# Prevalence and target attainment of traditional cardiovascular risk factors in patients with systemic lupus erythematosus: a cross-sectional study including 3401 individuals from 24 countries

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## Summary

**Background** Systemic lupus erythematosus (SLE) is characterised by increased cardiovascular morbidity and mortality risk. We aimed to examine the prevalence of traditional cardiovascular risk factors and their control in an international survey of patients with systemic lupus erythematosus.

**Methods** In this multicentre, cross-sectional study, cardiovascular risk factor data from medical files of adult patients (aged ≥18) with SLE followed between Jan 1, 2015, and Jan 1, 2020, were collected from 24 countries, across five continents. We assessed the prevalence and target attainment of cardiovascular risk factors and examined potential differences by country income level and antiphospholipid syndrome coexistence. We used the Systemic Coronary Risk Evaluation algorithm for cardiovascular risk estimation, and the European Society of Cardiology guidelines for assessing cardiovascular risk factor target attainment. People with lived experience were not involved in the research or writing process.

**Findings** 3401 patients with SLE were included in the study. The median age was 43·0 years (IQR 33–54), 3047 (89·7%) of 3396 patients were women, 349 (10.3%) were men, and 1629 (48·1%) of 3390 were White. 556 (20·7%) of 2681 patients had concomitant antiphospholipid syndrome. We found a high cardiovascular risk factor prevalence (hypertension 1210 [35·6%] of 3398 patients, obesity 751 [23·7%] of 3169 patients, and hyperlipidaemia 650 [19·8%] of 3279 patients), and suboptimal control of modifiable cardiovascular risk factors (blood pressure [target of <130/80 mm Hg], BMI, and lipids) in the entire SLE group. Higher prevalence of cardiovascular risk factors but a better blood pressure (target of <130/80 mm Hg; 54·9% [1170 of 2132 patients] *vs* 46·8% [519 of 1109 patients]; p<0·0001), and lipid control (75·0% [895 of 1194 patients] *vs* 51·4% [386 of 751 patients], p<0·0001 for high-density lipoprotein [HDL]; 66·4% [769 of 1158 patients] *vs* 60·8% [453 of 745 patients], p=0·013 for non-HDL; 80·9% [1017 of 1257 patients] *vs* 61·4% [486 of 792 patients], p<0·0001 for triglycerides]) was observed in patients from high-income versus those from middle-income countries. Patients with SLE with antiphospholipid syndrome had a higher prevalence of modifiable cardiovascular risk factors, and significantly lower attainment of BMI and lipid targets (for low-density lipoprotein and non-HDL) than patients with SLE without antiphospholipid syndrome.

**Interpretation** High prevalence and inadequate cardiovascular risk factor control were observed in a large multicentre and multiethnic SLE cohort, especially among patients from middle-income compared with high-income countries and among those with coexistent antiphospholipid syndrome. Increased awareness of cardiovascular disease risk in SLE, especially in the above subgroups, is urgently warranted.

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## Introduction

Systemic lupus erythematosus (SLE) is a complex systemic autoimmune disorder affecting mostly young women. Patients with SLE have a two-to-ten-fold higher risk for cardiovascular events compared with the general population,[1] and cardiovascular disease, along with infections, represents a leading cause of mortality in these patients.[2]

Several disease-related risk factors have been associated with high risk of cardiovascular disease in SLE, including

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## Research in context

### Evidence before this study

Cardiovascular disease, driven by an interplay between disease-related and traditional cardiovascular risk factors, is a leading cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE). Although highly prevalent, data from mostly single-centre studies have shown that traditional cardiovascular risk factors are frequently overlooked and undertreated in patients with SLE. In the 2022 European Alliance of Associations for Rheumatology (EULAR) recommendations for the management of cardiovascular risk in rheumatic and musculoskeletal diseases including SLE and antiphospholipid syndrome, rigorous screening and control of traditional cardiovascular risk factors using guidelines for the general population was stressed in the overarching principles. However, cardiovascular risk factor control in patients with SLE according to established general population guidelines has not been evaluated in large multicentre and multiethnic studies, based on our search of the literature. We searched PubMed and Google Scholar from database inception to Dec 31, 2023, using the search terms "traditional cardiovascular risk factors", "cardiovascular risk management", "hypertension control", "hyperlipidemia control" and "systemic lupus erythematosus", without any language restrictions.

### Added value of this study

We found a high prevalence of traditional cardiovascular risk factors and inadequate attainment of targets for several cardiovascular risk factors such as blood pressure, lipids and body weight in patients with SLE. Additionally, suboptimal cardiovascular risk factor control was observed in patients from lower income countries and those with SLE and coexistent antiphospholipid syndrome. These data support the need for better awareness of cardiovascular disease risk among physicians and patients with SLE, and for thorough screening and control of traditional cardiovascular risk factors according to established guidelines. This approach is important to improve cardiovascular health in SLE, especially in high-risk groups such as individuals from lower income countries and those with antiphospholipid syndrome.

### Implications of all the available evidence

Benefits of traditional cardiovascular risk factor assessment and control are well-documented in the general population. Rheumatology societies, national strategies, and policy makers have a crucial role in ensuring that early detection and management of cardiovascular disease risk in people with SLE becomes an important part of the healthcare development agenda.

disease duration and activity, renal involvement, treatment-associated factors (eg, prolonged exposure to glucocorticoids), and antiphospholipid antibodies.[3] The presence of persistently positive antiphospholipid antibodies in association with arterial or venous thrombosis, characterised as antiphospholipid syndrome, has been linked to high cardiovascular-related morbidity risk in patients with SLE.[4] Increasing evidence has also shown an independent association between traditional cardiovascular risk factors and cardiovascular events in patients with SLE. The 2022 European Alliance of Associations for Rheumatology (EULAR) recommendations for the management of cardiovascular risk in rheumatic and musculoskeletal diseases including SLE and antiphospholipid syndrome, highlighted the importance strict control of traditional cardiovascular risk factors in these patients.[5] For the management of most traditional cardiovascular risk factors in SLE, the implementation of the established guidelines for the general population was recommended, emphasising also the importance of a blood pressure target of lower than 130/80 mm Hg.[5] However, reports originating mostly from single-centre studies, have shown that cardiovascular risk factors are often unrecognised and undertreated in patients with SLE.[6]

Furthermore, cardiovascular disease burden in the general population has been inversely associated with country income level, likely to be mediated by inadequate management of traditional cardiovascular risk factors.[7] Although it has been argued that low socioeconomic status is a determinant of adverse cardiovascular outcomes in patients with SLE,[8] the association between country income level and cardiovascular risk factors prevalence and control in SLE has not been thoroughly evaluated in multicentre and multiethnic studies.

Surveys are important tools in the evaluation of implementation of guideline-recommended measures at the international level. Survey of cardiovascular disease risk factors (SURF) projects have been or are currently performed in the general population examining cardiovascular risk factor prevalence and control in patients with coronary heart disease, stroke, chronic obstructive pulmonary disease, and recently, in rheumatoid arthritis (SURF-RA).[9]

Here, in the context of the newly developed survey of cardiovascular disease risk factors-SLE and antiphospholipid syndrome (SURF-SLE and APS) project, we aimed to assess the prevalence of modifiable cardiovascular risk factors and their target attainment in a multicentre and multiethnic group of patients with SLE, according to established guidelines for the general population. We also evaluated potential differences among the participating centres based on country income level, and among patients with or without antiphospholipid syndrome.

## Methods

### Study design and participants

In this cross-sectional, multicentre study, adult patients (aged ≥18 years) who fulfilled the 2012 classification criteria

for SLE[10] were eligible for inclusion; there was no exclusion criteria. Patients were recruited from 27 international centres with experience on SLE or antiphospholipid syndrome, or both, across five continents (Europe, North America, South America, Asia, and Australia; appendix p 6). Consecutive patients from teaching and non-teaching hospitals were recorded. Grupo Latino Americano de Estudio del Lupus (GLADEL) was counted as one centre but collected data from ten countries (Argentina, Brazil, Chile, Colombia, Dominican Republic, Ecuador, Mexico, Paraguay, Peru, and Uruguay), which were included in the total number of participating countries (n=24; appendix p 6).

