

Systematic Review on Cost and Healthcare Resource Utilization in Immunoglobulin A Nephropathy (IgAN)

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Introduction

- Immunoglobulin A nephropathy (IgAN) is the most common form of primary glomerulonephritis worldwide and is characterized by the presence of predominant IgA1 deposits in the glomerular mesangium.¹
- The incidence of IgAN is estimated to be 2.5 per 100,000 population per year worldwide,² with the peak incidence observed in young adults aged 20-30 years.³
- Approximately 50% of IgAN patients with proteinuria ≥ 1 g/day progress to kidney failure in 15 years, irrespective of being on current standard of care like renin-angiotensin aldosterone system inhibitors and corticosteroids or other immunosuppressive agents.⁴
- Common signs and symptoms of IgAN include proteinuria, hematuria, hypertension, fatigue, pain and deteriorating kidney function (estimated glomerular filtration rate; eGFR),^{5,6} which can lead to a need for hospitalization, dialysis and kidney transplantation which are associated with economic burden.

Objective

- The aim of this systematic literature review (SLR) was to identify, collate and assess evidence related to costs and healthcare resource utilization (HCRU) associated with IgAN.

Methods

- The SLR was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta Analysis guidelines.⁷
- The following databases were searched to identify relevant publications from 1st January 2000 to 1st April 2021. Inclusion criteria are provided in **Table 1**.
 - Embase and Pubmed not MEDLINE (through embase.com)
 - Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily (through OVIDSP.com)
 - Cochrane database (through cochranelibrary.com)
- Additionally, key conferences, health technology assessment websites and bibliographies of included publications were hand-searched for relevant publications.
- The quality of included publications was assessed using the US National Heart, Lung, and Blood Institute study quality assessment tool for observational cohort and cross-sectional studies.⁸

Table 1: Inclusion Criteria

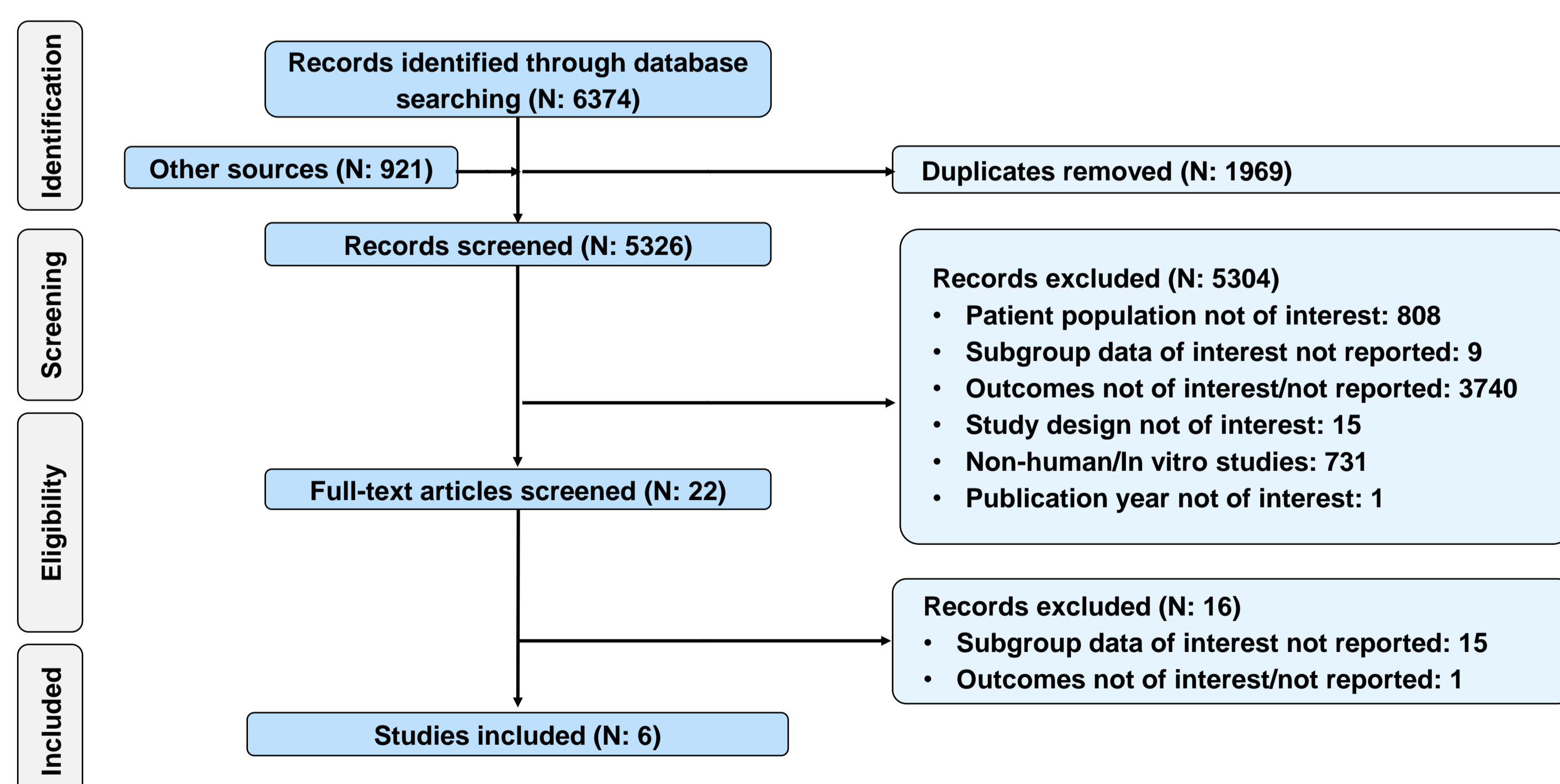
Criterion	Inclusion
Patient population	• Patients diagnosed with IgAN
Interventions	• Any intervention/no intervention for IgAN patients
Comparator	• Any other intervention/no intervention for IgAN patients; placebo, standard of care
Outcomes	• Cost (direct and indirect) • HCRU
Study designs	• Cost studies/surveys/analyses • Database studies collecting cost data • Burden of illness • Resource surveys
Language	• No restriction
Publication timeframe	• 1 st January 2000 to 1 st April 2021
Country	• No restriction

