No Effect of Glucomannan on Body Weight Reduction in Children and Adolescents with Overweight and Obesity: A Randomized Controlled Trial

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Objective To assess the efficacy of water-soluble dietary fiber, glucomannan supplementation, on the body mass index (BMI) in children with overweight or obesity.

Study design In this randomized, double-blind, placebo-controlled trial, we enrolled 96 children aged 6-17 years with overweight or obesity based on the World Health Organization growth criteria (>+1 SD or >+2 SD, respectively). Participants were assigned to receive glucomannan or placebo (maltodextrin), both at a dose of 3 g/d for 12 weeks and were followed up for the next 12 weeks. Concomitant care included dietary and lifestyle advice. The primary outcome was the difference in the BMI-for-age z score change between the groups at 12 weeks.

Results Compared with the placebo, glucomannan had no effect on the BMI-for-age z score at 12 weeks (mean difference: 0.0, 95% CI −0.1 to 0.1). Compared with the placebo, the glucomannan group had lower total and low-density lipoprotein cholesterol concentrations at 12 weeks. In addition, the blood pressure was greater at 12 weeks (systolic) and at 24 weeks (diastolic) in the glucomannan group. No differences between the groups in adverse events and other secondary outcomes were observed.

Conclusions Glucomannan supplementation compared with placebo had no effect on weight reduction in children with overweight and obesity. *(J Pediatr 2019;211:85-91)*.

Trial registration ClinicalTrials.gov NCT02280772.

Childhood obesity remains a major public health problem worldwide.[1-4] It is associated with an increased risk for physical and psychological comorbidities related to almost every system in the body.[5] One of the dietary supplements marketed for weight reduction is glucomannan, a viscous dietary fiber that is derived from the plant *Amorphophallus konjac*.[6] The exact mechanism by which glucomannan decreases weight is still unknown. However, it has been reported that glucomannan slows gastric emptying by forming a viscous gel of large volume, which tends to increase the feeling of satiety.[7]

In 2010, the European Food Safety Authority concluded that glucomannan contributes to the reduction of body weight in the context of an energy-restricted diet in adults who are overweight.[7] The findings from systematic reviews performed in 2008 and 2015 confirmed that, in the short term, glucomannan has the potential to reduce body weight, although not body mass index (BMI).[8-10] However, a systematic review in 2014 found a nonsignificant difference in weight loss between glucomannan and placebo.[11] In regard to children, a systematic review in 2015 concluded that data were too limited to draw any conclusions about the effects of glucomannan on weight reduction.[8] Considering that current evidence on the effectiveness of glucomannan administration in children is sparse, we developed a protocol for a randomized controlled trial (RCT) to assess the effects of glucomannan supplementation in children with overweight and obesity.[12] A BMI-related outcome instead of body weight change was used as the primary outcome, in accordance with the European Medicines Agency addendum on trials assessing weight control in children.[13] We hypothesized that, compared with placebo, glucomannan administration would decrease the BMI-for-age z score in children and adolescents with overweight and obesity.

Methods

This randomized, double-blind, parallel-group, placebo-controlled trial was conducted at the Department of Paediatrics of the Medical University of Warsaw, Poland. The protocol was published before the enrollment of the first patient.[12] The study protocol was

MD	Mean difference
BMI	Body mass index
DBP	Diastolic blood pressure
FPG	Fasting plasma glucose
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
MVPA	Moderate-to-vigorous physical activity
RCT	Randomized controlled trial
SBP	Systolic blood pressure
WHO	World Health Organization

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approved by the Bioethics Committee of the Medical University of Warsaw. Informed consent was obtained from all parents. The reporting is in line with the CONSORT statement.[14] The trial was registered at ClinicalTrials.gov (NCT02280772).

Children between 6 and 17 years of age with a BMI of >+1 SD or >+2 SD (ie, with overweight or obesity, respectively, according to the World Health Organization [WHO] growth reference) were eligible for inclusion. Exclusion criteria included drug therapy for a chronic disease (including drugs that influence appetite or weight), type 1 or 2 diabetes, history of surgical treatment of obesity, participation in another obesity treatment program during the project and/or 3 months before recruitment, secondary obesity, and pregnancy.

Patients were assigned randomly to 1 of the groups using a computer-generated schedule, stratified by sex and age (6-11 years; 12-17 years) using permuted blocks of size 4.[15] Allocation concealment was ensured by using opaque, sealed, and numbered envelopes. Both products were identically packaged in blister packs manufactured and supplied by Dicofarm S.p.A. (Rome, Italy). The manufacturer and funders did not have any role in the design or conduct of the trial or the analyses. The randomization sequence, codes, and treatment allocation were secured until data had been analyzed.

