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Title

Detectability of medication errors with a STOPP/START-based medication review in older people prior to a potentially preventable drug-related hospital admission

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Electronic supplementary material 2 – Adjudication guide for drug-related hospital admissions

A standardized chart review method previously published by Thevelin *et al.* was used for the adjudication of drug-related hospital admissions (DRAs) and related medication errors within the OPERAM trial [1-2]. The three-step approach for identifying DRAs (Figure 1) and the trigger tool with 26 explicit screening questions and 2 implicit screening questions (Table 1) are reprinted with permission of Thevelin *et al.* [1]

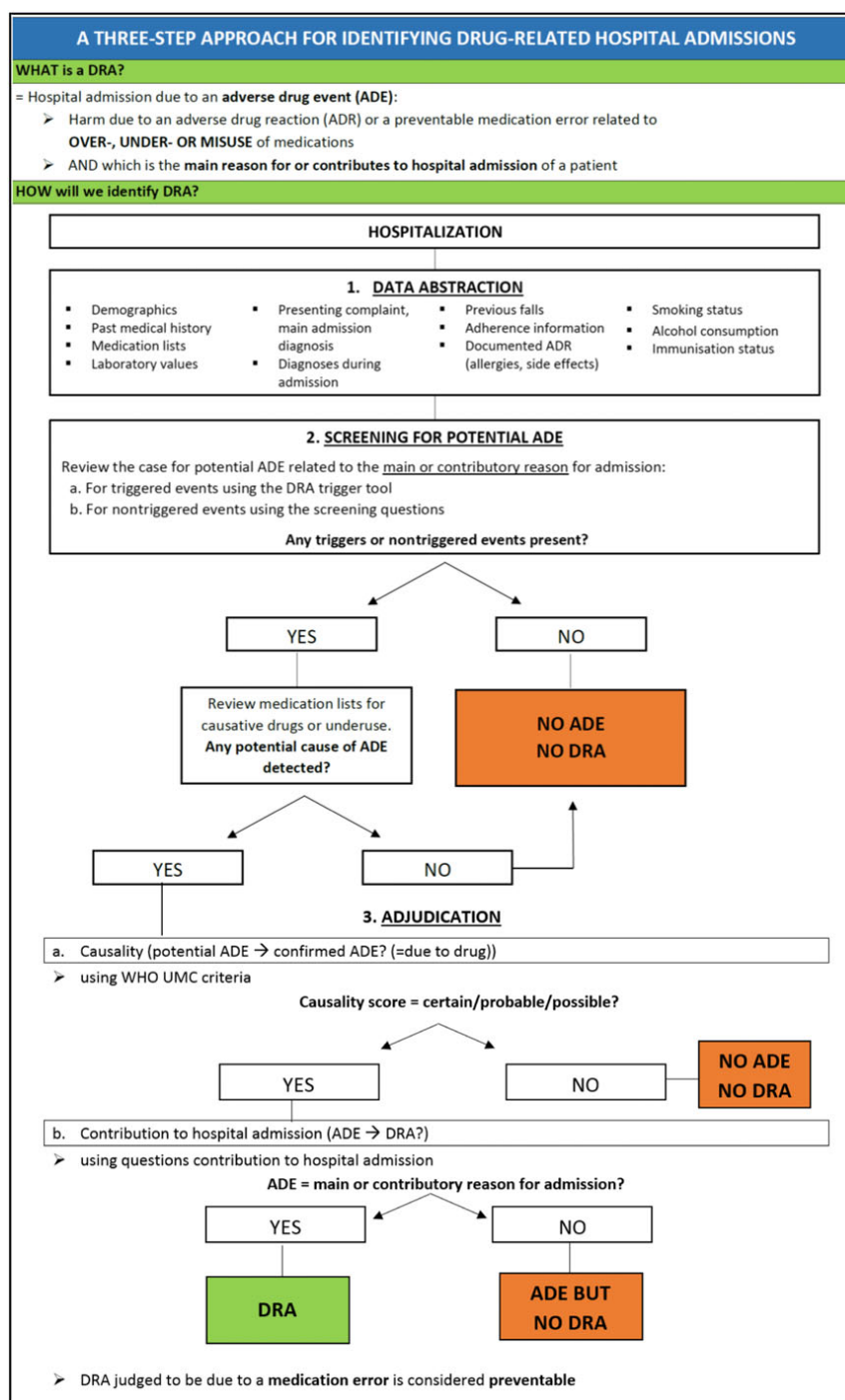


Figure 1. Three-step approach for identifying DRAs [1].

