KDIGO GN Guideline update – Evidence summary

IgA nephropathy and IgA vasculitis - IgA nephropathy

Non-immunosuppressive therapy for IgA nephropathy

PICO question

In patients with biopsy-proven IgA nephropathy, what non-immunosuppressive agents (fish oil, anticoagulants/antiplatelet, antioxidant, tonsillectomy, statins, traditional Chinese medicine, vitamin D, vitamin E, allopurinol, etc.) compared to no treatment/placebo or standard of care improve efficacy (all-cause mortality, end-stage kidney disease, ≥50% loss of GFR, annual loss of GFR, complete remission) outcomes and reduce adverse effects (infection, and malignancy)?

* Note – antihypertensive medication was not covered in this review

Search strategy and selection

Keywords for IgA nephropathy and fish oil, anticoagulant agents, tonsillectomy and other non-immunosuppressive treatments were used to search the Cochrane Kidney and Transplant Specialized Register for all randomized controlled trials (RCTs) published up to May 2018.

Search results

The non-immunosuppressive Cochrane review published in 2011, identified 2872 relevant citations with 433 duplicate reports, 2305 citations were excluded because they were not RCTs, did not include patients with biopsy-proven IgA nephropathy, had less than 75% of patients with IgA nephropathy in the trial, or were the wrong intervention. The review identified 56 primary studies with 56 secondary publications (112 reports) with 2838 participants.

The May 2018 search update for the Cochrane Kidney and Transplant Specialized Register identified 51 citations, of which 15 were excluded because they were not RCTs, did not include patients with biopsy-proven IgA nephropathy, had less than 75% of patients with IgA nephropathy in the trial, or were the wrong intervention. Thirty-six reports were included, of these four reports were of antihypertensive therapy leaving 31 reports (19 primary studies and 12 secondary publications) with 1210 participants that were included in the update for this review.

Overall 75 primary studies (68 secondary publications) with 4048 participants were included.

There were six ongoing studies identified from clinicaltrials.gov

Twenty-one comparisons for induction therapy were included for the following:

1. Fish oil versus placebo (5 studies, 169 participants)
2. Fish oil versus symptomatic treatment (1 study, 34 participants)
3. High dose fish oil versus low dose fish oil (1 study, 73 participants)
4. Anticoagulant versus placebo or no treatment (3 studies, 110 participants)
5. Anticoagulant versus other treatment (2 studies, 52 participants)
6. Anticoagulant plus angiotensin receptor blocker (ARB) versus ARB alone (3 studies, 331 participants)
7. Anticoagulant plus prednisone versus prednisone alone (1 study, 20 participants)
8. Antioxidant versus ARB (1 study, 68 participants)
9. Tonsillectomy plus standard of care versus standard of care alone (3 studies, 177 participants)
10. Statins versus placebo (1 study, 21 participants)
11. Statins plus antiplatelet therapy versus antiplatelet therapy alone (1 study 30 participants)

12. Phenytoin versus no treatment (2 studies, 83 participants)
13. Herbal medicine versus placebo or no treatment (3 studies, 176 participants)
14. Traditional Chinese medicine versus western medicine (3 studies, 205 participants)
15. Traditional Chinese medicine plus western medicine versus western medicine alone (2 studies, 157 participants)
16. Urokinase plus angiotensin converting enzyme inhibitor (ACEi) versus ACEi alone (1 study, 71 participants)
17. Vitamin D versus no treatment (1 study, 50 participants)
18. Vitamin E versus placebo (1 study, 55 participants)
19. Sodium cromoglycate versus placebo/no treatment (1 study, 30 participants)
20. Low-calorie diet versus usual diet (1 study, 26 participants)
21. Allopurinol versus no treatment (1 study, 40 participants)

Summary of the main findings

Fish oil

- Compared with placebo or no treatment, treatment with fish oil may decrease a >50% increase in serum creatinine. There were uncertain effects on other critical and important outcomes because the certainty of the evidence was very low due to study limitations and imprecise effect estimates.
    - The effects of high versus low dose fish oil were uncertain as only end-stage kidney disease was examined in RCTs and the certainty of the evidence was very low.
- Fish oil compared to symptomatic treatment, may slightly decrease the > 50% loss in GFR slightly. However, the effect estimate crosses the line of no effect (RR 0.14, 95%CI 0.02 to 1.01; 1 study, 28 participants).
- Fish oil combined with antihypertensive medication compared to antihypertensive medication alone may improve creatinine clearance (ml/min) (MD 26.20, 95%CI 1.01 to 51.39; 1 study, 30 participants).
    - We are uncertain if fish oil compared to symptomatic treatment increases or decreases other critical or important outcomes, as they were not examined in studies or the certainty of the evidence was very low due to study limitations and imprecise effect estimates.

Anticoagulant therapy

- We are uncertain if treatment with an anticoagulant compared to placebo or no treatment improves critical or important outcomes because the certainty of the evidence is very low (study limitations and imprecision in the effect estimate).
- Compared to hirudin, dipryidamole may increase complete remission (RR 0.27, 95% CI 0.16 to 0.46) but it may decrease creatinine clearance (ml/min) (MD 15.90, 95%CI 19.9 to 11.81 lower). However, its effects on other critical or important outcomes are unclear because the certainty of the evidence was very low, due to study limitations and very serious imprecision (1 study, 262 participants).
- Similarly, we are uncertain if the use of dipyridamole combined with aspirin compared to vitamin B increased or decreased critical or important outcomes because the certainty of the evidence was very low (1 study, 38 participants).
- Compared to treatment with ACEi or ARB alone, the addition of an ACEi or ARB to anticoagulant therapy may have little or no difference on end-stage kidney disease and eGFR. However, the effects on other critical and important outcomes are unclear because the certainty of the evidence is very low.

Antioxidant therapy

- Treatment with an antioxidant (probucol) compared to ARB alone may increase the annual loss of GFR (ml/min/1.73m^2) at three years (MD 1.36 higher, 95%CI 0.32 to 2.40 higher). RCTs did not report other critical, or important outcomes or there were too few events.

Tonsillectomy

- The addition of tonsillectomy to standard of care may increase the remission of proteinuria (RR 1.90, 95%CI 1.45 to 2.47) compared to standard of care alone. It may also increase the remission of microscopic hematuria (RR 1.93 95%CI 1.47 to 2.53) (2 studies, 143 participants). Tonsillectomy may also decrease relapse of proteinuria and hematuria. These trials have only been conducted in patients of Asian ethnicity, and hence the generalizability of these findings are unclear.
    - RCTs did not examine other critical or important outcomes.

Herbal medicine

- Treatment with Huai Qi Huang compared to no treatment may increase remission of proteinuria (RR 2.35, 95%CI 1.30 to 4.26; 1 study, 45 participants). There were uncertain effects on the remission of hematuria and other critical and important outcomes were not examined.
- Traditional Chinese medicine compared to western medicine had uncertain effects on critical and important outcomes because the certainty of the evidence was very low due to study limitations and imprecise effect estimates.

Effect modifiers

The following effect modifiers were considered

- Kidney function (GFR, proteinuria, the presence of albuminuria, the presence of macroscopic hematuria)
- Histopathological class of disease
- Relapse
- Primary versus secondary forms of the disease
- Age (adult versus pediatric)

However, because of a lack of data, subgroup analyses were not possible.

Immunosuppressive therapy of IgA nephropathy

PICO question

In patients with biopsy-proven IgA nephropathy, what immunosuppressive agents compared to no treatment/placebo or other immunosuppressive therapies efficacy (all-cause mortality, end-stage kidney disease, ≥50% loss of GFR, annual loss of GFR, complete remission) outcomes and reduce adverse effects (infection, and malignancy)?

Search strategy and selection

Keywords for IgA nephropathy and immunosuppressive therapy were used to search the Cochrane Kidney and Transplant Specialized Register for all RCTs published up to May 2018.

Search results

The immunosuppressive treatment Cochrane review published in 2011, identified 1196 relevant citations from relevant medical databases, 1159 citations were excluded because they were not RCTs, did not include patients with biopsy-proven IgA nephropathy, had less than 75% of patients with IgA nephropathy in the trial, or were the wrong intervention. The review identified 13 primary studies (21 reports). The 2015 Cochrane review update identified 103 relevant reports from the Cochrane Kidney and Transplant Specialized Register, 19 primary studies (41 reports) were included.

The May 2018 search update for the Cochrane Kidney and Transplant Specialized Register identified 68 reports, seven were excluded because they were duplicates, not RCTs, did not include patients with biopsy-proven IgA nephropathy, had less than 75% of patients with IgA nephropathy in the trial, or were the wrong intervention. The 2018 review update found 22 primary studies (46 reports), four reports of studies already included in the previous Cochrane review, and ten reports of ongoing studies.

Overall 53 primary studies (132 reports) with 3690 participants were included.

There were ten ongoing studies identified from clinicaltrials.gov

Twenty comparisons for induction therapy were included for the following:

1. Steroids (oral, oral + IV, oral + RASi) versus no steroid regimen (placebo/no treatment, usual care) (13 studies, 1110 participants)
2. Steroids plus non-immunosuppressive (RAS, RAS + tonsillectomy) versus steroid (2 studies, 117 participants)
3. Cyclophosphamide then azathioprine plus steroid versus usual care (2 studies, 200 participants)
4. Cyclophosphamide plus steroid versus steroid alone (1 study, 24 participants)
5. Cyclophosphamide plus antiplatelet/anticoagulant versus usual care (3 studies, 178 participants)
6. Azathioprine plus steroids versus placebo/ usual care (1 study, 43 participants)
7. Azathioprine plus steroids versus steroids alone (2 studies, 68 participants)
8. Azathioprine plus anticoagulant/antiplatelet versus anticoagulant/antiplatelet (1 study, 78 participants)
9. Calcineurin inhibitors plus steroids versus steroid alone (1 study, 51 participants)
10. Cyclosporin versus placebo/usual care (1 study, 22 participants)
11. Mycophenolate mofetil versus placebo/usual care (3 studies, 118 participants)
12. Mycophenolate mofetil plus steroids versus steroid alone (1 study, 176 participants)
13. Mycophenolate mofetil plus RASi versus RASi alone (1 study, 40 participants)
14. Mizoribine versus placebo/usual care (1 study, 42 participants)
15. Mizoribine plus steroid versus steroid alone (1 study, 40 participants)
16. Mizoribine plus RASi versus RASi alone (1 study, 99 participants)
17. Leflunomide versus placebo (1 study, 360 participants)
18. Leflunomide plus steroid versus steroid alone (2 studies, 85 participants)
19. Leflunomide plus low dose steroid versus high dose steroid alone (2 studies, 192 participants)
20. Leflunomide versus RASi alone (1 study, 49 participants)

Summary of the main findings

<u>Steroid versus no steroid regimen</u>

- Compared to no steroid regimen, treatment with steroids probably decreased end-stage kidney disease (RR 0.41, 95%CI 0.26 to 0.65; 10 studies, 825 participants) and annual GFR loss (ml/min) (MD 5.40 lower, 95%CI 2.25 lower to 8.55 lower; 2 studies, 359 participants). Also, steroid treatment compared with no steroid treatment may increase complete remission (RR 1.76, 95%CI 1.03 to 3.01). The effects on other critical and important outcomes are unclear because studies did not examine these outcomes or due to study limitations or imprecision in the effect estimate.
    - The protective effects of steroid use on end-stage kidney disease are seen in the use of oral steroids compared to placebo/usual care (RR 0.48, 95%CI 0.29 to 0.79; 7 studies,

579 participants) and steroid plus RASi compared with RASi alone (RR 0.16, 95%CI 0.04 to 0.59; 2 studies, 160 participants).
    - An increase in complete remission was not observed in the comparison of oral steroid with placebo or usual care or steroid plus RASi versus RASi alone. Although, it may decrease annual GFR loss.
    - The use of oral steroids compared with placebo / usual care may decrease doubling serum creatinine (RR 0.45, 95%CI 0.29 to 0.69; 6 studies, 341 participants)
    - Only one study examined the use of oral plus IV steroids compared to no treatment, and the effects were uncertain because studies did not examine critical or important outcomes or due to study limitations and imprecision.

<u>Cytotoxic regimens versus non-cytotoxic regimens</u>

Cyclophosphamide

- The use of cyclophosphamide then azathioprine plus corticosteroids versus supportive therapy may make no difference on end-stage kidney disease or annual loss of GFR, although it increases complete remission (RR 3.41, 95%CI 1.17 to 9.93; 1 study, 162 participants). The effect on other critical and important outcomes are unclear because either RCTs did not look at these outcomes or due to imprecision in the effect estimate and study limitations.
    - Treatment with cyclophosphamide plus steroid compared to steroids alone made no difference to complete remission and we are uncertain about the other critical and important outcomes because the certainty of the evidence was very low.
    - Treatment with cyclophosphamide plus antiplatelet/anticoagulant compared to usual care made no difference to end-stage kidney disease and we are uncertain about the other critical and important outcomes because the certainty of the evidence was very low.

