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Assessment and management of obesity and metabolic syndrome in children with CKD stages 2–5 on dialysis and after kidney transplantation–clinical practice recommendations from the Pediatric Renal Nutrition Taskforce

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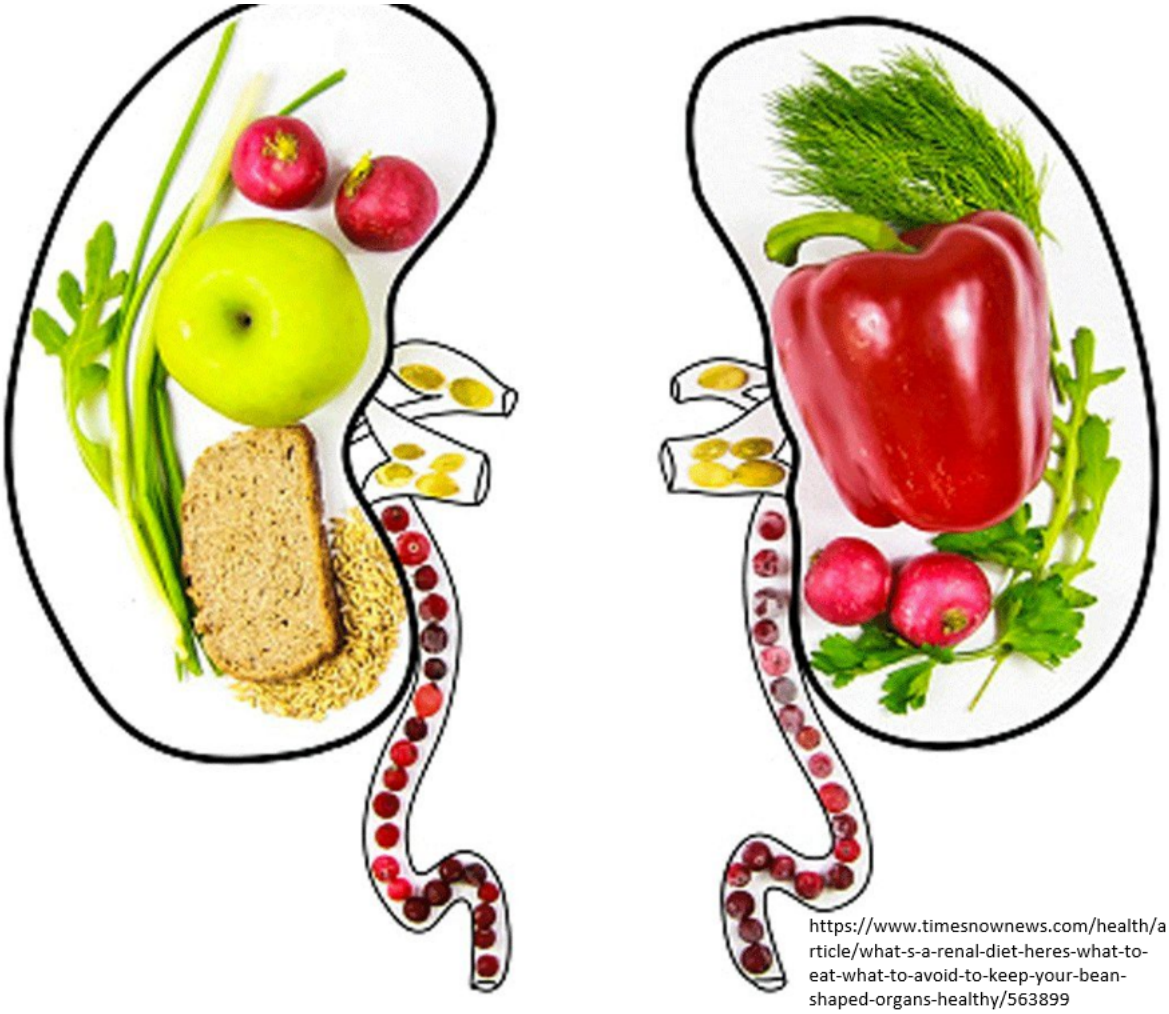


Additional Suggested Reads:

- Nutritional management of the infant with chronic kidney disease stages 2–5 and on dialysis PMID:35378603
- Assessment of nutritional status in children with kidney diseases—clinical practice recommendations from the Pediatric Renal Nutrition Taskforce. PMID:33319327
- Energy and protein requirements for children with CKD stages 2-5 and on dialysis-clinical practice recommendations from the Pediatric Renal Nutrition Taskforce PMID:31845057

Introduction:

Obesity can impair kidney function, even in children without chronic kidney disease (CKD). Inturn, children with CKD are at an increased risk of cardiovascular outcomes

such as hypertension, obesity, dyslipidemia, and abnormal glucose metabolism. To reduce morbidity and mortality due to cardiovascular disease (CVD), it is imperative to address these risk factors.

Metabolic syndrome (MS) includes obesity, hypertension, dyslipidemia and abnormal glucose metabolism. MS affects children of all ages, including children with CKD, those undergoing dialysis, and those following kidney transplantation. Additionally, MS in children can increase the prevalence of MS as an adult.

In children with CKD, the prevalence of MS is 15-30% compared to the average prevalence in the US and Europe of 3.8-9.8%. Despite the increased prevalence of obesity and metabolic syndrome (O&MS) in children and the evidence linked to adverse CKD and CV outcomes, appropriate guidelines to diagnose or treat these patients do not exist.

