**Supplemental materials for:**

Hanlon P, Quinn TJ, Gallacher KI, et al. assessing risks of polypharmacy involving medications with anticholinergic properties. *Ann Fam Med*. 2020;18(3):148-155.

# Supplementary appendix

## Contents

# Main analysis

## Hazard ratios per one-point increase in scale

### Model 1 - Adjusted for age, sex, and socioeconomic status

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| ARS | 1.21 ( 1.19 to 1.23 ) | 1.22 ( 1.2 to 1.24 ) | 1.21 ( 1.17 to 1.25 ) | 1.15 ( 1.12 to 1.19 ) | 1.38 ( 1.23 to 1.55 ) |
| CrAS | 1.21 ( 1.2 to 1.23 ) | 1.22 ( 1.2 to 1.24 ) | 1.25 ( 1.22 to 1.27 ) | 1.17 ( 1.14 to 1.19 ) | 1.36 ( 1.24 to 1.49 ) |
| AAS-r | 1.22 ( 1.2 to 1.23 ) | 1.22 ( 1.21 to 1.24 ) | 1.27 ( 1.25 to 1.3 ) | 1.17 ( 1.15 to 1.2 ) | 1.28 ( 1.17 to 1.41 ) |
| AAS | 1.23 ( 1.22 to 1.25 ) | 1.24 ( 1.22 to 1.25 ) | 1.29 ( 1.27 to 1.32 ) | 1.17 ( 1.15 to 1.2 ) | 1.39 ( 1.28 to 1.51 ) |
| m-ARS | 1.24 ( 1.22 to 1.25 ) | 1.24 ( 1.23 to 1.26 ) | 1.23 ( 1.2 to 1.27 ) | 1.17 ( 1.14 to 1.2 ) | 1.41 ( 1.28 to 1.56 ) |
| ALS | 1.24 ( 1.23 to 1.26 ) | 1.25 ( 1.23 to 1.26 ) | 1.28 ( 1.25 to 1.31 ) | 1.18 ( 1.16 to 1.21 ) | 1.41 ( 1.29 to 1.53 ) |
| AIS | 1.26 ( 1.24 to 1.28 ) | 1.27 ( 1.25 to 1.29 ) | 1.28 ( 1.24 to 1.31 ) | 1.24 ( 1.21 to 1.27 ) | 1.51 ( 1.38 to 1.66 ) |
| AEC | 1.26 ( 1.24 to 1.29 ) | 1.27 ( 1.25 to 1.3 ) | 1.28 ( 1.25 to 1.32 ) | 1.23 ( 1.2 to 1.27 ) | 1.61 ( 1.47 to 1.77 ) |
| ACOB | 1.28 ( 1.27 to 1.3 ) | 1.29 ( 1.28 to 1.31 ) | 1.38 ( 1.35 to 1.4 ) | 1.21 ( 1.18 to 1.24 ) | 1.43 ( 1.32 to 1.55 ) |
| ADS | 1.29 ( 1.28 to 1.31 ) | 1.3 ( 1.29 to 1.32 ) | 1.37 ( 1.34 to 1.39 ) | 1.22 ( 1.2 to 1.25 ) | 1.43 ( 1.32 to 1.55 ) |

### Model 2 - adjusted for age, sex, socioeconomic status, BMI, smoking, alchohol and phyiscal activity

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| ARS | 1.14 ( 1.12 to 1.16 ) | 1.14 ( 1.12 to 1.17 ) | 1.11 ( 1.08 to 1.15 ) | 1.12 ( 1.08 to 1.16 ) | 1.34 ( 1.18 to 1.52 ) |
| CrAS | 1.14 ( 1.12 to 1.16 ) | 1.15 ( 1.13 to 1.16 ) | 1.14 ( 1.11 to 1.17 ) | 1.14 ( 1.12 to 1.17 ) | 1.34 ( 1.21 to 1.47 ) |

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| AAS-r | 1.14 ( 1.13 to 1.16 ) | 1.15 ( 1.13 to 1.17 ) | 1.17 ( 1.14 to 1.2 ) | 1.14 ( 1.12 to 1.17 ) | 1.26 ( 1.14 to 1.4 ) |
| AAS | 1.15 ( 1.14 to 1.17 ) | 1.16 ( 1.15 to 1.18 ) | 1.19 ( 1.16 to 1.21 ) | 1.15 ( 1.12 to 1.17 ) | 1.35 ( 1.23 to 1.48 ) |
| ALS | 1.16 ( 1.14 to 1.18 ) | 1.17 ( 1.15 to 1.19 ) | 1.17 ( 1.14 to 1.2 ) | 1.16 ( 1.13 to 1.19 ) | 1.38 ( 1.25 to 1.52 ) |
| m-ARS | 1.16 ( 1.14 to 1.18 ) | 1.17 ( 1.15 to 1.19 ) | 1.13 ( 1.1 to 1.17 ) | 1.14 ( 1.11 to 1.17 ) | 1.38 ( 1.24 to 1.54 ) |
| AEC | 1.17 ( 1.15 to 1.19 ) | 1.18 ( 1.16 to 1.2 ) | 1.16 ( 1.12 to 1.2 ) | 1.19 ( 1.15 to 1.23 ) | 1.57 ( 1.42 to 1.73 ) |
| AIS | 1.18 ( 1.16 to 1.2 ) | 1.19 ( 1.17 to 1.21 ) | 1.16 ( 1.12 to 1.2 ) | 1.2 ( 1.17 to 1.23 ) | 1.5 ( 1.35 to 1.66 ) |
| ACOB | 1.21 ( 1.19 to 1.22 ) | 1.22 ( 1.2 to 1.24 ) | 1.27 ( 1.24 to 1.3 ) | 1.17 ( 1.15 to 1.2 ) | 1.38 ( 1.26 to 1.51 ) |
| ADS | 1.21 ( 1.2 to 1.23 ) | 1.22 ( 1.21 to 1.24 ) | 1.25 ( 1.23 to 1.28 ) | 1.19 ( 1.16 to 1.21 ) | 1.4 ( 1.28 to 1.53 ) |

## Model 3 - adjuted for age, sex, socioeconomic status, BMI, smoking, alchohol, physical activity and number of long-term conditions

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| CrAS | 1.05 ( 1.03 to 1.07 ) | 1.05 ( 1.04 to 1.07 ) | 1.03 ( 1 to 1.06 ) | 1.09 ( 1.06 to 1.11 ) | 1.23 ( 1.1 to 1.36 ) |
| ARS | 1.05 ( 1.03 to 1.08 ) | 1.06 ( 1.04 to 1.08 ) | 1.01 ( 0.97 to 1.05 ) | 1.06 ( 1.03 to 1.1 ) | 1.23 ( 1.07 to 1.4 ) |
| AAS-r | 1.06 ( 1.04 to 1.08 ) | 1.07 ( 1.05 to 1.08 ) | 1.07 ( 1.04 to 1.09 ) | 1.09 ( 1.06 to 1.12 ) | 1.14 ( 1.02 to 1.28 ) |
| ALS | 1.06 ( 1.04 to 1.08 ) | 1.07 ( 1.05 to 1.08 ) | 1.04 ( 1.01 to 1.07 ) | 1.1 ( 1.07 to 1.13 ) | 1.26 ( 1.14 to 1.41 ) |
| AAS | 1.06 ( 1.05 to 1.08 ) | 1.07 ( 1.05 to 1.09 ) | 1.07 ( 1.05 to 1.1 ) | 1.09 ( 1.06 to 1.12 ) | 1.24 ( 1.11 to 1.37 ) |
| AEC | 1.07 ( 1.05 to 1.1 ) | 1.08 ( 1.06 to 1.1 ) | 1.04 ( 1 to 1.08 ) | 1.12 ( 1.09 to 1.16 ) | 1.45 ( 1.3 to 1.61 ) |
| m-ARS | 1.07 ( 1.06 to 1.09 ) | 1.08 ( 1.06 to 1.1 ) | 1.02 ( 0.99 to 1.06 ) | 1.08 ( 1.05 to 1.12 ) | 1.27 ( 1.13 to 1.43 ) |
| AIS | 1.08 ( 1.06 to 1.1 ) | 1.09 ( 1.07 to 1.11 ) | 1.04 ( 1.01 to 1.08 ) | 1.14 ( 1.1 to 1.17 ) | 1.38 ( 1.24 to 1.54 ) |
| ACOB | 1.12 ( 1.1 to 1.14 ) | 1.13 ( 1.11 to 1.15 ) | 1.17 ( 1.14 to 1.2 ) | 1.11 ( 1.08 to 1.14 ) | 1.26 ( 1.14 to 1.4 ) |
| ADS | 1.12 ( 1.11 to 1.14 ) | 1.13 ( 1.12 to 1.15 ) | 1.15 ( 1.12 to 1.17 ) | 1.13 ( 1.1 to 1.16 ) | 1.29 ( 1.16 to 1.42 ) |

# Predictive accuracy of fully adjusted model

The predictive accuracy of model 3 was assessed using Harrell's C-statistic with ten-fold internal cross-validation. C-statistic is an extension of the area under the curve for time-to-event data. A value of 1 indicates perfect prediction and a value of 0.5 no better than chance. The C-statistic of a base model (including all covariates except the anticholinergic scale) was calculated for comparison.

