Medicine optimisation and deprescribing intervention outcomes for older people with dementia or mild cognitive impairment: a systematic review

Drugs & Aging

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Medication-related outcomes data

Outcome: Psychotropic medication	
Medication Review and Healthcare Professional Education Intervention	Ballard et al 2016 There was a significant reduction in antipsychotic use in those in the antipsychotic review group compared with the non-review group (odds ratio 0.17, 95% CI 0.05 to 0.60, p=0.006). The intervention significantly reduced antipsychotic use in people with dementia by 50%, even in a population with a baseline antipsychotic use below 20%.
	Brodaty et al 2018 There was a significant reduction in antipsychotic use after the intervention with 81.7% (95% CI: 72.4-89.0) of participants (n=76/93) having their regular antipsychotics deprescribed at 12 months.
	Cossette et al 2020 Antipsychotic deprescribing was attempted for 220/344 (64%) residents, with complete cessation observed in 116 (52.7%) and dose reduction in 72 (32.7%) for a total of 188 residents (85.5%, 95% CI: 80.1%, 89.8%). Antipsychotic re-prescription occurred at 6 months in 7 of the 59 residents who had complete cessation from baseline to 3 months, and at 9 months in 7 of 36 residents with complete cessation from 3 to 6 months.
	Cossette et al 2022 Antipsychotic deprescribing was attempted between baseline and 9 months for 46.8% of residents in phase 2, decreasing from 64.0% in phase 1. For residents for whom deprescribing was attempted, achievement of cessation or dose reduction decreased from 85.5% (95% CI 80.1%-89.8%) in phase 1 to 77.1% (95% CI 74.8% - 79.2%) in phase 2. The small decreases from phase 1 to phase 2 should be interpreted in the context of a single optimal long-term care centre being selected per region in phase 1 compared with the selection of multiple long term care centres centres reaching 30% of the region's residents in phase 2. In both phases successful antipsychotic deprescribing was associated with significantly greater cessation than initiation of benzodiazepines; a small decrease in cessation occurred in phase 2 and similar results were found for antidepressants.

	Kroger et al 2023 Residents in the intervention nursing home were receiving approximated twice the mean regular number of antipsychotics (0.64) as residents in the control nursing homes (0.39). There was a significant decrease at the of follow-up in the control sites (mean number of regular antipsychotics per resident = 0.30, p=0.02) but there was not significant change in the intervention nursing homes (mean number of regular antipsychotics per resident = 0.58, p = 0.21). p = 0.27 for the difference in differences.
	Massot Mesquida et al 2019 The number of psychotropic drugs prescribed was reduced by 28% (from 636 before to 458 after the intervention; p<0.0001). The pre and post intervention difference in the number of drugs prescribed per patient was 0.755 (95% CI 0.624 - 0.886), 0.771 (95% CI 0.635-0.908) at 1 month and 0.634 (95% CI 0.474-0.794) at 6 months (p=0.000 in all cases). At 1 month after discontinuation, 4 (2%) discontinued psychotropic drugs were reintroduced and 12% of drugs (n=22) were restarted at 6 months. The mean number of psychotropic drugs prescribed per patient decreased from 2.71 (SD 1.47) at baseline to 1.95 (1.26) at 1 month post intervention and 2.01 at 6 months (SD 1.36) (p < 0.001 for both time points).
	Muniz et al 2020 For residents with dementia who remained in the nursing home during the complete study period (n=107), a significant reduction of psychotropic medication was confirmed for atypical neuroleptics (42.7% to 18.7% of prescription frequency), for hypnotics (47.7% to 12.1%) and for long half-life benzodiazepines (25.2% to 6.5%) (p<0.0005).
	Muniz et al 2021 The mean number of psychotropic prescriptions was reduced from 1.9 (SD 1.1) to 0.9 (1.0) representing an absolute reduction of one medication per patient and a relative reduction of 52.6%.
	Smeets et al 2021 The prescription of any type of psychotropic drugs increased in the intervention group, and decreased in the control group, with an estimated difference of 3.9 percentage points per 6 months (p = 0.01).
	Wilchesky et al 2018 Reduction in the use of antipsychotic agents was minimal; three antipsychotic agents were stopped, two were increased and for one the dosage was reduced. There were very few prescriptions for cholinesterase inhibitors or memantine with only five at baseline and four at end of follow-up
Medication Review Intervention	Bravo-José et al 2019 For 80% patients (n=28) antipsychotic treatment completely withdrawn and in 20% reduced to minimum effective dose in (n=7). Treatment was resumed in 2 patients due to worsening symptoms.
	Kable et al 2023 There were no differences in the proportion of participants on at least one psychotropic medication between sites and phases at each timepoint (admission to discharge p = 0.275, discharge to three months p = 0.915).
	Liu et al 2022 There were significant decreases in the number of prescriptions for benzodiazepines (−0.05; 95% CI, −0.09 to −0.01; p = 0.008) but no significant decreases in antipsychotics compared to usual care (−0.03; 95% CI, −0.08 to 0.00; p = 0.126),
	Weeks et al 2019 All three interventions were associated with statistically significant lower milligram-equivalent daily dose of antipsychotic, anxiolytic and antidepressant at T2 when compared to T0 (pre-intervention). STOPP/START was more consistently effective than the other tools.

