Table S10

Included randomized controlled studies (RCTs); Characteristics and outcomes (n= 18)

Estimates are reported for safety outcomes and adverse effects. For other outcomes, information is given if outcomes were significantly worse, significantly better, or no significant differences

	Study Design RCT = randomized controlled trial RCT- I = **individuals randomized** RCT-C = RCT, cluster randomized Unit(s) of randomization	**Setting**	**Intervention** CDSS = computerised clinical decision support system EHR: electronic health record E-Rx: electronic prescribing eGPP = electronically generated paper prescription	**Comparison**	***á priori* specified monitoring for safety outcomes or risks** **Adverse events (AE) reported?** **Risks to patient safety reported?**	**Process outcomes**	**For safety outcomes: Change in process outcomes consistent with (↑) or non-consistent with (↓) intent of intervention** * : p calculated by reviewers **For other outcomes:** W: significantly worsened B: significantly better NS: no significant differences	**Patient outcomes**	**For safety outcomes: Change in patient outcomes consistent with (↑) or non-consistent with (↓) intent of intervention** * : P calculated by reviewers **For other outcomes:** W: significantly worsened B: significantly better NS: no significant differences	**Uptake of e-intervention** non-use, override or rejection of CDSS suggestion:
1	**Ansari 2003** - β-blocker use in heart failure RCT-C Patients randomized to prescriber Prescriber randomized to intervention	Hospital out-patient clinic	CDSS in EHR System initiated eGPP Computerized provider guideline based reminders (and patient letters advocating beta-blockers) to improve guideline adherence for β-blocker use in heart failure patients	Control and nurse facilitator	*á priori* specified-Information was collected on hospitalizations, emergency room visits, and deaths during follow-up as indicators of safety AE reported: no Risks to patient safety: See patient outcomes	% patients initiated or up-titrated and maintained on β-blockers % patients initiated on β-blockers % patients at target β-blockers doses at end of study Time to reach target dose	W W W W	Hospitalizations ER visits during follow-up Median hospitalizations or ER visits per patient Deaths during follow-up	↑ 6%, p = 0.56 (*) 43% vs. 49% ↑ 1%, p = 1.0 (*) 9% vs. 10% ↓4% vs 2% ↑ 5%, p = 0.55 (*) 9% vs. 14%	33% of intervention group (physicians) started or adjusted medications compared to 67% in no CDSS groups (nurse and control)
2	**Berner 2006** - NSAIDs	Hospital out-patient clinic	CDSS only User initiated	Usual care	*á priori* specified-Yes, unsafe prescribing main	Mean proportion of patients per MD with unsafe prescribing	↑ effect size = 0.54, p < 0.05			not reported

	RCT- I Prescriber randomized to intervention		Point-of-care hand-held risk assessment and treatment with NSAIDs		outcome AE reported: no		0.23 vs. 0.45, p<0.05 This does not make sense.			
3	**Dainty 2011** - Non-specific prescribing RCT- C Randomized by time period	Hospital out-patient clinic	E-Rx in conjunction with CDSS facility for computer-generated paper prescription User initiated Facility to transmit prescription to hospital or community pharmacy; pick-lists of medications for prescription writing	usual prescribing methods	*á priori* specified-no AE reported: no	Total prescription error ratio Pharmacy call-backs/week for clarification	↓ 0.1%, p = 0.91 6% vs. 5.9% ↓ 5.6%, p <0.001 1.89% vs. 1.45%			Low uptake of e-Rx, around 6%
4	**Feldstein 2006c** -Warfarin medication interaction RCT- C Practices randomized to intervention	Doctor's office	CDSS in EHR System initiated Alerts for warfarin medication interactions	No alerts	*á priori* specified-yes; main outcome AE reported: no	Total interacting prescription rate per month Absolute Risk Reduction (RRR) per month at 12 months	↑ slope -22.4/10000 patients, P = 0.01 ↑ 489.8 95%CI: -664.9 to – 314.7 (14.9%,95%CI:19.5% to -10.2%)			Not reported
5	**Fitzmaurice 1996** - Oral anticoagulation therapy RCT- I Patient randomized to intervention	Doctor's office	CDSS System initiated Dosing of oral anticoagulants	Hospital clinic dosing	*á priori* specified-Yes, deaths and adverse events AE reported: Yes, one unconfirmed thrombotic episode in intervention vs. none in control. Otherwise, intervention overall had fewer adverse events.			INR control Adverse events - deaths - thrombotic episodes - hemorrhagic episodes	NS ↑ 1 vs. 2 ↓ 1 (unconfirmed) vs. 2 ↑ 3 (2 epistaxes; 1 bruising) vs. 5 (3 epistaxes; 1 gum bleed; 1 haematoma)	Not reported
6	**Fitzmaurice 2000**	Hospital out-	CDSS	Hospital clinic	*á priori* specified-			Results given for intervention		

