## **Supplementary Online Content 2**

Bieleninik Ł, Geretsegger M, Mössler K, et al; TIME-A Study Team. Effects of improvisational music therapy vs enhanced standard care on symptom severity among children with autism spectrum disorder: the TIME-A randomized clinical trial. *JAMA*. doi:10.1001/jama.2017.9478

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

eTable 1. Changes to the Study Protocol

Domain	From	То	Rationale
Population	No prior experience of music therapy	Limited experience of music therapy if that was more than 12 months ago	In response to a request from a site
Baseline data	IQ level assessed by K-ABC or, when not possible, clinical judgment	IQ level assessed by K-ABC, other standardized test, or, when not possible, clinical judgment	In response to requests from sites
Interventions - improvisational music therapy	Music therapists with master degree or equivalent	Trained music therapists with a degree that is recognized in the country	Not applicable in all countries
Interventions – improvisational music therapy	No improvisational music therapy offered after completion of the study	At some sites: improvisational music therapy offered after the last wave of data collection (12 months) to those assigned to enhanced standard care	To maintain equipoise
Interventions – enhanced standard care	3 sessions of parent counseling	At one site: 3 or 10 sessions of parent counseling (balanced across the groups of the trial)	In response to a request from a site
Outcomes – primary	ADOS Social Communication	ADOS Social Affect	Name change only, to reflect current ADOS terminology
Outcomes – secondary		Two 100mm visual analogue scales were added to assess the quality of life of the child and of the family as a whole	Primarily to help with cost-effectiveness analyses

eTable 1. Changes to the Study Protocol (Continued)

Domain	From	То	Rationale
Outcomes – time points	0, 2, 5, and 12 months	At one site: The 2- months assessment for existing participants was regarded as optional when recruitment of new participants was high.	To avoid waiting times for participants
Statistical analyses – main	Longitudinal analysis using generalized estimating equations	Longitudinal analysis using linear mixed- effects models	Linear mixed-effects models require fewer assumptions (missing at random rather than missing completely at random) and have somewhat better power.
Statistical analyses – exploratory		A binary analysis of response (improved/not improved) was added.	To identify the proportion who improved.
Statistical analyses – subgroups	Relevant subgroups "such as" age or ASD subtype	Age, sex, ASD subtype, verbal ability, ASD severity, IQ level, country, time of enrolment in the study	Implied in the protocol.

Note. Abbreviations: ADOS – Autism Diagnostic Observation Schedule; ASD – Autism Spectrum Disorder; IQ – Intelligence Quotient K-ABC – Kaufman Assessment Battery for Children.

eTable 2. Baseline Characteristics of Those Observed Versus Those Who Dropped Out at 5 Months

	Followed	up at 5 months	Dropped		
Characteristics	N		N		P-value
Age (years), Mean (SD)	314	5.4 (0.9)	50	5.3 (0.9)	.517
Sex (male), No. (%)	314	266 (84.7%)	50	36 (72%)	.044
Native speaker of the country's main language, No. (%)	314	275 (87.6%)	50	46 (92%)	.507
Education mother, No. (%)	311		47		.562
<12years (less than high school)		33 (10.6%)		3 (6.4%)	
≥12years (equivalent to high school)		115 (37%)		17 (36.2%)	
University		139 (44.7%)		25 (53.2%)	
Unknown		24 (7.7%)		2 (4.3%)	
Education father, No. (%)	307		47		.274
<12years (less than high school)		46 (15%)		4 (8.5%)	
≥12years (equivalent to high school)		102 (33.2%)		13 (27.7%)	
University		125 (40.7%)		26 (55.3%)	
Unknown		34 (11.1%)		4 (8.5%)	
Employment mother, No. (%)	311		47		.392
Unemployed or social support		39 (12.5%)		9 (19.1%)	
Working part-time		80 (25.7%)		12 (25.5%)	
Working full time		55 (17.7%)		12 (25.5%)	
Homemaker		111 (35.7%)		12 (25.5%)	
Other		7 (2.3%)		0 (0%)	
Unknown		19 (6.1%)		2 (4.3%)	
Employment father, No. (%)	309		47		.715
Unemployed or social support		18 (5.8%)		1 (2.1%)	
Working part-time		16 (5.2%)		2 (4.3%)	
Working full time		225 (72.8%)		39 (83%)	
Homemaker		5 (1.6%)		0 (0%)	

eTable 2. Baseline Characteristics of Those Observed Versus Those Who Dropped Out at 5 Months (Continued)

	Followed	up at 5 months	Dropped		
Characteristics	N	Value	N	Value	P-value
Other		10 (3.2%)		1 (2.1%)	
Unknown		35 (11.3%)		4 (8.5%)	
Adults in the household, No. (%)	300		45		.343
1 adult		44 (14.7%)		3 (6.7%)	
2 adults		233 (77.7%)		38 (84.4%)	
>2 adults		23 (7.7%)		4 (8.9%)	
Siblings in the family, No. (%)	298		44		.423
No siblings		80 (26.8%)		10 (22.7%)	
1 sibling		144 (48.3%)		19 (43.2%)	
>1 sibling		74 (24.8%)		15 (34.1%)	
Diagnosis, No. (%)	314		50		.645
Childhood autism (ICD-10 code F84.0)		257 (81.8%)		44 (88%)	
Atypical autism (ICD-10 code F84.1)		3 (1%)		0 (0%)	
Asperger syndrome (ICD-10 code F84.5)		12 (3.8%)		2 (4%)	
PDD (ICD-10 code F84.9) <sup>1</sup>		42 (13.4%)		4 (8%)	
Previous music therapy, No. (%)	306	9 (2.9%)	50	3 (6%)	.491
ADOS module, No. (%)	314		50		.864
Module 1		192 (61.1%)		32 (64%)	
Module 2		112 (35.7%)		17 (34%)	
Module 3		10 (3.2%)		1 (2%)	
ADOS Total, Mean (SD)	313	17.6 (5.3)	50	18.1 (5)	.554
ADOS Social Affect, Mean (SD)	314	13.7 (4.4)	50	14.1 (4.5)	.569
ADOS Language and Communication, Mean (SD)	314	3.3 (1.5)	50	3.1 (1.4)	.318
ADOS Reciprocal Social Interaction, Mean (SD)	314	10.4 (3.5)	50	11 (3.7)	.285

eTable 2. Baseline Characteristics of Those Observed Versus Those Who Dropped Out at 5 Months (Continued)

		wed up at 5 Dropped out at 5 months months			
Characteristics	N	Value	N	Value	P-value
ADOS Restricted and Repetitive Behavior, Mean (SD)	313	3.9 (2.1)	50	4 (1.6)	.830
SRS Total, Mean (SD)	310	95.7 (28.1)	49	98.2 (30.3)	.599
SRS Social Awareness, Mean (SD)	314	12.3 (4.1)	49	12.1 (3.7)	.777
SRS Social Cognition, Mean (SD)	314	18.5 (5.9)	50	17.9 (6.4)	.540
SRS Social Communication, Mean (SD)	314	31.9 (9.9)	50	33.3 (11.3)	.395
SRS Social Motivation, Mean (SD)	314	14.7 (5.7)	50	16 (6.2)	.178
SRS Autistic Mannerisms, Mean (SD)	314	17.9 (7.1)	50	18.4 (7)	.660
Quality of life, participant, Mean (SD)	307	71.4 (18.7)	50	72.7 (17.5)	.624
Quality of life, family, Mean (SD)	307	68.4 (20.2)	50	66.7 (17.7)	.557
Parent working reduced hours due to the child's needs (in percent of full-time work), Mean (SD)	158	69.2 (30.3)	23	66.6 (32.6)	.714
IQ source, No. (%)	314		50		.161
K-ABC <sup>2</sup>		7 (2.2%)		1 (2%)	
Other standardized test	İ	175 (55.7%)		35 (70%)	
Clinical judgment <sup>3</sup>		132 (42%)		14 (28%)	

eTable 2. Baseline Characteristics of Those Observed Versus Those Who Dropped Out at 5 Months (Continued)