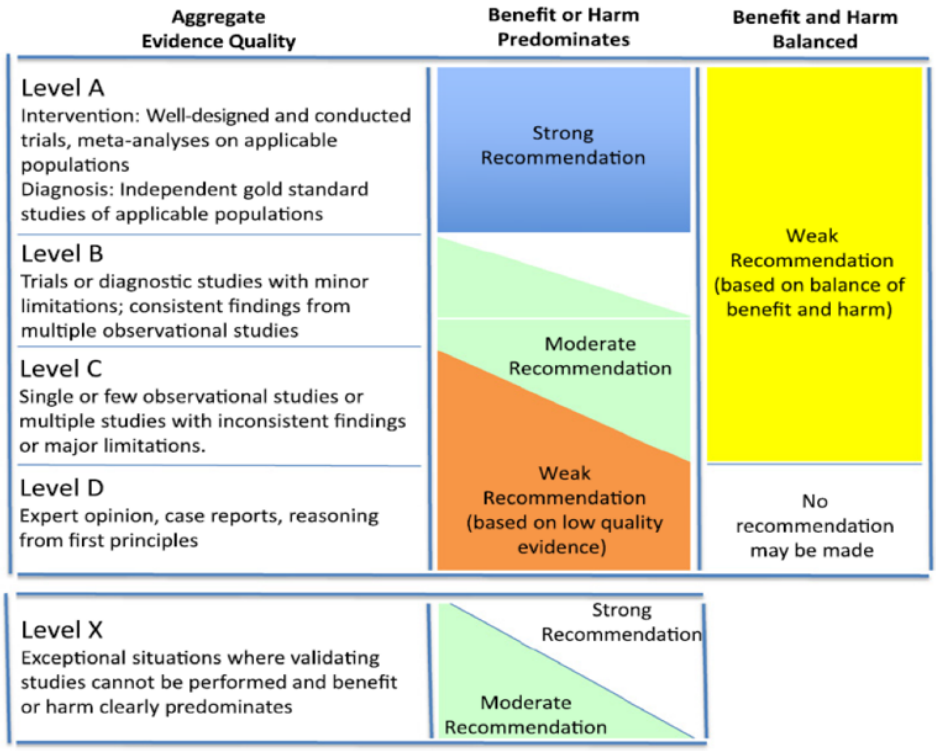
To address this issue, the Pediatric Renal Nutrition Taskforce (PRNT), which is an international group of pediatric renal dieticians and nephrologists, developed clinical practice recommendations (CPRs) for non-pharmacologic adjustments in diet, physical activity, and behavior modifications as key areas of improvement for children with kidney disease, which will be discussed in this month's journal club.

Methods:

In this clinical practice recommendations (CPRs), PRNT discusses the assessment and management of obesity and metabolic syndrome (O&MS) in children and adolescents with CKD stages 2–5 and on dialysis, as well as after kidney transplantation, focusing on non-pharmacological treatment (diet, physical activity and behavior modification) in the context of age and CKD stage. As with all CPRs produced by the PRNT, resources for the practical management of O&MS will be developed by the Taskforce during the dissemination phase of the guideline.

The statements have been graded using the American Academy of Pediatrics grading matrix. Statements with a low grade or those that are opinion-based must be carefully considered and adapted to individual patient needs based on the clinical judgment of the treating physician and dietitian. Research recommendations are provided

Supplementary Table 2 American Academy of Pediatrics grading matrix



PICO questions were developed in order to develop recommendations that provide specific actionable advice, with specification of the patient group (P) to whom the statement would apply; the intervention (I) being considered; the comparator (C) (which may be “no action” or an alternative intervention); and the outcomes (O) affected by the intervention. The PICO terms in this guidelines were:

Population: Children from 2 years to 18 years of age with CKD 2-5, on dialysis, and after kidney transplantation. Children with CKD1 have been excluded.

Intervention: Prevention or treatment of O&MS in children with CKD2-5D and after transplantation.

Comparator: Strategies for prevention or management of O&MS in age- and sex-matched general pediatric populations, adults with CKD who have O&MS, or no comparator.

Outcome: Weight reduction, regression of O&MS and associated adverse outcomes, including CV risk factors, CV target organ damage, CKD progression, access to transplantation, graft function, mortality.

Currently there is no accepted definition for adiposity in children <2y as there are no outcome measures in this age group and hence it has only briefly been addressed in this article. The International Pediatric Peritoneal Dialysis Network (IPPDN) has shown that 20% of infants receiving PD have a BMI-SDS > 95th centile (> 1.645 SDS) with highest prevalence in the Middle East and US, in keeping with national obesity prevalence rates. Gastrostomy feeding was considered the most significant risk factor for obesity. In addition, obesity is also associated with increased mortality in children under 5 years on PD and hence a careful attention to the nutritional management of those fed by enteral tube is required.

Literature Search:

An evidence search was performed for papers published from 1980 through September 2020 in Medline, Pubmed, Embase and Cochrane libraries (supplementary table 1). In children with CKD, all studies pertaining to O&MS were included, with retrospective studies limited to those with more than 20 children. The literature search was expanded to include meta-analyses in adults with obesity and/or MS and CKD2-5D and after transplantation, as well as meta-analyses and randomized controlled trials (RCTs) conducted in the general pediatric population with O&MS. The management of hypertension beyond its relation with dietary sodium and the management of sodium and fluid in children with CKD2-5D and after transplantation are not discussed in this article.

Given the very low grade of evidence for most recommendations, a Delphi survey (e-questionnaire) was conducted to attain consensus from experts in the field.

According to the results of the Delphi survey there were 50 responses to the electronic survey with joint responses by some dietitians and physicians from the same facility. All professionals who completed the survey were listed in “Participants in the Delphi survey.”

