Table 1. Children and parents baseline characteristics for overall and by intervention assignment

	Amount (%)			*χ^2/ t test*	P-*value*
	Intervention (n = *194)*	*Control* (n = *195)*	*Total* (n = *389)*		
Children's Characteristics					
Mean Age (s.e.)	3.39 (0.02)	3.43 (0.01)	3.41 (0.09)	t = 1.22	0.22
Sex					
Female	98 *(50.5%)*	89 *(45.6%)*	187 (48%)	$\chi^2 = 0.926$	0.336
Male	96 *(49.5%)*	106 *(54.4%)*	202 (52%)		
Race/Ethnicity					
Italian	175 *(90.7%)*	178 *(91.8%)*	353 (91.2%)	$\chi^2 = 0.141$	0.708
Foreign	18 *(9.3%)*	16 *(8.2%)*	34 (8.8%)		
Mean BMI (s.e.)	16.2 (0.10)	16.2 (0.10)	16.2 (0.07)	t = 0.33	0.74
Mean BMI z-score (s.e.)	0.27 (0.07)	0.28 (0.08)	0.28 (0.03)	t = 0.09	0.92
BMI category (cut-offs IOTF 2012)					
Normal	156 *(84.7%)*	162 *(84.8%)*	318 (84.8%)	$\chi^2 = 1.07$	0.59
Overweight	25 *(13.6%)*	23 *(12.0%)*	48 (12.8%)		
Obese	3 *(1.6%)*	6 *(3.1%)*	9 (2.4%)		
Children's healthy behaviours:					
FV intake s per d	2.4 (0.9)	2.3 (0.9)	2.4 (0.7)	t = − 0.288	0.773
Active playtime min per d	134.7 (5.6)	133.3 (5.8)	134 (4.0)	t = − 0.16	0.866
TV-watching min/d	97.8 (4.3)	104.5 (4.6)	101.1 (3.2)	t = 1.069	0.286
SSB intake s per d	0.38 (0.04)	0.35 (0.04)	0.36 (0.03)	t = − 0.51	0.608
TV in children's bedrooms					
No	149 (83.7%)	150 (89.8%)	299 (86.7)	$\chi^2 = 2.79$	0.095
Yes	29 (16.3%)	17 (10.2%)	46 (13.3)		
Parents' Characteristics					
Mothers					
Mean BMI (s.e.)	22.4 (0.28)	22.80 (0.32)	22.6 (0.21)	t = 1.18	0.23
BMI category					
Normal (BMI $<$ 25 kg m^{-2})	139 (80.4%)	127 (73.8%)	266 (77.7%)	$\chi^2 = 5.51$	0.111
Overweight (BMI 25–29.9 kg m^{-2})	26 (15.1%)	36 (20.9%)	62 (18.0%)		
Obese (BMI $\geqslant$ 30 kg m^{-2})	8 (4.6%)	9 (5.2%)	17 (4.9%)		
Level of education					
None	5 (2.6%)	0 (0%)	5 (1.3%)	$\chi^2 = 7.493$	0.112
Primary school	1 (0.5%)	2 (1.1%)	3 (0.8%)		
Secondary school	39 (20.2%)	28 (15.0%)	67 (17.6%)		
High school	96 (49.8%)	98 (52.4%)	194 (51.1%)		
Graduation	52 (26.9%)	59 (31.5%)	111 (29.2%)		
Employment status					
Working full-time	87 (47.8%)	73 (42.0%)	160 (44.9%)	$\chi^2 = 5.063$	0.08
Working part-time	48 (26.4%)	65 (37.3%)	113 (31.7%)		
Unemployed	47 (25.8%)	36 (20.7%)	83 (23.3%)		
Fathers					
Mean BMI (s.e.)	26.0 (0.23)	25.2 (0.22)	25.6 (0.16)	t = − 2.44	0.01
BMI category					
Normal (BMI $<$ 25 kg m^{-2})	63 (37.3%)	85 (43.6%)	148 (44.4%)	$\chi^2 = 7.34$	0.025
Overweight (BMI 25–29.9 kg m^{-2})	93 (55.0%)	71 (36.4%)	164 (49.3%)		
Obese (BMI $\geqslant$ 30 kg m^{-2})	13 (7.7%)	8 (4.1%)	21 (6.3%)		
Level of education					
None	5 (2.8%)	0 (0%)	5 (1.4%)	$\chi^2 = 9.018$	0.061
Primary school	0 (0.0%)	3 (1.8%)	3 (0.9%)		
Secondary school	57 (31.7%)	58 (34.5%)	115 (33.1%)		
High school	83 (46.1%)	69 (41.1%)	152 (43.7%)		
Graduation	35 (19.4%)	38 (22.6%)	73 (21.0%)		
Employment status					
Working full-time	170 (93.4%)	154 (90.6%)	324 (92.1%)	$\chi^2 = 2.784$	0.249
Working part-time	6 (3.3%)	12 (7.1%)	18 (5.1%)		
Unemployed	6 (3.3%)	4 (2.3%)	10 (2.8%)		

