Outcome measures for interventions to reduce inappropriate prescribing of chronic drugs: a narrative review

SUPPLEMENTARY INFORMATION

Search strategy, list of articles and details on studies and measures

Carole E. Aubert, MD, Eve A. Kerr, MD, MPH, Jennifer K. Maratt, MD, MS, Mandi L. Klamerus, MPH, Timothy P. Hofer, MD, MSc.

Supplementary Text S1. Search strategy

Concepts #1 and #2 were combined with the Boolean operator "AND". Concept #3 was added with the Boolean operator "OR" (i.e. (Concept #1 AND Concept#2) OR Concept #3).

Concept #1: low-value prescribing

(("low-value" or harmful or "low value" or inappropriate or unnecessary or wasteful or waste or overus* or futile or futility or "non-essential" or "non essential" or nonessential or "non-beneficial" or nonbeneficial or "not appropriate" or "no indication" or "not indicated" or "without indication" or overtreat* or "over-treat*" or "absence of indication" or "absence of proper indication" or "absence of a proper indication" or "absence of an indication" or "appropriateness of indication" or "appropriateness of polypharmacy" or "appropriate indication" or "appropriate polypharmacy") adj3 (therapeutic* or drug* or medication* or medicine* or prescription* or prescrib* or pharmaceutical* or polypharmacy or antidepressant* or "anti-depressant*" or antidepressive* or "anti-depressive*" or PPI* or "proton-pump inhibitor*" or antacid* or "proton pump inhibitor*" or "beta-blocker*" or betablocker* or laxative* or benzodiazepine* or hypnotic* or "z-drug*" or neuroleptic* or antipsychotic* or phenothiazine* or antihistamine* or "anti-histamine*" or "loop diuretic*" or "cholinesterase inhibitor*" or "acetylcholinesterase inhibitor*" or diltiazem or verapamil or amiodarone or digoxin or alphablocker* or "alpha-blocker*" or statin* or anticholinergic* or "anti-cholinergic*" or antimuscarinic* or "anti-muscarinic*" or levodopa or "dopamine agonist*" or nsar* or nsaid* or "non-steroidal antirheumatic*" or "non-steroidal anti-rheumatic*" or "non steroidal antirheumatic" or "non steroidal anti-rheumatic*" or "non-steroidal antiinflammatory" or "non steroidal antiinflammatory" or "non-steroidal anti-inflammatory*" or "non steroidal anti-inflammatory" or oestrogen* or androgen* or theophylline or thiazolidenedione or metformin or prochlorperazine or metoclopramide or "anti-emetic*" or antiemetic or antihypertensive or "anti-hypertensive" or (hypertension adj2 (therapeutic* or drug* or medication* or medicine* or prescription* or prescrib* or pharmaceutical* or treatment*)) or (diabetes adj2 (therapeutic* or drug* or medication* or medicine* or prescription* or prescrib* or pharmaceutical* or treatment*)) or ("blood pressure" adj2 (therapeutic* or drug* or medication* or medicine* or prescription* or prescrib* or pharmaceutical* or treatment*)) or antidiabetic or "anti-diabetic")).ab,ti.

OR

(overprescription* or overprescrib* or over-prescription* or over-prescrib* or "beers criteria" or STOPP).ab,ti.

OR

Inappropriate Prescribing/

OR

Potentially Inappropriate Medication List/

Concept #2: intervention to reduce concept low-value prescribing

Deprescriptions/

OR

Withholding Treatment/

OR

(reduce or reducing or reduction or reduced or withdraw* or withhold* or stop or stopped or stopping or elimin* or tapering or taper or cease or ceasing or ceased or cessation* or de-intensif* or deintensif* or deprescribing or deprescrib* or "de-prescribing" or "de-prescrib*" or "de-implementation*" or "de-implement*" or deimplement* or discontinue* or discontinuation* or curb or curbing or curbed).ab,ti.

Concept #3: additional short-cuts to broaden the search on specific issues not identified through (Concept #1 AND Concept #2)

((benzodiazepine* or "z-drug*" or hypnotic*) and (intervention or deprescribing)).ab,ti.

OR

("medication review" and (outcome or intervention)).ab,ti.

OR

(polypharmacy and intervention).ab,ti.

OR

(deprescribing and (guideline* or recommendation* or outcome* or intervention*)).ab,ti.

Supplementary Text S2. Complete list of articles

1. Rognstad S, Brekke M, Fetveit A, Dalen I, Straand J. Prescription peer academic detailing to reduce inappropriate prescribing for older patients: a cluster randomised controlled trial. The British journal of general practice : the journal of the Royal College of General Practitioners. 2013;63(613):e554-62.
2. Clyne B, Smith SM, Hughes CM, Boland F, Bradley MC, Cooper JA, et al. Effectiveness of a Multifaceted Intervention for Potentially Inappropriate Prescribing in Older Patients in Primary Care: A Cluster-Randomized Controlled Trial (OPTI-SCRIPT Study). Annals of family medicine. 2015;13(6):545-53.
3. Clyne B, Cooper JA, Hughes CM, Fahey T, Smith SM, team O-Ss. A process evaluation of a cluster randomised trial to reduce potentially inappropriate prescribing in older people in primary care (OPTI-SCRIPT study). Trials. 2016;17(1):386.
4. Clyne B, Smith SM, Hughes CM, Boland F, Cooper JA, Fahey T, et al. Sustained effectiveness of a multifaceted intervention to reduce potentially inappropriate prescribing in older patients in primary care (OPTI-SCRIPT study). Implementation science : IS. 2016;11(1):79.
5. Gillespie P, Clyne B, Raymakers A, Fahey T, Hughes CM, Smith SM. REDUCING POTENTIALLY INAPPROPRIATE PRESCRIBING FOR OLDER PEOPLE IN PRIMARY CARE: COST-EFFECTIVENESS OF THE OPTI-SCRIPT INTERVENTION. International journal of technology assessment in health care. 2017;33(4):494-503.
6. Eveleigh R, Grutters J, Muskens E, Oude Voshaar R, van Weel C, Speckens A, et al. Cost-utility analysis of a treatment advice to discontinue inappropriate long-term antidepressant use in primary care. Family practice. 2014;31(5):578-84.
7. Eveleigh R, Muskens E, Lucassen P, Verhaak P, Spijker J, van Weel C, et al. Withdrawal of unnecessary antidepressant medication: a randomised controlled trial in primary care. BJGP open. 2018;1(4):bjgpopen17X101265.
8. Eveleigh R, Speckens A, van Weel C, Oude Voshaar R, Lucassen P. Patients' attitudes to discontinuing not-indicated long-term antidepressant use: barriers and facilitators. Therapeutic advances in psychopharmacology. 2019;9:2045125319872344.
9. Luymes CH, Poortvliet RKE, van Geloven N, de Waal MWM, Drewes YM, Blom JW, et al. Deprescribing preventive cardiovascular medication in patients with predicted low cardiovascular disease risk in general practice - the ECSTATIC study: a cluster randomised non-inferiority trial. BMC medicine. 2018;16(1):5.
10. Vicens C, Bejarano F, Sempere E, Mateu C, Fiol F, Socias I, et al. Comparative efficacy of two interventions to discontinue long-term benzodiazepine use: cluster randomised controlled trial in primary care. The British journal of psychiatry : the journal of mental science. 2014;204(6):471-9.
11. Vicens C, Sempere E, Bejarano F, Socias I, Mateu C, Fiol F, et al. Efficacy of two interventions on the discontinuation of benzodiazepines in long-term users: 36-month follow-up of a cluster randomised trial

in primary care. The British journal of general practice : the journal of the Royal College of General Practitioners. 2016;66(643):e85-91.