ADE = adverse drug event; DRA = drug-related hospital admission.

Table 1. Trigger tool for identifying DRAs in older persons [1].

TRIGGER TOOL TO SCREEN FOR DRUG-RELATED HOSPITAL ADMISSIONS IN OLDER PERSONS	
Trigger on admission up to 48h of admission	Suspected causative drugs or causes for underuse
<i>Diagnoses</i>	
Fall and/or fracture	Use of any of the following drugs? ☐ Benzodiazepines ☐ Non-benzodiazepine hypnotics e.g. zopiclone, zolpidem ☐ Antipsychotics ☐ Antidepressants ☐ Sedating antihistamines ☐ Opioids ☐ Anticholinergic drugs^a ☐ Other (<i>Please specify</i>):
	Use of any drugs causing orthostatic hypotension? ☐ Calcium channel blockers ☐ Diuretics ☐ α1-receptor blockers ☐ Nitrates ☐ β-blockers ☐ ACE-inhibitors ☐ Angiotensin receptor blockers ☐ Direct renin inhibitors (e.g. aliskiren) ☐ Anti-Parkinson drugs ☐ Antidepressants (mainly tricyclic) ☐ Antipsychotics ☐ Gliflozines (SGLT2-inhibitors) ☐ Other (<i>Please specify</i>):
	If a fall is caused by hypoglycaemia, look for use of drugs contributing to hypoglycaemia (check trigger hypoglycaemia)
	Underuse of any of the following drugs in patients with known osteoporosis and/or history of fragility fracture(s) and/or Bone Mineral Density T-scores of -2.5 or lower in multiple sites? ☐ 800 IU Vitamin D/day (+ 1000-1200 mg calcium/day if dietary intake is <1200-1000mg/day) ☐ Bone anti-resorptive therapy (e.g. bisphosphonates, strontiumranelate,teriparatide, denosumab)
	Underuse of any of the following drugs in patients on corticosteroid therapy $\geq$ 3 months? ☐ 800 IU Vitamin D/day (+ 1000-1200 mg calcium/day if dietary intake is <1200-1000mg/day) ☐ Bisphosphonates
	Underuse of vitamin D in patients who are housebound and/or experiencing falls or with osteopenia with Bone Mineral Density T-score between -1 and -2.5 in multiple sites?
Confusion/delirium ^b	Use of any of the following drugs? ☐ Benzodiazepines ☐ Non-benzodiazepine hypnotics e.g. zopiclone, zolpidem ☐ Antipsychotics ☐ Anti-epileptics ☐ Antihistamines (H1- and H2-receptor blockers) ☐ Antidepressants ☐ Opioids ☐ Dopaminergic agonists ☐ Digoxin ☐ Fluoroquinolones (<i>dose adjustment in renal impairment required</i>) ☐ Acetylcholinesterase-inhibitors (new onset confusion in patients with dementia) ☐ Other anticholinergic drugs^a (<i>Please specify</i>):
	Abrupt discontinuation/rapid dose reduction of any of the following drugs? ☐ Benzodiazepines ☐ Non-benzodiazepine hypnotics e.g. zopiclone, zolpidem ☐ Corticosteroids ☐ Dopaminergic agonists ☐ Antidepressants ☐ Opioids ☐ Lithium ☐ Antipsychotics ☐ Other (<i>Please specify</i>):
Acute renal impairment ^b	☐ Non-steroidal anti-inflammatory drugs ☐ ACE-inhibitors ☐ Angiotensin receptor blockers ☐ Diuretics ☐ Sulphonamides ☐ Cephalosporins ☐ Quinolones (ciprofloxacin) ☐ Aminoglycosides ☐ Vancomycin ☐ Pentamidine ☐ Rifampicin ☐ Acyclovir, valacyclovir, gancyclovir, valgancyclovir, foscarnet, cidofovir ☐ Lithium ☐ Calcineurin Inhibitors (e.g. cyclosporine, tacrolimus) ☐ Cisplatin ☐ Radiology contrast medium ☐ Amphotericin ☐ Bisphosphonates ☐ Other nephrotoxic drugs (<i>Please specify</i>):
Dehydration	Use of any of the following drugs? ☐ Diuretics ☐ Gliflozines (SGLT2-inhibitors) ☐ Laxatives ☐ Any drugs causing vomiting ☐ Any drugs causing diarrhoea ☐ Other (<i>Please specify</i>):

(Table continues)

Bleeding ^b	Use of any of the following drugs? ☐ Antiplatelets ☐ Vitamin K antagonists ☐ Direct oral anticoagulants ☐ Unfractionated heparin ☐ Low molecular weight heparins ☐ Selective serotonin reuptake inhibitors ☐ Non-steroidal anti-inflammatory drugs ☐ Other (Please specify):
	☐ Underuse of proton pump inhibitors prophylaxis while - NSAIDs monotherapy (≥ 70 years old) or on concurrent NSAIDs and/or antiplatelets and/or corticosteroids - NSAIDs or antiplatelet or corticosteroids monotherapy with a history of peptic ulcer disease/gastrointestinal bleeding while on these drugs
Stroke	Underuse of any of the following drugs in patients with known chronic atrial fibrillation? ☐ Vitamin K antagonists ☐ Direct oral anticoagulants (except valvular atrial fibrillation)
	Underuse of adequate antihypertensive therapy? * Note: Adequate antihypertensive therapy is defined according to the recommendations for older patients in the 2013 European ESH/ESC guidelines for the management of arterial hypertension. Underuse of any of the following drugs in patients with history of coronary, cerebral or peripheral vascular disease? ☐ Antiplatelets ☐ Statins** (unless end-of-life or > 85 years old) **Note: Evidence for statin treatment above the age of 80-85 years is limited and clinical judgement should guide decisions in the very old, taking into account life expectancy, serious adverse events, possible drug interactions. Low to moderate intensity statin regimens are recommended. (low: simvastatin 10mg, pravastatin 10-20mg, fluvastatin 20-40 moderate: atorvastatin 10-20mg, Rosuvastatin 5-10mg, Simvastatin 20-40mg, pravastatin 40-80 mg, Fluvastatin 80 mg, Fluvastatin 40 mg BID)
Thromboembolic event (DVT or PE)	Underuse of adequate anticoagulation? ☐ Unfractionated heparin ☐ Low molecular weight heparins ☐ Direct oral anticoagulants ☐ Vitamin K antagonists
(Recurrent) myocardial infarction or ischaemic disease	Underuse of cardiovascular secondary prevention? ☐ Antiplatelets (unless already anticoagulated) ☐ Statins** (unless end-of-life or > 85 years old) ☐ β-blocker/ACE-inhibitor or angiotensin receptor blocker /adequate anti-anginal therapy in case of ischaemic disease Underuse of adequate antihypertensive therapy? *
Heart failure exacerbation	Use of any drugs that could precipitate heart failure exacerbation? ☐ Non-steroidal anti-inflammatory drugs ☐ Corticosteroids ☐ Thiazolidinediones (glitazones) ☐ Non-dihydropyridine calcium channel blockers (verapamil, diltiazem) ☐ Sodium-containing formulations (effervescent, dispersible and soluble medications) ☐ Other (Please specify):
	Underuse of any of the following drugs? ☐ β-blockers^x ☐ ACE-inhibitors^x ☐ Diuretics Note: ^x β-blocker and ACE-inhibitors in heart failure due to left ventricular dysfunction
COPD exacerbation	Use of any drugs that could precipitate COPD exacerbation? ☐ Benzodiazepines with acute or chronic respiratory failure ☐ Opioids ☐ Other (Please specify):
	Underuse of any of the following drugs? ☐ Single or dual inhaled bronchodilator therapy i.e. a β2 agonist and/or anticholinergic bronchodilator according to the GOLD (Global Initiative for Chronic Obstructive Lung Disease) grade
Uncontrolled (non-neuropathic) pain	Underuse of adequate pain treatment (according to the WHO analgesic ladder)? ☐ A strong opioid in moderate to severe pain if paracetamol, NSAIDs or weak opioids are not appropriate (e.g. because of insufficient pain relief) ☐ Short-acting opioids for break-through pain during treatment with long acting opioids ☐ Other (Please specify):
Gastrointestinal disorders (severe diarrhoea, vomiting)	Use of any of the following drugs? ☐ Antibiotics ☐ Laxatives ☐ Selective serotonin reuptake inhibitors ☐ Digoxin ☐ Cholinesterase-inhibitors ☐ Opioids ☐ Non-steroidal anti-inflammatory drugs ☐ Chemotherapy (Please specify): ☐ Other (Please specify):
Major constipation or faecal impaction	Use of any of the following drugs? ☐ Chronic (stimulant) laxative use ☐ Opioids (look for underuse of laxatives with regular opioid use) ☐ Calcium antagonists (Mainly verapamil) ☐ Calcium ☐ Oral iron ☐ Aluminium antacids ☐ Atypical antipsychotics ☐ Tricyclic antidepressants ☐ Bladder antimuscarinics ☐ Other anticholinergic drugs^a ☐ Other (Please specify):

(Table continues)

Laboratory values	
INR > 5	Look for evidence of bleeding (see trigger) to determine if an adverse drug event (ADE) has occurred. A raised INR in itself is not an ADE.
Digoxin level > 2ng/ml	Look for signs or symptoms of digoxin toxicity (bradycardia, nausea, diarrhoea, confusion) to determine if a potential ADE has occurred. Not all levels above normal will result in an ADE.
Hypoglycaemia (blood glucose < 4 mmol/L or 72 mg/dl)	Look for symptoms such as lethargy, tremor, confusion, faintness or administration of intravenous or oral glucose. Use of any of the following drugs? ☐ Insulin ☐ MAO – inhibitors ☐ Oral hypoglycaemic agents (except metformin in monotherapy) ☐ β-blockers (masking symptoms of hypoglycaemia)
Hyperglycaemia (blood glucose > 11 mmol/L or 198 mg/dl)	Use of any drugs that may cause or worsen hyperglycaemia? ☐ Corticosteroids ☐ Protease-inhibitors ☐ Atypical antipsychotics (mainly olanzapine & clozapine) ☐ Calcineurin Inhibitors (cyclosporine, sirolimus, tacrolimus) ☐ Thiazide diuretics <i>less frequent</i> ☐ β-blockers (except carvedilol and nebivolol) <i>less frequent</i> ☐ Other (Please specify): In case hyperglycaemia is part of diabetic ketoacidosis or hyperosmolar hyperglycaemic state in a patient, review for underuse of insulin or oral hypoglycaemic agents.
Hyperkalaemia (K ⁺ > 5.5 mmol/L)	Use of any the following drugs? ☐ Intravenous or oral potassium ☐ Heparins (seldom, mainly when treated > 7 days and concomitant other risk factors) ☐ Potassium-sparing diuretics ☐ Trimethoprim-sulfamethoxazole ☐ ACE-inhibitors ☐ Cyclosporine ☐ Angiotensin receptor blockers ☐ Tacrolimus ☐ Direct renin inhibitors (e.g. aliskiren) ☐ Other (Please specify): ☐ Non-steroidal anti-inflammatory drugs
Hypokalaemia (K ⁺ < 3 mmol/L)	Use of any of the following drugs? ☐ Loop diuretics ☐ Laxatives ☐ Thiazide and thiazide-like diuretics ☐ Salbutamol (IV or aerosol) ☐ Corticosteroids ☐ Theophylline ☐ Other (Please specify):
Hyponatraemia (Na ⁺ < 130 mmol/L)	Use of any of the following drugs? ☐ Diuretics ☐ Angiotensin receptor blockers ☐ Selective serotonin reuptake inhibitors ☐ Carbamazepine & oxcarbazepine ☐ Tricyclic antidepressants ☐ High dose cyclophosphamide ☐ ACE-inhibitors ☐ Other (Please specify):
White blood cells < 3000 /mm ³ or < 3 x 10 ³ / μ L	Use of any of the following drugs? ☐ Carbamazepine & oxcarbazepine ☐ Chemotherapy (Please specify): ☐ Antipsychotics (mainly clozapine) ☐ Mirtazapine (first 6 weeks of treatment) ☐ Thyreostatics ☐ Voriconazole ☐ Ganciclovir ☐ Other (Please specify): ☐ Immunosuppressants
Platelet count < 50000 /mm ³ or < 50 x 10 ³ / μ L	Use of any of the following drugs? ☐ Carbamazepine & oxcarbazepine ☐ Quinine sulfate ☐ Ganciclovir ☐ Sulfamides <i>Less frequent</i> ☐ Unfractionated heparin ☐ Chemotherapy (Please specify): ☐ Low molecular weight heparins ☐ Other (Please specify): ☐ Immunosuppressants ☐ Thienopyridines (mainly ticlopidine)
Neutrophils < 1400/mm³ or < 1.4 x 10 ³ / μ L	Use of any of the following drugs? ☐ Ganciclovir ☐ Chemotherapy (Please specify): ☐ Antipsychotics (mainly clozapine) ☐ Other (Please specify): ☐ Thyreostatics ☐ Thienopyridines (mainly ticlopidine)