## C statistics for model 3

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| Base model (add covariates minus anticholinergic score) | 0.737 | 0.741 | 0.757 | 0.623 | 0.820 |
| CrAS | 0.737 | 0.741 | 0.757 | 0.624 | 0.822 |
| ARS | 0.737 | 0.741 | 0.757 | 0.624 | 0.822 |
| AAS-r | 0.737 | 0.741 | 0.757 | 0.625 | 0.822 |
| ALS | 0.737 | 0.741 | 0.757 | 0.625 | 0.822 |
| AAS | 0.737 | 0.741 | 0.757 | 0.625 | 0.822 |
| AEC | 0.737 | 0.741 | 0.757 | 0.625 | 0.823 |
| m-ARS | 0.737 | 0.741 | 0.757 | 0.624 | 0.823 |
| AIS | 0.737 | 0.742 | 0.757 | 0.625 | 0.823 |
| ACOB | 0.738 | 0.743 | 0.758 | 0.625 | 0.822 |
| ADS | 0.738 | 0.742 | 0.758 | 0.626 | 0.822 |

# Sensitivity analysis 1: Excluding events occurring in the first 12 months of follow-up (limits bias from reverse causality)

## Hazard ratios per one-point increase in scale

### Model 1 - Adjusted for age, sex, and socioeconomic status

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| ARS | 1.21 ( 1.19 to 1.23 ) | 1.21 ( 1.19 to 1.24 ) | 1.22 ( 1.17 to 1.26 ) | 1.17 ( 1.13 to 1.22 ) | 1.28 ( 1.1 to 1.49 ) |
| CrAS | 1.21 ( 1.2 to 1.23 | 1.22 ( 1.2 to | 1.26 ( 1.23 | 1.18 ( 1.15 | 1.28 ( 1.14 to 1.44 |

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| | ) | 1.23 ) | to 1.29 ) | to 1.21 ) | ) |
| AAS-r | 1.22 ( 1.2 to 1.23 ) | 1.22 ( 1.2 to 1.24 ) | 1.29 ( 1.26 to 1.32 ) | 1.18 ( 1.15 to 1.21 ) | 1.26 ( 1.13 to 1.41 ) |
| AAS | 1.23 ( 1.21 to 1.24 ) | 1.23 ( 1.22 to 1.25 ) | 1.31 ( 1.28 to 1.34 ) | 1.18 ( 1.15 to 1.21 ) | 1.34 ( 1.22 to 1.49 ) |
| ALS | 1.24 ( 1.22 to 1.26 ) | 1.24 ( 1.23 to 1.26 ) | 1.3 ( 1.27 to 1.33 ) | 1.2 ( 1.17 to 1.24 ) | 1.33 ( 1.2 to 1.49 ) |
| m-ARS | 1.24 ( 1.22 to 1.26 ) | 1.24 ( 1.22 to 1.26 ) | 1.24 ( 1.2 to 1.28 ) | 1.19 ( 1.15 to 1.23 ) | 1.32 ( 1.16 to 1.5 ) |
| AEC | 1.26 ( 1.24 to 1.28 ) | 1.27 ( 1.24 to 1.29 ) | 1.3 ( 1.26 to 1.35 ) | 1.25 ( 1.2 to 1.29 ) | 1.5 ( 1.33 to 1.69 ) |
| AIS | 1.26 ( 1.24 to 1.28 ) | 1.27 ( 1.25 to 1.29 ) | 1.29 ( 1.26 to 1.33 ) | 1.24 ( 1.2 to 1.28 ) | 1.47 ( 1.31 to 1.65 ) |
| ACOB | 1.28 ( 1.26 to 1.3 ) | 1.29 ( 1.27 to 1.3 ) | 1.4 ( 1.37 to 1.43 ) | 1.22 ( 1.19 to 1.26 ) | 1.34 ( 1.2 to 1.49 ) |
| ADS | 1.29 ( 1.27 to 1.3 ) | 1.3 ( 1.28 to 1.31 ) | 1.39 ( 1.36 to 1.42 ) | 1.24 ( 1.21 to 1.27 ) | 1.36 ( 1.23 to 1.51 ) |

**Model 2 - adjusted for age, sex, socioeconomic status, BMI, smoking, alchohol and phyiscal activity**

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| ARS | 1.14 ( 1.12 to 1.16 ) | 1.14 ( 1.12 to 1.17 ) | 1.12 ( 1.08 to 1.17 ) | 1.14 ( 1.1 to 1.19 ) | 1.24 ( 1.05 to 1.46 ) |
| CrAS | 1.14 ( 1.12 to 1.16 ) | 1.15 ( 1.13 to 1.16 ) | 1.16 ( 1.13 to 1.19 ) | 1.16 ( 1.12 to 1.19 ) | 1.27 ( 1.12 to 1.43 ) |
| AAS-r | 1.14 ( 1.13 to 1.16 ) | 1.15 ( 1.13 to 1.16 ) | 1.19 ( 1.16 to 1.22 ) | 1.15 ( 1.12 to 1.19 ) | 1.24 ( 1.1 to 1.4 ) |
| AAS | 1.15 ( 1.14 to 1.17 ) | 1.16 ( 1.14 to 1.17 ) | 1.21 ( 1.18 to 1.24 ) | 1.16 ( 1.13 to 1.2 ) | 1.31 ( 1.17 to 1.47 ) |
| ALS | 1.16 ( 1.14 to 1.18 ) | 1.17 ( 1.15 to 1.18 ) | 1.19 ( 1.15 to 1.22 ) | 1.19 ( 1.15 to 1.22 ) | 1.31 ( 1.16 to 1.48 ) |
| m-ARS | 1.16 ( 1.14 to 1.18 ) | 1.17 ( 1.15 to 1.19 ) | 1.14 ( 1.1 to 1.18 ) | 1.16 ( 1.12 to 1.2 ) | 1.29 ( 1.13 to 1.49 ) |
| AEC | 1.17 ( 1.15 to 1.19 ) | 1.17 ( 1.15 to 1.2 ) | 1.18 ( 1.14 to 1.23 ) | 1.21 ( 1.16 to 1.26 ) | 1.47 ( 1.29 to 1.68 ) |
| AIS | 1.18 ( 1.16 to 1.2 ) | 1.18 ( 1.16 to 1.2 ) | 1.18 ( 1.14 to 1.22 ) | 1.21 ( 1.17 to 1.25 ) | 1.47 ( 1.3 to 1.66 ) |
| ACOB | 1.21 ( 1.19 to 1.22 ) | 1.21 ( 1.2 to 1.23 ) | 1.29 ( 1.26 to 1.32 ) | 1.19 ( 1.15 to 1.22 ) | 1.29 ( 1.14 to 1.45 ) |
| ADS | 1.21 ( 1.19 to 1.23 ) | 1.22 ( 1.2 to 1.24 ) | 1.28 ( 1.25 to 1.31 ) | 1.21 ( 1.17 to 1.24 ) | 1.32 ( 1.18 to 1.48 ) |

**Model 3 - adjuted for age, sex, socioeconomic status, BMI, smoking, alchohol, physical activity and number of long-term conditions**

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| CrAS | 1.06 ( 1.04 to 1.07 ) | 1.06 ( 1.04 to 1.07 ) | 1.04 ( 1.01 to 1.08 ) | 1.1 ( 1.06 to 1.14 ) | 1.15 ( 1 to 1.31 ) |
| ARS | 1.06 ( 1.04 to 1.08 ) | 1.06 ( 1.04 to 1.08 ) | 1.02 ( 0.98 to 1.06 ) | 1.09 ( 1.04 to 1.13 ) | 1.12 ( 0.94 to 1.33 ) |
| AAS-r | 1.06 ( 1.05 to 1.08 ) | 1.06 ( 1.05 to 1.08 ) | 1.09 ( 1.06 to 1.12 ) | 1.1 ( 1.06 to 1.13 ) | 1.11 ( 0.97 to 1.27 ) |
| AAS | 1.07 ( 1.05 to 1.08 ) | 1.07 ( 1.05 to 1.09 ) | 1.09 ( 1.06 to 1.13 ) | 1.11 ( 1.07 to 1.14 ) | 1.18 ( 1.04 to 1.34 ) |
| ALS | 1.07 ( 1.05 to 1.08 ) | 1.07 ( 1.05 to 1.09 ) | 1.06 ( 1.03 to 1.09 ) | 1.12 ( 1.09 to 1.16 ) | 1.18 ( 1.03 to 1.35 ) |
| AEC | 1.08 ( 1.05 to 1.1 ) | 1.08 ( 1.06 to 1.1 ) | 1.06 ( 1.02 to 1.1 ) | 1.14 ( 1.1 to 1.19 ) | 1.34 ( 1.16 to 1.54 ) |
| m-ARS | 1.08 ( 1.06 to 1.1 ) | 1.08 ( 1.06 to 1.1 ) | 1.03 ( 0.99 to 1.07 ) | 1.1 ( 1.06 to 1.14 ) | 1.18 ( 1.01 to 1.36 ) |
| AIS | 1.09 ( 1.07 to 1.11 ) | 1.09 ( 1.07 to 1.11 ) | 1.06 ( 1.02 to 1.1 ) | 1.14 ( 1.1 to 1.19 ) | 1.35 ( 1.18 to 1.54 ) |
| ACOB | 1.12 ( 1.1 to 1.14 ) | 1.13 ( 1.11 to 1.14 ) | 1.19 ( 1.16 to 1.22 ) | 1.13 ( 1.09 to 1.16 ) | 1.15 ( 1 to 1.32 ) |
| ADS | 1.13 ( 1.11 to 1.14 ) | 1.13 ( 1.11 to 1.15 ) | 1.17 ( 1.14 to 1.2 ) | 1.15 ( 1.11 to 1.18 ) | 1.19 ( 1.05 to 1.35 ) |

