

# MEDICAL AND NUTRITIONAL APPROACHES IN CHILDHOOD OBESITY

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## ABSTRACT

Obesity is a metabolic disorder, characteristic of countries where the nutritional transition process occurs more intensely. Currently, the number of obese children and adolescents has grown ominously, and the emergence of this disorder in childhood can result in negative consequences for adult life. In our review, a search for selected keywords in indexed databases was performed, inclusion/exclusion of selected works were applied for the acquisition of relevant documents, moreover, practices and standards of the PRISMA model (Preferring Reporting Items for Systematic Reviews and Meta-Analyses) were used to optimize the procedures for search and analysis of original content. This narrative review highlights the main representative aspects in the matter of antiobesogenic approaches in childhood, also highlighting the importance of prevention in pregnancy and post-natal periods, as well as indicating the role of a multidisciplinary team in this process.

Keywords: Obesity; Pediatrics; Weight Management; Sugar-sweetened Beverages.

## **1. INTRODUCTION**

Obesity is a medical disorder that has acquired great epidemiological significance over the years. Currently, at least 1.1 billion people are overweight, and 312 million of them may already be classified as obese individuals. If the Asian anthropometric standards for normal body mass index (23.0 kg/m<sup>2</sup>) are considered, this number would increase to 1.7 billion overweight people around the world (HASLAM & JAMES, 2005). Data from the last 5 years indicate that the increase in global obesity is slowing for some European countries and the US, however, population-based studies suggest that the current high body-mass index (BMI) is a global burden, mainly due to the number of cancer cases attributable to such anthropometric status (ARNOLD *et al.*, 2015). In the US, between the years 1999-2010, about 35.5 to 35.8% of the adult population and 16.9% of children and adolescents were obese (FLEGAL *et al.*, 2012; OGDEN *et al.*, 2012). Although obesity is a growing problem, large population studies have indicated a reduction in fast food and sugary drinks consumption, which may promote a prospective reduction in the prevalence of obesity among children and adolescents (DIETZ & ECONOMOS, 2015).

Data from the beginning of the century warn us about the significant increase in weight and BMI in children under four years old, anthropometric phenomenon that tends to grow over the years, especially in developed countries (BUNDRED, KITCHINER & BUCHAN, 2001). Studies also indicate that, in European countries, the prevalence of obesity and overweight among children aged less than 10 years tend to follow a social gradient where children placed in households with lower income and education tend to show a higher prevalence of obesity (AHRENS *et al.*, 2014).

Parallel to obesity, disorders such as type 2 diabetes are emerging as a regular affection in the obese pediatric public. According to Drake *et al.* (2002), the existence of diabetic and obese pediatric patients will

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become increasingly common, requiring professionals who are prepared to identify and initiate the correct therapeutic process in this population. Despite efforts, obesity numbers in pediatric groups throughout the US remains high (OGDEN *et al.*, 2014), and authors now strongly consider the benefits and outcomes of surgical procedures, such as bariatric surgery in adolescente patients (BRANDT *et al.*, 2010). Silverberg *et al.* (2015) points out that other manifestations occurring in obese children and adolescents, such as atopic dermatitis, may be associated with high blood pressure and central obesity, which can also be included in assessment diagnostic parameters for this audience. Kools and colleagues (2008) highlights, however, that adherence to dietary therapy is influenced by the individual characteristics in the context of social interactions.

To treat obese children and adolescents, health professionals tend to opt for subtler approaches such as promotion of changes in dietary parameters, limiting consumption of specific foods and modest calorie restriction, usually avoiding the use of highly restrictive diets or prescription medications (BARLOW *et al.*, 2002; PANDITA *et al.*, 2016). Some professionals, however, prefer not to treat obese individuals who do not present associated diseases and/or complications, factor which is exhausted by the low level of motivation and/or perception of parents in relation to the real state of obesity of their children (JONIDES; BUSCHBACHER & BARLOW, 2002). In a study conducted in 2003, about a third (32.1%) of the mothers interviewed erroneously classified the anthropometric status of their children (MAYNARD *et al.*, 2003). Recent reports, however, indicate a positive trend in physician knowledge of communication and weight management counseling rates (SHUE *et al.*, 2015), which may help parents in the process of detecting obesity and health risks whithin their family circle.

Our study, therefore, sought to conduct literature review of narrative character, with systematic search for recent and relevant literature on disorders, therapeutic and new approaches in pediatric patients with overweight or obesity, highlighting the role of family involvement and multidisciplinary strategies during pregnancy and postnatal periods.

#### 2. METHODOLOGY

#### 2.1 Bibliographic search

To search for original documents that met the study criteria, we used indexed electronic databases (*e.g.* PubMed, LILACS and PubMed Central) and manual in the following university libraries: Central Library of the Federal University of the State of Rio de Janeiro (UNIRIO) and Central Library of the Federal University of Rio de Janeiro (UFRJ). Search for printed and electronic periodic articles obeid to the following keywords: "childhood obesity", "cardiovascular disease", "childhood overweight", "eating disorders", "metabolic programming", "diabetes" and "dyslipidemia", including terms of lexical proximity and articles written in the English or Portuguese laguages.

Application of methodological procedures in this narrative review aimed the acquisition, analysis and discussion of works representative of the "state of the art" in the issue of childhood obesity. The search for narrative and systematic reviews, with or without meta-analysis, was limited to papers published from January 2004, while experimental studies, clinical interventions and original experimental works were selected if published from January 2000. Documents were obtained and analyzed in several steps of selection process. A total of 14535 documents were found by keywords search, of which 418 met the language, year of publication and/or experimental design requirements.

The remaining publications were fully read according to the specific selection criteria, and only 39 studies met the final requirements for this work. We also excluded patents, unpublished works, abstracts, monographs, dissertations, theses, books and other documents with poor methodological quality.

## 2.2 Selection Criteria

Articles were excluded if not met the following inclusion criteria: obesity and associated diseases OR eating and metabolic disorders OR drug therapy AND dietary weight disorders AND individuals aged 0 to 18 years, except for studies using *in vivo* and *in vitro* experimental models (non-human), which were also considered for the purposes of this review. This study followed three major stages of document analysis:

- 1. Search by keyword indexed in electronic databases and printed documents (n = 14535);
- 2. Analysis title and summary, to exclude unrelated studies (n = 418);
- 3. Careful selection, followed by individual article reading (n = 37).

