# **Supplementary Online Content**

Keller MS, Qureshi N, Mays A, Sarkisian C, Pevnick J. Cumulative update of a systematic overview evaluating interventions addressing polypharmacy. *JAMA Netw Open*. 2024;7(1):e2350963. doi:10.1001/jamanetworkopen.2023.50963

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## eReferences

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Full search strategy for updated systematic overview of systematic reviews evaluating interventions addressing polypharmacy

PubMed search strategy:

(("2017"[Date - Publication] : "3000"[Date - Publication]) AND english[Language])

AND

("Systematic Review"[ti] OR "Systematic Review"[tiab] OR "health technology assessment"[tiab] OR

"metaanalysis"[tiab] OR "meta-analysis"[tiab] OR "Systematic Review"[Publication Type])

AND

((polypharmacy[tiab] OR deprescribing[tiab] OR deprescriptions[MeSH Terms] OR polypharmacy[MeSH

Terms] OR "potentially inappropriate medication list" [MeSH Terms] OR "inappropriate prescribing" [MeSH

Terms]) AND (intervention\* or program\* or monitor\* or tool\*[tiab])) AND #1 AND #2)

Cochrane database search strategy:

#1 "polypharmacy":ti,ab,kw OR "deprescribing":ti,ab,kw Publication Year from 2017 to 2022

DARE search strategy:

(polypharmacy) IN DARE FROM 2017 TO 2022

#### eAppendix 2: Selection strategy

Similar to a previously published systematic overview,<sup>1</sup> we considered an SR to be a summary of outcomes resulting from a detailed and comprehensive plan and search strategy for relevant evidence derived *a priori*. We included SRs of studies with any study design (e.g., randomized clinical trials and observational studies) and outcome. SRs were included if they included a definition of polypharmacy or "polypharmacy" in the search criteria. We included SRs regardless of setting (e.g., inpatient, outpatient, nursing home) or population (e.g., frail older adults, patients with specific chronic diseases).

Exclusion criteria: We excluded SRs focusing exclusively on interventions implemented in low- to middle-income countries, where the average annual income level is under \$14,000,<sup>2</sup>due to differences in care practices and healthcare infrastructure. We excluded SRs focused on antibiotic stewardship, solely about inappropriate prescribing, or medication adherence, as we felt these topics merited separate systematic overviews. Finally, we excluded SRs focused on interventions aimed at reducing or managing only one medication class (e.g., benzodiazepines, proton pump inhibitors), as we considered these to be outside of the scope of polypharmacy-related interventions. This resulted in a more focused systematic overview compared to the previously published paper.<sup>1</sup> eAppendix 3: Standardized abstraction form for updated systematic overview of systematic reviews evaluating interventions addressing polypharmacy.

Article Data	Article ID
	Abstractor
	Authors
	First Author Last Name
	Year
	Title
	Abstract
AMSTAR2	1. Did the research questions and inclusion criteria for the review include the components of PICO?
(1 or 0)	2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of
	the review and did the report justify any significant deviations from the protocol?
	3. Did the review authors explain their selection of the study designs for inclusion in the review?
	4. Did the review authors use a comprehensive literature search strategy?
	5. Did the review authors perform study selection in duplicate?
	6. Did the review authors perform data extraction in duplicate?
	7. Did the review authors provide a list of excluded studies and justify the exclusions?
	8. Did the review authors describe the included studies in adequate detail?
	9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were
	included in the review?
	10. Did the review authors report on the sources of funding for the studies included in the review?
	11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?
	12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the
	results of the meta-analysis or other evidence synthesis?
	13. Did the review authors account for RoB in primary studies when interpreting/discussing the results of the review?
	14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the
	results of the review?
	15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias
	(small study bias) and discuss its likely impact on the results of the review?
	16. Did the review authors report any potential sources of conflict of interest, including any funding they received for
	conducting the review?
	SUM AMSTAR2
Study Data	
Study Data	Objective Number in shule disturble
	Number included studies
	Number and types of studies (RCT and non-RCT)
	Intervention type(s)
	Description of Interventions?
	Intervention target (pharmacist, physician, patient, other?)
	Single versus multi-component interventions
	Study (changed from patient) population(s)
	Analyses of subpopulation(s)
	Setting(s)
	Primary outcome measure(s)
	Presence of meta-analytic techniques and any pooled estimates
	Major conclusions regarding intervention effectivenes
Outcomes	(1) a positive association between intervention strategy and outcome
by Category	(2) a negative association between intervention strategy and outcome
2, Calogory	(2) a negative association between intervention strategy and outcome
	(4) preclusion from drawing conclusions due to limited or low-guality studies
	(4) preclusion from drawing conclusions due to inflited of low-quality studies (5) mixed results
Quality	
Quality	GRADE Score

