Real-world evidence for baricitinib in the treatment of rheumatoid arthritis in Spain: a systematic literature review

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Supplementary materials

Table S1. Search strategy for MEDLINE/EMBASE

	Search terms
	Disease terms
#1	*Arthritis, Rheumatoid/
#2	Rheumatoid.mp. or *Arthritis, Rheumatoid/
#3	*Arthritis, Rheumatoid/ or Arthritis.mp
#4	1 or 2 or 3
#5	*Arthritis, Rheumatoid/ and Seropositive.mp.
#6	*Arthritis, Rheumatoid/ and Seronegative.mp.
#7	*Arthritis, Rheumatoid/ or Seropositive Rheumatoid Arthritis.mp
#8	*Arthritis, Rheumatoid/ or Seronegative Rheumatoid Arthritis.mp.
#9	or/5-8
#10	Baricitinib.mp. and *Arthritis, Rheumatoid/
#11	*Janus Kinase Inhibitors/ or Baricitinib.mp. or *Treatment Outcome/ or *Arthritis, Rheumatoid/
#12	Baricitinib.mp
#13	or/10-12
	Observational study terms
#14	Observational.mp. or *Observational Study/
#15	Cohort.mp. or *Cohort Studies/
#16	Epidemiological.mp.
#17	Epidemiological study.mp. or *Epidemiologic Studies/
#18	*Follow-Up Studies/ or Follow-up.mp.
#19	Correlation.mp.

#20	Correlational.mp.
#21	Ecological.mp.
#22	Descriptive.mp.
#23	*Prospective Studies/ or Prospective.mp.
#24	*Retrospective Studies/ or Retrospective.mp.
#25	Longitudinal study.mp. or *Longitudinal Studies/
#26	*Cross-Sectional Studies/ or Cross-sectional.mp.
#27	Survey.mp. or *"Surveys and Questionnaires"/
#28	Questionnaires.mp. or *"Surveys and Questionnaires"/
#29	*Case-Control Studies/ or case-control.mp.
#30	*Observational Studies as Topic/mt [Methods]
#31	Observational study.mp. or *Observational Study/
#32	cohort studies.mp. or *Cohort Studies/
#33	longitudinal studies.mp. or *Longitudinal Studies/
#34	or/14-34
#35	meta-analysis/
#36	randomized controlled trial/
#37	review/
#38	systematic review/
#39	practice guideline/
#40	clinical trial/
#41	or/36-41
	Country terms
#42	*Spain/
#43	Spain.mp. or *Spain/
#44	*Spain/ or Andalucia.mp.
#45	*Spain/ or Andalusia.mp.

#46	*Spain/ or Aragon.mp.
#47	*Spain/ or Asturias.mp.
#48	*Spain/ or Balear.mp.
#49	*Spain/ or Canarias.mp.
#50	Canary.mp. or *Canaries/
#51	*Spain/ or Cantabria.mp.
#52	*Spain/ or Castilla.mp.
#53	*Spain/ or Castile.mp.
#54	*Spain/ or Cataluna.mp.
#55	*Spain/ or Catalonia.mp.
#56	Barcelona.mp. or *Spain/
#57	*Spain/ or Valencia.mp.
#58	*Spain/ or Extremadura.mp.
#59	*Spain/ or Galicia.mp.
#60	*Spain/ or Madrid.mp.
#61	*Spain/ or Murcia.mp.
#62	*Spain/ or Navarre.mp.
#63	Vasco.mp.
#64	*Spain/ or Basque.mp.
#65	*Spain/ or Rioja.mp.
#66	or/42-65
#67	Chile/
#68	Mexic/
#69	Colombia/
#70	Latin/
#71	or/67-70

Final

#72	66 not 71
#73	34 not 41
#74	4 and 9 and 13 and 72 and 73
#75	limit 74 to yr="2016–2023"

