# Brigham and Women's Hospital Founding Member, Mass General Brigham

## **Comorbidities associated with discoid lupus erythematosus: A case-control study in the All of Us** research program

## Mihir K. Patil<sup>1,2</sup>, Carlos E Salazar<sup>1,3#</sup>, Krithika Nayudu<sup>1,4#</sup>, Thomas Z Rohan<sup>1,5#</sup>, Vinod E Nambudiri<sup>1,3</sup>

<sup>1</sup>Department of Dermatology, Brigham and Women's Hospital, Boston, Massachusetts, <sup>2</sup>Carle Illinois College of Georgia, Augusta University, <sup>1</sup>Department of Dermatology, Brigham and Women's Hospital, Boston, Massachusetts, <sup>2</sup>Carle Illinois, <sup>3</sup>Harvard Medical School, Boston, Massachusetts, <sup>4</sup>Medical College of Georgia, Augusta University, Augusta, Georgia, <sup>5</sup>Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania, # - These authors contributed equally to this work and should be considered co-see

## Introduction

- Lupus erythematosus (LE) is a chronic autoimmune disorder that frequently involves the skin and predominantly affects women.<sup>1</sup>
- While the most common chronic cutaneous lupus subtype is discoid LE (DLE),<sup>1</sup> its common comorbidities are undercharacterized.<sup>2</sup> Prior research has demonstrated several cardiovascular comorbidities exist within the DLE population,<sup>4</sup> yet other domains have been relatively underexplored.
- We sought to explore the **potential comorbidities associated with DLE patients** using electronic health record (EHR) data from the All of Us Research Program, a National Institutes of Health database that include participants from groups historically to strives underrepresented in biomedical research.

## Methods

#### **Overview:**

- We conducted a nested, case-control study on adults (aged 18+) within the All of Us research program from May 2018 to July 2022.
- The Mass General Brigham IRB deemed the study to be non-human subjects' research. Cases of DLE were identified using Observational Medical Outcomes Partnership (OMOP) Common Data Model code 4066824, including ICD-10CM code L93.0 and SNOMED diagnostic code 200938002. Each DLE case was matched with four controls of the same age, race/ethnicity, and gender (all P = 1.000). Comorbidities were assessed using OMOP (please see Table 1 for complete list).

#### **Data Analysis Procedure:**

- **Pearson χ2** was used to compare data between cases and controls.
- Conditional logistic regression was used to calculate odds ratios (ORs) to evaluate DLE-associated comorbidities. Data analysis was performed using Python version 3.7.12. Significance was determined with two-sided P < .05.