Abbreviations: BMI, body mass index; FV, fruit and vegetable; SSB, sugar-sweetened beverages.

Then, we measured the percentage of children with a TV in their bedrooms as well.

Our secondary outcomes included anthropometrical parameters, such as:

- Change in BMI *z* score: we used CDC 2000 Reference to convert BMI into an age- and sex-specific BMI *z*-score;
- Change in BMI units;[24] and
- Percentage of children showing a BMI increase $\geqslant 0.1$ kg m^{-2} and $\geqslant 1$ standard deviation (the latter value indicates a *rapid weight gain*-RWG[25]). A BMI increase during a growth span, in which BMI normally physiologically decreases, is useful to detect a risky weight gain in early childhood even before a child reaches overweight or obesity cut-offs.

Sample size calculation

We calculated sample size with a method that takes into account the intracluster correlation coefficient (ICC) of the dichotomized primary outcome, the average number of children per cluster, the outcome odds in both control and intervention groups and $Z_{a/2}$ and Z_b on the basis of a normal distribution.[26–28]

We assumed an intracluster correlation coefficient ($P = 0.012$[14]), a minimum number of participants (at least 15 children) per cluster and an expected rate of 45% of intervention group children and 30% of control group children showing a low-risk CHBS (our primary outcome) with 80% power at an alpha level of 0.05 after 1 and 2 years from baseline. On the basis of those assumptions, we needed eight clusters for both groups.[14]

Statistical methods

We performed descriptive statistical analyses to sum up the main characteristics of the study sample. To test differences in baseline distribution of outcomes and other predictors of interest, we used χ^2 or *t*-test, according to the type of variable, with the appropriate degrees of freedom.

To examine the hierarchical data structure (children's measurements, child, childcare centres), we applied a three-level linear model, though preferring a two-level model that used children as random effect because of a school random effect near to 0. We provided both multilevel models: a random intercept model and a random intercept and slope model. We chose the first model in order to apply a principle of parsimony. To compare both the models, children's ICC was reported along with a likelihood ratio test.

CHBS, a model for binary data, was adjusted for mothers' levels of education (low level: $\leqslant 8$ years at school; mid/high level: >8 years at school), children's gender and baseline BMI. A model for the continuous data was fitted for BMI and BMI *z*-score, adjusted for mothers' levels of education and children's gender.

We carried out a sensitivity analysis and replaced any missing data in the intervention group with average values from CHBS, BMI, BMI *z*-scores in the control group for the same sex, age and the mothers' levels of education. Our results were the same.

We used STATA 12 (STATA Corp LLC, College Station, TX, USA) to perform every analysis.

RESULTS

Figure 1 shows the participant flow through the trial. We conducted our c-RCT on 425 three-year-old children at 16 childcare centres—out of 27 potentially eligible ones—that met our eligibility criteria and are based in Cesena, Forlì-Cesena, Italy. We randomly allocated eight childcare centres (199 children) to the intervention group and eight childcare centres (226 children) to the control group.

All the randomized childcare centres completed our study protocol.

Five children (3%) in the intervention group and 31 children (14%) in the control group were not involved in our trial because their parents did not allow them to take part into our c-RCT.

Table 1 shows no differences between the groups in the children's baseline characteristics. 48% were girls. Almost all the children were Italian.