22 clinical practice recommendation statements received an overall 87% consensus with a “strongly agree” or “agree” response and 11% with a “neutral”response; these largely reflected the wide variations in practice in the absence of robust evidence. Two statements did not reach the stipulated 70% level of consensus. The Taskforce members reviewed the comments and agreed that the statements did not require

changing as the GRADE clearly reflects the low level of evidence, indicating that these statements are based on expert opinion.

The highest “disagree and strongly disagree” rate was in response to statements on bariatric surgery. On careful review of the literature and discussion within the Task Force team, it was agreed that despite country policy, legal stipulations and few centers with the relevant experience, bariatric surgery may be considered in a selected subgroup of children with CKD2-5D or with a kidney transplant and O&MS when all other interventions have failed. Based on suggestions from Delphi respondents, minor rewording of statements and further clarification to the text were done.

Supplementary Table 3 Agreement and disagreement responses to the Delphi survey

Recommendations	Agree/Disagree*
1.1 We recommend using BMI-height-age to define overweight or obesity in children who are below the 3rd centile for height and have not reached their final adult height	83%/3%
2.1. Calculate BMI or weight-for-height and plot on centile growth charts.	93%/0%
2.1.1. Calculate z-scores [standard deviation scores (SDS)] to complement growth chart plots.	90%/3%
2.1.2. Utilize trends in growth parameters to assist clinical decision-making.	86%/0%
2.2. Measure BP, fasting TG, HDL and glucose levels in children with CKD2-5D and after transplantation if BMI > +1 SD.	93%/0%
2.3. Evaluate for MS risk factors, including focused history and physical exam, biochemical measurements for comorbidities and assessment of cardio-metabolic risk factors.	90% /3%
2.4. Evaluate lifestyle habits, including diet, physical activity, sleep and screen time.	93%/0%
2.5. The frequency of assessment should be individualized based on the child’s CV risk factors, disease severity and progression and the presence of comorbidities	86%/3%
3.1. We suggest a comprehensive multicomponent intervention that includes a nutrition care plan, physical activity prescription and behavioral modification to reduce BMI and improve components of the MS.	97%/0%
3.2.1. We recommend an individualized energy intake, adjusted for age, CKD stage, dialysis and comorbidities, to achieve weight loss or weight maintenance in children without compromising their nutrition.	97%/0%
3.2.2. The nutrition care plan should aim to improve the overall diet quality, with an emphasis on an intake comprised primarily of fruits and vegetables, whole grains, low- or non-fat dairy products, pulses (peas, beans, lentils), fish and lean meat, and avoidance of sugar-sweetened beverages, highly processed foods and foods high in saturated fat.	93%/3%

Funding: None

Recommendations:

Definition of O&MS:

Age	Overweight	Obese	Metabolic Syndrome (2-18 years)
			(Overweight or obesity) + 2 of 4 additional Cardiovascular (CV) risk factors
2-5 years	Weight-for-height for age > +2 SD, using World Health Organization (WHO) child growth standard chart	Weight-for-height for age > +3 SD, using WHO child growth standard chart	1) Systolic and/or diastolic office **blood pressure (BP)** ≥ 90th centile for age, sex, and height or ≥ 130/80 mmHg, whichever is lower, or on an anti-hypertensive medication 2) **Fasting triglycerides** ≥ 100 mg/dL (1.1 mmol/L) if age <10 years, or ≥ 130 mg/dL (1.5 mmol/L) if age ≥ 10 years 3) **Fasting** high-density lipoprotein (**HDL**) < 40 mg/dL (1.03 mmol/L) 4) **Fasting serum glucose** ≥ 100 mg/dL (5.6 mmol/L) or known type 2 diabetes mellitus (T2DM)
> 5 years	Body mass index (BMI) for age > +1 SD, equivalent to BMI 25 kg/m2 at 19 years, using the WHO growth reference chart or a country-specific growth chart	BMI for age > +2 SD, equivalent to BMI > 30 kg/m2 at 19 years, using the WHO growth reference chart or a country-specific growth chart	

by @NicoleSchmidt47

Here is the table comparing various definitions of O&MS:

Table 1 Definitions of metabolic syndrome used in studies in children with CKD

	Weiss et al. [20]	Cruz et al. [21]	International Diabetes Federation [18]	Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents [19]	Pediatric Renal Nutrition Taskforce 2021 In children with CKD2-5, on dialysis and after transplantation
Definition	Any ≥ 3 of 5 criteria	Any ≥ 3 of 5 criteria	WC ≥ 90th plus any 2 ≥ criteria	Any ≥ 3 of 5 criteria	Overweight or obesity plus any 2 ≥ criteria
Overweight/obesity	BMI > 97th centile for age and sex (or BMI z score ≥ 2)	WC ≥ 90th centile for age, sex, and Hispanic ethnicity from NHANES III	6- < 10 yrs: WC ≥ 90th centile 10- < 16 yrs: WC ≥ 90th centile or adult cut off if lower > 16 yrs: WC ≥ 94 cm in Europid males or ≥ 80 cm in females or other ethnic specific values	BMI ≥ 85th centile or WC ≥ 90th centile	2-5 yrs: BMI > +2SD on growth charts > 5 yrs: BMI > +1SD on growth charts
High TG	> 95th age and sex centile	≥ 90th age and sex centile	10–< 16 yrs: ≥ 150 mg/dL > 16 yrs: ≥ 150 mg/dL or treatment for high TG	≥ 75 mg/dL if 0–9 years ≥ 90 mg/dL if ≥ 10 years	< 10 yrs: TG ≥ 100 mg/dL ≥ 10 yrs: ≥ 130 mg/dL
Low HDL	< 5th age and sex centile	≤ 10th age and sex centile	10–< 16 yrs: < 40 mg/dL > 16 yrs: < 40 mg/dL in males < 50 mg/dL in females or treatment for low HDL	≤ 40 mg/dL	≤ 40 mg/dL
High BP	> 95th age, sex and height centile	≥ 95th age, sex and height centile	10–< 16 yrs: ≥ 130/85 mmHg > 16 yrs: ≥ 130/85 mmHg or diagnosis of HTN	≥ 90th age, sex and height centile	≥ 90th age, sex, and height centile or ≥130/80 mmHg or on antihypertensive medication
Glucose intolerance	Glucose ≥ 140 mg/dL at 2 h OGTT	Glucose > 140 mg/dL (3 h OGTT)	FG ≥ 100 mg/dL or known T2DM	FG ≥ 100 mg/dL	FG ≥ 100 mg/dL

