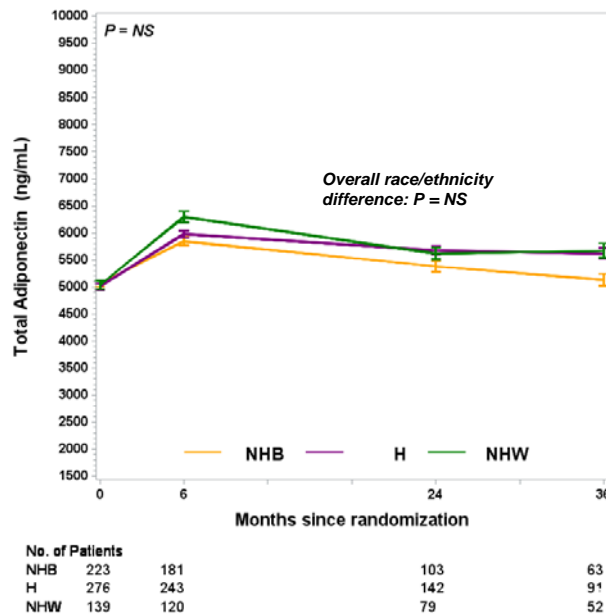


SUPPLEMENTARY DATA

Supplementary Figure S1. Temporal patterns of total adiponectin in the three race/ethnicity groups with the three treatment groups combined*



* Baseline adjusted geometric mean \pm SE asymmetric limits (obtained as $\exp[\text{mean} \pm \text{SE of log values}]$ of total adiponectin measures in the three racial/ethnic groups [NHB: non-Hispanic black; H: Hispanic; NHW: non-Hispanic white] over 36 months of follow-up in TODAY, analyzed using log transformed values. The P-value refers to the overall effect of race/ethnicity in the longitudinal models, adjusted for the baseline value of the outcome, sex, baseline BMI, age at randomization, medication adherence, and treatment group.

SUPPLEMENTARY DATA

Supplementary Table S1. Model-adjusted means and changes in insulin sensitivity, C-peptide index, C-peptide oDI, total adiponectin, and high molecular weight adiponectin (HMWA) in the three race/ethnicity groups over 36 months of follow-up in TODAY, based on longitudinal adjusted models*

	NHB (n=227)	H (n=278)	NHW (n=142)	P-value
Insulin sensitivity (mL/μU)				
Absolute mean				
Baseline	0.039 (0.037, 0.040)	0.039 (0.038, 0.041)	0.040 (0.038, 0.041)	† P = ns
6 month	0.040 (0.039, 0.041)	0.040 (0.039, 0.041)	0.043 (0.041, 0.045)	
24 month	0.043 (0.041, 0.045)	0.041 (0.040, 0.043)	0.041 (0.039, 0.043)	
36 month	0.042 (0.039, 0.044)	0.041 (0.039, 0.043)	0.039 (0.037, 0.042)	
Percent change				
0-6 month change (%)	+2.9 (-1.3, 7.3)	+1.4 (-2.2, 5.1)	+8.0 (2.6, 13.7)	‡ P = ns
6-36 month rate of change (%/yr)	+3.5 (-0.9, 8.1)	+1.8 (-1.9, 5.6)	-6.2 (-10.8, -1.4)	‡ P = ns
C-peptide index (ng/mL per mg/dL)				
Absolute mean				
Baseline	0.063 (0.060, 0.066)	0.062 (0.060, 0.065)	0.061 (0.057, 0.064)	† P = ns
6 month	0.052 (0.049, 0.054)	0.053 (0.051, 0.055)	0.055 (0.052, 0.058)	
24 month	0.040 (0.038, 0.042)	0.043 (0.041, 0.045)	0.043 (0.040, 0.045)	
36 month	0.043 (0.040, 0.046)	0.044 (0.041, 0.046)	0.043 (0.040, 0.047)	
Percent change				
0-6 month change (%)	-17.8 (-22.3, -13.1)	-15.6 (-19.5, -11.5)	-9.6 (-15.6, -3.1)	‡ P = ns
6-36 month rate of change (%/yr)	-13.4 (-18.3, -8.1)	-13.3, (-17.5, -9.0)	-16.6 (-21.9, -10.8)	‡ P = ns
oDI (mL/μU * ng/mL per mg/dL)				
Absolute mean				
Baseline	0.0025 (0.0023, 0.0026)	0.0024 (0.0023, 0.0026)	0.0024 (0.0022, 0.0026)	† P = ns
6 month	0.0021 (0.0020, 0.0022)	0.0022 (0.0020, 0.0023)	0.0024 (0.0022, 0.0025)	
24 month	0.0017 (0.0016, 0.0019)	0.0018 (0.0017, 0.0019)	0.0017 (0.0016, 0.0019)	

