

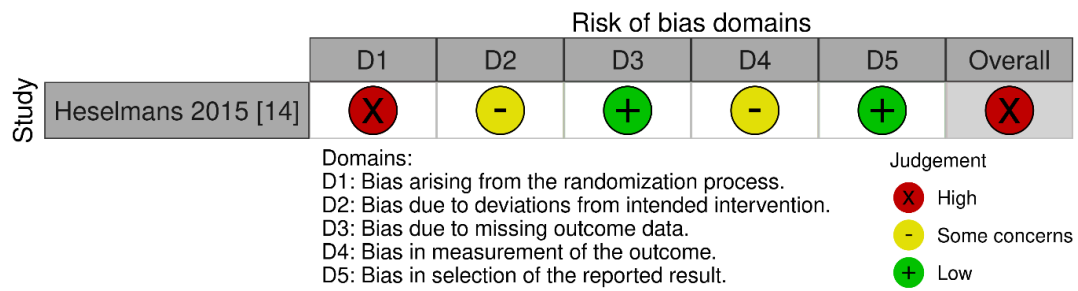
## Additional File 4: Risk of Bias and GRADE assessments

		Risk of bias domains							Overall
		D1	D2	D3	D4	D5	D6	D7	
Study	Anstey 2019 [54]	⊗	+	+	+	+	-	+	⊗
	Bosma 2018 [13]	-	+	+	+	+	-	+	-
	Buckley 2015 [55]	⊗	+	+	+	+	-	+	⊗
	Coon 2015 [56]	⊗	+	+	+	+	-	+	⊗
	D'Angelo 2019 [57]	-	+	+	+	+	-	-	⊗
	Hammond 2017 [58]	⊗	+	+	+	+	-	+	⊗
	Hatch 2010 [59]	⊗	+	+	+	-	-	+	⊗
	Kram 2019 [60]	⊗	+	+	+	+	-	+	⊗
	Medlock 2011 [61]	-	+	+	+	+	-	+	-
	Meena 2015 [47]	⊗	+	+	+	+	-	+	⊗
	Parsons Leigh 2020 [48]	⊗	-	+	+	+	-	+	⊗
	Pavlov 2014 [49]	-	+	+	+	+	-	-	⊗
	Pronovost 2003 [50]	⊗	+	⊗	+	⊗	-	+	!
	Stuart 2020 [53]	⊗	+	+	+	-	-	+	⊗
	Tasaka 2014 [51]	⊗	+	+	+	+	-	+	⊗
Zeigler 2008 [52]	⊗	+	+	+	+	-	+	⊗	

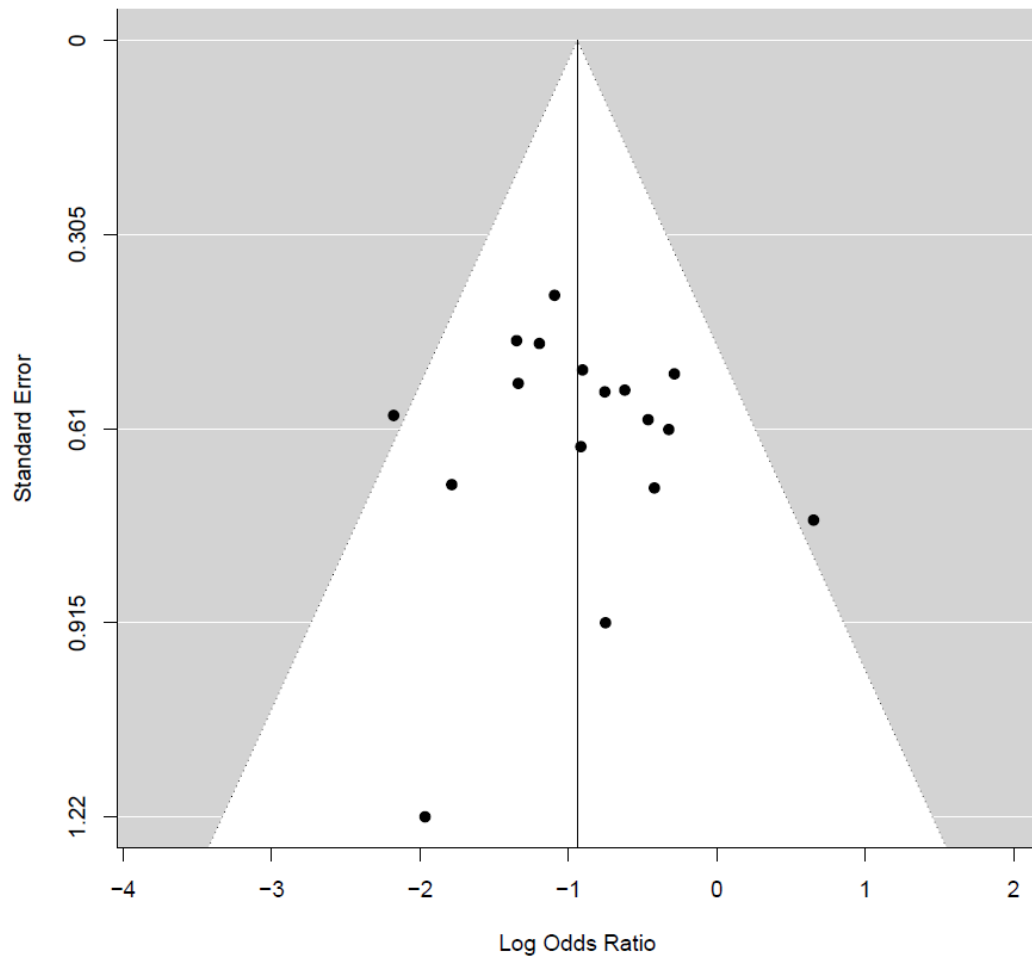
Domains:  
D1: Bias due to confounding.  
D2: Bias due to selection of participants.  
D3: Bias in classification of interventions.  
D4: Bias due to deviations from intended interventions.  
D5: Bias due to missing data.  
D6: Bias in measurement of outcomes.  
D7: Bias in selection of the reported result.