Participants were assigned randomly to receive glucomannan or placebo (maltodextrin) with a 1:1 allocation. Both products were administered orally, at a dose of 3 g/d, for 3 months, combined with a glass of water before main meals. Patients were followed up for the next 3 months to assess the retention of an effect. All patients received concomitant care at baseline and at 12 and 24 weeks. In brief, individual consultation with a dietitian was offered. It consisted of advice on achieving a normocaloric diet (ie, by identifying and decreasing foods with added sugars or low nutrients and promoting vegetable and water intake). Participants also were encouraged to complete ≥60 min/d of moderate-to-vigorous physical activity (MVPA). Finally, the limitation of sedentary time to ≤2 hours/day was advised. To increase study retention, visits at 6 and 18 weeks were arranged. Adherence to therapy was discussed and assessed by direct interview at 6 and 12 weeks. Parents were asked to bring remaining capsules at that time.

The primary outcome was the difference in the BMI-for-age z score change (baseline vs end of the intervention) between the glucomannan and placebo groups at 12 weeks. The secondary outcome measures included anthropometry and body composition, physical activity, food intake, and cardiometabolic factors. In addition to preplanned outcomes,[12] we included the following exploratory outcomes: body fat percentage, fat mass index, fasting plasma glucose (FPG), total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglyceride concentrations, and the triglyceride/HDL cholesterol ratio.[16]

Weight and height measurements were obtained at every study visit. The subject's weight was measured using the Radwag digital scale (Radwag Balances and Scales, Radom, Poland) to the nearest 0.1 kg, without shoes, and in underwear. Their height was measured using a Holtain stadiometer (Holtain Ltd, Pembrokeshire, Wales, United Kingdom), to the nearest 0.1 cm, barefoot and with the head in the Frankfurt horizontal plane. The BMI-for-age z scores were computed using the WHO macro.[17] Central body fat, whole body fat, and fat-free mass as well as body fat percentage (calculated as fat mass multiplied by 100 and divided by body weight) and fat-mass index (calculated as fat mass in kilograms divided by height in meters squared) were assessed at the baseline and after the intervention with dual-energy X-ray absorption technology, which is a valid and reliable for quantifying body fat.[18] Participants were positioned on the scanner table, and total body cuts were positioned as per standard specifications using the Lunar Prodigy (GE Healthcare, Amersham, United Kingdom) in the Department of Medical Imaging at the Children's Memorial Health Institute in Warsaw.

Physical activity was measured using a wrist-worn accelerometer (GENEActiv Original; Activinsights, London, United Kingdom) at the baseline and after the intervention. Acceleration was recorded at 75 Hz and quantified with the use of Euclidean norm minus one, averaged over the 5-second epoch intervals.[19] Validated cut points of acceleration associated with children's MVPA were used.[20] To remove random signals, only activities lasting for ≥1 minute and satisfying the ≥191.6-mg threshold for at least 80% of activity time were retained. Analysis of MVPA included only participants with ≥16 hours of wear time during every 24 hours of ≥3 days. The time in MVPA was calculated as the mean of measures over 7 valid days or when fewer days were available with the previously used equation.[21] Data were analyzed using R-package GGIR v.1.6-0 (http://cran.r-project.org).[22]

Daily energy intake calculations were based on 3-day food records (2 weekdays and 1 weekend day), reviewed by a dietitian using the computer software DIETA (http://www.izz.waw.pl) at baseline and at weeks 12 and 24.

Systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse rate were assessed at each visit, with 3 individual measurements taken in the sitting position according to standards, using an automatic oscillometer.[23] Total, HDL, and LDL cholesterol, triglyceride, and FPG concentrations were obtained at baseline and at weeks 12 and 24 after an overnight fast in all participants with the use of standard methods at the Medical University of Warsaw laboratory. The numbers and proportions of participants with impaired fasting glucose and dyslipidemia from baseline to week 12 and 24, as well as changes in lipid concentrations between groups, were evaluated. Dyslipidemia was defined as a disturbance in at least 1 of the following: total (≥200 mg/dL), LDL cholesterol (≥130 mg/dL), HDL cholesterol (<40 mg/dL), or triglycerides (up to 9 years: ≥100 mg/dL; from 10 years of age: ≥130 mg/dL).[24] Impaired fasting glucose was defined as an FPG concentration of >99 mg/dL.