## Sensitivity analysis 2: Follow-up truncated at 24 months, with participants censored at first event or 24 months follow-up, whichever happened first (to limit bias from unmeasured change in anticholinergic burden)

## Hazard ratios per one-point increase in scale

**Model 1 - Adjusted for age, sex, and socioeconomic status**

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| ARS | 1.23 ( 1.18 to 1.27 ) | 1.23 ( 1.18 to 1.28 ) | 1.19 ( 1.13 to 1.25 ) | 1.13 ( 1.09 to 1.18 ) | 1.38 ( 1.18 to 1.61 ) |
| CrAS | 1.24 ( 1.21 to 1.27 ) | 1.26 ( 1.23 to 1.3 ) | 1.21 ( 1.16 to 1.25 ) | 1.15 ( 1.12 to 1.18 ) | 1.35 ( 1.19 to 1.52 ) |
| m-ARS | 1.24 ( 1.21 to 1.28 ) | 1.26 ( 1.21 to 1.31 ) | 1.2 ( 1.15 to 1.26 ) | 1.15 ( 1.12 to 1.19 ) | 1.42 ( 1.24 to 1.62 ) |
| AAS-r | 1.25 ( 1.22 to 1.28 ) | 1.28 ( 1.24 to 1.31 ) | 1.24 ( 1.2 to 1.28 ) | 1.17 ( 1.14 to 1.2 ) | 1.27 ( 1.12 to 1.44 ) |

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| AAS | 1.26 ( 1.23 to 1.29 ) | 1.3 ( 1.26 to 1.33 ) | 1.24 ( 1.2 to 1.29 ) | 1.16 ( 1.13 to 1.19 ) | 1.39 ( 1.24 to 1.55 ) |
| ALS | 1.26 ( 1.23 to 1.3 ) | 1.29 ( 1.25 to 1.33 ) | 1.23 ( 1.18 to 1.27 ) | 1.17 ( 1.14 to 1.2 ) | 1.39 ( 1.23 to 1.56 ) |
| AIS | 1.3 ( 1.26 to 1.34 ) | 1.33 ( 1.29 to 1.38 ) | 1.23 ( 1.17 to 1.29 ) | 1.23 ( 1.19 to 1.27 ) | 1.52 ( 1.35 to 1.72 ) |
| AEC | 1.31 ( 1.27 to 1.35 ) | 1.34 ( 1.29 to 1.39 ) | 1.25 ( 1.19 to 1.31 ) | 1.22 ( 1.18 to 1.27 ) | 1.65 ( 1.47 to 1.86 ) |
| ACOB | 1.33 ( 1.3 to 1.36 ) | 1.35 ( 1.32 to 1.39 ) | 1.32 ( 1.28 to 1.36 ) | 1.2 ( 1.17 to 1.23 ) | 1.47 ( 1.33 to 1.63 ) |
| ADS | 1.33 ( 1.31 to 1.36 ) | 1.38 ( 1.34 to 1.41 ) | 1.31 ( 1.26 to 1.35 ) | 1.21 ( 1.18 to 1.24 ) | 1.45 ( 1.31 to 1.61 ) |

## Model 2 - adjuted for age, sex, socioeconomic status, BMI, smoking, alchohol and phyiscal activity

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| ARS | 1.14 ( 1.1 to 1.18 ) | 1.14 ( 1.09 to 1.19 ) | 1.1 ( 1.04 to 1.16 ) | 1.09 ( 1.05 to 1.14 ) | 1.33 ( 1.12 to 1.58 ) |
| CrAS | 1.15 ( 1.11 to 1.18 ) | 1.17 ( 1.13 to 1.21 ) | 1.1 ( 1.05 to 1.15 ) | 1.12 ( 1.09 to 1.16 ) | 1.31 ( 1.15 to 1.5 ) |
| m-ARS | 1.15 ( 1.12 to 1.19 ) | 1.17 ( 1.12 to 1.21 ) | 1.1 ( 1.05 to 1.16 ) | 1.12 ( 1.08 to 1.16 ) | 1.38 ( 1.2 to 1.58 ) |
| AAS-r | 1.16 ( 1.12 to 1.19 ) | 1.19 ( 1.15 to 1.22 ) | 1.13 ( 1.09 to 1.18 ) | 1.13 ( 1.1 to 1.17 ) | 1.25 ( 1.09 to 1.43 ) |
| ALS | 1.16 ( 1.13 to 1.2 ) | 1.19 ( 1.15 to 1.23 ) | 1.11 ( 1.07 to 1.16 ) | 1.14 ( 1.11 to 1.18 ) | 1.36 ( 1.2 to 1.55 ) |
| AAS | 1.17 ( 1.14 to 1.2 ) | 1.2 ( 1.16 to 1.24 ) | 1.14 ( 1.09 to 1.18 ) | 1.13 ( 1.1 to 1.16 ) | 1.36 ( 1.2 to 1.53 ) |
| AIS | 1.19 ( 1.15 to 1.23 ) | 1.23 ( 1.18 to 1.28 ) | 1.12 ( 1.06 to 1.18 ) | 1.19 ( 1.15 to 1.23 ) | 1.48 ( 1.29 to 1.7 ) |
| AEC | 1.2 ( 1.15 to 1.24 ) | 1.22 ( 1.17 to 1.28 ) | 1.13 ( 1.07 to 1.2 ) | 1.18 ( 1.14 to 1.22 ) | 1.59 ( 1.4 to 1.81 ) |
| ACOB | 1.23 ( 1.2 to 1.26 ) | 1.26 ( 1.22 to 1.3 ) | 1.21 ( 1.17 to 1.26 ) | 1.16 ( 1.13 to 1.2 ) | 1.42 ( 1.27 to 1.59 ) |
| ADS | 1.23 ( 1.2 to 1.26 ) | 1.27 ( 1.24 to 1.31 ) | 1.19 ( 1.15 to 1.24 ) | 1.18 ( 1.14 to 1.21 ) | 1.43 ( 1.28 to 1.6 ) |

## Model 3 - adjuted for age, sex, socioeconomic status, BMI, smoking, alchohol, physical activity and number of long-term conditions

| scales | MACE/mortality | All-cause mortality | MACE | Fall or fracture | Dementia/delirium |
|---|---|---|---|---|---|
| CrAS | 1.03 ( 1 to 1.07 ) | 1.05 ( 1.01 to 1.09 ) | 0.99 ( 0.94 to 1.04 ) | 1.06 ( 1.03 to 1.1 ) | 1.22 ( 1.05 to 1.41 ) |

| | | | | | |
|---|---|---|---|---|---|
| ALS | 1.04 ( 1 to 1.07 ) | 1.06 ( 1.02 to 1.1 ) | 0.99 ( 0.94 to 1.03 ) | 1.08 ( 1.04 to 1.11 ) | 1.26 ( 1.09 to 1.46 ) |
| ARS | 1.04 ( 1 to 1.08 ) | 1.03 ( 0.98 to 1.08 ) | 1 ( 0.95 to 1.06 ) | 1.04 ( 0.99 to 1.08 ) | 1.23 ( 1.03 to 1.48 ) |
| m-ARS | 1.05 ( 1.01 to 1.08 ) | 1.05 ( 1 to 1.09 ) | 1 ( 0.95 to 1.06 ) | 1.06 ( 1.02 to 1.1 ) | 1.28 ( 1.1 to 1.49 ) |
| AAS-r | 1.05 ( 1.02 to 1.08 ) | 1.08 ( 1.04 to 1.11 ) | 1.03 ( 0.99 to 1.07 ) | 1.08 ( 1.05 to 1.11 ) | 1.13 ( 0.97 to 1.32 ) |
| AAS | 1.05 ( 1.02 to 1.09 ) | 1.08 ( 1.04 to 1.12 ) | 1.02 ( 0.98 to 1.07 ) | 1.07 ( 1.04 to 1.1 ) | 1.25 ( 1.09 to 1.44 ) |
| AEC | 1.08 ( 1.04 to 1.12 ) | 1.1 ( 1.05 to 1.15 ) | 1.02 ( 0.96 to 1.08 ) | 1.11 ( 1.07 to 1.16 ) | 1.5 ( 1.3 to 1.72 ) |
| AIS | 1.08 ( 1.04 to 1.12 ) | 1.1 ( 1.06 to 1.15 ) | 1 ( 0.95 to 1.06 ) | 1.12 ( 1.08 to 1.17 ) | 1.38 ( 1.19 to 1.61 ) |
| ACOB | 1.12 ( 1.09 to 1.15 ) | 1.14 ( 1.1 to 1.18 ) | 1.11 ( 1.06 to 1.15 ) | 1.1 ( 1.07 to 1.14 ) | 1.33 ( 1.17 to 1.51 ) |
| ADS | 1.12 ( 1.09 to 1.15 ) | 1.16 ( 1.12 to 1.2 ) | 1.08 ( 1.04 to 1.13 ) | 1.12 ( 1.08 to 1.15 ) | 1.34 ( 1.17 to 1.52 ) |

**Sensitivity analysis 3: Model adjusted for all covariates of model 2 plus hypertension, coronary heart disease, diabetes, previous stroke/transient ischaemic attack, and heart failure at baseline, instead of adjusting for morbidity count. For primary outcome (cardiovascular event or death), all-cause mortality, and MACE**

### Hazard ratios per one-point increase in scale

| scales | MACE/mortality | All-cause mortality | MACE |
|---|---|---|---|
| CrAS | 1.1 ( 1.09 to 1.12 ) | 1.11 ( 1.09 to 1.13 ) | 1.06 ( 1.03 to 1.09 ) |
| ARS | 1.11 ( 1.09 to 1.14 ) | 1.12 ( 1.1 to 1.14 ) | 1.07 ( 1.03 to 1.11 ) |
| AAS | 1.11 ( 1.1 to 1.13 ) | 1.12 ( 1.1 to 1.14 ) | 1.1 ( 1.08 to 1.13 ) |
| AAS-r | 1.11 ( 1.1 to 1.13 ) | 1.12 ( 1.11 to 1.14 ) | 1.11 ( 1.09 to 1.14 ) |
| ALS | 1.12 ( 1.1 to 1.13 ) | 1.13 ( 1.11 to 1.14 ) | 1.09 ( 1.06 to 1.12 ) |
| m-ARS | 1.14 ( 1.12 to 1.16 ) | 1.15 ( 1.13 to 1.17 ) | 1.09 ( 1.05 to 1.12 ) |
| AEC | 1.15 ( 1.13 to 1.17 ) | 1.16 ( 1.13 to 1.18 ) | 1.11 ( 1.08 to 1.15 ) |
| AIS | 1.15 ( 1.13 to 1.17 ) | 1.16 ( 1.14 to 1.18 ) | 1.11 ( 1.08 to 1.15 ) |
| ACOB | 1.16 ( 1.14 to 1.18 ) | 1.17 ( 1.16 to 1.19 ) | 1.17 ( 1.14 to 1.2 ) |
| ADS | 1.17 ( 1.16 to 1.19 ) | 1.19 ( 1.17 to 1.2 ) | 1.17 ( 1.14 to 1.2 ) |

## Post-hoc analyses:

### Excluding participants with a prior history of fall or fracture

| scales | Fall/fracture |
|--------|---------------|
| CrAS | 1.09 (1.05-1.12) |
| ARS | 1.06 (1.02-1.1) |
| AAS | 1.09 (1.06-1.12) |
| AAS-r | 1.09 (1.06-1.12) |
| ALS | 1.1 (1.07-1.14) |
| m-ARS | 1.08 (1.04-1.12) |
| AEC | 1.13 (1.09-1.17) |
| AIS | 1.13 (1.1-1.17) |
| ACOB | 1.11 (1.08-1.14) |
| ADS | 1.12 (1.09-1.15) |

### Delirium as outcome, including participants with dementia at baseline

| scales | Delirium |
|--------|----------|
| CrAS | 1.09 (1.05-1.14) |
| ARS | 1.12 (1.07-1.18) |
| AAS | 1.10 (1.06-1.14) |
| AAS-r | 1.14 (1.10-1.18) |
| ALS | 1.11 (1.06-1.16) |
| m-ARS | 1.15 (1.10-1.20) |
| AEC | 1.20 (1.14-1.26) |
| AIS | 1.20 (1.15-1.25) |
| ACOB | 1.12 (1.07-1.16) |
| ADS | 1.12 (1.07-1.16) |

## Scales treated as categorical variables (score 1-2, and score ≥3)

The main analysis assessed the hazard ratio associated with one-point increase in each scale. We also analysed each scale as a categorical variable, the results of which are shown below. There is no generally accepted convention or cut-offs used to categorise anticholinergic scales. For consistency, we applied the same cut-offs to each scale:

- Score 1 – 2 (low)

- Score 3 or more

A score of 0 was the reference group

# Hazard ratio for categorised scales

## Model 1 - Adjusted for age, sex, and socioeconomic status
Primary outcome (MACE or death)

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 1.83 ( 1.76 to 1.9 ) | 2.17 ( 2.04 to 2.31 ) |
| AAS-r | 1.88 ( 1.8 to 1.97 ) | 2.08 ( 1.96 to 2.21 ) |
| ACOB | 1.8 ( 1.73 to 1.87 ) | 2.36 ( 2.23 to 2.49 ) |
| ADS | 1.89 ( 1.82 to 1.96 ) | 2.55 ( 2.42 to 2.69 ) |
| AEC | 1.89 ( 1.79 to 1.98 ) | 1.96 ( 1.83 to 2.1 ) |
| AIS | 1.88 ( 1.78 to 1.97 ) | 2.01 ( 1.89 to 2.14 ) |
| ALS | 1.68 ( 1.62 to 1.74 ) | 2.15 ( 2.03 to 2.28 ) |
| ARS | 1.52 ( 1.43 to 1.61 ) | 1.88 ( 1.75 to 2.01 ) |
| CrAS | 1.54 ( 1.48 to 1.6 ) | 2.04 ( 1.92 to 2.16 ) |
| m-ARS | 1.66 ( 1.58 to 1.74 ) | 1.99 ( 1.86 to 2.12 ) |

All-cause mortality

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 1.85 ( 1.78 to 1.93 ) | 2.21 ( 2.07 to 2.36 ) |
| AAS-r | 1.93 ( 1.84 to 2.02 ) | 2.11 ( 1.98 to 2.26 ) |
| ACOB | 1.82 ( 1.75 to 1.9 ) | 2.43 ( 2.29 to 2.57 ) |
| ADS | 1.93 ( 1.86 to 2.01 ) | 2.64 ( 2.49 to 2.79 ) |
| AEC | 1.92 ( 1.82 to 2.02 ) | 2.01 ( 1.87 to 2.16 ) |
| AIS | 1.94 ( 1.84 to 2.04 ) | 2.06 ( 1.93 to 2.2 ) |
| ALS | 1.71 ( 1.65 to 1.78 ) | 2.19 ( 2.06 to 2.33 ) |
| ARS | 1.52 ( 1.43 | 1.91 ( 1.77 |

| scales | | |
|---|---|---|
| | to 1.62 ) | to 2.05 ) |
| CrAS | 1.56 ( 1.5 to 1.63 ) | 2.06 ( 1.93 to 2.19 ) |
| m-ARS | 1.68 ( 1.59 to 1.77 ) | 2.03 ( 1.9 to 2.18 ) |

MACE

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 2.34 ( 2.19 to 2.5 ) | 2.69 ( 2.41 to 3 ) |
| AAS-r | 2.39 ( 2.22 to 2.58 ) | 2.59 ( 2.32 to 2.88 ) |
| ACOB | 2.34 ( 2.19 to 2.5 ) | 3.21 ( 2.92 to 3.52 ) |
| ADS | 2.21 ( 2.07 to 2.37 ) | 3.38 ( 3.08 to 3.7 ) |
| AEC | 2.11 ( 1.92 to 2.31 ) | 2.01 ( 1.77 to 2.29 ) |
| AIS | 1.99 ( 1.81 to 2.18 ) | 2.07 ( 1.84 to 2.32 ) |
| ALS | 1.91 ( 1.79 to 2.05 ) | 2.48 ( 2.22 to 2.76 ) |
| ARS | 1.52 ( 1.37 to 1.69 ) | 1.9 ( 1.67 to 2.17 ) |
| CrAS | 1.73 ( 1.61 to 1.85 ) | 2.26 ( 2.02 to 2.51 ) |
| m-ARS | 1.62 ( 1.47 to 1.78 ) | 1.99 ( 1.76 to 2.25 ) |

Fall or fracture

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 1.55 ( 1.45 to 1.67 ) | 1.77 ( 1.59 to 1.97 ) |
| AAS-r | 1.63 ( 1.51 to 1.76 ) | 1.78 ( 1.6 to 1.98 ) |
| ACOB | 1.5 ( 1.4 to 1.61 ) | 1.83 ( 1.66 to 2.01 ) |
| ADS | 1.72 ( 1.61 to 1.84 ) | 1.9 ( 1.72 to 2.1 ) |
| AEC | 1.88 ( 1.73 to 2.04 ) | 1.69 ( 1.5 to 1.9 ) |
| AIS | 1.93 ( 1.78 to 2.1 ) | 1.75 ( 1.57 to 1.96 ) |

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| ALS | 1.59 ( 1.49 to 1.7 ) | 1.71 ( 1.54 to 1.9 ) |
| ARS | 1.39 ( 1.26 to 1.54 ) | 1.55 ( 1.37 to 1.75 ) |
| CrAS | 1.49 ( 1.39 to 1.59 ) | 1.67 ( 1.51 to 1.86 ) |
| m-ARS | 1.45 ( 1.32 to 1.58 ) | 1.63 ( 1.45 to 1.83 ) |

