Weight change in the management of youth-onset type 2 diabetes: the TODAY clinical trial experience

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For the TODAY Study Group*
* A listing of the TODAY Study Group is included in the online appendix materials

Figure S1. Change from baseline in percent overweight (A) and percent of youth who achieved a drop ≥ 7% since baseline (B) across study visits (at 6, 12, and 24 months) by treatment group[*]
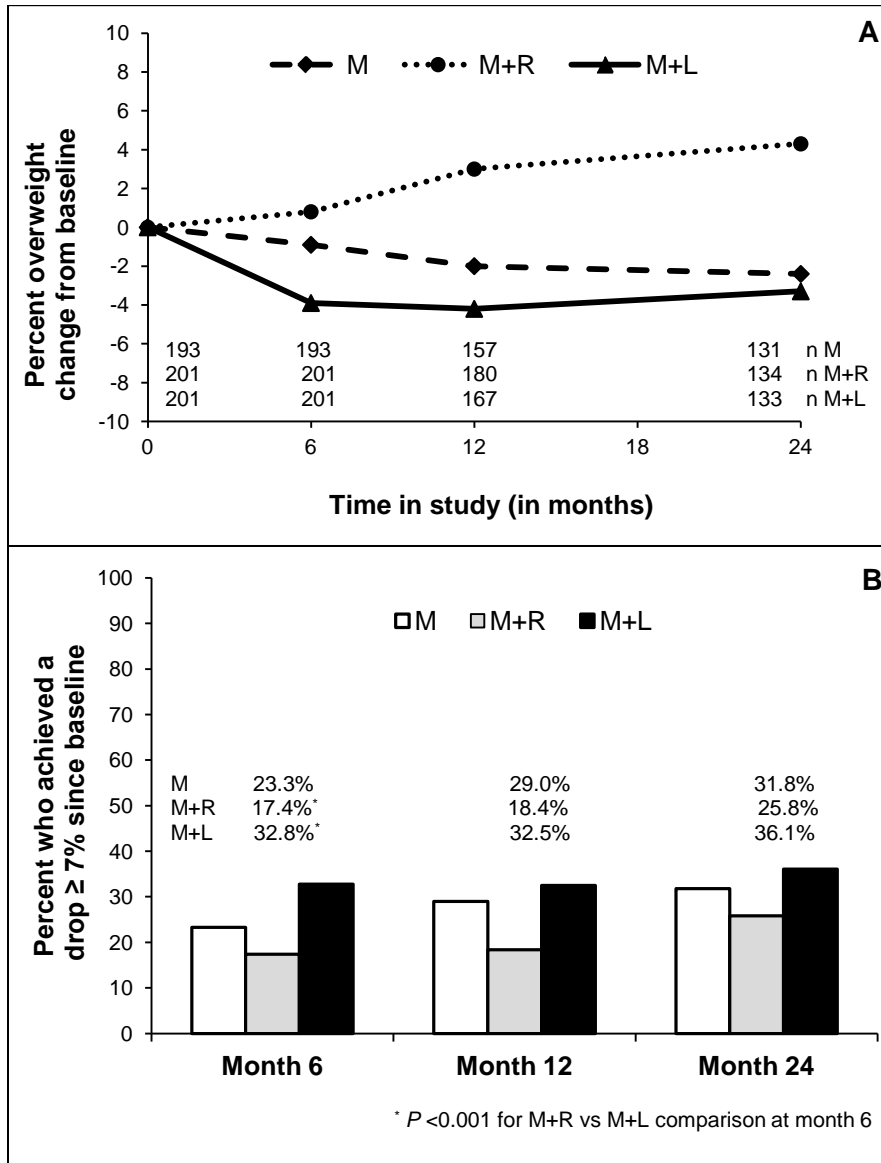
[*] The three treatment groups are: metformin monotherapy (M), metformin plus rosiglitazone (M+R), and metformin plus intensive lifestyle (M+L). 'n' represents the number of participants with data available.

