

# Onychomycosis in Underrepresented Groups: An All of Us Database Analysis

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## Short Report

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# Abstract

Few research studies evaluating the impact of dermatologic diseases in the United States (US) have adequately included underrepresented groups. All of Us (AoU) is an ongoing precision medicine-based research initiative by the National Institutes of Health (NIH) that facilitates research in populations traditionally underrepresented in biomedical research by prioritizing them for data collection. Our objective was to evaluate the burden of onychomycosis in underrepresented groups defined by the framework provided by AoU. The AoU Registered Tier dataset version 5 was used which includes data collected between May 30, 2017 and April 1, 2021. We conducted a cross-sectional analysis linking survey and electronic health record (EHR) data to estimate the prevalence of onychomycosis in underrepresented groups defined by race, ethnicity, age ( $\geq 75$  years), disability, sexual orientation/gender identity (LGBTQIA+), income (annual household income  $\leq$  \$35 000) and education (less than a high school degree). The latest All of Us data release includes 329,038 participants. Of these, 251,597 (76%) had EHR data and 13,874 had onychomycosis (overall prevalence, 5.5%; 95% CI, 5.4– 5.6). Multivariate analyses adjusted by tinea pedis, diabetes mellitus, immune compromise, nail psoriasis, and insurance status, in addition to the aforementioned variables, revealed that, compared with White participants, Black and Hispanic participants had a higher adjusted odds of onychomycosis (OR, 1.29; 95% CI, 1.23–1.36 and OR, 1.24; 95% CI, 1.17–1.31, respectively). Higher adjusted odds of onychomycosis were also observed in underrepresented groups. Our findings suggest a disproportionately high burden of onychomycosis in underrepresented groups, although further studies are needed to replicate our findings and address this disparity.

## Introduction

Onychomycosis was traditionally defined as a nondermatophytic infection of the nail, but the term has since been expanded to include all fungal infections of the nail caused by dermatophytes, yeasts, or nondermatophyte molds [1]. Onychomycosis may involve any component of the nail unit, including the matrix, bed, or plate, causing pain, discomfort, and/or disfigurement, resulting in physical and occupational limitations [1]. Prior studies have estimated the overall prevalence of onychomycosis in the North American population as between 2% and 9% [2–4]. Additionally, an increased prevalence of onychomycosis among elderly patients has been identified [1–3, 5, 8–9]. Underrepresented groups defined by features other than age may also be at an increased risk of onychomycosis; however, this has never been evaluated in a US-based epidemiologic study. All of Us (AoU) is an ongoing precision medicine-based research initiative by the NIH that includes participants from populations traditionally underrepresented in biomedical research [6]. The novel AoU framework defines underrepresented groups, which are prioritized for data collection and analysis, not only by race/ethnicity but by age ( $\geq 75$  years), physical disability (unable to perform everyday physical activities), sexual orientation/gender identity (LGBTQIA+), income (annual household income  $\leq$  \$35 000 US dollars), and education (less than a high school degree) [7]. Here we evaluate the burden of onychomycosis in underrepresented groups defined by the AoU framework.

## Methods

We evaluated AoU Registered Tier dataset version 5, which includes data collected between May 30, 2017 and April 1, 2021. We conducted a cross-sectional analysis linking survey and electronic health record (EHR) data to estimate the prevalence of onychomycosis in underrepresented groups defined by race, ethnicity, age ( $\geq 75$  years), disability (unable to perform everyday physical activities), sexual orientation/gender identity (LGBTQIA+), income (annual household income  $\leq$ \$35 000) and education (less than a high school degree).

We estimated the prevalence of onychomycosis as the number of study participants with onychomycosis divided by the total number of study participants with EHR data available and calculated the 95% CI for the proportion using the formula  $p \pm 1.96 \times \sqrt{\frac{p \times (1 - p)}{n}}$  where  $p$  is the proportion and  $n$  is the sample size. Age-adjusted univariate and multivariable logistic regression were used to estimate the odds ratios (ORs) of an onychomycosis diagnosis for participants in each category. Multivariable regression controlled for age category, race/ethnicity, gender identity, sexual orientation, household income, educational attainment, physical disability, health insurance status, tinea pedis, diabetes mellitus, immune compromise, and nail psoriasis. A 2-tailed  $P$  value of  $< 0.05$  was considered statistically significant. Analysis was conducted using R version 4.0.5 in the Jupyter Notebook environment.

