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Improvements in body mass index of children with cystic fibrosis following implementation of a standardized nutritional algorithm: A quality improvement project

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Abstract

Background: A collaboration between the University of Michigan (UM) Cystic Fibrosis Center (CFC) and Marmara University (MU) CFC was initiated in MU through conducting Quality Improvement projects (QIP). The global aim was to improve nutritional status of children with CF (cwCF), with a specific aim to increase the mean BMI percentile (BMIp) for cwCF by 10 percentile points in 12 months.

Methods: Body mass index (BMI) percentiles of cwCF were categorized as: nutritionally adequate (BMIp ≥ 50%); at risk (BMIp 25%–49%); urgently at risk (BMIp 10%–25%); critically at risk (BMIp < 10%). Appropriate interventions were made according to BMIp category every three months. Forced expiratory volume in one-second percent predicted (FEV1pp), and health-related quality of life (HRQoL) were evaluated.

Results: One hundred and eight-two cwCF with a mean age of 9.1 ± 4.3 years were included in the project. Baseline BMIp increased from 25.6 to 37.2 at the 12th month ($p < 0.001$). In the critically at-risk group BMIp increased from 3.6 to 20.5 ($p < 0.001$), in the urgently at risk group from 15.9 to 30.8 ($p < 0.001$), in the at risk group from 37.0 to 44.2 ($p < 0.079$) and in the nutritionally adequate group the increase was from 66.8 to 69.5 ($p < 0.301$). FEV1pp also improved significantly, from 81.3 ± 20.6 to 85.9 ± 20.8 ($p < 0.001$). Physical functioning, eating problems, and respiratory symptoms domains of the HRQoL evaluation improved ($p < 0.05$).

Conclusion: This project has led to significant improvements in BMIp, FEV1pp and HRQoL of cwCF; similar projects could easily be implemented by centers in other developing countries.

KEYWORDS

body mass index, children, cystic fibrosis, nutrition

Abbreviations: BMI, body mass index; BMIp, BMI percentile; CFC, Cystic Fibrosis Center; CFF, Cystic Fibrosis Foundation; CFQ-R, Cystic Fibrosis Questionnaire-Revised; cwCF, children with cystic fibrosis; ECFSPR, European Cystic Fibrosis Society Patient Registry; FEV1pp, forced expiratory volume at 1 s, percent predicted; HRQoL, health-related quality of life; MECFA, Middle East Cystic Fibrosis Association; MRSA, methicillin-resistant *Staphylococcus aureus*; MUCFC, Marmara University Cystic Fibrosis Center; PA, *Pseudomonas aeruginosa*; PEG, percutaneous endoscopic gastrostomy; PEx, pulmonary exacerbation; PFT, pulmonary function testing; QI, quality improvement; QIP, quality improvement project; UMCFC, University of Michigan Cystic Fibrosis Center.

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1 | BACKGROUND

The nutritional status of people with cystic fibrosis (CF) is closely associated with pulmonary function, respiratory status, and survival. Body mass index (BMI) and BMI percentile (BMIp) for age are the most commonly used measurements of nutritional status in CF.[1]

BMIp is a CF quality of care indicator, and it has been used as a benchmark for comparison between CF centers (CFC).[2–8] Most of the patients with CF in Turkey are children, and many have low BMIp values.[9] Delayed diagnosis due to the lack of a national newborn screening program before 2015, inadequate nutritional support, and lack of standardized follow-up protocols were the main reasons for low BMIp levels in Turkey. Caregivers and children's attitudes toward invasive procedures such as the insertion of gastrostomy tubes also played an important role in low BMIp in cwCF.

Marmara University (MU) CFC, where 311 pediatric CF patients are followed, is one of the largest centers in Turkey. It has participated in the European Cystic Fibrosis Patient Registry (ECFSPR) since 2015.[9] The BMIp values of MU CFC patients were significantly lower compared to those of cwCF in other CFCs in the ECFSPR and their US peers.[10] So, there was an urgent need to improve BMI values in MU CFC patients.

In recent years, there has been significant growth in CFF's international collaborations aimed at identifying barriers to CF care in different centers worldwide and improving the care for patients.[11] With the support of the CFF and the Middle East CF Association (MECFA) the University of Michigan (UM) CFC and MU CFC began collaborating in 2018. As part of this collaboration, a BMI quality improvement project (QIP) was launched in 2019. The objective was to improve the nutritional status of cwCF through the implementation of a nutritional algorithm adopted from UM CFC.[12] The specific aim was an increase of 10 percentile points in mean BMIp in cwCF. Secondary outcomes were lung function, specifically forced expiratory volume in one-second percent predicted (FEV1pp), and health-related quality of life (HRQoL).

