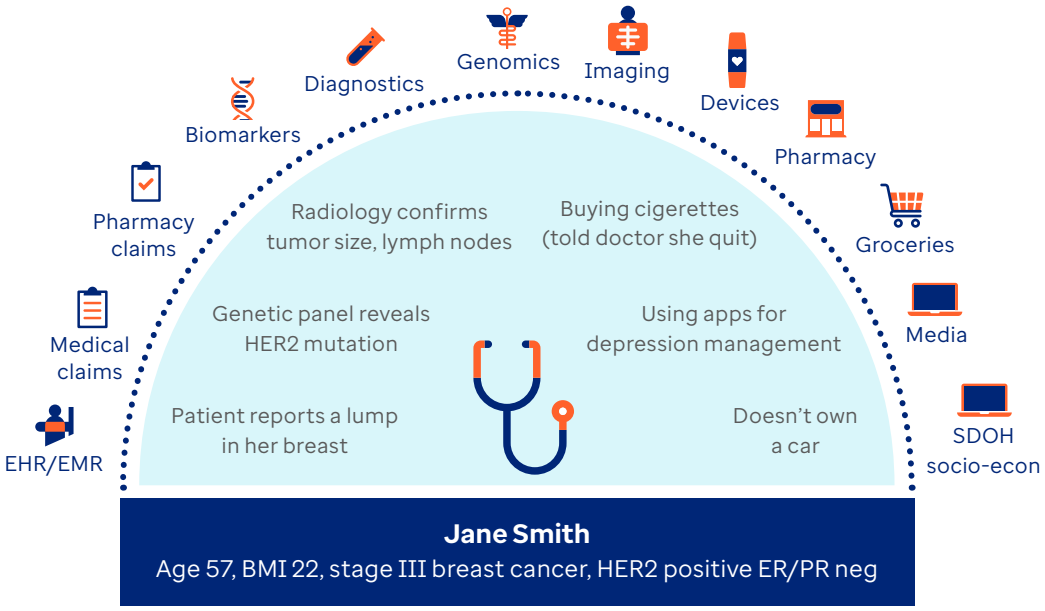
Optum

Patient journey as a foundation for insight: A lupus nephritis case study

The patient journey is a term broadly referring to tracking a given patient or a cohort of patients throughout their health care encounters. The journey is understood through data that tracks the patient's clinical trajectory from wellness to illness. It includes data related to risk factors for, development of, and the clinical course of their disease. The entire journey could include endogenous to exogenous data from the patient's molecular profile, clinical encounters, adjudicated claims, social determinants of health, lifestyle choices and digital behavior. It could even include environmental data like weather or allergens. Lastly, it's longitudinal, observing a patient over time.



There are many articles on the patient journey. Mapping the journey is one of the most valuable exercises we undertake because it answers critical questions of interest to all health care stakeholders. We all seek to understand how patients are diagnosed and treated, and whether they respond to therapy. The questions often center around factors that influence key decisions (such as symptoms that trigger testing), the time to critical events (diagnosis, surgery, mortality, etc.), and how care decisions impact patient outcomes. Some of the questions most often asked include:

Testing and diagnosis

- How does a given disease manifest in patients and what are the risk factors?
- What symptoms drive a patient to present to a care provider?
- What diagnostics and tests do providers administer?
- What test results, clinical assessments or symptoms lead to specific diagnoses?

Treatment selection, change and adherence

- What drives providers to initiate, discontinue or switch treatment?
- How are procedures, therapeutics and devices combined during treatment?
- How do specific care choices compare in improving outcomes?
- To what extent are treatment guidelines followed in real-world practice?
- What factors influence adherence to the therapeutic regimen?

Inpatient and outpatient care decisions, prescribing and transitions of care

- What types of care decisions are made in the inpatient care setting?
- Which inpatient departments are part of the care journey?
- What factors put patients at greater risk for inpatient adverse events (such as infections, falls or sepsis)?
- What tests, drugs and procedures are used during inpatient confinement?
- What interventions are prescribed at discharge?
- What factors influence adherence to the therapeutic regimen?
- Where and when is patient follow-up taking place?
- What is the average length of stay? How often are patients readmitted and why?

