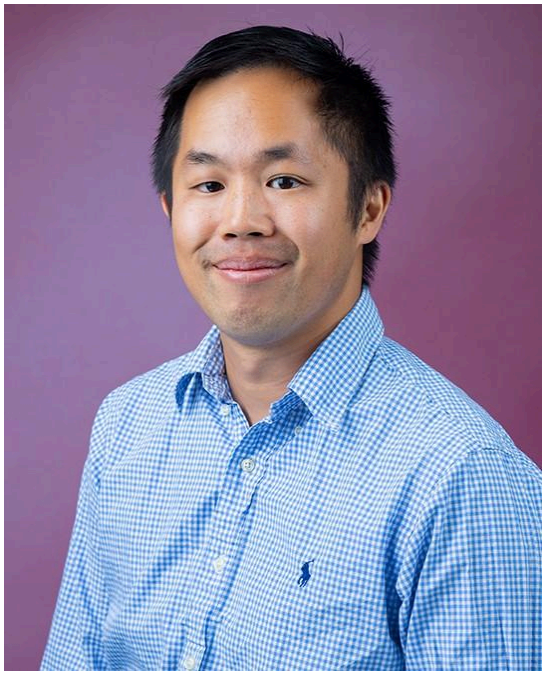
Article
https://pmc.ncbi.nlm.nih.gov/articles/PMC12925401/

🧵 Tweetorial Alert 🧵

1/
Hey #NephTwitter!
Welcome to a 🆕 #tweetorial #xtorial brought to you by @KIReports

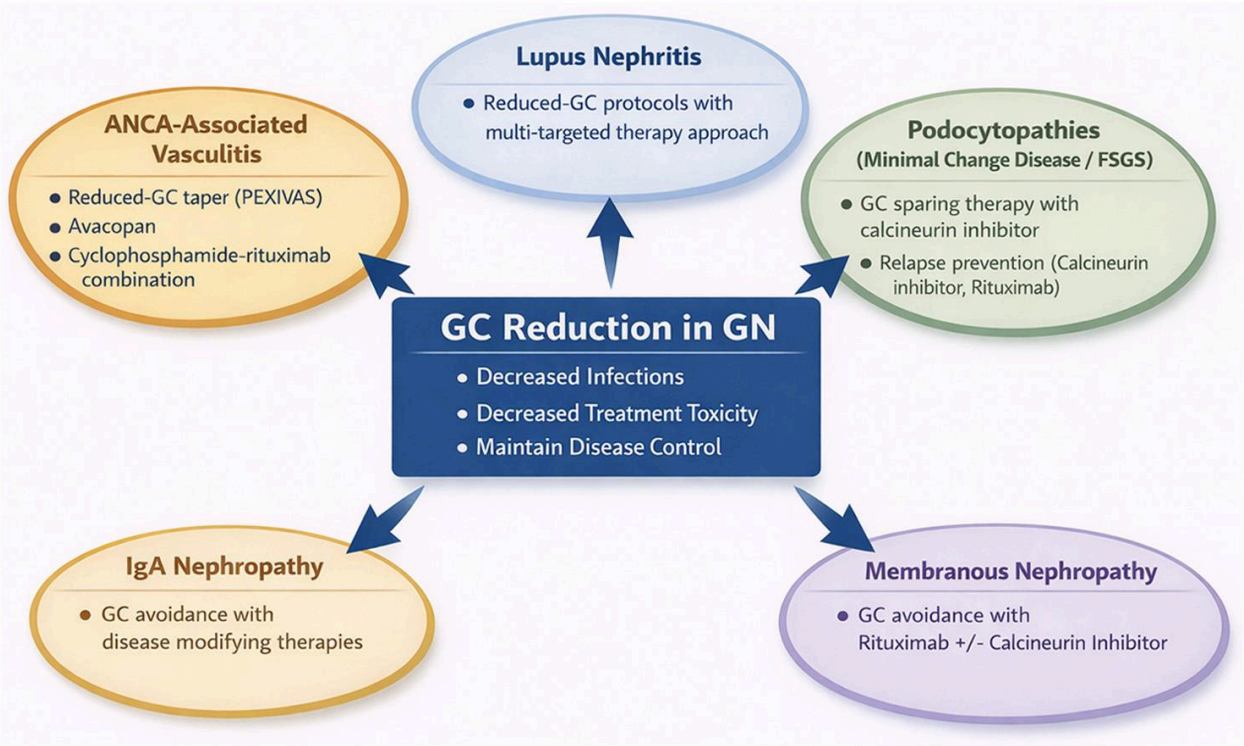
2/
Our author is Melvin @MChanMD (pediatric nephrologist)
Our topic: Corticosteroid Reduction in Glomerular Disease

#MedTwitter #nephtwitter @ISNkidneycare #XTwitter



3/
There are no conflicts of interest. Please also check out #KIReportsCommunity educational #blogposts at https://www.kireportscommunity.org/. FOLLOW US at @KIReports for more expert #MedEd in #kidneydisease. #FOAMed @MedTweetorials

4/ Our #Tweetorial is based on a recent publication by @michael-toal.bsky.social and VA: Glucocorticoid reduction in Glomerular Diseases
🔗https://www.kireports.org/article/S2468-0249(26)00027-6/fulltext