	Followed	up at 5 months	Dropped		
Characteristics	N	Value	N	Value	P-value
IQ, standardized test, Mean (SD)	178	75.9 (26.3)	33	72.8 (25.7)	.539
Mental retardation (IQ<70), No. (%) <sup>3</sup>	309	144 (46.6%)	47	21 (44.7%)	.929
ADI-R A: Reciprocal Social Interaction, Mean (SD)	314	18.2 (5.8)	50	18.6 (5.5)	.698
ADI-R B: Language and Communication, Mean (SD)	314	13.1 (4.2)	50	12.6 (3.9)	.453
ADI-R C: Repetitive Behaviors and Interests, Mean (SD)	314	5.9 (2.5)	50	5.3 (1.9)	.032
ADI-R D: Early Onset, Mean (SD)	314	4 (1.1)	50	3.8 (1.1)	.395
Child care, No. (%)	314		50		.037
Attends school		195 (62.1%)		34 (68%)	
Full-time care (≥7h per day)		76 (24.2%)		4 (8%)	
Part-time care (<7h per day)		30 (9.6%)		8 (16%)	
None of the above		13 (4.1%)		4 (8%)	

<sup>&</sup>lt;sup>1</sup>Pervasive developmental disorder unspecified. <sup>2</sup>Kaufman Assessment Battery for Children. <sup>3</sup>IQ was assessed with standardized scales. If the child was unable to complete a standardized test, no quantitative IQ assessment was made, but only a categorical clinical judgment whether mental retardation (i.e. IQ<70) was present.

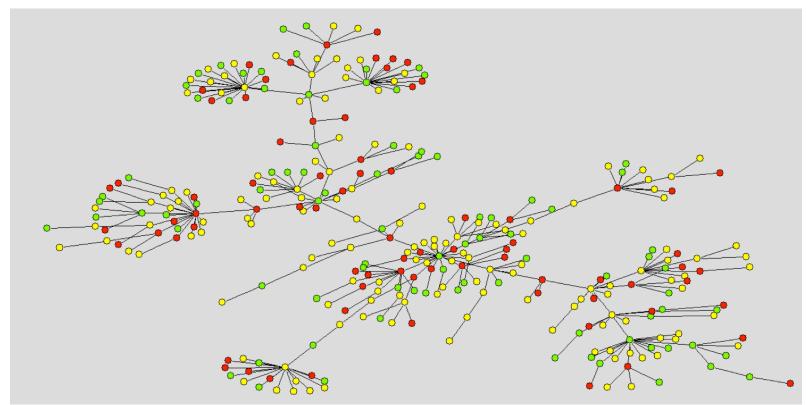
Measures: ADOS – Autism Diagnostic Observation Schedule. Higher scores indicate greater severity. Possible range: Total 0-37; Social Affect 0-27; Language and Communication 0-9; Reciprocal Social Interaction 0-19; Restricted and Repetitive Behavior 0-10.

SRS – Social Responsiveness Scale. Higher scores indicate greater severity. Possible range: Total 0-195; Social Awareness 0-24; Social Cognition 0-36; Social Communication 0-66; Social Motivation 0-33; Autistic Mannerisms 0-36.

Quality of life, participant and family: Visual analog scale. Higher scores indicate better quality of life. Possible range: 0-100, where 0 indicates worst possible and 100 best possible quality of life.

IQ – Intelligence Quotient. Higher scores indicate greater cognitive ability. Scores around 100 indicate normal intelligence; scores below 70 indicate mental retardation.

ADI-R – Autism Diagnostic Interview-Revised. Higher scores indicate greater severity. Possible range: Reciprocal Social Interaction 0-30; Language and Communication 0-26; Repetitive Behaviors and Interests 0-12; Early Onset 0-5.



eFigure 1. Multidimensional Scaling of Baseline Characteristics by Treatment Group

Note. This figure shows the clustering of records according to their multidimensional similarity. Yellow – enhanced standard care; red – high-intensity music therapy; green – low-intensity music therapy.

Explanation: The map in this figure represents the natural clustering of participants enrolled in the study obtained with minimum spanning tree algorithm. Each participant is described by 24 baseline variables (demographic characteristics and concomitant treatments). The figure shows the projection of all patients in a multidimensional space related to these variables. Natural clustering emerges bottom-up. Each node represents a participant. Participants are linked directly when their multidimensional similarity is very high. The closeness between participants is inversely proportional to separation degrees of the representing nodes.

Interpretation: In each cluster of participants the three groups are represented, suggesting that randomization created a multidimensional balance between the groups.

eTable 3. Concomitant Treatments Provided as Part of Enhanced Standard Care

Intervention	Baseline	2 months	5 months	12 months
	n (%)	n (%)	n (%)	n (%)
Specialist autism services tutoring of parents or school or day care centre	123 (34%)	99 (36%)	100 (32%)	90 (30%)
Sensory-motor therapy (incl. occupational & physiotherapy)	151 (41%)	112 (41%)	109 (34%)	104 (35%)
Speech and language therapy and communication training	210 (58%)	150 (55%)	163 (52%)	155 (52%)
Play therapy or Floortime approach	35 (10%)	24 (9%)	28 (9%)	18 (6%)
Behavioral/educational intervention (e.g. TEACCH or ABA)	55 (15%)	38 (14%)	45 (14%)	48 (16%)
Social skills training	31 (9%)	36 (13%)	43 (14%)	46 (15%)
Therapeutic leisure activities (e.g. horse riding)	47 (13%)	50 (18%)	55 (17%)	49 (16%)
Other interventions	60 (16%)	58 (21%)	63 (20%)	67 (23%)
No specific therapy or intervention (outside of this study)	55 (15%)	38 (14%)	45 (14%)	37 (12%)
Institutional stay	12 (3%)	9 (3%)	9 (3%)	8 (3%)
Outpatient treatment	38 (10%)	23 (8%)	19 (6%)	25 (8%)
Supplement or medication	110 (30%)	74 (27%)	74 (23%)	75 (25%)
Special diet	61 (17%)	32 (12%)	32 (10%)	31 (10%)

Note. n = 364 (baseline), 272 (2 months), 316 (5 months), 297 (12 months). At each time point, parents were asked to report interventions received during past two months.

Abbreviations: ABA – Applied Behavior Analysis; DIR – Developmental, Individual-differences, & Relationship-based Model; TEACCH – Treatment and Education of Autistic and Communication Handicapped Children.

## eTable 4. Mean Scores of Improvisational Music Therapy and Parent Counselling Principles

## a) Parent counseling

	(05)	Much or very much used, number of
Parent counselling principle	Mean (SD)	sessions (%)
Creating a safe place	2.97 (0.17)	33 (100%)
Discussing concerns regarding the present	2.76 (0.44)	33 (100%)
time		
Discussing concerns regarding the child's	2.52 (0.62)	31 (94%)
developmental process		
Providing information on various aspects of	1.30 (0.77)	10 (30%)
ASD		
Providing information on social communication and ASD	1.76 (0.71)	22 (67%)

Note. Based on 33 parent counseling sessions, one rater per session. Scores for each item were 0 (not used at all), 1 (a little), 2 (much), or 3 (used very much). All 33 sessions (100%) were rated as adequate overall.

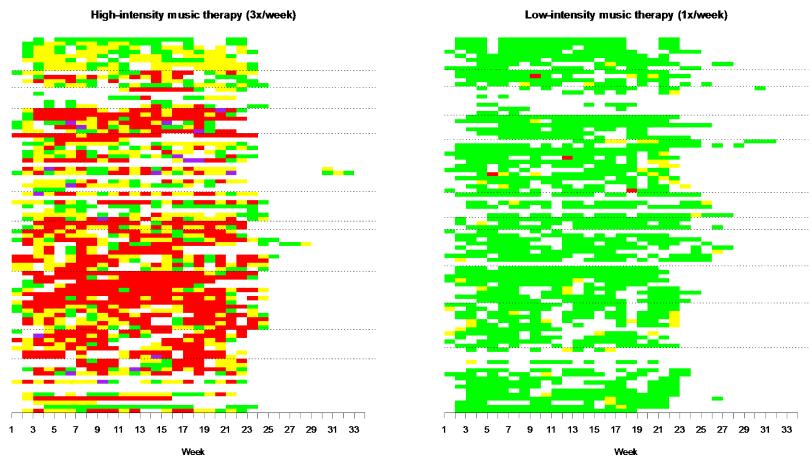
Abbreviations: ASD – Autism Spectrum Disorder.

