Supplementary Online Content

Rooney MR, Rawlings AM, Pankow JS, et al. Risk of progression to diabetes among older adults with prediabetes. *JAMA Intern Med.* Published online February 8, 2021. doi:10.1001/jamainternmed.2020.8774

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Supplemental Methods

Inverse Probability of Attrition Weights Details

We generated stabilized inverse probability of attrition weights (IPAW) for each person and used weighted analyses to obtain estimates "adjusted" for attrition. These weights were calculated from predicted probability of attrition estimated from two logistic models for 1) dropout not due to death and 2) dropout due to death (1; 2).

We modeled the probabilities of withdrawal not due to death and withdrawal due to death between visits 5 and 6 based on demographic characteristics (age, sex, race-center), and other covariates (hypertension, hypercholesterolemia, history of cardiovascular disease, history of cancer, eGFR<60 ml/min/1.73m^2).

To calculate the stabilized weights, we ran another set of logistic regression models to predict dropout not due to death and drop out due to death using a subset of covariates (age, age^2, sex, race-center). We multiplied the marginal probabilities from this model by the weights we calculated earlier to create stabilized weights [(marginal probability of attending visit 6) * (marginal probability of death)] / [(probability of attending visit 6) * (probability of death)]. The stabilized weights ideally have a mean of 1 to reflect the original population distribution (without inflating the sample size).

Distribution of our stabilized weights:

	Mean	**SD**	**Minimum**	**5th percentile**	**Median**	**95th percentile**	**Maximum**
Stabilized Weights	1.002	0.130	0.610	0.811	0.992	1.230	1.807

1. Cole SR, Hernan MA. Constructing inverse probability weights for marginal structural models. Am J Epidemiol 2008;168:656-664
2. Weuve J, Tchetgen Tchetgen EJ, Glymour MM, Beck TL, Aggarwal NT, Wilson RS, Evans DA, Mendes de Leon CF. Accounting for bias due to selective attrition: The example of smoking and cognitive decline. Epidemiology (Cambridge, Mass) 2012;23:119-128

eTable 1. Baseline (Visit 5, 2011-2013) characteristics of participants by attendance at visit 6 (2016-2017)

Characteristic (Visit 5)*	Overall	Attended Visit 6	Did not Attend Visit 6	
			Alive	Dead
N	3412	2089	915	408
Age	75.6 (5.2)	74.6 (4.7)	76.3 (5.2)	78.9 (5.5)
Women	59.8%	59.4%	63.7%	53.2%
Black	16.8%	16.9%	15.3%	19.4%
Hypertension	67.0%	65.6%	67.9%	72.1%
Hypercholesterolemia	49.7%	50.1%	49.3%	48.1%
eGFR <60 ml/min/1.73m^2	32.6%	27.9%	34.4%	52.2%
History of cardiovascular disease	18.4%	16.1%	17.5%	32.1%
History of cancer	3.3%	2.7%	3.1%	6.6%
Prediabetes definitions				
A1C 5.0-5.6% *and* IFG 100-125 mg/dL	29.4%	29.6%	29.5%	28.4%
A1C 5.7-6.4% *or* IFG 100-125 mg/dL	72.7%	73.1%	71.8%	73.0%
A1C 5.7-6.4%	43.7%	43.3%	43.0%	47.3%
IFG 100-125 mg/dL	58.5%	59.4%	58.4%	54.2%

Abbreviations: ARIC, Atherosclerosis Risk in Communities; FG, fasting glucose; IFG, impaired fasting glucose; eGFR, estimated glomerular filtration rate

***** % or Mean (standard deviation)

eTable 2. Cumulative incidence over 6.5 years (maximum) of A1C-defined and impaired fasting glucose (IFG)-defined progression to prediabetes, total diabetes, or mortality, overall and according to age, sex, and race: The ARIC Study (2011-2017), n=2497