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Table 1. Characterization between any series of the series of th	Results								
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Table 1. Charad	cteristics o	f DLE patients	and Contro	ol group in All of Us				
interaction of the second se		DLE	, No. (%) (n= 9	19) Con	Control. No. (%)(n=3676)				
White         339 (36.5)         1355 (36.5)           Black of African American         200 (22.6)         800 (22.6)           Mian         200 (22.6)         800 (22.6)           Other         30 (33.3)         120 (33.3)           Other         30 (33.1)         200 (33.6)           Other         30 (31.2)         412 (11.2)           Male         133 (12.2)         412 (11.2)           Female         739 (86.6)         3322 (86.8)           Other         180 (2.0)         72 (2.0)           Average         52.2         55.2           Standard Devisition         14.7         16.7           Defer         140 (12.0)         200 (8.2)         15.5 (1.24-1.98)           Alopecia arceta         141935         110 (12.0)         300 (8.2)         1.5 (1.24-1.98)           Alopecia arceta         141935         124 (2.6)         78 (2.1)         1.32 (0.83-2.11)         0.239           Contact dermatitis (Iritant)         400452         224 (2.6)         78 (2.1)         1.32 (0.83-2.11)         0.031           Ecrode skin         411925         24 (2.6)         78 (2.1)         1.32 (0.83-2.11)         0.001           BC of skin         41192752         24 (2.6)         <	Race/Ethnicity					1.00			
Jobustor         Jobustor         Jobustor         Jobustor         Jobustor           Aian         30(3.3)         120(3.3)         120(3.3)         100           Other         30(3.3)         120(3.3)         100           Gender         780 (68.8)         3192 (68.8)         100           Male         18(2.0)         72 (2.0)         100           Average         55.2         55.2         55.2         55.2           Sendard Deviation         14.7         14.7         14.7         100           Average         55.2	White Block on African America		339 (36.9)		1356 (36.9)				
Adom         Total	Black of African American Hispanic		300 (32.6) 200 (21.8)		1200 (32.6) 800 (21.8)				
Other         30(54)         200(54)         200(54)           Male         133(12)         412(12)         100           Male         1392(86.8)         3192(86.8)         100           Other         182(20)         72(20)         100           Age (v)         55.2         55.2         55.2         100           Standard Deviation         11.7         11.7         11.7         11.7           Dermatological Comorbidities         OMOP         DLE, No. (%)         Control, No. (%)         odds Ratio (95% C)         p-value*           Dermatological Comorbidities         Uncertant (11.2)         24 (2.6)         520 (50.5)         7.56 (3.83-14.9)         <0.001	Asian		30 (3.3)		120 (3.3)				
Gender         1.00           Mile         133(11.2)         412(11.2)           Female         3128(86.8)         3122(86.8)           Other         18(2.0)         721(2.0)           Age (n)         52.2         55.2           Average         55.2         55.2           Standard Deviation         14.7         14.7           Table 2. Comorbidities of UE patients and Control group in All of US           Dermatological Comorbidities           Anne         141095         110(12.0)         300(8.2)         1.57(1.24.1-98)         <0.001	Other		50 (5.4)		200 (5.4)				