2 | METHODS

The QIP was carried out between June 2019 and September 2020.

2.1 | MU-UM CFC collaboration and QI education

The UM CFC director visited MU CFC in person in 2018, and there was a follow-up visit in 2019 by the UMCFC team (center director, dietitian, respiratory therapist, and physical therapist). The MUCFC team (center director, three pediatric pulmonologists, dietitian, physical therapist, and rehabilitation specialist) went to the UM CFC in late 2019. During 2020 and 2021 physical visits were impossible because of travel restrictions due to the coronavirus pandemic, but online meetings between the two centers took place regularly. Areas for improvement were identified, and viable solutions were proposed by using QI techniques including fishbone diagrams, flow charts, and Plan Do Study Act (PDSA) cycles[13] (Table 1).

2.2 | Patient population

CwCF aged 2–18 years who were followed up routinely at MU CFC in the previous year were included by consecutive sampling. A CF diagnosis was confirmed through positive sweat chloride testing of

TABLE 1 Plan Do Study Act (PDSA) cycle-BMI Improvement project.

	PDSA 1	PDSA 2	PDSA 3	PDSA 4
Description	Implement the Michigan University nutritional algorithm	Determine the patients eligible for The QI project	Establish formal previsit planning meetings (PVP)	Provide standardized nutritional care to each patient at each visit
Population	All patients aged 2–18 years followed in MUCFC (*n*:274)	Patients aged 2–18 years followed in MUCFC and came to routine visits regularly and were eligible for inclusion (*n*:182, 66%)	All eligible patients aged 2–18 years followed in MUCFC (*n*:182, 66%)	All eligible patients aged 2–18 years followed in MUCFC (*n*:182, 66%)
Location	MUCFC	MUCFC	MUCFC	MUCFC
Duration	1 month	1 month	1 month	12 months
Executed by:	MUCFC and UMCFC team members	MUCF nurses	MUCFC team members	MUCFC dietitian and other team members
Results:	Flowcharts were reviewed/approved by entire CF team	182 patients fulfilled the criteria	PVP meetings were conducted weekly, and patients were classified according to their BMI percentile	Patients' BMI percentile was assessed at each visit, and necessary adjustments were made
Action (adapt, adopt, abandon)	Adopt	Adopt	Adopt	Adopt

Abbreviations: BMI, body mass index; MUCFC, Marmara University Cystic Fibrosis Center; PDSA, Plan Do Study Act; UMCFC, University of Michigan Cystic Fibrosis Center.

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60 mmol/L and/or two CF disease-causing mutations. Exclusion criteria included cirrhosis or/and portal hypertension and any other bowel disease other than those caused by CF. Patients with severe disease and approaching end of life within 6 months and those who did not agree to participate were also excluded.

2.3 | Interventions

This project was introduced to the parents of the cwCF through face-to-face meetings where they were encouraged to participate. The patient-family organization (KIFDER) played an active role in informing patients and caregivers about the project. The KIFDER representative set up a WhatsApp social texting group between the patients and the MU CFC staff to foster communication. Since 61% of the patients had a BMIp in the risk and critically at-risk categories, families were invited to an educational meeting about G-tube feeding.

The nutritional status of patients was assessed at their regular follow-up visit by the MU CFC dietitian. The BMIp of patients were categorized as nutritionally adequate (BMIp ≥ 50%), at-risk (BMIp 25%–49%), urgently at risk (BMIp 10%–25%), and critically at risk (BMIp < 10%).