Table S1. BMI and change from baseline (Δ) across study visits by treatment group[*]

|	BMI and Δ			Pairwise comparison *P* value		
	M	**M+R**	**M+L**	**M vs. M+R**	**M vs. M+L**	**M+R vs. M+L**
Baseline	35.3 ± 7.9	35.2 ± 7.8	33.8 ± 7.3			
n at baseline	193	201	105			
Month 6	35.6 ± 8.0	36.0 ± 8.1	33.6 ± 7.7			
Δ 6-0	*+0.4 ± 1.6*	*+0.7 ± 1.8*	*-0.2 ± 1.8*	0.1254	0.0128	<.0001
Month 12	35.6 ± 8.4	37.1 ± 8.4	33.9 ± 8.1			
Δ 12-0	*+0.7 ± 2.2*	*+1.7 ± 2.5*	*+0.2 ± 2.3*	<.0001	0.1479	<.0001
Month 24	36.6 ± 9.1	38.2 ± 8.2	35.3 ± 8.4			
Δ 24-0	*+1.6 ± 2.9*	*+3.0 ± 3.6*	*+1.4 ± 3.0*	<.0001	0.5990	<.0001

[*] Mean ± SD are presented. The three treatment groups are: metformin monotherapy (M), metformin plus rosiglitazone (M+R), and metformin plus intensive lifestyle (M+L). *P* values were calculated from repeated measures models testing for pairwise treatment differences in BMI change during the first 2 years of the study. *P* values presented are from adjusted models for baseline BMI, time, treatment, sex, age at baseline, race-ethnicity, percent overweight change during run-in, and an interaction term for time-by-treatment.

Table S2. Percent overweight and change from baseline (Δ) across study visits, among youth in the M+L group who attended at least 75% of the intensive lifestyle change phase sessions, by treatment group[*]

	Percent overweight and Δ			Pairwise comparison *P* value		
	M	**M+R**	**M+L**	**M vs. M+R**	**M vs. M+L**	**M+R vs. M+L**
Baseline	80.1 ± 38.1	80.2 ± 38.3	75.4 ± 39.2			
n at baseline	193	201	105			
Month 6	79.2 ± 38.3	81.1 ± 39.3	70.5 ± 40.2			
Δ 6-0	*-0.9 ± 8.3*	*+0.8 ± 8.9*	*-4.9 ± 9.7*	0.1383	0.0048	<.0001
Month 12	76.8 ± 40.0	84.1 ± 41.1	69.6 ± 41.0			
Δ 12-0	*-2.0 ± 10.9*	*+3.0 ± 12.4*	*-5.3 ± 11.5*	0.0001	0.0266	<.0001
Month 24	77.4 ± 41.8	85.6 ± 38.9	71.7 ± 40.9			
Δ 24-0	*-2.4 ± 14.4*	*+4.3 ± 17.4*	*-5.5 ± 15.0*	<.0001	0.0686	<.0001

[*] Mean ± SD are presented. The three treatment groups are: metformin monotherapy (M), metformin plus rosiglitazone (M+R), and metformin plus intensive lifestyle (M+L). *P* values were calculated from repeated measures models testing for pairwise treatment differences in percent overweight change during the first 2 years of the study. *P* values presented are from adjusted models for baseline percent overweight, time, treatment, sex, age at baseline, race-ethnicity, percent overweight change during run-in, and an interaction term for time-by-treatment.

Figure S2. Percent (%) of youth who achieved a drop ≥ 7% since baseline across study visits, by treatment group, among youth in the M+L group who attended at least 75% of the intensive lifestyle change phase sessions[*]
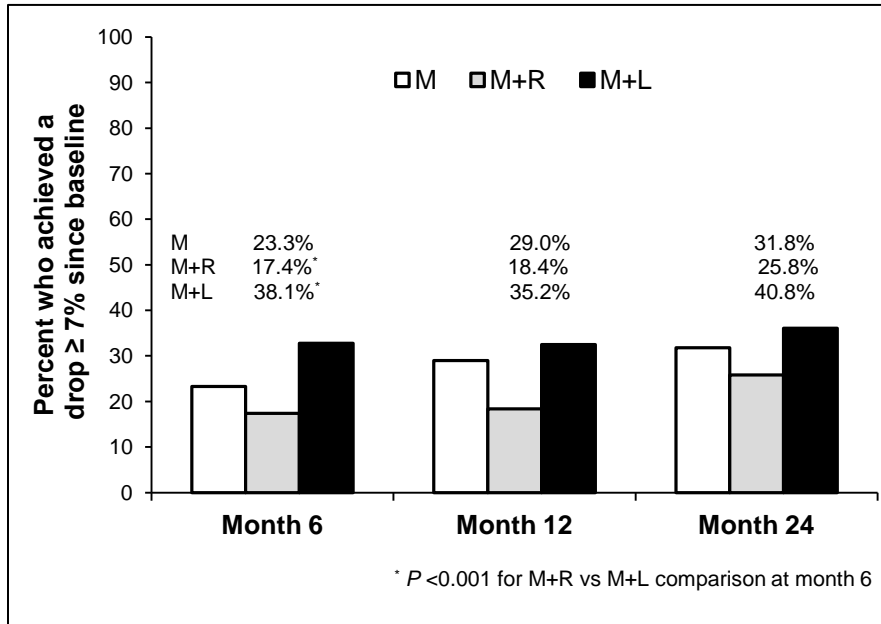
[*] The three treatment groups are: metformin monotherapy (M), metformin plus rosiglitazone (M+R), and metformin plus intensive lifestyle (M+L). P values were calculated from GEE repeated measures models testing for pairwise treatment differences in participants who achieved a 7% drop in percent overweight over time. P values presented are from adjusted models for baseline percent overweight, time, treatment, sex, age at baseline, race-ethnicity, percent overweight change during run-in, and an interaction term for time-by-treatment.