Instruct	Gender		102 (11.2)		112 (11 2)	1.00			
Other         18 (20)         72 (20)           Age (v)         55.2         55.2           Stendard Deviation         1.7         14.7           Table 2. Comorbidities of DLE patients and Control group in All of Us           Odds P DLE, NO. (%) Code         Control, NO. (%) (n=3676)         Odds Ratio (95% CI) p-value*           Dermatological Comorbidities           Acne         141993         24 (2.6)         520 (s0.5)         7.56 (3.83-14.9)         <0.001	Female		798 (86.8)		412 (11.2) 3192 (86.8)				
Age (n)         55.2         55.2         55.2           Standard Deviation         14.7         14.7         14.7           Table 2. Comorb. Mo. (%) Code         Control. Mo. (%) (n=3676)         Odds Ratio (95% C)         p-value*           Dermatological Comorblidites         Control. Mo. (%) (n=3676)         Odds Ratio (95% C)         p-value*           Acne         141095         110 (12.0)         300 (8.2)         1.57 (1.241.98)         <0.001	Other		18 (2.0)		72 (2.0)				
Wrenge Standard Deviation         55.2         55.2           Standard Deviation         14.7         14.7         14.7           Table 2. Comorbidities of DLE patients and Control group in All of Us           Control, No. (%) (n=3076)         Odds Ratio (95% CI) (n=3676)         p-value*           Dermatological Comorbidities           Acne         141095         110 (12.0)         300 (8.2)         1.57 (1.24-1.98)         <0.001           BC of skin         4112752         24 (2.6)         520 (s0.5)         7.56 (3.83-14.9)         <0.001	Age (y)								
Table 2. Comorbidities of DLE patients and Control, No. (%) Code         Control, No. (%) Code         Control, No. (%) Control, No.	Average Standard Doviation		55.2		55.2				
Table 2. comovidities of DLE potents and Control No. (No. 300)         Control, No. (No. (No. 60)         Control, No. (No. (No. 60)         Control, No. (No. (No. 60)         Control Alopecia areata         141093         24 (2.6)         AR (2.1)         1.32 (0.83-2.11)         0.0033           Contract dermatitis (Allergic)         40011         2.20 (8.2.2)         2.00 (1.2.6.3, 8.3.1.4.1)         0.001           Contract dermatitis (Irritant)         400215 (2.5)         3.55 (5.77-41.6.2)         0.001           Contract dermatitis (Irritant)         400122         220 (5.2)         2.20 (1.2.6.3, 1.3.2         0.001           Lichen planus         132703         2.10 (1.1)         2.22 (1.2.1         2.20 (2.2)         2.20 (0.1)         1.27 (2.2.7.4.0)         0.001           Lichen planus         2.20 (2.2)         2.20 (2.2)         2.20 (2.2)         2.20 (2.2)	Stanuaru Deviation		14./		14./				
OMOP Code         DLE, No. (%) (n=3979)         Control, No. (%) (n=3676)         Odds Ratio (95% CI)         p-value*           Dermatological Comorbidities         Acne         141095         110 (12.0)         300 (8.2)         1.57 (1.24-1.98)         <0.001	Table 2. Comorbidities of DLE patients and Control group in All of Us								