The sample size needed to detect an effect on the primary outcome (ie, the difference in BMI-for-age z score change [baseline vs 12 weeks]) was defined considering data from the literature.[25] It was calculated that 96 participants would be sufficient to detect a mean difference of 0.17 between groups in BMI-for-age z score change, with a power of 80% and a significance level of 5%, considering 20% of patients

Table I. Participants' characteristics at baseline

Characteristics	n	Intervention group	n	Placebo group
Female participants, %	27	54%	26	57%
Race, white, %	49	98%	46	100%
Age, y	50	10.0 (9.0-13.8)	46	10.5 (9.0-13.0)
Tanner, stage, n (%)				
1	50	23 (46%)	46	23 (50%)
2		9 (18%)		5 (11%)
3		5 (10%)		6 (13%)
4		8 (16%)		8 (17%)
5		5 (10%)		4 (9%)
Weight, kg	50	56.6 (43.9-77.7)	46	62.7 (46.0-80.7)
Height, cm	50	151.2 ± 15.3	46	151.2 ± 15.6
BMI-for-age z score	50	2.5 (2.2-3.1)	46	2.7 (2.2-3.1)
Energy intake, kJ/d	45	5515 (4661-6987)	44	4761 (4040-5794)
Central body fat, kg	50	1.9 (1.5-3.0)	46	2.0 (1.5-2.9)
Whole body fat, kg	50	22.0 (16.7-34.0)	46	24.6 (18.6-36.0)
Fat-free mass, kg	50	32.7 (26.5-40.6)	46	33.1 (26.5-39.9)
Body fat, %	50	41 ± 5	46	42 ± 6
FMI, kg/m^2	50	10.6 (8.5-13.0)	46	10.9 (8.8-13.3)
MVPA, min/d	45	23.1 (15.2-33.2)	39	23.6 (11.7-42.6)
Fasting glucose, mg/dL	50	86.8 ± 6.0	46	87.2 ± 5.7
Total cholesterol, mg/dL	50	169.6 ± 29.2	46	160.0 ± 24.2
LDL cholesterol, mg/dL	50	99.4 ± 27.7	46	90.3 ± 24.2
HDL cholesterol, mg/dL	50	50.5 (44.5-57.5)	46	50.5 (41.5-58.0)
TG, mg/dL	50	83.0 (61.3-117.3)	46	95.9 (64.5-114.8)
Dyslipidemia, n (%)	50	21 (42%)	46	19 (41%)
TG to HDL cholesterol ratio	50	1.6 (1.0-2.5)	46	1.9 (1.2-2.6)
TG to HDL cholesterol ratio (≥2.2), n (%)	50	17 (34.0%)	46	16 (34.8%)
IFG, n (%)	50	0 (0%)	46	0 (0%)
Systolic blood pressure, mm Hg	50	110.1 ± 11.4	45	113.5 ± 12.9
Diastolic blood pressure, mm Hg	50	66.6 ± 8.4	45	68.4 ± 8.1
Heart rate, beats/min	50	81.4 ± 12.0	45	81.5 ± 11.4

IFG, impaired fasting glucose; *TG*, triglyceride.
Data are presented as the mean (SD) or IQR (25th-75th percentile) unless otherwise indicated. Baseline data were analyzed using the independent-samples *t* test for continuous variables and the χ^2 test for categorical variables.

would be lost to follow-up. The sample size calculation was performed using statistical software (StatsDirect Ltd, Cambridge, United Kingdom). We used a calculation formula for sample size for an unpaired 2-sample Student *t* test, which assumes a specified level of difference between population means to be detected in the analysis, a normal distribution of population means, and a known estimate of the population SD.

All analyses followed intention-to-treat principles, including all randomized patients with available data. Data were assessed for normality with the Shapiro–Wilk test. Non-normally distributed data were log-transformed and retested. If a given variable still did not follow a normal distribution after log transformation, other transformations were tested. Nonparametric analyses (eg, Mann–Whitney *U* test) were applied only if data did not conform to a normal distribution after transformation. Baseline characteristics were compared between (1) study groups and (2) completers and those lost to follow-up at 12 weeks using the independent-samples *t* tests for continuous variables and the χ^2 test or Fisher exact test for nominal variables. Primary and secondary outcomes were calculated for each participant as the difference between the values at follow-up (12 weeks and/or 24) and the baseline at the start of the study. These changes were assessed with the use of independent-samples *t* tests or the Mann–Whitney *U* test to detect significant differences between groups (separately for week 12 and 24). Differences between groups in nominal secondary outcomes were assessed with the χ^2 test or Fisher exact test. Data are expressed as means (95% CIs), medians (95% CIs), or numbers (n [% of total]). Two-sided *P* values < .05 were considered significant.

