Supplementary Table I Grading of Evidence [i]

Grade	*Quality of evidence*
A	Well designed and controlled studies; meta-analysis on applicable population; true effect lies close to the estimate of the effect
B	Studies with minor limitations; consistent findings from multiple observational studies; true effect is likely to be close to estimate of the effect, but there is a possibility that it is substantially different
C	Single, few or multiple studies with inconsistent findings or major limitations; confidence in the effect estimate is limited, the true effect may be substantially different from estimate of the effect
D	Expert opinion, case reports; very little confidence in effect estimate, true effect likely to be substantially different from the estimate of effect
X	Situations where validating studies cannot be performed, and benefit or harm clearly predominates
Level	*Strength of recommendation*
1	"We recommend": Most patients should receive the recommended course of action
2	"We suggest": Different choices will be appropriate for different patients

Supplementary Table II Recent Randomized Controlled Trials, with Low Risk of Bias, for Initial Episode of Nephrotic Syndrome

Author, yr	*Type, N*	*Predniso(lo)ne (Intervention)*	*Predniso(lo)ne (Control)*	*Follow up, yr*	*Outcomes at 1-2 yr*			
					% relapsing; time to relapse; HR (95% CI)	*% frequent relapsers; HR (95% CI)*	*Relapse rate; RRR (95% CI)*	*Cumulative prednisone, g/m²/yr; MD (95% CI)*
Teeninga 2013 [ii]	Placebo controlled, randomized N=150	60 mg/m² D till remission; 50 mg/m² D for 6-wk; 40 and 20 mg/m² AD for 4-wk each; 10 mg/m² AD for 10-wk [3.4 g/m² in 24-wk]	60 mg/m² D for 6-wk; 40 mg/m² AD for 6-wk; placebo for 12-wk [3.4 g/m² in 24-wk]	≥1.5	80% *vs*. 77%; 8 *vs*. 6 months; NA	59% *vs*. 50%; 1.1 (0.7, 1.8)	1.0 *vs*. 0.6 per yr; 1.2 (0.9, 1.7)	Not available
Sinha 2014 [iii]	Placebo controlled, randomized N=181	2 mg/kg D for 6-wk; 1.5 mg/kg AD for 6-wk; 1, 0.75 & 0.5 mg/kg AD each for 4-wk [3.5 g/m² in 24-wk]	2 mg/kg D for 6-wk; 1.5 mg/kg AD for 6-wk; placebo for 12-wk [2.8 g/m² in 12-wk]	1	53% *vs*. 63%; 9 *vs*. 7 months; 0.57 (0.36, 1.07)	38% *vs*. 40% 1.0 (0.6, 1.7)	1.3 *vs*.1.5 per yr; 0.7 (0.5, 1.1)	2.3 *vs.* 1.9; 0.45 (-0.12, 1.02)
Yoshikawa 2014 [iv]	Open label, randomized N=255	60 mg/m² D for 4-wk; then 60, 45, 30, 15, 7.5 mg/m² AD for 4-wk each [3.9 g/m² in 24-wk]	60 mg/m² D for 4-wk; 40 mg/m² AD for 4-wk [2.2 g/m² in 8-wk]	2	~70% *vs.* 63%; 8 months each; 1.03 (0.76, 1.39)	~50% *vs*. 45%; 1.16 (0.86, 1.56)	1.3 per person-yr each; 1.1 (0.8, 1.4)	6.5 *vs.* 4.6 in 2-yr; *P*<0.001
Webb 2019 [v]	Placebo controlled, randomized N=237	60 mg/m² D for 4-wk; 60, 50, 40, 30, 20, 10 mg/m² AD, 2-wk each [3.2 g/m² in 16-wk]	60 mg/m² D for 4-wk; 40 mg/m² AD 4-wk; placebo 8-wk [2.2 g/m² in 8-wk]	2	80% *vs*. 81%; ~4.5 *vs*. 3.5 months; 0.87 (0.65, 1.17)	50% *vs*. 53%; 1.04 (0.81, 1.35)	3.6 *vs.* 4.0 at 2-yr; 1.1 (0.9, 1.4)	5.5 *vs.* 6.7 at 2-yr; 1.2 (-0.1, 2.5; *P*=0.07)
Sinha 2019 [vi]	Open label, randomized N=160; <4 yr	60 mg/m² D for 6-wk; 40 mg/m² AD 6-wk; 30, 20, 10 mg/m² AD, 4-wk each [4.6 g/m²]	60 mg/m² D for 6-wk; 40 mg/m² AD for 6-wk [3.4 g/m² in 12-wk]	2	Proportions with relapse, other outcomes; results awaited CTRI/2015/06/005939; NCT03141970			
Xu 2020	Placebo controlled, randomized N=154; 1-6 yr	Daily for 6-wk; AD for 6-wk; taper for 12-wk	Daily for 6-wk; AD for 6-wk; placebo for 12-wk	2	Proportions with frequent relapses, other outcomes; results awaited NCT04536181			

AD alternate days; CI confidence interval; D daily; HR hazards ratio; MD mean difference; RRR relative relapse rate; wk weeks; ^rates adjusted for stratifying variables, where reported