Code         (n=319)         (n=3676)         Odds Ratio (95% CI)         p-value*           Dermatological Comorbidities         141095         110 (12.0)         300 (8.2)         1.57 (1.24-1.98)         <0.001		OMOP	DLE, No. (%)	Control, No.	. (%)				
Dermatological Comorbidities           Arne         141095         110 (12.0)         300 (8.2)         1.57 (1.24-1.98)         <0.001		Code	(n=919)	(n=3676	) Odds Ratio (95% CI)	p-value*			
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Alopecia areata         141933         24 (2.6)         ≤20 (s0.5)         7.56 (3.83-14.9)         <0.001           BCC of skin         4112752         24 (2.6)         78 (2.1)         1.32 (0.83-2.11)         0.239           Contact dermatitis (Allergic)         4001352         24 (2.6)         47 (1.3)         2.07 (1.26-3.4)         0.004           Dermatomyositis         80182         ≤20 (s2.2)         ≤20 (s0.5)         15.5 (5.77-41.62)         <0.001	Acne	141095	110 (12.0)	300 (8.2)	1.57 (1.24-1.98)	< 0.001			
BCC of skin         4112752         24 (2.6)         78 (2.1)         1.32 (0.83-2.11)         0.239           Contact dermatitis (Allergic)         4031019         27 (2.9)         69 (1.9)         1.56 (0.99-2.45)         0.003           Contact dermatitis (Irritant)         4004352         24 (2.6)         47 (1.3)         2.07 (1.26-3.4)         0.004           Dermatomyositis         80182         520 (52.2)         520 (55.5)         15.5 (5.77-4.16.2)         <0.001	Alopecia areata	141933	24 (2.6)	≤20 (≤0.5)	7.56 (3.83-14.9)	< 0.001			
Contact dermatitis (Allergic)         4031019         27 (2.9)         69 (1.9)         1.56 (0.99-2.45)         0.053           Contact dermatitis (Irritant)         4004352         24 (2.6)         47 (1.3)         2.07 (1.26-3.4)         0.004           Dermatomyositis         80182         ≤20 (s0.5)         15.5 (5.77-41.62)         <0.001	BCC of skin	4112752	24 (2.6)	78 (2.1)	1.32 (0.83-2.11)	0.239			
Contact dermatitis (Irritant)400435224 (2.6)47 (1.3)2.07 (1.26-3.4)0.004Dermatomyositis80182 $\leq 20$ ( $\leq 2.2$ ) $\leq 20$ ( $\leq 0.5$ )15.5 (5.77-41.62)<0.001	Contact dermatitis (Allergic)	4031019	27 (2.9)	69 (1.9)	1.56 (0.99-2.45)	0.053			
Dermatomyositis         80182         ≤20 (≤2.2)         ≤20 (≤0.5)         15.5 (5.77-41.62)         <0.001           Eczema         133835         152 (16.5)         357 (9.7)         1.88 (1.53-2.31)         <0.001	Contact dermatitis (Irritant)	4004352	24 (2.6)	47 (1.3)	2.07 (1.26-3.4)	0.004			
Eczema133835152 (16.5)357 (9.7)1.88 (1.53-2.31)<0.001Hidradenitis suppurativa424122325 (2.7)40 (1.1)2.42 (1.47-3.99)<0.001	Dermatomyositis	80182	≤20 (≤2.2)	≤20 (≤0.5)	) 15.5 (5.77-41.62)	< 0.001			
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Lichen planus132703 $21 (2.3)$ $22 (0.5)$ $4.07 (2.21-7.49)$ $<0.001$ Localized scleroderma441928 $24 (2.6)$ $24 (0.7)$ $4.45 (2.49-7.98)$ $<0.001$ Melanoma of skin141232 $\leq 20 (\leq 2.2)$ $23 (0.6)$ $1.57 (0.72-3.41)$ $0.253$ Psoriasis140168 $56 (6.1)$ $104 (2.8)$ $2.14 (1.54-2.99)$ $<0.001$ SCC of skin4111921 $\leq 20 (\leq 2.2)$ $24 (0.6)$ $2.53 (1.32-4.83)$ $0.005$ Seborrheic dermatitis137053 $126 (13.7)$ $190 (5.2)$ $2.95 (2.32-3.74)$ $<0.001$ Vitiligo138502 $\leq 20 (\leq 2.2)$ $22 (0.6)$ $2.22 (1.06-4.64)$ $0.035$ Non-dermatological ComorbiditieAlcoholism4218106 $61 (6.6)$ $282 (7.7)$ $0.88 (0.66-1.17)$ $0.380$ Anxiety441542 $477 (51.9)$ $1358 (36.9)$ $1.86 (1.61-2.15)$ $<0.001$ Cardiovascular disorder134057 $836 (91.0)$ $2531 (68.9)$ $4.61 (3.64-5.84)$ $<0.001$ Depressive disorder440383 $480 (52.2)$ $1324 (36.0)$ $1.97 (1.7-2.28)$ $<0.001$ Diabetes mellitus (Type 1)201254 $37 (4.0)$ $90 (2.4)$ $1.67 (1.13-2.47)$ $0.010$ Diabetes mellitus (Type 2)201826 $259 (28.2)$ $821 (22.3)$ $1.38 (1.81-6.3)$ $<0.001$ End stage renal disease193782 $70 (7.6)$ $65 (1.8)$ $4.97 (3.49-7.07)$ $<0.001$ Gingivitis $4281516$ $32 (3.5)$ $94 (2.6)$ $1.52 (1.01-2.3)$ $0.04$	Hidradenitis suppurativa	4241223	25 (2.7)	40 (1.1)	2.42 (1.47-3.99)	< 0.001			
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Melanoma of skin $141232$ $\leq 20$ ( $\leq 2.2$ ) $23$ (0.6) $1.57$ (0.72-3.41) $0.253$ Psoriasis14016856 (6.1)104 (2.8) $2.14$ (1.54-2.99) $<0.001$ SCC of skin4111921 $\leq 20$ ( $\leq 2.2$ )24 (0.6) $2.53$ (1.32-4.83) $0.005$ Seborrheic dermatitis137053126 (13.7)190 (5.2) $2.95$ (2.32-3.74) $<0.001$ Vitiligo138502 $\leq 20$ ( $\leq 2.2$ )22 (0.6) $2.22$ (1.06-4.64) $0.035$ Non-dermatological Comorbidities $<$ $<$ $<$ $<$ $<$ $<$ Alcoholism421810661 (6.6)282 (7.7) $0.88$ (0.66-1.17) $0.380$ Anxiety441542477 (51.9)1358 (36.9) $1.86$ (1.61-2.15) $<$ $<$ Cardiovascular disorder134057836 (91.0) $2531$ (88.9) $4.61$ (3.64-5.84) $<$ $<$ Depressive disorder440383480 (52.2)1324 (36.0) $1.97$ ( $1.72$ .28) $<$ $<$ Diabetes mellitus (Type 1)20125437 (4.0)90 (2.4) $1.67$ ( $1.13$ -2.47) $0.010$ Diabetes mellitus (Type 2)201826259 (28.2) $821$ (22.3) $1.38$ ( $1.81$ - $1.63$ ) $<$ $<$ Hyperthyroidism414247969 (7.5) $145$ (3.9) $1.92$ ( $1.43$ - $2.58$ ) $<$ $<$ Hyperthyroidism140673265 (28.8)586 (15.9) $2.15$ ( $1.01$ - $2.3$ ) $0.001$ Hyperthyroidism140673265 (28.8)586 (15.9) $2.15$ ( $1.32$ - $2.54$ ) $<$ $<$ Infammato	Localized scleroderma	441928	24 (2.6)	24 (0.7)	4.45 (2.49-7.98)	< 0.001			
Psoriasis14016856 (6.1)104 (2.8)2.14 (1.54-2.9)<0.001SCC of skin4111921<20 (<2.2)	Melanoma of skin	141232	≤20 (≤2.2)	23 (0.6)	1.57 (0.72-3.41)	0.253			
SCC of skin $4111921$ $\leq 20 (\leq 2.2)$ $24 (0.6)$ $2.53 (1.32-4.83)$ $0.005$ Seborrheic dermatitis $137053$ $126 (13.7)$ $190 (5.2)$ $2.95 (2.32-3.74)$ $<0.001$ Vitiligo $138502$ $\leq 20 (\leq 2.2)$ $22 (0.6)$ $2.22 (1.06-4.64)$ $0.035$ Non-dermatological Comorbidities $220 (\leq 2.2)22 (0.6)2.22 (1.06-4.64)0.035Non-dermatological Comorbidities421810661 (6.6)282 (7.7)0.88 (0.66-1.17)0.380Anxiety441542477 (51.9)1358 (36.9)1.86 (1.61-2.15)<0.001Cardiovascular disorder134057836 (91.0)2531 (68.9)4.61 (3.64-5.84)<0.001Celiac disease194992**220 (\leq 2.2)21 (\leq 0.6)3.83 (1.97-7.46)<0.001Depressive disorder440383480 (52.2)1324 (36.0)1.97 (1.7-2.28)<0.001Diabetes mellitus (Type 1)20125437 (4.0)90 (2.4)1.67 (1.13-2.47)0.010Diabetes mellitus (Type 2)201826259 (28.2)821 (22.3)1.38 (1.18-1.63)<0.001End stage renal disease19378270 (7.6)65 (1.8)4.97 (3.49-7.07)<0.001Gingivitis428151632 (3.5)94 (2.6)1.52 (1.01-2.3)0.046Hyperthyroidism140673265 (28.8)586 (15.9)2.15 (1.82-2.54)<0.001Inflammatory bowel disease407481525 (2.7)29 (0.8)$	Psoriasis	140168	56 (6.1)	104 (2.8)	2.14 (1.54-2.99)	< 0.001			