12. Moga DC, Abner EL, Rigsby DN, Eckmann L, Huffmyer M, Murphy RR, et al. Optimizing medication appropriateness in older adults: a randomized clinical interventional trial to decrease anticholinergic burden. Alzheimer's research & therapy. 2017;9(1):36.

13. van der Meer HG, Wouters H, Pont LG, Taxis K. Reducing the anticholinergic and sedative load in older patients on polypharmacy by pharmacist-led medication review: a randomised controlled trial. BMJ open. 2018;8(7):e019042.

14. Kuntz JL, Kouch L, Christian D, Hu W, Peterson PL. Patient Education and Pharmacist Consultation Influence on Nonbenzodiazepine Sedative Medication Deprescribing Success for Older Adults. The Permanente journal. 2019;23:18-161.

15. Navy HJ, Weffald L, Delate T, Patel RJ, Dugan JP. Clinical Pharmacist Intervention to Engage Older Adults in Reducing Use of Alprazolam. The Consultant pharmacist : the journal of the American Society of Consultant Pharmacists. 2018;33(12):711-22.

16. Salonoja M, Salminen M, Aarnio P, Vahlberg T, Kivela S-L. One-time counselling decreases the use of benzodiazepines and related drugs among community-dwelling older persons. Age and ageing. 2010;39(3):313-9.

17. Keith SW, Maio V, Dudash K, Templin M, Del Canale S. A physician-focused intervention to reduce potentially inappropriate medication prescribing in older people: a 3-year, Italian, prospective, proof-of-concept study. Drugs & aging. 2013;30(2):119-27.

18. Lopatto J, Keith SW, Del Canale S, Templin M, Maio V. Evaluating sustained quality improvements: long-term effectiveness of a physician-focused intervention to reduce potentially inappropriate medication prescribing in an older population. Journal of clinical pharmacy and therapeutics. 2014;39(3):266-71.

19. Cossette B, Taseen R, Roy-Petit J, Villemure M-P, Grondin M, Ricard G, et al. A pharmacist-physician intervention model using a computerized alert system to reduce high-risk medication use in primary care. European journal of clinical pharmacology. 2019;75(7):1017-23.

20. Roughead EE, Kalisch Ellett LM, Ramsay EN, Pratt NL, Barratt JD, LeBlanc VT, et al. Bridging evidence-practice gaps: improving use of medicines in elderly Australian veterans. BMC health services research. 2013;13:514.

21. Morrison C, MacRae Y. Promoting Safer Use of High-Risk Pharmacotherapy: Impact of Pharmacist-Led Targeted Medication Reviews. Drugs - real world outcomes. 2015;2(3):261-71.

22. Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: addressing polypharmacy. Archives of internal medicine. 2010;170(18):1648-54.

23. Park M-J, Kim M-H, Shin SM, Chung SY. Effect of providing drug utilization review information on tricyclic antidepressant prescription in the elderly. Journal of medical systems. 2018;42(10):198.

24. Lasota ST, Merrey W, Ross PA, Martin A, Feeser SA. Provider Responsiveness to Pharmacist Recommendations in a Population Health Setting. The Senior care pharmacist. 2019;34(5):308-16.
25. de Gier NAH, Gorgels WJMJ, Lucassen PLBJ, Oude Voshaar R, Mulder J, Zitman F. Discontinuation of long-term benzodiazepine use: 10-year follow-up. Family practice. 2011;28(3):253-9.
26. Lopez-Peig C, Mundet X, Casabella B, del Val JL, Lacasta D, Diogene E. Analysis of benzodiazepine withdrawal program managed by primary care nurses in Spain. BMC research notes. 2012;5:684.
27. Jorgensen VRK. Benzodiazepine and cyclopyrrolone reduction in general practice--does this lead to concomitant change in the use of antipsychotics? A study based on a Danish population. Journal of affective disorders. 2010;126(1-2):293-8.
28. Jorgensen VRK. Benzodiazepine reduction in general practice. Are the elderly neglected? Journal of affective disorders. 2012;136(3):1216-21.
29. Kalisch Ellett LM, Lim R, Pratt NL, Kerr M, Ramsay EN, LeBlanc TV, et al. Reducing hypnotic use in insomnia management among Australian veterans: results from repeated national interventions. BMC health services research. 2018;18(1):626.
30. Crabtree A, Rose C, Chong M, Smolina K. Effects of the new prescribing standards in British Columbia on consumption of opioids and benzodiazepines and z drugs. Canadian family physician. 2019;65(5):e231-e7.
31. Shayegani R, Pugh MJ, Kazanis W, Wilkening GL. Reducing coprescriptions of benzodiazepines and opioids in a veteran population. The American journal of managed care. 2018;24(8):e265-e9.
32. Al Achkar M, Grannis S, Revere D, MacKie P, Howard M, Gupta S. The effects of state rules on opioid prescribing in Indiana. BMC health services research. 2018;18(1):29.
32. Murie J, Allen J, Simmonds R, de Wet C. Glad you brought it up: a patient-centred programme to reduce proton-pump inhibitor prescribing in general medical practice. Quality in primary care. 2012;20(2):141-8.
34. Quinn R, Park KM, Bodine R. Pharmacist-Driven Step-Down of Long-Term Proton-Pump Inhibitor Therapy. The Senior care pharmacist. 2019;34(8):520-8.
35. Reeve E, Andrews JM, Wiese MD, Hendrix I, Roberts MS, Shakib S. Feasibility of a patient-centered deprescribing process to reduce inappropriate use of proton pump inhibitors. The Annals of pharmacotherapy. 2015;49(1):29-38.
36. Walsh K, Kwan D, Marr P, Papoushek C, Lyon WK. Deprescribing in a family health team: a study of chronic proton pump inhibitor use. Journal of primary health care. 2016;8(2):164-71.
37. Ammerman CA, Simpkins BA, Warman N, Downs TN. Potentially Inappropriate Medications in Older Adults: Deprescribing with a Clinical Pharmacist. Journal of the American Geriatrics Society. 2019;67(1):115-8.

