HHS Public Access

Author manuscript

Arthritis Care Res (Hoboken). Author manuscript; available in PMC 2021 April 01.

Published in final edited form as:

Arthritis Care Res (Hoboken). 2020 April ; 72(4): 525–533. doi:10.1002/acr.23878.

Relationships Between Adverse Childhood Experiences and Health Status in Systemic Lupus Erythematosus

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Abstract

Purpose—Adverse childhood experiences (ACEs) are associated with poor adult health and immune dysregulation. The impact of ACEs on patients with autoimmune disease is unknown. We

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Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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compared the prevalence of ACEs in Systemic Lupus Erythematosus (SLE) patients to population-based survey estimate and investigated relationships between ACEs and SLE outcomes.

Methods—Data derive from the California Lupus Epidemiology Study (CLUES), a sample of adult SLE patients. Participants completed a 10-item ACE questionnaire covering 3 domains (abuse, neglect, household challenges). We estimated ACEs prevalence in 269 CLUES participants compared to 2015 California Behavioral Risk Factor Surveillance System (BRFSS) geographically matched respondents, standardized (age, sex, race/ethnicity) to CLUES participant characteristics. We examined associations for patient-reported and physician-assessed health status measures with overall ACE levels and domains using multivariable linear regression, controlling for socio-demographics, nephritis, and childhood onset SLE.

Results—Though specific domains varied, overall ACE levels were similar for CLUES and BRFSS respondents. Among SLE patients, 63.2% had ≥1 ACE and 19.3% had ≥4. ACEs were more prevalent in those who were older, women, Latino or African American, without college degrees, and with lupus nephritis. In adjusted models, higher ACE levels and ACE domains were associated with worse patient-reported SLE activity, depression, and health status, but were not significantly associated with physician-assessed SLE activity, damage, or severity.

Conclusions—Given the association between ACE levels and important patient-reported outcomes in SLE, our study reinforces the need for prevention of ACEs in childhood and for clinical interventions to promote resilience among adults who have experienced ACEs.

Keywords

Adverse Childhood Experiences; Systemic Lupus Erythematosus; Patient Reported Outcomes

Introduction

Systemic lupus erythematosus (SLE) is a complex chronic, multisystem autoimmune disease. Development of SLE is influenced by genetic susceptibility as well as environmental interactions (1–3). Stress has been implicated as a potential trigger of disease onset and flares (4–7) as well as chronic disability (8). Exploring how a history of major stress, such as childhood abuse and neglect, impacts outcomes may inform the association between stress and SLE.

Accelerated inflammation, immune dysregulation, and the onset of rheumatic diseases have been described in the context of adverse life events (7,9–14). One form of such events is adverse childhood experiences (ACEs) which encompass traumas such as abuse, neglect, and household challenges. The seminal ACEs study of adults in a large health management organization (Kaiser Permanente) found that ACEs were common (15), with a dose response for number of ACEs and negative adult health outcomes (16). Population-based studies show that a large percentage of adults experienced ACEs. For example, in a large prevalence study of ACEs in 2018 from the 2011–2014 Behavioral Risk Factor Surveillance Surveys (BRFSS)—state-level population-based surveys that included an ACE questionnaire in 23 states—more than 60% of respondents recalled at least one ACE and >15% more than four, prior to age 18 (17).

For individuals with autoimmune disease, the prevalence of ACEs and the association with disease status are not known. We aimed to determine ACE prevalence among patients with known SLE in comparison with population-based participants and to examine the association between ACEs with patient-reported and physician-assessed health status.

Patients and Methods

Data Source

This is a cross-sectional analysis of data derived from the California Lupus Epidemiology Study (CLUES), a prospective longitudinal sample of individuals with SLE. Briefly, starting in 2015, participants for CLUES were recruited through the California Lupus Surveillance Project, which used outpatient, hospital, and laboratory records to identify all SLE patients residing in San Francisco County from 2007–2009 (18). Additional participants in the geographic region were identified through academic and community rheumatology clinics, and from earlier studies of genetic risk factors for SLE outcomes (19,20). SLE diagnoses were confirmed by study physicians based on (a) ≥4 of the 11 American College of Rheumatology (ACR) revised criteria for the classification of SLE (21,22), (b) meeting 3 of the 11 ACR criteria with a documented rheumatologist's diagnosis of SLE, or (c) a confirmed diagnosis of lupus nephritis. This combined definition of SLE has been used in prior population-based studies (20).