The SURF-SLE and APS project was approved by the Data Protection Officer at the Diakonhjemmet Hospital in Oslo, Norway (17/10-2019–00150). Ethics committee approval was obtained at each participating centre. Only data that were already available from patient records were used, anonymity was preserved and there were no interventions, as mentioned in detail in Procedures section. Therefore, verbal consent, and not signed informed consent, was usually all that was required from patients.

## Procedures

The project protocol (appendix pp 22–32), a pre-specified questionnaire, and definitions of the included parameters and instructions for completion (appendix pp 33–36) were sent by the principal investigator (MGT) to all participating centres. Each centre completed the survey using data from their medical files (Jan 1, 2015–Jan 1, 2020, extended to Dec 31, 2022 for the centres that were unable to complete the survey by the end of 2020 due to the COVID-19 pandemic). Data were transferred to the data handling centre at the Diakonhjemmet Hospital, Oslo, Norway, following the approval of the survey (protocol number: 17/10-2019–00150) by the Data Protection Officer of this hospital. A data transfer agreement was signed between the party transferring the personal data (principal investigator from each participating centre) and the data receiver (AGS) at the Preventive Cardio-Rheuma clinic, Diakonhjemmet Hospital, Oslo, Norway. Data were transferred either through an electronic platform or an encrypted Microsoft Excel (version 16.0) sheet. Only data that were available from patient records were used and anonymity was preserved without direct or indirect identifying characteristics.

The following data were retrieved from medical files at the time of the patients' visit: (1) demographics and general characteristics: year of birth, sex (self-reported: male or female), ethnicity, type of health care (public or private), and level of education; (2) disease-related characteristics: disease duration, presence anti-double-stranded DNA antibodies or low complement (C3 or C4) concentration within the past year, history of lupus nephritis, current SLE activity as measured at the time of the patients' visit by the SLE Disease Activity Index-2000 (SLEDAI-2K) and damage as assessed by the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index, and coexistence of antiphospholipid syndrome according to the revised Sapporo classification criteria for antiphospholipid syndrome;[11] and (3) traditional cardiovascular risk factors: smoking status (never, previous, and current), known history of hypertension (patient was told of diagnosis previously) based on blood pressure of at least 140/90 mm Hg or use of anti-hypertensives, known history of hyperlipidaemia (patient was told of diagnosis previously) based on LDL of at least 190 mg/dL or use of lipid-lowering agents, diabetes (type 1 or 2), chronic kidney disease (defined as estimated glomerular filtration rate <60 mL/min per 1·73 m² for >3 months), obesity (defined as a BMI ≥30 kg/m²), physical activity (30 min per day or 30 min three to five times per week or less than 30 min three to five times per week), diet (daily consumption of vegetables, fruit, or berries), family history of coronary vascular disease (defined as diagnosis of coronary heart disease in a first-degree male relative occurring before the age of 55 years or in a female first-degree relative occurring before the age of 65 years), known history of atherosclerotic cardiovascular disease (coronary heart disease, cerebrovascular disease, or peripheral artery disease), and thrombotic events (arterial or venous thrombosis). The following cardiovascular risk factor measurements were recorded at the time of the patients' visit: systolic and diastolic blood pressure, heart rate, BMI, waist circumference (cm), total cholesterol, LDL and HDL, non-HDL (calculated by subtracting HDL from total cholesterol), triglycerides, fasting glucose, serum creatinine, and haemoglobin A1c (HbA1C). Medications were also recorded; antiplatelets, anticoagulants, antihypertensives, lipid-lowering agents, disease-related treatments (corticosteroids, hydroxychloroquine, immunosuppressants, and biological agents), and hormone replacement therapy. Other information such as known history of solid organ cancer and severe mental illness was also recorded.

## Outcomes

The main outcomes were the prevalence of cardiovascular risk factors and the the attainment of cardiovascular risk factor targets according to the 2016 European Society of Cardiology guidelines for cardiovascular disease prevention,[12] as the corresponding guidelines for the study period (appendix p 5). An additional blood pressure target level of lower than 130/80 mm Hg for all patients with SLE as recommended by the 2022 EULAR recommendations for cardiovascular risk factor management in people with rheumatic diseases[5] was also assessed. Cardiovascular risk factor target attainment was defined according to individuals' cardiovascular disease risk classification (low, moderate, high, or very high), as assessed by the Systemic Coronary Risk Evaluation. Further details about the Systemic Coronary

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See Online for appendix

| | All patients (N=3401) |
|---|---|
| Age (years) | 43 (33–54; n=3398) |
| Sex | |
| Male | 349/3396 (10·3%) |
| Female | 3047/3396 (89·7%) |
| Ethnicity | |
| Asian | 380/3390 (11·2%) |
| Black | 428/3390 (12·6%) |
| Hispanic | 834/3390 (24·6%) |
| White | 1629/3390 (48·1%) |
| Other | 119/3390 (3·5%) |
| Education completed | |
| None | 32/2629 (1·2%) |
| First level (7 years) | 269/2629 (10·2%) |
| Second level (10-14 years) | 1139/2629 (43·3%) |
| Third level (University or Technical School) | 1189/2629 (45·2%) |
| Access to public healthcare | 2305/3342 (69·0%) |
| Disease characteristics | |
| Disease duration (years) | 9·5 (4·5–17·0; n=3331) |
| Anti-dsDNA antibody positivity (within the past 12 months) | 2030/3320 (61·1%) |
| Low C3 or C4 (within the past 12 months) | 2223/3342 (66·5%) |
| Lupus nephritis (ever) | 1461/3374 (43·3%) |
| SLEDAI-2K score | 2 (0–6; n=3371) |
| SLICC/ACR Damage Index score | 1 (0–2; n=2955) |
| Concomitant antiphospholipid syndrome | 556/2681 (20·7%) |
| Thrombotic antiphospholipid syndrome | 482/556 (86·7%) |
| Obstetric antiphospholipid syndrome | 51/556 (9·2%) |
| Thrombotic and obstetric antiphospholipid syndrome | 23/556 (4·1%) |
| Anti-cardiolipin IgG positivity (moderate to high titres) | 888/3067 (29·0%) |
| Anti-cardiolipin IgM positivity (moderate to high titres) | 790/3031 (26·1%) |
| Anti-β2-glycoprotein 1 IgG positivity (moderate to high titres) | 276/2877 (9·6%) |
| Anti-β2-glycoprotein 1 IgM positivity (moderate to high titres) | 363/2867 (12·7%) |
| Lupus anticoagulant positivity | 655/2921 (22·4%) |
| Double antiphospholipid antibody positivity | 358/2930 (12·2%) |
| Triple antiphospholipid antibody positivity | 250/3087 (8·1%) |
| Cardiovascular risk factors and measurements | |
| Smoking status | |
| Current | 393/3281 (12·0%) |
| Previous | 581/3281 (17·7%) |
| Never | 2307/3281 (70·3%) |

