J01CA15	J01CA15	J01CA15	1
Ampicillin 2	J01CA51	J01CA51	J01CA51	J01CA51	1
Ampicillin 3	J01CR01	J01CR01	J01CR01	J01CR01	1
Piperacillin 2	J01CR05	J01CR05	J01CR05	J01CR05	1
Cefalexin	J01DB01	J01DB01	J01DB01	J01DB01	0
Cefalotin	J01DB03	J01DB03	J01DB03	J01DB03	1
Cefoxitin	J01DC01	J01DC01	J01DC01	J01DC01	1
Cefamandole	J01DC03	J01DC03	J01DC03	J01DC03	1
Trimethoprim	J01EA01	J01EA01	J01EA01	J01EA01	0
Clindamycin	J01FF01	J01FF01	J01FF01	J01FF01	1
Gentamicin 1	J01GB03	J01GB03	J01GB03	J01GB03	1
Gentamicin 2	J01GB53	J01GB53	J01GB53	J01GB53	1
Levofloxacin	J01MA12	J01MA12	J01MA12	J01MA12	0
Vancomycin 1	J01XA01	J01XA01	J01XA01	J01XA01	1
Cycloserine	J04AB01	J04AB01	J04AB01	J04AB01	1
Amantadine 2	J05AC04	J05AC04	J05AC04	J05AC04	1
Celecoxib 2	L01XX33	L01XX33	L01XX33	L01XX33	0

Tamoxifen	L02BA01	L02BA01	L02BA01	L02BA01	0
Ciclosporine	L04AD01	L04AD01	L04AD01	L04AD01	1
Azathioprine	L04AX01	L04AX01	L04AX01	L04AX01	1
Methotrexate	L04AX03	L04AX03	L04AX03	L04AX03	0
Piroxicam 1	M01AC01	M01AC01	M01AC01	M01AC01	0
Ibuprofen	M01AE01	M01AE01	M01AE01	M01AE01	0
Ketoprofen 1	M01AE03	M01AE03	M01AE03	M01AE03	0
Ketoprofen 2	M01AE53	M01AE53	M01AE53	M01AE53	0
Celecoxib 1	M01AH01	M01AH01	M01AH01	M01AH01	0
Piroxicam 2	M02AA07	M02AA07	M02AA07	M02AA07	0
Ketoprofen 3	M02AA10	M02AA10	M02AA10	M02AA10	0
Pancuronium	M03AC01	M03AC01	M03AC01	M03AC01	1
Carisoprodol 1	M03BA02	M03BA02	M03BA02	M03BA02	0
Carisoprodol 2	M03BA52	M03BA52	M03BA52	M03BA52	0
Carisoprodol 3	M03BA72	M03BA72	M03BA72	M03BA72	0
Orphenadrine 1	M03BC01	M03BC01	M03BC01	M03BC01	3
Orphenadrine 2	M03BC51	M03BC51	M03BC51	M03BC51	3
Baclofen	M03BX01	M03BX01	M03BX01	M03BX01	0
Cyclobenzaprine	M03BX08	M03BX08	M03BX08	M03BX08	2
Allopurinol	M04AA01	M04AA01	M04AA01	M04AA01	0
Colchicine	M04AC01	M04AC01	M04AC01	M04AC01	0
Fentanyl 2	N01AH01	N01AH01	N01AH01	N01AH01	1
Fentanyl 3	N01AH51	N01AH51	N01AH51	N01AH51	1
Diphenhydramine 4	N01BX06	N01BX06	N01BX06	N01BX06	3
Morphine 1	N02AA01	N02AA01	N02AA01	N02AA01	1
Oxycodone 1	N02AA05	N02AA05	N02AA05	N02AA05	1
Codeine 10 (Dihydrocodeine 1)	N02AA08	N02AA08	N02AA08	N02AA08	1
Morphine 3	N02AA51	N02AA51	N02AA51	N02AA51	1
Oxycodone 2	N02AA55	N02AA55	N02AA55	N02AA55	1
Codeine 11 (Dihydrocodeine 2)	N02AA58	N02AA58	N02AA58	N02AA58	1
Codeine 2	N02AA59	N02AA59	N02AA59	N02AA59	1
Codeine 3	N02AA64	N02AA64	N02AA64	N02AA64	1
Codeine 4	N02AA65	N02AA65	N02AA65	N02AA65	1
Codeine 5	N02AA66	N02AA66	N02AA66	N02AA66	1
Codeine 6	N02AA69	N02AA69	N02AA69	N02AA69	1
Codeine 7	N02AA79	N02AA79	N02AA79	N02AA79	1
Pethidine (=Meperidine) 1	N02AB02	N02AB02	N02AB02	N02AB02	2
Fentanyl 1	N02AB03	N02AB03	N02AB03	N02AB03	1
Pethidine (=Meperidine) 2	N02AB52	N02AB52	N02AB52	N02AB52	2
Pethidine (=Meperidine) 3	N02AB72	N02AB72	N02AB72	N02AB72	2
Morphine 4	N02AG01	N02AG01	N02AG01	N02AG01	1
Pethidine (=Meperidine) 4	N02AG03	N02AG03	N02AG03	N02AG03	2
Tramadol 1	N02AX02	N02AX02	N02AX02	N02AX02	1
Tramadol 2	N02AX52	N02AX52	N02AX52	N02AX52	1

Acetylsalicylicacid	N02BA01	N02BA01	N02BA01	N02BA01	0
Paracetamol	N02BE01	N02BE01	N02BE01	N02BE01	0
Topiramate 2	N02CX12	N02CX12	N02CX12	N02CX12	0
Codeine 8	N02CX58	N02CX58	N02CX58	N02CX58	1
Metoclopramide 3	N02CX59	N02CX59	N02CX59	N02CX59	0
Phenobarbital 1	N03AA02	N03AA02	N03AA02	N03AA02	0
Phenytoin 1	N03AB02	N03AB02	N03AB02	N03AB02	0
Phenytoin 3 (Fosphenytoin)	N03AB05	N03AB05	N03AB05	N03AB05	0
Phenytoin 2	N03AB52	N03AB52	N03AB52	N03AB52	0
Clonazepam	N03AE01	N03AE01	N03AE01	N03AE01	1
Midazolam 2	N03AE02	N03AE02	n/a	n/a	1
Carbamazepine	N03AF01	N03AF01	N03AF01	N03AF01	2
Oxcarbazepine	N03AF02	N03AF02	N03AF02	N03AF02	2
Valproic acid / Sodium Valproate	N03AG01	N03AG01	N03AG01	N03AG01	1
Topiramate 1	N03AX11	N03AX11	N03AX11	N03AX11	0
Trihexyphenidyl	N04AA01	N04AA01	N04AA01	N04AA01	3
Procyclidine	N04AA04	N04AA04	N04AA04	N04AA04	3
Orphenadrine 3	N04AB02	N04AB02	N04AB02	N04AB02	3
Benzatropine 1	N04AC01	N04AC01	N04AC01	N04AC01	3
Benzatropine 2 (Etybenzatropin)	N04AC30	N04AC30	N04AC30	N04AC30	3
Levodopa 1	N04BA01	N04BA01	N04BA01	N04BA01	0
Entacapone 2 + Levodopa 3	N04BA03	N04BA03	N04BA03	N04BA03	0
Levodopa 6 (Melevodopa 1)	N04BA04	N04BA04	N04BA04	N04BA04	0
Levodopa 7 (Melevodopa 2)	N04BA05	N04BA05	N04BA05	N04BA05	0
Levodopa 5 (Etilevodopa)	N04BA06	N04BA06	N04BA06	N04BA06	0
Levodopa 2	N04BA10	N04BA10	N04BA10	N04BA10	0
Levodopa 4	N04BA11	N04BA11	N04BA11	N04BA11	0
Amantadine 1	N04BB01	N04BB01	N04BB01	N04BB01	1
Bromocriptine 1	N04BC01	N04BC01	N04BC01	N04BC01	1
Ropinirole	N04BC04	N04BC04	N04BC04	N04BC04	0
Pramipexol	N04BC05	N04BC05	N04BC05	N04BC05	0
Selegiline	N04BD01	N04BD01	N04BD01	N04BD01	0
Entacapone 1	N04BX02	N04BX02	N04BX02	N04BX02	0
Chlorpromazine	N05AA01	N05AA01	N05AA01	N05AA01	3
Levomepromazine	N05AA02	N05AA02	N05AA02	N05AA02	2
Fluphenazine	N05AB02	N05AB02	N05AB02	N05AB02	1
Perphenazine	N05AB03	N05AB03	N05AB03	N05AB03	1
Prochlorperazine	N05AB04	N05AB04	N05AB04	N05AB04	1
Trifluoperazine	N05AB06	N05AB06	N05AB06	N05AB06	1
Thioridazine	N05AC02	N05AC02	N05AC02	N05AC02	3
Haloperidol	N05AD01	N05AD01	N05AD01	N05AD01	0
Molindone	N05AE02	N05AE02	N05AE02	N05AE02	2
Tiotixene	N05AF04	N05AF04	N05AF04	N05AF04	1
Pimozide	N05AG02	N05AG02	N05AG02	N05AG02	2