Table S2. Search strategy for IBECS and MEDES

Database	Search strategy
IBECS	ARTRITIS and BARICITINIB [Palabras] and OBSERVACIONALES or COHORTE or RETROSPECTIVO or PROSPECTIVO or CUESTIONARIO or TRANSVERSAL or EPIDEMIOLOGICO or DESCRIPTIVO or REGISTRO [Palabras] and not ENSAYO CLINICO or ENSAYO CLINICO CONTROLADO or ENSAYO CLINICO CONTROLADO ALEATORIO or ENSAYO CLINICO FASE I or ENSAYO CLINICO FASE II or ENSAYO CLINICO FASE III or ENSAYO CLINICO FASE IV or REVISION [Tipo de publicación]
MEDES	(artritis reumatoide[título]) and (Baricitinib[título]) AND ((observacional[título] OR observacional[resumen]) OR (cohorte[título] OR cohorte[resumen]) OR (prospectivo[título] OR prospectivo[resumen]) OR (retrospectivo[título] OR retrospectivo[resumen]) OR (longitudinal[título] OR longitudinal[resumen]) OR ("caso control"[título] OR "caso control"[resumen]) OR (epidemiológico[título] OR epidemiológico[resumen]) OR (cuestionario[título] OR cuestionario[resumen]) OR (descriptivo[título] OR descriptivo[resumen]) OR (registro[título] OR registro[resumen]))

Table S3. Study eligibility criteria

Study characteristic	Eligible	Ineligible
Patient population	• Adults ≥18 years old diagnosed with RA • Treated with baricitinib	• Patients younger than 18 years • Patients with other types of arthritis
Intervention, Comparator	• Treated with baricitinib, including comparative studies where specific baricitinib data is available	• Any study not including baricitinib as a treatment option
Outcomes (any)	• Patient characteristics at baseline: age, sex, time to diagnosis, baseline scores: DAS28-ESR, CDAI, SDAI, SJC, TJC, HAQ, VAS pain, C-reactive protein, RF and comorbidities • Prescription and treatment patterns (mean number of previous bDMARDs, csDMARDs and/or JAKis, dosing: percentage of patients initiating at 2 or 4 mg dose, characteristics of patients initiating each dose, percentage of patients receiving treatment optimisation, time to optimisation, line of treatment, monotherapy and concomitant treatment, percentage of patients switching to cycling or other JAKi) • Effectiveness (DAS28-ESR, CDAI, SDAI, SJC, TJC, HAQ, VAS pain, persistence, percentage of patients with disease improvement, percentage of patients in remission, reasons for treatment discontinuation: loss of effectiveness, adverse events, other) • Safety (serious infection, Zoster virus rate, MACE, thromboembolisms, malignancies, and death)	• NA
Time Frame	• March 2017–June 2023 (EMBASE, MEDLINE, MEDES, IBECS)	• Publications prior to March 2017

	• May 2021–June 2023 (Spanish national congresses)	
Study design (any)	• Observational studies • Cohort studies • Epidemiological studies • Follow-up studies • Correlational studies • Ecological studies • Descriptive studies • Prospective studies • Retrospective studies • Longitudinal studies • Cross-sectional studies • Surveys • Questionnaires • Case-control studies	• Systematic review • Meta-analysis • Randomized controlled study • Review • Guidelines or standards or recommendations
Language	• English • Spanish	• Non-English or non-Spanish

bDMARD, biologic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic disease-modifying antirheumatic drug DAS28; DAS28-ESR, Disease Activity Score 28 joints with erythrocyte sedimentation rate; IBEC, *Índice Bibliográfico Español en Ciencias de la Salud;* JAKi, Janus kinase inhibitor; HAQ, Health Assessment Questionnaire; MACE, Major adverse cardiovascular events; MEDES, *Medicina en Español*; NA, not applicable; RA, rheumatoid arthritis; RF, rheumatoid factor; SDAI, Simplified Disease Activity Index; SJC, swollen joint count; TJC, tender joint count; VAS, visual analogue scale.