Study procedures included an in-person research clinic visit, which comprised collection and review of medical records prior to the visit, a history and physical examination conducted by a physician specializing in lupus, collection of clinical labs and stored biospecimens, and a structured interview with questionnaires administered by a research assistant. Research clinic visits and interviews were conducted in English, Spanish, Cantonese, or Mandarin. A total of 332 SLE patients completed the baseline in-person CLUES study visit.

Variables

Identification of ACEs—To quantify the lasting effects of childhood trauma, an ACE questionnaire was introduced in 1998 (15). Multiple iterations of ACE questionnaires have been used since that time; one version was validated for use by the BRFSS (23).

CLUES: Participants completed a 10-item ACE questionnaire covering three domains: household challenges (five items), neglect (two items), and abuse (three items). The questionnaire was completed on paper in English or Spanish. For each ACE question, a response of "yes" was equivalent to a score of 1; a response of "no" or a skipped response was treated as a score of zero. Thus, overall ACE scores range from 0 – 10 with higher scores reflecting greater ACE exposure. The overall ACE score, the sum of the responses to ACE questions, was categorized into 4 groups (0, 1, 2–3, and ≥4) to derive the ACE level. Scores ≥4 denote severe exposure to ACEs (16). Throughout the text, 'overall ACE score' refers to the sum of individual ACE question items (0 – 10); 'ACE level' reflects one of 4 categorized ACE scores (0, 1, 2–3 or ≥4); 'ACE domain' describes question types of household challenges, neglect, and abuse.

A total of 269 completed the ACE questionnaire resulting in an 81% (269/332) response rate. Chinese speakers (n=23) were excluded because the ACE questionnaire was offered in only English or Spanish, 37 did not complete the ACE questionnaire and 3 were excluded for missing patient-reported outcomes.

BRFSS: Since 2009, the BRFSS survey includes an optional module in which states can administer items of the ACE questionnaire. We analyzed the 2015 California BRFSS survey data; 2015 was selected to match the year of CLUES sample initiation. The BRFSS ACE questionnaire, administered in English by telephone, differed from the CLUES version in several ways. For example, questions about neglect were absent from the 2015 California BRFSS ACE questionnaire. The CLUES and BRFSS ACE questions are in Supplemental Table 1.

Patient-Reported Outcomes—SLE disease activity was measured with the Systemic Lupus Activity Questionnaire (SLAQ) (24,25), a validated measure of SLE disease activity (range 0–44). The Brief Index of Lupus Damage (BILD) was used to estimate organ damage (26). The BILD is a proxy for the physician-assessed Systemic Lupus International Cooperating Clinics/American College of Rheumatology Damage Index (SDI) (27), and consists of 28 items capturing information on 26 SDI items including determinations of important comorbid conditions such as diabetes as well as cardiovascular disease and events (range 0 – 6). Depressive symptoms were measured with the eight-item version of the Patient Health Questionnaire (PHQ; range 0 – 24) (28). PHQ items correspond to the DSM-IV diagnostic criteria for depression. We assessed physical function with the National Institutes of Health Patient-Reported Outcomes Measurement Information System Physical Function measure (PROMIS-PF) (29). PROMIS-PF is a 10-item subscale (range 14 – 62) with a population mean of 50 and standard deviation of 10 (30). The Physical Component Score (PCS), calculated from the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), was examined as a composite generic measure of physical health status with a population mean of 50 and a standard deviation of 10 (31). For measures of disease activity (SLAQ), damage (BILD), and depression (PHQ), higher scores reflected worse outcomes. For physical function (PROMIS-PF) and generic health status (SF-36 PCS), higher scores reflected better outcomes.

