Risk of coronary heart disease and stroke in a large British cohort of patients with systemic lupus erythematosus

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Objectives. Patients with systemic lupus erythematosus (SLE) are at increased risk of myocardial infarction and stroke. We sought to determine how much of this risk was dependent on recognized cardiovascular risk factors.

Methods. Initially a software package ‘Cardio-Risk-Manager’, which utilizes Framingham data, was used to calculate a 10-yr risk of coronary heart disease (CHD) and stroke for 202 patients with SLE (Group 1) in comparison with hypothetical age- and sex-matched comparators. Subsequently 47 patients who had been followed since 1991 (Group 2) were studied to compare their predicted risks in 1991 with the actual number of cardiovascular events that occurred during the subsequent decade.

Results. Patients in Group 1 had a higher predicted 10-yr risk of stroke (\(P<0.0001\)), but not of CHD, than their comparators. However, following age stratification, traditional risk factors predicted a higher risk of CHD (\(P<0.0001\)) and of stroke (\(P<0.0001\)) in patients under 40 with SLE compared with age-matched comparators. The predicted 10-yr risks of CHD and stroke for patients aged 40 and above were not significantly different from those of their comparators. Predicted risks, however, were lower than the true 10-yr event rate for CHD and stroke in patients in Group 2. In this group, during the 10 yr of follow-up four patients (8.5%) suffered a CHD event and five patients (10.6%) had a stroke, significantly more than were predicted by the presence of conventional risk factors (\(P<0.001\) for CHD and \(P<0.001\) for stroke, respectively).

Conclusions. Conventional risk factors predicted an increased risk of stroke and CHD in younger patients. They do not, however, fully explain the high risk of cardiovascular disease in patients with SLE. Although it is important to address the management of orthodox risk factors for cardiovascular disease in patients with SLE, other causes must be sought to explain the increased incidence of CHD and stroke, especially in those aged over 40.

Key words: Systemic lupus erythematosus, Risk, Coronary heart disease, Stroke, Cardiovascular disease.

In spite of considerable improvements in treatment, morbidity and mortality in patients with systemic lupus erythematosus (SLE) are substantial, with mortality rates of 5–10% at 5 yr and 15–30% at 10 yr [1–6]. Patients with SLE have a nearly 5-fold increased risk of death compared with the general population. The standardized mortality ratio is particularly high, 9.16, in patients aged less than 55 yr [1]. A bimodal pattern of mortality has been described, with early deaths predominantly due to active SLE and intercurrent infection and late deaths principally due to atherosclerotic disease [1, 7, 8]. Cardiovascular disease (CVD) currently accounts for between 20 and 30% of deaths in patients with SLE, but is responsible for a proportionately greater percentage of deaths in late disease [1, 8, 9]. As the anti-inflammatory/immunosuppressive treatment of patients with SLE continues to improve [10], the contribution of cardiovascular disease to morbidity and mortality is likely to increase.

Jonsson et al. [11] showed that the myocardial infarction (MI) rate in Swedish patients with SLE was increased 9-fold. Whilst clinical evidence of coronary disease is found in 6.7 to 8.3% of patients with SLE [9, 12], subclinical atherosclerosis is far more common. Atheromatous carotid plaques have been demonstrated by ultrasonography in 25–40% of patients with SLE [13, 14]. Myocardial single photon emission computed tomography (SPECT) scanning has revealed coronary disease in 40% of such patients [15]. Autopsy studies have demonstrated a prevalence of 41–53% for moderate to severe atherosclerosis affecting the aorta, coronary, renal and cerebral vessels [1, 8].

Stroke occurs in up to 15% of patients with SLE, with some suffering multiple events. The majority of these events occur within the first 5 yr of the diagnosis of SLE [16, 17]. Although there is an increased relative risk for atherosclerotic CVD in patients with SLE, there is less agreement about the relative contributions of orthodox risk factors, such as hypertension, diabetes, smoking and hypercholesterolaemia and of lupus-specific risk factors (Table 1). This conflict may partly arise from the differences between study cohorts. Studies have suggested that not all of the increased risk of CVD seen in patients with SLE is attributable to orthodox risk factors [18, 19]. Esdaile et al. [18] showed that, after removing the effect of these known risk factors, there is still a 7.9-fold increase in the risk of stroke and a 10.1-fold increase in the risk of non-fatal myocardial infarction (MI) in patients with SLE.

