SUPPLEMENTAL MATERIALS

Supplementary material for SR1: Prevalence of Manifestations

Supplementary Table 1. PubMed search (28/Oct/2022)……2

Supplementary Table 2. Embase search (28/Oct/2022)……..3

Supplementary Table 3. Cochrane Library search (28/Oct/2022)…….....4

Supplementary Table 4. Outcomes of the review (SR1) ……..5

Supplementary Table 5. Quality assessment: adapted Hoy scale for prevalence studies……6

Supplementary Figure 1. PRISMA flow chart of included studies in SR1 on the Prevalence of Manifestations……7

Supplementary Figures 2, 3 and 4. Forest plots of proportions……..8

- Supplementary figure 2. Frequencies of clinical manifestations in sJIA and AOSD……8
- Supplementary figures 3. Frequencies of biological abnormalities in sJIA and AOSD……...15
- Supplementary figures 4. Frequencies of complications in sJIA and AOSD……20

Supplementary Table 6. Weighted percentage of treatment used in sJIA and AOSD……23

Supplementary material for SR2: Diagnostic Biomarkers for sJIA and AOSD

Supplementary Table 7. PubMed search (23/Feb/2023)……24

Supplementary Table 8. Embase search (23/Feb/2023)……..……..27

Supplementary Table 9. Cochrane Library search (18/Feb/2023)……..…28

Supplementary Figure 5. PRISMA flow chart of included studies in SR2……..……..…..29

Supplementary Figure 6. Overview of the diagnostic biomarkers for sJIA and AOSD retrieved by the SR2…….30

Supplementary Table 10. Studies retrieved reporting other diagnostic biomarkers in sJIA and AOSD and associated performance……..31

Supplementary table 11. Details of QUADAS- 2 results evaluating the global risk of bias of the selected studies on biomarkers…… 33

Supplementary material for SR3: Diagnostic Biomarkers for MAS

Supplementary figure 7. PRISMA flow chart of included studies in SR3……..……35

Supplementary table 12: Existing “classical” biomarkers for MAS……..36

De Matteis A, *et al. Ann Rheum Dis* 2024;0:1–14. doi: 10.1136/ard-2024-225853

Supplementary material for SR1: Prevalence of Manifestations

Supplementary Table 1. PubMed search (28th October 2022)

No.	Query	Results
#1	"Still's Disease, Adult-Onset"[Mesh]	1,620
#2	"Still's Disease, Adult-Onset/classification"[Mesh]	17
#3	"Still's Disease, Adult-Onset/epidemiology"[Mesh]	89
#4	#2 OR #3 ("Still's Disease, Adult-Onset/classification"[Mesh]) OR ("Still's Disease, Adult-Onset/epidemiology"[Mesh])	105
#5	#1 OR #4 ("Still's Disease, Adult-Onset"[Mesh]) OR (("Still's Disease, Adult-Onset/classification"[Mesh]) OR ("Still's Disease, Adult-Onset/epidemiology"[Mesh]))	1,620
#6	"adult-onset Still's disease"[Text Word]	1,579
#7	adult[Title/Abstract] AND onset[Title/Abstract] AND Still[Title/Abstract] AND disease[Title/Abstract]	2,524
#8	adult[Title/Abstract] AND onset[Title/Abstract] AND Still's[Title/Abstract] AND disease[Title/Abstract]	1,642
#9	(#1 OR #6) OR #8 (("Still's Disease, Adult-Onset"[Mesh]) OR ("adult-onset Still's disease"[Text Word])) OR (adult[Title/Abstract] AND onset[Title/Abstract] AND Still's[Title/Abstract] AND disease[Title/Abstract])	2,146
#10	"Arthritis, Juvenile/epidemiology"[Mesh]	823
#11	"systemic"[Title/Abstract] AND "juvenile"[Title/Abstract] AND (rheumatoid[Title/Abstract] OR idiopathic[Title/Abstract] OR chronic[Title/Abstract]) AND "arthritis"[Title/Abstract]	3,336
#12	("juvenile"[Title/Abstract]) AND "onset"[Title/Abstract] AND "Still"[Title/Abstract] AND "disease"[Title/Abstract]	445
#13	("juvenile"[Title/Abstract]) AND "onset"[Title/Abstract] AND "Still's"[Title/Abstract] AND "disease"[Title/Abstract]	212
#14	"systemic juvenile idiopathic arthritis"[Text Word]	705
#15	(#10 OR #11) OR (#12 OR #14) ((("Arthritis, Juvenile/epidemiology"[Mesh]) OR ("systemic"[Title/Abstract] AND "juvenile"[Title/Abstract] AND (rheumatoid[Title/Abstract] OR idiopathic[Title/Abstract] OR chronic[Title/Abstract]) AND "arthritis"[Title/Abstract])) OR (("juvenile"[Title/Abstract]) AND "onset"[Title/Abstract] AND "Still's"[Title/Abstract] AND "disease"[Title/Abstract])) OR ("systemic juvenile idiopathic arthritis"[Text Word])	4,000
#16	("adult"[Title/Abstract] OR "juvenile"[Title/Abstract]) AND "onset"[Title/Abstract] AND "Still's"[Title/Abstract] AND "disease"[Title/Abstract]	1,665
#17	#9 AND #15 ((("Still's Disease, Adult-Onset"[Mesh]) OR ("adult-onset Still's disease"[Text Word])) OR (adult[Title/Abstract] AND onset[Title/Abstract] AND Still's[Title/Abstract] AND disease[Title/Abstract])) AND ((((("Arthritis, Juvenile/epidemiology"[Mesh]) OR ("systemic"[Title/Abstract] AND "juvenile"[Title/Abstract] AND (rheumatoid[Title/Abstract] OR idiopathic[Title/Abstract] OR chronic[Title/Abstract]) AND "arthritis"[Title/Abstract])) OR (("juvenile"[Title/Abstract]) AND "onset"[Title/Abstract] AND "Still's"[Title/Abstract] AND "disease"[Title/Abstract])) OR ("systemic juvenile idiopathic arthritis"[Text Word]))	208

Supplementary table 2. Embase search (28th October 2022)

No.	Query	Results
#1	'systemic juvenile idiopathic arthritis'/exp OR 'systemic juvenile idiopathic arthritis'	2,536
#2	'adult onset still disease'/exp OR 'adult onset still disease'	2,811
#3	#1 AND #2	**202**

De Matteis A, *et al. Ann Rheum Dis* 2024;0:1–14. doi: 10.1136/ard-2024-225853

Supplementary table 3. Cochrane Library search (28th October 2022)

ID	Search	Hits
#1	MeSH descriptor: [Still's Disease, Adult-Onset] explode all trees	9
#2	"adult-onset Still's disease" OR (adult AND onset AND Still's AND disease)	1374
#3	MeSH descriptor: [Arthritis, Juvenile] explode all trees	337
#4	(systemic AND juvenile) AND (rheumatoid OR idiopathic OR chronic) AND "arthritis"	332
#5	"juvenile" AND "onset" AND "Still's" AND "disease"	119
#6	"systemic juvenile idiopathic arthritis"	138
#7	#1 OR #2	1374
#8	#3 OR #4 OR #5 OR #6	664
#9	#7 AND #8	**105**

Supplementary table 4. Outcomes of the review (SR1)

Main outcomes	
Clinical manifestations and their prevalence	Fever, joint involvement (arthritis, arthralgia, erosive arthritis,), skin rash, pharyngitis or sore throat, lymphadenopathy, splenomegaly, hepatomegaly, muscle involvement (myalgia, myositis), serositis (pericarditis, pleuritic), pericardial effusion, pulmonary involvement (pleuritis, interstitial lung disease), malaise, altered general condition, weight loss, abdominal pain.
Biological findings and their prevalence	Leukocytosis, neutrophilia, anaemia, elevated platelet count, elevated ESR, elevated CRP, altered liver function tests, elevated ferritin, elevated D-Dimers, immunological status for RF and ANA, IL-18, IL-1, IL-6, TNFα
Complications and their prevalence	Mortality, macrophage activation syndrome (MAS), disseminated intravascular coagulation, thrombotic microangiopathy, fulminant hepatitis, myocarditis, cardiac tamponade, endocarditis, pulmonary arterial hypertension, interstitial lung disease, acute respiratory distress syndrome, aseptic empyema, diffuse alveolar haemorrhage, amyloid A amyloidosis.
Additional outcomes	
Fever	Temperature threshold ☐ ≥ 38.0°C ☐ ≥ 38.5°C ☐ ≥ 39.0°C ☐ ≥ 39.5°C ☐ Unclear or not reported Duration in definition ☐ At least 3 days ☐ At least 5 days ☐ At least 1 week ☐ At least 2 weeks ☐ Unclear or not reported Spiking and hectic ☐ Yes ☐ No ☐ Unclear or not reported Spikes' predominance in the evening ☐ Yes ☐ No ☐ Unclear or not reported Other:
Joint involvement	Topography[1] of arthralgia and arthritis among knee, wrist, ankle, elbow, MCP, PIP, DIP, shoulder, MTP, hip, cervical spine, TMJ.
Skin rash	☐ Evanescent ☐ Salmon-pink ☐ Maculo-papular or popular ☐ Predominating on trunk and proximal limbs ☐ Urticarial ☐ Meet at least 1 feature ☐ Meet at least 2 features ☐ Unclear or not reported Other:
Hepatomegaly	☐ by imaging[2] ☐ by clinical palpation ☐ Unclear or not reported Other:
Splenomegaly	☐ by imaging[2] ☐ by clinical palpation ☐ Unclear or not reported Other:
Lymphadenopathies	☐ by imaging[2] ☐ by clinical palpation ☐ Unclear or not reported Number of lymphadenopathies had to be: ☐ At least 1 lymphadenopathy ☐ At least 2 lymphadenopathies ☐ At least 3 lymphadenopathies ☐ At least 4 lymphadenopathies ☐ At least 5 lymphadenopathies ☐ Unclear or not reported Number of sites with lymphadenopathies had to be: ☐ 1 or 2 sites ☐ 3 sites or more ☐ Unclear or not reported Other:

[1]MCP, metacarpophalangeal; PIP, proximal interphalangeal; DIP, distal interphalangeal; MTP, metatarsophalangeal; TMJ, temporomandibular joint.

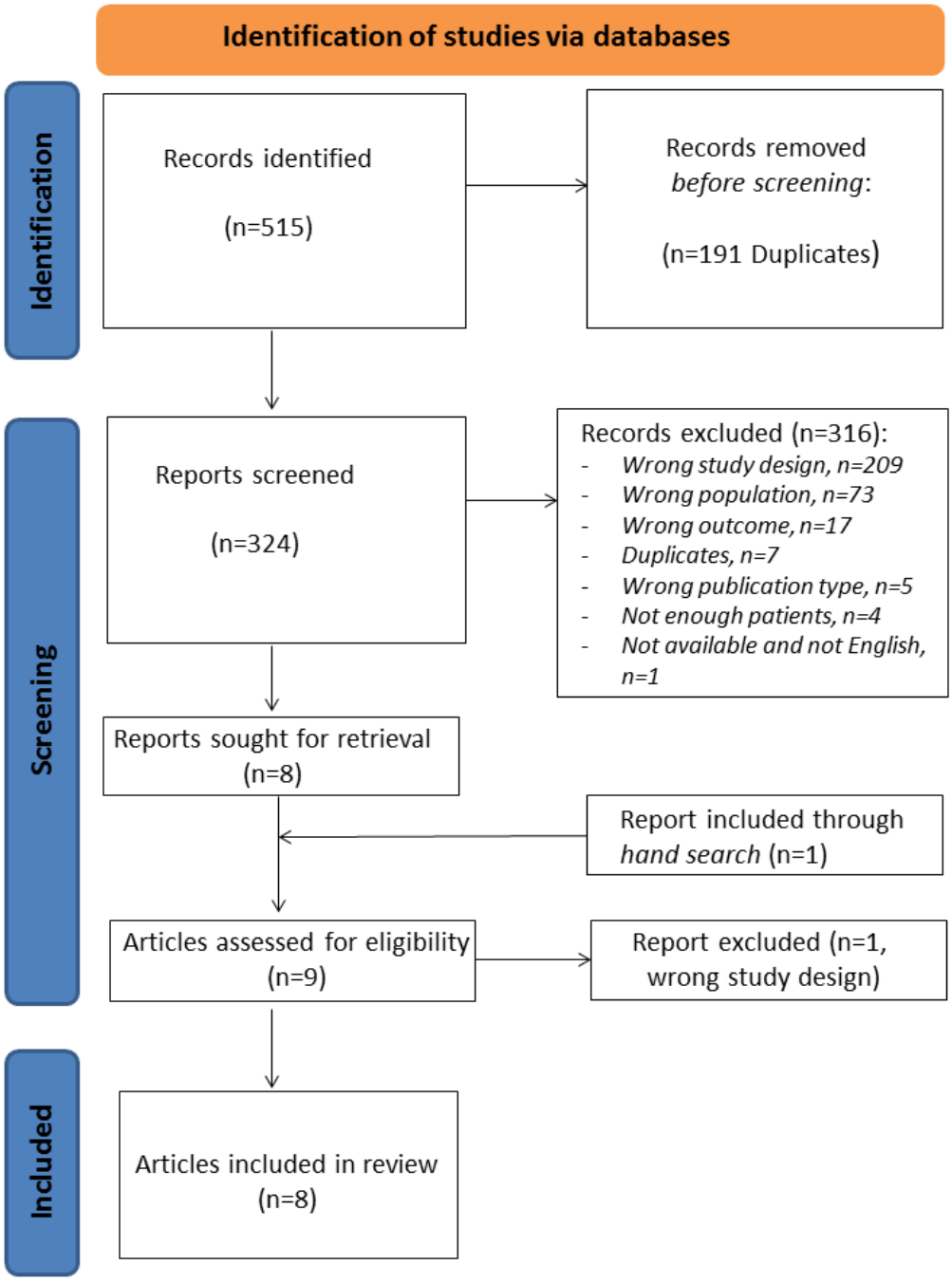
[2]Ultrasound, scanner and/or MRI.