A1C					
Normoglycemia A1C <5.7% at Baseline (2011-2013)					
		Status at Follow-up (2016-2017)			
	Baseline N	**Normoglycemia A1C <5.7%**	**Prediabetes A1C 5.7-6.4%**	**Total Diabetes** [a]	**Mortality**
Overall	1400	893 (64%)	239 (17%)	41 (3%)	227 (16%)
Age					
≥75 years	677	380 (56%)	111 (16%)	19 (3%)	167 (25%)
<75 years	723	513 (71%)	128 (18%)	22 (3%)	60 (8%)
Sex					
Men	594	359 (60%)	106 (18%)	19 (3%)	110 (19%)
Women	806	534 (66%)	133 (17%)	22 (3%)	117 (15%)
Race					
Black	173	106 (61%)	29 (17%)	6 (3%)	32 (19%)
White	1227	787 (64%)	210 (17%)	35 (3%)	195 (16%)
Prediabetes A1C 5.7-6.4% at Baseline (2011-2013)					
		Status at Follow-up (2016-2017)			
	Baseline N	**Normoglycemia A1C <5.7%**	**Prediabetes A1C 5.7-6.4%**	**Total Diabetes** [a]	**Mortality**
Overall	1097	148 (13%)	645 (59%)	97 (9%)	207 (19%)
Age					
≥75 years	558	73 (13%)	294 (53%)	39 (7%)	152 (27%)
<75 years	539	75 (14%)	351 (65%)	58 (11%)	55 (10%)
Sex					
Men	446	55 (12%)	262 (59%)	36 (8%)	93 (21%)
Women	651	93 (14%)	383 (59%)	61 (9%)	114 (18%)
Race					
Black	259	14 (5%)	165 (63%)	29 (11%)	51 (20%)
White	838	134 (16%)	480 (57%)	68 (8%)	156 (19%)
Fasting Glucose					
Normoglycemia FG <100 mg/dL at Baseline (2011-2013)					
		Status at Follow-up (2016-2017)			
	Baseline N	**Normoglycemia FG <100 mg/dL**	**Prediabetes IFG 100-125 mg/dL**	**Total Diabetes** [a]	**Mortality**
Overall	1035	731 (71%)	80 (8%)	26 (3%)	198 (19%)
Age					
≥75 years	518	316 (61%)	40 (8%)	14 (3%)	148 (29%)
<75 years	517	415 (81%)	40 (8%)	12 (2%)	50 (10%)
Sex					
Men	343	227 (66%)	31 (9%)	7 (2%)	78 (23%)
Women	692	504 (73%)	49 (7%)	19 (3%)	120 (17%)
Race					
Black	195	130 (67%)	13 (7%)	8 (4%)	44 (23%)
White	840	601 (72%)	67 (8%)	18 (2%)	154 (18%)
Prediabetes IFG 100-125 mg/dL at Baseline (2011-2013)					
		Status at Follow-up (2016-2017)			
	Baseline N	**Normoglycemia FG <100 mg/dL**	**Prediabetes IFG 100-125 mg/dL**	**Total Diabetes** [a]	**Mortality**
Overall	1462	647 (44%)	467 (32%)	112 (8%)	236 (16%)
Age					

≥75 years	717	290 (40%)	212 (30%)	44 (6%)	171 (24%)
<75 years	745	357 (48%)	255 (35%)	68 (9%)	65 (9%)
Sex					
Men	697	284 (41%)	240 (34%)	48 (7%)	125 (18%)
Women	765	363 (47%)	227 (30%)	64 (8%)	111 (15%)
Race					
Black	237	96 (41%)	75 (32%)	27 (11%)	39 (16%)
White	1225	551 (45%)	392 (322%)	85 (7%)	197 (16%)

Abbreviation: FG, fasting glucose; IFG, impaired fasting glucose.