Table 2. Amount and percentage of children with a low risk of CHBS and SHBS, TV in bedroom, mean values (95% C.I.), BMI score and BMI *z*-score (at baseline and follow-up)

	Baseline			*1 year*			*2 years*		
	Intervention N (%)	*Control* N (%)	P-*value*[a]	*Intervention* N (%)	*Control* N (%)	P-*value*[a]	*Intervention* N (%)	*Control* N (%)	P-*value*[a]
Primary outcome CHBS (low risk = 0–2)	70 (37.8%)	63 (35.4%)	0.629	80 (49.4%)	59 (36.4%)	0.018	78 (48.4%)	47 (28.0%)	0.000
Secondary outcome									
SHBS (low risk = 0)									
FV intake per day $\geqslant 4$ servings/d	25 (13.5%)	18 (10.1%)	0.316	27 (16. 7%)	23 (14.1%)	0.538	32 (19.9%)	16 (9.5%)	0.008
Active playtime per day $\geqslant 120$ min per day	102 (55.1%)	92 (51.7%)	0.510	132 (81.5%)	108 (66.7%)	0.002	121 (74.7%)	124 (73.8%)	0.855
TV-watching per day $\leqslant 60$ min per day	58 (31.4%)	56 (31.5%)	0.982	37 (22.8%)	26 (16.5%)	0.123	34 (21.0%)	23 (13.7%)	0.080
SSB intake per day, Glasses per day	157 (85.9%)	149 (84.7%)	0.762	148 (91.4%)	132 (81.5%)	0.009	147 (90.7%)	132 (78.6%)	0.002
TV in bedroom	29 (16.3%)	17 (10.1%)	0.095	23 (15.1%)	19 (13.1%)	0.616	28 (18.1%)	13 (8.8%)	0.019
	Mean Value (95% CI)	Mean Value (95% CI)		Mean Value (95% CI)	Mean Value (95% CI)		Mean Value (95% CI)	Mean Value (95% CI)	
BMI score	16.2 (15.9–16.4)	16.2 (16.0–16.4)	0.739	16.1 (15.9–16.3)	16.0 (15.8–16.2)	0.631	16.1 (15.8–16.4)	16.3 (16.0–16.6)	0.399
BMI *z*-score	0.27 (0.13–0.42)	0.28 (0.13–0.44)	0.929	0.38 (0.22–0.53)	0.33 (0.18–0.47)	0.671	0.38 (0.23–0.54)	0.44 (0.27–0.60)	0.644

Abbreviations: BMI, body mass index; CHBS, combined health behaviour score; CI, confidence intervals; FV, fruit and vegetable; OR, odds ratio; SHBS, single health behaviour score; SSB, sugar-sweetened beverages. [a]χ^2 test.

Table 3. Unadjusted and adjusted odds ratios (95% CI) for low-risk combined health behavior score (CHBS) and beta-coefficient (95% CI) for BMI and BMI z-score in the intervention group compared to the control group at 1 and to 2-year follow-ups

	One year				*Two years*			
	OR unadjusted (95% CI)	*P-value*	*OR adjusted*[a] *(95% CI)*	*P-value*	*OR unadjusted (95% CI)*	*P-value*	*OR adjusted*[a] *(95% CI)*	*P-value*
Primary outcome								
Combined health behaviour score (low risk = score 0–2)	1.96 (0.88–4.36)	0.101	2.09 (0.92–4.77)	0.078	3.43 (1.52–7.77)	0.003	3.41 (1.48–7.88)	0.004
	β unadjusted (95% CI)	P-value	*β adjusted* [b] *(95% CI)*	P-value	*β unadjusted (95% CI)*	P-value	*β adjusted* [b] *(95% CI)*	P-value
BMI outcomes								
BMI score	0.12 (−0.09–0.32)	0.261	0.10 (−0.10–0.31)	0.332	0.06 (−0.27–0.15)	0.569	−0.07 (−0.30–0.14)	0.537
BMI z-score	0.07 (−0.05–0.19)	0.277	0.06 (−0.06–0.19)	0.334	0.011 (−0.11–0.14)	0.868	0.006 (−0.12–0.14)	0.926

Abbreviations: ß unadjusted, ß coefficient not corrected for potential confounders; BMI, body mass index; CI, confidence intervals, OR, odds ratio; OR unadjusted, odds ratio not corrected for potential confounders. [a]OR adjusted for the following potential confounders: gender, mother's level of education, child's BMI. [b]β-coefficient adjusted for the following potential confounders: gender, mother's level of education.

