The Life-long Economic Burden of Immunoglobulin A Nephropathy (IgAN) Patients in Chinese Adults

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Background

- IgA nephropathy(IgAN) is a primary glomerulonephritis (PGN) characterized by the deposition of the IgA antibody in the glomerulus, and it is one of the most important causes of end-stage renal disease (ESRD). After 10 to 20 years of follow-up, the rate of progression to ESRD is 17% to 36% in China [1].
- Globally, about one-third of PGN patients have been diagnosed with IgAN, and the proportion is higher in Asia. It is estimated that the number of adult patients with IgA nephropathy is about 4.6 million in China[2-3].
- IgAN occurs frequently in young adults. The patients aged 25~44 years account for 57.1%~67.0% of all patients, resulting in huge loss of productivity to the society[4-6].
- For patients progressed to ESRD, the annual direct medical expenses for peritoneal dialysis (PD), hemodialysis (HD) and renal transplant (RT) bring heavy economic burden to patients, families and the society[7-10].
- Due to the large number of IgAN patients and the heavier economic burden of treatment after disease progression, it is essential to predict the lifelong economic burden of IgAN patients in China.

Objective

Our study aims to estimate the total life-long cost of IgAN treatment and to quantify potential years of delayed to ESRD if risk of progression could be reduced in China.

Methods

Model Construction

- A three-state (IgAN, End-stage renal disease/ESRD, Death) Markov model was developed to estimate the total cost of IgAN with a life-long (45 years) time horizon from society perspective in China.
- The patients enter into the IgAN state, and then they can either remain with IgAN, progress to the ESRD or die in each cycle of the model. Patients who have progressed to ESRD cannot return to IgAN and can only remain in the ESRD state until the end of life. The death was the absorption state(Fig 1).
- The simulation for each cycle was 1-year duration with half-cycle correction, and the discount rate was 5%.
- The model was constructed and analyzed using Microsoft Excel 2016.

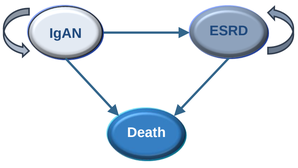


Fig 1. Markov model

Baseline characteristics

- The baseline characteristics of IgAN patients used in Markov Model were based on a Chinese IgAN Cohort study, which is the largest longitudinal study in China and more details as shown in Table 1[1].
- The age of kidney biopsy was 33 years, which was simulated to reach the national average life expectancy of 78 years after 45 years simulation (life-long) [11].

Table 1: Baseline characteristics of IgAN patients in China

Nanjing Glomerulonephritis Registry Database: IgAN Cohort			
Sample Sizes (n.)	1,126	**Urinary protein (g/day)**	
Female(%)	50.50%	**<1.0 (%)**	56.6%
Median Follow-up Time (years)	5.5	**≥1.0 (%)**	43.4%
Age of Kidney biopsy (years)	33	**＞3.5 (%)**	6.5%

Transition Probabilities

- The transition probabilities of IgAN state to ESRD state were based on Le's study[1], presenting in Fig 2. The best fit distribution for renal survival curve simulation was selected according to Akaike information criterion (AIC) and Bayesian information criterion (BIC).
- The age-adjusted all-cause mortality rate of IgAN was assumed equally to that of the natural population[12].
- The all-cause mortality rate of ESRD was calculated by adding ESRD-associated mortality to natural mortality. ESRD-associated mortality was from the published literature [13].
- Patients with IgAN could achieve remission or not after initial treatment. Based on the literature, the 6-month remission rate and non-remission rate of IgA patients were 74.40% and 25.6% [14].
- Patients after remission could relapse, and the 66-month relapse rate was 15.5% based on the published literature [14].

Interventions

- Based on literature review and experts' survey, 31.3% of patients use Renin-Angiotensin-Aldosterone System (RAAS) inhibitors + traditional Chinese medicine (TCM), 49.3% use RAAS inhibitors + TCM + glucocorticoid (GC) and 19.4% use RAAS inhibitors + TCM + GC + immunosuppress (IS).
- Patients achieved remission were assumed to continue use RAAS inhibitors + TCM for maintain treatment.
- Patients relapsed after initial treatment were assumed to use RAAS inhibitors + TCM + GC or RAAS inhibitors + TCM + GC + IS treatment.
- Patients with ESRD were treated by HD, PD and RT, accounted for 71.25%, 15.68% and 13.07%, respectively [9].

Costs

- The costs consist of direct medical costs, direct non-medical costs and indirect costs.
- The drug costs for IgAN patients were calculated based on the average bidding price of the drug multiplied by daily dose and the duration of treatment (DOT). The average bidding price came from Yaozhi Website[15].
- The direct medical costs of ESRD patients consist of the first-year costs and the follow-up year costs. The costs of HD, PD, and kidney transplantation were from the published literatures[8].
- The direct non-medical costs were calculated through the days of absence from work multiplied by the cost of transportation. The indirect costs were calculated through the days of absence from work multiplied by the China's GDP per capita in 2019 [16].
- According to the China Health Statistics Yearbook 2019 [17], the medical expenses of patients were increasing year by year. In this study, based on the literature data [9], the treatment expenses of patients with IgAN and ESRD and per capita GDP [16] are projected for long-term simulation.