Abbreviations: *WC* waist circumference, *BMI* body mass index, *TG* triglycerides, *HDL* high-density lipoprotein, *BP* blood pressure, *HTN* hypertension, *OGTT* oral glucose tolerance test, *FG* fasting glucose, *T2DM* type 2 diabetes mellitus

Recommendation : Authors/PNRT recommend using BMI-height-age to define overweight or obesity in children who are below the 3rd centile for height and have not reached their final adult height (Level B; moderate recommendation).

Assessment of O&MS:

BMI or weight for height is calculated and then plotted on growth charts (Level A; strong recommendation)

A. Z scores are calculated as well to aid with the growth charts (Level X; strong recommendation)
B. Growth parameter trends are used to aid in clinical decision making (Level D; weak recommendation)

In children with CKD2-5D and those after transplantation if BMI > +1SD, measure BP, fasting TG, HDL and glucose levels. (Level A; strong recommendation)

Complete an H&P, biochemical measurements for comorbidities, assessment for cardiometabolic risk factors in order to evaluate for metabolic syndrome risk factors. (Level C; weak recommendation)
Assess children's lifestyle habits such as sleep, exercise, diet, and screen time. (Level C; weak recommendation)
Based on each child's individual assessment of cardiovascular risk factors, severity of disease and progression and presence of comorbidities, decide on the necessary frequency of assessment. (Ungraded)

Table 3 Assessment of patients with CKD stages 2–5 on dialysis and after kidney transplantation with O&MS

Assess	Suggested minimum Interval	
	CKD2-5 and kidney transplants	CKD5D
Anthropometry		
Euvolemic weight, height, length, weight-for-height, BMI for age, BMI-height-age, SDS	1–3 months	Monthly
BMI trends plotted on centile growth charts	1–3 months	Monthly
Medical history		
Family history of obesity, diabetes, hypertension, hyperlipidemia, cardiovascular disease	Yearly	Yearly
Perinatal history, primary disease, age of disease onset	At initial visit	At initial visit
Snoring and sleep apnea history, sleep duration, history of NAFLD, PCOS, mental disorders, concurrent disease (endocrine, cardiac, neurological, systemic, e.g., lupus), symptoms or history of target organ damage, past and current treatments, compliance and side effects	6–12 months	6–12 months
Physical exam		
Assessment may include for cushingoid features, skin for acanthosis nigricans, acne, hirsutism, eye examination for cataract or pseudotumor cerebri, ankle, foot, knee pain, joint dysfunction,	6–12 months	6–12 months
neurodevelopmental assessment, features of syndromic obesity (e.g., Bardet-Biedl syndrome)	At initial visit	At initial visit
Cardio-metabolic risk factors		
BP:		
Office BP measurement	At each visit	At each visit
ABPM	6–12 months	6–12 months
Lipids:		
Triglycerides	3–4 months	3–4 months
HDL		
Glucose metabolism:		
Fasting glucose	3–4 months	3–4 months
HbA1C	If glucose > 100 mg/dL, reassess every 6–12 months	If glucose > 100 mg/dL, reassess every 6–12 months
Additional risk factors:		
Transaminases	6–12 months	6–12 months
Uric acid	3–4 months	3–4 months
Dietary assessment		
Food record or food recalls	3–6 months	3–4 months
Dietetic contact	At each visit	At each visit
Physical activity		
Record frequency, duration, intensity of PA	3–4 months	1–3 months
Lifestyle habits		
Daily screen time, leisure activities	3–4 months	3–4 months
Echocardiography		
Evaluation for LVH	Yearly	Yearly

Abbreviations: *BMI* body mass index, *SDS* standard deviation score, *NAFLD* nonalcoholic fatty liver disease, *PCOS* polycystic ovary syndrome, *BP* blood pressure, *ABPM* ambulatory BP monitoring, *HDL* high-density lipoprotein, *HgA1C* hemoglobin A1c, *PA* physical activity, *LVH* left ventricular hypertrophy

Management of O&MS:

A comprehensive multicomponent intervention which includes behavioral modification, exercise prescription and nutrition care plan should be performed to reduce their BMI as well as CV risk factors over time. (Ungraded)

Diet Management. (Ungraded)

A. Evaluate an individualized energy intake per child which should be adjusted by age, CKD stage, dialysis, and comorbidities. This should aid in weight loss or weight maintenance without compromising nutrition.
B. Emphasize dietary intake of fruits and vegetables, whole grains, low or non-fat dairy products, peas, beans, lentils, fish, lean meat. Encourage avoidance of processed foods, foods with high saturated fats, and sugar sweetened beverages. Both of these recommendations should help to improve the overall quality of diet. (Level B; weak recommendation)
C. For children who are enterally tube fed, frequently review the energy content of the formula and adjust accordingly to avoid development of overweight or underweight. (Level B; moderate recommendation)

Management of physical activity.

