Progression to Diabetes Among Older Adults With Hemoglobin A1c-Defined Prediabetes in the US

Alain K. Koyama, ScD; Kai McKeever Bullard, PhD; Meda E. Pavkov, MD; Joohyun Park, PhD; Russ Mardon, PhD; Ping Zhang, PhD

Introduction

Data on progression to diabetes in older adults are essential to guide policy because lifestyle intervention programs may not be cost-effective when progression rates are low. Existing data are limited and show a wide range of progression rates. Although recommendations for using hemoglobin A1c (HbA1c) to diagnose prediabetes are common, the progression rate of HbA1c-defined prediabetes in clinical settings among older US adults remains unclear. We estimated the annual

| Table 1. Baseline Characteristics of Study Patients With Prediabetes |
|------------------------|------------------------|
| Characteristic         | Patients, No. (%) (N = 50 152) |
| Age, y                 |                                      |
| 65-69                  | 18 075 (36.0)               |
| 70-74                  | 13 088 (26.1)               |
| 75-79                  | 9 210 (18.4)                |
| ≥80                    | 9 779 (19.5)                |
| Sex                    |                                      |
| Female                 | 29 372 (58.6)               |
| Male                   | 20 780 (41.4)               |
| Race and ethnicityb    |                                      |
| Asian/Pacific Islander | 1 408 (2.8)                 |
| Hispanic               | 5 537 (11.0)                |
| Non-Hispanic Black     | 4 857 (9.7)                 |
| Non-Hispanic White     | 36 361 (72.5)               |
| Otherc                 | 638 (1.3)                   |
| Unknown                | 1 351 (2.7)                 |
| Social vulnerability index scored |          |
| 0-0.24                 | 11 607 (23.1)               |
| 0.25-0.49              | 14 906 (29.7)               |
| 0.50-0.74              | 10 151 (20.2)               |
| 0.75-1.00              | 6 843 (13.6)                |
| Missing                | 6 645 (13.3)                |
| Body mass indexe       |                                      |
| <18.5                  | 789 (1.6)                   |
| 18.5-24.9              | 11 496 (22.9)               |
| 25.0-29.9              | 18 173 (36.2)               |
| 30.0-34.9              | 11 624 (23.2)               |
| 35.0-39.9              | 4 733 (9.4)                 |
| ≥40.0                  | 2 566 (5.1)                 |
| Missing                | 771 (1.5)                   |
| HbA1c level, %         |                                      |
| 5.7-5.9                | 27 204 (54.2)               |
| 6.0-6.4                | 22 948 (45.8)               |
| Family history of diabetesf |        |
|                       | 2929 (5.8)                  |
| Hypertension diagnosis | 29 918 (59.7)               |

Abbreviation: HbA1c, hemoglobin A1c.

SI conversion factor: To convert percentage of total HbA1c to proportion of total HbA1c, multiply by 0.01; to convert glucose to mmol/L, multiply by 0.0555.

* Prediabetes was defined as baseline HbA1c level of 5.7% to 6.4%.

b Self-reported race and ethnicity are reported because they are socioeconomic factors that may be associated with progression to diabetes.

c Other data were from the electronic health record and included Alaska Native, American Indian, American Indian or Alaska Native, multiple race, other, or other race.

d Derived from US census measures of the patient’s zip code and comprises socioeconomic status, household composition and persons with disability, racial and ethnic minority group and language, and housing and transportation. The overall score represents a sum of the 4 categories, with higher values indicating greater social vulnerability.

e Calculated as weight in kilograms divided by height in meters squared.

f Cases documented in the electronic health record. The Longitudinal Epidemiologic Assessment of Diabetes Risk data set excludes patients with prevalent diabetes at their first encounter or in the following 12 months based on a diabetes diagnosis, prescription for an antidiabetic agent, or laboratory results (HbA1c level ≥6.5%, fasting plasma glucose level ≥126 mg/dL, or random blood glucose level ≥200 mg/dL).

