

# The landscape of systemic lupus erythematosus in Brazil: An expert panel review and recommendations

Lupus

2021, Vol. 30(10) 1684–1695

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DOI: 10.1177/09612033211030008

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Evandro Mendes Klumb<sup>1</sup> , Morton Scheinberg<sup>2</sup>,  
Viviane Angelina de Souza<sup>3</sup>, Ricardo Machado Xavier<sup>4</sup>,  
Valderilio Feijo Azevedo<sup>5</sup>, Elizabeth McElwee<sup>6</sup>,  
Mariana Rico Restrepo<sup>7</sup> and Odirlei André Monticielo<sup>4</sup>

## Abstract

**Purpose:** The objective of this review is to address the barriers limiting access to diagnosis and treatment of systemic lupus erythematosus (SLE) and lupus nephritis (LN) in Brazil, specifically for patients in the public healthcare system, arguably those with the least access to innovation.

**Design:** A selected panel of Brazilian experts in SLE/LN were provided with a series of relevant questions to address in a multi-day conference. During the conference, responses were discussed and edited by the entire group through numerous drafts and rounds of discussion until a consensus was achieved.

**Results:** The authors propose specific and realistic recommendations for implementing access to innovative diagnostic tools and treatment alternatives for SLE/LN in Brazil. Moreover, in creating these recommendations, the authors strived to address barriers and impediments for technology adoption. The multidisciplinary care required for SLE/LN necessitates the collective participation of all involved stakeholders.

**Conclusion:** A great need exists to expand the adoption of innovative diagnostic tools and treatments for SLE/LN not only in Brazil but also in most countries, as access issues remain an urgent demand. The recommendations presented in this article can serve as a strategy for new technology adoption in other countries in a similar situation.

## Keywords

Systemic lupus erythematosus, Brazil, SLE, lupus nephritis, LN, innovative treatments

Date received: 4 May 2021; accepted: 9 June 2021

## Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease with a significant disease burden. Lupus nephritis (LN), which is associated with greater disease severity and mortality, occurs in more than half of SLE patients. Limited healthcare access can delay diagnosis and treatment of both, increasing progression and severity. In Brazil, socioeconomic factors, health system particularities, and scarce specialists create substantial barriers to diagnostic and treatment options. In addition to addressing these obstacles, greater access is urgently needed to create a path forward for innovative medicines. Efforts in surveillance, awareness, diagnostic criteria, access, and physician education are crucial

<sup>1</sup>Rheumatology Department, Universidade do Estado do Rio de Janeiro (UERJ), Rio de Janeiro, Brazil

<sup>2</sup>Hospital Israelita Albert Einstein, São Paulo, Brazil

<sup>3</sup>Faculty of Medicine, Universidade Federal de Juiz de Fora, Juiz de Fora, Brazil

<sup>4</sup>Faculty of Medicine, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil

<sup>5</sup>Rheumatology Unit, Universidade Federal do Paraná, Curitiba, Brazil

<sup>6</sup>Americas Health Foundation (AHF), USA

<sup>7</sup>Americas Health Foundation (AHF), Colombia

## Corresponding author:

Evandro Mendes Klumb. Blvd Vinte e Oito de Setembro, 77, Sala 333. Vila Isabel. Rio de Janeiro, RJ. Brazil. CEP: 20551-030.

Email: klumb@uol.com.br

to reduce health disparities and improve patient outcomes.

## Methodology

To address these issues, the Americas Health Foundation (AHF) identified clinicians and scientists with an academic or hospital affiliation, who are experts in the field and have published since 2016. As a result, AHF convened a six-member panel of clinical and scientific experts from Brazil. Great attention was paid to ensure a diverse group representing various disciplines.

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### Search Strategy and Selection Criteria

Manuscripts referenced in this paper were identified through searches of PubMed and Embase with the terms “systemic lupus erythematosus”, “lupus nephritis”, “Brazil”, “innovative treatments in SLE” and “SLE in Brazil” from January 2016 to January 2021. Articles were also identified through the bibliographies of the papers identified and from the authors’ own files. Particular attention was paid to papers that reviewed or summarized the topic or that were related to activities in Brazil. The final reference list was generated based on the relevance to the broad scope of this consensus.

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To better focus discussion, AHF independently developed specific questions, addressing the central issues for the Panel to address. Each Panel member initially wrote a response to each question. During the multiday meeting, the entire group discussed and edited each response through numerous drafts and rounds of discussion until consensus was obtained. The objective of this article was to create a practical document with standardized, Brazil-specific recommendations for SLE and LN.