eTable 1. AMSTAR2 scores for systematic reviews of studies examining polypharmacy interventions.

Systematic Review Author and Date	Johansson et al (2016)	Page <i>et al</i> (2016)	Thillainadesan <i>et al</i> (2018)	Rankin <i>et al</i> (2018)	Mizokami <i>et al</i> (2019)	Ali <i>et al</i> (2020)	Lum <i>et</i> <i>al</i> (2020)	Hasan Ibrahim <i>et al</i> (2021)	Laberge <i>et al</i> (2021)	Lee <i>et</i> <i>al</i> (2021)	Tasai <i>et al</i> (2021)	O'Shea <i>et al</i> (2022)	Reeve et al (2022)	Stozner <i>et al</i> (2022)
1. Did the research questions and inclusion criteria for the review include the components of PICO?	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	1	1	1	1	1	1	0	1	0	1	0	1	1	1
3. Did the review authors explain their selection of the study designs for inclusion in the review?	1	1	0	0	0	0	0	0	1	1	0	1	1	1
4. Did the review authors use a comprehensive literature search strategy?	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5. Did the review authors perform study selection in duplicate?	1	1	1	1	1	0	1	1	1	1	1	1	1	1
6. Did the review authors perform data extraction in duplicate?	1	1	0	1	1	0	1	1	1	1	1	1	1	1
7. Did the review authors provide a list of excluded studies and justify the exclusions?	1	0	0	1	0	0	0	1	0	1	0	0	1	0
8. Did the review authors describe the included studies in adequate detail?	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	1	1	1	1	1	1	1	1	1	1	1	1	0	1
10. Did the review authors report on the sources of funding for the studies included in the review?	0	1	0	0	0	0	0	0	0	0	0	0	0	0
11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?	1	1	NA	1	1	1	NA	NA	NA	1	1	NA	NA	NA

12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta- analysis or other evidence synthesis?	1	1	NA	1	0	1	NA	NA	NA	1	0	NA	NA	NA
13. Did the review authors account for RoB in primary studies when interpreting/discussing the results of the review?	1	1	1	1	0	1	0	1	0	1	0	0	0	0
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	1	1	1	1	1	1	0	0	0	1	1	1	1	1
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	1	1	NA	1	0	0	NA	NA	NA	1	0	NA	NA	NA
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	1	1	1	1	1	1	1	1	1	1	1	0	1	1
SUM AMSTAR2	15	15	9	14	10	10	7	10	8	15	9	9	10	10

Notes: AMSTAR2: A MeaSurement Tool to Assess systematic Reviews

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				(2021
13 studies (3 studies implemented compliance-		9 (2 studies included Type I CMR, which involves a prescription review only, 3 studies included a Type II CMR, which includes a prescription review and a medication adherence review, 4 studies		(202
improving strategies, 3 studies		included a Type III CMR, which includes the	5 studies (some	
included discussions		Type II elements and a face-to-	which	