Open Access. This is an open access article distributed under the terms of the CC-BY License.
progression rate (APR) of HbA1c-defined prediabetes in adults 65 years or older from the Longitudinal Epidemiologic Assessment of Diabetes Risk (LEADR) study.5

Methods

The LEADR study comprises longitudinal outpatient electronic health record (EHR) data on 2,045,999 adults between January 2010 and December 2018 across 10 geographically diverse US health care networks.5 Analyses were completed in October 2021. The Centers for Disease Control and Prevention institutional review board deemed the study exempt from review, with a waiver of informed consent because LEADR data are deidentified. Incident diabetes was ascertained using

| Characteristic                  | Diabetes cases, No. | Person-years, No. | Annual progression rate, % (95% CI) |
|---------------------------------|---------------------|-------------------|------------------------------------|
| Overall                         | 7161               | 136,058           | 5.3 (5.1-5.4)                      |
| Age, y                          |                     |                   |                                    |
| 65-69                           | 2735               | 51,047            | 5.4 (5.2-5.6)                      |
| 70-74                           | 1946               | 35,050            | 5.5 (5.2-5.7)                      |
| 75-79                           | 1290               | 25,698            | 5.0 (4.8-5.3)                      |
| ≥80                             | 1190               | 23,807            | 5.0 (4.7-5.3)                      |
| Sex                             |                     |                   |                                    |
| Female                          | 4029               | 80,629            | 5.0 (4.8-5.2)                      |
| Male                            | 3132               | 55,429            | 5.7 (5.5-5.9)                      |
| Race and ethnicitya             |                     |                   |                                    |
| Asian/Pacific Islander          | 246                | 4293              | 5.7 (5.1-6.5)                      |
| Hispanic                        | 956                | 17,977            | 5.3 (5.0-5.7)                      |
| Non-Hispanic Black             | 841                | 14,427            | 5.8 (5.5-6.2)                      |
| Non-Hispanic White             | 4848               | 94,837            | 5.1 (5.0-5.3)                      |
| Otherc                          | 94                 | 1497              | 6.3 (5.1-7.7)                      |
| Unknown                         | 176                | 3026              | 5.8 (5.0-6.7)                      |
| Social vulnerability index scored |                     |                   |                                    |
| 0-0.24                          | 1408               | 32,408            | 4.3 (4.1-4.6)                      |
| 0.25-0.49                       | 2149               | 42,537            | 5.1 (4.8-5.3)                      |
| 0.50-0.74                       | 1786               | 28,287            | 6.3 (6.0-6.6)                      |
| 0.75-1.00                       | 1209               | 20,502            | 5.9 (5.6-6.2)                      |
| Missing                         | 609                | 12,324            | 4.9 (4.6-5.4)                      |
| Body mass indexe                |                     |                   |                                    |
| <18.5                           | 77                 | 1964              | 3.9 (3.1-4.9)                      |
| 18.5-24.9                       | 1105               | 31,862            | 3.5 (3.3-3.7)                      |
| 25-29.9                         | 2416               | 49,768            | 4.9 (4.7-5.1)                      |
| 30-34.9                         | 2009               | 31,231            | 6.4 (6.2-6.7)                      |
| 35-39.9                         | 922                | 12,598            | 7.3 (6.9-7.8)                      |
| ≥40                             | 510                | 66,999            | 7.6 (7.0-8.3)                      |
| Missing                         | 122                | 1936              | 6.3 (5.3-7.5)                      |
| HbA1c, %                         |                     |                   |                                    |
| 5.7-5.9                         | 2078               | 73,729            | 2.8 (2.7-2.9)                      |
| 6.0-6.4                         | 5083               | 62,328            | 8.2 (7.9-8.4)                      |
| Family history of diabetes4     |                     |                   |                                    |
| No                              | 6748               | 130,117           | 5.2 (5.1-5.3)                      |
| Yes                             | 413                | 5940              | 7.0 (6.3-7.7)                      |
| Hypertension diagnosis          |                     |                   |                                    |
| No                              | 3106               | 61,596            | 5.0 (4.9-5.2)                      |
| Yes                             | 4055               | 74,462            | 5.4 (5.3-5.6)                      |

Abbreviation: HbA1c, hemoglobin A1c.