	- Oral anticoagulation therapy RCT- I Patients randomized to intervention	patient clinic and doctor's office	System initiated Dosing recommendations for patients taking oral anticoagulation therapy (Warfarin)	dosing	Yes; adverse events, particularly hemorrhagic and thromboembolic episodes AE reported: yes, see patient outcomes			(number of patients= 122) vs. intra-practice control (number of patients= 102) Proportion of patients achieving individual INR targets Percentage of time in INR range Adverse events: thromboembolic episodes - Deep venous thrombosis - Transient ischemic attack - Fatal CVA - Non-fatal CVA (infarct) - Saddle embolus - Epistaxis Death rates - Stroke - CHF - Ischemic heart disease - Left ventricular failure . Renal failure - Carcinoma	 NS B ↓ 1 vs. 0 ↑ 0 vs. 1 ↓ 1 vs. 0 ↑ 0 vs. 1 ↑ 0 vs. 1 ↓ 1 vs. 0 ↓ 1 vs. 0 ↓ 1 vs. 0 0 vs 0 ↑ 0 vs. 1 ↑ 0 vs. 1 1 vs. 1	Not reported
7	**Fortuna 2009** - Hypnotics for elderly patients RCT- C Practices randomized to intervention	Doctor's office	CDSS with EHR System initiated Alerts to support evidence based prescribing with and without physician-led educational sessions, to reduce prescribing of certain hypnotics	Usual care	*á priori* specified- Risk of prescribing certain hypnotics AE reported: no	Ratio of relative risk of prescriptions for certain hypnotics Changes in proportion of prescriptions for certain hypnotics	Ratio of adjusted RR (95% CI) 0.74(0.57 to 0.96) ↑ Adjusted RR (95% CI) 0.97 (0.82 to 1.14) vs. 1.31 (1.08 to 1.60)			Not reported
8	**Holt 2010** - Risk alerts for CVD	Doctor's office	CDSS in EHR	No alerts	*á priori specified:* Yes, main outcome			annual cardiovascular event rate	↑Rate ratio 0.96, p= 0.02 (95%	Not reported

	RCT- I Patients randomized to intervention		System initiated alerts of risk of coronary vascular disease		AE reported: no				C.I.0.85 to 1.10)	
9	**McCowan 2001** - Asthma RCT- C Practices randomized to intervention	Doctor's office	CDSS System initiated e-delivery of guidelines for asthma	Usual care	*á priori* specified- Yes: hospital admissions, A&E attendances, outpatient consultation, acute exacerbations of asthma AE reported: Yes, see patient outcomes	Level of maintenance prescribing	NS	Percent of patients who initiated an asthma consultation Acute exacerbation of asthma Need for acute prescription for oral corticosteroids Need for emergency nebulisations Admittance to hospital Need to attend ER Need to attend outpatient departments	↑ OR 0.59 (95% C.I. 0.37 to 0.95) 22% vs. 34% ↑ OR 0.43 (95% C.I. 0.21 to 0.85) 8% vs.1 7% ↑OR 0.42 (95% C.I. 0.14 to 1.29) 5% vs. 11% ↑ OR 0.13 (95% C.I. 0.01 to 0.91) 1% vs. 5% ↑ OR 0 (95% C.I. 0 to 3.44) 0% vs. 1% ↑ OR 0 (95% C.I 0 to 9.16) 0 vs. 1% ↑ OR 0.64 (95% C.I 0.09 to 3.38) 1% vs. 2%	Not reported
10	**Montgomery 2000** - Hypertension RCT- C Practices randomized to intervention	Doctor's office	CDSS and user or system initiated EHR CDSS system initiated CDSS cardiac risk calculation and cardiovascular risk chart combined for appropriate prescribing for	Traditional prescribing or Risk Chart Risk chart alone	*á priori* specified- Yes, high risk of cardiovascular event, see patient outcomes AE reported: no, only proportion of patients with high risk			Proportion of patients with high risk of cardiovascular event - vs Traditional dosing - vs Risk chart only	↓ OR = 1.7 (95% C.I 0.7 to 3.9) p = 0.43 ↓ OR = 2.3 (95% C.I 1.1 to 4.8) p = 0.02	Not reported