Table 4 shows only the cost breakdown associated with our intervention, should it be carried out again in the future. However, it does not show one-off costs, such as project planning, database management, statistical analysis, production of education materials.

DISCUSSION

This is the first c-RCT that aims at assessing the effects of a combined educational intervention carried out by primary care pediatricians and childcare centre teachers on an unparalleled large population of 3-year-old children and their parents. On the basis of evidence, it successfully changed four energy-related behaviours in the medium and long term: FV intake, physical activity, TV-watching time and SSB intake. After 2 years from baseline—18 months after the intervention end—significant and beneficial changes in target behaviours and their CHBS took place among those intervention children whose mothers had a medium/high level of education. However no significant change in BMI outcomes occurred. Our study confirmed that it is difficult to successfully bring about anthropometric changes, as a systematic review of intervention studies for preventing obesity among preschool children[29] aged 3–6 years has recently reported. Nevertheless, we found that a lower, yet statistically insignificant, percentage of intervention group children showed RWG in comparison with usual care children.

We observed a lack of significant changes in behaviour among those children whose mothers had a low level of education (23% of mothers had $\leqslant 8$ years of education). This result compels for the planning of educational programmes specifically designed for mothers with low levels of education.

Moreover, future investigation should use reliable indicators for preschool children's physical activity and FV intake to minimise any risk of bias, such as parents self-reporting their children's behaviours, and to appropriately assess relationships between parents'/childcare teachers' specific activities and subjects and children's behaviour changes. For this reason, we suggest two validated methods for preschool children: accelerometers and Resonance Raman Spectroscopy (RRS) technology. On the one side accelerometers can detect low, medium, and high levels of physical activity as well as sedentary time.[30] On the other side, RRS is an inexpensive, noninvasive technique for measuring carotenoid status in the skin (hand palms) and it is used as valid biomarker of FV intake.[31]

Our study has strengths and weaknesses

Its strengths include:

(1) The design of c-RCT provides a gold standard for studies to establish the relationship between cause and effect, and in particular between an intervention aimed at promoting health in a community and its outcomes at group level; (2) Its sample size is large; (3) it has a long-term follow-up. Most intervention studies assess behavioural outcomes in the short term so that it is very likely they show beneficial changes in children's lifestyles. Unlike those studies, our study revealed that children led healthy behaviours until at least 18 months from the intervention's end; (4) Our study launched an unprecedented education initiative: district nurses, primary care pediatricians and childcare centre teachers received a professional training course to improve their basic educational skills. They experienced a new way of co-working and formed a multilevel educational network in routine local health-promotion services; (5) Scientific research has recently revealed that multidimensional and multi-component interventions are especially effective in early childhood;[32] (6) it can achieve great generalizability in developed countries because primary care pediatricians/general practitioners examine all preschool children and most of those children attend a childcare centre; and (7) all the parents and

Table 4. Breakdown of costs associated with the intervention (intervention group: eight childcare centres and 199 children)[a]

Item	*Unit Price h/€ (price in € in 2012)*
Training	
1 psychiatrist leading a total 20-h-long training program (4 sessions) on MI for paediatricians	3500 €
2 psychologists leading a 20-h-long training program (4 sessions) on MI for paediatric nurses	1500 €
2 experts in early childhood physical activity who led a 10-h-long training program (3 sessions) for childcare centre teachers	500.00 €
Time for carrying out the intervention study	
Time devoted by 22 paediatricians:	
to receive a 20-h-long training on MI	440 h
to conduct 180 face-to-face interviews with parents (of ~20 min. each)	60 h
Time devoted by 9 nurses:	
to receive a 20-h-long training on MI	180 h
to conduct 180 face-to-face interviews with parents (of ~20 min. each)	60 h
Time devoted by 3 health professionals (research team) to hold 3 meetings (of ~2 h each) with teachers to encourage education initiatives at childcare centres	18 h
Time devoted by 21 teachers at 8 childcare centres	
to receive the overall 10-h-long training on early childhood physical activity	210 h
to participate in the overall 6-h-long meetings held by research team professionals	126 h
Cost of materials	
Printed education materials (30 posters, 200 leaflets for parents, 220 manuals for parents and teachers)	4000 €

[a]Additional costs for the intervention study: time for preliminary consultation with participants; phone bills for appointments with parents at paediatricians offices; costs and expenses covered by healthcare providers for study-related examinations; costs and expenses covered by parents (that is, time and travelling expenses to undergo the study examinations); and time devoted by teachers to arrange learning experiences at childcare centres (included in the year education plan without additional workload for teachers).

teachers expressed a medium/high degree of appreciation about our intervention.