Table S3. Descriptive statistics for percent overweight and change from baseline (Δ) across study visits, by treatment group and sex

	Female			Male		
	M	**M+R**	**M+L**	**M**	**M+R**	**M+L**
Baseline	80.3 ± 36.1	79.0 ± 39.2	75.7 ± 35.3	79.8 ± 41.4	82.4 ± 36.9	72.7 ± 38.3
n at baseline	121	128	129	72	73	72
Month 6	79.3 ± 36.6	81.0 ± 39.5	72.6 ± 36.6	79.2 ± 41.2	81.2 ± 39.3	67.3 ± 38.8
Δ 6-0	*-1.1 ± 7.6*	*+2.0 ± 8.9*	*-3.2 ± 9.0*	*-0.6 ± 9.4*	*-1.2 ± 8.5*	*-5.4 ± 9.5*
Month 12	77.1 ± 38.8	84.5 ± 41.3	71.4 ± 38.6	76.5 ± 42.1	83.4 ± 40.8	69.5 ± 39.3
Δ 12-0	*-2.1 ± 10.3*	*+4.7 ± 12.0*	*-3.5 ± 11.2*	*-1.7 ± 11.8*	*-0.1 ± 12.5*	*-5.4 ± 12.3*
Month 24	82.0 ± 42.0	87.1 ± 40.8	76.5 ± 41.0	69.5 ± 40.8	82.5 ± 35.1	65.3 ± 36.8
Δ 24-0	*-0.9 ± 15.0*	*+7.1 ± 17.0*	*-1.4 ± 14.8*	*-5.0 ± 13.1*	*-1.5 ± 16.9*	*-6.5 ± 13.5*

Table S4. Descriptive statistics for percent (%) of youth who achieved a ≥ 7% drop in percent overweight since baseline across study visits, by treatment group and sex

	Female			Male		
	M	**M+R**	**M+L**	**M**	**M+R**	**M+L**
Month 6	22.3%	14.1%	29.5%	25.0%	23.3%	38.9%
Month 12	30.9%	12.8%	33.3%	26.2%	29.0%	31.1%
Month 24	29.6%	16.9%	29.8%	35.4%	44.2%	46.9%

Table S5. Association between changes in percent overweight and cardiometabolic outcomes during the first 2 years of the study*

Cardiometabolic outcome	Estimate of change in cardiometabolic outcome associated with 1% decrease in percent overweight *(increase if estimate is positive, decrease if negative)*	*P* value for association
HbA1c	-0.0136 %	<.0001
Systolic blood pressure	-0.1054 mmHg	<.0001
Diastolic blood pressure	-0.0461 mmHg	0.0146
LDL	-0.0049 mmol L^{-1}	<.0001
HDL	+0.0017 mmol L^{-1}	<.0001
Total cholesterol	-0.0069 mmol L^{-1}	<.0001
Triglycerides	-0.0086 mmol L^{-1}	<.0001
C-peptide oDI	+0.0001	<.0001

*Association (dose-response) between change in metabolic outcome and change in percent overweight since baseline corresponding to the same time period, during the first 2 years of the study. *P* values are obtained from repeated-measures models adjusted for the baseline value of the cardiometabolic outcome, treatment, sex, race-ethnicity, age at baseline, and change in percent overweight during run-in. Associations of change at month 6, 12, and 24 were considered for all outcomes except for oral disposition index, as OGTTs were not obtained at month 12 per study protocol.