(Table 1 continues in next column)

| | All patients (N=3401) |
|---|---|
| (Continued from previous column) | |
| Physical activity | |
| 30 min daily | 267/1136 (23·5%) |
| 30 min three to five times per week | 290/1136 (25·5%) |
| Less than 30 min three to five times per week | 579/1136 (51·0%) |
| Diet including daily consumption of vegetables, fruits, or berries | 627/949 (66·1%) |
| Known family history of coronary vascular disease | 283/1566 (18·1%) |
| Hypertension | 1210/3398 (35·6%) |
| Systolic blood pressure (mmHg) | 120 (110–130; n=3241) |
| Diastolic blood pressure (mmHg) | 73 (66–80; n=3241) |
| Hyperlipidaemia | 650/3279 (19·8%) |
| Total cholesterol (mg/dL) | 175 (151–204; n=2652) |
| LDL (mg/dL) | 99 (79–124; n=1977) |
| HDL (mg/dL) | 52 (41–64; n=1945) |
| Triglycerides (mg/dL) | 107 (75–152; n=2049) |
| Non-HDL (mg/dL) | 122 (99–150; n=1938) |
| Type 1 diabetes | 8/2595 (0·3%) |
| Type 2 diabetes | 185/3348 (5·5%) |
| Fasting glucose (mg/dL) | 88 (81–95; n=2404) |
| $HbA_{1c}$ (mmol/mol) | 36·6 (32·2–39·9; n=537) |
| Obesity (BMI ≥30 kg/m²) | 751/3169 (23·7%) |
| BMI (kg/m²) | 25·2 (22·0–29·6; n=3169) |
| Waist circumference (cm) | 84 (75–93; n=1050) |
| Heart rate (beats per min) | 78 (70–86; n=1487) |
| Chronic kidney disease | 114/2141 (5·3%) |
| Serum creatinine (mg/dL) | 0·8 (0·6–0·9; n=3332) |
| Known cardiovascular events | |
| Coronary heart disease | 150/3393 (4·4%) |
| Cerebrovascular ischaemic disease | 202/3397 (5·9%) |
| Haemorrhagic cerebrovascular insult | 43/3344 (1·3%) |
| Peripheral artery disease | 58/3396 (1·7%) |
| Known thrombotic events* | |
| Arterial thrombosis | 218/3352 (6·5%) |
| Venous thrombosis | 379/3352 (11·3%) |
| Known history of solid organ cancer | 126/3385 (3·7%) |
| Severe mental illness | 154/3347 (4·6%) |
| Cardiovascular disease risk class, according to the Systemic Coronary Risk Evaluation and risk modifiers† | |
| Low-to-moderate risk | 2390/3015 (79·3%) |
| High risk | 211/3015 (7·0%) |
| Very high risk | 414/3015 (13·7%) |

(Table 1 continues in next column)

Risk Evaluation algorithm and the cardiovascular disease risk classification in specific patient groups in the appendix (p 3). The above outcomes were also examined in high-income versus middle-income countries and in patients with or without coexistent antiphospholipid syndrome.

## Statistical analysis

Quantitative variables are presented as medians with IQR due to deviation from normality (evaluated by the Kolmogorov–Smirnov test) and categorical variables as absolute numbers and percentages (relative frequencies).

| | All patients (N=3401) |
|---|---|
| (Continued from previous column) | |
| Cardiovascular disease-related medication (current use) | |
| Any antiplatelet agents (aspirin, dipyridamole, or clopidogrel) | 961/3171 (30·3%) |
| Any anticoagulants (Vitamin K antagonist, direct oral anticoagulant, or heparin) | 454/3089 (14·7%) |
| Antihypertensive agents | |
| Any angiotensin-converting enzyme inhibitor | 776/3177 (24·4%) |
| Any angiotensin receptor blocker | 541/3159 (17·1%) |
| Any calcium channel blocker | 474/2959 (16·0%) |
| Any beta-blocker | 399/2943 (13·6%) |
| Any diuretic | 380/2948 (12·9%) |
| Any other antihypertensive | 118/2998 (3·9%) |
| Lipid-lowering treatment | |
| Any statin | 661/3176 (20·8%) |
| Any other lipid-lowering agent | 32/1944 (1·6%) |
| Hormone replacement therapy | 93/2334 (4·0%) |
| Disease-related medication | |
| Corticosteroids (current use) | 1876/3391 (55·3%) |
| Corticosteroids (ever) | 2882/3366 (85·6%) |
| Hydroxychloroquine (current use) | 2820/3366 (83·8%) |
| Hydroxychloroquine (ever) | 3060/3359 (91·1%) |
| Any immunosuppressive agent (current use) | 1976/3384 (58·4%) |
| Any biological DMARD (current use) | 252/3262 (7·7%) |

Data are reported as median (IQR; n), or n/N (%). SLEDAI-2K=Systemic Lupus Erythematosus Disease Activity Index-2000. SLICC/ACR Damage Index=Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index. Anti-dsDNA=anti-double stranded DNA. C3=Complement 3. C4=Complement 4. LDL=low density lipoprotein. HDL=high-density lipoprotein. $HbA_{1c}$=haemoglobin A1c. DMARD=disease-modifying anti-rheumatic drug. *Arterial thrombosis includes non-atherosclerotic stroke or transient ischaemic attack, myocardial infarction, and peripheral, splanchnic, or retinal artery thrombosis. Venous thrombosis includes deep venous thrombosis, pulmonary embolism, splanchnic vein thrombosis, cerebral venous thrombosis, or retinal vein thrombosis. †Cardiovascular disease risk modifiers include the presence of atherosclerotic cardiovascular disease, diabetes, or markedly elevated single risk factors.

***Table 1:*** **Demographics, disease-related characteristics, cardiovascular risk factors, and medications**

We also assessed differences between country income subgroups (appendix pp 3–4) and between SLE with antiphospholipid syndrome and SLE without antiphospholipid syndrome subgroups, using Mann-Whitney *U* test for quantitative variables and Pearson's $\chi^2$ or Fisher's exact tests for categorical outcomes. Pearson's $\chi^2$ or Fisher's exact tests were also used to compare cardiovascular risk factor target attainment between these subgroups. Univariate and multivariate logistic regression analysis was also performed for the blood pressure target of less than 130/80 mm Hg. No imputation for missing data was done and we summarised each variable using all available data. A p value of less than 0·05 was considered statistically significant. p values have not been corrected for multiple comparisons as the design of the study was mainly descriptive and exploratory. STATA (version 16.1) statistical software was used for all analyses.

### Role of the funding source

There was no funding source for this study.

## Results

A total of 3401 patients with SLE (both inception and prevalent cases) from 27 centres across 24 countries were included in the study (appendix pp 6, 21). 3047 (89·7%) of 3396 patients were women, 349 (10·3%) were male, 1629 (48·1%) of 3390 were White, and the median age was 43 years (IQR 33–54; table 1). The differences in demographics and disease-related characteristics between patients from high-income countries and middle-income countries, and between SLE with antiphospholipid syndrome and SLE without antiphospholipid syndrome subgroups are presented in the appendix (pp 7–10).

The median disease duration was 9·5 years (IQR 4·5–17·0), the median SLEDAI-2K was 2 (0–6), and the median SLICC/ACR Damage Index score was 1 (0–2). 556 (20·7%) of 2681 patients fulfilled the classification criteria for antiphospholipid syndrome (table 1).[11] Patients with SLE from high-income countries had longer disease duration than those from middle-income countries (11·0 *vs* 6·0 years; p<0·0001) and less active disease as reflected by the SLEDAI-2K scores (2 *vs* 4; p<0·0001), were treated less frequently with corticosteroids and immunosuppressants (44·0% [997 of 2265 patients] *vs* 78·1% [879 of 1126 patients] for corticosteroids, 46·6% [1057 of 2266] *vs* 82·2% [919 of 1118 patients] for immunosuppressants; p<0·0001 for both), and more frequently with hydroxychloroquine (84·8% [1918 of 2261 patients] *vs* 81·6% [902 of 1105 patients]; p=0·018; appendix pp 7–8). Prevalence of antiphospholipid syndrome was comparable between patients from middle-income countries and high-income countries. No significant difference was observed between patients from middle-income countries and those from high-income countries regarding the type of health care (public *vs* private; public health care for middle-income countries 70·0% [790 of 1128 patients] *vs* high-income countries 68·4% [1515 of 2214 patients]; p=0·34; appendix pp 7–8).

Hypertension (1210 [35·6%] of 3398 patients), obesity (751 [23·7%] of 3169 patients), hyperlipidaemia (650 [19·8%] of 3279 patients), and current smoking (393 [12·0%] of 3281 patients) were the most common cardiovascular risk factors in the entire group of patients with SLE (table 1). 185 (5·5%) of 3348 patients had type 2 diabetes and eight (1%) of 2595 had type 1 diabetes. Statins were used by 661 (20·8%) of 3176 of patients with SLE. Regarding atherosclerotic cardiovascular events, coronary heart disease (150 [4·4%] of 3393 patients), ischaemic cerebrovascular disease (202 [5·9%] of 3397 patients), and

peripheral artery disease (58 [1·7%] of 3396 patients) were reported. In total, 2390 (79·3%) of 3015 patients were classified as having a low-to-moderate cardiovascular disease risk, whereas 211 (7·0%) 211 (7·0%) were classified as high-risk and 414 (13·7%) as very-high risk (table 1). Higher prevalence of cardiovascular risk factors and high to very high cardiovascular disease risk was observed in people older than 50 years versus people aged 50 years and younger, and in men versus women (appendix pp 11–13).