Due to the large number of initial documents, we used a software (Zotero Standalone 4.0) to organize and select references. Considering the methodological limitations of this narrative review, we have adapted our search procedures from Freitas *et al.* (2015) and from the PRISMA (*i.e.* Preferring Reporting Items for Systematic Reviews and Meta-Analyses) norms and standards, allowing systematic search, optimization of analysis and discussion of the data obtained (FREITAS; PEREIRA & RAMOS, 2015).

## 3. RESULTS

Due to the large number of obtained works after the first selection step, papers were firstly sorted according to date of publication, title and keywords. After the initial stage of selection, it was possible to carry out the reading of summary and text body, resulting in a total of 26 articles of narrative and systematic review with or without meta-analysis and 13 experimental human studies, which were able to met the minimum criteria of methodological quality, as indicated in **Table 1**.

Keywords	Literature reviews	Experimental works
"childhood obesity"	249	100
"cardiovascular disease"	1093	737
"childhood overweight"	94	563
"eating disorders"	1333	4915
"metabolic programming"	51	26
"diabetes"	2525	1858
"dyslipidemia"	524	467
Total <sup>a</sup>	5869	8666
Total <sup>b</sup>	245	173
Total <sup>c</sup>	24	13

Table 1. Quantification of obtained articles according to keyword and methodological model.

<sup>a</sup>Total number of selected documents after first step of bibliographic search. <sup>b</sup>Compiled articles after judicious reading of title and abstract. <sup>c</sup>Total works selected after reading, at least, title, abstract and part of the text body.

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**Table 2** presents the quantification of review articles obtained were classified according to their thematic approach (*e.g.* cardiovascular disease, diabetes, psychopathology). All obtained papers were published from January 2014 and attended the minimum selection criteria. Works with more than one thematic approach were discriminated in table legend.

to the specific theme in childhood obesity.		
Ayer et al., 2015		
Barraco et al., 2014	Cardiovascular diseases, endothelial disorders and infant dyslipidemia (n=11)	
D'Adamo et al., 2015		
Franks and Estampador, 2014 <sup>a</sup>		
Falkner, 2015		
Kelishadi et al., 2015		
McCrindle, 2015		
Pires <i>et al.</i> , 2015		
Pollock, 2015 <sup>b</sup>		
Voortman et al., 2015		
Wiegman et al., 2015		
Bergh and Södersten, 2004		
Foster <i>et al.</i> , 2015		
Habib-Mourad and Ghandour, 2015		
Kar & Kar, 2015	Pharmacological, dietetic, psychological approaches and/or physical activity practice (n=9)	
Kelishadi and Azizi-Soleiman, 2014		
Magrone and Jirillo, 2015 <sup>e</sup>		
Sabin <i>et al.</i> , 2015		
Sypniewska, 2015		
Tremblay et al., 2015		
Benton, Skouteris and Hayden, 2015	Psycological disorders	
El-Behadli et al., 2015	(n=2)	
Franks and Estampador, 2014 <sup>a</sup>	Genetic mechanisms (n=1)	
Magrone and Jirillo, 2015 <sup>c</sup>	Immune system (n=1)	
Onge et al., 2015	Diabetes (n=1)	
Munyaka, Khafipour and Ghia, 2014	Gut microbiota (n=1)	
Pollock, 2015 <sup>b</sup>	Childhood bone development (n=1)	

**Table 2.** Distribution of the selected narrative and systematic reviews according to the specific theme in childhood obesity.

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<sup>a</sup>Estampador and Franks (2014) explore the effects of genetic and epigenetic mechanisms active during childhood on cardiovascular outcomes in adult age. <sup>b</sup>Pollock (2015) compile data related to the influence of childhood obesity on bone development arrest and risk of cardiovascular disorders. <sup>c</sup>Magrone and Jirillo (2015) investigate the consequences of childhood obesity on immune system and possible nutritional approaches in these patients.

**Table 3** summarizes information about sampling units (*e.g.* children and/or adolescents), objectives, methodology and results of experimental studies obtained, separated according to the applied model (*i.e.* supplementation, dietary approach, physical activity protocol). Information obtained from the analysis of experimental studies were subsequently pared with proposals and perspectives presented in the selected review articles (see **Table 2**).

Study	Characteristics	Subjects	Methodology	Results
Daley <i>et al.</i> , 2006 (United Kingdom) <sup>1</sup>	Prescription of physical activity as a therapeutic resource in the treatment of morbid obese and obese teenagers.	Morbid obese and obese teenagers (n=81) ageing between 11-16 years old.	Patients were selected randomly for periodic execution of a physical activity protocol during 8 weeks followed by an additional non- supervised 6-week practice.	Significative improvements in psycophatological patterns and frequency of physical activity practice among morbid obese and obese teenagers.
Reilly <i>et al.</i> , 2006 (United Kingdom) <sup>1</sup>	Utilization of a physical activity protocol to prevent or reduce obesity outcome in children in pre-school age.	Children (n=545) in pre-school age $(4.2 \pm 0.2 \text{ y.o.})$ , with or without weight disorders.	Individuals from experimental group started a supervisioned exercise protocol, three sessions a week, 30 minutes/session during 24 weeks. Participants were also guided to follow a less sedentary routine when at home.	Data indicate that moderate physical activity practice and promotion of a more active routine promoted a significative gain in motor skills. No changes in antropometric measurements were observed.
Ford <i>et al.</i> , 2009 (United Kingdom) <sup>2</sup>	Aplication of a feeding control protocol using a computadorized equipment ( <i>i.e.</i> mandometer).	Obese children and teenagers (n=106) aging between 9-17 y.o.	Using a computadorized equipment, capable of regulating volume and frequency of ingestion, subjects were evaluated throughout 12 weeks of dietary control.	Use of a computadorized equipment demonstrated therapeutic efficacy as a resource in modifying the feeding habits among children and teenagers.
James, 2004 (United Kingdom) <sup>3</sup>	Establishment of an educational scholar program aiming to reduce weight gain and ingestion of soft drinks in a children population.	Overweight, obese or eutrophic children and teenagers (n=644) aging between 7- 11 y.o.	Educational intervention in six primary schools from South England. Approach aimed to discourage the intake of soft drinks and stimulate balanced feeding throughout an academic	The application of an educational program was able to reduce the intake of soft drinks and the number of overweight/obese children throughout the academic

Table 3. General characteristics, methodology and results obtained in the selected experimental works.