Table S6. Descriptive statistics for cardiometabolic outcomes and change from baseline (Δ) for all visits combined, by treatment group and by percent (%) of youth who achieved a ≥ 7% drop in percent overweight since baseline

| | M | | | | M+R | | | | M+L | | | | P-value[*] for interaction between 7% weight drop and treatment group |
| | Did not achieve 7% drop | | Achieved 7% drop | | Did not achieve 7% drop | | Achieved 7% drop | | Did not achieve 7% drop | | Achieved 7% drop | | |
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	
HbA1c	6.2	(0.9)	6.1	(1.3)	6.0	(1.0)	5.8	(1.0)	6.1	(1.0)	5.7	(0.8)	
Δ from baseline	0.4	(0.7)	0.1	(1.2)	0.2	(0.9)	-0.1	(0.9)	0.4	(0.8)	-0.1	(0.6)	*P=0.4483*
SBP (mmHg)	115.1	(10.9)	111.6	(11.7)	114.7	(10.8)	115.3	(10.9)	114.2	(10.8)	112.8	(11.7)	
Δ from baseline	2.5	(9.4)	-1.4	(9.5)	2.2	(9.5)	-2.0	(9.9)	2.5	(10.0)	0.8	(10.6)	*P=0.1231*
DBP (mmHg)	67.5	(8.3)	65.8	(9.1)	68.2	(8.7)	68.2	(7.8)	67.3	(9.4)	66.7	(8.6)	
Δ from baseline	1.8	(8.7)	-0.3	(9.1)	1.6	(8.5)	-1.0	(8.3)	1.1	(9.3)	0.8	(9.3)	*P=0.2315*
LDL (mmol L^{-1})	2.30	(0.69)	2.34	(0.78)	2.28	(0.72)	2.01	(0.63)	2.30	(0.65)	2.19	(0.70)	
Δ from baseline	0.21	(0.46)	0.05	(0.42)	0.05	(0.51)	-0.03	(0.44)	0.14	(0.48)	-0.04	(0.42)	*P=0.7535*
HDL (mmol L^{-1})	1.01	(0.22)	1.09	(0.27)	1.09	(0.27)	1.14	(0.29)	1.06	(0.22)	1.12	(0.26)	
Δ from baseline	0.05	(0.14)	0.11	(0.17)	0.07	(0.20)	0.13	(0.23)	0.05	(0.17)	0.09	(0.16)	*P=0.9757*
Total cholesterol (mmol L^{-1})	3.95	(0.78)	3.96	(0.93)	4.00	(0.85)	3.64	(0.77)	3.93	(0.79)	3.88	(0.90)	
Δ from baseline	0.31	(0.54)	0.16	(0.54)	0.17	(0.61)	0.08	(0.53)	0.25	(0.59)	0.05	(0.49)	*P=0.8669*
Triglyceride (mmol L^{-1})	1.40	(0.74)	1.16	(0.65)	1.43	(1.06)	1.08	(0.69)	1.25	(0.78)	1.24	(1.04)	
Δ from baseline	0.12	(0.65)	-0.00	(0.47)	0.15	(0.70)	-0.02	(0.48)	0.13	(0.54)	-0.01	(0.60)	*P=0.8612*
C-peptide oDI	0.0024	(0.0021)	0.0040	(0.0042)	0.0041	(0.0057)	0.0051	(0.0037)	0.0024	(0.0023)	0.0062	(0.0066)	
Δ from baseline	-0.0008	(0.0024)	0.0005	(0.0037)	0.0003	(0.0057)	0.0015	(0.0041)	-0.0009	(0.0030)	0.0012	(0.0059)	*P=0.0525*

[*] Mean ± SD collapsed across the 3 visits (month 6, 12, and 24) are presented. The three treatment groups are: metformin monotherapy (M), metformin plus rosiglitazone (M+R), and metformin plus intensive lifestyle (M+L). *P* values were calculated from GEE repeated measures models evaluating the relation between change from baseline in cardiometabolic outcome and weight change based on the dichotomized measure (i.e., percent overweight decrease ≥ 7%), adjusted for the baseline value of the cardiometabolic oucome, visit, treatment, sex, race-ethnicity, age at baseline, and change in percent overweight during run-in. The *P* value represents the interaction between the dichotomized weight change measure and treatment group.

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The following individuals and institutions constitute the TODAY Study Group (* indicates principal investigator or director):

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