# eTable 2. Intervention types by systematic review.

Systematic Review Author and Date	Johansson <i>et</i> <i>al</i> (2016)	Page <i>et al</i> (2016)	Thillainades an <i>et al</i> (2018)	Rankin <i>et al</i> (2018)	Mizokami <i>et al</i> (2019)	Ali <i>et al</i> (2020)	Lum <i>et</i> <i>al</i> (2020)	Hasan Ibrahim <i>et al</i> (2021)	Laberge <i>et al</i> (2021)	Lee <i>et</i> <i>al</i> (2021)	Tasai <i>et al</i> (2021)	O'Shea <i>et al</i> (2022)	Reeve <i>et al</i> (2022)	Stozner <i>et al</i> (2022)
					9 (2 studies included Type I CMR, which involves a prescription review only, 3									
					studies included a Type II CMR, which includes a prescription									
	13 studies (3 studies implemented compliance- improving				review and a medication adherence review, 4 studies included a Type		5			3 studies				
Pharmacist-led	strategies, 3 studies included discussions with patients about				III CMR, which includes the Type II elements and a face-to- face review of medicines and		studies (some which include d patient			(studie s focuse d on fall-risk increas				
medication reviews	medication changes)	2 studies	4 studies	17 studies	conditions with the patient.)		educati on)	5 studies	10 studies	ing drugs) 2 studies (studie	7 studies	7 studies	5 studies	
Dhusisian lad										s focuse d on fall-risk				
Physician-led medication reviews	3 studies	11 studies	4 studies	5 studies				2		increas ing drugs)		2 studies	11 studies	
								studies (delivere d in collabor ation						
Nurse-led medication reviews		1 study		3 studies				with pharmac ists)						44
														studies (36 studies used a
Medication review (unspecified						4								compreh ensive medicati on
deliverer)						4 studies								review)

Multi-disciplinary team-led interventions	(1 study included medication changes related to the patient)	4 studies	1 study			1 study	1 study				4 studies	
Geriatric assessment and screening				4 studies included	2 studies							
Educational programs to reduce polypharmacy	4 studies also included patient education	3 studies		patient education, 10 studies included education to providers 31 studies		1 study						
Complex, multi- faceted interventions				(including computerized decision support)								
Pharmacogeneti c interventions								1 study	stu	12 Idies		
Shared decision making/patient involvement											17 studies	16 studies

# eTable 3. Citation matrix

Systematic Review Author and Date	Johansson <i>et</i> al (2016)	Page <i>et al</i> (2016)	Thillainades an <i>et al</i> (2018)	Rankin <i>et al</i> (2018)	Mizokami <i>et al</i> (2019)	Ali <i>et al</i> (2020)	Lum <i>et</i> <i>al</i> (2020)	Hasan Ibrahim <i>et al</i> (2021)	Laberge <i>et al</i> (2021)	Lee <i>et</i> <i>al</i> (2021)	Tasai <i>et al</i> (2021)	O'Shea <i>et al</i> (2022)	Reeve et al (2022)	Stozner et al (2022)
Abdool 2019 Ailabouni 2019 Allard 2001	х	Х						(2021)						X X
Avorn 1992 Baqir 2014	X	~		×										X X
Basger 2015 Beer 2011 Bernsten 2001	х	х		x							х			
Bladh 2011 Blalock 2010 Blenke 2018			Х	х		Х				Х			X	х
Boersma 2019 Boyé 2017 Bregnhøj 2009	x									Х			Х	
Briggs 2015 Brixner 2016 Brophy 2014					Х				х			х		X
Brulhart 2011 Bryant 2011 Bucci 2003 Caffiero 2017				х							Х		х	Х
Calbelguenne 2019 Campbell 1999		Х				х				х			X	х
Campins 2017 Casper 2019 Chan 2009				Х			Х	х	Х				х	х
Chiarelli 2020 Chiu 2018 Christensen				Х									Х	X
2004 Claesson 1998 Clyne 2015	х			х										X
Cool 2018 Craig 1984 Crotty 2004a Crotty 2004b	x			x x										X X X
Curtin 2020 Dahl 2008 Dalleur 2014		Х	Х	x									х	х
Davidsson 2011 Denneboom 2007		~	~	~					х					х
Elliott 2017 Ewan 2001 Finkelstein									7			Х		х
2016a Finkelstein 2016b												x x		
Finkers 2007 Fog 2017 Foubert 2020														X X X
Franchi 2016				Х										