Baseline visits for all cwCF that are included in this project were completed within 3-months of enrollment. Parents were asked to write a 3-day diet history before each visit. Appropriate interventions were selected according to a patient's BMIp category (Figure 1). The dose of pancreatic enzymes was adjusted according to a patient's current weight. Subjects were followed for 12 months and assessed at clinical visits every 3 months. The algorithm used included the evaluation by MU CFC's dietitian, at each visit, of the patient's nutritional status. A high-calorie diet (120%–150% of the recommended dietary allowance (RDA) per day) was recommended for all cwCF. Oral supplements were recommended for patients with BMIp < 50. The recommended amount of oral supplement per day was determined by the caloric deficit to reach the patient's daily

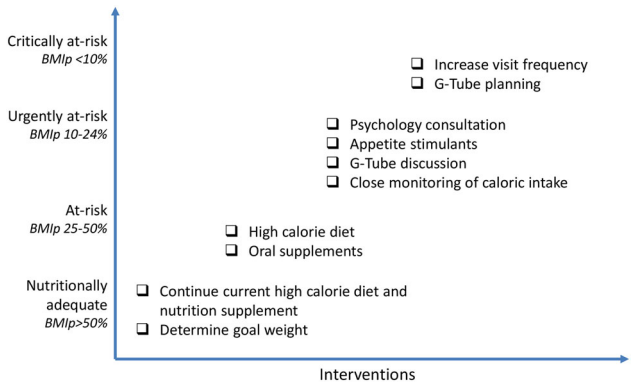

FIGURE 1 UM CFC standardized nutritional algorithm according to the patients' BMIp. BMIp, body mass index percentile; UM CFC, University of Michigan Cystic Fibrosis Center. [Color figure can be viewed at wileyonlinelibrary.com]

energy needs. Type of supplement and caloric density per kilogram were determined by our CFC dietitian. An appetite stimulant (cyproheptadine) was recommended for cwCF with poor appetite.[14] Patients who required psychological support were referred to a psychologist that works specifically with cwCF. Weekly meetings were held by the dietitian and MU CFC team to discuss patient progress. All patients were given a monthly weight gain goal at each clinic visit; these ranged from 0.5 to 1.0 kg per month depending on the patient's age and weight. Patients who could not gain weight with standard measures were referred to the MU Pediatric Gastroenterology Department to be evaluated for gastrostomy tube placement.

Patients diagnosed with diabetes were monitored by the pediatric endocrinologist every 3 months; the remainder of the patients over 10 years of age were evaluated for CF-related diabetes by oral glucose tolerance testing and were referred to a pediatric endocrinologist as needed.

Subjects who did not respond well to the standard nutritional protocols during the project period were also confidentially discussed with the UM CFC team via online meetings or e-mail. QIP results were also shared with the UM CFC team at 3, 6, and 12-month joint online meetings.

The COVID-19 pandemic, first reported in March 2020 in Turkey, meant the cancellation of many regular follow-up visits, particularly at the 6th and 9th months. Canceled clinic visits were replaced by phone calls and/or virtual visits with cwCF and their families to encourage adherence to the protocol and included updates on diet history and weight gain.

2.4 | Outcome measures

The primary outcome was the change in BMIp for age and BMIp was calculated by an online program.[15] Weight and height of the CF patients were measured every 3 months during routine clinical care. When cwCF could not attend the clinic, their weight was measured using a home scale and recorded by the dietitian. Secondary outcomes were changes in FEV1pp and HRQoL.

A pulmonary function test (PFT) was carried out using a spirometer (WinspiroPRO 2.8 MIR) in accordance with internationally agreed standards. PFT was performed in an upright sitting position after the application of a nose clip using the same device for all patients. Only results that met ERS/ATS standards for interpretation were included in the project for analysis.[16] PEx was defined as the need for additional antibiotic treatment (both IV and oral) as indicated by a recent change in at least two of the following: change in sputum volume or color; increased cough; increased malaise, fatigue or lethargy; anorexia or weight loss; decrease in FEV1pp by 10% or radiographic changes in the lungs; increased dyspnea.[17] PEx rate was calculated for both the previous year and the year of the project period.

HRQoL was measured by the validated CF Questionnaire-Revised (CFQ-R).[18] CFQ-R was completed twice; at baseline before of the QIP started and again at the conclusion of the project. Older

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children and parents completed the questionnaire themselves, while younger children were interviewed by one of the researchers. Both parent and child questionnaires were completed at the same outpatient clinic visit.

2.5 | Statistical analysis

Statistical analysis was carried out with SPSS for Windows, version 23.0. Continuous variables were described through means, standard deviations, and medians, whereas categorical variables were presented as proportions. Categorical variables were compared with Chi-square or with Fisher's exact test when 20% of the expected frequencies were less than five. Parameters with normal distribution were compared by independent groups (independent samples) *t*-test. Wilcoxon test was performed for comparing two dependent variables with non-normal distribution. Friedman test was performed for three or more repeated measures without normal distribution. Results were evaluated in 95% confidence interval, and significance level was set at *p*-value of 0.05.

