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# Economic evaluation of lupus nephritis in the Systemic Lupus International Collaborating Clinics inception cohort using a multistate model approach

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**Running Head:** Economic Evaluation of Lupus Nephritis in an International Inception Cohort

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## Abstract

### Objective

Little is known about the long-term costs of lupus nephritis (LN). These were compared between patients with and without LN based on multistate modelling.

### Methods

Patients from 32 centres in 11 countries were enrolled in the Systemic Lupus International Collaborating Clinics (SLICC) inception cohort within 15 months of diagnosis and provided annual data on renal function, hospitalizations, medications, dialysis, and selected procedures. LN was diagnosed by renal biopsy or the American College of Rheumatology classification criteria. Renal function was assessed annually using estimated glomerular filtration rate (eGFR) or proteinuria (ePrU). A multistate model was used to predict 10-year cumulative costs by multiplying annual costs associated with each renal state by the expected state duration.

### Results

1,545 patients participated, 89.3% female, mean age at diagnosis 35.2 years (SD 13.4), 49.0% Caucasian, and mean follow up 6.3 years (SD 3.3). LN developed in 39.4% by the end of follow up. Ten-year cumulative costs were greater in those with LN and an eGFR < 30 ml/min ($310 579 2015 Canadian dollars versus $19 987 if no LN and eGFR > 60 ml/min) or with LN and ePrU > 3 g/d ($84 040 versus $20 499 if no LN and ePrU < 0.25 g/d).

### Conclusion


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Patients with eGFR < 30 ml/min incurred 10-year costs 15-fold higher than those with normal eGFR. By estimating the expected duration in each renal state and incorporating associated annual costs, disease severity at presentation can be used to anticipate future healthcare costs. This is critical knowledge for cost-effectiveness evaluations of novel therapies.

**Significance and Innovations**

- We are providing the first estimates of annual and 5 and 10-year cumulative costs stratified by baseline renal function in an international, multi-ethnic inception SLE cohort.

- An inception cohort allows for the development of multistate modeling, which provides a dynamic representation of both improvement and deterioration of renal disease in continuous time.

- Patients with lupus nephritis and a baseline eGFR < 30 ml/min incurred ten-year costs of $310 579 (2015 Canadian dollars) versus $19 987 if they did not have lupus nephritis and their baseline eGFR was > 60 ml/min.

- Similarly, patients with lupus nephritis and a baseline ePrU > 3 g/d incurred ten-year costs of $84 040 (2015 Canadian dollars) versus $20 499 if they did not have lupus nephritis and their baseline ePrU was <0.25 g/d.

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## Introduction

Renal disease in SLE patients is associated with significant morbidity and mortality, and is extremely costly (1). Approximately 40% of SLE patients develop lupus nephritis (LN), although in African descendants and Hispanics of predominantly Amerindian ancestry the frequency may be as high as 60% (2–4). Lupus nephritis varies from clinically silent pathology to end-stage renal disease (ESRD), and is often present at the time of SLE diagnosis (2). The current standard of care includes induction with corticosteroids and mycophenolate mofetil, cyclophosphamide, or rituximab and long-term maintenance therapy with mycophenolate mofetil or azathioprine (5,6). Despite receiving treatment according to established guidelines, a significant proportion of patients still progress to ESRD, requiring dialysis or transplantation. Recent studies including a 30-year single centre study (7) indicate that the 5-year risk of ESRD in SLE patients with renal disease ranges between 6.9% to 8.1% and a meta-analysis (8) reports that the 5-year risk of ESRD in those with LN decreased from 16% in the 1970s to 11% in the mid-1990s. These rates have plateaued for at least the past two decades. The presence of renal damage is the most important predictor of early mortality in SLE patients (9); in fact, it has been shown that renal damage reduces the survival of SLE patients by approximately 24 years, compared to the general population (10) and LN patients who develop ESRD have a 26-fold increased risk of mortality (11). Hence, numerous studies demonstrate significantly higher costs in patients with LN versus those without LN (1,12–14).