Loxapine	N05AH01	N05AH01	N05AH01	N05AH01	2
Clozapine	N05AH02	N05AH02	N05AH02	N05AH02	3
Olanzapine	N05AH03	N05AH03	N05AH03	N05AH03	1
Quetiapine (fumarate)	N05AH04	N05AH04	N05AH04	N05AH04	0
Lithium	N05AN01	N05AN01	N05AN01	N05AN01	0
Diazepam	N05BA01	N05BA01	N05BA01	N05BA01	1
Chlordiazepoxide	N05BA02	N05BA02	N05BA02	N05BA02	1
Oxazepam	N05BA04	N05BA04	N05BA04	N05BA04	1
Clorazepate	N05BA05	N05BA05	N05BA05	N05BA05	1
Lorazepam 1	N05BA06	N05BA06	N05BA06	N05BA06	1
Alprazolam	N05BA12	N05BA12	N05BA12	N05BA12	1
Lorazepam 2	N05BA56	N05BA56	N05BA56	N05BA56	1
Hydroxyzine 1	N05BB01	N05BB01	N05BB01	N05BB01	3
Hydroxyzine 3	N05BB51	N05BB51	N05BB51	N05BB51	3
Phenobarbital 2	N05CA24	N05CA24	N05CA24	N05CA24	0
Flurazepam	N05CD01	N05CD01	N05CD01	N05CD01	1
Estazolam	N05CD04	N05CD04	N05CD04	N05CD04	1
Triazolam	N05CD05	N05CD05	N05CD05	N05CD05	1
Temazepam	N05CD07	N05CD07	N05CD07	N05CD07	1
Midazolam 1	N05CD08	N05CD08	N05CD08	N05CD08	1
Zopiclone	N05CF01	N05CF01	N05CF01	N05CF01	0
Zolpidem	N05CF02	N05CF02	N05CF02	N05CF02	0
Scopolamine 3 (=Hyoscin)	N05CM05	N05CM05	N05CM05	N05CM05	3
Diphenhydramine 5	N05CM20	N05CM20	N05CM20	N05CM20	3
Promethazine 4	N05CM22	N05CM22	N05CM22	N05CM22	3
Diphenhydramine 2	N05CX07	N05CX07	N05CX07	N05CX07	3
Promethazine 5	N05CX13	N05CX13	N05CX13	N05CX13	3
Desipramine	N06AA01	N06AA01	N06AA01	N06AA01	3
Imipramine 1	N06AA02	N06AA02	N06AA02	N06AA02	3
Imipramine 2	N06AA03	N06AA03	N06AA03	N06AA03	3
Clomipramine	N06AA04	N06AA04	N06AA04	N06AA04	3
Trimipramine	N06AA06	N06AA06	N06AA06	N06AA06	3
Amitriptyline 1	N06AA09	N06AA09	N06AA09	N06AA09	3
Nortriptyline 1	N06AA10	N06AA10	N06AA10	N06AA10	3
Protriptyline	N06AA11	N06AA11	N06AA11	N06AA11	3
Doxepin	N06AA12	N06AA12	N06AA12	N06AA12	3
Amitriptyline 3	N06AA25	N06AA25	N06AA25	N06AA25	3
Fluoxetine 1	N06AB03	N06AB03	N06AB03	N06AB03	1
Citalopram	N06AB04	N06AB04	N06AB04	N06AB04	0
Paroxetine	N06AB05	N06AB05	N06AB05	N06AB05	1
Fluvoxamine	N06AB08	N06AB08	N06AB08	N06AB08	1
Escitalopram	N06AB10	N06AB10	N06AB10	N06AB10	0
Phenelzine	N06AF03	N06AF03	N06AF03	N06AF03	1
Trazodone	N06AX05	N06AX05	N06AX05	N06AX05	0
Nefazodone	N06AX06	N06AX06	N06AX06	N06AX06	0
Mirtazapine	N06AX11	N06AX11	N06AX11	N06AX11	0
Bupropion 1	N06AX12	N06AX12	N06AX12	N06AX12	0
Venlafaxine 1	N06AX16	N06AX16	N06AX16	N06AX16	0
Duloxetine	N06AX21	N06AX21	N06AX21	N06AX21	0

Venlafaxine 2 (Desvenlafaxine)	N06AX23	N06AX23	N06AX23	N06AX23	0
Amitriptyline 2	N06CA01	N06CA01	N06CA01	N06CA01	3
Fluoxetine 2	N06CA03	n/a	n/a	n/a	1
Nortriptyline 2	N06CA06	N06CA06	N06CA06	N06CA06	3
Donepezil	N06DA02	N06DA02	N06DA02	N06DA02	0
Galantamine	N06DA04	N06DA04	N06DA04	N06DA04	0
Bupropion 2	N07BA02	N07BA02	N07BA02	N07BA02	0
Pseudoephedrine 1	R01BA02	R01BA02	R01BA02	R01BA02	0
Pseudoephedrine 2	R01BA52	R01BA52	R01BA52	R01BA52	0
Terbutaline (oral) 2	R03AC03	R03AC03	R03AC03	R03AC03	0
Fluticasone-salmeterol	R03AK06	R03AK61	R03AK61	R03AK61	1
Ipratropium	R03BB01	R03BB01	R03BB01	R03BB01	0
Terbutaline (oral) 1	R03CC03	R03CC03	R03CC03	R03CC03	0
Terbutaline (oral) 3	R03CC53	R03CC53	R03CC53	R03CC53	0
Theophylline 1	R03DA04	R03DA04	R03DA04	R03DA04	1
Theophylline 4	R03DA54	R03DA54	R03DA54	R03DA54	1
Theophylline 5	R03DA74	R03DA74	R03DA74	R03DA74	1
Theophylline 6	R03DB04	R03DB04	R03DB04	R03DB04	1
Guaifenesin	R05CA03	R05CA03	R05CA03	R05CA03	0
Hydrocodone	R05DA03	R05DA03	R05DA03	R05DA03	0
Codeine 1	R05DA04	R05DA04	R05DA04	R05DA04	1
Morphine 5	R05DA05	R05DA05	R05DA05	R05DA05	1
Codeine 12 (Dihydrocodeine 3)	R05DA14	R05DA14	R05DA14	R05DA14	1
Codeine 9	R05DA54	R05DA54	R05DA54	R05DA54	1
Codeine 13 (Dihydrocodeine 4)	R05DA64	R05DA64	R05DA64	R05DA64	1
Ampicillin 4	R05GB05	R05GB05	R05GB05	R05GB05	1
Diphenhydramine 1	R06AA02	R06AA02	R06AA02	R06AA02	3
Clemastine 1	R06AA04	R06AA04	R06AA04	R06AA04	3
Carbinoxamine	R06AA08	R06AA08	R06AA08	R06AA08	3
Diphenhydramine 7	R06AA52	R06AA52	R06AA52	R06AA52	3
Clemastine 2	R06AA54	R06AA54	R06AA54	R06AA54	3
Brompheniramine 1	R06AB01	R06AB01	R06AB01	R06AB01	3
Chlorpheniramine (=Chlorphenamine) 1	R06AB04	R06AB04	R06AB04	R06AB04	3
Brompheniramine 2	R06AB51	R06AB51	R06AB51	R06AB51	3
Chlorpheniramine (=Chlorphenamine) 2	R06AB54	R06AB54	R06AB54	R06AB54	3
Pyrilamine	R06AC01	R06AC01	R06AC01	R06AC01	3
Promethazine 1	R06AD02	R06AD02	R06AD02	R06AD02	3
Promethazine 8 (Hydroxyethylpromethazin 1)	R06AD05	R06AD05	R06AD05	R06AD05	3
Promethazine 7 (Dioxopromethazin)	R06AD10	R06AD10	R06AD10	R06AD10	3
Promethazine 2	R06AD52	R06AD52	R06AD52	R06AD52	3

Promethazine 9 (Hydroxyethylpromethazin 2)	R06AD55	R06AD55	R06AD55	R06AD55	3
Meclozine 1	R06AE05	R06AE05	R06AE05	R06AE05	3
Cetirizin 1	R06AE07	R06AE07	R06AE07	R06AE07	0
Cetirizin 3 (Enantiomer Levocetirizin)	R06AE09	R06AE09	R06AE09	R06AE09	0
Meclozine 2	R06AE55	R06AE55	R06AE55	R06AE55	3
Cetirizin 2	R06AE57	R06AE57	R06AE57	R06AE57	0
Cyproheptadine 1	R06AX02	R06AX02	R06AX02	R06AX02	2
Loratadine 1	R06AX13	R06AX13	R06AX13	R06AX13	0
Ketotifen	R06AX17	R06AX17	R06AX17	R06AX17	1
Fexofenadine	R06AX26	R06AX26	R06AX26	R06AX26	0
Loratadine 2 (Enantiomer Desloratadin)	R06AX27	R06AX27	R06AX27	R06AX27	0
Hydroxyzine 2	R06AX32	R06AX32	R06AX32	R06AX32	3
Promethazine 6	V03AB05	V03AB05	V03AB05	V03AB05	3

Drug Burden Index

Medication IDIS ingredient code (IDIS=Iowa Drug Information System)	**Medication**	**ATC-Code 2014**	**ATC-Code 2013**	**ATC-Code 2012**	**ATC-Code 2011**
Dicyclomine 12080005	Dicycloverine	A03AA07	A03AA07	A03AA07	A03AA07
Propantheline 12080008	Propantheline 1	A03AB05	A03AB05	A03AB05	A03AB05
Papaverine 86000007	Papaverine 1	A03AD01	A03AD01	A03AD01	A03AD01
	Belladonna alkaloids 2	A03BA01	A03BA01	A03BA01	A03BA01
Hyoscyamine 12080079	Hyoscyamine 1 + Belladonna alkaloids 3	A03BA03	A03BA03	A03BA03	A03BA03
	Belladonna alkaloids 4	A03BA04	A03BA04	A03BA04	A03BA04
	Belladonna alkaloids 5	A03BA20	A03BA20	A03BA20	A03BA20
	Belladonna alkaloids 6	A03BB01	A03BB01	A03BB01	A03BB01
	Belladonna alkaloids 7	A03BB02	A03BB02	A03BB02	A03BB02
Methscopolamine 12080007	Methscopolamine 1 (Belladonna alkaloids 8)	A03BB03	A03BB03	A03BB03	A03BB03
	Belladonna alkaloids 9	A03BB04	A03BB04	A03BB04	A03BB04
	Belladonna alkaloids 10	A03BB05	A03BB05	A03BB05	A03BB05
Clidinium 12080047	Clidinium	A03CA02	A03CA02	A03CA02	A03CA02
	Propantheline 2	A03CA34	A03CA34	A03CA34	A03CA34
	Methscopolamine 2 (Belladonna alkaloids 11)	A03CB01	A03CB01	A03CB01	A03CB01
	Belladonna alkaloids 12	A03CB02	A03CB02	A03CB02	A03CB02
	Belladonna alkaloids 13	A03CB03	A03CB03	A03CB03	A03CB03
	Belladonna alkaloids 14	A03CB04	A03CB04	A03CB04	A03CB04
	Hyoscyamine 2 (Belladonna alkaloids 15)	A03CB31	A03CB31	A03CB31	A03CB31
	Belladonna alkaloids 16	A03CB37	A03CB37	A03CB37	A03CB37
	Belladonna alkaloids 17	A03CB38	A03CB38	A03CB38	A03CB38
	Belladonna alkaloids 18	A03DB04	A03DB04	A03DB04	A03DB04
Metoclopramide 56220098	Metoclopramide 1	A03FA01	A03FA01	A03FA01	A03FA01
	Metoclopramide 2	A03FA51	A03FA51	A03FA51	A03FA51
Dimenhydrinate 56220003	Dimenhydrinate 1	A04AB02	A04AB02	A04AB02	A04AB02
	Meclozine 3	A04AB04	A04AB04	A04AB04	A04AB04
	Diphenhydramine 3	A04AB05	A04AB05	A04AB05	A04AB05
	Dimenhydrinate 2	A04AB52	A04AB52	A04AB52	A04AB52
	Meclozine 4	A04AB54	A04AB54	A04AB54	A04AB54
	Diphenhydramine 6	A04AB55	A04AB55	A04AB55	A04AB55
	Doxylamine 4	A04AB56	A04AB56	A04AB56	A04AB56
	Promethazine 3	A04AB58	A04AB58	A04AB58	A04AB58
	Triflupromazine 2	A04AD06	A04AD06	A04AD06	A04AD06
Belladonna 12080002	Belladonna alkaloids 1	A06AB30	A06AB30	A06AB30	A06AB30
Diphenoxylate 56080005	Diphenoxylate	A07DA01	A07DA01	A07DA01	A07DA01
Opium 28080881	Opium 1	A07DA02	A07DA02	A07DA02	A07DA02
Loperamide 56080009	Loperamide 1	A07DA03	A07DA03	A07DA03	A07DA03
	Morphine 2	A07DA52	A07DA52	A07DA52	A07DA52
	Loperamide 2	A07DA53	A07DA53	A07DA53	A07DA53
	Cyproheptadine 2	A15AA01	A15AA01	A15AA01	A15AA01
	Cyproheptadine 3	A15AA51	A15AA51	A15AA51	A15AA51
Disopyramide 24040024	Disopyramide	C01BA03	C01BA03	C01BA03	C01BA03