Patient, Carer and/or Healthcare Professional Education Intervention	Martin and Tannenbaum 2017 Complete discontinuation of benzodiazepines was achieved in 39 participants with MCI (32% of MCI participants). 16 additional MCI participants (13.1% of MCI participants) significantly reduced their benzodiazepine dose. 55 (45.1%) of MCI participants achieved cessation or dose reduction compared to 65 (46.8%) of participants with normal cognition.
	Pasina et al 2016 The number of patients with dementia receiving at least one antipsychotic agent reduced significantly from 66 (36.5%) at T0 (pre-intervention) to 50 (27.6%) at T1 (5 months post intervention) (p=.001) and 40 (22.1% at T2 (9 months post intervention) (p=.007). The number of patients with dementia receiving duplicates of antipsychotics decreased from 15 (8.3%) at T0 to 1 (0.6% at T1 (p=.0002) and T2.
	Walsh et al 2022 The levels of prescribing remained relatively stable for all classes of psychotropics in residents with dementia during the period from 3 months pre intervention to 3 months after, except antipsychotics which decreased slightly from 44% at baseline (n=19) to 36% at T3 (3 months post intervention) (n=14). The level of month psychotropic PRN administrations to residents with dementia fell substantially from 90 incidences/month at T0 to 69 incidences/month at T3
Outcome: Potentially Inappropriate Medications (PIMs)	
Medication Review and Healthcare Professional Education Intervention	Kröger et al 2023 The proportion of residents receiving “sometimes” appropriate medications stayed the same from baseline to end of follow-up and the proportion of residents receiving “exceptionally” appropriate medications reduced from 19% to 17% in the intervention sites (p=0.43) and 28% to 21% (p = 0.007) in the control sites.
	Wilchesky et al 2018 There was a significant decrease in the total number of "sometimes" appropriate medications (from 194 pre to 167 post intervention, p=0.0003). The odds ratios estimating the risks of having at least one prescription of “exceptionally appropriate” or “sometimes appropriate” medication post-intervention were 0.82 (95% CI: 0.52–1.30) and 0.83 (95% CI: 0.74–0.94), respectively.
Medication Review Intervention	Coli et al 2022 There was a statistically significant post intervention reduction in frequency of total PIMS from mean of 1.8 [SD 1.6] per patient to 1.7 [SD 1.6], p<0.01 and actionable PIMS from 0.6 [SD 1.0] to 0.5 [1.0], p<0.01. Patients with any PIMS reduced from 141 (78%) to 134 (74%), p=0.02.
	Gustafsson et al 2018 PIMS decreased significantly in the intervention group from 20.3% to 14.2% (p=0.002) between admission and discharge. In the control group, the overall percentage decreased significantly from 20.7% to 18.4% (p=0.025). The decrease in overall number of PIMs in the intervention group was significantly larger than in the control group (p = 0.011).
	Kable et al 2023 There was a significant decrease in the mean number of PIMs at all sites from admission to discharge, but after adjusting for age, gender and discharge destination, there was no significant treatment effect for PIMs at admission compared to discharge (p-0.366) or at discharge compared to 3 months (p=0.391).