Seborrheic dermatitis137053126 (13.7)190 (5.2)2.95 (2.32-3.74)<0.001Vitiligo138502 $\leq 20 (\leq 2.2)$ 22 (0.6)2.22 (1.06-4.64)0.035Non-dermatological ComorbiditiesAlcoholism421810661 (6.6)282 (7.7)0.88 (0.66-1.17)0.380Anxiety441542477 (51.9)1358 (36.9)1.86 (1.61-2.15)<0.001	SCC of skin	4111921	≤20 (≤2.2)	24 (0.6)	2.53 (1.32-4.83)	0.005			
Vitiligo $138502$ $\leq 20 (\leq 2.2)$ $22 (0.6)$ $2.22 (1.06-4.64)$ $0.035$ Non-dermatological ComorbiditiesAlcoholism $4218106$ $61 (6.6)$ $282 (7.7)$ $0.88 (0.66-1.17)$ $0.380$ Anxiety $441542$ $477 (51.9)$ $1358 (36.9)$ $1.86 (1.61-2.15)$ $<0.001$ Cardiovascular disorder $134057$ $836 (91.0)$ $2531 (68.9)$ $4.61 (3.64-5.84)$ $<0.001$ Celiac disease $194992$ ** $\leq 20 (\leq 2.2)$ $21 (\leq 0.6)$ $3.83 (1.97-7.46)$ $<0.001$ Depressive disorder $440383$ $480 (52.2)$ $1324 (36.0)$ $1.97 (1.7-2.28)$ $<0.001$ Diabetes mellitus (Type 1) $201254$ $37 (4.0)$ $90 (2.4)$ $1.67 (1.13-2.47)$ $0.010$ Diabetes mellitus (Type 2) $201826$ $259 (28.2)$ $821 (22.3)$ $1.38 (1.18-1.63)$ $<0.001$ End stage renal disease $193782$ $70 (7.6)$ $65 (1.8)$ $4.97 (3.49-7.07)$ $<0.001$ Gingivitis $4281516$ $32 (3.5)$ $94 (2.6)$ $1.52 (1.01-2.3)$ $0.046$ Hyperthyroidism $4142479$ $69 (7.5)$ $145 (3.9)$ $1.92 (1.43-2.58)$ $<0.001$ Hypethyroidism $140673$ $225 (2.2)$ $32 (0.9)$ $3.4 (1.99-5.81)$ $<0.001$ Inflammatory bowel disease $4074815$ $25 (2.7)$ $29 (0.8)$ $3.4 (1.99-5.81)$ $<0.001$ Interstitial lung disease $4119786$ $109 (11.9)$ $93 (2.5)$ $5.24 (3.93-6.99)$ $<0.001$ Lung cancer $443388$ $\leq 20 (\leq 2.2)$	Seborrheic dermatitis	137053	126 (13.7)	190 (5.2)	2.95 (2.32-3.74)	< 0.001			
Non-dermatological Comorbidities           Alcoholism         4218106         61 (6.6)         282 (7.7)         0.88 (0.66-1.17)         0.380           Anxiety         441542         477 (51.9)         1358 (36.9)         1.86 (1.61-2.15)         <0.001	Vitiligo	138502	≤20 (≤2.2)	22 (0.6)	2.22 (1.06-4.64)	0.035			
Alcoholism421810661 (6.6)282 (7.7)0.88 (0.66-1.17)0.380Anxiety441542477 (51.9)1358 (36.9)1.86 (1.61-2.15)<0.001	Non-dermatological Comorbiditi	es							
Anxiety441542477 (51.9)1358 (36.9)1.86 (1.61-2.15)<0.001Cardiovascular disorder134057836 (91.0)2531 (68.9)4.61 (3.64-5.84)<0.001	Alcoholism	4218106	61 (6 6)	282 (7 7)	0 88 (0 66-1 17)	0 380			
Cardiovascular disorder134057836 (91.0)2531 (68.9)4.61 (3.64-5.84)<0.001Celiac disease194992**<20 (≤2.2)	Anxiety	441542	477 (51 9)	1358 (36 9	1.86(1.61-2.15)	<0.001			
Celiac disease194992**<20 (51.6)2531 (50.5)1101 (30.5)1001 (30.5)Depressive disorder440383480 (52.2)21 (≤0.6)3.83 (1.97-7.46)<0.001	Cardiovascular disorder	134057	836 (91.0)	2531 (68 9	$\begin{array}{c} 1.00 (1.01 \ 2.13) \\ 4.61 (3 \ 64 \ 5 \ 84) \end{array}$	<0.001			
Depressive disorder440383480 (52.2)1324 (36.0)1.97 (1.7-2.28)<0.001Diabetes mellitus (Type 1)20125437 (4.0)90 (2.4)1.67 (1.13-2.47)0.010Diabetes mellitus (Type 2)201826259 (28.2)821 (22.3)1.38 (1.18-1.63)<0.001	Celiac disease	194992	**≤20 (<2.2)	21 (<0.6)	3.83 (1.97-7.46)	< 0.001			
Diabetes mellitus (Type 1)20125437 (4.0)90 (2.4)1.67 (1.13-2.47)0.010Diabetes mellitus (Type 2)201826259 (28.2)821 (22.3)1.38 (1.18-1.63)<0.001	Depressive disorder	440383	480 (52 2)	1324 (36.0)	1.97 (1.7-2.28)	<0.001			