Reserpine 24080010	Reserpine 1	C02AA02	C02AA02	C02AA02	C02AA02
	Reserpine 2	C02AA52	C02AA52	C02AA52	C02AA52
Methyldopa 24080006	Methyldopa 1	C02AB01	C02AB01	C02AB01	C02AB01
	Methyldopa 2	C02AB02	C02AB02	C02AB02	C02AB02
Clonidine 24080064	Clonidine 1	C02AC01	C02AC01	C02AC01	C02AC01
Guanfacine 24080063	Guanfacine	C02AC02	C02AC02	C02AC02	C02AC02
Prazosin 12160404	Prazosin 1	C02CA01	C02CA01	C02CA01	C02CA01
Doxazosin 12160419	Doxazosin 1	C02CA04	C02CA04	C02CA04	C02CA04
	Terazosin 2	C02CA08	C02CA08	C02CA08	C02CA08
Guanethidine 24080003	Guanethidine 1	C02CC02	C02CC02	C02CC02	C02CC02
Guanabenz 24080084	Guanoxabenz	C02CC07	C02CC07	C02CC07	C02CC07
	Reserpine 3	C02LA01	C02LA01	C02LA01	C02LA01
	Reserpine 4	C02LA51	C02LA51	C02LA51	C02LA51
	Reserpine 5	C02LA71	C02LA71	C02LA71	C02LA71
	Methyldopa 3	C02LB01	C02LB01	C02LB01	C02LB01
	Clonidine 2	C02LC01	C02LC01	C02LC01	C02LC01
	Clonidine 3	C02LC51	C02LC51	C02LC51	C02LC51
	Prazosin 2	C02LE01	C02LE01	C02LE01	C02LE01
	Guanethidine 2	C02LF01	C02LF01	C02LF01	C02LF01
Flavoxate 12080039	Flavoxate	G04BD02	G04BD02	G04BD02	G04BD02
Oxybutynin 86000004	Oxybutynin	G04BD04	G04BD04	G04BD04	G04BD04
Tolterodine 86000047	Tolterodine	G04BD07	G04BD07	G04BD07	G04BD07
	Papaverine 2	G04BE02	G04BE02	G04BE02	G04BE02
Tamulosin 12160411	Tamsulosin 1	G04CA02	G04CA02	G04CA02	G04CA02
Terazosin 12160401	Terazosin 1	G04CA03	G04CA03	G04CA03	G04CA03
	Doxazosin 2	G04CA05	G04CA05	G04CA05	G04CA05
	Tamsulosin 2	G04CA52	G04CA52	G04CA52	G04CA52
	Tamsulosin 3	G04CA53	G04CA53	G04CA53	G04CA53
Carisoprodol 12200001	Carisoprodol 1	M03BA02	M03BA02	M03BA02	M03BA02
Methocarbamol 12200005	Methocarbamol 1	M03BA03	M03BA03	M03BA03	M03BA03
	Carisoprodol 2	M03BA52	M03BA52	M03BA52	M03BA52
	Methocarbamol 2	M03BA53	M03BA53	M03BA53	M03BA53
	Meprobamate 4	M03BA57	M03BA57	M03BA57	M03BA57
	Carisoprodol 3	M03BA72	M03BA72	M03BA72	M03BA72
	Methocarbamol 3	M03BA73	M03BA73	M03BA73	M03BA73
Chlorzoxazone 12200091	Chlorzoxazone 1	M03BB03	M03BB03	M03BB03	M03BB03
	Chlorzoxazone 3	M03BB53	M03BB53	M03BB53	M03BB53
	Chlorzoxazone 2	M03BB73	M03BB73	M03BB73	M03BB73
Orphenadrine 12080804	Orphenadrine 1	M03BC01	M03BC01	M03BC01	M03BC01
	Orphenadrine 2	M03BC51	M03BC51	M03BC51	M03BC51
Cyclobenzaprine 12200009	Cyclobenzaprine	M03BX08	M03BX08	M03BX08	M03BX08
Hexobarbital 28240405	Hexobarbital 1	N01AF02	N01AF02	N01AF02	N01AF02
	Fentanyl 2	N01AH01	N01AH01	N01AH01	N01AH01
	Fentanyl 3	N01AH51	N01AH51	N01AH51	N01AH51
	Diphenhydramine 4	N01BX06	N01BX06	N01BX06	N01BX06
Morphine 28080819	Morphine 1	N02AA01	N02AA01	N02AA01	N02AA01
	Opium 2	N02AA02	N02AA02	N02AA02	N02AA02
Oxycodone 28080883	Oxycodone 1	N02AA05	N02AA05	N02AA05	N02AA05
	Codeine 10 (Dihydrocodeine 1)	N02AA08	N02AA08	N02AA08	N02AA08

	Morphine 3	N02AA51	N02AA51	N02AA51	N02AA51
	Oxycodone 2	N02AA55	N02AA55	N02AA55	N02AA55
	Codeine 11 (Dihydrocodeine 2)	N02AA58	N02AA58	N02AA58	N02AA58
	Codeine 2	N02AA59	N02AA59	N02AA59	N02AA59
	Codeine 3	N02AA64	N02AA64	N02AA64	N02AA64
	Codeine 4	N02AA65	N02AA65	N02AA65	N02AA65
	Codeine 5	N02AA66	N02AA66	N02AA66	N02AA66
	Codeine 6	N02AA69	N02AA69	N02AA69	N02AA69
	Codeine 7	N02AA79	N02AA79	N02AA79	N02AA79
Fentanyl 28080810	Fentanyl 1	N02AB03	N02AB03	N02AB03	N02AB03
Propoxyphene 28080840	Propoxyphene	N02AC04	N02AC04	N02AC04	N02AC04
	Methadone 3 (Levomethadone)	N02AC06	N02AC06	N02AC06	N02AC06
	Methadone 2	N02AC52	N02AC52	N02AC52	N02AC52
Pentazocine 28080892	Pentazocine	N02AD01	N02AD01	N02AD01	N02AD01
	Morphine 4	N02AG01	N02AG01	N02AG01	N02AG01
Tramadol 28080854	Tramadol 1	N02AX02	N02AX02	N02AX02	N02AX02
	Tramadol 2	N02AX52	N02AX52	N02AX52	N02AX52
	Clonidine 4	N02CX02	N02CX02	N02CX02	N02CX02
	Codeine 8	N02CX58	N02CX58	N02CX58	N02CX58
	Metoclopramide 3	N02CX59	N02CX59	N02CX59	N02CX59
Phenobarbital 28120405	Phenobarbital 1	N03AA02	N03AA02	N03AA02	N03AA02
Primidone 28120407	Primidone	N03AA03	N03AA03	N03AA03	N03AA03
Phenytoin 28120805	Phenytoin 1	N03AB02	N03AB02	N03AB02	N03AB02
	Phenytoin 3 (Fosphenytoin)	N03AB05	N03AB05	N03AB05	N03AB05
	Phenytoin 2	N03AB52	N03AB52	N03AB52	N03AB52
Clonazepam 28240212	Clonazepam	N03AE01	N03AE01	N03AE01	N03AE01
Carbamazepine 28122007	Carbamazepine	N03AF01	N03AF01	N03AF01	N03AF01
Oxcarbazepine 28122011	Oxcarbazepine	N03AF02	N03AF02	N03AF02	N03AF02
Valproic acid 28122015	Valproic acid / Sodium Valproate	N03AG01	N03AG01	N03AG01	N03AG01
Tiagabine 28122034	Tiagabine	N03AG06	N03AG06	N03AG06	N03AG06
Lamotrigine 28122024	Lamotrigine	N03AX09	N03AX09	N03AX09	N03AX09
Gabapentin 28122020	Gabapentin	N03AX12	N03AX12	N03AX12	N03AX12
Levetiracetam 28122040	Levetiracetam	N03AX14	N03AX14	N03AX14	N03AX14
Trihexyphenidyl 12080802	Trihexyphenidyl	N04AA01	N04AA01	N04AA01	N04AA01
	Orphenadrine 3	N04AB02	N04AB02	N04AB02	N04AB02
Benztropine 12080806	Benzatropine 1	N04AC01	N04AC01	N04AC01	N04AC01
	Benzatropine 2 (Etybenzatropin)	N04AC30	N04AC30	N04AC30	N04AC30
Ropinerole 28280011	Ropinerole	N04BC04	N04BC04	N04BC04	N04BC04
Pramipexole 28280013	Pramipexole	N04BC05	N04BC05	N04BC05	N04BC05
Selegiline 28160520	Selegiline	N04BD01	N04BD01	N04BD01	N04BD01
Chlorpromazine 56220089	Chlorpromazine	N05AA01	N05AA01	N05AA01	N05AA01
Triflupromazine 28160996	Triflupromazine 1	N05AA05	N05AA05	N05AA05	N05AA05
Fluphenazine 28160906	Fluphenazine	N05AB02	N05AB02	N05AB02	N05AB02
Perphenazine 28160909	Perphenazine	N05AB03	N05AB03	N05AB03	N05AB03
Prochlorperazine 56220096	Prochlorperazine	N05AB04	N05AB04	N05AB04	N05AB04
Trifluoperazine 28160913	Trifluoperazine	N05AB06	N05AB06	N05AB06	N05AB06

