Supplementary Online Content

Ali MK, Chwastiak L, Poongothai S, et al. Effect of a collaborative care model on depressive symptoms and glycated hemoglobin, blood pressure, and serum cholesterol among patients with depression and diabetes in india: the INDEPENDENT randomized clinical trial. *JAMA*. doi:10.1001/jama.2020.11747

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

eTable 1. Completed CONSORT checklist for Pragmatic Trials

Section	Item	CONSORT description specific to Pragmatic Trials	Page
Title and abstract	1	How participants were allocated to interventions (eg, “random allocation,” “randomised,” or “randomly assigned”)	1, 2-3
Introduction			
Background	2	Describe the health or health service problem that the intervention is intended to address and other interventions that may commonly be aimed at this problem	2
Methods			
Participants	3	Eligibility criteria should be explicitly framed to show the degree to which they include typical participants and/or, where applicable, typical providers (eg, nurses), institutions (eg, hospitals), communities (or localities eg, towns) and settings of care (eg, different healthcare financing systems)	2
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.Describe extra resources added to (or resources removed from) usual settings in order to implement intervention. Indicate if efforts were made to standardise the intervention or if the intervention and its delivery were allowed to vary between participants, practitioners, or study sites Describe the comparator in similar detail to the intervention	3 3
Objectives	5	Specific objectives and hypotheses	2
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (eg, multiple observations, training of assessors) Explain why the chosen outcomes and, when relevant, the length of follow-up are considered important to those who will use the results of the trial	4
Sample size	7	How sample size was determined; explanation of any interim analyses and stopping rules when applicable If calculated using the smallest difference considered important by the target decision maker audience (the minimally important difference) then report where this difference was obtained	4
Randomisation—sequence generation	8	Method used to generate the random allocation sequence, including details of any restriction (eg, blocking, stratification)	2
Randomisation—allocation concealment	9	Method used to implement the random allocation sequence (eg, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned	2
Randomisation—implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups	2
Blinding (masking)	11	Whether participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment	2

Section	Item	CONSORT description specific to Pragmatic Trials	Page
		If blinding was not done, or was not possible, explain why	
Statistical methods	12	Statistical methods used to compare groups for primary outcomes; methods for additional analyses, such as subgroup analyses and adjusted analyses	4-5
Results			
Participant flow	13	The number of participants or units approached to take part in the trial, the number which were eligible, and reasons for non-participation should be reported	5 Fig. 1
Recruitment	14	Dates defining the periods of recruitment and follow-up	2
Baseline data	15	Baseline demographic and clinical characteristics of each group	5 Table 1
Numbers analysed	16	Number of participants (denominator) in each group included in each analysis and whether analysis was by “intention-to-treat”; state the results in absolute numbers when feasible (eg, 10/20, not 50%)	4-5
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group and the estimated effect size and its precision (eg, 95% CI)	5-8 Fig. 2 Table 2
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating which are prespecified and which are exploratory	8-10 Fig. 3 eTables eFigures
Adverse events	19	All important adverse events or side effects in each intervention group	10 eTable10
Discussion			
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision, and the dangers associated with multiplicity of analyses and outcomes	10-11
Generalisability	21	Generalisability (external validity) of the trial findings Describe key aspects of the setting which determined the trial results. Discuss possible differences in other settings where clinical traditions, health service organisation, staffing, or resources may vary from those of the trial	10-11
Overall evidence	22	General interpretation of the results in the context of current evidence	10-11

Zwarenstein M, Treweek S, Gagnier JJ, Altman DG, Tunis S, Haynes B, Oxman AD, Moher D for the CONSORT and Pragmatic Trials in Healthcare (Practihc) group. Improving the reporting of pragmatic trials: an extension of the CONSORT statement. BMJ 2008; 337;a2390

eTable 2. Adjusted Risk Differences in Multiple and Single Care Improvements and Goal Achievement by Treatment Group at 12- and 24-months, and Overall

	12 months		RD (95% CI) at 12-month	24 Months		RD (95% CI) at 24-month	Overall RD (95% CI) [c]	p-value[d]
	Collaborative Care	Usual Care		Collaborative Care	Usual Care			
Primary Outcome [a]								
≥50% improvement in SCL-20 [b] plus either ≥0.5ppt HbA1c reduction, ≥5mmHg SBP reduction, or ≥10mg/dl LDLc reduction, %	67.8	42.8	25.1 (16.2; 33.9)	73.3	55.0	18.3 (10.0; 26.5)	20.2 (14.7; 25.7)	<.001
Secondary Outcomes								
≥50% improvement in SCL-20, % [b]	73.6	46.4	27.2 (18.8; 35.6)	79.8	64.2	15.7 (8.4; 22.9)	19.6 (14.2; 24.9)	<.001
≥0.5ppt reduction in HbA1c, %	61.8	47.2	14.7 (5.5; 23.8)	51.3	45.4	5.9 (-2.9; 14.7)	11.5 (5.2; 17.9)	<.001
≥5mmHg reduction in SBP, %	55.0	48.5	6.5 (-2.4; 15.4)	55.0	53.0	1.9 (-7.1; 10.9)	5.6 (-0.1; 11.4)	0.05
≥10 mg/dl reduction in LDLc, %	44.3	42.2	2.2 (-6.1; 10.4)	41.9	44.2	-2.3 (-10.9; 6.4)	0.5 (-4.8; 5.9)	0.84
HbA1c <7%, %	30.7	21.8	8.9 (0.8; 17.0)	14.8	16.2	-1.3 (-8.3; 5.6)	4.3 (-1.2; 9.8)	0.12
SBP <130mmHg, %	61.4	59.9	1.5 (-7.5; 10.6)	64.1	63.6	0.5 (-8.5; 9.6)	0.9 (-5.0; 6.7)	0.78
LDLc <100mg/dl (<70mg/dl with history of CVD), %	59.8	53	6.9 (-2.3; 16.1)	54.8	53.5	1.3 (-7.9; 10.6)	4.2 (-2.2; 105)	0.20
Achieving either ≥0.5ppt reduction or HbA1c<7%, %	69.6	55.2	14.5 (5.0; 24.0)	55.0	51.9	3.1 (-6.3; 12.5)	10.4 (3.6; 17.3)	<.001
Achieving either ≥5mmHg reduction of SBP<130mmHg, %	70.8	72.4	-1.6 (-10.3; 7.1)	73.3	76.3	-3.0 (-11.6; 5.5)	-0.9 (-6.6; 4.9)	0.77
Achieving either ≥10mg/dl reduction or LDLc<100mg/dl (<70mg/dl with history of CVD), %	71.9	67.7	4.2 (-5.0; 13.5)	65.7	66.4	-0.7 (-10.1; 8.7)	3.1 (-3.3; 9.4)	0.34
Achieving HbA1c <7%, SBP <130mmHg, and LDLc <100mg/dl (<70mg/dl with history of CVD), %	13.5	4.2	9.3 (3.7; 14.8)	5.7	4.5	1.3 (-3.2; 5.8)	3.9 (0.5; 7.4)	0.03
Post Hoc Outcomes								
PHQ-9 <10, % [b]	88.1	65.5	22.6 (15.0; 30.2)	94.1	78.1	16.0 (9.9; 22.1)	16.0 (9.9; 22.1)	<.001