Frankethal 2014	Х			X X		Х							
Fried 2017				Х			Х					Х	
Furniss 2000													Х
Gallagher 2011		Х	Х	Х									
García-Gollarte													
2014		X		Х									Х
Garfinkel 2010		X X		X									Х
Garfinkel 2018		~				Х							
Gerety 1993		х				~							
Gelety 1995		^			X								
Gillespie 2009			X		Х								
Gillespie 2013			Х										
Gillespie 2017									Х				
Gnjidic 2010		Х											
Granas 2019													X X
Gurwitz 2008													Х
Haag 2016				Х									
Hahn 2018													Х
Halvorsen 2010													Х
Hanlon 1996	Х	Х		Х									
Herbert 2017													X X
Hernandez 2020													Х
Hogg 2009								Х					
Holland 2005													
Jodar-Sanchez													
2015										х			
Jordan 2015										Λ			Х
Keine 2019											Y		X
Kim 2018											X X		
Kiili 2010 King 2004	х										^		
King 2001	^												
Köberlein-Neu				V			V					V	
2016				Х			Х					Х	
Komagamine													
2017													
												Х	
Komagamine													
Komagamine 2018												x x	
Komagamine 2018 Kroenke 1990	х	х											
Komagamine 2018 Kroenke 1990 Krska 2001		х			x			х					
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010	x x	x			x			x					
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012		X			x			х					X
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980		x			x			х					X X
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019		x						х			x		X X
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980	x	x						х			x		X X
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019 Lenaghan 2007 Lenaghan 2008	x	x			x x						x		X X
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019 Lenaghan 2007 Lenaghan 2008 Lenander 2014		x									x		
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019 Lenaghan 2007 Lenaghan 2008 Lenander 2014	x	Х						x x			x		
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019 Lenaghan 2007 Lenaghan 2007 Lenander 2014 Lepler 1993	x	X			х				x		x		x x x
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Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019 Lenaghan 2007 Lenaghan 2008 Lenander 2014 Lepler 1993 Lin 2018 Lisby 2010	x	X						x	x		x		
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019 Lenaghan 2007 Lenaghan 2008 Lenander 2014 Lepler 1993 Lin 2018 Lisby 2010 Lowrie 2012	x	X			х				x		x		x
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019 Lenaghan 2007 Lenaghan 2008 Lenander 2014 Lepler 1993 Lin 2018 Lisby 2010 Lowrie 2012 Lupu 2017	x	X			х			x	x		x		x
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Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019 Lenaghan 2007 Lenaghan 2008 Lenander 2014 Lepler 1993 Lin 2018 Lisby 2010 Lowrie 2012 Lupu 2017 Maidment 2020 Malet-Larrea 2016 Martin Lesende	x	X			x x			x			x	x	x x x
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019 Lenaghan 2007 Lenaghan 2008 Lenander 2014 Lepler 1993 Lin 2018 Lisby 2010 Lowrie 2012 Lupu 2017 Maidment 2018 Maidment 2020 Malet-Larrea 2016 Martin Lesende 2013	x	Х			x x			x			x		x x x
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019 Lenaghan 2007 Lenaghan 2007 Lenaghan 2008 Lenander 2014 Lepler 1993 Lin 2018 Lisby 2010 Lowrie 2012 Lupu 2017 Maidment 2018 Maidment 2020 Malet-Larrea 2016 Martin Lesende 2013 Massot	x	X			x x			x			x	x	X X X X
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Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019 Lenaghan 2007 Lenaghan 2007 Lenaghan 2007 Lenaghan 2008 Lenander 2014 Lepler 1993 Lin 2018 Lisby 2010 Lowrie 2012 Lupu 2017 Maidment 2020 Malet-Larrea 2016 Martin Lesende 2013 Massot Mesquida 2019 Mathys 2015 McCarthy 2017	x	X			x x			x			x	x x	X X X X
Komagamine 2018 Kroenke 1990 Krska 2001 Lampela 2010 Lang 2012 Laska 1980 Lee 2019 Lenaghan 2007 Lenaghan 2007 Lenaghan 2008 Lenander 2014 Lepler 1993 Lin 2018 Lisby 2010 Lowrie 2012 Lupu 2017 Maidment 2018 Maidment 2020 Malet-Larrea 2016 Martin Lesende 2013 Massot Mesquida 2019 Mathys 2015	x	X			x x			x			x	x	X X X X