## Results

The latest All of Us data release includes 329,038 participants. Of these, 251,597 (76%) had EHR data and 13,874 had onychomycosis (overall prevalence, 5.5%; 95% CI, 5.4– 5.6). Multivariate analyses adjusted by aforementioned demographic factors revealed that, compared with White participants, Black and Hispanic participants had a higher adjusted odds of onychomycosis (OR, 1.29; 95% CI, 1.23–1.36 and OR, 1.24; 95% CI, 1.17–1.31, respectively; Table 1). Higher adjusted odds of onychomycosis were also observed in underrepresented groups defined by: age  $\geq 75$  years (OR, 1.85; 95% CI, 1.75–1.96), LGBTQIA+ status (OR, 1.12; 95% CI, 1.05–1.19), less than a high school education (OR, 1.05; 95% CI, 0.98–1.13), income  $\leq$ \$35,000 (OR, 1.04; 95% CI, 0.99–1.09), and physical disability (OR, 1.14; 95% CI, 1.08–1.20; Table 2).

Table 1  
Underrepresented Populations in the All of Us Cohort

	All Enrolled (n = 315297)		No EHR Data (n = 124418)		EHR Data (n = 190576)		Onychomycosis (n = 7244)	
	n	%	n	%	n	%	n	%
Race/Ethnicity								
White	172753	52.50	33960	43.85	138793	55.16	7244.0	44.87
Black	67897	20.64	20333	26.26	47564	18.90	3171	19.64
Hispanic	60535	18.40	15340	19.81	45195	17.96	2584	16.00
Other	21726	6.60	6086	7.86	15640	6.22	563	3.49
Age								
< 75	309632	94.11	74251	95.88	235381	93.57	12132	87.44
≥ 75	19375	5.89	3189	4.12	16186	6.43	11742	12.56
Gender								
M	124196	37.75	31341	40.47	92855	36.91	5992	43.19
F	197949	60.17	44159	57.02	153790	61.13	7606	54.82
Other <sup>a</sup>	6862	2.09	1940	2.51	4922	1.96	276	1.99
LGBTQIA + Status								
N	290158	88.19	67205	86.78	222953	88.63	1467	10.57
Y	38849	11.81	10235	13.22	28614	11.37	12407	89.43
Education								
Completed College	140529	42.71	28258	36.49	112271	44.63	5512	39.73
Completed High School	148725	45.20	37446	48.35	111279	44.23	6391	46.06
Less than High School	32177	9.78	9303	12.01	22874	9.09	1639	11.81
Income <sup>b</sup>								
> 35K	191368	58.17	40190	51.90	151178	60.09	8078	58.22
≤ 35k	73942	22.47	20571	26.56	53371	21.22	3026	21.81
Health insurance								

	All Enrolled (n = 315297)		No EHR Data (n = 124418)		EHR Data (n = 190576)		Onychomycosis (n = 7244)	
Yes	296627	90.16	65896	85.09	230731	91.72	13194	95.10
No	23235	7.06	8314	10.74	14921	5.93	387	2.79
Disability <sup>c</sup>								
w/o disability	284833	86.59	61596	79.54	223287	88.76	11416	84.23
w/ disability	31413	9.55	6862	8.86	24551	9.76	2138	15.77
Columns for risk factors present the prevalence of each risk factor in each subgroup. BMI indicates body mass index; EHR indicates electronic health record; LGBTQIA+, lesbian, gay, bisexual, transgender, queer, intersex, and asexual.								
<sup>a</sup> The "other" category comprises the following categories from All of Us questionnaires: Another single population: participants self-reporting either Middle Eastern or North African or Native Hawaiian or other Pacific Islander (please note All of Us does not provide disaggregated data on these yet). None of these populations: participants self-reporting "None of these fully describe me" (options are White, Black, African American, or African, Asian, Middle Eastern or North African, Native Hawaiian or other Pacific Islander). > 1, non-Hispanic > 1 race selected.								
<sup>b</sup> Income corresponds to annual household income.								
<sup>c</sup> Disability indicates physical disability (participants who answered that they cannot carry out every day physical activities at all or only a little).								

