Table 3. Characteristics of included research

Author	Location	No. of patients	No. of drugs	Rates of primary outcome	Drugs most frequently associated with outcomes	Validation	Most frequent body system affected by ADRs	Selection was not biased	Acceptability low rates of Loss to follow-up	Blinding outcome
Nishtala et al, 2009	Australia – database reported ADRs of psychiatric medications collected from TGA, PBS, health care professional (including hospitals and aged care facilities), consumers	150475 (6751 cases and 123334 non-cases) Case is a report that include 1 or more neuropsychiatric ADRs. The non-case is a report that does not include any neuropsychiatric medication	Benzodiazepines, Anticholinergics, TCAs, and other 24 medications (CVDs, neurological, and pain management)	The following medications results reported as 95%Cl: Antipsychotics 1.50 (1.35-1.68) Benzodiazepines 1.85 (1.69-2.02), Anticholinergics 2.18 (1.87-2.55), TCAs 2.01 (1.79-2.26), Atenolol 0.76 (0.62-0.95), Captopril 0.66 (0.53-0.83), Codeine 1.68 (1.15-2.46), Cimetidine 1.56 (1.24-1.96), Diltiazem 0.93 (0.74-1.18), Digoxin 1.11 (0.97-1.28), Dipyridamole 0.83 (0.47-1.45), Dyazide 1.07 (0.74-1.57), Furosemide 0.91 (0.78-1.07), HCTs 0.31 (0.04-2.27), Ibuprofen 0.84 (0.61-1.16), Isosorbide dinitrate 0.87 (0.63-1.20), Insulin 0.82 (0.58-1.16), Methyldopa 0.79 (0.61-1.00), Metoprolol 1.10 (0.83-1.46), Nifedepine 0.80 (0.62-1.04), Nitroglyceride 0.87 (0.66-1.15), Prednisolone 0.97 (0.82-1.14), Propranolol 1.28 (1.04-1.58), Ranitidine 1.40 (1.23-1.60), Theophyline 0.95 (0.71-1.26), Timolol 1.42 (1.00-2.02), Warfarin 0.63 (0.49-0.80)	The following medications are results of 95% Cl for older + drug/older-drug. These medications producing more ADRs effects with older people than younger people: Cimetidine 2.24(1.7-3.0); Anticholinergic drugs 3.12(2.53-3.85); Antipsychotics 2.73(2.21-3.37); TCAs 2.31(1.93-2.77).	ADRs reports were validated by inclusion and exclusion criteria. Reports were excluded from the analysis if data for age or DOB were absent. Also a combination of drugs including drug of interest had excluded as well from analysis. The 25 drugs of interest identified and assessed by Tune and co-workers method.	CNS with major reports of agitation, anxiety, cognitive impairment, confusion, delirium, hallucinations, psychosis	The selection of report based on CNS signs such as history of hallucination, anxiety, agitation, depression, delirium and cognitive impairment. The association observed between drug exposure to the observed outcome may have been biased or distorted. Also, confounding by concomitant drug use gives concern of bias. In addition, the ADRs database are consist of reported adverse events information, thus subject to differential reporting are clearly biases. However, the authors minimised bias in this study by applying the drug of interest were not typically viewed as possessing anticholinergic characters. Furthermore, all reporting and coding had included in the analysis (not just those drugs that were coded as suspect drug for the reactions).	Not mentioned	Blinding was not reported in any stage.
Harrison et al, 2018	Australia – cross-sectional analysis of 541 older people recruited from 17 residential aged care facilities around Australia.	541	The criteria regarding drugs of interest based on Beers criteria and PIMs for all older people exposed for more than 8 weeks: PPIs 41.5%, Benzodiazepine 30.5%, Antipsychotics 24.8%, Antidepressants (mirtazapine 17.1%, sertraline 9.5%, escitalopram 8.6%, citalopram 7.1%) , and Opioids (buprenorphine 14.3%, fentanyl 9.7%, oxycodone 8.2%). Benzodiazepine 9.9%. Antipsychotics (risperidone 12.7%)	82.8% had mild to severe cognitive impairment. 64.3% diagnosed with dementia. 74.5% were female. Co-morbidity mean: 3.7 (+/- 1.4). Median: 10 (3-17) of totally different medications per person. 38.2% exposed to 5-9 medications, while 52.3% exposed to 10 or more medications. DBI and Beers criteria analysis: 83.1% exposed to at least one medication contributed to DBI. DBI Median: 0.86 (0.36-1.52). According to Beers criteria 73% exposed to PIM.	Benzodiazepine, antipsychotics, antidepressants, and opioids	PIMs identified in this study by using validated measures of Beers criteria for older people. The facilities candidates have characteristic-levels were determined from information collected in a standardised questionnaire that was validated in older residential care population. This questionnaire includes 33 questions (asked about facility-level, location, No. of direct care hours per resident, size of facility, age, sex, marital status). The measures of EQ-5D-5L which completed by proxy has been validated in residential living in aged care facilities with dementia.	CNS and musculoskeletal system	Not mentioned	Not mentioned	Not mentioned
Turner at al, 2016	Australia, cross-sectional study at referral hospitals in Adelaide,	383	Psychotropics, opioids, anxiolytics, hypnotics, sedatives, antidepressant, vasodilators in cardiac diseases, antihypertensives,	From the total number of participants (383), the following medications causing fall: opioids: 26%, anxiolytics: 4.3%, hypnotics & sedatives: 7.6%, antidepressant 22.8%, psychotropics: 47.8%, vasodilators in cardiac diseases: 8.7%, antihypertensives: 3.3%, diuretics:	Psychotropics, opioids, anxiolytics, hypnotics, sedatives, antidepressant, vasodilators in cardiac diseases, antihypertensives, diuretics, B-blockers, CCB, Renin-angiotension system	This study is well-characterized cohort for older people with cancer. The validation stated from the initial appointment, and all data contained within the structured collection sheet which verified by nurses have access to participant's medical	CNS and CVD	Not mentioned	Not mentioned	Not mentioned