Most studies of this nature have been carried out in North America and a calculation of risk of CVD in a European population has not been published to date. We carried out an analysis in a large British cohort. We calculated the predicted 10-yr...
risk of CHD and stroke for each member of a cohort of 202 patients with SLE, using a software package that utilizes data from the Framingham study, to investigate whether management designed to target orthodox cardiovascular risk factors would be predicted to reduce risk of CVD significantly in patients with SLE. We then sought to determine, in a smaller group of patients, how the predicted 10-yr risk of CHD and stroke compared with the number of CHD and stroke events that were actually observed during a 10-yr follow-up period.

Methods

Cross-sectional study: comparison of patients with SLE with hypothetical comparators

Group 1 consisted of 202 consecutive patients (186 female, 16 male) attending a specialist SLE clinic over a period of 12 months in 2001, all of whom fulfilled the revised American College of Rheumatology (ACR) criteria for the classification of SLE [20]. Four patients aged over 70 yr were not included because the software package used is not validated for patients older than 70. Analysis of this group was designed to determine whether these individuals had a greater predicted risk of CVD than age- and sex-matched comparators, when prediction is based on orthodox risk factors only.

Cardio Risk Manager program

The ‘Cardio Risk Manager’ computer program, which is based upon Microsoft Excel Version 5.0, was developed by Hingorani and Vallance [21] for use in primary prevention of atherosclerotic events. This interactive program makes risk calculations utilizing logistic regression equations derived from the Framingham populations [22–24]. The program has been validated against published data for large intervention studies [25–27], and against the risk estimates provided by the Sheffield tables [28, 29], which are also based on Framingham data. The fact that the Framingham data were used successfully to predict the event rate in the placebo arm of the West of Scotland Coronary Prevention Study [30] suggests that the Framingham equations are directly applicable to a UK population. For each patient, data are entered on the following risk factors: systolic and diastolic blood pressure, total serum cholesterol and high-density lipoprotein (HDL) cholesterol, blood glucose, history of smoking, previous cardiovascular disease, left ventricular hypertrophy (LVH) and diabetes. The presence of left ventricular hypertrophy was determined by electrocardiography and defined by the sum of the R wave in lead V5 or V6 and the S wave in lead V1 or V2 being greater than 35 mm. Patients were considered to have a positive smoking history if they were current smokers or had given up smoking in the preceding 12 months.

The software package then calculates a 10-yr risk of coronary heart disease (CHD) and CVD (stroke) for each patient, and for a hypothetical age- and sex-matched comparator. The program assumes that the hypothetical comparators are healthy individuals with mean population levels of blood pressure, total cholesterol and HDL cholesterol for an age- and sex-matched population. They are also assumed to be non-smokers, free of diabetes, LVH and previous CVD. The risk for the comparator thus shows the possible reduction in the patient’s risk of CVD which might be achieved by ideal management of orthodox risk factors.

The predicted CHD and stroke risks for the patients and the comparators were then compared using the Wilcoxon signed ranks test for two related samples. Similar analyses were performed following age stratification of Group 1 into those under 40 yr of age and those aged 40 and above.

Longitudinal study: comparison of predicted risk with actual cardiovascular events

Group 2 was drawn from a sample of 64 patients, also fulfilling the revised ACR criteria, who had attended the same specialist SLE clinic in 1991 and were originally recruited for a study of lipid levels and anti-cardiolipin antibodies in patients with SLE [34]. Sufficient data to permit the calculation of a 10-yr predicted risk of CHD and stroke in 1991, together with continuous follow-up data for the succeeding 10 yr (or to the time of death), were available for 47 of these patients. Four patients had moved away, and for the remaining 13 baseline data were insufficient. One of these 13 patients suffered a myocardial infarction between 1991 and 2001. The 10-yr risks of CHD and stroke predicted for the remaining 47 patients were compared with the number of cardiovascular events that actually took place during this 10-yr period (or until the time of death) using a Hosmer–Lemeshow analysis. The great majority of patients from Group 2 remained as current patients in 2001 and were, therefore, also included in Group 1.