Thioridazine 28160912	Thioridazine	N05AC02	N05AC02	N05AC02	N05AC02
Haloperidol 28161014	Haloperidol	N05AD01	N05AD01	N05AD01	N05AD01
Ziprasidone 28160844	Ziprasidone	N05AE04	N05AE04	N05AE04	N05AE04
Chlorprothixine 28160804	Chlorprothixene	N05AF03	N05AF03	N05AF03	N05AF03
Loxapine 28160858	Loxapine	N05AH01	N05AH01	N05AH01	N05AH01
Olanzapine 28160836	Olanzapine	N05AH03	N05AH03	N05AH03	N05AH03
Quetiapine 28160834	Quetiapine	N05AH04	N05AH04	N05AH04	N05AH04
Risperidone 28160822	Risperidone	N05AX08	N05AX08	N05AX08	N05AX08
	Reserpine 6	N05AX15	N05AX15	N05AX15	N05AX15
Diazepam 28240205	Diazepam	N05BA01	N05BA01	N05BA01	N05BA01
Chlordiazepoxide 28240202	Chlordiazepoxide	N05BA02	N05BA02	N05BA02	N05BA02
Oxazepam 28240215	Oxazepam	N05BA04	N05BA04	N05BA04	N05BA04
Clorazepate 28240228	Clorazepate	N05BA05	N05BA05	N05BA05	N05BA05
Lorazepam 28240276	Lorazepam 1	N05BA06	N05BA06	N05BA06	N05BA06
Alprazolam 28240232	Alprazolam	N05BA12	N05BA12	N05BA12	N05BA12
	Lorazepam 2	N05BA56	N05BA56	N05BA56	N05BA56
Hydroxyzine 28160807	Hydroxyzine 1	N05BB01	N05BB01	N05BB01	N05BB01
	Hydroxyzine 3	N05BB51	N05BB51	N05BB51	N05BB51
Meprobamate 28240820	Meprobamate 1	N05BC01	N05BC01	N05BC01	N05BC01
	Meprobamate 2	N05BC51	N05BC51	N05BC51	N05BC51
Buspirone 28240837	Buspirone	N05BE01	N05BE01	N05BE01	N05BE01
	Hexobarbital 2	N05CA16	N05CA16	N05CA16	N05CA16
	Phenobarbital 2	N05CA24	N05CA24	N05CA24	N05CA24
Dichloralphenazone 28240828	Dichloralphenazone	N05CC04	N05CC04	N05CC04	N05CC04
Flurazepam 28240206	Flurazepam	N05CD01	N05CD01	N05CD01	N05CD01
Estazolam 28240216	Estazolam	N05CD04	N05CD04	N05CD04	N05CD04
Triazolam 28240222	Triazolam	N05CD05	N05CD05	N05CD05	N05CD05
Temazepam 28240231	Temazepam	N05CD07	N05CD07	N05CD07	N05CD07
Zolpidem 28240834	Zolpidem	N05CF02	N05CF02	N05CF02	N05CF02
Zaleplon 28240856	Zaleplon	N05CF03	N05CF03	N05CF03	N05CF03
	Diphenhydramine 5	N05CM20	N05CM20	N05CM20	N05CM20
	Doxylamine 3	N05CM21	N05CM21	N05CM21	N05CM21
	Promethazine 4	N05CM22	N05CM22	N05CM22	N05CM22
	Meprobamate 3	N05CX01	N05CX01	N05CX01	N05CX01
	Diphenhydramine 2	N05CX07	N05CX07	N05CX07	N05CX07
	Promethazine 5	N05CX13	N05CX13	N05CX13	N05CX13
Desipramine 28160689	Desipramine	N06AA01	N06AA01	N06AA01	N06AA01
Imipramine 28160602	Imipramine 1	N06AA02	N06AA02	N06AA02	N06AA02
	Imipramine 2	N06AA03	N06AA03	N06AA03	N06AA03
Clomipramine 28160688	Clomipramine	N06AA04	N06AA04	N06AA04	N06AA04
Trimipramine 28160650	Trimipramine	N06AA06	N06AA06	N06AA06	N06AA06
Amitriptyline 28160601	Amitriptyline 1	N06AA09	N06AA09	N06AA09	N06AA09
Nortryptyline 28160695	Nortriptyline 1	N06AA10	N06AA10	N06AA10	N06AA10
Doxepin 28160681	Doxepin	N06AA12	N06AA12	N06AA12	N06AA12
	Amitriptyline 3	N06AA25	N06AA25	N06AA25	N06AA25
Fluoxetine 28160701	Fluoxetine 1	N06AB03	N06AB03	N06AB03	N06AB03
Citalopram 28160705	Citalopram	N06AB04	N06AB04	N06AB04	N06AB04
Paroxetine 28160702	Paroxetine	N06AB05	N06AB05	N06AB05	N06AB05

Sertraline 28160703	Sertraline	N06AB06	N06AB06	N06AB06	N06AB06
Ecitalopram 28160711	Escitalopram	N06AB10	N06AB10	N06AB10	N06AB10
Phenelzine 28160505	Phenelzine	N06AF03	N06AF03	N06AF03	N06AF03
Tranylcypromine 28160601	Tranylcypromine 1	N06AF04	N06AF04	N06AF04	N06AF04
Trazodone 28160415	Trazodone	N06AX05	N06AX05	N06AX05	N06AX05
Nefazodone 28160486	Nefazodone	N06AX06	N06AX06	N06AX06	N06AX06
Mirtazepine 28160617	Mirtazapine	N06AX11	N06AX11	N06AX11	N06AX11
Venlafaxine 28160458	Venlafaxine 1	N06AX16	N06AX16	N06AX16	N06AX16
	Venlafaxine 2 (Desvenlafaxine)	N06AX23	N06AX23	N06AX23	N06AX23
	Amitriptyline 2	N06CA01	N06CA01	N06CA01	N06CA01
	Fluoxetine 2	N06CA03	n/a	n/a	n/a
	Nortriptyline 2	N06CA06	N06CA06	N06CA06	N06CA06
	Tranylcypromine 2	N06CA07	N06CA03	N06CA03	N06CA03
	Clonidine 5	N07BB06	N07BB06	N07BB06	N07BB06
Methadone 28080818	Methadone 1	N07BC02	N07BC02	N07BC02	N07BC02
	Dextrometorphan 2	N07XX59	n/a	n/a	n/a
Hydrocodone 48000072	Hydrocodone	R05DA03	R05DA03	R05DA03	R05DA03
Codeine 48000063	Codeine 1	R05DA04	R05DA04	R05DA04	R05DA04
	Morphine 5	R05DA05	R05DA05	R05DA05	R05DA05
Dextromethorphan 48000069	Dextrometorphan 1	R05DA09	R05DA09	R05DA09	R05DA09
	Codeine 12 (Dihydrocodeine 3)	R05DA14	R05DA14	R05DA14	R05DA14
	Codeine 9	R05DA54	R05DA54	R05DA54	R05DA54
	Dextrometorphan 3	R05DA59	R05DA59	R05DA59	R05DA59
	Codeine 13 (Dihydrocodeine 4)	R05DA64	R05DA64	R05DA64	R05DA64
Benzonatate 48000054	Benzonatate	R05DB01	R05DB01	R05DB01	R05DB01
Diphenhydramine 4000006	Diphenhydramine 1	R06AA02	R06AA02	R06AA02	R06AA02
Clemastine 4000054	Clemastine 1	R06AA04	R06AA04	R06AA04	R06AA04
Doxylamine 4000068	Doxylamine 1	R06AA09	R06AA09	R06AA09	R06AA09
Trimethobenzamide 56220006	Trimethobenzamide	R06AA10	R06AA10	R06AA10	R06AA10
	Diphenhydramine 7	R06AA52	R06AA52	R06AA52	R06AA52
	Clemastine 2	R06AA54	R06AA54	R06AA54	R06AA54
	Doxylamine 2	R06AA59	R06AA59	n/a	n/a
Brompheniramine 4000078	Brompheniramine 1	R06AB01	R06AB01	R06AB01	R06AB01
Dexchlorpheniramine 4000084	Dexchlorpheniramine 1	R06AB02	R06AB02	R06AB02	R06AB02
Chlorpheniramine (=Chlorphenamine) 4000003	Chlorpheniramine (=Chlorphenamine) 1	R06AB04	R06AB04	R06AB04	R06AB04
Pheniramine 4000092	Pheniramine	R06AB05	R06AB05	R06AB05	R06AB05
Dexbrompheniramine 4000083	Dexbrompheniramine 1	R06AB06	R06AB06	R06AB06	R06AB06
	Brompheniramine 2	R06AB51	R06AB51	R06AB51	R06AB51
	Dexchlorpheniramine 2	R06AB52	R06AB52	R06AB52	R06AB52
	Chlorpheniramine (=Chlorphenamine) 2	R06AB54	R06AB54	R06AB54	R06AB54

	Dexbrompheniramine 2	R06AB56	R06AB56	R06AB56	R06AB56
Tripelennamine 4000013	Tripelennamine	R06AC04	R06AC04	R06AC04	R06AC04
Promethazine 4000010	Promethazine 1	R06AD02	R06AD02	R06AD02	R06AD02
	Promethazine 8 (Hydroxyethylpromethazin 1)	R06AD05	R06AD05	R06AD05	R06AD05
	Promethazine 7 (Dioxopromethazin)	R06AD10	R06AD10	R06AD10	R06AD10
	Promethazine 2	R06AD52	R06AD52	R06AD52	R06AD52
	Promethazine 9 (Hydroxyethylpromethazin 2)	R06AD55	R06AD55	R06AD55	R06AD55
Meclizine 56220005	Meclozine 1	R06AE05	R06AE05	R06AE05	R06AE05
Cetirizine 4000031	Cetirizin 1	R06AE07	R06AE07	R06AE07	R06AE07
	Cetirizin 3 (Enantiomer Levocetirizin)	R06AE09	R06AE09	R06AE09	R06AE09
	Meclozine 2	R06AE55	R06AE55	R06AE55	R06AE55
	Cetirizin 2	R06AE57	R06AE57	R06AE57	R06AE57
Cyproheptadine 4000012	Cyproheptadine 1	R06AX02	R06AX02	R06AX02	R06AX02
Triprolidine 4000099	Triprolidine 1	R06AX07	R06AX07	R06AX07	R06AX07
Azatadine 4000018	Azatadine	R06AX09	R06AX09	R06AX09	R06AX09
Astemizole 4000022	Astemizole	R06AX11	R06AX11	R06AX11	R06AX11
Loratadine 4000029	Loratadine 1	R06AX13	R06AX13	R06AX13	R06AX13
	Loratadine 2 (Enantiomer Desloratadin)	R06AX27	R06AX27	R06AX27	R06AX27
	Hydroxyzine 2	R06AX32	R06AX32	R06AX32	R06AX32
	Triprolidine 2	R06AX57	R06AX57	R06AX57	R06AX57
	Promethazine 6	V03AB05	V03AB05	V03AB05	V03AB05