[a] Incident total diabetes includes diagnosed diabetes identified during semiannual telephone calls or at visit 6 (self-reported physician diagnosis of diabetes, glucose-lowering medication use), visit 6 A1C ≥6.5%, or visit 6 FG ≥126 mg/dL.

eTable 3. Incidence rates and adjusted hazard ratios (95% CIs) for incident total diabetes, incident diagnosed diabetes, and mortality according to international definitions of prediabetes status at baseline in older adults, the ARIC Study (2011-2017)

Prediabetes Criteria	Events/Participants	Incidence Rate per 1000 Person-Years (95% CI)	HR (95% CI) [a]	Subhazard Ratio (95% CI) [b]
Incident total diabetes				
Normoglycemia (A1C <6.0%)	82/2122	8.5 (6.9, 10.6)	1 (Ref)	1 (Ref)
Prediabetes (A1C 6.0-6.4%)	74/375	46.2 (36.8, 58.0)	5.86 (4.20, 8.17)	5.83 (4.12, 8.23)
Normoglycemia (FG <110 mg/dL)	82/1925	9.5 (7.6, 11.8)	1 (Ref)	1 (Ref)
Prediabetes (FG 110-125 mg/dL)	74/572	28.9 (23.0, 36.3)	3.21 (2.33, 4.41)	3.24 (2.35, 4.45)
Incident diagnosed diabetes				
Normoglycemia (A1C <6.0%)	68/2122	7.1 (5.6, 9.0)	1 (Ref)	1 (Ref)
Prediabetes (A1C 6.0-6.4%)	50/375	31.2 (23.6, 41.1)	4.61 (3.13, 6.78)	4.60 (3.05, 6.92)
Normoglycemia (FG <110 mg/dL)	67/1925	7.7 (6.1, 9.8)	1 (Ref)	1 (Ref)
Prediabetes (FG 110-125 mg/dL)	51/572	19.9 (15.2, 26.2)	2.74 (1.89, 3.96)	2.76 (1.90, 4.03)
All-cause mortality				
Normoglycemia (A1C <6.0%)	368/2122	32.8 (29.6, 36.3)	1 (Ref)	-
Prediabetes (A1C 6.0-6.4%)	66/375	33.7 (26.5, 42.9)	0.90 (0.69, 1.17)	-
Normoglycemia (FG <110 mg/dL)	345/1925	34.1 (30.7, 37.9)	1 (Ref)	-
Prediabetes (FG 110-125 mg/dL)	89/572	29.0 (23.6, 35.7)	0.84 (0.67, 1.06)	-

[a] Adjusted for age, sex, and race-center

[b] Subhazard ratio incorporates competing risk of death

[c] Incident total diabetes includes diagnosed diabetes identified during semiannual telephone calls or at visit 6 (self-reported physician diagnosis of diabetes, glucose-lowering medication use), visit 6 A1C ≥6.5%, or visit 6 FG ≥126 mg/dL

[d] Incident diagnosed diabetes includes diagnosed diabetes identified use during semiannual follow-up calls or at visit 6 (self-reported physician diagnosis of diabetes, glucose-lowering medication use)

eTable 4. Cumulative incidence over 6.5 years maximum and hazard ratios (95% CIs) for incident total diabetes and incident diagnosed diabetes with inverse probability of attrition weighting according to prediabetes status at baseline in older adults: The ARIC Study (2011-2017)