	Liu et al 2022 The intervention resulted in significantly fewer PIMs prescriptions compared to usual care after 12 months (-0.35 PIMs; 95% CI -0.49 - -0.20, p<0.0001). The intervention group received fewer PIMs for dementia or cognitive impairment (−0.14; 95% CI, −0.23 to −0.05; p = 0.002) and CNS-active PIMs (−0.28; 95% CI, −0.42 to −0.14; p < 0.0001) than those receiving usual care at 12-months. The total number of PIMs for dementia or cognitive impairment decreased in the intervention group and increased in the usual care group.
	Pearson et al 2021 (Living with Dementia clinical initiative) The 6-month PIM discontinuation rate was 60.0% (9 out of 15). This contributed to a 6-month reduction in baseline PIM usage from 1.5 PIMs per patient to 0.9 PIMs per patient
	Silva-Almodóvar, 2020 45% (n=8002/ 17933) patients discontinued at least 1 medication. In the year 11608 PIMs were discontinued as a result of the automated targeted medication review.
Patient, Carer and/or Healthcare Professional Education Intervention	Bayliss et al 2022 At 6 months, the estimated percentages of patients in the intervention and control groups taking 1 or more PIMs were similar (17.8% [95% CI, 15.4%-20.5%] vs 20.9% [95% CI, 18.4%-23.6%]; p = .08).
Outcome: Total medications	
Medication Review and Healthcare Professional Education Intervention	Kroger et al 2023 The mean number of regular medications per participant decreased from 7.69 to 5.90 in the control nursing homes (p < 0.05) and from 7.1 to 6.6 (p = 0.21) in the intervention nursing homes.
	Wilchesky et al 2018 The total number of regular medications decreased by 12.1%, from 372 at baseline to 327 at the end of follow-up (odds ratio: 0.81; 95% CI: 0.70–0.92). The mean number of regular medications per participant decreased from 7.86 to 6.81 (p = 0.007).
Medication Review Intervention	Andrew et al 2018 Residents with dementia were taking fewer medications following the intervention (mean 15.9, SD 0.6 pre-intervention versus 14.4, SD 0.4 post-intervention; p = 0.04).
	Liu et al 2022 The total number of medications increased significantly less in the intervention when compared with usual care (-.053; 95% CI -0.92 - -0.14, p =0.008).
	Molist Brunet et al 2014 There was a decrease of an average of 2.45 medications per person (66.30%) to 4.8 at discharge, excluding medications initiated to address the complaint they were admitted for (p < 0.05).
	Sakakibara et al 2015 From initial visit to 3 months, the number of prescription drugs in the intervention group reduced by an average of 2.6 drugs from 7.1±2.3 to 4.5±2.1 (p<0.01), whereas it increased slightly from 6.0±2.7 to 6.7±2.4 in the non-intervention group.

Patient, Carer and/or Healthcare Professional Education Intervention	Bayliss et al 2022 At baseline a similar mean number of long-term medications were prescribed in the intervention group (7.0 [SD 2.1]) and in the control group (7.0 [2.2]). At 6 months, the adjusted mean number of long-term medications was similar in the intervention and control groups (6.4 [95% CI, 6.3-6.5] vs 6.5 [95% CI, 6.4-6.6]; p=.14).
Outcome: Anticholinergic burden	
Medication Review and Healthcare Professional Education Intervention	Yeh et al 2013 Compared with baseline, anticholinergic burden (measured using the Clinician-Rated Anticholinergic Score) was significantly reduced at 12-week follow up in the intervention group (mean difference = -0.5, 95% CI = -0.9-0.1, p=0.038) and it remained unchanged in the reference group (mean difference = 0.1, 95% CI = -0.2 -0.3, p=0.414).
Medication Review Intervention	Coli et al 2022 There was a significant reduction in anticholinergic burden scores among all patients (mean 1.5 [SD 1.8] to 1.3 [1.7], n=180, p<0.01), patients for whom pharmacist recommendations were made (2.2 [2.0] to 1.9 [2.0], n=89, p<0.01) and patients for whom the recommendations were acted upon (2.5 [1.8] to 1.3 [1.7], n=19, p<0.01). The decrease was not significant (0.8 [SD 1.2] to 0.7 [1.2], n=91, p=0.4) for patients for whom pharmacist recommendations were not made.
	Jaidi et al 2018 Anticholinergic burden score was successfully reduced by at least 20% in 78 patients (62.4%).
	Kable et al 2023 The mean mean anticholinergic burden score (mACB) score decreased for all phase/site combinations from admission to discharge, however, no treatment effect was seen (p=0.086). The mean mACB score increased from discharge to 3 months at the control site in both phases, and did not change significantly at the intervention site, and no overall treatment effect was seen (p=0.608). Reduced PIMs at discharge were correlated with reduced anticholinergic burden (rho = 0.48–0.55, p < 0.001).
	Liu et al 2022 There was a significant increase in anticholinergic burden score of 0.20 points more after 12 months for those receiving usual care compared to those receiving the intervention (95% CI, −0.39 to −0.01; p = 0.035), with no effect on the anticholinergic burden score of those receiving the intervention.