## SLE/LN in Brazil

SLE is an inflammatory, multisystem autoimmune disease with protean clinical and laboratory manifestations and a variable course that most commonly affects women between 15-44 years of age.<sup>1</sup> Some Brazil-specific aspects like African descendancy and high tuberculosis incidence may increase SLE incidence and severity.<sup>2,3</sup> SLE is associated with a host of autoantibodies directed against nuclear antigens, and many other innate and adaptive immune system abnormalities.<sup>4,5</sup> These characteristics, combined with the absence of pathognomonic features and established diagnostic tests, make defining and diagnosing SLE challenging.

LN, a severe organ manifestation of SLE, is the most frequent cause of disease morbimortality.<sup>6-8</sup> It is marked by a complex, wide range of inflammatory renal lesions, with predominant immune-mediated

glomerular damage that progresses to end-stage renal disease (ESRD) within 10 years of SLE diagnosis in 5–20% of patients.<sup>9</sup>

Brazil is a country of continental dimensions, diverse climatic conditions, varied socioeconomic status (SES), and a high rate of racial miscegenation.<sup>10,11</sup> Brazilian data on SLE are scarce and generally limited to the south and southeastern regions or Latin American (LA) cohort studies.<sup>10</sup> In the northeastern city of Natal, SLE incidence was 8.7 cases/100,000/year, and a much lower incidence of 4.2 cases/100,000/year was found in southern Brazil.<sup>12,13</sup> Based on SLE prevalence in the United States and Europe for those of LA and Hispanic origins (100–200/100,000 people) and on data obtained in a COPCORD study, an estimated 150,000–300,000 adult SLE patients exist in Brazil.<sup>14,15</sup>

Data regarding mortality in SLE patients in Brazil are scarce, but regional differences are evident. Mortality in South and Southeast is lower than in the North, possibly reflecting inherent ethnic differences in disease severity, SES, healthcare services and priorities, and other comorbidities associated with poor survival.<sup>16</sup> In contrast to high-income country data, the main mortality causes among SLE patients in Brazil are renal failure and infections.<sup>17</sup> A study analyzed 2,200 deaths that included SLE among other systemic connective tissue diseases and found that infection was the most frequent underlying cause of death (53.7%).<sup>18</sup> Independent mortality predictors for SLE patients are higher damage index score, cyclophosphamide use, methylprednisolone pulse therapy, and antiphospholipid antibody syndrome.<sup>19</sup> In São Paulo state, the 5-year survival rate is 88% and the 10-year is 80%, and in southern Brazil 96% and 93%, respectively.<sup>20,21</sup>

SLE-specific registries collect, code, and classify data to produce relevant statistics and provide a framework for assessing disease burden and course. In Brazil, no regional or national SLE registries exist. Data on clinical course are obtained through patient series from SLE reference centers which are typically tertiary centers linked to the public health system, where mostly complex cases are treated.<sup>22</sup> This reinforces the urgent need for reliable, local data on SLE disease course and LN severity among Brazilian patients, particularly for inception cohorts such as the SLICC Cohort.<sup>23</sup> Barriers to SLE registries are the lack of a specialized workforce and long follow-up times required for reliable data collection.

### Brazilian health system

Brazil’s public health system (SUS) is the national, publicly funded healthcare system, which covers 100% of Brazil’s 220 million people. Government

activities are based on multiyear plans that are approved by national congress for four-year periods under control of the Health Surveillance Agency (ANVISA), an autonomous government agency.<sup>24</sup> Adoption of new diagnostic tools and treatments are possible as long as there is a specific incorporation request for a specific technology. The National Committee for the Incorporation of Technologies in the Public Health System (CONITEC) is the health technology evaluation (HTA) body created to guide the Ministry of Health in decisions regarding the incorporation or exclusion of health technologies in SUS. Recommendations are based on HTA evidence regarding efficacy, effectiveness, safety, health economics, and budget impact.<sup>25</sup>

Often, the only way to access certain tests, drugs, and procedures not covered is “judicialization.” This practice uses individual litigation to enforce the right to health. Although it provides an alternative route to access,<sup>26</sup> it favors those who are financially able to hire private attorneys. Thus, in addition to the high costs of litigation (for both state and patient), judicialization could widen the social gap in Brazil and further accentuate inequities.

Approximately 25% of the population purchases private insurance and is entitled to undergo all medically necessary procedures included in a list published by the National Regulatory Agency for Private Health Insurance and Plans (ANS), an autonomous government body that regulates Brazil’s private health insurance plans.<sup>26</sup> A diverse expert committee reviews this list biennially, considering factors such as budget impact and clinical effectiveness, on which inclusion is based.<sup>27</sup>

Although Brazil’s health systems have made great strides, serious challenges remain in ensuring universal access to comprehensive care and improving quality and effectiveness of services offered in the private and public systems. Currently, vast disparities exist in healthcare access throughout Brazil, with poorer regions and lower socioeconomic populations suffering the most disadvantages.