Physician-Assessed Status—The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) (32) is a frequently used measure of disease activity that ranges from 0 – 105. The Systemic Lupus Collaborating Clinics/American College of Rheumatology Damage Index (SDI) (27) is a measure of organ damage over time (range 0 – 47). The Lupus Severity Index (LSI) (33) is a validated tool that utilizes ACR criteria and sub-criteria for SLE and predicts morbidity and mortality (range 0 – 100). All physician-assessed outcomes were collected by study rheumatologists during the in-person study visit. For each instrument, higher scores represent poorer outcomes.

Covariates—We considered potential correlates of SLE outcomes and selected the following baseline characteristics (i.e., collected at the initial interview): age, sex, race/ethnicity (Latino of any race, Non-Hispanic White, Non-Hispanic African American, Asian/

Pacific Islander, Other), pediatric onset disease prior to age 18 (yes/no), lupus nephritis (yes/no), and educational attainment (high school or less, some college/associate degree, college graduate).

Statistical Analyses

Comparison with the geographically matched population—To increase comparability of ACE prevalence estimates from the BRFSS and the CLUES sample, we standardized BRFSS estimates to the age- (18–37, 38–53, >54 years), sex-, and racial/ethnic distribution to 269 CLUES participants. The BRFSS sample was also limited to the California counties represented in the CLUES sample (the San Francisco Bay Area), resulting in a sample size of 6,107 BRFSS respondents. Differences in the item and domain responses were calculated using a 2-sample t-test, assuming independence of the BRFSS and CLUES samples. For these comparisons, we excluded the neglect domain items from calculation of CLUES patients' ACE scores because neglect data were not collected in BRFSS; scores for both samples ranged from 0–8. In all analyses of BRFSS data, we accounted for its complex design (34).

Analysis of ACE among CLUES Sample—Descriptive statistics were calculated for the total sample and by overall ACE level categories. Differences in group characteristics were evaluated using linear contrast trend tests for continuous (35) and chi-square tests for categorical variables. We developed unadjusted and multivariable linear regression models of patient-reported and physician-assessed measures to examine differences in these outcomes by overall ACE level (0, 1, 2–3, ≥4). Adjustment variables were age, sex, race/ethnicity, pediatric onset disease, and educational attainment. Next, we looked at differences in the patient-reported and physician-assessed measures by ACE domain through separate models for each domain where respondents were categorized into the following 3 groups: ≥1 items in the domain, 0 items in the domain but ≥1 items in other domains, and 0 ACEs (i.e., no items in any domain; referent group). We created a referent group comprising those who were not exposed to any ACEs to isolate the specific effects of the domain of interest. The ACE domain models were run with and without adjustment for the variables listed above. All statistical tests were conducted at $\alpha = 0.05$. Analyses were performed with Stata (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

Results

Estimates for overall ACE levels and ACE domains from CLUES and BRFSS are shown in Table 1. The distribution of overall ACE levels was similar for the two study populations (p=0.42) with severe ACE exposure (i.e., ACEs ≥ 4) of 15.2% in CLUES and 17.2% in BRFSS). In this table, the neglect domain was excluded from the overall CLUES ACE levels, to be consistent with the BRFSS questionnaire. For analysis of ACEs by domain, the prevalence of household challenges overall was similar for the CLUES and BRFSS populations (53.0% vs. 49.5%, p=0.32). However, there was a higher prevalence of abuse in the BRFSS population than in CLUES patients (45.2% vs 34.2%, p<0.001). For the specific domain items, there were more reports of emotional abuse (36.5% vs 21.6%, p<0.001) and

domestic violence (21.0% vs 10.0%, p<0.001) in BRFSS than CLUES. In contrast, sexual abuse was reported somewhat more frequently by CLUES patients than BRFSS participants (19.0% vs 14.1%, p=0.06). Among the CLUES participants, approximately one-quarter reported neglect, with most of that being emotional neglect (lack of care and support) rather than physical deprivation.