CI	Confidence Interval
CNS	Central Nervous System
MCI	Mild Cognitive Impairment
PIMs	Potentially Inappropriate Medications
SD	Standard Deviation
STOPP/START	Screening Tool of Older Person's Prescriptions / Screening Tool to Alert to Right Treatment

Clinical-related outcomes data

Outcome: Behavioural and Psychological Symptoms of Dementia (BPSD)	
Medication Review and Healthcare Professional Education Intervention	Ballard et al 2016 Those in the antipsychotic review group experienced a significantly worse outcome on overall neuropsychiatric symptoms in comparison to those not assigned to antipsychotic review. Hallucinations and delusions were absent at baseline and 9 months in more than 85% of residents.
	Brodaty et al 2018 There was no significant behavioural and social withdrawal over the study period on deprescription of regular antipsychotics.
	Cossette et al 2020 In the antipsychotic cessation sub-group, a decrease of 30% or greater (improvement) in the CMAI score was observed more frequently than an increase of 30% or greater (worsening).
	Cossette et al 2022 In both phases, a greater percentage of residents were observed to have clinically significant (≥30%) decreases in CMAI scores (indicating improvement) than clinically significant increases in CMAI scores. In phase 2 (scale-up study), a slight decrease in the percentage of residents with improved BPSD was observed compared with phase1 (initial study).
	Kroger et al 2023 There was an 8.3% reduction in levels of agitation in the intervention group, with a decrease in mean CMAI score of 3.2 points (p=.0002), compared to a decrease of 1.4% in the control group (p=.026).
	Maidment et al 2020 An increase of 0.9 points in the NPI total score from baseline to 3 months for the group whose medication changed (at baseline mean 17.4, SD 13.9; at 3 months mean 18.3, SD 12.3). This compared to increase of 22.8 points for those with no changes to medication (at baseline mean 22.3, SD 24.0; at 3 months mean 45.1, SD 32.0; p=.03).
	Muniz et al 2021 Neuropsychiatric symptoms improved (pre-intervention mean NPI-Q score 2.5 [SD 3.1], post-intervention mean 2.1 [SD 2.5], p = .008). Doctors spontaneously shared positive subjective experiences during the intervention period. Patients seemed to be more aware, and improvements in the home's atmosphere were reported.
	Smeets et al 2021 NPI-Q scores remained fairly constant, not showing statistically significant differences. NPI cluster and symptom scores did not show significant differences either. CMAI scores showed a slight but not statistically significant increase of 2.6 points (SD 15.5) in the intervention group and 0.5 points (SD 10.0) in the control group.
	Wilchesky et al 2018 Levels of agitation did not change, 6/44 showing severe agitation pre-intervention compared to 5/39 post-intervention.
Medication Review Intervention	Bravo-Jose et al 2019 No statistically significant changes in neuropsychiatric symptoms between pre- and post-intervention were found, assessed with the NPI-NH (12.91 ± 12.80 vs 13.76 ± 16.68; p = 0.124). Worsening symptoms led to treatment being resumed in two patients, but significant behavioural abnormalities were not experienced by the remaining patients.