SUPPLEMENTARY DATA

Supplementary Table S1. Model-adjusted means and changes in insulin sensitivity, C-peptide index, C-peptide oDI, total adiponectin, and high molecular weight adiponectin (HMWA) in the three race/ethnicity groups over 36 months of follow-up in TODAY, based on longitudinal adjusted models*

	NHB (n=227)	H (n=278)	NHW (n=142)	P-value
36 month	0.0019 (0.0017, 0.0021)	0.0018 (0.0017, 0.0020)	0.0017 (0.0015, 0.0019)	
Percent change				
0-6 month change (%)	-15.1 (-21.3, -8.3)	-11.9 (-17.4, -6.0)	-1.0 (-9.7, 8.6)	‡ P = ns
6-36 month rate of change (%/yr)	-8.6 (-15.6, -0.9)	-11.6 (-17.3, -5.6)	-22.3 (-29.0, -15.0)	‡ P = ns
Total Adiponectin (ng/mL)				
Absolute mean				
Baseline	5062 (4954, 5171)	5007 (4915, 5101)	5034 (4903, 5169)	† P = ns
6 month	5844 (5712, 5978)	5976 (5862, 6093)	6294 (6123, 6470)	
24 month	5377 (5221, 5539)	5671 (5533, 5813)	5617 (5433, 5808)	
36 month	5132 (4942, 5329)	5618 (5447, 5795)	5666 (5439, 5902)	
Percent change				
0-6 month change (%)	+15.4 (12.5, 18.5)	+19.3 (16.7, 22.0)	+25.0 (21.1, 29.1)	‡ NHB vs H p=0.0376
6-36 month rate of change (%/yr)	-8.9 (-11.5, -6.2)	-4.4 (-6.7, -2.1)	-7.6 (-10.6, -4.6)	‡ P = ns
HMWA (ng/mL)				
Absolute mean				
Baseline	2357 (2288, 2427)	2338 (2279, 2398)	2367 (2283, 2455)	† P = 0.0104
6 month	2764 (2679, 2852)	3038 (2958, 3119)	3166 (3048, 3288)	
24 month	2616 (2512, 2724)	2956 (2858, 3058)	2788 (2663, 2919)	
36 month	2540 (2412, 2675)	2918 (2797, 3045)	2944 (2784, 3114)	
Percent change				
0-6 month change (%)	+17.3 (13.2, 21.5)	+29.9 (26.0, 33.9)	+33.7 (28.0, 39.7)	‡ NHB vs H p=0.0281 NHB vs NHW p=0.0190
6-36 month rate of change (%/yr)	-5.9 (-9.5, 2.0)	-2.8 (-6.0, 0.5)	-5.8 (-9.9, 1.4)	‡ P = ns