38. Hui RL, Chang CC, Niu F, Tang YK, Harano D, Deguzman L, et al. Evaluation of a Pharmacist-Managed Antidiabetic Deprescribing Program in an Integrated Health Care System. Journal of managed care & specialty pharmacy. 2019;25(8):927-34.
39. Weatherburn CJ. Benzodiazepines and non-benzodiazepine hypnotics - impact of a cluster adopted protocol on primary care prescribing. Scottish medical journal. 2019;64(3):97-102.
40. Ragan AP, Aikens GB, Bounthavong M, Brittain K, Mirk A. Academic Detailing to Reduce Sedative-Hypnotic Prescribing in Older Veterans. Journal of pharmacy practice. 2019:897190019870949.
41. Patel S, Carmichael JM, Taylor JM, Bounthavong M, Higgins DT. Evaluating the Impact of a Clinical Decision Support Tool to Reduce Chronic Opioid Dose and Decrease Risk Classification in a Veteran Population. The Annals of pharmacotherapy. 2018;52(4):325-31.
42. Santolaya-Perrin R, Calderon-Hernanz B, Jimenez-Diaz G, Galan-Ramos N, Moreno-Carvajal MT, Rodriguez-Camacho JM, et al. The efficacy of a medication review programme conducted in an emergency department. International journal of clinical pharmacy. 2019;41(3):757-66.
43. Stevens MB, Hastings SN, Powers J, Vandenberg AE, Echt KV, Bryan WE, 3rd, et al. Enhancing the Quality of Prescribing Practices for Older Veterans Discharged from the Emergency Department (EQUiPPED): Preliminary Results from Enhancing Quality of Prescribing Practices for Older Veterans Discharged from the Emergency Department, a Novel Multicomponent Interdisciplinary Quality Improvement Initiative. Journal of the American Geriatrics Society. 2015;63(5):1025-9.
44. Tannenbaum C, Martin P, Tamblyn R, Benedetti A, Ahmed S. Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: the EMPOWER cluster randomized trial. JAMA internal medicine. 2014;174(6):890-8.
45. Martin P, Tannenbaum C. A realist evaluation of patients' decisions to deprescribe in the EMPOWER trial. BMJ open. 2017;7(4):e015959.
46. Martin P, Tannenbaum C. Use of the EMPOWER brochure to deprescribe sedative-hypnotic drugs in older adults with mild cognitive impairment. BMC geriatrics. 2017;17(1):37.
47. Kouladjian O'Donnell L, Gnjidic D, Chen TF, Hilmer SN. Integration of an electronic Drug Burden Index risk assessment tool into Home Medicines Reviews: deprescribing anticholinergic and sedative medications. Therapeutic advances in drug safety. 2019;10:2042098619832471.
48. Luchen GG, Prohaska ES, Ruisinger JF, Melton BL. Impact of community pharmacist intervention on concurrent benzodiazepine and opioid prescribing patterns. Journal of the American Pharmacists Association : JAPhA. 2019;59(2):238-42.
49. Dormuth CR, Miller TA, Huang A, Mamdani MM, Juurlink DN, Canadian Drug S, et al. Effect of a centralized prescription network on inappropriate prescriptions for opioid analgesics and benzodiazepines. CMAJ. 2012;184(16):E852-6.
50. Gomes T, Juurlink D, Yao Z, Camacho X, Paterson JM, Singh S, et al. Impact of legislation and a prescription monitoring program on the prevalence of potentially inappropriate prescriptions for monitored drugs in Ontario: a time series analysis. CMAJ open. 2014;2(4):E256-61.

51. Hurmuz MZM, Janus SIM, van Manen JG. Changes in medicine prescription following a medication review in older high-risk patients with polypharmacy. International journal of clinical pharmacy. 2018;40(2):480-7.
52. McNicholl IR, Gandhi M, Hare CB, Greene M, Pierluissi E. A Pharmacist-Led Program to Evaluate and Reduce Polypharmacy and Potentially Inappropriate Prescribing in Older HIV-Positive Patients. Pharmacotherapy. 2017;37(12):1498-506.
53. McIntyre C, McQuillan R, Bell C, Battistella M. Targeted Deprescribing in an Outpatient Hemodialysis Unit: A Quality Improvement Study to Decrease Polypharmacy. American journal of kidney diseases : the official journal of the National Kidney Foundation. 2017;70(5):611-8.
54. Shilpa HSS, Kumar NN, Maheswari E, Virupaksha HS, Subeesh V, Saraswathy GR, et al. Deprescribing of benzodiazepines and Z-drugs amongst the psychiatric patients of a tertiary care Hospital. Asian journal of psychiatry. 2019;44:189-94.
55. Erwin WJ, Goodman C, Smith T. Effectiveness of a direct-to-consumer written health education program in the reduction of benzodiazepine and sedative-hypnotic use in an elderly population at a single Veterans Affairs medical center. The mental health clinician. 2018;8(3):100-4.
56. Avdagic K, Geier M, Coralic Z, Finley P. Evaluation of the Impact of a Multimodel Intervention on Prescribing Patterns of Sedative-Hypnotics in a Behavioral Health System. The primary care companion for CNS disorders. 2018;20(3).
57. Lenander C, Bondesson A, Viberg N, Jakobsson U, Beckman A, Midlov P. Effects of an intervention (SAKLAK) on prescription of potentially inappropriate medication in elderly patients. Family practice. 2017;34(2):213-8.
58. Coffey CP, Barnette DJ, Wenzke JT, Lawrence J. Implementing a Systematic Approach to Deprescribing Proton Pump Inhibitor Therapy in Older Adults. The Senior care pharmacist. 2019;34(1):47-55.
59. Avraham O, Biglow M. Implementation of Proton Pump Inhibitor Deprescription Protocol in Geriatric Residents. The Annals of pharmacotherapy. 2018;52(8):747-53.
60. Smith AJ, Tett SE. An intervention to improve benzodiazepine use--a new approach. Family practice. 2010;27(3):320-7.
61. Patterson SM, Hughes CM, Crealey G, Cardwell C, Lapane KL. An evaluation of an adapted U.S. model of pharmaceutical care to improve psychoactive prescribing for nursing home residents in northern ireland (fleetwood northern ireland study). Journal of the American Geriatrics Society. 2010;58(1):44-53.
62. Wouters H, Scheper J, Koning H, Brouwer C, Twisk JW, van der Meer H, et al. Discontinuing Inappropriate Medication Use in Nursing Home Residents: A Cluster Randomized Controlled Trial. Annals of internal medicine. 2017;167(9):609-17.
63. Pitkala KH, Juola A-L, Kautiainen H, Soini H, Finne-Soveri UH, Bell JS, et al. Education to reduce potentially harmful medication use among residents of assisted living facilities: a randomized controlled trial. Journal of the American Medical Directors Association. 2014;15(12):892-8.

64. Juola A-L, Bjorkman MP, Pylkkanen S, Finne-Soveri H, Soini H, Kautiainen H, et al. Nurse Education to Reduce Harmful Medication Use in Assisted Living Facilities: Effects of a Randomized Controlled Trial on Falls and Cognition. Drugs & aging. 2015;32(11):947-55.
65. Kirkham J, Maxwell C, Velkers C, Leung R, Moffat K, Seitz D. Optimizing Prescribing of Antipsychotics in Long-Term Care (OPAL): A Stepped-Wedge Trial. Journal of the American Medical Directors Association. 2019.
66. Potter K, Flicker L, Page A, Etherton-Beer C. Deprescribing in Frail Older People: A Randomised Controlled Trial. PloS one. 2016;11(3):e0149984.
67. de Souto Barreto P, Lapeyre-Mestre M, Cestac P, Vellas B, Rolland Y. Effects of a geriatric intervention aiming to improve quality care in nursing homes on benzodiazepine use and discontinuation. British journal of clinical pharmacology. 2016;81(4):759-67.
68. Carnahan RM, Brown GD, Letuchy EM, Rubenstein LM, Gryzlak BM, Smith M, et al. Impact of programs to reduce antipsychotic and anticholinergic use in nursing homes. Alzheimer's & dementia (New York, N Y). 2017;3(4):553-61.
69. Massot Mesquida M, Tristany Casas M, Franzi Siso A, Garcia Munoz I, Hernandez Vian O, Toran Monserrat P. Consensus and evidence-based medication review to optimize and potentially reduce psychotropic drug prescription in institutionalized dementia patients. BMC geriatrics. 2019;19(1):7.
70. Lapane KL, Hughes CM, Christian JB, Daiello LA, Cameron KA, Feinberg J. Evaluation of the fleetwood model of long-term care pharmacy. Journal of the American Medical Directors Association. 2011;12(5):355-63.
71. Pruskowski J, Handler SM. The DE-PHARM Project: A Pharmacist-Driven Deprescribing Initiative in a Nursing Facility. The Consultant pharmacist : the journal of the American Society of Consultant Pharmacists. 2017;32(8):468-78.
72. Blozik E, Born AM, Stuck AE, Benninger U, Gillmann G, Clough-Gorr KM. Reduction of inappropriate medications among older nursing-home residents: a nurse-led, pre/post-design, intervention study. Drugs & aging. 2010;27(12):1009-17.
73. Garcia-Caballero TM, Lojo J, Menendez C, Fernandez-Alvarez R, Mateos R, Garcia-Caballero A. Polimedication: applicability of a computer tool to reduce polypharmacy in nursing homes. International psychogeriatrics. 2018;30(7):1001-8.
74. Sasson E, James M, Wubshet B, Todorov D, Cohen H. Implementing Psychopharmacology Rounds in a Nursing Facility to Improve Antipsychotic Usage. The Consultant pharmacist : the journal of the American Society of Consultant Pharmacists. 2017;32(6):352-9.
75. Bravo-Jose P, Saez-Lleo CI, Peris-Marti JF. Deprescribing antipsychotics in long term care patients with dementia. Deprescribing antipsychotics in long term care patients with dementia. 2019;43(4):140-5.
76. Brodaty H, Aerts L, Harrison F, Jessop T, Cations M, Chenoweth L, et al. Antipsychotic Deprescription for Older Adults in Long-term Care: The HALT Study. Journal of the American Medical Directors Association. 2018;19(7):592-600.e7.