	geriatric oncology outpatients clinics,		diuretics, B-blockers, CCB, Renin-angiotension system inhibitors, Alpha-antagonists, Dopaminergic agents.	20%, B-blockers: 27.2%, CCB: 15.2%, Renin-angiotension system inhibitors: 48.9%, Alpha-antagonists: 0%, Dopaminergic agents: 4.3%.	inhibitors, Alpha-antagonists, Dopaminergic agents	records to allow any omitted data to be collected. Also the validation of this study found that 77% concordance for self-reported prescription medication use when compared with participants obtained in an interview conducted by clinical pharmacist, which also comparable with medication has been taken routinely in hospital wards.				
Basger et al, 2008	Australia – cross-referenced treatment of the common medical conditions with the highest 50 PBS-medications prescribed to Australians in 2006.	50 highest used PBS-prescribed medications / documentations.	Top 50 prescribed medications in 2006 for Australian older people (>65 years old)	48 indicators developed. 18 cases of avoidance of psychotropic medications due to develop risk of fall. 19 concerned recommender treatment of anti-platelet or anticoagulant agents to patients suffered type 2 diabetes and CVDs. 4 cases of analgesic monitoring for non-pain conditions. 3 cases drug-drug interactions.	ACEI, ARB, Aspirin, B-adrenoceptor antagonists, Biphosphonates, Bupropion, Calcitriol, Calcium, Clopidogrel, Dipyridamole, inhaled corticosteroids, Intravaginal estrogen, Nicotine replacement medications, Paracetamol, Raloxifene, HMG-CoA (statins), Strontium, Teriparatide, Varenicline, Vitamin D, Warfarin.	The indicators of this study need to be tested and validated for relevance. However, the common anticipation is an identification of inappropriate medication use for commonly used medications in elderly Australians.	Heart failure, URI, depression, anxiety, arthritis, back pain, osteoporosis, falls, CVDs, renal impairment, GIT diseases (including GORD and ulcers), Type 2 diabetes mellitus, thyroid and parathyroid disorders, hepatic impairments, asthma and COPD, coagulation disorders.	Not mentioned	Not mentioned	Not mentioned
Ashoorian et al, 2015 (M3Q Tool)	Australia-adult people diagnosed with mental health condition(s) and they taking at least one or more psychotropic medications. Participants data collected from community and clinic public mental health services in west Australia.	205 patients: >50 % male, Mean = 43 years, SD = 13. 73% reported taking multiple psychotropic medications.	All psychotropic PBS approvals	Average time of M3Q tool was 15 mins (SD=6.5), 10 cases reported severe side effects of medications, 40% participants reported health-medication interactions, 52.7% reported thinking to stop their medications due to intolerance side effects, 63.9% stopped their medication already.	All psychotropic PBS approvals	M3Q tool was validated by provided participants an opportunity to express the impact of psychotropic medications side effects on their lives. Furthermore, the validation pf this tool passed through rigorous process: including eight focus groups with experts stakeholders to develop items followed by psychometric testing assessing the validity and reliability of the M3Q questionnaire	Schizophrenia, bipolar disorder, depression, anxiety. These diseases usually associated with more or more comorbidities	Not mentioned	Follow-up after 3 months from the date of collection. Loss to follow-up had reported as 3 interviews abandoned to answer questions, 2 patients deceased and 14 decline to participate after 3 months from the first interview.	Not mentioned
Horne, Weinman & Hankins. 1999 (BMQ Tool)	This study had done in UK's clinics and hospitals, but using in Australia as a part of cognitive representation of medication assessment in older people	524 participants for MBQ general, and then assessed MBQ specific thereafter.	Non-drugs tools. This study contains only two sets of questionnaires: Specific MBQ (for representation of personal use) and General MBQ (assess believe about their medications)	Confirmatory factor analysis for MBQ general (overuse medications): cardiac 0.9, asthma: zero, Renal: zero, general medicine: 0.7, Psychotropic: 0.88, diabetes: zero. BMQ-General (Harm of medications): cardiac: 0.93, Asthma: zero, Renal: zero, general medicine: 0.73, psychiatry: 0.83, diabetes: zero. BMQ-Specific (Necessity of medications): cardiac: 0.98, Asthma: 0.92, Renal: 0.88, general medicine: 0.95, psychiatry: 0.83, diabetes: 0.9. BMQ-specific (concerns about medications): cardiac: 0.98, asthma: 0.88, renal: 0.88,	All medications are related with chronic conditions	The validity of BMQ-general scales was tested on basis on ability to distinguish between a personal prescription at community pharmacy and those seeking complementary therapies. The validity of BMQ-specific scales was tested on basis of participants ability to distinguish between different illness and treatment modalities.	CVDs, mental health, Asthma and COPD, type 2 diabetes, renal issues.	Not mentioned	Not mentioned	Not mentioned