			year.	year.
Kalarchian <i>et al.</i> , 2009 (United States) <sup>3</sup>	Application of a family- based treatment protocol to reduce severe pediatric obesity through changings within the family feeding patterns.	Obese (BMI <sup>a</sup> ≥ 95 percentile) children and teenagers (n=192) aging between 8- 12 y.o.	Family members were selected to follow guidelines for a correction in feeding habits, receiving a directed nutritional plan. Subjects were evaluated in four occasions: months 0 (baseline), 6, 12 and 18.	Interventions were significantly effective in attenuating weight parameters and improving health markers. Benefits were sustained for long- term periods if the selected family members had a minimum 75% frequency in orientations meetings.
West <i>et al.</i> , 2010 (Australia) <sup>3</sup>	Intervention program to promote health feeding within family members of overweight children and teenagers.	Obese or overweight children and teenagers (n=101) aging between 4- 11 y.o.	Selected group received instructions to promote adaptations in feeding habits, physical activity and to improve the control over the food intake of their offspring. Intervention occurred during a 12-week period.	During the intervention period, children reduced "score z" and BMI <sup>a</sup> indexes, as well as body weight-related behavioral disorders.
Wilfley <i>et</i> <i>al.</i> , 2007 (United States) <sup>3</sup>	Efficacy analisys of approaches to maintain and control results obtained from a previous short-term weight loss program.	Children teenagers and (n=204), with or without weight disorders, aging between 7-12 y.o.	Groups were submitted to a 5-month weight loss program followed or not by one of the long-term maintenance protocols (1 or 2 years follow up).	Application of a maintenance program after a short-term weight loss program is an effective strategy to optimize interventive results.
Javed <i>et al.</i> , 2015 (Italy) <sup>4</sup>	Evaluate the relationship of oral glucose tolerance test (OGTT)-induced insulin secretion and vitamin D status. Authors also investigated the effects of variable vitamin D supplement doses in modifying these parameters.	Obese (BMI <sup>a</sup> ≥ 95 percentile) teenagers (n=51) aging between 12- 18 y.o.	Individuals instructed to supplement vitamin $D_3$ for a 12-week period. After supplementation protocol, subjects were evaluated according to anthropometric and plasmatic standards.	High-dose supplementation of vitamin D <sub>3</sub> (2000 UI/day) for a 12-week period did not modify insulin sensitivity, β-cell function or lipid profile in the experimental group.
Liber and Szajewska, 2014 (Poland) <sup>4</sup>	Oligofructose supplementation effects on body weight and BMI <sup>a</sup> of overweight and obese children and teenagers.	Obese (BMI <sup>a</sup> ≥ percentile 85) children and teenagers (n=97) aging between 7- 11 y.o.	Subjects received physical activity and dietetic counseling before supplementing with age-dependent doses of oligofructose (8g/day or 15g/day) during 12 weeks.	Supplementation with age-dependent doses of oligofructose weren't effective in reducing body weight or BMI <sup>a</sup> in children and teenager subjects.



López- Alarcón <i>et</i> <i>al.</i> , 2011 (Mexico) <sup>4</sup>	Impact of omega-3 fatty acid supplementation on parameters of insulin resistance and body weight of children and teenager individuals.	Overweight and insulin resistant children and teenagers (n=76), aging between 9- 18 y.o.	Intervention group were supplemented with omega-3 fatty acids (900mg/day) for 1 month, without further dietetic interventions.	Significant differences were observed in fasting insulin levels, insulin resistance indexes ( <i>i.e.</i> HOMA-IR), TNF- $\alpha$ , leptin and adiponectin of supplemented subjects. Statistical adjustments also demonstrated a significant weight loss within experimental group.
Nader <i>et al.</i> , 2014 (United States) <sup>4</sup>	Effectivity of vitamin D <sub>3</sub> supplementation on 25(OH)D <sup>b</sup> plasma levels, lipid fractions and insulin resistance markers of teenager individulals.	Obese (BMI <sup>a</sup> ≥ 95 percentile) teenagers (n=44) aging 12-18 y.o.	Subjects were supplemented with high doses (2000 UI/day) of vitamin D <sub>3</sub> for 12 weeks. Plasma levels of 25(OH)D <sup>b</sup> , fasting glucose, insulin and lipid profile were measured.	Supplementation with high doses of vitamin $D_3$ induced moderate elevations in 25(OH)D <sup>b</sup> levels, however, no changes in lipid profile, insulin resistance and inflammatory markers were observed.
De Ruyter <i>et</i> <i>al.</i> , 2012 (Holland) <sup>4</sup>	Comparative study of the effects exerted by sugary (caloric) or artificially sweetened (non-caloric) drinks in chronic (18 months) weight gain whithin children and teenager subjects.	Eutrophic children and teenagers (n=474) aging between 4.1-11.1 y.o.	Groups received 250mL of either caloric (104Kcal) or non-caloric beverages for 18 months.	Substituition of caloric by non-caloric drinks allowed for a reduction in weight gain among participant children during execution of the experimental protocol.
Yanovski <i>et al.</i> , 2011 (United States) <sup>5</sup>	Effect of metformin therapy in weight modulation and obesity- related markers among insulin-dependent obese children.	Severely obese (BMI <sup>a</sup> 34.6 $\pm$ 6.6 Kg/m <sup>2</sup> ) and insulin-resistant children and teenagers (n=100).	Experimental group received twice-a-day 1000mg doses of metformin during 6 months, followed by an additional free prescription of up to 2000mg/day of the drug.	There was a moderate but significant effect of metformin on body weight, body composition and glucose homeostasis within enrolled patients.

<sup>a</sup>Body Mass Index. <sup>b</sup>25-hydroxyvitamin D. <sup>1</sup>Application of physical activity protocols. <sup>2</sup>Electronic equipament as therapeutic resource. <sup>3</sup>Educational/family interventions. <sup>4</sup>Interventions with dietary supplements and dietetic approaches. <sup>5</sup>Drug therapy to promote weight loss or reduce gain weight.

## 4. **DISCUSSION**

## 4.1 Physical activity in childhood obesity

Daley and colleagues (2006) conducted a proof-of-concept, randomized, controlled-trial study to investigate the practical involvement of supervised physical activity in 81 obese adolescents (11-16 years) with psychopathological disorders. Participants selected for the study were presented in the percentile group  $\geq$  98 (for BMI), and were designed to follow a protocol consisting of hiking, cycling, dancing and other

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activities, which should be carried out in 30-minute daily sessions, three days a week for 8 weeks (24 sessions). The placebo group was instructed to only perform light activity and stretching during the observation period. Patients were assessed for anthropometric parameters (*i.e.* weight, height and BMI) and various psychological/behavioral features (*e.g.* physical self perception, depression and affective).