We did not perform the originally planned ANCOVA adjusted for the baseline value, as the average baseline scores were not statistically different between groups.[26] Data from baseline and weeks 12 and 24, across the placebo and glucomannan groups, were assessed for violations of assumptions of ANOVA with repeated measures. Due to numerous violations in normality, not solved via data transformation, as well as in sphericity of variance, it was also not performed. Multiple imputation was considered but not done at 12 weeks, as 16% of the lost observations for most of the characteristics were within the 20% assumption of follow-up losses in the sample size calculation. The multiple imputation approach (5 imputed datasets, data assumed to be missing at random) was used to handle missing data for most outcomes at week 24 (33% of missing observations). The only exception was energy intake at week 24, for which imputation could not be done, as the proportions of missing data were too large.[27] Analyses were carried out with the statistical software R v.3.4.4 (R Foundation for Statistical Computing, Vienna, Austria). All analyses, except for the primary outcome, were considered as exploratory, and no correction for multiple comparisons was made.

Table II. Changes in continuous outcome measures between baseline and 12/24 weeks

Characteristics	Week	n	Intervention group change from baseline	n	Placebo group change from baseline	Mean difference*	P
BMI-for-age z score	12	41	−0.2 (−0.3 to −0.1)	40	−0.2 (−0.3 to −0.2)	0.0 (−0.1 to 0.1)	.99
	24†	50	−0.3 (−0.4 to −0.2)	46	−0.3 (−0.4 to −0.2)	0.1 (−0.1 to 0.2)	.42
Energy intake, kJ/d	12†	29	−732 (−1387 to −161)	30	2 (−640 to 492)	−734 (−1577 to 201)	.21
	24†	15	−814 (−1773 to 146)	13	−399.0 (−1639 to 841)	−415 (−1910 to 1081)	.57
Central body fat, kg	12†	41	0.0 (−0.2 to 0.0)	39	−0.1 (−0.2 to −0.1)	0.1 (−0.1 to 0.1)	.37
Whole body fat, kg	12†	41	−0.6 (−2.5 to −0.5)	39	−1.6 (−2.1 to −0.6)	1.0 (−1.1 to 1.1)	.85
Fat free mass, kg	12†	41	0.8 (0.5 to 1.3)	39	0.6 (0.3 to 1.2)	0.2 (−0.5 to 0.8)	.98
Body fat, %	12‡	41	−2.0 (4 to −2)	39	−2.0 (−3 to −1)	0.0 (−0.02 to 0.01)	.64
FMI, kg/m^2	12	41	−0.9 (−1.2 to −0.5)	39	−0.8 (−1.1 to 0.3)	−0.1 (−0.6 to 0.4)	.73
MVPA, min/d	12†	30	1.0 (−7.0 to 5.5)	28	−3.5 (−6.5 to 6.5)	4.5 (−8.0 to 8.0)	.15
Fasting glucose, mg/dL	12	41	2.4 (0.1 to 4.8)	40	2.0 (−0.2 to 4.1)	0.5 (−2.7 to 3.6)	.77
	24†	50	1.6 (−0.0 to 4.6)	46	1.2 (−1.3 to 3.5)	0.4 (−2.0 to 3.8)	.50
Total cholesterol, mg/dL	12	41	−12.8 (−17.9 to −7.8)	40	1.0 (−6.1 to 8.1)	−13.8 (−22.4 to −5.2)	.002
	24†	50	−3.5 (−12.8 to 4.2)	46	−3.8 (−12.8 to 2.9)	0.2 (−10.5 to 12.2)	.68
LDL cholesterol, mg/dL	12	41	−12.1 (−17.4 to −6.8)	40	0.8 (−5.2 to 6.8)	−12.8 (−20.7 to −5.0)	.002
	24†	50	−4.3 (−12.8 to 2.9)	46	−6.9 (−13.8 to −1.9)	2.5 (−6.6 to 12.6)	.36
HDL cholesterol, mg/dL	12	41	−0.8 (−3.0 to 1.4)	40	1.7 (−0.7 to 4.0)	−2.5 (−5.6 to 0.7)	.12
	24‡	50	1.8 (−1.1 to 5.4)	46	3.2 (0.8 to 6.4)	−1.4 (−4.0 to 2.8)	.62
TG, mg/dL	12‡	41	−4.0 (−18.5 to 5.5)	40	−8.0 (−17.5 to 5.1)	4.0 (−16.3 to 16.7)	.97
	24†	50	−5.7 (−22.7 to 5.4)	46	−4.8 (−22.0 to 8.1)	−0.9 (−21.8 to 17.4)	.55
TG to HDL-C ratio	12‡	41	−0.2 (−0.8 to −0.1)	40	−0.3 (−0.7 to −0.1)	0.1 (−0.4 to 0.2)	.99
	24‡	50	−0.2 (−0.6 to 0.1)	46	−0.3 (−0.6 to 0.1)	0.1 (−0.6 to 0.1)	.60
Blood pressure, mm Hg, systolic	12	41	3.7 (1.0 to 6.4)	39	−0.7 (−3.5 to 2.1)	4.4 (0.5 to 8.2)	.03
	24†	50	4.6 (2.4 to 7.7)	46	−0.3 (−4.2 to 2.7)	4.9 (1.5 to 9.7)	.15
Blood pressure, mm Hg, diastolic	12‡	41	3.0 (−0.5 to 4.5)	39	−3.0 (−4.5 to 1.0)	6.0 (−0.00001 to 7.0)	.05
	24‡	50	3.0 (1.2 to 5.7)	46	−2.1 (−5.6 to −0.1)	5.0 (2.4 to 8.6)	.012

