Fixed regimen		
5–10 mg/day	29 (37%)	23 (37%)
10–15 mg/day	22 (28%)	15 (24%)
Intramuscular glucocorticoids	15 (19%)	11 (18%)
No glucocorticoids	12 (15%)	13 (21%)
Moderate flare		
Weigh regimen		
0.1–0.25 mg/kg/day	17 (17%)	11 (13%)
0.25–0.3 mg/kg/day	47 (48%)	33 (40%)
0.5 mg/kg/day	27 (28%)	31 (37%)
Intramuscular glucocorticoids	3 (3%)	5 (6%)
Pulse therapy	4 (4%)	2 (2%)
No glucocorticoids	0 (0%)	0 (0%)
Fixed regimen		
7.5–15 mg/day	16 (21%)	14 (23%)
15–20 mg/day	31 (40%)	22 (35%)
20–40 mg/day	13 (17%)	12 (19%)
Intramuscular glucocorticoids	8 (10%)	3 (5%)
Pulse therapy	10 (13%)	11 (18%)
No glucocorticoids	0 (0%)	0 (0%)
Severe flare		
Weight regimen		
Pulse therapy	78 (80%)	54 (65%)
1 mg/kg/day	18 (18%)	22 (27%)
0.3–0.5 mg/kg/day	2 (2%)	6 (7%)
Fixed regimen		
Pulse therapy	61 (78%)	39 (63%)
40–80 mg/day	12 (15%)	14 (23%)
20–40 mg/day	5 (6%)	9 (15%)
Pulse therapy		
125 mg	6 (3%)	10 (7%)
250 mg	16 (9%)	17 (12%)
500 mg	65 (37%)	38 (27%)
750 mg	23 (13%)	12 (8%)
1000 mg	49 (28%)	30 (21%)
No pulses	16 (9%)	33 (23%)
Other	1 (0.5%)	4 (3%)
N° days for pulses		
1 day	3 (2%)	21 (19%)
3 days	119 (74%)	85 (77%)
5 days	25 (16%)	5 (5%)
7 days	13 (8%)	0 (0%)
Taper dose for glucocorticoids		
>12.5 mg/day	0 (0%)	0 (0%)
12.5 mg/day	1 (0.6%)	0 (0%)
10 mg/day	18 (10%)	10 (7%)
7.5 mg/day	28 (16%)	18 (12.5%)
6 mg/day	18 (10%)	17 (12%)
5 mg/day	88 (50%)	68 (47%)
0 mg/day	23 (13%)	31 (22%)
Determining factors for withdrawing glucocorticoids		
Organ involvement	78 (44%)	73 (51%)
Disease activity	114 (65%)	96 (67%)
Time since latest flare	63 (36%)	36 (25%)

moderate flares. The most common dose was 0.10 mg/kg/day or 5–10 mg/day in mild flares, and 0.25–0.3 mg/kg/day or 15–20 mg/day in moderate flares. In severe flares, pulse therapy was used more often by SE physicians (79% vs 65%, p=0.01). The commonest dose was 500 mg/day for both groups over 3 days. SE physicians more frequently prescribed pulse doses >500 mg/day (41% vs 29%, p=0.02), and pulses for >3 days (24% vs 5%, p<0.001).

The most frequently reported target dose for tapering steroids was ≤5mg/day in both groups, however LE physicians targeted 0 mg/day more frequently (22% vs 13%, p=0.04). Steroid withdrawal >12 months after achieving remission/LLDAS was preferred by both groups.

Both groups agreed that current disease activity, and type of organ involvement, were the main deciding factors for selecting steroid dose. LE physicians rated comorbidities as their third key driver (39%), whereas SE physicians ranked the course of the disease (44%). There was agreement that infection, cushingoid features, and osteoporosis were the most influencing factors for withdrawing steroids.

Conclusions The years of experience influence the use of glucocorticoid therapy in severe flare management, tapering protocols, and steroid withdrawal. These differences underscore the need for wide-reaching dissemination and implementation strategies to ensure the adoption of evidence-based care practices across all levels of clinical experience.

04 CLINICAL CHARACTERISTICS OF PATIENTS WITH HIGH SLE-SPECIFIC AND HIGH MULTITRAIT POLYGENIC RISK – AN INVESTIGATION OF SLE RISK LOCI

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Objective Some genome-wide significant SLE risk loci associate with SLE development only while other associate with other diseases, such as type 1 diabetes (T1DM) and rheumatoid arthritis (RA). Our objective: to investigate what clinical phenotype associate with high polygenic scores (PRSs) for SLE-specific and multitrait-associated SLE loci.

Methods Patients with SLE (ACR-97 or SLICC-12, n=1498) and healthy controls (n=1947) were genotyped using Illumina's Global Screening Array. SLE-associated single nucleotide variants (SNVs) (European ancestry) at GWAS significance ($p<5\times10–8$) were identified through the GWAS catalog. After filtering 112 SNVs were identified. SNVs were considered multitrait if associated with ≥1 additional disease. Two PRSs were constructed; one including SLE specific SNVs (n=79) and one including multitrait SNVs (n=33). Groups were compared using logistic regression, adjusting for age and sex. 50% of patients with the highest SLE-specific PRS were selected and from them the 50% with the lowest multitrait PRS were selected. This group (highSLE-lowMultitrait, 25% of total) was then compared with the other patients (75% of total). The same method was used for the highMultitrait-lowSLE group.