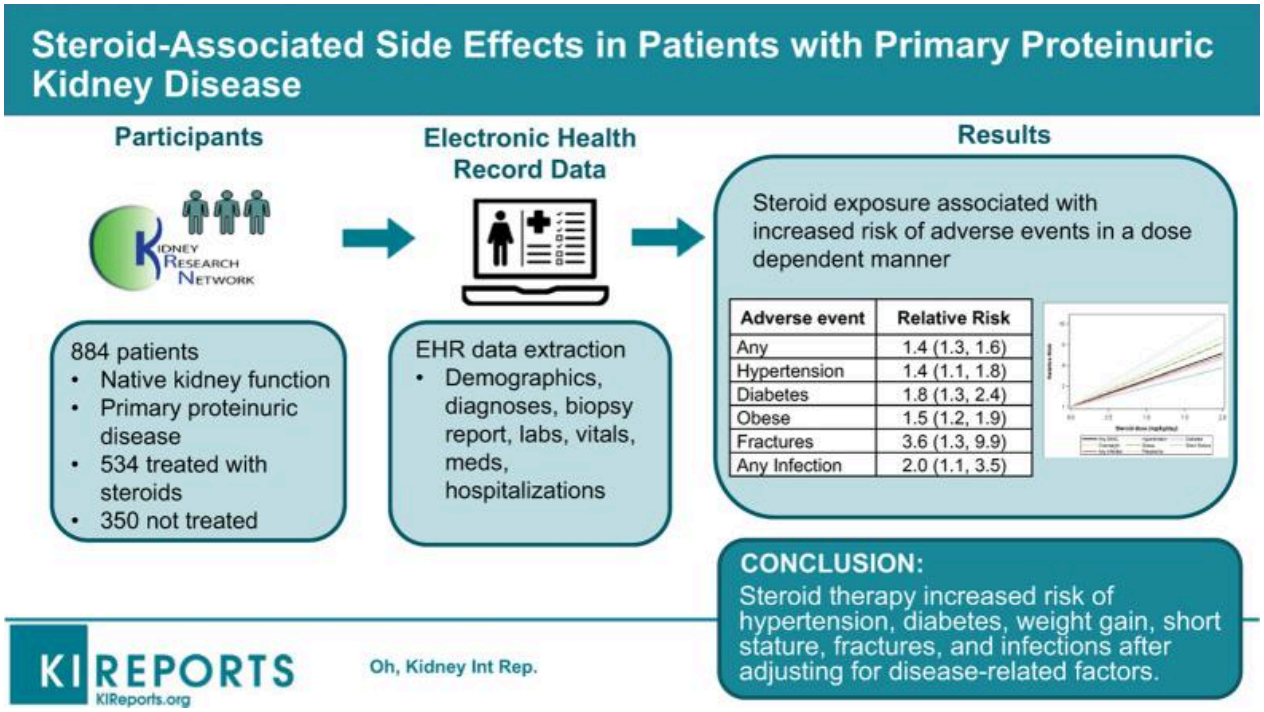
5/ Intro

⚡Steroids are a cornerstone for multiple glomerular diseases.

⚡However, side effects are well documented (see VA).

⚡Contemporary steroid reduction strategies include faster taper or steroid sparing combinations.

