Table 2. Study characteristics	and outcomes for the outcom	ne measure immunogenicity
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First author, year	Vaccine	Patients	Medication used <sup>a</sup>	Follow-up	Result	Effect of medication on results
DPT						
Brunner, 2020	DT	IG: n=29 JIA patients CG: n=17 JIA patients not vaccinated	29 ABT, 22 MTX, 3 LD-GC	24 months	100% SP tetanus, 90% SP diphtheria 2 m post vaccine.	All patients had protective antibody levels to tetanus after ≥2 months of abatacept treatment and 26/29 (89.7%) patients had protective antibody levels to diphtheria.
Ingelman- Sundberg, 2016 <sup>b</sup>	DTP	IG: n=50 in total, 46 JIA patients CG: n=31 HC	10 NSAID, 8 MTX, 32 MTX+TNFi	Not applicable	lgG-TT reduced in MTX+TNFi group.	Patients treated with any DMARD had lower tetanus serum IgG compared to healthy controls and NSAID-treated patients.
Heijstek, 2012 <sup>b</sup>	DT	IG: n=400 JIA patients CG: n=2176 HC	93 MTX, 8 TNFi, 28 GC 10 mg/day	Not applicable	Reduced SP and GMT for tetanus.	Methotrexate use and glucocorticosteroid use did not have any effect on pathogen- specific GMT or seroprotection rates.
HPV						
Heijstek, 2014	HPV- b(Cervarix vaccine)	IG: n=68 JIA patients CG: n=55 HC	24 MTX, 9 TNFi, 6 other DMARD	12 months	Equal SC and GMT in JIA and HC.	Methotrexate did not affect HPV16 or HPV18 antibodies. No difference in antibody concentrations in patient with anti- TNF, but the sample size was too small to draw definite conclusions.
Esposito, 2014	HPV-b (Cervarix vaccine)	IG: n=21 JIA patients CG: n=55 HC	10 NSAID, 5 MTX, 6 TNFi	7 months	100% SC. Reduced titers 1 month post 3th vaccine in JIA vs HC. No effect of medication.	No effect on immune response of NSAIDs, methotrexate, and etanercept.
HBV/HAV	1		1	1	1	
Çakmak, 2022	Hepatitis B	IG: n=262 JIA patients CG: n=274 HC	Not reported	Not applicable	Anti-Hbs antibody: JIA patients: 59.1% Control: 72.9%, p=0.002. HbsAG positivity: N=0 in both groups	Four patients were negative for anti-Hbs and were receiving DMARDs (methotrexate=1, sulfasalazine=1) and biological agents (etanercept=1, adalimumab=1)

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Image: Control: 43.3 (range 0.1000) IU/L, p=0.01Control: 43.3 (range 0.1000) IU/L, p=0.01Anti-nuclear antibody positivity IA patients: 27.1%. Among these, anti-Hos antibody seropositivity rate while this rate wass 56.2% (n=104) In the remaining ANA negative cases (n=185) (p=0.04).Erguven, 2010Hepatitis A patients CG: n=67 HC4 anti-TWF, 5 NSADS, 29 MTX, 12 predinsione2 months second positivity rate second (100%)Four patients (3.5%) had negative titers, had negative titers, these were all male patients (4.3 %).MenCIG: n=47 JIA patients CG: n=67 HC4 anti-TWF, 5 NSADS, 29 MTX, 12 predinsione2 months second predinsionePositive anti-HAV patients (4.3 %).MenCIG: n=127 JIA patients Conjugate (conjugate (conjugate Conjugate Conjugate (conjugate Conjugate<						IU/L	
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CG: n=67 HCMTX, 12 prednisolone, 19 salazopyrine, 11 MTX- prednisolonesecond doseJJA: 43 (91.5%) Control: 67 (100%)these were all male patients with active systemic JIA and using anti-TNF.MenCIG: n=127 JIA patients (NeisVac-C) vaccineIG: n=127 JIA patients CG: n=1527 HC42 MTX, 66 pre-MTX, 7 NA bDMARD, 53 pre-, 4 GC, 10 pre-GCNot applicableEqual SP 4 years post vaccine JIA ws HC. MenC-lgG decrease over time.Starting methotrexate treatment did not affect the decline of MenC-specific IgG concentrations. However, starting