



Published in final edited form as:

Diabetes Obes Metab. 2025 June ; 27(6): 3536–3541. doi:10.1111/dom.16365.

Incidence of chronic kidney disease among adults with prediabetes in the CURE-CKD registry, 2013–2020

Radica Z. Alicic, MD^{1,2}, Obidiugwu K. Duru, MD³, Cami R. Jones, PhD¹, Lindsey M. Kornowske, MS¹, Kenn B. Daratha, PhD¹, Christina L. Reynolds, PhD¹, Meda E. Pavkov, MD⁴, Alain K. Koyama, ScD⁴, Fang Xu, PhD⁴, Susanne B. Nicholas, MD^{3,5}, Joshua J. Neumiller, PharmD^{1,6}, Keith C. Norris, MD^{3,5}, Kelly A. Hennessey, MD⁷, Katherine R. Tuttle, MD^{1,8}

¹Providence Medical Research Center, Providence Inland Northwest Health, Spokane, Washington, USA

²Department of Medicine, University of Washington School of Medicine, Seattle, Washington, USA

³Division of General Internal Medicine & Health Services Research, David Geffen School of Medicine, University of California, Los Angeles, California, USA

⁴Division of Diabetes Translation, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

⁵Division of Nephrology, David Geffen School of Medicine, University of California, Los Angeles, California, USA

⁶College of Pharmacy and Pharmaceutical Sciences, Washington State University, Spokane, Washington, USA

⁷Department of Internal Medicine, Yale School of Medicine, New Haven, Connecticut, USA

⁸Division of Nephrology, University of Washington School of Medicine, Seattle, Washington, USA

Keywords

chronic kidney disease; observational study; prediabetes

Correspondence Radica Z. Alicic, Providence Medical Research Center, Providence Inland Northwest Health, Spokane, WA, USA. radica.alicic@providence.org.

AUTHOR CONTRIBUTIONS

All authors met the International Committee of Medical Journal Editors criteria for authorship for this article. RZA, OKD and KRT led project development from concept through data acquisition, curation, analyses, interpretation and drafting the manuscript. CRJ, LMK, KBD, CLR, SBN and KCN contributed to data acquisition, curation, analyses and drafting the manuscript. MEP, AKK, FX, JJN and KAH provided feedback on the manuscript. RZA is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

PEER REVIEW

The peer review history for this article is available at <https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.16365>.

1 | BACKGROUND

Prediabetes is a common condition characterized by sustained sub-diabetic hyperglycaemia that is on the rise globally.¹ In the United States, one in three adults, or approximately 98 million individuals, had prediabetes in 2021.² People with prediabetes have heightened risks of diabetes and cardiovascular disease (CVD).³ Emerging data suggest that prediabetes may also lead to chronic kidney disease (CKD), a major public health problem that may be attenuated by control of hyperglycaemia and other risk factors such as hypertension.⁴⁻⁷ The study aim was to estimate CKD incidence in a large real-world population with prediabetes.

2 | METHODS

2.1 | Data source

The study population was drawn from the Providence and University of California Los Angeles Health (UCLA) electronic health records (EHRs) based Center for Kidney Disease Research, Education, and Hope (CURE-CKD) Registry that includes persons with or at risk for CKD from diabetes mellitus, hypertension and prediabetes.⁸ The study was approved by Providence and UCLA Health institutional review boards and conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines for cohort studies. Demographic data were abstracted from the EHR; race categories include only non-Hispanic individuals.

2.2 | Study population and design

Between 1 January 2013, and 31 December 2020, adults (≥ 18 years) were identified with prediabetes by the American Diabetes Association definition-based criteria: HbA1c of 5.7%–6.4%, two fasting blood glucose measures of 100–125 mg/dL or two random blood glucose measures of 140–199 mg/dL. Individuals were included in the analysis at the first identification of prediabetes any time during 2013–2020, regardless of the date of entry, if they were tested for CKD and diabetes at baseline and during follow-up. Laboratory evidence of CKD, an administrative CKD code, or kidney failure were exclusionary (Table S1). Baseline demographic and clinical characteristics were obtained during the 6 months following the identification of prediabetes. The index date for follow-up started 6 months after entry into the cohort and ended at the onset of CKD or diabetes, or the last encounter before 31 December 2020, whichever came first (Figure S1). Individuals who developed diabetes before CKD were removed from the risk set at the time of diabetes identification. Those included in the study had more frequent hypertension but were otherwise similar to those excluded from the study for missing measures (Table S2).