Table 2 shows baseline characteristics among the 269 CLUES participants who completed the ACE questionnaire. Mean age was 45.2 years, 89.6% were women and 16.4% were diagnosed with SLE in childhood, consistent with the epidemiology of SLE. Reflecting the diverse population of the study area, 31.6% were Non-Hispanic White, 29.4% Asian/Pacific Islander, 25.7% Latino, 11.9% Non-Hispanic African American, and 1.5% Other. The median overall ACE score, which includes neglect, was 1, and 19.3% had ≥4 ACEs. Those with ACE scores > 0 were older, more likely to be women, of Hispanic ethnicity or African American race, more likely to have less than a four-year college degree, and more likely to have a history of SLE nephritis than those with ACE scores = 0. Pediatric onset disease was less common among those with ACE scores > 0. There were no differences in ACE scores by disease duration.

Analysis of patient-reported health outcomes by overall ACE level demonstrated a dose-response where patient-reported SLE disease activity, damage, depression were higher, and physical function and health status were lower, with increasing ACE levels. These relationships persisted after adjusting for age, sex, race, childhood onset, and educational attainment (Table 3), although the PROMIS-PF measure of functioning and the BILD score measuring damage were not statistically significant. After multivariable adjustments, for each of the three domains, ACE exposure (household challenges, neglect, abuse) was consistently associated with poor patient-reported outcomes, with all but BILD reaching statistical significance. In contrast with patient-reported outcomes, multivariable adjusted analyses of physician-assessed measures (Table 4) did not show the same trends for ACE level or any of the ACE domains.

Discussion

This is the first study to identify the prevalence of ACEs in persons with SLE and to examine associations between ACEs and health status in a sample with SLE. Analyses suggest that ACEs are common in persons with SLE, and that ACE scores for overall ACE level and all 3 ACE domains were significantly associated with worse patient-reported outcomes (SLAQ, PHQ, SF-36 PCS) in a dose-response pattern. These associations persisted after adjustment for age, sex, race/ethnicity, disease onset <18 years, and educational attainment. Patients who report life stressors often perceive worse SLE symptoms (36,37). Although ACEs were not significantly associated with SLE outcomes deriving from physician assessments, they may play a role in patient perception of disease activity, depression, and overall health status.

In the more than twenty years that the ACE questionnaire has been used in population studies, multiple studies have revealed that having a history of ACE exposures is associated with poor long-term health and impaired quality of life in adulthood (12,16,38). Estimates

from large surveys (Kaiser Permanente and BRFSS in multiple states) conducted from 1998–2014 showed a range in prevalence of ACE exposures; 50.5–63.9% of individuals had ACE scores ≥1 and 6.2–15.8% had ACE scores ≥4. ACE domains such as abuse and household challenges were also frequently documented in these studies (abuse prevalence=10.6–35.0%; household challenge prevalence=3.4–26.9%, respectively) (15–17,39,40). We found that for CLUES and BRFSS participants, overall ACE levels were generally comparable: more than 60% identified at least 1 ACE (60.4 and 65.6%, respectively) and more than 15% indicated ≥4 ACEs (15.0 and 19.6%, respectively). The BRFSS respondents reported significantly more domestic violence, overall abuse, and emotional abuse than the CLUES sample.

The similar prevalence of overall ACE levels and the high prevalence of ACEs for specific domains among BRFSS respondents is inconsistent with prior findings of an association between immune dysregulation and childhood trauma (12). For example, we found a trend toward higher exposure to childhood sexual abuse among the SLE sample than in the population-based participants, though this did not reach statistical significance. There may be several reasons for these results. One possibility is potential selection bias in the CLUES sample as patients with a childhood history of low socioeconomic status and/or more severe disease may be less able to participate in research studies due to social stressors (41); furthermore, the BRFSS is designed to be representative of the civilian, non-institutionalized population for the geographic target area. Survival bias may also be present here if those with more severe ACE exposure were more susceptible to potentially life-threatening SLE manifestations. Thus, those with the most exposure to ACEs and those with the most severe disease may not be represented in the CLUES sample. Finally, recall bias may be differential across the two data sources because the CLUES ACE questions are more specific than the BRFSS questions which may have prompted increased reporting of ACEs among CLUES respondents.