Values are mean differences (95% CI) or median differences (95% CI) between baseline and follow-up measures (at 12th or 24th week). Data were tested with the use of the independent-samples *t* test or Mann−Whitney *U* test. Missing data for week 24 were imputed with the multiple imputation method.
*Mean difference represents intervention group change from baseline minus placebo group change from baseline (95% CI).
†Log-transformation was applied before running the independent-samples *t* test.
‡The Mann−Whitney *U* test was applied if data did not conform to a normal distribution after transformation.

Results

A flow diagram of the trial is shown in the **Figure** (available at www.jpeds.com). Eligible patients were recruited between April 2015 and January 2018. After screening, 96 children fulfilling the inclusion criteria were randomized. A total of 81 completed the 12-week intervention, and 64 remained for analysis at 24 weeks (after 12 weeks of observation). The characteristics of the patients were similar between the groups at baseline (**Table I**), as well as between those who completed the intervention (n = 81) and those who were lost to follow-up (n = 15) (data not shown). In detail, the glucomannan group consisted of 9 patients who were overweight and 41 patients who were obese, including 14 patients (34%) with severe obesity (defined as BMI z score >3 SD, based on WHO growth reference). Similarly, the placebo group consisted of 9 patients who were overweight and 37 patients who were obese, including 15 patients (41%) with severe obesity. At 12 and 24 weeks, 15 (16%) and 32 (33%) of patients, respectively, were lost to follow-up. If reported, the reasons for attrition included parents' work commitments. The number of patients lost to follow-up did not differ significantly between the study groups (**Figure**).

For the primary outcome, the BMI-for-age z-score change at 12 weeks, no difference in the change between follow-up and baseline values was found between the glucomannan and placebo groups. The intervention effects on the primary and secondary outcomes are presented in **Table II** and **Table III**. There was also no difference between the groups for any of the secondary outcomes, with 3 exceptions. We found significantly lower total cholesterol (mean difference [MD], −13.8 mg/dL; 95% CI −22.4 to −5.2) and LDL cholesterol (MD, −12.8 mg/dL; 95% CI −20.7 to −5.0) concentrations in the glucomannan group compared with the placebo group at the end of the intervention (12 weeks). In addition, we observed a statistically significant greater SBP at 12 (MD, 4.4 mm Hg; 95% CI 0.5-8.2) and DBP at 24 (MD, 5.0 mm Hg; 95% CI 2.4-8.6) weeks in the glucomannan group compared with the placebo group.

Adverse events were similar in both groups, both after 6 and 12 weeks of the intervention (**Table III**). One patient in the glucomannan group noticed transient head hair loss. Detailed data about adverse events are presented in **Table IV**.

After 12 weeks of the intervention, the calculated percentage of adherence to therapy was similar between groups (mean compliance: 80% in glucomannan and 84% in placebo groups).