SUPPLEMENTARY DATA

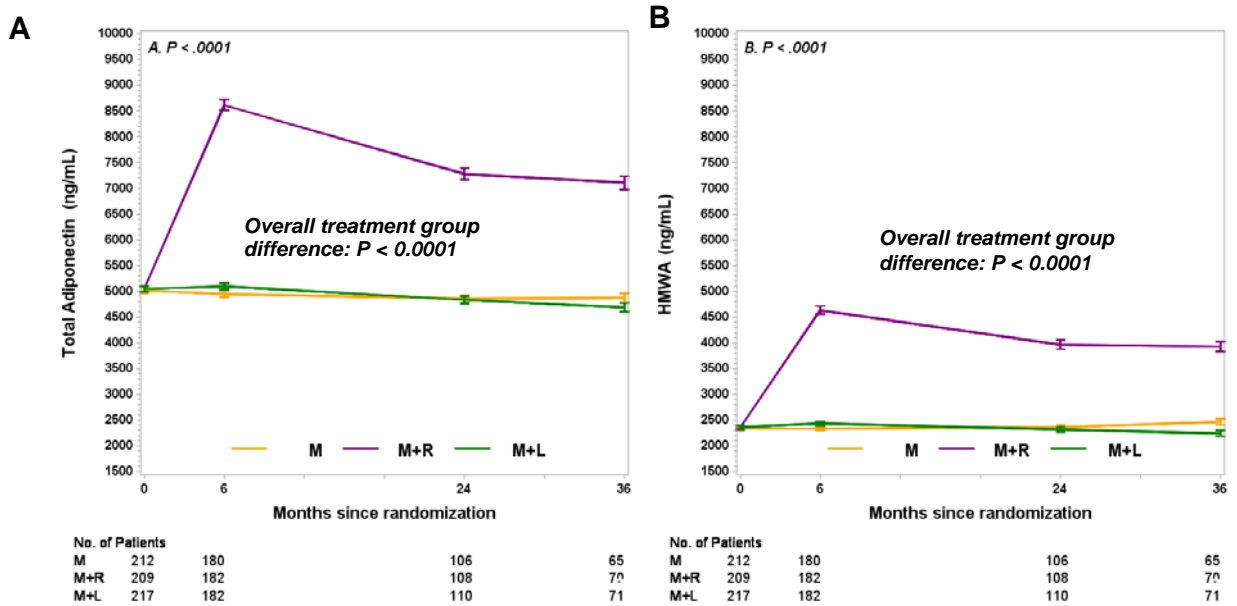
* Data presented are model-adjusted geometric means (95% CI) at baseline, month 6, 24, and 36, model-adjusted 0-6 month mean percent change (95% CI), and model-adjusted 6-36 month mean percent annual rate of change (95% CI) in the three racial/ethnic groups [NHB: non-Hispanic black; H: Hispanic; NHW: non-Hispanic white]. Because these are model adjusted data the baseline numbers are different from the raw data in table 1.

† Overall P-value refers to the effect of race/ethnicity over time from longitudinal models, adjusted for the baseline value of the outcome, sex, baseline BMI, age at randomization, medication adherence, and treatment group. Variables were log-transformed prior to testing.

‡ P-values evaluating differences by race/ethnicity in the 0-6 month percent change and in the 6-36 month mean rate of change, from models adjusted for the baseline value of the outcome, sex, baseline BMI, age at randomization, medication adherence, and treatment group. Variables were log-transformed prior to testing.

SUPPLEMENTARY DATA

Supplementary Figure S2. Temporal patterns of total adiponectin and high molecular weight adiponectin (HMWA) in the three treatment groups with the three race/ethnic groups combined (Figure S2A-B)*



* Baseline adjusted geometric mean \pm SE asymmetric limits (obtained as $\exp[\text{mean} \pm \text{SE of log values}]$ of measures of total adiponectin (A) and HMWA (B) in the three treatment groups [M: metformin only; M+R: metformin+rosiglitazone; M+L: metformin+intensive lifestyle] over 36 months of follow-up in TODAY, analyzed using log transformed values. The P-value refers to the overall effect of treatment group in the longitudinal models, adjusted for the baseline value of the outcome, sex, baseline BMI, age at randomization, medication adherence, and race/ethnicity.

SUPPLEMENTARY DATA

Supplementary Table S2. Model-adjusted means and changes in total adiponectin and high molecular weight adiponectin (HMWA) in the three treatment groups over 36 months of follow-up in TODAY, based on longitudinal adjusted models*