2.6 | Ethics committee approval

The project was approved by the Marmara University Faculty of Medicine Research Ethics Committee (No: 09.2021.534).

3 | RESULTS

3.1 | Process outcomes

Of the 274 patients between 2 and 18 years of age that were followed in the MU CFC, 43 did not meet eligibility criteria for the project, and 49 had not attended regular clinical visits every three visits in the previous year and therefore, were not included in the QIP. The remaining 182 patients were included. Mean age was 9.1 ± 4.1 years. All 182 patients underwent the baseline BMI assessment by the MU CFC dietitian. Median (25th-75th percentile) BMIp of the whole group was 14.1 (3.9–44.5). Although the median BMIp was lower in males (*p*:0.02), this was not significant according to age groups (*p*:0.85). Table 2 shows the baseline demographics of the patients.

TABLE 2 Patient characteristics according to the BMIp groups.

Patient characteristic	Total *n*:182	Group 1 (BMI: < 10%ile) *n*:76 (42%)	Group 2 (BMI:10%–24%ile) *n*:35 (19%)	Group 3 (BMI:25%–49%ile) *n*:33 (18%)	Group 4 (BMI: ≥ 50%ile) *n*:38 (21%)	*p* value
Age at CF diagnosis, years, median (25–75 p)	4.0 (2.0–7.0)	3.0 (2.0–6.8)	4.0 (2.0–14.0)	4.0 (2.0–5.0)	4.5 (2.8–8.0)	0.820
Age, years, mean ± SD (2–18 years)	9.0 ± 4.3	8.9 ± 4.5	9.1 ± 4.1	8.5 ± 4.3	9.6 ± 4.1	0.490
Age, years (%)						0.850
2–6	72	33	12	16	11	
7–12	65	24	16	9	17	
13–18	45	19	7	8	10	
Gender, *n* (%)						**0.020**
Male	102 (56)	49 (64.5)	20 (57.1)	20 (60.6)	13 (34.2)	
Female	80 (44)	27 (35.5)	15 (42.9)	13 (39.4)	25 (65.8)	
Height percentile, median (25–75 p)	36 (9.8–65.6)	30.9 (5.6–62.8)	40.2 (8.9–70.2)	41.9 (22.5–55.1)	40.1 (14.7–82.4)	0.370
Weight percentile, median (25–75 p)	23.1 (4.3–42.0)	15.3 (0.73–16.9)	19.7 (7.0–40.1)	36.4 (26–7-47.6)	54.5 (38.3–83.5)	**0.022**
BMI percentile, median (25–75 p)	14.1 (3.9–44.5)	3.1 (0.6–6.3)	15.0 (12.6–18.9)	38.2 (30.8–43.8)	66.0 (55.6–74.5)	**0.001**
FEV1, (mean ± SD)	81.7 ± 22.0	71.5 ± 22.8	84.3 ± 20.2	91.9 ± 14.5	90.4 ± 13.9	0.390
Pseudomonas colonization, *n* (%)	42 (23.1)	25 (32.9)	6 (17.1)	8 (24.2)	3 (7.9)	0.070
Pancreatic status, *n* (%) Insufficient	133 (73.1)	64 (84.2)	26 (74.3)	25 (75.8)	19 (50.0)	**0.010**
Genetic category, *n* (%)						0.231
Homozygous dF508	33 (18.1)	18 (23.7)	6 (17.1)	6 (18.2)	3 (7.9)	
Heterozygous dF508	47 (25.8)	20 (26.3)	5 (14.3)	9 (27.3)	13 (34.2)	
Other	101 (55.5)	38 (50.0)	23 (65.7)	18 (54.5)	22 (57.9)	
Not found	1 (0.5)		1 (2.9)			

Abbreviations: BMI, body mass index; BMIp, body mass index percentile; CF, cystic fibrosis; FEV1, forced expiratory volume at 1 second; SD, standard deviation.

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At baseline, 128 (70.3%) patients were taking oral supplements, but none of them were using appetite stimulants. One patient had a percutaneous endoscopic gastrostomy (PEG) tube. An appetite stimulant (Cyproheptadine) was added on to the treatment regimen of 113 (62.1%) patients at the initial visit, and oral supplements were introduced in 33 (18.2%) patients; the latter was in addition to the aforementioned 128 cwCF who were already taking them. The personalized nutritional intervention plan was reviewed every 3 months and adjusted according to patient needs, preferences, and BMIp. According to BMIp classification, PEG tube placement was recommended for 17 patients at follow-up, but only one child's parent accepted. All others refused to proceed with the PEG procedure.