Discussion

In a previous RCT involving otherwise healthy children with obesity, there was no difference between the glucomannan and placebo groups in the percentage change of "overweight individuals."[28] In our trial, the duration of the intervention was longer (3 vs 2 months) and the daily dose of glucomannan was increased (from 2 to 3 g/d, as suggested by the European Food Safety Authority),[7] but no effect on the BMI-for-age z score was observed. In adults, the only

Table III. Nominal secondary outcome measures

Characteristics	Week	n	Intervention group	n	Placebo group	*P*	RR (95% CI)
Dyslipidemia, n (%)	12	41	15 (37%)	40	12 (30%)	.69*	0.82 (0.44-1.53)
	24	50	20 (40%)	46	18 (39%)	>.99*	0.98 (0.60-1.61)
IFG, n (%)	12	41	3 (7%)	40	2 (5%)	>.99†	0.68 (0.12-3.88)
	24	50	3 (6%)	46	2 (4%)	>.99†	0.73 (0.12-4.14)
TG to HDL-C ratio (≥2.2), n (%)	12	50	9 (18%)	46	13 (28%)	.341*	1.57 (0.74-3.32)
Adverse events, n (%)	6	50	16 (32%)	46	15 (33%)	>.99*	1.02 (0.57-1.82)
	12	50	7 (14%)	46	12 (26%)	.22*	1.86 (0.80-4.32)

RR, risk ratio.
*χ^2 test.
†Fisher exact test.

comparable trial in terms of dose and time of the intervention also showed no effect of glucomannan on both BMI and weight reduction.[8,29] Of note, when interpreting the results, a high placebo effect in our trial should be considered. We observed a significant mean difference in the BMI-for-age z score within the placebo group from baseline to 12 weeks (−0.2; 95% CI −0.3 to −0.2) and from baseline to 24 weeks (−0.3; 95% CI −0.4 to −0.2). In the Cochrane Collaboration meta-analysis, the mean effect of the lifestyle intervention in children aged 12 years and more was reported to be −0.14 (95% CI −0.17 to −0.12) of the BMI z score after 6 months, which is almost 2 times less than our effect.[30]

The reduction in LDL and total cholesterol concentrations with glucomannan administration are in line with the results of a recent meta-analysis of RCTs that documented that effect of glucomannan on blood lipids in both adults and children. The authors concluded that the intake of approximately 3 g/d of glucomannan reduced LDL cholesterol by about 10%.[6] In our trial, despite the observed differences in total and LDL cholesterol concentrations between groups, no change in the prevalence of dyslipidemia or the triglyceride/HDL-C ratio[16] in favor of the glucomannan group was found after the intervention. This may be partly explained by the lack of an additional effect of glucomannan on triglyceride concentrations. Our findings are in line with a 2008 meta-analysis in which a subgroup of 3 pediatric studies found no effect of glucomannan on triglyceride concentrations (MD, −10.8; 95% CI −34.3 to 12.9).[10] In addition, no retention of this effect was observed after another 12 weeks. Blood pressure differences between groups were unexpected, given the within-group reductions in the BMI-for-age z scores observed during the whole trial. Previous trials assessing the effects of glucomannan interventions in children with dyslipidemia[31] and in adults with dyslipidemia[10] demonstrated no effect on blood pressure. We found a greater SBP (after the intervention) and DBP (after the observation) in the glucomannan compared with the placebo group.

Table IV. Adverse events

Adverse events	Intervention group (n = 41), n (%)	Placebo group (n = 40), n (%)	Difference* (95% CI)
Patients reporting ≥1 adverse event	11 (27%)	11 (28%)	−1 (−20 to 19)
Abdominal pain	11 (27%)	11 (28%)	−1 (−20 to 19)
Loose stools	9 (22%)	5 (13%)	9 (−7 to 26)
Fullness and/or lack of appetite	8 (20%)	11 (28%)	−8 (−26 to 10)
Headache	2 (5%)	3 (8%)	−3 (−13 to 80)
Hard stools	3 (7%)	2 (5%)	2 (−8 to 13)
Dizziness	0 (0%)	2 (5%)	−5 (−12 to 2)
Borborygmus	5 (12%)	2 (5%)	7 (−5 to 19)
Abdominal distension	3 (7%)	4 (10%)	−3 (−15 to 10)
Nausea	0	3 (8%)	−8 (−16 to 10)
Heartburn	0	2 (5%)	−5 (−12 to 2)

*Values are the difference (reported in percentage points) calculated as intervention group minus placebo group.