The attainment of cardiovascular risk factor targets in the entire group of patients with SLE is presented in table 2. Targets were attained by 1542 (48·7%) of 3169 patients for BMI, 1159 (59·7%) of 1942 patients for LDL, 1281 (65·9%) of 1945 patients for HDL, 1222 (64·2%) of 1903 patients for non-HDL, 1503 (73·4%) of 2049 patients for triglycerides, and 2888 (88·0%) of 3281 patients for smoking. When using the target of lower than 130/80 mm Hg for the blood pressure goal (blood pressure-2),[5] target attainment was 1689 (52·1%) of 3241 patients and 2607 (80·4%) of 3241 patients when applying the 2016 European Society of Cardiology guidelines blood pressure target of lower than 140/90 mm Hg (blood pressure-1).[12] Cardiovascular risk factor target attainment was worse for most cardiovascular risk factors in patients older than those 50 years versus 50 years and younger, in men versus women, and those with a SLEDAI-2K of more than 4 versus 4 or less (appendix p 14). In multivariate logistic regression analysis, age, country income level, SLEDAI-2K, lupus nephritis (ever), current hydroxychloroquine and corticosteroids use, smoking status, BMI, and non-HDL were independently associated with attainment of blood pressure lower than 130/80 mm Hg (appendix p 15).

We also examined cardiovascular risk factor prevalence, cardiovascular disease risk classification, and cardiovascular risk factor target attainment in patients from high-income countries versus those from middle-income countries. A significantly higher prevalence of hypertension (39·0% [884 of 2268 patients] *vs* 28·8% [326 of 1130 patients]; p<0·0001), hyperlipidaemia (26·1% [584 of 2236 patients] *vs* 6·3% [66 of 1043 patients]; p<0·0001), obesity (27·3% [565 of 2072 patients] *vs* 17·0% [186 of 1097 patients]; p<0·0001), and smoking (current smoking 13·7% [296 of 2155 patients] *vs* 8·6% [97 of 1126 patients], previous smoking 22·1% [477 of 2155 patients] *vs* 9·2% [104 of 1126 patients]; p<0·0001) was observed in patients from high-income countries compared with those from middle-income countries (table 3; figure 1). There was no uniform trend concerning the use of different classes of anti-hypertensives between the two subgroups and use of statins was similar, whereas antiplatelet use was higher in patients with SLE from high-income countries versus middle-income countries (31·6% [695 of 2199 patients] *vs* 27·4% [266 of 972 patients]; p=0·017). In addition, the prevalence of cardiovascular events, namely coronary heart disease, ischaemic cerebrovascular disease and haemorrhagic cerebrovascular disease, was higher in patients with SLE from high-income countries compared with those from middle-income countries (table 3).

A higher cardiovascular disease risk was observed in high-income countries versus middle-income countries according to the Systemic Coronary Risk Evaluation and risk modifiers (table 3; appendix p 3). Concerning cardiovascular risk factor target attainment, a significantly lower percentage of patients with SLE from high-income countries attained the BMI (45·6% [944 of 2072 patients] *vs* 54·5% [598 of 1097 patients]; p<0·0001) and smoking targets compared with those from middle-income countries (86·3% [1859 of 2155 patients] *vs* 91·4% [1029 of 1126 patients]; p=0·0002; figure 1; appendix p 16). Blood pressure target attainment was comparable between the two subgroups when the blood pressure target was set according to the 2016 European Society of Cardiology guidelines (blood pressure-1).[12] Using the blood pressure target of lower than 130/80 mm Hg (blood pressure-2) based on the 2022 EULAR recommendations for cardiovascular risk factor management,[5] blood pressure

| | All patients (N=3401) |
|---|---|
| **Smoking** | |
| Yes | 2888/3281 (88·0%) |
| No | 393/3281 (12·0%) |
| **BMI** | |
| Yes | 1542/3169 (48·7%) |
| No | 1627/3169 (51·3%) |
| **Blood pressure-1*** | |
| Yes | 2607/3241 (80·4%) |
| No | 634/3241 (19·6%) |
| **Blood pressure-2†** | |
| Yes | 1689/3241 (52·1%) |
| No | 1552/3241 (47·9%) |
| **LDL‡** | |
| Yes | 1159/1942 (59·7%) |
| No | 783/1942 (40·3%) |
| **HDL‡** | |
| Yes | 1281/1945 (65·9%) |
| No | 664/1945 (34·1%) |
| **Non-HDL‡** | |
| Yes | 1222/1903 (64·2%) |
| No | 681/1903 (35·8%) |
| **Triglycerides‡** | |
| Yes | 1503/2049 (73·4%) |
| No | 546/2049 (26·6%) |

Data are reported as n/N (%). LDL=low-density lipoprotein. HDL=high-density lipoprotein. SLE=systemic lupus erythematosus. *Blood pressure-1 refers to a blood pressure lower than 140/90 mm Hg as a general target, lower than 130/80 mmHg for type 1 diabetes, and lower than 140/85 mm Hg for type 2 diabetes. †Blood pressure-2 refers to a blood pressure lower than 130/80 mmHg target for all patients with systemic lupus erythematosus. ‡Lipid targets were evaluated according to the 2016 European Society of Cardiology guidelines (as defined in the appendix p 5).

***Table 2*: Cardiovascular risk factor target attainment in patients with SLE**

control was significantly better in high-income countries than in middle-income countries (54·9% [1170 of 2132 patients] *vs* 46·8% [519 of 1109 patients]; p<0·0001). In addition, target attainment for HDL (75·0% [895 of 1194 patients] vs 51·4% [386 of 751 patients]; p<0·0001), non-HDL (66·4% [769 of 1158 patients] vs 60·8% [453 of 745 patients]; p=0·013), and triglycerides (80·9% [1017 of 1257 patients] *vs* 61·4% [486 of 792 patients]; p<0·0001) was significantly better in high-income countries than in middle-income countries (figure 1).

Considering the large number of included patients from the USA (998 [29·3%] of 3401 patients) and the high

| | Middle-income countries (N=1132) | High-income countries (N=2269) | p value |
|---|---|---|---|
| **Cardiovascular risk factors and measurements** | | | |
| Smoking status | | | <0·0001 |
| Current | 97/1126 (8·6%) | 296/2155 (13·7%) | .. |
| Previous | 104/1126 (9·2%) | 477/2155 (22·1%) | .. |
| Never | 925/1126 (82·1%) | 1382/2155 (64·1%) | .. |
| Physical activity | | | <0·0001 |
| 30 min daily | 111/567 (19·6%) | 156/569 (27·4%) | .. |
| 30 min three to five times per week | 123/567 (21·7%) | 167/569 (29·3%) | .. |
| Less than 30 min three to five times per week | 333/567 (58·7%) | 246/569 (43·2%) | .. |
| Diet including daily consumption of vegetables, fruits, or berries | 359/569 (63·1%) | 268/380 (70·5%) | 0·018 |
| Known family history of coronary vascular disease | 155/583 (26·6%) | 128/983 (13·0%) | <0·0001 |
| Hypertension | 326/1130 (28·8%) | 884/2268 (39·0%) | <0·0001 |
| Systolic blood pressure (mmHg) | 120 (110–130; n=1109) | 121 (111–131; n=2132) | <0·0001 |
| Diastolic blood pressure (mmHg) | 78 (70–82; n=1109) | 71 (64–80; n=2132) | <0·0001 |
| Hyperlipidaemia | 66/1043 (6·3%) | 584/2236 (26·1%) | <0·0001 |
| Total cholesterol (mg/dL) | 176 (148–208; n=809) | 175 (152–203; n=1843) | 0·74 |
| LDL (mg/dL) | 100 (79–125; n=758) | 98 (79–123; n=1219) | 0·35 |
| HDL (mg/dL) | 45 (37–57; n=751) | 56 (45–69; n=1194) | <0·0001 |
| Triglycerides (mg/dL) | 128 (92–185; n=792) | 96 (67–136; n=1257) | <0·0001 |
| Non-HDL (mg/dL) | 126 (103–156; n=748) | 119 (97–145; n=1190) | <0·0001 |
| Type 1 diabetes | 2/636 (0·3%) | 6/1959 (0·3%) | 0·99 |
| Type 2 diabetes | 67/1130 (5·9%) | 118/2218 (5·3%) | 0·47 |
| Fasting glucose (mg/dL) | 86 (79–94; n=943) | 89 (83–96; n=1461) | <0·0001 |
| $HbA_{1c}$ (mmol/mol) | 36·6 (32·2–41·0; n=270) | 36·6 (32·2–40·0; n=267) | 0·82 |
| Obesity (BMI ≥30 kg/m²) | 186/1097 (17·0%) | 565/2072 (27·3%) | <0·0001 |
| BMI (kg/m²) | 24·5 (21·8–27·8; n=1097) | 25·7 (22·2–30·6; n=2072) | <0·0001 |
| Waist circumference (cm) | 83 (75–92; n=515) | 85 (75–94; n=535) | 0·088 |
| Heart rate (bpm) | 82 (75–90; n=617) | 74 (67–81; n=870) | <0·0001 |
| Chronic kidney disease | 54/1039 (5·2%) | 60/1102 (5·4%) | 0·80 |
| Serum creatinine (mg/dL) | 0·7 (0·6–0·9; n=1108) | 0·8 (0·7–0·9; n=2224) | 0·0019 |
| Known cardiovascular events | | | |
| Coronary heart disease | 21/1131 (1·9%) | 129/2262 (5·7%) | <0·0001 |
| Cerebrovascular ischaemic disease | 44/1131 (3·9%) | 158/2266 (7·0%) | 0·0003 |
| Haemorrhagic cerebrovascular insult | 5/1131 (0·4%) | 38/2213 (1·7%) | 0·0017 |
| Peripheral artery disease | 15/1131 (1·3%) | 43/2265 (1·9%) | 0·23 |
| Known thrombotic events* | | | |
| Arterial thrombosis | 49/1131 (4·3%) | 169/2221 (7·6%) | 0·0003 |
| Venous thrombosis | 91/1131 (8·0%) | 288/2221 (13·0%) | <0·0001 |
| Known history of solid organ cancer | 16/1127 (1·4%) | 110/2258 (4·9%) | <0·0001 |
| Severe mental illness | 34/1131 (3·0%) | 120/2216 (5·4%) | 0·0017 |
| Cardiovascular disease risk class, according to the Systemic Coronary Risk Evaluation and risk modifiers† | | | <0·0001 |
| Low-to-moderate risk | 847/1020 (83·0%) | 1543/1995 (77·3%) | .. |
| High risk | 84/1020 (8·2%) | 127/1995 (6·4%) | .. |
| Very high risk | 89/1020 (8·7%) | 325/1995 (16·3%) | .. |

(Table 3 continues on next page)

| | Middle-income countries (N=1132) | High-income countries (N=2269) | p value |
|---|---|---|---|
| (Continued from previous page) | | | |
| **Current cardiovascular disease-related medication use** | | | |
| Any antiplatelet agents (aspirin, dipyridamole, or clopidogrel) | 266/972 (27·4%) | 695/2199 (31·6%) | 0·017 |
| Any anticoagulants (vitamin K antagonist, direct oral anticoagulant, or heparin) | 133/920 (14·5%) | 321/2169 (14·8%) | 0·81 |
| Antihypertensive agents | | | |
| Any angiotensin-converting enzyme inhibitor | 246/976 (25·2%) | 530/2201 (24·1%) | 0·50 |
| Any angiotensin receptor blocker | 236/980 (24·1%) | 305/2179 (14·0%) | <0·0001 |
| Any calcium channel blocker | 147/865 (17·0%) | 327/2094 (15·6%) | 0·35 |
| Any beta-blocker | 80/849 (9·4%) | 319/2094 (15·2%) | <0·0001 |
| Any diuretic | 80/856 (9·3%) | 300/2092 (14·3%) | 0·0002 |
| Any other antihypertensive | 62/879 (7·1%) | 56/2119 (2·6%) | <0·0001 |
| Lipid-lowering treatment | | | |
| Any statin | 193/975 (19·8%) | 468/2201 (21·3%) | 0·35 |
| Any other lipid-lowering agent | 9/611 (1·5%) | 23/1333 (1·7%) | 0·69 |
| Hormone replacement therapy | 0/538 (0%) | 93/1796 (5·2%) | <0·0001 |

Data are reported as median (IQR; n) or n/N (%). LDL=low-density lipoprotein. HDL=high-density lipoprotein. $HbA_{1c}$=haemoglobin A1c. SLE=systemic lupus erythematosus. *Arterial thrombosis includes non-atherosclerotic stroke or transient ischaemic attack, myocardial infarction, and peripheral, splanchnic, or retinal artery thrombosis. Venous thrombosis includes deep venous thrombosis, pulmonary embolism, splanchnic vein thrombosis, cerebral venous thrombosis, or retinal vein thrombosis. †Cardiovascular disease risk modifiers include the presence of atherosclerotic cardiovascular disease, diabetes, or markedly elevated single risk factors.

***Table 3*: Prevalence of cardiovascular risk factors, cardiovascular disease risk classification, and cardiovascular disease-related medications in patients with SLE according to country income subgroup**

prevalence of some cardiovascular risk factors (eg, obesity) in the USA according to the literature, we assessed the differences between high-income countries and middle-income countries after excluding centres from the USA from the analysis. Current smoking (19·3% [224 of 1158 patients] *vs* 8·6% [97 of 1126 patients]) and hyperlipidaemia (13·8% [171 of 1243 patients] *vs* 6·3% [66 of 1043 patients]), but not hypertension and obesity, remained significantly higher in high-income countries versus middle-income countries, as well as the percentage of HDL (76·8% [630 of 820 patients] *vs* 51·4% [386 of 751 patients]; p<0·0001) and triglycerides (81·4% [716 of 880 patients] *vs* 61·4% [486 of 792 patients]; p<0·0001) target attainment.

In the high cardiovascular disease risk group, no significant difference was observed between high-income countries and middle-income countries for the targets of smoking, BMI, blood pressure (either according to the 2016 European Society of Cardiology guidelines or 2022 EULAR recommendations), LDL, non-HDL, and triglycerides; the HDL target was attained more frequently in high-income countries than in middle-income countries subgroup (71·6% [58 of 81 patients] vs 53·8% [35 of 65 patients]; p=0·027; appendix p 17). In the very high risk group, cardiovascular risk factor target attainment remained suboptimal in both income subgroups. A significantly higher percentage of patients from high-income countries fulfilled the HDL, non-HDL, and triglyceride targets than those from middle-income countries (figure 1; appendix p 17).

A subgroup analysis including 2681 patients with available data on coexistent antiphospholipid syndrome was also done. Differences in cardiovascular risk factor prevalence, cardiovascular disease risk classification, and use of cardiovascular disease preventive medications between the two subgroups are shown in appendix (pp 18–19). A higher percentage of patients with antiphospholipid syndrome had hypertension (47·1% [262 of 556 patients] *vs* 34·6% [736 of 2125 patients]; p<0·0001), hyperlipidaemia (34·6% [189 of 547] *vs* 21·2% [447 of 2105 patients]; p<0·0001), obesity (29·0% [150 of 518 patients] *vs* 24·0% [471 of 1960 patients]; p=0·021), and type 2 diabetes (7·9% [43 of 547 patients] *vs* 5·1% [107 of 2084 patients]; p=0·014) than those without antiphospholipid syndrome (figure 2; appendix pp 18–19). Generally, similar trends apply when comparing traditional cardiovascular risk factor prevalence between patients with SLE with antiphospholipid syndrome and those without antiphospholipid syndrome, according to country income level (figure 2). Statins, antihypertensives (including angiotensin-converting enzyme inhibitors, calcium channel blockers, beta-blockers, diuretics, and other agents), and antiplatelet agents were used more frequently among patients with SLE with antiphospholipid syndrome versus those without antiphospholipid syndrome (appendix pp 18–19).

The prevalence of all recorded types of atherosclerotic cardiovascular events was higher in patients with SLE with antiphospholipid syndrome than those without antiphospholipid syndrome (p<0·0001 for all types of events) and more individuals with coexistent

antiphospholipid syndrome were classified as having very high cardiovascular disease risk (appendix pp 18–19).

Cardiovascular risk factor target attainment was significantly lower in patients with SLE with antiphospholipid syndrome compared to those without antiphospholipid syndrome, across all countries, for BMI (37·1% [192 of 518 patients] *vs* 50·5% [989 of 1960 patients]; p<0·0001), LDL (48·3% [156 of 323 patients] *vs* 61·7% [771 of 1249 patients]; p<0·0001), and non-HDL (55·7% [175 of 314 patients] *vs* 65·9% [807 of 1224 patients]; p=0·0008; figure 2; appendix p 20).

## Discussion

To our knowledge, this is the first international study examining the prevalence of cardiovascular risk factors and their control in patients with SLE from 24 countries across five continents, and according to country income level and the coexistence of antiphospholipid syndrome. We found a high prevalence and inadequate control of traditional cardiovascular risk factors in the entire SLE cohort, and suboptimal cardiovascular risk factor target attainment in patients from middle-income countries and in those with coexistent antiphospholipid syndrome, supporting the need for increased cardiovascular disease risk awareness in patients with SLE and especially in high-risk subgroups.

Reports from meta-analyses have showed a higher risk of stroke and myocardial infarction in patients with SLE than the general population.[1] The increased cardiovascular disease risk in SLE seems to be driven by an inter-relationship between innate and adaptive immune dysregulation, several disease-related characteristics, and the traditional cardiovascular risk factors.[3] The traditional cardiovascular risk factors, although more prevalent in people with SLE than in the general population, are often overlooked and undermanaged.[6,13] The results from this study confirm a high prevalence of modifiable cardiovascular risk factors in the patients with SLE. Notably, 35·6% of patients with SLE in our sample study were hypertensive in accordance with previous findings from regional observational studies[13] and the reported 33% prevalence of hypertension in the international inception cohort study by the SLICC group.[14]

Comparing patients from high-income countries and middle-income countries, we found a higher cardiovascular risk factor prevalence in those from high-income countries in accordance with large cohort studies in the general population, such as those by the Prospective Urban Rural Epidemiology research group.[15] The Prospective Urban Rural Epidemiology research group showed that the INTERHEART risk score—a validated tool for cardiovascular risk factor burden quantification including a sum of several traditional cardiovascular risk factors—was significantly higher among individuals from high-income countries than those from middle-income countries.

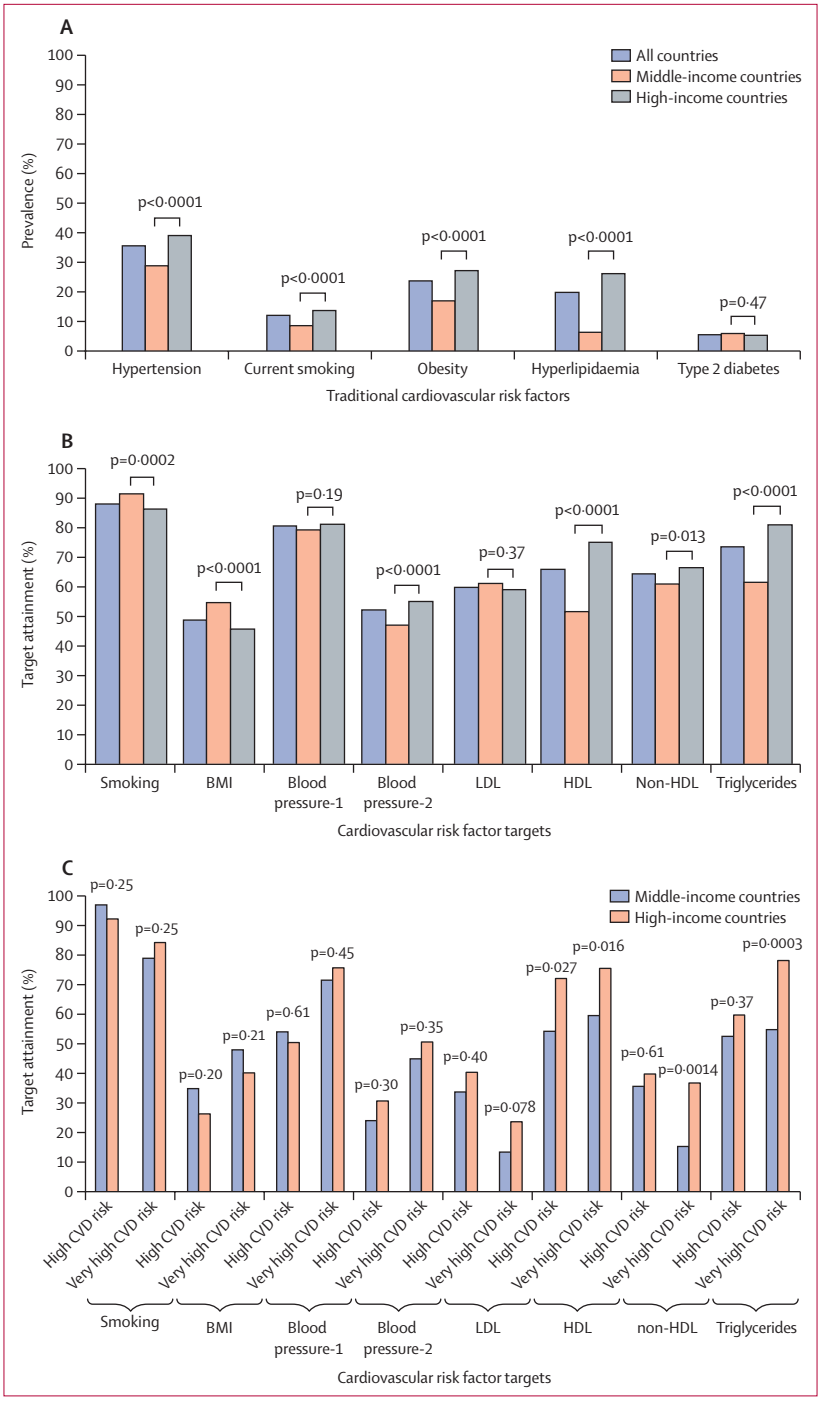


***Figure 1:*** **Prevalence and target attainment of cardiovascular risk factors in patients with SLE according to country income level**

Prevalence of traditional cardiovascular risk factors (A), cardiovascular risk factor target attainment (B) in patients with SLE in the entire group (all countries) and in middle-income countries versus high-income countries, and cardiovascular risk factors target attainment (C) in patients with SLE in middle-income versus high-income countries in the high and very high CVD risk groups. Blood pressure-1 refers to blood pressure lower than 140/90 mm Hg as a general target, blood pressure lower than 130/80 mm Hg for type 1 diabetes, and blood pressure lower than 140/85 mm Hg for type 2 diabetes. Blood pressure-2 refers to blood pressure lower than 130/80 mm Hg target for all patients with SLE. Lipid targets were evaluated according to the 2016 European Society of Cardiology guidelines (as defined in the appendix p 5). CVD=cardiovascular disease. SLE=systemic lupus erythematosus.

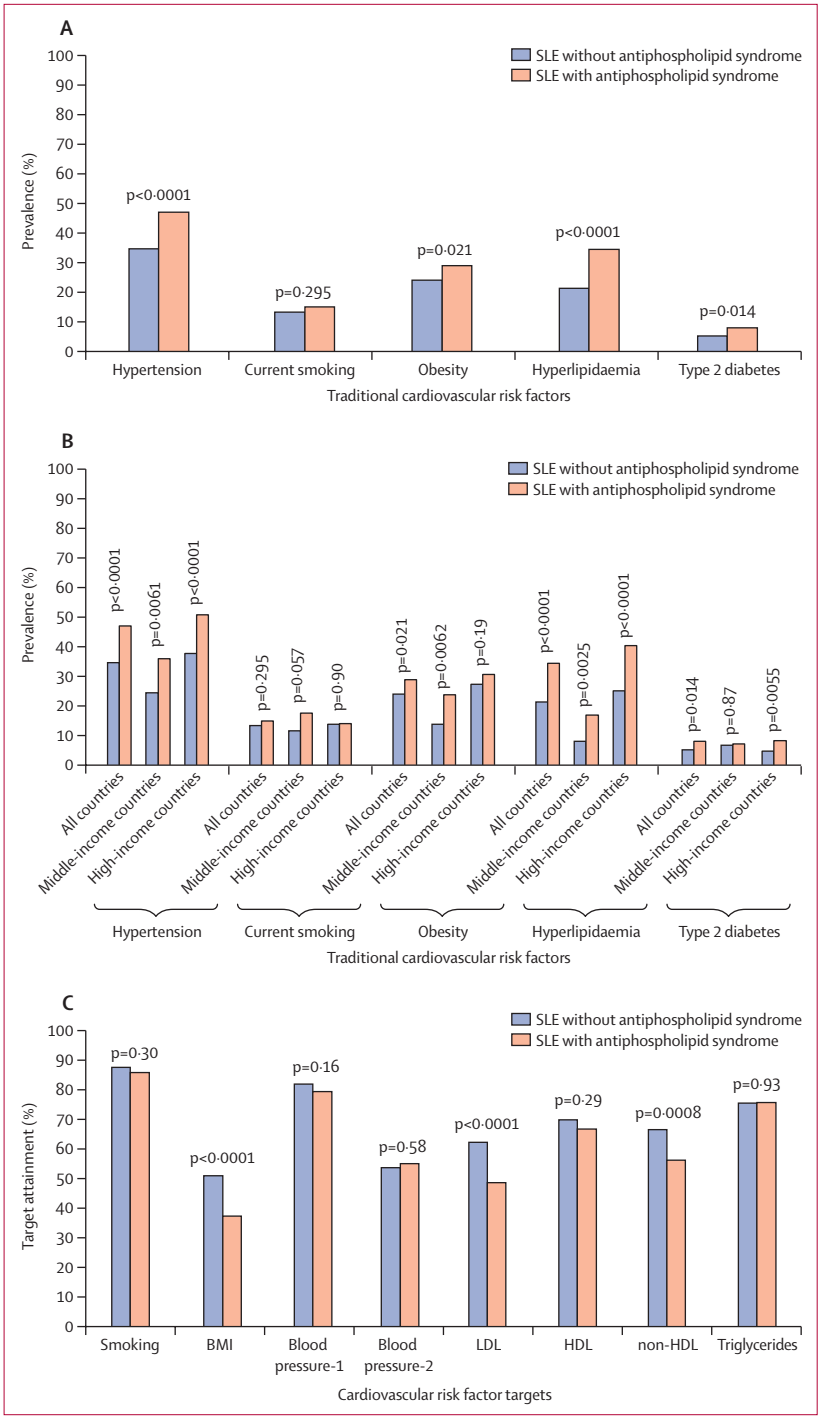


***Figure 2:*** **Prevalence and target attainment of cardiovascular risk factors in patients with SLE according to antiphospholipid syndrome coexistence**

Prevalence of traditional cardiovascular risk factors in patients with SLE with coexistent antiphospholipid syndrome versus patients with SLE without antiphospholipid syndrome in the entire group (A), by country income level (B), and cardiovascular risk factors target attainment (C) in patients with SLE with antiphospholipid syndrome versus patients with SLE without antiphospholipid syndrome, in the entire group. Blood pressure-1 refers to blood pressure lower than 140/90 mm Hg as a general target, blood pressure lower than 130/80 mm Hg for type 1 diabetes, and blood pressure lower than 140/85 mm Hg for type 2 diabetes. Blood pressure-2 refers to blood pressure lower than 130/80 mm Hg target for all patients with SLE. Lipid targets were evaluated according to the 2016 European Society of Cardiology guidelines (as defined in the appendix p 5). SLE=systemic lupus erythematosus.

Adequate control of traditional cardiovascular risk factors has been inversely associated with cardiovascular disease risk in the general population and in patients with SLE.[16,17] Notably, a 7-year follow-up study of patients with SLE published in 2023, showed a 50% reduction in atherosclerotic plaque progression for every modifiable cardiovascular risk factor fulfilling European Society of Cardiology targets (odds ratio [OR] 0·56 [95% CI 0·34–0·93]; p=0·026).[6] In the present study, we found suboptimal cardiovascular risk factor control in the entire SLE cohort, with target attainment ranging from 48·7% to 65·9% for the BMI, blood pressure (for <130/80 mm Hg), LDL, HDL, and non-HDL targets. Our results are congruent with those from previous cross-sectional studies in patients with SLE,[18] which report poor rates of control for hypertension and hyperlipidaemia according to established guidelines.

Focusing on blood pressure target attainment, a previous study showed a lower incidence of cardiovascular events in the group of patients with SLE with a blood pressure of lower than 130/80 mm Hg compared with the groups with a blood pressure of at least 140/90 mm Hg and 130–139/80–89 mm Hg,[19] whereas in another study,[20] systolic blood pressure of at least 132 mm Hg was associated with higher risk of cardiovascular events in patients with SLE. The findings of these studies support the suggested blood pressure target of lower than 130/80 mm Hg for patients with SLE in the 2022 EULAR recommendations for cardiovascular risk factor management in rheumatic diseases.[5] The 130/80 mm Hg blood pressure target was recommended for all adults by the updated 2018 European Society of Cardiology[21] and the American College of Cardiology and American Heart Association guidelines for hypertension management.[22] We showed that only 52·1% of patients with SLE in this study met this target. Notably, in addition to traditional cardiovascular risk factors, disease-related factors such as SLEDAI-2K, lupus nephritis, and corticosteroids were found to be independently associated with blood pressure lower than 130/80 mm Hg target attainment in our multivariate analysis, highlighting the need for low disease activity and remission, and withdrawal of corticosteroids.

The importance of LDL as a primary lipid target has been highlighted by the 2016 European Society of Cardiology guidelines,[12] the updated 2019 European Society of Cardiology guidelines,[23] and the 2018 American Heart Association and American College of Cardiology guidelines[24] for the management of dyslipidaemia in the general population. We found that only 59·7% of patients with SLE in our study met the LDL target according to the 2016 European Society of Cardiology guidelines. High LDL has been associated with increased coronary risk in SLE and the beneficial effect of lipid-lowering treatment on cardiovascular disease morbidity and mortality in patients with SLE with hyperlipidaemia has also been documented.[25]

Comparing cardiovascular risk factor control by country income level, patients with SLE from

high-income countries had suboptimal but substantially better target attainment than those from middle-income countries for several cardiovascular risk factors, such as blood pressure (for the target of <130/80 mm Hg), HDL, non-HDL, and triglycerides. In the general population, a better control of blood pressure[7] and lipids[26] in higher income settings has been attributed to increased awareness, more efficient implementation of primary and secondary cardiovascular disease prevention measures, and better access to health-care resources.[15] In this study, we detected a more widespread use of antiplatelet agents in high-income countries compared with middle-income countries, but no differences in statins and antihypertensive medications. The differences between patients from high-income countries and middle-income countries in our study might be explained by different access to health care, with less detected risk-factors and less financial possibilities to control risk in lower income countries. Among patients classified in the high and very high cardiovascular disease risk categories, cardiovascular risk factor target attainment was suboptimal in both income subgroups, indicating that cardiovascular disease prevention is probably based on a single cardiovascular risk factor approach rather than a more global cardiovascular disease risk assessment and management.

Our results also suggest that patients with SLE and concomitant antiphospholipid syndrome represent a subset of patients with additional cardiovascular disease burden compared with those without antiphospholipid syndrome, highlighting the importance of inclusion of disease characteristics in cardiovascular disease risk estimation and management in SLE.[5]

Previous studies[3,4] have showed an association between the presence of antiphospholipid antibodies or antiphospholipid syndrome and cardiovascular events in SLE,[3,4] stressing the role of antiphospholipid antibody-mediated thrombo-inflammation and atherogenesis in cardiovascular disease pathophysiology in this group of patients.[27] Evidence has shown an increased cardiovascular disease burden and inadequate cardiovascular risk factor target attainment in primary antiphospholipid syndrome and SLE with coexistent antiphospholipid syndrome.[28,29] However, data directly comparing patients with SLE with concomitant antiphospholipid syndrome versus patients with SLE without antiphospholipid syndrome, and especially at an international level, are scarce. In our study, a significantly higher prevalence of hypertension, hyperlipidaemia, obesity, and type 2 diabetes was detected in SLE with antiphospholipid syndrome versus the SLE without antiphospholipid syndrome subgroup. These findings are in agreement with the results from a multicentre cross-sectional study reporting that hypertension, dyslipidaemia, and diabetes were significantly more frequent in patients with SLE with antiphospholipid syndrome than in patients with SLE without antiphospholipid syndrome (40·8%, 42% and 7·9% *vs* 27·8%, 29·7% and 4·7%, respectively).[30]

Regarding cardiovascular risk factor target attainment, we observed that BMI control was worse in patients with antiphospholipid syndrome than in those without. In addition, a lower percentage of patients with SLE and antiphospholipid syndrome met the LDL and non-HDL targets compared with patients with SLE without antiphospholipid syndrome. Because there was no significant difference in lipid measurements between the two subgroups, this finding could be explained by the higher percentage of patients with very high cardiovascular disease risk in the SLE with antiphospholipid syndrome subgroup, to whom a stricter lipid control is usually applied.

This study has several strengths. First, the assessment of cardiovascular risk factor prevalence and recommended cardiovascular risk factor target attainment according to established guidelines a large, international, sample of patients with SLE. Second, the comparison for the first time of cardiovascular risk factor prevalence and control between patients from different income country levels and between patients with and without antiphospholipid syndrome. Third, the contemporary collection of data; and fourth, the representativeness of our sample as patient demographics (age and sex) and the percentage of patients with concomitant antiphospholipid syndrome are similar to those reported by large SLE studies.[14,16] The cross-sectional design of our study is a limitation, including the inability to assess incidence, the production of time-limited results (eg, SLEDAI-2K measurements or complement concentrations at one point in time) and the difficulty in inferring causal and temporal associations. However, we highlight the importance of surveys such as ours to evaluate the implementation of guideline-recommended cardiovascular risk factor goals. The use of a European cardiovascular disease risk stratification tool (ie, Systemic Coronary Risk Evaluation) for all countries might be considered a limitation, but all (except the more recent Globorisk score) clinical prediction scores are non-universal and validation efforts of the Systemic Coronary Risk Evaluation tool in non-European populations have been published. Furthermore, our main objective was to evaluate cardiovascular risk factor target attainment that has been defined based on the Systemic Coronary Risk Evaluation. Although data availability was more than 85% for most parameters (eg, known hypertension, blood pressure measurements, hyperlipidaemia, smoking, obesity, cardiovascular disease-related medications, corticosteroids, and hydroxychloroquine), some variables (eg, lipids including HDL and non-HDL) had a higher percentage of missingness. However, we believe that data were likely to be missing at random, reflecting the limited recording of cardiovascular risk factors for rheumatic and musculoskeletal diseases in daily practice at some centres and highlighting the importance of implementing cardiovascular disease risk management recommen-

dations. It is noteworthy that demographic and several clinical characteristics (eg, age, sex, disease activity and use of antihypertensives, statins, and hydroxychloroquine) did not differ substantially between those with available data and those with missing data. Thus, subsets with available data for specific analyses are likely to be representative of the whole study population. People with lived experience were not involved in the research and writing process of this survey, which is another limitation.

In conclusion, our study showed a high prevalence and inadequate control of traditional cardiovascular risk factors in the entire SLE group, and mostly in subgroups of patients from middle-income countries and those with concomitant antiphospholipid syndrome. Better awareness of cardiovascular disease risk among physicians and patients with SLE, especially in lower income countries, is recommended. Comprehensive risk evaluation including specific disease characteristics such as antiphospholipid syndrome coexistence, and thorough screening and control of traditional cardiovascular risk factors according to established guidelines are warranted to reduce cardiovascular disease burden in patients with SLE.

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**Contributors**

EB did the data acquisition, analysis, interpretation, drafting, and critical revision of the manuscript. AGS, EI, and AMK did the study design and critical revision of the manuscript. MP, GJP-E, GAK, PPS, RQ, DPM, EFB, IG-dlT, TVP, BA-E, ATr, HF-L, SA, AY, GA-M, HD, MFU-G, MM, MG, ES, CM, AH, KL, NC-C, ATi, EM, IAC, AD, LM, JB, NY, DT, SY, CK, EH, MJMA, RM-L did the data acquisition and critical revision of the manuscript. NP did the analysis, interpretation, and critical revision of the manuscript. MGT did the conception, study design, supervision, data acquisition, analysis, interpretation, drafting, and critical revision of the manuscript. EB, AGS, and MGT accessed and verified the underlying data. All authors had full access to the data in the study, gave final approval of the manuscript, and had final responsibility to submit for publication. All SURF-SLE and APS Collaborators were also responsible for data acquisition and critical revision of the manuscript. GJP-E and RQ (Argentina), EFB (Brazil), IG-dlT (Mexico), GA-M (Colombia), MFU-G (Peru), IAC (Paraguay), AD (Uruguay), LM (Chile), MJMA (Ecuador), and RM-L (Dominican Republic), and the SURF-SLE and APS Collaborators OAM and ACSM (Brazil), MPH and MASS (Mexico), and MS (Argentina) are members of GLADEL (Grupo Latino Americano de Estudio del Lupus), an international group formed by experts in the field of SLE.

**Declaration of interests**

AGS has received speaker fees from Merck and Schering-Plough, Bristol Myers Squibb, UCB, Pfizer, Novartis, Lilly and Women's College Hospital, Toronto, ON, Canada. AMK has received speaker fees from Boehringer Ingelheim and Sanofi; has participated on advisory boards for Pfizer, Gilead, and Boehringer Ingelheim; and has received congress sponsorship from Pfizer, Celgene, UCB, Mylan, and Roche. GJP-E has received grants from Janssen; consulting fees from GSK, AstraZeneca, Janssen, Novartis, and Bago; speakers fees from GSK, Werfen, Janssen, AstraZeneca, and Novartis; support for attending meetings and travel from GSK, AstraZeneca, and Boehringer Ingelheim; and for participation on a data safety monitoring board or advisory board from RemeGen, AstraZeneca, and Janssen. GAK has received consulting fees from Janssen and Scipher; and for participation on a data safety monitoring board or advisory board from Janssen. MFU-G has received grant support from Janssen and Pfizer; has been a speaker for GSK and AstraZeneca; and has been a member of advisory boards for AstraZeneca and Ferrer. NC-C has received grants from Roche and UCB. EH has received consulting fees and meeting fees from Johnson & Johnson, Boehringer Ingelheim, Bayer, GSK, Roche-Chugai, and Sanofi-Genzyme; speaking fees from Johnson & Johnson, GSK, and Roche-Chugai; and research funding from Commonwealth Serum Laboratories Behring, GSK, Roche-Chugai, and Johnson & Johnson. NP has received grants from Gilead Sciences Hellas and the European Centre for Disease Prevention and Control. OAM has received speaker's fees or payment for advisory boards from AbbVie, APSEN, AstraZeneca, Boehringer Ingelheim, Celltrion, GSK, and Janssen. MS has received research grants and consulting fees, and has participated as a speaker for: AbbVie, Bristol Myers Squibb, GSK, Janssen, Lilly, Pfizer, Roche, and AstraZeneca. ACSM has received speaker fees from GSK and AstraZeneca. All other authors and SURF-SLE and APS Collaborators declare no competing interests.

**Data sharing**

All data relevant to the study have been included in the Article or uploaded as supplementary information. The data were pseudonymised by each centre before transferred to the data handling centre at Diakonhjemmet hospital, Oslo, Norway where it is stored on a central server. Data for this study are available from the authors upon reasonable request and with permission of the data provider.

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