In contrast to SUS, that is conceptually a sociodemocratic system, other countries have more restrictive health systems.<sup>28,29</sup> Most countries in LA employ a combination of public partial coverage and private access through the Bismarckian proposal. However, in Colombia, Mexico, and the United States, market-oriented systems predominate, characterized by liberal policy. Despite Brazil’s particularities, the chronic underfunding and fragmentation of health systems endemic in LA poses major obstacles to proper treatment and management of SLE and LN. Therefore, the analysis conducted in this manuscript alongside the

recommendations provide a framework for many of the Region’s countries.

### **National clinical practice guidelines**

SLE and LN clinical practice guidelines (CPGs) were published by the Brazilian Society of Rheumatology (SBR). In 2008, the SLE Consensus formally addressed aspects of SLE treatment.<sup>30</sup> In 2015, the SBR Lupus Committee published the Consensus of the Brazilian Society of Rheumatology, which focused on LN diagnosis, treatment, and management. This document highlighted recommendations concerning renal biopsy indications, inference of LN histological classes, care for immunosuppressed patients, response criteria, and protocols for induction and remission maintenance.<sup>22</sup> GLADEL and PANLAR guidelines complement the therapeutic measures established for current recommended SLE/LN management in LA. Of note, Brazilian experts were included in the curation of these guidelines.<sup>31</sup>

Within SUS, SLE treatment is based in part on the clinical protocol for therapeutic guidelines (PCDT) developed by the Ministry of Health in 2013.<sup>32</sup> This protocol is primarily used by rheumatologists but must be encouraged among primary care physicians (PCPs). The PCDT does not include all therapeutic options available and internationally indicated for SLE/LN.<sup>33</sup>

### **SLE and LN diagnosis**

SLE presents a large diagnostic challenge for reasons intrinsic to its complex nature. SLE onset may be insidious, with a wide spectrum of vague clinical and immunological findings, making early and accurate diagnosis difficult.<sup>34</sup> Polyarthritis or morning stiffness may be mistaken for rheumatoid arthritis, the most common rheumatologic misdiagnosis in SLE patients, especially when patients are not seen by specialists. Further, no pathognomonic clinical sign or gold standard test exists for SLE diagnosis confirmation and diagnosis primarily depends upon clinical judgment, often occurring when organ damage is already present.

Diagnostic methods are based on immunological changes (i.e., antinuclear antibody (ANA), anti-DNA, low complement, antiphospholipid antibodies) and involvement of diverse organ systems. A patient workup with possible SLE requires a case-by-case approach through critical analysis and treating physician expertise.

LN poses a more critical diagnostic challenge because these patients can be asymptomatic in the early stages when treatment is most effective. Therefore, some patients may quickly progress from

the absence of overt symptoms to late-stage renal disease and require kidney replacement therapy (KRT). Subtle changes indicating LN should be promptly recognized (e.g., proteinuria, mild arterial hypertension, small increases in serum creatinine). Although LN may be clinically silent, it occurs in over half of SLE patients and tends to present in the first 5 years of SLE onset.<sup>35</sup>

Renal biopsy is a definitive disease marker; however, it is costly, not widely available, an invasive procedure with complication risks, and cannot be repeated as frequently as LN flares are suspected.<sup>6</sup> Except for biopsy, there are no accurate confirmatory studies that can identify early LN. Although biomarkers such as specific cytokines, anti-nucleosome antibodies, and serum anti-C1q antibodies may serve as a surrogate diagnostic method for renal biopsy and for activity tracking, these are largely unavailable in practice due to the limited number of laboratories that offer them.<sup>36–38</sup>

### Histological classifications in Brazil

In 603 SLE patients from southern Brazil, LN was present in 41% of patients, and classes III, IV, and V were the most common.<sup>39</sup> In Brazil, chronic glomerulopathies represent a major cause of ESRD, accounting for 11% of dialysis patients.<sup>40</sup> A study conducted in the northeastern region demonstrated that secondary glomerulopathies, including LN, were present in 42% of cases.

In an LN patient cohort from northeastern Brazil, progressive chronic kidney disease occurred in 25% of patients and ESRD occurred in 7% of patients after 5 years. Despite adequate treatment, remission was not achieved by a significant number of patients and more than 50% of them relapsed during follow-up.<sup>41</sup> Another analysis of this cohort concluded that predictors of worse long-term outcomes were class IV LN, chronic interstitial damage at initial renal biopsy, non-response after one year of therapy, and relapse.<sup>41</sup>

### Treatment and management

Ideally, SLE/LN management should involve a multidisciplinary approach, including rheumatologists, pathologists, nephrologists, and radiologists.<sup>6,42</sup> However, in Brazil, specialists are disproportionately located in main cities, leaving large areas underserved. Thus, education for medical personnel in the primary setting can improve diagnosis, treatment, outcomes, and increase appropriate referrals.