Results

Cross-sectional study: characteristics of patients

The characteristics of the 202 patients in Group 1 are shown in Table 2. Their mean values for blood pressure and serum cholesterol are not elevated, but there was a wide range of values. Thirty-four patients were considered to be hypertensive (systolic blood pressure (SBP) >140 mmHg and/or diastolic blood pressure (DBP) >90 mmHg), 45 had hypercholesterolaemia (serum total cholesterol >5.2 mmol/l) and 45 smoked. One hundred and thirty-four of these patients were of Caucasian origin, 35 were black
African or Afro-Caribbean, 21 were Asian, four were Chinese and eight were from other ethnic groups or of mixed race.

Comparison of patients with SLE with hypothetical comparators

The median predicted 10-yr risk of CHD for the 202 patients with SLE, calculated by the 'Cardio Risk Manager' program, was 1.2% (interquartile range (IQR) 0.1 to 4.2). This risk was similar to the median CHD risk of 1.0% (IQR 0.0 to 4.0) predicted for the hypothetical matched comparators (Table 3). In contrast, the SLE cohort's median risk of stroke was 0.8% (IQR 0.3 to 1.7), while the median risk for the comparators was 1.0% (IQR 0.1 to 1.0).

Analysis by the Wilcoxon signed rank test showed that patients with SLE had significantly higher predicted risk of stroke ($P < 0.0001$), but not of CHD, than their comparators.

Since previous studies had suggested a particularly increased relative risk of CVD in younger patients with SLE, Group 1 was also stratified by age into patients aged under 40 ($n = 93$) and those aged 40 or over ($n = 109$). This analysis revealed that traditional risk factors predicted a higher risk of CHD (median 0.1% compared with 0; $P < 0.0001$) and of stroke (median 0.4% compared with 0.1%; $P < 0.0001$) in patients with SLE aged under 40 than in age- and sex-matched comparators. The 10-yr risks of CHD and stroke for older patients were not significantly different from those of the comparators.

Longitudinal study: characteristics of patients

The characteristics of this group were very similar to those of Group 1. The mean age of the 47 patients in Group 2 was 43 yr (range 24–67 yr). Forty-five were female and two male. Nine patients smoked.

Table 2. Patient data for Group 1

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Mean (standard deviation)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>42.2 (±12.1)</td>
<td>17–69</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>123 (±16)</td>
<td>91–205</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>79 (±9)</td>
<td>60–102</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>5.0 (±1.1)</td>
<td>2.6–8.7</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>1.6 (±0.5)</td>
<td>0.5–3.5</td>
</tr>
<tr>
<td>History of smoking</td>
<td>45 (21.2%)</td>
<td></td>
</tr>
<tr>
<td>Diabetic patients</td>
<td>2 (1.0%)</td>
<td></td>
</tr>
<tr>
<td>ECG changes of LVH</td>
<td>15 (7.4%)</td>
<td></td>
</tr>
<tr>
<td>History of CVD</td>
<td>13 (6.4%)</td>
<td></td>
</tr>
<tr>
<td>Hypertensive$^a$</td>
<td>34 (16.8%)</td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolaemia$^b$</td>
<td>65 (32.2%)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Female 186 (92.1%), Male: 16 (7.9%)</td>
<td></td>
</tr>
</tbody>
</table>

$^a$Hypertension was defined as a systolic blood pressure >140 mmHg and/or a diastolic blood pressure >90 mmHg.

$^b$Hypercholesterolaemia was defined as a serum total cholesterol >5.2 mmol/l.

Comparison of predicted risk with actual cardiovascular events

The median predicted 10-yr risks of CHD (1.4%, IQR 0.2 to 3.4) and stroke (0.6%, IQR 0.4 to 1.3) for the patients with SLE in this group were similar to the median CHD (1.0%, IQR 0 to 3.0) and stroke (1.0%, IQR 0.1 to 1.0) risks predicted for the hypothetical matched comparators. Analysis by the Wilcoxon signed rank test showed no significant difference in risk of CHD or stroke between the patients with SLE and their comparators. This is, however, probably due in part to the small sample size of Group 2.