Supplementary Table III Studies on Predniso(lo)ne Therapy of Infrequent Relapses

Author, yr	*Type*	*N*	*Prednisone (Intervention)*	*Prednisone (Control)*	*Follow up, months*	*Time to remission; MD (95% CI)*	*% Frequent relapses*	*Cumulative prednisone*
Raja, 2017 [vii]	Retrospective	50	1 mg/kg/d until remission (minimum 7 d), tapered <1-mo	NA	6	<7 days in 70%; 7-10 days in 7%	NA; 0.9±0.8 relapses in 6-mo	0.75±0.25 mg/kg
Fujinaga, 2018 [viii]	Retrospective	49	60 mg/m^2 until remission; tapered AD <6-mo	Comparison: ≤1.8, 1.8-2 and >2 mg/kg/d	12	7, 7.5 & 7 days	39%, 43%, & 55%	NA
Kainth, 2020 [ix]	Open label, randomized	114	60 mg/m^2/d until remission; 40 mg/m^2 AD for 2-wk	60 mg/m^2/d until remission; 40 mg/m^2 AD for 2-wk	12	Not available	23% *vs*. 22%; RD -1 (-17, 14); HR 1.0 (0.8, 1.2)	1.2 (0.3-1.8) *vs*. 1.8 (1.2-2.4) g/m^2***
Borovitz, 2019 [x]	Open label, not randomized	30	1.5 mg/kg/d (A); 1 mg/kg/d (B) until remission; taper 8-10 wk	2 mg/kg/d until remission; tapered 10-12 wk (C)	6	10±5 (A) & 9±3 (B) *vs*. 7±1 days (C)*	NA	43±26 (A), 25±7 (B) *vs*. 46±3 mg/kg*
Sheikh, 2019 [xi]	Open label, randomized	60	1 mg/kg/d until remission; 1.5 mg/kg AD for 4-wk	2 mg/kg/d until remission; 1.5 mg/kg AD for 4-wk	12	9±2 *vs*. 9±2 days; 0.4 (0.7, 1.6) days	NA	12.5 (9-18) *vs.* 17 (14-21) mg/kg**
Kansal, 2019 [xii]	Open label, randomized	40	2 mg/kg/d until remission; 1 mg/kg AD for 4-wk	2 mg/kg/d until remission; 1.5 mg/kg AD for 4-wk	3	Not available	Relapse at 3 months: HR 1.1 (0.4, 3.2)	NA
Raman, 2017 [xiii]	Open label, randomized, equivalence	52[#]	60 mg/m^2/d until remission; 40 mg/m^2 AD for 4-wk	2 mg/kg/d until remission; 1.5 mg/kg AD for 4-wk	6	6.5 *vs.* 6 days	Similar relapse rate	Similar cumulative prednisolone
PROPINE, [xiv]	Open label, randomized, superiority	78	60 mg/m^2/d until remission; 40 mg/m^2 AD for 36 days	60 mg/m^2/d until remission; 40 mg/m^2 AD for 72 days	6	5 (4-7) *vs*. 6 (5-8) days	Not reported; any relapse: 42% *vs*. 58%	1.29 (1.16-1.64) *vs*. 1.33 (127-1.51) g/m^2
Schijvens, 2018 [xv]	Placebo controlled, randomized	144	60 mg/m^2/d until remission; 40 mg/m^2 AD for 2-wk; placebo at 40 mg/m^2 AD for 4-wk	60 mg/m^2/d until remission; 40 mg/m^2 AD for 6-wk	24	Time to first relapse & other outcomes awaited [Reducing STEroids in Relapsing Nephrotic syndrome, RESTERN; NTR5670, EudraCT 2016-002430-76]		

AD alternate days; /d per day; HR hazard ratio; MD mean difference; mo months; NA not applicable; RD risk difference; RR risk ratio; wk weeks; yr year
P<0.05, **<0.01 and ***<0.0001*
[#]*Number of infrequent relapsers among 100 patients randomized*

Supplementary Table IV Controlled Trials on Efficacy of Predniso(lo)ne on Alternate Days (AD) for Frequent Relapses

Author, yr (reference)	*Type of study*	*N*	*Prednisone AD*	*Comparator*	*Follow up, yr*	*Outcomes at 12-24 mo*				*Adverse events*
						Relapses, n or rate	*Proportion (%) with relapses*	*% with frequent relapses*	*Cumulative predniso(lo)ne*	
APN, 1981 [xvi]	Open label RCT	64[#1]	35 mg/m^2	Prednisone at 40 mg/m^2 on 3 consecutive days each week	0.5 (1)[^]	0.9±0.3 *vs*. 1.9±0.4 in 6 months*	43% *vs*. 72%*		3.9±0.2 *vs*. 3.8±0.2 g/m^2 in 6 months	Obesity 57% *vs*. 52%; hirsutism 13% vs. 20%; psychosis 0% *vs*. 8%; infections 17% *vs*. 12%; 4 in each group withdrawn for steroid toxicity
Broyer, 1997 [xvii]	Open label RCT	40	15-20 mg/m^2	Deflazocort in equivalent dose AD	1	3±2 *vs*. 1±1**	88% *vs*. 42%**		5.1 *vs* 5.7 g/m^2	Mean change in height -0.4 *vs*. -0.2 SDS, weight 3.9 *vs*. 1.7 kg & BMD -12 *vs*. -6%; Cushingoid 7 *vs*. 11
Mattoo, 2000 [xviii]	Prospective study	36	0.5-0.8 mg/kg	Prednisolone at same dose; given daily for 5 days during URTI	2	5.5±1.3 *vs*. 2.2±0.9*	Non-relapsers excluded	Not reported	Not reported	Not reported
Jayantha, 2002 [xix]	Open label RCT	129[#2@]	60 mg/m^2 AD, tapered q 4 wk by 10 mg/m^2 (total 7 months)	Prednisolone 40 mg/m^2 AD for 4 wk (total 2 months)	0.5	0.4±0.5 *vs*. 2.1±1.5*	38% *vs*. 88%*	17.5% *vs*. 40.6%*	3.3±1.2 *vs*. 2.7±1.3	Hypertension 30% *vs*. 12.5%; slow growth 35% *vs*. 28.1%
Al Saran, 2006 [xx]	Open label, not randomized	56	<0.5 mg/kg	Levamisole 2.5 mg/kg AD	1	2.6±1.8 *vs*. 1.0±1.8*	100% *vs*. 37.5%*	50% *vs*. 9.4%*	3.9±1.2 *vs*. 3.1±1.9 g/m^2	None *vs*. gastrointestinal symptoms in one patient
Abeyagunawardena, 2008 [xxi]	Placebo-controlled cross-over RCT	40[@]	0.1-0.5 mg/kg; given 5 mg daily for 7 days in URTI	Prednisone at same dose; given placebo daily for 7 days in URTI	2 URTI	Not reported	48% *vs*. 18%*	Not reported	Not reported	No significant events
Gulati, 2011 [xxii]	Open label RCT	100[!]	0.5–0.75 mg/kg	Prednisolone at same dose; daily during infections	1	1.8±0.5 *vs*. 0.9±0.4*	85% *vs*. 61%*	8% *vs*. 4%	138±22 *vs*. 120±32 mg/kg	Not reported
Yadav, 2019 [xxiii]	Open label RCT	61	0.5–0.7 mg/kg	Prednisolone at 0.2-0.3 mg/kg daily	1	1.94 *vs*. 0.55 per person-yr	71% *vs*. 40%	57% *vs*. 7%[$*]	0.39±0.19 *vs*. 0.27±0.07 mg/kg/day	Cataract & glaucoma 6.5% *vs*. 0% each

BMD bone mineral density; NS not significant; RCT randomized controlled trial; SDS standard deviation score; URTI upper respiratory tract infection
[#]Outcomes reported for [1]48 and [2]90 patients; [^]therapy for 6 months; follow up for 6 months more off therapy; [@]included patients with infrequent relapses; [!]includes 32 patients that also received levamisole; [$]includes patients with infrequent relapses with steroid toxicity
*P *<0.05*

Supplementary Table V Studies on Low-dose Predniso(lo)ne Administered Daily at Onset of or During Infections[@]