To further examine this association, SBP and DBP were converted to blood pressure z scores as described previously[32] and based on the most recent Centers for Disease Control and Prevention growth charts.[33] After this transformation, an additional statistically significant difference between groups was observed after 24 weeks for SBP (**Table V**; available at www.jpeds.com). As this is an exploratory analysis, caution is needed when interpreting these findings. In our opinion, blood pressure should be considered as an additional safety outcome in potential glucomannan trials, especially in children with overweight or obesity.

The strengths of this trial include trial design (investigator-initiated, randomized, double-blind, placebo-controlled), with a study protocol that was peer-reviewed and published in advance.[12] Our population included a wide age range of pediatric patients (ie, children and adolescents). We used objective methods to assess body composition (with dual-energy X-ray absorption technology) and physical activity (accelerometers). Still, there are some study limitations. The use of the 3-day food record to measure energy intake is one of these, as underreporting of food intake is a well-recognized problem.[34] To minimize the risk of bias, a dietitian interviewed parents and patients. However, a large number of participants did not provide the 3-day food record (only 59 and 28 records were available for the analysis at 12 and 24 weeks, respectively). The attrition rate of 16% at the intervention (12 weeks) and 33% after the observation (24 weeks) is another limitation of this trial. However, the loss to follow-up during the intervention was lower than projected, and we used a multiple imputation approach to minimize the effect of missing outcome data for the observation time point (24 weeks) only. Nevertheless, due to larger attrition at 24 weeks and non-normality of the data, these findings are less robust. Although we observed a powerful placebo effect on BMI z score, no differences in energy intake and MVPA duration between and within groups after 12 weeks of the intervention were noted. Other factors,

not assessed in this RCT, could be responsible for the observed BMI z score reduction. These include routine physical activities performed over the day, such as walking up the stairs, walking/cycling instead of driving, or limiting sedentary behaviors such as decreased use of electronic media. One can question whether improved diet quality (without caloric intake changes) is responsible for our observed placebo effect on weight reduction.[35] We do not support the use of glucomannan to reduce weight in the pediatric population. ■

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Data Statement

Data sharing statement available at www.jpeds.com.

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50 Years Ago in *The Journal of Pediatrics*

Lung Expansion and Ventilation During Resuscitation of Asphyxiated Newborn Infants

Hull D. J Pediatr 1969;75:47-58.

In this study, Hull presented 42 asphyxiated term neonates who were intubated and ventilated with positive pressure ventilation. He used a device consisting of a flow meter, a spirometer, a pressure manometer, and a foot-driven lever for ventilating the neonates. An airtight seal was established between the endotracheal tube and the larynx, making accurate measurements of the intrathoracic pressure possible. The study revealed a high gas uptake in the first two minutes after delivery while the functional residual capacity was formed. This was more delayed in severely asphyxiated infants. It was demonstrated that the mean total static compliance changed from 1.0 to 1.5 mL/cm/H_2O over the first minute. Thus, the lungs of most infants would be adequately ventilated using a pressure of 30 cmH_2O delivering tidal volumes of in mean 10-13 mL in the 2 first minutes.

Several studies emerged in the late 1950s and the 1960s on lung mechanics and oxygen uptake in the neonate.[1,2] Hull's study combined the measurements of oxygen uptake and the assessment of ventilation pressure needed for adequate lung ventilation, thus adding to the knowledge regarding what pressure to use for adequate ventilation of asphyxiated neonates. The suggested pressure in Hull's study is similar to the pressure now recommended in most resuscitation guidelines (ILCOR, ANZCOR) since 2015.[3] The resuscitation of asphyxiated neonates has changed since the late 1960s. Hull's findings are, however, still valid and offer insight into the physiology of formation of functional residual capacity, oxygen uptake, and lung expansion.