biological treatment induced a trend towards accelerated decay rate in 92.6% of patients.Additional methotrexate second towards accelerated decay in MenC- specific antibodies, with a faster predicted decay rate in 92.6% of patients.PCV/PPVPV23IG: n=17 JIA patients using wTXIG: MTX HD 2 WTX12 monthsEqual SC at 2 (53 vs. 30%) and 12 months (36 vs. 40%) in JIA with and without TNFi.Adequate vaccine response was similar between patients with and without TNFi.InfluenzaH1N1IG: n=237 in total, 93 JIA patients CG: n=91 HC90 GC, MTX FL, 43 AZA, 23 CYC, 13 MMFF,21 daysSubgroup analysis: N=93 Before Before immunization %Not reported	2010		patients	NSAIDs, 29	after	IgG (n (%)):	had negative titers,
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PCV/PPVAikawa, 2015PPV23IG: n=17 JIA patients pre- etanercept CG: n=10 JIA MTXIG: MTX HD 2 weeks before ETA CG: 10 LD MTX12 months response vas similar between patients 40%) in JIA with and without TNFi.Adequate vaccine response was similar between patients with anti-TNF and without anti-TNF.Aikawa, 2015PPV23IG: n=237 in total, 93 JIA patients90 GC, MTX CY, 13 MMF, CY, 13 MMF,21 daysSubgroup analysis: N=93 BeforeNot reported	MenC Stoof, 2014	MenC conjugate (NeisVac-C) vaccine	IG: n=127 JIA patients CG: n=1527 HC	11 MTX- prednisolone 42 MTX, 66 pre-MTX, 7 NA bDMARD, 53 pre-, 4 GC, 10 pre-GC	Not applicable	Equal SP 4 years post vaccine JIA vs HC. MenC-IgG decrease over time.	Starting methotrexate treatment did not affect the decline of MenC-specific IgG concentrations. However, starting biological treatment induced a trend towards accelerated decay in MenC- specific antibodies,
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etanercept CG: n=10 JIA patients using MTXETA CG: 10 LD MTXmonths (36 vs. 40%) in JIA with and without TNFi.between patients with anti-TNF and without anti-TNF.InfluenzaIG: n=237 in total, 93 JIA patients90 GC, MTX 74, 43 AZA, 23 patients21 days Before immunization. %Subgroup analysis: N=93 BeforeNot reported	MenC Stoof, 2014 PCV/PPV Aikawa,	MenC conjugate (NeisVac-C) vaccine PPV23	IG: n=127 JIA patients CG: n=1527 HC IG: n=17 JIA	11 MTX- prednisolone 42 MTX, 66 pre-MTX, 7 NA bDMARD, 53 pre-, 4 GC, 10 pre-GC IG: MTX HD 2	Not applicable 12 months	Equal SP 4 years post vaccine JIA vs HC. MenC-IgG decrease over time.	Starting methotrexate treatment did not affect the decline of MenC-specific IgG concentrations. However, starting biological treatment induced a trend towards accelerated decay in MenC- specific antibodies, with a faster predicted decay rate in 92.6% of patients.
CG: n=10 JIA patients using MTXCG: 10 LD MTX40%) in JIA with and without TNFi.with anti-TNF and without anti-TNF.InfluenzaAikawa, 2012H1N1IG: n=237 in total, 93 JIA patients90 GC, MTX 74, 43 AZA, 23 patients21 daysSubgroup analysis: N=93 Before immunization. %Not reported	MenC Stoof, 2014 PCV/PPV Aikawa, 2015	MenC conjugate (NeisVac-C) vaccine PPV23	IG: n=127 JIA patients CG: n=1527 HC IG: n=17 JIA patients pre-	11 MTX- prednisolone 42 MTX, 66 pre-MTX, 7 NA bDMARD, 53 pre-, 4 GC, 10 pre-GC IG: MTX HD 2 weeks before	Not applicable 12 months	Equal SP 4 years post vaccine JIA vs HC. MenC-IgG decrease over time. Equal SC at 2 (53 vs. 30%) and 12	Starting methotrexate treatment did not affect the decline of MenC-specific IgG concentrations. However, starting biological treatment induced a trend towards accelerated decay in MenC- specific antibodies, with a faster predicted decay rate in 92.6% of patients.