Dementia or delirium

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 2.38 ( 1.71 to 3.29 ) | 4.46 ( 2.95 to 6.73 ) |
| AAS-r | 2.03 ( 1.4 to 2.93 ) | 3.24 ( 2.08 to 5.04 ) |
| ACOB | 2.08 ( 1.51 to 2.86 ) | 3.29 ( 2.17 to 5.01 ) |
| ADS | 2.24 ( 1.62 to 3.1 ) | 4.1 ( 2.77 to 6.07 ) |
| AEC | 4.64 ( 3.31 to 6.52 ) | 4.42 ( 2.81 to 6.94 ) |
| AIS | 4.93 ( 3.52 to 6.9 ) | 3.97 ( 2.57 to 6.14 ) |
| ALS | 2.13 ( 1.55 to 2.93 ) | 4.27 ( 2.84 to 6.42 ) |
| ARS | 2.36 ( 1.55 to 3.59 ) | 2.52 ( 1.48 to 4.28 ) |
| CrAS | 2.2 ( 1.61 to 3.02 ) | 3.63 ( 2.37 to 5.55 ) |
| m-ARS | 3.02 ( 2.11 to 4.33 ) | 2.63 ( 1.57 to 4.42 ) |

**Model 2 - Adjusted for age, sex, socioeconomic status, BMI, smoking, alcohol and physical activity**

Primary outcome (MACE or death)

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 1.59 ( 1.53 to 1.66 ) | 1.67 ( 1.57 to 1.79 ) |
| AAS-r | 1.64 ( 1.56 to 1.71 ) | 1.61 ( 1.51 to 1.72 ) |
| ACOB | 1.59 ( 1.53 to 1.65 ) | 1.86 ( 1.75 to 1.97 ) |
| ADS | 1.64 ( 1.57 | 1.98 ( 1.86 |

| scales | | |
|---|---|---|
| | to 1.71 ) | to 2.09 ) |
| AEC | 1.63 ( 1.54 to 1.72 ) | 1.5 ( 1.39 to 1.61 ) |
| AIS | 1.6 ( 1.51 to 1.69 ) | 1.59 ( 1.48 to 1.7 ) |
| ALS | 1.46 ( 1.4 to 1.52 ) | 1.65 ( 1.55 to 1.77 ) |
| ARS | 1.36 ( 1.28 to 1.44 ) | 1.47 ( 1.36 to 1.59 ) |
| CrAS | 1.37 ( 1.31 to 1.42 ) | 1.6 ( 1.51 to 1.71 ) |
| m-ARS | 1.45 ( 1.37 to 1.53 ) | 1.56 ( 1.46 to 1.68 ) |

**All-cause mortality**

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 1.62 ( 1.55 to 1.7 ) | 1.7 ( 1.59 to 1.83 ) |
| AAS-r | 1.68 ( 1.61 to 1.77 ) | 1.64 ( 1.53 to 1.76 ) |
| ACOB | 1.61 ( 1.54 to 1.68 ) | 1.91 ( 1.8 to 2.03 ) |
| ADS | 1.68 ( 1.61 to 1.75 ) | 2.05 ( 1.93 to 2.18 ) |
| AEC | 1.65 ( 1.56 to 1.75 ) | 1.54 ( 1.42 to 1.66 ) |
| AIS | 1.64 ( 1.55 to 1.74 ) | 1.62 ( 1.51 to 1.74 ) |
| ALS | 1.5 ( 1.43 to 1.56 ) | 1.68 ( 1.57 to 1.8 ) |
| ARS | 1.37 ( 1.28 to 1.46 ) | 1.49 ( 1.38 to 1.62 ) |
| CrAS | 1.39 ( 1.33 to 1.45 ) | 1.62 ( 1.52 to 1.74 ) |
| m-ARS | 1.47 ( 1.39 to 1.55 ) | 1.6 ( 1.48 to 1.72 ) |

**MACE**

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 1.9 ( 1.77 to 2.05 ) | 1.91 ( 1.69 to 2.14 ) |
| AAS-r | 1.97 ( 1.82 to 2.14 ) | 1.84 ( 1.64 to 2.07 ) |

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| ACOB | 1.96 ( 1.83 to 2.11 ) | 2.35 ( 2.12 to 2.6 ) |
| ADS | 1.84 ( 1.71 to 1.98 ) | 2.41 ( 2.18 to 2.67 ) |
| AEC | 1.75 ( 1.59 to 1.93 ) | 1.41 ( 1.23 to 1.63 ) |
| AIS | 1.62 ( 1.46 to 1.79 ) | 1.49 ( 1.31 to 1.7 ) |
| ALS | 1.55 ( 1.44 to 1.66 ) | 1.73 ( 1.54 to 1.95 ) |
| ARS | 1.32 ( 1.18 to 1.47 ) | 1.37 ( 1.19 to 1.58 ) |
| CrAS | 1.44 ( 1.33 to 1.54 ) | 1.63 ( 1.45 to 1.84 ) |
| m-ARS | 1.37 ( 1.24 to 1.51 ) | 1.43 ( 1.25 to 1.64 ) |

Fall or fracture

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 1.51 ( 1.4 to 1.63 ) | 1.59 ( 1.41 to 1.79 ) |
| AAS-r | 1.53 ( 1.41 to 1.67 ) | 1.61 ( 1.44 to 1.81 ) |
| ACOB | 1.46 ( 1.35 to 1.57 ) | 1.63 ( 1.46 to 1.81 ) |
| ADS | 1.67 ( 1.56 to 1.79 ) | 1.68 ( 1.51 to 1.88 ) |
| AEC | 1.78 ( 1.63 to 1.94 ) | 1.49 ( 1.3 to 1.69 ) |
| AIS | 1.82 ( 1.67 to 1.98 ) | 1.59 ( 1.41 to 1.79 ) |
| ALS | 1.57 ( 1.46 to 1.68 ) | 1.56 ( 1.39 to 1.76 ) |
| ARS | 1.37 ( 1.24 to 1.52 ) | 1.37 ( 1.2 to 1.56 ) |
| CrAS | 1.46 ( 1.36 to 1.56 ) | 1.53 ( 1.37 to 1.72 ) |
| m-ARS | 1.41 ( 1.28 to 1.55 ) | 1.45 ( 1.28 to 1.65 ) |

Dementia or delirium

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 2.2 ( 1.54 to 3.15 ) | 3.91 ( 2.48 to 6.16 ) |

| scales | | |
|---|---|---|
| AAS-r | 1.85 ( 1.24 to 2.78 ) | 3.03 ( 1.89 to 4.86 ) |
| ACOB | 1.98 ( 1.4 to 2.8 ) | 2.88 ( 1.81 to 4.57 ) |
| ADS | 2.16 ( 1.52 to 3.07 ) | 3.9 ( 2.55 to 5.98 ) |
| AEC | 4.28 ( 2.96 to 6.19 ) | 4.15 ( 2.56 to 6.74 ) |
| AIS | 4.6 ( 3.19 to 6.64 ) | 4.04 ( 2.56 to 6.38 ) |
| ALS | 2.01 ( 1.42 to 2.84 ) | 3.99 ( 2.55 to 6.22 ) |
| ARS | 2.19 ( 1.4 to 3.44 ) | 2.21 ( 1.24 to 3.93 ) |
| CrAS | 2.17 ( 1.55 to 3.05 ) | 3.53 ( 2.24 to 5.57 ) |
| m-ARS | 2.96 ( 2.02 to 4.33 ) | 2.37 ( 1.35 to 4.14 ) |

**Model 3 - Adjusted for age, sex, socioeconomic status, BMI, smoking, alcohol, physical activity and number of long-term conditions**

Primary outcome (MACE or death)

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 1.28 ( 1.22 to 1.34 ) | 1.24 ( 1.16 to 1.33 ) |
| AAS-r | 1.32 ( 1.26 to 1.39 ) | 1.22 ( 1.14 to 1.31 ) |
| ACOB | 1.32 ( 1.27 to 1.38 ) | 1.44 ( 1.35 to 1.53 ) |
| ADS | 1.36 ( 1.3 to 1.42 ) | 1.52 ( 1.43 to 1.62 ) |
| AEC | 1.29 ( 1.22 to 1.36 ) | 1.18 ( 1.09 to 1.27 ) |
| AIS | 1.26 ( 1.19 to 1.33 ) | 1.25 ( 1.17 to 1.34 ) |
| ALS | 1.18 ( 1.13 to 1.23 ) | 1.22 ( 1.14 to 1.31 ) |
| ARS | 1.13 ( 1.06 to 1.2 ) | 1.17 ( 1.08 to 1.26 ) |
| CrAS | 1.13 ( 1.08 to 1.18 ) | 1.21 ( 1.13 to 1.29 ) |
| m-ARS | 1.19 ( 1.13 to 1.26 ) | 1.22 ( 1.14 to 1.32 ) |