Table S4. Patient characteristics

Reference	Number of patients receiving baricitinib, n	Age, mean (SD), or median (range), years	Female sex, %	Disease duration, mean (SD), or median (range), years	RF+, %, or median (Q1, Q3) titre	Anti-CCP +, %, or median (Q1, Q3) titre	CRP, mean (SD), or median (Q1, Q3), mg/dL	ESR, mean (SD), or median (Q1, Q3) mm/hour	DAS28-ESR, mean (SD), or median (Q1, Q3) score	CDAI, mean (SD)	SDAI, mean (SD)	SJC mean (SD), or median (Q1, Q3)	TJC mean (SD), or median (Q1, Q3)	HAQ-DI/HAQ mean (SD), or median (Q1, Q3)	VAS pain	Comorbidities
Velez, 2019 [42] [ABSTRACT]	38	52 (12)	74	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Calvo-García, 2020 [29] [ABSTRACT]	30	63.3 (49.7–74.8)	87	NR	77	70	2.2 (0.3, 1.0)	NR	5.5 (3.6, 4.3)	NR	NR	NR	NR	NR	NR	NR
Velloso-Feijoo, 2020 [43] [ABSTRACT]	13	57.8 (10.8)[a]	75[a]	8.7 (6.54)[a]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Egües-Dubuc, 2021 [31] [ABSTRACT]	101	58 (13)	82	6.3 (5.7) years	76	82	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
González-Freire, 2021 [35]	20	61 (41–79)	70	NR	85	80	NR	NR	4.4 (2.7, 6.3)	NR	NR	7 (2, 10)	7 (2, 12)	NR	8.8 (7, 10)	NR
Loricera García, 2021 [38] [ABSTRACT]	9	64 (7)	67	NR	NR	78	0.83 (0.77)	32.70 (17, 20)	3.10 (2.60, 3.50)	NR	NR	0 (0, 2)	0 (0, 2)	0.63 (0.40, 1.30)	NR	NR
Retuerto, 2021 [39]	15[b]	62 (51-67)	81	11 (6, 18) (IQR) unit not specified	81	71	8.7 (estimated from a graph)	NR	DAS28-CRP, 5.3 (5, 5.9). At the	NR	NR	6 (4, 10)	10 (7.24, 14.3)	NR	NR	NR

									start of 2nd JAKi							
Codes-Mendez, 2022 [30] [ABSTRACT]	75[c]	63 (13)	87	NR	NR	NR	NR	NR	5.1 (1.2)	NR	NR	NR	NR	NR	NR	NR
Font Urgelles, 2022 [32] [ABSTRACT]	49[d]	56 (10.3)	86	13.9 (8.1)	73	74	NR	NR	4.7 (1.0)	20.2 (8.5)	NR	NR	NR	NR	NR	NR
Fragío Gil, 2022 [33] [ABSTRACT]	59	54.5 (22.7)	95	NR	45 (10, 189)	263.5 (29.75. 340)	9.2 (2.6, 19.6)[e]	28 (16.75, 48)[e]	DAS-28, 4.99 (1.01)	NR	25.45 (9.86)	NR	NR	1.56 (0.46)	NR	Hypertension : 17 (29) Diabetes: 1 (2) Dyslipidaemia: 18 (31)
González-Mazarío, 2022 [34]	32	53.2 (13.1)	97	NR	95 (17, 294)	192 (90, 340)	9 (2.2, 19)	28.5 (16.75, 51)	4.88 (1)	NR	28.72 (9.55)	NR	NR	1.56 (0.45)	NR	High blood pressure: 8 (25) Dyslipidaemia: 9 (28) Diabetes mellitus: 0 (0)
Hernandez-Cruz, 2022 [36]	182	62.2 (12.3)	84	14.6 (10.8) [n=177]	79	80	8.6 (15.8) [n=176]	29.7 (24.0) [n=171]	4.4 (1.1)	23.6 (10.5)	25 (10.4)	4.4 (3.7)	6.7 (5.8)	NR	6.6 (2.0)	CCI mean (SD), 2.4 (2.0)
Rosas 2022 [28] [ABSTRACT][h]	63	63 (6)	89	NR	86	79	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Rosas, 2022 [26] [LETTER TO THE EDITOR][h]	50 (n=40 for the analysis)	59 (10.5)	84	10.5 (8.5)	80	82	NR	NR	bDMARD naïve = 5.1 bDMARD experienced = 5.6	bDMARD naïve = 23.3 bDMARD experienced = 29.8	NR	NR	NR	NR	NR	NR

