

# Supplementary Material

## Declining Use of Potentially Inappropriate Medication in People with Dementia from 2000 to 2015: A Repeated Cross-Sectional Nationwide Register-Based Study

### Identification of People with Dementia in the Registers: Diagnosis Codes and Available Dementia Medications

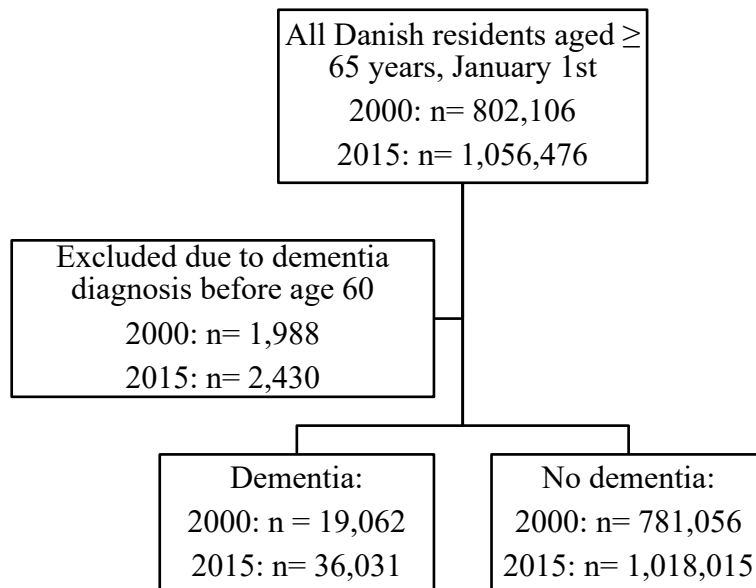
**Supplementary Table 1A.** ICD-8 and ICD-10 diagnosis codes used to identify dementia status. Diagnoses were coded as A- or B-diagnoses. H-diagnoses were not used.

	ICD-8	ICD-10
Alzheimer's disease	290.10	F00.0, F00.1, F00.2, F00.9, G30.0, G30.1, G30.8, G30.9
Vascular dementia	293.09-19	F01.0, F01.1, F01.2, F01.3, F01.8, F01.9
Frontotemporal dementia	290.11	F02.0, G31.8
Dementia without specification	290.09-19	F03.9, G31.9

**Supplementary Table 1B.** Anti-dementia medication used to identify persons with dementia.

Drug name	ATC
Donepezil	N06DA02
Rivastigmine	N06DA03
Galantamine	N06AD04
Memantine	N06DX01

**Supplementary Figure 1.** Formation of the study population in 2000 and 2015.



## Comorbidities

**Supplementary Table 2.** Diagnosis codes used to define comorbidities

Charlson Comorbidity Index (weight)	ICD-10 codes
Myocardial infarct (1)	I21-22, I25.2
Congestive heart failure (1)	I50
Peripheral vascular disease (1)	I71, I73.9, I79.0
Cerebrovascular disease (1)	I60-69, G45-46
Chronic pulmonary disease (1)	J40-47, J60-67
Connective tissue disease (1)	M05, M06.0, M06.3, M06.9, M32, M33.2, M34, M35.3
Ulcer disease (1)	K25-28
Mild liver disease (1)	K70.2-70.3, K71.7, K73, K74
Diabetes mellitus (1)	E10.1, E10.5, E10.9, E11.1, E11.5, E11.9, E12.1, E12.5, E12.9, E13.1, E13.5, E13.9, E14.1, E14.5, E14.9
Hemiplegia (2)	G81, G82.0-82.2
Moderate or severe renal disease (2)	N01, N03, N05.2-05.6, N07.3-07.4, N18, N19, N25
Diabetes with end-organ damage (2)	E10.2-10.4, E11.2-11.4, E13.2-13.4, E14.2-14.4
Any tumor (2)	C00-76, C80
Leukemia (2)	C90.0-90.2, C91-96, C97X
Lymphoma (2)	C81-85, C88
Moderate or severe liver disease (3)	K72.1, K72.9, K76.6-76.7
Metastatic solid tumor (6)	C77-79
AIDS (6)	B20-24

## The Red-Yellow-Green List

Red and yellow categories of the Danish red-yellow-green list of “drugs, where the indication should be reassessed in people  $\geq 65$  years” published by the Institute for Rational Pharmacotherapy. ATC stands for Anatomical Therapeutic Chemical Classification system.