🔗https://pmc.ncbi.nlm.nih.gov/articles/PMC6933464/



6/ Methods

🧱Review of Randomized Controlled Trials/Observational Studies

🎗️Inclusion: Reduced steroid exposure with either lower dosage or duration

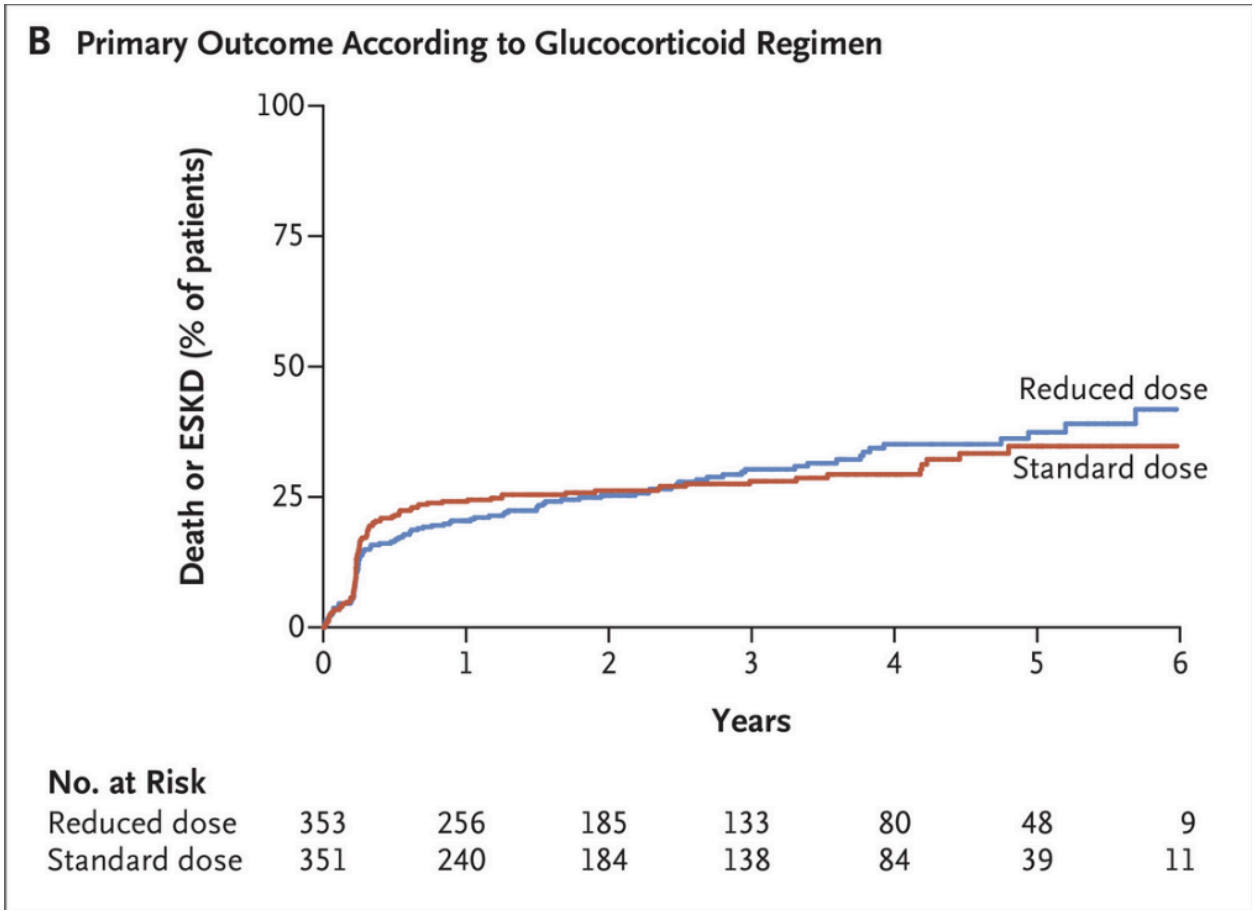
⚕️Two reviewers evaluate studies to make sure were included and 35 studies were included

7/ ANCA-Vasculitis

🏛️Historically, management has been dedicated by expert opinions. Emerging clinical trials are guiding treatment.

🫘PEXIVAS show that reduced steroids is non-inferior to standard steroids to primary outcome (ESKD or death), with 40% reduced cumulative steroid dosage.

PMID: 32053298



8/ ANCA-Vasculitis

🫘LOVAS evaluated the role of reduced steroids to standard dose with rituximab showed non-inferior outcomes, with 75% reduced cumulative steroid dosage.

👎Limitation: Population is in Japanese patients with a predominance of microscopic polyangitis.

PMID: 34061144

Table 2. Primary and Secondary Outcomes at 6 Months

Outcomes	Reduced-dose glucocorticoid plus rituximab (n = 69)		High-dose glucocorticoid plus rituximab (n = 65)		Absolute difference (95% CI)	*P* value[a]
	No. (%) with data	Median (IQR)	No. (%) with data	Median (IQR)		
Primary outcomes						
Remission[b]	49 (71.0)		45 (69.2)		1.8 (−13.7 to ∞)[c]	.003[d]
Secondary outcomes						
Remission[b,e]	49 (71.0)		45 (69.2)		0.6 (−15.3 to ∞)[c,f]	.005[d]
Relapse[b]	3 (4.3)		0		4.4 (−0.5 to 9.2)	.24
Deaths[b]	2 (2.9)		3 (4.6)		−1.7 (−4.7 to 8.2)	.67
End-stage kidney disease[b]	0		1 (1.5)		−1.5 (−4.5 to 1.5)	.48
Prednisolone, mg						
Cumulative dose	65 (94.2)	1318 (989 to 1770)	62 (95.4)	4151.25 (3795.25 to 4376)	−2599.3 (−2856 to −2342)[g]	<.001
Dose at 6 mo	65 (94.2)	2.0 (0 to 7.5)	62 (95.4)	10.0 (9.0 to 10.0)	−5.5 (−7.0 to −4.0)[g]	<.001
SF-36 component summary						
Physical[h]	54 (78.2)	38.3 (21.1 to 47.4)	49 (75.3)	31.7 (22.0 to 49.4)	6.3 (−2.6 to 15.2)	.43
Mental[i]	54 (78.2)	49.8 (45.1 to 56.6)	49 (75.3)	50.4 (46.3 to 57.2)	−0.4 (−4.7 to 4.0)	.65
Birmingham Vasculitis Activity Score[j]	65 (94.2)	0 (0 to 1)	58 (89.2)	0 (0 to 0)	0 (0 to 0)	.65
Patient visual analog scale						
Disease activity, mm[k]	55 (79.7)	12 (0 to 50)	49 (75.3)	24 (7 to 55)	−12.0 (−29.4 to 5.4)	.17
Treatment toxicity, mm[l]	54 (78.2)	2.5 (0 to 24)	49 (75.3)	26 (5 to 53)	−23.0 (−39.1 to −6.8)	.003

Abbreviations: IQR, interquartile range; SF-36, Medical Outcomes Study 36-Item Short Form.