There is mounting evidence that links a history of life stressors with autoimmune disease onset and flares (13,42,43). A recent retrospective cohort of primarily male veterans (Operation Enduring Freedom, Operation Iraqi Freedom, Operation New Dawn Roster) and a prospective trial of women nurses (Nurses' Health Study II) found that individuals with post-traumatic stress disorder (PTSD) had an increased likelihood of a new diagnosis of SLE (Adjusted Rate Ratio=1.65, 95% CI 1.14–2.24, $p<0.008$; Hazard Ratio (HR)=2.94 95% CI 1.19–7.26, $p<0.05$, respectively) (42,43). Trauma exposure, regardless of PTSD status, was strongly associated with incident autoimmune disease (HR=2.83, 95% CI 1.29–6.21, $p<0.01$) (43). Our findings align with these recent associations between stress and SLE in suggesting that ACEs may result in poorer patient-reported outcomes among those with autoimmune disease.

We showed a significant association between high overall ACE score level and poor patient-reported disease activity, depression, and overall health status. Depression across the lifespan has been reported in those with high ACE exposure and SLE diagnosis (44). A previous study found a strong inverse relationship between ACEs and health status in adulthood as measured by the SF-36 (45), that corresponds to findings in this study. Therefore, there may be value for clinicians to regularly screen SLE patients for ACEs,

along with depression, and overall perceived health status, whether they meet the individual early or later in the disease course. There may be particular utility in screening near the time of diagnosis to identify those at higher risk for subsequent poor outcomes.

Greater presence of household challenges, neglect, and abuse were significantly associated with worse patient reported outcomes across all patient-reported measures except SLE damage. These findings support the notion by Dong et al. that ACEs often occur concurrently; i.e., self-report of an ACE in one domain may increase the likelihood that an individual has a history of additional ACEs, possibly in another domain (46). This suggests a parallel concept seen in this study: if a history of ACEs affects one patient-reported outcome measure, multiple measures may in fact be impacted. Therefore, examination of a constellation of patient-reported outcomes permits a more granular understanding of ACEs' effects on SLE patient experience which in turn may enable more tailored strategies for coping and resilience. For example, the strong relationship with ACE levels and current depression, as measured through the PHQ, suggests that those with depression may benefit from learning behavioral coping strategies.

Patient-reported outcome measures have long been recognized as critical to capture the patient experience in parallel with disease management (47), and our data suggest that the ACE questionnaire aligns with health status in SLE patients. However, while we found a strong association of ACE history with patient-reported outcomes, we did not find an association with physician-assessed outcomes. This pattern is consistent with other studies in the SLE literature, whereby quality of life and other patient-reported outcomes often show little relationship to physician-assessed measures of disease activity and damage (48,49).

This disconnect may stem from differences in the way items are explored in physician-assessed versus patient-reported questionnaires. Physician-assessed items focus on quantifying overt physical findings on exam, history, or laboratory results. In contrast, patient-reported outcomes expand on how a disease affects daily life activities like walking, bathing, and work. For example, associations of arthritis and poor sleep, anhedonia, or pain are not measurable by the clinician-assessed SLEDAI but are identified by patient-reported surveys like the SLAQ, SF-36 PCS, and PHQ. Physician-assessments quantify a physical impairment while patient-reported outcomes include the patient's experience of that physical impairment. Therefore, patient-reported measures are more suited to effectively capture ACE impact on overall health in SLE patients than physician-assessed outcomes and should continue to be utilized to understand ACEs in the context of chronic illness.