All-cause mortality

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 1.3 ( 1.24 to 1.36 ) | 1.25 ( 1.16 to 1.35 ) |
| AAS-r | 1.35 ( 1.28 to 1.42 ) | 1.24 ( 1.15 to 1.33 ) |
| ACOB | 1.34 ( 1.28 to 1.4 ) | 1.47 ( 1.38 to 1.57 ) |
| ADS | 1.39 ( 1.33 to 1.46 ) | 1.57 ( 1.47 to 1.68 ) |
| AEC | 1.3 ( 1.22 to 1.38 ) | 1.2 ( 1.11 to 1.3 ) |
| AIS | 1.29 ( 1.22 to 1.37 ) | 1.27 ( 1.18 to 1.37 ) |
| ALS | 1.21 ( 1.15 to 1.26 ) | 1.23 ( 1.15 to 1.33 ) |
| ARS | 1.13 ( 1.05 to 1.2 ) | 1.18 ( 1.09 to 1.28 ) |
| CrAS | 1.15 ( 1.1 to 1.2 ) | 1.21 ( 1.13 to 1.3 ) |
| m-ARS | 1.2 ( 1.13 to 1.27 ) | 1.24 ( 1.15 to 1.34 ) |

MACE

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 1.47 ( 1.36 to 1.59 ) | 1.32 ( 1.16 to 1.49 ) |
| AAS-r | 1.52 ( 1.4 to 1.66 ) | 1.32 ( 1.17 to 1.49 ) |
| ACOB | 1.6 ( 1.48 to 1.72 ) | 1.74 ( 1.56 to 1.94 ) |
| ADS | 1.47 ( 1.36 to 1.59 ) | 1.75 ( 1.57 to 1.95 ) |
| AEC | 1.3 ( 1.17 to 1.43 ) | 1.04 ( 0.9 to 1.2 ) |
| AIS | 1.19 ( 1.07 to 1.32 ) | 1.09 ( 0.96 to 1.25 ) |
| ALS | 1.18 ( 1.1 to 1.28 ) | 1.16 ( 1.02 to 1.32 ) |
| ARS | 1.04 ( 0.93 to 1.17 ) | 1.02 ( 0.88 to 1.18 ) |
| CrAS | 1.14 ( 1.05 to 1.23 ) | 1.13 ( 1 to 1.27 ) |
| m- | 1.06 ( 0.96 | 1.04 ( 0.9 |

| ARS | to 1.17 ) | to 1.19 ) |

**Fall or fracture**

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 1.31 ( 1.21 to 1.42 ) | 1.31 ( 1.16 to 1.49 ) |
| AAS-r | 1.33 ( 1.22 to 1.45 ) | 1.35 ( 1.2 to 1.53 ) |
| ACOB | 1.29 ( 1.19 to 1.39 ) | 1.38 ( 1.23 to 1.54 ) |
| ADS | 1.48 ( 1.38 to 1.6 ) | 1.44 ( 1.29 to 1.62 ) |
| AEC | 1.53 ( 1.4 to 1.68 ) | 1.28 ( 1.12 to 1.47 ) |
| AIS | 1.58 ( 1.44 to 1.73 ) | 1.37 ( 1.21 to 1.55 ) |
| ALS | 1.38 ( 1.28 to 1.48 ) | 1.32 ( 1.17 to 1.49 ) |
| ARS | 1.21 ( 1.09 to 1.35 ) | 1.17 ( 1.02 to 1.34 ) |
| CrAS | 1.29 ( 1.2 to 1.39 ) | 1.29 ( 1.14 to 1.45 ) |
| m-ARS | 1.23 ( 1.12 to 1.36 ) | 1.23 ( 1.08 to 1.4 ) |

**Dementia or delirium**

| scales | Score 1 to 2 | Score 3 or more |
|---|---|---|
| AAS | 1.72 ( 1.18 to 2.51 ) | 2.65 ( 1.61 to 4.35 ) |
| AAS-r | 1.4 ( 0.92 to 2.13 ) | 2.01 ( 1.21 to 3.35 ) |
| ACOB | 1.53 ( 1.07 to 2.2 ) | 2.05 ( 1.25 to 3.35 ) |
| ADS | 1.73 ( 1.2 to 2.5 ) | 2.75 ( 1.73 to 4.38 ) |
| AEC | 3.33 ( 2.25 to 4.93 ) | 3.3 ( 2 to 5.45 ) |
| AIS | 3.6 ( 2.44 to 5.32 ) | 3.26 ( 2.03 to 5.24 ) |
| ALS | 1.56 ( 1.08 to 2.26 ) | 2.86 ( 1.78 to 4.62 ) |
| ARS | 1.75 ( 1.1 to 2.77 ) | 1.66 ( 0.92 to 2.98 ) |

| CrAS | 1.74 ( 1.22 to 2.48 ) | 2.59 ( 1.6 to 4.19 ) |
| m-ARS | 2.38 ( 1.6 to 3.52 ) | 1.79 ( 1.01 to 3.17 ) |

**Categorisation of Long-Term Conditions**

| Morbidity grouping* | Conditions included |
| --- | --- |
| **Hypertension** | Hypertension<br>Essential hypertension |
| **Coronary heart disease** | Heart attack/MI<br>Angina |
| **Diabetes** | Diabetic nephropathy<br>Diabetic neuropathy/ulcers<br>Diabetes<br>Type 1 diabetes<br>Type 2 diabetes<br>Diabetic eye disease |
| **Stroke/TIA** | Stroke<br>TIA<br>Subarachnoid haemorrhage<br>Brain haemorrhage<br>Ischaemic stroke |
| **Atrial fibrillation** | Atrial fibrillation |
| **Heart failure** | Cardiomyopathy<br>Hypertrophic cardiomyopathy<br>Heart failure/pulmonary oedema |
| **Peripheral vascular disease** | Peripheral vascular disease<br>Leg claudication/intermittent claudication |
| **COPD** | COPD/Chronic obstructive pulmonary disease<br>Emphysema/Chronic bronchitis<br>Emphysema |
| **Asthma** | Asthma |
| **Bronchiectasis** | Bronchiectasis |
| **Cancer** | "yes"/"no" to "have you ever had cancer?" |
| **Dyspepsia** | Gastro-oesophageal reflux (GORD)<br>Oesophagitis/Barrett's oesophagus<br>Gastric stomach ulcers<br>Gastric erosions/gastritis<br>Duodenal ulcer |

|  | Dyspepsia/indigestion<br>Hiatus hernia<br>Helicobacter pylori |
|---|---|
| **Diverticular disease** | Diverticular disease/diverticulitis |
| **Irritable bowel syndrome** | Irritable bowel syndrome |
| **Chronic liver disease** | Oesophageal varices<br>Non infective hepatitis<br>Liver failure/cirrhosis<br>Primary biliary cirrhosis |
| **Inflammatory bowel disease** | Inflammatory bowel disease<br>Crohn's disease<br>Ulcerative colitis |
| **Constipation** | Constipation |
| **Viral hepatitis** | Hepatitis B<br>Hepatitis C<br>Hepatitis D |
| **Depression** | Depression<br>Postnatal depression |
| **Anxiety** | Anxiety/panic attacks<br>Nervous breakdown<br>Post-traumatic stress disorder<br>Obsessive compulsive disorder<br>Stress<br>Insomnia<br>Psychological/psychiatric problem |
| **Schizophrenia/Bipolar affective disorder Bipolar** | Scizophrenia<br>Mania<br>Bipolar disorder<br>Manic depression |
| **Connective tissue diseases** | Myositis/myopathy<br>Systemic lupus erythematosus/SLE<br>Connective tissue disorder<br>Sjogren's syndrome.sicca syndrome<br>Dermatopolymyositis<br>Scloeroderma/systemic sclerosis<br>Rheumatoid arthritis<br>Psoriatic arthropathy<br>Dermatomyositis<br>Polymyositis<br>Polymyalgia rheumatica |

| | |
|---|---|
| **Painful conditions** | Back pain<br>Joint pain<br>Headaches (not migraine)<br>Sciatica<br>Plantar fasciitis<br>Carpal tunnel syndrome<br>Fibromyalgia<br>Arthritis<br>Shingles<br>Disc problem<br>Prolapsed disc/slipped disc<br>Spine arthritis/spondylitis<br>Ankylosing spondylitis<br>Back problem<br>Osteoarthritis<br>Gout<br>Cervical spondylosis<br>Trigeminal neuralgia<br>Disc degeneration<br>Trapped nerve/compressed nerve |
| **Osteoporosis** | Osteoporosis |
| **Thyroid disorders** | Thyroid problem (not cancer<br>Hyperthroidism/thyrotoxicosis<br>Hypothyroidism/myxoedema<br>Grave's disease<br>Thyroid goitre<br>Thyroititis |
| **Alcohol problems** | Alcohol dependency<br>Alcoholic liver disease/alcoholic cirrhosis |
| **Chronic kidney disease** | Polycystic kidney<br>Diabetic nephropathy<br>Renal/kidney failure<br>Renal failure requiring dialysis<br>Renal failure not requiring dialysis<br>Kidney nephropathy<br>Immunoglobulin A (IgA) nephropathy |
| **Prostate disorders** | Prostate problem (not cancer)<br>Enlarged prostate<br>Benign prostatic hypertrophy |
| **Glaucoma** | Glaucoma |
| **Epilepsy** | Epilepsy |
| **Dementia** | Dementia/Alzheimer/cognitive impairment |

| | |
|---|---|
| **Psoriasis or eczema** | Eczema/dermatitis<br>Psoriasis |
| **Migraine** | Migraine |
| **Chronic sinusitis** | Chronic sinusitis |
| **Anorexia or bulimia** | Anorexia, bulimia/other eating disorder |
| **Parkinson's disease** | Parkinson's disease |
| **Multiple sclerosis** | Multiple sclerosis |
| **Chronic fatigue syndrome** | Chronic fatigue syndrome |
| **Endometriosis** | Endometriosis |
| **Meniere disease** | Meniere disease |
| **Pernicious anaemia** | Pernicious anaemia |
| **Polycystic ovaries** | Polycystic ovaries |
| *Self-report lifetime diagnosis by doctor recorded by nurse-led interview (UK Biobank data field 20002), except cancer diagnosis which was reported by touch-screen questionnaire. The list of disease groupings was based on Barnett et al (2012) | |