ICD-10-Code (Source: ICD-10-GM). 1 = yes, 0 = no

2014	2013	2012	2011	Schaefer et al. (mod.)	Diederich	Charlson	HRQoL-Index	Excluded diagnoses
B15	B15	B15	B15	0	0	0	1	0
B16	B16	B16	B16	0	0	0	1	0
B17	B17	B17	B17	0	0	0	1	0
B18	B18	B18	B18	0	0	0	1	0
B19	B19	B19	B19	0	0	0	1	0
B20	B20	B20	B20	0	0	1	1	0
B21	B21	B21	B21	0	0	1	1	0
B22	B22	B22	B22	0	0	1	1	0
B23	B23	B23	B23	0	0	1	1	0
B24	B24	B24	B24	0	0	1	1	0
C00	C00	C00	C00	1	1	1	0	0
C01	C01	C01	C01	1	1	1	0	0
C02	C02	C02	C02	1	1	1	0	0
C03	C03	C03	C03	1	1	1	0	0
C04	C04	C04	C04	1	1	1	0	0
C05	C05	C05	C05	1	1	1	0	0
C06	C06	C06	C06	1	1	1	0	0
C07	C07	C07	C07	1	1	1	0	0
C08	C08	C08	C08	1	1	1	0	0
C09	C09	C09	C09	1	1	1	0	0
C10	C10	C10	C10	1	1	1	0	0
C11	C11	C11	C11	1	1	1	0	0
C12	C12	C12	C12	1	1	1	0	0
C13	C13	C13	C13	1	1	1	0	0
C14	C14	C14	C14	1	1	1	0	0
C15	C15	C15	C15	1	1	1	0	0
C16	C16	C16	C16	1	1	1	0	0
C17	C17	C17	C17	1	1	1	0	0
C18	C18	C18	C18	1	1	1	0	0
C19	C19	C19	C19	1	1	1	0	0
C20	C20	C20	C20	1	1	1	0	0
C21	C21	C21	C21	1	1	1	0	0
C22	C22	C22	C22	1	1	1	0	0
C23	C23	C23	C23	1	1	1	0	0
C24	C24	C24	C24	1	1	1	0	0
C25	C25	C25	C25	1	1	1	0	0
C26	C26	C26	C26	1	1	1	0	0
C30	C30	C30	C30	1	1	1	0	0
C31	C31	C31	C31	1	1	1	0	0
C32	C32	C32	C32	1	1	1	0	0
C33	C33	C33	C33	1	1	1	0	0
C34	C34	C34	C34	1	1	1	0	0
C37	C37	C37	C37	1	1	1	0	0
C38	C38	C38	C38	1	1	1	0	0
C39	C39	C39	C39	1	1	1	0	0
C40	C40	C40	C40	1	1	1	0	0

C41	C41	C41	C41	1	1	1	0	0
C43	C43	C43	C43	1	1	1	0	0
C44	C44	C44	C44	1	1	1	0	0
C45	C45	C45	C45	1	1	1	0	0
C46	C46	C46	C46	1	1	1	0	0
C47	C47	C47	C47	1	1	1	0	0
C48	C48	C48	C48	1	1	1	0	0
C49	C49	C49	C49	1	1	1	0	0
C50	C50	C50	C50	1	1	1	0	0
C51	C51	C51	C51	1	1	1	0	0
C52	C52	C52	C52	1	1	1	0	0
C53	C53	C53	C53	1	1	1	0	0
C54	C54	C54	C54	1	1	1	0	0
C55	C55	C55	C55	1	1	1	0	0
C56	C56	C56	C56	1	1	1	0	0
C57	C57	C57	C57	1	1	1	0	0
C58	C58	C58	C58	1	1	1	0	0
C60	C60	C60	C60	1	1	1	0	0
C61	C61	C61	C61	1	1	1	0	0
C62	C62	C62	C62	1	1	1	0	0
C63	C63	C63	C63	1	1	1	0	0
C64	C64	C64	C64	1	1	1	0	0
C65	C65	C65	C65	1	1	1	0	0
C66	C66	C66	C66	1	1	1	0	0
C67	C67	C67	C67	1	1	1	0	0
C68	C68	C68	C68	1	1	1	0	0
C69	C69	C69	C69	1	1	1	0	0
C70	C70	C70	C70	1	1	1	0	0
C71	C71	C71	C71	1	1	1	0	0
C72	C72	C72	C72	1	1	1	0	0
C73	C73	C73	C73	1	1	1	0	0
C74	C74	C74	C74	1	1	1	0	0
C75	C75	C75	C75	1	1	1	0	0
C76	C76	C76	C76	1	1	1	0	0
C77	C77	C77	C77	1	1	1	0	0
C78	C78	C78	C78	1	1	1	0	0
C79	C79	C79	C79	1	1	1	0	0
C80	C80	C80	C80	1	1	1	0	0
C81	C81	C81	C81	1	1	1	0	0
C82	C82	C82	C82	1	1	1	0	0
C83	C83	C83	C83	1	1	1	0	0
C84	C84	C84	C84	1	1	1	0	0
C85	C85	C85	C85	1	1	1	0	0
C86	C86	C86	C86	1	1	1	0	0
C88	C88	C88	C88	1	1	1	0	0
C90	C90	C90	C90	1	1	1	0	0
C91	C91	C91	C91	1	1	1	0	0
C92	C92	C92	C92	1	1	1	0	0
C93	C93	C93	C93	1	1	1	0	0
C94	C94	C94	C94	1	1	1	0	0

C95	C95	C95	C95	1	1	1	0	0
C96	C96	C96	C96	1	1	1	0	0
C97	C97	C97	C97	1	1	1	0	0
D00	D00	D00	D00	1	1	1	0	0
D01	D01	D01	D01	1	1	1	0	0
D02	D02	D02	D02	1	1	1	0	0
D03	D03	D03	D03	1	1	1	0	0
D04	D04	D04	D04	1	1	1	0	0
D05	D05	D05	D05	1	1	1	0	0
D06	D06	D06	D06	1	1	1	0	0
D07	D07	D07	D07	1	1	1	0	0
D09	D09	D09	D09	1	1	1	0	0
D37	D37	D37	D37	1	1	1	0	0
D38	D38	D38	D38	1	1	1	0	0
D39	D39	D39	D39	1	1	1	0	0
D40	D40	D40	D40	1	1	1	0	0
D41	D41	D41	D41	1	1	1	0	0
D42	D42	D42	D42	1	1	1	0	0
D43	D43	D43	D43	1	1	1	0	0
D44	D44	D44	D44	1	1	1	0	0
D45	D45	D45	D45	1	1	1	0	0
D46	D46	D46	D46	1	1	1	0	0
D47	D47	D47	D47	1	1	1	0	0
D48	D48	D48	D48	1	1	1	0	0
D50	D50	D50	D50	1	0	0	1	0
D51	D51	D51	D51	1	0	0	1	0
D52	D52	D52	D52	1	0	0	1	0
D53	D53	D53	D53	1	0	0	1	0
D55	D55	D55	D55	1	0	0	1	0
D56	D56	D56	D56	1	0	0	1	0
D57	D57	D57	D57	1	0	0	1	0
D58	D58	D58	D58	1	0	0	1	0
D59.0	D59.0	D59.0	D59.0	1	0	0	1	0
D59.1	D59.1	D59.1	D59.1	1	0	0	1	0
D59.2	D59.2	D59.2	D59.2	1	0	0	1	0
D59.4	D59.4	D59.4	D59.4	1	0	0	1	0
D59.5	D59.5	D59.5	D59.5	1	0	0	1	0
D59.6	D59.6	D59.6	D59.6	1	0	0	1	0
D59.8	D59.8	D59.8	D59.8	1	0	0	1	0
D59.9	D59.9	D59.9	D59.9	1	0	0	1	0
D60.0	D60.0	D60.0	D60.0	1	0	0	1	0
D60.8	D60.8	D60.8	D60.8	1	0	0	1	0
D60.9	D60.9	D60.9	D60.9	1	0	0	1	0
D61	D61	D61	D61	1	0	0	1	0
D63	D63	D63	D63	1	0	0	1	0
D64	D64	D64	D64	1	0	0	1	0
D66	D66	D66	D66	1	0	0	0	0
D67	D67	D67	D67	1	0	0	0	0
D68	D68	D68	D68	1	0	0	0	0
D69	D69	D69	D69	1	0	0	0	0

E01	E01	E01	E01	1	0	0	1	0
E02	E02	E02	E02	1	0	0	1	0
E03	E03	E03	E03	1	0	0	1	0
E04	E04	E04	E04	1	0	0	1	0
E05	E05	E05	E05	1	0	0	1	0
E06.1	E06.1	E06.1	E06.1	1	0	0	1	0
E06.2	E06.2	E06.2	E06.2	1	0	0	1	0
E06.3	E06.3	E06.3	E06.3	1	0	0	1	0
E06.5	E06.5	E06.5	E06.5	1	0	0	1	0
E06.9	E06.9	E06.9	E06.9	1	0	0	1	0
E07	E07	E07	E07	1	0	0	1	0
E10.0	E10.0	E10.0	E10.0	1	1	1	1	0
E10.1	E10.1	E10.1	E10.1	1	1	1	1	0
E10.2	E10.2	E10.2	E10.2	1	1	1	1	0
E10.3	E10.3	E10.3	E10.3	1	1	1	1	0
E10.4	E10.4	E10.4	E10.4	1	1	1	1	0
E10.5	E10.5	E10.5	E10.5	1	1	1	1	0
E10.6	E10.6	E10.6	E10.6	1	1	1	1	0
E10.7	E10.7	E10.7	E10.7	1	1	1	1	0
E10.8	E10.8	E10.8	E10.8	1	1	1	1	0
E10.9	E10.9	E10.9	E10.9	1	1	1	1	0
E11.0	E11.0	E11.0	E11.0	1	1	1	1	0
E11.1	E11.1	E11.1	E11.1	1	1	1	1	0
E11.2	E11.2	E11.2	E11.2	1	1	1	1	0
E11.3	E11.3	E11.3	E11.3	1	1	1	1	0
E11.4	E11.4	E11.4	E11.4	1	1	1	1	0
E11.5	E11.5	E11.5	E11.5	1	1	1	1	0
E11.6	E11.6	E11.6	E11.6	1	1	1	1	0
E11.7	E11.7	E11.7	E11.7	1	1	1	1	0
E11.8	E11.8	E11.8	E11.8	1	1	1	1	0
E11.9	E11.9	E11.9	E11.9	1	1	1	1	0
E12.0	E12.0	E12.0	E12.0	1	1	1	1	0
E12.1	E12.1	E12.1	E12.1	1	1	1	1	0
E12.2	E12.2	E12.2	E12.2	1	1	1	1	0
E12.3	E12.3	E12.3	E12.3	1	1	1	1	0
E12.4	E12.4	E12.4	E12.4	1	1	1	1	0
E12.5	E12.5	E12.5	E12.5	1	1	1	1	0
E12.6	E12.6	E12.6	E12.6	1	1	1	1	0
E12.7	E12.7	E12.7	E12.7	1	1	1	1	0
E12.8	E12.8	E12.8	E12.8	1	1	1	1	0
E12.9	E12.9	E12.9	E12.9	1	1	1	1	0
E13.0	E13.0	E13.0	E13.0	1	1	1	1	0
E13.1	E13.1	E13.1	E13.1	1	1	1	1	0
E13.2	E13.2	E13.2	E13.2	1	1	1	1	0
E13.3	E13.3	E13.3	E13.3	1	1	1	1	0
E13.4	E13.4	E13.4	E13.4	1	1	1	1	0
E13.5	E13.5	E13.5	E13.5	1	1	1	1	0
E13.6	E13.6	E13.6	E13.6	1	1	1	1	0
E13.7	E13.7	E13.7	E13.7	1	1	1	1	0
E13.8	E13.8	E13.8	E13.8	1	1	1	1	0