A. Children should engage in exercise with individualized intensity and duration according to their age, CKD stage, physical tolerance, and comorbidities. (Level B; moderate recommendation)

Behavior modification.

A. Inclusive of regular and adequate sleep as well as reduced screen time.
B. Management of psychosocial stressors according to the individual need and family need. Counseling or psychosocial support may be appropriate. (Level D; weak recommendation)

Medication considerations: it is not recommended to use anti-obesity medications in children with CKD2-5D or those with kidney transplant and O&MS. (Ungraded)

Bariatric surgery recommendations:

A. In a certain subset of children with CKD2-5D or with a kidney transplant and O&MS, it can be appropriate to undertake bariatric surgery when all other interventions have failed.
B. Those who may be considered for surgery include:
    a. Adolescents with extreme obesity (BMI greater than or equal to 40 kg/m2) and other comorbidities associated with long-term risks (Level C; weak recommendation)
    b. Adolescents with BMI greater than or equal to 35 kg/m2 with specific obesity related comorbidities such as T2DM, severe steatohepatitis, pseudotumor cerebri, and moderate to severe obstructive sleep apnea (Level C; weak recommendation)

Management of components of Metabolic Syndrome

Management of hypertension

A. In all children with CKD2-5D or those with a kidney transplant and O&MS, it is suggested to avoid excess sodium intake to prevent hypertension and to reduce dietary sodium intake in those with hypertension (WHO recommends that the max level of sodium in adults- 2g/day- should be adjusted downward in children based upon their energy requirements) (Level B; moderate recommendation)

Management of dyslipidemia

A. Dietary interventions and lifestyle modifications to treat dyslipidemia (Level D; weak recommendation)
B. It is not suggested to routinely use statins or other lipid lowering agents (National Heart, Lung, and Blood Institute and KDIGO clinical practice guidelines) (Level D; weak recommendation)

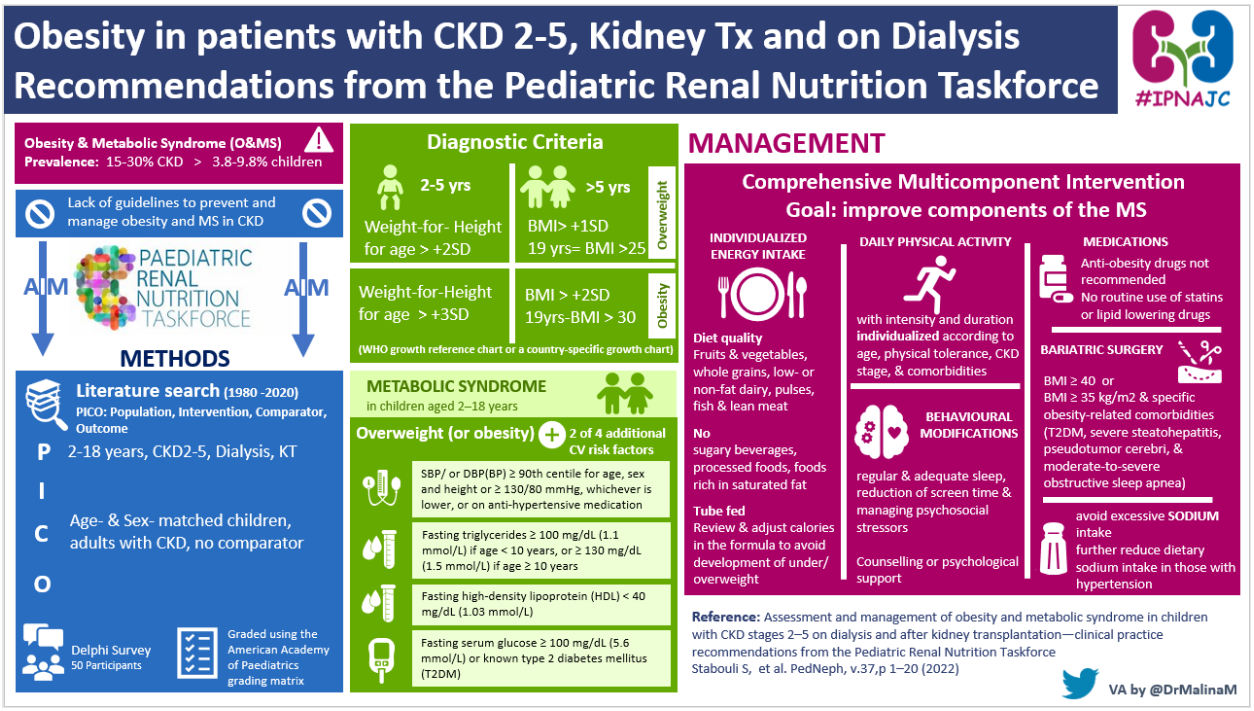
Management of diabetes/glucose intolerance

A. All children with CKD2-5D or those with kidney transplantation and O&MS should receive comprehensive education to manage abnormal glucose metabolism (Level D; weak recommendation)
B. Review medications that are known to cause abnormal glucose metabolism and adjust the dosing accordingly (Ungraded)

Prevention of O&MS:

A healthy diet, regular exercise, and behavioral modifications are recommended to help prevent O&MS in those with CKD2-5D or those with kidney transplantation. (Level D; weak recommendation)

Here is the infographic by Michal M. Malina, summarizing the recommendations.