Messerli 2016					Х									
Michalek 2014			Х	X X										
Milos 2013	Х			X										Х
Matt 0040	~			~						V				Λ
Mott 2016										Х				
Muir 2001		Х												
Muñiz 2020														Х
Muth 2016				Х									х	
Muth 2018				X X									X X	
Nulli 2010	V			~									~	
Naunton 2003	Х													
Nishtala 2009														Х
O'Brien 2018									Х					
Olsson 2010	Х													
Olsson 2012	X			Х										
Ortega Blanco	X			X										
Onega Blanco	^													
Papastergiou														
2017												Х		
Pasina 2016														Х
Patterson 2010										Х				X X
Patterson 2011									Х	~				~
									~				V	
Petersen 2018													Х	
Pitkala 2014	Х	Х		Х										
Pope 2011	Х													
Potter 2015		Х												
Potter 2016		~				Х								
						~							V	
Potter 2019													Х	
Reynolds 2017												Х		
Roberts 2001														Х
Russell 2019													Х	
Saldivar 2016												Х		
Saluivar 2010								v				~		
Salisbury 2018								Х						
Salonoja 2012		Х				Х								
San-José 2020													Х	
Sano 2017														X X
Scheifes 2016														Х
Schmader 2004				х										~
				^										V
Schmidt 1998														X X
Schorr 1994														Х
Sellors 2003	Х													
Shorr 1994														Х
Siaw 2015							x							
Siaw 2017							X X							
Olaw 2017							^	X						
Sloeserwij 2019								Х						
Smeets 2021														X X
Soeresnen 2018														Х
Sorensen 2004									х					
Spinewine 2007			Х	х					~					
Sturgood 2002	v		~	~										
Sturgess 2003	Х													
Sugarman 2016												Х		
Tabloski 1998		Х												
Tamblyn 2003				Х										
Tamura 2011														Х
Taylor 2003				×										~
				х										N/
Thompson														Х
Thyrian 2017				Х										
Touchette 2012											Х			
Trygstad 2005				Х										
Trygstad 2009				~										
Twigg 2015									Х					
van der Heijden														
2019									Х					

van der Linden 2017			V	х						
van der Meer			Х	^						
2018						Х				
van der Spek						^				
2018										Х
van der Velde										^
2007		Х				Х				
Van der Wouden		Л				Λ				
2019								Х		
van Summeren								Λ		
2017									Х	
Verrue 2012									χ	х
Vinks 2009	Х									~
Watson 2014										Х
Weber 2008		Х				Х				
Weber 2007	Х									
Wehling 2016			Х	Х						
Westbury 2010										Х
Wilchesky 2018										Х
Williams 2004	Х									
Wolf 2015										Х
Wouters 2017										Х
Yeh 2013		Х								
Zaal 2016										Х
Zechmann 2019									Х	
Zermansky 2006	Х				Х					Х

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