			hypertension							
11	**Poller 2009** - Oral anticoagulation therapy RCT- I Patients randomized to intervention	Hospital out-patient clinic	CDSS System initiated Computer-generated dosing of anti-coagulant therapy	Traditional dosing	*á priori* specified-Major bleeds, thrombotic events, death. AE reported: Higher risk (NS) for major bleeds (1.4 versus 0.9 events per 100 patient years) with computer-assisted anticoagulant dosing			Overall time in target range Events per 1000 patient years - Major bleeds - Minor bleeds - Thrombotic events - Deaths	B ↓ 1.4 vs. 0.9 (p = 0.404)* ↑ 2.5 vs. 2.7 (p = 0.8896)* ↑ 0.9 vs. 1.4 9 (p = 0.404)* 0.8 vs. 0.8 * 2-tailed chi-squared with Yate's correction	27.2% of computer dosing advice was not taken.
12	**Tamblyn 2003** - Elderly patients RCT- I Prescribers randomized to intervention	Doctor's offices	CDSS with EHR System initiated Alerts identifying potential prescribing problems, consequences and alternative suggestions to reduce inappropriate prescribing in elderly patients for selected drugs	No CDSS	*á priori* specified-no AE reported: no	Initiation rate of inappropriate prescribing - Overall - Drug - disease contraindications - Drug-age contraindication - Excessive duration of therapy - Therapeutic duplication - Drug interaction - Discontinuation of inappropriate prescribing Discontinuation of inappropriate prescribing - Overall - For drug-disease contraindication - For drug-age contraindication	RR (95% C.I.) ↑ 0.8 (0.69 to 0.98) ↑ 0.89 (0.72 to 1.10) ↑ 0.77 (0.59 to 1.00) ↑ 0.78 (0.61 to 0.99) ↑ 0.78 (0.61 to 0.99) ↓1.12 (0.68 to 1.87) ↓1.06 (0.89 to 1.26) RR (95% C.I.) ↑ 1.06 (0.89 to 1.26) ↑ 1.08 (0.85 to 1.36) ↓0.94 (0.79 to 1.1)			Not clear

						- For excessive duration of therapy - For therapeutic duplication - For drug interaction	1.00 (0.77 to 1.29) ↓0.94 (0.54 to 1.51) ↑ 1.33 (0.90 to 1.95)			
13	**Tamblyn 2012** - Psychotropics for elderly patients RCT- I) Prescribers randomized to intervention	Doctor's office	CDSS: patient-specific risk of injury alert upon prescribing of psychotropics to elderly patients System initiated	No alert	*á priori specified:* yes, main outcome "risk of injury" AE reported: no	Physician's response to the injury risk alert (observational, non-comparative) Changes in the use and dose of psychotropic medications (observational, non-comparative)	83.3% 41%	Reduction in risk of injury per 1000 patients	↑1.7 (95% C.I. 0.2 to 3.2; p= 0.02)	yes, process outcomes: 41% alerts not followed
14	**Terrell 2009** - Elderly patients RCT- I Prescribers randomized to intervention	Emergency room	CDSS with EHR-CPOE—emergency room) System initiated CDSS triggered upon tentatively inappropriate prescribing for patients over 64 to reduce potentially inappropriate prescribing	Usual care	*á priori* specified: no AE reported: no	Visits with an inappropriate medication prescription Prescriptions that were inappropriate	↑ 2.6% vs. 3.9%, p = 0.02, OR: 0.55 (C.I. 0.34 to 0.89) ↑ 3.4% vs. 5.4%, p = 0.006, OR: 0.59 (C.I. 0.41 to 0.85)			57% of intervention suggestions rejected
15	**Terrell 2010** - Renal insufficiency RCT- I Prescribers randomized to intervention	Emergency room	CDSS integrated in EHR System initiated To facilitate appropriate dosing of targeted medications for adult patients with renal insufficiency	Usual care	*á priori* specified-excessive dosing AE reported: no	Rate of excessive prescribing of targeted medications overall	↑ Effect Size 31% (95% C.I. 14% to 49%) 43% vs. 74%, p = 0.0012*			Prescribers did not follow suggestions for 43% of prescriptions