DISCUSSION

The global obesity and MS pandemic has affected healthy as well as children with chronic diseases world over. Children with CKD have pre-existing cardiometabolic risk factors that are compounded by obesity. Defining O&MS is important for these guidelines and two different definitions are used: BMI for age (used in the US to screen children ages 2-20 for obesity, overweight or underweight) and BMI-height for age. Neither of these take central obesity/waist circumference into account when defining metabolic syndrome which can be difficult in patients receiving peritoneal dialysis (PD), those on steroids or those with nephrotic syndrome to name a few causes. However, data from the US Renal Data System (USRDS) has shown increased mortality rates and decreased access to transplant when BMI SDS (Standardized BMI) are used for drawing conclusions making it more objective for use. Irrespective of used definitions, O&MS is associated with decline in kidney function and poor CV outcome. Lower thresholds of all parameters including blood pressure (90th percentile for age and gender), triglycerides and HDL have been proposed as targets in children with CKD. Similar diagnostic criteria for glucose metabolism as diabetes have been used.

Reevaluation of all parameters (BP, lipid panel, etc) is important in transplanted children when BMI crosses +>1SD. The frequency of assessment should be individualized based on the child's CV risk factors, disease severity and progression and the presence

of comorbidities. Here is a table describing a few studies on CV and renal outcomes in children with CKD and after kidney transplantation-

Table 2 Studies on CV and renal outcomes of MS in children with CKD and after kidney transplantation

Study/country/ design	Population	MS definition	Risk factors for MS	MS prevalence	MS Outcome
Lalan et al. [5] USA Multi-center, observational prospective cohort study	472 children, median age ~12 years from the CKiD study (eGFR 30–90 mL/min/1.73 m^2)	Overweight plus ≥ 2 criteria Expert Panel 2011	NR	15.1% (40% among OW, 60% among OB)	2 times greater OR of decline in eGFR >10% per year
Sgambat et al. [26] USA Single-center prospective, longitudinal cohort study	42 kidney transplant recipients from single center aged 3-20 years (mean eGFR at end of study 90.3 ± 3.1 mL/min/1.73 m^2) 24 healthy controls	Abdominal obesity plus ≥ 2 criteria Modified Expert Panel 2011 ATP-III if > 19 yrs	The prevalence of obesity as detected by WHr was significantly higher (2.3–5.1 times) than by WC alone	33.3%, 29.7%, 30.3% at 1, 18, and 30 months post-transplant	- BMI-obesity, WHr-obesity and MS had 3.7 ± 1.9, 2.8 ± 1.3, and 3.6 ± 1.8 times higher ORs for post-transplant LVH. WC-obesity was not a predictor. - BMI-obesity, WHr-obesity, WC-obesity, and MS had 1.5 ± 0.39, 1.4 ± 0.49, 1.6 ± 0.51, and 1.3 ± 0.58 times higher ORs for post-transplant worse myocardial longitudinal strain (%). - In the models, there were also higher ORs for high BP for LVH and high BP and eGFR for strain.

Sgambat et al. [27] USA Single-center prospective, longitudinal cohort study	42 kidney transplant recipients from single center aged 3–20 years (mean eGFR at end of study 90.3 ± 3.1 mL/min/1.73 m^2) 24 healthy controls	Abdominal obesity plus ≥ 2 criteria Modified Expert Panel 2011 ATP-III if > 19 yrs	NR	33.3%, 29.7%, 30.3% at 1, 18, and 30 months post-transplant	Among the 21 AA transplant patients, MS was independently associated with a 0.03 ± 0.01-mm increase in cIMT.
Tainio et al. [12] Finland Single-center retrospective cohort study	210 kidney transplant recipients from single center median age 4.5 years (range 0.7–18.2)	Any of ≥ 3 criteria Modified for the study AHA 200	NR	19% at 1.5 years and 14.2 at 5 years post-transplant	Higher ^{51}Cr-EDTA GFR decline in MS at 1.5 years (ml/min/1.73 m^2), but no difference at 5 years post-transplant
Wilson et al. [2] USA Multi-center, observational prospective cohort study	586 children 1–16 years from the CKiD study (eGFR 30–90 mL/min/1.73 m^2)	≥ 3 CV risk factors	NR	13%	Nephrotic-range proteinuria was associated with 2.04 higher odds of having more CV risk factors.
Wilson et al. [13] USA Retrospective multi-center study	234 kidney transplant recipients from 6 centers in the Midwest Pediatric Nephrology Consortium aged 12.1 ± 5.16 years (mean eGFR at end of study 87.3 ± 28.3 mL/min/1.73 m^2)	Any of ≥ 3 criteria Weiss 2004 [20]	Factors associated with incident metabolic syndrome included pretransplant BMI > 85th centile and cyclosporine	18.8% at time of transplant 37.6% at 1-year post-transplant (40% among overweight and 74.5% among obese)	- 2.6 times higher OR for post-transplant LVH - 3 times higher OR of eccentric LVH hypertrophy post-transplant - 55% in MS vs. 32% in those without - Mean LVMI was 48.3 $g/m^{2.7}$ in MS vs. 40.0 $g/m^{2.7}$ (p = 0.0008) without MS

Table 2 (continued)

