(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

[1]Olivia Castellini-Pérez*, [1,2]Elena Povedano-Espejo*, [1,3]Guillermo Barturen, [1,4]Abir Azri, [1]Ruth Dominguez, [1]Marta E Alarcón-Riquelme*, [1,3]Elena Carnero-Montoro*. *Shared first authors, ** Shared last senior authors; [1]Pfizer – University of Granada – Andalusian Government Center for Genomics and Oncological Research (GENYO), Granada, Spain; [2]Spanish National Research Council (CSIC), Institute of Economy, Geography and Demography, Madrid (IEGD), Madrid, Spain; [3]University of Granada (UGR), Granada, Spain; [4]Research unit of Genomics, Biotechnology and Antiviral Strategies, Higher institute of biotechnology of Monastir, Tunisia

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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

[1]Martina Frodlund, [2]Dag Leonard, [3]Thomas Haugli-Stephens, [4]Lauren Remkus, [5]Daniel Eek, [6]Fabian Söderdahl, [7]Andreas Jönsen. [1]Dept. of Biomedical and Clinical Sciences, Division of Inflammation and Infection/Rheumatology, Linköping University, Linköping, Sweden; [2]Dept. of Medical Sciences, Rheumatology, Uppsala University, Uppsala, Sweden; [3]AstraZeneca AS, Oslo, Norway; [4]AstraZeneca A/S, Copenhagen, Denmark; [5]AstraZeneca AB, Södertälje, Sweden; [6]Statisticon AB, Uppsala, Sweden; [7]Dept. of Clinical Sciences, Section of Rheumatology, Lund University, Skåne University Hospital, Lund, Sweden

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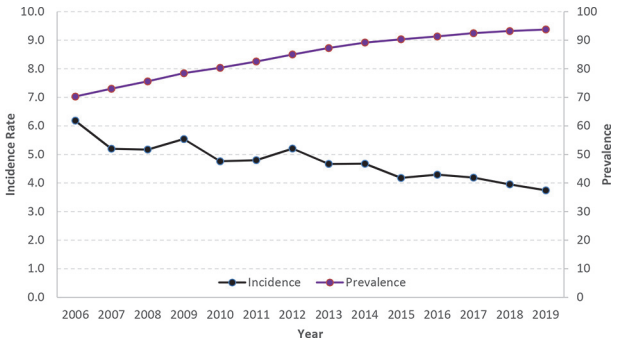
Objective To estimate the prevalence and incidence of SLE in Sweden using a recent patient cohort, and to estimate the proportion and survival of patients with moderate-to-severe disease defined from register data.

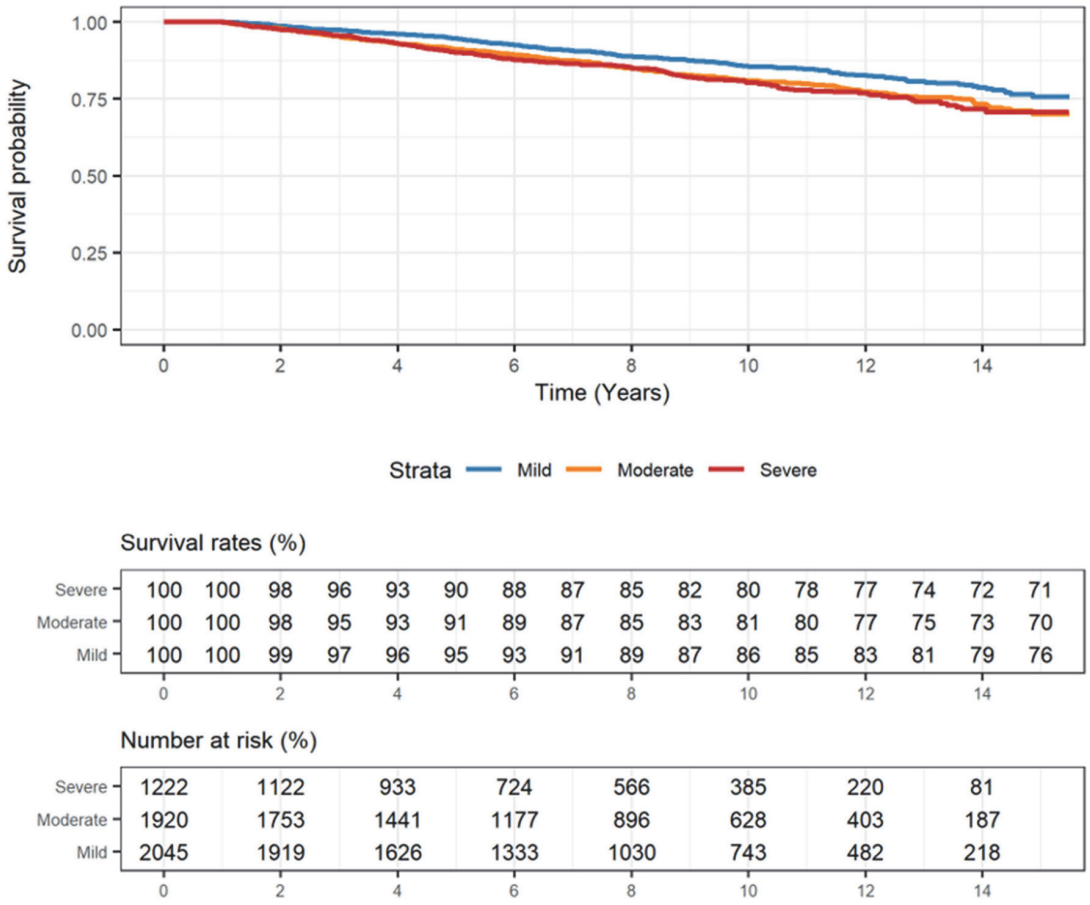
Methods This observational cohort study utilized data from national registries. Adult patients were included if they had at least two secondary care visits with a primary diagnosis of SLE from 1 July 2005 to 31 December 2020.