Abbreviations: %, percentage achieving; RD, risk difference; MD, mean difference; 95% CI, 95% confidence intervals; ppt, percentage point; SCL-20, 20-item symptoms checklist; PHQ-9, 9-item patient health questionnaire; HbA1c, glycated hemoglobin; SBP, systolic blood pressure; LDLc, low-density lipoprotein cholesterol; CVD, cardiovascular disease

Risk differences and proportions estimated with Gaussian models using an identity-link and a generalized estimating equation approach to account for correlation of observations within participants over time. Model effects are treatment group, time, treatment-by-time interaction, age, sex, respective baseline values and site

[a] *Study was powered to detect a between-group difference in primary outcome at 24 months; 12-month primary outcome estimates are post hoc findings*

[b] *SCL-20 range: 0 (best) – 4 (worst); PHQ-9 range: 0 (best) – 27 (worst) where ≥10 signifies moderate-to-severe depressive symptoms*

[c] *post-hoc analysis*

[d] *p-values represent statistical significance of overall between-group RD*

eTable 3. Adjusted Between-Group Differences and Means of Continuous Measures by Treatment Group at 12- and 24-months, and Overall

	Baseline		12 months		MD (95% CI) at 12-month	24 months		MD (95% CI) at 24-month	Overall MD (95% CI)[a]	p-value[b]
	Collaborative Care	Usual Care	Collaborative Care	Usual Care		Collaborative Care	Usual Care			
SCL-20, mean score [c]	1.3	1.4	0.5	0.8	-0.3 (-0.4; -0.2)	0.4	0.6	-0.1 (-0.2; -0.1)	-0.2 (-0.3; -0.2)	<.001
PHQ-9, mean score [c]	13.0	13.4	5.2	7.3	-2.2 (-2.9; -1.4)	4.7	5.7	-1.0 (-1.7; -0.4)	-1.7 (-2.2; -1.2)	<.001
HbA1c, mean (ppt)	9.3	9.0	8.0	8.5	-0.4 (-0.7; -0.1)	8.6	8.7	-0.1 (-0.4; 0.2)	-0.3 (-0.5; -0.1)	0.02
SBP, mean (mmHg)	132.0	133.0	125.0	126.8	-1.7 (-4.7; 1.2)	122.2	123.1	-0.9 (-4.5; 2.7)	-1.7 (-4.0; 0.6)	0.15
LDLc, mean (mg/dl)	101.0	101.0	91.7	93.7	-1.9 (-8.2; 4.3)	97.2	95.3	1.9 (-5.2; 9.0)	-0.7 (-5.3; 3.9)	0.78

Abbreviations: %, percentage achieving; MD, mean difference; 95% CI, 95% confidence intervals; ppt, percentage point; SCL-20, 20-item symptoms checklist; PHQ-9, 9-item patient health questionnaire; HbA1c, glycated hemoglobin; SBP, systolic blood pressure; LDLc, low-density lipoprotein cholesterol

Differences in means estimated with Gaussian models using an identity-link and a generalized estimating equation approach to account for correlation of observations within participants over time. Model effects are treatment group, time, treatment-by-time interaction, age, sex, respective baseline values and site

[a] *post-hoc analysis*

[b] *p-values represent statistical significance of overall between-group RD*

[c] *SCL-20 range: 0 (best) – 4 (worst); PHQ-9 range: 0 (best) – 27 (worst) where ≥10 signifies moderate-to-severe depressive symptoms*

eTable 4. Post Hoc Sensitivity Analyses Using Alternative Models for Primary Outcome Analysis at 12- and 24-months, and Overall

	12 Month			24 Month			Overall[a]			
	RD	**SE**	**95% CI**	**RD**	**SE**	**95% CI**	**RD**	**SE**	**95% CI**	**p value[b]**
GEE	23.7%	4.6	(14.7; 32.6)	16.9%	4.3	(8.5; 25.2)	18.7%	2.9	(13.1; 24.4)	<0.001
GEE-cl	24.0%	4.8	(14.5; 33.4)	17.2%	4.7	(7.9; 26.4)	19.1%	3.4	(12.4; 25.7)	<0.001
LMM	23.7%	4.4	(14.9; 32.4)	16.9%	4.5	(8.1; 25.6)	18.8%	2.9	(13.1; 24.5)	<0.001