While SLE patients with renal injury are known to have increased healthcare costs compared to those without renal involvement (15), there is very little data on the long-term healthcare costs of LN patients (12). Between 1999 and 2011, the Systemic Lupus International Collaborating Clinics (SLICC) enrolled patients into an inception cohort to study long-term clinical outcomes. In previous research on this cohort, reversible multistate modeling has

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been used to estimate transitions (improvement or deterioration) between multiple states of renal function (16). This type of modeling is unique in that it provides a dynamic representation of renal dysfunction in continuous time as opposed to the typical static cross-sectional view provided by conventional regression analyses. In the current study, multistate modeling was used to forecast the duration in each renal state and the annual direct costs associated with each renal state were calculated. Five and ten-year cumulative costs were then estimated by multiplying the annual costs associated with each renal state with the expected duration in that state and were compared between patients with and without renal involvement. This methodology allows for prediction of costs for renal states in which there are few observations.

Understanding how patients progress through states of renal disease and the costs associated with each state will allow for cost-effectiveness analyses of novel emerging therapies.

## Patients and Methods

### *Inception cohort*

The SLICC network includes 32 academic centres from 11 countries (17). Members of this network enrolled patients fulfilling the American College of Rheumatology (ACR) revised classification criteria for SLE (18) into an inception cohort within 15 months of SLE diagnosis (i.e., date at which criteria were met). For this study, data collection extended from 1999 through to 2013. Data were collected at enrollment on demographics (age, sex, race/ethnicity) and at enrollment and annually (± 6 months) on disease activity [SLE Disease Activity Index – 2000 (SLEDAI-2K) (19)], disease damage [SLICC/ ACR Damage Index (SDI) (20)], smoking history, and alcohol consumption [high risk consumption defined as

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greater than 10 units per week for females and 15 units per week for males (21)]. Data were also collected annually on all hospitalizations, medications (including corticosteroids, antimalarials, immunosuppressives, biologics, antihypertensives, lipid-lowering agents, anti-epileptics, anti-psychotics and other psychoactive drugs, anticoagulants, and antiplatelets), and dialysis from any time since the previous assessment. The initial focus of the inception cohort was on cardiovascular and neuropsychiatric outcomes and later, on renal outcomes, and as part of the data collection protocol, diagnostic procedures related only to these outcomes were also recorded (e.g. ECGs, echocardiograms, stress tests, neuroimaging, and renal biopsies) and used for resource use and cost estimation. The study was approved by the institutional research ethics review board at each site and each participant provided written informed consent.

*Renal status*

Lupus nephritis was diagnosed by renal biopsy or fulfillment of the renal item on the ACR classification criteria for SLE (18).

Renal function was also assessed annually based on estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) equation (22), or on estimated proteinuria (ePrU) as measured by either 24 hour urine collection or spot urine total protein to creatinine ratio (23). eGFR was divided into three states: state 1 (eGFR > 60 ml/min), state 2 (eGFR 30-60 ml/min) and state 3 (eGFR < 30 ml/min). ePrU was stratified as: state 1 (ePrU < 0.25 g/d), state 2 (ePrU 0.25-3 g/d), or state 3 (ePrU > 3g/d). End stage renal disease (ESRD) was identified based on the SDI renal variable (20).

*Statistical Analysis*

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*Multistate Modelling*

At each assessment, patients were assessed for the presence of LN and state of eGFR and ePrU and were assigned to one of six states in Markov models (Figure 1) for either eGFR or ePrU. Within the eGFR model, it was clinically sensible to assume that a patient could not move from an eGFR state 1 or 2 to ESRD without first having transitioned through eGFR state 3 with LN. However, within the ePrU model, it was clinically reasonable to assume that a patient could develop ESRD from any ePrU state with LN. Further, in both models, direct transition from one state to a non-adjacent state was not permitted in continuous time (except for transition of ePrU state 1 or state 2 with LN to ESRD) and transitions could occur into adjacent higher or lower states, except for ESRD or LN where the transitions were unidirectional. However, changes between non-adjacent states could be observed between assessments, with the transition being assumed to occur through a set of adjacent transitions. Death was regarded as a censoring event consistent with the collection of cost data only in years when death did not occur.

Due to small numbers of transitions into less frequent states, the transition rates between observed states were estimated with a null multistate model without explanatory variables [full details provided in (16)]. This model can account for intermittent observations and, through conditioning on current states, for the correlation between observations within the same patient. The correlation among the states of a patient at the different assessment visits was characterized through the Markov assumption that the future evolution of a patient's renal function depends only on his/her current state and not on his/her previous history. Transition rates were estimated through maximum likelihood estimation and expected state occupancy times over fixed follow-up periods were also obtained.