SI conversion factor: To convert percentage of total HbA1c to proportion of total HbA1c, multiply by 0.01; to convert glucose to mmol/L, multiply by 0.0555.

* Incident diabetes required a minimum of 2 records of diabetes diagnoses, diabetes drug prescriptions, and/or laboratory measurements (HbA1c level ≥6.5%, fasting blood glucose level ≥126 mg/dL, or random blood glucose level ≥200 mg/dL) occurring within 2 years of each other. Events had to occur on separate days, and prescriptions for metformin, thiazolidinediones, and glucagon-like peptide 1 agonists had to be combined with another type to count.

b Self-reported race and ethnicity are reported because they are socioeconomic factors that may be associated with progression to diabetes.

c Other data were from the electronic health record and included Alaska Native, American Indian, American Indian or Alaska Native, multiple race, other, or other race.

d Derived from US census measures of the patient’s zip code and comprises socioeconomic status, household composition and persons with disability, racial and ethnic minority group and language, and housing and transportation. The overall score represents a sum of the 4 categories, with higher values indicating greater social vulnerability.

* Calculated as weight in kilograms divided by height in meters squared.

f Cases documented in the electronic health record.

The Longitudinal Epidemiologic Assessment of Diabetes Risk data set excludes patients with prevalent diabetes at their first encounter or in the following 12 months based on diabetes diagnosis, prescription for an antidiabetic agent, or laboratory results (HbA1c level ≥6.5%, fasting plasma glucose level ≥126 mg/dL, or random blood glucose level ≥200 mg/dL).
previously published criteria. This cohort study included patients 65 years or older with HbA1c level of 5.7% to 6.4% (ie, prediabetes), with 3 months or more follow-up after HbA1c-based prediabetes diagnosis, and without kidney failure. The APR was estimated from mean 1-year cumulative incidence (eg, [cases/patients]/mean follow-up years), and 95% CIs were derived from Poisson regression models. Estimates were stratified by baseline variables: age group, sex, race and ethnicity, social vulnerability index (SVI), body mass index (BMI), HbA1c level, family history of diabetes, and hypertension diagnosis. Analyses were performed using SAS, version 9.4. This study followed the STROBE reporting guideline.

Results

A total of 50,152 patients were included in the study (Table 1). Median follow-up was 2.3 years (IQR, 1.2-3.7 years). Crude diabetes incidence was 53 per 1000 person-years (APR, 5.3%; 95% CI, 5.1%-5.4%) (Table 2). APRs were 5.0% or greater for all groups except patients with the lowest SVI, BMI less than 30, or baseline HbA1c level of 5.7% to 5.9%. The most pronounced differences in progression were for BMI and HbA1c. The APR among patients with BMI of 18.5 to 24.9 was 3.5% (95% CI, 3.3%-3.7%), whereas it was 7.6% (95% CI, 7.0%-8.3%) among those with BMI of 40 or greater. Patients with HbA1c levels of 5.7% to 5.9% had an APR of 2.8% (95% CI, 2.7%-2.9%) compared with 8.2% (95% CI, 7.9%-8.4%) among patients with HbA1c levels of 6.0% to 6.4%.

Discussion

The estimated APR to diabetes among older adults with prediabetes in this study was 5.3%, differing from previous US studies, likely owing to different study designs and populations. A study of community-dwelling Black and White adults 70 years or older with HbA1c-defined prediabetes reported approximately half the APR in our study and substantial regression to normoglycemia, recommending against prediabetes screening and intervention in older adults. The results of that study may be attributed to an older, less diverse sample and self-selection bias from an observational design. Using HbA1c and fasting blood glucose levels to define prediabetes, a study of primary care patients reported an APR of 4.7% among individuals aged 65 to 75 years and 4.1% among those 75 years or older. Another study of a nationally representative population reported APRs of 4.5% among those aged 65 to 79 years and 1.8% among those 80 years or older, both with HbA1c-defined prediabetes.