Adverse Events

- Few studies have reported adverse events (AEs) of RAAS inhibitors, so this study mainly considered the AEs of Grade 3/4 severity of glucocorticoid and immunosuppressants, such as diabetes, infection, femoral head necrosis and insomnia [18-20].
- The costs of AEs treatments in patients with IgAN were mainly derived from literature and expert survey[21-26].

Results

Base-Case Result

- The cumulative renal survival rate of IgA patients at the 10th, 20th year were 83% and 64% based on the results from cohort, and projected to 30th ,40th and 45th years were 51.3%, 41.3%, and 37. 3%, respectively (Fig 2) .

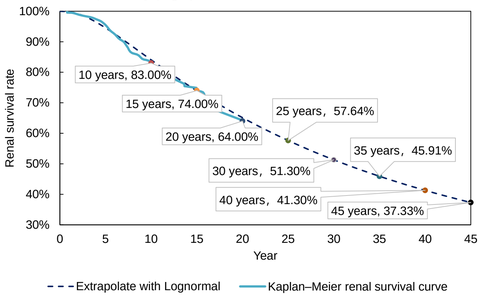
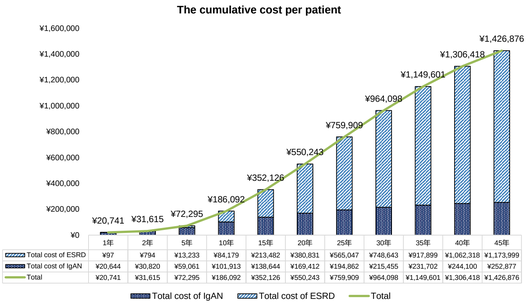


Fig 2. Renal survival curve

- **The average life-long cost of each patient with IgAN is RMB 1,426,876 (219,519 USD; exchange rate 1:6.5)** (Fig 3) from society perspective in China.
- More than 80% of total cost was attributed to the treatment cost of ESRD.



	1年	2年	5年	10年	15年	20年	25年	30年	35年	40年	45年
Total cost of ESRD	¥97	¥794	¥13,233	¥84,179	¥213,482	¥380,831	¥565,047	¥748,643	¥917,899	¥1,062,318	¥1,173,999
Total cost of IgAN	¥20,644	¥30,820	¥59,061	¥101,913	¥138,644	¥169,412	¥194,862	¥215,455	¥231,702	¥244,100	¥252,877
Total	¥20,741	¥31,615	¥72,295	¥186,092	¥352,126	¥550,243	¥759,909	¥964,098	¥1,149,601	¥1,306,418	¥1,426,876

Fig 3. The average life-long cost of per IgAN patient

Sensitivity Analyses

- Cost, transition probability, and other clinical parameters were considered in univariate sensitivity analysis. The parameters ranged from ±20% of the base case, and discount rate ranged from 0% to 8%.
- Univariate sensitivity analysis showed that the three main factors were the **discount rate**, **direct medical cost of ESRD** and **average annual all-cause mortality of ESRD** (Fig 4).

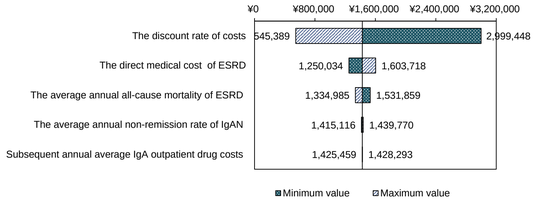


Fig 4. Univariate sensitivity analysis

Scenario Analyses

- If the risk of progression to ESRD could reduced by 10%, 20%, 30% by a new intervention compared to current IgAN treatment, **4, 8 and 14 years of ESRD will be delayed** (Table 2).

Table 2: Scenario analyses

Ratio of risk reduction of IgAN progression to ESRD	Median time of renal survival (Years)	Delayed progression to ESRD (Years)
Baseline	**31**	**Baseline**
10%	**35**	**4**
20%	**39**	**8**
30%	**45**	**14**

Conclusion

- **From society perspective, the lifelong cost of IgAN per patient is about 1.42 million in China, bringing heavy economic burden to the patients, families and healthcare system;**
- **In the scenario analysis, if a new treatment could reduce the risk of IgAN disease progressed to ESRD by 10%-30%, the time of progression to ESRD was significantly delayed by about 4-14 years;**
- **It has a huge unmet medical need to reduce the risk of patients progressing to ESRD, and then further reduce the financial burden on the healthcare system and improve patients' quality of life.**

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