E13.9	E13.9	E13.9	E13.9	1	1	1	1	0
E14.0	E14.0	E14.0	E14.0	1	1	1	1	0
E14.1	E14.1	E14.1	E14.1	1	1	1	1	0
E14.2	E14.2	E14.2	E14.2	1	1	1	1	0
E14.3	E14.3	E14.3	E14.3	1	1	1	1	0
E14.4	E14.4	E14.4	E14.4	1	1	1	1	0
E14.5	E14.5	E14.5	E14.5	1	1	1	1	0
E14.6	E14.6	E14.6	E14.6	1	1	1	1	0
E14.7	E14.7	E14.7	E14.7	1	1	1	1	0
E14.8	E14.8	E14.8	E14.8	1	1	1	1	0
E14.9	E14.9	E14.9	E14.9	1	1	1	1	0
E16.0	E16.0	E16.0	E16.0	1	1	0	1	0
E16.1	E16.1	E16.1	E16.1	0	1	0	1	0
E16.2	E16.2	E16.2	E16.2	0	1	0	1	0
E16.3	E16.3	E16.3	E16.3	0	1	0	1	0
E16.4	E16.4	E16.4	E16.4	0	1	0	1	0
E16.5	E16.5	E16.5	E16.5	0	1	0	1	0
E16.6	E16.6	E16.6	E16.6	0	1	0	1	0
E16.7	E16.7	E16.7	E16.7	0	1	0	1	0
E16.8	E16.8	E16.8	E16.8	0	1	0	1	0
E16.9	E16.9	E16.9	E16.9	0	1	0	1	0
E66	E66	E66	E66	1	0	0	0	0
E73	E73	E73	E73	1	0	0	0	0
E78	E78	E78	E78	1	0	0	0	0
E79	E79	E79	E79	1	0	0	0	0
F00	F00	F00	F00	0	0	0	0	1
F01	F01	F01	F01	0	0	0	0	1
F02	F02	F02	F02	0	0	0	0	1
F03	F03	F03	F03	0	0	0	0	1
F05.1	F05.1	F05.1	F05.1	0	0	0	0	1
F10	F10	F10	F10	1	0	0	0	0
F13	F13	F13	F13	1	0	0	0	0
F17	F17	F17	F17	1	0	0	0	0
F20	F20	F20	F20	0	0	0	1	0
F21	F21	F21	F21	0	0	0	1	0
F22	F22	F22	F22	0	0	0	1	0
F23	F23	F23	F23	0	0	0	1	0
F24	F24	F24	F24	0	0	0	1	0
F25	F25	F25	F25	0	0	0	1	0
F28	F28	F28	F28	0	0	0	1	0
F29	F29	F29	F29	0	0	0	1	0
F30	F30	F30	F30	0	0	0	1	0
F31	F31	F31	F31	0	0	0	1	0
F32	F32	F32	F32	1	1	0	1	0
F33	F33	F33	F33	1	1	0	1	0
F34	F34	F34	F34	0	0	0	1	0
F38	F38	F38	F38	0	0	0	1	0
F39	F39	F39	F39	0	0	0	1	0
F40	F40	F40	F40	1	0	0	1	0
F41	F41	F41	F41	1	0	0	1	0

F45	F45	F45	F45	1	0	0	0	0
F51	F51	F51	F51	1	0	0	0	0
F52	F52	F52	F52	1	0	0	0	0
G20	G20	G20	G20	1	0	0	1	0
G21	G21	G21	G21	1	0	0	1	0
G22	G22	G22	G22	1	0	0	1	0
G30	G30	G30	G30	0	0	0	0	1
G31	G31	G31	G31	0	0	0	0	1
G35	G35	G35	G35	0	0	0	1	0
G40	G40	G40	G40	1	0	0	1	0
G41	G41	G41	G41	1	0	0	1	0
G43	G43	G43	G43	1	0	0	1	0
G44	G44	G44	G44	1	0	0	1	0
G45	G45	G45	G45	1	1	1	1	0
G47	G47	G47	G47	1	0	0	0	0
G50	G50	G50	G50	1	0	0	0	0
G51	G51	G51	G51	1	0	0	0	0
G52	G52	G52	G52	1	0	0	0	0
G53	G53	G53	G53	1	0	0	0	0
G54	G54	G54	G54	1	0	0	0	0
G55	G55	G55	G55	1	0	0	0	0
G56	G56	G56	G56	1	0	0	0	0
G57	G57	G57	G57	1	0	0	0	0
G58	G58	G58	G58	1	0	0	0	0
G59	G59	G59	G59	1	0	0	0	0
G60	G60	G60	G60	1	0	0	0	0
G61	G61	G61	G61	1	0	0	0	0
G62	G62	G62	G62	1	0	0	0	0
G63	G63	G63	G63	1	0	0	0	0
G64	G64	G64	G64	1	0	0	0	0
G80.0	G80.0	G80.0	G80.0	0	0	1	1	0
G80.1	G80.1	G80.1	G80.1	0	0	1	1	0
G80.2	G80.2	G80.2	G80.2	0	0	1	1	0
G81	G81	G81	G81	0	0	1	1	0
G82	G82	G82	G82	0	0	1	1	0
G83.0	G83.0	G83.0	G83.0	0	0	1	1	0
H01.1	H01.1	H01.1	H01.1	1	0	0	0	0
H17	H17	H17	H17	1	1	0	1	0
H18	H18	H18	H18	1	1	0	1	0
H25	H25	H25	H25	1	1	0	1	0
H26	H26	H26	H26	1	1	0	1	0
H27	H27	H27	H27	1	1	0	1	0
H28	H28	H28	H28	1	1	0	1	0
H31	H31	H31	H31	1	1	0	1	0
H33	H33	H33	H33	1	0	0	1	0
H34.1	H34.1	H34.1	H34.1	1	1	0	1	0
H34.2	H34.2	H34.2	H34.2	1	1	0	1	0
H34.8	H34.8	H34.8	H34.8	1	1	0	1	0
H34.9	H34.9	H34.9	H34.9	1	1	0	1	0
H35	H35	H35	H35	1	1	0	1	0

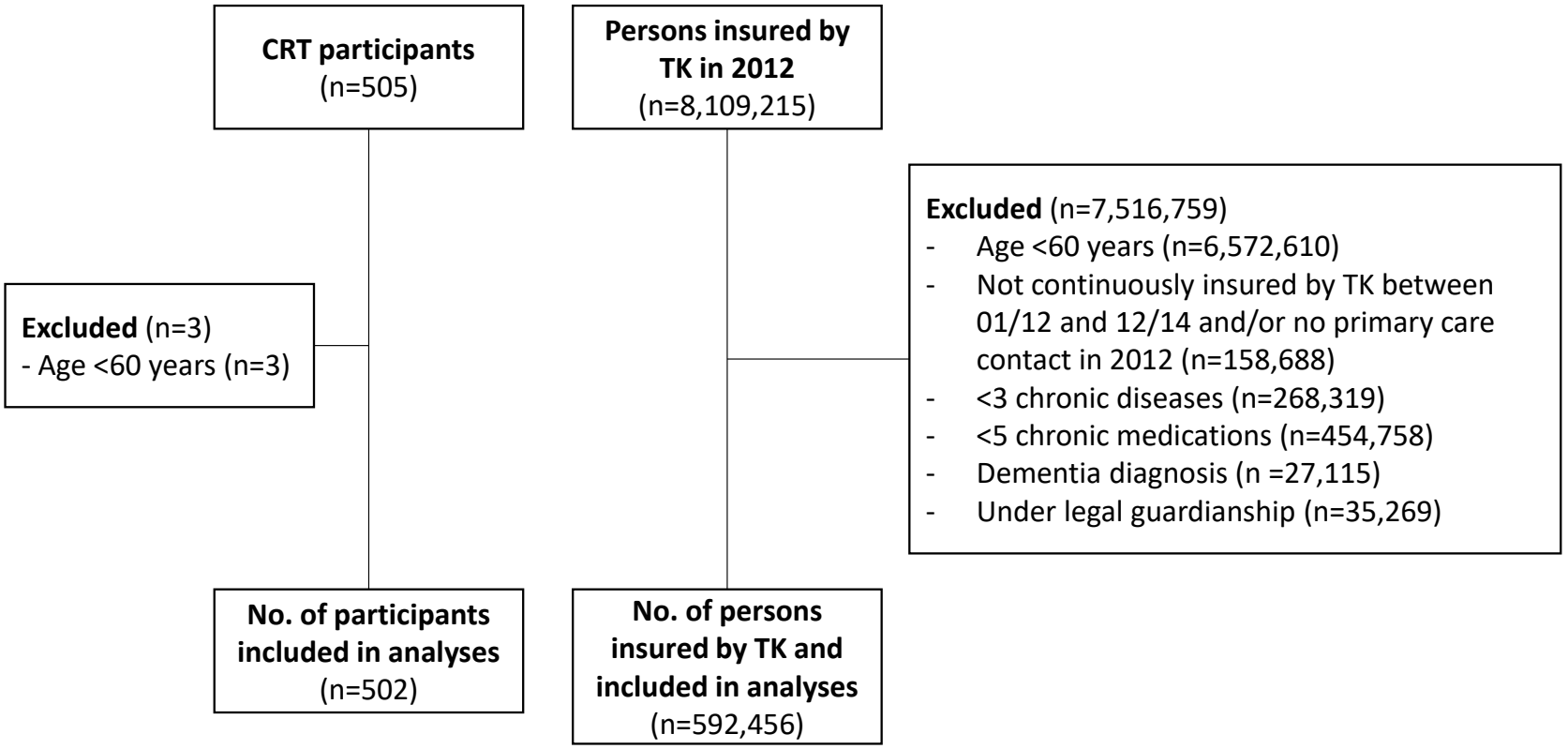
H36	H36	H36	H36	1	1	0	1	0
H40	H40	H40	H40	1	1	0	1	0
H43	H43	H43	H43	1	1	0	1	0
H47	H47	H47	H47	1	1	0	1	0
H54	H54	H54	H54	1	1	0	1	0
H81	H81	H81	H81	1	0	0	0	0
H82	H82	H82	H82	1	0	0	0	0
H90	H90	H90	H90	1	1	0	0	0
H91.0	H91.0	H91.0	H91.0	1	1	0	0	0
H91.1	H91.1	H91.1	H91.1	1	1	0	0	0
H91.3	H91.3	H91.3	H91.3	1	1	0	0	0
H91.8	H91.8	H91.8	H91.8	1	1	0	0	0
H91.9	H91.9	H91.9	H91.9	1	1	0	0	0
I10	I10	I10	I10	1	1	0	1	0
I11	I11	I11	I11	1	1	0	1	0
I12	I12	I12	I12	1	1	0	1	0
I13	I13	I13	I13	1	1	0	1	0
I15	I15	I15	I15	1	1	0	1	0
I20	I20	I20	I20	1	1	0	1	0
I21	I21	I21	I21	1	1	1	1	0
I22	I22	I22	I22	1	0	0	1	0
I23	I23	I23	I23	1	0	0	1	0
I24	I24	I24	I24	1	0	0	1	0
I25	I25	I25	I25	1	1	0	1	0
I26	I26	I26	I26	1	0	0	0	0
I34	I34	I34	I34	1	0	0	0	0
I35	I35	I35	I35	1	0	0	0	0
I36	I36	I36	I36	1	0	0	0	0
I37	I37	I37	I37	1	0	0	0	0
I44	I44	I44	I44	1	0	0	1	0
I45	I45	I45	I45	1	0	0	1	0
I46.0	I46.0	I46.0	I46.0	1	0	0	1	0
I46.9	I46.9	I46.9	I46.9	1	0	0	1	0
I47	I47	I47	I47	1	0	0	1	0
I48	I48	I48	I48	1	0	0	1	0
I49.1	I49.1	I49.1	I49.1	1	0	0	1	0
I49.2	I49.2	I49.2	I49.2	1	0	0	1	0
I49.3	I49.3	I49.3	I49.3	1	0	0	1	0
I49.4	I49.4	I49.4	I49.4	1	0	0	1	0
I49.5	I49.5	I49.5	I49.5	1	0	0	1	0
I49.8	I49.8	I49.8	I49.8	1	0	0	1	0
I49.9	I49.9	I49.9	I49.9	1	0	0	1	0
I50	I50	I50	I50	1	1	1	1	0
I60	I60	I60	I60	1	1	1	1	0
I61	I61	I61	I61	1	1	1	1	0
I62	I62	I62	I62	1	1	1	1	0
I63	I63	I63	I63	1	1	1	1	0
I64	I64	I64	I64	1	1	1	1	0
I65	I65	I65	I65	1	1	1	1	0
I66	I66	I66	I66	1	1	1	1	0