	Metformin only (M, n=217)	Metformin + rosiglitazone (M+R, n=212)	Metformin + intensive lifestyle (M+L, n=218)	P-value
Total Adiponectin (ng/mL)				
Absolute mean				
Baseline	5015 (4917, 5116)	5046 (4945, 5148)	5048 (4950, 5148)	† P < .0001
6 month	4949 (4847, 5054)	8620 (8442, 8802)	5095 (4992, 5201)	
24 month	4853 (4727, 4983)	7283 (7095, 7476)	4835 (4713, 4961)	
36 month	4873 (4712, 5040)	7107 (6881, 7340)	4686 (4539, 4838)	
Percent change				
0-6 month change (%)	-1.3 (-3.5, 0.9)	+70.8 (67.0, 74.7)	+0.9 (-1.3, 3.2)	‡ M+R vs M p<.0001 M+R vs M+L p<.0001
6-36 month rate of change (%/yr)	-1.2 (-3.7, 1.4)	-13.3 (-15.4, -11.1)	-5.8 (-8.1, -3.4)	‡ M+R vs M p=0.0003 M+R vs M+L p=0.0197
HMWA (ng/mL)				
Absolute mean				
Baseline	2339 (2275, 2404)	2350 (2285, 2417)	2362 (2299, 2428)	† P < .0001
6 month	2331 (2264, 2400)	4634 (4502, 4771)	2435 (2366, 2506)	
24 month	2364 (2278, 2452)	3966 (3824, 4113)	2319 (2237, 2403)	
36 month	2463 (2350, 2581)	3926 (3752, 4107)	2241 (2143, 2343)	
Percent change				
0-6 month change (%)	-0.3 (-3.4, 2.9)	+97.2 (91.1, 103.5)	+3.1 (-0.1, 6.4)	‡ M+R vs M p<.0001 M+R vs M+L p<.0001
6-36 month rate of change (%/yr)	+3.8 (0.1, 7.6)	-11.6 (-14.7, -8.5)	-5.7 (-9.0, -2.4)	‡ M+R vs M p=0.0015

SUPPLEMENTARY DATA

* Data presented are model-adjusted geometric means (95% CI) at baseline, month 6, 24, and 36, and model-adjusted 0-6 month mean percent change (95% CI), and model-adjusted 6-36 month mean percent annual rate of change (95% CI) in the three treatment groups [M: metformin only; M+R: metformin+rosiglitazone; M+L: metformin+intensive lifestyle].

† Overall P-value refers to the effect of treatment group over time from longitudinal models, adjusted for the baseline value of the outcome, sex, baseline BMI, age at randomization, medication adherence, and race/ethnicity. Variables were log-transformed prior to testing.

‡ P-values evaluating differences by treatment group in the 0-6 month percent change and in the 6-36 month mean rate of change, from models adjusted for the baseline value of the outcome, sex, baseline BMI, age at randomization, medication adherence, and race/ethnicity. Variables were log-transformed prior to testing.

SUPPLEMENTARY DATA

Supplementary Table S3. Demographic and metabolic characteristics of TODAY participants at baseline by race/ethnicity and by those who failed versus those who did not fail treatment (primary outcome reached yes/no)*

	Failed	Did Not Fail	Unadjusted P-value [†]	Adjusted P-value [†]
Non-Hispanic black	n=120	n=107		
Age at randomization (yr)	13.8 ± 2.0	14.0 ± 1.9	ns	-
Female (%)	68.3%	71.0%	ns	-
Months since diagnosis	6 (4,11)	6 (4,9)	ns	-
BMI (kg/m ²)	36.1 ± 7.9	37.0 ± 8.3	ns	-
BMI Z-score	2.30 ± 0.43	2.35 ± 0.38	ns	-
Waist circumference (cm)	109.5 ± 16.6	113.4 ± 18.2	ns	-
HbA1c (%)	6.5 ± 0.7	5.9 ± 0.6	<.0001	<.0001
Fasting glucose (mg/dL)	121.6 ± 27.1	100.5 ± 18.3	<.0001	<.0001
Fasting insulin (μU/mL) [‡]	36.8 ± 24.1	31.7 ± 23.1	0.0257	0.0082
Fasting C-peptide (ng/mL) [‡]	3.9 ± 1.6	3.5 ± 1.5	ns	0.0118
Insulin sensitivity [1/I _F] (mL/μU) [‡]	0.039 ± 0.024	0.044 ± 0.027	ns	0.0435
C-peptide index ΔC ₃₀ /ΔG ₃₀ (ng/mL per mg/dL) [‡]	0.066 ± 0.070	0.103 ± 0.075	<.0001	<.0001
oDI 1/I _F x ΔC ₃₀ /ΔG ₃₀ [‡]	0.002 ± 0.002	0.004 ± 0.004	<.0001	<.0001
Total adiponectin (ng/mL) [‡]	4960 ± 2237 ^a	5050 ± 2146 ^b	ns	ns
HMWA (ng/mL) [‡]	2466 ± 1610 ^c	2349 ± 1308 ^d	ns	ns
Hispanic	n=125	n=153		
Age at randomization (yr)	14.1 ± 2.0	13.8 ± 2.0	ns	-
Female (%)	56.0%	65.4%	ns	-
Months since diagnosis	6 (4,12)	5 (4,8)	0.0055	-
BMI (kg/m ²)	34.8 ± 7.1	34.3 ± 7.7	ns	-
BMI Z-score	2.24 ± 0.47	2.20 ± 0.46	ns	-
Waist circumference (cm)	110.5 ± 16.6	107.7 ± 15.6	ns	-
HbA1c (%)	6.3 ± 0.8	5.7 ± 0.6	<.0001	<.0001
Fasting glucose (mg/dL)	120.3 ± 29.1	101.9 ± 17.4	<.0001	<.0001
Fasting insulin (μU/mL) [‡]	28.6 ± 19.0	31.2 ± 21.1	ns	ns
Fasting c-peptide (ng/mL) [‡]	3.9 ± 1.4	3.9 ± 1.5	ns	ns
Insulin sensitivity [1/I _F] (mL/μU) [‡]	0.050 ± 0.043	0.050 ± 0.034	ns	ns
C-peptide index ΔC ₃₀ /ΔG ₃₀ (ng/mL per mg/dL) [‡]	0.053 ± 0.050	0.098 ± 0.073	<.0001	<.0001
oDI 1/I _F x ΔC ₃₀ /ΔG ₃₀ [‡]	0.002 ± 0.002	0.004 ± 0.003	<.0001	<.0001
Total adiponectin (ng/mL) [‡]	5742 ± 2526	5893 ± 2489	ns	ns
HMWA (ng/mL) [‡]	3062 ± 1877	3100 ± 1865	ns	ns
Non-Hispanic white	n=52	n=90		
Age at randomization (yr)	14.3 ± 2.2	14.0 ± 2.0	ns	-
Female (%)	61.5%	60.0%	ns	-
Months since diagnosis	7 (4,12)	5 (3,8)	0.0029	-