Abbreviations: HCRU: Healthcare Resource Utilization; IgAN: Immunoglobulin A Nephropathy

Results

- A total of six studies from 7,295 identified citations met the inclusion criteria (**Table 1**) and were included in this review (**Figure 1**)

Figure 1: Study selection using PRISMA flow diagram



Study characteristics:

- Sample size:** The number of IgAN patients ranged from 12 to 11,569;^{13,11} one study did not report sample size.¹²
- Country:** Out of six studies, the majority (5) were from Asia (three studies were conducted in China,^{9,10,11} two studies in Japan^{12,13}) and one study was conducted in Canada.¹⁴
- Study design:** Four studies were retrospective analyses^{9,10,11,14}, one study used a prospective design¹³, and one was a cost analysis study using a decision model.¹²
- Publication type:** Most of the included studies were full-text publications (5).^{9,10,11,13,14}

Patient characteristics:

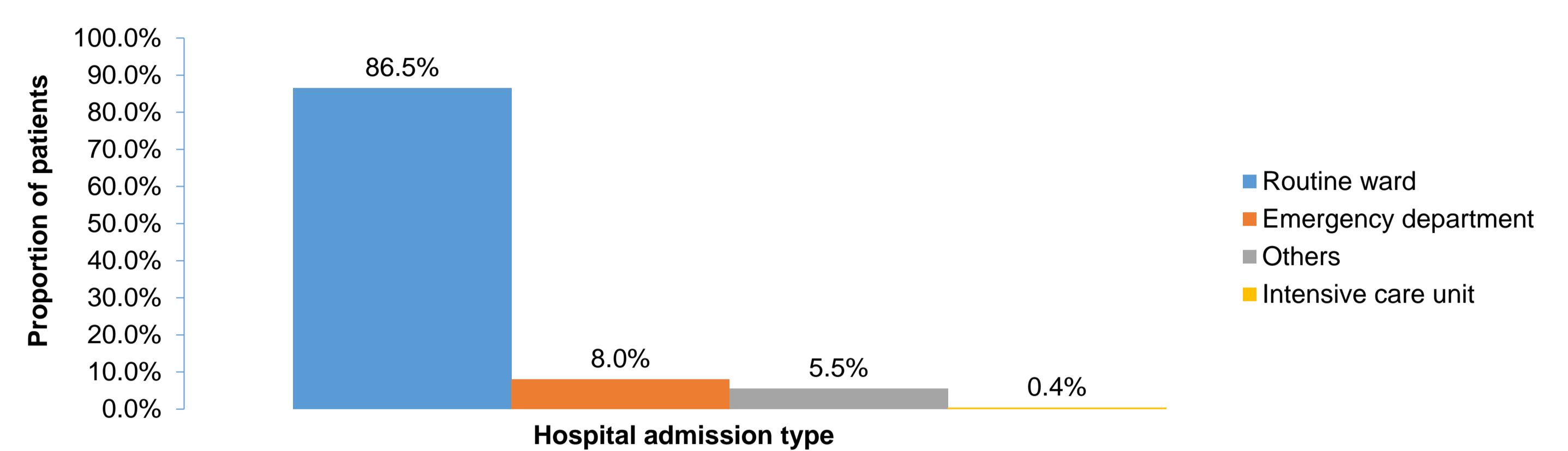
- Age:** The mean patient age ranged from 35 to 45 years.^{13,14}
- Gender:** The proportion of female patients ranged from 24.2% to 75.0%.^{9,13}
- eGFR:** Mean eGFR was only reported in three studies and ranged from 38 to 58.5 mL/min/1.73m².^{9,14}
- Proteinuria:** Mean/median proteinuria was only reported in two studies and ranged from 1.9 to 2.3 g/day.^{9,14}

HCRU:

- Four studies reported data on HCRU, including data on hospitalizations^{9,11} and length of stay (LOS).^{10,11,13}
- Hospitalizations:** Two studies from China reported data on hospitalization.^{9,11}

- Among 11,569 hospitalized IgAN patients in a national database analysis in China, 86.5% were admitted to a routine ward, 8.0% to the emergency department and the remaining patients (5.5%) to other wards. An intensive care unit (ICU) stay was reported for 0.4% of patients (**Figure 2**).¹¹

Figure 2: Types of hospital admission among 11,569 hospitalized IgAN patients in China¹¹