2.3 | Outcomes

The primary outcome was CKD onset identified by two estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m² (CKD Epidemiology Collaboration 2021 equation with serum creatinine), urine albumin-to-creatinine ratio (UACR) ≥ 30 mg/g, urine protein-to-creatinine ratio (UPCR) ≥ 0.15 g/g for ≥ 90 days, or by a new administrative code for CKD. Diabetes was identified by HbA1c $\geq 6.5\%$, two blood glucose measures (≥ 126 mg/dL fasting/ ≥ 200 mg/dL random), administrative codes or a prescription for blood

glucose-lowering medication. Hypertension was identified by two blood pressures $\geq 140/90$ mmHg or administrative codes (Table S1).

2.4 | Statistical analysis

Baseline characteristics were reported overall and by hypertension or atherosclerotic CVD (ASCVD) status. Descriptive measures are reported as mean $\pm$ standard deviation (SD) for normally distributed variables, median and interquartile range (IQR) for skewed variables or frequencies for categorical variables.

The overall incidence of CKD was calculated as the number of CKD cases/1000 person-years at risk and directly standardized by age (reference: 18–39), race and ethnicity (reference: non-Hispanic [NH] White), and sex (reference: men) to the 2020 U.S. Census Bureau population. Estimates by demography were standardized by the remaining variables, for example, age estimates were standardized by sex, race and ethnicity. CKD incidence was also assessed by hypertension or ASCVD status at cohort entry. Incidence rate ratios (IRRs) and 95% confidence intervals (CIs) were estimated relative to the reference group for each demographic category. The threshold for statistical significance was selected at $p < 0.05$. Bonferroni correction for demographic categories resulted in significance threshold adjustments for age ($p < 0.02$) and race and ethnicity ($p < 0.01$). Incidence was computed using the procedure PROC STDRA in SAS version 9.4. All other analyses were completed in R version 4.2.2.

3 | RESULTS

3.1 | Characteristics of the study population

The study included 281 933 individuals with prediabetes. Mean $\pm$ SD age was 57 ± 15 years, and 55% were women. Baseline HbA1c was $5.9 \pm 0.2\%$, BMI was 30 ± 7 kg/m² and eGFR was 93.3 ± 15.7 mL/min/1.73 m². Persons with hypertension or ASCVD had a similar level of HbA1c but higher BMI and lower eGFR than those without (Table 1).

3.2 | CKD incidence

Over a median follow-up of 2.5 (IQR 1.3–4.2) years, 3.6% ($n = 10\,104$) of persons with prediabetes developed CKD, mostly ascertained by eGFR < 60 mL/min/1.73 m² (81.4%, $n = 8221$; Figure S2). The overall age-, sex- and race and ethnicity-standardized CKD incidence was 10.9 (95% CI 10.5–11.2) cases/1000 person-years. The incidence of CKD was lower for women compared with men (IRR 0.92, [95% CI: 0.87–0.98], $p = 0.009$). It increased exponentially with age and was higher among Native Hawaiian/Pacific Islander (7.94, [1.66–37.95], $p = 0.01$) and NH Black (1.56, [1.36–1.78], $p < 0.001$) populations compared with the NH White population (Figure 1). Incidence was higher in participants with hypertension or ASCVD at baseline, 11.9 (95% CI 11.5–12.3) cases/1000 person-years. In persons without hypertension or ASCVD, CKD incidence was 9.4 (8.9–9.9) cases/1000 person-years (Table S3).

4 | CONCLUSIONS

Onset of CKD was common within a short timeframe among persons with prediabetes. Incident CKD was more frequent in the presence of hypertension or ASCVD. CKD incidence was higher in men, in older age and in Native Hawaiian or Pacific Islander or NH Black groups.