Supplementary table 5. Quality assessment, adapted from the Hoy scale for prevalence studies[1]

External validity		
Risk of bias item	**Risk of bias level**	**Points**
1. Was the study's target population a close representation of the sJIA/AOSD population in relation to relevant variables, e.g., age and sex?[2]	☐ **Yes (LOW RISK) 0** ☐ **No (HIGH RISK) 1**	
2. Was the sampling frame[3] a true or close representation of the target population?	☐ **Yes (LOW RISK) 0** ☐ **No (HIGH RISK) 1**	
3. Was some form of random selection (e.g., simple random sampling, stratified random sampling, cluster sampling, systematic sampling) used to select the sample, OR, was a list of ALL ever existing patients with sJIA/AOSD undertaken?	☐ **Yes (LOW RISK) 0** ☐ **No (HIGH RISK) 1**	
4. Was the likelihood of nonresponse bias minimal? i.e., the response rate (or complete data) for the study was ≥75%, OR, an analysis was performed that showed no significant difference in relevant characteristics between responders and non- responders (or between those with complete or incomplete data	☐ **Yes (LOW RISK) 0** ☐ **No (HIGH RISK) 1**	
Internal validity		
5. Were data collected directly from the subjects (as opposed to a proxy)? (In the case of retrospective data collection, low risk would be if the researchers crossed checked with the patients for symptoms)	☐ **Yes (LOW RISK) 0** ☐ **No (HIGH RISK) 1**	
6. Was an acceptable case definition used in the study? (NOTE: Owing to the multiple features we are interested in knowing their prevalence, we will consider high risk if only one of the main features (i.e., fever, joint involvement, or MAS) is not well defined)	☐ **Yes (LOW RISK) 0** ☐ **No (HIGH RISK) 1**	
7. Was the study instrument that measured the parameter of interest shown to have validity and reliability? (Make a general judgement of data collection; if there was some sort of standardisation give it a low).	☐ **Yes (LOW RISK) 0** ☐ **No (HIGH RISK) 1**	
8. Was the same mode of data collection used for all subjects?	☐ **Yes (LOW RISK) 0** ☐ **No (HIGH RISK) 1**	
Summary on the overall risk of study bias **LOW RISK (0-3)**	**MODERATE RISK (4-5)** **HIGH RISK (6-8)**	

[1] Hoy D, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. J Clin Epidemiol. 2012;65: 934-9.
It does not include item 9 on shortest prevalence period or the denominators, as no population samples were foreseen to be included.
[2] Basically, not skewed, like all men or all women, or a single occupation, like nurses.
[3] It refers to the source of patients. If they come from a referral hospital of terrible cases=> this is not a representative sampling frame; if they come from the consultation of many different centres, internal medicine and Rheumatology, the sampling frame has a low risk of bias.

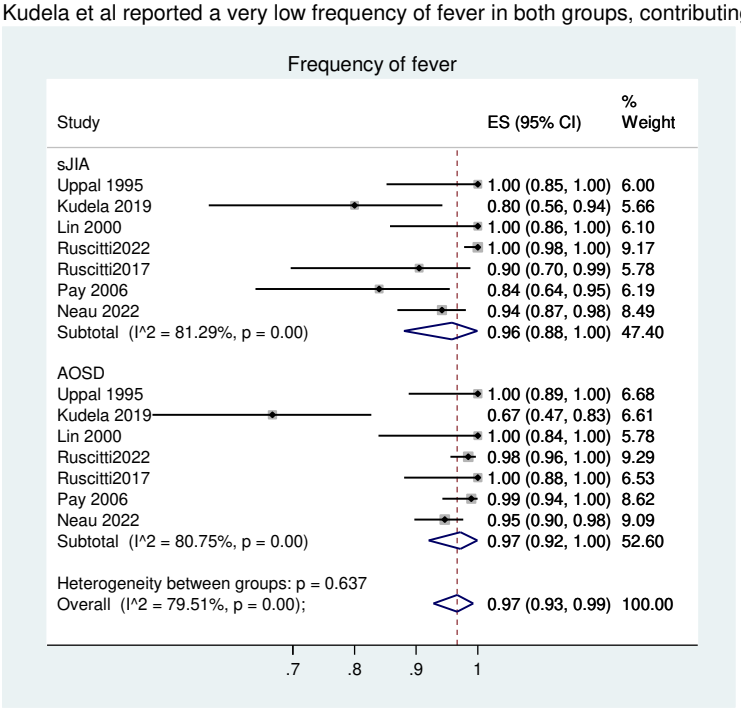
Supplementary figure 1. PRISMA flow chart of included studies in SR1 on the Prevalence of Manifestations



Supplementary figures 2. Frequencies of clinical manifestations in sJIA and AOSD

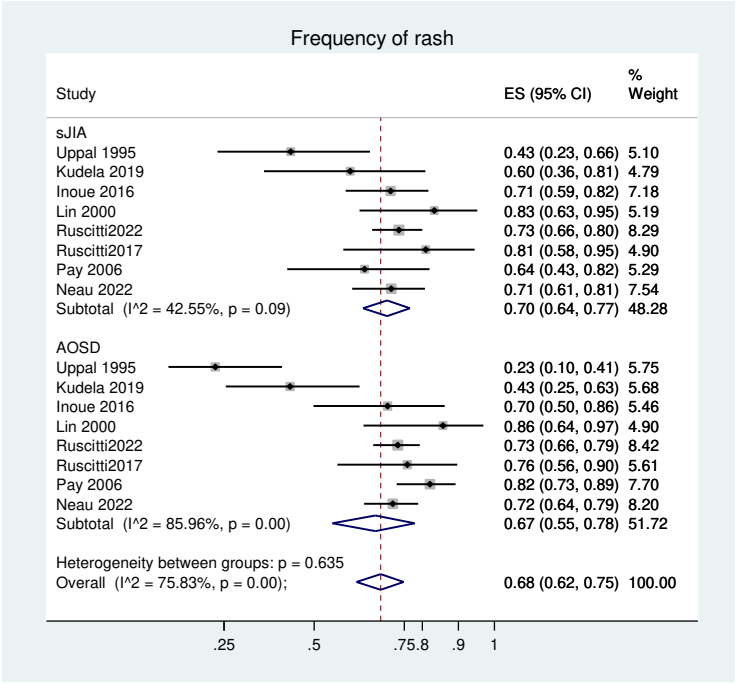
Supplemental Figure 2a: Fever

Seven studies reported a frequency for fever in both age groups. The pooled frequency was similar. The study by Kudela et al reported a very low frequency of fever in both groups, contributing to heterogeneity.

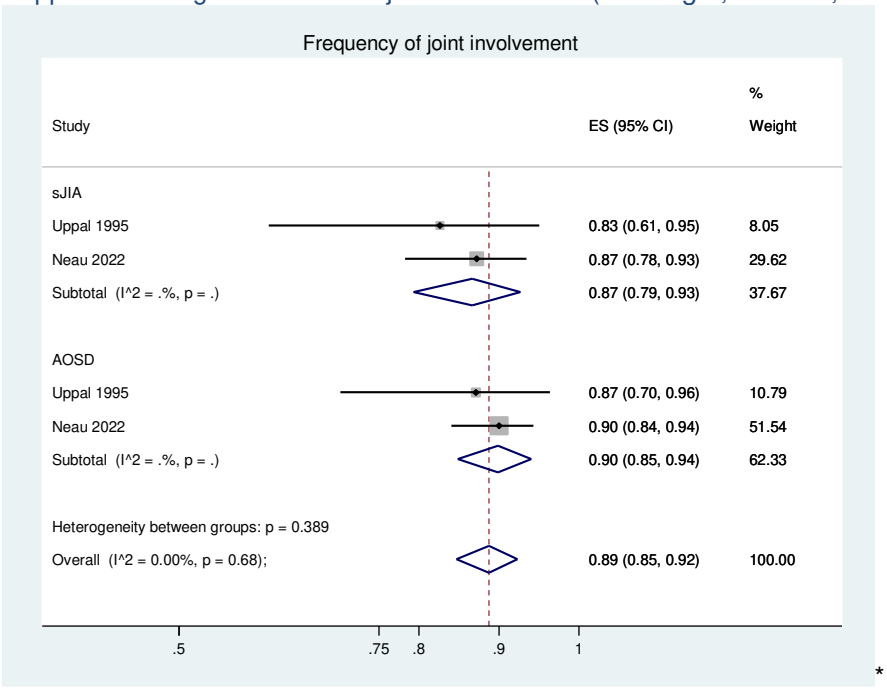


Supplemental Figure 2b: Rash

Eight studies reported a frequency for fever in both age groups. The pooled frequency was similar. The studies by Uppal and Kudela *et al* reported a very low frequency of rash in both groups, contributing to heterogeneity.



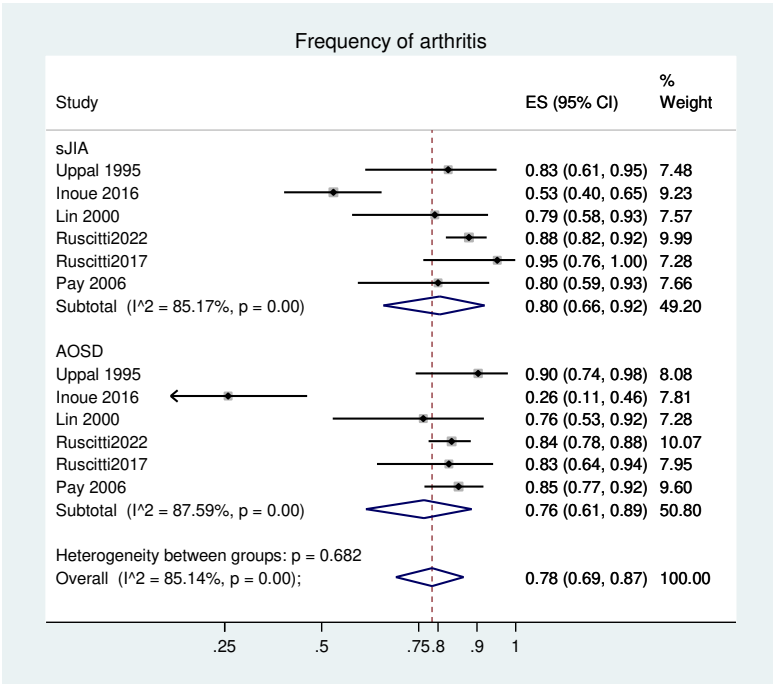
Supplemental Figure 2c: Overall joint involvement (arthralgia, arthritis, erosive arthritis)



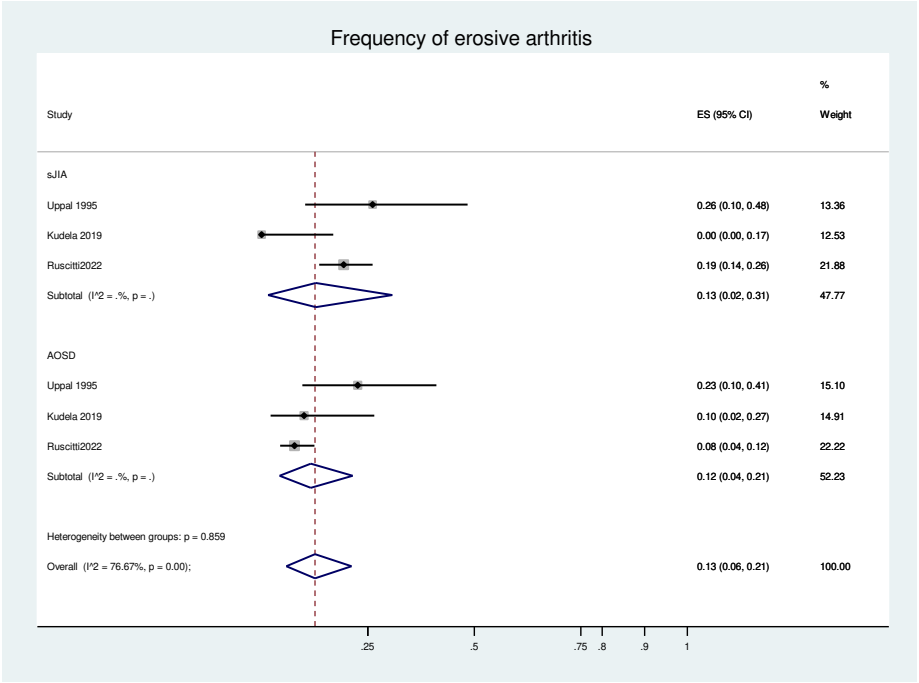
*

Supplemental Figure 2d: Overall joint involvement (arthralgia, arthritis, erosive arthritis)

Some assumptions were made: 1) In Ruscitti 2017 the authors do not make any distinction between arthralgia and arthritis, so we took the same value (n=20) for each parameter (arthralgia and arthritis). 2) In Kudela 2019, the authors provide the n of patients with "swollen joints" and "tender joints", but do not use the term "arthritis". We considered that "arthritis" corresponds to "swollen joints". 3) In Ruscitti 2022: for sJIA and arthrtitis, there were 146 patients (88.0%) at time of diagnosis with arthritis, but 20 patients developed arthritis during follow-up, so 166 (100%) had arthritis during follow-up. We took all arthritis (at onset and during follow up).