Abbreviations: RD, risk difference; SE, standard error; 95% CI, 95% confidence intervals; GEE, generalized estimating equations; GEE-cl, GEE additionally accounting for clustering of observations at clinic-level; LMM, linear mixed model

*GEE: Gaussian models using an identity-link and a generalized estimating equation approach to account for correlation of observations within participants over time. Model effects are treatment group, time, treatment*time interaction and site.*

*GEE-cl: Gaussian models using an identity-link and a generalized estimating equation approach to account for correlation of observations within participants and sites over time. Model effects are treatment group, time and treatment*time interaction.*

*LMM: Linear mixed effects models with nested random effects to account for participants within sites over time. Model effects are treatment group, time and treatment*time interaction.*

[a] *post-hoc analysis*

[b] *p-values represent statistical significance of overall between-group RD within the type of models used; p-values do not indicate differences between models*

eTable 5. Unadjusted Risk Differences in Multiple and Single Care Improvements and Goal Achievement by Treatment Group at 12- and 24-months

	12 months		RD (95% CI) at 12-month	24 Months		RD (95% CI) at 24-month
	Collaborative Care	Usual Care		Collaborative Care	Usual Care	
Primary Outcome [a]						
50% improvement in SCL-20 [b] plus either ≥0.5ppt HbA1c reduction, ≥5mmHg SBP reduction, or ≥10mg/dl LDLc reduction, %	66.1	42.4	23.7 (14.7; 32.6)	71.6	54.7	16.9 (8.5; 25.2)
Secondary Outcomes						
≥50% improvement in SCL-20, % [b]	71.5	45.8	25.7 (17.0; 34.4)	77.7	63.6	14.1 (6.7; 21.6)
≥0.5ppt reduction in HbA1c, %	62.2	44.7	17.5 (7.8; 27.2)	51.9	43.2	8.7 (-0.9; 18.4)
≥5mmHg reduction in SBP, %	55.1	50.3	4.8 (-5.1; 14.7)	54.8	54.5	0.3 (-9.6; 10.2)
≥10 mg/dl reduction in LDLc, %	42.9	41.0	1.9 (-7.9; 11.7)	40.5	43.0	-2.5 (-12.3; 7.2)
HbA1c <7%, %	29.6	22.3	7.3 (-1.3; 15.8)	13.7	16.6	-3.0 (-10.1; 4.2)
SBP <130 mmHg, %	61.4	60.2	1.2 (-8.1; 10.7)	63.7	63.4	0.3 (-9.1; 9.7)
LDLc <100 mg/dl (<70 with history of CVD), %	61.4	54.6	6.7 (-2.9; 16.4)	56.3	55.1	1.2 (-8.6; 11.0)
Achieving either ≥0.5ppt reduction or HbA1c<7%, %	69.4	53.3	16.1 (6.5; 25.7)	55.1	50.4	4.7 (-5.0; 14.5)
Achieving either ≥5mmHg reduction of SBP<130mmHg, %	71	73.1	-2.1 (-10.8; 6.7)	73.1	76.6	-3.5 (-12.1; 5.1)
Achieving either ≥10mg/dl reduction or LDLc<100 mg/dl (<70 with history of CVD), %	72.2	68	4.1 (-5.2; 13.4)	66	66.8	-0.8 (-10.3; 8.7)
Achieving HbA1c <7%, SBP <130 mmHg, and LDLc <100 mg/dl (<70 with history of CVD)%	13.3	4.7	8.6 (3.0; 14.3)	5.4	4.8	0.6 (-4.0; 5.2)
	12 months		MD (95% CI) at 12-month	24 Months		MD (95% CI) at 24-month
SCL-20, mean score [b]	0.5	0.8	-0.3 (-0.4; -0.2)	0.4	0.6	-0.2 (-0.2; -0.1)
PHQ-9, mean score [b]	5.0	7.4	-2.4 (-3.2; -1.6)	4.5	5.7	-1.2 (-1.9; -0.6)
HbA1c, mean (ppt)	8.1	8.4	-0.3 (-0.6; 0.1)	8.7	8.6	0.0 (-0.3; 0.4)
SBP, mean (mmHg)	125.0	126.7	-1.7 (-4.8; 1.5)	122.4	123.2	-0.8 (-4.6; 2.9)
LDLc, mean (mg/dl)	90.6	92.5	-1.9 (-8.5; 4.8)	95.9	94.0	2.0 (-5.6; 9.6)

Post Hoc Outcomes	12 Months		RD (95% CI) at 12-month	24 Months		RD (95% CI) at 24-month
PHQ-9 <10, % [b]	89.3	65.5	23.8 (16.2; 31.4)	95.2	78.0	17.2 (11.2; 23.2)

Abbreviations: %, percentage achieving; RD, risk difference; MD, mean difference; 95% CI, 95% confidence intervals; ppt, percentage point; SCL-20, 20-item symptoms checklist; PHQ-9, 9-item patient health questionnaire; HbA1c, glycated hemoglobin; SBP, systolic blood pressure; LDLc, low-density lipoprotein cholesterol; CVD, cardiovascular disease