Authors point out that the supervised practice of physical activity was able to optimize self-esteem measurements and stimulate independent physical activity, however, results for anthropometric parameters and conditioning were modest, indicating that the practice of moderate physical activity, in short-term interventions, is effective in stimulating changes in psychopathological parameters associated with obesity, but not sufficient to promote significant changes in body composition in adolescents with severe obesity (DALEY *et al.*, 2006). It is possible that combining short and long-term strategies may prove effective in altering anthropometric conditions of young people with obesity, as shown by Wilfley and colleagues (2007) and briefly presented in **Table 3**.

In a systematic review, Benton *et al.* (2015) evaluated 20 studies exploring the relationship between maternal depression and childhood obesity. Their study emphasizes that maternal depressive disorders are positively related to the incidence of obesity in preschool age. El-Behadli *et al.* (2015) point out, however, that studies of maternal depression and childhood obesity are inconsistent in demonstrating the direct dependence of many variables, and that they should now take into consideration aspects such as culturality, beliefs, practices, stress and eating habits.

Reilly and colleagues (2006) conducted an interventional study with regular physical activity for a total of 545 children with a mean age of 4.2 ( $\pm$  0.2) years. The model used by the authors resembles that proposed by Daley and colleagues (2006). Participants were asked to carry out 30-minute sessions of physical activity, three times a week for 24 months, three times the period of study used by Daley *et al.* (2006)<sup>14</sup>. The placebo group, however, was not encouraged to make changes in the level of daily physical activity and continued on regular monitoring during the study. Parameters such as total physical capacity and essential anthropometric data (*i.e.* weight, height and BMI) were assessed during the study. Data collected has shown significant improvement in motor skills, also suggesting small but significant gender-specific difference, as female children have benefited more positively from motor conditioning strategies. Anthropometric variables did not differ between experimental and placebo groups, however, authors highlight the important variation of several environmental factors, largely responsible for the emergence and continuation of weight disorders. Eating habits, availability of healthy foods and psychosocial condition of the individual and the family core are examples of variables to be controlled (REILLY *et al.*, 2006).

According to Foster *et al.* (2015), in a systematic review of interventional works with obese preschool age, studies where multidisciplinary approaches were applied and parental guidance had positive results in reduction of overall adiposity, whereas works where motivational interviewing and guidelines were used as the main tool failed to present similar results. Such statements corroborate with data from a systematic review by Kelishadi and Azizi-Soleiman (2014) and a narrative review by Kar and Kar (2015), which highlight the importance of conducting multidisciplinary approaches in schools, counting with active participation of the family members involved in the children's daily routine. Authors suggest that this model approach is able to promote better changes in dietary patterns and physical activity performed by obese children and adolescents.

#### 4.2 Electronics and food education

Ford and colleagues (2009) investigated the effectiveness of electronic equipment (*i.e.* Mandometer) for the treatment of obesity and food training of 106 children and adolescents aged 9 to 17 years, classified in the percentile  $\geq$  95 (for BMI). The equipment consists of a scale attached to a small computer, capable of generating indicative graphs of variation in the content of food on the plate and its relation to the time consumption, allowing control of the total time to perform meals and indicating the time necessary to



generate a feeling of fullness. The equipment was used for a period of 12 months, and data were collected for a period of 18 months after the start of the intervention protocol.

The study was not able to "blind" the differences between the experimental and placebo condition due to the presence of the interventional material (*i.e.* using or not the equipment), revealing a limitation of the work. Authors highlight, however, that life quality measurements during the study were maintained optimal for both groups. Nutritional education and counseling on the practice of physical activities, associated with the use of the electronic equipment was effective in modulating the time and size of meals consumed, suggesting that the use of similar resources may represent an alternative to pharmacotherapy (FORD *et al.*, 2009).

Use of electronic equipment and non-traditional resources have been criticized in the clinical and academic environments, however, researchers reinforce its effectiveness in treating weight disorders and regulating food behavior (BERGH & SÖDERSTEN, 2004). As discussed by Franks and Estampador (2014), Ayer *et al.* (2015), and Sabin and Kiess (2015), the influence of obesogenic disorders during childhood on the prevalence of comorbidities in adult life is undeniable, and the low effectiveness of therapeutic/dietetic protocols extenuate the negative outcomes observed. Sabin *et al.* (2015) indicates, however, that the preferred approach for weight reduction in children and adolescents should target the maternal public, acting through preventive child health in the familial environment.

## 4.3 Direct and familiar dietary guidance

James (2004) has established an intervention program in the school environment, aiming to reduce the consumption of carbonated drinks and therefore prevent excessive weight gain among children and adolescents (n = 644) aging between 7-11 years throughout a school year. The intervention protocol consisted of the visit of a researcher in the classrooms of six primary schools in the South West England. During the visits, the consumption of carbonated drinks, sugared or sweetened, was discouraged, while the consumption of balanced meals was stimulated based on claims of improvements in wellness and dental health.

Application an instructional program showed modest effectiveness in reducing the consumption of carbonated beverages, however, it was able to attenuate the number of overweight and obesity in the participating schools. Authors highlight that the participation of schools in stimulating the intake of a balanced diet and discouraging the consumption of carbonated drinks is of deep importance (JAMES, 2004). The use of complementary proposals, such as those from Habib-Mourad *et al.* (2015) and Mistry and Puthussery (2015), may induce additional improvements in the feeding patterns and weight status among young subjects. Authors present several recommendations, including training of school staff, maintainance of a healthy-food supply in school cafeterias, encouraging family/local community and making intervention protocols fun, interactive and relevant to the social context of the participants.

Kalarchian and colleagues (2009) carried out educational/instructional intervention in family groups with the aim to control the occurrence of severe obesity in pediatric patients. Children and adolescents (n = 192) aging between 8-12 years and an average of 99.18 percentile (for BMI), participated in the study intervention, which lasted six months. Specific evaluations occured 0, 6, 12 and 18 months after baseline. Several anthropometric parameters (*e.g.* BMI), physiological (*e.g.* blood pressure) and social (*e.g.* quality of life) were analyzed throughout the study. Data obtained indicate that familial interventions are effective in reducing the percentage of overweight and attenuating risk factors. Authors also highlight the importance of demonstrating the link between adherence to the study and optimization of the parameters evaluated, suggesting that these changes are pivotal to achieving positive results.