The Framingham Heart Study offspring cohort previously reported that impaired fasting glucose and impaired glucose tolerance conferred 25% higher odds of developing CKD compared with normoglycaemia.⁴ The Renal Iohexol Clearance Survey in Tromsø 6 (RENIS-T6) and the RENIS Follow-Up Study of a general population found nearly twofold higher odds of glomerular hyperfiltration and high-normal albuminuria in participants with prediabetes.⁹ Furthermore, higher eGFR levels across the spectrum of hyperglycaemia have been demonstrated in prediabetes.¹⁰ Since glomerular hyperfiltration is a mediator of progressive kidney damage, these observations offer a plausible mechanistic explanation for CKD onset in prediabetes.^{11,12}

Our study has notable strengths, including assessment for CKD in a large, real-world population with prediabetes. Persistence of abnormal laboratory measures for ≥ 90 days increases the reliability of the CKD incidence estimates. To support the identification of CKD without diabetes, glycaemic measures were required for individuals to be included in the risk set. However, the study is limited by the use of data from the CURE-CKD Registry. Therefore, our findings may not be generalizable to geographical regions with different populations or to individuals who have not interacted with these U.S. health systems. We also did not have a normoglycaemic group for comparison. Lack of death data and unmeasured confounders are further limitations. Although inferences can be made about associations between prediabetes and CKD, they do not establish causality by this observational analysis.

In conclusion, relatively rapid-onset CKD was common in persons with prediabetes, especially if they also had hypertension or ASCVD. The population with prediabetes, and certain subgroups characterized by older age, male sex, Native Hawaiian or Pacific Islander or NH Black race, may benefit from proactive monitoring and interventions to reduce CKD risks such as the control of glycaemia and hypertension.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

This manuscript was written and processed by authors, and no assistance was received by any other individual.

CONFLICT OF INTEREST STATEMENT

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. RZA is supported by NIH research grants OT2HL161847, OT2OD032581, U24TR001608 and CDC project numbers 75D301-21-P-12254 and 75D301-23-C-18264 and reports other support from Benaroya Research Institute, Travele Therapeutics Inc., the Doris Duke Charitable Foundation, Bayer AG, AstraZeneca, Novo Nordisk, the George Institute for Global Health, CareDx

