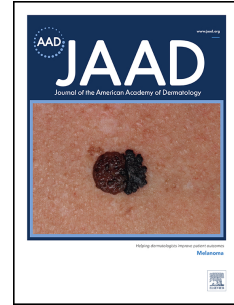# Journal Pre-proof

Prevalence of calcinosis cutis in the United States using the All of Us research database

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Please cite this article as: Kam O, Osborne S, Wescott R, Vo C, Thacker S, George SE, Wu JJ, Prevalence of calcinosis cutis in the United States using the All of Us research database, *Journal of the American Academy of Dermatology* (2023), doi: https://doi.org/10.1016/j.jaad.2023.09.076.

1   **Article type:** Research Letter

2   **Title:** Prevalence of calcinosis cutis in the United States using the All of Us research database

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25 **Conflicts of Interest:**

26 Dr. Wu is or has been an investigator, consultant, or speaker for AbbVie, Almirall, Amgen,

27 Arcutis, Aristea Therapeutics, Bausch Health, Boehringer Ingelheim, Bristol-Myers Squibb,

28 Dermavant, DermTech, Dr. Reddy's Laboratories, Eli Lilly, EPI Health, Galderma, Janssen, LEO

29 Pharma, Mindera, Novartis, Pfizer, Regeneron, Samsung Bioepis, Sanofi Genzyme, Solius, Sun

30 Pharmaceutical, UCB, and Zerigo Health.

31

32 **IRB approval status:** not applicable

33 **Reprint requests:** not available

34 **Patient consent on file:** not applicable

35 **Manuscript word count:** 410

36 **References:** 4

37 **Figures and tables:** 2

38 Figures: 1

39 Tables: 1

40 Supplementary figures: 0

41 Supplementary tables: 0

42

43 **Key words**: calcinosis cutis; calcification; connective tissue disease; autoimmune; systemic

44 sclerosis

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48 *To the Editor*: Calcinosis cutis (CC) is characterized by the deposition of calcium in the skin and

49 subcutaneous tissues. It is often associated with rheumatologic diseases, most commonly,

50 systemic sclerosis (SSc)/CREST syndrome [1-3]. Pathogenesis of CC can also be idiopathic,

51 iatrogenic, or secondary to disruptions in calcium homeostasis [3]. Currently, there is a lack of

52 literature addressing the prevalence of CC. The aim of our study was to estimate the prevalence

53 of CC in the general US population using the National Institute of Health's *All of Us* database

54 [4].

55

56 Our analysis identified cases of CC, SSc, and CREST syndrome using the *International*

57 *Classification of Diseases, Tenth Revision, Clinical Modification* codes L94.2, M34.9, M34.1,

58 and *SNOMED* codes 21323007, 89155008/299279006/298285004/128460000, 31848007,

59 respectively. Prevalence was calculated using the Wald test with a 95% confidence interval (CI).

60

61 As of August 15, 2023, there were 407,333 participants in the *All of Us* database. CC comprised

62 107 cases (overall prevalence 0.026%; 95% CI 0.02-0.03), of which the majority were female

63 (72%). The mean and median age of calcinosis cutis patients were 60 (SD 14.7) and 62 years old,

64 respectively. The mean and median ages at diagnosis were 56 (SD 14.7) and 57 years old,

65 respectively. CC was most prevalent in patients ages 55-64 (0.035%; 95% CI 0.02-0.05) (*Figure*

66 *1*), particularly in females of this age group (89.7%). Amongst the racial/ethnic groups, Asians

67 had the highest prevalence (0.042%; 95% CI 0.02-0.09), followed by Black patients (0.031%;

68 95% CI 0.02-0.05) (*Table 1*). Approximately half of CC patients had at least one autoimmune

69 disease (n=52, 48.6%) and 23 had a diagnosis of SSc and/or CREST syndrome (21.5%).

70 Our estimation indicates that CC affects 260 out of every million individuals in the US. Previous

71 research has examined the prevalence of CC in patients with autoimmune disorders; CC has been

72 shown to affect up to 50% of SSc patients [1, 2]. To our knowledge, this is the first large

73 population-based study to examine the prevalence of CC in the general US population.

74 Interestingly, our findings suggest that all-cause CC is most common in Asians despite their

75 underrepresentation in the *All of Us* database.

76

77 Limitations include reliance on EMR data, which is subject to inter-provider coding variability.

78 As a result, our estimate could be an underestimation as patients without records of an *ICD-*

79 *10/SNOMED* code for CC were excluded from our calculations. Given the rarity of this disease,

80 misclassification or underdiagnosis is probable. Future studies are warranted to further

81 characterize the epidemiology of calcinosis cutis.

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93   Table 1. Prevalence of calcinosis cutis in All of Us across age and racial/ethnic groups

Group	Total population, n	CC cases, n	Prevalence % (95% CI)	Female, n (%)
Overall	407,333	107	0.026 (0.02-0.03)	77 (72)
Age group, y				
18-44	129,508 (31.8)	16	0.012 (0.01-0.02)	9 (56.3)
45-54	61,957 (15.2)	17	0.027 (0.02-0.04)	10 (58.8)
55-64	82,337 (20.2)	29	0.035 (0.02-0.05)	26 (89.7)
65-74	81,810 (20.1)	27	0.033 (0.02-0.05)	21 (77.8)
75+	51,721 (12.7)	18	0.035 (0.02-0.06)	11 (61.1)
Racial/ethnic group				
Asian	14,162 (3.5)	6	0.042 (0.02-0.09)	3 (50)
Black	73,321 (18.0)	23	0.031 (0.02-0.05)	18 (78.3)
Hispanic/Latino	73,945 (18.1)	17	0.023 (0.01-0.04)	13 (76.5)
White	226,615 (55.6)	58	0.026 (0.02-0.03)	37 (63.8)

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Distribution of Calcinosis Cutis Cases by Age Group