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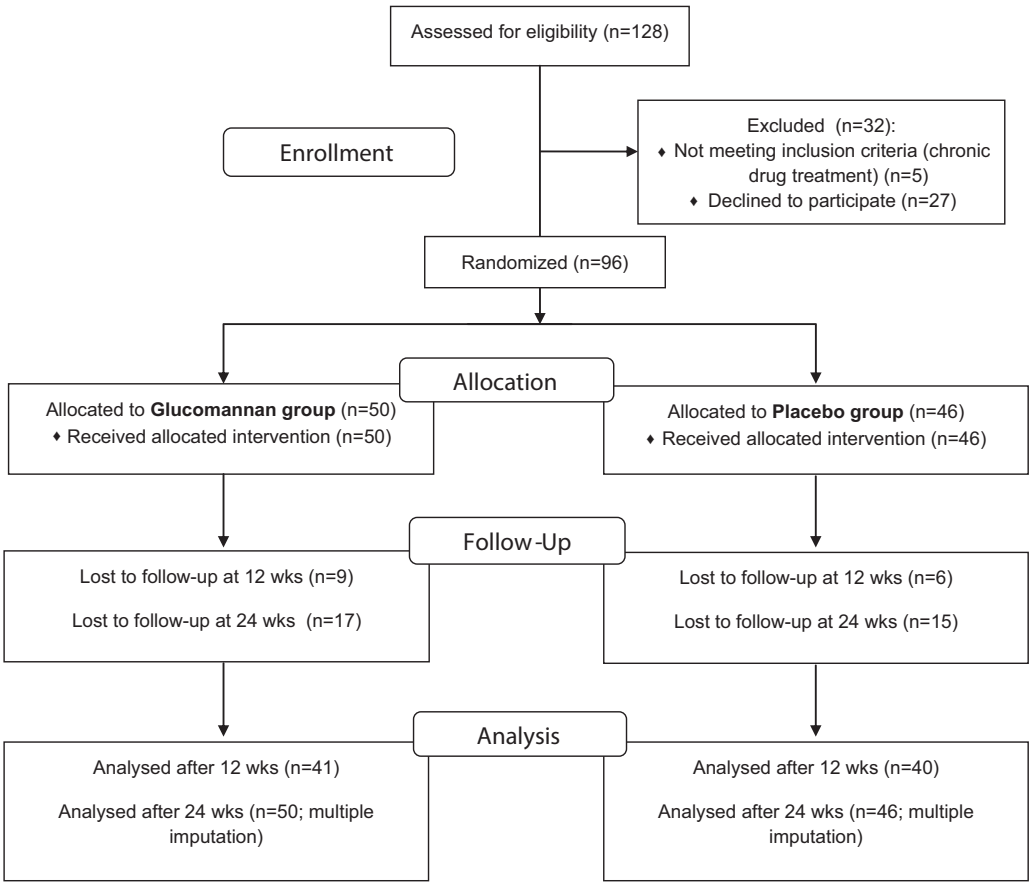

Figure. Flow diagram of the inclusion of participants and observations.

Table V. Changes in blood pressure between baseline and 12/24 weeks*

Characteristics	Week	n	Intervention group change from baseline	n	Placebo group change from baseline	*P*	Mean difference†
Systolic blood pressure, mm Hg	12	41	3.7 (1.0 to 6.4)	39	−0.7 (−3.5 to 2.1)	.026	4.4 (0.5 to 8.2)
	24‡	50	4.6 (2.4 to 7.7)	46	−0.3 (−4.2 to 2.7)	.150	4.9 (1.5 to 9.7)
Diastolic blood pressure, mm Hg	12§	41	3.0 (−0.5 to 4.5)	39	−3.0 (−4.5 to 1.0)	.053	6.0 (−0.00001 to 7.0)
	24§	50	3.0 (1.2 to 5.7)	46	−2.1 (−5.6 to −0.1)	.012	5.0 (2.4 to 8.6)
Systolic blood pressure, z score	12	41	0.3 (0.1 to 0.6)	39	−0.1 (−0.4 to 0.2)	.020	0.4 (0.1 to 0.8)
	24§	50	0.3 (0.1 to 0.6)	46	−0.1 (−0.5 to 0.1)	.019	0.4 (0.2 to 0.9)
Diastolic blood pressure, z score	12	41	0.1 (−0.1 to 0.3)	39	−0.2 (−0.4 to 0.02)	.0502	0.3 (−0.0002 to 0.6)
	24§	50	0.2 (0.0 to 0.4)	46	−0.2 (−0.5 to 0.1)	.002	0.4 (0.2 to 0.8)

*Values are mean differences (95% CI) or median differences (95% CI) between baseline and follow-up measure (in 12th or 24th week). Data were tested with the use of independent-samples *t* test or Mann−Whitney *U* test. Missing data for week 24 imputed with multiple imputation method.
†Mean difference represents intervention group change from baseline minus placebo group change from baseline (95% CI).
‡Nonparametric data, values are median differences (95% CI). Log-transformation or square root transformation applied before running independent-samples *t* test.
§Nonparametric data, values are median differences (95% CI). Mann−Whitney *U* test applied, as data did not conform to a normal distribution after transformation.