Diabetes mellitus (Type 2)       201826       259 (28.2)       821 (22.3)       1.38 (1.18-1.63)       <0.001	Diabetes mellitus (Tyne 1)	201254	37 (4 0)	90 (2.4)	1.67 (1.13-2.20)	0.010			
End stage renal disease19378270 (7.6)651 (1.8)4.97 (3.49-7.07)<0.001Gingivitis428151632 (3.5)94 (2.6)1.52 (1.01-2.3)0.046Hypertensive disorder316866636 (69.2)1698 (46.2)2.62 (2.25-3.06)<0.001	Diabetes mellitus (Type 2)	201826	259 (28.2)	821 (22 3)	) $1.38(1.18-1.63)$	<0.001			
Single Function of StateFist (Fist)Sist (Fist)Fist (Site Fist)Sist (Site Fist)Gingivitis428151632 (3.5)94 (2.6)1.52 (1.01-2.3)0.046Hypertensive disorder316866636 (69.2)1698 (46.2)2.62 (2.25-3.06)<0.001	End stage renal disease	193782	70 (7.6)	65 (1 8)	4.97 (3 49-7 07)	<0.001			
Hypertensive disorder316866636 (69.2)1698 (46.2)2.62 (2.25-3.06)<0.001Hyperthyroidism414247969 (7.5)145 (3.9)1.92 (1.43-2.58)<0.001	Gingivitis	4281516	32 (3 5)	94 (2.6)	1.52 (1.01-2.3)	0.046			
Hyperthyroidism414247969 (7.5)145 (3.9)1.92 (1.43-2.58)<0.001Hypothyroidism140673265 (28.8)586 (15.9)2.15 (1.82-2.54)<0.001	Hypertensive disorder	316866	636 (69.2)	1698 (46.2	2.62(1.012.3)	<0.01			
Hypothyroidism1412173265 (7.5)145 (3.5)1.52 (1.45 2.56)<0.001Hypothyroidism140673265 (28.8)586 (15.9)2.15 (1.82-2.54)<0.001	Hyperthyroidism	4142479	69 (7 5)	145 (3 9)	1.92 (1 43-2 58)	<0.001			
Inflammatory bowel disease4074815 $25 (2.7)$ $29 (0.8)$ $3.4 (1.99-5.81)$ <0.001Interstitial lung disease4119786109 (11.9)93 (2.5) $5.24 (3.93-6.99)$ <0.001	Hypothyroidism	140673	265 (28.8)	586 (15 9)	) $2.15(1.82-2.50)$	<0.001			
Interstitial lung disease       4119786       109 (11.9)       93 (2.5)       5.24 (3.93-6.99)       <0.001	Inflammatory howel disease	4074815	255 (20.0)	29 (0.8)	3 4 (1 99-5 81)	<0.001			
Lung cancer443388 $\leq 20 (\leq 2.2)$ $32 (0.9)$ $1.83 (0.99-3.39)$ $0.054$ Lymphoma432571 $33 (3.6)$ $35 (1.0)$ $3.57 (2.22-5.72)$ $<0.001$ Nephritis193253243 (26.4)127 (3.5) $10.38 (8.23-13.09)$ $<0.001$ Rheumatoid arthritis80809247 (26.9) $134 (3.6)$ $9.87 (7.87-12.38)$ $<0.001$ Seizure377091148 (16.1)208 (5.7) $3.17 (2.53-3.97)$ $<0.001$	Interstitial lung disease	4119786	109 (11 9)	93 (2.5)	5.24 (3.93-6.99)	<0.001			
Lymphoma43257133 (3.6)35 (1.0)3.57 (2.22-5.72)<0.001Nephritis193253243 (26.4)127 (3.5)10.38 (8.23-13.09)<0.001		ΔΔ2288	<20 (<2 2)	32 (0 0)	1 83 (0 90-3 30)	0.051			
Nephritis       193253       243 (26.4)       127 (3.5)       10.38 (8.23-13.09)       <0.001	Lymnhoma	422571	33 (3 6)	32 (0.9)	2 57 (2 22-5 72)	<0.004			
Reprintis       103233       243 (20.4)       127 (3.3)       10.38 (8.23-13.03)       <0.001         Rheumatoid arthritis       80809       247 (26.9)       134 (3.6)       9.87 (7.87-12.38)       <0.001	Nenhritis	102252	243 (26 A)	127 (2 5)	10 38 (8 22-12 00)				
Seizure       377091       148 (16.1)       208 (5.7)       3.17 (2.53-3.97)       <0.001         Siögren syndrome       254/43       171 (18.6)       57 (1.6)       14.02 (10.22.10.04)       <0.001	Rheumatoid arthritic	80800	243 (20.4)	127 (3.3)	Q Q7 (7 Q7_12 20)				
Siögren syndrome 25///2 171 (18.6) 57 (1.6) 1/ 02 (10.22 10.0/) <0.001	Seizure	377001	247 (20.3) 148 (16 1)	208 (5.0)	2 17 (2 52-2 07)				
	Sjögren syndrome	254443	171 (18.6)	57 (1.6)	14.02 (10.32-19.04)	< 0.001			