## b) Improvisational music therapy

		Frequently used, number of sessions
Improvisational music therapy principle	Mean (SD)	(%)
Facilitate musical and emotional attunement	3.45 (0.74)	495 (82%)
Scaffold flow of interaction musically	3.16 (0.79)	426 (70%)
Tap into shared history of musical interaction	2.98 (0.93)	363 (60%)
Build and maintain a positive therapeutic	3.67 (0.78)	529 (87%)
relationship		
Provide a secure environment	3.7 (0.71)	548 (91%)
Follow the child's lead	3.08 (0.87)	408 (67%)
Set treatment goals and evaluate progress	3.24 (0.76)	454 (75%)
Facilitate enjoyment	2.97 (0.92)	372 (61%)

Note. Based on 606 randomly selected therapy sessions, average of two independent raters. Scores could range from 0 (not used at all) to 5 (used frequently and with mastery); scores  $\geq$  3 represented frequently used. Detailed definitions of principles, see ref. 15 in the main article. The mean sum score was 26.26 (SD 5.67); a total of 410 sessions (68%) had scores  $\geq$  24. This cutoff was derived theoretically (i.e. 8 items with an average of  $\geq$  3), but was also justified by the ROC curve (see eFigure 3). Raters also provided a binary rating of whether the session was adequate overall: rater 1, 604/606 (100%) yes; rater 2, 566/606 yes (94%).

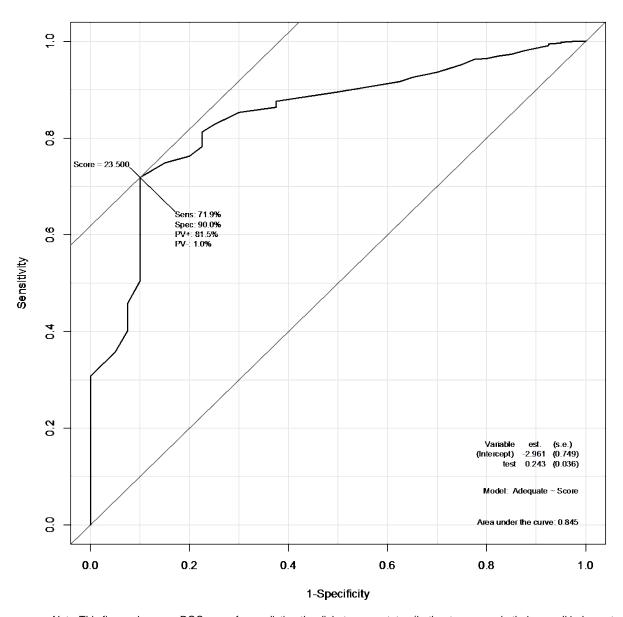
eFigure 2. Patterns of Improvisational Music Therapy Sessions Received Per Week



Note. Figure depicts number of sessions conducted with each participant per seven-day period (purple = 4, red = 3, yellow = 2, green = 1, white = 0). Each line represents one participant; sites are separated by dotted lines. It can be seen that patterns of missingness are irregular, suggesting holidays or illness as plausible causes rather than declining attendance over time.

Abbreviations: IMT - Improvisational music therapy.

eFigure 3. ROC Curve for Optimal Treatment Fidelity Cutoffs



Note. This figure shows an ROC curve for predicting the dichotomous status (both raters agree in their overall judgment that the improvisational music therapy session was conducted adequately) from the continuous score (the mean of two raters' sum score of ratings of improvisational music therapy principles). The cutoff that maximized specificity and sensitivity was ≥ 24 versus <24.

Abbreviations: PV- – negative predictive value; PV+ – positive predictive value; ROC – received operating characteristic; Sens – sensitivity; Spec – specificity; Variables: Adequate – overall rating of adequacy (1 if judged as adequate by two independent raters; 0 if judged as

Variables: Adequate – overall rating of adequacy (1 if judged as adequate by two independent raters; 0 if judged as inadequate or uncertain by at least one of two raters); Score – sum score of 8 improvisational music therapy principles (see eTable 4b).

eTable 5. Linear Mixed-Effects Analyses—All Outcomes, Two Groups

	Unadjusted			Adjusted for site		
ADOS Social Affect (Primary outcome)	Beta coefficient	CI	P- value	Beta coefficient	CI	P- value
Intercept	13.49	(12.82, 14.16)	<0.00 1	13.67	(12.53, 14.81)	<0.00 1
Group (improvisational music therapy)	0.59	(-0.37, 1.54)	0.23	0.45	(-0.45, 1.36)	0.32
2 months vs. BL	-0.38	(-0.96, 0.21)	0.21	-0.33	(-0.91, 0.25)	0.27
5 months vs. BL	-0.91	(-1.45, - 0.36)	0.001	-0.9	(-1.45, - 0.36)	0.001
12 months vs. BL	-1.63	(-2.2, -1.07)	<0.00 1	-1.62	(-2.19, - 1.06)	<0.00 1
Group * (2 months vs. BL)	0.21	(-0.59, 1.01)	0.61	0.18	(-0.62, 0.98)	0.66
Group * (5 months vs. BL)	0.06	(-0.7, 0.81)	0.88	0.05	(-0.71, 0.81)	0.90
Group * (12 months vs. BL)	0.16	(-0.62, 0.94)	0.69	0.14	(-0.64, 0.92)	0.73
Social Responsiveness (SRS) Total (Prespecified secondary outcome)	Beta coefficient	CI	P- value	Beta coefficient	CI	P- value
Intercept	95.81	(91.58, 100.04)	<0.00	95.62	(88.73, 102.52)	<0.00
Group (improvisational music therapy)	0.05	(-5.94, 6.03)	0.99	-0.37	(-5.99, 5.26)	0.90
2 months vs. BL	0.47	(-2.67, 3.61)	0.77	0.81	(-2.33, 3.95)	0.61
5 months vs. BL	-1.81	(-4.87, 1.26)	0.25	-1.53	(-4.59, 1.53)	0.33
12 months vs. BL	-4.61	(-7.7, -1.52)	0.004	-4.35	(-7.44, - 1.26)	0.006
Group * (2 months vs. BL)	-2.37	(-6.7, 1.95)	0.28	-2.65	(-6.97, 1.66)	0.23
Group * (5 months vs. BL)	-3.32	(-7.56, 0.91)	0.13	-3.57	(-7.8, 0.66)	0.10
Group * (12 months vs. BL)	-2.47	(-6.77, 1.84)	0.26	-2.67	(-6.97, 1.64)	0.23

eTable 5. Linear Mixed-Effects Analyses—All Outcomes, Two Groups (Continued)

	Unadjusted			Adjusted for site			
SRS Social Awareness	Beta coefficient	CI	P-value	Beta coefficient	CI	P-value	
(Prespecified secondary outcome)							
Intercept	12.39	(11.8, 12.99)	<0.001	12.42	(11.42, 13.43)	<0.001	
Group (improvisational music therapy)	-0.3	(-1.14, 0.55)	0.49	-0.38	(-1.17, 0.41)	0.34	
2 months vs. BL	0.43	(-0.1, 0.96)	0.11	0.51	(-0.01, 1.04)	0.06	
5 months vs. BL	-0.16	(-0.67, 0.35)	0.53	-0.1	(-0.61, 0.41)	0.70	
12 months vs. BL	-0.57	(-1.08, -0.05)	0.03	-0.51	(-1.02, 0.01)	0.05	
Group * (2 months vs. BL)	-0.58	(-1.3, 0.14)	0.12	-0.64	(-1.36, 0.08)	0.08	
Group * (5 months vs. BL)	-0.18	(-0.89, 0.52)	0.61	-0.23	(-0.94, 0.47)	0.52	
Group * (12 months vs. BL)	0.13	(-0.58, 0.85)	0.72	0.1	(-0.62, 0.81)	0.79	
SRS Social Cognition	Beta coefficient	CI	P-value	Beta coefficient	CI	P-value	
(Prespecified secondary outcome)							
Intercept	18.65	(17.78, 19.53)	<0.001	18.56	(17.3, 19.82)	<0.001	
Group (improvisational music therapy)	-0.48	(-1.73, 0.76)	0.45	-0.53	(-1.73, 0.67)	0.39	
2 months vs. BL	-0.33	(-1.1, 0.44)	0.40	-0.25	(-1.02, 0.52)	0.52	
5 months vs. BL	-0.45	(-1.19, 0.3)	0.24	-0.39	(-1.14, 0.35)	0.30	
12 months vs. BL	-1.25	(-2, -0.5)	0.001	-1.2	(-1.95, -0.45)	0.002	
Group * (2 months vs. BL)	0.4	(-0.66, 1.45)	0.46	0.34	(-0.71, 1.4)	0.52	
Group * (5 months vs. BL)	-0.38	(-1.41, 0.65)	0.47	-0.42	(-1.45, 0.61)	0.42	
Group * (12 months vs. BL)	0.11	(-0.94, 1.16)	0.84	0.07	(-0.97, 1.12)	0.89	

eTable 5. Linear Mixed-Effects Analyses—All Outcomes, Two Groups (Continued)