				general medicine: 0.9, psychiatry: 0.96, diabetes: 0.95.						
(Lee at al. 2017) M-DRAW Tool	This study designed in USA-California and used in Australia. The study conducted in academic medical centres pharmacy in south California.	26	This study is non-drug focused. This study assesses factors contributing to medication non-adherence	Rate of response 48.1% out of 54. 65.4% out of 26 recruited are self-reported adherence level. Number of participants with health conditions (control and intervention respectively: hypertension 14, 8. Dyslipidaemia: 11, 4. Diabetes: 9, 4. Chronic back pain: 5, 2.	PBS-approved medication prescribed in chronic condition in adult and older people.	The validity been examined by applied pilot study of the psychometric properties of the M-DRAW tool to check the tool's reliability. The validity of the tool was examined by priming question in 4-fold number of barriers to adherence within the self-selected intervention group and control group. However, confirmed validity not clearly stated because of small sample size and lost follow-up	CVDs (hypertension and dyslipidaemia), type 2 diabetes, and chronic pain conditions.	Not mentioned	Loss follow-up reported in this study. For this reason, the validity of this study not been completely confirmed. The follow-up assessments were not collected as planned at the initial stage of the study protocol development because of short duration of this study time.	Not mentioned
McLeod et al. 1997 (McLeod Tool)	This study designed in Canada and using as a tool of older people I Australia. The participants from health professional of 32 specialities (7 clinical pharmacists, 9 geriatrics, 8 family GPs, and 8 community pharmacists)	32 health specialities recruited in academic medical centres across Canada.	CVDs drugs, psychotropic drugs, pain management drugs, and other miscellaneous drugs in older people	First mailing of preliminary list of 38 inappropriate practices in prescribing and respondents' suggestions of total 51 additional list.	B-blockers, AECIs, diuretics, CCB, benzodiazepine, TCA, barbiturate, antipsychotics, NSAIDs, phenylbutazone, warfarin, pentazocine, cimetidine, anticholinergics, antispasmodics, dipyridamole, diphenoxylate, cyclobenzaprine, methocarbamol.	Not mentioned	CVDs (including heart failure), asthma, COPD, mental issues (including dementia and insomnia), back pain, and osteoarthritis.	Not mentioned	Not mentioned	The collected list of inappropriate practice in prescribed medication underwent modifications before it is used in double-blinded controlled trial of a computer-based intervention for improving prescribing for older people.