	Jaidi et al 2018 Reduction of anticholinergic burden by at least 20% led to a significant reduction in both the frequency x severity NPI-NH score (odds ratio adjusted: 3.5, 95% CI: 1.6 - 7.9; Wald X2 = 9.32, df = 1, p = .002) and the occupational disruptiveness score (odds ratio adjusted: 9.9, 95% CI: 3.6 - 27.3; Wald X2 = 19.94, df = 1, p < .0001). There was also an association between a reduction of the frequency x severity score and a high probability of depression (odds ratio adjusted: 3.6, 95% CI: 1.6 - 8.0; Wald X2 = 9.61, df = 1, p = .002).
Patient, Carer and/or Healthcare Professional Education Intervention	Walsh et al 2022 There was minimal change in the total NPI-NH score and total occupational disruptiveness score between baseline and 3 months post-intervention.
Outcome: Falls	
Medication Review and Healthcare Professional Education Intervention	Brodaty et al 2018 Deprescribing regular antipsychotics was not associated with significant changes in falls over the study period.
	Cossette et al 2020 Decreases and increases in falls were observed for similar numbers of residents.
	Cossette et al 2022 A higher percentage of residents had a decrease in falls (p<.05) in phase 2 compared to phase 1.
Medication Review Intervention	Coli et al 2022 A significant increase in the proportion of the 111 patients included in falls risk analysis who reported feeling unsteady post-intervention was found both overall (47 to 53%, p=.02) and among those in the recommendation group (50 to 60%, n=60, p=.04). However, for the subset of patients for whom PIMs had been acted on no significant difference was found (38 to 46%, n=13, p = 1).
	Weeks et al 2019 Interventions were not associated with higher rates of falls.
Patient, Carer and/or Healthcare Professional Education Intervention	Walsh et al 2022 Numbers of residents experiencing a fall in the previous 24 days remained static at between 7 and 10 from month to month.

Outcome: Health-Related Quality of Life (HRQOL)	
Medication Review and Healthcare Professional Education Intervention	Ballard et al 2017 Those receiving antipsychotic review showed a 4.54 (95% CI - 9.26 to 0.19) point worsening in DEMQOL-Proxy scores (p=.06), approaching statistical significance (Cohen's d effect size 0.32), driven by a significant decrease in the DEMQOL domains of negative emotion (mean difference - 1.60, 95% CI -2.89 to -0.31; p=0.02) and appearance (mean difference -0.49, 95% CI -0.94 to -0.04, p=0.04). Sensitivity analyses showed statistical significance for worsening of total DEMQOL-Proxy in the best-case scenario analysis.
	Muniz et al 2021 Total HRQOL score did not change significantly (p=.541) but there was significant improvement in response to surroundings (p<.0005) and a trend of improvement in feelings and mood (p = .037).
Medication Review Intervention	Sakakibara et al 2015 HRQOL scores were maintained in the intervention group (differences in scores -0.03 ± 0.29) but decreased slightly in the non-intervention group (differences in scores -0.13 ± 0.29). There were significant differences in HRQOL between the benzodiazepine reduction group from initial visit to 6 months (p<.05) and compared to both the benzodiazepine non-reduction group and the non-intervention groups six months after initial visit (p<.05).
Outcome: Cognition	
Medication Review and Healthcare Professional Education Intervention	Brodaty et al 2018 There were no significant improvements in cognition over the study period following deprescription of regular antipsychotics.
	Yeh et al 2013 MMSE in both the intervention and reference groups remained similar between baseline and post-intervention (Intervention group MMSE mean difference = -0.1, 95% CI: -0.9-0.6, p=.947; Reference group: MMSE = -0.9, 95% CI: -1.8-0, p=0.073).
Medication Review intervention	Coli et al 2022 A statistically significant decrease in converted MMSE scores was found for the 41 patients who had both pre- and post-intervention cognitive tests (mean 20.5 [SD 5.6] to 18.0 [SD 8.4], p<.01) and for the 21 of these patients in the recommendation group (mean 21.5 [SD 5.6] to 18.8 [SD 7.1], p=.01).

