KDIGO GN Guideline update – Evidence summary

Patient preferences for glomerulonephritis treatment

**PICO question**
In patients with glomerulonephritis what are patient preferences and values for immunosuppressive and non-immunosuppressive therapy?

**Search strategy and selection**
MeSH sub-headings and text words associated with glomerulonephritis, non-immunosuppressive and immunosuppressive treatment and patient preferences were searched using relevant medial databases for studies published up to July 2018.

**Search results**
The search strategy identified 279 relevant citations, from these 272 were excluded on the basis of being either the incorrect study design, wrong population, wrong intervention, and one was excluded as it was in Spanish and due to a lack of resources we were unable to translate this study. Overall the search found seven relevant studies. There were a total of 708 participants, and study-types included five cross-sectional studies, and two mixed method studies, using nominal group technique.

All seven studies addressed lupus nephritis.

**Summary of the main findings**

**Patient and physician preferences for lupus nephritis treatment**

*Mycophenolate mofetil versus cyclophosphamide*

- Two studies by De Abreu et al. (1, 2) looked at patient and physician preferences for treatment options for lupus nephritis. Both studies had 172 female systemic lupus erythematosus patients from Brazil and the second study had the addition of 202 physicians to compare patient to physician preferences. The mean age of the patients was 34 ± 8 years, physicians 31 ± 7 years. Seventy-five percent had lupus nephritis, 39.9% of patients and physicians were Caucasian and 60.5% were non-Caucasian. Patients were given information about the efficacy and toxicity of the two medications (blinded to treatment names to reduce bias) and asked to rank the worst side-effects, and asked to justify treatment preference.
- Out of a list of side effects, the three worst side effects selected by patients were: cancer caused by the drug (44.2%), hair loss (21.6%), and severe infection (19.1%).
- Most patients preferred oral medication (mycophenolate mofetil) (68%) rather than intravenous cyclophosphamide.
  - The justification for the preference (patients vs. physicians), were risk (47.7% and 68.9%), effectiveness (12.2% and 2.0%), risk/benefit trade-offs (2.3% and 22.3%), and practicality (37.8% and 5.9%) (P < 0.001).
- Multivariate analysis suggest that patient decisions were steered by the risk associated with the drug, compared to an effectiveness-based justification (OR 31.8; 95%CI 8.2 to 122.9) or a practicality based justification compared to an effectiveness-based justification (OR 6.0; 95%CI 2.5 to 14.2).
- Patients with prior joint involvement were less likely to select mycophenolate mofetil, compared with patients with no joint involvement (OR 5.3; 95%CI 1.4 to 19.5).
Womens preferences for cyclophosphamide versus azathioprine

- Two studies looked at the preferences of women with lupus for cyclophosphamide or azathioprine using adaptive conjoint analysis (3) and the Health State Scenario Description and Preference questionnaire (4). The study participants were taken from New Haven, New London, and Danbury, USA.
- Premenopausal women who wanted more children were less likely to choose cyclophosphamide compared to azathioprine (56% vs. 80%, P= 0.04) (3).
- Ninety-eight percent of the participants chose azathioprine over cyclophosphamide when there was an equal probability of maintaining kidney survival. Of those initially preferring azathioprine, required probabilities greater 33% than conferred by cyclophosphamide after 15 years before they would choose to change medications.
- Thirty-one per cent were unwilling to switch from azathioprine to cyclophosphamide for improved short-term renal survival, and 15% were unwilling to switch to cyclophosphamide even if it offered maintenance of complete kidney survival at 15 years (4).
- Participants preferred medication with high efficacy and low risk of infection (each accounting for 20% of the variation in preferences) and were considered as important as differences in the probability of loss of kidney survival (3).
- Overall there was high individual variability in treatment preferences between participants and 91% preferred a collaborative role in their medication decision-making (4).
- The results found that those identified as risk-seeking participants had a preference for cyclophosphamide, while more risk-averse patients had a preference for treatments that were less effective but less toxic (5).

Barriers & facilitators to medication decision-making (non-specific lupus nephritis medication)

- There were two relevant studies (6, 7), one evaluating patients barriers and another looking at facilitators of medication decision-making. These US studies included 52 women (mean age 40.6 ±13.3) and used the nominal group technique (NGT) to acquire both qualitative and quantitative valuations.
- The study took participants from two different centres (eight NGTs at University of Alabama at Birmingham and University of California, San Francisco clinics) and had included participants with both low and high socioeconomic background, including a mix of ethnicity: Caucasian (23%), African American (52%) and Hispanic (25%) participants, this increases the generalizability of the findings.
- Side-effects were the most influential barrier chosen by the groups. Seven out of eight groups selected two to four side effect related barriers. Known or anticipated side effects had the highest weighted vote (15.4%), followed by medication expense/ability to pay for them (8.2%) and the fear that the medication could cause other diseases (7.8%) for most prominent perceived barriers.
  - There was no difference reported between ethnicities.
  - Participants expressed concerns about the impact that medication had on physical appearance, the impact on pregnancy, the practicalities of taking medications (IV compared to oral administration) affecting a normal life. Additionally, the cost of medication, and the perceived side-effects of medication influenced participant’s decisions.
- Patients generated 35 medication decision-making facilitators. Seven key facilitators were identified: effective patient-physician communication regarding benefits/harms, patients desire to live a normal life and concern for their dependents, experience benefits including improved quality of life, symptom relief and few/infrequent harms, and affordability (7).
  - Group responses according to ethnicity were unable to be achieved because of the variability of prioritized responses.
  - However, the benefit of effective communication with their health-care provider was brought up in all groups as a key facilitator.
References