77. Westbury J, Jackson S, Gee P, Peterson G. An effective approach to decrease antipsychotic and benzodiazepine use in nursing homes: the RedUSe project. International psychogeriatrics. 2010;22(1):26-36.
78. Westbury J, Tichelaar L, Peterson G, Gee P, Jackson S. A 12-month follow-up study of "RedUSe": a trial aimed at reducing antipsychotic and benzodiazepine use in nursing homes. International psychogeriatrics. 2011;23(8):1260-9.
79. Westbury JL, Gee P, Ling T, Brown DT, Franks KH, Bindoff I, et al. RedUSe: reducing antipsychotic and benzodiazepine prescribing in residential aged care facilities. The Medical journal of Australia. 2018;208(9):398-403.
80. Pasina L, Marengoni A, Ghibelli S, Suardi F, Djade CD, Nobili A, et al. A Multicomponent Intervention to Optimize Psychotropic Drug Prescription in Elderly Nursing Home Residents: An Italian Multicenter, Prospective, Pilot Study. Drugs & aging. 2016;33(2):143-9.
81. Farrell B, Richardson L, Raman-Wilms L, de Launay D, Alsabbagh MW, Conklin J. Self-efficacy for deprescribing: A survey for health care professionals using evidence-based deprescribing guidelines. Research in social & administrative pharmacy : RSAP. 2018;14(1):18-25.
82. Ailabouni N, Mangin D, Nishtala PS. DEFEAT-polypharmacy: deprescribing anticholinergic and sedative medicines feasibility trial in residential aged care facilities. International journal of clinical pharmacy. 2019;41(1):167-78.
83. Mestres Gonzalvo C, Milosevic V, van Oijen BPC, de Wit HAJM, Hurkens KPGM, Mulder WJ, et al. The use of an electronic clinical rule to discontinue chronically used benzodiazepines and related Z drugs. European journal of clinical pharmacology. 2018;74(2):227-31.
84. Gemelli MG, Yockel K, Hohmeier KC. Evaluating the Impact of Pharmacists on Reducing Use of Sedative/Hypnotics for Treatment of Insomnia in Long-Term Care Facility Residents. The Consultant pharmacist : the journal of the American Society of Consultant Pharmacists. 2016;31(11):650-7.
85. Lee C, Lo A, Ubhi K, Milewski M. Outcome after Discontinuation of Proton Pump Inhibitors at a Residential Care Site: Quality Improvement Project. The Canadian journal of hospital pharmacy. 2017;70(3):215-23.
86. Weeks WB, Mishra MK, Curto D, Petersen CL, Cano P, Hswen Y, et al. Comparing Three Methods for Reducing Psychotropic Use in Older Demented Spanish Care Home Residents. Journal of the American Geriatrics Society. 2019;67(7):1444-53.
87. Bounthavong M, Lau MK, Popish SJ, Kay CL, Wells DL, Himstreet JE, et al. Impact of academic detailing on benzodiazepine use among veterans with posttraumatic stress disorder. Substance abuse. 2019:1-9.
88. Pope G, Wall N, Peters CM, O'Connor M, Saunders J, O'Sullivan C, et al. Specialist medication review does not benefit short-term outcomes and net costs in continuing-care patients. Age and ageing. 2011;40(3):307-12.

89. Dalleur O, Boland B, Losseau C, Henrard S, Wouters D, Speybroeck N, et al. Reduction of potentially inappropriate medications using the STOPP criteria in frail older inpatients: a randomised controlled study. Drugs & aging. 2014;31(4):291-8.
90. Edey R, Edwards N, Von Sychowski J, Bains A, Spence J, Martinusen D. Impact of deprescribing rounds on discharge prescriptions: an interventional trial. International journal of clinical pharmacy. 2019;41(1):159-66.
91. Gnjidic D, Ong HMM, Leung C, Jansen J, Reeve E. The impact of in hospital patient-education intervention on older people's attitudes and intention to have their benzodiazepines deprescribed: a feasibility study. Therapeutic advances in drug safety. 2019;10:2042098618816562.
92. Van der Linden L, Decoutere L, Beerten L, Delva T, Spriet I, Flamaing J, et al. External validation of a clinical pharmacy intervention in geriatric inpatients: a controlled study. International journal of clinical pharmacy. 2019;41(4):853-8.
93. Van der Linden L, Decoutere L, Walgraeve K, Milisen K, Flamaing J, Spriet I, et al. Combined Use of the Rationalization of Home Medication by an Adjusted STOPP in Older Patients (RASP) List and a Pharmacist-Led Medication Review in Very Old Inpatients: Impact on Quality of Prescribing and Clinical Outcome. Drugs & aging. 2017;34(2):123-33.
94. Grion AM, Gallo U, Tinjala DD, Daragjati J, Loreggian M, Cardaci G, et al. A New Computer-Based Tool to Reduce Potentially Inappropriate Prescriptions in Hospitalized Geriatric Patients. Drugs & aging. 2016;33(4):267-75.
95. McKean M, Pillans P, Scott IA. A medication review and deprescribing method for hospitalised older patients receiving multiple medications. Internal medicine journal. 2016;46(1):35-42.
96. Kashyap M, D'Cruz S, Sachdev A, Tiwari P. Evidence-based information leads to reduction in inappropriate drug prescribing: Results from Indian older inpatients. The International journal of risk & safety in medicine. 2015;27(4):209-17.
97. Kimura T, Ogura F, Yamamoto K, Uda A, Nishioka T, Kume M, et al. Potentially inappropriate medications in elderly Japanese patients: effects of pharmacists' assessment and intervention based on Screening Tool of Older Persons' Potentially Inappropriate Prescriptions criteria ver.2. Journal of clinical pharmacy and therapeutics. 2017;42(2):209-14.
98. Potter EL, Lew TE, Sooriyakumaran M, Edwards AM, Tong E, Aung AK. Evaluation of pharmacist-led physician-supported inpatient deprescribing model in older patients admitted to an acute general medical unit. Australasian journal on ageing. 2019;38(3):206-10.
99. Hashimoto Y, Tensho M. Effect of pharmacist intervention on physician prescribing in patients with chronic schizophrenia: a descriptive pre/post study. BMC health services research. 2016;16:150.
100. Pellicano OA, Tong E, Yip G, Monk L, Loh X, Ananda-Rajah M, et al. Geriatric Psychotropic Stewardship Team to de-escalate inappropriate psychotropic medications in general medicine inpatients: An evaluation. Australasian journal on ageing. 2018;37(2):E37-E41.