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)



Abstract O6 Figure 2 Kaplan-Meier for mortality by disease severity

per 100,000 (figure 1). Of incident patients (mean age 49.9, 85% females), 61% had a clinical presentation of moderate-to-severe SLE at some point during the year following diagnosis, however patients can transition between severity states over time. The proportion of patients with moderate-to-severe disease stabilised at around 45% by 4 years after diagnosis until the end of follow-up. Compared to mild SLE patients, moderate-to-severe patients had poorer survival. After 10 years, patients with severe SLE in the year following diagnosis had an 80% survival probability compared to 86% for those with mild SLE (HR 1.49, P<0.001). Patients with moderate SLE had an 81% survival probability (HR vs. mild 1.42, P<0.001) (figure 2).

Conclusions The estimated incidence and prevalence of SLE in Sweden is consistent with previous studies. This is the first study to evaluate moderate-to-severe SLE in Sweden from registers. Previous research has shown that survival in SLE is poorer than for controls, and we show that survival is poorer in patients presenting with moderate-to-severe disease than in mild disease, highlighting the importance of improving care for this patient group.

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O7 HIGH INCIDENCE OF BOTH SPONTANEOUS AND INDICATED PRETERM BIRTH IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW AND META-ANALYSIS

[1]Birgit Blomjous, [2]Carolien Abheiden, [3]Ciska Slaager, [1]Anadeijda Landman, [4]Johannes Ket, [5]Jane Salmon, [6]Jill Buyon, [7]Martijn Heymans, [2]Johanna de Vries, [1]Irene Bultink, [2]Marjon de Boer. *[1]Dept. of Rheumatology and Clinical Immunology, Amsterdam Rheumatology and immunology Center, Amsterdam institute for Infection and Immunity, Amsterdam University Medical Center, Amsterdam, The Netherlands; [2]Dept. of Obstetrics and Gynecology, Amsterdam Reproduction and Development research institute, Amsterdam University Medical Center, Amsterdam, The Netherlands; [3]Dept. of Gynecology, Erasmus University Medical Center, Rotterdam, The Netherlands; [4]Medical Library, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands; [5]Hospital for Special Surgery and Weill Cornell Medical College, New York, USA; [6]New York University Grossman School of Medicine, New York, USA; [7]Dept. of Epidemiology and Data Science, Amsterdam Public Health research institute, Amsterdam University Medical Center, Amsterdam, The Netherlands*

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Objective Preterm birth (PTB) is a frequent complication of pregnancy in women with systemic lupus erythematosus (SLE). The high indicated PTB rate due to hypertensive disorders of pregnancy and/or fetal growth restriction in women with SLE is well known. Preventive measures are taken and screening for early detection are performed, but the risk of spontaneous PTB is less well recognized. The objective of this study is to determine the rates of both spontaneous and indicated PTB in pregnancies of women with SLE.

Methods A systematic literature search using Pubmed, Embase, Web of Science and Google Scholar was performed in June