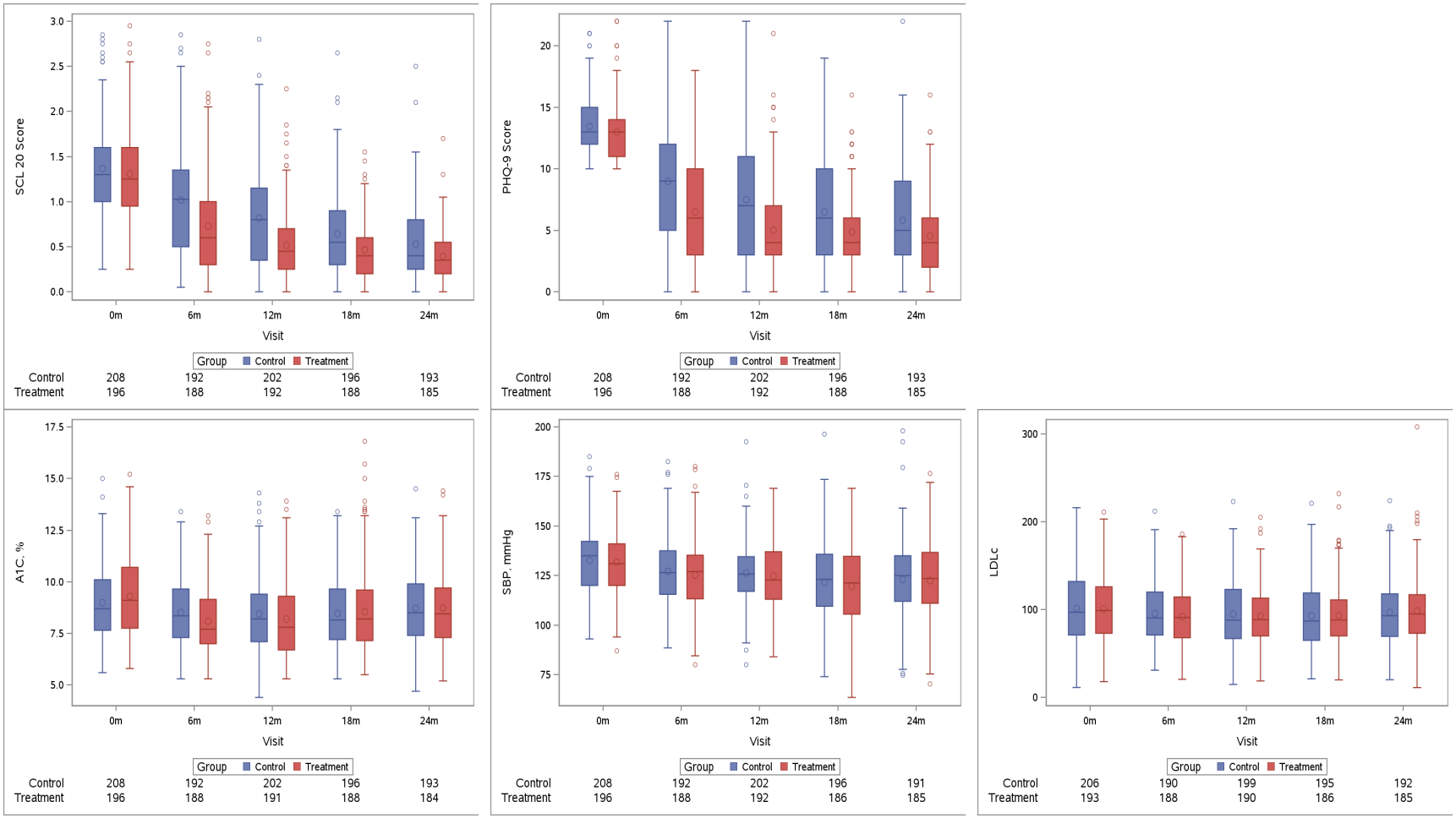
Risk differences and proportions estimated with Gaussian models using an identity-link and a generalized estimating equation approach to account for correlation of observations within patients over time. Model effects are treatment group, time, treatment-by-time interaction, and site.

Differences in means estimated with Gaussian models using an identity-link and a generalized estimating equation approach to account for correlation of observations within patients over time. Model effects are treatment group, time, treatment-by-time interaction, and site.

[a] Study was powered to detect a between-group difference in primary outcome at 24 months; 12-month primary outcome estimates are post-hoc findings

[b] SCL-20 range: 0 (best) – 4 (worst); PHQ-9 range: 0 (best) – 27 (worst) where ≥10 signifies moderate-to-severe depressive symptoms

eFigure 1. Within- and Between-Group Changes in Mean Levels of Depressive Symptom Scores and Cardiometabolic Indices



Abbreviations: SCL-20, 20-item symptoms checklist (range: 0 [best] – 4 [worst]); PHQ-9, 9-item patient health questionnaire (range: 0 [best] – 27 [worst] where score ≥10 signifies moderate-to-severe depressive symptoms); HbA1c, glycated hemoglobin; SBP, systolic blood pressure; LDLc, low-density lipoprotein cholesterol

Graphs show observed unadjusted values by treatment over time. Box represents interquartile range (IQR) with median (line) and mean (point), whiskers are defined by 1.25 times IQR and points beyond whiskers represent observations falling outside of this range

Ns by treatment over time are observed values

eTable 6. Within-group Mean Changes between Baseline and End-of-Study and Between-group Differences by Outcome