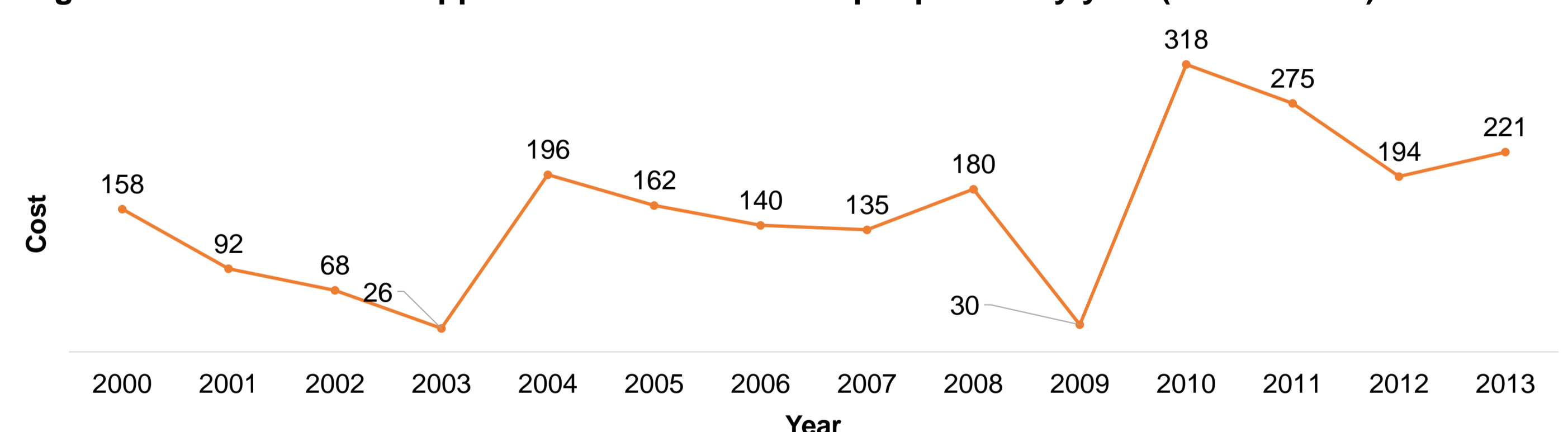


- In a retrospective single-center Chinese study among 132 IgAN patients with stage 3 or 4 chronic kidney disease (CKD) and proteinuria ≥ 1.0 g/d, a lower hospitalization rate due to infections was reported in patients who did not receive immunosuppressants compared to patients who received immunosuppressants (2.4% vs 8.8%; $p = 0.407$). Hospitalizations in patients treated with immunosuppressants were mainly due to pulmonary infections.⁹
- Length of stay:** Three studies (two from China and one from Japan) reported data on LOS.^{10,11,13}
 - Mean/median LOS in the Chinese studies ranged from 10.0 days ($n=11,569$) to 10.6 days ($n=1,350$).^{10,11} Reason for hospitalization of these patients was not reported.
 - Mean LOS in the Japanese study was 11.4 days ($n=12$). Patients in this study were hospitalized to undergo palate tonsillectomy for treatment of IgAN followed by a high-dose (1,000 mg) intravenous methylprednisolone pulse therapy for three consecutive days and oral prednisolone at a daily dose of 20 mg, gradually tapered and discontinued after one year.¹³

Cost:

- Four studies reported data on costs.^{10,11,12,14}
- Cost of treating IgAN patients:** Two studies from China reported data on costs.^{10,11}
 - A cross-sectional survey conducted between 2012 and 2017 using electronic medical records of hospitalized IgAN patients with CKD ($n=1,350$) reported mean per capita cost for treating IgAN as 14,900 CNY.¹⁰
 - A comprehensive retrospective analysis of a national Chinese database using data from IgAN patients ($n=11,569$) hospitalized between 2010 and 2015 reported median costs of treating hospitalized IgAN patients in 2015 as 8,000 CNY per patient.¹¹
- Cost of immunosuppressants:** One study from Canada reported cost of immunosuppressants (prednisone, azathioprine, cyclophosphamide, rituximab, mycophenolate mofetil, calcineurin inhibitors).¹⁴
 - A population-level retrospective cohort study using administrative health data of adult IgAN patients in Canada ($n=756$) reported a high variation in mean cost of immunosuppressants per patient over the 14-year period from 2000 to 2013 (**Figure 3**).
 - While for other types of glomerulonephritis costs of immunosuppressants significantly increased between 2000 and 2013, for patients with IgAN the mean change in per patient medication cost between year 2000 (158 CAD) and year 2013 (221 CAD) was not significant ($p = 0.08$). IgAN patients were mainly treated with prednisone (89-100%), whereas the use of other immunosuppressants remained low over the 2000-2013 study period.

Figure 3: Mean immunosuppressant cost in Canada per patient by year (in 2016 CAD)¹⁴



Cost analysis study using a decision model:

- A Japanese cost analysis study using a decision-analytic model with a societal perspective estimated a reduction of lifetime medical expenses per person by 20,633 USD when screened for IgAN using novel biomarkers versus conventional screening (novel: 287,270 USD vs conventional: 307,903 USD).¹²

Quality assessment:

- The included studies were judged to be of moderate quality since the publications did not provide sufficient information to respond to all of the quality assessment questions.

Conclusions

- There is scarce evidence on costs and resource use in IgAN patients.
- Existing evidence shows that currently used treatments like immunosuppressants and tonsillectomy are burdensome to the healthcare system and this warrants the need for improved, disease-specific therapy in IgAN.

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Conflict of Interest: George A, Akkapantula S, Kolli NR and Pannagl K are all permanent employees of Novartis. Doherty J was an employee of Novartis at the time of conducting this SLR.

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