**Supplementary Table 3A.** Red drugs: “drugs to avoid in older people unless under special circumstance”

Subgroup	Drug name	ATC
<i>Digestive</i>	Sodium picosulfate	A06AB08
	Butylscopolamine	A03BB01
	Propantheline	A03AB05
	Bisacodyl	A06AB02, A06AG02
<i>Cardiovascular</i>	Digoxin	C01AA05
<i>Urological</i>	Tolterodine	G04BD07
	Fesoterodine	G04BD11
	Solifenacin	G04BD08
<i>Analgesics</i>	NSAIDs	M01A
	Quinine	P01BC01
<i>Sleep and anxiety</i>	Nitrazepam	N05CD02
	Diazepam	N05BA01
<i>Antipsychotics</i>	Aripiprazole	N05AX12
	Zuclopenthixol	N05AF05
	Flupentixol	N05AF01
	Levomepromazine	N05AA02
	Haloperidol	N05AD01
	Quetiapine	N05AH04
	Chlorprothixene	N05AF03
	Olanzapine	N05AH03
	Biperiden	N04AA02
	Orphenadrine	N04AB02
	<i>Antidepressants</i>	Amitriptyline
Clomipramine		N06AA04
Imipramine		N06AA02
Nortriptyline		N06AA10

**Supplementary Table 3B.** Yellow drugs: “drugs where correct and current indication should be reassessed”

Subgroup	Drug name	ATC
<i>Digestive</i>	Metoclopramide	A03FA01
<i>Cardiovascular</i>	Furosemide	C03CA01
<i>Analgesics</i>	Oxycodone	N02AA05
	Ketobemidone, comb. antispasmodics	N02AG02
	Morphine	N02AA01
<i>Sleep and anxiety</i>	Zopiclone	N05CF01
	Zolpidem	N05CF02
	Promethazine	R06AD02
	Oxazepam	N05BA04
<i>Antipsychotics</i>	Risperidone	N05AX08

\*Drugs excluded due to extra requirements such as dosage: Asasantin® Retard (B01AC30, Platelet aggregation inhibitors excluding heparin, combinations) and acetylsalicylic acid (B01AC06).

## Detailed Results from the Logistic Regression

**Supplementary Table 4A.** Odds ratio (OR) with 95% confidence intervals (CI) for filling prescriptions for **at least one red drug** in 2005, 2010, or 2015 versus 2000 for people  $\geq 65$  years with dementia

<b>Age groups</b>		<b>Crude</b>	<b>Adjusted for sex</b>	<b>adjusted for age, sex, and Charlson Comorbidity Index</b>
<b>65-69 years</b>	2000:	1.0	1.0	1.0
	2005:	1.07 (0.92-1.25)	1.08 (0.92-1.26)	1.04 (0.89-1.22)
	2010:	0.99 (0.86-1.16)	0.99 (0.86-1.15)	0.97 (0.83-1.13)
	2015:	0.82 (0.71-0.96)	0.82 (0.71-0.96)	0.80 (0.68-0.92)
<b>70-74 years</b>	2000:	1.0	1.0	1.0
	2005:	1.09 (0.97-1.21)	1.09 (0.97-1.21)	1.07 (0.96-1.19)
	2010:	0.91 (0.82-1.01)	0.91 (0.82-1.02)	0.89 (0.80-0.98)
	2015:	0.72 (0.65-0.80)	0.72 (0.65-0.80)	0.70 (0.63-0.77)
<b>75-79 years</b>	2000:	1.0	1.0	1.0
	2005:	1.10 (1.02-1.19)	1.10 (1.02-1.19)	1.08 (1.00-1.17)
	2010:	0.84 (0.78-0.91)	0.84 (0.78-0.91)	0.81 (0.75-0.88)
	2015:	0.62 (0.57-0.67)	0.62 (0.57-0.67)	0.60 (0.55-0.65)
<b>80-84 years</b>	2000:	1.0	1.0	1.0
	2005:	1.13 (1.05-1.22)	1.14 (1.06-1.22)	1.12 (1.04-1.20)
	2010:	0.80 (0.74-0.86)	0.80 (0.75-0.86)	0.78 (0.72-0.84)
	2015:	0.60 (0.56-0.65)	0.60 (0.56-0.65)	0.58 (0.54-0.63)
<b>85-89 years</b>	2000:	1.0	1.0	1.0
	2005:	1.08 (1.00-1.17)	1.08 (1.00-1.17)	1.06 (0.99-1.15)
	2010:	0.82 (0.77-0.88)	0.82 (0.77-0.88)	0.79 (0.74-0.85)
	2015:	0.59 (0.55-0.64)	0.60 (0.55-0.64)	0.57 (0.53-0.61)
<b>90-94 years</b>	2000:	1.0	1.0	1.0
	2005:	1.10 (0.98-1.23)	1.10 (0.98-1.24)	1.09 (0.97-1.22)
	2010:	0.82 (0.74-0.91)	0.82 (0.74-0.91)	0.80 (0.72-0.90)
	2015:	0.64 (0.57-0.71)	0.64 (0.58-0.71)	0.61 (0.55-0.68)
<b>95-99 years</b>	2000:	1.0	1.0	1.0
	2005:	1.39 (1.08-1.79)	1.39 (1.08-1.79)	1.39 (1.08-1.79)
	2010:	1.01 (0.80-1.28)	1.02 (0.81-1.29)	1.00 (0.79-1.27)
	2015:	0.75 (0.59-0.94)	0.74 (0.59-0.94)	0.75 (0.59-0.95)

**Supplementary Table 4B.** Odds ratio (OR) with 95% confidence intervals (CI) for filling prescriptions for at least one red drug in 2005, 2010, or 2015 versus 2000 for people  $\geq 65$  years without dementia

<b>Age groups</b>		<b>Crude</b>	<b>Adjusted for sex</b>	<b>Adjusted for age, sex, and Charlson Comorbidity Index</b>
<b>65-69 years</b>	2000:	1.0	1.0	1.0
	2005:	1.22 (1.21-1.24)	1.23 (1.21-1.24)	1.20 (1.18-1.21)
	2010:	1.01 (1.00-1.02)	1.02 (1.01-1.03)	0.98 (0.96-0.99)
	2015:	0.75 (0.74-0.76)	0.75 (0.74-0.76)	0.71 (0.70-0.71)
<b>70-74 years</b>	2000:	1.0	1.0	1.0
	2005:	1.16 (1.14-1.17)	1.16 (1.15-1.18)	1.12 (1.11-1.14)
	2010:	1.00 (0.99-1.01)	1.01 (0.99-1.02)	0.95 (0.94-0.96)
	2015:	0.66 (0.66-0.67)	0.67 (0.66-0.68)	0.62 (0.61-0.63)
<b>75-79 years</b>	2000:	1.0	1.0	1.00
	2005:	1.08 (1.06-1.09)	1.09 (1.07-1.10)	1.04 (1.03-1.06)
	2010:	0.89 (0.88-0.90)	0.90 (0.89-0.91)	0.84 (0.83-0.85)
	2015:	0.60 (0.59-0.61)	0.61 (0.60-0.62)	0.56 (0.55-0.56)
<b>80-84 years</b>	2000:	1.0	1.0	1.0
	2005:	1.03 (1.01-1.04)	1.03 (1.01-1.05)	0.98 (0.97-1.00)
	2010:	0.81 (0.79-0.82)	0.81 (0.80-0.83)	0.75 (0.74-0.77)
	2015:	0.53 (0.52-0.54)	0.54 (0.53-0.55)	0.49 (0.48-0.50)
<b>85-89 years</b>	2000:	1.0	1.0	1.0
	2005:	1.00 (0.98-1.02)	1.01 (0.98-1.03)	0.97 (0.94-0.99)
	2010:	0.77 (0.75-0.78)	0.77 (0.76-0.79)	0.72 (0.70-0.73)
	2015:	0.51 (0.50-0.53)	0.52 (0.51-0.53)	0.47 (0.46-0.48)
<b>90-94 years</b>	2000:	1.0	1.0	1.0
	2005:	1.03 (1.00-1.07)	1.04 (1.00-1.08)	1.01 (0.97-1.05)
	2010:	0.78 (0.75-0.81)	0.79 (0.76-0.82)	0.74 (0.71-0.77)
	2015:	0.55 (0.53-0.57)	0.55 (0.53-0.57)	0.50 (0.48-0.52)
<b>95-99 years</b>	2000:	1.0	1.0	1.0
	2005:	1.07 (0.99-1.16)	1.07 (0.99-1.16)	1.04 (0.96-1.12)
	2010:	0.82 (0.76-0.88)	0.82 (0.76-0.88)	0.77 (0.71-0.83)
	2015:	0.59 (0.55-0.64)	0.59 (0.55-0.64)	0.55 (0.51-0.60)

**Supplementary Table 4C.** Odds ratio (OR) with 95% confidence intervals (CI) for filling prescriptions for at least one red drug, excluding N05A from the analysis in 2015 versus 2000 for people  $\geq 65$  years with dementia