West *et al.* (2010) explored the effects of family intervention, considering family members the exclusive agents of changing in the obesity condition of their offspring. Overweight and obese children (n = 101), aging between 4-11 years, participated in 12 weeks of intervention. In the experimental group, the

protocol used consisted of nine guided group meetings of 90 minutes and three phone sessions of 20 minutes to provide further training, in addition, parents received printed materials to guide them about the sessions and to recommend daily tasks aiming to improve results.

Authors indicate three limitations of their study: (1) parents were responsible for reporting the progress of their children when during telephone sessions and (2) the households surveyed were homogeneous and at low social risk, thus restricting the possibility to extrapolate the obtained results. Final data indicate that treatment mediated by familial counseling was effective when parents showed clear concern with the anthropometric status of their children and were willing to make the changes suggested by the researchers (WEST *et al.*, 2010). As noted by Kalarchian and colleagues (2009), significant changes in anthropometric indices and feeding behavior heavily depends on adherence to therapy proposed.

Wilfley *et al.* (2007), unlike other researchers, explored the effectiveness of treatment directed towards the maintenance of the results obtained in previously applied approaches. Children and adolescents (n = 204), with or without weight disorders, aging between 7-12 years, participated in the study. All subjects underwent five months of treatment and then stratified into three groups: (1) maintenance of behavioral skills; (2) maintenance of sociability and (3) control group, in which the intervention was discontinued after the first 5 months of treatment. Groups (1) and (2) underwent interventions and behavioral therapy sessions, respecting age and specific characteristics of each stratum. Progress was evaluated for two years after the start of the intervention protocol.

Both continued intervention groups were able to promote the maintenance of weight loss promoted by the initial program, however, no significant relationship was found among intervention groups (WILFLEY *et al.*, 2007). As discussed above, several studies could benefit from the use of continuous therapy, the control of weight disorders, feeding behavior and physical activity necessarily rely on long-term interventions, as clearly highlighted in Tremblay *et al.* In recent reviews, McCrindle (2015) and Wiegman *et al.* (2015) also reveal the need for interventions to prevent, as soon as possible, childhood obesity to be initiated, avoiding the emergence of cardiometabolic and vascular diseases in adulthood.

#### 4.4 Dietary interventions and supplemental

In a recent study, Javed *et al.* (2015) investigated the extra skeletal effects of vitamin D, specifically on the development of insulin resistance and diabetes in 51 adolescents aging between 12-18 years and  $\geq$  95 percentile for BMI. After random layering experimental groups, authors provided doses of 400 or 2000 IU/day for 12 weeks, evaluating parameters such as serum level of 25-hydroxyvitamin D (*i.e.* 25(OH)D), insulin, glucose and C-peptide after an oral glucose tolerance test (*i.e.* OGTT). As expected, 25(OH)D were significantly higher in serum of subjects supplementing 2000 IU/day doses of vitamin D, however, regardless of dose or evaluated intervention period, parameters related to pancreatic function and insulin resistance remained unchanged with the vitamin D supplementation. Authors suggest that future research should explore the consequences of the nutritional deficiency of vitamin D on insulin sensitivity parameters and pre-diabetes risk.

In the same period, Nader *et al.* (2014) performed a similar study with 44 adolescents aging between 12-18 years and  $\geq$  95 percentile for BMI, in a 12-week interventional work. In their study, however, patients received doses of 2000 IU/day or placebo only, evaluating serum 25(OH)D levels, fasting glucose, insulin, and lipid concentrations without the use of a OGTT. Corroborating with the study from Javed *et al.* (2014), serum levels of 25(OH)D rose modestly, but significantly in the supplemented group, while parameters such as C-reactive protein, insulin, fasting glucose and lipid profile weren't modified between groups. Together, these studies confirm, consistently, that vitamin D supplementation do not influence insulin resistance and diabetes mechanisms in adolescent subjects.

López-Alarcón and colleagues (2011) provided 900 mg of polyunsaturated omega-3/day for a period of one month to children and adolescents (n = 76) aging between 9-18 years, with overweight status and

insulin resistance. Anthropometric measurements, adipokine levels and insulin resistance were accessed after the intervention period. Short-term supplementation with omega-3 fatty acids was able to significantly reduce insulin levels, fasting insulin resistance, TNF- $\alpha$ , leptin and adiponectin. After statistical adjustments, the authors also showed significant influence of omega-3 supplementation on weight loss in experimental group.

In a recent review, Voortman *et al.* (2015) highlight the need for further evidence on the effectiveness of omega-3 when provided during infancy or fetal period. According Magrone and Jirillo (2015), however, diets rich in antioxidants, anti-inflammatory nutrients and/or supplements rich in polyphenols, omega-3, symbiotic and vitamins are advantageous strategies for the prevention of symptoms and disorders related to childhood obesity.

Based on previous allegations about the use of oligofructose as satiety enhancer, thus reducing total calorie intake and weight loss in adults, Liber and Szajewska (2014) investigated the effectiveness of oligofructose supplementation for overweight and obesity ( $\geq$  85 percentile for BMI) children and adolescents (n = 97), aging between 7-18 years. During the intervention period (12 weeks), participants consumed either oligofructose or maltodextrin (placebo), individuals aging between 7-11 years received 8g/day oligofructose, while participants aging between 12-18 years were supplemented with 15g/day of the supplement. All participants were encouraged to perform regular physical activity during the intervention period, *z* score values for the BMI/age ratio was used to compare groups. Authors found no significant differences in BMI/age values, reduction in weight or body fat percentage.

De Ruyter *et al.* (2012) conducted an experimental study with 474 children and adolescents (4.1-11.1 years) in ideal weight. Lasting for 18 months, the intervention consisted in providing drinks sweetened with table sugar (caloric) or artificial sweetener (non-caloric) to randomly stratified groups. The group responsible for consuming caloric beverages was instructed to drink 250 ml of the product (equivalent to 104 Kcal), while those receiving non-caloric beverages should consume the same volume of an artificially sweetened product, without significant energy content. BMI, skinfold thickness, waist-to-height ratio and fat percentage returned significantly smaller values in the group consuming a non-caloric drink, indicating that restricting the consumption of sugary drinks may serve as a therapeutic resource, reducing the progression of obesogenic indicators in children and adolescents.

#### 4.5 Drug therapy

The use of drug therapy in the treatment of obesity in pediatric patients is unusual, and few studies have explored the effects of classic drugs on weight disorders. Yanovski *et al.* (2011) conducted drug intervention in severely obese (BMI  $34.6 \pm 6.6 \text{ kg/m}^2$ ) and insulin resistant children and adolescents (n = 85) aging between 6-12 years old. The experimental group was assigned to intake two doses of metformin (1000mg) a day for 6 months, plus 6 additional months of use according to the provided prescription (up to 2000mg/day). During the program, subjects received professional dietary monitoring.