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL X

## Discussion

- Our case-control study reports on several comorbidities of DLE, which remain under-characterized in the literature, and reinforces a known link between DLE and cardiovascular disease in a dataset enriched with individuals from diverse backgrounds historically underrepresented in biomedical research.<sup>3,4</sup>
- Cardiovascular risks in DLE are hypothesized to arise from skinspecific inflammation (i.e., chronic elevation of pro-inflammatory cytokines like interleukin-17).<sup>4</sup>
- Significant associations were also found between DLE and several other **autoimmune conditions** noted in patients with CLE without concurrent SLE,<sup>5</sup> which may be explained by overlapping genetic and environmental factors.
- The increased odds of **depression and anxiety** may reflect severe quality-of-life impairments from chronic autoimmune diseases like DLE.
- Limitations include reliance on EHR and lack of DLE severity data. Clinical similarities between dermatomyositis, lichen planus, and DLE may contribute to their respective increased odds of concurrent diagnosis with DLE and warrant further analyses in settings with detailed chart reviews and clinical images.
- Our study underscores the need for further DLE research to enhance disease pathophysiology understanding, patient management, and avenues for DLE-specific treatment, particularly among individuals from diverse backgrounds.

## References

- Uva L, Miguel D, Pinheiro C, Freitas JP, Marques Gomes M, Filipe P. Cutaneous Manifestations of Systemic Lupus Erythematosus. Autoimmune Diseases. 2012;2012:e834291. doi:10.1155/2012/834291
- 2. McDaniel B, Sukumaran S, Koritala T, Tanner LS. Discoid Lupus Erythematosus. In: StatPearls. StatPearls Publishing; 2023. Accessed June 28, 2023 http://www.ncbi.nlm.nih.gov/books/NBK493145/
  - All of Us Research Program Investigators, Denny JC, Rutter JL, et al. The "All of Us" Research Program. N Engl J Med. 2019;381(7):668-676. doi:10.1056/NEJMsr1809937
- 4. Olbrich H, Kridin K, Zirpel H, et al. Cutaneous lupus erythematosus is associated with an increased risk of cardiac and vascular diseases: a large-scale, propensity-matched global retrospective cohort study. eBioMedicine. 2023;93. doi:10.1016/j.ebiom.2023.104639 5. Kunzler E, Hynan LS, Chong BF. Autoimmune Diseases in Patients With Cutaneous Lupus Erythematosus. JAMA Dermatol. 2018;154(6):712-716. doi:10.1001/jamadermatol.2018.0616

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