101. Wilson MG, Lee TC, Hass A, Tannenbaum C, McDonald EG. EMPOWERing Hospitalized Older Adults to Deprescribe Sedative Hypnotics: A Pilot Study. Journal of the American Geriatrics Society. 2018;66(6):1186-9.
102. Hamzat H, Sun H, Ford JC, Macleod J, Soiza RL, Mangoni AA. Inappropriate prescribing of proton pump inhibitors in older patients: effects of an educational strategy. Drugs & aging. 2012;29(8):681-90.
103. McDonald EG, Jones J, Green L, Jayaraman D, Lee TC. Reduction of inappropriate exit prescriptions for proton pump inhibitors: A before-after study using education paired with a web-based quality-improvement tool. Journal of hospital medicine. 2015;10(5):281-6.
104. Tay HS, Soiza RL, Mangoni AA. Minimizing anticholinergic drug prescribing in older hospitalized patients: a full audit cycle. Therapeutic advances in drug safety. 2014;5(3):121-8.
105. Carr F, Tian P, Chow J, Guzak J, Triscott J, Mathura P, et al. Deprescribing benzodiazepines among hospitalised older adults: quality improvement initiative. BMJ open quality. 2019;8(3):e000539.

Supplementary Table S1. Measure categorization and assessment

Measure specification
Count
Scale - existing/validated vs. non-validated
Proportion (numerator/denominator)
Other
Measure type
Appropriateness (overuse, underuse, other) - cessation, dose reduction, new prescription, switch for another drug
Utilization/ordering - cessation, dose reduction, new prescription, switch for another drug
Intermediate outcome
Outcome
Patient reported: - outcome measure (PROM) - experience measure (PREM) - preferences
Provider-reported experience
Patient-provider interaction
Cost-related - value (outcome/cost) - cost
Other
Measure of unintended consequence type (if applicable)
Substitution of an alternative drug
Underuse of the drug being intervened upon
Underuse of a related drug
Patient-reported experience
Provider-reported experience
Harm (outcome)
Other
Measure source
Patient-reported
Provider-reported
Medical/pharmacy record
Validated scale/questionnaire
Not validated scale/questionnaire
Blinded assessment

Supplementary Table S2. Detailed study characteristics

	First author, year	**Setting**	**Design (*qualitative assessment*)**	**Control group**	**Elderly only**	**N of drug(s)**	**Drug class(es)**	**Patient intervention**	**Provider intervention**
1	Rognstad, 2013	Outpatient, general care	Cluster RCT *(No)*	Yes	Yes	≥4	Multiple PIMs	-	Education, drug review, feedback and audit
2-5	Clyne, 2015, 2016, 2016; Gillespie, 2017	Outpatient, general care	Cluster RCT *(Yes)*	Yes	Yes	≥4	Multiple PIMs	Education	Education, drug review
6-8	Eveleigh, 2014, 2018, 2019	Outpatient, general care	Cluster RCT *(Yes)*	Yes	No	1	Antidepressant	-	Education, guideline
9	Luymes, 2018	Outpatient, general care	Cluster RCT *(No)*	Yes	No	2	Antihypertensive & lipid-lowering drugs	Education, advice to discuss with GP, SDM process	Education, guideline
10-11	Vicens, 2016, 2019	Outpatient, general care	Cluster RCT *(No)*	Yes	No	1	BZD	Education	Education
12	Moga, 2017	Outpatient, general care	RCT *(No)*	Yes	Yes	1	Anticholinergic	Education, drug plan, discussion, alternative drug	Drug review
13	Van der Meer, 2018	Outpatient, general care	RCT *(No)*	Yes	Yes	2	BZD/SH, anticholinergic	Preferences and action plan discussion	Drug review, action plan discussion
14	Kuntz, 2019	Outpatient, general care	RCT *(No)*	Yes	Yes	1	SH, not BZD	Education, phone call with pharmacist, physician's letter, drug substitution	-
15	Navy, 2018	Outpatient, general care	RCT *(No)*	Yes	Yes	1	Alprazolam	Education	-
16	Salonoja, 2010	Outpatient, general care	RCT *(No)*	Yes	Yes	≥4	Fall-risk increasing drugs	Education	-
17-18	Keith, 2013; Lopatto, 2014	Outpatient, general care	Prospective pre/post *(No)*	Yes	Yes	≥4	Multiple PIMs	-	Education, guideline, brochure with alternative drugs
19	Cossette, 2019	Outpatient, general care	Prospective interventional pilot *(No)*	No	Yes	≥4	Multiple PIMs	-	Education, guideline, checklist, drug review, computer alert
20	Roughead, 2013	Outpatient, general care	Prospective pre/post & time series *(Yes)*	No	Yes	≥4	Multiple PIMs	Educational brochure encouraging dialogue	Education
21	Morrison, 2015	Outpatient, general care	Prospective cohort *(No)*	No	No	≥4	Multiple PIMs	-	Checklist, drug review
22	Garfinkel, 2010	Outpatient, general care	Prospective cohort *(No)*	No	Yes	≥4	PIMs	Education, explanation of deprescribing rationale	Checklist, Good Palliative-Geriatric Practice algorithm

23	Park, 2018	Outpatient, general care	Prospective pre/post, time series *(No)*	No	Yes	1	Antidepressant	-	Drug utilization review
24	Lasota, 2019	Outpatient, general care	Prospective quality improvement *(Yes)*	No	Yes	2	BZD, antidepressant	-	Guideline with deprescribing algorithm, drug review, phone call to inform provider about PIMs
25	De Gier, 2010	Outpatient, general care	Prospective matched-control *(No)*	Yes	No	1	BZD	Group psychotherapy	Pay for performance, discontinuation letter, consultation to discuss tapering
26	Lopez-Peig, 2012	Outpatient, general care	Prospective pre/post *(Yes)*	No	No	1	BZD	Education, drug substitution	Education, feedback
27-28	Jorgensen, 2010, 2012	Outpatient, general care	Prospective pre/post *(No)*	No	No	1	BZD/SH	-	Prescription rules
29	Kalisch Ellet, 2018	Outpatient, general care	Prospective pre/post *(No)*	No	Yes	1	BZD/SH	Education, tailored letter recommending dialogue with doctor	Education
30	Crabtree, 2019	Outpatient, general care	Prospective time series *(No)*	Yes	No	2	BZD, SH, opioid	-	Guideline
31	Shayegani, 2018	Outpatient, general care	Prospective cohort *(No)*	No	No	2	BZD with opioid	-	Drug review, recommendations sent to prescriber
32	Al Achkar, 2018	Outpatient, general care	Retrospective time-series *(No)*	No	No	1	Opioid	Signed controlled-substance agreement	Drug review, prescribing rules
33	Murie, 2012	Outpatient, general care	Prospective cohort *(Yes)*	No	No	1	PPI	Education, drug substitution (sodium alginate, bicarbonate)	-
34	Quinn, 2019	Outpatient, general care	Prospective cohort *(No)*	No	No	1	PPI	Education, tapering protocol, drug substitution	Deprescribing algorithm
35	Reeve, 2015	Outpatient, general care	Prospective feasibility study *(No)*	No	No	1	PPI	Education, consent for withdrawal	Guideline, drug review, physician approval for withdrawal
36	Walsh, 2016	Outpatient, general care	Prospective cohort *(Yes)*	No	No	1	PPI	Education	Deprescribing tool, reminders in electronic medical record
37	Ammerman, 2019	Outpatient, general care	Retrospective matched control *(No)*	Yes	Yes	≥4	Multiple PIMs	-	Drug review
38	Hui, 2019	Outpatient, general care	Retrospective matched control *(No)*	Yes	Yes	1	Antidiabetic	Shared-decision discussion of best action plan according to lifestyle and preferences	Deprescribing algorithm