and KBP BioSciences and personal fees from Boehringer Ingelheim, Bayer Pharmaceuticals and Eli Lilly. She also reports being a member of the Executive Council for the American College of Physicians, Washington Chapter. OKD is supported by NIH research grants R25HL161609, R18DK122372, R01DK124503, R01DK127733, R01AI135029, P30AG021684 and the CDC cooperative agreement U18DP006535 and receives research support from the Patient-Centered Outcomes Research Institute and the Terasaki Institute of Biomedical Innovation. CRJ is supported by NIH research grants R01MD014712, OT2OD032581 and CDC project numbers 75D301-21-P-12254 and 75D301-23-C-18264 and reports other support from Benaroya Research Institute, Traverre Therapeutics Inc. and the Doris Duke Charitable Foundation. LMK is supported by an NIH research grant OT2OD032581 and CDC project numbers 75D301-21-P-12254 and 75D301-23-C-18264; and reports other support from Benaroya Research Institute and Traverre Therapeutics Inc. KBD is supported by NIH research grants R01MD014712, OT2OD032581 and CDC project numbers 75D301-21-P-12254 and 75D301-23-C-18264; and reports other support from Benaroya Research Institute, Traverre Therapeutics Inc. and the Doris Duke Charitable Foundation. CLR is supported by NIH research grant OT2OD032581 and CDC project numbers 75D301-21-P-12254 and 75D301-23-C-18264 and reports other support from Traverre Therapeutics Inc. and the Doris Duke Charitable Foundation. MEP has no disclosures to report. AAK has no disclosures to report. FX has no disclosures to report. SBN is supported by NIH research grants R01MD014712, RF00250-2022-0038, U2CDK129496 and P50MD017366 and CDC project number 75D301-21-P-12254 and received research support from Traverre Therapeutics Inc., Terasaki Institute of Biomedical Innovation and personal fees and other support from AstraZeneca, Bayer AG, Gilead, Novo Nordisk, Boehringer Ingelheim, Eli Lilly and Vertex. She also reports having a pending US Patent Provisional Application for a Novel Small Molecule Drug to Treat Diabetic Kidney Disease. Additionally, she participates in an NIH/NIDDK and PCORI advisory board for Health System Outreach to Eliminate Disparities in Living Kidney Transplants (STEPS) and is President of Women in Nephrology and a board member of the National Kidney Foundation of Southern California. JJN is supported by an NIH research grant OT2OD032581 and reports personal fees and other support from the American College of Clinical Pharmacy, Bayer AG, Sanofi, Novo Nordisk, Boehringer Ingelheim, Eli Lilly, Proteomics International and Dexcom. He also reports being on the Board of Directors for the American Diabetes Association. KCN is supported in part by NIH research grants UL1TR001881, P30AG021684, U2CDK129496 and P50MD017366 and reports personal fees from Atlantis Dialysis Inc. and AstraZeneca. KAH has no disclosures to report. KRT is supported by NIH research grants R01MD014712, U2CDK114886, UL1TR002319, U54DK083912, U01DK100846, OT2HL161847, UM1AI109568 and OT2OD032581 and CDC project numbers 75D301-21-P-12254 and 75D301-23-C-18264. She has also received investigator-initiated grant support from Traverre Therapeutics Inc., Bayer, Benaroya Research Institute and the Doris Duke Charitable Foundation. She reports consultancy fees from AstraZeneca, Boehringer Ingelheim, Eli Lilly, Novo Nordisk, Traverre Therapeutics Inc. and Pfizer and speaker fees from Novo Nordisk. Additionally, she reports being chair of data safety monitoring boards for the National Institute of Diabetes and Digestive and Kidney Diseases and George Clinical Institute, and member of the data safety monitoring board for AstraZeneca. She reports leadership roles as chair for the Diabetic Kidney Disease Collaborative for the American Society of Nephrology, chair for the Kidney Week 2025 Program Committee and a member of the American Heart Association/American College of Cardiology Cardiovascular-Kidney-Metabolic Guideline Committee.