		Unadjusted		Adjusted for site			
SRS Social Communication (Prespecified secondary outcome)	Beta coefficient	CI	P-value	Beta coefficient	CI	P-value	
Intercept	32.06	(30.55, 33.57)	<0.001	31.91	(29.79, 34.04)	<0.001	
Group (improvisational music therapy)	0.06	(-2.08, 2.2)	0.96	-0.03	(-2.1, 2.04)	0.98	
2 months vs. BL	-0.15	(-1.45, 1.16)	0.82	-0.02	(-1.32, 1.29)	0.98	
5 months vs. BL	-1.13	(-2.4, 0.13)	0.08	-1.04	(-2.3, 0.23)	0.11	
12 months vs. BL	-2.09	(-3.37, -0.82)	0.001	-2	(-3.28, -0.73)	0.002	
Group * (2 months vs. BL)	-0.48	(-2.27, 1.32)	0.60	-0.58	(-2.37, 1.21)	0.53	
Group * (5 months vs. BL)	-1.19	(-2.95, 0.56)	0.18	-1.28	(-3.03, 0.47)	0.15	
Group * (12 months vs. BL)	-0.38	(-2.16, 1.4)	0.68	-0.46	(-2.24, 1.32)	0.62	
SRS Social Motivation	Beta coefficient	CI	P-value	Beta coefficient	CI	P-value	
(Prespecified secondary outcome)							
Intercept	15.01	(14.18, 15.83)	<0.001	15.03	(13.78, 16.28)	<0.001	
Group (improvisational music therapy)	-0.19	(-1.36, 0.98)	0.75	-0.28	(-1.39, 0.84)	0.63	
2 months vs. BL	-0.21	(-0.94, 0.53)	0.58	-0.14	(-0.87, 0.6)	0.72	
5 months vs. BL	-0.59	(-1.31, 0.12)	0.10	-0.55	(-1.26, 0.17)	0.13	
12 months vs. BL	-1.04	(-1.75, -0.32)	0.005	-0.99	(-1.71, -0.28)	0.007	
Group * (2 months vs. BL)	-0.36	(-1.37, 0.64)	0.48	-0.41	(-1.42, 0.6)	0.43	
Group * (5 months vs. BL)	-0.95	(-1.94, 0.03)	0.06	-0.99	(-1.97, -0.01)	0.05	
Group * (12 months vs. BL)	-0.78	(-1.78, 0.22)	0.13	-0.81	(-1.81, 0.19)	0.12	

eTable 5. Linear Mixed-Effects Analyses—All Outcomes, Two Groups (Continued)

		Unadjusted			Ad	justed for site	
SRS Autistic Mannerisms (Prespecified secondary outcome)	Beta coefficient	CI	P-value	Bet	a coefficient	CI	P-value
Intercept	17.57	(16.53, 18.6)	<0.001		17.63	(15.98, 19.28)	<0.001
Group (improvisational music therapy)	0.85	(-0.62, 2.32)	0.26		0.78	(-0.61, 2.18)	0.27
2 months vs. BL	0.38	(-0.48, 1.25)	0.39		0.47	(-0.39, 1.34)	0.28
5 months vs. BL	0.13	(-0.71, 0.97)	0.76		0.2	(-0.64, 1.04)	0.64
12 months vs. BL	-0.19	(-1.03, 0.66)	0.66		-0.12	(-0.96, 0.72)	0.78
Group * (2 months vs. BL)	-1.12	(-2.3, 0.07)	0.07		-1.2	(-2.39, -0.02)	0.05
Group * (5 months vs. BL)	-1.05	(-2.21, 0.1)	0.08		-1.13	(-2.29, 0.03)	0.06
Group * (12 months vs. BL)	-1.13	(-2.31, 0.05)	0.06		-1.19	(-2.37, -0.01)	0.05
ADOS Total (Post hoc outcome)	Beta coefficient	CI	P-value	Bet	a coefficient	CI	P-value
Intercept	17.37	(16.56, 18.19)	<0.001		17.43	(16.26, 18.59)	<0.001
Group (improvisational music therapy)	0.65	(-0.51, 1.8)	0.27		0.54	(-0.58, 1.66)	0.34
2 months vs. BL	-0.45	(-1.11, 0.21)	0.19		-0.4	(-1.06, 0.26)	0.24
5 months vs. BL	-1.08	(-1.7, -0.46)	<0.001		-1.07	(-1.69, -0.45)	<0.001
12 months vs. BL	-2.03	(-2.67, -1.39)	<0.001		-2.01	(-2.65, -1.37)	<0.001
Group * (2 months vs. BL)	0.24	(-0.67, 1.14)	0.61		0.21	(-0.7, 1.11)	0.65
Group * (5 months vs. BL)	0.11	(-0.75, 0.97)	0.81		0.1	(-0.76, 0.95)	0.83
Group * (12 months vs. BL)	0.33	(-0.55, 1.22)	0.46		0.31	(-0.57, 1.2)	0.49

eTable 5. Linear Mixed-Effects Analyses—All Outcomes, Two Groups (Continued)

		Unadjusted		A	Adjusted for site				
ADOS Language and Communication (Post hoc outcome)	Beta coefficient	CI	P-value	Beta coefficient	CI	P-value			
Intercept	3.25	(3.03, 3.48)	<0.001	3.31	(2.84, 3.78)	<0.001			
Group (improvisational music therapy)	0.1	(-0.22, 0.43)	0.52	0.05	(-0.24, 0.33)	0.75			
2 months vs. BL	-0.27	(-0.5, -0.04)	0.02	-0.23	(-0.46, -0.01)	0.04			
5 months vs. BL	-0.4	(-0.62, -0.19)	<0.001	-0.39	(-0.6, -0.17)	<0.001			
12 months vs. BL	-0.54	(-0.76, -0.32)	<0.001	-0.52	(-0.74, -0.3)	<0.001			
Group * (2 months vs. BL)	0.18	(-0.13, 0.49)	0.26	0.15	(-0.16, 0.46)	0.35			
Group * (5 months vs. BL)	0.13	(-0.17, 0.42)	0.41	0.11	(-0.19, 0.4)	0.49			
Group * (12 months vs. BL)	0.16	(-0.14, 0.47)	0.30	0.13	(-0.17, 0.44)	0.39			
ADOS Reciprocal Social Interaction (Post hoc outcome)	Beta coefficient	CI	P-value	Beta coefficient	CI	P-value			
Intercept	10.24	(9.7, 10.78)	<0.001	10.34	(9.58, 11.1)	<0.001			
Group (improvisational music therapy)	0.48	(-0.28, 1.25)	0.22	0.41	(-0.33, 1.16)	0.28			
2 months vs. BL	-0.12	(-0.6, 0.37)	0.64	-0.09	(-0.57, 0.39)	0.71			
5 months vs. BL	-0.5	(-0.96, -0.05)	0.03	-0.5	(-0.96, -0.05)	0.03			
12 months vs. BL	-1.09	(-1.56, -0.63)	<0.001	-1.09	(-1.56, -0.62)	<0.001			
Group * (2 months vs. BL)	0.04	(-0.62, 0.7)	0.90	0.03	(-0.63, 0.69)	0.94			
Group * (5 months vs. BL)	-0.06	(-0.69, 0.56)	0.84	-0.07	(-0.69, 0.56)	0.84			
Group * (12 months vs. BL)	-0.01	(-0.66, 0.64)	0.98	-0.02	(-0.66, 0.63)	0.96			

eTable 5. Linear Mixed-Effects Analyses—All Outcomes, Two Groups (Continued)