New referral policies have been implemented at municipal and state levels with clear referral protocols and “teleregulation” adoption. “Teleregulation” encompasses the complete and formal process in

which a physician in Brazil requests and attains a physician-to-physician teleconsultation regarding medical procedures, health actions, and issues related to work processes, as well as guidance when the patients should be referred to secondary or tertiary care center. These initiatives, while not yet widespread, have significantly reduced wait times.<sup>43</sup>

### Treatment

In recent decades, there have been significant advances in SLE treatment, leading to increased survival. Despite this progress, the toxicity burden of SLE treatments remains relatively stagnant, and patients with SLE and LN continue to have a high morbimortality risk. Successful SLE therapy relies on treating both disease symptoms and the underlying inflammation<sup>44</sup> and involves both non-pharmacologic and pharmacologic approaches.

#### Non-pharmacologic therapy

Non-pharmacologic approaches are fundamental in a holistic approach to treating SLE patients. The importance of adequately controlling comorbidities cannot be underestimated, and treatment requires a multidisciplinary approach.<sup>45</sup>

In Brazil, the SLE PCDT includes several well-defined, non-pharmacologic approaches, including physical, psychological, and integrative interventions to complement pharmacologic therapy.<sup>46,47</sup> These interventions include counseling and support regarding smoking cessation, contraceptive use, and protection against exposure to sunlight. Infection risk must be addressed through vaccination and screening for tuberculosis, HPV, Hepatitis B and C, HIV, infectious diseases, and opportunistic microorganisms. Additionally, several approaches are outlined for control of cardiovascular risk and other comorbidities through improved diet and routine exercise.

#### Pharmacologic treatment

Pharmacologic treatment revolves around four drug classes: glucocorticoids (GCS), antimalarials, immunosuppressants, and targeted biological therapies, often in combination. Before initiating pharmacological treatment, it is necessary to rule out infection and antiphospholipid syndrome as symptom cause. Challenges lie in finding the most appropriate drug regimen to achieve disease control, adequate tolerability, and utmost safety, considering potential long-term side effects of these agents.

**Glucocorticosteroids.** GCSs have been the mainstay of SLE treatment for over 50 years and remain first arm



of SLE treatment.<sup>48</sup> High-dose GCS or “pulse therapy” is used to rapidly control the autoimmune response during renal flares, hemolytic anemia, neuropsychiatric manifestations, among other life-threatening situations.<sup>49</sup>

In GCS therapy, the concept of less is more proves to be true. Daily GCS doses vary according to disease severity and due to adverse effects, such as increased infection risk and irreversible damage accrual, the lowest effective dose should be used. Progressively reducing the dose to a maintenance level of prednisone of less than 5–7.5 mg/day is indicated as early as possible.<sup>50</sup> Prednisone dosage greater than 6 mg/day increases risk of organ damage, iatrogenic osteoporosis, avascular necrosis, cardiovascular events, cataracts, glaucoma, and psychiatric events.<sup>51</sup>

In the past decade, safety concerns arising from long-term GCS use have prompted recommendations for methylprednisolone pulses to control acute disease as a more effective and less toxic alternative in moderate to severe renal flares. In general, patients with frequent flares and high disease activity should be treated with combination therapy that includes antimalarial and other immunosuppressive medications.<sup>52–54</sup>

**Antimalarials.** Antimalarial therapy has long been indicated for SLE patients and continues to be a treatment cornerstone. Hydroxychloroquine, the preferred antimalarial therapy, is recommended for all patients, and its long-term use and safety is well established. A simple ophthalmologic evaluation and ophthalmologic computer tomography, when appropriate, can be performed before initiating treatment. Patients on antimalarial therapy should have periodic follow-up visits.<sup>51,55</sup> When antimalarial therapy does not achieve remission, switching to or supplementing steroid use with immunosuppressant or biologic therapy may be recommended.

**Immunosuppressants.** Some approaches to reduce treatment-related toxicity include immunosuppressant medications such as azathioprine and methotrexate, which have proven steroid-sparing mechanisms.<sup>56,57</sup> In refractory cases, other immunosuppressive agents (e.g., cyclophosphamide, mycophenolate mofetil, mycophenolate sodium, cyclosporine, tacrolimus, leflunomide), immunomodulating agents (e.g., thalidomide, dapson), or a combination may be indicated. Adverse effects include teratogenicity, infertility, severe infections, and peripheral axonal neuropathy.