*Calculating costs*

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Costs included all hospitalizations, medications, dialysis, and diagnostic procedures related to cardiovascular, neuropsychiatric, and renal manifestations. Costs were calculated from the Canadian national health insurance perspective by multiplying each health resource by its corresponding Canadian unit cost at the 2015 price level. Except for hospitalizations, national estimates for unit costs were based on provincial price data from the Ontario and Quebec Ministries of Health, adjusted to reflect average Canadian prices. The unit cost for medications was sourced from the Quebec List of Medications (published by the Régie de l'assurance maladie du Québec). Reimbursement for physician services related to investigations, dialysis and other procedures was based on the Ontario fee schedule (published by the Ontario Health Insurance Plan), and hospital costs for dialysis and day procedures were sourced from the Ontario Case Costing Initiative (OCCI) (24). Costs for hospitalizations were developed through the Case-Mix Group method from the Canadian Institute for Health Information (CIHI). This methodology adjusts for the case complexity through resource intensity weights. Appropriate weights were identified using data from previous research on reasons for hospitalizations in a representative sample of lupus patients (25). Cost per in-patient day was derived from this data, which also incorporated physician reimbursements during hospital stays, based on fee schedules from Ontario and Quebec. Adjustment to average Canadian 2015 price levels was done, in the case of medications, using the Consumer Price Index (http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/econ09a-eng.htm) ratio of provincial to national price indices for prescribed medicines, and for all other health services, using similar wage ratios for labour in the healthcare sector across provinces and calendar years (http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/health23-eng.htm).

To compute estimates of 5 and 10-year cumulative costs, annual costs associated with each state of renal function, defined as presence of LN and state of eGFR or ePrU or ESRD, were first estimated. Generalized least squares regression modeling with random effects was

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used to account for possible confounding of the relationship between annual costs and state of renal function. Potential confounding covariates included age, sex, race/ethnicity, geographic region (i.e. within versus outside of North America), disease duration, smoking, and high-risk alcohol use. Adjusted annual cost estimates were predicted using the average values of relevant confounders, and confidence intervals (CI) were calculated using the bootstrapping method, accounting for the non-normal distribution of healthcare costs. Five and ten-year cumulative costs stratified by baseline renal state were calculated by multiplying the adjusted annual cost estimates associated with each renal state by the expected duration in each state over five and ten years. However, accurate discounting of future costs required this calculation to be done for each consecutive year, using expected duration over one-year and repeating the process for longer term estimates. The year-to-year change in state was approximated using transition probabilities estimated after one year. The one-year state durations and transition probabilities were both derived from multistate modelling (16). Future annual costs for each baseline renal state were discounted at a yearly rate of 3% and annual costs were summed over the five-or-ten year period. Note that since the null multistate model does not include adjustment variables, predicted long-term costs can be compared based on this model, but will only reflect partial adjustment for confounders.

## Results

### *Patients*

A total of 1826 patients were recruited from 32 SLICC centres in 11 countries. Of these, 1545 patients (United States, n= 426; Europe, n=405; Canada, n=372; Mexico, n=184; and Korea, n=158) (Table 1) had at least an enrollment and one follow up assessment, allowing for costing analysis, and were therefore included in the analysis. Patients were 89.3% female, with a mean age at diagnosis of 35.2 years (SD 13.4), mean disease duration at

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enrollment of 0.47 years (SD 0.35), and mean follow up of 6.3 years (SD 3.3) (range: 0.6 to 13.7 years); 49.0% of the patients were Caucasian. These characteristics are similar to those for the entire cohort (2).

*Renal status*

Lupus nephritis was diagnosed in 609/1545 patients (39.4%). It was present at enrollment in 466/1545 patients (30.2%) and developed during follow up in another 143/1545 patients (9.3%).

*Annual costs and predictors*

For the eGFR model examining the association between annual costs and state of renal function, age greater than 65 years [regression coefficient $1700 (95% CI $8, $3392)] and region outside of North America [regression coefficient $1183 (95% CI $409, $1956)] were associated with higher annual costs and Caucasian race/ethnicity [regression coefficient -$870 (95% CI -$1653, -$88)] was associated with lower costs. For the ePrU model, the same variables were associated with annual costs [age > 65 years: regression coefficient $2229 (95% CI $601, $3858), region outside of North America regression coefficient $1110 (95% CI $337, $1884) and Caucasian race/ethnicity regression coefficient -$789 (95% CI -$1573, $-4)].