[a] Relapse, deaths, and end-stage kidney disease were compared by Fisher exact test. Dose of prednisolone was compared by Wilcoxon rank-sum test. SF-36, the Birmingham Vasculitis Activity Score, and visual analog scales were compared by analysis of covariance.

[b] No. (%) with event.

[c] Difference (97.5% CI).

[d] *P* values for noninferiority.

[e] Covariate (age, estimated glomerular filtration rate, antineutrophil cytoplasm antibody)-adjusted analysis by Mantel-Haenszel methods.

[f] Adjusted difference.

[g] Estimated difference with 95% CI using quantile regression.

[h] SF-36 physical component summary is an assessment tool of physical health status and its scores range from 0 to 100, with higher scores indicating better health. A median of 31.7 to 38.3 indicates physically bad condition.

[i] SF-36 mental component summary is an assessment tool of mental health status and its scores range from 0 to 100, with higher scores indicating better health. A median of 49.8 to 50.4 indicates normal mental health status.

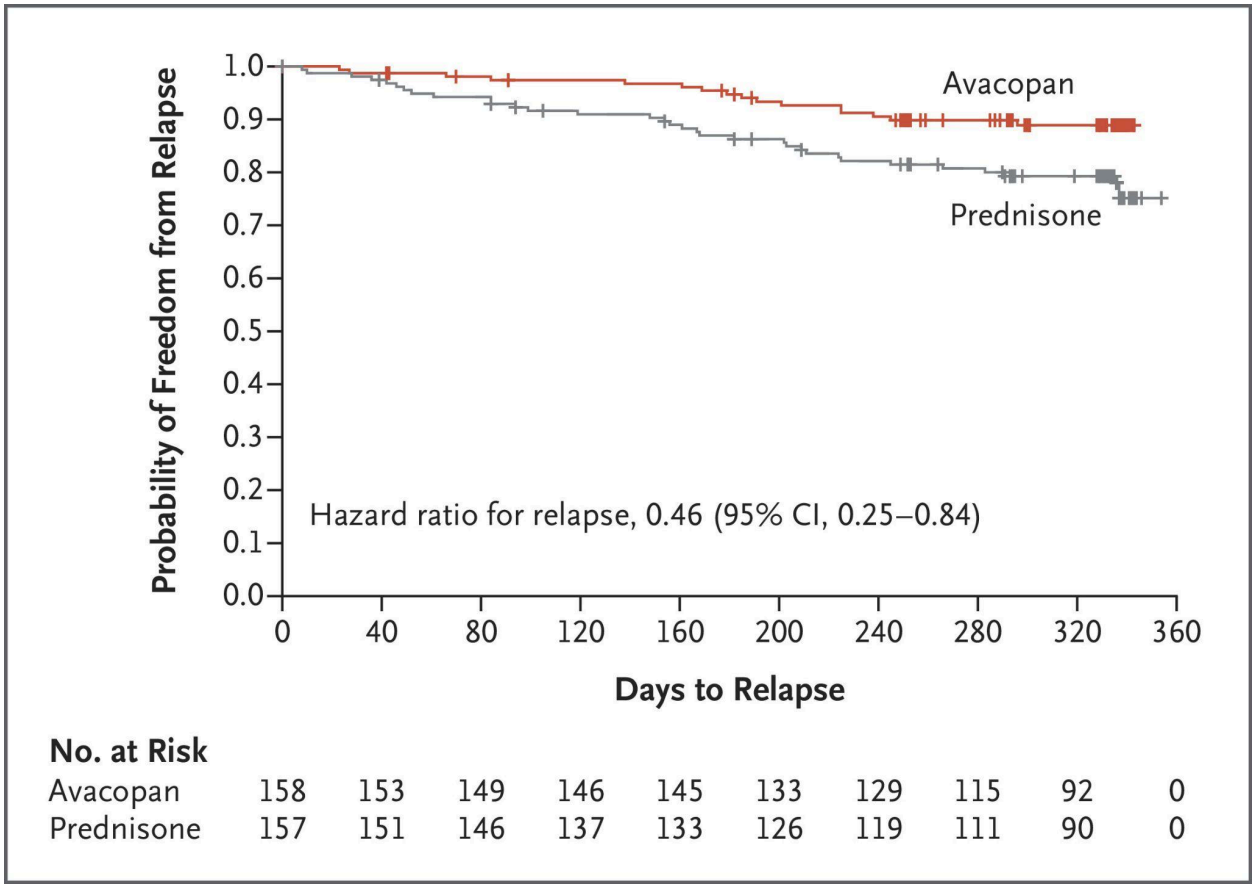
[j] The Birmingham Vasculitis Activity Score is an assessment tool for disease activity of systemic vasculitis and its scores range from 0 to 63, with higher scores indicating more active disease. A median of 0 points indicates disease remission.

[k] Visual analog scale for disease activity of vasculitis is a self-assessment by patients and its scores range from 0 mm to 100 mm, with higher scores indicating more severe disease activity. A median of 12 mm to 24 mm indicates very low disease activity.