Judgement  
! Critical  
⊗ Serious  
- Moderate  
+ Low

**Figure S1. Robvis representation of ROBINS-I risk of bias assessments of non-randomised controlled trial studies**



**Figure S2. Robvis representation of ROB2.0 risk of bias assessments of the randomised controlled trial study**



**Figure S3.** Funnel plot of the treatment effect estimates from individual studies included in the meta-analysis

No of studies	Study design	Certainty assessment					Effect (OR) (95% CI)	Certainty
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Main meta-analysis. All de-escalation studies - ICU discharge inappropriate medication therapy								
9	observational studies	very serious <sup>a</sup>	not serious	serious <sup>b</sup>	not serious	strong association <sup>c</sup>	OR 0.45 (0.31 to 0.63)	⊕⊕○○ LOW
Main meta-analysis. All de-escalation studies - Hospital discharge inappropriate medication therapy								
9	observational studies	very serious <sup>a</sup>	serious <sup>d</sup>	serious <sup>b</sup>	not serious	strong association <sup>c</sup>	OR 0.39 (0.2 to 0.76)	⊕○○○ ○ VERY LOW
Sub-group meta-analysis. Multicomponent de-escalation studies - ICU discharge inappropriate medication therapy								
3	observational studies	very serious <sup>a</sup>	not serious	not serious	not serious	strong association <sup>c</sup>	OR 0.37 (0.23 to 0.59)	⊕⊕⊕○ MODERATE
Subgroup meta-analysis. Multicomponent de-escalation studies - Hospital discharge inappropriate medication therapy								
6	observational studies	very serious <sup>a</sup>	not serious	not serious	not serious	strong association <sup>c</sup>	OR 0.26 (0.13 to 0.55)	⊕⊕⊕○ MODERATE
Subgroup meta-analysis. Single component de-escalation studies - ICU discharge inappropriate medication therapy								
5	observational studies	very serious <sup>a</sup>	not serious	serious <sup>b</sup>	not serious	strong association <sup>c</sup>	OR 0.42 (0.24 to 0.74)	⊕⊕○○ LOW
Subgroup meta-analysis. Single component de-escalation studies - Hospital discharge inappropriate medication therapy								
3	observational studies	very serious <sup>a</sup>	not serious	serious <sup>b</sup>	not serious	None	OR 0.77 (0.16 to 3.74)	⊕○○○ ○ VERY LOW

**Table S3: Meta-analysis GRADE assessments****Explanations**<sup>a</sup>High-risk of bias on ROBINS-I (downgraded 2 levels)<sup>b</sup>Significant variability in intervention components and timing of delivery (downgraded 1 level)<sup>c</sup>Large effect – OR <0.5 (upgraded 1 level)<sup>d</sup>Heterogeneity ( $I^2 \geq 75\%$ ) (downgraded 1 level)