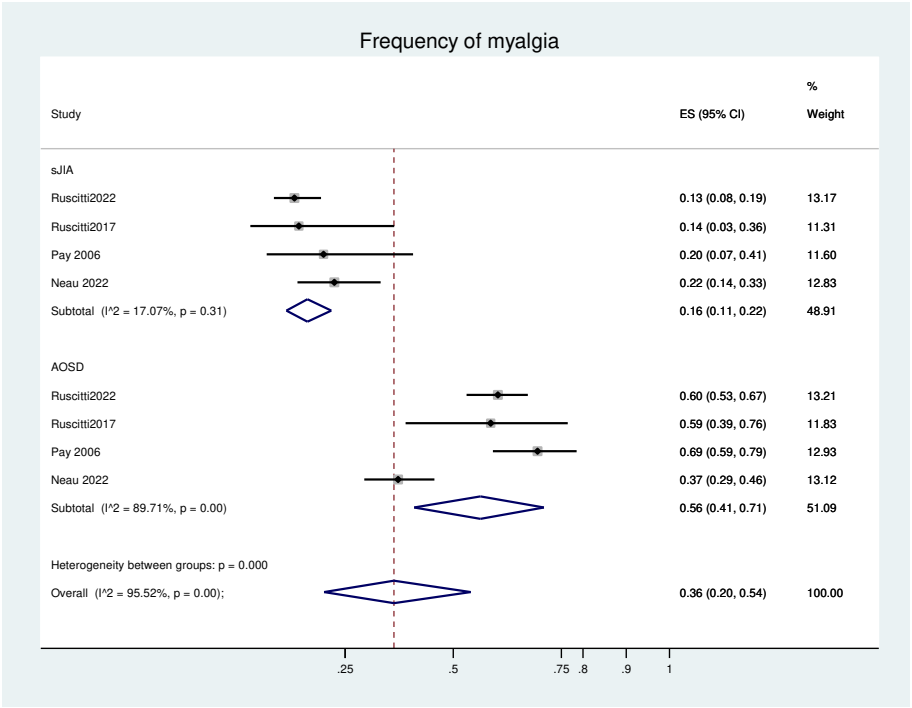


Supplemental Figure 2e: Erosive arthritis

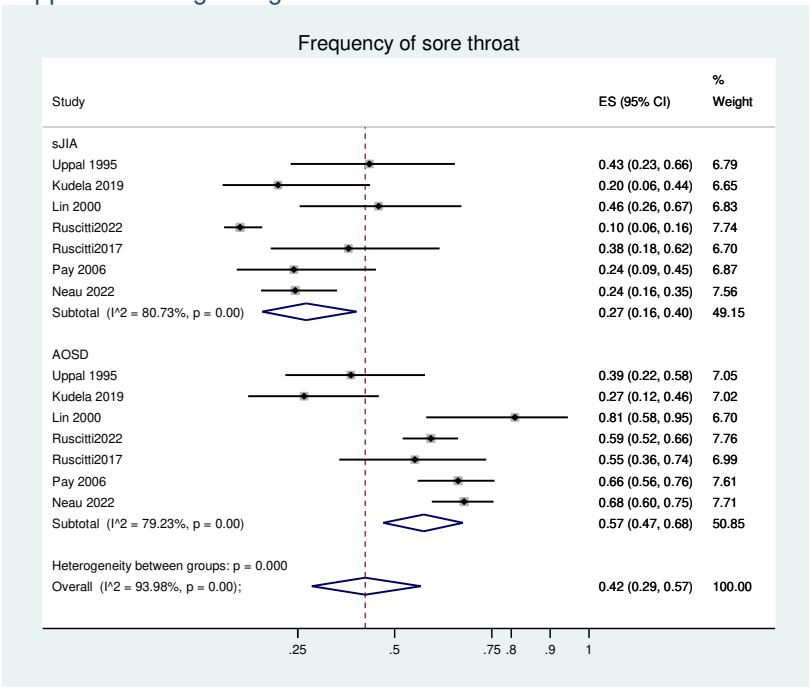


Supplemental Figure 2f: Myalgia

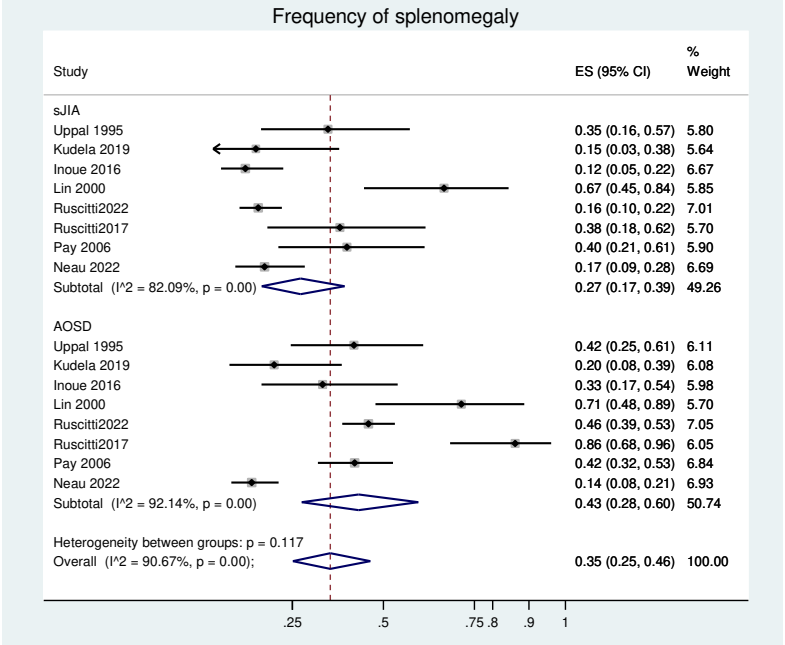
The difference between groups is significant, 16% in sJIA vs 56% in AOSD.



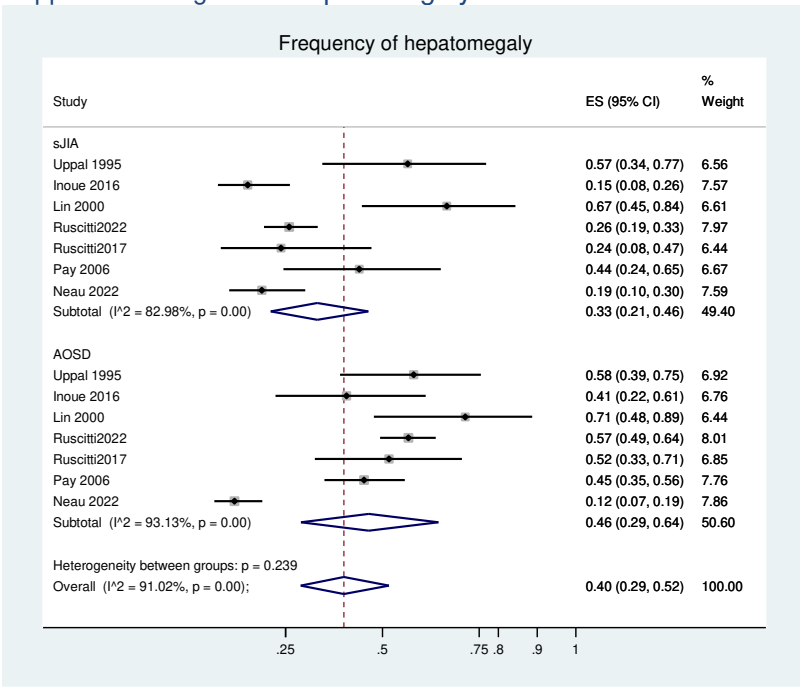
Supplemental Figure 2g: Sore throat



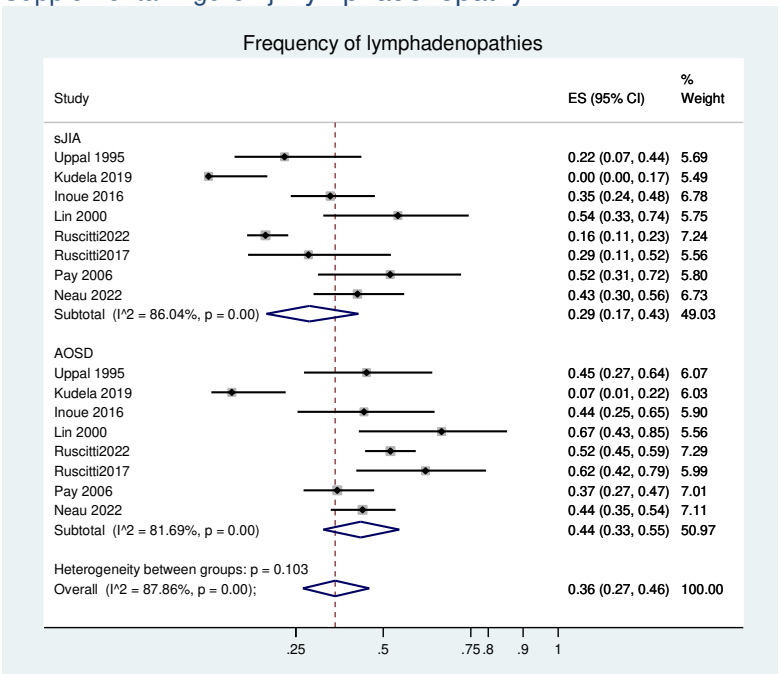
Supplemental Figure 2h: Splenomegaly



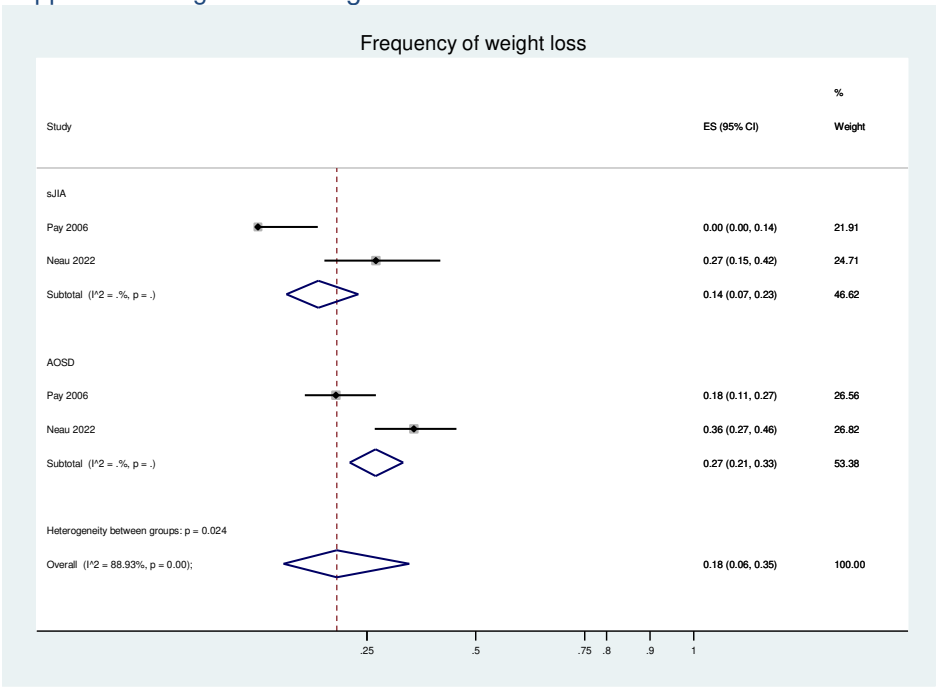
Supplemental Figure 2i: Hepatomegaly



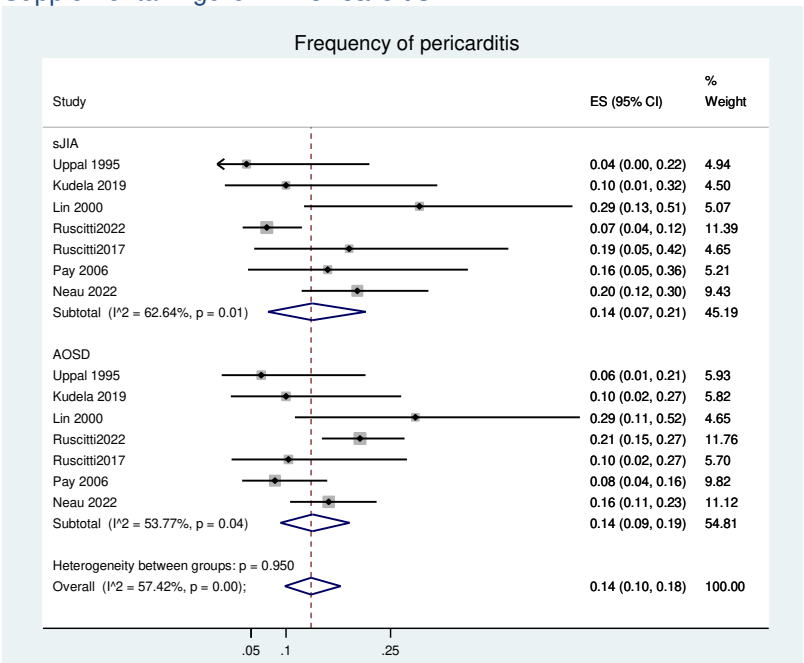
Supplemental Figure 2j: Lymphadenopathy



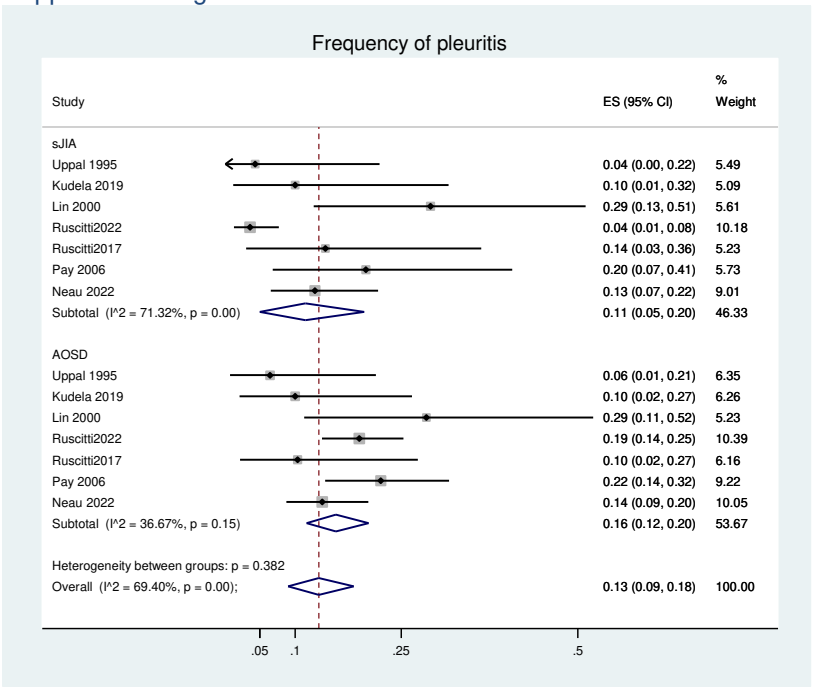
Supplemental Figure 2k: Weight loss



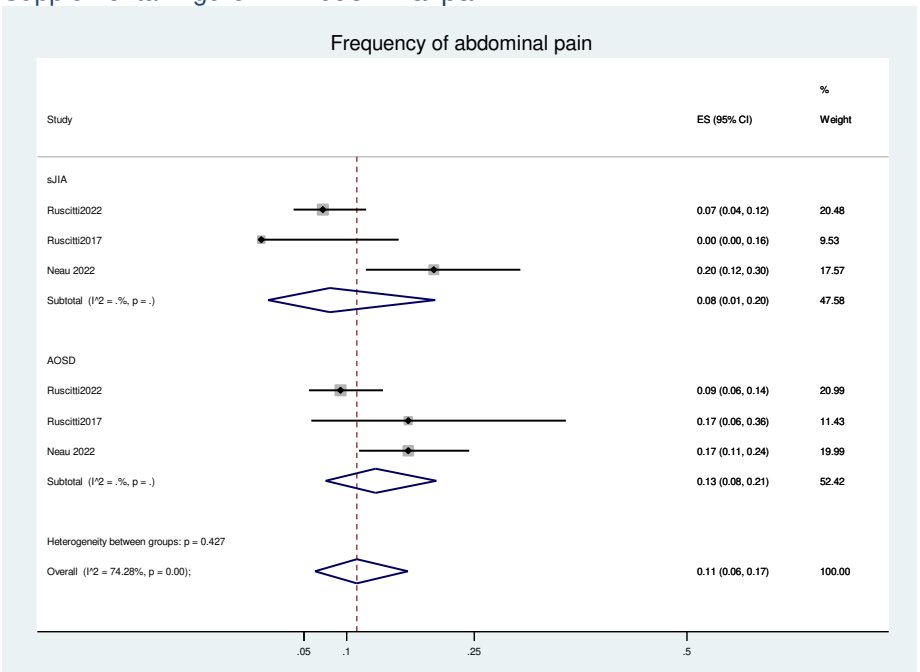
Supplemental Figure 2l: Pericarditis



Supplemental Figure 2m: Pleuritis

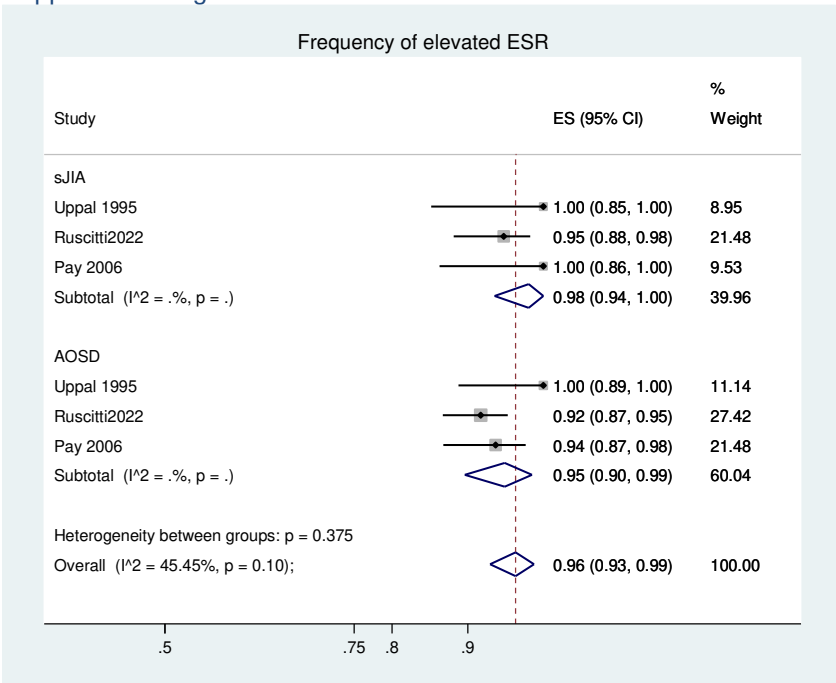


Supplemental Figure 2n: Abdominal pain



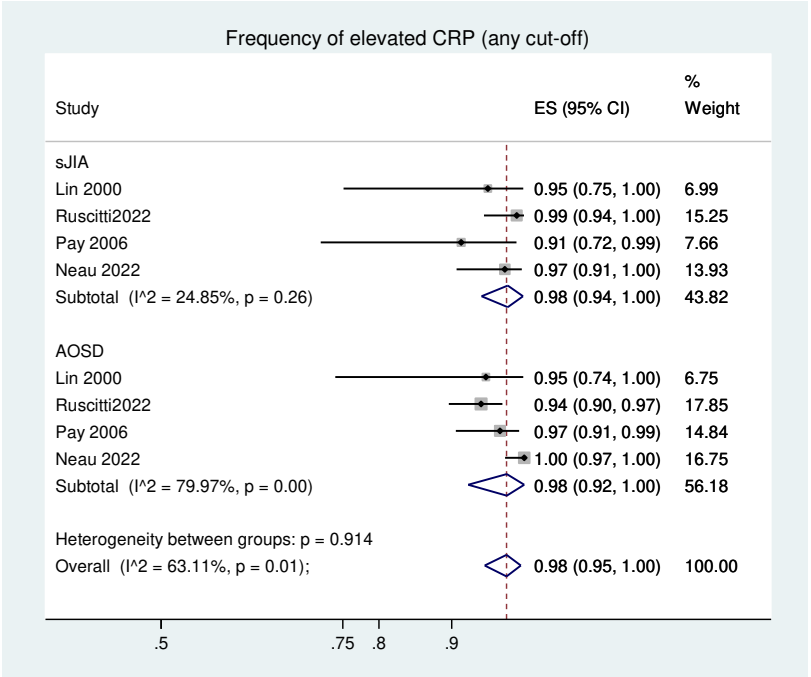
Supplementary figures 3. Frequencies of biological abnormalities in sJIA and AOSD

Supplemental Figure 3a: Elevated ESR

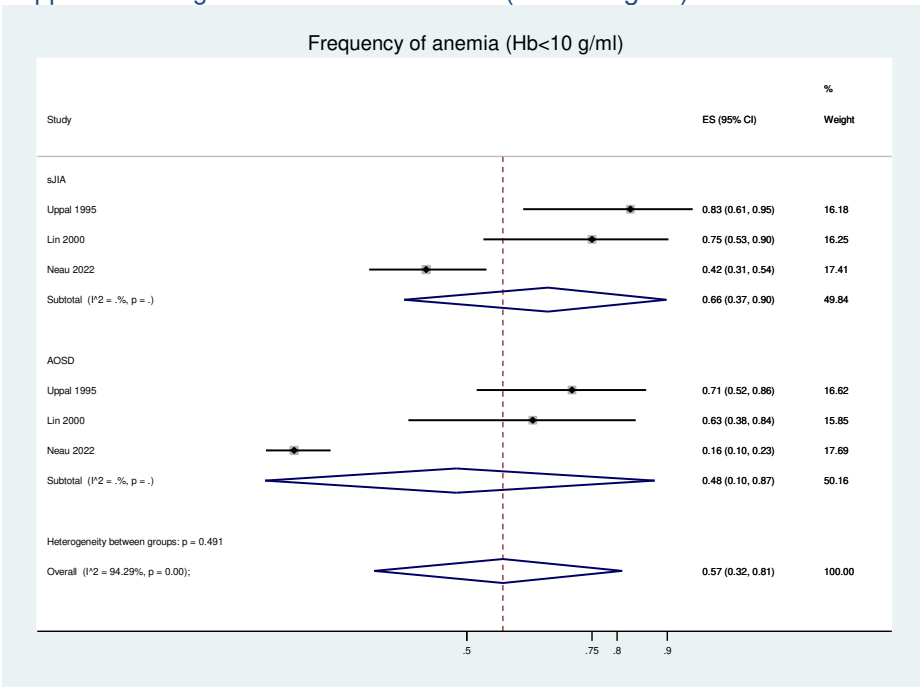


Supplemental Figure 3b: Elevated CRP

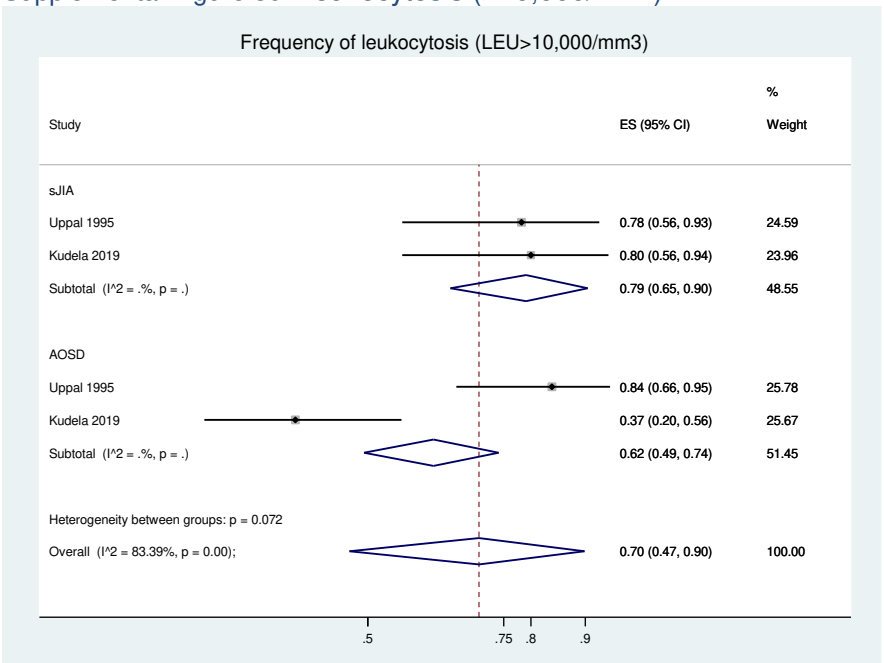
Variability is low and there is not marked difference between the groups, neither with a more open definition (any cut-off) nor with the most common cut-off of 6 mg/dL (only two studies).



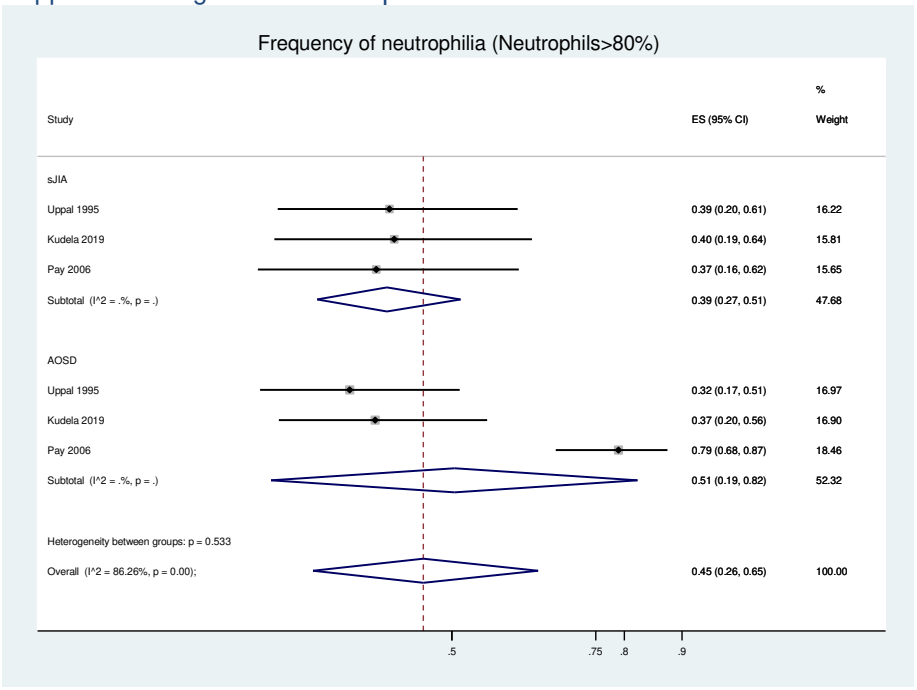
Supplemental Figure 3c: Severe anaemia (Hb < 10 g/dL)



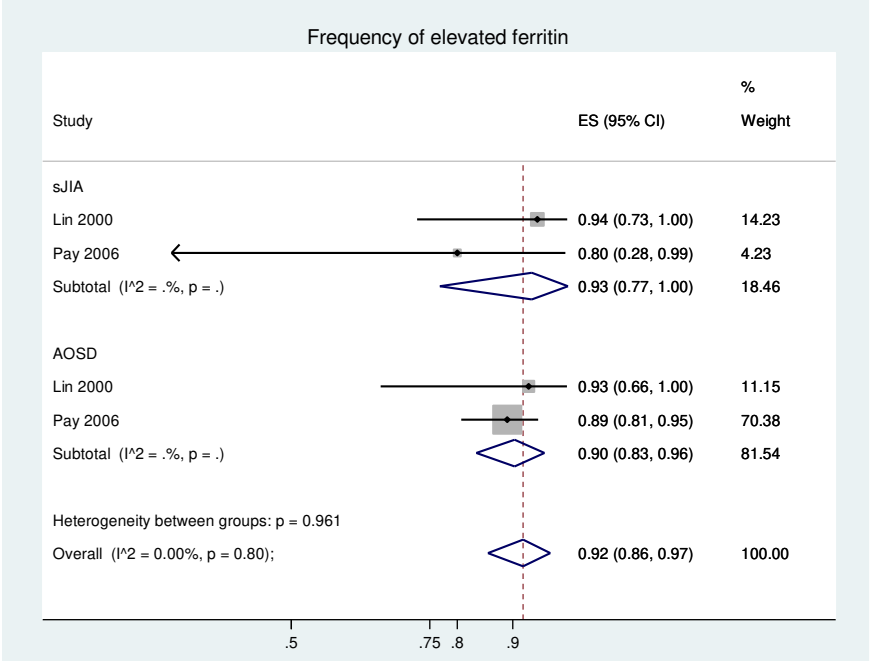
Supplemental Figure 3d: Leukocytosis (>10,000/mm^3)



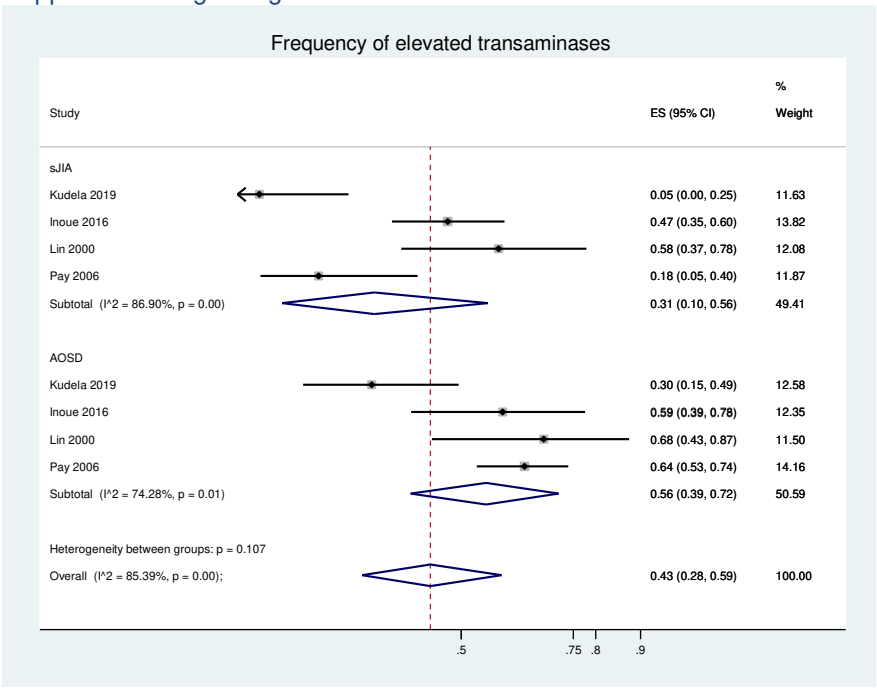
Supplemental Figure 3e: Neutrophilia < 80%



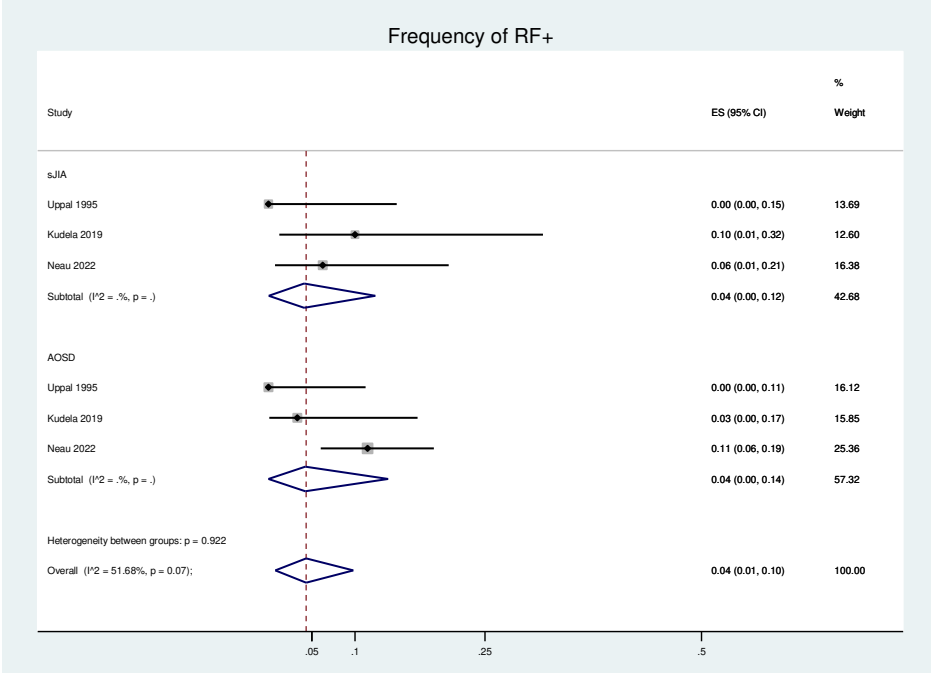
Supplemental Figure 3f: Elevated ferritin



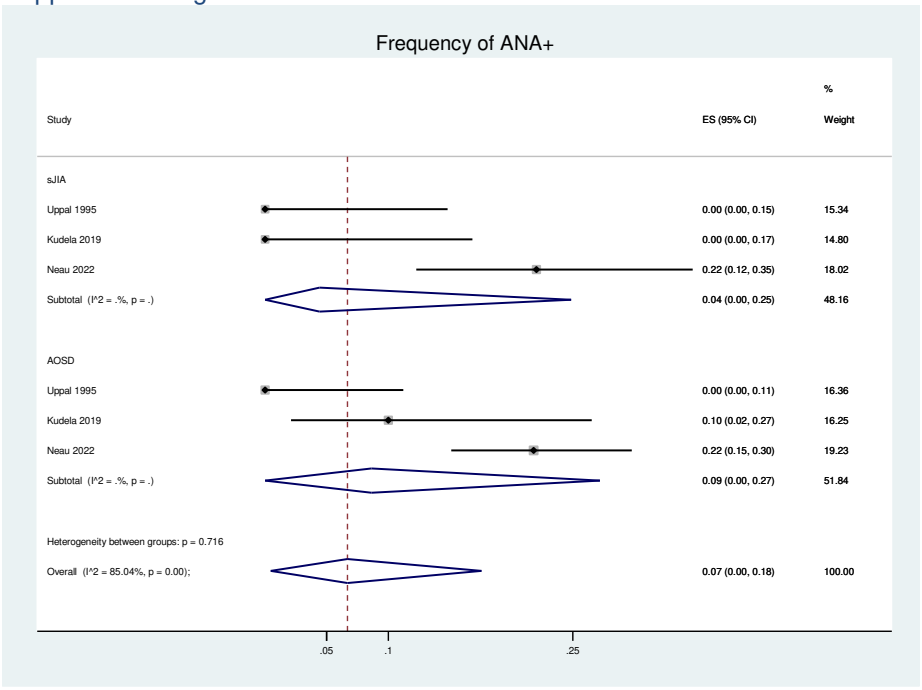
Supplemental Figure 3g: Elevated transaminases



Supplemental Figure 3h: RF+

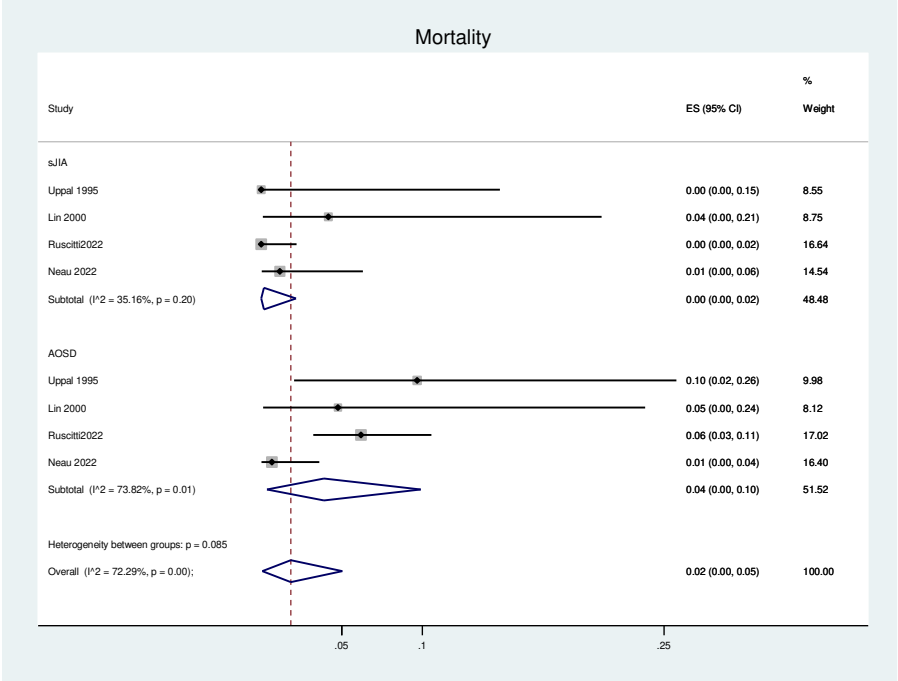


Supplemental Figure 3i: ANA+



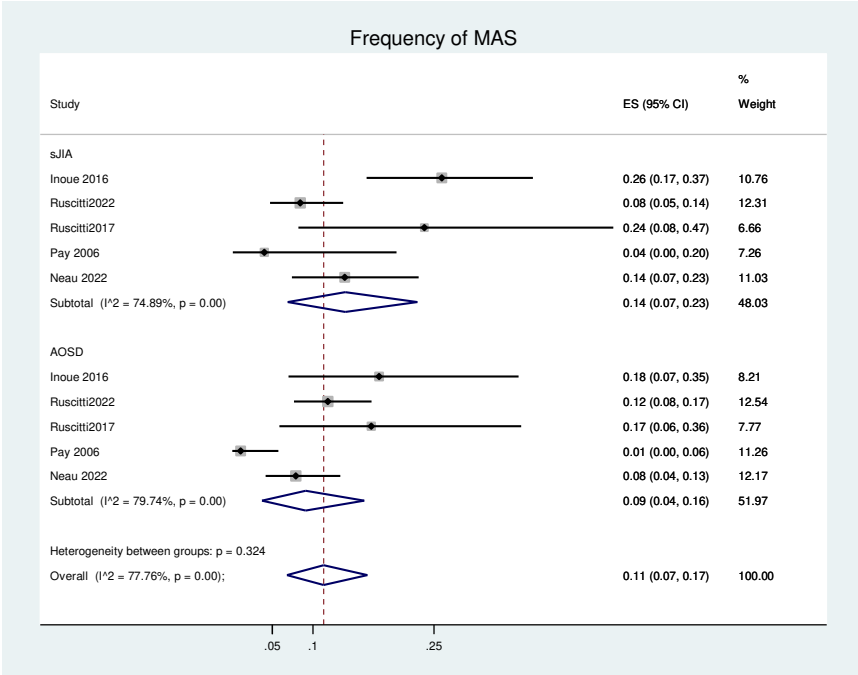
Supplementary figures 4. Frequencies of complications in sJIA and AOSD

Supplemental Figure 4a: Mortality

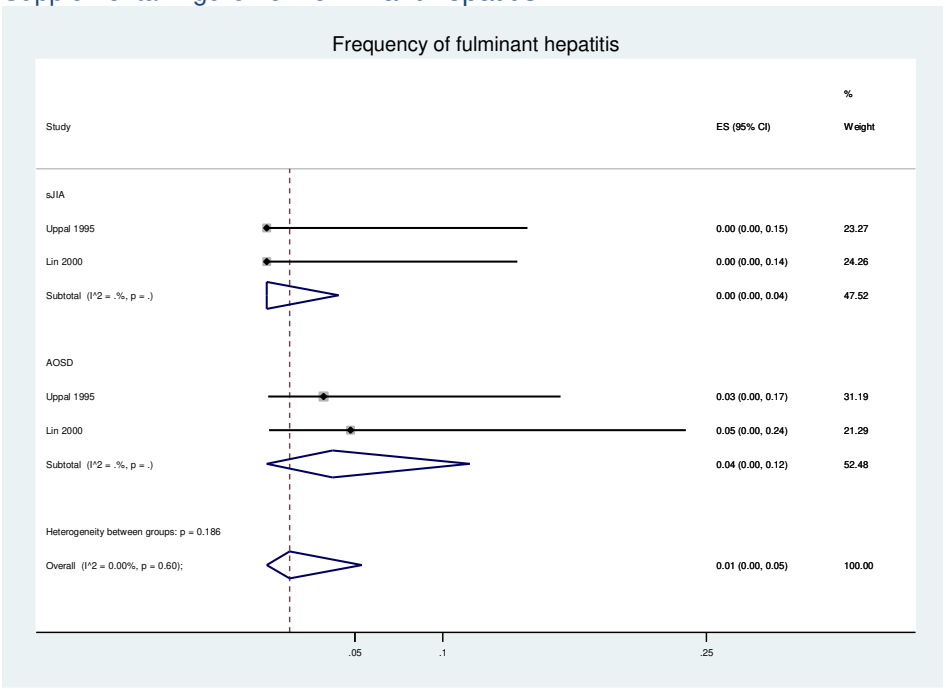


Supplemental Figure 4b: MAS

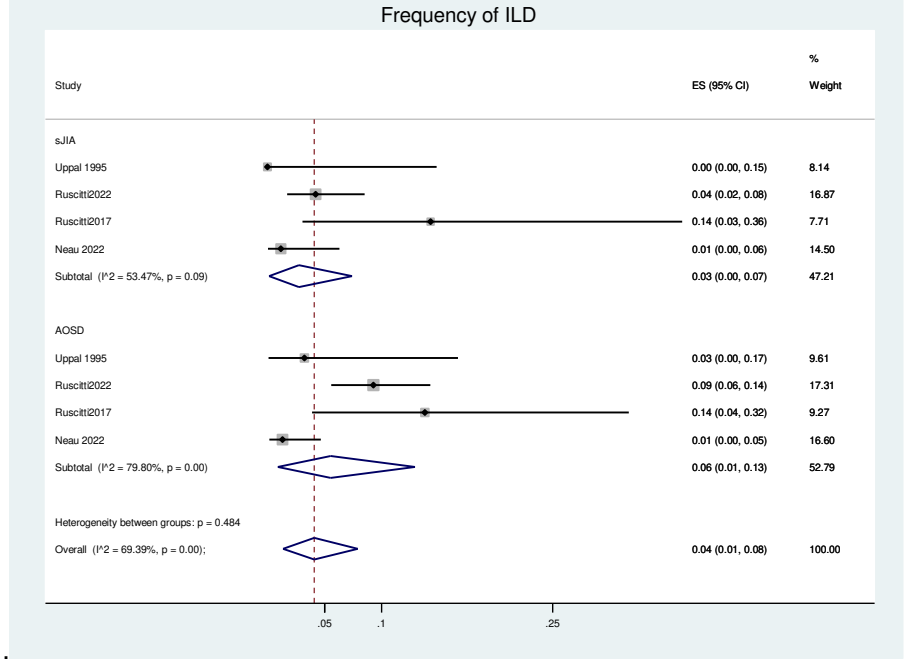
Note that for Neau 2022, in the paper the authors report a total n=26 but in their Excel file it is n=24 (12 in sJIA group, 12 in AOSD group), so we considered n=24 for our metanalysis.



Supplemental Figure 4c: Fulminant hepatitis



Supplemental Figure 4d: lung disease



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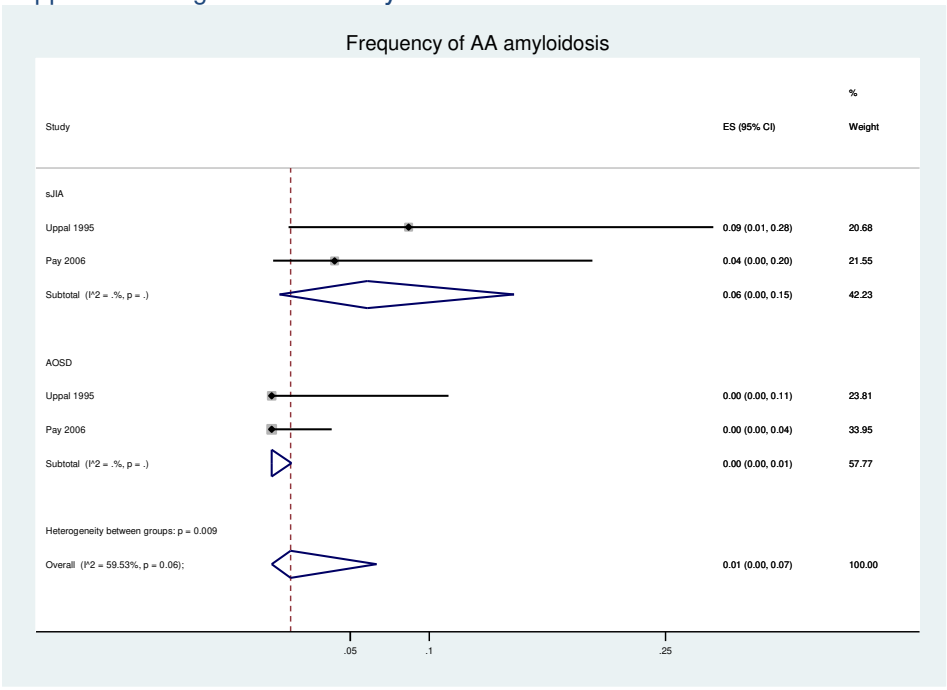
Supplemental Figure 4e: AA amyloidosis



Thrombotic microangiopathy

Only one study reported on the frequency of thrombotic microangiopathy (Neau, 2022), and so metanalysis was not performed. The prevalence reported was 1.4% in sJIA and 0.8% in AOSD. Numbers are too low and similar to draw any conclusions.

Tamponade

Only one study reported on the frequency of tamponade (Neau, 2022), and so metanalysis was not performed. The prevalence reported was 4.8% in sJIA and 1.3% in AOSD. Numbers are too low to draw any conclusions.

Myocarditis

Only one study reported on the frequency of myocarditis (Neau, 2022), and so metanalysis was not performed. The prevalence reported was 1.2% in sJIA and 6.0% in AOSD. The frequency seems large in AOSD.

Pulmonary arterial hypertension

Only one study reported on the frequency of pulmonary arterial hypertension (Neau, 2022), and so metanalysis was not performed. No cases were reported in the sJIA group and only 2 (1.8%) in AOSD. Numbers are too low to draw any conclusions.

Supplementary table 6. Weighted percentage of treatment used in sJIA and AOSD

Treatment	Number of articles	Total number of patients	Number of sJIA patients	Number of AOSD patients	Weighted treatment used (%), sJIA	Weighted treatment used (%), AOSD
NSAIDs alone	3	149	68	81	26	4
Glucocorticoids	5	607	296	311	71	86
csDMARDs	3	464	210	254	40	65
Methotrexate[1]	5	602	299	303	20	38
bDMARDs[2]	2	410	187	223	68	40
IL-1 inhibitors[2]	2	410	186	224	37	26
IL-6 inhibitors[2] (1st line)	1	360	166	194	2	7
TNF inhibtors[2]	3	530	211	319	26	4

[1]Inoue study was not very precise reporting data on treatment, as it was not the purpose of the study.

[2]In the paper by Ruscitti 2022, the proportion of bDMARDs 'IL1-inhibitors, IL6-inhibitors and TNFi agents) are all in first line. Ruscitti 2017 provides total bDMARDs.

csDMARDS, conventional synthetic Disease Modifying Anti-Rheumatic Drugs; IL, interleukin; NSAIDs, non-steroidal anti-inflammatory drugs; TNF inhibitors, tumour necrosis factor inhibitors.

Supplementary material for SR2: Diagnostic Biomarkers for sJIA and AOSD

Supplementary table 7. Search strategy for SR2 on PubMed (23rd February 2023)

N°	Query	Results
#1	((biomarker[Title/Abstract]) OR (biomarker[Text Word])) OR (biomarker[MeSH Terms])	975,610
#2	"biomarker s"[All Fields] OR "biomarkers"[MeSH Terms] OR "biomarkers"[All Fields] OR "biomarker"[All Fields]	1,109,464
#3	(((biomarker[Title/Abstract]) OR (biomarker[Text Word])) OR (biomarker[MeSH Terms])) OR (biomarkers)	1,109,464
#4	"interleukine"[All Fields] OR "interleukines"[All Fields] OR "interleukins"[MeSH Terms] OR "interleukins"[All Fields] OR "interleukin"[All Fields]	405,279
#5	interleukins[Title/Abstract]	8,261
#6	interleukins[Text Word]	25,616
#7	interleukins[MeSH Terms]	268,316
#8	(((interleukins) OR (interleukins[Title/Abstract])) OR (interleukins[Text Word])) OR (interleukins[MeSH Terms])	405,279
#9	interferons	224,262
#10	interferons[MeSH Terms]	143,887
#11	interferons[Text Word]	35,438
#12	interferons[Title/Abstract]	13,233
#13	(((interferons) OR (interferons[MeSH Terms])) OR (interferons[Text Word])) OR (interferons[Title/Abstract])	224,262
#14	"ferritin s"[All Fields] OR "ferritine"[All Fields] OR "ferritins"[MeSH Terms] OR "ferritins"[All Fields] OR "ferritin"[All Fields]	38,811
#15	ferritins[MeSH Terms]	22,324
#16	ferritins[Text Word]	21,731
#17	ferritins[Title/Abstract]	1,034
#18	(((ferritins) OR (ferritins[MeSH Terms])) OR (ferritins[Text Word])) OR (ferritins[Title/Abstract])	38,811
#19	"s100 proteins"[MeSH Terms] OR ("s100"[All Fields] AND "proteins"[All Fields]) OR "s100 proteins"[All Fields]	28,373
#20	S100 proteins[MeSH Terms]	25,324
#21	S100 proteins[Title/Abstract]	972
#22	S100 proteins[Text Word]	12,421
#23	(((S100 proteins) OR (S100 proteins[MeSH Terms])) OR (S100 proteins[Title/Abstract])) OR (S100 proteins[Text Word])	28,373
#24	(((((((biomarker[Title/Abstract]) OR (biomarker[Text Word])) OR (biomarker[MeSH Terms])) OR (biomarkers)) OR ((((interleukins) OR (interleukins[Title/Abstract])) OR (interleukins[Text Word])) OR (interleukins[MeSH Terms]))) OR ((((interferons) OR (interferons[MeSH Terms])) OR (interferons[Text Word])) OR (interferons[Title/Abstract]))) OR ((((ferritins) OR (ferritins[MeSH Terms])) OR (ferritins[Text Word])) OR (ferritins[Title/Abstract]))) OR ((((S100 proteins) OR (S100 proteins[MeSH Terms])) OR (S100 proteins[Title/Abstract])) OR (S100 proteins[Text Word]))	1,641,454

N°	Query	Results
#25	((("Still's Disease, Adult-Onset"[Mesh]) OR ("adult-onset Still's disease"[Text Word])) OR (adult[Title/Abstract] AND onset[Title/Abstract] AND Still's[Title/Abstract] AND disease[Title/Abstract])) OR ((((("Arthritis, Juvenile/epidemiology"[Mesh]) OR ("systemic"[Title/Abstract] AND "juvenile"[Title/Abstract] AND (rheumatoid[Title/Abstract] OR idiopathic[Title/Abstract] OR chronic[Title/Abstract]) AND "arthritis"[Title/Abstract])) OR (("juvenile"[Title/Abstract]) AND "onset"[Title/Abstract] AND "Still's"[Title/Abstract] AND "disease"[Title/Abstract])) OR ("systemic juvenile idiopathic arthritis"[Text Word]))	6540
#26	(((macrophage activation syndrome[Title/Abstract]) OR (macrophage activation syndrome[Text Word])) OR (macrophage activation syndrome[MeSH Terms])) OR ((((Lymphohistiocytosis, Hemophagocytic) OR (Lymphohistiocytosis, Hemophagocytic[MeSH Terms])) OR (Lymphohistiocytosis, Hemophagocytic[Title/Abstract])) OR (Lymphohistiocytosis, Hemophagocytic[Text Word]))	6,068
#27	((((("Still's Disease, Adult-Onset"[Mesh]) OR ("adult-onset Still's disease"[Text Word])) OR (adult[Title/Abstract] AND onset[Title/Abstract] AND Still's[Title/Abstract] AND disease[Title/Abstract])) OR ((((("Arthritis, Juvenile/epidemiology"[Mesh]) OR ("systemic"[Title/Abstract] AND "juvenile"[Title/Abstract] AND (rheumatoid[Title/Abstract] OR idiopathic[Title/Abstract] OR chronic[Title/Abstract]) AND "arthritis"[Title/Abstract])) OR (("juvenile"[Title/Abstract]) AND "onset"[Title/Abstract] AND "Still's"[Title/Abstract] AND "disease"[Title/Abstract])) OR ("systemic juvenile idiopathic arthritis"[Text Word]))) OR ((((macrophage activation syndrome[Title/Abstract]) OR (macrophage activation syndrome[Text Word])) OR (macrophage activation syndrome[MeSH Terms])) OR ((((Lymphohistiocytosis, Hemophagocytic) OR (Lymphohistiocytosis, Hemophagocytic[MeSH Terms])) OR (Lymphohistiocytosis, Hemophagocytic[Title/Abstract])) OR (Lymphohistiocytosis, Hemophagocytic[Text Word]))	11,943
#28	(((((((((biomarker[Title/Abstract]) OR (biomarker[Text Word])) OR (biomarker[MeSH Terms])) OR (biomarkers)) OR ((((interleukins) OR (interleukins[Title/Abstract])) OR (interleukins[Text Word])) OR (interleukins[MeSH Terms]))) OR ((((interferons) OR (interferons[MeSH Terms])) OR (interferons[Text Word])) OR (interferons[Title/Abstract]))) OR ((((ferritins) OR (ferritins[MeSH Terms])) OR (ferritins[Text Word])) OR (ferritins[Title/Abstract]))) OR ((((S100 proteins) OR (S100 proteins[MeSH Terms])) OR (S100 proteins[Title/Abstract])) OR (S100 proteins[Text Word]))))) AND (((((("Still's Disease, Adult-Onset"[Mesh]) OR ("adult-onset Still's disease"[Text Word])) OR (adult[Title/Abstract] AND onset[Title/Abstract] AND Still's[Title/Abstract] AND disease[Title/Abstract])) OR ((((("Arthritis, Juvenile/epidemiology"[Mesh]) OR ("systemic"[Title/Abstract] AND "juvenile"[Title/Abstract] AND (rheumatoid[Title/Abstract] OR idiopathic[Title/Abstract] OR chronic[Title/Abstract]) AND "arthritis"[Title/Abstract])) OR (("juvenile"[Title/Abstract]) AND "onset"[Title/Abstract] AND "Still's"[Title/Abstract] AND "disease"[Title/Abstract])) OR ("systemic juvenile idiopathic arthritis"[Text Word]))) OR ((((macrophage activation syndrome[Title/Abstract]) OR (macrophage activation syndrome[Text Word])) OR (macrophage activation syndrome[MeSH Terms])) OR ((((Lymphohistiocytosis, Hemophagocytic) OR (Lymphohistiocytosis, Hemophagocytic[MeSH Terms])) OR (Lymphohistiocytosis, Hemophagocytic[Title/Abstract])) OR (Lymphohistiocytosis, Hemophagocytic[Text Word]))))	3,057
#29	"Diagnostic Tests, Routine"[Mesh]	15,054
#30	"Data Accuracy"[Mesh]	3,865
#31	accuracy[Text Word]	530,319
#32	"Dimensional Measurement Accuracy"[Mesh]	646
#33	"Area Under Curve"[Mesh]	45,404
#34	"Area Under Curve"[Text Word]	53,407
#35	AUC[Text Word]	113,618
#36	"Sensitivity and Specificity"[Mesh]	644,066
#37	"Sensitivity"[Text Word]	1,320,311
#38	"Specificity"[Text Word]	1,142,707

N°	Query	Results
#39	"ROC Curve"[Mesh]	70,392
#40	"ROC Curve"[Text Word]	98,056
#41	precision[Text Word]	195,129
#42	((((((((((("Diagnostic Tests, Routine"[Mesh]) OR ("Data Accuracy"[Mesh])) OR (accuracy[Text Word])) OR ("Dimensional Measurement Accuracy"[Mesh])) OR ("Area Under Curve"[Mesh])) OR ("Area Under Curve"[Text Word])) OR (AUC[Text Word])) OR ("Sensitivity and Specificity"[Mesh])) OR ("Sensitivity"[Text Word])) OR ("Specificity"[Text Word])) OR ("ROC Curve"[Mesh])) OR ("ROC Curve"[Text Word])) OR (precision[Text Word])	2,713,393
#43	((((((((((biomarker[Title/Abstract]) OR (biomarker[Text Word])) OR (biomarker[MeSH Terms])) OR (biomarkers)) OR ((((interleukins) OR (interleukins[Title/Abstract])) OR (interleukins[Text Word])) OR (interleukins[MeSH Terms]))) OR ((((interferons) OR (interferons[MeSH Terms])) OR (interferons[Text Word])) OR (interferons[Title/Abstract]))) OR ((((ferritins) OR (ferritins[MeSH Terms])) OR (ferritins[Text Word])) OR (ferritins[Title/Abstract]))) OR ((((S100 proteins) OR (S100 proteins[MeSH Terms])) OR (S100 proteins[Title/Abstract])) OR (S100 proteins[Text Word]))))) AND (((((("Still's Disease, Adult-Onset"[Mesh]) OR ("adult-onset Still's disease"[Text Word])) OR (adult[Title/Abstract] AND onset[Title/Abstract] AND Still's[Title/Abstract] AND disease[Title/Abstract])) OR ((((("Arthritis, Juvenile/epidemiology"[Mesh]) OR ("systemic"[Title/Abstract] AND "juvenile"[Title/Abstract] AND (rheumatoid[Title/Abstract] OR idiopathic[Title/Abstract] OR chronic[Title/Abstract]) AND "arthritis"[Title/Abstract])) OR (("juvenile"[Title/Abstract]) AND "onset"[Title/Abstract] AND "Still's"[Title/Abstract] AND "disease"[Title/Abstract])) OR ("systemic juvenile idiopathic arthritis"[Text Word]))) OR ((((macrophage activation syndrome[Title/Abstract]) OR (macrophage activation syndrome[Text Word])) OR (macrophage activation syndrome[MeSH Terms])) OR ((((Lymphohistiocytosis, Hemophagocytic) OR (Lymphohistiocytosis, Hemophagocytic[MeSH Terms])) OR (Lymphohistiocytosis, Hemophagocytic[Title/Abstract])) OR (Lymphohistiocytosis, Hemophagocytic[Text Word])))))) AND ((((((((((("Diagnostic Tests, Routine"[Mesh]) OR ("Data Accuracy"[Mesh])) OR (accuracy[Text Word])) OR ("Dimensional Measurement Accuracy"[Mesh])) OR ("Area Under Curve"[Mesh])) OR ("Area Under Curve"[Text Word])) OR (AUC[Text Word])) OR ("Sensitivity and Specificity"[Mesh])) OR ("Sensitivity"[Text Word])) OR ("Specificity"[Text Word])) OR ("ROC Curve"[Mesh])) OR ("ROC Curve"[Text Word])) OR (precision[Text Word]))	310