Metformin-treated group have suffered more frequently with symptoms of gastrointestinal discomfort, however, the use of drug therapy with metformin was able to significantly reduce parameters such as BMI, body weight, *z* score for BMI and body fat percentage. As noted, the use of pharmacotherapy for the control of obesogenic disorders in childhood is unusual, however, in cases where the drug is intended to regulate an already present disease, such as diabetes type 2 (ONGE *et al.*, 2015), there is the possibility that this approach promotes improvements in anthropometric/aesthetic parameters in the pediatric public.

#### 4.6 Health perspectives on infant obesity

One of the main consequences of childhood obesity is the strong impact this has on the occurrence of cardiovascular disorders in adulthood. Authors have investigated several parameters related to causality or consequences of these dysfunctions (SYPNIEWSKA, 2015). Barraco *et al.* (2014) explored the effects of

newly discovered adipokines in the pathogenesis of cardiovascular disorders in obese children (BARRACO *et al.*, 2014). D'Adamo *et al.* (2015) and Pires *et al.* (2015) highlight aspects of atherogenic dyslipidemia, endothelial dysfunction and risk factors for obese pediatric patients (D'ADAMO *et al.*, 2015; PIRES *et al.*, 2015).

Kelishadi *et al.* (2015), in a systematic review, shows the strong direct relationship between central obesity in children/adolescents and cardiometabolic risks (KELISHADI *et al.*, 2015). Falkner (2015) highlights important epidemiological, physiological and genetic disorders of blood pressure, scoring about its synergism with childhood obesity (FALKNER, 2015). Pollock (2015) investigates the strong relationship between body mass and mass/bone quality as determinants of bone growth mechanisms in childhood and adolescence (POLLOCK, 2015).

During pregnancy and post-natal period, the organism has a great ability to respond to an almost ubiquitous array of environmental stimuli, and the essential components of plasticity and adaptations remain deeply active during the anatomical, physiological and biochemical development of the infant (MACAULAY *et al.*, 2014). A strong example of this "window" of opportunity is the establishment of the intestinal microbiota, which occurs mainly during early childhood. Profiling of bacterial colonization becomes responsible for communication of metabolic, immune and neurophysiological pathways, essential for the control of obesogenic disorders in young and adult individuals (MUNYAKA, KHAFIPOUR & GHIA, 2014).

## 5. CONCLUSIONS

Childhood and adolescence are critical periods of development, and the presence of obesogenic disorders in this age may induce consequences in adult life, such as cardiovascular disease, type 2 diabetes, disorders of the oxidative metabolism and inflammatory reactivity. Data compiled in this study indicate the strong role of family and the multidisciplinary team in treatment and prevention of weight disorders in children and adolescents. However, preventive approaches, carried out preferably during pregnancy and post-natal care, appear to be necessary to attenuate the epidemic impact caused by weight disorders in pediatric patients.

Other concerns relly on the fact that a gowing food industry facilitates the acess to heavly processed meals and snacks, reducing the time parents have to invest in preparing unprocessed natural food at home. In fact, it's hard to reconcile urban work routines with house and offspring responsabilities, but an integration between health care practioneers, such as dietitians/pediatritians, and the family is the key to develop strategies for healthy eating and adequate body development during childhood and adolescence.

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## 5.2 Author disclosure statement

No competing financial interests exist.

## 6. **REFERENCES**

AHRENS, W.; PIGEOT, I.; POHLABELN, H.; HENAUW, S.; LISSNER, L.; MOLNÁR, D. *et al.* on behalf of the IDEFICS consortium. Prevalence of overweight and obesity in European children below the age of 10. International Journal of Obesity (2014) 38, S99–S107.

ARNOLD, M.; PANDEYA, N.; BYRNES, G.; RENEHAN, A. G.; STEVENS, G. A.; EZZATI, M. *et al.* Global burden of cancer attributable to high body-mass index in 2012: a population-based study. Lancet Oncol 2015; 16: 36–46.

AYER, J.; CHARAKIDA, M.; DEANFIELD, J. E. & CELERMAJER, D. S. Lifetime risk: childhood obesity and cardiovascular risk. European Heart Journal. 2015 Jun 2;36(22):1371–6.

BARLOW, S. E.; TROWBRIDGE, F. L.; KLISH, W. J. & DIETZ, W. H. Treatment of Child and Adolescent Obesity: Reports From Pediatricians, Pediatric Nurse Practitioners, and Registered Dietitians. PEDIATRICS Vol. 110 No. 1 July 2002.

BARRACO, G.; LUCIANO, R.; SEMERARO, M.; PRIETO-HONTORIA, P. & MANCO, M. Recently Discovered Adipokines and Cardio-Metabolic Comorbidities in Childhood Obesity. International Journal of Molecular Sciences. 2014 Oct 29;15(11):19760–76.

BENTON, P. M.; SKOUTERIS, H. & HAYDEN, M. Does maternal psychopathology increase the risk of pre-schooler obesity? A systematic review. Appetite. 2015 Apr;87:259–82.

BERGH, C. & SÖDERSTEN, P. Mandometer treatment of eating disorders; a reply. European Eating Disorders Review Volume 12, Issue 6, pages 333–336, November/December 2004.

BRANDT, M. L.; HARMON, C. M.; HELMRATH, M. A.; INGE, T. H.; MCKAY, S. V. & MICHALSKY, M. P. Morbid obesity in pediatric diabetes mellitus: surgical options and outcomes. Nature Reviews Endocrinology 6, 637-645 (November 2010) | doi:10.1038/nrendo.2010.167.

BUNDRED, P.; KITCHINER, D. & BUNCHAN, I. Prevalence of overweight and obese children between 1989 and 1998: population based series of cross sectional studies. BMJ 2001 v. 322.

D'ADAMO, E.; GUARDAMAGNA, O.; CHIARELLI, F.; BARTULI, A.; LICCARDO, D.; FERRARI, F. *et al.* Atherogenic Dyslipidemia and Cardiovascular Risk Factors in Obese Children. International Journal of Endocrinology. 2015;2015:1–9.

DALEY, A. J.; COPELAND, R. J.; WRIGHT, N. P.; ROALFE, A. & WALES, J. K. H. Exercise Therapy as a Treatment for Psychopathologic Conditions in Obese and Morbidly Obese Adolescents: A Randomized, Controlled Trial. PEDIATRICS. 2006 Nov 1;118(5):2126–34.