**Targeted therapies.** Progress in understanding SLE pathogenesis has led to the development of several biologic agents specifically targeting disease pathways. Some agents, such as rituximab and belimumab, are available

in clinical practice, while others are in ongoing clinical trials.

There is widespread off-label use of rituximab, a chimeric monoclonal antibody, to treat SLE even though in two clinical trials this biologic agent did not achieve primary clinical and laboratory outcomes.<sup>58,59</sup> In contrast, rituximab utility is widely established for patients with severe disease refractory to conventional management, especially in cases with renal involvement (also musculoskeletal, hematological, cutaneous, and neurological involvement).<sup>60–63</sup> Rituximab reduces steroid dosage in more than 50% of patients with higher dose of steroids and disease activity.<sup>64</sup>

Belimumab, a monoclonal antibody, became the only biologic agent approved for SLE treatment after reaching primary efficacy goals in the BLISS trials. The primary clinical endpoints were reached in a metanalysis and four independent phase III trials resulting in extensive evidence that SLE patients treated with belimumab in combination with standard of care have reductions in disease activity and lower daily GCS dosage.<sup>65,66</sup>

The BLISS-NL study recently confirmed the efficacy of belimumab in LN patients, prompting FDA approval. The overall effect is small to moderate, depending on disease activity, presence or absence of anti-dsDNA, and intensity of complement consumption. However, the outcome evaluated is critically important because maintenance of disease activity determines the continuous need for GCS and irreversible damage accrual, which is directly related to decreased survival.<sup>67</sup>

The mean steroid reduction induced by belimumab was around 50% compared to treatment start. In that sense, SLE treatment with biologic agents in patients that fail on standard-of-care therapy may be considered in new guidelines on combination therapy of active SLE.<sup>68</sup> This approach further supports current treatment trends of reduced GCS doses. For now, belimumab is recommended for patients with persistently active LN/SLE, particularly with musculoskeletal or skin conditions and whose combination treatment of antimalarial therapies, low-dose GCS, and at least two immunosuppressants used in adequate doses for 3–6 months has failed.

The time has come to incentivize SLE therapy guided by frequent disease activity evaluations and successfully reducing steroids to a minimal daily dose. New agents in combination therapies may be recommended for longer and healthier patient lives.<sup>69–71</sup> Larger studies are needed to consolidate findings that indicate the early use of new agents is a safe and effective strategy to avoid higher steroid doses and prevent significant toxicity risk.<sup>72,73</sup>

Among the new potential targets are IFN activation axis inhibitors,<sup>74,75</sup> CD40L/CD40 pathway,<sup>76</sup> BAFF/APRIL, T-cell activation pathways, and second-generation calcineurin inhibitors.<sup>77</sup> New drugs that deplete B lymphocytes and small molecules that interfere in intracellular signaling axes, especially JAK inhibitors, also represent potential treatments with further study. For instance, Bruton's tyrosine kinase (BTK) inhibition that has proven efficacy in B cell malignancies are well established in hematology and may be a possible SLE treatment.<sup>78</sup>

## LN

Objectives of LN treatment have been recently updated with new proteinuria cut-offs and time of treatment to reach goals. Classes III, IV, and V are the most severe with a high risk for ESRD progression. Treatment consists of two phases: induction and maintenance with the goal of achieving complete or partial remission. Induction includes immunosuppressants and high-dose GCS. Maintenance aims to achieve lower GCS doses and should be continued for 5–6 years.<sup>9</sup> Immunosuppressor withdrawal should be considered only after achieving complete long-term remission. Without remission, the renal lesion is considered refractory and a different induction scheme, including therapies with new agents, should be initiated. Adjuvant therapy, which includes hydroxychloroquine in combination with angiotensin-converting enzyme inhibitors and/or angiotensin-receptor blockers, is also indicated for all LN patients. This therapy acts as an anti-proteinuric agent and promote systemic arterial blood pressure control, which is required to preserve renal function.

## Access to therapy in Brazil

The medications used for SLE/LN treatment that are available within SUS are outlined in Table 1.

Patients in the private system may be eligible to access rituximab and belimumab in some situations. However, ANS has not yet included immunobiological therapy for SLE patients in its list of approved medications.

Some evidence from randomized clinical trials has shown that the subgroups of SLE patients in Brazil have higher cumulative doses of GCS compared with North American or European populations.<sup>66</sup> These findings may result from the greater disease severity in these patients, aspects related to access to healthcare services, and delayed access to treatment. Early access to other therapeutic groups such as immunosuppressants and biologics may contribute to achieving reduced GCS doses.

Access to SLE therapies is limited both in the private and public health systems. A lag in updating the PCDT limits the availability of medications in the public sphere. In the private system, biologic therapy is not included in the list of procedures controlled by ANS, limiting their availability. As a result, medications such as mycophenolate mofetil, belimumab, rituximab, and tacrolimus are obtained primarily through a judicial proceeding. Some Brazilian states and health medical organizations have decided to provide access to certain drugs, acknowledging that legal costs ultimately exceed the costs of providing the drugs. This dynamic further exacerbates inequalities in the supply of medicines to SLE patients in Brazil.

## Barriers to SLE/LN early diagnosis and treatment in Brazil

In line with global trends, delayed diagnosis of SLE often occurs in Brazil, resulting in the grave consequences of delays in treatment initiation.<sup>79–81</sup> Early diagnosis and prompt treatment are crucial to ensure patient health and avoid the high societal and health system costs associated with SLE complications. Although some causes of these delays are intrinsic to the complex nature of the disease, there are also extrinsic causes that can be more readily addressed. The principal barriers to the early diagnosis and treatment of SLE/LN in Brazil are as follows:

### *Limited access to specialized care*

Although the number of rheumatologists in Brazil increased significantly during the past decade, the proportion of rheumatologists for the population remains insufficient. Currently, 2,380 certified rheumatologists exist in Brazil, translating into 1 rheumatologist for more than 77,000 Brazilians.<sup>82,83</sup> More important, specialists involved in SLE care, including rheumatologists, pathologists, and nephrologists, are largely concentrated in state capitals and large municipalities,<sup>90</sup> creating significant geographic disparities in access, as shown in Figure 1. Not unexpectedly, data obtained from the government regulation system in the city of Rio de Janeiro show that there are approximately 6,000 patients referred by a PCP waiting for a rheumatologic evaluation.<sup>84</sup> This specialist shortage further embeds long delays in diagnosis and treatment.

### *Lack of awareness and training in primary care settings*

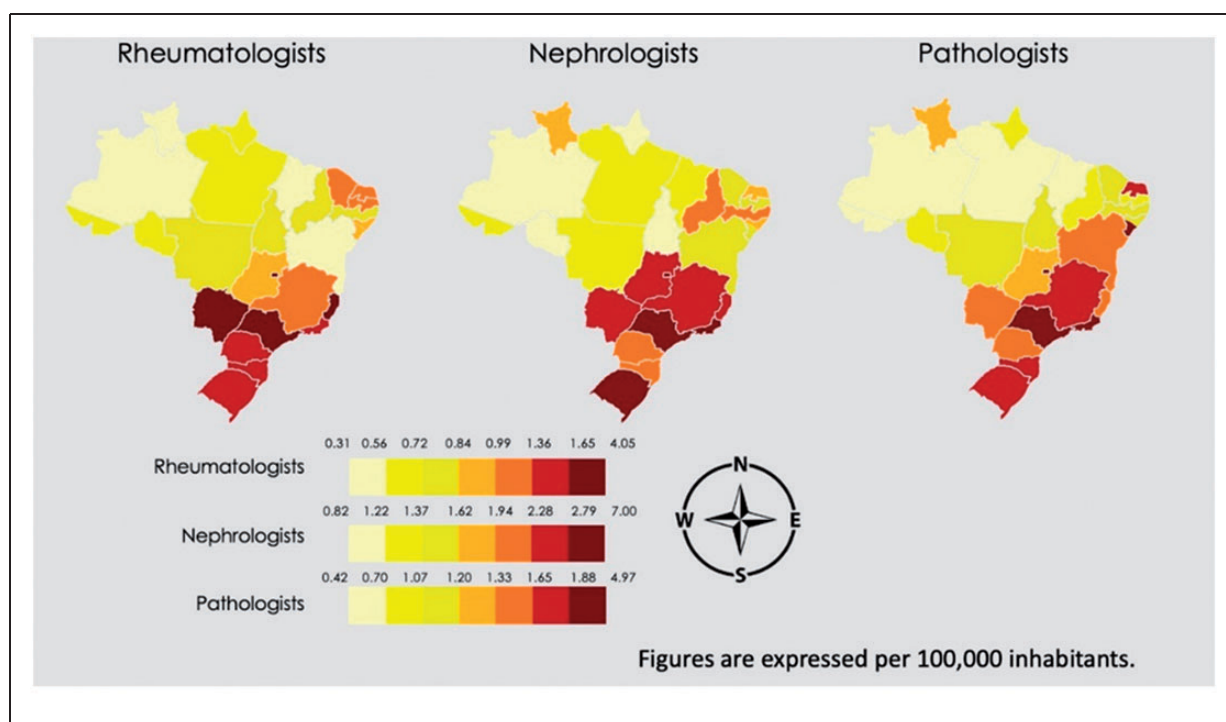
PCPs and family doctors often lack in basic training and disease awareness to properly diagnose and treat SLE and LN, contributing to delayed referrals to specialists,

**Table 1.** Drugs available for SLE treatment in Brazil<sup>a</sup>, according to current PCDT.

Active substance	Route and pharmaceutical formulation
Chloroquine	Oral: 150 mg tablet
Hydroxychloroquine	Oral: 400 mg tablet
Azathioprine	Oral: 50 mg tablet
Betamethasone	Intravenous: 6 mg injectable suspension
Cyclophosphamide	Oral: 50 mg tablet Intravenous: 200 and 1000 mg solution reconstituted
Cyclosporine	Oral: 10, 25, 50 and 100 mg capsule
Danazol	Oral: 100 and 200 mg capsule
Dexamethasone	Oral: 4 mg tablet
Methotrexate	Oral: 2.5 mg tablet Subcutaneous: 25 mg/mL injectable suspension
Methylprednisolone	Intravenous: 500 mg solution reconstituted
Prednisone	Oral: 5 and 20 mg tablet
Thalidomide	Oral: 100 mg tablet

<sup>a</sup>These drugs are available within SUS.

Source: Literature.<sup>32</sup>

**Figure 1.** Geographic distribution of Brazilian rheumatologists, nephrologists, and pathologists.

suboptimal management, or both.<sup>85</sup> Because of the limited access to specialists, PCPs, and family doctors are often responsible for managing SLE/LN patients; therefore, they must be adequately trained to diagnose SLE, identify early stages of LN, and initiate treatment.

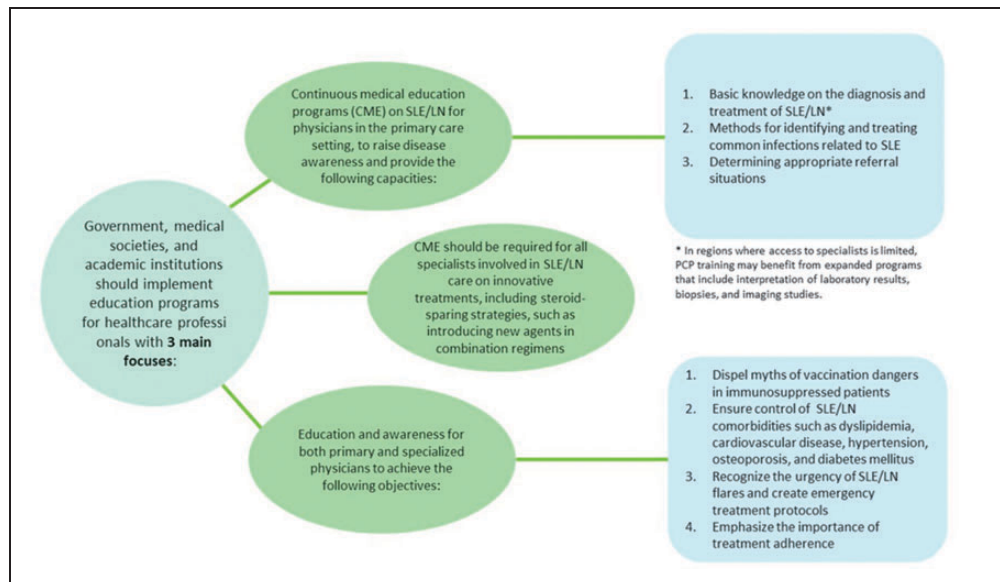
#### Out-of-date government treatment guidelines

The PCDT, which dictates the drugs that can be used in the treatment of SLE and LN in the public system have

not been updated since 2013 and currently do not include the most innovative diagnosis methods and treatments recommended by national and international clinical practice guidelines.

#### Limited access to diagnostic testing and therapies

Vast disparities exist in access and availability to testing and therapies between the private and public system in Brazil. Common testing, such as renal



**Figure 2.** Recommendations for SLE/LN education programs in Brazil.

biopsies and antibodies, are necessary to evaluate and confirm systemic disease involvement but are not widely available throughout the country. Further, access to treatments proven to be effective for SLE, such as mycophenolate mofetil, belimumab, rituximab, and tacrolimus, is very restricted by high costs and other limitations imposed by the national health system.<sup>86</sup> Although some of these barriers apply to both the private and public systems, patients in the private system may have better access to more regular clinical follow-up, testing, and emergency care.

**Lack of local data**

There is a lack of country-specific data to provide insight into the epidemiologic behavior and burden of disease of SLE/LN, in part due to the absence of disease-specific registries. This affects clinical and policy decision-making on numerous levels because such information is crucial for health technology evaluations. Furthermore, clinical trials on treatment options for SLE/LN have included few representative samples of Brazilian patients; therefore, results obtained in these protocols cannot always be extrapolated to the country’s population. Trial designs can also limit the patient profile studied since these patients often differ significantly in complexity from those seen in routine clinical practice.

**Treatment difficulties**

In at least 25% of SLE patients who have renal involvement, current treatment is not effective for long-term GFR preservation.<sup>7,22,87</sup> Treatment failure

may be related to disease severity, interruptions to treatment because of infections, and poor adherence to treatment. In Brazilian SLE patients, adherence was found to be notably low, with only one third of patients taking 80% of prescribed drugs.<sup>6</sup> Notwithstanding, drug adherence should not be interpreted as an immutable condition but rather as an opportunity to optimize therapeutic results, if properly addressed.<sup>6</sup>

**Conclusions and recommendations**

SLE has a high morbimortality, and the Brazilian health system has not yet prioritized its diagnosis and treatment. This panel addressed specific issues related to the access disparity in diagnostic tools, treatments, and specialized care for SLE/LN in both the public and private healthcare systems in Brazil. Access to SLE/LN care is a concern worldwide; therefore, the issues discussed are not exclusive to this country. With increasing healthcare costs and limited resources, there is an opportunity to examine the current reality of SLE patients and to comprehensively address access to care. The recommendations below were developed to address the principal barriers identified in Brazil and are not one-size-fits-all; however, these can be adapted to each country’s SLE reality.

**Recommendations**

**Implement national SLE program**

- The government, health institutions, and medical societies should support the development and



implementation of a national program focused on early diagnosis and treatment of SLE patients. The Brazilian Society of Rheumatology should be considered the reference institution to guide this effort.

### **Increase education**

Medical professionals, PCPs, and family doctors in the primary care setting must be trained in the basics of SLE and LN diagnosis and care, as many Brazilians do not have access to the necessary specialists. Recommendations for education programs can be found in Figure 2.

### **Reduce diagnosis and treatment delays**

- Governments, medical societies, and health institutions should:
  1. Address the unequal geographic distribution of specialists by providing incentives for rheumatologists, pathologists, and nephrologists to accommodate underserved areas, and guarantee the necessary resources to provide adequate care
  2. Promote a multidisciplinary approach that includes a network of experienced PCPs, rheumatologists, pathologists, nephrologists, radiologists, dermatologists, neurologists, cardiologists, hematologists, and pulmonologists, among other supporting specialties<sup>22,42</sup>
  3. Implement an organized assistance network with an effective referral system that includes clear referral protocols and the widespread adoption of telemedicine solutions such as a “teleregulation” program

### **Increase access to new diagnostic and therapeutic methods**

- The government should systematically update PCDT guidelines and protocols with the support of medical societies to include the most current recommendations from the Brazilian Society of Rheumatology, EULAR/ACR, and GLADEL/PANLAR and promote guideline adherence among all treating physicians
- Government, medical societies, academic institutions, private HMOs, and Industry must conduct more comprehensive pharmacoeconomic evaluations as part of guideline optimization
- The government should increase the allocation of designated resources for SUS to diagnose and treat SLE/LN and to address specifically the existing inequalities among regions
- The private and public healthcare sectors should optimize dialogues in order to develop sustainable funding mechanisms that support access to modern and innovative agents

### **Increase country-specific data**

- With funding from the government, medical societies and health institutions should establish SLE/LN-specific data registries in order to characterize the disease course and develop strategies for affected populations
- All stakeholders should prioritize funding and urge the importance of SLE/LN research to generate local data, monitor quality metrics, and track treatment outcomes that will drive the inclusion of new diagnosis and treatment methods
- Research institutions should prioritize and conduct prevalence and incidence studies of SLE/LN specific to the country with support of government funding

### **Declaration of conflicting interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### **Funding**

The author(s) received no financial support for the research, authorship, and/or publication of this article. The organization and implementation of the consensus conference and manuscript was carried out by the Americas Health Foundation (AHF), a 501(c)3 nonprofit organization dedicated to improving healthcare throughout the Latin American Region and was supported by unrestricted grants from Roche. The AHF independently selected the experts to serve on the panel. The AHF had no role deciding the content of the manuscript and the recommendations are those solely of the panel members.

### **Contributorship**

All authors participated and made significant contributions to the data search, drafting, and discussion of the topic and all subtopics provided in this manuscript.

### **Acknowledgements**

To Dr. Mariana Rico, Elizabeth McElwee MPH, and Elizabeth Moran from the Americas Health Foundation (AHF) for the valuable help in the design and development of the manuscript.

### **ORCID iD**

Evandro Mendes Klumb  <https://orcid.org/0000-0001-9546-3144>

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