	Ų	<b>Jnadjusted</b>		Adj	usted for site	
ADOS Restricted and Repetitive Behavior	Beta coefficient	CI	P-value	Beta coefficient	CI	P-value
(Post hoc outcome)						
Intercept	3.91	(3.62, 4.2)	<0.001	3.77	(3.26, 4.29)	<0.001
Group (improvisational music therapy)	0.03	(-0.38, 0.44)	0.87	0.06	(-0.33, 0.45)	0.76
2 months vs. BL	-0.11	(-0.4, 0.18)	0.47	-0.09	(-0.38, 0.2)	0.56
5 months vs. BL	-0.21	(-0.48, 0.07)	0.14	-0.2	(-0.48, 0.07)	0.15
12 months vs. BL	-0.48	(-0.76, -0.2)	<0.001	-0.47	(-0.75, -0.18)	0.001
Group * (2 months vs. BL)	0.06	(-0.34, 0.46)	0.78	0.05	(-0.35, 0.45)	0.80
Group * (5 months vs. BL)	0.08	(-0.3, 0.46)	0.67	0.08	(-0.3, 0.46)	0.68
Group * (12 months vs. BL)	0.26	(-0.13, 0.65)	0.19	0.25	(-0.14, 0.64)	0.20
Quality of life, participant	Beta coefficient	CI	P-value	Beta coefficient	CI	P-value
(Post hoc outcome)						
Intercept	71.13	(68.66, 73.6)	<0.001	71.01	(68.01, 74.01)	<0.001
Group (improvisational music therapy)	1.19	(-2.32, 4.7)	0.51	1.13	(-2.33, 4.58)	0.52
2 months vs. BL	1.83	(-0.56, 4.21)	0.13	1.76	(-0.63, 4.15)	0.15
5 months vs. BL	3.4	(1.11, 5.68)	0.004	3.39	(1.11, 5.68)	0.004
12 months vs. BL	4.9	(2.6, 7.21)	<0.001	4.91	(2.6, 7.22)	<0.001
Group * (2 months vs. BL)	-0.35	(-3.67, 2.97)	0.84	-0.33	(-3.65, 2.99)	0.85
Group * (5 months vs. BL)	2.73	(-0.49, 5.94)	0.10	2.71	(-0.5, 5.93)	0.10
Group * (12 months vs. BL)	0.4	(-2.87, 3.66)	0.81	0.36	(-2.9, 3.62)	0.83

eTable 5. Linear Mixed-Effects Analyses—All Outcomes, Two Groups (Continued)

		Unadjusted		Adjusted for site			
Quality of life, family (Post hoc outcome)	Beta coefficient	CI	P-value	Beta coefficient	CI	P-value	
Intercept	68.02	(65.25, 70.79)	<0.001	68	(64.53, 71.48)	<0.001	
Group (improvisational music therapy)	0.39	(-3.55, 4.33)	0.84	0.31	(-3.58, 4.2)	0.88	
2 months vs. BL	2.01	(-0.51, 4.52)	0.12	2.02	(-0.5, 4.54)	0.12	
5 months vs. BL	2.77	(0.35, 5.19)	0.03	2.79	(0.37, 5.21)	0.02	
12 months vs. BL	3.55	(1.1, 5.99)	0.005	3.56	(1.11, 6.01)	0.005	
Group * (2 months vs. BL)	-1.16	(-4.66, 2.35)	0.52	-1.13	(-4.64, 2.37)	0.53	
Group * (5 months vs. BL)	0.88	(-2.51, 4.27)	0.61	0.9	(-2.48, 4.29)	0.60	
Group * (12 months vs. BL)	-0.15	(-3.6, 3.31)	0.93	-0.15	(-3.6, 3.31)	0.93	

Abbreviations: BL - Baseline.

Measures: ADOS – Autism Diagnostic Observation Schedule. Higher scores indicate greater severity. Possible range: Total 0-37; Social Affect 0-27; Language and Communication 0-9; Reciprocal Social Interaction 0-19; Restricted and Repetitive Behavior 0-10.

SRS – Social Responsiveness Scale. Higher scores indicate greater severity. Possible range: Total 0-195; Social Awareness 0-24; Social Cognition 0-36; Social Communication 0-66; Social Motivation 0-33; Autistic Mannerisms 0-36.

Quality of life, participant and family: Visual analog scale. Higher scores indicate better quality of life. Possible range: 0-100, where 0 indicates worst possible and 100 best possible quality of life.

Explanation of the model: Intercept – mean value in enhanced standard care at baseline. Group (Music therapy) – difference from Intercept if in music therapy. 2/5/12 months vs. BL – difference from baseline in enhanced standard care at 2, 5 or 12 months. Group \* (2 months vs. BL) – interaction effect, representing the difference between Music therapy and enhanced standard care change from baseline at 2 months (i.e. the treatment effect); similar for 5 and 12 months. The beta coefficients can be added to predict values for each group and time point. For example, the value of the primary outcome in music therapy at 5 months is 13.49+0.59+(-0.91)+0.06=13.23.

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups

	U	nadjusted		Adjusted for site			
ADOS Social Affect (Primary outcome)	Beta coefficient	CI	P- value	Beta coefficient	CI	P- value	
Intercept	13.49	(12.82, 14.16)	<0.001	13.68	(12.53, 14.82)	<0.001	
High-intensity MT vs. standard care	0.91	(-0.26, 2.08)	0.13	0.86	(-0.25, 1.96)	0.13	
Low-intensity MT vs. standard care	0.27	(-0.89, 1.43)	0.65	0.06	(-1.04, 1.16)	0.92	
2 months vs. BL	-0.38	(-0.96, 0.21)	0.21	-0.33	(-0.91, 0.25)	0.27	
5 months vs. BL	-0.91	(-1.45, -0.36)	0.001	-0.9	(-1.45, -0.36)	0.001	
12 months vs. BL	-1.63	(-2.2, -1.07)	<0.001	-1.62	(-2.19, -1.06)	<0.001	
(High-intensity MT vs. standard care) * (2 months vs. BL)	0.21	(-0.78, 1.2)	0.68	0.18	(-0.8, 1.17)	0.72	
(Low-intensity MT vs. standard care) * (2 months vs. BL)	0.22	(-0.73, 1.17)	0.65	0.19	(-0.76, 1.14)	0.70	
(High-intensity MT vs. standard care) * (5 months vs. BL)	-0.24	(-1.18, 0.69)	0.61	-0.26	(-1.19, 0.68)	0.59	
(Low-intensity MT vs. standard care) * (5 months vs. BL)	0.34	(-0.57, 1.24)	0.47	0.33	(-0.57, 1.24)	0.48	
(High-intensity MT vs. standard care) * (12 months vs. BL)	0.18	(-0.78, 1.14)	0.72	0.16	(-0.8, 1.12)	0.75	
(Low-intensity MT vs. standard care) * (12 months vs. BL)	0.15	(-0.78, 1.08)	0.76	0.13	(-0.8, 1.06)	0.78	

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups (Continued)

	U	<b>Inadjusted</b>		Adjusted for site		
Social Responsiveness (SRS) Total	Beta	CI	P-	Beta	CI	P-
(Prespecified secondary outcome)	coefficient		value	coefficient		value
Intercept	95.81	(91.58,	<0.001	95.62	(88.73,	<0.001
		100.04)			102.52)	
High-intensity MT vs. standard care	-0.27	(-7.62, 7.09)	0.94	-0.63	(-7.53, 6.28)	0.86
Low-intensity MT vs. standard care	0.35	(-6.95, 7.64)	0.93	-0.11	(-6.98, 6.76)	0.97
2 months vs. BL	0.47	(-2.67, 3.6)	0.77	0.81	(-2.32, 3.95)	0.61
5 months vs. BL	-1.81	(-4.86, 1.25)	0.25	-1.53	(-4.59, 1.52)	0.33
12 months vs. BL	-4.61	(-7.69, -1.52)	0.004	-4.35	(-7.43, -1.27)	0.006
(High-intensity MT vs. standard care) * (2 months vs. BL)	-1.54	(-6.89, 3.81)	0.57	-1.84	(-7.18, 3.5)	0.50
(Low-intensity MT vs. standard care) * (2 months vs. BL)	-3.11	(-8.25, 2.03)	0.24	-3.37	(-8.51, 1.77)	0.20
(High-intensity MT vs. standard care) * (5 months vs. BL)	-4.52	(-9.81, 0.76)	0.10	-4.79	(-10.07, 0.48)	0.08
(Low-intensity MT vs. standard care) * (5 months vs. BL)	-2.39	(-7.41, 2.63)	0.35	-2.61	(-7.63, 2.4)	0.31
(High-intensity MT vs. standard care) * (12 months vs. BL)	-1.52	(-6.87, 3.84)	0.58	-1.75	(-7.1, 3.6)	0.52
(Low-intensity MT vs. standard care) * (12 months vs. BL)	-3.29	(-8.43, 1.85)	0.21	-3.46	(-8.6, 1.67)	0.19