SUPPLEMENTARY DATA

BMI (kg/m ²)	34.8 ± 7.2	32.8 ± 6.8	ns	-
BMI Z-score	2.21 ± 0.51	2.07 ± 0.51	ns	-
Waist circumference (cm)	110.9 ± 18.0	103.6 ± 14.7	0.0103	-
HbA1c (%)	6.3 ± 0.8	5.7 ± 0.6	<.0001	<.0001
Fasting glucose (mg/dL)	126.7 ± 27.7	104.3 ± 16.1	<.0001	<.0001
Fasting insulin (μU/mL) [‡]	29.5 ± 18.1	26.6 ± 23.3	ns	ns
Fasting c-peptide (ng/mL) [‡]	4.1 ± 1.8	3.6 ± 1.5	ns	ns
Insulin sensitivity [1/I _F] (mL/μU) [‡]	0.053 ± 0.040	0.051 ± 0.028	ns	ns
C-peptide index ΔC ₃₀ /ΔG ₃₀ (ng/mL per mg/dL) [‡]	0.036 ± 0.031	0.082 ± 0.080	<.0001	<.0001
oDI 1/I _F × ΔC ₃₀ /ΔG ₃₀ [‡]	0.002 ± 0.003	0.003 ± 0.003	<.0001	<.0001
Total adiponectin (ng/mL) [‡]	5847 ± 2100	5674 ± 2424	ns	ns
HMWA (ng/mL) [‡]	3212 ± 1586	3073 ± 1741	ns	ns

* Data are presented as mean ± SD, % or median (first, third quartile).

[†] Unadjusted p-values were calculated from F-tests and/or Kruskal Wallis tests for continuous variables; and from chi-square tests for categorical variables. Adjusted p-values are adjusted by sex, baseline BMI, and age at randomization. Significant differences (P<0.05) among the 3 racial/ethnic groups for adiponectin were: (^a) p=0.0032 within the failed category and (^b) p=0.0127 within the 'did not fail' category. Significant differences among the 3 racial/ethnic groups for high-molecular weight adiponectin (HMWA) were: (^c) p=0.0004 within the failed category and (^d) p=0.0030 within the 'did not fail' category. For all 4 (^a, ^b, ^c, and ^d), non-Hispanic blacks were different from Hispanics and non-Hispanic whites.

[‡] Variables were log-transformed prior to testing.

SUPPLEMENTARY DATA

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