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Editorial: Advancements and challenges in epidemiology of lupus

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Editorial on the Research Topic
Advancements and challenges in epidemiology of lupus

Systemic Lupus Erythematosus (SLE) is the prototypical autoantibody-mediated systemic autoimmune disease. SLE is a chronic, disabling, potentially life-threatening disease, characterized by heterogeneity and unpredictability. The significant challenges of SLE include inaccurate/delayed diagnosis, years of exposure to toxic or partially effective medications, and a relentless impact on quality of life, family, relationships, and career. It primarily affects young women, particularly women of color, and is up to three times more prevalent in historically underrepresented groups (1). Substantial advances in understanding the pathophysiology and management of lupus have led to tremendous improvements in survival over the past 50 years (2). The epidemiology of lupus reflects the heterogeneity of the disease and is influenced by genetic, environmental, and socio-economic factors. Improving our understanding of these factors would allow for earlier diagnosis and tailored, individualized treatment, improving both survival and quality of life.

The research topic "*Advancements and challenges in epidemiology of lupus*," featured in *Frontiers in Lupus*, brings together four studies that explore the genetic underpinnings of lupus, barriers to clinical trial recruitment, and evolving treatment paradigms. Together, these studies illuminate the multifaceted nature of lupus and underscore the need for continued research and innovation.

Genetic insights: the APOL1 gene and osteonecrosis

The Apolipoprotein L1 (APOL1) high-risk genotype (HRG) is present in 13% of African Americans. This HRG increases the risk of lupus nephritis progression, hypertension, cardiovascular disease, and organ damage, and is considered one of the causes of increased disease severity in patients of African descent (3). Osteonecrosis, the atraumatic necrosis of bone due to insufficient blood supply, is prevalent in lupus patients, affecting up to 29% of patients (4). The study by Yip et al., "*Osteonecrosis is associated with APOL1 variants in African Americans with systemic lupus*

erythematosus," found that the APOL1 HRG is independently associated with osteonecrosis in lupus patients.

Understanding genetic risk factors in lupus is critical. Identifying APOL1 HRG as a risk factor for osteonecrosis offers a pathway for early intervention and personalized treatment. Recognizing individuals at higher risk for osteonecrosis allows clinicians to further increase efforts, such as minimizing corticosteroid exposure, to mitigate the risk of osteonecrosis, prevent disease-related damage and improve the quality of life for lupus patients. Additionally, ongoing studies of APOL1-directed therapy are paving the way for personalized treatments based on individual risk.

Barriers to clinical trial recruitment

Two studies focus on the barriers to clinical trial recruitment in lupus. Clinical trials are essential for medical advancements, providing the evidence needed to develop new treatments and improve patient outcomes. However, recruiting participants for lupus clinical trials, especially from historically underrepresented groups, has been challenging (5). Marginalized communities, particularly those with lower socioeconomic status and minority backgrounds, are underrepresented in lupus clinical trials, limiting the generalizability of trial results and perpetuating health disparities. Financial and logistical barriers, lack of awareness and access to studies, systemic racism, and mistrust of the medical system are often thought to be key culprits (6).

The study by Scofield et al., "*Impact of race and ethnicity on family participation in systemic lupus erythematosus genetic studies*," explores the reasons for non-participation in a genetic registry for families affected by SLE. The majority of families approached either declined or were excluded across all groups, but the authors found insightful differences in the reasons for non-participation among different racial and ethnic groups. Namely, while white non-Hispanic families were often excluded for not meeting lupus diagnostic criteria, black families' participation was dependent on factors related to trust in the medical system. White Hispanic families' recruitment was thought to be associated with the family's level of acculturation, as well as the availability of Spanish-speaking recruiters and Spanish-language study materials. The differences between the groups highlight that recruitment strategies cannot be one-size-fits-all. Strategies that are culturally sensitive, acknowledge past injustices, and actively aim to be inclusive need to be employed to achieve representative enrollment.

Educating patients about the procedures, rights and protections available is crucial to increasing trust and promoting clinical trial participation. The second study by Khalili et al., "*Development of the lupus clinical trials enrollment decision aid: a pilot study*," tackles low recruitment rates through a decision aid developed with patient and physician input. This tool informs patients about clinical trial processes, such as placebo use, the standard of care, and the risks and benefits of participation, providing an accessible, informational resource for shared decision-making between patients and physicians. Disseminating such educational tools can empower patients and improve study participation rates, enhancing our ability to explore the full range and impact of the disease.

Evolving treatment paradigms: lupus nephritis

The final study, "*Insights into future management of lupus nephritis*," by Askanase et al., reviews current treatments for lupus nephritis (LN), a severe manifestation of SLE that can lead to end-stage renal disease and death. Despite recent advances in the treatment of LN, achieving complete remission and significantly reducing the rate of progressive kidney disease remain challenging. This review summarizes existing therapies, including newly-approved medications like belimumab and voclosporin, and discusses their strengths and weaknesses in specific clinical scenarios. Importantly, the authors highlight the recent EULAR 2023 SLE guidelines, which suggest utilizing either of these agents as a triple therapy regimen in combination with lower dose steroids and mycophenolate mofetil to improve kidney outcomes (7). Promising future treatments, such as chimeric antigen receptor T-cell (CAR T-cell) therapy and treatments targeting B cells, specific cytokines, immunoproteasomes, and components of the complement system are also discussed.

This review emphasizes the need for personalized treatment approaches based on individual disease pathophysiology, aggressive steroid tapering and combination therapies, and lower thresholds for kidney biopsies to achieve better outcomes and improve patients' quality of life.

Conclusion

The studies presented in this research topic underscore the complexity of lupus and the multifaceted approach required to address its challenges. Identifying APOL1 gene variants as a risk factor for osteonecrosis highlights the critical role of genetics in disease manifestation. Exploring barriers to clinical trial recruitment reveals the socioeconomic and logistical hurdles that must be overcome to ensure equitable access to medical advancements. Finally, reviewing lupus nephritis treatments, and incorporating new guidelines and medications, marks significant progress in the quest for individualized medicine and better patient outcomes.

Researchers, clinicians, patients, and policymakers must work together to address the genetic, socio-economic, and clinical complexities of the disease. By fostering a culturally sensitive, inclusive research environment and embracing new therapeutic strategies, we can continue to make strides toward better understanding and managing lupus.

The advancements and challenges in the epidemiology of lupus presented in this issue of *Frontiers in Lupus* offer a glimpse into recent developments in lupus research and treatment. The journey is just beginning; continued dedication and collaboration

will ensure that lupus is no longer a chronic formidable illness but a curable one.

Author contributions

NS: Writing – original draft, Writing – review & editing. AA: Writing – original draft, Writing – review & editing.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Publisher's note

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