At the 6th and 9th months, 1/3–1/2 of the patients could not be seen in person at the outpatient clinic due to the pandemic restrictions. At the 12th month, 103 (59.2%) patients were using cyproheptadine, and 136 (78.2%) patients were using oral supplements.

3.2 | Patient outcomes

At the 12th month, the number of critically at-risk patients decreased from 76 (41.8%) to 40 (22.0%), and the nutritionally adequate patients increased from 38 (20.9%) to 61 (33.5%) ($p < 0.05$). Mean BMIp had risen from 25.6 to 37.2 at the 12th month ($p < 0.001$). A significant increase in BMIp was noted in both the BMIp < 10% and the BMIp 10%–24% subgroups ($p < 0.001$, $p < 0.001$). Although BMIp increased in patients with or without pancreatic insufficiency (PI), it was only significant in the PI group ($p < 0.001$). Table 3 and Figure 2 show the mean BMIp for each BMIp group over the project period from baseline to the 12th month.

Significant FEV1pp increase, from 81.3 ± 20.6 to 85.9 ± 20.8 ($p < 0.001$), was detected in the total population at the 12th month.

During the project period, the hospitalization rate due to acute PEx was similar ($p = 0.73$) to that before the start of the project. However, oral antibiotic usage rate due to PEx was significantly higher ($p = 0.01$) than the previous year. There was no difference between baseline and 12th month *Pseudomonas aeruginosa* (PA) [42 (23.1%) versus 41 (22.5%) *p*:0.35] and methicillin-resistant *Staphylococcus aureus* (MRSA) colonization rates [17 (8.8%) versus 19 (9.9%); *p*:0.19].

According to the HRQoL questionnaire analyses, scores for physical functioning, eating problems, and respiratory symptoms domains of CFQ-R improved significantly at the end of the 1-year period, for both the 6–13 year old (*p*:0.005, *p*:0.004, *p*:0.004) and 14–18 year old age groups (*p*:0.040, *p*:0.040, *p*:0.010). Additionally, scores in the body image domain increased significantly in the 6–13-year-old age group (*p*:0.030).

4 | DISCUSSION

Despite the problems caused by the COVID-19 pandemic, this QIP led to significant improvement in mean BMIp in the cwCF who participated over the 12-month period, and this BMIp increase was above the target-specific aim by 10p. FEV1pp values also increased significantly. In terms of HRQoL, scores in physical functioning, eating problems, and respiratory symptoms domains of CFQ-R had also improved at the end of the 12 months in the 6–13 and 14–18-year-old age groups; in addition, body image score was significantly higher in the 6–13 age group.

Many factors contributed to the success of the project. First, a personalized nutritional plan was provided to each patient according to the patient's baseline nutritional status, specific needs, and preferences. Close monitoring of patients by all MU CFC team members and discussion of all subjects after routine clinic visits at

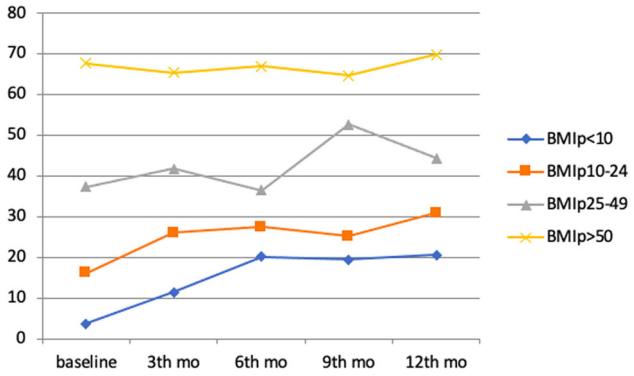

FIGURE 2 Mean BMIps for each initial BMIp group over the project period at baseline and 12th months. BMIp, body mass index percentile. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Mean BMIp values for each BMIp sub-group over the project period at baseline and 12th months.