**Outcome**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preference for medication: All patients</td>
<td>Based on data from 172 patients in 2 studies</td>
<td>Most female patients with SLE preferred mycophenolate mofetil compared to IV cyclophosphamide. Their justification for medications (compared to physician) was determined by the risk of therapy (48% vs. 69%), the effectiveness of medication (12% vs. 2.0%), risk/benefit trade-off (2% vs. 22%) and practicality of treatment (38% vs. 6%). All comparisons were statistically significant (P&lt;0.001). The risk of treatment (OR 31.8, 95%CI 8.2 to 122.9) and the practicality of therapy (OR 6.0, 95%CI 2.5 to 14.2) was considered more important than the effectiveness of treatment for patients.</td>
<td>Low</td>
<td>Patients were blinded to the name of therapies, and preferred MMF over IV cyclophosphamide. Patients compared to physicians placed more emphasis on the practicality of oral therapy compared to IV therapy. The practicality and risk of therapy were considered the most important factors in medication decision-making.</td>
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<td>Preference for medication: Patients with joint involvement</td>
<td>Based on data from 172 patients in 2 studies</td>
<td>Patients with joint involvement compared to patients with no joint involvement were less likely to choose mycophenolate mofetil over IV cyclophosphamide (OR 5.3, 95%CI 1.4 to 19.5)</td>
<td>Low</td>
<td>Patients with joint involvement compared to patients with no joint involvement preferred MMF over IV cyclophosphamide.</td>
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<td>Side-effects</td>
<td>Based on data from 172 patients in 2 studies</td>
<td>In two brazilian observation studies, 172 female patients with lupus nephritis considered the worst side-effects of treatment with either MMF or cyclophosphamide as cancer (44%), alopecia (22%), and severe infection (19%).</td>
<td>Low</td>
<td>Patients with lupus nephritis emphasised the importance of treatment-related side-effects of cancer, alopecia and severe infection.</td>
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## PICO (10.2)
Population: Females with lupus nephritis - patient preferences
Intervention: Cyclophosphamide
Comparator: Azathioprine

<table>
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<td><strong>Patient preferences</strong>&lt;br&gt;Equal probability of kidney survival</td>
<td>Based on data from 215 patients in 2 studies</td>
<td>98% of patients preferred azathioprine over cyclophosphamide when there was an equal probability of renal survival</td>
<td><strong>Very Low</strong>&lt;br&gt;Due to serious indirectness&lt;sup&gt;1&lt;/sup&gt;</td>
<td>The majority of patients with SLE in these studies of mainly Caucasian, high-income Americans preferred treatment for lupus nephritis with azathioprine compared to IV cyclophosphamide when there was an equal probability of kidney survival. This finding may not be representative of all patients with lupus nephritis.</td>
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<td><strong>Patient preferences</strong>&lt;br&gt;Different probabilities of kidney survival</td>
<td>Based on data from 265 patients in 3 studies</td>
<td>When cyclophosphamide conferred a 15% improved short-term kidney survival, 31% of patients still preferred azathioprine compared to cyclophosphamide. Of those initially preferring azathioprine, required probabilities greater than 33% than conferred by cyclophosphamide after 15 years before they would choose to change medications. However, 15% were unwilling to switch to cyclophosphamide even if it offered complete kidney survival at 15 years.</td>
<td><strong>Very Low</strong>&lt;br&gt;Due to serious indirectness&lt;sup&gt;2&lt;/sup&gt;</td>
<td>When the probability of short-term or long-term kidney survival was improved for cyclophosphamide not azathioprine, 15% of patients were still preferred azathioprine compared to cyclophosphamide. However, these findings may not be representative of the wider lupus nephritis population, as they are largely of Caucasian American patients from high SES backgrounds.</td>
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<td><strong>Patient preferences - Premenopausal women wanting children</strong></td>
<td>Based on data from 215 patients in 2 studies</td>
<td>Premenopausal women who wanted more children were less likely to choose cyclophosphamide compared to azathioprine (56% vs. 80%, P= 0.04).</td>
<td><strong>Very Low</strong>&lt;br&gt;Due to serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>In premenopausal women who wanted more children, azathioprine is the preferred therapy over cyclophosphamide.</td>
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1. **Indirectness: Serious.** Differences between the population of interest and those studied; Differences between the population of interest and those studied;
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<td><strong>Barriers</strong></td>
<td>Based on data from 52 patients in 1 studies</td>
<td>A representative sample of US patients with lupus nephritis indicated that side-effects were the most influential barrier to medication-decision making, with known or anticipated side-effects having the highest weighted vote using nominal group technique. Participants explained that this related to its effect on physical appearance, perceived side-effects impact on daily life and its effect on pregnancy and starting a family. Additionally, the cost and practical implications of treatment on daily life were considered important barriers to medication.</td>
<td>Low</td>
<td>In patients with lupus nephritis, side-effects either real or perceived influence there medication decision-making. With a focus on its impact on physical appearance and fertility. Costs and the implications on daily life (i.e. IV versus oral drug administration) were also important barriers to medication use.</td>
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<td><strong>Facilitators</strong></td>
<td>Based on data from 52 patients in 1 studies</td>
<td>A representative US sample of patients with lupus nephritis, using nominal group technique indicated that key facilitators to medication decision-making included: effective patient-physician communication regarding benefits and harms, a desire to live a normal life and impact on their families/dependents, improved quality of life, symptom relief and affordability</td>
<td>Low</td>
<td>In patients with lupus nephritis, good communication between patient and physician about benefits and harms and the impact of therapy on everyday life, and their families, as well as affordability are key facilitators to medication decision-making.</td>
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