			being discharged home from the ER							
16	**Tierney 2003** - Heart failure and ischemic heart disease RCT- C Time periods randomized to intervention	Doctor's office	CDSS withEHR System initiated Evidence-based medication management suggestions for patients with heart failure and ischemic heart disease	Usual care	*á priori* specified: Yes, clinic visits, hospitalizations and other adverse events AE reported: not other than as prespecified patient outcomes	Adherence to suggestion to - start or increase an ACE inhibitor - prescribe pneumococcal vaccination -start or increase a β-blocker -start low-dose aspirin -start or increase a diuretic -start or increase a long-acting nitrate -start an antihyperlipidemic drug -start or increase a calcium channel blocker:	 NS NS NS NS NS NS NS	Adverse events - Number of all emergency department visits - Number of heart disease specific emergency department visits - Number of all hospitalizations - Number of heart disease specific hospitalizations	mean/person ↓ 1.1 (SD 1.9) vs. 1.0 (SD 1.7) 0.2 (SD 0.4) vs. 0.2 (SD 0.5) 0.2 (SD 0.4) vs. 0.2 (SD 0.5) 0.2 (SD 0.45) vs. 0.2 (SD 0.6)	Not reported
17	**Tierney 2005** - Medication and vaccination suggestions for asthma and COPD RCT- C Time periods randomized to intervention	Hospital out-patient clinic	CDSS with EHR System initiated Patient-specific medication and vaccination suggestions based on evidence-based guidelines for asthma and COPD	No suggestions	*á priori* specified: Yes, clinic visits, hospitalizations and other adverse events AE reported: not other than as prespecified patient outcomes .	Compliance with medication treatment guidelines for medication to - prescribe influenza vaccination - prescribe pneumococcal vaccination - Start ipratropium - Start inhaled β-agonist - Increase/ decrease theophylline dose - Stop ipratropium	 NS NS NS NS NS NS	Number of all emergency department visits Number of emergency department visits for reactive airways disease Number of all hospitalizations Number of hospitalizations for reactive airways disease	1.4 (SD 1.7) vs. 1.4 (SD 1.59) 0.3 (SD 0.7) vs. 0.3 (SD 0.8) ↑ 0.5 (SD 1.6) vs. 0.4 (SD 0.8) ↓ 0.5 (SD 0.5) vs. 0.1 (SD 0.3)	Physicians did not adhere to 68% of suggestions overall.

						- Start inhaled corticosteroid - Start oral corticosteroid	NS NS			
18	**Vadher 1997** - Oral anticoagulant control RCT- I Patients randomized to intervention	Hospital out-patient clinic	CDSS for nurses System initiated Oral anticoagulant control by nurse using CDSS	Trainee doctors without CDSS	*á priori* specified- YES, thrombosis, hemorrhage AE reported: Yes, patient outcomes	Adherence to guidelines for - INR range group (2-3) - INR range group (3-4.5)	B NS	Time (days per 100 patient days of treatment) in INR therapeutic range - range group (2-3) - range group (3-4.5) Thrombotic events Hemorrhagic events	B NS intervention: 1 vs. control : 2 intervention: 2 vs. control : 1	Adherence to guideline in lower INR group intervention 88% vs. control 60%; P = <0.01 Adherence to guideline in higher INR group intervention 67% vs. control 73%; P =0.18