BMIp subgroups	Baseline BMIp (mean ± SD) (*n*:182)	12th month BMIp (mean ± SD) (*n*:174)	*p*-value
Critically at-risk (<10%)	3.6 ± 3.2	20.5 ± 22.9	**<0.001**
Urgently at-risk (10%–24%)	15.9 ± 4.1	30.8 ± 20.1	**<0.001**
At risk (25%–49%)	37.0 ± 6.7	44.2 ± 16.9	0.079
Nutritionally adequate (≥50%)	66.8 ± 13.9	69.5 ± 18.1	0.301
All participants	25.6 ± 14.5	37.2 ± 18.2	**<0.001**

Abbreviations: BMIp, body mass index percentile; SD, standard deviation.

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weekly meetings were vital to the success of this project. MU CFC team members worked in collaboration with patients and families to overcome obstacles in obtaining supplements or medications. Also of primary importance during the project were the discussions with the UM CFC team via online meetings or e-mail about individuals who did not meet appropriate weight gain targets despite their following the standard nutritional protocol. QIP results were also shared with the UM CFC team at 3, 6, and 12-month joint online meetings.

Current QIP on nutrition varies somewhat compared to previous nutritional improvement studies in cwCF. Some previous studies have attempted to raise BMI by concentrating on behavioral therapies.[18–20] In addition, a recent study assessed the effectiveness of a self-management mobile telephone application in achieving the dietary goals set by the CF nutrition guidelines.[21]

This project was also one of the first of its kind conducted in a low-to-middle income country and the average BMIp values of the participants before the QIP were much lower than in previously published studies.[9]

In MU CFC, the principal reasons for the low BMIp were the lack of a standardized nutritional protocol, the non-use of appetite stimulant, and a lack of social workers or psychologist in the CF team. With the implementation of this standardized protocol, there was a significant improvement in BMIp of cwCF at MU CFC despite the rejection of G-tube placement by most caregivers. Of the 17 cwCF for whom a gastrostomy tube was recommended, permission was given for the G-tube place by only one caregiver. The reason for this is be likely related to negative perceptions in our population regarding G-tube insertion.

One of the secondary outcomes of the project was a change in FEV1pp and, indeed, a significant increase in FEV1pp was demonstrated. We believe that the improvement was due to both better nutrition and the close monitoring of patients throughout the project. Previous studies also indicate that higher lung function outcomes are associated with better nutrition.[22,23]

During the project period, Pa and MRSA colonization and hospitalization rates did not change compared to the previous year; this may be due to its relatively short duration. On the other hand, oral antibiotic usage for PEx increased, though this could be attributed to closer monitoring and the more aggressive treatment which may also have contributed to the observed increases in FEV1pp.[24] Patient-reported outcomes, such as HRQoL, are important indicators of patient benefit in clinical trials. CFQ-R is frequently used in pre-post intervention studies to determine the HRQoL in CF. It is also employed to assess the efficacy of pharmacological interventions such as treatment with CFTR modulators or other medications.[25,26] Although several studies that evaluate nutritional status and relation to HRQoL have been published, only two of them were longitudinal cohort studies that included analyses of participant data collected before the study start.[27–32] Neither of these studies in the literature evaluated HRQoL before and after nutritional intervention. At the end of this QIP physical functioning, eating problems and respiratory symptoms domains of CFQ-R were significantly better in the 6–13 and 14–18 year-age groups and body image was significantly better in the 6–13 year-age group.

There are several limitations to the current project. The first is associated with the COVID-19 pandemic and the impossibility for almost half of the patients to attend, in-person, the 6th and 9th month outpatient clinic. We partially overcame this issue through online interviews or phone calls with the cwCF and their caregivers. Another limitation was the rejection of G-tube insertion by the great majority of the parents causing a failure in adherence to the full protocol. Despite the latter, the biggest BMIp increase was still in cwCF with BMI < 10% and 10%–24%, which we believe is a further indication of the efficacy of implementing a rigorously controlled, high-calorie diet and the use of an appetite stimulant. The lack of social workers and psychologists in the CFC team was another limitation. Although the additional efforts of other team members minimized this problem, this QIP would have been more successful if there had been a social worker and a psychologist at our CFC. Notwithstanding the limitations, to our knowledge, this is the first nutritional QIP using a standardized algorithm that has been carried out in a country with limited resources and showing proven effectiveness. Current significant improvements in BMIp, FEV1pp, and HRQoL have been demonstrated in those who took part despite some operational deficiencies. QIPs can be easily implemented in other countries where resources are limited, and we urge support for this type of QIP as an integral element in improving the quality of CF care all over the world.

AUTHOR CONTRIBUTIONS

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data is available on request from the authors.

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