Prediabetes Criterion	6.5-year Cumulative Incidence, %, (95% CI)	HR (95% CI) [a]
	Incident total diabetes [b]	
Normoglycemia (A1C <5.7%)	3.1 (2.4, 4.0)	1 (Ref)
Prediabetes (A1C 5.7-6.4%)	9.3 (7.9, 10.9)	3.06 (2.22, 4.21)
Normoglycemia (FG <100 mg/dL)	2.9 (2.1, 3.9)	1 (Ref)
Prediabetes (FG 100-125 mg/dL)	7.5 (6.4, 8.7)	2.61 (1.84, 3.69)
Normoglycemia (A1C <5.7% and FG <100 mg/dL)	1.1 (0.6, 2.1)	1 (Ref)
Prediabetes (A1C 5.7-6.4% or FG 100-125 mg/dL)	7.3 (6.4, 8.4)	6.77 (3.55, 12.89)
Normoglycemia (A1C <5.7% or FG <100 mg/dL)	3.7 (3.0, 4.6)	1 (Ref)
Prediabetes (A1C 5.7-6.4% and FG 100-125 mg/dL)	10.4 (8.7, 12.5)	2.73 (2.05, 3.64)
	Incident diagnosed diabetes [c]	
Normoglycemia (A1C <5.7%)	2.8 (2.1, 3.7)	1 (Ref)
Prediabetes (A1C 5.7-6.4%)	7.0 (5.8, 8.5)	2.57 (1.83, 3.63)
Normoglycemia (FG <100 mg/dL)	2.6 (1.9, 3.6)	1 (Ref)
Prediabetes (FG 100-125 mg/dL)	5.8 (4.9, 6.9)	2.30 (1.58, 3.35)
Normoglycemia (A1C <5.7% and FG <100 mg/dL)	1.1 (0.6, 2.1)	1 (Ref)
Prediabetes (A1C 5.7-6.4% or FG 100-125 mg/dL)	5.8 (4.9, 6.8)	5.51 (2.88, 10.56)
Normoglycemia (A1C <5.7% or FG <100 mg/dL)	3.3 (2.7, 4.1)	1 (Ref)
Prediabetes (A1C 5.7-6.4% and FG 100-125 mg/dL)	7.6 (6.1, 9.4)	2.25 (1.63, 3.10)

Abbreviation: FG, fasting glucose; IPAW, inverse probability of attrition weighting.

IPAW weights for dropout not due to death at the follow-up (visit 6, 2016-2017) and dropout due to death by December 31, 2017.

[a] Adjusted for age, sex, and race-center

[b] Incident total diabetes includes diagnosed diabetes identified during semiannual telephone calls or at visit 6 (self-reported physician diagnosis of diabetes, glucose-lowering medication use), visit 6 A1C ≥6.5%, or visit 6 FG ≥126 mg/dL.

[c] Incident diagnosed diabetes includes diagnosed diabetes identified use during semiannual follow-up calls or at visit 6 (self-reported physician diagnosis of diabetes, glucose-lowering medication use)

eTable 5. Performance of alternative international definitions of prediabetes in older adults for 6.5-year prediction of incident total diabetes and incident diagnosed diabetes: The ARIC Study (2011-2017)