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups (Continued)

	U	nadjusted		Adjusted for site			
SRS Social Awareness (Prespecified secondary outcome)	Beta coefficient	CI	P- value	Beta coefficient	CI	P- value	
Intercept	12.39	(11.8, 12.99)	<0.001	12.42	(11.42, 13.43)	<0.001	
High-intensity MT vs. standard care	-0.21	(-1.25, 0.82)	0.69	-0.25	(-1.22, 0.72)	0.61	
Low-intensity MT vs. standard care	-0.38	(-1.41, 0.65)	0.47	-0.51	(-1.48, 0.45)	0.30	
2 months vs. BL	0.43	(-0.09, 0.96)	0.11	0.51	(-0.01, 1.04)	0.06	
5 months vs. BL	-0.16	(-0.67, 0.35)	0.53	-0.1	(-0.61, 0.41)	0.70	
12 months vs. BL	-0.57	(-1.08, - 0.05)	0.03	-0.51	(-1.02, 0)	0.05	
(High-intensity MT vs. standard care) * (2 months vs. BL)	-0.29	(-1.18, 0.61)	0.53	-0.35	(-1.24, 0.54)	0.44	
(Low-intensity MT vs. standard care) * (2 months vs. BL)	-0.83	(-1.69, 0.03)	0.06	-0.88	(-1.74, -0.03)	0.04	
(High-intensity MT vs. standard care) * (5 months vs. BL)	-0.11	(-0.99, 0.77)	0.81	-0.16	(-1.04, 0.72)	0.73	
(Low-intensity MT vs. standard care) * (5 months vs. BL)	-0.24	(-1.08, 0.59)	0.57	-0.29	(-1.12, 0.54)	0.49	
(High-intensity MT vs. standard care) * (12 months vs. BL)	0.01	(-0.88, 0.91)	0.98	-0.03	(-0.91, 0.86)	0.96	
(Low-intensity MT vs. standard care) * (12 months vs. BL)	0.23	(-0.62, 1.09)	0.59	0.21	(-0.65, 1.06)	0.64	

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups (Continued)

	U	nadjusted		Adju	sted for site	
SRS Social Cognition (Prespecified secondary outcome)	Beta coefficient	CI	P- value	Beta coefficient	CI	P- value
Intercept	18.65	(17.78, 19.53)	<0.001	18.56	(17.3, 19.82)	<0.001
High-intensity MT vs. standard care	-0.68	(-2.2, 0.85)	0.39	-0.72	(-2.19, 0.76)	0.34
Low-intensity MT vs. standard care	-0.3	(-1.81, 1.22)	0.70	-0.34	(-1.81, 1.13)	0.65
2 months vs. BL	-0.33	(-1.09, 0.44)	0.40	-0.25	(-1.02, 0.51)	0.52
5 months vs. BL	-0.45	(-1.19, 0.3)	0.24	-0.39	(-1.14, 0.35)	0.30
12 months vs. BL	-1.25	(-2, -0.51)	0.001	-1.2	(-1.95, - 0.45)	0.002
(High-intensity MT vs. standard care) * (2 months vs. BL)	0.86	(-0.45, 2.16)	0.20	0.81	(-0.5, 2.11)	0.23
(Low-intensity MT vs. standard care) * (2 months vs. BL)	-0.02	(-1.27, 1.24)	0.98	-0.07	(-1.32, 1.19)	0.92
(High-intensity MT vs. standard care) * (5 months vs. BL)	-0.32	(-1.61, 0.97)	0.63	-0.36	(-1.65, 0.92)	0.58
(Low-intensity MT vs. standard care) * (5 months vs. BL)	-0.45	(-1.67, 0.77)	0.47	-0.49	(-1.71, 0.72)	0.43
(High-intensity MT vs. standard care) * (12 months vs. BL)	0.53	(-0.78, 1.83)	0.43	0.48	(-0.82, 1.79)	0.47
(Low-intensity MT vs. standard care) * (12 months vs. BL)	-0.27	(-1.52, 0.98)	0.67	-0.3	(-1.55, 0.96)	0.64

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups (Continued)

	U	Inadjusted		Adjusted for site			
SRS Social Communication	Beta	CI	P-	Beta	CI	P-	
(Prespecified secondary outcome)	coefficient		value	coefficient		value	
Intercept	32.06	(30.55,	<0.001	31.91	(29.79,		
		33.57)			34.04)	<0.001	
High-intensity MT vs. standard care	-0.18	(-2.82, 2.45)	0.89	-0.29	(-2.83, 2.26)	0.83	
Low-intensity MT vs. standard care	0.3	(-2.32, 2.91)	0.82	0.22	(-2.31, 2.75)		
,						0.87	
2 months vs. BL	-0.15	(-1.45, 1.15)	0.82	-0.02	(-1.32, 1.28)		
						0.98	
5 months vs. BL	-1.13	(-2.4, 0.13)	0.08	-1.04	(-2.3, 0.22)		
						0.11	
12 months vs. BL	-2.09	(-3.36, -0.82)	0.001	-2	(-3.27, -0.73)		
						0.002	
(High-intensity MT vs. standard care) * (2 months vs.	0.4	(-1.81, 2.62)	0.72	0.32	(-1.9, 2.53)		
BL)						0.78	
(Low-intensity MT vs. standard care) * (2 months vs.	-1.25	(-3.38, 0.88)	0.25	-1.37	(-3.5, 0.76)		
BL)		(2.22.2.11)			( 1 2 2 2 )	0.21	
(High-intensity MT vs. standard care) * (5 months vs.	-1.74	(-3.93, 0.44)	0.12	-1.82	(-4, 0.37)		
BL)		(0.05.4.00)	0.40		( 0 0 7 1 10)	0.10	
(Low-intensity MT vs. standard care) * (5 months vs.	-0.78	(-2.85, 1.29)	0.46	-0.88	(-2.95, 1.19)	0.44	
BL)	0.04	( 0 0 0 00)	0.00	0.07	(0.00, 0.44)	0.41	
(High-intensity MT vs. standard care) * (12 months vs.	0.01	(-2.2, 2.23)	0.99	-0.07	(-2.28, 2.14)	0.05	
BL)	0.75	( 0 00 4 00)	0.40	0.00	( 0 0F 4 04)	0.95	
(Low-intensity MT vs. standard care) * (12 months vs.	-0.75	(-2.88, 1.38)	0.49	-0.82	(-2.95, 1.31)	0.45	
BL)						0.45	

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups (Continued)

	U	nadjusted		Adjusted for site		
SRS Social Motivation (Prespecified secondary outcome)	Beta coefficient	CI	P- value	Beta coefficient	CI	P- value
Intercept	15.01	(14.18, 15.83)	<0.001	15.03	(13.78, 16.28)	<0.001
High-intensity MT vs. standard care	0.03	(-1.41, 1.46)	0.97	-0.05	(-1.42, 1.32)	0.94
Low-intensity MT vs. standard care	-0.41	(-1.83, 1.02)	0.58	-0.5	(-1.86, 0.87)	0.47
2 months vs. BL	-0.21	(-0.94, 0.53)	0.58	-0.14	(-0.87, 0.6)	0.72
5 months vs. BL	-0.59	(-1.3, 0.12)	0.10	-0.55	(-1.26, 0.17)	0.13
12 months vs. BL	-1.04	(-1.75, -0.32)	0.005	-0.99	(-1.71, -0.28)	0.007
(High-intensity MT vs. standard care) * (2 months vs. BL)	-0.77	(-2.02, 0.48)	0.23	-0.81	(-2.06, 0.43)	0.20
(Low-intensity MT vs. standard care) * (2 months vs. BL)	-0.01	(-1.21, 1.19)	0.98	-0.06	(-1.26, 1.14)	0.92
(High-intensity MT vs. standard care) * (5 months vs. BL)	-0.98	(-2.22, 0.25)	0.12	-1.02	(-2.25, 0.21)	0.11
(Low-intensity MT vs. standard care) * (5 months vs. BL)	-0.91	(-2.08, 0.25)	0.13	-0.95	(-2.11, 0.22)	0.11
(High-intensity MT vs. standard care) * (12 months vs. BL)	-0.6	(-1.84, 0.65)	0.35	-0.63	(-1.87, 0.62)	0.32
(Low-intensity MT vs. standard care) * (12 months vs. BL)	-0.93	(-2.13, 0.27)	0.13	-0.95	(-2.15, 0.25)	0.12

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups (Continued)

	U	nadjusted		Adjusted for site		
SRS Autistic Mannerisms (Prespecified secondary outcome)	Beta coefficient	CI	P- value	Beta coefficient	CI	P- value
Intercept	17.57	(16.53, 18.6)	<0.001	17.63	(15.99, 19.27)	<0.001
High-intensity MT vs. standard care	0.53	(-1.27, 2.34)	0.56	0.49	(-1.21, 2.19)	0.57
Low-intensity MT vs. standard care	1.16	(-0.63, 2.95)	0.20	1.08	(-0.62, 2.77)	0.21
2 months vs. BL	0.38	(-0.48, 1.24)	0.39	0.47	(-0.39, 1.33)	0.28
5 months vs. BL	0.13	(-0.7, 0.97)	0.76	0.2	(-0.64, 1.03)	0.64
12 months vs. BL	-0.19	(-1.03, 0.65)	0.66	-0.12	(-0.96, 0.72)	0.78
(High-intensity MT vs. standard care) * (2 months vs. BL)	-1.06	(-2.52, 0.41)	0.16	-1.15	(-2.61, 0.31)	0.12
(Low-intensity MT vs. standard care) * (2 months vs. BL)	-1.18	(-2.59, 0.23)	0.10	-1.25	(-2.66, 0.15)	0.08
(High-intensity MT vs. standard care) * (5 months vs. BL)	-1.84	(-3.29, -0.4)	0.01	-1.93	(-3.37, -0.48)	0.009
(Low-intensity MT vs. standard care) * (5 months vs. BL)	-0.43	(-1.8, 0.94)	0.54	-0.5	(-1.86, 0.87)	0.48
(High-intensity MT vs. standard care) * (12 months vs. BL)	-0.89	(-2.36, 0.57)	0.23	-0.98	(-2.44, 0.49)	0.19
(Low-intensity MT vs. standard care) * (12 months vs. BL)	-1.34	(-2.75, 0.07)	0.06	-1.38	(-2.79, 0.02)	0.06

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups (Continued)

	U	Inadjusted		Ad	Adjusted for site			
	Beta	CI	P-	Beta	CI	P-		
	coefficient		value	coefficient		value		
ADOS Total (Post hoc outcome)								
Intercept	17.37	(16.56, 18.18)	<0.001	17.43	(16.26, 18.6)	<0.001		
High-intensity MT vs. standard care	0.97	(-0.44, 2.39)	0.18	0.94	(-0.43, 2.31)	0.18		
Low-intensity MT vs. standard care	0.33	(-1.08, 1.73)	0.65	0.15	(-1.21, 1.52)	0.83		
2 months vs. BL	-0.45	(-1.11, 0.21)	0.19	-0.4	(-1.06, 0.26)	0.24		
5 months vs. BL	-1.08	(-1.7, -0.46)	<0.001	-1.07	(-1.69, - 0.45)	<0.001		
12 months vs. BL	-2.03	(-2.67, -1.39)	<0.001	-2.01	(-2.65, - 1.37)	<0.001		
(High-intensity MT vs. standard care) * (2 months vs. BL)	0.2	(-0.92, 1.32)	0.72	0.18	(-0.94, 1.3)	0.75		
(Low-intensity MT vs. standard care) * (2 months vs. BL)	0.28	(-0.8, 1.35)	0.61	0.25	(-0.83, 1.32)	0.66		
(High-intensity MT vs. standard care) * (5 months vs. BL)	-0.18	(-1.24, 0.88)	0.74	-0.19	(-1.25, 0.87)	0.72		
(Low-intensity MT vs. standard care) * (5 months vs. BL)	0.37	(-0.65, 1.4)	0.48	0.36	(-0.66, 1.39)	0.49		
(High-intensity MT vs. standard care) * (12 months vs. BL)	0.22	(-0.87, 1.31)	0.70	0.2	(-0.89, 1.29)	0.72		
(Low-intensity MT vs. standard care) * (12 months vs. BL)	0.44	(-0.61, 1.5)	0.41	0.43	(-0.63, 1.48)	0.43		

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups (Continued)

	Unadjusted			Adjusted for site		
ADOS Language and Communication (Post hoc outcome)	Beta coefficient	CI	P- value	Beta coefficient	CI P-v	alue
Intercept	3.25	(3.03, 3.48)	<0.001	3.31	(2.84, 3.78)	<0.00 1
High-intensity MT vs. standard care	0.13	(-0.27, 0.52)	0.53	0.1	(-0.25, 0.45)	0.58
Low-intensity MT vs. standard care	0.08	(-0.31, 0.48)	0.67	0	(-0.36, 0.35)	0.98
2 months vs. BL	-0.27	(-0.5, -0.04)	0.02	-0.23	(-0.46, - 0.01)	0.04
5 months vs. BL	-0.4	(-0.62, - 0.19)	<0.001	-0.39	(-0.6, -0.17)	<0.00 1
12 months vs. BL	-0.54	(-0.76, - 0.32)	<0.001	-0.52	(-0.74, -0.3)	<0.00 1
(High-intensity MT vs. standard care) * (2 months vs. BL)	0.25	(-0.13, 0.64)	0.20	0.23	(-0.16, 0.61)	0.25
(Low-intensity MT vs. standard care) * (2 months vs. BL)	0.12	(-0.26, 0.49)	0.54	0.09	(-0.29, 0.46)	0.66
(High-intensity MT vs. standard care) * (5 months vs. BL)	0.09	(-0.28, 0.46)	0.62	0.07	(-0.3, 0.44)	0.70
(Low-intensity MT vs. standard care) * (5 months vs. BL)	0.16	(-0.2, 0.51)	0.40	0.14	(-0.22, 0.49)	0.45
(High-intensity MT vs. standard care) * (12 months vs. BL)	0.16	(-0.22, 0.54)	0.41	0.13	(-0.25, 0.51)	0.50
(Low-intensity MT vs. standard care) * (12 months vs. BL)	0.17	(-0.2, 0.53)	0.38	0.14	(-0.23, 0.5)	0.46

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups (Continued)

	Unadjusted			Adju		
ADOS Reciprocal and Social Interaction	Beta	CI	P-	Beta	CI	P-
(Post hoc outcome)	coefficient		value	coefficient		value
Intercept	10.24	(9.7, 10.78)	<0.001	10.34	(9.58, 11.1)	<0.001
High-intensity MT vs. standard care	0.79	(-0.15, 1.73)	0.10	0.76	(-0.16, 1.67)	0.10
Low-intensity MT vs. standard care	0.19	(-0.75, 1.12)	0.69	0.07	(-0.84, 0.98)	0.87
2 months vs. BL	-0.12	(-0.6, 0.36)	0.64	-0.09	(-0.57, 0.39)	0.71
5 months vs. BL	-0.5	(-0.96, - 0.05)	0.03	-0.5	(-0.96, - 0.05)	0.03
12 months vs. BL	-1.09	(-1.56, - 0.63)	<0.001	-1.09	(-1.56, - 0.62)	<0.001
(High-intensity MT vs. standard care) * (2 months vs. BL)	-0.03	(-0.85, 0.79)	0.95	-0.04	(-0.86, 0.78)	0.93
(Low-intensity MT vs. standard care) * (2 months vs. BL)	0.11	(-0.67, 0.9)	0.78	0.1	(-0.69, 0.88)	0.81
(High-intensity MT vs. standard care) * (5 months vs. BL)	-0.34	(-1.11, 0.44)	0.40	-0.34	(-1.11, 0.44)	0.40
(Low-intensity MT vs. standard care) * (5 months vs. BL)	0.19	(-0.57, 0.94)	0.63	0.19	(-0.57, 0.94)	0.63
(High-intensity MT vs. standard care) * (12 months vs. BL)	0.02	(-0.78, 0.82)	0.96	0.01	(-0.78, 0.81)	0.97
(Low-intensity MT vs. standard care) * (12 months vs. BL)	-0.03	(-0.8, 0.74)	0.95	-0.03	(-0.8, 0.74)	0.94