BPSD	Behavioural and psychological symptoms of dementia
CI	Confidence Interval
CMAI	Cohen-Mansfield Agitation Inventory
DEMQOL-Proxy	Proxy measure of quality of life in dementia
HRQOL	Health-Related Quality of Life
MMSE	Mini Mental State Examination
NPI	Neuropsychiatric Inventory
NPI-NH	Neuropsychiatric Inventory – Nursing Home
NPI-Q	Neuropsychiatric Inventory - Questionnaire
PIMs	Potentially Inappropriate Medications
SD	Standard Deviation

Safety-related outcomes data

Outcome: Mortality	
Medication Review and Healthcare Professional Education Intervention	Ballard et al 2016 Antipsychotic review conferred a non-significant reduction in mortality (odds ratio 0.67, 95% CI 0.39-1.14, p=0.15).
	Cossette et al 2020 Death was less frequent in residents who had their antipsychotics deprescribed (n=17, 7.5% vs n=8, 19.5%; p=.04).
Medication Review Intervention	Weeks et al 2019 Interventions were not associated with mortality rate.
Patient, Carer and/or Healthcare Professional Education Intervention	Bayliss et al 2022 No differences in mortality rates between the intervention and control clinics were found during the 4 months after the index date (adjusted risk ratio for mortality, 1.24 [95% CI, 0.82-1.88]).
	Boyd et al 2024 Both groups had zero deaths "likely" attributed to a medication change.
Outcome: Hospital attendance	
Medication Review and Healthcare Professional Education Intervention	Brodaty et al 2018 Deprescribing regular antipsychotics was not associated with significant changes in hospitalisations over the study period.
	Yeh et al 2013 Hospitalisation rates were similar between groups (20% vs 22.2%, p=.99).

Medication Review Intervention	Gustafsson et al 2017 18.9% (40/212) of patients in the intervention group and 23.0% (50/217) in the control group readmitted (HR 0.80, 95% CI 0.53–1.21, p = .28, univariable Cox regression). A Kaplan-Meier survival analysis showed no significant difference in time to drug-related readmission within 180 days between the intervention and control groups (160.0 (SD 3.3) days vs 150.1 (4.0) days, Mantel-Cox log rank test, p = .28). The intervention group had a significantly higher prevalence of heart failure (p = .04), with this associated with a higher risk of drug-related readmissions (HR 2.48, 95% CI 1.64–3.76, p < .001). After adjustment for heart failure as a potential confounder and an interaction term, multiple Cox regression analysis indicated that the risk of drug-related admissions significantly decreased with the intervention (HR = 0.49, 95% CI = 0.27–0.90, p = .02). In subgroup analyses for patients without heart failure (140 intervention and 163 control), the drug-related readmission rate at 180 days was significantly lower in the intervention group compared to the control group (11% [15/140] and 20% [33/163], p = .02). Also, significantly longer time to drug-related readmission within 180 days for the intervention group than the control group (171.2 [SD 2.7] days vs 153.1 [4.5] days, Mantel-Cox log rank test, p = .02). For drug-related readmissions within 30 days of discharge in the total population, a significant difference between the groups was found both in frequency (intervention group 5% [11/212]; control group 11% [24/217], p = .03) and in time to readmission (29.1 [SD 0.30] days vs 28.1 [0.43] days, Mantel-Cox log rank test, p = .03). However, no difference between the groups was found in analyses for certain and probable (but not possibly) drug-related readmissions, adjusting for heart failure (HR = 0.46, 95% CI = 0.18–1.18, p = .10).
	Gustafsson et al 2018 No significant difference was found between the groups in drug-related readmissions within 180 days. No significant difference was found in all-cause emergency department (ED) visits within 180 days or time to first all-cause ED visits.
Patient, Carer and/or Healthcare Professional Education Intervention	Bayliss et al 2022 No differences in hospitalisation rates between the intervention or control clinics for individuals in the full cohort during the 4 months after the index date (adjusted risk ratio 0.92 [95% CI, 0.77-1.09]).
	Boyd et al 2024 Rates for hospitalisations were insignificantly lower for intervention vs delated control [risk ration 0.92 (95% CI 0.72, 1.16)]. Emergency Department visits (during the 8 months for which they were assessed) were insignificantly lower for patients in the intervention clinics [risk ratio 0.87 (95% CI 0.67, 1.14)]. Across all event types, medication changes preceding events that were found to be potentially related to the event were often titrations for managing chronic illness, such as diuretic management for congestive heart failure.

CI	Confidence Interval
HR	Hazard ratio
SD	Standard Deviation

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