Background Systemic lupus erythematosus (SLE) is a chronic autoimmune disease. Genetics play a role in SLE susceptibility, with >100 risk single nucleotide polymorphisms (SNPs) from genome wide association studies (GWAS). Approximately 20% of SLE patients have childhood-onset SLE (cSLE) diagnosed <18 years. These patients are at risk for reduced bone mineral density (BMD) due to disease activity and chronic glucocorticoid exposure. Our aim was to assess the genetic contribution to bone mineral density among a multi-ethnic cohort of patients with cSLE.

Methods All patients were diagnosed and followed for cSLE at the SickKids Lupus Clinic. Patients were genotyped on the multiethnic Multiethnic Genotyping Array or the Infinium Global Screening Array. Those with baseline Lumbar Spine (LS) BMD dual-energy X-ray absorptiometry (DXA) scan were included in analysis. Baseline was defined as 1 month prior, or up to one year after cSLE diagnosis. Patients with bony abnormalities and with DXA scans due to medical conditions other than SLE were excluded. We extracted demographics, clinical features, and medication use from the Lupus database. The main outcome of interest was LS (L1-L4) BMD z scores. Two weighted polygenic risk scores (PRs) were calculated. 1.) BMD PRS was calculated using alleles associated with low LS from the largest LS BMD meta-GWAS of BMD to date. 2.) SLE PRS was also calculated using one of the largest SLE GWAS. We regressed BMD and SLE PRs with baseline BMD z-scores in linear models adjusted for sex, ancestry, glucocorticoid exposure, height percentile, and an indicator for lupus nephritis and/or neuropsychiatric lupus.

Results Our study included 283 patients, 82% female, 30% of European and 28% of East Asian ancestry. The median age of cSLE diagnosis was 13.3 years [IQR 10.8, 15.1]. In univariate and multivariate adjusted models, a higher BMD PRS was significantly associated with low BMD at a univariate level but was not significant in the adjusted model. Height percentile was significantly associated with BMD z-score (β: 0.01; 95%CI: 0.01, 0.02; P=5.09e-10), yet the presence of LN and/or NPSLE was not (β: 0.06; 95%CI: 0.21, 0.33; P=0.67).

Conclusions Our study found that a low-BMD PRS was significantly associated with lower LS BMD z-score in cSLE patients at baseline. BMD PRS may be used to stratify patients with cSLE who are at greatest risk of reduced BMD. We hope to expand this to long term LS BMD z-scores and explore BMD PRS predicts long term BMD z scores among cSLE patients.