DE RUYTER, J. C.; OLTHOF, M. R.; SEIDELL, J. C. & KATAN, M. B. A Trial of Sugar-free or Sugar-Sweetened Beverages and Body Weight in Children. New England Journal of Medicine. 2012 Oct 11;367(15):1397–406.

DIETZ, W. H. & ECONOMOS, C.D. Progress in the Control of Childhood Obesity. PEDIATRICS. 2015 Mar 1;135(3):e559–61.

DRAKE, A. J.; SMITH, A.; BETTS, P. R.; CROWNE, E. C. & SHIELD, J. P. H. Type 2 diabetes in obese white children. Arch Dis Child 2002;86:207–208.

EL-BEHADLI, A. F.; SHARP, C.; HUGHES, S. O.; OBASI, E. M. & NICKLAS, T. A. Maternal depression, stress and feeding styles: towards a framework for theory and research in child obesity. British Journal of Nutrition. 2015 Jan;113(S1):S55–71.

FALKNER, B. Recent Clinical and Translational Advances in Pediatric Hypertension. Hypertension. 2015;65(5):926–31.

Persp. online: biol. & saúde, Campos dos Goytacazes, 22 (6),1-16, 2016 seer.perspectivasonline.com.br

FLEGAL, K. M.; CARROLL, M. D.; KIT, B. K. & OGDEN C.L. Prevalence of Obesity and Trends in the Distribution of Body Mass Index Among US Adults, 1999-2010. JAMA. 2012;307(5).

FORD, A. L.; BERGH, C.; SODERSTEN, P.; SABIN, M. A.; HOLLINGHURST, S.; HUNT, L. P. *et al.* Treatment of childhood obesity by retraining eating behaviour: randomised controlled trial. BMJ. 2009 Jan 5;340(jan05 1):b5388–b5388.

FOSTER, B. A.; FARRAGHER, J.; PARKER, P. & SOSA, E. T. Treatment Interventions for Early Childhood Obesity: A Systematic Review. Academic PEDIATRICS. 2015;15(4):353–61.

FRANKS, P.; ESTAMPADOR, A. Genetic and epigenetic catalysts in early-life programming of adult cardiometabolic disorders. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2014 Dec;575.

FREITAS, H. R.; PEREIRA, A. S. & RAMOS, T. S. The Effects of Acute/Chronic Glutamine and Glutamine Peptide Supplementation on the Performance and Immune Function in Young Active Adult Athletes. Current Nutrition & Food Science, v. 11, p. 1-1, 2015.

HABIB-MOURAD, C. & GHANDOUR, L. A. Time to Act: Lessons Learnt from the First Pilot School-Based Intervention Study from Lebanon to Prevent and Reduce Childhood Obesity. Frontiers in Public Health [Internet]. 2015 Apr 15 [cited 2015 Jul 15];3. Available from: http://journal.frontiersin.org/article/10.3389/fpubh.2015.00056/abstract

HASLAM, D. W. & JAMES W. P. T. Obesity. Lancet 2005; 366: 1197-209.

JAMES, J. Preventing childhood obesity by reducing consumption of carbonated drinks: cluster randomised controlled trial. BMJ. 2004 May 22;328(7450):1237–0.

JAVED, A.; VELLA, A.; BALAGOPAL, P. B.; FISCHER, P. R.; WEAVER, A. L.; PICCININI, F. *et al.* Cholecalciferol Supplementation Does Not Influence -Cell Function and Insulin Action in Obese Adolescents: A Prospective Double-Blind Randomized Trial. Journal of Nutrition. 2015 Feb 1;145(2):284–90.

JONIDES, L.; BUSCHBACHER, V. & BARLOW, S. E. Management of Child and Adolescent Obesity: Psychological, Emotional, and Behavioral Assessment. PEDIATRICS 2002 Vol. 110 No. 1 July.

KALARCHIAN, M. A.; LEVINE, M. D.; ARSLANIAN, S. A.; EWING, L. J.; HOUCK, P. R.; CHENG, Y. *et al.* Family-Based Treatment of Severe Pediatric Obesity: Randomized, Controlled Trial. PEDIATRICS. 2009 Oct 1;124(4):1060–8.

KAR, S. & KAR, S. Prevention of childhood obesity in India: Way forward. Journal of Natural Science, Biology and Medicine. 2015;6(1):12.

KELISHADI, R. & AZIZI-SOLEIMAN, F. Controlling childhood obesity: A systematic review on strategies and challenges. Journal of Research in Medical Science. 2014 Oct; 19(10): 993–1008.

KELISHADI, R.; MIRMOGHTADAEE, P.; NAAFI, A. & KEIKHA, M. Systematic review on the association of abdominal obesity in children and adolescents with cardio-metabolic risk factors. Journal of Research in Medical Science. 2015 Mar; 20(3): 294–307.

KOOLS, S.; KENNEDY, C.; ENGLER, M. & ENGLER, M. Pediatric Hyperlipidemia: Child and Adolescent Disease Understandings and Perceptions About Dietary Adherence. JSPN Vol. 13, No. 3, July 2008.

Persp. online: biol. & saúde, Campos dos Goytacazes, 22 (6),1-16, 2016 seer.perspectivasonline.com.br

LIBER, A. & SZAJEWSKA, H. Effect of oligofructose supplementation on body weight in overweight and obese children: a randomised, double-blind, placebo-controlled trial. British Journal of Nutrition. 2014 Dec;112(12):2068–74.

LÓPEZ-ALARCÓN, M.; MARTÍNEZ-CORONADO, A.; VELARDE-CASTRO, O.; RENDÓN-MACÍAS, E. & FERNÁNDEZ, J. Supplementation of n3 Long-chain Polyunsaturated Fatty Acid Synergistically Decreases Insulin Resistance with Weight Loss of Obese Prepubertal and Pubertal Children. Archives of Medical Research. 2011 Aug;42(6):502–8.

MACAULAY, E. C.; DONOVAN, E. L.; LEASK, M. P.; BLOOMFIELD, F. H.; VICKERS, M. H., DEARDEN, P. K. *et al.* The importance of early life in childhood obesity and related diseases: a report from the 2014 Gravida Strategic Summit. Journal of Developmental Origins of Health and Disease. 2014 Dec;5(06):398–407.