Once adjusted accordingly, i.e., calculated at cohort average values (in this case, the observed proportions of patients older than 65 years, residing outside of North America, and of Caucasian race/ethnicity in the sample), annual costs by renal state were markedly higher in those with ESRD than in those without LN and eGFR > 60 ml/min (state 1, no LN) or ePrU

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< 0.25 g/d (state 1, no LN) [($51 313 (95% CI $38 645, $63 982) versus $1813 (95% CI $1034, $2593) versus $1797 (95% CI $995, $2599)] (Table 2).

Annual unadjusted component costs are provided in Supplementary Table 1. In patients without LN, medications were the most costly component, whereas in those patients with LN and eGFR < 30 ml/min or with ESRD, dialysis was the most costly component. In patients with ePrU 0.25 g/d or more, with or without LN, hospitalization was the most costly component. In all other renal states, medications were the most costly component.

*Transition probabilities and expected state durations*

Based on the estimated transition rates between states, the probability and expected duration for each state of eGFR and ePrU in the absence and presence of LN after 1 year is shown in Table 3. As anticipated, for example, patients with LN and a baseline eGFR > 60 ml/min (state 1, LN) had a much lower probability of transitioning to ESRD (0.1%) than those with LN and a baseline eGFR < 30 ml/min (state 3, LN) (37.6%). Accordingly, patients with LN and an eGFR > 60 mL/min (state 1, LN) were forecasted to spend none of the next year in ESRD, whereas patients with LN and an eGFR <30 mL/min (state 3, LN) were forecasted to spend one fifth of the next year in ESRD (Table 3). Transition probabilities after 1 year and expected state durations over 1 year are also shown for ePrU in Table 3.

*Five and ten-year cumulative costs*

Five-year cumulative costs were predicted to be substantially higher in patients with LN and an eGFR < 30 mL/min (state 3, LN) or with ESRD at baseline (Table 4). Patients with LN and an eGFR < 30 mL/min (state 3, LN) had 5-year cumulative costs of $154 320 (95% CI

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$100 919, $207 721) and those with ESRD had costs of $242 196 (95% CI $182 407, $301 985) while those without LN and eGFR > 60 mL/min (state 1, no LN) at baseline were expected to accrue 5-year cumulative costs of $9536 (95% CI $5246, $13 825) (Table 4).

Ten-year cumulative costs were also greater in those with LN and an eGFR < 30 mL/min (state 3, LN) or with ESRD at baseline. Patients with LN and an eGFR < 30 mL/min (state 3, LN) had 10-year cumulative costs of $310 579 (95% CI $217 631, $403 528) and those with ESRD had costs of $451 406 (95% CI $339 977, $562 835) while those without LN and eGFR > 60 mL/min (state 1, no LN) at baseline had 10-year cumulative costs of only $19 987 (95%CI $11 061, $28 913) (Table 4).

Similarly, when renal function was stratified by ePrU, five-year cumulative costs were highest in those with LN and an ePrU of >3 g/d (state 3, LN) or with ESRD at baseline. Patients with LN and an ePrU of > 3g/d (state 3, LN) had 5-year cumulative costs of $39 638 (95% C1 $27 834, $51 441) while those without LN and ePrU of <0.25 g/d (state 1, no LN) at baseline had 5-year cumulative costs of only $9651 (95% CI $5393, 13 909) (Table 4). Ten-year cumulative costs were also greater in those with LN and an ePrU of > 3 g/d (state 3, LN) or with ESRD at baseline (Table 4).

**Discussion**

We have provided the first comparison of annual and 5 and 10-year cumulative costs stratified by baseline renal function in an international, multi-ethnic inception cohort of SLE patients. The use of an inception cohort allows for the development of multistate modeling, which can be used to forecast expected duration in each renal state. By incorporating annual costs associated with each renal state, long-term cumulative costs can be estimated

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stratified by baseline renal status. The regression model examining the association between annual costs and state of renal function produced point estimates of higher annual costs by an average of $870 in non-Caucasians compared to Caucasians in the eGFR model and an average of $789 in the ePrU model, consistent with literature on poorer health outcomes in non-Caucasians (26). As anticipated, worsening renal disease resulted in higher healthcare costs, with patients with ESRD projected to incur 10-year cumulative costs almost 23-fold that of patients with no LN and normal eGFR [($451 406 (95% CI $339 977, $562 835) versus $19 987 (95% CI $11 061, $28 913)]. Even patients with LN with eGFR < 60 ml/min who did not have ESRD still incurred substantial costs [($111 326 (95% CI $76 466, $146 185) to $310 579 (95% CI $217 631, $403 528)]. Patients with an eGFR < 30 ml/min and LN are substantially more expensive than patients with ePrU > 3 g/L and LN (10-year costs of $310 579 versus $84 040), because the former represent a sicker group of patients.