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups (Continued)

	Unadjusted			Adjusted for site		
ADOS Restricted and Repetitive Behavior	Beta	CI	P-	Beta	CI	P-value
(Post hoc outcome)	coefficient		value	coefficient		
Intercept	3.91	(3.62, 4.2)	<0.001	3.77	(3.26, 4.29)	<0.001
High-intensity MT vs. standard care	0.04	(-0.47,	0.88	0.06	(-0.41, 0.54)	
		0.54)				0.79
Low-intensity MT vs. standard care	0.03	(-0.47,	0.91	0.06	(-0.42, 0.53)	0.81
		0.53)				
2 months vs. BL	-0.11	(-0.4, 0.18)	0.47	-0.09	(-0.38, 0.2)	
						0.56
5 months vs. BL	-0.21	(-0.48,	0.14	-0.2	(-0.48, 0.07)	
		0.07)				0.15
12 months vs. BL	-0.48	(-0.76, -0.2)	0.001	-0.47	(-0.75, -	0.001
					0.18)	
(High-intensity MT vs. standard care) * (2 months vs. BL)	0.03	(-0.46,	0.89	0.04	(-0.46, 0.53)	
		0.53)				0.89
(Low-intensity MT vs. standard care) * (2 months vs. BL)	0.08	(-0.39,	0.74	0.07	(-0.41, 0.54)	
		0.56)				0.78
(High-intensity MT vs. standard care) * (5 months vs. BL)	0.09	(-0.37,	0.69	0.09	(-0.37, 0.56)	
		0.56)				0.70
(Low-intensity MT vs. standard care) * (5 months vs. BL)	0.08	(-0.38,	0.75	0.07	(-0.38, 0.52)	
		0.53)				0.76
(High-intensity MT vs. standard care) * (12 months vs.	0.12	(-0.37, 0.6)	0.64	0.11	(-0.37, 0.59)	
BL)						0.65
(Low-intensity MT vs. standard care) * (12 months vs.	0.38	(-0.08,	0.11	0.38	(-0.09, 0.84)	0.11
BL)		0.85)				

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups (Continued)

	Uı	nadjusted		Adjı	sted for site	ted for site	
Quality of life, participant	Beta	CI	P-	Beta	CI	P-	
(Post hoc outcome)	coefficient		value	coefficient		value	
Intercept	71.13	(68.67, 73.6)	<0.001	71.01	(68.01, 74.01)	<0.001	
High-intensity MT vs. standard care	1.55	(-2.76, 5.85)	0.48	1.52	(-2.72, 5.75)	0.48	
Low-intensity MT vs. standard care	0.85	(-3.44, 5.15)	0.70	0.75	(-3.48, 4.98)	0.73	
2 months vs. BL	1.83	(-0.55, 4.21)	0.13	1.76	(-0.62, 4.15)	0.15	
5 months vs. BL	3.4	(1.12, 5.68)	0.004	3.4	(1.11, 5.68)	0.004	
12 months vs. BL	4.9	(2.6, 7.21)	<0.001	4.91	(2.61, 7.22)	<0.001	
(High-intensity MT vs. standard care) * (2 months vs. BL)	-0.67	(-4.78, 3.44)	0.75	-0.64	(-4.75, 3.47)	0.76	
(Low-intensity MT vs. standard care) * (2 months vs. BL)	-0.08	(-4.06, 3.89)	0.97	-0.08	(-4.05, 3.9)	0.97	
(High-intensity MT vs. standard care) * (5 months vs. BL)	4.4	(0.38, 8.43)	0.03	4.41	(0.39, 8.44)	0.03	
(Low-intensity MT vs. standard care) * (5 months vs. BL)	1.37	(-2.46, 5.2)	0.48	1.34	(-2.49, 5.17)	0.50	
(High-intensity MT vs. standard care) * (12 months vs. BL)	0.61	(-3.45, 4.68)	0.77	0.62	(-3.45, 4.69)	0.77	
(Low-intensity MT vs. standard care) * (12 months vs. BL)	0.21	(-3.7, 4.13)	0.92	0.14	(-3.78, 4.06)	0.94	

eTable 6. Linear Mixed-Effects Analyses—All Outcomes, Three Groups (Continued)

	Unadjusted Adjusted for si			usted for site	Э	
Quality of life, family (Post hoc outcome)	Beta coefficient	CI	P- value	Beta coefficient	CI	P-value
Intercept	68.02	(65.25, 70.79)	<0.001	68.01	(64.53, 71.48)	<0.001
High-intensity MT vs. standard care	0.73	(-4.12, 5.58)	0.77	0.56	(-4.22, 5.34)	0.82
Low-intensity MT vs. standard care	0.07	(-4.74, 4.88)	0.98	0.07	(-4.68, 4.82)	0.98
2 months vs. BL	2.01	(-0.5, 4.52)	0.12	2.02	(-0.49, 4.54)	0.12
5 months vs. BL	2.77	(0.36, 5.18)	0.03	2.79	(0.37, 5.2)	0.02
12 months vs. BL	3.55	(1.1, 5.99)	0.005	3.56	(1.11, 6)	0.005
(High-intensity MT vs. standard care) * (2 months vs. BL)	-1.85	(-6.2, 2.5)	0.41	-1.8	(-6.15, 2.55)	0.42
(Low-intensity MT vs. standard care) * (2 months vs. BL)	-0.54	(-4.72, 3.64)	0.80	-0.54	(-4.73, 3.64)	0.80
(High-intensity MT vs. standard care) * (5 months vs. BL)	2.02	(-2.22, 6.25)	0.35	2.06	(-2.18, 6.3)	0.34
(Low-intensity MT vs. standard care) * (5 months vs. BL)	-0.02	(-4.05, 4.01)	0.99	-0.02	(-4.06, 4.01)	0.99
(High-intensity MT vs. standard care) * (12 months vs. BL)	-1.15	(-5.48, 3.18)	0.60	-1.13	(-5.45, 3.2)	0.61
(Low-intensity MT vs. standard care) * (12 months vs. BL)	0.72	(-3.41, 4.85)	0.73	0.69	(-3.44, 4.83)	0.74

Abbreviations: BL – Baseline; MT – music therapy.

Measures: ADOS – Autism Diagnostic Observation Schedule. Higher scores indicate greater severity. Possible range: Total 0-37; Social Affect 0-27; Language and Communication 0-9; Reciprocal Social Interaction 0-19; Restricted and Repetitive Behavior 0-10.

SRS – Social Responsiveness Scale. Higher scores indicate greater severity. Possible range: Total 0-195; Social Awareness 0-24; Social Cognition 0-36; Social Communication 0-66; Social Motivation 0-33; Autistic Mannerisms 0-36.

Quality of life, participant and family: Visual analog scale. Higher scores indicate better quality of life. Possible range: 0-100, where 0 indicates worst possible and 100 best possible quality of life.

Explanation of the model: Intercept – mean value in enhanced standard care at baseline. High/low-intensity music therapy vs. standard care – difference from Intercept if in high- or low-intensity music therapy. 2/5/12 months vs. BL – difference from baseline in enhanced standard care at 2, 5 or 12 months. (High/low-intensity music therapy vs. standard care) \* (2/5/12 months vs. BL) – interaction effect, representing the difference between high- or low-intensity music therapy and enhanced standard care change from baseline at 2, 5 or 12 months (i.e. the treatment effect). The beta coefficients can be added to predict values for each group and time point. For example, the value of the primary outcome in high-intensity music therapy at 5 months is 13.49+0.91+(-0.91)+(-0.24)=13.25.