39	Weatherburn, 2019	Outpatient, general care	Retrospective pre/post, time series *(No)*	Yes	No	1	BZD/SH	-	Prescribing protocol
40	Ragan, 2019	Outpatient, general care	Retrospective pre/post, time series *(No)*	No	Yes	1	BZD/SH	Education	Education, guideline, Academic detailing
41	Patel, 2018	Outpatient, general care	Retrospective time series, matched control *(No)*	Yes	No	1	Opioid	-	Clinical reminder
42	Santolaya-Perrin, 2019	Outpatient, general care; ED	RCT *(No)*	Yes	Yes	≥4	Multiple PIMs	-	Checklist, drug review, recommendations sent to GP
43	Stevens, 2015	Outpatient, general care; ED	Prospective pre/post *(No)*	No	Yes	≥4	Multiple PIMs	-	Checklist, informatics-based guideline, feedback
44-46	Tannenbaum, 2014; Martin, 2017, 2017	Outpatient, general care; pharmacy	Cluster RCT *(Yes)*	Yes	Yes	1	BZD	Education, patient asked to discuss with physician/pharmacist	-
47	Kouladjian O'Donnell, 2019	Outpatient, general care; pharmacy	Prospective pre/post *(Yes)*	Yes	Yes	≥4	Drugs with sedative or anticholinergic effect	Patient version of Drug Burden Index report	Education, drug review, integration of Drug Burden Index in medical record
48	Luchen, 2018	Outpatient, general care; pharmacy	Prospective cohort *(No)*	No	No	2	BZD, opioid	-	Guideline, drug review, letter with prescription recommendation
49	Dormuth, 2012	Outpatient, general care; pharmacy	Retrospective pre/post *(No)*	Yes	No	2	BZD, opioid	-	Centralized prescription network (PharmaNet)
50	Gomes, 2014	Outpatient, general care; pharmacy	Retrospective time series *(No)*	Yes	No	3	BZD/SH, opioid, stimulant	-	Legislation for physicians and pharmacists
51	Hurmuz, 2018	Outpatient, general care; pharmacy	Retrospective pre/post *(Yes)*	No	Yes	≥4	Multiple PIMs	-	Drug review
52	McNicholl, 2017	Outpatient, HIV care	Prospective cohort *(No)*	No	Yes	≥4	Multiple PIMs	Discussion of patient perception of drug use and indication	Checklist, drug review, drug interaction according to Center for Disease Control and Prevention
53	McIntyre, 2017	Outpatient, dialysis unit	Prospective quality improvement *(No)*	No	No	≥4	Quinine, PPI, diuretic, alpha-blocker, statin	-	Deprescribing algorithm
54	Shilpa, 2019	Psychiatric in- and outpatient care	Prospective cohort *(No)*	No	No	1	BZD/SH	Education, SDM process	SDM process

55	Erwin, 2018	Outpatient, mental health care	Prospective cohort *(No)*	No	Yes	1	BZD/SH	Education letter	-
56	Avgadic, 2018	Outpatient, mental health care	Retrospective pre/post *(No)*	No	No	1	BZD/SH	Education	Education, guidelines
57	Lenander, 2017	Outpatient general care, home care, long-term care	Cluster RCT *(No)*	Yes	No	≥4	Multiple PIMs	-	Questionnaire to fulfil, followed by review and feedback,
58	Coffey, 2019	Outpatient, general care; long-term care	Prospective interventional pilot *(Yes)*	No	Yes	1	PPI	Education, drug substitution (anti-H2)	Drug review, tapering recommendation from pharmacist to physician
59	Avraham, 2018	Outpatient, general care; long-term care	Prospective interventional pilot study *(Yes)*	No	Yes	1	PPI	Interactions about triggers, history, symptoms drug substitution (anti-H2)	Education, drug review, qualitative interactions
60	Smith, 2010	Outpatient, general care; long-term care	Prospective pre/post and matched control *(Yes)*	Yes	No	1	BZD	Education	Education
61	Patterson, 2010	Long-term care; pharmacy	Cluster RCT *(No)*	Yes	Yes	3	Anxiolytic, BZD/SH, antipsychotic	Discussion	Discussion, drug review, algorithm on appropriateness and alternatives
62	Wouters, 2018	Long-term care	Cluster RCT *(No)*	Yes	Yes	≥4	Multiple PIMs	Discussion of experience and preferences	Checklist, drug review
63-64	Pitkälä, 2014; Juola, 2015	Long-term care	Cluster RCT *(No)*	Yes	Yes	≥4	Multiple PIMs	-	Education, checklist, list of harmful drugs provided by nurses to physicians
65	Kirkham, 2019	Long-term care	Cluster RCT *(No)*	Yes	No	1	Antipsychotic	-	Education, monitoring tools, interprofessional meetings
66	Potter, 2016	Long-term care	RCT *(No)*	Yes	Yes	≥4	Multiple PIMs	Discussion about symptoms	Deprescribing algorithm, medical and drug review, discussion between providers, GP suggestions
67	De Souto Barreto, 2016	Long-term care	Quasi-experimental *(No)*	Yes	Yes	1	BZD/SH	-	Audit and feedback, drug review, identification of quality indicators
68	Carnahan, 2017	Long-term care	Quasi-experimental *(No)*	Yes	Yes	2	Antipsychotic, anticholinergic	-	Education, guideline
69	Massot Mesquida, 2019	Long-term care	Quasi-experimental pre/post *(No)*	No	Yes	1	Antipsychotic	-	Guideline, drug review based on patient needs and guidelines

70	Lapane, 2011	Long-term care	Prospective pre/post *(No)*	Yes	No	≥4	Multiple PIMs	-	Education, guideline, computer communication between providers
71	Pruskowski, 2017	Long-term care	Prospective quality improvement pilot study *(No)*	No	No	≥4	Multiple PIMs	Discussion of drug changes	Drug review, recommendations to physicians/nurses
72	Blozik, 2010	Long-term care	Prospective pre/post *(No)*	No	Yes	≥4	Multiple PIM	-	Education, checklist, other recommendations
73	Garcia-Caballero, 2018	Long-term care	Prospective cohort *(No)*	No	No	≥4	PIMs	-	Checklist, computer alert
74	Sasson, 2017	Long-term care	Prospective pre/post *(No)*	No	No	1	Antipsychotic	-	Drug review, interdisciplinary psychopharmacology rounds
75	Bravo-José, 2019	Long-term care	Prospective pre/post *(No)*	No	Yes	1	Antipsychotic	-	Guideline
76	Brodaty, 2018	Long-term care	Prospective pre/post *(No)*	No	Yes	1	Antipsychotic	-	Education
77-78	Westbury, 2010, 2011	Long-term care	Prospective matched control *(No)*	Yes	Yes	2	Antipsychotic, BZD	-	Education, guideline, audit and feedback, drug review, Academic detailing consciousness raising
79	Westbury, 2018	Long-term care	Prospective cohort *(No)*	No	Yes	2	Antipsychotic, BZD	-	Education, guideline, audit and feedback, drug review, Academic detailing consciousness raising
80	Pasina, 2016	Long-term care	Prospective pre/post *(No)*	No	Yes	3	BZD, antipsychotic, antidepressant	-	Education, computerized prescription support system
81	Farrell, 2017	Long-term care	Prospective pre/post *(No)*	No	No	3	Antipsychotic, BZD/SH, PPI	-	Education, guideline
82	Ailabouni, 2019	Long-term care	Prospective pre/post *(No)*	No	Yes	2	BZD/SH, anticholinergic	Discussion with patient to assess concerns	Guidelines, drug review
83	Mestres Gonzalvo, 2018	Long-term care	Prospective cohort *(No)*	No	Yes	1	BZD/SH	-	Drug alert with report sent to physician
84	Gemelli, 2016	Long-term care	Prospective intervention pilot study *(Yes)*	No	Yes	1	BZD/SH	-	Drug review, pharmacist recommendations to physician