However, during the 10 yr of follow-up four patients (8.5%) suffered a CHD event and five patients (10.6%) had a stroke. Using the binomial distribution, we calculate that the observed incidences of both CHD and stroke over this 10-yr period are significantly greater than would be predicted by the Cardio Risk Manager program ($P < 0.001$ for CHD and $P < 0.001$ for stroke).

Four patients died during this 10-yr period: two following a stroke, one as a result of an infection and one due to a malignancy.

Figure 1 illustrates the excess of observed CHD and stroke over the number of expected events based on the risk predictions using data collected in 1991. The solid line indicates the number of observed events over the 10-yr period, whereas the broken line shows the number of expected events.

Characteristics of patients who suffered a cardiovascular event

The characteristics of these patients are summarized in Table 4. Two of the nine patients who suffered CHD or stroke were aged under 40 yr in 1991. Two were hypertensive, five had raised cholesterol and one was a smoker in 1991. The predicted risk of suffering the event that actually occurred in these patients was higher than that of the comparator in five cases, and lower in four cases. The mean age of these nine individuals was 48.0 yr, compared with 40.2 yr for the remaining 38 patients.

The mean duration of SLE for the 47 patients in Group 2 was 7.3 yr. The mean disease duration was greater in the nine individuals who suffered a cardiovascular event (11.3 yr) than in the remaining 38 (6.3 yr).

Fifteen of the 47 patients in Group 2 (32%) had either IgG or IgM anti-cardiolipin antibodies. Anti-cardiolipin antibodies were measured by enzyme-linked immunosorbent assay (ELISA) (Shield Diagnostics, Dundee) [34]. Whilst only two of the five patients who suffered a stroke had anti-cardiolipin antibodies (40%), these were present in three out of the four patients who had a CHD event (75%). Lupus anticoagulant was present in eight patients, only one of whom had a cardiovascular event.

Eleven of the 47 patients had evidence of lupus nephritis (grades 3 to 5) on renal biopsy. Of these 11 patients three suffered a cardiovascular event (all of whom had grade 4 nephritis). The mean total cumulative corticosteroid dose at enrolment for the nine individuals who suffered a cardiovascular event (19.7 g) was slightly greater than that for the remaining 38 subjects (16.0 g). Four of these nine individuals (44.4%) had been on hydroxychloroquine or chloroquine treatment at or prior to enrolment, compared with 25 of the remaining 38 (65.8%).
Five of the nine individuals who suffered a cardiovascular event were using aspirin (55.6%), compared with only four of the remaining 38 (10.5%). One of the nine (11.1%) and four of the remaining 38 (10.5%) were anticoagulated with warfarin. Only one patient, who went on to have a CHD event, was using a statin in 1991. Statins were introduced in three further patients after they had suffered a cardiovascular event.

Due to the small sample size of Group 2 there were insufficient data to make any statistically significant conclusions regarding the effects of lupus-specific risk factors, such as disease duration and anti-cardiolipin antibodies, on the risk of suffering a cardiovascular event.

**Discussion**

The Cardio Risk Manager program predicts the reduction in the risk of CHD or stroke that could be achieved in individual patients by successfully reducing orthodox risk factors. Our analysis suggests that managing these risk factors could reduce the predicted risk of CHD and stroke significantly in patients with SLE under the age of 40, but not in older patients.

SLE has been shown to result in the premature onset of both stroke and CHD [12, 35, 36]. Bruce *et al.* [36] found that the mean age at a first coronary event was 49 yr in patients with SLE compared with 65–74 yr in the general population. Manzi *et al.* [12] investigated cardiovascular disease in 498 women with SLE, and found that the risk of MI relative to age-matched controls was highest, at 52.4, in those aged 35–44 yr. Two thirds of all cardiovascular events in this cohort occurred in patients aged less than 55 yr. Ward [35] also found the relative risk of MI, congestive heart failure and stroke to be greatest in young patients with SLE (aged 18–44 yr).