Study/country/design	Population	MS definition	Risk factors for MS	MS prevalence	MS Outcome
Maduram et al. [14] USA Retrospective single-center cohort study	58 kidney transplant recipients from single center aged 11.2 ± 5.1 years	Any of ≥ 3 criteria Age-modified ATP-III	Prevalence significantly higher 68% in steroid group vs. 15% in steroid withdrawal group	38%	Lower GFR in children at 1-year post-transplant (65) vs those without MS (65 ± 19 vs. 88 ±25 mL/min/1.73 m^2) in both steroid and steroid withdrawal groups

Abbreviations: *GFR* glomerular filtration rate, *OW* overweight, *WHr*, waist-to-height ratio, *WC* waist circumference, *BMI* body mass index, *BP* blood pressure, *LVH* left ventricular hypertrophy, *cIMT* carotid intima media thickness, *CV* cardiovascular, *LVMI* left ventricular mass index

Non-modifiable risk factors for O&MS include maternal obesity and gestational diabetes, low birth weight and rapid catch-up growth. These are also associated with a higher risk of developing congenital anomalies of kidney and urinary tract (CAKUT). Awareness and vigilance may positively affect these populations. Hyperuricemia,

enteral tube-feeding and steroid and mTOR inhibitor use are additional risk factors for O&MS. Certain ***underlying kidney diseases*** including cystic kidney diseases, nephropathic cystinosis, and Bardet–Biedl and Alstrom syndromes, are at greater risk of developing new onset diabetes after transplantation as well as other cardio-metabolic risk factors and subsequently O&MS. ***Obese Sarcopenia*** (progressive and generalized loss of muscle mass and strength) in children with CKD due to several factors including the kidney disease itself, dialysis, metabolic acidosis and Vitamin D deficiency besides adipocyte dysfunction should be paid attention to. Resistance training is advised to improve muscle strength in sarcopenic obesity. MS is associated with 2-3 times higher risk of **left ventricular hypertrophy** and annual echocardiography is recommended. Clinical value of carotid intima media thickness (cIMT) & pulse wave velocity (PWV) needs validation.

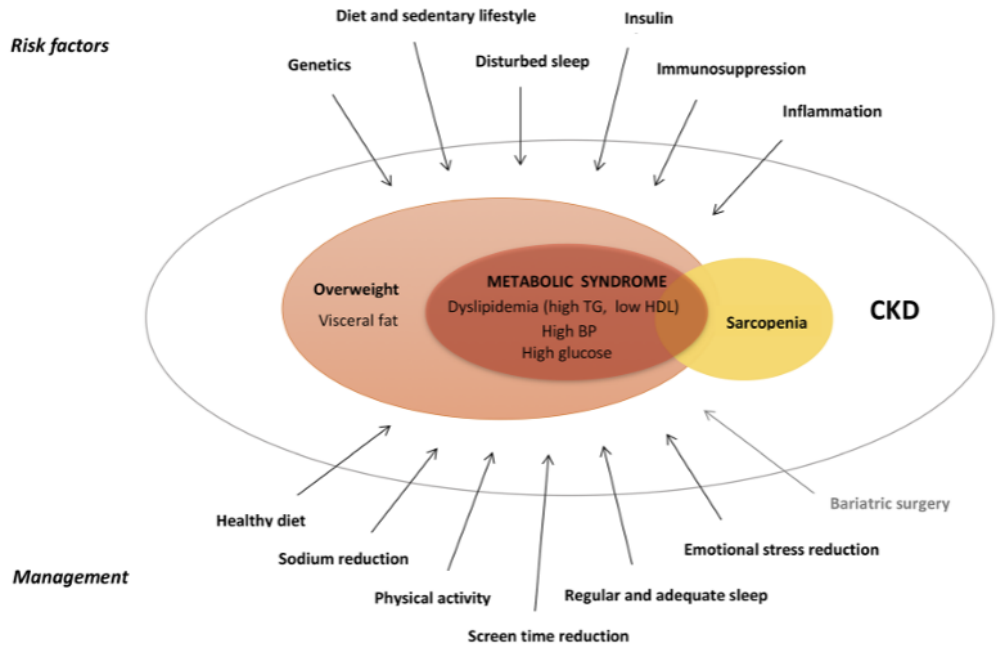


Fig. 1 Traditional and disease-related risk factors and management of O&MS in CKD patients. First line (black) and second line (gray) treatment

Multidisciplinary approach with interventions including modification of diet plan, physical activity and behavioral modifications is key for treatment of O&MS in children. **Diet** must be individualized to take into account mode of feeding, age, CKD stage, comorbidities and need for weight gain or weight loss. The current evidence demonstrates that the Mediterranean diet is preferred for adults with CKD and that the Mediterranean, DASH, and Nordic diets have lowered systolic and diastolic BPs in adults. Further studies must be completed in children comparing the Mediterranean and

the DASH diet for treatment of O&MS in CKD and renal transplant with particular emphasis on reduction in caloric, sodium and phosphorus intake. DASH diet and low-salt diet are recommended in children with *O&MS and HTN*. Children with *glucose intolerance* or those at high-risk of *new onset diabetes after transplantation (NODAT)* should receive self-management information including healthy eating habits, portion sizes, and reading food labels and should be referred to an endocrinologist if lifestyle modifications are not effective. Medications that cause abnormal glucose metabolism including steroids and CNIs may need dose reduction or change to a different medication. However, tailored dietary assessment and counseling has so far not proven useful in children post-transplant.

Nutrition and exercise are the corner-stones of management of *dyslipidemias* with no proven role of **statins.**

There isn't much evidence supporting the use of statins in children with O&MS with or without kidney disease. Two small RCTs have compared statins to placebo in children with various kidney disorders (mainly nephrotic syndrome), with conflicting results in terms of lipid profile improvement. There is a lack of consensus among current guidelines.