Strengths of this study include a diverse sample with an array of clinically relevant outcome measures. There are several limitations as well. First, as noted above, our sample may not be representative of patients with the most severe SLE due to either presence of fewer patients with clinically active disease or survival bias. Second, while there is ongoing research to investigate links between ACE and poverty, the CLUES questionnaire did not include measures of childhood socioeconomic status, for example, whether the family received government benefits or parental education levels. However, patient educational attainment was used as a proxy for socioeconomic status that would pre-date disease onset in most individuals; all models of the association between ACEs and disease status controlled for

educational attainment. Third, reporting of ACEs may vary for different reasons. We previously suggested reporting may depend on specificity of ACE questionnaires. On the other hand, there may be overall underreporting of ACEs, due both to reluctance to report childhood traumatic experiences in adulthood (16) as well as to limitations of the ACE questionnaire itself, which excludes such adverse experiences as accidental/injurious trauma, bullying, discrimination, and community-level trauma. Additionally, the ways in which race, ethnicity, and culture play a role in SLE and ACEs reporting are unclear and deserve future dedicated study. Furthermore, it is not possible to rule out additional sources of bias, such as recall bias, in which people with poor health are more likely to report prior negative experiences. We also cannot confirm causal associations between remote ACEs and disease outcomes. However, there is some evidence for a causal association, including the lasting effects of ACEs and the graded associations between ACEs and poor adult health (16).

Conclusion

While the prevalence of adverse childhood experiences varies by domain, and in some domains BRFSS respondents actually reported more ACEs, overall, ACEs are frequently reported both in individuals with SLE and in the population at large. Higher overall ACE score levels and scores in each domain are associated with greater patient-reported SLE activity and damage, higher levels of depressive symptoms, poorer physical function, and worse overall health status. Clinical measures of activity, damage, and severity do not parallel patient-reported trends of cumulative ACEs. Cumulative ACE exposure may be relevant to patient perceptions of SLE activity, depression, and physical function. Although this study exposes relationships between ACEs and patient-reported health outcomes, definitive means to successfully prevent or repair long-term effects of ACEs are less clear. Prevention of ACEs and promotion of safe, stable, nurturing relationships and environments for children are vital (50). This work lends support for ACE prevention during childhood as well as clinical and mental health interventions that focus on resilience in adulthood after a history of ACE has been established.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This work is supported by CDC 5U01DP005120 (Dall'Era, Katz, Trupin, Rush, Li); NIH/NIAMS P30AR070155 (Criswell, Lanata), P60AR053308 (Katz, Lanata, Yelin, Trupin, Rush), 2R01AR056476 (Yelin) T32AR00730439 (DeQuattro); Rheumatology Research Foundation Scientist Development Award 128849A (Lanata), Robert L. Kroc Chair in Rheumatic and Connective Tissue Diseases (Yazdany); Robert Wood Johnson Investigator Health Policy Award (Yelin); Russell/Engleman Medical Research Center for Arthritis (Dall'Era, Yazdany).

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Significance & Innovations

- This study is the first to assess ACE levels in an SLE sample and examine SLE outcomes associated with childhood trauma. Findings reinforce the need for prevention of ACEs and promotion of resilience-informed clinical interventions in those who have experienced ACEs.
- ACEs were common in patients with SLE and a geographically matched population.
- Higher ACE levels and presence of ACEs from each domain (abuse, neglect, and household challenges) were associated with worse patient-reported disease activity, depression, and health status, but not physician-assessed measures.

Table 1.

Comparison of California Lupus Epidemiology Study (CLUES) 2015–2018 participants and California Behavioral Risk Factor Surveillance System Survey (BRFSS) 2015 respondents in Adverse Childhood Experiences (ACE) levels, domains, and items.