The most likely explanation for the results obtained by age stratification in the current study is that risk factors such as hypertension and hypercholesterolaemia are relatively uncommon in people under 40. The increased incidence of these risk factors in young patients with SLE therefore makes a significant difference to their risk of CVD compared with other people of the same age. The same is not true of patients over 40, because those risk factors are also fairly common in the general population of that age group and this is reflected in the values that the computer program uses to generate the level of risk for the age-matched hypothetical comparator.

One limitation of our analysis is that the comparators are assumed to be free of risk factors such as smoking, diabetes and previous history of CVD. Therefore the predicted risk of the hypothetical comparators will be lower than an actual population of people without SLE. Given this fact, the predicted risks in our patients over 40 are surprisingly low. Long-term management in a hospital setting may have resulted in the recognition and treatment

![Fig. 1. Kaplan–Meier plots illustrating the excess of observed CHD (a) and stroke (b) over the number of expected events based on the risk predictions using data collected in 1991. The solid line indicates the number of observed events over the 10-yr period, whereas the broken line shows the number of expected events.](https://academic.oup.com/rheumatology/article-abstract/43/7/924/1788366/fig1)

**Table 4. Clinical details at enrolment of patients who subsequently suffered a cardiovascular event**

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Event type</th>
<th>Ethnic origin</th>
<th>Blood pressure</th>
<th>Total cholesterol</th>
<th>ACL status</th>
<th>Renal disease*</th>
<th>Steroid dose (g)*</th>
<th>Hydroxychloroquine*</th>
<th>Risk factors</th>
<th>Predicted risk of event (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37</td>
<td>F</td>
<td>CHD</td>
<td>Caucasian</td>
<td>120/80</td>
<td>5.2</td>
<td>IgG</td>
<td>4</td>
<td>15.45</td>
<td></td>
<td></td>
<td>H&lt;sub&gt;s&lt;/sub&gt; CVD</td>
</tr>
<tr>
<td>2</td>
<td>46</td>
<td>F</td>
<td>CHD</td>
<td>Caucasian</td>
<td>115/75</td>
<td>6.0</td>
<td>–</td>
<td>4</td>
<td>19.8</td>
<td></td>
<td></td>
<td>H&lt;sub&gt;s&lt;/sub&gt; smoking</td>
</tr>
<tr>
<td>3</td>
<td>37</td>
<td>F</td>
<td>CHD</td>
<td>Indian</td>
<td>135/85</td>
<td>7.9</td>
<td>IgG</td>
<td>4</td>
<td>18.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>54</td>
<td>F</td>
<td>CHD</td>
<td>Caucasian</td>
<td>120/80</td>
<td>6.1</td>
<td>IgM</td>
<td>2.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>45</td>
<td>F</td>
<td>Stroke</td>
<td>Caucasian</td>
<td>120/70</td>
<td>4.0</td>
<td>–</td>
<td>4</td>
<td>61.65</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>58</td>
<td>F</td>
<td>Stroke</td>
<td>Caucasian</td>
<td>125/75</td>
<td>3.1</td>
<td>–</td>
<td>–</td>
<td>10.86</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>65</td>
<td>F</td>
<td>Stroke</td>
<td>West Indian</td>
<td>155/85</td>
<td>5.0</td>
<td>–</td>
<td>–</td>
<td>15.66</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>42</td>
<td>F</td>
<td>Stroke</td>
<td>Indian</td>
<td>110/65</td>
<td>5.9</td>
<td>IgG/IgM</td>
<td>0.5</td>
<td></td>
<td></td>
<td></td>
<td>H&lt;sub&gt;s&lt;/sub&gt; CVD</td>
</tr>
<tr>
<td>9</td>
<td>48</td>
<td>F</td>
<td>Stroke</td>
<td>Caucasian</td>
<td>155/95</td>
<td>5.4</td>
<td>IgG/IgM</td>
<td>13.89</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Age is age at enrolment in 1991.

*Number indicates grade of lupus nephritis.

*Total cumulative corticosteroid dose at enrolment.

*Yes indicates usage at or prior to enrolment.

*Predicted risk of event relates to the 10-yr risk of the actual event suffered by the subject, namely CHD or stroke. The patient’s risk is given, followed by the comparator’s risk (in brackets).