Various systematic reviews have assessed the role of statin therapy in adult patients with CKD or following kidney transplantation. Only in patients with CKD not on dialysis and without CV disease at baseline was statin therapy found to reduce death, major CV events, and myocardial infarction. It is hard to extrapolate these adult studies to pediatric patients.

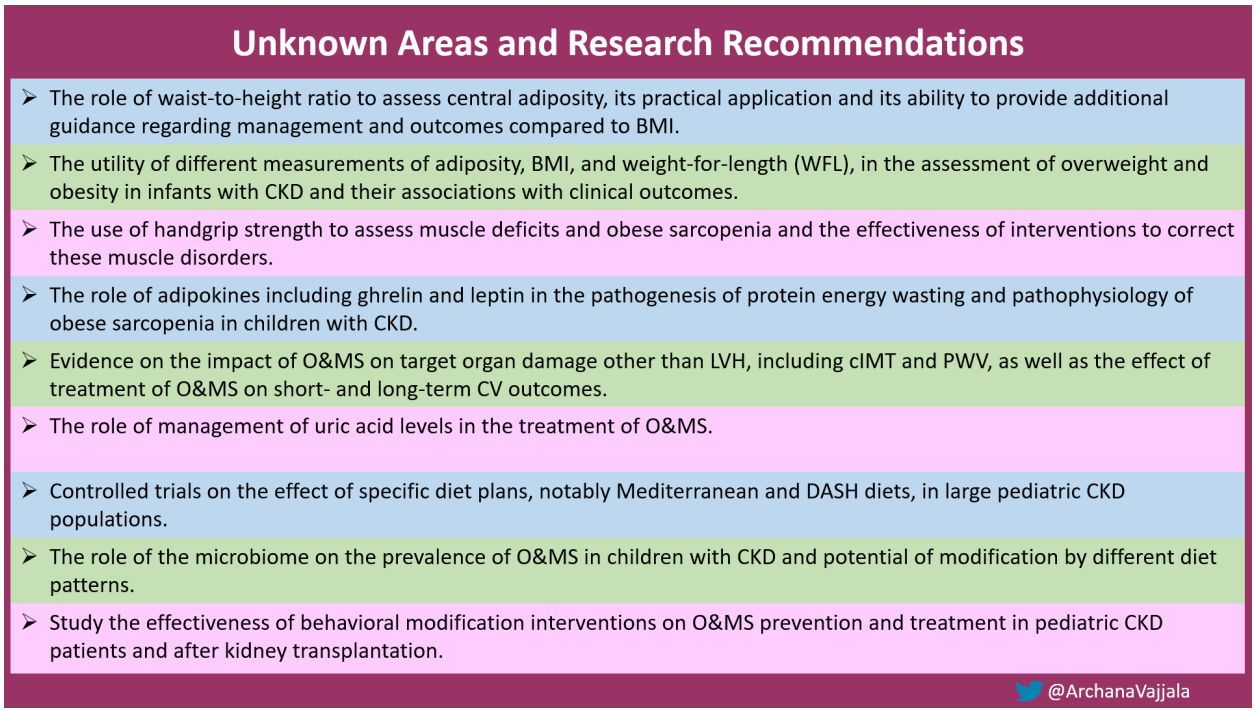
The 2013 KDIGO clinical practice guideline for lipid management in CKD don't suggest the initiation of statins or a statin/ ezetimibe combination in CKD patients under 18 years due to the lack of long-term safety data and the low level of evidence for benefit. Pharmacological treatment of hypertriglyceridemia in children with CKD, with fibric acid derivatives, niacin, and fish oil is debated. Finally, the evidence regarding the use of statins is extremely scarce and not specific for children with O&MS and CKD.

Bariatric surgery has been recommended by this taskforce in refractory cases (extreme obesity and associated co-morbidities including T2DM, severe steatohepatitis, pseudotumor cerebri, and moderate-to severe obstructive sleep apnea)when all other interventions have failed. Local expertise and legality may vary across countries.

Physical activity also needs to be tailored according to physical tolerance and should be individualized. Poor kidney function leads to reduced exercise tolerance due to the effect of anemia, ongoing inflammation and acidosis on skeletal and cardiac muscles. While, most adolescents agree to have increased screen time and less physical activity

as compared to their peers, nonetheless, strenuous exercise may result in worsening of preexisting metabolic acidosis.

Interventions in behavioral modification are currently a weak/ungraded recommendation by the PRNT. **Behavioral modifications** include regularized sleep, reduction in screen time, and psychosocial stressors as these factors can interplay with each other. Further studies need to be completed on poor sleep duration/quality in children with CKD in regards to O&MS. Currently, general pediatric studies have shown that longer sleep durations have been associated with lower adiposity scores. There is also limited evidence showing a direct correlation between increased screen time and cardiometabolic outcomes in those with CKD. Studies done in the adult population have also demonstrated the effects of **psychological stress** and emotional response on O&MS in those with CKD, but no assessment of these factors has been done in the pediatric population. **Anti- obesity medications** are not recommended. Orlistat is specifically associated with deposition of calcium oxalate crystals in kidney tubules.



To sum up-
Obesity and metabolic syndrome can impact kidney function and increase prevalence of CV risk factors, thus having a larger impact on children with CKD and those who have undergone kidney transplants. The PRNT has put forth CPRs defining, assessing,

managing, and preventing O&MS. A healthy diet, regular exercise, and behavioral modifications are recommended to help prevent and treat O&MS. Pharmacological and surgical treatment is recommended only in patients refractory to therapy. A multidisciplinary team based individualized approach is recommended.

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