## Selection of anticholinergic scales

The identification of anticholinergic scales included in this analysis was based on searches for a systematic literature review (registered on PROSPERO: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017076510). The review itself is ongoing, and findings will be published elsewhere. Search strategy and identification of scales is summarized here briefly to explain the choice of scales included in this review.

Medline and Embase were searched up until September 2017 using the following terms:

anticholinergic*.mp or anti-cholinergic*.mp or cholinergic antagonist*.mp or antimuscarinic*.mp or anti-muscarinic*.mp or muscarinic antagonist*.mp

AND

scale*.mp or score*.mp or rank*.mp or rating*.mp or grading*.mp or index.mp or classification.mp

Titles and abstracts here screened by 2 reviewers to identify studies in which anticholinergic medication scales have been validated.

From 6558 abstracts screened, 377 full texts were identified as potentially relevant and screened for inclusion. From these, 14 anticholinergic scales were identified.

Of these 14 scales, 4 were excluded from this UK Biobank analysis:
- Summers' list (Summers 1978): This was not specifically an anticholinergic scale, and also was likely to exclude many more recent medications.
- Ancelin 2006: This was not a scale constructed for this study, but rather the application of an existing scale to a new cohort of patients. Only those medication found in the cohort were listed in the paper, hence we could not re-create the full scale from this text.
- Ellett 2014: This paper listed anticholinergic medication identified from a range of existing scales (all of which were included in our analysis). Medications scoring "1" were also excluded. This was therefore not a distinct anticholinergic scale, rather a collection of medicaitons from existing scales already included in our analysis.
- MARANTE (Klamer 2017): This scale was based on daily dosage calculations. As UK Biobank did not collect data on medication dosage we were unable to include this scale.

This left 10 anticholinergic scales which were included in our analysis: Anticholinergic Drug Scale (ADS),[8] Clinician-rated Anticholinergic Scale (CrAS),[5] Anticholinergic Risk Scale (ARS),[4] Anticholinergic Cognitive Burden (ACoB),[3] Anticholinergic Activity Scale (AAS),[6] revised Anticholinergic Activity Scale (AAS-r),[7] Anticholinergic Loading Scale (ALS),[9] Modified Anticholinergic Risk Scale (m-ARS),[12] Anticholinergic Effect on Cognition (AEC),[10] Anticholinergic Impregnation Scale (AIS).[11]

**Anticholinergic medications and their classification according to each anticholinergic medication scale.**

| Medication | AIS | AEC | mARS | ACoB | AAS (Chew) | ALS | AAS (Ehrt)† | CrAS | ARS | ADS |
|---|---|---|---|---|---|---|---|---|---|---|
| Alimemazine | 1 | 3 | | 1 | | | | | | |
| Alprazolam | 1 | | | 1 | | 1 | | 1 | | 1 |
| Alverine | 1 | | | 1 | | | | | | |
| Amantadine | 2 | 2 | 2 | 2 | | | | | 2 | 1 |
| Amiodarone | | 1 | | | | | | | | |
| Amitriptyline | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Amoxapine | 3 | | | 3 | | | | | | |
| Ampicillin | 1 | | | | | | | | | 1 |
| Aripiprazole | | 1 | | | | | | | | |
| Atenolol | 1 | | | 1 | | | | 1 | | |
| Atropine | 3 | 3 | 3 | 3 | 3 | 3 | | 3 | 3 | 3 |
| Azathioprine | 1 | | | | | | | | | 1 |
| Baclofen | 2 | | 2 | | | | | 2 | 2 | |
| Belladonna | | | | 2 | | | | 3 | | |
| Benazepril | | | | | | | | 1 | | |
| Benztropine | | 3 | 3 | 3 | | | 3 | | 3 | 3 |
| Betaxolol | | | | | | | | 1 | | |
| Biperiden | 3 | | | | | | | | | |
| Bisacodyl | | | | | | 1 | | | | |
| Bromocriptine | 1 | 1 | | | | | | | | 1 |
| Brompheniramine | 3 | | | 3 | | | | | | 3 |
| Bupropion | 1 | | | 1 | | | | 1 | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Captopril | 1 | | | 1 | | | | | | 1 |
| Carbamazepine | 2 | 1 | | 2 | | | | 1 | | 2 |
| Carbidopa ± levodopa | 1 | | 1 | | | 1 | | 1 | 1 | |
| Carbinoxamine | | | | 3 | | | | | | 3 |
| Carisoprodol | | | | | | | | | 3 | |
| Cefamandole | | | | | | | | | | 1 |
| Cefoxitin | 1 | | | | | | | | | 1 |
| Celecoxib | | | | | | 1 | | | | |
| Cephalothin | | | | | | | | | | 1 |
| Cetirizine | 2 | | 2 | | | 2 | | 2 | 2 | |
| Chlordiazepoxide | 1 | | | | | | | 1 | | 1 |
| Chlorphenamine | 3 | 2 | 3 | 3 | | 3 | | 3 | 3 | 3 |
| Chlorpromazine | 3 | 3 | 3 | 3 | 2 | | | 3 | 3 | 3 |
| Chlorthalidone | 1 | | | 1 | | | | | | 1 |
| Cimeditine | 2 | | 2 | 1 | | | | | 2 | 2 |
| Citalopram | 1 | 1 | | | 1 | 1 | 1 | | | |
| Clemastine | | 3 | 3 | 3 | | | | | | 3 |
| Clindamycin | 1 | | | | | | | | | 1 |
| Clomipramine | 3 | 3 | 2 | 3 | | | | | | 3 |
| Clonazepam | 1 | | | | | 1 | | | | 1 |
| Clorazepate | 1 | | | 1 | | | | | | 1 |
| Clozapine | 3 | 3 | 2 | 3 | 3 | | 3 | | 2 | 3 |
| Co-codamol | | | | 2 | | | | | | |
| Codeine | 1 | | | 1 | | 1 | | 1 | | 1 |
| Colchicine | 1 | | | 1 | | | | | | |
| Cortisone | | | | | | | | | | 1 |
| Cyamemazine | 3 | | | | | | | | | |
| Cyclobenzaprine | | | | 2 | | | | 1 | 2 | 2 |
| Cycloserine | | | | | | | | | | 1 |
| Cyclosporine | 1 | | | | | | | | | 1 |
| Cyproheptadine | 3 | 3 | 3 | 2 | | 3 | | | 3 | 2 |
| Darifenacin | | | 2 | 3 | | | | | | 3 |
| Desipramine | | 2 | 2 | 3 | | | | 2 | 2 | 3 |
| Desloratadine | 3 | | | | | | | | | |
| Dexamethasone | 1 | | | | | | | | | 1 |
| Dexchlorpheniramine | 3 | | | | | 3 | | | | |
| Dextromethorphan | | | | | | | | 1 | | |
| Diazepam | 1 | 1 | | 1 | | 1 | 1 | 1 | | 1 |
| Dicycloverine/dicyclomine | | 2 | 3 | 3 | 3 | | | | 3 | 3 |
| Digitoxin | | | | | | | 1 | | | 1 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Digoxin | 1 | | | 1 | | 1 | 1 | | | 1 |
| Diltiazem | 1 | | | | | | | | | 1 |
| Dimenhydrinate | 3 | 2 | | 3 | | | | | | 3 |
| Diphenhydramine | 3 | 2 | | 3 | 2 | | | 3 | 3 | 3 |
| Dipyridamole | | | | 1 | | | | | | 1 |
| Disopyramide | 2 | 2 | | 1 | | | | | | 2 |
| Divalproex sodium | 1 | | | | | | | | | 1 |
| Domperidone | 1 | 1 | | | | 1 | | | | |
| Dothiepin/dosulepin | 2 | 3 | 2 | | | 2 | | | | |
| Doxepin | 3 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | | 3 |
| Doxylamine | 2 | | | | | | | | | |
| Duloxetine | 1 | | | | | | | | | |
| Emepronium | | | | | | | 3 | | | |
| Entacapone | 1 | | 1 | | | | | | 1 | |
| Escitalopram | | | | | 1 | 1 | | | | |
| Estazolam | | | | | | | | | | 1 |
| Famotidine | 1 | | | | | | | | | 1 |
| Fentanyl | 1 | 1 | | 1 | | | | | | 1 |
| Fesoterodine | | 2 | | | | | | | | |
| Fexofenadine | 2 | | | | | 2 | | 2 | | |
| Flavoxate | 3 | | 2 | 3 | | | | | | 3 |
| Flunitrazepam | | | | | | | 1 | | | |
| Fluoxetine | 1 | 1 | | | 1 | 1 | 1 | 1 | | 1 |
| Fluphenazine | 3 | 1 | 3 | | | 3 | | | 3 | 1 |
| Flurazepam | | | | | | | | | | 1 |
| Fluticasone-salmeterol | | | | | | | | | | 1 |
| Fluvoxamine | 1 | | | 1 | | 1 | 1 | | | 1 |
| Furosemide | | | | 1 | | | 1 | | | 1 |
| Gentamicin | 1 | | | | | | | | | 1 |
| Guaifenesin | | | | | | | | 1 | | |
| Haloperidol | 1 | | 1 | 1 | | 2 | | | 1 | |
| Homatropine | | | | | | | | 3 | | |
| Hydralazine | | | | 1 | | | | | | 1 |
| Hydrocodone/dihydrocodeinone | | | | | | | | 2 | | |
| Hydrocortisone | 1 | | | 1 | | | | | | 1 |
| Hydroxyzine | 3 | 1 | 3 | 3 | | | | | 3 | 3 |
| Hyoscine/scopolamine | 3 | 3 | | 3 | | | | 3 | | 3 |
| Hyoscyamine/L-hyoscyamine | | | 3 | 3 | 3 | | | | 3 | 3 |
| Iloperidone | | 1 | | | | | | | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Imipramine | 3 | 3 | 3 | 3 | | 3 | | 3 | 3 | 3 |
| Ipratropium | 3 | | | | | | 3 | | | |
| Isosorbide | 1 | | | 1 | | | | | | 1 |
| Isosorbide dinitrate | | | | | | | | | | 1 |
| Isosorbide mononitrate | | | | | | | | | | 1 |
| Ketorolac | | | | | | | | 1 | | |
| Ketotifen* | | | | | | | | | | 1 |
| Lansoprazole | | | | | | | 1 | | | |
| Levodopa | 1 | | | | | | | | | |
| Levomepromazine/methotrimeprazine | 2 | 2 | 2 | 2 | | | | | | 2 |
| Lithium | 1 | 1 | | | 1 | 1 | | | | |
| Lofepramine | | 3 | 1 | | | | | | | |
| Loperamide | 2 | | 2 | 1 | | 1 | | 1 | 2 | 1 |
| Loratadine | 2 | | 2 | | | 1 | | 1 | 2 | |
| Lorazepam | 1 | | | | | | | | | 1 |
| Loxapine | 2 | | | 2 | | | | | | 2 |
| Lumiracoxib | | | | | | 1 | | | | |
| Maprotiline | 3 | | | | | | | | | |
| Meclozine/meclizine | | | | 3 | | | | | 3 | 3 |
| Meperidine/pethidine | 2 | 2 | | 2 | | | | | | 2 |
| Mequitazine | 3 | | | | | | | | | |
| Metformin | | | | | | 1 | | | | |
| Methadone | 2 | | | | | | | 2 | | |
| Methocarbamol | 1 | | 1 | | | | | 1 | 1 | |
| Methotrexate | | | | | | 1 | | | | |
| Methylprednisolone | 1 | | | | | | | | | 1 |
| Metoclopramide/Reglan | 1 | | 1 | | | 1 | | 3 | 1 | |
| Metoprolol | 1 | | | 1 | | | | 1 | | |
| Midazolam | 1 | | | | | | | | | 1 |
| Mirtazapine | 1 | 1 | 1 | | 1 | | | | 1 | |
| Molindone | | | | 2 | | | | | | 2 |
| Morphine | 1 | | | 1 | | | | 1 | | 1 |
| Naratriptan | | | | | | 1 | | | | |
| Nefazodone | | | | | | | | 1 | | |
| Nifedipine | 1 | | | 1 | | | | | | 1 |
| Nizatidine | 1 | | | | | | | | | 1 |
| Nortriptyline | 3 | 3 | 2 | 3 | 2 | | 2 | 3 | 2 | 3 |
| Olanzapine | 2 | 2 | 2 | 3 | 2 | | 2 | 1 | 2 | 1 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Orphenadrine | | 3 | 3 | 3 | | | 3 | | | 3 |
| Oxazepam | 1 | | | | | 1 | | | | 1 |
| Oxcarbazepine | 2 | | | 2 | | | | | | 2 |
| Oxybutynin | 3 | 3 | 3 | 3 | 2 | 2 | 3 | | 3 | 3 |
| Oxycodone | 1 | | | | | 1 | | 1 | | 1 |
| Pancuronium | | | | | | | | | | 1 |
| Paroxetine | 2 | 2 | 1 | 3 | 2 | 2 | 2 | 2 | 1 | 1 |
| Perphenazine | 3 | 1 | 3 | 3 | | | | 2 | 3 | 1 |
| Phenelzine | 1 | | | | | | | | | 1 |
| Phenobarbital | | | | | | | 1 | 1 | | |
| Pimozide | 2 | 2 | | 2 | | | | | | 2 |
| Piperacillin | 1 | | | | | | | | | 1 |
| Pipotiazine | 1 | | | | | | | | | |
| Pramipexole | 1 | | 1 | | | | | | 1 | |
| Prednisolone | 1 | 1 | | | | | | | | 1 |
| Prednisone | 1 | | | 1 | | | | | | 1 |
| Prochlorperazine | 2 | 2 | 2 | | | 2 | | 2 | 2 | 1 |
| Procyclidine | | 3 | 3 | 3 | | | | | | 3 |
| Promazine | | 2 | | 3 | | | 2 | | | |
| Promethazine | 3 | 3 | 3 | 3 | | | | | 3 | 3 |
| Propantheline | | 2 | | 3 | | | | 2 | | 3 |
| Propericiazine/pericyazine | 1 | | 2 | | | | | | | |
| Propiverine | | | 2 | | | | | | | |
| Propoxyphene | | | | | | | 1 | 2 | | |
| Protriptyline | | | | | | 3 | | | | 3 |
| Pseudoephedrine ± triprolidine | 2 | | 2 | | | 2 | | | 2 | |
| Pyrilamine/mepryamine | | | | 3 | | | | | | 3 |
| Quetiapine | 2 | 2 | 1 | 3 | 1 | | 1 | 2 | 1 | |
| Quinidine | 1 | 1 | | 1 | | | | | | |
| Ranitidine | 1 | | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 2 |
| Reboxetine | | 1 | | | | | | | | |
| Risperidone | 1 | | 1 | 1 | | 1 | | 1 | 1 | |
| Robitussin | | | | | | | | 1 | | |
| Selegiline | 1 | | 1 | | | | | | 1 | |
| Sertindole | | 1 | | | | | | | | |
| Sertraline | 1 | 1 | | | | | | 1 | | 1 |
| Solifenacin | 3 | 1 | 2 | | | | | | | |
| Sumatriptan | | | | | | 1 | | | | |
| Temazepam | 1 | 1 | | | 1 | 1 | | | | 1 |
| Theophylline | 1 | | | 1 | | 2 | 1 | | | 1 |
| Thioridazine | | | 3 | 3 | 3 | | 3 | 3 | 3 | 3 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Thiothixine | | | | | | | | | 3 | 1 |
| Tiotropium | | | 2 | | | | | | | |
| Tizanidine | 3 | | 3 | | | | | | 3 | |
| Tolterodine | 3 | 2 | 2 | 3 | 3 | 3 | | 3 | 2 | 3 |
| Tramadol | 1 | | | | | 2 | | 2 | | 1 |
| Trandolapril | | | | | | | | 1 | | |
| Trazodone | 1 | | 1 | 1 | | | | 1 | 1 | |
| Triamcinolone | 1 | | | | | | | | | 1 |
| Triamterene | 1 | | | 1 | | | | | | 1 |
| Triazolam | | | | | | | | 1 | | 1 |
| Trifluoperazine | | 2 | 3 | 3 | | | | | 3 | 1 |
| Trihexyphenidyl /Benzhexol | 3 | 3 | | 3 | | | 3 | 3 | | 3 |
| Trimipramine | 3 | 3 | 2 | 3 | | | 3 | | | 3 |
| Triprolidine | 2 | | | | | | | | | |
| Tropatepine | 3 | | | | | | | | | |
| Trospium | 3 | | 2 | | | | | | | |
| Valproic acid | 1 | | | | | | | | | 1 |
| Vancomycin | 1 | | | | | | | | | 1 |
| Venlafaxine | | | | | 1 | | | 1 | | |
| Warfarin | 1 | | | 1 | | | | | | 1 |
| Ziprasidone | | | | | | | | | 1 | |
| Zolmitriptan | | | | | 1 | | | | | |

*Ophthalmic preparation.

†Original 4-point scale modified by combining scores '1' or '2' to score as '1', scoring '3' as '2', and '4' as '3' to fit the 3-point scale system of other scales.