[l] Visual analog scale for glucocorticoid/rituximab-related treatment toxicity is a self-assessment by patients and its scores range from 0 mm to 100 mm, with higher scores indicating more severe toxicity. A median of 2.5 mm indicates almost no toxicity and a median of 26 mm indicates mild toxicity.

9a/ ANCA-Vasculitis

🫘ADVOCATE showed non-inferior outcome with patients on treatment with avacopan and fast steroid with taper over 4 weeks or standard steroid with taper over 26 weeks. All patients also got rituximab or cyclophosphamide.



PMID: 33596356

9b/ ANCA-Vasculitis

👎Limitation: This difference was only seen in those who got rituximab. Those receiving rituximab only got induction dose and not maintenance, which is not standard of care. Furthermore, there have been concerns over the data integrity of this trial.

https://www.fda.gov/drugs/drug-alerts-and-statements/cder-proposes-withdraw-approval-tavneos

10/ SLE

🏛️Steroids have improved short-term outcomes. Increased survival has shifted to using steroids for maintenance, increasing lifetime steroid burden.

🫘A meta-analysis of RCTs show that high dose steroids improve renal remission but does have significant side effects.

PMID: 38766897

Supplementary Table 4. Meta-regression predicted rates
Meta-regression predicted rates of complete response, serious infections, and death at six months according to glucocorticoid starting dose (mg/day) and use or not of glucocorticoid pulses.

	Complete Response, % (95% CI)		Serious Infections, % (95% CI)		Death, % (95% CI)	
Dose, mg/day	Non-GC Pulses	GC Pulses	Non-GC Pulses	GC Pulses	Non-GC Pulses	GC Pulses
20	17.8 (6.5–29.2)	22.9 (9.2–36.7)	2.6 (2.0, 3.3)	2.9 (2.2, 3.6)	0.1 (0.0–0.3)	0.2 (0.0–0.4)
25	19.5 (7.3–31.5)	25.0 (10.4–39.6)	3.2 (2.4–4.0)	3.5 (2.6–4.4)	0.2 (0.0–0.4)	0.3 (0.0–0.6)
30	21.3 (8.3–34.4)	27.1 (11.7–42.5)	3.9 (3.0–4.9)	4.3 (3.2–5.3)	0.3 (0.0–0.6)	0.4 (0.0–0.8)
35	23.3 (9.4–37.2)	29.4 (13.2–45.6)	4.7 (3.5–6.0)	5.2 (3.9–6.5)	0.4 (0.0–0.8)	0.6 (0.0–1.2)
40	25.3 (10.6–40.0)	31.7 (14.8–48.7)	5.7 (4.3–7.1)	6.3 (4.7–7.8)	0.6 (0.0–1.2)	0.9 (0.0–1.8)
45	27.5 (11.9–43.0)	34.2 (16.6–51.8)	6.9 (5.2–8.6)	7.6 (5.8–9.4)	0.9 (0.0–1.7)	1.3 (0.0–2.6)
50	29.8 (13.4–46.1)	36.7 (18.5–55.0)	8.4 (6.4–10.4)	9.2 (7.0–11.3)	1.3 (0.0–2.5)	1.9 (0.0–3.8)
55	32.1 (15.1–49.2)	39.4 (20.6–58.1)	10.1 (7.7–12.4)	11.0 (8.4–13.6)	1.8 (0.0–3.6)	2.8 (0.1–5.6)
60	34.6 (16.9–52.3)	42.1 (22.9–61.2)	12.1 (9.3–14.9)	13.1 (10.1–16.2)	2.7 (0.0–5.3)	4.0 (0.1–7.9)

GC: glucocorticoids; CI: confidence interval.

11/ SLE

🫘Impact of reduced steroid dosage during induction has only been studied in small cohorts.

🫘One study of 81 patients showed that reduced steroids was comparable to standard steroids (19% vs 20%) in terms of complete remission.

🫘Other smaller studies have been mixed.

Table 2. Summary of steroid-sparing trials in lupus nephritis

Author (year, location)	Duration	Primary outcome	Intervention	Comparator	Key findings
Zeher (2011, International)	24 wks	CR UPCR < 0.5 with normalized urine sediment and serum creatinine within 10% of baseline value	Weight-based prednisolone starting at 22.5–35 mg/d reducing to 2.5–5 mg/d by week 24 ($n = 39$)	Weight-based prednisolone starting at 45–70 mg/d reducing to 5–10 mg/d by week 24 ($n = 42$)	Equivalent rates of CR (20.5% reduced dose vs. 19% standard dose.) Increased infection rates in standard dose (57%) compared with reduced dose (36%)
Bharati (2019, India)	24 wks	CR (> 50% reduction of proteinuria and stabilization of creatinine)	Prednisone 0.5 mg/kg/d for 8 wks, then reduced by 0.1 mg/kg every 4 wks to 0.1 mg/kg maintenance ($n = 10$)	Prednisone 1 mg/kg/d for 8 wks, then reduced by 0.2 mg/kg every 4 wks to 0.1 mg/kg maintenance ($n = 10$)	CR rates higher in standard dose (70%) regimen compared with the reduced dose (10%). More infections in standard-dose group (30% vs. 0%)
Bandhan (2021, Bangladesh)	24 wks	CR (UPCR < 500 mg/d and return to baseline creatinine)	Prednisone 0.5 mg/kg/d for 4 wks, tapered by 5 mg/wk until 10 mg, then 2.5 mg to 7.5 mg maintenance ($n = 15$)	Prednisone 1 mg/kg/d for 4 wks, tapered by 10 mg every 2 wks to 40 mg, then 5 mg every 2 wks to 10 mg, then tapered by 2.5 mg to maintenance 7.5 mg ($n = 12$)	Complete renal remission achieved in 66.7% in each group No significant difference in adverse events

CR, complete remission; KRT, kidney replacement therapy; UPCR, urine protein-to-creatinine ratio.

12/ SLE

🫘More recent studies have shown that reduced doses of steroids in induction combined with novel immunosuppressives like obinutuzumab and voclosporin can also achieve comparable remission.

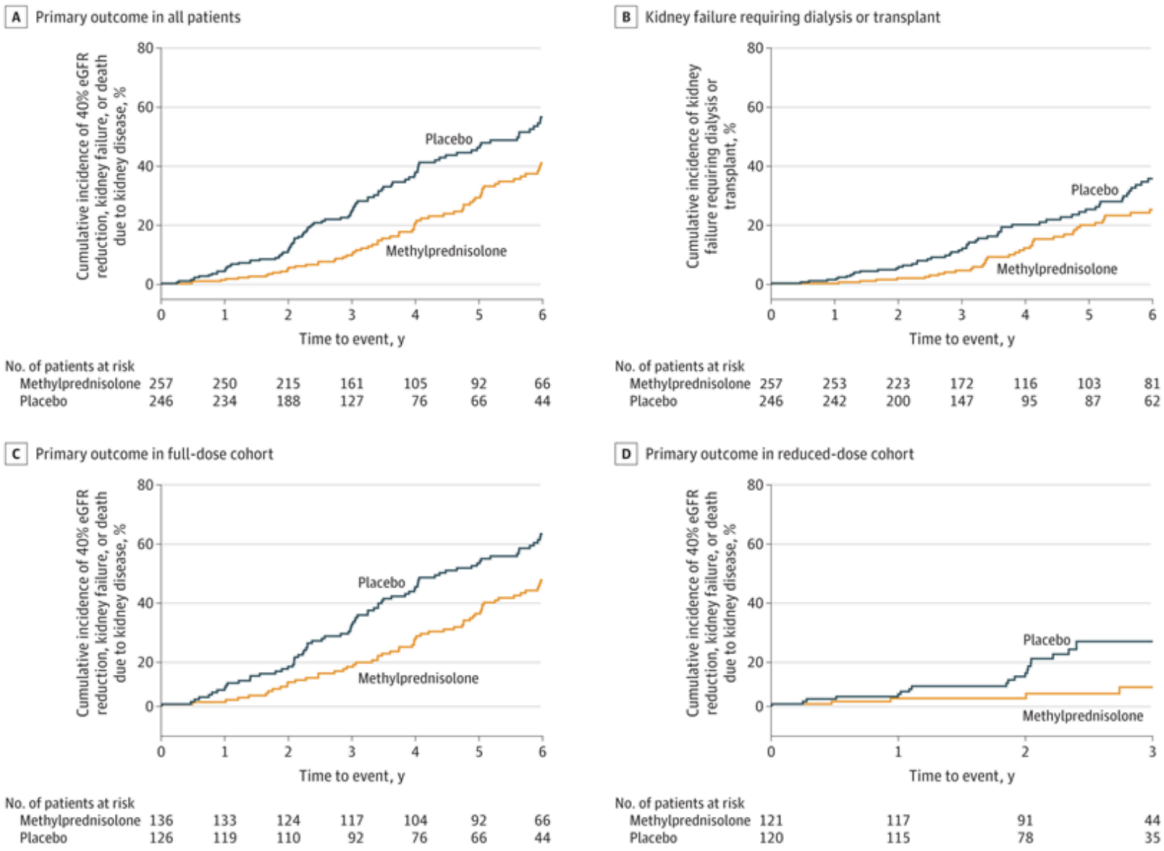
👎Limitation: These studies do not report cumulative steroid dose.