Strengths of this study include the large sample of diverse patients. Limitations include patients’ unknown duration of prediabetes, possible incomplete capture of health care utilization resulting in under-ascertainment of prediabetes or diabetes, and the inability to distinguish between type 1 and type 2 diabetes. Owing to inherent selection bias, the EHR-based sample was representative of patients comprising the health care organizations contributing data and may not be representative of the general US population. Our findings may provide important information to evaluate the cost-effectiveness of lifestyle interventions in older adults with prediabetes identified by HbA1c testing in clinical settings.

ARTICLE INFORMATION

Accepted for Publication: March 02, 2022.
Published: April 20, 2022. doi:10.1001/jamanetworkopen.2022.8158
Open Access: This is an open access article distributed under the terms of the CC-BY License. © 2022 Koyama AK et al. JAMA Network Open.
Corresponding Author: Alain K. Koyama, ScD, Division of Diabetes Translation, Centers for Disease Control and Prevention, 4770 Buford Hwy, HE, MS-S107-3, Atlanta, GA 30341-3724 (akoyama@cdc.gov).


Author Affiliations: Division of Diabetes Translation, Centers for Disease Control and Prevention, Atlanta, Georgia (Koyama, Bullard, Pavkov, Park, Zhang); Westat, Rockville, Maryland (Mardon).

Author Contributions: Dr Koyama 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. Concept and design: Koyama, McKeever Bullard, Park, Zhang. Acquisition, analysis, or interpretation of data: Koyama, Pavkov, Mardon, Zhang. Drafting of the manuscript: Koyama, Pavkov, Zhang. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Koyama, Mardon, Zhang. Administrative, technical, or material support: Koyama, Park. Supervision: Koyama, Pavkov.

Conflict of Interest Disclosures: Dr Mardon reported receiving funding from Westat during the conduct of the study. No other disclosures were reported. Funding/Support: This study was supported under contract HHSD200201587699 from the Centers for Disease Control and Prevention to Westat. Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: 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.

REFERENCES

1. Park J, Zhang P, Shao HUI, Laxy M, Imperatore G. 141-OR: selecting intervention population for lifestyle program for type 2 diabetes prevention (LPT2DP): a cost-effectiveness perspective. Diabetes. 2021;70(suppl 1):141-OR. doi:10.2337/db21-141-OR

2. Rooney MR, Rawlings AM, Pankow JS, et al. Risk of progression to diabetes among older adults with prediabetes. JAMA Intern Med. 2021;181(4):511-519. doi:10.1001/jamainternmed.2020.8774

3. DeJesus RS, Breitkopf CR, Rutten LJ, Jacobson DJ, Wilson PM, Sauver JS. Incidence rate of prediabetes progression to diabetes: modeling an optimum target group for intervention. Popul Health Manag. 2017;20(3):216-223. doi:10.1089/pop.2016.0067

4. Bardenheier BH, Wu WC, Zullo AR, Gravenstein S, Gregg EW. Progression to diabetes by baseline glycemic status among middle-aged and older adults in the United States, 2006-2014. Diabetes Res Clin Pract. 2021;174:108726. doi:10.1016/j.diabres.2021.108726

5. Fishbein HA, Birch RJ, Mathew SM, et al. The Longitudinal Epidemiologic Assessment of Diabetes Risk (LEADR): unique 1.4 M patient electronic health record cohort. Healthc (Amst). 2020;8(4):100458. doi:10.1016/j.hjdsi.2020.100458

6. Nichols GA, Desai J, Elston Lafata J, et al; SUPREME-DM Study Group. Construction of a multisite DataLink using electronic health records for the identification, surveillance, prevention, and management of diabetes mellitus: the SUPREME-DM project. Prev Chronic Dis. 2012;9:E11Q. doi:10.5888/pcd9.110311