Author, yr	*Type of study*	*N*[#]	*Intervention: Prednisone*	*Control*	*Duration*	*Outcomes*	
						Relapse rate [RR (95% CI)] or %	*Proportion (%) with relapses*
Mattoo 2000 [xviii]	Non-randomized, prospective study	36	0.5 mg/kg daily x 5 days	Prednisolone 0.5-0.8 mg/kg AD	2 yr	2.2±0.9 *vs*. 5.5±1.3*	Non-relapsers excluded
Abeyagunawardena 2008 [xxi]	Placebo-controlled cross-over RCT	40[$]	5 mg daily x 7 days[@1]	Placebo for 7 days[@1]	2 URTI	Not available	18% *vs*. 48%*
Gulati 2011 [xxii]	Open label RCT	100[^]	0.5-0.8 mg/kg AD; daily x 7 days[@2]	Prednisolone 0.5-0.8 mg/kg AD[@2]	2 yr	0.9±0.4 *vs*. 1.8±0.5 [0.9 (0.4, 1.4)]***	61% *vs*. 85%*
Abeyagunawardena 2017 [xxiv]	Placebo-controlled cross-over RCT	48[#1]	0.5 mg/kg daily x 5 days	Placebo for 5 days	2 yr	Not available	33% *vs*. 58%*
PREDNOS 2 [xxv]	Placebo-controlled RCT	300[#2]	15 mg/m^2 x 6 days (maximum 40 mg)	Placebo for 6 days	Until first infection: 1 yr	Occurrence of relapse [ISRCTN10900733]	

AD on alternate days; CI confidence interval; RR rate ratio; URTI upper respiratory tract infection; yr year
[@]Refers to URTI, except [@1]viral infections and [@2]any infections
[$]While on prednisolone AD
[#]These studies included patients with frequent relapses, except two that also enrolled patients with [1]infrequent relapses and [2]relapsing nephrotic syndrome (≥2 relapses in previous year) while on/off maintenance immunosuppression
[^]Patients requiring prednisolone AD at >1 mg/kg to maintain remission additionally received levamisole at 2-2.5 mg/kg AD
*P *<0.05, **<0.01, and ***<0.0001*

Supplementary Table VI Randomized Controlled Trials Examining Efficacy of Levamisole Administered on Alternate Days

Author, Year	*Type of RCT*	*Comparison**	*N*	*Follow up, months*	*Outcomes at 6-12 months*		
					Proportion (%) with relapse	*Frequency of relapses*	*Relative risk of relapse (95% CI)*
BAPN, 1991 [xxvi]	Placebo controlled	Placebo	61	6	87.1 *vs*. 93.3	Not reported	0.93 (0.79, 1.1)
Weiss, 1993 [xxvii]	Placebo controlled	Placebo	49	12	93.4 *vs*. 88.9	0.7±0.2 *vs*. 0.6±0.3	1.05 (0.86, 1.3)
Abeyagunawardena, 2006 [xxviii]	Open label	No treatment	76	12	19.0 *vs*. 76.5*	Not reported	0.25 (0.13, 0.48)
Gruppen, 2018 [xxix]	Placebo controlled	Placebo	99	12	66.0 *vs*. 85.7*	Not reported	0.77 (0.61, 0.97)
Dayal, 1994 [xxx]	Open label	Prednisone	61	12	40.9 *vs*. 71.4	Not reported	0.57 (0.31, 1.05)
Rashid, 1996 [xxxi]	Open label	Prednisone	40	10	55 *vs*. 90*	Not reported	0.61 (0.4, 0.93)
Sural, 2001 [xxxii]	Open label	Prednisone	58	12	56.7 *vs*. 82.1*	Not reported	0.69 (0.48, 0.99)
Al-Saran, 2006 [xx]	Open label	Prednisone	56	12	41.2 *vs*. 100*	0.1±0.2 *vs*. 0.2±0.2*	0.42 (0.28, 0.63)
Sural, 2001 [xxxii]	Open label	Oral cyclophosphamide	57	12	56.7 *vs*. 37	Not reported	1.53 (0.85, 2.74)
Donia, 2005 [xxxiii]	Open label	Intravenous cyclophosphamide	40	22	64 *vs*. 72	Not reported	0.89 (0.68, 1.16)
Sinha, 2019 [xxxiv]	Open label	Mycophenolate mofetil	149	12	59.2 *vs*. 65.8	1.3 (1.1, 1.7) *vs*. 1.1 (0.3, 1.3)	1.11 (0.86, 1.43)

*P *<0.05*

Supplementary Table VII Non-Randomized Studies Examining Efficacy of Levamisole Administered Daily

Author, Year	*Type of study*	*Dose of levamisole, mg/kg per day*	*Comparison, if any*	*N*	*Follow up, months*	*Outcomes at 6-12 months*			
						Proportion (%) with relapse; frequent relapses	*Frequency of relapses*	*Cumulative prednisone*	*Adverse events (AE)*
Abeyagunawardena, 2017 [xxxv]	Prospective	2.5[#]	AD levamisole (received historically)	58	12	79.3% *vs*. 100%; not reported	2.8±0.8 vs. 1.3±0.9	Median 154.1 *vs*. 254.2 mg/kg	No major AE
Ekambaram, 2014 [xxxvi]	Retrospective	2	Prior year	97	6-24	Effective in 77%	1.3±0.7 vs. 2.4±0.5	2.5±0.69 g/m^2 *vs*. 4.1±0.1 g/m^2	Not reported
Chen, 2010 [xxxvii]	Retrospective	2-3.3	Other agents	12	NA	93.3%; no effect 66.7%	Not reported	Not reported	Not reported
Sumegi, 2004 [xxxviii]	Retrospective	2	Prior year	34	60	32.4% *vs*. 100%; not reported	0.41 vs. 4.4	1.5±1.7 g/yr; 23 off steroids	Neutropenia in 14.7%
Fu, 2004 [xxxix]	Prospective	2-3[#]	AD levamisole, 2-3 mg/kg	36	4-36	17% *vs*. 49%; response in 69% *vs*. 80%	1.3±2.1 vs. 2.0±2.5	0.2±0.4 *vs*. 0.2±0.3 mg/kg/day	Leukopenia in 20% *vs*. 31.3%
La Manna, 1988 [xl]	Prospective	2.5	Levamisole, 2.5 mg/kg, given 2/wk	8	2-16	Response in 25%	Not reported	Not reported	Minimal

NA not available
[#]*Having failed AD levamisole*

Supplementary Table VIII Non-Randomized Studies on Mycophenolate Mofetil (MMF) in Nephrotic Syndrome