patients using MTXMTXand without INFi.without anti-TNF.InfluenzaAikawa, 2012H1N1IG: n=237 in total, 93 JIA90 GC, MTX 74, 43 AZA, 2321 daysSubgroup analysis: N=93Not reported analysis: N=93patientsCYC, 13 MMF, CG; n=91 HC6 LEF. 3 Cyimmunization. %	MenC Stoof, 2014 PCV/PPV Aikawa, 2015	MenC conjugate (NeisVac-C) vaccine	IG: n=127 JIA patients CG: n=1527 HC IG: n=17 JIA patients pre- etanercept	11 MTX- prednisolone 42 MTX, 66 pre-MTX, 7 NA bDMARD, 53 pre-, 4 GC, 10 pre-GC IG: MTX HD 2 weeks before ETA	Not applicable 12 months	Equal SP 4 years post vaccine JIA vs HC. MenC-IgG decrease over time. Equal SC at 2 (53 vs. 30%) and 12 months (36 vs.	Starting methotrexate treatment did not affect the decline of MenC-specific IgG concentrations. However, starting biological treatment induced a trend towards accelerated decay in MenC- specific antibodies, with a faster predicted decay rate in 92.6% of patients.
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Aikawa, H1N1 IG: n=237 in 90 GC, MTX 21 days Subgroup Not reported   2012 total, 93 JIA 74, 43 AZA, 23 analysis: N=93 patients CYC, 13 MMF, Before   CG: n=91 HC 6 LEF. 3 Cy immunization. %	MenC Stoof, 2014 PCV/PPV Aikawa, 2015	MenC conjugate (NeisVac-C) vaccine	IG: n=127 JIA patients CG: n=1527 HC IG: n=17 JIA patients pre- etanercept CG: n=10 JIA patients using	11 MTX- prednisolone 42 MTX, 66 pre-MTX, 7 NA bDMARD, 53 pre-, 4 GC, 10 pre-GC IG: mTX HD 2 weeks before ETA CG: 10 LD MTX	Not applicable 12 months	Equal SP 4 years post vaccine JIA vs HC. MenC-IgG decrease over time. Equal SC at 2 (53 vs. 30%) and 12 months (36 vs. 40%) in JIA with and without TNFi.	Starting methotrexate treatment did not affect the decline of MenC-specific IgG concentrations. However, starting biological treatment induced a trend towards accelerated decay in MenC- specific antibodies, with a faster predicted decay rate in 92.6% of patients. Adequate vaccine response was similar between patients with anti-TNF and without anti-TNF.
2012 Interported I	MenC Stoof, 2014 PCV/PPV Aikawa, 2015	MenC conjugate (NeisVac-C) vaccine PPV23	IG: n=127 JIA patients CG: n=1527 HC IG: n=17 JIA patients pre- etanercept CG: n=10 JIA patients using MTX	11 MTX- prednisolone 42 MTX, 66 pre-MTX, 7 NA bDMARD, 53 pre-, 4 GC, 10 pre-GC IG: MTX HD 2 weeks before ETA CG: 10 LD MTX	Not applicable 12 months	Equal SP 4 years post vaccine JIA vs HC. MenC-IgG decrease over time. Equal SC at 2 (53 vs. 30%) and 12 months (36 vs. 40%) in JIA with and without TNFi.	Starting methotrexate treatment did not affect the decline of MenC-specific IgG concentrations. However, starting biological treatment induced a trend towards accelerated decay in MenC- specific antibodies, with a faster predicted decay rate in 92.6% of patients. Adequate vaccine response was similar between patients with anti-TNF and without anti-TNF.
patients CYC, 13 MMF, Before CG: n=91 HC 6 LEF. 3 Cv immunization. %	MenC Stoof, 2014 PCV/PPV Aikawa, 2015 Influenza	MenC conjugate (NeisVac-C) vaccine PPV23	IG: n=127 JIA patients CG: n=1527 HC IG: n=17 JIA patients pre- etanercept CG: n=10 JIA patients using MTX	11 MTX- prednisolone 42 MTX, 66 pre-MTX, 7 NA bDMARD, 53 pre-, 4 GC, 10 pre-GC IG: MTX HD 2 weeks before ETA CG: 10 LD MTX	Not applicable 12 months	Equal SP 4 years post vaccine JIA vs HC. MenC-IgG decrease over time. Equal SC at 2 (53 vs. 30%) and 12 months (36 vs. 40%) in JIA with and without TNFi.	Starting methotrexate treatment did not affect the decline of MenC-specific IgG concentrations. However, starting biological treatment induced a trend towards accelerated decay in MenC- specific antibodies, with a faster predicted decay rate in 92.6% of patients. Adequate vaccine response was similar between patients with anti-TNF and without anti-TNF.
CG: n=91 HC 6 LEF. 3 Cv immunization. %	MenC Stoof, 2014 PCV/PPV Aikawa, 2015 Influenza Aikawa, 2012	MenC conjugate (NeisVac-C) vaccine PPV23	IG: n=127 JIA patients CG: n=1527 HC IG: n=17 JIA patients pre- etanercept CG: n=10 JIA patients using MTX	11 MTX- prednisolone 42 MTX, 66 pre-MTX, 7 NA bDMARD, 53 pre-, 4 GC, 10 pre-GC IG: mTX HD 2 weeks before ETA CG: 10 LD MTX 90 GC, MTX 74, 43 A7A, 22	Not applicable 12 months 21 days	Equal SP 4 years post vaccine JIA vs HC. MenC-IgG decrease over time. Equal SC at 2 (53 vs. 30%) and 12 months (36 vs. 40%) in JIA with and without TNFi.	Starting methotrexate treatment did not affect the decline of MenC-specific IgG concentrations. However, starting biological treatment induced a trend towards accelerated decay in MenC- specific antibodies, with a faster predicted decay rate in 92.6% of patients. Adequate vaccine response was similar between patients with anti-TNF and without anti-TNF.
	MenC Stoof, 2014 PCV/PPV Aikawa, 2015 Influenza Aikawa, 2012	MenC conjugate (NeisVac-C) vaccine PPV23	IG: n=127 JIA patients CG: n=1527 HC IG: n=17 JIA patients pre- etanercept CG: n=10 JIA patients using MTX IG: n=237 in total, 93 JIA patients	11 MTX- prednisolone 42 MTX, 66 pre-MTX, 7 NA bDMARD, 53 pre-, 4 GC, 10 pre-GC IG: mTX HD 2 weeks before ETA CG: 10 LD MTX 90 GC, MTX 74, 43 AZA, 23 CYC. 13 MMF	Not applicable 12 months 21 days	Equal SP 4 years post vaccine JIA vs HC. MenC-IgG decrease over time. Equal SC at 2 (53 vs. 30%) and 12 months (36 vs. 40%) in JIA with and without TNFi. Subgroup analysis: N=93 Before	Starting methotrexate treatment did not affect the decline of MenC-specific IgG concentrations. However, starting biological treatment induced a trend towards accelerated decay in MenC- specific antibodies, with a faster predicted decay rate in 92.6% of patients. Adequate vaccine response was similar between patients with anti-TNF and without anti-TNF.

Aikawa, 2013	H1N1	IG: n=95 JIA patients CG: n=91 HC	16 TNFi, 63 DMARD(s)	3 weeks	(95%CI) 20.4 (12.2–28.6) After immunization, % (95%CI) 88.2 (81.6–94.8) Seroconversation rate, % (95%CI) 82.8 (75.1–90.5) (p<0.05) Equal SP and GMT. Reduced SC in pts, irresp.of TNF/MTX	No difference in immunogenicity between patients with and without immunosuppressive drugs, and with and without MTX and with and without TNF blockers.