<b>Age groups</b>		<b>Crude</b>	<b>Adjusted for sex</b>
<b>65-69 years</b>	2000:	1.0	1.0
	2005:	1.10 (0.94-1.29)	1.11 (0.95-1.30)
	2010:	0.97 (0.83-1.13)	0.97 (0.83-1.13)
	2015:	0.75 (0.65-0.88)	0.76 (0.65-0.88)
<b>70-74 years</b>	2000:	1.0	1.0
	2005:	1.14 (1.02-1.27)	1.14 (1.02-1.28)
	2010:	0.94 (0.85-1.05)	0.94 (0.85-1.05)
	2015:	0.70 (0.63-0.77)	0.70 (0.63-0.77)
<b>75-79 years</b>	2000:	1.0	1.0
	2005:	1.19 (1.10-1.29)	1.19 (1.10-1.29)
	2010:	0.91 (0.84-0.98)	0.91 (0.84-0.99)
	2015:	0.66 (0.61-0.71)	0.66 (0.61-0.72)
<b>80-84 years</b>	2000:	1.0	1.0
	2005:	1.21 (1.12-1.30)	1.21 (1.12-1.30)
	2010:	0.87 (0.81-0.93)	0.87 (0.81-0.93)
	2015:	0.63 (0.59-0.68)	0.64 (0.59-0.68)
<b>85-89 years</b>	2000:	1.0	1.0
	2005:	1.24 (1.15-1.34)	1.24 (1.15-1.34)
	2010:	0.95 (0.88-1.02)	0.95 (0.88-1.02)
	2015:	0.67 (0.62-0.72)	0.67 (0.63-0.73)
<b>90-94 years</b>	2000:	1.0	1.0
	2005:	1.27 (1.14-1.42)	1.28 (1.14-1.43)
	2010:	0.98 (0.88-1.09)	0.98 (0.88-1.09)
	2015:	0.73 (0.66-0.82)	0.74 (0.66-0.82)
<b>95-99 years</b>	2000:	1.0	1.0
	2005:	1.53 (1.19-1.96)	1.53 (1.19-1.96)
	2010:	1.20 (0.95-1.52)	1.21 (0.96-1.54)
	2015:	0.89 (0.71-1.13)	0.90 (0.71-1.13)



**Supplementary Table 4D.** Odds ratio (OR) with 95% confidence intervals (CI) for filling prescriptions for at least one red drug excluding N05A in 2005, 2010, or 2015 versus 2000 for people 65 years or older without dementia

<b>Age groups</b>		<b>Crude</b>	<b>Adjusted for sex</b>
<b>65-69 years</b>	2000:	1.0	1.0
	2005:	1.24 (1.22-1.25)	1.24 (1.22-1.26)
	2010:	1.02 (1.01-1.04)	1.03 (1.02-1.04)
	2015:	0.75 (0.74-0.76)	0.75 (0.74-0.76)
<b>70-74 years</b>	2000:	1.0	1.0
	2005:	1.17 (1.16-1.19)	1.18 (1.16-1.19)
	2010:	1.01 (1.00-1.02)	1.02 (1.00-1.03)
	2015:	0.66 (0.66-0.67)	0.67 (0.66-0.68)
<b>75-79 years</b>	2000:	1.0	1.0
	2005:	1.09 (1.07-1.11)	1.10 (1.08-1.11)
	2010:	0.90 (0.89-0.91)	0.91 (0.90-0.92)
	2015:	0.60 (0.59-0.61)	0.61 (0.60-0.62)
<b>80-84 years</b>	2000:	1.0	1.0
	2005:	1.04 (1.03-1.06)	1.05 (1.03-1.06)
	2010:	0.82 (0.80-0.83)	0.82 (0.81-0.84)
	2015:	0.54 (0.53-0.54)	0.54 (0.53-0.55)
<b>85-89 years</b>	2000:	1.0	1.0
	2005:	1.02 (1.00-1.05)	1.03 (1.00-1.05)
	2010:	0.79 (0.77-0.80)	0.79 (0.77-0.81)
	2015:	0.52 (0.51-0.53)	0.53 (0.51-0.54)
<b>90-94 years</b>	2000:	1.0	1.0
	2005:	1.07 (1.03-1.11)	1.08 (1.04-1.11)
	2010:	0.81 (0.78-0.84)	0.82 (0.79-0.85)
	2015:	0.56 (0.54-0.58)	0.57 (0.55-0.59)
<b>95-99 years</b>	2000:	1.0	1.0
	2005:	1.12 (1.04-1.21)	1.12 (1.04-1.21)
	2010:	0.87 (0.81-0.94)	0.87 (0.81-0.94)
	2015:	0.62 (0.58-0.67)	0.62 (0.58-0.67)