(Table continues)

Other	
Antidote use or treatments that suggest a potential ADE	Use of any of the following drugs on the day of admission? ☐ Flumazenil in a patient on benzodiazepines ☐ Naloxone in a patient on opioids ☐ Adrenaline, antihistamines and corticosteroids (general drug allergy) ☐ Phytanadione (vitamin K) in a patient on VKA ☐ Protamine sulphate in a patient on heparins ☐ Acetylcysteine (paracetamol overdose) ☐ Oral or intravenous glucose or glucagon in a patient taking hypoglycaemic drugs ☐ Potassium supplements in case of hypokalaemia ☐ Digoxin antibodies in a patient with supratherapeutic digoxin levels ☐ Sodium polystyrene (Kayexalate) in case of hyperkalaemia ☐ Oral metronidazole or vancomycin in a patient who has recently been treated with an antibiotic that may cause <i>Clostridium difficile</i> associated diarrhoea
Mention of a (potential) ADE in the medical record	Assess causality using the WHO-UMC criteria
Abrupt medication stop within 24h of admission	When medications are stopped or withheld as compared to medications taken at home, look for reasons why this was done. Abruptly stopping medications is a trigger requiring further investigation for cause. A sudden change in patient condition requiring adjustment of medications is often related to an ADE.

ADE, adverse drug event; ADR, adverse drug reaction; COPD, chronic obstructive pulmonary disease; DVT, deep vein thrombosis; FEV₁, forced expiratory volume in 1 second; ESH/ESC, European Society of Hypertension/European Society of Cardiology; INR, international normalised ratio; NSAIDs, non-steroidal anti-inflammatory drugs; PE, pulmonary embolism; VKA, Vitamin K antagonists
 *A list of medications with clinically relevant anticholinergic properties is available in the DRA adjudication guide; *Detailed definition of trigger available in the DRA adjudication guide

SCREENING QUESTIONS FOR NON-TRIGGERED, SPONTANEOUSLY DETECTED EVENTS	
1. Could the main or contributory reason for admission be related to a drug or recent change in medications?	☐ Adverse drug reaction (non-preventable side effect, first allergic reaction) ☐ Wrong drug ☐ Overuse of medication(s) (drug without an indication, too long duration of therapy, therapeutic duplication) ☐ Wrong dose (supratherapeutic or subtherapeutic) ☐ Inappropriate discontinuation (removal or dosage decrease) leading to physiological withdrawal signs/symptoms or return of the underlying disease signs/symptoms ☐ Clinically significant drug-drug or drug-food interactions ☐ Inappropriate monitoring ☐ Other (e.g. drug not correctly dispensed/prepared/administered)
2. Could the main or contributory reason for admission be related to underuse?	☐ Omission of an indicated drug ☐ Suspected adherence concerns ☐ Too short duration of medication therapy

References

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