Carvalho, 2013	Influenza (H1N1, H3N2, B/Florida)	IG: n=44 JIA patients CG: n=10 healthy controls	IS, DMARDs, or anti-TNFα ranging from 55.7% to 70%	180 days	Equal SP & SC in JIA and HC. TNFi lower SP and SC for H1N1 but SP for h3N2 &B/Florida was normal (N = not reported).	Patients on anti- TNF $\alpha$ drugs presented lower seroconversion (p = 0.03) and seroprotection (60%) responses to H1N1 strain, but the seroprotection above the cut-off levels to the other strains: H3N2 (100%) and B/Florida (80%).
Toplak, 2012	Influenza (H1N1, H3N2, Influenza B)	IG: n=31 JIA patients CG: n=14 HC and n=31 not vaccinated JIA patients	18 NSAID, 2 DMARD, 7 DMARD + GC, 4 TNF	6 months	Equal SP pts and HC	GMTs for all vaccine viruses were significantly elevated 1 months after vaccination in patients using DMARDs. The group of 4 children with anti-TNF treatment did not respond significantly to any of the vaccine viruses. After 6 months, all 4 children with anti- TNF had protective titers but did not respond significantly as a group. Compared to the GMTs before vaccination, the values after 6 months were still significantly

						elevated for the Influenza B vaccine virus in both study groups including children treated with DMARDs, but not in a subgroup of 4 children also receiving anti-TNF-α therapy.
Woerner, 2011	Influenza (H1N1, H3N2, H1N1 MDCK cell adapted, H3N2 MDCK adapted, and influenza B MDCK adapted)	IG: n=34 in total, of which n=25 JIA patients CG: n=16 HC	18 MTX, 10 TNFi, 8 MTX+TNFi	4-8 weeks after single dose or after the second of two doses.	Equal SP pts vs. HC, reduced GMT.	Subgroup analysis for immunosuppressive medication (MTX vs. TNF $\alpha$ inhibitors vs. MTX and TNF $\alpha$ inhibitors) showed no significant differences between the treatment groups in seroprotection, seroconversion or post-vaccination GMTs. Treatment with TNF $\alpha$ inhibitors showed a trend toward a lower relative change between pre- vaccination and post-vaccination titers in comparison to treatment with MTX (p 0.06 resp. 0.66).
Dell'Era, 2012	Influenza (M59 adjuvanted, with H1N1, H3N2, and influenza B)	IG: n=60 JIA patients CG: n=30 HC	30 DMARD vs. 30 aTNF (Etanercept)	3 months	Equal SP & SC in JIA and HC. TNFi lower H1N1-GMT & more rapid decline in H3N2- GMT	All, except in one, 100% seroconversation and seroprotection in JIA patients treated with etanercept and DMARDs after follow-up. There was no difference in the B antigen immunogenicity endpoints between the DMARD-treated JIA patients and HC
Camacho- Lovillo, 2017	Influenza (H1N1, H3N2, B)	IG: n=25 JIA patients CG: n=6 healthy siblings	15 anti-TNFα (11 etanercept and 4 adalimumab),	1 year	SP after 4–8 weeks: 97.8% H1N1, 95.6% H3N2, 91.1% B.	No differences were observed in the short-time and long- time (after 1 year) antibody response

			4 anti-IL-1R			and postvaccination
			(anakinra), 6			seroprotection,
			anti-IL-6R			GMT, and
			(tocilizumab)			seroconversion rates
			(,			to vaccination based
						on treatment
						No difference in
						seronrotection or
						antibody titors in
						nationts with
						biological treatment
						systemic steroids
						(n=2), compared
						with patients with
						biological treatment
						with no steroids
MMR (live-a	attenuated vaco	cine)				
Heijstek,	MMR	IG: n=68	60 MTX, 15	12 months	SP and GMT	Revaccinated
2013	(MMR-NVI	vaccinated	biologicals, 3		higher in vacc. vs.	patients taking
	and M-M-	JIA patients	GC		controls	biologics at the time
	RVAXPRO)	CG: n=69				of revaccination
		unvaccinated				were seroprotected.
		JIA patients				
						One patient was
						taking
						methotrexate. 9.3
						mg/m2 per week, at
						the time of
						vaccination and
						showed a small
						increase in mumns-
						spacific antibadias
						specific antiboules
						at 3 months, but
						antibodies dropped
						below
						seroprotection
						levels at 12 months.
						Another patient
						using methotrexate
						was started just
						after vaccination,
						followed by
						etanercept at 9
						months. This patient
						was seronegative for
						measles, mumps,
						and rubella at
						baseline and failed
						to produce a
						serologic response
						to mumps. whereas
						measles-specific
						antibodies increased
						17-fold and rubella-
						specific antihodies
						179-fold
Hojistok	MMR	IG: n=400 IIA	03 MTY 0	Not	Reduced SP and	Methotrevato uso
2012b		natients		annlicable	GMT for mumps	and
2012-		$CG \cdot p = 2176$	10 mg/day	applicable	rubella but not	anu
			TO IIIR/ UAY		monocles	giucocor ticosteroiu
		пс			measies.	use did not nave any

						effect on pathogen- specific GMT or
						seroprotection.
Ingelman-	MMR	IG: n=50 in	10 NSAID, 8	Not	Equal IgG titers	No difference in
Sundberg,		total, 46 JIA	MTX, 32	applicable	MV and RV, IgG-	measles and rubella
2016 <sup>b</sup>		patients	MTX+TNFi		TT reduced in	titers rates between
		CG: n=31 HC			MTX+iTNF group.	patients using
					Vaccspec. mem.	DMARDs and
					B cells preserved	patients using
					in patients with	NSAIDs and HC.
					booster	
VZV (live-at	tenuated vaccir	ne)				
Groot,	VZV (Oka	IG: n=49 in	49 MTX, 16	4-6 weeks	Equal GMT in pts	Type of
2017	strain,	total, 39 JIA	GCs, 3	after	& HC, more VZV-	immunosuppressive
	Varilrix as	patients	biologics	vaccination	spec. T cells.	drug did not have a
	second	CG: n=18 HC				significant effect on
	dose)					humoral response (p
						= 0.203) but patients
						who used biologics
						at time of
						vaccination of the
						first vaccination (n =
						<ol><li>did not show an</li></ol>
						increase in antibody
						concentrations after
						vaccination. Of the
						two patients who
						used biologics and
						received two
						vaccines, one (using
						etanercept)
						responded to the
						second vaccine and
						one (using
						abatacept) did not.

AB, antibody; ABT, abatacept; ADA, adalimumab; AE, ad verse event;ANR, Anakinra; AZA, azathioprine; bDMARD, biological disease modifying anti-rheumatic drugs;CAM, canakinumab; CG, control group; Cy, cyclophosphamide; CYC, cyclosporine; DTP, diphtheria tetanus pertussis; ETN, etanercept; GC, glucocorticosteroids; GMT, geometric mean titer; HAV, hepatitis A virus; HBV, hepatitis B virus; HC, healthy controls; IBD, inflammatory bowel disease; IFX, infliximab; IG, intervention group; IgG, immunoglobulin G; HCQ, hydroxychloroquine; IRD, immune rheumatic diseases; IS, immunosuppression; IVIG, intravenous immunoglobulines; JIA, juvenile idiopathic arthritis; LEF, leflunomide; MMF, mycophenolic acid; MMR(/V), measles mumps rubella (/varicella); 6-MP, 6-mercaptopurine; MTX, methotrexate; MV, measles vaccine; NSAID, non-steroid anti-inflammatory drug; pts, patients; RAI, relative avidity index; RD, rheumatic diseases; TBE, tick-borne-encephalitis; TBEV, tick-borne-encephalitis virus; TCZ, tocilizumab; Thiopur, thiopurine; TNFi, tumor necrosis factor inhibitor; TT, tetanus toxoid; vacc, vaccine; VZV, varicella zoster virus

<sup>a</sup>Medication used in the intervention group, unless reported different. Numbers represent amount of patients using that medication.

<sup>b</sup> Studies are reported twice due to use of two different vaccines