However, our study has some limitations. The SLICC network is based within tertiary care academic centres and therefore our patient population may not represent the entire spectrum of SLE patients and likely overestimates the hospitalization, medication, and dialysis costs incurred by SLE patients in a community practice. Further, we did not capture indirect costs due to lost productivity in paid and unpaid endeavors. Additionally, our assessment of healthcare resource utilization was incomplete and therefore we have underestimated total direct costs. While we did capture the most costly components of health resource use – hospitalizations, medications, dialysis, and physician visits associated with these services, we did not collect data on other physician or emergency room visits and our assessment of diagnostic procedures was restricted to those related to cardiovascular, neuropsychiatric, and renal disease. Based on our previous work (27) estimating long-term costs for Canadian lupus patients, where all components of direct costs were included, our current estimates would represent, on average, 68% of total direct costs. Our costs were also based only on data that was recorded while patients survived and incurred costs for the whole period preceding questionnaire administration. There were 36 deaths in the study

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(Supplemental Table 2) and because of our study design, we have no data on resource use in the year preceding death.

The substantial cost of LN has been reported by others, primarily through the use of insurance claims databases. Studies from the US have shown that patients with LN incurred annual costs that are 2.5 to 6-fold higher than patients without LN (1,12–14). Carls et al. reported annual costs were almost 4-fold higher in US patients with LN [$83 869 versus $ 22 188 in those without LN][1] (1) while Furst *et al.* reported that patients with LN incurred annual costs of $44 524 versus $7113 in matched controls without SLE (14). A Medicaid study reported lower annual costs, but the differential between those with LN and matched controls without SLE was almost 3-fold [$38 401 versus $12 945] (12). These annual costs for patients with LN are substantially higher than our estimates, which range between $3858 and $20 837 depending on the eGFR. However, our cost estimates for ESRD of $ 51 313 are more comparable to the estimates for LN based on insurance data. It is to be expected that our estimates are lower as we did not include all healthcare resources and we used Canadian prices for healthcare, which are much lower than in the US, relative to other consumer goods.

However, use of insurance claims data is limited by reliance on diagnostic codes, which may lead to inclusion of patients who do not have LN, and the lack of detailed data on renal pathology and renal function. Other studies have employed self-reported healthcare utilization in a clinical cohort to estimate the direct costs associated with LN (15), demonstrating almost 5-fold higher costs in ESRD patients compared to SLE patients without any renal damage as defined on the SDI ($144 389 versus $29 499). In our current study, we observed an over 25-fold difference in 5-year costs between those with ESRD and an eGFR > 60 ml/min and no LN ($242 196 versus $9536). This much higher differential in

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our current study is attributable to two factors: 1) the costs of ESRD are higher in the current study because they are more precise and 2) the costs incurred by patients without renal damage as defined by the SDI are higher than in our current study because these patients were older, had accrued more non-renal damage, and also had renal dysfunction not sufficient to fulfill the SDI renal criteria.

A recent Swedish study estimated both the annual direct and indirect costs of LN compared to all SLE patients by linking well-defined clinical cohorts to national registries and the social insurance system. SLE patients with LN incurred direct costs of $18 579 compared to $13 339 in all SLE patients (28), with indirect costs comprising approximately 60% of total costs for those with LN and 70% for those without LN. These direct cost estimates for patients with LN are reasonably comparable to ours where annual costs ranged between $3858 and $20 837 for those with LN, but without ESRD.