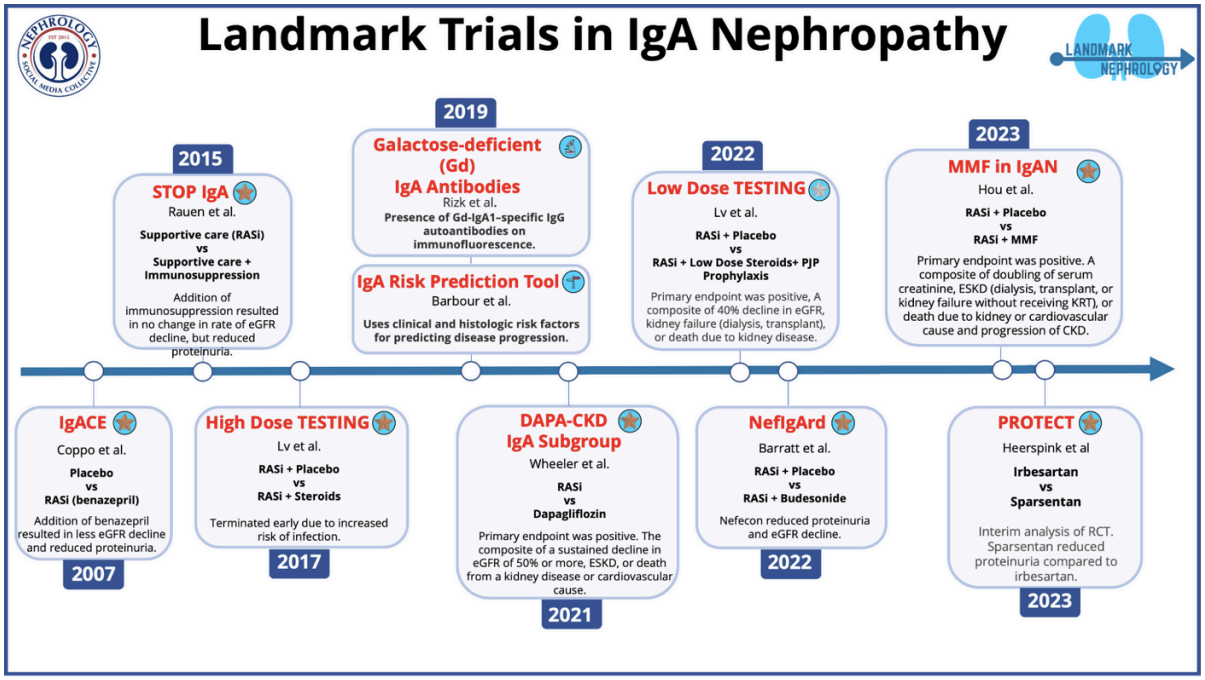
13/ IgAN

🏛️Both standard dose steroids and reduce dose (panel D) have shown improvement in renal outcomes at the measurable cost of infection.

🫘However, we may be able to forgo steroids altogether with the number of treatments available.

👉A great review: https://www.nephjc.com/news/igan-kdigo-2025





14/ Nephrotic Syndrome

🏛️Pediatric patients typically are exposed to steroids for 8-10 weeks, whereas in adults 1-2 years. However, shorter course have been linked to earlier relapse.

🫘Multiple studies have found addition of tacro to low dose steroids is noninferior for new or relapsing disease.

15/ Nephrotic Syndrome

🫘One study with tacro monotherapy have found it to be non-inferior, with continued improvements in remission months later.

🫘Other studies have looked at mycophenolate and rituximab but data is limited to small trials.

Table 3. Summary of randomized controlled trials examining GC-sparing strategies for treating nephrotic syndrome due to minimal change disease in adult patients

Author (year, location)	Duration	Primary outcome	Intervention	Comparator	Key findings
Calcineurin inhibitor					
Miao (2006, China)	24 wks	CR (proteinuria < 0.3 g/d) or PR (proteinuria 0.3–2.9 g/d and serum albumin ≥ 30 g/l)	Tacrolimus 2 g/d plus prednisone 30 mg/d ($n = 30$)	Prednisone 1 mg/kg/d to a max of 60 mg/d ($n = 30$)	All patients achieved CR/PR in both groups CR achieved in 29 (97%) patients in intervention and 27 (90%) in control Less weight gain in intervention group
Eguchi (2010, Japan)	24 wks	CR (proteinuria < 0.3 g/d)	Cyclosporine to target C2 level 600–800 ng/ml (mean dose: 1.8 mg/kg/d) plus prednisone 0.8 mg/kg/d ($n = 26$)	Prednisone 1 mg/kg/d ($n = 26$)	Numerically higher CR rate in cyclosporine/prednisone group at 4 wks (96% vs 77%) Similar rates of CR at 3 mos and 6 mos in both groups Faster mean time to remission in intervention group (13 d vs. 20 d) No reporting of AEs
Li (2017, China)	64 wks	CR (proteinuria < 0.3 g/d) or PR (proteinuria < 3.5 g/d but > 0.3 g/d)	i.v. MP 0.8 mg/kg/d for 10 d followed by tacrolimus 0.05 daily ($n = 63$)	i.v. MP 0.8 mg/kg/d for 10 d followed by prednisone 1 mg/kg/d ($n = 56$)	Similar remission rates in both groups (98% in intervention and 96% in control) Tacrolimus was noninferior to prednisone Similar time to remission in both groups Similar relapse rate in both groups More SAEs in prednisone arm (7 vs. 2)
Medjeral-Thomas (2020, UK)	Median 44 wks	CR at 8 wks (UPCR < 50 mg/mmol)	Tacrolimus 0.1 mg/kg/d ($n = 27$)	Prednisone 1 mg/kg/d to a max of 60 mg daily ($n = 25$)	Lower remission rate in tacrolimus group (63%) than in prednisone (84%) Similar rates of relapses in both groups Similar rates of AEs
Chin (2021, South Korea)	24 wks	CR within 8 weeks (UPCR <0.2 g/g)	Tacrolimus 0.1 mg/kg per day plus prednisone 0.5 mg/kg per day (n=67)	Prednisone 1 mg/kg per day (n=69)	Similar CR rate in tacrolimus/prednisone (79%) and high-dose prednisone (77%) Fewer relapses observed in intervention group (5.7% vs. 22.6%) Similar rate of AEs in both groups

AE, adverse event; CR, complete remission; MP, methylprednisolone; PR, partial remission; SAE, serious AE; UPCR, urine protein-to-creatinine ratio.

16/ FSGS

🏛️High dose steroids are used first line for primary FSGS.

🫘A single-center trial of mycophenolate and reduced steroids compared to standard dose steroids found similar efficacy.

👎Limitation: This study was small with mixed disease population. Additionally, it had not yet been replicated.

17/ Membranous Nephropathy

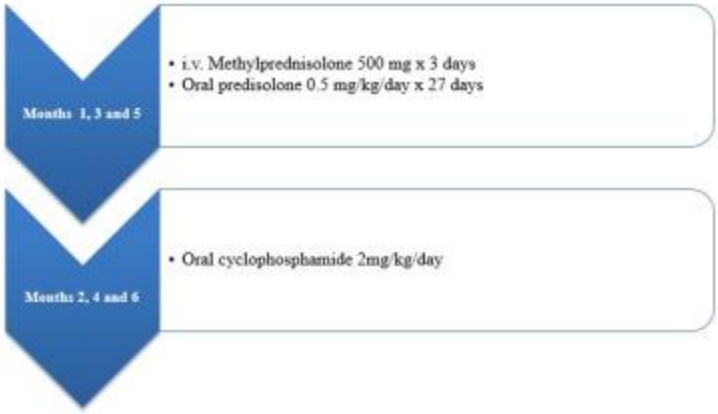
🏛️Steroids have been reserved for severe cases. If they are used, the Ponticelli protocol is typically used.

🫘With discovery of auto-antibodies, rituximab is the preferred treatment.

https://www.kireports.org/article/S2468-0249(19)30625-4/fulltext

https://pubmed.ncbi.nlm.nih.gov/38766897/

Figure 1. A lower-than-standard dose pulse steroid based modification of the conventional 'modified Ponticelli' regimen



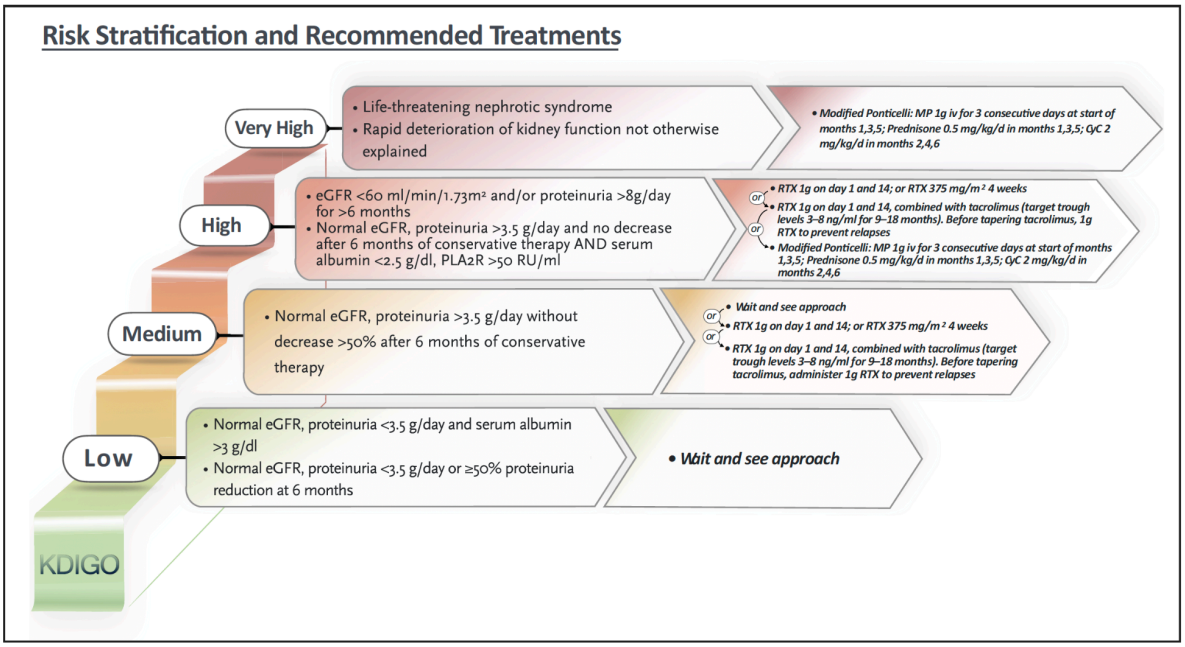


FIGURE 1. Risk stratification proposed on KDIGO guidelines and selection of the most commonly prescribed treatment regimens for each of the immunosuppressants. CyC, cyclophosphamide; RTX, rituximab.

18/ Based on this evidence, what are your thoughts on reduced steroid inductions? Please comment!

19/ The topic remains developing. We hope this #tweetorial has improved your knowledge on the effects of reduced steroids on glomerular diseaess. Please share this #tweetorial with your followers and friends! Thanks to @MChanMD for authoring & *** for great feedback! @ISNkidneycare @KIReports