	Data Source		
	CLUES (n= 269)	**BRFSS[1] (n= 6,107)**	**p-value**
	% (95% Confidence Intervals)		
Overall ACE Level[2]			0.42
0	39.8 (34.1, 45.8)	37.3 (34.7, 40.0)	
1	23.4 (18.7, 28.9)	21.4 (19.3, 23.7)	
2–3	21.6 (17.0, 26.9)	24.1 (22.0, 26.4)	
≥4	15.2 (11.4, 20.1)	17.2 (15.5, 18.9)	
Domain			
Abuse	34.2 (28.8, 40.1)	45.2 (42.6, 47.9)	<0.001
Emotional	21.6 (17.0, 26.9)	36.5 (34.0, 39.0)	<0.001
Physical	17.1 (13.0, 22.1)	21.6 (19.6, 23.8)	0.08
Sexual	19.0 (14.7, 24.1)	14.1 (12.2, 16.1)	0.06
Household Challenges	53.0 (47.0, 58.9)	49.5 (46.9, 52.1)	0.32
Separation/Divorce	33.1 (27.7, 39.0)	27.3 (25.3, 29.5)	0.06
Substances in Home	23.0 (18.4, 28.5)	24.2 (22.5, 26.1)	0.66
Mental Illness in Home	19.0 (14.7, 24.1)	15.2 (13.6, 17.0)	0.14
Incarcerated Household Member	5.6 (3.4, 9.1)	7.3 (6.4, 8.4)	0.24
Domestic Violence in Home	10.0 (7.0, 14.3)	21.0 (19.1, 23.1)	<0.001
Neglect	24.2 (19.4, 29.7)	--	
Emotional	23.4 (18.7, 28.9)	--	
Physical	3.7 (2.0, 6.8)	--	

[1]BRFSS responses account for complex survey design and are standardized to CLUES demographic distribution on age (18–37, 38–53, >54 years), sex, and race/ethnicity.

[2]BRFSS ACE questionnaire does not include two “Neglect” items. Overall ACE levels for CLUES patients do not include the two neglect items.

Table 2.

Characteristics of California Lupus Epidemiology Study (CLUES) participants, 2015–2018, by Adverse Childhood Experiences (ACE) level

	Overall CLUES Participants	CLUES Participants with ACE Responses				
		ACE Level				
Demographics		**ACE 0**	**ACE 1**	**ACE 2–3**	**ACE ≥4**	**p-value** *
n, (row %)	269	99 (36.8)	59 (21.9)	59 (21.9)	52 (19.3)	
Age, mean (sd)	45.2 (13.9)	43.7 (15.3)	43.6 (13.5)	46.0 (13.2)	48.9 (11.7)	0.02
Women	241 (89.6)	82 (82.8)	56 (94.9)	53 (89.8)	50 (96.2)	0.03
Race/ethnicity						0.001
Non-Hispanic White	85 (31.6)	25 (25.3)	20 (33.9)	24 (40.7)	16 (30.8)	
Latino	69 (25.7)	19 (19.2)	19 (32.2)	16 (27.1)	15 (28.9)	
Non-Hispanic African American	32 (11.9)	8 (8.1)	5 (8.5)	7 (11.9)	12 (23.1)	
Asian/Pacific Islander	79 (29.4)	45 (45.5)	15 (25.4)	12 (20.3)	7 (13.5)	
Other	4 (1.5)	2 (2.0)	0	0	2 (3.9)	
Education						0.02
High school or less	42 (15.6)	9 (9.1)	14 (23.7)	8 (13.6)	11 (21.2)	
Some college/AA	90 (33.5)	28 (28.3)	17 (28.8)	27 (45.8)	18 (34.6)	
College graduate	137 (50.9)	62 (62.6)	28 (47.5)	24 (40.7)	23 (44.2)	
Disease duration, mean (sd)	16.7 (10.4)	16.2 (11.0)	16.0 (10.9)	18.0 (9.0)	17.1 (10.2)	0.41
Childhood onset <18 years	44 (16.4)	24 (24.2)	10 (17.0)	8 (13.6)	2 (3.9)	0.01
Lupus Nephritis	120 (44.6)	50 (50.5)	32 (54.2)	24 (40.7)	14 (26.9)	0.01

AA – Associate Degree.

Note: cells are n (column %), unless indicated.

* P-values for age and disease duration based on linear contrasts for trend. All others from chi-square tests. Comparison to ACE = 0.

Table 3.