Its weaknesses include:

(1) Parents self-reported their children's behaviours. This indicator is not objective and can have a potential bias; (2) we could not validate our primary outcome of CHBS although it is based on an evidence-based approach to four energy balance-related behaviours;[2,7–11] (3) Nurses and paediatricians had no or poor previous experience in MI. This could have limited the effectiveness of the intervention; and (4) We suffered a significant loss of the data at follow-up. Nevertheless, the ITT approach is likely to have successfully accounted for potential attrition bias.

CONCLUSIONS

Scientific research has shown that early childhood obesity prevention interventions (0–5 years) are associated with more effectiveness, and in particular, when they combine home and school.[5,32] However, clear insights in basic behavioural and biological mechanisms of obesity development during the first years of life are still lacking and most obesity prevention programs have been focusing on school children. Our study was a multicomponent/multidimensional educational intervention that focused on preschool children and their parents. It was included in routines for local healthcare services and childcare centres, and it consisted of motivational interviews with parents and teacher-led learning experiences for children. On this basis, we found that it improved preschool children's CHBS in the long term, but it achieved no significant improvement in BMI outcomes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

We are grateful to the following primary care pediatricians and pediatric nurses who work in Cesena, Forlì-Cesena, Italy, carried out MI's with parents and completed a crucial component of our intervention trial. Pediatricians: Arturo Alberti, Antonio Belluzzi, Rita Casalboni, Giancarlo Cerasoli, Antonella De Pascale, Mila Degli Angeli, Paolo Faberi, Clara Faedi, Alessandra Foschi, Maurizio Iaia, Elide Lucchi, Marna Mambelli, Franco Mazzini, Marco Minghetti, Giuseppina Mingozzi, Loreta Piccolo, Barbara Poggioli, Antonella Stazzoni, Pierluigi Tonti, Miro Trebbi, Francesca Vaienti, Silvia Valentini. Nurses: Tosca Alessandrini, Patrizia Amaduzzi, Monica Bertozzi, Flavia Bonavita, Roberta Bracci, Barbara Gori, Fiammetta Mazzotti, Roberta Ruffilli, Milva Silvani. We thank the following colleagues for their effective cooperation that helped us conduct our study: Gianpaolo Guelfi, psychiatrist who led the Motivational Interviewing training for primary care paediatricians; Francesca Castoldi and Emanuela Baldassarri, psychologists who led a similar training course for nurses; Dr Lorena Quaranta, Health Education Office Coordinator, who gave her support to planning information tools for parents and teachers; Dr Rita Scalambra, Uisp (Unione Italiana Sport per tutti—Italian Sports Union for Everyone), who led a training course about the Promotion of Physical Activity among Preschool Children for childcare centre teachers; and all the directors and teachers of the 16 randomized childcare centres. We are also grateful to Leonardo Grilli, Associated Professor in Statistics, Department of Statistics, Information Technology, Applications 'G.Parenti' University of Florence, for his helpful suggestions on designing the statistical analysis model. Dr Iaia is grateful to Giancarlo Biasini, Senior Professor of Pediatrics, for his constructive suggestions. In September 2012, OROGEL S.p.A., a company based in via Dismano 2600, I-47522, Cesena, Forlì Cesena, Italy, granted €10 000 in support of our educational intervention. This sponsor had no role in designing and conducting our study; collecting, managing, analysing and interpreting its data; and preparing, reviewing and approving our paper.

AUTHOR CONTRIBUTIONS

Dr MI promoted the idea for this study and its design, and developed its score system for the evaluation of the intervention's effects on behaviours. He drafted the manuscript, coordinated the implementation of the intervention study and he is also the author of two versions of a manual guide '*5210 messaggi in codice per crescere in salute*' (one for medical staff and one for parents and teachers). Drs MP, AB contributed to the study design and coordinated its implementation. They also measured children's weight and height at child care centres, and they entered all the data into our database for statistical analysis. Dr PV contributed to the statistical analysis model and carried out the statistical analysis of the results. Dr EA contributed to our statistical analysis model and thoroughly reviewed our paper. Dr MF contributed to our study design and