Sarabia de Ardanaz, 2022 [40] [ABSTRACT]	42	56.2 (11.8)	88	NR	74	72	NR	NR	DAS28, 4.4 (estimated from a graph)	20 (estimated from a graph)	23 (estimated from a graph)	NR	NR	NR	NR	Hypertension: 11 (28) Diabetes type 1: 1 (10) Diabetes type 2: 4 (38)
Valera Ribera, 2022 [41] [ABSTRACT]	41	65.4 (NR)	76	12.27 (0.96)	68	63	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Charca-Benavente, 2023 [44] [ABSTRACT]	34	61.5 (11)	68%[f]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Lorenzo, 2023 [37] [ABSTRACT]	185	63.2 (12.79)	80	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	Hypertension: 53 (29) Diabetes: 23 (12) HDL-C <40 mg/dL: 182 (98) Coronary history: 11 (6)
Rosas 2023 [27] [ABSTRACT][h]	81	60 (1)[g]	95[g]	7.2[g]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

CDAI, Clinical Disease Activity Index; CRP, C-reactive protein, DAS28-ESR; Disease Activity Score 28 joints using erythrocyte sedimentation rate; ESR, erythrocyte sedimentation rate; mo, months; HAQ, Health Assessment Questionnaire; HAQ-DI, Health Assessment Questionnaire Disability Index; HDL-C, high-density lipoprotein cholesterol; JAKi, Janus kinase inhibitor, NR, not reported; Q1-Q3, 1st, 3rd quartile; RA, rheumatoid arthritis; RF, Rheumatoid factor; SDAI, Simplified Disease Activity Index; SJC, swollen joint count; TJC, tender joint count; VAS, visual analogue scale.

[a]All data are reported for the entire patient cohort of 58 patients, which includes 45 patients treated with tofacitinib.

[b]All data is reported for the entire patient cohort of 31 patients, which include 16 patients treated with tofacitinib who then switched to baricitinib.

[c]Includes 31 patients who received treatment with both baricitinib and tofacitinib.

[d]All data are reported for the entire patient cohort of 78 patients, which includes 45 patients treated with tofacitinib.

[e]It has been assumed that these data points represent median and 1st, 3rd quartile, based on other data presented in this abstract, but this is not explicitly stated for these data points.

[f]Data reported for the entire patient cohort of 164 patients, which includes 45 patients treated with tofacitinib, 60 treated with upadacitinib and 25 with filgotinib.

[g]All data are reported for the entire patient cohort of 129 patients, which includes 48 patients treated with tumour necrosis factor inhibitors.

[h]These publications report data from the same study at different timepoints.

Table S5. Treatment outcomes

First author	Number of patients receiving baricitinib, n	DAS28 mean change	Remission, low disease activity, %	CDAI mean (SD) change	SDAI mean (SD) change	SJC mean change	TJC mean change
Velez, 2019 [42] [ABSTRACT]	38	NR	NR	NR	NR	NR	NR
Calvo-García, 2020 [29] [ABSTRACT]	30	Baseline DAS28-ESR [median (IQR)] 5.5 (3.6-4.3), final 3.9 (2.2-2.8)	DAS28-ESR remission 33 DAS28-ESR LDA 27	NR	NR	NR	NR
González-Freire, 2021 [35]	20	Median (range) 6 mo = 2.1 (0.6-4.1) Change from BL = -2.3 12 mo = 2.7 (1.1-3.5) Change from BL = - 1.7	NR	NR	NR	6 and 12 mo = 0 (0-0) Change from BL = - 7	6 and 12 mo = 0 (0-0) Change from BL = - 7
Loricera García, 2021 [38] [ABSTRACT]	9	Median (IQR) At 1 mo: 2.60 (2.40-3.60) At 3 mo: 3.50 (2.60-4.00) At 6 mo: 3.60 (2.60-4.60)	NR	NR	NR	Median (IQR) At 1 mo: 0 (0-3) At 3 mo: 0 (0-3) At 6 mo: 0 (0) No change from BL	Median (IQR) At 1 mo: 0 (0-2) At 3 mo: 1 (0-7) At 6 mo: 1 (0-7) Change from BL = 1
Fragío Gil, 2022 [33]	59	NR	Remission or LDA 3 mo = 31 6 mo = 49 12 mo = 58 24 mo = 85	NR	NR	NR	NR