Patient-reported SLE activity and damage, depression, physical function and quality of life among 269 California Lupus Epidemiology Study participants, by Adverse Childhood Experiences (ACE) level and domain from linear regression models adjusted for covariates[1]

Patient-Reported Measures					
Overall ACE Level	**SLAQ Disease Activity**	**BILD Disease Damage**	**PHQ Depression**	**PROMIS-PF Physical Function**	**SF-36 PCS Health Status**
	Adjusted means (95% CI)				
0	7.7 (6.3–9.1)	1.6 (1.2–2.1)	5.1 (4.1–6.1)	48.9 (47.2–50.7)	44.0 (41.9–46.2)
1	8.2 (6.5–9.9)	2.0 (1.4–2.5)	5.4 (4.1–6.7)	48.4 (46.2–50.6)	42.6 (39.9–45.3)
2–3	9.5 (7.8–11.2)	1.9 (1.3–2.4)	7.3 (6.1–8.6)	46.9 (44.7–49.2)	41.1 (38.4–43.8)
≥4	13.1 (11.2–15.0)	2.6 (2.0–3.2)	8.1 (6.7–9.5)	44.8 (42.4–47.2)	38.0 (35.1–41.0)
p-value	<0.001	0.10	0.01	0.050	0.01
ACE Domain					
None	7.7 (6.3–9.1)	1.6 (1.2–2.1)	5.1 (4.1–6.1)	48.9 (47.2–50.7)	44.0 (41.9–46.2)
Household Challenges	10.0 (8.9–11.2)*	2.1 (1.8–2.5)	6.8 (6.0–7.7)*	46.5 (45.1–48.0)*	40.7 (38.9–42.4)*
Neglect	10.9 (9.2–12.5)*	2.0 (1.4–2.5)	7.6 (6.4–8.8)*	45.7 (43.6–47.9)*	39.7 (37.1–42.3)*
Abuse	11.7 (10.3–13.1)*	2.2 (1.8–2.7)	7.7 (6.7–8.7)*	46.1 (44.3–48.0)*	39.2 (37.0–41.4)*

SLAQ - Systemic Lupus Activity Questionnaire; BILD - Brief Index of Lupus Damage; PHQ - Patient Health Questionnaire depression scale; PROMIS PF – Patient-Reported Outcomes Measurement Information System Physical Function; SF-36 PCS – Short Form, Physical Component Scale.

[1] Adjusted for age, gender, race, disease onset <18 years, education level.

Domain effects estimated in separate models, using a 3-level variable: 1+ items in the given domain; 1+ items in any other domain (not shown in table); no items (i.e., ACE=0).

* p<0.05 for comparison of domain effect to ACE=0.

Table 4.

Physician-assessed outcomes of activity, damage and severity by Adverse Childhood Experiences (ACE) level and domain, adjusted models

Physician-Assessed Outcomes			
Overall ACE Level	**SLEDAI Disease Activity**	**SDI Disease Damage**	**LSI Disease Severity**
	Adjusted means (95% CI)		
0	2.5 (1.9–3.2)	1.7 (1.3–2.1)	6.9 (6.6–7.2)
1	2.6 (1.8–3.4)	2.2 (1.7–2.7)	7.0 (6.6–7.4)
2–3	3.7 (2.9–4.5)	2.1 (1.6–2.6)	6.8 (6.4–7.2)
≥4	2.4 (1.6–3.3)	1.9 (1.3–2.4)	6.4 (6.0–6.8)
p-value *	0.08	0.49	0.18
ACE Domain			
None	2.5 (1.9–3.2)	1.7 (1.3–2.1)	6.9 (6.6–7.2)
Household Challenges	3.0 (2.5–3.6)	2.1 (1.8–2.4)	6.8 (6.5–7.0)
Neglect	2.6 (1.9–3.4)	1.7 (1.2–2.2)	6.7 (6.3–7.1)
Abuse	3.0 (2.4–3.7)	2.1 (1.6–2.5)	6.7 (6.4–7.0)

SLEDAI - Systemic Lupus Erythematosus Disease Activity Index; SDI - Systemic Lupus Collaborating Clinics Damage Index; LSI - Lupus Severity Index

[1] Adjusted for age, gender, race, disease onset <18 years, education level.

Domain effects estimated in separate models, using a 3-level variable: 1+ items in the given domain; 1+ items in any other domain (not shown in table); no items (i.e., ACE=0).

* $p<0.05$ for comparison of domain effect to ACE=0.