Outcome	Within Intervention[a]		Within Control[a]		Between-group MD at EO[b]			Difference-in-Difference[c]	
	MD	95% CI	MD	95% CI	MD	95% CI	p-value	MD	95% CI
SCL-20, mean score[d]	-0.9	(-0.9; -0.8)	-0.8	(-0.9; -0.7)	-0.1	(-0.3; 0.0)	0.04	-0.1	(-0.2; -0.0)
PHQ-9, mean score[d]	-8.4	(-9.0; -7.9)	-7.6	(-8.2; -6.9)	-1.5	(-2.7; -0.3)	0.01	-1.2	(-1.8; -0.5)
HbA1c, mean (ppt)	-0.6	(-0.8; -0.3)	-0.3	(-0.6; 0.0)	-0.1	(-0.8; 0.6)	0.72	-0.6	(-1.0; -0.3)
SBP, mean (mmHg)	-9.7	(-12.8; -6.6)	-9.6	(-12.8; -6.4)	-2.9	(-11.3; 5.5)	0.49	0.3	(-3.6; 4.2)
LDLc, mean (mg/dl)	-3.1	(-9.0; 2.9)	-5.4	(-11.4; 0.5)	-3.0	(-19.5; 13.5)	0.71	0.6	(-6.6; 8.0)

Abbreviations: MD, mean difference; SCL-20, 20-item symptoms checklist; PHQ-9, 9-item patient health questionnaire; HbA1c, glycated hemoglobin; SBP, systolic blood pressure; LDLc, low-density lipoprotein cholesterol; EOS, end-of-study; ppt, percentage points

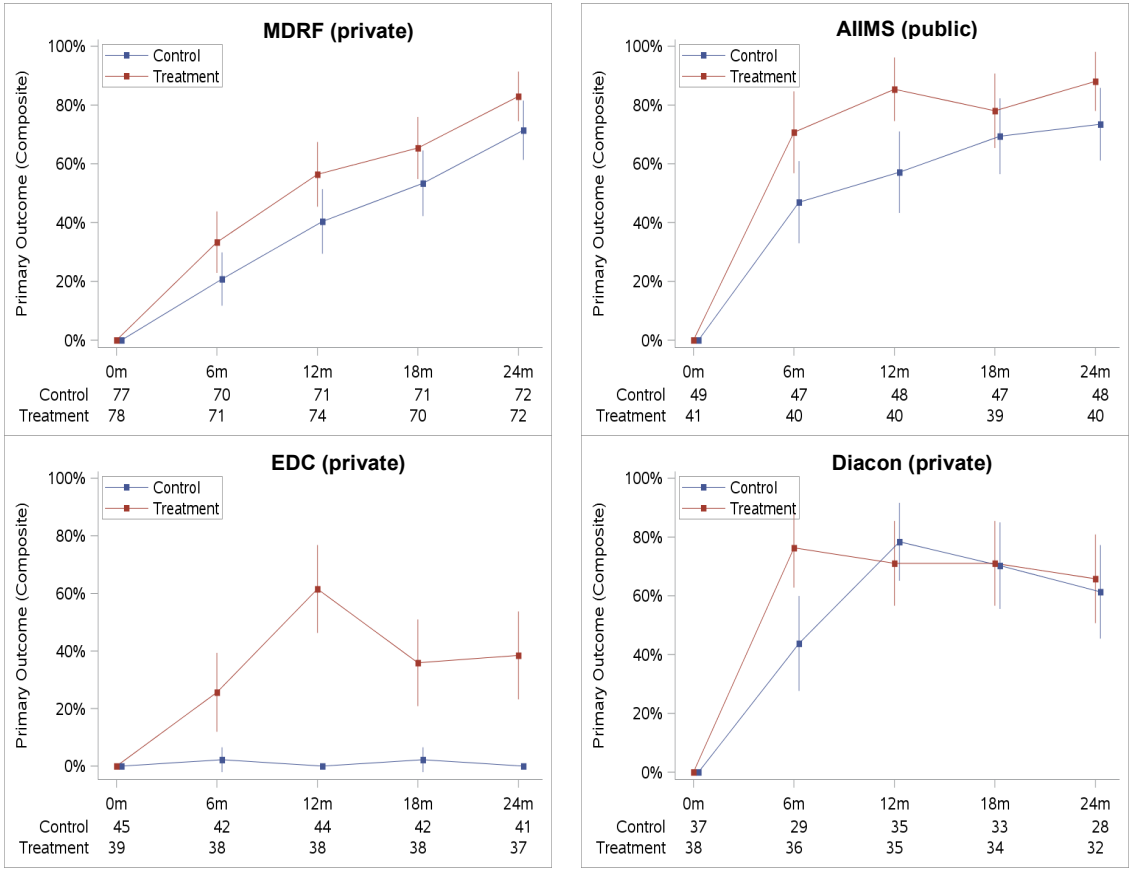
[a] *Paired multiple imputation t-test per group EOS - baseline*

[b] *Multiple imputation t-test between groups at EOS*

[c] *Between-group difference of within-group differences (EOS-baseline) estimated as average population means with Gaussian models using an identity-link and a generalized estimating equation approach to account for correlation of observations within participants over time. Models were adjusted for study site. Confidence intervals are generated using a cluster-bootstrap procedure with 1000 replications across all 10 imputations. No p-values provided*

[d] *SCL-20 range: 0 (best) – 4 (worst); PHQ-9 range: 0 (best) – 27 (worst) where ≥10 signifies moderate-to-severe depressive symptoms*

eFigure 2. Achievement of Primary Outcome by Treatment Group and Study Site



Abbreviations: SCL-20, 20-item symptoms checklist (range: 0-4); HbA1c, glycated hemoglobin; SBP, systolic blood pressure; LDLc, low density lipoprotein cholesterol

Graphs show unadjusted proportions of patients (square markers) by treatment achieving the primary outcome over time by study site. Vertical bars indicate the 95% confidence interval of the point estimate. Estimates generated with Gaussian models using an identity-link and a generalized estimating equation approach to account for correlation of observations within patients over time, separately for each site. Model effects are treatment group, time, treatment-by-time interaction. Sample size by treatment group reflects the number of participants observed at each time point.