Results Both PRSs were higher in patients in comparison with healthy controls, $p<2\times10–6$. Besides SLE, the most common diseases associated with the multitrait SNVs were RA

(SNV=10), T1DM (SNV=8), multiple sclerosis and ulcerative colitis (SNV=6).

The highSLE-lowMultitrait group had higher prevalence of malar rash (OR 1.28(1.00–1.66), p=0.04), neurologic manifestations (OR 1.44(1.10–2.08), p=0.048), thrombocytopenia (OR 1.47(1.06–2.04), p=0.022), anti-Sm antibodies (OR 1.80 (1.12–2.80), p=0.009), low complement (OR 1.70(1.25–2.30), p <0.001) and lower prevalence of hemolytic anemia (OR 0.55(0.32–0.97), p=0.038) compared with the other group.

The highMultitrait-lowSLE group had higher prevalence of anti-SSA (OR 1.49 (1.14–1.94), p= 0.003) and anti-SSB antibodies (OR 1.79 (1.34–2.39), p <0.001) and lower prevalence of discoid rash (OR 0.72(0.52–1.0), p=0.038) compared with the other group.

Conclusions Comparative analysis of multitrait and SLE-specific SNVs shed light on SLE heterogeneity. Leveraging data for shared genetic associations can be important for determining the genetic background influencing SLE subphenotypes, but also common disease manifestations among autoimmune diseases.

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05 EXPLORING THE IMPACT OF GENOME-WIDE DNA METHYLATION ALTERATIONS ON CHROMOSOME X INACTIVATION AND FEMALE LUPUS

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Objective Lupus, an autoimmune disease primarily affecting women, is influenced by genetics and the environment. Recent research suggests that epigenetic changes play a role in connecting these factors. In females, a process called X chromosome inactivation (XCI) helps balance X chromosome dosage. However, some X-linked genes escape this process, which is associated with aging and immune-related conditions. This study proposes that DNA methylation changes on the X chromosome may disrupt XCI control, leading to lupus in women by affecting the regulation of immune genes and accelerating aging.

Methods We used DNAm data obtained from Illumina EPIC and 450K arrays on 310 SLE and 358 CTRLS. Firstly, we ran epigenome-wide association studies separately on females (N=556) and males (N= 112) to identify lupus associated DNAm differential positions on chrX (lupus chrX-DMPs). Secondly, we estimated epigenetic age acceleration using machine-learning algorithms such as Horvath, Hannum, and Levine's epigenetic clocks and studied their associations with DNAm. Finally, we ran trans methylation quantitative methylation loci mapping to identify genetic variants influencing lupus DNAm at lupus chrX-DMP.

Results Our preliminary results show vast alteration of chrX DNAm in lupus females (N=298 DMPs at FDR < 5%), many of them were not present in men (P > 0.05) and were enriched in genes known to escape XCI (Chi-square, P = 5x10E-5). Some of the greatest DNAm changes were observed in relevant genes such as BCOR, AP1S2 and IQSEC2. Although we discovered fewer alterations in males, DNAm differences were greater between cases and controls, probably due to men only carrying one chromosome X. Interestingly, a high proportion of female lupus chrX DMPs do also show strong associations with epigenetic age acceleration measurements and a strong autosomic genetic control.

Conclusion Most EWAS ignore chrX DNAm changes between sexes, leaving the genetic and epigenetic factors of diseases like lupus in women unexplored. Our findings show that chrX epigenetic alterations contribute to aging and female lupus by impacting X chromosome inactivation and immune-related gene dysregulation.

06 EPIDEMIOLOGY OF MODERATE-TO-SEVERE SLE IN SWEDEN

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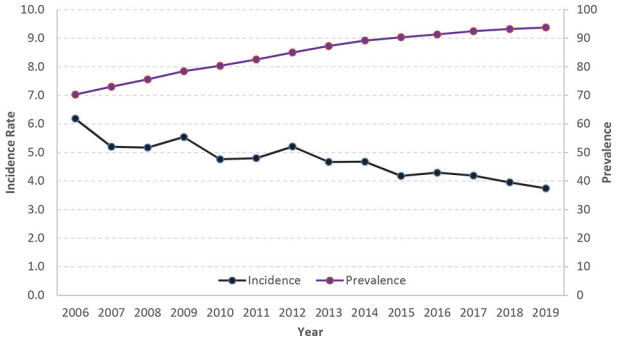
Objective To estimate the prevalence and incidence of SLE in Sweden using a recent patient cohort, and to estimate the proportion and survival of patients with moderate-to-severe disease defined from register data.

Methods This observational cohort study utilized data from national registries. Adult patients were included if they had at least two secondary care visits with a primary diagnosis of SLE from 1 July 2005 to 31 December 2020.

Incident patients were defined as those with no prior visits for SLE in at least the previous 4 years. Disease severity was defined using an algorithm based on previous studies.[1 2] Overall survival was defined for incident patients from date of first SLE visit (presumed diagnosis date) until death, stratified by severity in the year after diagnosis.

Results In total, 10,186 patients were identified, of which 5,076 were diagnosed after 2006. Prevalence increased from 2006 to 2019. The estimated point prevalence of adult SLE was 93.8 per 100,000 on 31 December 2019, and the estimated average incidence rate between 2015 and 2019 was 4.1



Abstract 06 Figure 1 Incidence and prevalence of SLE (per 100 000)