Table 4: Auditing and Critical appraisal of included studies

Tool	Current use in practice	Used by	Evaluation	When not used and why?	Limitations in practice
DBI study (Nishtala et al. 2009) [14]	62 aged-care facilities in NSW. Determine DBI scores in older people in aged-care homes; and evaluate the impact of RMMR on DBI score after uptake of pharmacist recommendations by GPs [14]	Consultant Pharmacists in community and hospital settings, HMR† and RMMR‡ accredited pharmacists [14]	N = 500 residents, SD of age = 84.0 years, 25% male. SD for medications per resident = 7.4, SD for anticholinergic and sedative =0.9 & 0.2 respectively. Reduction in prescribed anticholinergic and sedative medications can be achieved in older people through using DBI [14].	DBI is a formula designed to measure the adverse effects of anticholinergic and sedative medication on the quality of life. A higher DBI score represents a lower quality of life. DBI is not a tool for frequent use. It provides a reference for developing a RMMR report and subsequent pharmacist recommendations to GPs and nursing staff [14]	This tool does not take into account differential pharmacokinetic properties of medications. No indication for drug-drug interactions provided and no pharmacodynamic profiles among aged-care home residents are developed [14]. No questionnaire; DBI calculations will be estimated as a liner dose-response relationship between drug classes. Predictive capacity of DBI not established. In this study the residents were not randomised into the intervention and control groups. This tool is applied retrospectively limiting any establishment of causality. No information about their health status or their disease severity was included [14].
INSPIRED study (Harrison et al. 2018) [7]	Cross-sectional study: analysis of 541 individuals recruited from 17 aged-care facilities in Australia (from NSW, QLD, SA, WA) [7]	Nurses and carers in aged-care facilities. This study was specific to older people living with cognitive impairment and dementia [7].	With respect to anticholinergic and sedative medications adverse effects, the PIM (Beers)§ criteria and DBI were highly prevalent in residential aged care at 73% and 83.1% respectively. Study confirmed higher exposure to these medications in inappropriate prescriptions were associated with a lower quality of life [7].	This study does not present a new tool. It is a comparison between DBI and PIM (Beer's criteria) to determine whether these tools are associated with quality of life in older adults living in aged-care facilities. It was only used in those with cognitive impairment and not for other medical conditions [7].	This study was unable to assess causality or the direction of any observed associated issues. In addition, these is no certainty of compatibility between the proxy measures that were used and what the individual would self-report if they able to do so [7].

FRIDs study Turner et al. 2016 [8]	Tertiary referral hospital in geriatric oncology outpatient multidisciplinary clinic [8].	Administrated by nurses, geriatricians, medical oncologists, geriatric oncology nurse, social workers, dietician, pharmacists, occupational therapists, and palliative care nurses [8].	Cohort study of older people with cancer. All data in this study verified by nurses with full access to patients' medical records. Enabled inclusion of any omitted data to be collected. There was 79% concordance for self-reported prescribed medications compared with those obtained in an interview with clinical pharmacists in hospital wards [8].	Study limited to older people newly diagnosed with cancer, and previous history of falls / or orthostatic hypotension, and administrating psychotropic medications. Not applicable to older people administered psychotropic medications [8].	Single site data collection and not generalisable to other settings. Some patients did not know what fall was, others did not remember having fallen or they underreported the number of falls (if they fell several times). Not possible to determine if FRIDs study used at the time of fall or initiated after fall [8]. In addition, the number of older people who were receiving more than 3 prescribed medications of antipsychotic was small. These factors impacted the results of the adjusted multi-variate regression analysis giving wider confidence intervals [8].
IMU-PI tool Basger et al. 2008 [9]	Study tool design informed by expert's review, international literatures, and clinical practice guidelines for medication use in elderly [9]. The tool used with Australian heathcare system data and cross-referenced with treatment of common medical conditions for those with the highest volume of Australian Pharmaceutical Benefits Scheme usage in 2006 and 2007 [9].	Experts from University of Sydney, NSW	Tool design is similar to Beers and McLeod tool. This tool had set out to develop an indicator list relevant to Australia the design did not involve an expert consensus process. Instead the tool was based on Australian healthcare data. Indicators had been selected from analysis of the most commonly dispensed PBS medications and based on the most common conditions for older people receiving medical care [9].	This study is NOT a specific tool or questionnaire used in age care facilities. This study performed only by collection of PBS data within only a 2 year window. As a result, this tool has no ability to determine or detect the adverse effects of medications nor be used in any aged-care facility [9].	The tool has not been validated yet. This tool was not designed to act as a preventative health tool to avoid adverse events. It indicates that either appropriate or inappropriate medication has been prescribed [9].