Unfortunately, the frequency and survival of SLE-related ESRD has not improved over several decades (7,8,29,30), highlighting the need for new therapies. Although numerous clinical trials of biologics have yielded disappointing results for LN, novel agents continue to emerge, and there is optimism that some will be proven effective (31). Koutsokeras and Healy (32,33) forecasted the LN market to be $505 million by 2022 for seven major international markets (United States, France, Germany, Italy, Spain, the United Kingdom, and Japan). As novel biologics become available, understanding the current costs of LN using standard of care is necessary for cost-effectiveness studies. Biologics are very costly, and are often utilized for only refractory or advanced disease. However, they are likely to become more cost-effective over time as their patents expire while the cost of dialysis is unlikely to decrease. Our study demonstrates the substantial cost increases in patients with

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more advanced renal disease, highlighting the cost savings potentially achieved by earlier aggressive therapy to prevent progression or induce remission of renal disease.

**Footnote**

[1]Currencies from publications have been converted to 2015 Canadian dollars using purchasing power parities data from the Organisation for Economic Cooperation and Development (https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm) and the consumer price index from Statistics Canada (http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/econ09a-eng.htm).

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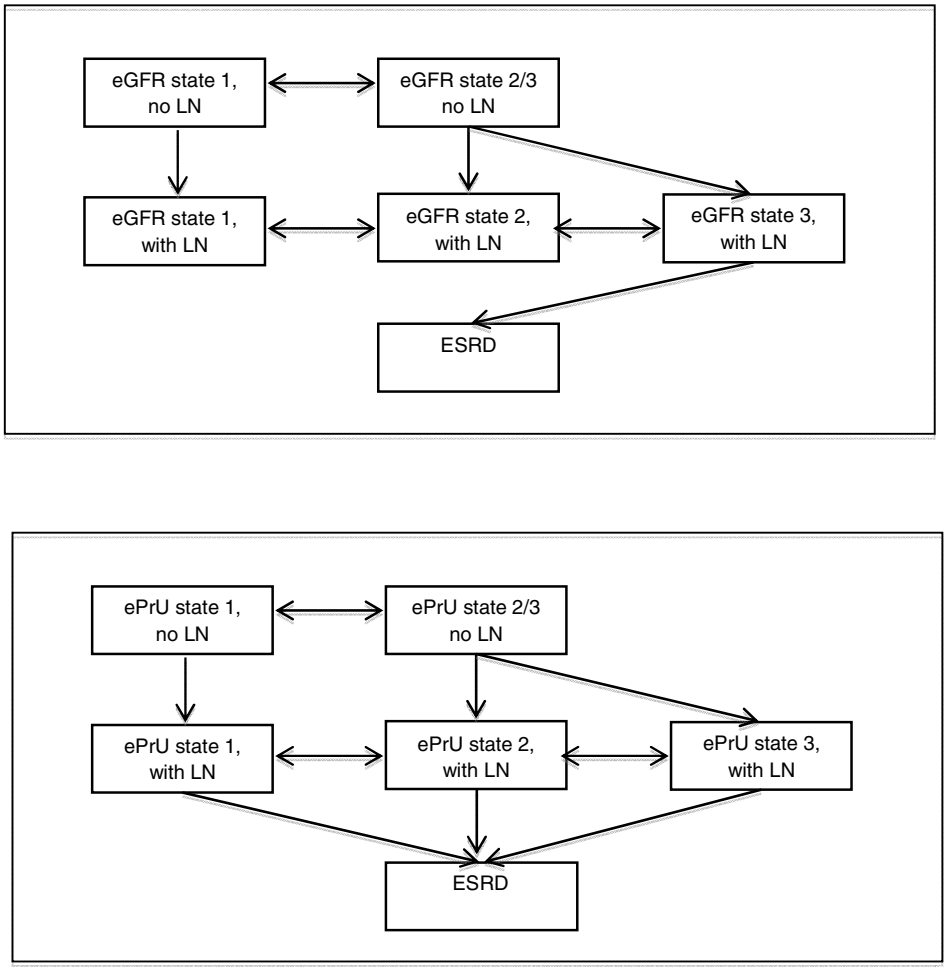