85	Lee, 2017	Long-term care	Prospective cohort *(No)*	No	Yes	1	PPI	Drug substitution (anti-H2), discussion of cessation	Pharmacist recommendation to physician, choice of tapering mode
86	Weeks, 2019	Long-term care	Retrospective matched control *(No)*	Yes	Yes	3	Anxiolytic, antidepressant, antipsychotic	Education	Checklist, drug review
87	Bounthavong, 2019	Long-term care	Retrospective pre/post *(No)*	No	Yes	1	BZD	-	Education, Academic detailing
88	Pope, 2011	Inpatient; long-term care	Cluster RCT *(No)*	Yes	Yes	≥4	Multiple PIMs	-	Checklist, drug review, clinical assessment
89	Dalleur, 2014	Inpatient	RCT *(No)*	Yes	Yes	≥4	Multiple PIMs	-	Recommendations to ward physicians, checklist
90	Edey, 2018	Inpatient	RCT *(Yes)*	Yes	No	≥4	Multiple PIMs	Education	Guideline, drug review, rounds to discuss discontinuation
91	Gnjidic, 2019	Inpatient	RCT *(Yes)*	Yes	Yes	1	BZD	Education	-
92	Van der Linden , 2017	Inpatient	Prospective cohort *(No)*	Yes	Yes	≥4	Multiple PIMs	-	Checklist, drug review
93	Van der Linden , 2019	Inpatient	Prospective cohort *(No)*	Yes	Yes	≥4	Multiple PIMs	-	Checklist, drug review
94	Grion, 2016	Inpatient	Prospective cohort *(No)*	No	Yes	≥4	Multiple PIMs	-	Computer tool integrating checklist, interaction tool, patient & prognostic data
95	McKean, 2015	Inpatient	Prospective pilot study *(No)*	No	Yes	≥4	Multiple PIMs	Discussion for cessation agreement	Education, discussions, decision support tool with 5-step deprescribing algorithm
96	Kashyap, 2015	Inpatient	Prospective cohort *(No)*	No	Yes	≥4	Multiple PIMs	-	Checklist, feedback to physician, education
97	Kimura, 2015	Inpatient	Prospective cohort *(No)*	No	Yes	≥4	Multiple PIMs	Discussion about intention to change	Checklist, discussion between pharmacists and physicians
98	Potter, 2019	Inpatient	Prospective cohort *(No)*	No	Yes	≥4	Multiple PIMs	-	Pharmacist-led, physician-supported drug review
99	Hashimoto, 2016	Inpatient	Prospective pre/post *(No)*	No	No	1	Antipsychotic	-	Drug review, pharmacist recommendations to physicians
100	Pellicano, 2018	Inpatient	Prospective cohort *(No)*	No	Yes	3	BZD/SH, antipsychotic, antidepressant	-	Recommendation on how to change prescription
101	Wilson, 2018	Inpatient	Prospective cohort *(No)*	Yes	Yes	1	BZD/SH	Educational booklet	-
102	Hamzat, 2012	Inpatient	Prospective pre/post *(No)*	No	Yes	1	PPI	Education	Education, drug review

103	McDonald, 2015	Inpatient	Prospective pre/post, time-series *(No)*	Yes	No	1	PPI	Education, counselling	Education, feedback
104	Tay, 2014	Inpatient	Prospective pre/post *(Yes)*	No	Yes	1	Anticholinergic	-	Drug review
105	Carr, 2019	Rehabilitation inpatient	Prospective interventional pilot study *(Yes)*	No	Yes	1	BZD	Education brief supportive counselling	Education, drug review, communication with GP

Abbreviations: anti-H2, histamine H2 antagonist; BZD, benzodiazepine; ED, emergency department; GP, general practitioner; N, number; PIMs, potentially inappropriate medications; PPI, proton pump inhibitor; pre/post, pre-/post-intervention study; RCT, randomized controlled trial; SDM, shared-decision making; SH, sedative-hypnotic other than benzodiazepine.
Legend: Eight studies published their results in different articles that were grouped for the analyses (105 articles, 93 original studies). We considered BZD and SH as a single drug class. First column numbers correspond to reference numbers in Supplementary Text S2. The studies were ordered according to 1) setting (outpatient general care, outpatient general care and other, outpatient specialized care, long-term care and other, long-term care, inpatient, rehabilitation inpatient); 2) design (cluster RCT, RCT, prospective, retrospective); 3) drug class(es) targeted.

Supplementary Table S3. Summary of measures for each study

	First author, year	N of measures	N of measures of unintended consequences	N of each measure category									N of each measure subcategory		
				Appropr-iateness	*Utilization/ ordering*	*Interme-diate outcome*	*Outcome*	*PREM /prefe-rences*	*PROM*	*Provider-reported experience*	*Patient-provider interaction*	*Value / Cost*	*Cessation*	*Dose reduction*	*Switch*
1	Rognstad, 2013	4	0	4	0	0	0	0	0	0	0	0	4	0	0
2-5	Clyne, 2015, 2016, 2016; Gillespie, 2017	20	0	6	0	0	2	1	3	1	1	5	6	1	1
6-8	Eveleigh, 2014, 2018, 2019	11	5	1	0	0	0	3	5	0	0	2	1	0	0
9	Luymes, 2018	11	2	0	1	0	8	0	1	0	0	1	1	1	0
10-11	Vicens, 2016, 2019	7	1	1	0	0	1	0	5	0	0	0	1	0	0
12	Moga, 2017	6	0	4	0	0	0	1	1	0	0	0	4	1	0
13	Van der Meer, 2018	10	0	1	0	0	2	0	7	0	0	0	1	1	0
14	Kuntz, 2019	5	0	2	0	0	3	0	0	0	0	0	1	0	0
15	Navy, 2018	4	0	2	1	1	0	0	0	0	0	0	1	1	1
16	Salonoja, 2010	2	0	2	0	0	0	0	0	0	0	0	2	0	0
17-18	Keith, 2013; Lopatto, 2014	3	0	3	0	0	0	0	0	0	0	0	2	0	0
19	Cossette, 2019	5	0	2	2	1	0	0	0	0	0	0	2	2	2
20	Roughead, 2013	4	0	1	0	0	0	1	0	1	0	0	1	0	0
21	Morrison, 2015	11	0	4	2	2	2	0	0	0	0	0	2	1	3
22	Garfinkel, 2010	15	7	3	2	2	4	0	4	0	0	0	3	1	1
23	Park, 2018	1	0	1	0	0	0	0	0	0	0	0	1	0	0
24	Lasota, 2019	5	0	3	0	0	0	0	0	2	0	0	3	3	0
25	De Gier, 2010	4	1	3	1	0	0	0	0	0	0	0	2	1	2
26	Lopez-Peig, 2012	4	1	1	0	0	0	0	3	0	0	0	1	0	0
27-28	Jorgensen, 2010, 2012	2	1	1	1	0	0	0	0	0	0	0	1	0	1