Author, yr (reference)	*Type of study*	*N*	*MMF, mg/m² per day*	*Follow up (range), yr*	*Outcomes at 12-24 months*				*Adverse events (AE)*
					Relapses, n or rate	*Proportion with relapses*	*Frequent relapses*	*Predniso(lo)ne, mg/kg per day*	
Bagga, 2003 [xli]	Prospective	19	29 (27.4-30.7)	1	2 (1.2-2.7)	78/9%	15.8%	0.3 (0.2-0.4)	Abdominal pain 26.3%
Gellermann, 2004 [xlii]	Prospective	6	1000	2.1 (1.3-3.3)	Not reported	16.7%	0%	Not reported	Juvenile conglobate acne in 16.7%
Novak, 2005 [xliii]	Retrospective	21	1200	1±0.5	0.47±0.43 per month	80.9%	24%	Not reported	Gastrointestinal AE common but mild; varicella in 4.7%
Al-Akash, 2005 [xliv]	Retrospective	11	948 (500-1087)	1 (0.3-2)	1.05 (0-4.5)	45.5%	18.2%	Not reported	Herpes stomatitis 9.1%; gastrointestinal AE 18.2%
Hogg, 2006 [xlv]	Prospective	33	1200	0.5	1 per 14.7 months	25%	Not reported	Not reported	Leukopenia 15.6%; varicella 3.1%; gastritis 3.1%
Okada, 2007 [xlvi]	Prospective	11	750-1000	1	Not reported	36.4%	9.1%	3.2±3.1 mg/kg/month	Gastrointestinal AE 18.2%; alopecia 9.1%
Fujinaga, 2007 [xlvii]	Prospective	12	1220±95	0.9 (0.5-6.5)	0.6±0.9	25% at 6 months	Not reported	0.21±0.11	None
Afzal, 2007 [xlviii]	Retrospective	42	26.5 (16.6-31.3) mg/kg	1.2 (0.5-6.8)	2.2 (1.4, 2.9)	78.6%	11.9%	0.3 (0.3, 0.4)	Abdominal pain 21.4%; infections 9.5%
Fujinaga, 2009 [xlix]	Retrospective	26	34±6 mg/kg	1.6 (0.6-6.5)	0.8±1.2	Not reported	Not reported	0.17±0.11	Anemia and herpes labialis in 3.8% each
Baudouin, 2012 [l][$]	Prospective	23	1200	1	Not reported	26.1%	Not reported	264 (196–306) mg/m²/month[^]	Gastrointestinal AE or infections in 26.1%; leukopenia or anemia in 30.4%
Hasan, 2013 [li]	Retrospective	61	1200	3.2 (1.7-4.7)	0.5 (0–0.87)[^]	51%	38%	Withdrawn in 56%	Gastrointestinal AE 13%; leukopenia or infections 11%; arthralgia 3%

Banerjee, 2013 [lii]	Retrospective	46	20-30 mg/g	3.6±1.8	Not reported	57%	No response in 33.3%	Reduced in 70%	Gastrointestinal AE 7.4%; neutropenia and elevated transaminases in 3.1% each
Jellouli, 2016 [liii]	Retrospective	30	1200	Not reported	0.45	Not reported	Not reported	0.2	Not reported
Basu, 2017 [liv]	Retrospective	130	1200	2.5	0.9±0.4	13.1% (at 1 yr)	6.1%	108.8±35.7 mg/kg	Gastrointestinal AE 3.8%; infections 6.2%; other minor 1.5%
Karunamoorthy, 2019 [lv]	Retrospective	87	28.5 mg/kg	3.3 (1.3-6.5)	Not reported	72.4%	17.2%	0.35^	Infections 12%; diarrhea 6%; leukopenia 3%; gastritis 2%

$Single limb Bayesian randomized controlled trial; ^Reported only for patients with response

Supplementary Table IX Randomized Controlled Trials (RCT) on Mycophenolate Mofetil (MMF) in Steroid Sensitive Nephrotic Syndrome

Author, yr [ref]	*Type of RCT*	*N*	*MMF dose, mg/m² per day*	*Comparator*	*Follow up, yr*	*Outcomes at 12-24 months*				*Adverse events (AE)*
						Relapses, n or rate (95% CI)	*Proportion with relapses*	*Frequent relapses*	*Cumulative predniso(lo)ne, mg/kg per day*	
Dorresteijn [lvi]	Open label	24	1200	Cyclosporine 4-5 mg/kg/day	1	0.83±1.3 *vs*. 0.08±0.3	41.7% *vs*. 8.3%	8.3% vs. 0%	0.13±0.16 *vs*. 0.08±0.12	First 3 studies: Hypertension 8.3% *vs*. 29.2%; hypertrichosis 6.9% *vs*. 40.3%; leukopenia 2.4% *vs*. 4.8%; gum hypertrophy 0% *vs*. 20.8%; reduced eGFR 0% *vs*. 8.3%; diarrhea 13.3% *vs*. 0%
Gellermann [lvii]	Cross-over, open label	60	1000; titrated to level	Cyclosporine 150 mg/m² per day	2	1.1±2 *vs*. 0.4±0.7*	42.9% *vs*. 30%	Not reported	1.83 *vs*. 0.99 g/m²	
Uddin [lviii]	Open label	60	800-1200	Cyclosporine 4-5 mg/kg/day	0.5	3±2.9 *vs*. 1.4±2.6	Not reported	Not reported	Not reported	
Wang [lix]	Not RCT	72	24.6±3.1 mg/kg/day	Tacrolimus 0.08±0.02 mg/kg/day	1	1.43 *vs*. 0.83	~58% *vs*. ~48%	12.2% *vs*. 0%	0.16±0.02 *vs*. 0.17±0.03	Infections 11.8% *vs*. 7.9%; gastrointestinal AE 11.8% *vs*. 2.6%; leukopenia 2.7% *vs*. 2.6%
Sinha [xlv]	Open label	149	750-1000	Levamisole 2-2.5 mg/kg on alternate days	1	1.1 (0.3, 1.3) *vs*. 1.3 (1.1, 1.7)	65.8% *vs*. 65.7%	16.4% *vs*. 14.5%	0.2 (0.1, 0.4) *vs*. 0.3 (0.2, 0.4)	Increased aminotransferases 2.6% *vs*. 2.7%; leukopenia 1.3% *vs*. none

AE adverse event; eGFR estimated glomerular filtration rate
**P <0.05; one Bayesian RCT is included in Web Table IX, since it lacked a comparator limb*

Supplementary Table X Determinants of Response to Therapy with Cyclophosphamide

Author, yr	*Cyclophosphamide cumulative dose*	*N*	*Age, yr*	*Follow up, yr*	*Proportion (%) in remission at 1, 2, 5 & 10 yr*[^]	*Factors associated with prolonged remission*
Latta 2001 [lx]	105-588 mg/kg	1504; 38 studies	NA	NA	Frequent relapses/dependence: NA/NA; 72/40; 36/24; NA/NA	Frequent relapses*; cumulative dose of cyclophosphamide
Vester 2003 [lxi]	165±33 mg/kg	106	7.3±3.8	NA	44; 34; 24; 24	Age >5.5-yr; frequent relapses*; cumulative dose >5 g/m^2; leukopenia
Kyrieleis 2007 [lxii]	~168 mg/kg	80	~4 (2-15)	6 (2-27)	NA; 35; ~48; ~60	Age >3-yr
Zagury 2011 [lxiii]	175 mg/kg	108	4.9	9.5 (5-29)	NA; 34; 25; 22	Relapse threshold <1.4 mg/kg; age >7-yr (univariate analysis)
Cammas 2011 [lxiv]	168 (157-197) mg/kg	143	7.9 (4.6-11.2)	7.8 (4-11.8)	44; 27; 13; 11[^1]	Age >5-yr; cumulative dose >170 mg/kg
Azib 2011 [lxv][#]	160 (149–170) mg/kg	90	5.3 (3.2–9.1)	5.5 (3.2-8.5)	57, 42, 31, NA[^2]	Age >7.5-yr
Berkane 2018 [lxvi]	168 mg/kg	50	8	1.6	52; 48; NA; NA	Age>8-yr; frequent relapses*

NA not available
**versus steroid dependence*
[^]Median time to relapse not reported, except [^1]10 months and [^2]0.8 (0.4-1.5) years
[#]All patients were steroid dependent

Supplementary Table XI Controlled Studies Examining Comparative Efficacy of Rituximab in Steroid Sensitive Nephrotic Syndrome

Author, yr	*Rituximab mg/m²; n*	*Control*	*N*	*Follow up, yr*	*Outcomes*				
					Relapse rate (RR)	*Proportion with relapse (HR; 95% CI)*	*Time to relapse, mo*	*% off steroids*	*% off all agents*
Randomized clinical trials									
Iijima 2014 [lxvii]	375, 4	Placebo	24; 24	1	1.5 *vs*. 4.2 per p-yr (0·37; 0·2, 0·6)	71% *vs*. 96% (0.27; 0.1, 0.5)	8.9 *vs*. 3.4	88% *vs*. 79%	NA
Boumediene 2018 [lxviii]	375, 2[#1]	Placebo[#1]	10; 13	0.5	NA	10% *vs*. 100%	NA	NA	NA
Ahn 2018 [lxix]	375, 1[#1]	None[#1]	40; 21	0.5	3.4 *vs*. 9.4 per p-yr	26% *vs*. 69%	9 *vs*. 2.9	NA	NA
Ravani 2020 [lxx]	375, 1[#]	None[#]	15; 15	1	NA	13% *vs*. 7%	NA *vs*. 1.5	NA	NA
Ravani 2015 [lxxi]	375, 1[#]	Prednisone[#]	15; 15	0.25 (1)	NA	20% *vs*. 93%[$] (0.02; 0.01, 0.15)	18 *vs*. NA	NA	NA
Ravani 2011 [lxxii]	375, 1-2	CNI alone	27; 27	0.25 (1)	NA	19% *vs*. 48% at 3-months	NA	78% *vs*. 7.4%	63% *vs*. 3.7%
Basu 2018 [lxxiii]	375, 2	Tacrolimus	60; 60	1	NA	10% *vs*. 37%	10 *vs*. 7	93% *vs*. 79%	NA
Single arm clinical trials									
Ruggenenti 2014 [lxxiv]	375, 1	None	30[^]	1	0.5 (0-1)	70% in children	7.5	NA	60%
Non-randomized prospective (P) or retrospective (R) comparisons									
Kari 2020 (P) [lxxv]	375, 2	Cyclophosphamide	19; 27	1	NA	16% *vs*. 41% (0.36; 0.1, 1.5)	NA[$]	74% *vs*. 30%	NA
Webb 2016 (R) [lxxvi]	750, 2	Cyclophosphamide	42; 79	≥1	NA	50% *vs*. 60%[$]	14 *vs*. 7	NA	69% *vs*. 84%

Sinha 2012 (R) [lxxvii]	375, 2-3	Tacrolimus	10; 13	1	0.8±1.0 *vs*. 0.9±1.1	50% *vs.* 54%[$]	8.5 *vs*. 9.8	80% *vs*. 46%	80% *vs*. 46%
Ongoing randomized clinical trials									
Nagano [lxxviii]	375, 2	Placebo	20; 20	1	Awaited; JMA-IIA00380				
Ravani [lxxix]	375, 1[#1]	Ofatumumab 1500 mg/m^2, 1[#1]	70; 70	2	Awaited; NCT02394119; Eudra-CT 2015-000624-28				
Mathew	375, 2	Tacrolimus	21; 20	1	Awaited; CTRI/2018/11/016342				

NA not available; p-yr person-year; yr year

[#]Steroids and [#1]CNI tapered; ^Includes 10 children; [$]Based on Kaplan Meier estimates of relapse-free survival at 1-yr

Supplementary Table XII Strategies to Maintain Remission Following Rituximab Administration

Author, year	*RTX* doses*	*Immunosuppression*	*N*	*Follow up, yr*	*Results*
Maintenance immunosuppression (mIS)					
Ito 2011 [lxxx]	1	MMF *vs*. none	9 *vs*. 7	1 yr	MMF therapy led to fewer relapses (0.4 *vs.* 2.3) and relapsers (33% *vs*. 86%) at 1-yr
Fujinaga 2013 [lxxxi]	1	CsA *vs*. MMF	13 *vs*. 16	1.5 yr	CsA *vs.* MMF led to fewer relapses (0.6±1.4 *vs.* 1.0±0.9); lower rates of relapse (25% *vs*. 45%) and lower treatment failure (15% *vs*. 44%); steroid sparing
Hourinouchi 2018 [lxxxii]	4	MMF *vs*. placebo	40 *vs*.40	1.4 yr	Awaited; UMIN000014347
Number of doses					
Hogan 2019 [lxxxiii]	1[*1] *vs*. 1 *vs*. 2	None	8 *vs*. 35 *vs*. 18	≥1 yr	Proportions in sustained remission at 1-yr higher by dose: 50 (58–77) % for 100 mg/m^2; 59 (42-76) % for 375 mg/m^2 and 72 (46-87) % for 750 mg/m^2 Low *vs.* high dose associated with risk of relapse: HR 5.0 (1.2, 21.6)
Maxted 2019 [lxxxiv]	1 *vs*. 2-3 *vs*. 4[*2]	Details not available	40 *vs.* 5 *vs*. 15	≥1 yr	1, 2-3 or 4 dose equivalents: Similar proportions in sustained remission at 1-yr (47%, 71%, 53%); similar time to relapse (334, >720, 344 days)
Number of doses and maintenance immunosuppression (mIS)					
Chan 2020 [lxxxv]	1 *vs*. 2 *vs*. 3-4	Prednisone, CNI or MMF [Continued *vs*. stopped]	191 *vs*. 208 *vs*. 112	≥0.5 yr	Time to relapse: *(i)* Similar for 1, 2 or 3-4 doses (11.8, 11.9, 13 months); *(ii)* similar among patients on mIS (11.8, 11.9, 13 months); *(iii)* lower for 1 vs. 2 or 3-4 doses if not given mIS (8.5, 12.7, 14.3 months); adjusted HR 0.5 & 0.6 (0.3-0.9)
Sequential administration of doses					
Takei 2013 [lxxxvi]	1 q 6 mo; 2 doses	Prednisone; CNI, MMF or mizoribine	25 adults^	1 yr	Before *vs*. after: Fewer relapses (62 *vs*. 4) and reduced prednisone (8.2±3.4 vs. 3.3±2.3 g/yr); 80% off prednisone and mIS; increased serum IgG (P=0.0005)
Miyabe 2016 [lxxxvii; lxxxviii]	1 q 6 mo; 4 doses	Prednisone; CNI, MMF or mizoribine	25^& 54^adults	2 yr	Before *vs*. after: Fewer relapses and reduced prednisone; all off prednisone and mIS; increased IgG; improved bone mineral density and blood pressure
Iwabuchi 2018 [lxxxix]	1 q 6 mo;4 doses	Prednisone; CNI, MMF or mizoribine	32 children & 19 adults^	2 yr	In children *vs*. adults: Few relapses and minimal prednisone dose (P <0.001); similar frequency of adverse reactions (21% *vs*.20%)
Papakrivopoulou 2016 [xc]	1 q 6 mo; 2-3 doses	Prednisone off by 3-mo; CNI tapered at >1-yr	15 adults	1.7 yr	Before *vs.* after: Fewer relapses (P <0.001); median remission 25 months; IgG levels unchanged

Taguchi 2020 [xci]	1 q 6 mo; 2-4 doses		13 adults	2 (1-5) yr	Before *vs.* after: Reduced relapses, and prednisone and cyclosporine dosage
Kim 2018 [xcii]	At B cell recovery[@1]	Details NA	12 children	2±1 yr	Before *vs.* after: Fewer relapses and off mIS (P <0.01)
Sellier-Leclerc 2012 [xciii]	At B cell recovery[@2]	MMF off; prednisone and CNI off by 3-mo	30 children	≥2 yr	Sustained remission in 63% at 3.2±0.1 yr; 37% relapsed 4.3 months after B cell recovery; 100% off mIS; transient adverse effects

CNI calcineurin inhibitor; HR hazards ratio; IgG immunoglobulin G; MMF mycophenolate mofetil; mo months; NA not available; yr year
**Each dose was 375 mg/m² except[*1] where it was 100 mg/m²or [*2]750 mg/m² x 2 or 375 mg/m² x 4 doses*
[^]Overlap of patients between studies is unclear
[@]Total doses and frequency were [1]3.9±1.6 doses q 6±2 months and [2]5±1.4 doses over 15 months

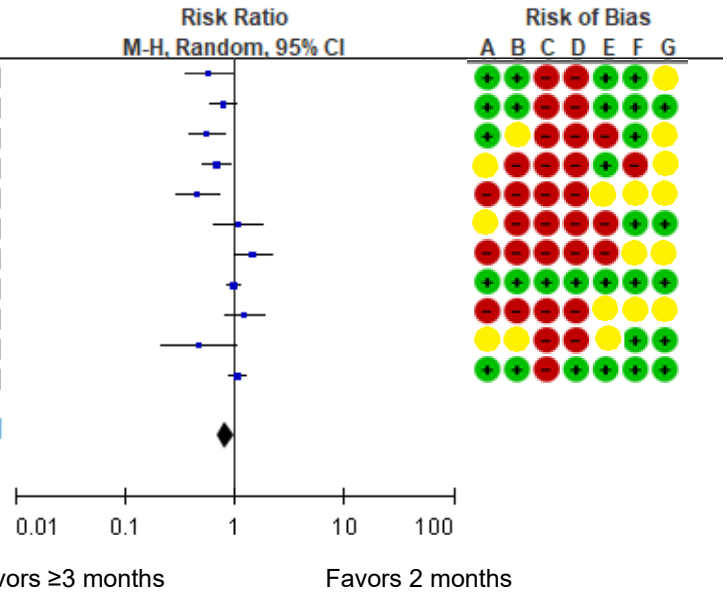
Supplementary Figure I Meta-analyses of Randomized Controlled Trials on Prednisone Therapy for First Episode of Nephrotic Syndrome

Comparison 1.1.1 3-months or longer versus 2-months: Occurrence of relapse (all studies)

Study or Subgroup	3 months or longer Events	Total	2 months Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
APN 1993	13	34	24	37	7.3%	0.59 [0.36, 0.96]
Bagga 1999	16	22	21	23	10.8%	0.80 [0.60, 1.06]
Jayantha 2002a	16	35	43	53	9.0%	0.56 [0.38, 0.83]
Ksiazek 1995	36	72	32	44	10.6%	0.69 [0.51, 0.92]
Moundekhel 2012	15	46	33	46	7.8%	0.45 [0.29, 0.72]
Norero 1996	15	29	13	27	6.8%	1.07 [0.63, 1.82]
Paul 2014	30	47	20	46	8.8%	1.47 [0.99, 2.18]
PREDNOS 2019	91	114	88	109	13.4%	0.99 [0.87, 1.13]
Satomura 2001	23	36	19	37	8.7%	1.24 [0.84, 1.85]
Ueda 1988	5	17	18	29	4.1%	0.47 [0.22, 1.04]
Yoshikawa 2014	83	122	80	124	12.7%	1.05 [0.88, 1.26]
Total (95% CI)		**574**		**575**	**100.0%**	**0.83 [0.69, 1.01]**
Total events	343		391			

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 38.65$, df = 10 ($P < 0.0001$); $I^2 = 74\%$

Test for overall effect: $Z = 1.91$ ($P = 0.06$)

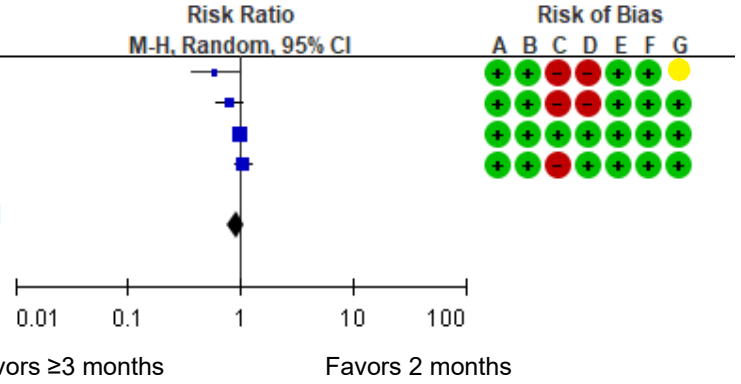


Comparison 1.1.2 3-months or longer versus 2-months: Occurrence of relapse in studies at low risk of bias