Table 2  
Prevalence of Onychomycosis in Underrepresented Groups Enrolled in All of Us

Group	Age (SD)	Prevalence estimate (95% CI)	Age-Adjusted Regression OR (95% CI)	Multivariate Regression OR (95% CI)
Race/Ethnicity				
White	55.18 (16.74)	0.052 (0.051–0.053)	Ref	Ref
Black	50.15 (14.48)	0.067 (0.064–0.069)	1.72 (1.65–1.80)	1.29 (1.23–1.36)
Hispanic	45.07 (15.72)	0.057 (0.055–0.059)	1.75 (1.66–1.83)	1.24 (1.17–1.31)
Other <sup>b</sup>	44.88 (16.85)	0.036 (0.033–0.039)	1.03 (0.94–1.13)	0.89 (0.81–0.98)
Age				
< 75	49.88 (15.55)	0.052 (0.051–0.052)	Ref	Ref
≥ 75	79.37 (2.87)	0.108 (0.103–0.112)	2.22 (2.10–2.34)	1.85 (1.75–1.96)
Gender				
M	54.14 (16.54)	0.065 (0.063–0.066)	Ref	Ref
F	50.48 (16.60)	0.049 (0.048–0.051)	0.86 (0.83–0.89)	0.86 (0.83–0.89)
Other	47.93 (17.71)		1.06 (0.93–2.00)	0.98 (0.85–1.11)

<sup>a</sup>Multivariate model adjusts for race, ethnicity, age, sex, household income, education, physical disability, and health insurance status.

<sup>b</sup>The "other" category comprises the following categories from All of Us questionnaires: Another single population: participants self-reporting either Middle Eastern or North African or Native Hawaiian or other Pacific Islander (please note All of Us does not provide disaggregated data on these yet). None of these populations: participants self-reporting "None of these fully describe me" (options are White, Black, African American, or African, Asian, Middle Eastern or North African, Native Hawaiian or other Pacific Islander). > 1, non-Hispanic > 1 race selected.

<sup>c</sup>LGBTQIA+ indicates lesbian, gay, bisexual, transgender, queer, intersex, and asexual; OR, odds ratio.

<sup>d</sup>Income corresponds to annual household income.

<sup>e</sup>Disability indicates physical disability (participants who answered that they cannot carry out every day physical activities at all or only a little).

Group	Age (SD)	Prevalence estimate (95% CI)	Age-Adjusted Regression OR (95% CI)	Multivariate Regression OR (95% CI)
LGBTQIA + Status <sup>c</sup>				
N	52.54 (16.57)	0.056 (0.055–0.057)	Ref	Ref
Y	45.86 (16.59)	0.051 (0.049–0.054)	1.87 (1.12–1.26)	1.12 (1.05–1.19)
Education				
Completed College	53.64 (16.96)	0.049 (0.048–0.050)	Ref	Ref
Completed High School	50.10 (16.69)	0.057 (0.056–0.059)	1.38 (1.33–1.43)	1.03 (0.89–1.14)
Less than High School	50.44 (14.79)	0.072 (0.068–0.075)	1.81 (1.70–1.91)	1.05 (0.98–1.13)
Income <sup>d</sup>				
> 35K	53.31 (16.56)	0.053 (0.052–0.055)	Ref	Ref
≤ 35k	47.50 (15.98)	0.057 (0.055–0.059)	1.36 (1.30–1.43)	1.04 (0.99–1.09)
Health insurance				
No	44.51 (13.03)	0.026 (0.023–0.028)	Ref	Ref
Yes	52.37 (16.79)	0.057 (0.056–0.058)	0.64 (0.57–0.70)	0.58 (0.52–0.64)

<sup>a</sup>Multivariate model adjusts for race, ethnicity, age, sex, household income, education, physical disability, and health insurance status.

<sup>b</sup>The "other" category comprises the following categories from All of Us questionnaires: Another single population: participants self-reporting either Middle Eastern or North African or Native Hawaiian or other Pacific Islander (please note All of Us does not provide disaggregated data on these yet). None of these populations: participants self-reporting "None of these fully describe me" (options are White, Black, African American, or African, Asian, Middle Eastern or North African, Native Hawaiian or other Pacific Islander). > 1, non-Hispanic > 1 race selected.