Primary outcome = proportion achieving ≥50% reductions in SCL-20 and ≥1 of: ≥0.5ppt HbA1c, ≥5mmHg SBP, or ≥10mg/dl LDLc reductions

eTable 7. Mean Differences in Primary and Secondary Outcomes Between Treatment and Control by Site and Sensitivity Analysis at 12 months

12 months	MDRF (N = 155)	AIIMS (N = 90)	EDC (N = 84)	Diacon (N = 75)	All 4 Sites (N = 404)	Without EDC (N = 320)
Primary Outcome	17.7 (6.3; 29.2)	23.8 (10.3; 37.3)	42.4 (30.5; 54.3)	14.8 (-1.1; 30.7)	23.7 (14.7; 32.6)	13.5 (2.9; 24.1)
≥50% improvement in SCL-20	16.6 (5.4; 27.9)	27.0 (13.8; 40.1)	49.0 (-12.4; 12.4)	17.0 (2.3; 31.7)	25.7 (17.0; 34.4)	15.6 (5.4; 25.7)
Mean SCL-20 score difference	-0.3 (-0.4; -0.1)	-0.3 (-0.5; -0.2)	-0.5 (-0.6; -0.3)	-0.2 (-0.3; -0.1)	-0.3 (-0.4; -0.2)	
≥0.5ppt reduction in HbA1c	21.6 (7.7; 35.4)	18.0 (2.1; 33.8)	14.4 (-2.6; 31.5)	12.0 (-6.2; 30.2)	17.5 (7.8; 27.2)	17.6 (6.7; 28.5)
HbA1c < 7.0%	7.6 (-4.1; 19.3)	9.5 (-3.6; 22.7)	7.8 (-8.0; 23.6)	3.4 (-10.6; 17.3)	7.3 (-1.2; 15.8)	7.4 (-1.8; 16.6)
≥0.5ppt reduction or HbA1c<7.0%	23.0 (9.4; 36.7)	16.1 (0.4; 31.7)	10.5 (-6.4; 27.4)	8.3 (-9.1; 25.7)	16.1 (6.5; 25.7)	16.6 (5.9; 27.3)
Mean HbA1c difference, ppt	-0.4 (-1.0; 0.1)	-0.4 (-1.0; 0.2)	-0.3 (-0.7; 0.2)	0.1 (-0.6; 0.9)	-0.3 (-0.6; 0.1)	-0.3 (-0.7; 0.2)
≥5mmHg reduction in SBP	3.4 (-10.4; 17.2)	-0.3 (-17.1; 16.5)	14.8 (-0.6; 30.2)	2.7 (-15.7; 21.1)	4.8 (-5.1; 14.7)	-1.8 (-12.8; 9.3)
SBP < 130 mmHg	0.1 (-13.2; 13.4)	0.9 (-13.6; 15.4)	8.6 (-6.6; 23.9)	-4.0 (-19.7; 11.8)	1.3 (-8.1; 10.7)	-4.6 (-15.0; 5.9)
≥5mmHg reduction or SBP<130	-2.2 (-13.8; 9.4)	-6.9 (-20.0; 6.2)	7.7 (-7.5; 22.8)	-6.8 (-20.8; 7.1)	-2.1 (-10.8; 6.7)	-8.7 (-18.1; 0.7)
Mean SBP difference, mmHg	-2.6 (-7.6; 2.4)	-0.7 (-6.0; 4.7)	-2.6 (-8.7; 3.4)	0.1 (-5.8; 6.1)	-1.7 (-4.9; 1.5)	0.0 (-3.5; 3.5)
≥10mg/dl reduction in LDL	6.2 (-7.3; 19.6)	-0.2 (-16.3; 16.0)	-2.3 (-20.2; 15.6)	0.2 (-17.9; 18.3)	1.9 (-7.9; 11.7)	2.4 (-8.6; 13.4)
LDLc < 100mg/dl (<70 if CVD)	7.7 (-6.3; 21.7)	20.0 (4.3; 35.8)	8.5 (-8.4; 25.5)	-13.1 (-28.4; 2.3)	6.7 (-2.9; 16.4)	3.1 (-7.9; 14.1)
≥10mg/dl reduction or LDLc<100	8.1 (-4.5; 20.6)	12.0 (-4.1; 28.1)	0.7 (-14.8; 16.1)	-9.5 (-24.8; 5.7)	4.1 (-5.2; 13.4)	2.9 (-7.5; 13.4)
Mean LDLc difference, mg/dl	-5.5 (-15.6; 4.7)	-6.7 (-16.4; 2.9)	-2.2 (-15.1; 10.6)	11.9 (-1.8; 25.6)	-1.9 (-8.5; 4.8)	0.6 (-7.3; 8.5)
All CVD Targets	9.7 (1.6; 17.9)	8.3 (-0.7; 17.3)	8.7 (2.2; 15.2)	6.6 (-2.3; 15.6)	8.6 (3.0; 14.3)	6.2 (-0.2; 12.6)
PHQ-9 < 10	15.2 (4.6; 25.7)	15.5 (5.8; 25.2)	63.2 (52.2; 74.2)	7.6 (-0.1; 15.3)	23.8 (16.2; 31.4)	11.4 (2.7; 20.1)
Mean PHQ-9 difference	-1.9 (-3.0; -0.8)	-2.2 (-3.4; -1.0)	-4.6 (-5.5; -3.6)	-1.3 (-2.3; -0.4)	-2.4 (-3.2; -1.6)	-1.4 (-2.3; -0.4)