I67.0	I67.0	I67.0	I67.0	0	1	0	0	0
I67.2	I67.2	I67.2	I67.2	1	1	1	1	0
I67.4	I67.4	I67.4	I67.4	1	1	0	1	0
I67.8	I67.8	I67.8	I67.8	0	1	0	0	0
I67.9	I67.9	I67.9	I67.9	0	1	0	0	0
I69	I69	I69	I69	1	1	1	1	0
I70	I70	I70	I70	1	1	1	1	0
I71	I71	I71	I71	1	1	1	1	0
I72	I72	I72	I72	1	1	1	1	0
I73.9	I73.9	I73.9	I73.9	1	1	1	1	0
I80	I80	I80	I80	1	0	0	0	0
I83	I83	I83	I83	1	0	0	0	0
I87.0	I87.0	I87.0	I87.0	1	0	0	0	0
I87.2	I87.2	I87.2	I87.2	1	0	0	0	0
I95	I95	I95	I95	1	0	0	0	0
J30	J30	J30	J30	1	0	0	0	0
J40	J40	J40	J40	1	1	1	0	0
J41	J41	J41	J41	1	1	1	1	0
J42	J42	J42	J42	1	1	1	1	0
J43	J43	J43	J43	1	1	1	1	0
J44	J44	J44	J44	1	1	1	1	0
J45	J45	J45	J45	1	1	1	1	0
J47	J47	J47	J47	1	1	1	1	0
K21	K21	K21	K21	1	0	0	1	0
K25.4	K25.4	K25.4	K25.4	1	0	1	1	0
K25.5	K25.5	K25.5	K25.5	1	0	1	1	0
K25.6	K25.6	K25.6	K25.6	1	0	1	1	0
K25.7	K25.7	K25.7	K25.7	1	0	1	1	0
K25.9	K25.9	K25.9	K25.9	1	0	1	1	0
K26.4	K26.4	K26.4	K26.4	1	0	1	1	0
K26.5	K26.5	K26.5	K26.5	1	0	1	1	0
K26.6	K26.6	K26.6	K26.6	1	0	1	1	0
K26.7	K26.7	K26.7	K26.7	1	0	1	1	0
K26.9	K26.9	K26.9	K26.9	1	0	1	1	0
K27.4	K27.4	K27.4	K27.4	1	0	1	1	0
K27.5	K27.5	K27.5	K27.5	1	0	1	1	0
K27.6	K27.6	K27.6	K27.6	1	0	1	1	0
K27.7	K27.7	K27.7	K27.7	1	0	1	1	0
K27.9	K27.9	K27.9	K27.9	1	0	1	1	0
K28.4	K28.4	K28.4	K28.4	1	0	1	1	0
K28.5	K28.5	K28.5	K28.5	1	0	1	1	0
K28.6	K28.6	K28.6	K28.6	1	0	1	1	0
K28.7	K28.7	K28.7	K28.7	1	0	1	1	0
K28.9	K28.9	K28.9	K28.9	1	0	1	1	0
K29.2	K29.2	K29.2	K29.2	1	0	1	1	0
K29.3	K29.3	K29.3	K29.3	1	0	1	1	0
K29.4	K29.4	K29.4	K29.4	1	0	1	1	0
K29.5	K29.5	K29.5	K29.5	1	0	1	1	0
K29.6	K29.6	K29.6	K29.6	1	0	1	1	0
K29.7	K29.7	K29.7	K29.7	1	0	1	1	0

K29.8	K29.8	K29.8	K29.8	1	0	1	1	0
K29.9	K29.9	K29.9	K29.9	1	0	1	1	0
K52.2	K52.2	K52.2	K52.2	1	0	0	0	0
K57	K57	K57	K57	1	0	0	0	0
K58	K58	K58	K58	1	0	0	0	0
K64	K64	I84	I84	1	0	0	0	0
K70.0	K70.0	K70.0	K70.0	1	0	1	1	0
K70.1	K70.1	K70.1	K70.1	1	0	1	1	0
K70.2	K70.2	K70.2	K70.2	1	0	0	1	0
K70.3	K70.3	K70.3	K70.3	1	0	0	1	0
K70.4	K70.4	K70.4	K70.4	1	0	1	1	0
K70.5	K70.5	K70.5	K70.5	1	0	0	1	0
K70.6	K70.6	K70.6	K70.6	1	0	0	1	0
K70.7	K70.7	K70.7	K70.7	1	0	0	1	0
K70.8	K70.8	K70.8	K70.8	1	0	0	1	0
K70.9	K70.9	K70.9	K70.9	1	0	1	1	0
K71.0	K71.0	K71.0	K71.0	0	0	1	0	0
K71.1	K71.1	K71.1	K71.1	0	0	1	0	0
K71.2	K71.2	K71.2	K71.2	0	0	1	0	0
K71.3	K71.3	K71.3	K71.3	1	0	0	1	0
K71.4	K71.4	K71.4	K71.4	1	0	0	1	0
K71.5	K71.5	K71.5	K71.5	1	0	0	1	0
K71.6	K71.6	K71.6	K71.6	0	0	1	0	0
K71.7	K71.7	K71.7	K71.7	1	0	0	1	0
K71.8	K71.8	K71.8	K71.8	0	0	1	0	0
K72.0	K72.0	K72.0	K72.0	0	0	1	0	0
K72.1	K72.1	K72.1	K72.1	1	0	1	1	0
K72.2	K72.2	K72.2	K72.2	0	0	1	0	0
K72.3	K72.3	K72.3	K72.3	0	0	1	0	0
K72.4	K72.4	K72.4	K72.4	0	0	1	0	0
K72.5	K72.5	K72.5	K72.5	0	0	1	0	0
K72.6	K72.6	K72.6	K72.6	0	0	1	0	0
K72.7	K72.7	K72.7	K72.7	1	0	1	1	0
K72.8	K72.8	K72.8	K72.8	0	0	1	0	0
K72.9	K72.9	K72.9	K72.9	1	0	1	1	0
K73	K73	K73	K73	1	0	1	1	0
K74	K74	K74	K74	1	0	1	1	0
K75.0	K75.0	K75.0	K75.0	0	0	1	0	0
K75.1	K75.1	K75.1	K75.1	0	0	1	0	0
K75.2	K75.2	K75.2	K75.2	0	0	1	0	0
K75.3	K75.3	K75.3	K75.3	0	0	1	0	0
K75.4	K75.4	K75.4	K75.4	0	0	1	0	0
K75.8	K75.8	K75.8	K75.8	0	0	1	0	0
K75.9	K75.9	K75.9	K75.9	0	0	1	0	0
K76.0	K76.0	K76.0	K76.0	0	0	1	1	0
K76.1	K76.1	K76.1	K76.1	0	0	1	1	0
K76.2	K76.2	K76.2	K76.2	1	0	0	1	0
K76.3	K76.3	K76.3	K76.3	1	0	0	1	0
K76.4	K76.4	K76.4	K76.4	1	0	0	1	0
K76.5	K76.5	K76.5	K76.5	1	0	0	1	0

K76.6	K76.6	K76.6	K76.6	1	0	0	1	0
K76.7	K76.7	K76.7	K76.7	1	0	0	1	0
K76.8	K76.8	K76.8	K76.8	1	0	0	1	0
K76.9	K76.9	K76.9	K76.9	1	0	0	1	0
K77	K77	K77	K77	0	0	1	0	0
K80	K80	K80	K80	1	0	0	1	0
K81.1	K81.1	K81.1	K81.1	1	0	0	1	0
K90.0	K90.0	K90.0	K90.0	1	0	0	0	0
L23	L23	L23	L23	1	0	0	0	0
L27.2	L27.2	L27.2	L27.2	1	0	0	0	0
L40	L40	L40	L40	1	0	0	0	0
L56.4	L56.4	L56.4	L56.4	1	0	0	0	0
M05	M05	M05	M05	1	1	0	1	0
M06	M06	M06	M06	1	1	0	1	0
M07	M07	M07	M07	1	1	0	1	0
M10	M10	M10	M10	1	0	0	0	0
M15	M15	M15	M15	1	1	0	1	0
M16	M16	M16	M16	1	1	0	1	0
M17	M17	M17	M17	1	1	0	1	0
M18	M18	M18	M18	1	1	0	1	0
M19	M19	M19	M19	1	1	0	1	0
M30	M30	M30	M30	1	0	1	1	0
M31	M31	M31	M31	1	0	1	1	0
M32	M32	M32	M32	1	0	1	1	0
M33	M33	M33	M33	1	0	1	1	0
M34	M34	M34	M34	1	0	1	1	0
M35	M35	M35	M35	1	0	1	1	0
M36	M36	M36	M36	1	0	1	1	0
M40	M40	M40	M40	1	0	0	1	0
M41	M41	M41	M41	1	0	0	1	0
M42	M42	M42	M42	1	0	0	1	0
M43	M43	M43	M43	1	0	0	1	0
M45	M45	M45	M45	1	0	0	1	0
M47	M47	M47	M47	1	0	0	1	0
M48.0	M48.0	M48.0	M48.0	1	0	0	1	0
M48.1	M48.1	M48.1	M48.1	1	0	0	1	0
M48.2	M48.2	M48.2	M48.2	1	0	0	1	0
M48.5	M48.5	M48.5	M48.5	1	0	0	1	0
M48.8	M48.8	M48.8	M48.8	1	0	0	1	0
M48.9	M48.9	M48.9	M48.9	1	0	0	1	0
M50	M50	M50	M50	1	0	0	1	0
M51	M51	M51	M51	1	0	0	1	0
M53	M53	M53	M53	1	0	0	1	0
M54	M54	M54	M54	1	0	0	1	0
M79.0	M79.0	M79.0	M79.0	1	1	0	0	0
M80	M80	M80	M80	1	1	0	0	0
M81	M81	M81	M81	1	1	0	0	0
M82	M82	M82	M82	1	1	0	0	0
N00	N00	N00	N00	1	1	1	0	0
N01	N01	N01	N01	1	1	1	0	0

N02	N02	N02	N02	1	1	1	0	0
N03	N03	N03	N03	1	1	1	0	0
N04	N04	N04	N04	1	1	1	0	0
N05	N05	N05	N05	1	1	1	0	0
N06	N06	N06	N06	1	1	1	0	0
N07	N07	N07	N07	1	1	1	0	0
N08	N08	N08	N08	1	1	1	0	0
N18	N18	N18	N18	1	1	1	0	0
N19	N19	N19	N19	1	1	1	0	0
N20	N20	N20	N20	1	0	0	0	0
N25	N25	N25	N25	1	1	1	0	0
N26	N26	N26	N26	1	1	1	0	0
N27	N27	N27	N27	1	1	1	0	0
N28	N28	N28	N28	1	1	1	0	0
N29	N29	N29	N29	1	1	1	0	0
N39.3	N39.3	N39.3	N39.3	1	0	0	0	0
N39.4	N39.4	N39.4	N39.4	1	0	0	0	0
N40	N40	N40	N40	1	0	0	0	0
N48.4	N48.4	N48.4	N48.4	1	0	0	0	0
N81	N81	N81	N81	1	0	0	0	0
N84	N84	N84	N84	1	0	0	0	0
N85	N85	N85	N85	1	0	0	0	0
N86	N86	N86	N86	1	0	0	0	0
N87	N87	N87	N87	1	0	0	0	0
N88	N88	N88	N88	1	0	0	0	0
N89	N89	N89	N89	1	0	0	0	0
N90	N90	N90	N90	1	0	0	0	0
N93	N93	N93	N93	1	0	0	0	0
N95	N95	N95	N95	1	0	0	0	0
R00	R00	R00	R00	1	0	0	1	0
R03.1	R03.1	R03.1	R03.1	1	0	0	0	0
R32	R32	R32	R32	1	0	0	0	0
R42	R42	R42	R42	1	0	0	0	0
R51	R51	R51	R51	1	0	0	1	0
R54	R54	R54	R54	0	0	0	0	1
T78.1	T78.1	T78.1	T78.1	1	0	0	0	0
T78.4	T78.4	T78.4	T78.4	1	0	0	0	0
T88.7	T88.7	T88.7	T88.7	1	0	0	0	0
U85	U85	U85	U85	0	0	1	0	0


CRT participants
(n=505)
Persons insured by TK in 2012
(n=8,109,215)
Excluded (n=3)
- Age <60 years (n=3)
Excluded (n=7,516,759)
- Age <60 years (n=6,572,610)
- Not continuously insured by TK between 01/12 and 12/14 and/or no primary care contact in 2012 (n=158,688)
- <3 chronic diseases (n=268,319)
- <5 chronic medications (n=454,758)
- Dementia diagnosis (n =27,115)
- Under legal guardianship (n=35,269)
No. of participants included in analyses
(n=502)
No. of persons insured by TK and included in analyses
(n=592,456)

Additional file 5: Univariate Analyses: Association between predictor variables and combined outcome in claims data

	combined outcome reached after 6 months				**combined outcome reached after 9 months**				**combined outcome reached after 24 months**			
	Yes (n = 192357)	**No (n = 400099)**	**Total (n = 592456)**		**Yes (n = 244190)**	**No (n = 348266)**	**Total (n = 592456)**		**Yes (n = 387951)**	**No (n = 204505)**	**Total (n = 592456)**	
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**p-value**
Age	72.2 (7.3)	70.8 (6.9)	71.3 (7.1)	<0.001	72.1 (7.3)	70.7 (6.9)	71.3 (7.1)	<0.001	71.8 (7.2)	70.2 (6.7)	71.3 (7.1)	<0.001
Disease count	10.5 (4.0)	9.3 (3.6)	9.7 (3.8)	<0.001	10.4 (3.9)	9.2 (3.5)	9.7 (3.8)	<0.001	10.2 (3.9)	8.8 (3.4)	9.7 (3.8)	<0.001
CCI	3.4 (2.8)	2.8 (2.4)	3.0 (2.5)	<0.001	3.4 (2.7)	2.8 (2.4)	3.0 (2.5)	<0.001	3.2 (2.7)	2.6 (2.3)	3.0 (2.5)	<0.001
No. of specific chronic diseases (Diederichs)	4.7 (2.1)	4.1 (1.9)	4.3 (2.0)	<0.001	4.7 (2.1)	4.1 (1.9)	4.3 (2.0)	<0.001	4.6 (2.0)	3.9 (1.8)	4.3 (2.0)	<0.001
No. of PIM (EU-PIM)	1.3 (1.2)	1.1 (1.1)	1.1 (1.2)	<0.001	1.3 (1.2)	1.1 (1.1)	1.1 (1.2)	<0.001	1.2 (1.2)	1.0 (1.0)	1.1 (1.1)	<0.001
ADS	1.2 (1.6)	0.9 (1.4)	1.0 (1.5)	<0.001	1.2 (1.6)	0.9 (1.3)	1.0 (1.5)	<0.001	1.1 (1.5)	0.8 (1.3)	1.0 (1.5)	<0.001
DBI	0.9 (1.2)	0.7 (1.0)	0.8 (1.0)	<0.001	0.9 (1.1)	0.7 (0.9)	0.8 (1.0)	<0.001	0.8 (1.1)	0.6 (0.9)	0.8 (1.0)	<0.001
Number of involved physicians	11.0 (5.6)	9.4 (5.0)	10.0 (5.3)	<0.001	10.9 (5.6)	9.3 (4.9)	10.0 (5.3)	<0.001	10.6 (5.4)	8.8 (4.7)	10.0 (5.3)	<0.001

Abbreviations: ACh burden – Anticholinergic drug burden, ADS – Anticholinergic Drug Scale, CCI - Charlson Comorbidity Index, DBI – Drug Burden Index, PIM – Potentially Inappropriate Medication.

		combined outcome reached after 6 months				combined outcome reached after 9 months				combined outcome reached after 24 months			
		Yes (n = 192357)	**No (n = 400099)**	**Total (n = 592456)**		**Yes (n = 244190)**	**No (n = 348266)**	**Total (n = 592456)**		**Yes (n = 387951)**	**No (n = 204505)**	**Total (n = 592456)**	
		n (%)	**n (%)**	**n (%)**	**p-value**	**n (%)**	**n (%)**	**n (%)**	**p-value**	**n (%)**	**n (%)**	**n (%)**	**p-value**
Sex	**Female**	90924 (47.3%)	182079 (45.5%)	273003 (46.1%)		114859 (47.0%)	158144 (45.4%)	273003 (46.1%)		180222 (46.5%)	92781 (45.4%)	273003 (46.1%)	
	Male	101433 (52.7%)	218020 (54.5%)	319453 (53.9%)	<0.001	129331 (53.0%)	190122 (54.6%)	319453 (53.9%)	<0.001	207729 (53.5%)	111724 (54.6%)	319453 (53.9%)	<0.001
Previous hospitalisation	**No**	107627 (56%)	289845 (72.4%)	397472 (67.1%)		141326 (57.9%)	256146 (73.5%)	397472 (67.1%)		240676 (62%)	156796 (76.7%)	397472 (67.1%)	
	yes	84730 (44%)	110254 (27.6%)	194984 (32.9%)	<0.001	102864 (42.1%)	92120 (26.5%)	194984 (32.9%)	<0.001	147275 (38%)	47709 (23.3%)	194984 (32.9%)	<0.001
Previous falls	**No**	103734 (53.9%)	325335 (81.3%)	429069 (72.4%)		142477 (58.3%)	286592 (82.3%)	429069 (72.4%)		255691 (65.9%)	173378 (84.8%)	429069 (72.4%)	
	yes	88623 (46.1%)	74764 (18.7%)	163387 (27.6%)	<0.001	101713 (41.7%)	61674 (17.7%)	163387 (27.6%)	<0.001	132260 (34.1%)	31127 (15.2%)	163387 (27.6%)	<0.001

Additional file 6: Univariate analyses

Table A6.1: Association between predictor variables and EQ5D-3L (Pearson Correlation)

Predictor variable	**EQ5D-3L (T1)**
Core predictors	
▪ Age	-0.09
▪ Disease count	-0.24
▪ Charlson Comorbidity Index (CCI)	-0.07
▪ No. of specific chronic diseases (Diederichs)	-0.19
▪ No. of drugs	-0.26
▪ No. of PIM (EU-PIM)	-0.18
▪ ACh burden (ADS)	-0.16
▪ Mod. Drug Burden Index	-0.20
▪ No. of involved physicians	-0.06
Additional predictors	
▪ No. of persons living in household	0.04
▪ CASMIN	0.09
▪ Alcohol intake (AUDIT C)	0.13
▪ Body Mass Index	-0.15
▪ MAI	-0.24
▪ CIRS sum score	-0.27
▪ CIRS, no. of organ systems	-0.22
▪ HRQoL-CI, mental	-0.24
▪ HRQoL-CI, physical	-0.20
▪ Depressive Symptoms (GDS)	-0.52

▪ EQ5D-3L (Baseline)	0.68

Abbreviations: ACh burden – Anticholinergic drug burden, ADS – Anticholinergic Drug Scale, AUDIT - Alcohol Use Disorders Identification Test (WHO), CASMIN - Comparative Analysis of Social Mobility in Industrial Nations, CCI - Charlson Comorbidity Index, CIRS – Cumulative Illness Rating Scale, GDS – Geriatric Depression Scale, HRQoL – Health-Related Quality of Life, HRQoL-CI – Health-Related Quality of Life Comorbidity Index, MAI – Medication Appropriateness Index, PIM – Potentially Inappropriate Medication.

Table A6.2: Association between predictor variables and EQ5D-3L (T-Test)

Predictor variable	**Mean (SD)**	**Mean (SD)**	**p-value**
Core predictors			
▪ Sex (female / male)	67.7 (25.77)	78.5 (22.97)	<0.001
▪ Previous hospitalisation (yes / no)	71.2 (26.76)	73.3 (24.67)	0.531
▪ Previous falls (yes/no)	65.9 (25.28)	74.3 (24.76)	0.011
Additional predictors			
▪ Smoker (yes / no)	74.1 (25.81)	73.1 (25.07)	0.807

Abbreviations: SD – Standard Deviation