**Figure 1: Multstate Markov model for observed transitions between estimated glomerular filtration rate (eGFR) and estimated proteinuria (ePrU) states**

eGFR: state 1 > 60 mL/min, state 2 30 – 60 mL/min, state 3 < 30 mL/min

ePrU: state 1 < 0.25 g/d, state 2 0.25 – 3.0 g/d, state 3 > 3.0 g/d

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## Tables

**Table 1 –** Baseline demographic and clinical manifestations of patients

| | |
|---|---|
| No. of patients: | 1545 |
| Age (years): (Mean ± SD) | 35.2 (13.4) |
| Gender (%): | |
| Female | 89.3 |
| Male | 10.7 |
| Race/Ethnicity (%): | |
| Caucasian | 49.0 |
| Hispanic | 14.9 |
| Asian | 16.1 |
| African | 16.2 |
| Other | 3.8 |
| Country (%): | |
| United States | 27.6 |
| Europe | 26.2 |
| Canada | 24.1 |
| Mexico | 11.9 |
| Korea | 10.2 |
| Disease Duration (yr) (Mean ± SD) | 0.47 (0.35) |
| ACR Classification Criteria (%): | |
| Malar Rash | 34.7 |

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| | |
|---|---|
| Discoid Rash | 11.4 |
| Photosensitivity | 34.4 |
| Oral/nasopharyngeal Ulcers | 36.1 |
| Serositis | 27.1 |
| Arthritis | 72.4 |
| Renal Disorder | 26.9 |
| Neurological Disorder | 4.9 |
| Hematologic Disorder | 61.1 |
| Immunologic Disorder | 73.4 |
| Antinuclear Antibody | 92.0 |
| SLEDAI-2K (Mean ± SD) | 5.3 (5.3) |
| SDI score (Mean ± SD) * | 0.32 (0.73) |
| Medications (%): | |
| Corticosteroids | 70.3 |
| Antimalarials | 67.3 |
| Immunosuppressants | 39.0 |
| Comorbidities/Lifestyle | |
| Current Smoker (%) | 14.7 |
| Alcohol (% with high risk consumption) | 1.2 |

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ACR = American College of Rheumatology; SDI = SLICC/ACR Damage index; SLEDAI-2K = SLE Disease Activity Index – 2000

* For patients with a disease duration of less than six months, SDI cannot be calculated – therefore at enrolment, SDI was available on 580 patients

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**Table 2 –** Predicted annual health costs stratified by state of eGFR and ePrU

| | eGFR | ePrU |
|---|---|---|
| eGFR/ePrU State* | Costs, 2015 CDN$ (Mean, 95% CI) | Costs, 2015 CDN$ (Mean, 95% CI) |
| State 1 (no LN) | 1813 (1034, 2593) | 1797 (995, 2599) |
| State 2/3 (no LN) | 2955 (37, 5873) | 2740 (1467, 4013) |
| State 1 (LN) | 3858 (2858, 4859) | 3768 (2341, 5194) |
| State 2 (LN) | 4012 (2362, 5662) | 4739 (3485, 5993) |
| State 3 (LN) | 20837 (3628, 38046) | 5643 (3302, 7984) |
| ESRD | 51313 (38645, 63982) | 50944 (38158, 63730) |

eGFR = estimated glomerular filtration rate; ePrU = estimated proteinuria; ESRD = end-stage renal disease; LN = lupus nephritis; CDN = Canadian

*eGFR: state 1 > 60 mL/min, state 2 30 – 60 mL/min, state 3 < 30 mL/min

ePrU: state 1 < 0.25 g/d, state 2 0.25 – 3.0 g/d, state 3 > 3.0 g/d

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**Table 3 –** Probabilities of transitioning between states and duration of eGFR and ePrU states over 1 year