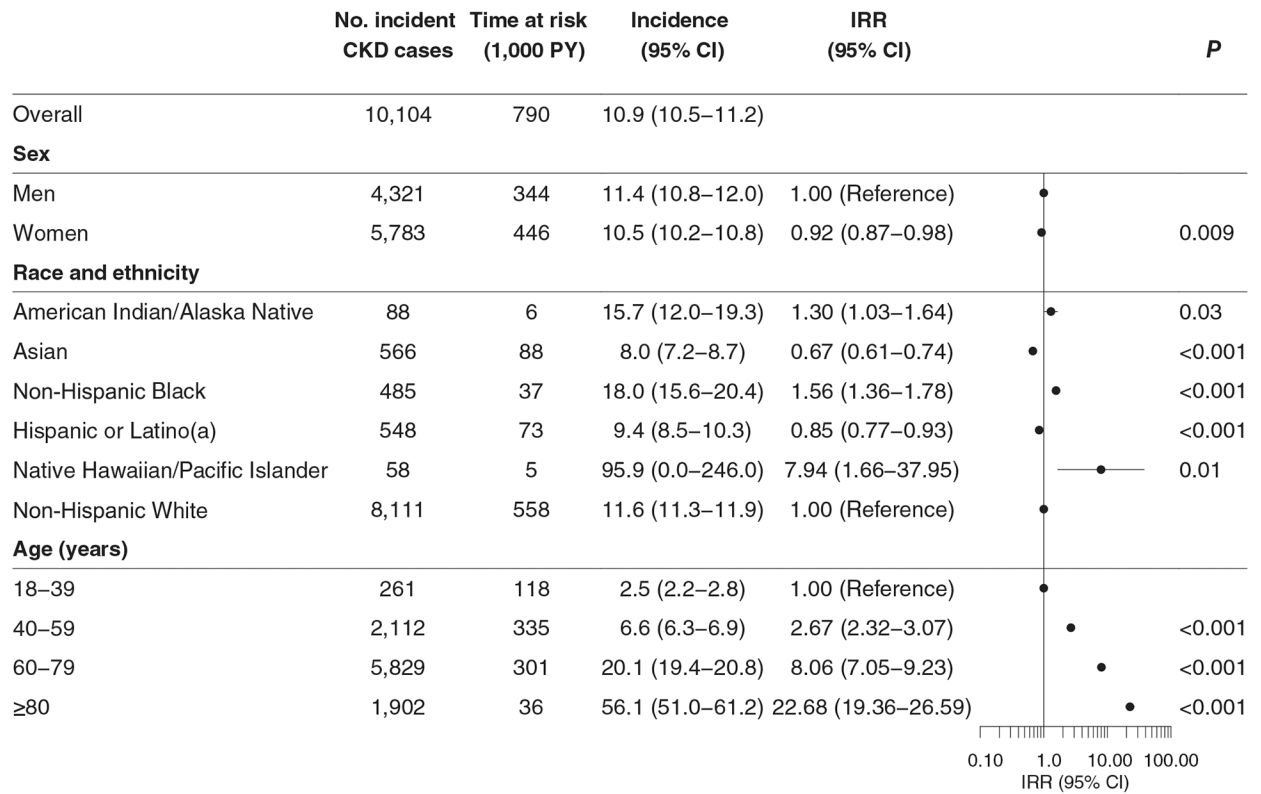
DATA AVAILABILITY STATEMENT

The dataset for this study are not publicly available due to privacy and ethical restrictions. The de-identified dataset may be available from the corresponding author upon request and the signing of a data use agreement.

REFERENCES

1. Rooney MR, Fang M, Ogurtsova K, et al. Global prevalence of prediabetes. *Diabetes Care*. 2023;46:1388–1394. [PubMed: 37196350]
2. Diabetes Statistics. Accessed July 1, 2024. <https://www.niddk.nih.gov/health-information/health-statistics/diabetes-statistics>.
3. Ali MK, Bullard KM, Saydah S, Imperatore G, Gregg EW. Cardiovascular and renal burdens of prediabetes in the USA: analysis of data from serial cross-sectional surveys, 1988–2014. *Lancet Diabetes Endocrinol*. 2018;6:392–403. [PubMed: 29500121]
4. Fox CS, Larson MG, Leip EP, Meigs JB, Wilson PW, Levy D. Glycemic status and development of kidney disease: the Framingham Heart Study. *Diabetes Care*. 2005;28:2436–2440. [PubMed: 16186276]
5. Echouffo-Tcheugui JB, Narayan KM, Weisman D, Golden SH, Jaar BG. Association between prediabetes and risk of chronic kidney disease: a systematic review and meta-analysis. *Diabetic Med*. 2016;33:1615–1624. [PubMed: 26997583]

6. Zivkovic M, Tonjes A, Baber R, Wirkner K, Loeffler M, Engel C. Prevalence of moderately increased albuminuria among individuals with normal HbA1c level but impaired glucose tolerance: results from the LIFE-adult-study. *Endocrinol Diabetes Metab.* 2018;1:e00030. [PubMed: 30815561]
7. Plantinga LC, Crews DC, Coresh J, et al. Prevalence of chronic kidney disease in US adults with undiagnosed diabetes or prediabetes. *Clinic J Am Soc Nephrol.* 2010;5:673–682.
8. Tuttle KR, Alicic RZ, Duru OK, et al. Clinical characteristics of and risk factors for chronic kidney disease among adults and children: an analysis of the CURE-CKD registry. *JAMA Netw Open.* 2019;2:e1918169. [PubMed: 31860111]
9. Melsom T, Schei J, Stefansson VT, et al. Prediabetes and risk of glomerular hyperfiltration and albuminuria in the general nondiabetic population: a prospective cohort study. *Am J Kidney Dis.* 2016;67:841–850. [PubMed: 26744126]
10. Okada R, Wakai K, Naito M, et al. Renal hyperfiltration in prediabetes confirmed by fasting plasma glucose and hemoglobin A1c. *Ren Fail.* 2012;34:1084–1090. [PubMed: 22978359]
11. Brenner BM, Lawler EV, Mackenzie HS. The hyperfiltration theory: a paradigm shift in nephrology. *Kidney Int.* 1996;49:1774–1777. [PubMed: 8743495]
12. Ruggenenti P, Porrini EL, Gaspari F, et al. Glomerular hyperfiltration and renal disease progression in type 2 diabetes. *Diabetes Care.* 2012;35:2061–2068. [PubMed: 22773704]

**FIGURE 1.**

Chronic kidney disease incidence standardized by age, sex, race and ethnicity, and incidence rate ratios in persons with prediabetes. Race categories include non-Hispanic individuals only. CI, confidence interval; CKD, chronic kidney disease; IRR, incidence rate ratio; PY, person-years.

