PEER REVIEW HISTORY

This paper was submitted to a another journal from The Lupus Science & Medicine but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received two reviews from its previous journal and two reviewers agreed to published their review.)

ARTICLE DETAILS

TITLE (PROVISIONAL)	Treatment Patterns and Control of Hypertension in Systemic Lupus Erythematosus (SLE): A Cross-Sectional Study
AUTHORS	Li Liu, Jia; Pineau, Christian; Grenier, Louis-Pierre; Vinet, Evelyne; Kalache, Fares; Lukusa, Luck; Bernatsky, Sasha

VERSION 1 – REVIEW

REVIEWER	Review #1

GENERAL COMMENTS	This study based on SLE patients in the McGill Lupus Clinic Registry is designed to describe treatment patterns and control of hypertension, identifying factors associated with uncontrolled hypertension by both the Canadian and ACC/AHA guidelines. The design is cross-sectional, assessing only the last annual visit during 2017-2019 in patients receiving antihypertensive medications. Interestingly, the major findings are that Caucasians have poorer BP control than other ethnic groups, while those with renal damage had better control, both results contradictory to most previously published studies. Given the prospectively collected data in the McGill Lupus registry, a number of questions need to be considered: 1) What is the definition of an annual visit? Are routine follow-up visits also included in the registry, so that a given patient would be likely to have more than one visit per year? IF so, how is the determination of the annual visit date made? 2) Why only use the last "annual visit"? Other demographic features may have changed over time. The authors do recognize as a limitation of the study that a repeated measures longitudinal analysis would likely have provided more precise answers. 3) If the primary objective was to identify patterns of antihypertensive use, why were patients with elevated BP on no antihypertensive medication excluded from study? How many patients with untreated HTN were identified at annual visits? Were medications prescribed but not taken? Was there any assessment of compliance with visits or prescribed medications? 4) Given that higher BMI was associated with uncontrolled HTN, is there any information regarding whether patients were receiving maximal doses of prescribed medications?

	Based on the demographic information provided in Table 1, it is interesting that the majority of SLE patients in the registry appear to have had long-standing SLE, with a mean duration of more than 23 years. Despite this, a high proportion of those with both controlled and uncontrolled BP had a SLEDAI-2K > 4. Were the majority of manifestations serologic, or did these patients also have clinically active features of lupus? Comments from the authors would be welcome.

REVIEWER	Garsshick, Michael

GENERAL COMMENTS	In this manuscript, Liu et al describe HTN treatment patterns in SLE and note that almost 2/3rds had elevated HTN. They then go on to state elevated BMI and Caucasian race is a risk factor undertreated HTN in SLE. It's a well written manuscript. Given the data presented, this may be best as a brief report, rather than full manuscript. Please look at race break down by renal disease, even though adjusted for, this may be confounding finding that Caucasian's have higher rate of uncontrolled HTN, if they also had less renal disease. Would include seperate analysis adjusting for SLICC. What was the percent taking chronic steroids, or percent taking chronic nsaid use. Many more items to put into table 1, first of all p-values for differences. Would calculate CV risk score for pts and include in table 1. In those under 40, can round up to calculate the score. Also include actual SBP and DBP in the table (by definition, the p-value would be significant). A better manuscript would be to include the entire cohort to look at undertreated HTN, not just those on treatment.

VERSION 1 – AUTHOR RESPONSE

Comments to the Author
This study based on SLE patients in the McGill Lupus Clinic Registry is designed to describe treatment patterns and control of hypertension, identifying factors associated with uncontrolled hypertension by both the Canadian and ACC/AHA guidelines. The design is cross-sectional, assessing only the last annual visit during 2017-2019 in patients receiving antihypertensive medications. Interestingly, the major findings are that Caucasians have poorer BP control than other ethnic groups, while those with renal damage had better control, both results contradictory to most previously published studies.
Given the prospectively collected data in the McGill Lupus registry, a number of questions need to be considered:

1) What is the definition of an annual visit? Are routine follow-up visits also included in the registry, so that a given patient would be likely to have more than one visit per year? IF so, how is the determination of the annual visit date made?

RESPONSE: Patients are scheduled once a year for an annual visit at which time data are collected in a standard manner.

2) Why only use the last "annual visit"? The authors do recognize as a limitation of the study that a repeated measures longitudinal analysis would likely have provided more precise answers.

RESPONSE: This study was designed as a cross-sectional study. With current limitations in our research resources due to the pandemic, it would be extremely difficult to go back to the drawing table. If a longitudinal design is required, we would have to withdraw our paper.

3) Why were patients with elevated BP on no antihypertensive medication excluded from study? How many patients with untreated HTN were identified at annual visits? Were medications prescribed but not taken? Was there any assessment of compliance with visits or prescribed medications?

RESPONSE: Patients with elevated BP on no antihypertensives were not in the scope of our research. We focused on patients with elevated BP despite already taking antihypertensives, to assess factors of poor control in this population.

4) Given that higher BMI was associated with uncontrolled HTN, is there any information regarding whether patients were receiving maximal doses of prescribed medications?

RESPONSE: We do not capture data on specific medication doses of antihypertensives.

5) Based on the demographic information provided in Table 1, it is interesting that the majority of SLE patients in the registry appear to have had long-standing SLE, with a mean duration of more than 23 years. Despite this, a high proportion of those with both controlled and uncontrolled BP had a SLEDAI-2K > 4. Were the majority of manifestations serologic, or did these patients also have clinically active features of lupus? Comments from the authors would be welcome.

RESPONSE: We set a SLEDAI-2K > 4 as an indication of high disease activity and did not examine the distribution of serologic or clinical features.

Reviewer: 2

Comments to the Author
In this manuscript, Liu et al describe HTN treatment patterns in SLE and note that almost 2/3rds had elevated HTN. They then go on to state elevated BMI and Caucasian race is a risk factor undertreated HTN in SLE. It's a well written manuscript.

1) Please look at race break down by renal disease, even though adjusted for, this may be confounding finding that Caucasian’s have higher rate of uncontrolled HTN, if they also had less renal disease.

RESPONSE: We added a description of renal disease in our cohort patients treated for HTN, comparing Caucasian to non-Caucasians. We found that renal disease was present in 21% (N=15) of Caucasian patients taking HTN medications, and in 46% (N=17) of patients of another race taking HTN medications. As suggested, fewer renal disease in Caucasian patients could contribute to their poorer BP control.

2) Would include separate analysis adjusting for SLICC DI.

RESPONSE: We did not include the SLICC damage index in the model because we already had the renal component of the SLICC DI in the model. Moreover, we found that if we substitute the total SLICC DI for the renal damage item, it does not improve the model.

3) What was the percent taking chronic steroids, or percent taking chronic nsaid use.

RESPONSE: In the uncontrolled HTN group, 11 (15.3%) were taking prednisone, and 4 (5.6%) NSAIDs. On logistic regression, their contribution to uncontrolled HTN was insignificant as both confidence intervals included the null value. With these two new variables, our results or conclusions did not significantly change.

4) Many more items to put into table 1. In those under 40, can round up to calculate the score. Also include actual SBP and DBP in the table.

RESPONSE: We have incorporated more data in Table 1, including a column showing differences between controlled and uncontrolled HTN groups, with confidence interval. We have also included the actual SBP and DBP.