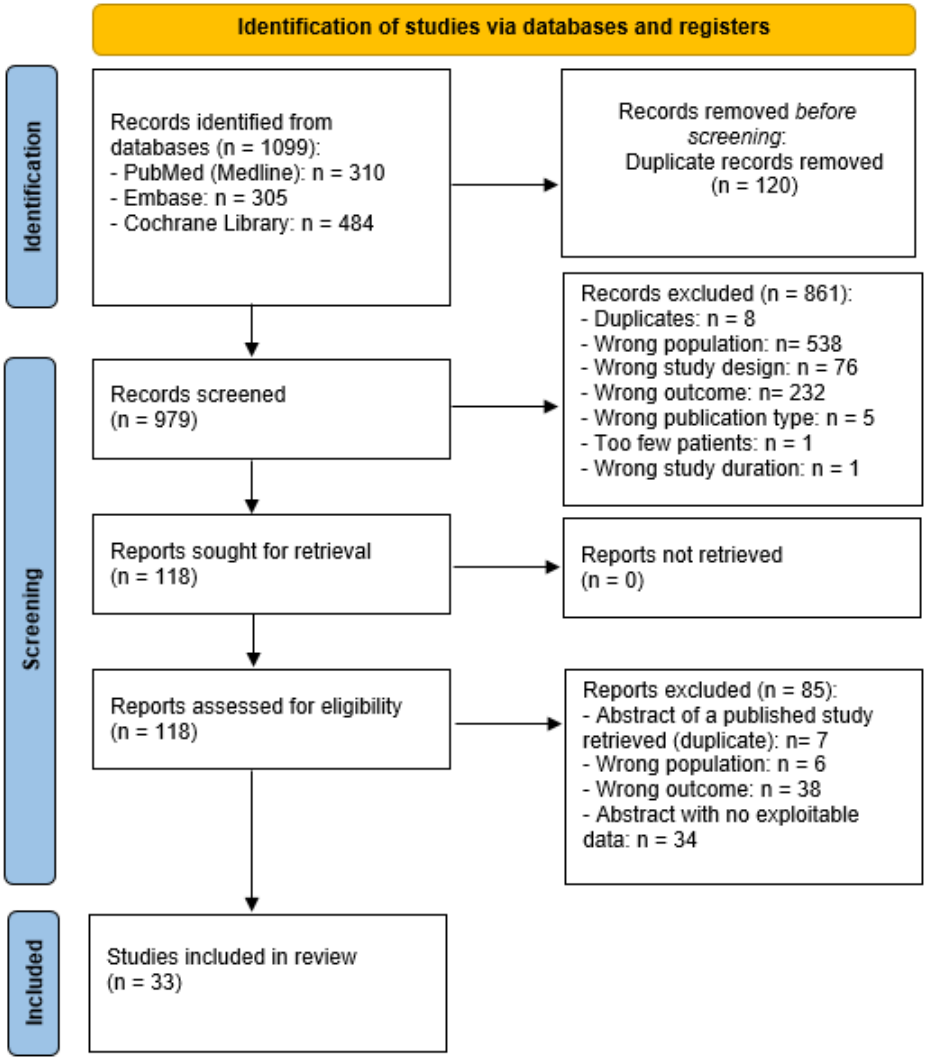
Supplementary table 8. Search strategy for SR2 on EMBASE (23rd February 2023)

No.	Query	Results
#1	'biological marker'/mj/exp OR 'biological marker' OR biomarker$ OR 'cytokine'/exp OR 'cytokine' OR 'interleukin'/exp OR 'interleukin' OR 'interferon'/exp OR 'interferon' OR 'ferritin'/exp OR 'ferritin' OR 'protein s 100'/exp OR 'protein s 100'	2,744,817
#2	'adult-onset still disease'/exp OR 'adult-onset still disease' OR 'adult onset still disease'/exp OR 'adult onset still disease' OR 'systemic juvenile idiopathic arthritis'/exp OR 'systemic juvenile idiopathic arthritis' OR 'macrophage activation syndrome'/exp OR 'macrophage activation syndrome'	8,069
#3	#1 AND #2	4,876
#4	'diagnostic accuracy'/exp OR 'diagnostic accuracy'	318,968
#5	'accuracy'/exp OR 'accuracy'	1,095,581
#6	'measurement precision'/exp OR 'measurement precision'	269,206
#7	'area under the curve'/exp OR 'area under the curve'	227,145
#8	'sensitivity and specificity'/exp OR 'sensitivity and specificity'	496,987
#9	'receiver operating characteristic'/exp OR 'receiver operating characteristic'	233,085
#10	#4 OR #5 OR #6 OR #7 OR #8 OR #9	1,759,165
#11	#3 AND #10	305

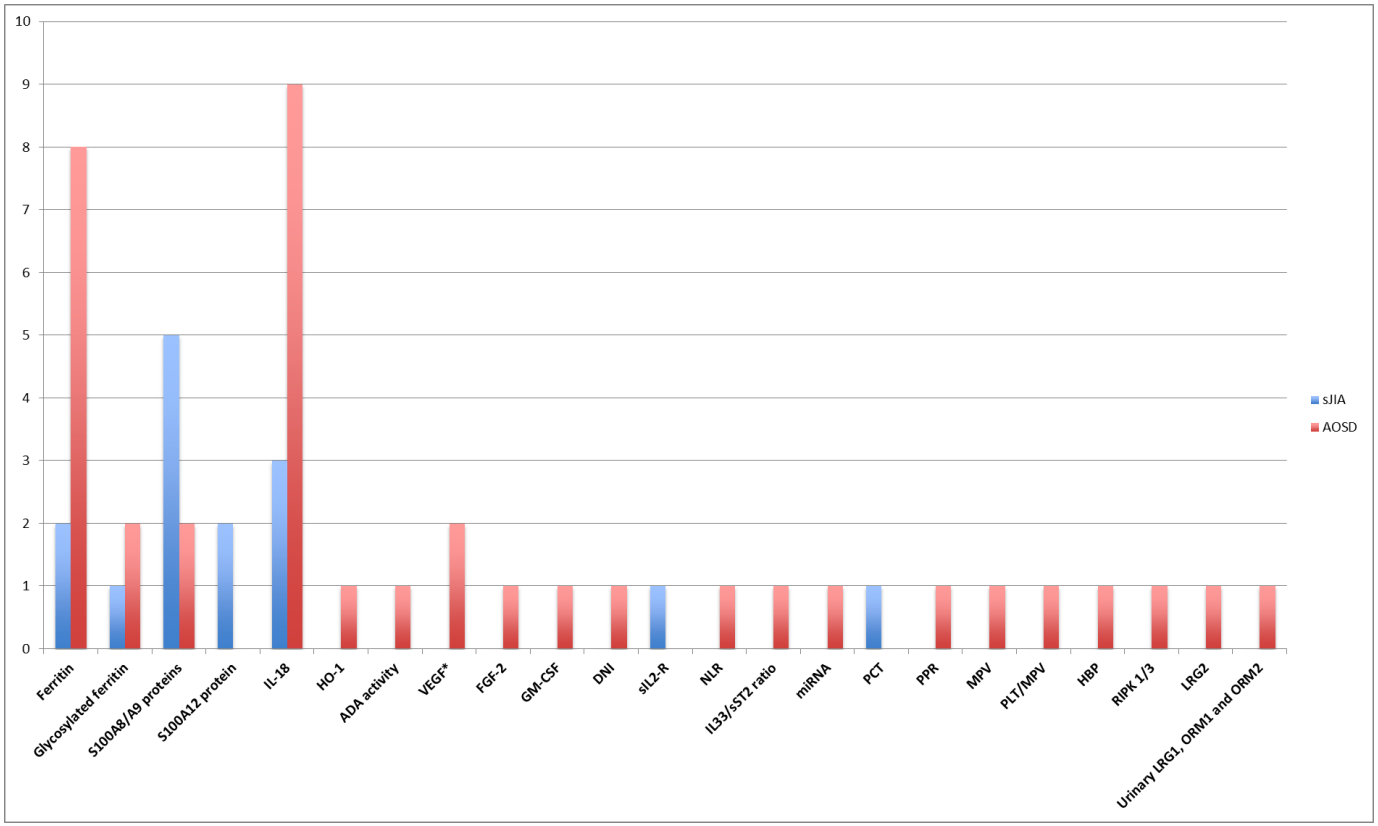
Supplementary table 9. Search strategy for SR2 on Cochrane Library (18th February 2023)

ID	Search	Hits
#1	MeSH descriptor: [Biomarkers] this term only	17908
#2	biomarker*	51992
#3	MeSH descriptor: [Interleukins] explode all trees	7636
#4	interleukin*	24620
#5	MeSH descriptor: [Interferons] explode all trees	6464
#6	interferon*	17225
#7	MeSH descriptor: [Ferritins] this term only	1174
#8	ferritin*	5363
#9	MeSH descriptor: [S100 Proteins] explode all trees	468
#10	S100 protein*	383
#11	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	90613
#12	MeSH descriptor: [Still's Disease, Adult-Onset] explode all trees	11
#13	"adult-onset Still's disease" OR (adult AND onset AND Still's AND disease)	1409
#14	MeSH descriptor: [Arthritis, Juvenile] explode all trees	379
#15	(systemic AND juvenile) AND (rheumatoid OR idiopathic OR chronic) AND "arthritis"	340
#16	"juvenile" AND "onset" AND "Still's" AND "disease"	121
#17	"systemic juvenile idiopathic arthritis"	141
#18	#12 OR #13 OR #14 OR #15 OR #16 OR #17	2005
#19	MeSH descriptor: [Macrophage Activation Syndrome] explode all trees	9
#20	("macrophage" AND "activation" AND "syndrome") OR "macrophage activation syndrome"	189
#21	#19 OR #20	189
#22	#18 OR #21	2157
#23	#11 AND #22	484

Supplementary figure 5. PRISMA flow chart of included studies in SR2: Diagnostic Biomarkers for sJIA and AOSD



Supplementary figure 6. Overview of the diagnostic biomarkers for sJIA and AOSD retrieved by SR2



The figure shows the number of articles (ordinate) found for each biomarker (abscissa). For each biomarker, the articles on sJIA are in blue, those on AOSD in red. Some studies reported several biomarkers. When not specified, all biomarkers are serum (or plasmatic).
*One study (Koga T, 2020) reported total VEGF, while the other (Chen X, 2022) reported VEGF-C.
ADA, adenosine deaminase – DNI, delta neutrophil index – FGF, fibroblast growth factor – GM-CSF, Granulocyte macrophage colony-stimulating factor – HBP, serum heparin Binding Protein – HO-1, heme oxygenase 1 – IFN-γ, interferon gamma – IL, interleukin – LRG1, α-1-acid glycoprotein 1 – LRG2, Serum leucine-rich α2-glycoprotein – MRP, myeloid-related protein – MPV, mean platelet volume –NLR, neutrophil to lymphocyte ratio – ORM1, orosomucoid 1 (alternatively named leucine-rich α-2-glycoprotein 1, AGP1) – ORM2, orosomucoid 2 (alternatively named AGP2) – PLT, platelet – PDW, platelet distribution width ratio – PPR, platelet to platelet distribution width ratio – RIPK, Receptor interacting serine/threonine kinase – sIL2-R, Soluble interleukin 2 receptor – VEGF, Vascular endothelial growth factor

Supplementary table 10. Studies retrieved reporting other diagnostic biomarkers in sJIA and AOSD and associated performance

Biomarker	Author, year	Population (n)	Controls (n)	Cut-off and unit	AUC	Sensitivity (%)	Specificity (%)
Serum Heme oxygenase 1 (HO-1)	Kirino, 2018	AOSD (42)	Sepsis and ANCA-vasculitis (46)	30.2 ng/mL	NA	85.7	83.3
Total serum Adenosine deaminase (ADA) activity	Xu, 2022	AOSD (53)	Healthy controls (60)	14.5 U/L	0.930	93.3	83.0
Serum VEGF-C	Chen, 2022	AOSD (80)	Healthy controls (31) Rheumatoid arthritis (26) and systemic lupus erythematosus (30)	NA NA	0.814 0.649	70.9 75.0	82.5 55.0
Serum total VEGF	Koga, 2020	AOSD (70)	Sepsis (22)	221 pg/mL	0.850	66.2	88.9
Serum fibroblast growth factor (FGF)-2	Koga, 2020	AOSD (70)	Sepsis (22)	36 pg/mL	0.864	82.4	88.9
Serum granulocyte macrophage colony-stimulating factor (GM-CSF)	Koga, 2020	AOSD (70)	Sepsis (22)	4.4 pg/mL	0.880	85.3	83.3
Delta neutrophil index	Park, 2014	AOSD (13)	Sepsis (33)	2.75%	0.896	82.1	84.6
Serum sIL2-R	Park, 2022	sJIA (102)	Untreated fever among infections (60), autoinflammatory diseases[a] (97) and miscellaneous[b] (98)	13420 pg/mL	0.560	56.1	55.2
Serum NLR	Seo, 20217	AOSD (127)	Initially suspected AOSD but finally not AOSD (37)[c]	3.08	0.967	91.7	68.4
Serum SL-33/sST2 ratio	Park, 2014	AOSD (52)	Healthy controls (26)	0.35 (ratio)	NA	80.0	72.2
miRNA	Hu, 2019	AOSD (25)	Sepsis (18)[d]	4-miRNA panel[c]	0.844	88.0	80.9
PCT	Park, 2022	sJIA (102)	Untreated fever among infections (60), autoinflammatory diseases[a] (97) and miscellaneous[b] (98)	0.005 ng/mL	0.623	79.3	44.3

Biomarker	Author, year	Population (n)	Controls (n)	Cut-off and unit	AUC	Sensitivity (%)	Specificity (%)
PPR (platelet to platelet distribution width ratio)	Liu, 2019	AOSD (82)	Sepsis (48)	16.8 (ratio)	0.733	61.0	68.0
MPV (mean platelet volume)	Luo, 1992	AOSD (68)	Sepsis (55)	10.9 fL	0.761	79.1	63.3
PMR (platelet to mean platelet volume ratio)	Ge, 2021	AOSD (73) AOSD (37)	Test cohort: sepsis (56) Validation cohort: sepsis (28)	PMR>25.06 PMR>25.06	0.735 0.712	54.1 88.9	80.4 42.9
Serum heparin-binding protein (HBP)	Tian, 2021	AOSD (30)	Sepsis (29)	65.1 ng/mL	0.653	75.9	55.2
RIPK1 in peripheral blood lymphocytes	Liu, 2020	AOSD (72)	Healthy controls (19)	33.7%	0.671	70.8	90.0
RIPK3 in peripheral blood lymphocytes	Liu, 2020	AOSD (72)	Healthy controls (19)	38.3%	0.813	66.7	95.0
Serum LRG2	Ha, 2015	AOSD (39) Act.AOSD (31)	Rheumatoid arthritis (47) Active rheumatoid arthritis (24)	67.9 ng/mL 67.9 ng/mL	0.966 0.992	92.3 96.8	97.9 95.8
Urinary LRG1	Sun, 2020	AOSD (70)	Non-AOSD: healthy controls (50), rheumatoid arthritis (24), sepsis (14), neoplastic (27)	NA	0.700	92.8	36.2
Urinary ORM1	Sun, 2020	AOSD (70)	Non-AOSD: healthy controls (50), rheumatoid arthritis (24), sepsis (14), neoplastic (27)	NA	0.837	78.3	83.8
Urinary ORM2	Sun, 2020	AOSD (70)	Non-AOSD: healthy controls (50), rheumatoid arthritis (24), sepsis (14), neoplastic (27)	NA	0.736	58.0	82.9
Combined urinary LRG1, ORM1 and ORM2	Sun, 2020	AOSD (70)	Non-AOSD: healthy controls (50), rheumatoid arthritis (24), sepsis (14), neoplastic (27)	NA	0.838	78.3	82.9