29	Kalisch Ellet, 2018	6	0	2	0	0	2	1	0	1	0	0	2	0	0
30	Crabtree, 2019	4	0	1	3	0	0	0	0	0	0	0	4	4	0
31	Shayegani, 2018	2	0	1	0	1	0	0	0	0	0	0	1	1	0
32	Al Achkar, 2018	1	0	1	0	0	0	0	0	0	0	0	1	1	0
33	Murie, 2012	5	0	2	1	0	0	1	0	0	0	1	1	1	0
34	Quinn, 2019	3	0	2	1	0	0	0	0	0	0	0	1	1	1
35	Reeve, 2015	4	1	2	0	0	0	1	1	0	0	0	1	1	0
36	Walsh, 2016	6	1	2	1	1	0	0	0	2	0	0	2	0	1
37	Ammerman, 2019	4	0	3	0	0	0	0	0	0	1	0	2	1	0
38	Hui, 2019	5	0	0	0	0	4	0	0	0	0	1	0	0	0
39	Weatherburn, 2019	1	0	1	0	0	0	0	0	0	0	0	1	1	0
40	Ragan, 2019	9	0	8	1	0	0	0	0	0	0	0	6	0	1
41	Patel, 2018	2	0	1	0	0	1	0	0	0	0	0	1	1	0
42	Santolaya-Perrin, 2019	2	0	1	0	0	1	0	0	0	0	0	1	1	1
43	Stevens, 2015	1	0	1	0	0	0	0	0	0	0	0	1	0	0
44-46	Tannenbaum, 2014; Martin, 2017, 2017	14	1	2	0	0	0	2	9	0	1	0	1	1	0
47	Kouladjian O'Donnell, 2019	3	0	1	0	0	0	1	0	1	0	0	1	1	0
48	Luchen, 2018	4	0	1	2	1	0	0	0	0	0	0	1	0	1
49	Dormuth, 2012	3	0	3	0	0	0	0	0	0	0	0	3	3	0
50	Gomes, 2014	2	0	2	0	0	0	0	0	0	0	0	2	0	0
51	Hurmuz, 2018	9	0	4	4	0	0	0	0	0	0	0	5	4	2
52	McNicholl, 2017	3	0	2	1	0	0	0	0	0	0	0	3	1	1
53	McIntyre, 2017	2	0	1	0	0	0	1	0	0	0	0	1	0	0
54	Shilpa, 2019	4	1	1	0	0	0	0	2	0	0	1	1	0	0
55	Erwin, 2018	4	0	1	0	3	0	0	0	0	0	0	1	1	0
56	Avgadic, 2018	3	0	3	0	0	0	0	0	0	0	0	3	0	0
57	Lenander, 2017	5	0	4	1	0	0	0	0	0	0	0	5	1	1

58	Coffey, 2019	6	1	3	1	0	0	1	0	0	0	0	1	1	0
59	Avraham, 2018	8	6	1	1	0	3	0	1	2	0	0	1	0	1
60	Smith, 2010	6	0	4	0	0	0	0	0	1	0	0	4	1	0
61	Patterson, 2010	3	0	2	0	0	1	0	0	0	0	0	2	0	0
62	Wouters, 2018	13	0	6	0	0	6	0	1	0	0	0	3	2	1
63-64	Pitkälä, 2014; Juola, 2015	12	0	6	0	0	5	0	1	0	0	0	6	1	1
65	Kirkham, 2019	6	3	1	0	0	3	0	2	0	0	0	1	0	0
66	Potter, 2016	15	0	2	2	1	6	0	4	0	0	0	2	1	0
67	De Souto Barreto, 2016	2	0	2	0	0	0	0	0	0	0	0	2	0	0
68	Carnahan, 2017	4	2	3	0	0	1	0	0	0	0	0	1	0	0
69	Massot Mesquida, 2019	5	0	3	2	0	0	0	0	0	0	0	3	1	0
70	Lapane, 2011	4	0	1	0	0	3	0	0	0	0	0	1	0	0
71	Pruskowski, 2017	4	0	1	1	0	2	0	0	0	0	0	2	1	1
72	Blozik, 2010	3	0	2	1	0	0	0	0	0	0	0	2	0	1
73	Garcia-Caballero, 2018	3	0	2	0	0	0	0	0	0	0	1	2	2	2
74	Sasson, 2017	8	0	4	0	0	4	0	0	0	0	0	1	1	0
75	Bravo-José, 2019	4	1	2	1	0	1	0	0	0	0	0	1	1	0
76	Brodaty, 2018	12	3	3	3	0	5	0	1	0	0	0	3	2	1
77-78	Westbury, 2010, 2011	8	0	6	2	0	0	0	0	0	0	0	4	4	0
79	Westbury, 2018	9	1	8	1	0	0	0	0	0	0	0	8	4	1
80	Pasina, 2016	4	0	3	1	0	0	0	0	0	0	0	3	0	0
81	Farrell, 2017	3	0	0	0	0	0	0	0	3	0	0	0	0	0
82	Ailabouni, 2019	11	0	1	1	2	2	0	5	0	0	0	2	1	0
83	Mestres Gonzalvo, 2018	2	0	1	0	0	0	0	0	0	0	0	1	0	0

84	Gemelli, 2016	6	2	3	0	2	0	0	0	0	0	0	1	1	1
85	Lee, 2017	5	2	2	1	0	1	0	1	0	0	0	1	0	1
86	Weeks, 2019	5	2	2	0	0	3	0	0	0	0	0	2	1	0
87	Bounthavong, 2019	4	0	4	0	0	0	0	0	0	0	0	4	3	0
88	Pope, 2011	7	0	1	0	0	5	0	0	0	0	1	1	0	0
89	Dalleur, 2014	5	0	3	0	0	0	0	0	0	0	0	3	1	0
90	Edey, 2018	6	0	2	0	0	1	1	0	1	0	0	2	0	0
91	Gnjidic, 2019	4	0	1	1	0	0	1	1	0	0	0	1	0	0
92	Van der Linden, 2017	12	0	3	0	0	8	0	1	0	0	0	2	2	0
93	Van der Linden, 2019	4	0	1	2	1	0	0	0	0	0	0	2	0	0
94	Grion, 2016	3	0	3	0	0	0	0	0	0	0	0	2	2	2
95	McKean, 2015	3	0	1	0	0	2	0	0	0	0	0	1	0	0
96	Kashyap, 2015	1	0	1	0	0	0	0	0	0	0	0	1	1	0
97	Kimura, 2015	3	0	2	0	1	0	0	0	0	0	0	2	2	2
98	Potter, 2019	3	0	1	0	2	0	0	0	0	0	0	1	0	0
99	Hashimoto, 2016	7	4	2	3	0	1	0	0	0	0	1	2	1	3
100	Pellicano, 2018	2	0	1	0	1	0	0	0	0	0	0	1	1	1
101	Wilson, 2018	4	0	3	0	0	0	0	1	0	0	0	3	0	0
102	Hamzat, 2012	4	1	2	0	1	0	0	1	0	0	0	1	1	0
103	McDonald, 2015	2	0	1	1	0	0	0	0	0	0	0	2	0	0
104	Tay, 2014	7	0	5	1	1	0	0	0	0	0	0	4	2	0
105	Carr, 2019	14	2	2	1	3	1	3	1	1	1	1	1	1	1
	Total (% of measures)	**511**	**52**	**211 (51)**	**52 (10)**	**27 (5)**	**94 (18)**	**19 (4)**	**62 (12)**	**16 (3)**	**4 (1)**	**15 (3)**	**187 (37)**	**79 (15)**	**39 (8)**

Abbreviations: N, number; PREM, patient-reported experience measure; PROM, patient-reported outcome measure.

Legend: Eight studies published their results in different articles that were grouped for the analyses (105 articles, 93 original studies). "Other type" measures are not listed, explaining that the total of the measures in each category doesn't match the total number of measures for studies 14, 16, 19, 22, 30, 36, 41, 65, 67, 87 (one "other type" measure for each, except for study 19 which had two "other type" measures). First column numbers correspond to reference numbers in Supplementary Text S2. The studies were ordered according to 1) setting (outpatient general care, outpatient general care and other, outpatient specialized care, long-term care and other, long-term care, inpatient, rehabilitation inpatient); 2) design (cluster RCT, RCT, prospective, retrospective); 3) drug class(es) targeted (see Table S2).