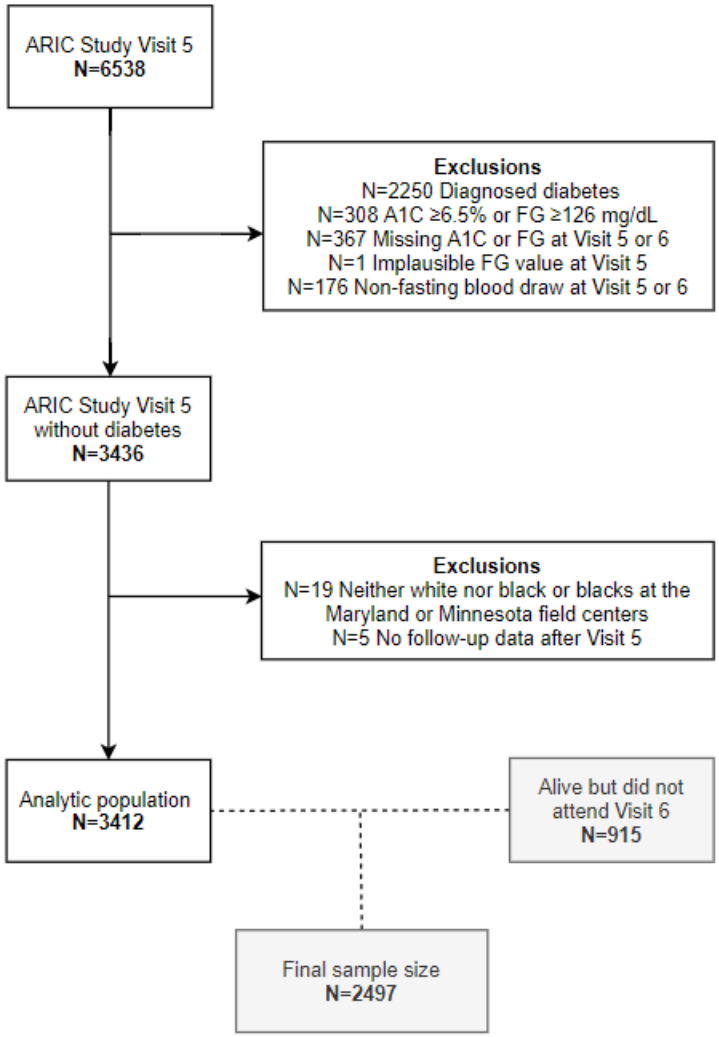
Prediabetes Criterion	6.5-year Risk of Total Diabetes			Diagnostic Performance for Incident Total Diabetes[a], % (95% CI)			
	Incident Total Diabetes[a]	No Incident Total Diabetes	%	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Prediabetes (IEC A1C)							
IEC A1C 6.0-6.4%	74	301	19.7	47.4 (39.4, 55.6)	87.1 (85.7, 88.5)	19.7 (15.8, 24.1)	96.1 (95.2, 96.9)
IEC A1C <6.0%	82	2040	3.9	-	-	-	-
Prediabetes (WHO IFG)							
WHO FG 110-125 mg/dL	74	498	12.9	47.4 (39.4, 55.6)	78.7 (77.0, 80.4)	12.9 (10.3, 16.0)	95.7 (94.7, 96.6)
WHO FG <110 mg/dL	82	1843	4.3	-	-	-	-
	6.5-year Risk of Diagnosed Diabetes			**Diagnostic Performance for Incident Diagnosed Diabetes[b], % (95% CI)**			
	Incident Diagnosed Diabetes[b]	No Incident Diagnosed Diabetes	%	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Prediabetes (IEC A1C)							
A1C 6.0-6.4%	50	325	13.3	42.4 (33.3, 51.8)	86.3 (84.9, 87.7)	13.3 (10.1, 17.2)	96.8 (96.0, 97.5)
A1C <6.0%	68	2054	3.2	-	-	-	-
Prediabetes (WHO IFG)							
FG 110-125 mg/dL	51	572	8.9	43.2 (34.1, 52.7)	78.1 (76.4, 79.7)	8.9 (6.7, 11.6)	96.5 (95.6, 97.3)
FG <110 mg/dL	67	1925	3.5	-	-	-	-

Abbreviations: ARIC, Atherosclerosis Risk in Communities; FG, fasting glucose; IEC, International Expert Committee; IFG, impaired fasting glucose; WHO, World Health Organization

[a] Incident total diabetes was defined as a self-reported physician diagnosis of diabetes, glucose-lowering medication use, A1C ≥6.5%, or FG ≥126 identified during semiannual follow-up calls or at visit 6 (2016-2017)

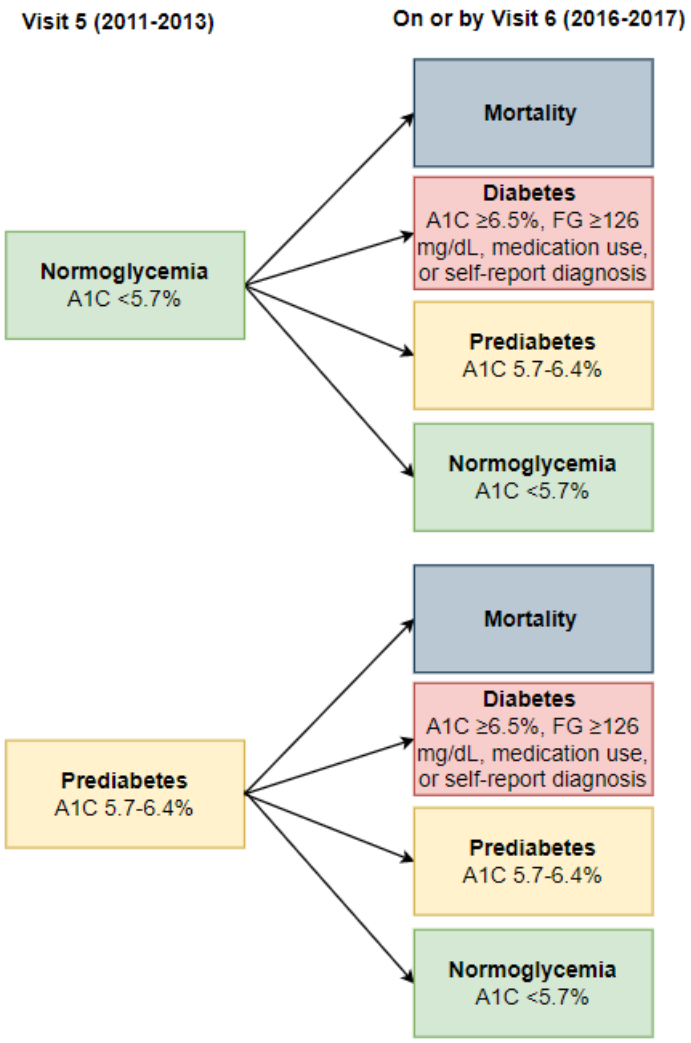
[b] Incident diagnosed diabetes was defined as a self-reported physician diagnosis of diabetes or glucose-lowering medication use identified during semiannual follow-up calls or at visit 6 (2016-2017)