Azathioprine

- The use of azathioprine combined with steroids compared to placebo or usual care increases complete remission (RR 5.94, 95%CI 2.03 to 17.34; 1 study, 43 participants) but we are uncertain of the effects on other critical and important outcomes as RCTs did not examine these outcomes or due to study limitations or two few events.
    - Azathioprine plus steroids plus anticoagulant/antiplatelet therapy compared to anticoagulant/antiplatelet alone may have little or no difference to end-stage kidney disease or complete remission. However, compared to steroids alone it probably increases complete remission (RR 1.24, 95%CI 1.01 to 1.52; 1 study, 78 participants). The effects on other outcomes are unclear because the certainty of the evidence is so low

Calcineurin inhibitors

- Calcineurin inhibitors plus steroids compared with steroids alone may make little or no difference to complete remission (RR 0.91, 95%CI 0.60 to 1.39; 2 studies, 72 participants). The effects on other critical and important outcomes are unclear because the certainty of the evidence is very low due to study limitations and imprecision in the effect estimates.

Mycophenolate mofetil

- Mycophenolate mofetil with or without steroids compared to either steroid or usual care has only been examined in a few small studies and the effects on critical and important outcomes are mostly uncertain
    - Mycophenolate mofetil plus steroids compared with steroids alone may have little or no difference on infection (RR 1.37, 95%CI 0.83 to 2.24; 1 study. 175 participants) and complete remission (RR 0.99, 95%CI 0.68 to 1.46; 1 study, 174 participants)

- Mycophenolate mofetil plus a RASi compared with a RASi alone may decrease end-stage kidney disease (RR 0.22, 95%CI 0.05 to 0.90; 1 study, 40 participants) but the effects on other outcomes are uncertain as other critical and important outcomes were not examined.

Other immunosuppressive agents

- The effects of a mizoribine regimen compared with no mizoribine on critical and important outcomes are uncertain because there have only been a few small RCTs.
- The effects of leflunomide with or without low dose steroids compared to a non-leflunomide regimen are uncertain due to study limitations and imprecision in the effect estimates. Many critical and important outcomes were not examined in these RCTs.

Effect modifiers

The following table lists the effect modifiers considered for comparisons. Only one comparison, steroid versus no steroid had sufficient data (13 trials, 1110 participants).

Effect modifier	Explanation/ results
Kidney function (GFR, presence of proteinuria, presence of albuminuria)	Subgroups determined by kidney function were no examined in many of the RCTs. However the TESTING 2017 (1) study had pre-specified subgroups for composite outcome (≥40% GFR loss, ESKD, death due to kidney failure): • Proteinuria - <3.0 g/day proteinuria (RR 0.2 95%CI 0.05 to 0.9); ≥3.0 g/day proteinuria (RR 0.4, 95%CI 0.17 to 0.97) • Baseline eGFR – <50 ml/min/1.73m^2 (RR 0.60, 95%CI 0.25 to 1.40); ≥50 ml/min/1.73m^2 (RR 0.12, 95%CI 0.02 to 0.97)
Relapse or resistant disease	RCTs did not examine the treatment of patients with relapsing or resistant IgA nephropathy.
Histopathological class of disease	RCTs did not examine results in regards to the class of IgA nephropathy.
Gender	The RCTs similarly included around 65% of male.
Age (adult vs. pediatric)	One trial Kobayashi 1996 (2), included children <15 years of age. Similar results to the overall effect estimate (included both adults and children) were reported. That treatment with steroids (oral) decreased ESKD and doubling serum creatinine compared to placebo or usual care.

1. Lv J, et al. Effect of oral methylprednisolone on clinical outcomes in patients with IgA nephropathy: the TESTING randomized clinical trial. JAMA 2017;318(5):432-42.
2. Koitabashi Y, et al. Randomized, prospective, multi-center trial for treatment of IgA nephropathy in children [abstract no: S-5]. Pediatric Nephrology 1996;10(1):C4.

Studies from the 2012 KDIGO GN guideline evidence tables not included in 2018 evidence review.

Non-immunosuppressive therapy

All RCTs included in the previous guideline evidence summary have been included in this evidence review, except for Walker RG et al 1990 (1) as this has been covered included in the immunosuppressive treatment for IgA nephropathy review.

Walker RG, et al. The treatment of mesangial IgA nephropathy with cyclophosphamide, dipyridamole and warfarin: a two-year prospective trial. Clinical Nephrology. 1990;34(3):103-7

Immunosuppressive therapy

Steroid versus no steroid regimen

1. Pozzi 2004 – Long-term follow-up study of Pozzi 1999 that has been included in the meta-analysis. All data from long-term follow-up studies are included in the meta-analysis if an attrition rate over 70% is maintained.

Pozzi C: Corticosteroid effectiveness in IgA nephropathy: long-term results of a randomized, controlled trial. *JASN.* 2004;*15(1):157-63*

2. Manno 2009 - Long-term follow-up study of Manno 2001 that has been included in the meta-analysis. All data from long-term follow-up studies are included in the meta-analysis if an attrition rate over 70% is maintained.

Manno C et al. Randomized controlled clinical trial of corticosteroids plus ACE-inhibitors with long-term follow-up in proteinuric IgA nephropathy. *NDT.* 2009;24(12):3694-701

PICO (18.1)
Population: Patients with IgA nephropathy
Intervention: Steroid regimen
Comparator: no steroid regimen

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** no steroid regimen	Steroid	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 1.85 (CI 95% 0.17 - 20.19) Based on data from 262 patients in 1 studies Follow up 25 months (estimated 5 years)	**8** per 1000	**15** per 1000 Difference: **7 more per 1000** (CI 95% 7 fewer - 154 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision,[1]	We are uncertain whether steroid improves or worsen all-cause mortality
End-stage kidney disease	Relative risk: 0.41 (CI 95% 0.26 - 0.65) Based on data from 825 patients in 10 studies Follow up 1-10 years, mean 21 months	**160** per 1000	**66** per 1000 Difference: **94 fewer per 1000** (CI 95% 118 fewer - 56 fewer)	**Moderate** Due to serious risk of bias[2]	Steroid probably decreases end stage kidney disease
≥50% GFR loss	Relative risk: 0.56 (CI 95% 0.25 - 1.24) Based on data from 326 patients in 2 studies Follow up 2-5 years, mean 24.5 months	**95** per 1000	**53** per 1000 Difference: **42 fewer per 1000** (CI 95% 71 fewer - 23 more)	**Low** Due to serious risk of bias, Due to serious imprecision[3]	Steroid (oral) versus placebo or usual care may have little or no difference on ≥50% GFR loss
Infection	Relative risk: 3.31 (CI 95% 0.14 - 76.58) Based on data from 412 patients in 2 studies[4] Follow up 1-5 years, mean 18.5	**17** per 1000	**56** per 1000 Difference: **39 more per 1000** (CI 95% 15 fewer - 1285 more)	**Very Low** Due to serious inconsistency, Due to serious risk of bias, Due to serious imprecision[5]	We are uncertain whether steroid (oral) versus placebo or usual care increases or decreases infection
Malignancy	Relative risk: 1.0 (CI 95% 0.06 - 15.48) Based on data from 86 patients in 1 studies Follow up 6 years	**23** per 1000	**23** per 1000 Difference: **0 fewer per 1000** (CI 95% 22 fewer - 333 more)	**Low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether steroid increases or decreases malignancy
Complete remission	Relative risk: 1.76 (CI 95% 1.03 - 3.01) Based on data from 305 patients in 4 studies Follow up 1-5 years, mean 30 months	**364** per 1000	**641** per 1000 Difference: **277 more per 1000** (CI 95% 11 more - 732 more)	**Low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision, Upgraded due to Large magnitude of effect[7]	Steroid compared to no steroid may increase complete remission
Annual GFR loss 5 years	Measured by: Scale: - Lower better Based on data from 359 patients in 2 studies Follow up 5 years	**6.56** Mean	**5.40** Mean Difference: **MD 5.40 lower** (CI 95% 2.25 lower - 8.55 lower)	**Low** Due to very serious risk of bias, Due to serious imprecision, Upgraded due to Large magnitude of effect[8]	Steroid compared to no steroid treatment may decrease annual GFR loss

1. **Risk of bias: Serious.** Trail terminated early due to excess serious adverse events; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, due to few events;
2. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias;
3. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Wide confidence intervals,;
4. Systematic review [26] with included studies: NEFIGAN 2017, TESTING 2017 **Baseline/comparator:** Control arm of reference used for intervention .
5. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome

assessors, resulting in potential for detection bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 76 %.; **Imprecision: Serious.** Wide confidence intervals, due to few infection events;

6. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, due to few malignancy events, Only data from one study;
7. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 69%.; **Imprecision: Serious.** Wide confidence intervals; **Upgrade: Large magnitude of effect.**
8. **Risk of bias: Very Serious.** due to Due to trial terminated early because of excess serious adverse events., Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Wide confidence intervals; **Upgrade: Large magnitude of effect.**

References

[26] Immunosuppressive agents for treating IgA nephropathy. 2018;

PICO (18.2)
Population: Patients with IgA nephropathy
Intervention: Steroid (oral)
Comparator: Placebo / usual care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** placebo / usual care	Steroid (oral)	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 1.85 (CI 95% 0.17 - 20.19) Based on data from 262 patients in 1 studies Follow up median 25 months (estimated 5 years)	**8** per 1000	**15** per 1000 Difference: **7 more per 1000** (CI 95% 7 fewer - 154 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether steroid (oral) versus placebo or usual care increases or decreases all-cause mortality
End-stage kidney disease	Relative risk: 0.48 (CI 95% 0.29 - 0.79) Based on data from 579 patients in 7 studies[2] Follow up 16 months average	**166** per 1000	**80** per 1000 Difference: **86 fewer per 1000** (CI 95% 118 fewer - 35 fewer)	**Moderate** Due to serious risk of bias[3]	Steroid (oral) versus placebo or usual care probably decreases end stage kidney disease
≥50% GFR loss	Relative risk: 0.56 (CI 95% 0.25 - 1.24) Based on data from 326 patients in 2 studies[4] Follow up 2-5 years, mean 24.5 months	**96** per 1000	**54** per 1000 Difference: **42 fewer per 1000** (CI 95% 72 fewer - 23 more)	**Low** Due to serious risk of bias[5]	Steroid (oral) versus placebo or usual care may have little or no difference on ≥50% GFR loss
Infection	Relative risk: 3.31 (CI 95% 0.14 - 76.58) Based on data from 412 patients in 2 studies[6] Follow up 1-5 years, mean 18.5 months	**17** per 1000	**56** per 1000 Difference: **39 more per 1000** (CI 95% 15 fewer - 1285 more)	**Very Low** Due to serious imprecision, Due to serious inconsistency[7]	We are uncertain whether - steroid (oral) versus placebo or usual care increases or decreases infection
Complete remission	Relative risk: 3.47 (CI 95% 0.71 - 17.08) Based on data from 145 patients in 2 studies[8] Follow up 1-5 years, mean 18.5 months	**167** per 1000	**579** per 1000 Difference: **412 more per 1000** (CI 95% 48 fewer - 2685 more)	**Very Low** Due to serious risk of bias, Due to serious imprecision, Due to serious inconsistency[9]	We are uncertain whether steroid (oral) versus placebo or usual care increases or decreases complete remission
Doubling of serum creatinine	Relative risk: 0.45 (CI 95% 0.29 - 0.69) Based on data from 341 patients in 6 studies[10] Follow up Mean 50 months	**326** per 1000	**147** per 1000 Difference: **179 fewer per 1000** (CI 95% 231 fewer - 101 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[11]	Steroid (oral) versus placebo or usual care slightly may increase doubling of serum creatinine
Annual GFR loss	Measured by: Scale: - Lower better Based on data from 262 patients in 1 studies[12]	ml/min/m^2Mean	ml/min/m^2Mean Difference: **MD 5.16 higher** (CI 95% 0.53 higher - 9.79 higher)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[13]	We are uncertain whether steroid (oral) versus placebo or usual care increases or decreases annual GFR loss

1. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals consistent appreciable or harm;
2. Systematic review [25] with included studies: TESTING 2017, Kobayashi 1996, NA IgAN 1995, Lai 1986, Shoji 2000, Katafuchi 2003, Julian 1993 **Baseline/comparator:** Control arm of reference used for intervention .
3. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting, due to other issue;
4. Systematic review [25] with included studies: TESTING 2017, NA IgAN 1995 **Baseline/comparator:** Control arm of reference used for intervention .

5. **Risk of bias: Very Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias;
6. Systematic review [25] with included studies: NEFIGAN 2017, TESTING 2017 **Baseline/comparator:** Control arm of reference used for intervention .
7. **Risk of bias: No serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting, Incomplete data and/or large loss to follow up; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high; **Imprecision: Serious.** Wide confidence intervals consistent with appreciable benefit or harm;
8. Systematic review [25] with included studies: TESTING 2017, Lai 1986 **Baseline/comparator:** Control arm of reference used for intervention .
9. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high; **Imprecision: Serious.** Wide confidence intervals;
10. Systematic review [25] with included studies: Julian 1993, Katafuchi 2003, Kobayashi 1996, Pozzi 1999, Shoji 2000, Lai 1986 **Baseline/comparator:** Control arm of reference used for intervention .
11. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Wide confidence intervals;
12. Systematic review [25] with included studies: TESTING 2017 **Baseline/comparator:** Control arm of reference used for intervention .
13. **Risk of bias: Serious.** Due to Trial terminated early because of excess serious adverse events.; **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals;

References

[25] Immunosuppressive agents for treating IgA nephropathy. 2018;

PICO (18.3)
Population: Patients with IgA nephropathy
Intervention: Steroid (IV + oral)
Comparator: placebo / usual care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** placebo / usual care	Steroid (IV + oral)	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	Relative risk: 0.14 (CI 95% 0.01 - 2.68) Based on data from 86 patients in 1 studies Follow up 6 years	**70** per 1000	**10** per 1000	**Very Low** Due to serious risk of bias, Due to serious imprecision[1]	We are uncertain whether steroid (iv + oral) versus placebo or usual care improves or worsen end-stage kidney disease
		Difference: **60 fewer per 1000** (CI 95% 69 fewer - 118 more)			
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Malignancy	Relative risk: 1.0 (CI 95% 0.06 - 15.48) Based on data from 86 patients in 1 studies Follow up 6 years	**23** per 1000	**23** per 1000	**Very Low** Due to serious risk of bias, Due to serious imprecision[2]	There were too few who experienced the malignancy to determine whether steroid made a difference
		Difference: **0 fewer per 1000** (CI 95% 22 fewer - 333 more)			
Infection	(CI 95% -)	Difference: **fewer**			No studies were found that looked at infection
Complete remission	(CI 95% -)	Difference: **fewer**			No studies were found that looked at complete remission
Annual GFR loss	Measured by: Scale: - Lower better	Difference: **null lower**			No studies were found that looked at annual GFR loss

1. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. Four patients in the control group received steroids as rescue therapy ; **Imprecision: Serious.** Only data from one study;
2. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals consistent with appreciable benefit or harm, Only data from one study, due to few events;

PICO (18.4)
Population: Patients with IgA nephropathy
Intervention: Steroid (oral) plus RASi
Comparator: RASi alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** no steroid regimen	**Absolute effect estimates** Steroid (oral) plus RASi	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Doubling of serum creatinine	Relative risk: 0.26 (CI 95% 0.06 - 1.15) Based on data from 63 patients in 1 studies[1] Follow up 48 months	**233** per 1000	**61** per 1000 Difference: **172 fewer per 1000** (CI 95% 219 fewer - 35 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether steroid (oral) plus RASi versus RASi alone increases or decreases doubling of serum creatinine
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Infection	(CI 95% -)	Difference: **fewer**			No studies were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies were found that looked at malignancy
End-stage kidney disease	Relative risk: 0.16 (CI 95% 0.04 - 0.59) Based on data from 160 patients in 2 studies[3] Follow up 42 months	**190** per 1000	**30** per 1000 Difference: **160 fewer per 1000** (CI 95% 182 fewer - 78 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Steroid (oral) plus RASi versus RASi alone may have little or no difference on end-stage kidney disease
Complete remission	Relative risk: 1.41 (CI 95% 0.8 - 2.48) Based on data from 160 patients in 2 studies[5] Follow up Mean 54 months	**544** per 1000	**767** per 1000 Difference: **223 more per 1000** (CI 95% 109 fewer - 805 more)	**Very Low** Due to serious risk of bias[6]	We are uncertain whether steroid plus RASi versus RASi alone increases or decreases complete remission
Annual GFR loss	Measured by: Scale: - Lower better Based on data from 97 patients in 1 studies[7] Follow up Median 60 months	Mean	Mean Difference: **MD 5.61 higher** (CI 95% 1.31 higher - 9.91 higher)	**Low** Due to serious risk of bias, Due to very serious imprecision, Upgraded due to Large magnitude of effect[8]	Steroid (oral) plus RASi versus RASi alone may improve annual GFR loss

1. Primary study Lv 2009 **Baseline/comparator:** Control arm of reference used for intervention .
2. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
3. Systematic review [25] with included studies: Lv 2009, Manno 2001 **Baseline/comparator:** Control arm of reference used for intervention .

4. **Risk of bias: Serious.** Due to inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study, Low number of patients;
5. Systematic review [25] with included studies: Manno 2001, Lv 2009 **Baseline/comparator:** Control arm of reference used for intervention .
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias;
7. Primary study Manno 2001 **Baseline/comparator:** Control arm of reference used for intervention .
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals; **Upgrade: Large magnitude of effect.**

References

[25] Immunosuppressive agents for treating IgA nephropathy. 2018;

PICO (18.5)
Population: Patients with IgA nephropathy
Intervention: Steroid plus RASi
Comparator: steroid alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** steroid alone	Steroid plus RASi	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Infection	(CI 95% -)	Difference: **fewer**			No studies were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies were found that looked at malignancy
Complete remission	Relative risk: 1.08 (CI 95% 0.84 - 1.39) Based on data from 38 patients in 1 studies	**833** per 1000	**900** per 1000 Difference: **67 more per 1000** (CI 95% 133 fewer - 325 more)	**Low** Due to serious risk of bias, Due to serious imprecision[1]	Steroid plus RASi compared with steroid alone may have little or no difference on complete remission
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference: **null lower**			No studies were found that looked at annual GFR loss
GFR	Measured by: Scale: - High better Based on data from 38 patients in 1 studies	Mean	Mean Difference: **MD 16 higher** (CI 95% 6.89 lower - 38.89 higher)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether steroid plus RASi increases or decreases GFR compared to steroid alone

1. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients;
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Only data from one study;

PICO (18.6)
Population: Patients with IgA nephropathy
Intervention: Steroid plus tonsillectomy plus angiotensin II receptor blockers
Comparator: steroid plus tonsillectomy

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** steroid plus tonsillectomy	Steroid plus tonsillectomy plus angiotensin II receptor blockers	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Infection	(CI 95% -)	Difference: **fewer**			No studies were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies were found that looked at malignancy
Complete remission	Relative risk: 0.93 (CI 95% 0.56 - 1.53) Based on data from 77 patients in 1 studies	**459.0** Difference: **32.0 fewer** (CI 95% 202.0 fewer - 243.0 more)	**427.0**	**Very Low** Due to serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether steroid plus tonsillectomy plus ARB increases or decreases complete remission compared to tonsillectomy alone
Annual GFR loss	Measured by: Scale: - Lower better	Difference: **null lower**			No studies were found that looked at annual GFR loss

1. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Low number of patients, Only data from one study, Wide confidence intervals;

PICO (18.7)
Population: Patients with IgA nephropathy
Intervention: Cytotoxic regimen
Comparator: no cytotoxic regimen

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** no cytotoxic regimen	Cytotoxic regimen	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.98 (CI 95% 0.06 - 15.33) Based on data from 162 patients in 1 studies Follow up 3 years	**13** per 1000	**13** per 1000 Difference: **0 fewer per 1000** (CI 95% 12 fewer - 186 more)	**Low** Due to serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether cyclophosphamide then azathioprine plus steroid versus steroid increases or decreases all-cause mortality
≥50% GFR loss	(CI 95% -)		Difference: **fewer**		No studies were found that looked at ≥50% GFR loss
End stage kidney disease	Relative risk: 0.63 (CI 95% 0.33 - 1.2) Based on data from 200 patients in 2 studies[2] Follow up 1-7 years	**166** per 1000	**105** per 1000 Difference: **61 fewer per 1000** (CI 95% 111 fewer - 33 more)	**Low** Due to serious risk of bias, Due to serious imprecision[3]	Cytotoxic regimen may have little or no difference on end stage kidney disease - cyclophosphamide then azathioprine plus steroid versus usual care
Infection	Relative risk: 1.7 (CI 95% 0.43 - 6.76) Based on data from 268 patients in 4 studies[4] Follow up 1 to 7 years	**22** per 1000	**37** per 1000 Difference: **15 more per 1000** (CI 95% 13 fewer - 127 more)	**Very Low** Due to very serious imprecision[5]	There were few patients who experienced infection, to determine whether cytotoxic regimen made a difference
Complete remission	Relative risk: 3.41 (CI 95% 1.17 - 9.93) Based on data from 162 patients in 1 studies Follow up 1-5 years	**50** per 1000	**171** per 1000 Difference: **121 more per 1000** (CI 95% 8 more - 447 more)	**Very Low** Due to serious inconsistency[6]	We are uncertain whether cytotoxic regimen increases or decreases complete remission
Malignancy[7]	Relative risk: 4.88 (CI 95% 0.24 - 100.08) Based on data from 162 patients in 1 studies Follow up 36 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (CI 95% 0 fewer - 0 fewer)	**Very Low** Due to serious risk of bias, Due to very serious imprecision,[8]	There were too few who experienced the malignancy - cyclophosphamide then azathioprine plus steroid versus usual care, to determine whether cytotoxic regimen made a difference
Annual GFR loss[9]	Measured by: Scale: - Based on data from 162 patients in 1 studies Follow up 36 months		Difference: **MD 0.01 lower** (CI 95% 0.03 lower - 0.01 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	We are uncertain whether cyclophosphamide then azathioprine plus steroid versus usual care regimen increases or decreases annual GFR loss, ml/min per 1.73 m2

1. **Risk of bias: No serious.** Due to open -label study, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study;
2. Systematic review [25] with included studies: Ballardie 2002, STOP-IgAN 2008 **Baseline/comparator:** Control arm of reference used for intervention .

3. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Selective outcome reporting; **Imprecision: Serious.**
4. Systematic review [25] with included studies: Ballardie 2002, STOP-IgAN 2008 **Baseline/comparator:** Control arm of reference used for intervention .
5. **Risk of bias: Very Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** due to low infection events, Low number of patients;
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2 72%., Point estimates vary widely; **Imprecision: Very Serious.** Wide confidence intervals; **Upgrade: Large magnitude of effect.**
7. Cyclophosphamide then azathioprine plus steroid versus usual care
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals, due to lack of events;
9. , ml/min per 1.73 m2 - Cyclophosphamide then azathioprine plus steroid versus usual care
10. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study;

References

[25] Immunosuppressive agents for treating IgA nephropathy. 2018;

PICO (18.8)
Population: Patients with IgA nephropathy
Intervention: Cyclophosphamide then azathioprine plus steroid
Comparator: Supportive therapy

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Supportive therapy	**Absolute effect estimates** Cyclophosphamide then azathioprine plus steroid	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.98 (CI 95% 0.06 - 15.33) Based on data from 162 patients in 1 studies Follow up 36 months	**13** per 1000	**13** per 1000 Difference: **0 fewer per 1000** (CI 95% 12 fewer - 186 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether cyclophosphamide then azathioprine plus steroid compared with usual care increases or decreases all-cause mortality
End-stage kidney disease	Relative risk: 0.49 (CI 95% 0.14 - 1.75) Based on data from 200 patients in 2 studies[2] Follow up Mean 42 months	**212** per 1000	**104** per 1000 Difference: **108 fewer per 1000** (CI 95% 182 fewer - 159 more)	**Low** Due to serious risk of bias, Due to serious imprecision[3]	Cyclophosphamide then azathioprine plus steroid versus usual care may have little or no difference on end-stage kidney disease
Malignancy	Relative risk: 4.88 (CI 95% 0.28 - 100.08) Based on data from 162 patients in 1 studies Follow up 36 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (CI 95% 0 fewer - 0 fewer)	**Very Low** Due to serious risk of bias, Due to very serious imprecision,[4]	There were too few who experienced the malignancy - cyclophosphamide then azathioprine plus steroid versus usual care, to determine whether cytotoxic regimen made a difference
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Infection	Relative risk: 4.65 (CI 95% 0.54 - 39.85) Based on data from 200 patients in 2 studies[5] Follow up Mean 42 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (CI 95% 0 fewer - 0 fewer)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[6]	There were too few infections in the usual care arm to determine whether cyclophosphamide then azathioprine plus steroid made a difference
Complete remission	Relative risk: 3.41 (CI 95% 1.17 - 9.93) Based on data from 162 patients in 1 studies Follow up 36 months	**50** per 1000	**171** per 1000 Difference: **121 more per 1000** (CI 95% 9 more - 447 more)	**High** Due to serious risk of bias, Due to serious imprecision, Upgraded due to Very large magnitude of effect[7]	Cyclophosphamide then azathioprine plus steroid compared to usual care increases complete remission
Annual GFR loss	Measured by: Scale: - Lower better Based on data from 162 patients in 1 studies Follow up 36 months	Mean	Mean Difference: **MD 0.01 lower** (CI 95% 0.03 lower - 0.01 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Cyclophosphamide then azathioprine plus steroid compared with usual care may have little or no difference on annual GFR loss

1. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

2. Systematic review [25] with included studies: Ballardie 2002, STOP-IgAN 2008 **Baseline/comparator:** Control arm of reference used for intervention .
3. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Selective outcome reporting; **Imprecision: Serious.** Wide confidence intervals;
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals, due to lack of events, Wide confidence intervals, Only data from one study, Low number of patients;
5. Systematic review [25] with included studies: Ballardie 2002, STOP-IgAN 2008 **Baseline/comparator:** Control arm of reference used for intervention .
6. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Wide confidence intervals;
7. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study; **Upgrade: Very large magnitude of effect.**
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study;

References

[25] Immunosuppressive agents for treating IgA nephropathy. 2018;

PICO (18.9)
Population: Patients with IgA nephropathy
Intervention: Cyclophosphamide plus steroid
Comparator: Steroid alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Steroid alone	Cyclophosphamide plus steroid	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Infection	(CI 95% -)	Difference: **fewer**			No studies were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies were found that looked at infection
Complete remission	Relative risk: 0.78 (CI 95% 0.44 - 1.39) Based on data from 24 patients in 1 studies Follow up 6 months	**750** per 1000	**585** per 1000 Difference: **165 fewer per 1000** (CI 95% 420 fewer - 292 more)	**Low** Due to serious risk of bias, Due to serious imprecision[1]	Cyclophosphamide plus steroid compared with steroid alone may have little or no difference on complete remission
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference: **null lower**			No studies were found that looked at annual GFR loss

1. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Wide confidence intervals, Low number of patients;

PICO (18.10)
Population: Patients with IgA nephropathy
Intervention: Cyclophosphamide plus antiplatelet/anticoagulant
Comparator: Usual care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Usual care	Cyclophosphamide plus antiplatelet/anticoagulant	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	Relative risk: 0.31 (CI 95% 0.03 - 2.85) Based on data from 100 patients in 2 studies[1] Follow up Mean 27 months	**42** per 1000	**13** per 1000 Difference: **29 fewer per 1000** (CI 95% 41 fewer - 78 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Cyclophosphamide plus antiplatelet/anticoagulant compared with usual care may have little or no difference on end-stage kidney disease
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Infection	(CI 95% -)	Difference: **fewer**			No studies were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**			No studies were found that looked at complete remission
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference: **null lower**			No studies were found that looked at annual GFR loss

1. Systematic review [25] with included studies: Woo 1987, Walker 1990 **Baseline/comparator:** Control arm of reference used for intervention .
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting (adverse events and all-cause mortality not reported (Walker 1990)), due to other bias (imbalance in duration of follow up and proteinuria between treatment groups, Woo 1987). ; **Imprecision: Serious.** Wide confidence intervals;

References

[25] Immunosuppressive agents for treating IgA nephropathy. 2018;

PICO (18.11)
Population: Patients with IgA nephropathy
Intervention: Azathioprine plus steroid
Comparator: placebo/usual care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** placebo/usual care	Azathioprine plus steroid	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Complete remission	Relative risk: 5.94 (CI 95% 2.03 - 17.34) Based on data from 43 patients in 1 studies Follow up Median 60 months	**136** per 1000	**808** per 1000 Difference: **672 more per 1000** (CI 95% 140 more - 2222 more)	**High** Due to serious risk of bias, Due to serious imprecision, Upgraded due to Very large magnitude of effect[1]	Azathioprine plus steroid compared with steroid alone increases complete remission
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Infection	(CI 95% -)	Difference: **fewer**			No studies were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies were found that looked at malignancy
End-stage kidney disease	Relative risk: 3.14 (CI 95% 0.13 - 72.96) Based on data from 43 patients in 1 studies Follow up Median 60 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (CI 95% 0 fewer - 0 fewer)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[2]	There were too few events of end-stage kidney disease in the placebo/usual care arm to determine whether azathioprine plus steroid made a difference
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference: **null lower**			No studies were found that looked at annual GFR loss

1. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients; **Upgrade: Very large magnitude of effect.**
2. **Risk of bias: Very Serious.** Selective outcome reporting, Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study, Wide confidence intervals, Only data from one study;

PICO (18.12)
Population: Patients with IgA nephropathy
Intervention: Azathioprine
Comparator: Steroid alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Steroid alone Azathioprine	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies were found that looked at all-cause mortality
Infection	Relative risk: 0.85 (CI 95% 0.14 - 5.1) Based on data from 68 patients in 2 studies[1] Follow up Mean 48 months	**83** per 1000 **71** per 1000 Difference: **12 fewer per 1000** (CI 95% 71 fewer - 340 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision,[2]	We are uncertain whether azathioprine compared with steroids alone increases or decreases infection
≥50% GFR loss	(CI 95% -)	Difference: **fewer**		No studies were found that looked at ≥50% GFR loss
End-stage kidney disease	Relative risk: 1.17 (CI 95% 0.59 - 2.32) Based on data from 46 patients in 1 studies Follow up 7 years	**385** per 1000 **450** per 1000 Difference: **65 more per 1000** (CI 95% 158 fewer - 508 more)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[3]	We are uncertain whether azathioprine compared with steroids alone increases or decreases end-stage kidney disease
Malignancy	(CI 95% -)	Difference: **fewer**		No studies were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**		No studies were found that looked at complete remission
Annual GFR loss	Measured by: Scale: - Lower better	Difference: **null lower**		No studies were found that looked at annual GFR loss

1. Systematic review [25] with included studies: Locatelli 1999, Stangou 2011 **Baseline/comparator:** Control arm of reference used for intervention .
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
3. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study, Wide confidence intervals;

References

[25] Immunosuppressive agents for treating IgA nephropathy. 2018;

PICO (18.13)
Population: Patients with IgA nephropathy
Intervention: Azathioprine plus steroid plus anticoagulant/antiplatelet
Comparator: anticoagulant/antiplatelet

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** anticoagulant/ antiplatelet	Azathioprine plus steroid plus anticoagulant/ antiplatelet	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Complete remission	Relative risk: 1.13 (CI 95% 0.76 - 1.7) Based on data from 74 patients in 1 studies Follow up 2 years	**529** per 1000	**598** per 1000 Difference: **69 more per 1000** (CI 95% 127 fewer - 370 more)	**Low** Due to serious risk of bias, Due to serious imprecision[1]	Azathioprine plus steroid plus anticoagulant/antiplatelet compared with anticoagulant/antiplatelet alone may have little or no difference on complete remission
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Infection	(CI 95% -)	Difference: **fewer**			No studies were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies were found that looked at malignancy
End-stage kidney disease	Relative risk: 0.34 (CI 95% 0.07 - 1.64) Based on data from 74 patients in 1 studies Follow up 2 years	**147** per 1000	**50** per 1000 Difference: **97 fewer per 1000** (CI 95% 137 fewer - 94 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Azathioprine plus steroid plus anticoagulant/antiplatelet compared with anticoagulant/antiplatlet alone may have little or no difference on end-stage kidney disease
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference: **null lower**			No studies were found that looked at annual GFR loss

1. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study, Low number of patients;
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Wide confidence intervals;

PICO (18.14)
Population: Patients with IgA nephropathy
Intervention: Azathioprine plus steroids plus anticoagulants
Comparator: Steroids alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Steroids alone	Azathioprine plus steroids plus anticoagulants	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Infection	(CI 95% -)	Difference: **fewer**			No studies were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies were found that looked at malignancy
Complete remission	Relative risk: 1.24 (CI 95% 1.01 - 1.52) Based on data from 78 patients in 1 studies Follow up 2 years	**744** per 1000	**923** per 1000 Difference: **179 more per 1000** (CI 95% 7 more - 387 more)	**Moderate** Due to serious risk of bias, Due to serious imprecision, Upgraded due to Large magnitude of effect[1]	Azathioprine plus steroids plus anticoagulants compared with steroids alone probably increases complete remission
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference: **null lower**			No studies were found that looked at annual GFR loss

1. **Risk of bias: Serious.** Selective outcome reporting, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study, Low number of patients; **Upgrade: Large magnitude of effect.**

PICO (18.15)
Population: Patients with IgA nephropathy
Intervention: Calcineurin inhibitor plus steroid
Comparator: Steroid alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Steroid alone	Calcineurin inhibitor plus steroid	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Infection	Relative risk: 0.31 (CI 95% 0.03 - 2.74) Based on data from 48 patients in 1 studies Follow up 12 months	**130** per 1000	**40** per 1000 Difference: **90 fewer per 1000** (CI 95% 126 fewer - 226 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether calcineurin inhibitor compared to steroids plus steroid versus steroid increases or decreases infection
Malignancy	Relative risk: 0.36 (CI 95% 0.02 - 8.45) Based on data from 48 patients in 1 studies Follow up 12 months	**40** per 1000	**14** per 1000 Difference: **26 fewer per 1000** (CI 95% 39 fewer - 298 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether calcineurin plus steroid versus steroid increases or decreases malignancy
Complete remission	Relative risk: 0.91 (CI 95% 0.6 - 1.39) Based on data from 72 patients in 2 studies[3] Follow up Mean 9 months	**541** per 1000	**492** per 1000 Difference: **49 fewer per 1000** (CI 95% 216 fewer - 211 more)	**Low** Due to very serious risk of bias[4]	Calcineurin inhibitor plus steroid compared with steroid alone may have little or no difference on complete remission
Annual GFR loss	Measured by: Scale: - Lower better Based on data from 1 patients in 22 studies	Mean	Mean Difference: **MD 4.50 higher** (CI 95% 7.36 lower - 16.36 higher)		No studies were found that looked at annual GFR loss

1. **Risk of bias: Serious.** Selective outcome reporting, Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Only data from one study, due to few infections, Low number of patients;
2. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Low number of patients, only data from one study, due to few malignancy events,;
3. Systematic review [25] with included studies: Liu 2014, Shen 2013 **Baseline/comparator:** Control arm of reference used for intervention .
4. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: No serious.** Low number of patients;

References

[25] Immunosuppressive agents for treating IgA nephropathy. 2018;

PICO (18.16)
Population: Patients with IgA nephropathy
Intervention: Mycophenolate mofetil
Comparator: steroid/usual care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Steroid/usual care	Mycophenolate mofetil	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -) Based on data from 0 patients in 0 studies	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	Relative risk: 2.37 (CI 95% 0.63 - 8.96) Based on data from 66 patients in 2 studies[1] Follow up Mean 24 months	**71** per 1000	**168** per 1000 Difference: **97 more per 1000** (CI 95% 26 fewer - 565 more)	**Very Low** Due to serious risk of bias, Due to serious imprecision, Due to very serious imprecision[2]	We are uncertain whether mycophenolate mofetil compared to placebo/usual care increases or decreases end-stage kidney disease
≥50% GFR loss	Relative risk: 2.21 (CI 95% 0.5 - 9.74) Based on data from 32 patients in 1 studies Follow up 12 months	**133** per 1000	**294** per 1000 Difference: **161 more per 1000** (CI 95% 67 fewer - 1162 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[3]	We are uncertain whether Mycophenolate mofetil plus placebo/usual care versus steroid alone increases or decreases ≥50% gfr loss
Infection	Relative risk: 1.35 (CI 95% 0.5 - 3.64) Based on data from 126 patients in 3 studies[4] Follow up Mean 22 months	**83** per 1000	**112** per 1000 Difference: **29 more per 1000** (CI 95% 42 fewer - 219 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[5]	We are uncertain whether mycophenolate mofetil versus placebo/usual care improves or worsen infection
Malignancy	Relative risk: 0.28 (CI 95% 0.03 - 2.54) Based on data from 86 patients in 2 studies[6] Follow up Mean 24 months	**50** per 1000	**14** per 1000 Difference: **36 fewer per 1000** (CI 95% 49 fewer - 77 more)	**Very Low** Due to very serious imprecision, Due to very serious risk of bias[7]	We are uncertain whether mycophenolate mofetil versus placebo/usual care increases or decreases malignancy
Complete remission	Relative risk: 2.02 (CI 95% 0.55 - 7.38) Based on data from 72 patients in 2 studies[8] Follow up Mean 15 months	**86** per 1000	**174** per 1000 Difference: **88 more per 1000** (CI 95% 39 fewer - 549 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[9]	We are uncertain whether Mycophenolate mofetil versus placebo/usual care increases or decreases complete remission
Annual GFR loss	Measured by: Scale: - Lower better Based on data from 28 patients in 1 studies[10] Follow up 12 months	Mean	Mean Difference: **MD 2 higher** (CI 95% 25.15 lower - 29.15 higher)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[11]	We are uncertain whether mycophenolate mofetil versus placebo/usual care increases or decreases annual GFR loss

1. Systematic review [25] with included studies: Frisch 2005, Maes 2004 **Baseline/comparator:** Control arm of reference used for intervention .
2. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, One trial (Frisch 2005) stopping earlier than scheduled, resulting in potential for overestimating benefits.; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients;
3. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Trial stopping earlier than scheduled, resulting in potential for overestimating benefits; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients, due to few events;
4. Systematic review [25] with included studies: 2nd NA IgAN 2004, Maes 2004, Tang 2005 **Baseline/comparator:** Control arm of reference used for intervention .
5. **Risk of bias: Very Serious.** Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting. Other bias due to termination of the trail after an independent Data and Safety Monitoring Committee met in person or by

teleconference recommended termination of the trial. There were no safety issues leading to this decision. Baseline characteristics were balanced across treatment groups(2nd NA IgAN, 2004); **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, few events ;

6. Systematic review [25] with included studies: Maes 2004, 2nd NA IgAN 2004 **Baseline/comparator:** Control arm of reference used for intervention .
7. **Risk of bias: Very Serious.** Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting. Other issue due to termination of the trail early without any safety issues for this (2nd NA IgAN 2004); **Imprecision: Very Serious.** Wide confidence intervals, due to few events;
8. Systematic review [25] with included studies: Frisch 2005, Tang 2005 **Baseline/comparator:** Control arm of reference used for intervention .
9. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting, Incomplete data and/or large loss to follow up. Due to other bias, The study was terminated early after the second scheduled interim analysis done by the independent study monitor revealed a trend towards a worse outcome in the mycophenolate mofetil group that would have made it highly unlikely to show a benefit for mycophenolate mofetil given our rate of recruitment and our target sample size (Frisch 2005); **Imprecision: Very Serious.** Wide confidence intervals, due to few events;
10. Systematic review [25] with included studies: 2nd NA IgAN 2004 **Baseline/comparator:** Control arm of reference used for intervention .
11. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study, Low number of patients;

References

[25] Immunosuppressive agents for treating IgA nephropathy. 2018;

PICO (18.17)
Population: Patients with IgA nephropathy
Intervention: Mycophenolate mofetil plus steroid
Comparator: Steroid alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Steroid alone	Mycophenolate mofetil plus steroid	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
Complete remission	Relative risk: 0.99 (CI 95% 0.68 - 1.46) Based on data from 174 patients in 1 studies[1] Follow up 12 months	**375** per 1000	**371** per 1000 Difference: **4 fewer per 1000** (CI 95% 120 fewer - 173 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Mycophenolate mofetil plus steroid versus steroid alone may have little or no difference on complete remission
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Malignancy	(CI 95% -)	Difference: **fewer**			No studies were found that looked at malignancy
End-stage kidney disease	Relative risk: 0.2 (CI 95% 0.01 - 4.2) Based on data from 174 patients in 1 studies Follow up 12 months	**23** per 1000	**5** per 1000 Difference: **18 fewer per 1000** (CI 95% 23 fewer - 74 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[3]	We are uncertain whether Mycophenolate mofetil plus steroid versus steroid alone increases or decreases end-stage kidney disease
Infection	Relative risk: 1.37 (CI 95% 0.83 - 2.24) Based on data from 175 patients in 1 studies Follow up 12 months	**227** per 1000	**311** per 1000 Difference: **84 more per 1000** (CI 95% 39 fewer - 281 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Mycophenolate mofetil plus steroid versus steroid alone may have little or no difference on infection
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference: **null lower**			No studies were found that looked at annual GFR loss

1. Systematic review [25] with included studies: Hou 2017 **Baseline/comparator:** Control arm of reference used for intervention .
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study;
3. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, due to few events;
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study;

References

[25] Immunosuppressive agents for treating IgA nephropathy. 2018;

PICO (18.18)
Population: Patients with IgA nephropathy
Intervention: Mycophenolate mofetil plus RASi
Comparator: RASi alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** RASi alone Mycophenolate mofetil RASi	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies were found that looked at all-cause mortality
End-stage kidney disease	Relative risk: 0.22 (CI 95% 0.05 - 0.9) Based on data from 40 patients in 1 studies Follow up 18 months	**450** per 1000 **99** per 1000 Difference: **351 fewer per 1000** (CI 95% 427 fewer - 45 fewer)	**Moderate** Due to serious risk of bias, Due to serious imprecision, Upgraded due to Large magnitude of effect[1]	Mycophenolate mofetil plus RASi versus a RASi alone probably decreases end-stage kidney disease
≥50% GFR loss	(CI 95% -)	Difference: **fewer**		No studies were found that looked at ≥50% GFR loss
Infection	(CI 95% -)	Difference: **fewer**		No studies were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**		No studies were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**		No studies were found that looked at complete remission
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference: **null lower**		No studies were found that looked at annual GFR loss

1. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study, Low number of patients, due to few events; **Upgrade: Large magnitude of effect.**

PICO (18.19)
Population: Patients with IgA nephropathy
Intervention: Mizoribine
Comparator: No mizoribine regimen

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** No mizoribine regimen / Mizoribine	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
Malignancy	Relative risk: 3.0 (CI 95% 0.13 - 69.7) Based on data from 42 patients in 1 studies Follow up 30 months	**466** per 1000 / **1398** per 1000 Difference: **932 more per 1000** (CI 95% 405 fewer - 32014 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether mizoribine improves or worsens malignancy
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies were found that looked at all-cause mortality
≥50% GFR loss	(CI 95% -)	Difference: **fewer**		No studies were found that looked at ≥50% GFR loss
End-stage kidney disease	Relative risk: 1.0 (CI 95% 0.07 - 14.95) Based on data from 42 patients in 1 studies[2] Follow up 30 months	**48** per 1000 / **48** per 1000 Difference: **0 fewer per 1000** (CI 95% 45 fewer - 670 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[3]	We are uncertain whether mizoribine improves or worsens end-stage kidney disease
Infection - Mizoribine plus RASi verus RASi	Relative risk: 0.59 (CI 95% 0.11 - 3.29) Based on data from 64 patients in 1 studies Follow up 12 months	**100** per 1000 / **59** per 1000 Difference: **41 fewer per 1000** (CI 95% 89 fewer - 229 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether mizoribine plus steroid compared with steroid alone increases or decreases infection
Infection - Mizoribine plus steroids versus steroid	Relative risk: 7.0 (CI 95% 0.38 - 127.32) Based on data from 104 patients in 2 studies[5] Follow up 24-25 months	**0** per 1000 / **0** per 1000 Difference: **0 fewer per 1000** (CI 95% 0 fewer - 0 fewer)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[6]	There were too few who experienced the infection to determine whether mizoribine plus steroid compared to steroid alone made a difference
Complete remission	Relative risk: 1.9 (CI 95% 1.06 - 3.43) Based on data from 24 patients in 1 studies Follow up 30 months	**466** per 1000 / **885** per 1000 Difference: **419 more per 1000** (CI 95% 28 more - 1132 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[7]	We are uncertain whether mizoribine improves or worsen complete remission
Annual GFR loss	Measured by: Scale: - Lower better	Difference: **null lower**		No studies were found that looked at annual GFR loss

1. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study, due to few patients with malignancy;
2. Systematic review [26] with included studies: Hirai 2017 **Baseline/comparator:** Control arm of reference used for intervention .

3. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study, due to few patients with end stage kidney disease;
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study;
5. Systematic review [26] with included studies: Masutani 2016 **Baseline/comparator:** Control arm of reference used for intervention .
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study, due to few infections;
7. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Low number of patients, Only data from one study;

References

[26] Immunosuppressive agents for treating IgA nephropathy. 2018;

PICO (18.20)
Population: Patients with IgA nephropathy
Intervention: Leflunomide
Comparator: No leflunomide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** No leflunomide Leflunomide	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**		No studies were found that looked at end-stage kidney disease
≥50% GFR loss	(CI 95% -)	Difference: **fewer**		No studies were found that looked at ≥50% GFR loss
Infection - versus placebo	Relative risk: 3.0 (CI 95% 0.12 - 72.77) Based on data from 200 patients in 1 studies[1] Follow up 6 months	**0** per 1000 **0** per 1000 Difference: **0 fewer per 1000** (CI 95% 0 fewer - 0 fewer)	**Low** Due to very serious imprecision[2]	There were too few who experienced the infection, to determine whether leflunomide compared to placebo made a difference
Malignancy	(CI 95% -)	Difference: **fewer**		No studies were found that looked at malignancy
Complete remission - versus RASi	Relative risk: 1.17 (CI 95% 0.68 - 2.0) Based on data from 46 patients in 1 studies Follow up 6 months	**500** per 1000 **585** per 1000 Difference: **85 more per 1000** (CI 95% 160 fewer - 500 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[3]	Compared to RASi, leflunomidemay have little or no difference on complete remission
Complete remission - versus steroid	Relative risk: 1.63 (CI 95% 0.56 - 4.7) Based on data from 49 patients in 1 studies Follow up 3 months	**500** per 1000 **585** per 1000 Difference: **85 more per 1000** (CI 95% 160 fewer - 500 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	Compared to steroid, leflunomidemay have little or no difference on complete remission
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference: **null lower**		No studies were found that looked at annual GFR loss

1. Primary study Wu 2016 **Baseline/comparator:** Control arm of reference used for intervention .
2. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, due to few/no infections;
3. **Risk of bias: Serious.** Selective outcome reporting, Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

4. **Risk of bias: Serious.** Selective outcome reporting, Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

PICO (18.21)
Population: Patients with IgA nephropathy
Intervention: Leflunomide plus low dose steroid
Comparator: High dose steroid

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** High dose steroid	**Absolute effect estimates** Leflunomide plus low dose steroid	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
≥50% GFR loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at ≥50% GFR loss
Complete remission	Relative risk: 1.0 (CI 95% 0.64 - 1.57) Based on data from 187 patients in 2 studies[1] Follow up Mean 18 months	**365** per 1000	**365** per 1000 Difference: **0 fewer per 1000** (CI 95% 131 fewer - 208 more)	**Very Low** Due to serious imprecision, Due to very serious risk of bias[2]	We are uncertain whether leflunomide plus low dose steroid versus high dose steroid increases or decreases complete remission
End stage kidney disease	Relative risk: 0.68 (CI 95% 0.17 - 2.65) Based on data from 85 patients in 1 studies Follow up 12 months	**111** per 1000	**75** per 1000 Difference: **36 fewer per 1000** (CI 95% 92 fewer - 183 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision,[3]	We are uncertain whether leflunomide plus low dose steroid versus high dose steroid increases or decreases end stage kidney disease
Malignancy	(CI 95% -)	Difference: **fewer**			No studies were found that looked at malignancy
Infection	Relative risk: 0.9 (CI 95% 0.41 - 1.99) Based on data from 187 patients in 2 studies[4] Follow up Mean 18 months	**115** per 1000	**103** per 1000 Difference: **12 fewer per 1000** (CI 95% 68 fewer - 114 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[5]	We are uncertain whether leflunomide plus low dose steroid versus high dose steroid increases or decreases infection
Annual GFR loss	Measured by: Scale: - Lower better	Difference: **null lower**			No studies were found that looked at annual GFR loss
GFR	Measured by: Scale: - High better Based on data from 85 patients in 1 studies Follow up 12 months	Mean	Mean Difference: **MD 3.77 higher** (CI 95% 8.82 lower - 16.36 higher)	**Very Low** Due to serious imprecision, Due to very serious risk of bias[6]	We are uncertain whether leflunomide plus low dose steroid versus high dose steroid increases or decreases GFR (any measure)

1. Systematic review [25] with included studies: Ni 2005, Min 2017 **Baseline/comparator:** Control arm of reference used for intervention .

2. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Imprecision: Serious.** Wide confidence intervals;
3. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** due to severe imprecision in treatment estimate (consistent with appreciable benefit or harm), due to only data from one study;
4. Systematic review [25] with included studies: Ni 2005, Min 2017 **Baseline/comparator:** Control arm of reference used for intervention .
5. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals;
6. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Serious.** Only data from one study;

References

[25] Immunosuppressive agents for treating IgA nephropathy. 2018;

PICO (18.22)
Population: Patients with IgA nephropathy
Intervention: Fish oil
Comparator: placebo/no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** placebo/no treatment	Fish oil	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	: 0.93 (CI 95% 0.06 - 14.44) Based on data from 106 patients in 1 studies Follow up 24 months	**20.0**	**19.0** Difference: **1.0 fewer** (CI 95% 19.0 fewer - 269.0 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether fish oil compared with placebo or no treatment increases or decreases end-stage kidney disease
End-stage kidney disease	Relative risk: 1.01 (CI 95% 0.34 - 2.97) Based on data from 143 patients in 2 studies[2] Follow up Mean 24 months	**85** per 1000	**86** per 1000 Difference: **1 more per 1000** (CI 95% 56 fewer - 167 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[3]	We are uncertain whether fish oil compared with placebo or no treatment increases or decreases end-stage kidney disease
> 50% loss in creatinine clearance	Relative risk: 1.87 (CI 95% 0.63 - 5.55) Based on data from 60 patients in 1 studies Follow up 24 months	**138** per 1000	**258** per 1000 Difference: **120 more per 1000** (CI 95% 51 fewer - 628 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether fish oil compared with placebo or no treatment increases or decreases >50% decrease in creatinine clearance
Infection	(CI 95% -)	Difference: **fewer**			No studies comparing fish oil with placebo or no treatment were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies comparing fish oil with placebo or no treatment were found that looked at malignancy
> 50% increase in serum creatinine	Relative risk: 0.2 (CI 95% 0.06 - 0.65) Based on data from 106 patients in 1 studies[5] Follow up 24 months	**275** per 1000	**55** per 1000 Difference: **220 fewer per 1000** (CI 95% 258 fewer - 96 fewer)	**Low** Due to serious risk of bias, Due to very serious imprecision, Upgraded due to Large magnitude of effect[6]	Fish oil may compared with placebo or no treatment decrease > 50% increase in serum creatinine
Complete remission	(CI 95% -)	Difference: **fewer**			No studies comparing fish oil with placebo or no treatment were found that looked at complete remission
Annual GFR loss (ml/min/1.73m^3) 3 years	Measured by: Scale: - Lower better	Difference: **null lower**			No studies comparing fish oil with placebo or no treatment were found that looked at annual GFR loss
Creatinine clearance	Measured by: Scale: -	Mean	Mean	**Very Low** Due to serious risk of bias, Due to	We are uncertain whether fish oil

(ml/min)	Based on data from 69 patients in 2 studies[7] Follow up Mean 15 months	Difference: **MD 15.57 lower** (CI 95% 34.94 lower - 3.79 higher)	very serious imprecision[8]	compared with placebo or no treatment increases or decreases creatinine clearance

1. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
2. Systematic review [27] with included studies: Bennett 1989, Donadio 1994 **Baseline/comparator:** Control arm of reference used for intervention .
3. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients;
4. **Risk of bias: Serious.** Large loss to follow up, 72% completed 2 years (67% prednisone, 80% O3FA, 83% placebo); **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
5. Systematic review [27] with included studies: Donadio 1994 **Baseline/comparator:** Control arm of reference used for intervention .
6. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Only data from one study, Low number of patients; **Upgrade: Large magnitude of effect.**
7. Systematic review [27] with included studies: Pettersson 1994, Bennett 1989 **Baseline/comparator:** Control arm of reference used for intervention .
8. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients;

References

[27] Non-immunosuppressive treatment for IgA nephropathy. 2018;

PICO (18.23)
Population: Patients with IgA nephropathy
Intervention: Fish oil
Comparator: Symptomatic treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** symptomatic treatment	Fish oil	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk (CI 95% -)	per 1000	per 1000		No studies comparing fish oil with symptomatic treatment were found that looked at all-cause mortality
		Difference: **fewer per 1000**			
End-stage kidney disease	Relative risk: 0.17 (CI 95% 0.02 - 1.21) Based on data from 28 patients in 1 studies[1] Follow up 4 years	**429** per 1000	**73** per 1000	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether fish oil compared with symptomatic treatment increases or decreases end-stage kidney disease
		Difference: **356 fewer per 1000** (CI 95% 420 fewer - 90 more)			
> 50% loss in GFR	Relative risk: 0.14 (CI 95% 0.02 - 1.01) Based on data from 28 patients in 1 studies[3] Follow up 4 years	**500** per 1000	**70** per 1000	**Low** Due to serious risk of bias, Due to very serious imprecision, Due to serious imprecision[4]	Fish oil compared to symptomatic treatment may decrease > 50% loss in GFR slightly. However, the effect estimates do cross the line of no effect.
		Difference: **430 fewer per 1000** (CI 95% 490 fewer - 5 more)			
Infection	Relative risk (CI 95% -)	per 1000	per 1000		No studies comparing fish oil with symptomatic treatment were found that looked at infection
		Difference: **fewer per 1000**			
Malignancy	Relative risk (CI 95% -)	per 1000	per 1000		No studies comparing fish oil with symptomatic treatment were found that looked at malignancy
		Difference: **fewer per 1000**			
Adverse events (corticosteroid related)	Relative risk (CI 95% -)	per 1000	per 1000		No studies comparing fish oil with symptomatic treatment were found that looked at corticosteroid-related adverse events
		Difference: **fewer per 1000**			
Complete remission	Relative risk (CI 95% -)	per 1000	per 1000		No studies comparing fish oil with symptomatic treatment were found that looked at complete remission
		Difference: **fewer per 1000**			
> 50% increase in serum creatinine	Relative risk: 0.17 (CI 95% 0.02 - 1.21) Based on data from 28 patients in 1 studies[5] Follow up 4 years	**429** per 1000	**73** per 1000	**Very Low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether fish oil compared with symptomatic treatment increases or decreases >50% increase in serum creatinine
		Difference: **356 fewer per 1000** (CI 95% 420 fewer - 90 more)			
Creatinine clearance	Measured by: Scale: - High better	Mean	Mean	**Very Low** Due to serious risk of bias, Due to	We are uncertain whether fish oil

	Based on data from 28 patients in 1 studies[7] Follow up 4 years	Difference: **7 higher** (CI 95% 10.13 lower - 24.13 higher)	very serious imprecision[8]	compared with symptomatic treatment increases or decreases >50% increase creatinine clearance
Annual GFR loss	Based on data from 28 patients in 1 studies Follow up 4 years	In the fish oil group (14), the mean annual change in GFR was -1.4 mL/min/1.73 m² per year (SD not reported) and in the Symtomatic treatment group (n=14), the the mean annual change in GFR was -3 mL/min/1.73 m² per year (SD not reported).)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[9]	We are uncertain whether fish oil compared with symptomatic treatment increases or decreases annual GFR loss

1. Systematic review [27] with included studies: Alexopoulos 2004 **Baseline/comparator:** Control arm of reference used for intervention .
2. **Risk of bias: Serious.** High lost to follow-up with 33% lost to follow-up in fish oil group and 22% in symptomatic treatment group. No intention-to-treat analysis undertaken; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
3. Systematic review [27] with included studies: Alexopoulos 2004 **Baseline/comparator:** Control arm of reference used for intervention .
4. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
5. Systematic review [27] with included studies: Alexopoulos 2004 **Baseline/comparator:** Control arm of reference used for intervention .
6. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
7. Systematic review [27] with included studies: Alexopoulos 2004 **Baseline/comparator:** Control arm of reference used for intervention .
8. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
9. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Only data from one study, Low number of patients and no measure of variance provided ;

References

[27] Non-immunosuppressive treatment for IgA nephropathy. 2018;

PICO (18.24)
Population: Patients with IgA nephropathy
Intervention: Fish oil: high dose
Comparator: Fish oil: low dose

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Fish oil: low dose Fish oil: high dose	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies comparing high dose versus low dose fish oil were found that looked at all-cause mortality
End-stage kidney disease	Relative risk: 0.82 (CI 95% 0.37 - 1.85) Based on data from 73 patients in 1 studies Follow up 2 years	**270** per 1000 **221** per 1000 Difference: **49 fewer per 1000** (CI 95% 170 fewer - 230 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether high dose versus low dose fish oil increases or decreases end-stage kidney disease
>50% loss in GFR	(CI 95% -)	Difference: **fewer**		No studies comparing high dose versus low dose fish oil were found that looked at >50% loss in GFR
Infection	(CI 95% -)	Difference: **fewer**		No studies comparing high dose versus low dose fish oil were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**		No studies comparing high dose versus low dose fish oil were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**		No studies comparing high dose versus low dose fish oil were found that looked at complete remission
Annual GFR loss	Measured by: Scale: - High better	Difference: **null lower**		No studies comparing high dose versus low dose fish oil were found that looked at Annual GFR loss

1. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

PICO (18.25)
Population: Patients with IgA nephropathy
Intervention: Fish oil plus ACEi and ARBs
Comparator: ACEi plus ARBs

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** ACEi plus ARBs	Fish oil plus ACEi and ARBs	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies comparing fish oil plus ACEi and ARBs with ACEi or ARBs alone were found that looked at mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies comparing fish oil plus ACEi and ARBs with ACEi or ARBs alone were found that looked at end-stage kidney disease
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			No studies comparing fish oil plus ACEi and ARBs with ACEi or ARBs alone were found that looked at ≥50% loss of GFR
Infection	(CI 95% -)	Difference: **fewer**			No studies comparing fish oil plus ACEi and ARBs with ACEi or ARBs alone were found that looked at infection
Malignancy[1]	(CI 95% -)	Difference: **fewer**			No studies comparing fish oil plus ACEi and ARBs with ACEi or ARBs alone were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**			No studies comparing fish oil plus ACEi and ARBs with ACEi or ARBs alone were found that looked at complete remission
Annual GFR loss	Measured by: Scale: - Lower better	Difference: **null lower**			No studies comparing fish oil plus ACEi and ARBs with ACEi or ARBs alone were found that looked at annual GFR loss
Creatinine clearance (mL/min)	Measured by: Scale: - High better Based on data from 30 patients in 1 studies Follow up 6 months	Mean	Mean Difference: **MD 26.20 higher** (CI 95% 1.01 higher - 51.39 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Fish oil plus ACEi and ARBs versus ACEi plus ARbs alone may improve creatinine clearance slightly

1. No studie
2. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

PICO (18.26)
Population: Patients with IgA nephropathy
Intervention: Anticoagulant
Comparator: Placebo/no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/no treatment	Anticoagulant	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulants with placebo or no treatment were found that looked at all-cause mortality
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulants with placebo or no treatment were found that looked at ≥50% loss of GFR
End-stage kidney disease[1]	Relative risk: 0.28 (CI 95% 0.04 - 2.07) Based on data from 21 patients in 1 studies[2] Follow up 3 years	**364** per 1000	**102** per 1000 Difference: **262 fewer per 1000** (CI 95% 349 fewer - 389 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[3]	We are uncertain whether anticoagulant versus placebo/no treatment increases or decreases end-stage kidney disease
Infection	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulants with placebo or no treatment were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulants with placebo or no treatment were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulants with placebo or no treatment were found that looked at complete remission
Remission of proteinuria[4]	Relative risk: 0.95 (CI 95% 0.19 - 4.6) Based on data from 49 patients in 1 studies[5] Follow up 6 months	**125** per 1000	**119** per 1000 Difference: **6 fewer per 1000** (CI 95% 101 fewer - 450 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether anticoagulant versus placebo/no treatment increases or decreases remission of proteinuria
Annual loss in GFR	Measured by: Scale: - Lower better	Difference: **null lower**			No studies comparing anticoagulants with placebo or no treatment were found that looked at annual loss in GFR
Creatinine clearance	Measured by: Scale: -	Mean	Mean	**Very Low** Due to serious risk of bias, Due to	We are uncertain whether anticoagulant

(mL/min)	Based on data from 21 patients in 1 studies Follow up 3 years	Difference: **MD 21 higher** (CI 95% 0.19 lower - 42.19 higher)	very serious imprecision[7]	versus placebo/no treatment increases or decreases creatinine clearance

1. Antiplatelet: DipyridamoleDose: 75 mg 3 times/dAnticoagulant: WarfarinDose: INR 1.3 to 1.5 versus no treatment
2. Systematic review [27] with included studies: Lee 1997 **Baseline/comparator:** Control arm of reference used for intervention .
3. **Risk of bias: Serious.** Selective outcome reporting, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
4. Sulodexide versus placebo 50% Reduction in UPCR proteinuria
5. Systematic review [27] with included studies: Bang 2011 **Baseline/comparator:** Control arm of reference used for intervention .
6. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
7. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

References

[27] Non-immunosuppressive treatment for IgA nephropathy. 2018;

PICO (18.27)
Population: Non-immunosuppressive treatment for IgA nephropathy
Intervention: Anticoagulant
Comparator: Other treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Other treatment	Anticoagulant	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulants with other treatments were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulants with other treatments were found that looked at end-stage kidney disease
Complete remission[1]	Relative risk: 0.27 (CI 95% 0.16 - 0.46) Based on data from 262 patients in 1 studies Follow up 6 months	**500** per 1000	**865** per 1000 Difference: **365 more per 1000** (CI 95% 230 more - 525 more)	**Low** Due to very serious risk of bias, Due to serious imprecision, Upgraded due to Large magnitude of effect[2]	Dipyridamole compared with hirudin may decrease complete remission
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulants with other treatments were found that looked at ≥50% loss of GFR
Malignancy	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulants with other treatments were found that looked at malignancy
Infection	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulants with other treatments were found that looked at infection
Adverse events	Relative risk: 1.38 (CI 95% 0.86 - 2.22) Based on data from 262 patients in 1 studies Follow up 6 months	**181** per 1000	**250** per 1000 Difference: **69 more per 1000** (CI 95% 25 fewer - 221 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[3]	We are uncertain whether dipyridamole versus hirudin increases or decreases adverse events
Annual GFR loss	Measured by: Scale: - Lower better	Difference: **null lower**			No studies comparing anticoagulants with other treatments were found that looked at annual GFR loss
Creatinine clearance[4]	Measured by: Scale: - High better	Mean	Mean	**Very Low** Due to very serious risk of bias,	We are uncertain whether dipyridamole +

	Based on data from 38 patients in 1 studies Follow up 33.2 months	Difference: **MD 6 higher** (CI 95% 17.60 lower - 29.60 higher)	Due to very serious imprecision[5]	aspirin versus vitamin B increases or decreases creatinine clearance
Creatinine clearance[6]	Measured by: Scale: - High better Based on data from 262 patients in 1 studies[7]	Mean Mean Difference: **MD 15.90 lower** (CI 95% 19.99 lower - 11.81 lower)	**Low** Due to very serious risk of bias, Due to serious imprecision, Upgraded due to Large magnitude of effect[8]	dipyridamole versus hirudin may decrease creatinine clearance

1. Dipyridamole versus Hirudin
2. **Risk of bias: Very Serious.** Selective outcome reporting, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study, Low number of patients; **Upgrade: Large magnitude of effect.**
3. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
4. Dipyridamole + aspirin versus Vitamin B
5. **Risk of bias: Very Serious.** Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
6. Dipyridamole versus hirudin
7. Systematic review [27] with included studies: Li 2008e **Baseline/comparator:** Control arm of reference used for intervention .
8. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients; **Upgrade: Large magnitude of effect.**

References

[27] Non-immunosuppressive treatment for IgA nephropathy. 2018;

PICO (18.28)
Population: Patients with IgA nephropathy
Intervention: Anticoagulant plus other treatment
Comparator: Other treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Other treatment	Anticoagulant plus other treatment	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk (CI 95% -) Based on data from 200 patients in 1 studies[1] Follow up 6 months	**0** per 1000	per 1000 Difference: **fewer per 1000**	**Low** Due to serious risk of bias, Due to serious imprecision[2]	There were too few who experienced the all-cause mortality, to determine whether clopidogrel plus telmisaratan versus telmisartan alone made a difference
End-stage kidney disease[3]	Relative risk: 0.32 (CI 95% 0.03 - 3.12) Based on data from 31 patients in 1 studies Follow up 36 months	**167** per 1000	**53** per 1000 Difference: **114 fewer per 1000** (CI 95% 162 fewer - 354 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether ticlopidine plus ACEi versus ACEi alone increases or decreases end-stage kidney disease
End-stage kidney disease[5]	Relative risk: 0.25 (CI 95% 0.03 - 2.14) Based on data from 84 patients in 1 studies[6] Follow up 24 months	**95** per 1000	**24** per 1000 Difference: **71 fewer per 1000** (CI 95% 92 fewer - 108 more)	**Low** Due to very serious imprecision[7]	Clopidine + ARB versus ARB alone may have little or no difference on end-stage kidney disease
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulant plus other treatment with other treatment alone were found that looked at ≥50% loss of GFR
Infection[8]	Relative risk: 1.0 (CI 95% 0.06 - 15.77) Based on data from 200 patients in 1 studies[9] Follow up 6 months	**10** per 1000	**10** per 1000 Difference: **0 fewer per 1000** (CI 95% 9 fewer - 148 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[10]	We are uncertain whether clopidogrel plus telmisaratan versus telmisartan alone increases or decreases infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulant plus other treatment with other treatment alone were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**			No studies comparing anticoagulant plus other treatment with other treatment alone were found that looked at complete remission
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference: **null lower**			No studies comparing anticoagulant plus other treatment with other treatment alone were found that looked at annual GFR loss
Change in creatinine	Measured by: Scale: - High better	Mean	Mean	**Very Low** Due to serious risk of bias, Due to	We are uncertain whether difibrotide plus

clearance	Based on data from 20 patients in 1 studies[11] Follow up 24 months	Difference: **MD 7 higher** (CI 95% 10.62 lower - 24.62 higher)	very serious imprecision[12]	prednisone versus predinsone alone improves or worsens change in creatinine clearance
eGFR	Measured by: Scale: - High better Based on data from 84 patients in 1 studies Follow up 24 months	Mean Mean Difference: **MD 1.28 lower** (CI 95% 6.73 lower - 4.17 higher)	**Low** Due to very serious imprecision[13]	Clopidine + ARB versus ARB alone may have little or no difference on eGFR

1. Primary study . **Baseline/comparator:** Control arm of reference used for intervention .
2. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Only data from one study, due to no events;
3. Ticlopidine +ACEi versus ACEi
4. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Unclear concealment of allocation during randomization process, resulting in potential for selection bias, Unclear blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
5. Clopidine + ARB versus ARB
6. Systematic review [27] with included studies: Cheng 2015 **Baseline/comparator:** Control arm of reference used for intervention .
7. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
8. Clopidogrel plus telmisaratan versus telmisartan alone
9. Systematic review [27] with included studies: Wu 2016 **Baseline/comparator:** Control arm of reference used for intervention .
10. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
11. Systematic review [27] with included studies: Frasca 1997 **Baseline/comparator:** Control arm of reference used for intervention .
12. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
13. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

References

[27] Non-immunosuppressive treatment for IgA nephropathy. 2018;

PICO (18.29)
Population: Patients with IgA nephropathy
Intervention: Antioxidant
Comparator: Other treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Other treatment Antioxidant	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies comparing antioxidants with other treatment were found that looked at all-cause mortality
End-stage kidney disease	Relative risk (CI 95% -) Based on data from 68 patients in 1 studies Follow up 36 months	**0** per 1000 per 1000 Difference: **fewer per 1000**	**Low** Due to serious risk of bias, Due to serious imprecision[1]	There were too few who experienced the end-stage kidney disease, to determine whether probucol compared to ARB made a difference
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**		No studies comparing antioxidants with other treatment were found that looked at ≥50% loss of GFR
Infection	(CI 95% -)	Difference: **fewer**		No studies comparing antioxidants with other treatment were found that looked at ≥50% loss of GFR
Malignancy	(CI 95% -)	Difference: **fewer**		No studies comparing antioxidants with other treatment were found that looked at ≥50% loss of GFR
Complete remission	(CI 95% -)	Difference: **fewer**		No studies comparing antioxidants with other treatment were found that looked at complete remission
Annual eGFR loss 3 years	Measured by: Scale: - Lower better Based on data from 68 patients in 1 studies Follow up 36 months	Mean Mean Difference: **MD 1.36 higher** (CI 95% 0.32 higher - 2.40 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Probucol compared with ARB alone may increase annual eGFR loss

1. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients;

PICO (18.30)
Population: Patients with IgA nephropathy
Intervention: Tonsillectomy plus other treatment
Comparator: Other treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Other treatment	Tonsillectomy plus other treatment	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies comparing tonsillectomy plus other treatments versus other treatments alone were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies comparing tonsillectomy plus other treatments versus other treatments alone were found that looked at end-stage kidney disease
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			No studies comparing tonsillectomy plus other treatments versus other treatments alone were found that looked at ≥50% loss of GFR
Infection	(CI 95% -)	Difference: **fewer**			No studies comparing tonsillectomy plus other treatments versus other treatments alone were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies comparing tonsillectomy plus other treatments versus other treatments alone were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**			No studies comparing tonsillectomy plus other treatments versus other treatments alone were found that looked at complete remission
Remission of proteinuria	Relative risk: 1.9 (CI 95% 1.45 - 2.47) Based on data from 143 patients in 2 studies[1] Follow up Mean 42 months	**441** per 1000	**838** per 1000 Difference: **397 more per 1000** (CI 95% 198 more - 648 more)	**Low** Due to very serious risk of bias, Due to serious imprecision, Upgraded due to Large magnitude of effect[2]	Tonsillectomy plus other treatment versus other treatment alone may increase remission of proteinuria
Remission of microscopic haematuria	Relative risk: 1.93 (CI 95% 1.47 - 2.53) Based on data from 143 patients in 2 studies[3] Follow up Mean 42 months	**456** per 1000	**880** per 1000 Difference: **424 more per 1000** (CI 95% 214 more - 698 more)	**Low** Due to very serious risk of bias, Due to serious imprecision, Upgraded due to Large magnitude of effect[4]	Tonsillectomy plus other treatment versus other treatment alone may increase remission of microscopic haematuria
Remission of macroscopic	Relative risk: 1.33 (CI 95% 0.8 - 2.23)	**563** per 1000	**749** per 1000	**Very Low** Due to serious risk of bias, Due to	We are uncertain whether tonsillectomy

haematuria	Based on data from 32 patients in 1 studies[5] Follow up 24 months	Difference: **186 more per 1000** (CI 95% 113 fewer - 692 more)	very serious imprecision[6]	plus other treatment versus other treatment alone increases or decreases remission of macroscopic haematuria
Relapse of proteinuria	Relative risk: 0.7 (CI 95% 0.57 - 0.85) Based on data from 73 patients in 1 studies Follow up 12 months	**1000** per 1000 **700** per 1000 Difference: **300 fewer per 1000** (CI 95% 430 fewer - 150 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[7]	Tonsillectomy plus other standard of care versus standard of care alone may decrease relapse of proteinuria
Relapse of hematuria	Relative risk: 0.7 (CI 95% 0.51 - 0.98) Based on data from 72 patients in 1 studies Follow up 12 months	**783** per 1000 **548** per 1000 Difference: **235 fewer per 1000** (CI 95% 384 fewer - 16 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Tonsillectomy plus other standard of care versus standard of care alone may decrease relapse of haematuria
Annual GFR loss	Measured by: Scale: - High better	Difference: **null lower**		No studies comparing tonsillectomy plus other treatments versus other treatments alone were found that looked at annual GFR loss
Creatinine clearance (mL/min)	Measured by: Scale: - High better Based on data from 77 patients in 2 studies[9] Follow up Mean 30 months	Mean Mean Difference: **MD 3.77 higher** (CI 95% 13.80 lower - 21.35 higher)	**Very Low** Due to very serious risk of bias, Due to very serious inconsistency, Due to very serious imprecision[10]	We are uncertain whether tonsillectomy plus treatment versus treatment alone increases or decreases creatinine clearance

1. Systematic review [27] with included studies: Hotta 1993, Yang 2016 **Baseline/comparator:** Control arm of reference used for intervention .
2. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Selective outcome reporting; **Imprecision: Serious.** Wide confidence intervals, Low number of patients; **Upgrade: Large magnitude of effect.**
3. Systematic review [27] with included studies: Hotta 1993, Yang 2016 **Baseline/comparator:** Control arm of reference used for intervention .
4. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Selective outcome reporting; **Imprecision: Serious.** Wide confidence intervals, Low number of patients; **Upgrade: Large magnitude of effect.**
5. Primary study Kawasaki 2006 **Baseline/comparator:** Control arm of reference used for intervention .
6. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
7. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients;
8. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients;
9. Systematic review [27] with included studies: Hotta 1993, Kawasaki 2006 **Baseline/comparator:** Control arm of reference used for intervention .
10. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Selective outcome reporting; **Inconsistency: Very Serious.** The magnitude of statistical heterogeneity was high, with I^2:76%., The direction of the effect is not consistent between the included studies; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients;

References

[27] Non-immunosuppressive treatment for IgA nephropathy. 2018;

PICO (18.31)
Population: Non-immunosuppressive treatment for IgA nephropathy
Intervention: Statins
Comparator: placebo/no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** placebo/no treatment Statins	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
Malignancy	(CI 95% -)	Difference: **fewer**		No studies comparing statins with placebo/no treatment were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**		No studies comparing statins with placebo/no treatment were found that looked at complete remission
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies comparing statins with placebo/no treatment were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**		No studies comparing statins with placebo/no treatment were found that looked at end-stage kidney disease
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**		No studies comparing statins with placebo/no treatment were found that looked at ≥50% loss of GFR
Infection	(CI 95% -)	Difference: **fewer**		No studies comparing statins with placebo/no treatment were found that looked at infection
Annual GFR loss	Measured by: Scale: - High better	Difference: **null lower**		No studies comparing statins with placebo/no treatment were found that looked at Annual GFR loss
eGFR (mL/min/1.73 m²)	Based on data from 21 patients in 1 studies Follow up 6 months	After the duration of therapy, the statins arm (n=13) had a eGFR of 85 mL/min/1.73 m²; interquartile range = 70-147; the placebo arm (n=8) had a eGFR of 77 mL/min/1.73 m²; interquartile range = 47-92	**Very Low** Due to serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether statins compared with placebo increases or decreases eGFR

1. **Risk of bias: Serious.** Selective outcome reporting, unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Very Serious.** Only data from one study, Low number of patients;

References

[27] Non-immunosuppressive treatment for IgA nephropathy. 2018;

PICO (18.32)
Population: Patients with IgA nephropathy
Intervention: Statins plus other treatment
Comparator: Other treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Other treatment / Statins plus other treatment	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies comparing statins plus other treatment versus other treatments alone were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**		No studies comparing statins plus other treatment versus other treatments alone were found that looked at end-stage kidney disease
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**		No studies comparing statins plus other treatment versus other treatments alone were found that looked at ≥50% loss of GFR
Infection	(CI 95% -)	Difference: **fewer**		No studies were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**		No studies comparing statins plus other treatment versus other treatments alone were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**		No studies comparing statins plus other treatment versus other treatments alone were found that looked at complete remission
Annual GFR loss	Measured by: Scale: - Lower better	Difference: **null lower**		No studies comparing statins plus other treatment versus other treatments alone were found that looked at annual GFR loss
Creatinine clearance	Measured by: Scale: - High better Based on data from 30 patients in 1 studies Follow up 12 months	mL/minMean / mL/minMean Difference: **MD 22.60 higher** (CI 95% 11.83 higher - 33.37 higher)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[1]	We are uncertain whether statins plus other treatment versus other treatment alone improves or worsen creatinine clearance

1. **Risk of bias: Very Serious.** Selective outcome reporting, unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study, Low number of patients;

PICO (18.33)
Population: Patients with IgA nephropathy
Intervention: Phenytoin
Comparator: Placebo/no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/no treatment	Phenytoin	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			No studies comparing phenytoin versus no treatment were found that looked at ≥50% loss of GFR
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies comparing phenytoin versus no treatment were found that looked at end-stage kidney disease
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies comparing phenytoin versus no treatment were found that looked at all-cause mortality
Infection	(CI 95% -)	Difference: **fewer**			No studies comparing phenytoin versus no treatment were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies comparing phenytoin versus no treatment were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**			No studies comparing phenytoin versus no treatment were found that looked at complete remission
Remission of haematuria	Relative risk: 4.47 (CI 95% 0.58 - 34.57) Based on data from 36 patients in 1 studies Follow up Not reported	**59** per 1000	**264** per 1000 Difference: **205 more per 1000** (CI 95% 25 fewer - 1981 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether phenytoin increases or decreases remission of haematuria
Creatinine clearance	Measured by: Scale: - High better Based on data from 47 patients in 1 studies[2] Follow up Not reported	Mean	Mean Difference: **MD 6.00 lower** (CI 95% 28.05 lower - 16.05 higher)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[3]	We are uncertain whether phenytoin compared with no treatment improves or worsens creatinine clearance

1. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias, unclear of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
2. Primary study . **Baseline/comparator:** Control arm of reference used for intervention .

3. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias, unclear of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

PICO (18.34)
Population: Patients with IgA nephropathy
Intervention: Herbal medicine
Comparator: Placebo/no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/no treatment	Herbal medicine	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies comparing herbal medicine with placebo were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies comparing herbal medicine with placebo were found that looked at end-stage kidney disease
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			No studies comparing herbal medicine with placebo were found that looked at ≥50% loss of GFR
Remission in proteinuria	Relative risk: 2.35 (CI 95% 1.3 - 4.26) Based on data from 45 patients in 1 studies[1] Follow up 3 months	**348** per 1000	**818** per 1000 Difference: **470 more per 1000** (CI 95% 104 more - 1134 more)	**Low** Due to very serious risk of bias, Due to serious imprecision, Upgraded due to Large magnitude of effect[2]	Huai Qi Huang (traditional chinese medicine) compared with no treatment may increase remission in proteinuria
Malignacy	(CI 95% -)	Difference: **fewer**			No studies comparing herbal medicine with placebo were found that looked at malignancy
Infection	(CI 95% -)	Difference: **fewer**			No studies comparing herbal medicine with placebo were found that looked at infecton
Complete remission	(CI 95% -)	Difference: **fewer**			No studies comparing herbal medicine with placebo were found that looked at complete remission
Remission in haematuria	Relative risk: 4.88 (CI 95% 1.62 - 14.68) Based on data from 45 patients in 1 studies Follow up 3 months	**130** per 1000	**634** per 1000 Difference: **504 more per 1000** (CI 95% 81 more - 1778 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision, Upgraded due to Large magnitude of effect[3]	We are uncertain whether Huai Qi Huang (traditional chinese medicine) versus no treatment increases or decreases remission in haematuria
Annual GFR loss	Measured by: Scale: - Lower better				No studies comparing herbal medicine with

		Difference: **null lower**		placebo were found that looked at annual GFR loss

1. Systematic review [27] with included studies: Li 2013d **Baseline/comparator:** Control arm of reference used for intervention .
2. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients; **Upgrade: Large magnitude of effect.**
3. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients; **Upgrade: Large magnitude of effect.**

References

[27] Non-immunosuppressive treatment for IgA nephropathy. 2018;

PICO (18.35)
Population: Patients with IgA nephropathy
Intervention: Traditional Chinese medicine
Comparator: Western medicine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Western medicine	Traditional Chinese medicine	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies comparing traditional Chinese medicine with western medicine were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies comparing traditional Chinese medicine with western medicine were found that looked at end-stage kidney disease
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			No studies comparing traditional Chinese medicine with western medicine were found that looked at ≥50% loss of GFR
Infection	(CI 95% -)	Difference: **fewer**			No studies comparing traditional Chinese medicine with western medicine were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies comparing traditional Chinese medicine with western medicine were found that looked at malignancy
Complete remission[1]	Relative risk: 3.09 (CI 95% 0.79 - 12.08) Based on data from 54 patients in 1 studies[2] Follow up 6 months	**35** per 1000	**108** per 1000 Difference: **73 more per 1000** (CI 95% 7 fewer - 388 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[3]	We are uncertain whether traditional Chinese medicine compared with western medicine increases or decreases complete remission
Annual loss in GFR	Measured by: Scale: - Lower better Based on data from 65 patients in 1 studies Follow up 12 months	Mean	Mean Difference: **MD 1.87 lower** (CI 95% 3.28 lower - 0.46 lower)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[4]	We are uncertain whether traditional Chinese medicine compared with ARBs improves or worsens annual loss in GFR
Creatinine clearance (mL/min)	Measured by: Scale: - Based on data from 65 patients in 1 studies Follow up 12 months	Mean	Mean Difference: **MD 3.91 higher** (CI 95% 2.11 lower - 9.93 higher)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[5]	We are uncertain whether traditional Chinese medicine compared with ARBs increases or decreases complete remission

1. Traditional medicine versus western medicine
2. Primary study Zhou 2011 **Baseline/comparator:** Control arm of reference used for intervention .

3. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients and few events;
4. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients;
5. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

PICO (18.36)
Population: Patients with IgA nephropathy
Intervention: Urokinase plus ACEi
Comparator: ACEi

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** ACEi	Urokinase plus ACEi	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies comparing urokinase plus ACEi versus ACEi alone were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies comparing urokinase plus ACEi versus ACEi alone were found that looked at end-stage kidney disease
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			No studies comparing urokinase plus ACEi versus ACEi alone were found that looked at ≥50% loss of GFR
Infection	(CI 95% -)	Difference: **fewer**			No studies comparing urokinase plus ACEi versus ACEi alone were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies comparing urokinase plus ACEi versus ACEi alone were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**			No studies comparing urokinase plus ACEi versus ACEi alone were found that looked at complete remission
> 50% increase in serum creatinine	Relative risk: 0.15 (CI 95% 0.01 - 2.74) Based on data from 71 patients in 1 studies Follow up 12 months	**83** per 1000	**12** per 1000 Difference: **71 fewer per 1000** (CI 95% 82 fewer - 144 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether urokinase plus ACEi compared with ACEi alone increases or decreases > 50% increase in serum creatinine
> 50% decrease in proteinuria	Relative risk: 1.61 (CI 95% 1.05 - 2.45) Based on data from 71 patients in 1 studies Follow up 12 months	**444** per 1000	**715** per 1000 Difference: **271 more per 1000** (CI 95% 22 more - 644 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision, Upgraded due to Large magnitude of effect[2]	We are uncertain whether urokinase plus ACEi compared with ACEi alone increases or decreases > 50% decrease in proteinuria
Annual loss in GFR[3]	Measured by: Creatinine clearance	(mL/min)Mean	(mL/min)Mean	**Very Low** Due to very serious risk of bias,	We are uncertain whether urokinase plus

	Scale: - Lower better Based on data from 71 patients in 1 studies Follow up 12 months	Difference: **6.92 higher** (CI 95% 2.90 lower - 16.74 higher)	Due to very serious imprecision[4]	ACEi compared with ACEi alone improves or worsens annual loss in GFR

1. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Unclear concealment of allocation during randomization process, resulting in potential for selection bias, Unclear blinding of participants and personnel, resulting in potential for performance bias, unclear of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
2. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Unclear concealment of allocation during randomization process, resulting in potential for selection bias, Unclear blinding of participants and personnel, resulting in potential for performance bias, unclear of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients; **Upgrade: Large magnitude of effect.**
3. Creatinine clearance (mL/min)
4. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Unclear concealment of allocation during randomization process, resulting in potential for selection bias, Unclear blinding of participants and personnel, resulting in potential for performance bias, unclear of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

PICO (18.37)
Population: Patients with IgA nephropathy
Intervention: Vitamin E
Comparator: Placebo/no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/no treatment	Vitamin E	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies comparing vitamin E with placebo/no treatment were found that looked at all-cause mortality
End-stage kidney disease	Relative risk (CI 95% -) Based on data from 55 patients in 1 studies Follow up 24 months	**0** per 1000	per 1000		There were too few who experienced the end-stage kidney disease, to determine whether vitamin E compared with placebo/no treatment made a difference
		Difference: **fewer per 1000**			
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			No studies comparing vitamin E with placebo/no treatment were found that looked at ≥50% loss of GFR
Infection	(CI 95% -)	Difference: **fewer**			No studies comparing vitamin E with placebo/no treatment were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies comparing vitamin E with placebo/no treatment were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**			No studies comparing vitamin E with placebo/no treatment were found that looked at complete remission
Annual loss of GFR 3 years	Measured by: Scale: - Lower better	Difference: **null lower**			No studies comparing vitamin E with placebo/no treatment were found that looked at annual loss of GFR
Creatinine clearance (mL/min)	Measured by: Scale: - High better Based on data from 55 patients in 1 studies Follow up 24 months	Mean	Mean	**Very Low** Due to serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether vitamin E versus placeboe increases or decreases creatinine clearance (ml/min)
		Difference: **MD 15 higher** (CI 95% 7.08 lower - 37.08 higher)			

1. **Risk of bias: Serious.** 69% completed study to at least 1 year; number not reported for each group. No intention-to-treat analysis was conducted; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

PICO (18.38)
Population: Patients with IgA nephropathy
Intervention: Vitamin D
Comparator: Placebo/no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/no treatment	Vitamin D	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies comparing vitamin D with placebo/ no treatment were found that looked at all-cause mortality
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			We are uncertain whether vitamin D compared with no treatment increases or decreases ≥50% loss of GFR
Adverse events	Relative risk: 0.72 (CI 95% 0.32 - 1.63) Based on data from 50 patients in 1 studies Follow up 11 months	**375** per 1000	**270** per 1000 Difference: **105 fewer per 1000** (CI 95% 255 fewer - 236 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether vitamin D compared with no treatment increases or decreases adverse events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies comparing vitamin D with placebo/ no treatment were found that looked at end-stage kidney disease
Malignancy	(CI 95% -)	Difference: **fewer**			No studies comparing vitamin D with placebo/ no treatment were found that looked at malignancy
Infection	Relative risk: 0.74 (CI 95% 0.22 - 2.43) Based on data from 50 patients in 1 studies Follow up 11 months	**208** per 1000	**154** per 1000 Difference: **54 fewer per 1000** (CI 95% 162 fewer - 297 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether vitamin D compared with no treatment increases or decreases infection
Complete remission	(CI 95% -)	Difference: **fewer**			No studies comparing vitamin D with placebo/ no treatment were found that looked at complete remission
Annual loss in eGFR (ml/min/1.73m^2)	Measured by: Scale: - Lower better Based on data from 50 patients in 1 studies Follow up 11 months	Mean	Mean Difference: **MD 0.00 higher** (CI 95% 16.61 lower - 16.61 higher)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[3]	We are uncertain whether vitamin D compared with no treatment improves or worsens annual loss in GFR

1. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
2. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;
3. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

PICO (18.39)
Population: Patients with IgA nephropathy
Intervention: Sodium cromoglycate
Comparator: placebo/no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** placebo/no treatment	Sodium cromoglycate	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies comparing sodium cromoglycate with placebo/no treatment were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies comparing sodium cromoglycate with placebo/no treatment were found that looked at end-stage kidney disease
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			No studies comparing sodium cromoglycate with placebo/no treatment were found that looked at end-stage kidney disease
Infection	(CI 95% -)	Difference: **fewer**			No studies comparing sodium cromoglycate with placebo/no treatment were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies comparing sodium cromoglycate with placebo/no treatment were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**			No studies comparing sodium cromoglycate with placebo/no treatment were found that looked at complete remission
Annual loss of GFR 3 years	Measured by: Scale: - High better	Difference: **null lower**			No studies comparing sodium cromoglycate with placebo/no treatment were found that looked at annual loss of GFR
Creatinine clearance (mL/min)	Measured by: Scale: - High better Based on data from 30 patients in 1 studies Follow up 3.5 months	Mean	Mean Difference: **8.4 higher** (CI 95% 10.19 lower - 26.99 higher)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether sodium cromoglycate compared with no treatment increases or decreases creatinine clearance

1. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;

PICO (18.40)
Population: Patients with IgA nephropathy
Intervention: Allopurinol
Comparator: Placebo/no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/no treatment	Allopurinol	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies comparing allopurinol with placebo/ no treatment were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies comparing allopurinol with placebo/ no treatment were found that looked at end-stage kidney disease
≥50% loss of GFR	(CI 95% -)	Difference: **fewer**			No studies comparing allopurinol with placebo/ no treatment were found that looked at ≥50% loss of GFR
Infection	(CI 95% -)	Difference: **fewer**			No studies comparing allopurinol with placebo/ no treatment were found that looked at infection
Malignancy	(CI 95% -)	Difference: **fewer**			No studies comparing allopurinol with placebo/ no treatment were found that looked at malignancy
Complete remission	(CI 95% -)	Difference: **fewer**			No studies comparing allopurinol with placebo/ no treatment were found that looked at complete remission
eGFR (mL/min/1.73m^2)	Measured by: Scale: - High better Based on data from 40 patients in 1 studies Follow up 6 months	Mean	Mean Difference: **MD 4.30 higher** (CI 95% 17.89 lower - 26.49 higher)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether allopurinol compared with no treatment improves or worsen eGFR
Annual GFR loss	Measured by: Scale: - High better	Difference: **null lower**			No studies comparing allopurinol with placebo/ no treatment were found that looked at annual GFR loss

1. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients;