event, from being event-free to experiencing death, and from experiencing an adverse renal event to experiencing death.

Results There were 38 deaths in a cohort of 615 patients with the mean follow-up time of 14.4 person years. The all-cause mortality rate was 3.36 per 1000 person-years. The rates for end- stage kidney disease (ESKD) requiring chronic dialysis and renal transplant were 3.87 and 2.43 per 1000 person-years, respectively. The rate for any type of cardiovascular event and cancer were 6.49 and 3.47 per 1000 person-years, respectively. The multi-state Cox model indicated that the Black ethnic group (HR, 3.58; 95% CI, 1.6-8.0) and the presence of renal involvement at baseline (HR, 2.19; 95% CI, 1.2-4.1) were significantly associated with higher rates of transition from event-free to adverse renal event. Additionally, the Black ethnic group (HR, 5.45; 95% CI, 1.6-18.8) was significantly associated with higher rates of transition from event-free to death.

Abstract 602 Table 2 Descriptive summary of major outcomes of cSLE

Outcomes	N (%)	Mean Years of Follow-Up to Event (SD)	Event Rate (per 1000 person-years)
Cause of Death			
All	38	14.41 (8.96)	3.36
SLE and Complications	14	11.53 (8.67)	1.24
Infection or Malignancy	10	14.45 (9.49)	0.89
Other or Unknown	14	17.27 (8.54)	1.24
Renal			
ESKD	43	13.26 (8.01)	3.87
Renal Transplant	27	17.86 (7.89)	2.43
Cardiovascular			
Any	69	9.42 (9.10)	6.49
Cerebrovascular Disease	36	9.81 (8.44)	3.39
Cancer	39	17.65 (8.22)	3.47

ESKD, End-Stage Kidney Disease requiring chronic dialysis; SD, standard deviation

None of the variables were significantly associated with higher rates of transition from adverse renal event to death.

Conclusion In this large Canadian multi-ethnic long-term cSLE cohort, ethnicity was associated with adverse outcomes including adverse renal events and death. Further analyses will help inform risk for adverse outcomes to improve clinical care for the highest risk patients.

603 REMISSION AND LOW DISEASE ACTIVITY ARE ASSOCIATED WITH LOWER HEALTH CARE COSTS IN AN INTERNATIONAL INCEPTION COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose Remission and low disease activity (LDA) are associated with decreased flares, damage, and mortality. However, little is known about the impact of disease activity

states (DAS) on health care costs. We determined the independent impact of different definitions of remission and LDA on direct and indirect costs (DC, IC) in a multicentre, multiethnic inception cohort.

Methods Patients fulfilling revised ACR classification criteria for SLE from 33 centres in 11 countries were enrolled within 15 months of diagnosis and assessed annually. Patients with ≥2 annual assessments were included. Five mutually independent DAS were defined:

Abstract 603 Table 1 Patient Characteristics

Panel A. At baseline (Number of patients = 1631)

Characteristic	Number of Patients (%) or Mean (SD)
Female sex	1446 (88.7%)
Age at diagnosis, years	34.5 (13.3)
Ethnicity	
White, North American	509 (31.2%)
White, other	289 (17.7%)
Black	268 (16.4%)
Hispanic	258 (15.8%)
Asian	250 (15.3%)
Other	57 (3.5%)
Disease duration at baseline, months	5.6 (4.2)

Panel B. Follow-up (Number of assessments = 12,281)

Disease Activity State	Number of Annual Assessments, (%)	Number of Patients,* (%)
Remission Off-Treatment	2566 (20.8%)	612 (37.5%)
Remission On-Treatment	2421 (19.7%)	771 (47.3%)
LDA-TC	556 (4.5%)	277 (17.0%)
mLLDAS	680 (5.5%)	430 (26.4%)
Active	6058 (49.3%)	1446 (88.7%)

*The number of patients exceeds 1631 as a single patient may have multiple disease activity states during the study and will contribute assessments to multiple states.
LDA-TC: Low Disease Activity-Toronto Cohort; mLLDAS: Modified Lupus Low Disease Activity State

1) Remission off-treatment: clinical (c) SLEDAI-2K=0, without prednisone or immunosuppressants

2) Remission on-treatment: cSLEDAI-2K=0, prednisone ≤5mg/d and/or maintenance immunosuppressants

3) LDA-Toronto Cohort (TC): cSLEDAI-2K≤2, without prednisone or immunosuppressants

4) Modified Lupus LDA State (mLLDAS): SLEDAI-2K≤4, no activity in major organs/systems, no new disease activity, prednisone ≤7.5mg/d and/or maintenance immunosuppressants

5) Active: all remaining assessments

Antimalarials were permitted in all DAS. At each assessment, patients were stratified into 1 DAS; if >1 definition was fulfilled per assessment, the patient was stratified into the most stringent. The proportion of time patients were in a specific DAS at each assessment since cohort entry was determined.

At each assessment, annual DC and IC were based on health resource use and lost workforce/non-workforce productivity over the preceding year. Resource use was costed using 2021 Canadian prices and lost productivity using Statistics Canada age-and-sex-matched wages.

To examine the association between the proportion of time in a specific DAS at each assessment since cohort entry and annual DC and IC, multivariable random-effects linear regression modelling was used. Potential covariates included age at diagnosis, disease duration, sex, race/ethnicity, education, region, smoking, and alcohol use.

Results 1631 patients (88.7% female, 48.9% White, mean age at diagnosis 34.5) were followed for a mean of 7.7 (SD 4.7) years (table 1, Panel A). Across 12,281 assessments, 49.3% were classified as active (table 1, Panel B). Patients spending <25% vs 75-100% of their time since cohort entry in an active DAS had lower annual DC and IC (DC $4042 vs $9101, difference - $5060, 95%CI -$5983, -$4136; IC $21,922 vs $32,049, difference -$10,127, 95% -$16,754, -$3499) (table 2, Panel B&C).

In multivariable models, remission and LDA (per 25% increase in time spent in specified DAS vs active) were associated with lower annual DC and IC: remission off-treatment (DC -$1296, 95%CI -$1800, -$792; IC -$3353, 95%CI -$5382, -$1323), remission on-treatment (DC -$987, 95%CI -

Abstract 603 Table 2 Annual Direct and Indirect Costs Stratified by Proportion of Time since Cohort Entry in Specified Disease Activity States

% of time since cohort entry in specified state	Remission Off- Treatment	Remission On- Treatment	LDA - TC	mLLDAS	Active
Panel A. Distribution of Assessments based on Percentage of Time in Specified Disease Activity States, n (%)					
< 25%	9215 (75.0)	9381 (76.4)	11355 (92.5)	11409 (92.9)	2701 (22.0)
25 - <50%	1184 (9.6)	1707 (13.9)	535 (4.4)	677 (5.5)	2286 (18.6)
50 - <75%	943 (7.7)	918 (7.5)	230 (1.9)	135 (1.1)	2248 (18.3)
75 - 100%	939 (7.6)	275 (2.2)	161 (1.3)	60 (0.5)	5046 (41.1)
Panel B. Annual Direct Costs (in 2021 Canadian dollars), mean (95% CI)					
< 25%	7812 (7275, 8348)	7055 (6578, 7532)	7085 (6644, 7526)	6996 (6555, 7437)	4042 (3540, 4543)
25 - <50%	5131 (4328, 5934)	7033 (5794, 8272)	4604 (3327, 5880)	4997 (4237, 5757)	4614 (4157, 5070)
50 - <75%	3650 (3016, 4284)	5026 (4289, 5764)	3328 (1967, 4688)	6357 (4093, 8621)	7633 (6503, 8763)
75 - 100%	3183 (2511, 3855)	5485 (4150, 6820)	3789 (1953, 5626)	4012 (2030, 5995)	9101 (8303, 9899)
Panel C. Annual Indirect Costs (in 2021 Canadian dollars), mean (95%CI)					
< 25%	29667 (25531, 33803)	29207 (25094, 33319)	29125 (25364, 32885)	29168 (25387, 32950)	21922 (16803, 27041)
25 - <50%	29074 (24217, 33931)	29137 (25731, 32544)	25792 (19158, 32425)	23965 (18644, 29285)	27122 (23233, 31010)
50 - <75%	26138 (21812, 30463)	25453 (20486, 30420)	22276 (15112, 29441)	18895 (8347, 29443)	30843 (27061, 34625)
75 - 100%	21100 (13680, 28519)	18807 (9964, 27650)	16344 (4057, 28630)	11821 (-11681, 35322)	32049 (26573, 37525)

LDA-TC: Low Disease Activity-Toronto Cohort; mLLDAS: Modified Lupus Low Disease Activity State

Abstract 603 Table 3 Multivariable Models of the Impact of Disease Activity States Since Cohort Entry on Annual Direct and Indirect Costs

Model A		
	Annual Direct Costs, coefficient (95%CI)	**Annual Indirect Costs, coefficient (95%CI)**
Active state*	1161 (743, 1579)	3390 (1424, 5356)
Disease duration	333 (249, 417)	1346 (652, 2040)
White race/ethnicity	-2049 (-3356, -742)	-
Residing outside North America	-	-13657 (-19202, -8112)
Model B		
Remission Off-Treatment**	-1296 (-1800, -792)	-3353 (-5382, -1323)
Remission On-Treatment	-987 (-1550, -424)	-3508 (-5761, -1256)
LDA-TC	-1037 (-1853, -222)	-3229 (-5681, -778)
mLLDAS	-1307 (-2194, -420)	-3822 (-6309, -1334)
Disease duration	330 (245, 415)	1353 (662, 2044)
White race/ethnicity	-1996 (-3319, -674)	-
Residing outside North America	-	-13569 (-19040, -8097)
Difference between disease activity state coefficients (95%CI)		
Remission On vs Remission Off-Treatment	309 (-304, 921)	-156 (-1680, 1369)
LDA-TC vs Remission Off-Treatment	259 (-660, 1117)	123 (-1812, 2058)
LDA-TC vs Remission On-Treatment	-50 (-924, 824)	279 (-1400, 1959)
mLLDAS vs Remission Off-Treatment	-11 (-902, 881)	-469 (-2259, 1321)
mLLDAS vs Remission On-Treatment	-320 (-1255, 616)	-313 (-2741, 2115)
mLLDAS vs LDA-TC	-270 (-1365, 826)	-592 (-3056, 1872)

*Reference group for active state in Model A is all other disease activity states
** Reference group for all disease activity states in Model B is active state
LDA-TC: Low disease activity – Toronto Cohort; mLLDAS: modified Lupus Low Disease Activity State

$1550, -$424; IC -$3508, 95%CI -$5761, -$1256), LDA-TC (DC -$1037, 95%CI -$1853, -$222; IC -$3229, 95%CI -$5681, -$778) and mLLDAS (DC -$1307, 95%CI -$2194, -$420; IC - $3822, 95%CI -$6309, $-1334) (table 3, Model B). There were no differences in costs between remission and LDA.

Conclusions Remission and LDA are associated with lower costs, likely mediated through the known association of these DAS with more favourable clinical outcomes.

604 PREDICTING ADVERSE PREGNANCY OUTCOMES IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: EXTERNAL VALIDATION OF THE PROMISSE MODEL USING MULTIPLE INDEPENDENT COHORTS

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Background Nearly 20% of pregnancies in patients with Systemic lupus erythematosus (SLE) result in an adverse pregnancy outcome (APO); early identification of women with SLE who are at high risk of APO is vital. We previously examined several regression and machine learning (ML) predictive models for APO using data from the PROMISSE Study, a large multi-center, multi-ethnic/racial study of APO in women with mild/moderate SLE and/or aPL. Penalized logistic regression (LASSO), as well as several "black box" ML algorithms (Random Forest, Support Vector Machine, and Super Learner) each achieved good internal cross-validated performance, with area under the receiver operating curve (AUC) of 0.77-0.78. The goal of this study was to externally validate the performance of these promising APO risk models using three independent, external cohorts.

Methods The PROMISSE data set used to develop the initial APO prediction models consisted of N=385 pregnancies, 71 APO events (18.4%), and 32 known or potential APO risk factors that are routinely measured in clinical practice early in pregnancy. APO was defined as preterm delivery due to placental insufficiency or preeclampsia, fetal or neonatal death, or fetal growth restriction. Three independent prospective cohorts were provided by a team of international investigators with expertise in SLE pregnancy (Bronx, NY: N=96; NYC, NY: N=62; Pisa, Italy: N=152). Patient demographics were summarized for each cohort and missing data handled using multiple imputation with chained equations. Using the APO risk models developed with the PROMISSE data, we computed for each cohort: 1) the standard deviation (SD) of predicted risk scores to summarize the degree of heterogeneity in patient characteristics and 2) the area under the receiver operating curve (AUC) to summarize the ability of each model to discriminate patients with and without APO.

Results The three external cohorts and the PROMISSE development cohort showed distributional differences in previously identified APO risk factors (table 1). Non-Hispanic White comprised 49.3% of the PROMISSE, compared to 98.7% in Pisa, 27.4% in NYC, and 0% in the Bronx. LAC positivity varied from 8.1% in PROMISSE to 22.6% in the NYC cohort, while PGA > 1 varied from 10.6% in the development cohort to 4.4% in the Bronx, NY cohort. Current antihypertensive use was 8.6% in PROMISSE, higher in the Bronx cohort (12.6%), and lower in the NYC (4.8%) and Pisa (5.3%) cohorts. APO rates were the same in PROMISSE and Pisa (18.4%) and higher in the Bronx (24%) and NYC cohorts (25.8%). Prediction risk score SD indicated similar levels of heterogeneity within each external cohort compared to the PROMISSE cohort. Model performance in external validation cohorts varied depending on the algorithm used. As expected, AUCs in the external cohorts were generally lower than cross-validated internal estimates, but still indicated satisfactory performance of the different models with the independent data sets (table 2). Super Learner, the highest performing algorithm in PROMISSE, performed well across all three external cohorts, with a minimum AUC of 0.63 in the NYC cohort and a maximum of 0.71 in the Pisa cohort (table 2). LASSO also maintained consistent external performance with minimum AUC of 0.60 and maximum of 0.66. Overall, performance was highest using data from the Pisa cohort, which was the largest and most complete of the three external validation data sets.

Conclusions Penalized regression and ML approaches using variables obtained early in pregnancy show potential in discriminating pregnancies with high APO risk from those pregnancies with lower risk. This study provides confirmation of the geographic transportability of the best performing algorithms developed with PROMISSE. While Super Learner