When not specified: all biomarkers are serum (or plasmatic).
[a]Autoinflammatory diseases (AIDs) included TRAPS, CAPS, HIDS, TRAPS+CAPS, PFAPA syndrome and undifferentiated AIDs (FMF excluded).
[b]Miscellaneous included Behçet's disease, connective tissue diseases, CRMO, haematological/oncological diseases, non-systemic JIA, reactive arthritis, vasculitis, other/unknown diagnoses.
[c] Viral infection, palindromic rheumatism, lupus-like disease, or Kikuchi's disease.
[d]miR-142-5p, miR-101-3p and miR-29c-3p and miR-141-3p

ADA, adenosine deaminase – DNI, delta neutrophil index – FGF, fibroblast growth factor – GM-CSF, Granulocyte macrophage colony-stimulating factor – HBP, serum heparin Binding Protein – HO-1, heme oxygenase 1 – IFN-γ, interferon gamma – IL, interleukin – LRG1, α-1-acid glycoprotein 1 – LRG2, Serum leucine-rich α2-glycoprotein – MRP, myeloid-related protein – MPV, mean platelet volume – NA, not available – NLR, neutrophil to lymphocyte ratio – ORM1, orosomucoid 1 (alternatively named leucine-rich α-2-glycoprotein 1, AGP1) – ORM2, orosomucoid 2 (alternatively named AGP2) – PLT, platelet – PDW, platelet distribution width ratio – PMR, platelet to mean platelet volume ratio –PPR, platelet to platelet distribution width ratio – RIPK, Receptor interacting serine/threonine kinase –sIL2-R, Soluble interleukin 2 receptor – sST2, soluble receptor ST2 of interleukin 33 – VEGF, Vascular endothelial growth factor

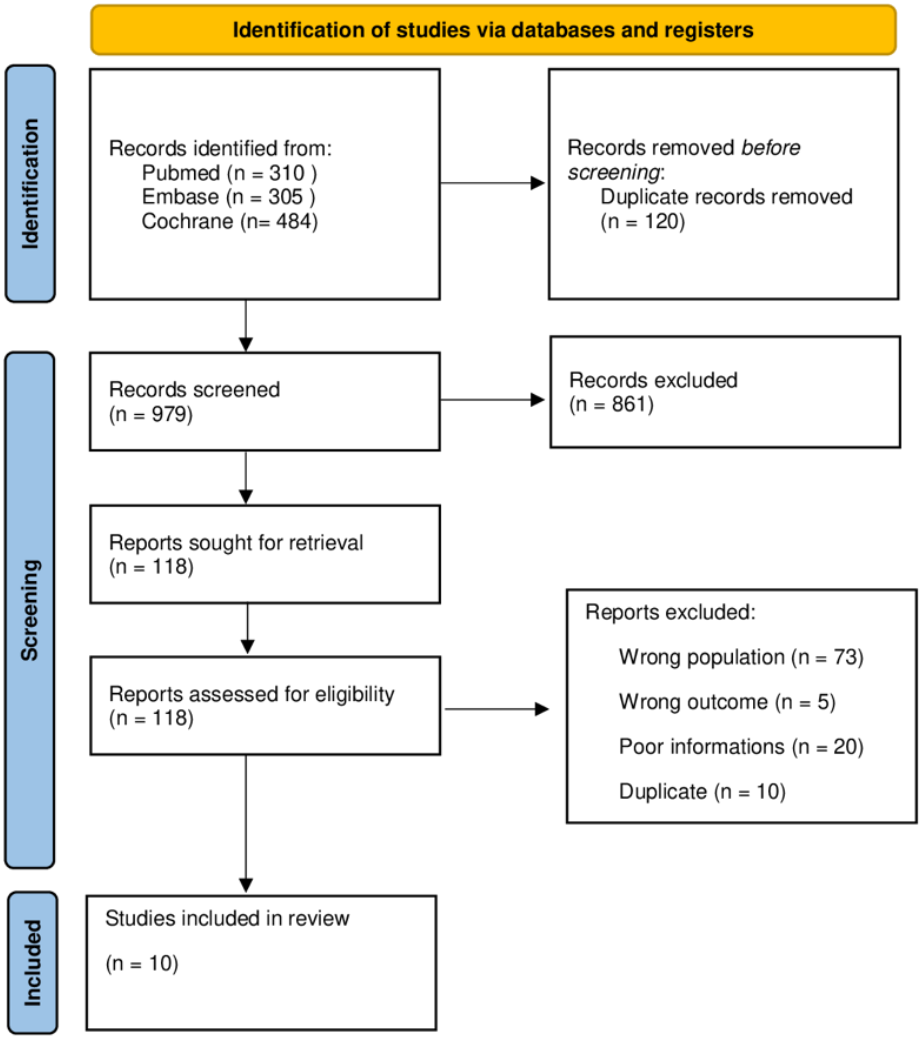
Supplementary table 11. Details of QUADAS- 2 results evaluating the global risk of bias of the selected studies on biomarkers

Study		Risk of bias			
First author, year	**DOI (or PMID if DOI not available)**	**Patient selection**	**Index test**	**Reference standard**	**Flow and timing**
Aljaberi N, 2020	https://doi.org/10.1186/s12969-020-0398-2	☹	☹	☹	☺
Chen PK, 2021 (Frontiers)	https://doi.org/10.3389/fimmu.2021.719544	☹	☹	☹	☹
Chen X, 2022 (Rheum Int)	https://doi.org/10.1007/s00296-021-04978-1	☹	☹	☹	☺
Colafrancesco S, 2012	https://doi:10.1155/2012/156890	☹	☹	☹	☹
Eraso R, 2021	https://doi.org/10.7705/biomedica.5849	☹	☹	☹	☹
Fautrel B 2001,	PMID: 11246670 J Rheumatol. 2001 Feb;28(2):322-9.	☹	☹	☹	☹
Frosch M 2009	https://doi:10.1002/15290131(200003)43:3<628::AID-ANR20>3.0.CO;2-X.	☹	☹	☺	☹
Ge S, 2021	https://doi.org/10.6061/clinics/2021/e2307	☹	☹	☹	☹
Guerber 2022	https://doi.org/10.3390/jcm11175012	☹	☺	☹	☹
Guo Q 2015	https://doi10.1007/s10067-015-3108-6	☹	☺	☺	☺
Ha YJ 2015	https://doi:10.3109/03009742.2015.1016103	☹	☹	☹	☹
Hu Q 2019	https://doi:10.3389/fimmu.2018.03099	☹	☹	☹	☹
Kim HA 2012	https://doi:10.3899/rheum.120079	☹	☹	☹	☹
Kirino Y, 2018	https://doi.org/10.1080/14397595.2017.1422231	☹	☹	☺	☹
Koga T 2020	https://doi.org/10.1186/s13075-020-02200-4	☹	☹	☹	☹
Kudela H 2019	https://doi.org/10.1186/s41927-019-0053-z	☹	☹	☹	☺
Liu JP 2019	PMID: 31814574 Neth J Med.2019 Oct;77(8):274-279.	☹	☹	☹	☹

Study		Risk of bias			
First author, year	**DOI (or PMID if DOI not available)**	**Patient selection**	**Index test**	**Reference standard**	**Flow and timing**
Liu X, 2020	https://doi:10.3389/fimmu.2020.560744	☹	☹	?	☺
Luo L 1992	https://doi.org/10.1590/1806-9282.20210649	☹	☹	☹	☹
Maruyama J, 2010	https://doi.org.10.1002/art.28471	☹	☹	☹	☹
Park C, 2022	https://doi:10.1093/rheumatology/keab729	☹	☺	☺	☹
Park HJ, 2014 (YMJ)	https://dx.doi.org/10.3349/ymj.2014.55.3.753	☹	☺	☹	☹
Park HJ 2014 ARD	https://doi:10.1136/annrheumdis-2014-eular.1411	☹	☹	☹	☺
Priori R, 2014	https://doi:10.3899/jrheum.130575	☹	☺	☺	☹
Sagy I, 2022	https://doi:10.1097/MD.0000000000030152	☹	☹	☹	☺
Seo JY, 2017	http://dx.doi.org/10.1097/MD.0000000000007546	☹	☺	☺	☹
Shiga T, 2021	https://doi.org/10.3389/fimmu.2021.750114	☹	☹	☹	☺
Sun Y, 2020	https://doi:10.3389/fimmu.2020.02112	☹	?	☺	☺
Tian R, 2021	https://doi:10.3389/fimmu.2021.654811	☹	☹	☹	☺
Wittkowski H, 2008	https://doi.org/10.1002/art.24137	☹	?	☺	☺
Xia Y, 2017	https://doi.org/10.1590/1414-431X20165958	?	?	☺	☺
Xu Z, 2022	https://doi.org/10.1186/s12865-022-00477-5	☹	☺	☺	☺
Zhang W, 2021	https://doi.org/10.1016/j.cyto.2021.155642	☹	☺	☹	☹

Supplementary material for SR3: Diagnostic Biomarkers for MAS

Supplementary figure 7. PRISMA flow chart of included studies in SR3 on MAS biomarkers



Supplementary table 12. Existing "classical" biomarkers for MAS

Biomarker	Outcome	Case (N)	Controls (N)	Cut-off	Se (%)	Sp (%)	AUC	First Author, year	Rob*
Ferritin	Diagnosis	AOSD-MAS (26)	AOSD (121)	1225 ng/ml	85.0	70.0	0.840	Di Benedetto, 2020	
Ferritin	Diagnosis	sJIA-MAS (262)	sJIA (262)	1045 mg/dl	84.0	66.0	0.810	Eloseily EMA, 2019	
			Infections (93)	396.6 mg/dl	92.0	95.0	0.970		
Ferritin	Diagnosis	sJIA-MAS (18)	Active sJIA (40)	>400 µg/l	100.0	76.0	0.920	Kostik MM, 2015	
Ferritin	Diagnosis	sJIA-MAS (23)	sJIA (65)	>731 ng/ml	100.0	88.0	0.955	Lee PY, 2020	
Ferritin	Diagnosis	AOSD-MAS (20)	AOSD (186)	> 3500 µg/ml	85.0	62.0	NA	Javaux C, 2021	
Ferritin	Diagnosis	sJIA-MAS (53)	sJIA (53)	12217.5 µg/l	80.0	88.0	0.871	Zou LX, 2020	
Ferritin/ESR	Diagnosis	sJIA-MAS (262)	sJIA (262)	21.5	82.0	78.0	0.870	Eloseily EMA, 2019	
			Infections (93)	11.3	91.0	93.0	0.950		
Ferritin/ESR	Diagnosis	sJIA-MAS (53)	sJIA (53)	267.5	91.0	87.0	0.878	Zou LX, 2020	
Glycosylated Ferritin	Diagnosis	AOSD-MAS (20)	AOSD (186)	<21 %	100.0	43.0	NA	Javaux C, 2021	
Albumin	Diagnosis	sJIA-MAS (18)	Active sJIA (40)	≤ 2.9 g/dl	100.0	96.0	0.980	Kostik MM, 2015	
AST	Diagnosis	sJIA-MAS (18)	Active sJIA (40)	>59.7 U/L	82.0	92.0	0.880	Kostik MM, 2015	
Soluble CD25	Diagnosis	sJIA-MAS (27)	FHL (90), VA-HLH (42)	≤7900 U/mL	79.0	86.0	0.790	Lehmberg, 2013	
CRP	Mortality	AOSD-MAS (26)	AOSD (121)	68.7 mg/L	80.0	65.0	0.735	Di Benedetto, 2020	
CRP	Diagnosis	sJIA-MAS (27)	FHL (90), VA-HLH (42)	≥90 mg/L	74.0	89.0	0.870	Lehmberg, 2013	
Fibrinogen	Diagnosis	sJIA-MAS (18)	Active sJIA (40)	≤ 1.8 g/l	64.0	100.0	0.880	Kostik MM, 2015	
LDH	Diagnosis	sJIA-MAS (18)	Active sJIA (40)	>882 U/L	75.0	100.0	0.910	Kostik MM, 2015	
Neutrophil	Diagnosis	sJIA-MAS (27)	FHL (90), VA-HLH (42)	≥1.8 x10^9/L	85.0	83.0	0.890	Lehmberg, 2013	
PLT	Diagnosis	sJIA-MAS (18)	Active sJIA (40)	≤211x10^9/l	89.0	100.0	0.980	Kostik MM, 2015	
WBC	Diagnosis	sJIA-MAS (18)	Active sJIA (40)	<9.9x10^9/l	83.0	90.0	0.920	Kostik MM, 2015	

*Risk of Bias: green = low, yellow= intermediate, red= high.

AOSD: adult onset Still's disease; AST: aspartate aminotransferase; AUC: area under the curve; CRP: C reactive protein; ESR: erythrocyte sedimentation rate; FHL: familiar hemophagocytic lymphohistiocytosis; LDH: lactic dehydrogenase; MAS: macrophage activation syndrome; NA: not available; PLT: platelet count; sJIA: systemic juvenile idiopathic arthritis; Se, sensitivity; Sp, specificity; VA-HLH: virus-associated hemophagocytic lymphohistiocytosis; WBC: white blood cells. The reference list (in alphabetic order) is as follows:

-Di Benedetto, Cipriani P, Iacono D, *et al*. Ferritin and C-Reactive Protein are predictive biomarkers of mortality and macrophage activation syndrome in adult-onset Still's disease. Analysis of the multicentre Gruppo Italiano di Ricerca in Reumatologia Clinica e Sperimentale (GIRRCS) cohort. *PloS One* 2020;15(7):e0235326.

-Eloisely EMA, Minoia F, Crayne CB, *et al.* Ferritin to Erythrocyte Sedimentation Rate Ratio: Simple Measure to Identify Macrophage Activation Syndrome in Systemic Juvenile Idiopathic Arthritis. *ACR Open Rheumatol* 2019;1(6):345-349.

-Javaux C, El-Jammal T, Neau PA*, et al.* Detection and Prediction of Macrophage Activation Syndrome in Still's Disease. *J Clin Med* 2021;11(1):206.

-Kostik MM, Dubko MF, Masalova VV, *et al*. Identification of the best cutoff points and clinical signs specific for early recognition of macrophage activation syndrome in active systemic juvenile idiopathic arthritis. *Semin Arthritis Rheum* 2015;44(4):417-22.

-Lee PY, Schulert GS, Canna SW *et al*. Adenosine deaminase 2 as biomarker of macrophage activation syndrome in systemic juvenile idiopathic arthritis. *Ann Rheum Dis* 2020;79(2):225-231.

-Lehmberg K, Pink I, Eulenburg C, *et al.* Differentiating macrophage activation syndrome in systemic juvenile idiopathic arthritis from other forms of hemophagocytic lymphohistiocytosis. *J Pediatr 2013*;162(6):1245-51.

-Zou LX, Zhu Y, Sun L, *et al*. Clinical and laboratory features, treatment, and outcomes of macrophage activation syndrome in 80 children: a multi-center study in China. *World J Pediatr* 2020;16(1):89-98.