			36 mo = 80				
González-Mazarío, 2022 [34]	32	3 mo: 4.5 12 mo: 4 24 mo: 2.8 Change from BL = -2 (estimated from a graph)	Remission or LDA 3 mo = 57 6 mo = 59 12 mo 55 18 mo = 68 24 mo = 69	NR	3 mo 15 12 mo 10 24 mo 8 Change from BL = -20 (estimated from a graph)	NR	NR
Hernandez-Cruz, 2022 [36]	182	6 mo score = 2.6 (1.2) Change from BL = -1.7 (1.4), p<0.0001 12 months score = 2.5 (1.2) Change from BL = -1.7 (1.5), p<0.0001	Remission or LDA 6 mo = 72 12 mo = 76	6 mo = 10.1 (9.9) Change from BL= -13 (11.4), p<0.0001 12 mo = 8.2 (8.5) Change from BL = -13.7 (11.8) p<0.001	6 mo = 10.9 (10.3), Change from BL = -13.4 (11.6), p<0.0001 12 mo = 8.9 (8.7), Change from BL = -14.4 (12.0), p<0.0001	Change from BL: 6 mo = -2.8 12 mo = -4.0	Change from BL: 6 mo = -4.4 12 mo -5.2
Rosas, 2022 [26]	50 (n=40 for analysis)	bDMARD naïve Change from BL = - 2.5 bDMARD experienced Change from BL = - 2.4	NR	bDMARD naïve Change from BL = - 17.8 bDMARD experienced Change from BL = - 21	NR	NR	NR
Sarabia de Ardanaz, 2022 [40] [ABSTRACT]	42	DAS28, At 12 mo: 2.2 Change from BL = -2 At 24 mo: 2.8 Change from BL = -1.4 (estimated from a graph)	NR	At 12 mo: 4 At 24 mo: 3 Change from BL = -17 (estimated from a graph)	At 12 mo: 4 At 24 mo: 4 Change from BL = - 18 (estimated from a graph)	NR	NR

AE, adverse event; BL, baseline; bDMARD, biologic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; CRP, C-reactive protein, DAS28, Disease Activity Score 28 joints; DAS28-ESR, Disease Activity Score 28 joints with erythrocyte sedimentation rate; ESR, erythrocyte sedimentation

rate; IQR, interquartile range; mo, months; NR, not reported; SDAI, Simplified Disease Activity Index; SJC, swollen joint count; TJC, tender joint count; VAS, visual analogue scale.

Table S6. Assessment of reporting quality of the included publications using the STROBE checklist

Publication	STROBE item number																																	
	1a	1b	2	3	4	5	6a	6b	7	8	9	10	11	12a	12b	12c	12d	12e	13a	13b	13c	14a	14b	14c	15	16a	16b	16c	17	18	19	20	21	22
Velez (2019) [42]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	Y	Y	NA	N	N	NA	N	N	N	Y	N	N	Y	Y	NA	NA	NA	N	N	Y	N	N
Calvo Garcia (2020) [29]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	Y	Y	NA	N	NA	NA	Y	N	N	Y	N	N	Y	Y	NA	NA	NA	N	Y	Y	N	N
Velloso Feijoo (2020) [43]	Y	Y	Y	Y	Y	Y	N	NA	N	N	N	N	N	N	NA	N	N	NA	Y	N	N	Y	N	N	Y	Y	NA	NA	NA	Y	N	Y	N	N
Egües Dubuc (2021) [31]	Y	Y	Y	Y	Y	Y	Y	NA	N	N	N	N	Y	Y	NA	N	NA	NA	N	N	N	Y	N	N	N	Y	NA	NA	NA	Y	N	Y	N	N
González-Freire (2021) [35]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	Y	Y	NA	N	NA	NA	Y	N	N	Y	N	N	Y	Y	NA	NA	NA	Y	Y	Y	Y	NA
Loricera García (2021) [38]	Y	Y	Y	Y	Y	N	Y	NA	Y	N	N	N	N	N	NA	N	NA	NA	Y	N	N	Y	N	Y	Y	Y	NA	NA	NA	Y	N	Y	N	N
Retuerto (2021) [39]	Y	Y	Y	Y	Y	Y	Y	NA	N	Y	N	N	N	Y	NA	N	NA	NA	Y	N	N	Y	N	Y	Y	Y	NA	NA	NA	Y	N	Y	Y	Y
Codes-Mendez (2022) [30]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	Y	Y	NA	N	NA	NA	Y	N	N	Y	N	N	Y	Y	NA	NA	NA	Y	N	N	N	N
Font Urgelles, 2022 [32]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	N	N	NA	N	NA	NA	Y	N	N	Y	N	N	Y	Y	NA	NA	NA	Y	N	N	N	N
Fragío Gil (2022) [33]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	Y	N	NA	N	N	NA	Y	N	N	N	N	N	N	Y	NA	NA	NA	Y	N	N	N	N
González Mazarío (2022) [34]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	Y	Y	NA	N	NA	NA	Y	N	N	Y	N	Y	Y	Y	NA	NA	NA	Y	Y	Y	N	NA
Hernández-Cruz (2022) [36]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	Y	Y	NA	N	NA	NA	Y	N	N	Y	N	Y	Y	Y	NA	NA	NA	Y	Y	Y	Y	Y
Rosas (2022a)[28]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	N	N	NA	N	N	NA	N	N	N	Y	N	N	Y	Y	NA	NA	NA	Y	N	N	N	Y
Rosas (2022b) [26]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	N	N	NA	N	N	NA	N	N	N	Y	N	N	Y	Y	NA	NA	NA	Y	N	N	N	Y
Sarabia de Ardanaz (2022)[40]	Y	Y	Y	Y	Y	N	Y	NA	Y	Y	N	N	Y	Y	NA	N	NA	NA	Y	N	N	Y	N	Y	Y	Y	NA	NA	NA	Y	N	N	N	N

Publication	STROBE item number																																
	1a	1b	2	3	4	5	6a	6b	7	8	9	10	11	12a	12b	12c	12d	12e	13a	13b	13c	14a	14b	14c	15	16a	16b	16c	17	18	19	20	21	22
Valera Ribera (2022) [41]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	Y	Y	NA	N	NA	NA	Y	N	N	Y	N	N	Y	Y	NA	NA	NA	Y	N	Y	N	N
Charca Benavente (2023) [44]	Y	Y	Y	Y	Y	Y	Y	NA	Y	N	N	N	N	N	NA	N	NA	NA	N	N	N	Y	N	N	Y	Y	NA	NA	NA	Y	N	Y	N	N
Lorenzo (2023) [37]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	Y	Y	NA	N	NA	NA	Y	N	N	Y	N	N	Y	Y	NA	NA	NA	Y	N	Y	N	N
Rosas (2023) [27]	Y	Y	N	Y	Y	Y	Y	NA	Y	Y	N	N	Y	Y	NA	N	NA	NA	N	N	N	Y	N	Y	Y	Y	NA	NA	Y	Y	N	Y	N	N

N, not reported; NA, not applicable; Y, reported

Table S7. Assessment of bias results for the included publications

Publication	D1	D2	D3	D4	D5	D6	D7	Overall
Velez (2019) [42]	-	+	+	+	+	-	+	-
Calvo Garcia (2020) [29]	-	+	-	+	+	-	+	-
Velloso Feijoo (2020) [43]	-	+	-	+	+	-	+	-
Egües Dubuc (2021) [31]	-	+	-	+	+	-	+	-
González-Freire (2021) [35]	-	+	+	+	+	-	+	-
Loricera García (2021) [38]	-	+	+	+	+	-	+	-
Retuerto (2021) [39]	-	+	+	+	-	-	+	-
Codes-Mendez (2022) [30]	-	+	-	+	+	-	+	-
Font Urgelles, 2022 [32]	-	-	-	+	+	-	+	-
Fragío Gil (2022) [33]	-	+	-	+	-	-	+	-
González Mazarío (2022) [34]	-	-	-	+	+	-	+	-
Hernández-Cruz (2022) [36]	-	+	+	+	+	-	+	-
Rosas (2022a)[28]	-	+	-	+	-	-	+	-
Rosas (2022b) [26]	-	+	-	+	-	-	+	-
Sarabia de Ardanaz (2022)[40]	-	+	+	+	+	-	+	-
Valera Ribera (2022) [41]	-	+	+	+	-	-	+	-
Charca Benavente (2023) [44]	-	-	-	+	-	-	+	-

Lorenzo (2023) [37]	-	+	+	+	-	-	+	-
Rosas (2023) [27]	-	+	-	+	-	-	+	-

Domains:
D1: Bias due to confounding
D2: Bias due to selection of participants for the study
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:
+ Low risk of bias
- Moderate risk of bias
x Serious risk of bias