M3Q Tool Ashoorian et al. 2015 [10]	Six public mental health clinics and one hospital in WA; 205 participants divided into intervention and control groups [10].	Nurses in mental health clinics	M3Q was designed specifically to assess the effects of antidepressants, antipsychotics, anxiolytic and mood stabilizers. This tool was developed to fill the gaps of lack communication between clinicians and patients. It contains closed and open response questions. It has been through rigorous validation processes; expert focus groups developed the design and psychometric testing. Focuses on patient's list of self-reported medications and dose and they rank three bothersome side effects. Checklist of 32 possible side effects under 11 domains [10].	M3Q tool not applicable for older people suffering from other co-morbidities. The assessment of the psychotropic medication side effects does not reflect the reality of comorbidities and increases risk of inaccuracy [10].	The participants were 18 years or more. This tool is not designed to objectively record the accurate number of psychotropic medications and their side effects [10]. No statistically significant change was demonstrated within each group. M3Q tool has used a non-randomized convenience sample of patients. Many patients suffered other co-morbidities and were taking a number of medications not related to psychotropic medications or mental illness which may confound the assessment of side effects by clinician. A wider cross-section of patients attending GPs, pharmacies and wider representations would be worthwhile [10].
BMQ Tool Horne, Weinman & Hankins. 1999 [11]	London's hospitals and in clinical settings. This tool is used in Australia as a part of Pharmacist consultant questionnaire for determining patient's adherence to medication regimes and estimating possible medication side effects [11].	Nurses and consultant pharmacists	BMQ scales assess commonly held beliefs by a patient about prescribed medications and about medicines in general. BMQ tool has ability to distinguish among: different illness groups, treatment groups, adherence behaviours, and using complementary medicines [11].	BMQ tool has no criteria or questionnaire to help to determine side effects, or detect new illness, or for dealing with data of residents in aged-care facilities. This tool is only designed to estimate and to determine the beliefs of patients against their medications. Also, this tool is very general and has no specificity to mental illness [11].	The results of this tool may be at risk of overestimation because some patients have strong beliefs about the potential of harm regarding their medications [11]. Also, the negative views about their medication tend to attach to the potential for harm rather than the lack of efficacy or lack of benefits as a focus for clinician's concern. Furthermore, the evaluation of the BMQ validity due to an absence of testing [11].

M-DRAW Tool Lee at al. 2017 [12]	Academic medical centre pharmacy in California-USA.	Pharmacists, nurses, social workers, and patient's carers.	M-DRAW uses a motivational interview-based intervention strategy for each identified barrier. M-DRAW provides recommendations to clinicians on how to systematically approach follow-up for each identified barrier, and also identify the root cause of non-adherence [12].	This tool has been designed only for identifying barriers of medication adherence. It consists of a 13-item checklist questionnaire, and the results of this tool is scaled from 1 = never to 4 = often [12].	The limitation of this study is small sample size which limits generalisation. Test and re-test reliability was NOT performed, short duration study, follow-up items were not well defined [12] No specific illness dealt with; any chronic conditions. This tool assesses only non-intentional and intentional non-adherence of medications. This tool is applicable for a pharmacist conducting RMMR for medication-adherence assessment only [12].
McLeod Tool McLeod et al. 1997 [13]	Academic medical centres across Canada.	Pharmacists, doctors' specialists, nurses, GPs, geriatricians.	New approach to identify inappropriate practice in prescribing medication for older people. This study has a list of 71 inappropriate practices in prescription for older people, and each practice rated from 1-not significant to 4 high significance. 3 major categories: drug contraindicated, drug-disease interactions and drug-drug interactions. The recommendation for each item could be generalisable [13].	This tool developed by Beers and collaborators resulting in considerable similarity between this tool and Beers criteria. This tool will be helpful for medication reviewing and preparing recommendations to GPs for consideration [13].	This study has no specific questionnaire and requires no interview with patients [13]. It was designed only for detecting frequent inappropriate prescriptions for older people. The recommendation for each item was general with no further details or explanation [13].

† - HMR: Home Medication Review

‡ - RMMR: Residential Medication Management Review

§ - PIM Beers criteria: Potentially inappropriate medicines