<sup>c</sup>LGBTQIA+ indicates lesbian, gay, bisexual, transgender, queer, intersex, and asexual; OR, odds ratio.

<sup>d</sup>Income corresponds to annual household income.

<sup>e</sup>Disability indicates physical disability (participants who answered that they cannot carry out every day physical activities at all or only a little).

Group	Age (SD)	Prevalence estimate (95% CI)	Age-Adjusted Regression OR (95% CI)	Multivariate Regression OR (95% CI)
Disability <sup>e</sup>				
w/o disability	51.55 (16.99)	0.051 (0.050–0.052)	Ref	Ref
w/ disability	53.64 (13.79)	0.087 (0.084–0.091)	1.74 (1.66–1.83)	1.14 (1.08–1.20)
<sup>a</sup> Multivariate model adjusts for race, ethnicity, age, sex, household income, education, physical disability, and health insurance status.				
<sup>b</sup> The "other" category comprises the following categories from All of Us questionnaires: Another single population: participants self-reporting either Middle Eastern or North African or Native Hawaiian or other Pacific Islander (please note All of Us does not provide disaggregated data on these yet). None of these populations: participants self-reporting "None of these fully describe me" (options are White, Black, African American, or African, Asian, Middle Eastern or North African, Native Hawaiian or other Pacific Islander). > 1, non-Hispanic > 1 race selected.				
<sup>c</sup> LGBTQIA+ indicates lesbian, gay, bisexual, transgender, queer, intersex, and asexual; OR, odds ratio.				
<sup>d</sup> Income corresponds to annual household income.				
<sup>e</sup> Disability indicates physical disability (participants who answered that they cannot carry out every day physical activities at all or only a little).				

## Discussion

Numerous prior studies have demonstrated that the prevalence of onychomycosis increases with age [1–3, 5, 8–9]. Welsh et al. reported an onychomycosis prevalence increased up to 30% in patients over 60 years old, and Mayo et al. reported a 50% prevalence in patients over 70 years old [8–9]. Proposed explanations for this association include aging-related reduction in peripheral circulation, increasing prevalence of diabetes, repeated nail trauma, slowing nail growth, longer exposure to pathogenic fungi, deteriorating immune function, inactivity, difficulty cutting toenails or maintaining good foot care, and stays at nursing homes [1, 10]. Similarly, we found that an increased prevalence of onychomycosis in participants aged 75 and over. Notably, in our analyses the association between age  $\geq$  75 years and onychomycosis decreased (but remained significant) after adjustment for diabetes, immune dysfunction, and physical disability. These findings suggest that diabetes, immune dysfunction, and physical disability may play a role in the increased risk of onychomycosis observed in older adults. We also found an independently increased risk of onychomycosis in participants with physical disabilities. Similar factors, such as inactivity and difficulty with nail and foot care likely explain this association.

Multivariate analysis also identified increased risk of onychomycosis among individuals with skin of color and those with low socioeconomic status (i.e. annual household income  $\leq$  \$35 000 or educational

attainment less than a high school degree). Although the association between race and onychomycosis risk in adults has not been specifically evaluated in any prior US-based epidemiologic study, other dermatophyte infections have been shown to disproportionately affect Black Americans [11]. Low socioeconomic status has also been demonstrated to increase the risk of other dermatophyte infections. Increasing societal crowding and sharing of clothes/shoes and personal hygiene products may explain this association [11].

Last, we report the novel finding of increased risk of onychomycosis among the LGBTQIA + population. Prior studies evaluating the epidemiology of fungal skin infections in the LGBTQIA + population have been limited to sexually transmitted diseases. As a result, we have no true basis of comparison for this finding.

Prior studies have reported the overall prevalence of onychomycosis in North America as between 2–9%, with an increased prevalence in the elderly [1–5]. The consistency of our findings with these prior studies indicates that the All of Us database provides scientifically consistent data that can be utilized to evaluate the burden of dermatologic disease among underrepresented groups. Our findings suggest that underrepresented groups may experience a disproportionately high burden of onychomycosis.

## Declarations

**Funding sources:** None

**Conflicts of Interest:** None declared.

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