eFigure 1. Participant flow chart

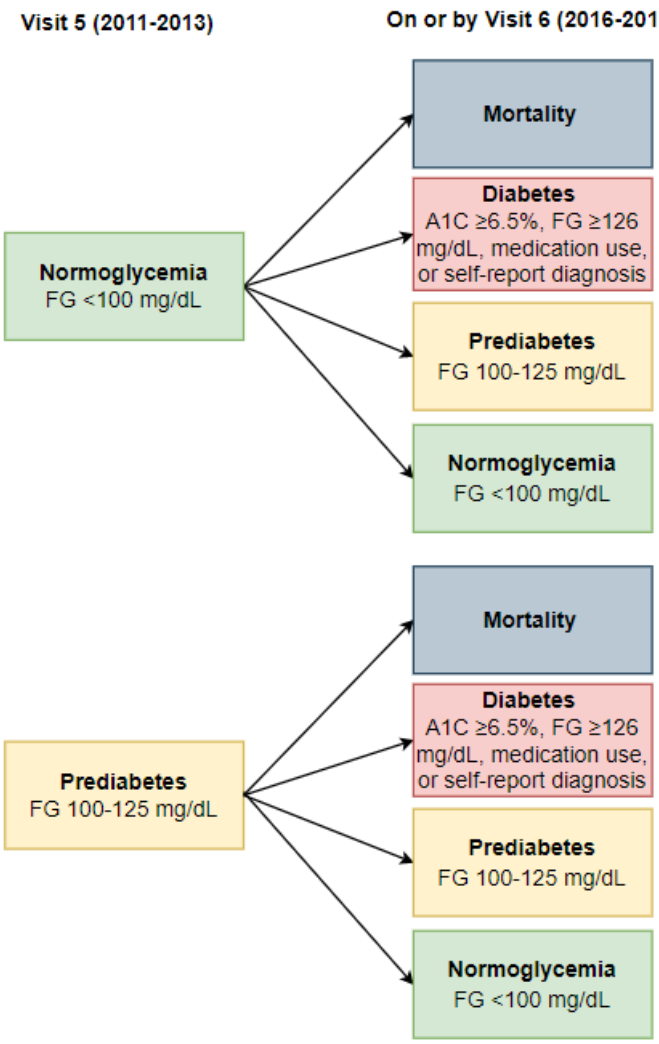


eFigure 2. Possible outcomes according to baseline status defined by A1C (Panel A) or defined by fasting glucose (Panel B). Abbreviation: FG, fasting glucose.

(A)



(B)



eFigure 3. Prevalence of prediabetes in older adults in the ARIC Study according to International Expert Committee (IEC) A1C 6.0-6.4% and World Health Organization (WHO) impaired fasting glucose (IFG, 110-125 mg/dL) definitions