MAGRONE, T. & JIRILLO, E. Childhood Obesity: Immune Response and Nutritional Approaches. Frontiers in Immunology [Internet]. 2015 Feb 24 [cited 2015 Jul 15];6. Available from: http://journal.frontiersin.org/Article/10.3389/fimmu.2015.00076/abstract

MAYNARD, L. M.; GALUSKA, D. A.; BLANCK, H. M. & SERDULA, M. K. Maternal Perceptions of Weight Status of Children. PEDIATRICS 2003 Vol. 111 No. 5 May.

MCCRINDLE, B. W. Cardiovascular Consequences of Childhood Obesity. Canadian Journal of Cardiology. 2015 Feb;31(2):124–30.

MISTRY, S. K. & PUTHUSSERY, S. Risk factors of overweight and obesity in childhood and adolescence in South Asian countries: a systematic review of the evidence. Public Health. 2015 Mar;129(3):200–9.

MUNYAKA, P. M.; KHAFIPOUR, E. & GHIA, J.E. External Influence of Early Childhood Establishment of Gut Microbiota and Subsequent Health Implications. Frontiers in Pediatrics [Internet]. 2014 Oct 9 [cited 2015 Jul 15];2. Available from: http://journal.frontiersin.org/article/10.3389/fped.2014.00109/abstract.

NADER, N. S.; AGUIRRE-CASTANEDA, R.; WALLACE, J.; SINGH, R.; WEAVER, A. & KUMAR, S. Effect of Vitamin D<sub>3</sub> Supplementation on Serum 25(OH)D, Lipids and Markers of Insulin Resistance in Obese Adolescents: A Prospective, Randomized, Placebo-Controlled Pilot Trial. Hormone Research in Paediatrics. 2014;82(2):107–12.

OGDEN, C. L.; CARROLL, M. D.; KIT, B. K. & FLEGAL, K. M. Prevalence of Childhood and Adult Obesity in the United States, 2011-2012. JAMA. 2014;311(8):806-814. doi:10.1001/jama.2014.732.

OGDEN, C.L.; CARROLL, M. D.; KIT, B. K. & FLEGAL, K. M. Prevalence of Obesity and Trends in Body Mass Index Among US Children and Adolescents, 1999-2010. JAMA. 2012;307(5):483-490.

ONGE, E. S.; MILLER, S. A.; MOTYCKA, C. & DEBERRY, A. A Review of the Treatment of Type 2 Diabetes in Children. The Journal of Pediatric Pharmacology and Therapeutics. 2015;20(1):4–16.

PANDITA, A.; SHARMA, D.; PANDITA, D.; PAWAR, S.; TARIQ, M. & KAUL, A. Childhood obesity: prevention is better than cure. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2016:9 83–89.

PIRES, A.; CASTELA, E.; SENA, C. & SEIÇA, R. Obesidade: Paradigma da Disfunção Endotelial em Idade Pediátrica. Acta Medica Portuguesa [Internet]. 2015 [cited 2015 Jul 15];28(2).

Persp. online: biol. & saúde, Campos dos Goytacazes, 22 (6),1-16, 2016 seer.perspectivasonline.com.br

POLLOCK, N. K. Childhood obesity, bone development, and cardiometabolic risk factors. Molecular and Cellular Endocrinology. 2015 Jul;410:52–63.

REILLY, J. J.; KELLY, L.; MONTGOMERY, C.; WILLIAMSON, A.; FISHER, A.; MCCOLL, J. H. *et al.* Physical activity to prevent obesity in young children: cluster randomised controlled trial. BMJ. 2006 Nov 18;333(7577):1041–1041.

SABIN, M. A. & KIESS, W. Childhood obesity: Current and novel approaches. Best Practice & Research Clinical Endocrinology & Metabolism. 2015 Jun;29(3):327–38.

SHUE, C. K.; WHITT, J. K.; DANIEL, L. & SHUE, C. B. Promoting conversations between physicians and<br/>families about childhood obesity: evaluation of physician communication training within a clinical practice<br/>improvement initiative. HEALTH COMMUNICATION, 2015.<br/>http://dx.doi.org/10.1080/10410236.2014.963785

SILVERBERG, J. I.; BECKER, L.; KWASNY, M.; MENTER, A.; CORDORO, K. M. & PALLER, A. S. Central Obesity and High Blood Pressure in Pediatric Patients With Atopic Dermatitis. JAMA Dermatol. 2015;151(2):144-152.

SYPNIEWSKA, G. Laboratory assessment of cardiometabolic risk in overweight and obese children. Clinical Biochemistry. 2015 Apr;48(6):370–6.

TREMBLAY, M.; GRAY, C.; BABCOCK, S.; BARNES, J.; BRADSTREET, C.; CARR, D. *et al.* Position Statement on Active Outdoor Play. International Journal of Environmental Research and Public Health. 2015 Jun 8;12(6):6475–505.

VOORTMAN, T.; VAN DEN HOOVEN, E. H.; BRAUN, K. V. E.; VAN DEN BROECK, M.; BRAMER, W. M.; CHOWDHURRY, R. *et al.* Effects of polyunsaturated fatty acid intake and status during pregnancy, lactation, and early childhood on cardiometabolic health: A systematic review. Progress in Lipid Research. 2015 Jul;59:67–87.

WEST, F.; SANDERS, M. R.; CLEGHORN, G. J. & DAVIES, P. S. W. Randomised clinical trial of a family-based lifestyle intervention for childhood obesity involving parents as the exclusive agents of change. Behaviour Research and Therapy. 2010 Dec;48(12):1170–9.

WIEGMAN, A.; GIDDING, S. S.; WATTS, G. F.; CHAPMAN, M. J.; GINSBERG, H. N.; CUCHEL, M. *et al.* Familial hypercholesterolaemia in children and adolescents: gaining decades of life by optimizing detection and treatment. European Heart Journal [Internet]. 2015 May 25 [cited 2015 Jul 15]; Available from: http://eurheartj.oxfordjournals.org/cgi/doi/10.1093/eurheartj/ehv157

WILFLEY, D. E.; STEIN, R. I.; SAELENS, B. E.; MOCKUS, D. S.; MATT, G. E.; HAYDEN-WADE, H. A. *et al.* Efficacy of maintenance treatment approaches for childhood overweight: a randomized controlled trial. JAMA. 2007;298(14):1661–73.

YANOVSKI, J. A.; KRAKOFF, J.; SALAITA, C. G.; MCDUFFIE, J. R.; KOZLOSKY, M.; SEBRING, N. G. *et al.* Effects of Metformin on Body Weight and Body Composition in Obese Insulin-Resistant Children: A Randomized Clinical Trial. Diabetes. 2011 Feb 1;60(2):477–85.