| | Probability of being in state after 1 year | | | | | |
|---|---|---|---|---|---|---|
| | State 1 | State 2/3 | State 1 | State 2 | State 3 | |
| Initial State* | no LN | no LN | LN | LN | LN | ESRD |
| eGFR | | | | | | |
| State 1 (no LN) | 0.955 | 0.020 | 0.024 | 0.001 | 0.000 | 0.000 |
| State 2/3 (no LN) | 0.364 | 0.598 | 0.011 | 0.025 | 0.002 | 0.000 |
| State 1 (LN) | 0 | 0 | 0.957 | 0.039 | 0.003 | 0.001 |
| State 2 (LN) | 0 | 0 | 0.314 | 0.557 | 0.096 | 0.033 |
| State 3 (LN) | 0 | 0 | 0.040 | 0.146 | 0.438 | 0.376 |
| ESRD | 0 | 0 | 0 | 0 | 0 | 1 |
| ePrU | | | | | | |
| State 1 (no LN) | 0.931 | 0.050 | 0.012 | 0.006 | 0.001 | 0.000 |
| State 2/3 (no LN) | 0.674 | 0.216 | 0.028 | 0.065 | 0.015 | 0.002 |
| State 1 (LN) | 0 | 0 | 0.814 | 0.171 | 0.011 | 0.004 |
| State 2 (LN) | 0 | 0 | 0.354 | 0.567 | 0.063 | 0.016 |
| State 3 (LN) | 0 | 0 | 0.162 | 0.467 | 0.314 | 0.057 |
| ESRD | 0 | 0 | 0 | 0 | 0 | 1 |
| | Expected duration in state over 1 year | | | | | |
| eGFR | | | | | | |
| State 1 (no LN) | 0.977 | 0.011 | 0.012 | 0.000 | 0.000 | 0.000 |
| State 2/3 (no LN) | 0.198 | 0.781 | 0.004 | 0.015 | 0.001 | 0.000 |
| State 1 (LN) | 0 | 0 | 0.977 | 0.022 | 0.001 | 0.000 |
| State 2 (LN) | 0 | 0 | 0.173 | 0.752 | 0.062 | 0.012 |
| State 3 (LN) | 0 | 0 | 0.014 | 0.093 | 0.684 | 0.209 |

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| | | | | | | |
|---|---|---|---|---|---|---|
| ESRD | 0 | 0 | 0 | 0 | 0 | 1 |
| ePrU | | | | | | |
| State 1 (no LN) | 0.960 | 0.032 | 0.006 | 0.002 | 0.000 | 0.000 |
| State 2/3 (no LN) | 0.434 | 0.499 | 0.011 | 0.044 | 0.010 | 0.001 |
| State 1 (LN) | 0 | 0 | 0.895 | 0.100 | 0.004 | 0.001 |
| State 2 (LN) | 0 | 0 | 0.206 | 0.743 | 0.043 | 0.008 |
| State 3 (LN) | 0 | 0 | 0.065 | 0.323 | 0.580 | 0.032 |
| ESRD | 0 | 0 | 0 | 0 | 0 | 1 |

eGFR = estimated glomerular filtration rate; ePrU = estimated proteinuria; ESRD = end-stage renal disease; LN = lupus nephritis;

*eGFR: state 1 > 60 mL/min, state 2 30 – 60 mL/min, state 3 < 30 mL/min

ePrU: state 1 < 0.25 g/d, state 2 0.25 – 3.0 g/d, state 3 > 3.0 g/d

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**Table 4 –** Predicted 5-year and 10-year cumulative health costs stratified by baseline state of renal function for eGFR and ePrU

| eGFR/ePrU State* | eGFR Costs, 2015 CDN$ (Mean, 95% CI) | ePrU Costs, 2015 CDN$ (Mean, 95% CI) |
|---|---|---|
| 5-year | | |
| State 1 (no LN) | 9536 (5246, 13825) | 9651 (5393, 13909) |
| State 2/3 (no LN) | 12641 (4340, 20941) | 12317 (7298, 17336) |
| State 1 (LN) | 20829 (14666, 26992) | 22479 (14924, 30034) |
| State 2 (LN) | 47486 (30248, 64723) | 27788 (19339, 36236) |
| State 3 (LN) | 154320 (100919, 207721) | 39638 (27834, 51441) |
| ESRD | 242196 (182407, 301985) | 240499 (180173, 300826) |
| 10-year | | |
| State 1 (no LN) | 19987 (11061, 28913) | 20499 (11681, 29318) |
| State 2/3 (no LN) | 25988 (12175, 39802) | 25997 (15747, 36247) |
| State 1 (LN) | 47524 (33158, 61891) | 50997 (34654, 67340) |
| State 2 (LN) | 111326 (76466, 146185) | 61030 (42667, 79394) |
| State 3 (LN) | 310579 (217631, 403528) | 84040 (59619, 108461) |
| ESRD | 451406 (339977, 562835) | 448336 (335942, 560730) |

eGFR = estimated glomerular filtration rate; ePrU = estimated proteinuria; ESRD = end-stage renal disease; LN = lupus nephritis; CDN = Canadian

*eGFR: state 1 > 60 mL/min, state 2 30 – 60 mL/min, state 3 < 30 mL/min
ePrU: state 1 < 0.25 g/d, state 2 0.25 – 3.0 g/d, state 3 > 3.0 g/d

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