Abbreviations: ACL status, anti-cardiolipin antibody status; H<sub>s</sub> CVD/smoking, previous history of CVD/smoking.
of orthodox risk factors in a proportion of patients. It is clear, however, that many of our patients do have potentially reversible risk factors for CVD. Twenty-two per cent of Group 1 smoked, 17% were hypertensive and 32% had raised cholesterol. In Group 2 consideration of orthodox risk factors alone did not predict the significantly increased risk of CHD and stroke that was actually observed in this cohort during the 10-yr follow-up period. Our results in a British cohort of patients with SLE are consistent with those previously obtained in North America.

Esdaile et al. [18] carried out a retrospective study of 263 patients with SLE at two Canadian centres. After excluding patients with a history of CVD pre-dating the baseline visit from the analysis, this study reported an increased relative risk of non-fatal MI of 10.1, of death due to CHD of 17.0 and of stroke of 7.9 in patients with SLE [18]. Although conservative assumptions were made, this study suffered from missing data on the presence of LVH in 26% and smoking history in 9% of patients. LVH, an important independent factor associated with an increase in cardiovascular mortality [39], occurs six times more frequently in patients with SLE than in the general population [40], and may amplify the global and regional myocardial ischaemia caused by any degree of coronary artery disease.

Rahman et al. [37] found that amongst patients with premature cardiovascular disease, those with SLE had fewer and less severe conventional risk factors (hypertension, hypercholesterolaemia, diabetes mellitus, smoking status and family history) than those without SLE. However, this study used only total cholesterol measurements, and it is possible that altered individual cholesterol fractions, such as HDL cholesterol, were not detected amongst the patients with SLE in this study [34, 41].

Our results support the hypothesis raised by these authors and others [18, 37, 38] that there are additional risk factors for increased rates of CVD in patients with SLE which are not considered by the Framingham equations.

A large prospective multicentre international study, coordinated from Toronto, is currently attempting to identify these factors by monitoring a cohort of patients with newly diagnosed SLE annually.

Further possible risk factors include the presence of anti-cardiolipin antibodies. Anti-cardiolipin antibodies were present in more than half of the nine patients from Group 2 who actually suffered a CVD event during the 10-yr follow-up period. The number of patients involved is too small to permit further statistical analysis of such risk factors.

Other suggested risk factors for CVD in patients with SLE include raised homocysteine levels, reduced physical activity due to fatigue, persistent inflammation and impaired endothelial function. Impaired endothelium-dependent vasodilatation (EDD), which was inversely correlated with total cholesterol levels, has been demonstrated in patients with SLE [42]. Endothelial function is also impaired in patients with primary systemic necrotizing vasculitis, but can be normalized following treatment of this condition [43], suggesting that early suppression of disease activity in chronic inflammatory rheumatic disorders may reduce long-term vascular damage. Another more recently identified risk factor is the reduced activity of paraoxonase in patients with SLE [44]. The physiological role of paraoxonase is to prevent low-density lipoprotein oxidation with its attendant atherogenic effects.

It is now accepted that cardiovascular disease is a common cause of morbidity and mortality in patients with SLE. As a reduction in the risk of CVD may be obtained by addressing the presence of orthodox risk factors, especially in those aged under 40, we suggest that all patients with SLE should be screened for these factors and offered appropriate intervention if indicated. Patients with hypercholesterolaemia, for example, may benefit from a reduction in the dose of steroid where possible and the introduction of steroid-sparing agents, especially anti-malarials, which have a lipid-lowering effect. Dietary advice and lipid-lowering drugs should be commenced early where indicated. Even aggressive management of these potentially reversible conventional risk factors, however, will not reduce the incidence of CHD and stroke to that of subjects without SLE. It is important to continue the international effort to identify other risk factors, which contribute to the high prevalence of CVD in patients with SLE.

Ethical approval and informed consent were not required because assessment of risk factors for cardiovascular disease is part of the standard management of all patients in our cohort of patients with SLE and is not a research procedure. We are presenting the risks of a whole cohort of patients without any identifiable information about single patients.

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