TABLE 1
Characteristics of patients identified with prediabetes in 2013–2020 ($n = 281\,933$).

	Overall cohort	Hypertension or ASCVD	
		Yes	No
Patients, n (% of total)	281 933 (100.0)	172 875 (61.3)	109 058 (38.7)
Demographics			
Sex, n (%)			
Men	126 344 (44.8)	82 556 (47.8)	43 788 (40.2)
Women	155 589 (55.2)	90 319 (52.2)	65 270 (59.8)
Age, years, mean, SD	57, 15	59, 14	53, 15
Age category, n (%)			
18–39	41 479 (14.7)	18 382 (10.6)	23 097 (21.2)
40–59	115 083 (40.8)	66 027 (38.2)	49 056 (45.0)
60–79	109 299 (38.8)	76 433 (44.2)	32 866 (30.1)
≥80	16 072 (5.7)	12 033 (7.0)	4039 (3.7)
Race and ethnicity, n (%)			
American Indian/Alaska Native	2112 (0.7)	1433 (0.8)	679 (0.6)
Asian	31 210 (11.1)	14 323 (8.3)	16 887 (15.5)
Non-Hispanic Black	12 981 (4.6)	8309 (4.8)	4672 (4.3)
Hispanic or Latino(a)	26 897 (9.5)	14 087 (8.1)	12 810 (11.7)
Native Hawaiian/other Pacific Islander	1671 (0.6)	1054 (0.6)	617 (0.6)
Multiple ^a	8378 (3.0)	4641 (2.7)	3737 (3.4)
Non-Hispanic White	198 684 (70.5)	129 028 (74.6)	69 656 (63.9)
Clinical characteristics			
Hypertension, n (%)	167 992 (59.6)	167 992 (97.2)	0 (0.0)
ASCVD, n (%)	31 850 (11.3)	31 850 (18.4)	0 (0.0)
BMI, kg/m ² , n (%)	223 015 (79.1)	149 003 (86.2)	74 012 (67.9)
Mean, SD	30, 7	30, 8	28, 7
eGFR, mL/min/1.73 m ² , n (%)	259 707 (92.1)	159 875 (92.5)	99 832 (91.5)
Mean, SD	93.3, 15.7	91.8, 15.1	95.5, 16.3
HbA1c, %, n (%)	196 299 (69.6)	115 246 (66.7)	81 053 (74.3)
Mean, SD	5.9, 0.2	5.9, 0.2	5.9, 0.2

	Hypertension or ASCVD	
	Overall cohort	No
FBG, mg/dL, <i>n</i> (%)	35 330 (12.5)	21 061 (12.2)
Mean, SD	102.5, 12.6	103.2, 11.6
RBG, mg/dL, <i>n</i> (%)	247 843 (87.9)	154 432 (89.3)
Mean, SD	111.2, 22.3	112.7, 21.3
SBP, mm Hg, <i>n</i> (%)	231 620 (82.2)	155 059 (89.7)
Mean, SD	127, 16	131, 15
UACR, mg/g, <i>n</i> (%)	8815 (3.1)	5733 (3.3)
Median, IQR	7.1 (4.0–13.7)	7.4 (4.2, 14.2)
UPCR, g/g, <i>n</i> (%)	618 (0.2)	493 (0.3)
Median (IQR)	0.2 (0.1–0.3)	0.16 (0.10, 0.29)
		0.17 (0.10, 0.33)

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; Hb, haemoglobin; IQR: interquartile range; RBG, random blood glucose; SBP, systolic blood pressure; SD, standard deviation; UACR, urine albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.

^aIncludes patients with two or more race categories.