Abbreviations: MDRF, Madras Diabetes Research Foundation; AIIMS, All India Institute of Medical Sciences; EDC, Endocrine and Diabetes Centre; Diacon, Diacon Diabetes Hospital; SCL-20, 20-item symptoms checklist (range: 0 [best] – 4 [worst]); PHQ-9, 9-item patient health questionnaire (range: 0 [best] – 27 [worst] where score ≥10 signifies moderate-to-severe depressive symptoms); HbA1c, glycated hemoglobin (%); SBP, systolic blood pressure (mmHg); LDLc, low-density lipoprotein cholesterol (mg/dl); ppt, percentage points; CVD, cardiovascular disease

Primary outcome = proportion achieving ≥50% reductions in SCL-20 and ≥1 of: ≥0.5ppt HbA1c, ≥5mmHg SBP, or ≥10mg/dl LDLc reductions

All estimates are risk differences between groups with 95% confidence intervals using the same unadjusted analysis approach as the main analysis additionally including a treatment-by-site interaction. Ns per site are sample sizes at baseline.

eTable 8. Mean Differences in Primary and Secondary Outcomes Between Treatment and Control by Site and Sensitivity Analysis at 24 months

24 months						
	MDRF (N = 155)	**AIIMS (N = 90)**	**EDC (N = 84)**	**Diacon (N = 75)**	**All 4 Sites (N = 404)**	**Without EDC (N = 320)**
Primary Outcome	10.9 (0.5; 21.3)	17.0 (3.8; 30.2)	35.6 (23.8; 47.5)	8.0 (-8.4; 24.4)	16.9 (8.5; 25.2)	10.4 (0.9; 19.8)
≥50% improvement in SCL-20	5.1 (-4.1; 14.2)	15.4 (3.0; 27.8)	37.4 (-12.4; 12.4)	5.4 (-9.7; 20.6)	14.1 (6.7; 21.6)	5.7 (-2.2; 13.6)
Mean SCL-20 score difference	-0.1 (-0.2; 0.0)	-0.2 (-0.3; -0.0)	-0.3 (-0.4; -0.2)	-0.1 (-0.2; 0.1)	-0.2 (-0.2; -0.1)	-0.1 (-0.2; 0.0)
≥0.5ppt reduction in HbA1c	12.8 (-0.8; 26.4)	9.2 (-6.9; 25.4)	5.7 (-11.0; 22.3)	3.2 (-15.3; 21.7)	8.7 (-0.9; 18.4)	10.7 (-0.3; 21.7)
HbA1c < 7.0%	-2.6 (-12.5; 7.3)	-0.7 (-12.9; 11.5)	-2.5 (-18.2; 13.2)	-6.9 (-20.6; 6.9)	-3 (-10.1; 4.2)	-2.9 (-10.3; 4.6)
≥0.5ppt reduction or HbA1c<7.0%	11.6 (-1.8; 25.0)	4.7 (-11.3; 20.6)	-0.9 (-18.3; 16.5)	-3.1 (-20.6; 14.5)	4.7 (-5.0; 14.5)	7.7 (-3.3; 18.7)
Mean HbA1c difference, ppt	-0.1 (-0.6; 0.4)	-0.1 (-0.7; 0.5)	0.1 (-0.4; 0.5)	0.4 (-0.3; 1.2)	0.0 (-0.3; 0.4)	0.1 (-0.3; 0.5)
≥5mmHg reduction in SBP	-1.2 (-15.1; 12.8)	-4.9 (-20.7; 10.9)	10.3 (-5.3; 25.9)	-1.8 (-20.9; 17.2)	0.3 (-9.6; 10.2)	-1.8 (-12.9; 9.4)
SBP < 130 mmHg	-0.9 (-13.8; 12.0)	-0.1 (-14.0; 13.8)	7.7 (-8.1; 23.5)	-5.0 (-21.6; 11.6)	0.3 (-9.1; 9.7)	-2.1 (-12.5; 8.3)
≥5mmHg reduction or SBP<130	-3.7 (-14.9; 7.5)	-8.3 (-20.4; 3.7)	6.2 (-9.0; 21.5)	-8.3 (-23.3; 6.7)	-3.5 (-12.1; 5.1)	-5.8 (-15.1; 3.5)
Mean SBP difference, mmHg	-1.7 (-6.7; 3.2)	0.2 (-6.1; 6.4)	-1.8 (-8.2; 4.6)	1.0 (-5.4; 7.4)	-0.8 (-4.6; 2.9)	-0.5 (-4.9; 3.9)
≥10mg/dl reduction in LDL	1.8 (-11.5; 15.1)	-4.6 (-20.7; 11.5)	-6.7 (-24.7; 11.3)	-4.2 (-22.3; 13.9)	-2.5 (-12.3; 7.2)	0.5 (-10.5; 11.4)
LDLc < 100mg/dl (<70 if CVD)	2.2 (-11.5; 15.9)	14.5 (-1.5; 30.5)	3.0 (-14.3; 20.2)	-18.6 (-34.1; -3.1)	1.2 (-8.6; 11.0)	4.7 (-6.4; 15.8)
≥10mg/dl reduction or LDLc<100	3.2 (-9.9; 16.3)	7.0 (-9.0; 23.1)	-4.3 (-19.7; 11.1)	-14.5 (-29.4; 0.5)	-0.8 (-10.3; 8.7)	3.7 (-7.2; 14.6)
Mean LDLc difference, mg/dl	-1.6 (-12.1; 8.9)	-2.9 (-12.9; 7.1)	1.6 (-11.7; 15.0)	15.7 (0.8; 30.7)	2.0 (-5.6; 9.6)	-0.8 (-9.6; 8.1)
All CVD Targets	1.7 (-4.7; 8.2)	0.3 (-8.6; 9.3)	0.7 (-4.6; 6.0)	-1.4 (-10.8; 8.1)	0.6 (-4.0; 5.2)	1.5 (-3.9; 7.0)
PHQ-9 < 10	8.6 (0.5; 16.6)	8.9 (0.0; 17.9)	56.6 (45.5; 67.8)	1.0 (-6.0; 8.1)	17.2 (11.2; 23.2)	3.1 (-2.0; 8.2)
Mean PHQ-9 difference	-0.7 (-1.7; 0.2)	-1 (-2.2; 0.1)	-3.4 (-4.3; -2.5)	-0.2 (-1.1; 0.7)	-1.2 (-1.9; -0.6)	-0.4 (-1.1; 0.2)