It is interesting to explore how the same patient journey exercise is relevant to every health care stakeholder. Let's use a lupus nephritis case study to illustrate:

The importance of the journey to each market participant

What the patient journey analysis can reveal

How each group acts on those insights

How major health care stakeholders may use the lupus patient journey

The Lupus Foundation of America estimates that 1.5 million Americans and at least 5 million people worldwide have a form of lupus.[1] Patients may report different types of initial symptoms of lupus, including fatigue, joint pain or photosensitivity.[2] A diagnosis of lupus requires a positive antinuclear antibody test and scoring 10 points or more across 10 different domains.[3] Patients often see their general physician first when experiencing symptoms, and symptoms may be present for as long as 5 years leading up to diagnosis[4]

In the United States, approximately 35% of adults with systemic lupus erythematosus (SLE) have clinical evidence of kidney nephritis at the time of diagnosis, with an estimated total of 50%–60% developing nephritis during the first 10 years of disease.[5] Lupus nephritis is a serious condition because when not controlled, patients can progress to chronic kidney disease (CKD) or end-stage renal disease (ESRD), which may require dialysis and/or a kidney transplant.[6]

Lupus patients with active nephritis at the start of treatment must be monitored carefully. Certain tests such as blood pressure monitoring, urinalysis, UACR and serum creatinine must be conducted on a monthly basis. Testing for complement C3/C4 and anti-DNA antibodies is recommended quarterly. In lupus patients with no prior or current nephritis, tests must be conducted twice in a year (with the exception of blood pressure monitoring, which is monitored on a quarterly basis).[5]

Lupus nephritis is classified histologically into 6 types according to the International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2003 classification. The ISN/RPS classes guide treatment decisions. It is believed that class I lupus nephritis often remains undiagnosed as there are frequently no clinical findings recorded. Class II lupus nephritis presents with mild proteinuria or renal insufficiency. Immunosuppressive therapy is not recommended for class I and class II.[5]

The proliferative classes III and IV are treated with anti-inflammatory and potent immunosuppressive agents. The induction of immunosuppressive therapy usually lasts 3 to 6 months, followed by a longer period of less intensive maintenance therapy. Even with available treatments, up to 50% of patients with lupus nephritis progress to ESRD within 5 years of diagnosis.[6]

The current guidelines recommend either mycophenolate mofetil (CellCept®) or cyclophosphamide with prednisone as first line therapy for class III or IV patients who experience lupus nephritis flares, confirmed through kidney function tests, urinalysis and/or kidney biopsies.[7] Recent scientific literature suggests that patients who experience complete renal response may be able to delay their progression to CKD/ESRD and a kidney transplant.[8]

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A life sciences organization working on a new therapy that delays kidney function decline in lupus nephritis may use patient journey insights to inform their strategy. For example, clinical real-world data (RWD) can help biopharma organizations:

1. Understand what proportion of patients with SLE develop lupus nephritis
2. Measure the time from the SLE diagnosis to development of lupus nephritis
3. Assess how often testing is conducted
4. Evaluate compliance with guideline recommendations on initial therapy
5. Quantify the time from the lupus nephritis diagnosis to CKD, ESRD and, ultimately, a kidney transplant
6. With medical and pharmacy claims one could also try to quantify the cost of patients who progress to CKD and ESRD and whether existing therapies reduce those costs

Providers may use the same insight in population health initiatives to increase screening. They may use medical education to improve adherence to guideline-recommended testing and initial choice of therapy. Payers will look at the total costs of lupus nephritis, including medical and pharmacy, and the largest cost drivers like dialysis and kidney transplant. They may identify points in the patient's care journey where they can help increase physician and patient engagement in testing kidney function and adherence to recommended therapies.

35%

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Tracing the development of lupus nephritis using Optum EHR data

We explored the journey of patients with a diagnosis of SLE who developed lupus nephritis to assess a) the proportion of patients who receive guideline recommended testing and treatment, and b) the proportion of those patients who progress to CKD/ESRD by testing and treatment status. We used the Optum electronic health record (EHR) data set, which is a de-identified longitudinal data set of more than 100 million patients treated mostly in practices that are part of integrated delivery networks (IDNs). We examined the period of 2015 to 2019 and identified 150,097 patients diagnosed with SLE (with no history in the prior 5 years).[9]

SLE patients with a high risk of renal involvement (males, juvenile lupus onset, serologically active, including positivity for anti-C1q antibodies) must be monitored at routine intervals (every 3 months) to detect any signs of kidney disease.[10] We looked at the number of patients assessed for markers suggestive of lupus nephritis using any of the following tests – serum creatinine, urinalysis, UACR, proteinuria (24 hours), complement C3/C4 and anti-DNA – either alone or together. We found that nearly half of SLE patients were screened (approximately 54.4%).[9]

As lupus nephritis does not have a dedicated ICD code other than SLE with organ involvement, we used markers for lupus nephritis to identify patients with the condition. We have defined the lupus nephritis population using SLE patients who also had ICD codes for proteinuria, nephritis and glomerular diseases in the SLE population. Using these criteria, nearly a quarter (22.6% or 34,072) of all SLE patients in the data appear to develop lupus nephritis. The average time to diagnosis was approximately 7 months.[9]

Kidney function testing frequency

Guidelines recommend that all lupus nephritis patients (SLE patients with renal involvement) are administered monthly kidney function tests including urinalysis, UACR and serum creatinine. Other tests (complement C3/C4 and anti-DNA antibodies) are recommended less frequently. Of all the lupus nephritis patients who met the guideline criteria for testing, 54% did not receive any test.[9] It is important to note that the EHR may not capture all lab tests and results. We used the data available in the structured fields to conduct this analysis.

Over the course of one year, only 2%–5% of patients received each of the recommended urine tests nearly every month. About half of patients did not have any urinalysis test and even higher rates received no UACR or creatinine clearance testing.[9]

	Urinalysis	UACR	Creatinine
(Guideline recommended test frequency)	Monthly	Monthly	Monthly
As recommended (%)	2.3	0.9	1
9-11 tests/year (%)	2.2	0.7	0.5
5-8 tests/year (%)	8.4	3.4	1.6
2-4 tests/year (%)	23.5	12.5	5.8
Once yearly (%)	17.1	9	6.7
No test (%)	46	73.3	84

Table shows the frequency of urinalysis, UACR and creatinine tests performed within one year after lupus nephritis diagnosis in 34,072 patients

Adherence to treatment guidelines

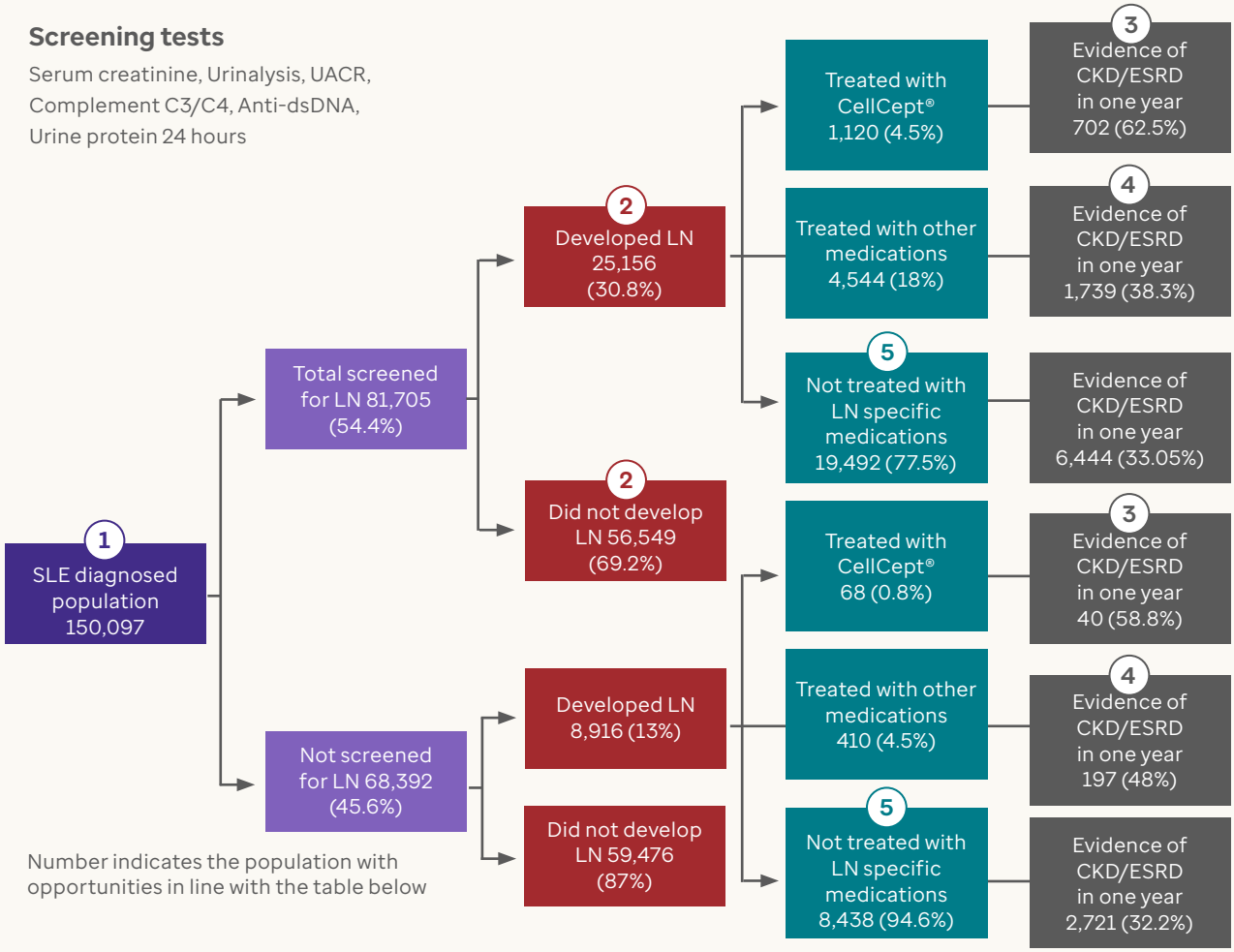
With regard to treatment, clinical guidelines recommend different treatment approaches based on ISN/RPS class of the disease. Class I and II patients are managed according to the treatment regimen for SLE and usually no immunosuppressive treatment is given. Class III and IV patients are managed with an induction therapy using either mycophenolate mofetil (CellCept®) or cyclophosphamide to control autoimmunity and high-dose corticosteroids for rapid control of inflammation. Induction therapy is given for the first 3 to 6 months, followed by a less intensive maintenance therapy to maintain autoimmunity and inflammation, thereby preventing a flare.[5]

Structured staging data are often not available in EHR data. Stratifying patients by lupus nephritis class could be done via kidney function and biopsies, but neither of those tests were prevalent enough in the data. Only 5% (1,595) of the total patients who developed lupus nephritis received a kidney biopsy in the year after diagnosis.[9] Therefore, we looked at those patients who received treatment and the treatment sequence as a measure to understand adherence to treatment guidelines. In the untreated population, we looked at the proportion of patients who progress to CKD or ESRD to ascertain the proportion of patients who are undertested and undertreated.

Nearly 35% of all lupus nephritis patients (11,843) progress to CKD or ESRD within a year of diagnosis irrespective of treatment.[9] Even when the guideline-recommended hyphenate therapy mycophenolate mofetil (CellCept®) is prescribed, more than 50% of patients taking the drug progress to kidney failure in less than one year.[9] A large proportion of patients remain untreated with any of the induction therapies or glucocorticoids, and 33% of these patients progressed to CKD or ESRD within a year of diagnosis.

Only 2%-5%

of patients received each of the recommended urine tests nearly every month over the course of one year.



For a life sciences company developing a new therapy for lupus nephritis, if validated, the following insights would be valuable to the commercial strategy:

Insight	Implication
1. Increase screening of SLE patients About one quarter of SLE patients develop lupus nephritis and up to 35% of those progress to kidney failure.	1. Quarterly screening of high-risk SLE patients (males, juvenile lupus onset, serologically active, including positivity for anti-C1q antibodies) should be reinforced to better detect development of lupus nephritis. 2. Treatment should be initiated upon diagnosis of a flare-up or kidney impairment with a goal of complete renal response.
2. Need for new lupus nephritis therapies Even when clinical guidelines are followed for treated patients, 50% of patients' kidney function continues to decline to ESRD within one year.	3. There is an unmet medical need in lupus nephritis for new therapies as significant numbers of patients on guideline-recommended therapy still develop significant kidney impairment. 4. The time to developing CKD or ESRD, suggesting that for a notable proportion of patients, existing therapies do little to delay the time to CKD or ESRD.
3. Increase monitoring and treatment rate of lupus nephritis patients • More than 50% of diagnosed patients do not receive any kidney function testing. Of those tested, only 1% or 2% received testing at the recommended frequency. • A significant number of diagnosed patients go untreated (77%). Of those, 33% progress to CKD or ESRD.	5. There is a need to increase the frequency of renal function testing to identify lupus nephritis patients whose disease progresses to the point of needing treatment. 6. With more testing, it is likely more patients will be eligible for treatment.

For providers, these insights may offer opportunities for increased monitoring and intervention. For diagnosed lupus nephritis patients, the importance of kidney function monitoring cannot be understated, and the effectiveness of CellCept® and prednisone should be determined by the extent to which patients experience complete renal response. Health systems may elect to benchmark the kidney function testing rate for affected patients and the rate of therapy initiation to closely monitor this population and reinforce testing and guideline recommended treatment. If new therapies emerge, it would be useful to understand if concomitant prescribing of CellCept® with the new therapy could better achieve full renal response and lengthen trajectory of kidney function decline.

Payers who estimate the total cost of care for lupus nephritis patients whose renal function declines and transition to ESRD (even when on CellCept®) may want to identify whether the right incentives are in place to a) evaluate the appropriate patients for lupus nephritis, b) prescribe guideline recommended drug combinations to achieve complete renal response, and c) monitor patient response to therapy to maintain complete renal response for as long as possible.

A life sciences company with a new lupus nephritis therapy should conduct an integrated EHR and claims-based study to estimate the real-world costs of managing lupus nephritis patients. This would include estimating the rate of those who progress to requiring renal replacement therapy (including kidney transplant or dialysis) and then estimating the value of their therapy based on clinical trial outcomes translated into cost savings from delay or avoidance of ESRD, dialysis and kidney transplant procedures. If their trial outcomes are positive, these data could be the basis of a value-based contract grounded in complete avoidance or forestalling of dialysis or kidney transplant. Alternatively, there could be an agreed upon "standard" cost of care and savings generated by using the new therapy within a cohort of targeted patients and shared by the payer and company.

The data needed for such a journey is likely a combination of clinical and claims data, ideally for the same known group of patients. The richness of the clinical data can help design balanced patient cohorts with similar clinical characteristics. Then one can track the vital signs, symptoms, lab results, biopsy results and other clinical measures that may more clearly signal lupus nephritis flares and kidney function decline. Linked medical and pharmacy claims data can reveal total health care utilization and identify the largest drivers of cost. With these data, life sciences companies, providers and payers can understand the disease trajectory of lupus nephritis patients, identify their rate of decline and measure the real-world use of, and effectiveness of, existing therapeutic options. Each group may act upon the data differently, but the foundational insights produced from the journey are valuable to all of them.

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