Appendix ii. Predictors used in univariate testing for the development of the algorithm, grouped by category, and reasons of exclusion for testing in the multivariate models

Predictor	Description	Univariate	P-value	Reason of exclusion			
		analysis	(algorithm				
			score)				
	Medication distribution						
Collects his/her	Medication is collected	T-test	0.0020	-			
own medication†	by the patient						
	him/herself at the						
	pharmacy.						
Sachet packed	Receives sachet packed	T-test	0.0045	-			
medication‡	medication						
	M	lobility	ı				
Diminished	Has no to seriously	T-test	<0.0001	-			
mobility†	impaired mobility						
Diminished	Diminished mobility in 5	Oneway	<0.0001	No difference in			
mobility	categories from not to	anova		complexity between			
(categorised)	seriously impaired			different categories			
	mobility						
	Bloo	d pressure					
Systolic blood	Systolic blood pressure	Linear	0.0053	-			
pressure†		regression					
Low systolic blood	Systolic blood pressure	T-test	0.0107	-			
pressure‡	below 120 mmHg when						
	under 80 years old and						
	below 140 mmHg when						
	80 years or older						
Diastolic blood	Diastolic blood pressure	Linear	0.2881	P-value >0.25			
pressure		regression					
High systolic blood	Systolic blood pressure	T-test	0.1077	Patients with high			
pressure	over 140 mmHg when			blood pressure had a			
	<80 years or Systolic			lower algorithm score			
	blood pressure over 160						
	mmHg when ≥80 years						

blood pressure       systolic blood pressure         High or low blood pressure + at least pressure + at least antihypertensive medications       systolic pressure in antihypertensive medications       0.7394       P-value >0.25         Low systolic blood pressure + at least pressure in combination antihypertensive medications       T-test pressure in combination antihypertensive medications       0.2841       P-value >0.25         Medications       Medication         Number of medications medications with a medications medications with a medications medications medications with a medication with a
pressure + at least 3 antihypertensive medications antihypertensive medications  Low systolic blood pressure in combination with ≥3 antihypertensive medications  T-test 0.2841 P-value >0.25 pressure + at least pressure in combination 3 antihypertensive with ≥3 antihypertensive medications  Medication  Number of A count of all medications with a regression
antihypertensive medications  Low systolic blood pressure + at least antihypertensive medications  T-test o.2841 P-value >0.25  pressure + at least pressure in combination antihypertensive medications  Medication  Number of Medications A count of all medications with a regression  medications  Combination with ≥3  antihypertensive medication  Medication  Linear <0.0001 -
medications  antihypertensive medications  Low systolic blood pressure + at least pressure in combination 3 antihypertensive medications  medications  Medication  Number of medications A count of all medications with a regression  medications  A medications with a regression  medications  T-test o.2841 prevalue >0.25  P-value >0.25  Medication combination antihypertensive medications  Linear co.0001 co.0001 co.0001
Low systolic blood   Low systolic blood   T-test   0.2841   P-value >0.25
Low systolic blood pressure + at least 3 antihypertensive medications       Low systolic blood pressure in combination with ≥3 antihypertensive medications       T-test       0.2841       P-value >0.25         Medications       Medication         Number of medications+       A count of all medications with a       Linear regression       <0.0001
pressure + at least 3 antihypertensive medications with ≥3 antihypertensive medications Medication  Number of A count of all Linear <0.0001 - medications with a regression - medication - medications with a regression - medications - medica
3 antihypertensive medications with ≥3 antihypertensive medications  Medication  Number of A count of all medications with a regression
medications  medications  Medication  Number of A count of all Linear <0.0001 - medications with a regression
Medications  Medication  Number of A count of all Linear <0.0001 - medications with a regression
Number of A count of all Linear <0.0001 - medications with a regression
Number of A count of all Linear <0.0001 - medications + medications with a regression
medications† medications with a regression
distinct ATC-code
Number of A count of Linear 0.3123 P-value >0.25
antihypertensive regression
medications medications
HARM medication A count of medications Linear 0.0816 -
(Leendertse et al., responsible for many regression
2008)‡ medication related
hospitalisations
according to the HARM
study, excluding
antibiotics
HARM+ narrow A count of medications Linear 0.0062 -
therapeutic index + responsible for many regression
high risk medication related
medication hospitalisations
(Barnett et al., according to the HARM
2011; Blix et al., study (excluding
2010; Leendertse antibiotics) plus other
et al., 2008) medications considered

2014)‡ medication   Linear   Cognitive Burden Scale   Cognitive Burden Scale   Linear   Cognitive Burden Scale   Cognitive Burden	Saedder et al.,	to be high risk			
score (Campbell et al., 2009)‡  anticholinergic load of the medications according to the Anticholinergic Cognitive Burden Scale  Number of A count of the medications that need requiring to be adjusted in the adjustment according to eGFR  MRCI (George et al., 2004)‡  Index (MRCI)  Number of units allow presence of low eGFR  With a count of all units (pills, inhalations, injections, etc.) to be used per day  Estimated Glomerular Filtration Rate regression ml/min/1,73m²  Eow eGFR in 3 categories: 30, 30-59 and >59 ml/min/1,73m²  Low eGFR in combination with a relevant combination with a medication allow in eGFR  Estimated Glomerular Filtration Rate regression ml/min/1,73m² in relevant combination with a medication allow in eGFR  Estimated Glomerular Filtration Rate regression ml/min/1,73m² in relevant combination with a medication allow in eGFR  Estimated Glomerular Filtration Rate regression ml/min/1,73m² in relevant combination with a medication allow in eGFR  Estimated Glomerular Filtration Rate regression shows anova ml/min/1,73m² in relevant combination with at medication allow in eGFR  Estimated Glomerular Filtration Rate regression shows anova ml/min/1,73m² in relevant combination with at medication allow in eGFR  Estimated Glomerular Filtration Rate regression shows anova ml/min/1,73m² in relevant combination with at medication that needs to be adjusted for eGFR	2014)‡	medication			
al., 2009)‡ the medications according to the Anticholinergic Cognitive Burden Scale  Number of A count of the medications medications that need requiring to be adjusted in the adjustment according to eGFR  MRCI (George et al., 2004)‡ (pills, inhalations, injections, etc.) to be used per day  Estimated Glomerular Filtration Rate regression injections act goals and ya ml/min/1,73m² (pills, inhalations) and	ACB anticholinergic	A score of the	Linear	0.0228	-
According to the Anticholinergic Cognitive Burden Scale	score (Campbell et	anticholinergic load of	regression		
Anticholinergic Cognitive Burden Scale  Number of Medications medications that need requiring adjustment according to eGFR  MRCI (George et al., 2004)‡ (pills, inhalations, injections, etc.) to be used per day  Kidner eGFR categorised eGFR in a categories:	al., 2009)‡	the medications			
Cognitive Burden Scale		according to the			
Number of medications medications that need requiring adjustment according to eGFR  MRCI (George et al., 2004)‡ regimen complexity index (MRCI)  Number of units a day‡  Estimated Glomerular Filtration Rate regression  eGFR categorised eGFR in 3 categories: <30, 30-59 and >59 ml/min/1,73m²  Low eGFR in combination with at relevant medication‡ least 1 medication that needs to be adjusted for the medication that needs to be adjusted for medications to be adjusted for medications adjusted for eGFR  MRCI (George et Adjusted Medication Linear regression index (MRCI)  Linear regression  Co.0001  - C.00001		Anticholinergic			
medications medications that need to be adjusted in the adjustment presence of low eGFR according to eGFR  MRCI (George et al., 2004)‡ regimen complexity index (MRCI)  Number of units a day‡ (pills, inhalations, injections, etc.) to be used per day  EStimated Glomerular Filtration Rate regression wil/min/1,73m²  EGFR categorised eGFR in 3 categories: <30, 30-59 and >59 ml/min/1,73m²  Low eGFR in combination with a relevant combination with a medication‡ least 1 medication that needs to be adjusted for eGFR  Hospitalisations  regression regression version adjusted for eGFR  Regression version		Cognitive Burden Scale			
requiring adjustment presence of low eGFR according to eGFR  MRCI (George et al., 2004)‡ regimen complexity index (MRCI)  Number of units a day‡ (pills, inhalations, injections, etc.) to be used per day  EGFR† Estimated Glomerular Filtration Rate regression anova ml/min/1,73m²  Low eGFR in combination with a medication‡ least 1 medication that needs to be adjusted for eGFR    Combination with a needs to be adjusted for eGFR   Complex of the presence of low eGFR in according to the beautiful presence of low eGFR in adjusted for eGFR   Complex of the presence of low eGFR in adjusted for eGFR   Complex of the presence of low eGFR in adjusted for eGFR   Complex of the presence of low eGFR in adjusted for eGFR   Complex of the presence of low eGFR in adjusted for eGFR   Complex of the presence of low eGFR in the presence of low eGFR in edging to the presence of low eGFR in edging to the presence of low eGFR   Complex of of low	Number of	A count of the	Linear	0.9853	P-value >0.25
adjustment according to eGFR  MRCI (George et al., 2004)‡ regimen complexity index (MRCI)  Number of units a day‡ (pills, inhalations, injections, etc.) to be used per day  **Kidner regression injection Rate  EStimated Glomerular Filtration Rate  eGFR categorised eGFR categorised eGFR in a categories:	medications	medications that need	regression		
according to eGFR  MRCI (George et al., 2004)‡ regimen complexity index (MRCI)  Number of units a day‡ (pills, inhalations, injections, etc.) to be used per day  Kidney function  EGFR† Estimated Glomerular Filtration Rate regression eGFR categorised eGFR in 3 categories: <a href="https://doi.org/10.2729">30, 30-59 and &gt;59 and &gt;59 and &gt;59 ml/min/1,73m² in relevant combination with a medication‡ least 1 medication that needs to be adjusted for eGFR  MRCI (George et Adjusted Medication al. Linear regression)  Elinear regression  **CO.0001* -* **</a>	requiring	to be adjusted in the			
MRCI (George et al., 2004)‡ regimen complexity regression index (MRCI)  Number of units a day‡  Regression injections, etc.) to be used per day  Regression injections, etc.) to be used	adjustment	presence of low eGFR			
al., 2004)‡ regimen complexity index (MRCI)  Number of units a day‡ (pills, inhalations, injections, etc.) to be used per day    Estimated Glomerular Filtration Rate Filtration Rate and individual i	according to eGFR				
Number of units a day‡	MRCI (George et	Adjusted Medication	Linear	<0.0001	-
Number of units a day‡  (pills, inhalations, injections, etc.) to be used per day    Combination with a relevant medication ‡ least 1 medication that needs to be adjusted for eGFR    Number of units a day	al., 2004)‡	regimen complexity	regression		
day‡ (pills, inhalations, injections, etc.) to be used per day    Composition   Compos		index (MRCI)			
injections, etc.) to be used per day    Combination with a relevant medication ‡ least 1 medication † least 1 medication that needs to be adjusted for eGFR   least 1 medication † least 1 medication	Number of units a	A count of all units	Linear	<0.0001	-
Setimated Glomerular   Linear   regression   P-value > 0.25	day‡	(pills, inhalations,	regression		
Estimated Glomerular   Linear   regression   P-value >0.25		injections, etc.) to be			
eGFR† Estimated Glomerular Filtration Rate regression		used per day			
Filtration Rate regression P-value >0.25  eGFR categorised eGFR in 3 categories:		Kidne	y function	L	
eGFR categorised eGFR in 3 categories:	eGFR†	Estimated Glomerular	Linear	0.2368	-
<pre></pre>		Filtration Rate	regression		
Low eGFR in eGFR <60 T-test 0.2448 -  combination with a relevant combination with at medication‡ least 1 medication that needs to be adjusted for eGFR  Hospitalisations	eGFR categorised	eGFR in 3 categories:	Oneway	0.2729	P-value >0.25
Low eGFR in eGFR <60 T-test 0.2448 -  combination with a ml/min/1,73m² in combination with at medication‡ least 1 medication that needs to be adjusted for eGFR  Hospitalisations		<30 , 30-59 and >59	anova		
combination with a ml/min/1,73m² in combination with at medication‡ least 1 medication that needs to be adjusted for eGFR  Hospitalisations		ml/min/1,73m <sup>2</sup>			
relevant combination with at medication ‡ least 1 medication that needs to be adjusted for eGFR  Hospitalisations	Low eGFR in	eGFR <60	T-test	0.2448	-
medication‡ least 1 medication that needs to be adjusted for eGFR  Hospitalisations	combination with a	ml/min/1,73m <sup>2</sup> in			
needs to be adjusted for eGFR  Hospitalisations	relevant	combination with at			
eGFR Hospitalisations	medication‡	least 1 medication that			
Hospitalisations		needs to be adjusted for			
		eGFR			
Hospitalisation in Has had at least 1 T-test 0.0047 -	Hospitalisations				
	Hospitalisation in	Has had at least 1	T-test	0.0047	-

the last 12	unplanned				
months†	hospitalisation is the				
	last 12 months				
Number of	Unplanned	Oneway	0.0253	No difference in	
unplanned	hospitalisations in 4	anova		complexity between 1	
hospitalisations in	categories: none; 1; 2 or			or more	
last 12 months	3; 4 or more			hospitalisations	
	Morb	idity scores			
QOF (Carey et al.,	Quality and Outcomes	Linear	<0.0001	-	
2013)‡	Framework score	regression			
QOF extended,	Quality and Outcomes	Linear	<0.0001	-	
excluding renal	Framework extended	regression			
disease (Carey et	score				
al., 2013)‡					
QOF extended	Quality and Outcomes	Linear	<0.0001	-	
excluding renal	Framework extended	regression			
disease (Carey et	score, excluding renal				
al., 2013)†	disease				
	Che	olesterol	<u> </u>		
Total cholesterol	Total cholesterol level	Linear	0.0511	Patients with a high	
		regression		cholesterol had a	
				lower algorithm score	
Total	Total cholesterol	Linear	0.9805	P-value >0.25	
cholesterol/HDL	divided by High-density-	regression			
	lipoprotein (HDL) level				
Fall incidents					
Fall incidents†	Has had at least 1	T-test	0.0006	-	
	severe fall incident is				
	the last 12 months				
Fall incidents	Number of fall incidents	Oneway	0.0018	No difference	
categorised	in 4 categories: no falls;	anova		between 1 or more fall	
	1; 2 or 3 ; 4 or more			incidents	
Age					

Age†	Age	Linear	0.0483	-	
		regression			
Age categorised	Age in 5 year classes	Oneway	0.0409	Differences between	
		anova		groups cannot be	
				explained by older age	
Other individual characteristics (not part of a category)					
Number of	A count of all active	Linear	<0.0001	-	
prescribers†	prescribers including	regression			
	the GP				
Diminished	Diminished eyesight in 5	Oneway	0.1190	Differences between	
eyesight	categories from not to	anova		groups cannot be	
	seriously diminished			explained by the	
	eyesight			severity of the	
				eyesight impairment	
Diminished social	Diminished social	Oneway	0.0353	Differences between	
network	network in 5 categories	anova		groups cannot be	
	from no to adequate			explained by more	
	social network			severely diminished	
				social network	
Adherence issue†	Patient has some form	T-test	0.1488	-	
	of adherence problems				
Believes that	Patient believes that	T-test	0.1683	-	
(some of the)	(some of) his/her				
medication does	medication does not				
not work†	work				
Worries about the	Patient worries about	T-test	0.1974	-	
amount of	the amount of				
medication†	medication he/she is				
	taking				
Difficulty in	Patient has difficulties in	T-test	0.0818	-	
communicating†	communicating (with				
	healthcare				
	professionals)				
Education	Level of education	Oneway	0.3089	P-value >0.25	

	divided in 5 categories	anova		
Deviating	Potassium or sodium	T-test	0.8062	P-value >0.25
potassium or	level is outside the			
sodium levels	reference value;			
	potassium [3.5-5.0			
	mmol/L]; sodium [135-			
	145 mmol/L]			
Side effect(s)	Reported at least 1 side	T-test	0.4841	P-value >0.25
	effect			
Intake problem(s)	At least 1 issue for	T-test	0.6834	P-value >0.25
	medication intake, e.g.			
	swallowing problem,			
	inhalation problem			
Diminished hearing	Diminished hearing in 5	Oneway	0.9416	P-value >0.25
	categories from not to	anova		
	seriously impaired			
	hearing			
Diminished	Diminished cognition in	Oneway	0.6479	P-value >0.25
cognition	5 categories from not to	anova		
	seriously impaired			
	cognition			
Sex	Male or female	T-test	0.6706	P-value >0.25
Contacts	Patient contacts	T-test	0.3407	P-value >0.25
healthcare	healthcare professionals			
professionals in	in time when needed			
time				

<sup>†</sup> Included in the first backward stepwise linear regression procedure,‡ Alternative predictor tested in the model

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