Study or Subgroup	3 months or longer Events	Total	2 months Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
APN 1993	13	34	24	37	9.7%	0.59 [0.36, 0.96]
Bagga 1999	16	22	21	23	20.6%	0.80 [0.60, 1.06]
PREDNOS 2019	91	114	88	109	37.9%	0.99 [0.87, 1.13]
Yoshikawa 2014	83	122	80	124	31.7%	1.05 [0.88, 1.26]
Total (95% CI)		**292**		**293**	**100.0%**	**0.92 [0.77, 1.09]**
Total events	203		213			

Heterogeneity: Tau² = 0.02; Chi² = 6.79, df = 3 (P = 0.08); I² = 56%

Test for overall effect: Z = 0.99 (P = 0.32)

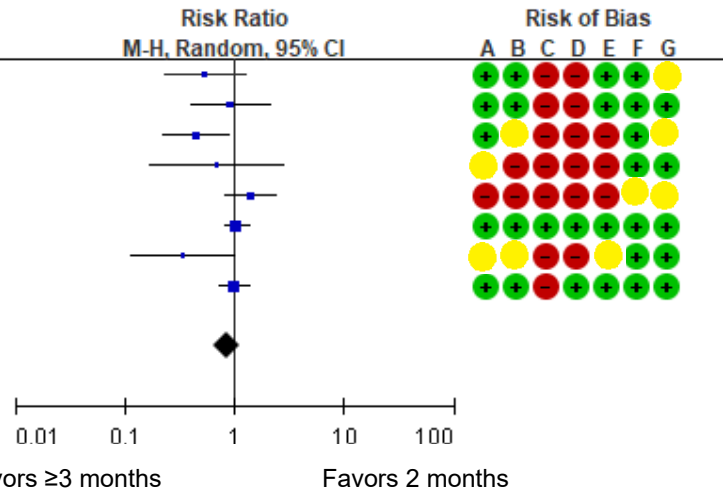


Comparison 1.2.1 3-months or longer versus 2-months: Occurrence of frequent relapses (all studies)

Study or Subgroup	3 months or longer Events	Total	2 months Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
APN 1993	6	34	12	37	7.9%	0.54 [0.23, 1.29]
Bagga 1999	7	22	8	23	8.4%	0.91 [0.40, 2.10]
Jayantha 2002a	8	48	26	70	10.7%	0.45 [0.22, 0.91]
Norero 1996	3	29	4	27	3.5%	0.70 [0.17, 2.84]
Paul 2014	20	47	14	46	14.6%	1.40 [0.81, 2.42]
PREDNOS 2019	60	114	55	109	26.4%	1.04 [0.81, 1.35]
Ueda 1988	3	17	15	29	5.5%	0.34 [0.12, 1.01]
Yoshikawa 2014	45	122	46	124	23.1%	0.99 [0.72, 1.38]
Total (95% CI)		**433**		**465**	**100.0%**	**0.86 [0.65, 1.13]**
Total events	152		180			

Heterogeneity: Tau² = 0.06; Chi² = 12.50, df = 7 (P = 0.09); I² = 44%

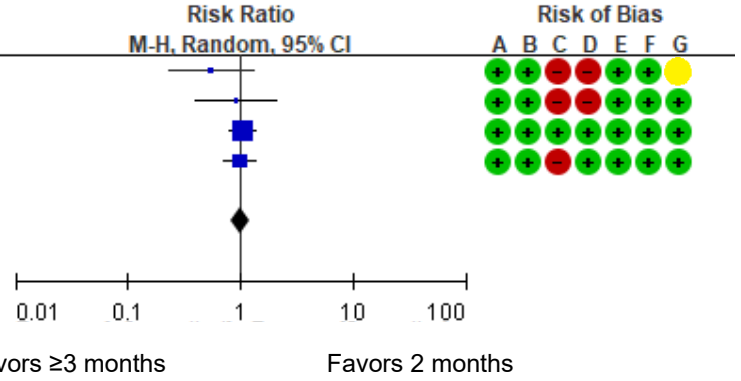
Test for overall effect: Z = 1.09 (P = 0.28)



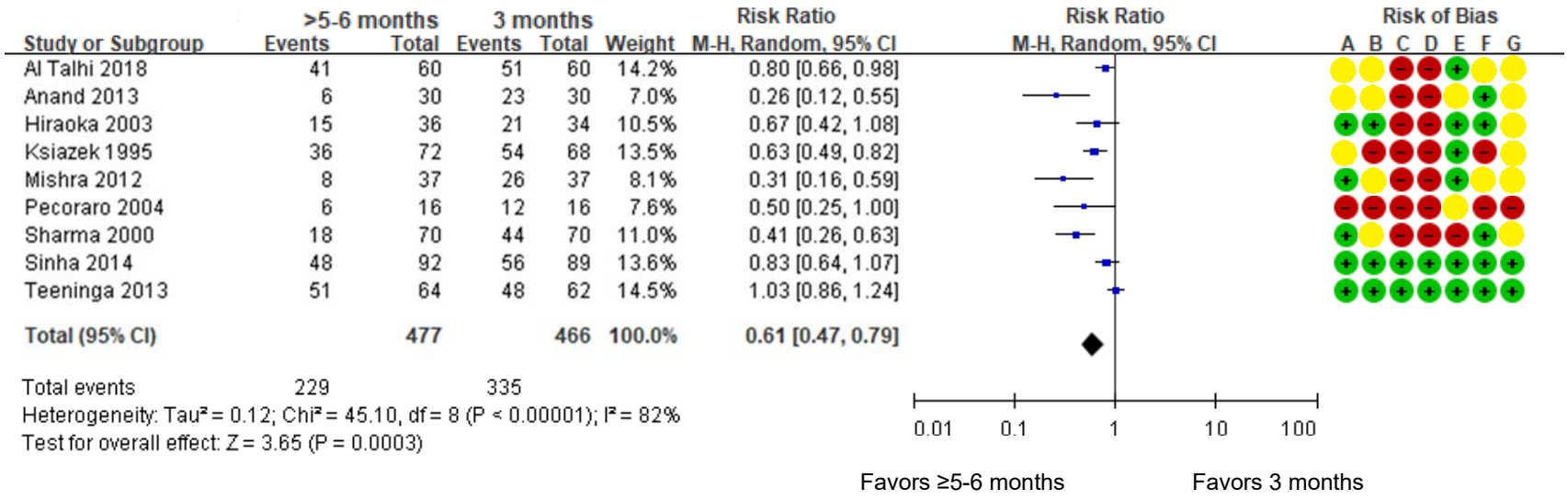
Comparison 1.2.2 3-months or longer versus 2-months: Occurrence of frequent relapses in studies at low risk of bias

Study or Subgroup	3 months or longer Events	Total	2 months Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
APN 1993	6	34	12	37	4.9%	0.54 [0.23, 1.29]
Bagga 1999	7	22	8	23	5.3%	0.91 [0.40, 2.10]
PREDNOS 2019	60	114	55	109	55.8%	1.04 [0.81, 1.35]
Yoshikawa 2014	45	122	46	124	34.1%	0.99 [0.72, 1.38]
Total (95% CI)		**292**		**293**	**100.0%**	**0.99 [0.82, 1.19]**
Total events	118		121			

Heterogeneity: Tau² = 0.00; Chi² = 2.08, df = 3 (P = 0.56); I² = 0%
Test for overall effect: Z = 0.13 (P = 0.90)



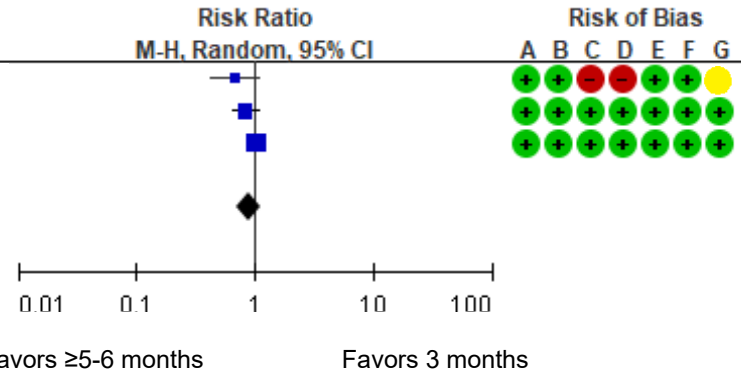
Comparison 2.1.1 5-6 months or longer versus 3 months: Occurrence of relapse (all studies)



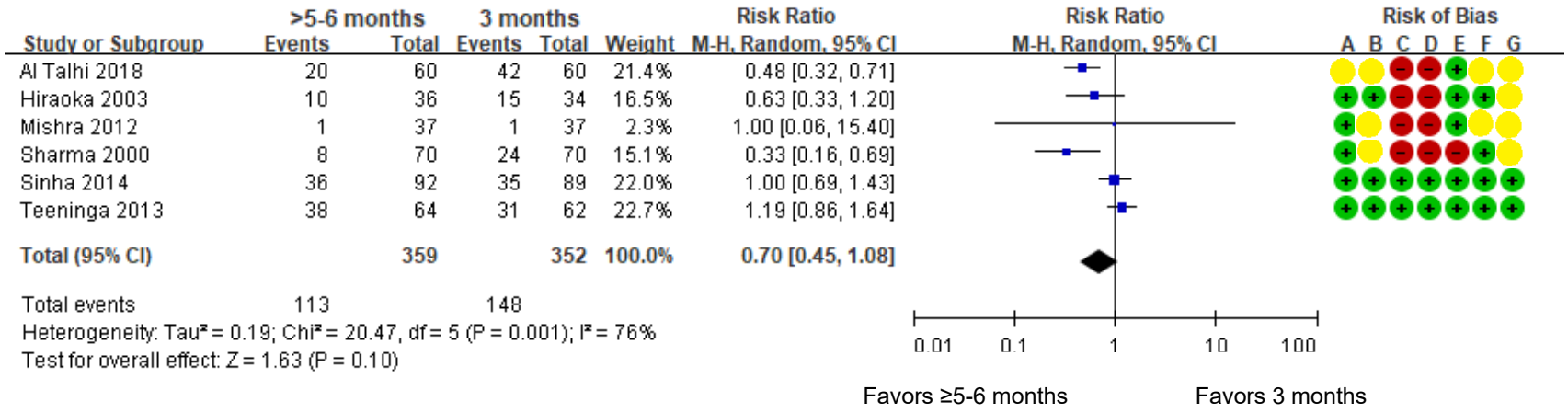
Comparison 2.1.2 5-6 months or longer versus 3-months: Occurrence of relapse in studies at low risk of bias

Study or Subgroup	>5-6 months Events	Total	3 months Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Hiraoka 2003	15	36	21	34	17.8%	0.67 [0.42, 1.08]
Sinha 2014	48	92	56	89	36.4%	0.83 [0.64, 1.07]
Teeninga 2013	51	64	48	62	45.8%	1.03 [0.86, 1.24]
Total (95% CI)		**192**		**185**	**100.0%**	**0.88 [0.70, 1.11]**
Total events	114		125			

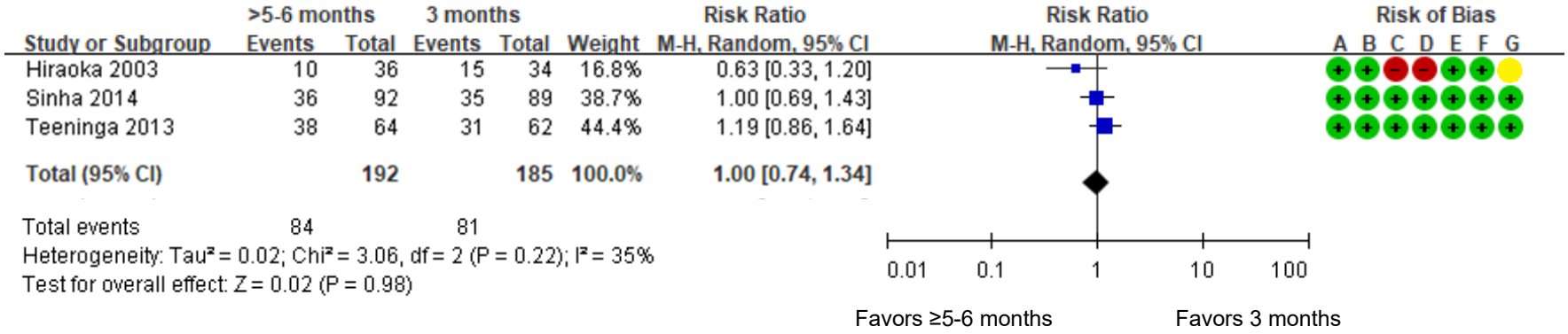
Heterogeneity: Tau² = 0.02; Chi² = 4.29, df = 2 (P = 0.12); I² = 53%
Test for overall effect: Z = 1.05 (P = 0.29)



Comparison 2.2.1 5-6 months or longer versus 3-months: Occurrence of frequent relapses (all studies)



Comparison 2.2.2 5-6 months or longer versus 3-months: Occurrence of frequent relapses in studies at low risk of bias



Legend for risk of bias assessment

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

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