Abbreviations: MDRF, Madras Diabetes Research Foundation; AIIMS, All India Institute of Medical Sciences; EDC, Endocrine and Diabetes Centre; Diacon, Diacon Diabetes Hospital; SCL-20, 20-item symptoms checklist (range: 0 [best] – 4 [worst]); PHQ-9, 9-item patient health questionnaire (range: 0 [best] – 27 [worst] where score ≥10 signifies moderate-to-severe depressive symptoms); HbA1c, glycated hemoglobin (%); SBP, systolic blood pressure (mmHg); LDLc, low-density lipoprotein cholesterol (mg/dl); ppt, percentage points; CVD, cardiovascular disease

Primary outcome = proportion achieving ≥50% reductions in SCL-20 and ≥1 of: ≥0.5ppt HbA1c, ≥5mmHg SBP, or ≥10mg/dl LDLc reductions

All estimates are risk differences between groups with 95% confidence intervals using the same unadjusted analysis approach as the main analysis additionally including a treatment-by-site interaction. Ns per site are sample sizes at baseline.

eTable 9. Post hoc Sensitivity Analysis examining Within-Group Mean Differences in HbA1c, SBP, and LDL-c in Patients with Elevated Levels at Baseline

	n	12 month		24 month		Overall[d]		
		MD	95% CI	MD	95% CI	MD	95% CI	p-value[e]
Unadjusted								
HbA1c, mean (ppt)[a]	288	-0.4	(-0.8; 0.0)	0.0	(-0.43; 0.36)	-0.3	(-0.6; 0.1)	0.10
SBP, mean (mmHg)[b]	170	-6.2	(-11.0; -1.4)	-2.7	(-8.5; 3.2)	-3.6	(-7.5; 0.4)	0.08
LDLc, mean (mg/dl)[c]	95	-13.9	(-26.8; -0.9)	13.9	(-3.0; 30.9)	-2.0	(-12.6; 8.5)	0.70
Adjusted								
HbA1c, mean (ppt)[a]	288	-0.5	(-0.9; -0.1)	-0.2	(-0.5; 0.2)	-0.4	(-0.7; -0.1)	0.009
SBP, mean (mmHg)[b]	170	-6.4	(-11.0; -1.9)	-2.9	(-8.4; 2.7)	-3.8	(-7.5; 0.0)	0.05
LDLc, mean (mg/dl)[c]	95	-15.3	(-28.4; -2.3)	12.5	(-4.9; 29.8)	-3.5	(-14.1; 7.1)	0.52

Abbreviations: MD, mean differences; 95% CI, 95% confidence intervals; HbA1c, glycated hemoglobin (%); SBP, systolic blood pressure (mmHg); LDLc, low-density lipoprotein cholesterol (mg/dl); ppt, percentage points

*Mean differences estimated with Gaussian models using an identity-link and a generalized estimating equation approach to account for correlation of observations within participants over time. Model effects in the unadjusted analysis are treatment group, time, treatment*time interaction and site. Adjusted analysis: additional adjustment for age, sex and respective baseline values*

[a] *only participants with PHQ-9 ≥ 10 & HbA1c ≥ 8% at baseline*

[b] *only participants with PHQ-9 ≥ 10 & SBP ≥ 140 mmHg at baseline*

[c] *Only participants with PHQ-9 ≥ 10 & LDLc ≥ 130 mg/dl at baseline*

[d] *post-hoc analysis*

[e] *p-values represent statistical significance of overall between-group RD*

eTable 10. Serious adverse effects by treatment group

Description	Incident Events, n			Total Events Reported in Trial, n[a]		
	Total	**Collaborative Care**	**Usual Care**	**Total**	**Collaborative Care**	**Usual Care**
Acute Coronary Syndrome	2	1	1	2	1	1
Amputation	1	1	0	2	2	0
CAD	7	4	3	7	4	3
CAD: Revascularization	6	3	3	6	3	3
CHF	2	0	2	2	0	2
CHF Hospitalization	1	0	1	1	0	1
Death	9	2	7	9	2	7
Diabetic Foot / Leg Ulcer	4	1	3	4	1	3
Diabetic Nephropathy	1	1	0	1	1	0
Diabetic Retinopathy	1	1	0	1	1	0
Hospitalization	3	3	0	3	3	0
Hyperglycemia	1	0	1	1	0	1
Hypoglycemia	8	8	0	8	8	0
Ischemic Stroke	3	0	3	3	0	3
Neuropathy	41	16	25	49	21	28
Peripheral Edema	6	3	3	7	4	3
Suicidal Ideation	2	0	2	2	0	2
Suicide Attempt	1	1	0	1	1	0

Numbers are counts

[a] Total reported events include those at baseline plus incident events during trial

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure