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CKJ Review

CKJ REVIEW

Expert guidance on the multidisciplinary management of cystinosis in adolescent and adult patients

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ABSTRACT

Cystinosis, a rare autosomal recessive lysosomal storage disorder, results in an abnormal accumulation of the amino acid cystine in multiple organs and tissues of the body. Renal symptoms typically develop in the first few months of life, with extra-renal manifestations becoming apparent over the next 10–20 years, which require coordinated multidisciplinary care. Here, we describe a consensus-based guidance to support the management of adolescents and adults living with cystinosis. The programme was led by a Steering Committee (SC) of six experts in the management of patients with cystinosis, who identified a list of 15 key questions reflecting the multi-organ effects of cystinosis. An Extended Faculty (EF) of eight additional specialists was invited to answer the questions via an online digital platform

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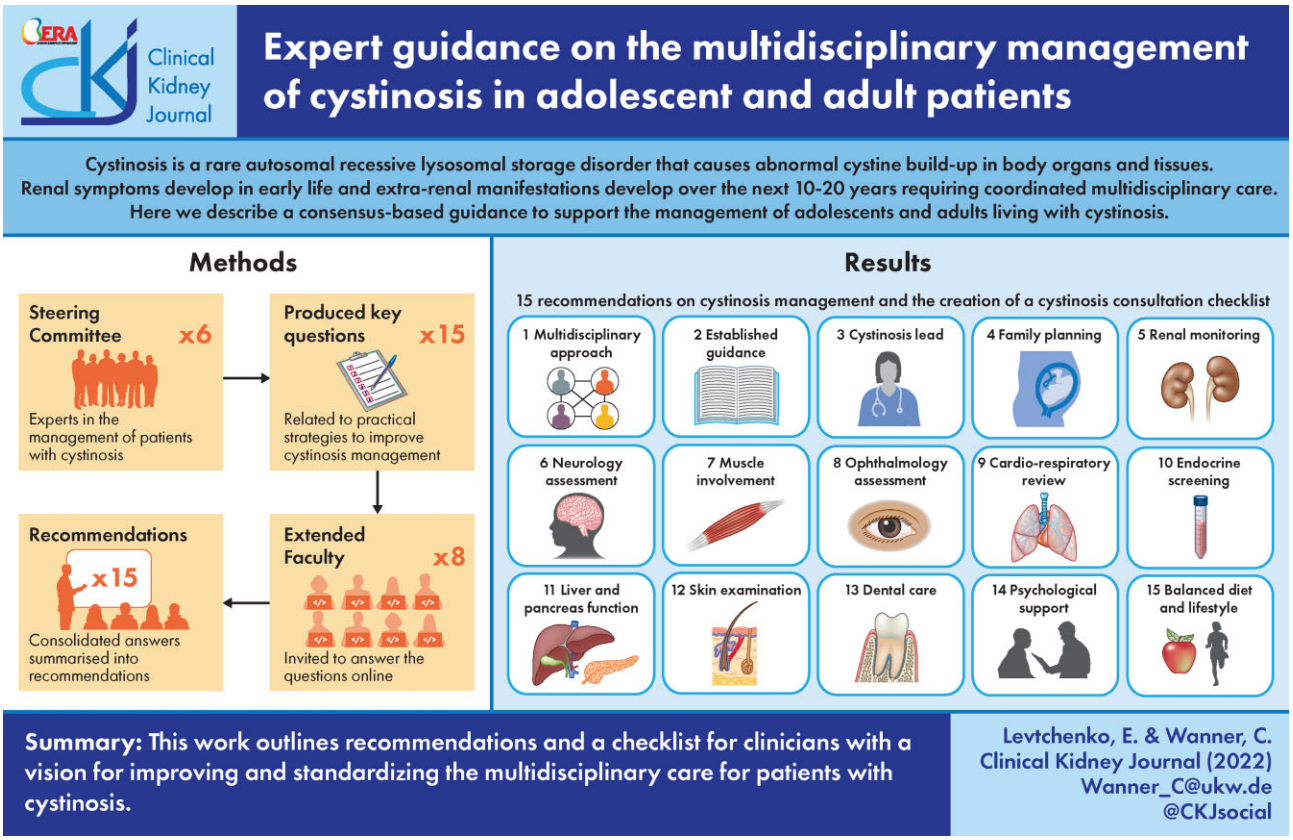
using a quasi-Delphi approach. The consolidated answers were summarized into recommendations. Where evidence was lacking, recommendations were developed using collective expert consensus. The EF was asked to agree/disagree with the clinical recommendations. The expert-agreed clinical recommendations provide guidance that considers both renal and extra-renal systems. The topics covered are advice on fertility and family planning, consideration of the nervous, muscular, ophthalmic, cardio-respiratory, endocrine, dermatological and gastrointestinal systems, as well as guidance on dental care, diet, lifestyle, and improving quality of life and psychological well-being. In summary, this work outlines recommendations and a checklist for clinicians with a vision for improving and standardizing the multidisciplinary care for patients with cystinosis.

GRAPHICAL ABSTRACT



Keywords: adult and adolescent, checklist, clinical recommendations, consensus statements, cysteamine, cystinosis, disease management, multidisciplinary care, rare diseases

INTRODUCTION

Cystinosis is a rare autosomal recessive lysosomal storage disease [1, 2], affecting between 1:150 000 and 1:200 000 live births, with a prevalence of approximately 1.6 per million [1]. The responsible gene, *CTNS*, encodes cystinosin, the lysosomal cystine carrier. As a result of a defective or absent cystinosin transporter, cystine accumulates within the lysosome, eventually precipitating as cystine crystals in almost all tissues and organs in the body, affecting their function [3, 4]. Cystine crystals have recently been shown to activate cells of the immune system potentially triggering a chronic inflammatory process, apoptosis and oxidative stress within affected cells [1, 5].

The *CTNS* gene is found on chromosome 17, and over 140 pathogenic mutations have been reported within the gene [6–8]. The most common mutation is a 57-kb deletion that encompasses the first nine exons and introns of *CTNS* and interrupts exon 10. This is present in >50% of patients of North European or North American origin [6].

Cystinosis can be classified into three main groups, largely based on the severity of symptoms and age of onset [6, 9, 10]:

- *Infantile nephropathic form:* The most frequent (95%) and severe presentation—includes renal Fanconi syndrome.
- *Juvenile nephropathic form:* Affects a small group of patients (~5%) and characteristically can present with proteinuria and mild or absent tubulopathy. It has a slower rate of progression but can still progress to kidney failure.
- *Ocular non-nephropathic form:* Rarely presents before adulthood. Typically involves presentation of photophobia due to corneal accumulation of cystine; however, the kidneys may still be affected.

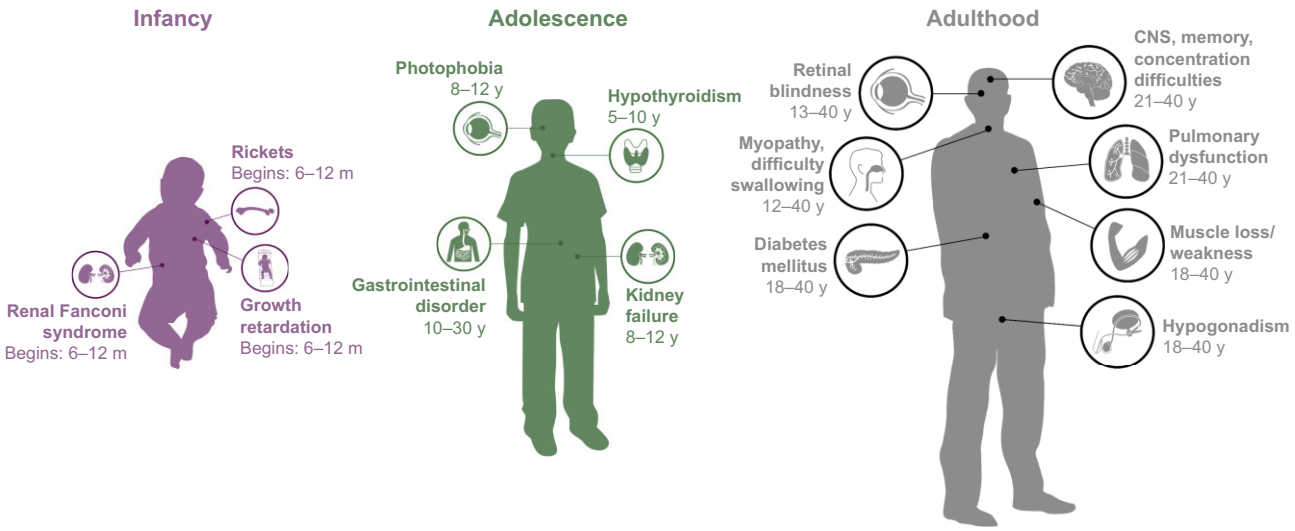


FIGURE 1: Typical progression of cystinosis that may be seen in patients who do not receive early and sustained cysteamine treatment.

The diagnosis is currently suggested by the detection of elevated cystine levels in white blood cells. Several biochemical methods are available to measure cystine levels, and this can give rise to variability in results across different test centres. Molecular testing of the *CTNS* gene is now a well-established diagnostic method [6, 9].

Cystinosis is a progressive disease that affects a number of organs (Figure 1). Typically, with the infantile nephropathic form of the disease, neonates have a normal birth weight and initial growth but begin to develop symptoms in the first few months of life. Their kidneys are the first organs to be affected with all cases developing renal Fanconi syndrome. Rickets and growth retardation are other common observations in the first 6–12 months of life, with corneal cystine deposits developing later [6]. If cystinosis is left untreated, or patients are treated late, or if the patient is non-adherent with treatment, end-stage kidney disease (ESKD) can develop before the 10th year of life [6]. The importance of these issues was recently demonstrated in a large cohort of cystinosis patients ($N = 453$), which highlighted the benefits of early diagnosis and cystine depletion therapy on patient growth and kidney function [11].

Throughout adolescence and into adulthood, extra-renal manifestations of cystinosis become apparent. These can include photophobia, thyroid dysfunction, hypogonadism and infertility (males), pancreatic dysfunction, hepatomegaly, splenomegaly, muscle atrophy/weakness, pulmonary dysfunction and neurocognitive abnormalities. These extra-renal complications of the disease often contribute to life-limiting disability and reduced life-expectancy [12].

There is a general lack of recognition of the systemic nature of cystinosis due to its rarity. Most individuals experience cystinosis metabolic bone disease often resulting in bone deformities, fractures, osteomalacia, osteoporosis and short stature in later life [13, 14]. Specific guidance on managing the effects of bone disease in cystinosis have been developed independently by a group of experts. They advise the rigorous treatment of rickets, the use of recombinant human growth hormone (rhGH) for short stature, physical therapy to strengthen musculature and improve skeletal deformities, and vitamin D supplementation in deficient patients, among their recommendations [14].

Not only does the systemic nature of cystinosis pose some challenges, but these effects often present during adolescence, creating further issues. Transition of adolescents from paediatric to adult services is often poor, particularly if there is limited knowledge of the disease due to its low prevalence. It can often occur during a period of fragility for patients and at a time when important choices such as transplantation are made. Adolescent-specific issues such as treatment adherence and an urge for independence can require an individualized approach, careful management and coordination. Consequently, during this specific period, it is vital that extrarenal disease complications are detected and monitored carefully. At present, advances on patient prognosis leads to a larger and increasing number of adolescents and adults with cystinosis. Thus, improvement of patient transition and multidisciplinary care has become a priority.

In order to address these unmet needs, we describe a Clinical Decision Support Programme (CDSP) led by an international group of experts, with the objective of creating guidance to support specialist and non-specialist clinicians in their daily clinical practice when treating adolescents and adults with cystinosis; thereby enhancing patient outcomes. The aim was to:

- Build upon existing guidance [1, 12–14] with practical advice and strategies that address the requirements of adolescents and adults living with the multi-organ effects of cystinosis.
- Provide knowledge for the healthcare professional on how best to support patients in the management of the disease and help to empower them as they grow older.

MATERIALS AND METHODS

The CDSP Programme was based on a quasi-Delphi methodology, which took place throughout 2018, 2019 and 2020. The process is outlined in Figure 2. A Steering Committee (SC) of six experts who treat patients with rare tubulopathies including cystinosis met together, and agreed that there was a need for a review of the existing guidance and to offer practical advice to improve clinical outcomes for adolescents and adults living with cystinosis.

The SC identified a list of 15 key questions related to practical strategies to improve the management of patients with this rare disease. An additional eight international experts (the Extended Faculty, EF) were invited to participate in the process by answering the questions via an online digital platform. Each EF member was able to review all comments and upload supporting

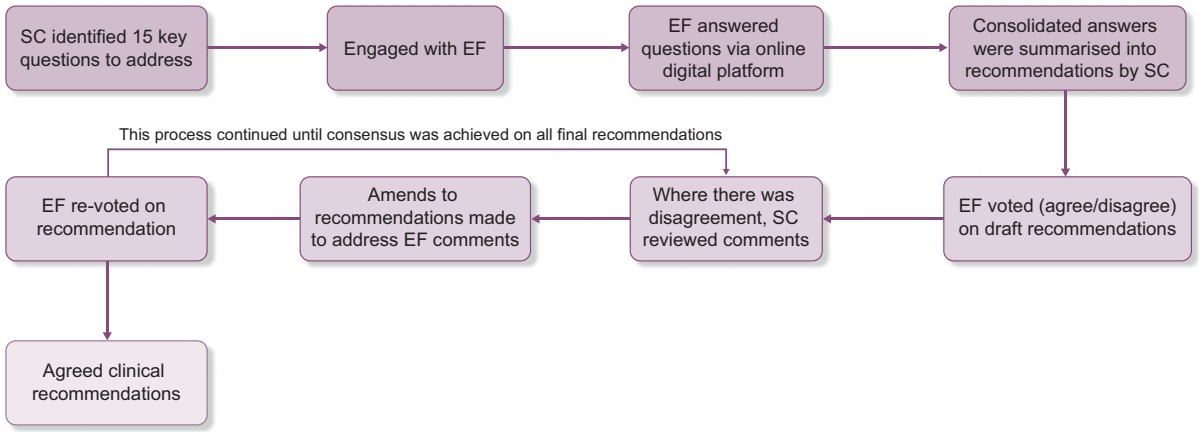


FIGURE 2: Consensus methodology overview; EF, extended faculty; SC, steering committee.

published evidence where available. The consolidated answers were summarized into recommendations by the SC.

Recommendations were supported by evidence-based clinical guidance and additional published data where possible. However, where such evidence was lacking, guidance was based on collective expert opinion. The EF was then invited to agree/disagree with the draft clinical recommendations. Where there was disagreement with the draft wording, the SC members reviewed the comments and made any necessary amendments. Recommendations were re-voted on, and this process continued until consensus was achieved on all final recommendations.

The Patient Advocacy Group, Cystinosis Network Europe (CNE), was asked to review the document and their suggestions were incorporated by the group of experts.

RESULTS

Consensus was achieved by the experts on all recommendations. In addition to the specific recommendations made here, all healthcare professionals caring for adults with cystinosis should consider each individual case on its own merits. For simplicity, the term 'adult' is further used to encompass both adolescents and adults.

In addition, a checklist based on these recommendations, to help clinicians during their routine consultations, has also been created. It is hoped that this checklist, combined with the recommendations outlined here, will provide a useful and valuable resource that helps clinicians to decide whether the patient requires further specialist care and support in addition to their regular disease management.

Recommendations

1. A multidisciplinary approach to cystinosis care

We recommend a multidisciplinary team to manage adult cystinosis patients, led by an identified clinical care coordinator (a nephrologist or metabolic specialist). We suggest that the following specialists comprise the team according to different healthcare systems: nephrologist, ophthalmologist, specialist renal nurse, metabolic specialist, neurologist and parent/family network. Others may include psychologist, pulmonologist, dietician (especially if the patient experiences weight loss, has diabetes mellitus and/or kidney failure), speech and language specialist, occupational therapist, orthopedic specialist, physiotherapist, a transition leader between paediatric and adult services, and a social worker as required. The recommended frequencies of review by key members of the multidisciplinary team are presented in Table 1.

However, we acknowledge that the frequency at which each specialist is involved should be tailored to the individual needs of the patient. We suggest that the patient should have regular consultations with a smaller core group of the team to foster a good relationship.

The patient themselves are central to any discussions and family/friends/caregivers should also be considered as part of the team, to be involved in decisions regarding their care with the consent of the patient.

Finally, good communication and networking between the local hospital and the specialist centre is crucial as patients may have to travel long distances to attend the specialist centre.

2. Recommended clinical guidance and resources around cystinosis

We suggest that healthcare professionals refer to previously published recommendations, such as the Nephropathic cystinosis Kidney Disease: Improving Global Outcomes (KDIGO 2016) [1] paper and Nephropathic cystinosis: an international consensus document [12] which together provide a good overview of the pathophysiology, diagnostics, monitoring and treatment of cystinosis in different age groups. In addition, specific recommendations should be used, such as those for adult and adolescent patients [13] and for the management of bone disease [14], as well as their own national guidance and local policies, to manage patients with cystinosis.

3. General considerations when treating a patient with cystinosis

There can be a lack of awareness of the short- and long-term consequences and multi-organ impact of cystinosis due to its rarity, even among adult nephrologists.

We advise that an identified adult nephrologist and/or specialist in metabolic diseases with specific experience of managing cystinosis, ideally based at a specialist centre, be responsible for the overall care of adults with cystinosis including coordinating extra-renal aspects. This will ensure that practical management strategies such as optimal cysteamine dosing regimens,

Table 1. Recommended frequencies of review by key members of the multidisciplinary team

Multidisciplinary team member	Frequency for review
Nephrologist	From 2 times/year to more if required
Metabolic specialist	At least annually, more frequently if required
Ophthalmologist	At least annually, more frequently if required
Specialist renal nurse	Always present to help coordinate and assist with patient queries and offer support (where available)
Cardiologist/cardiology input	As appropriate
Neurologist	At least annually, more frequently if required (unless no problem identified)

regular measuring of white blood cell (WBC) cystine levels, as well as awareness of the long-term consequences of the disease in the different organ systems, are adequately monitored. Other healthcare specialties may also be involved, for example to provide education and support post-transplant or to optimize patient adherence for the long-term.

All young adults with cystinosis should be transitioned from paediatric to adult care through a formal paediatric to adult transition service. This way, the impact of the disease in patients together with their adherence to therapy can be optimized to improve long-term outcomes.

4. Fertility and family-planning considerations

We recommend the following advice is offered to those persons with cystinosis wishing to start a family:

Women should be advised that the likelihood of becoming pregnant, including potential for a successful pregnancy outcome, is dependent upon their renal health. Women should be advised that they are fertile [15–18] and be signposted to appropriate contraception where indicated. A successful pregnancy outcome is achievable (dependent upon kidney health), but pre-pregnancy counselling is essential and should be provided by an experienced combined renal-obstetric service. They should be counselled in time that they will need to stop cysteamine treatment during pregnancy. Medications for all, including those who have been transplanted, will require adjustments throughout the pregnancy and will require experienced obstetric and nephrologist care. This care should be tailored throughout according to the individual patient's kidney function and extra-renal manifestations, as per conventional chronic kidney disease and post-transplant advice. Cysteamine treatment should be avoided during breastfeeding.

Males with infantile cystinosis were previously thought to be infertile, but some have fathered children through *in vitro* fertilization (IVF), after percutaneous epididymal sperm aspiration, using their own sperm [19]. A few male patients with cystinosis were reported to have viable sperm in ejaculate [20].

Additionally, potential preservation in a sperm bank could be a possibility. We advise that this option is considered early in selected patients wishing to have children. Sperm can be collected using testis or epididymis biopsy, or from ejaculate in a small selection of patients not having complete azoospermia.

We would also advise involving colleagues from other specialties, such as fertility specialists, endocrinologist and urologist, for further support and advice.

5. Renal considerations

We recommend routinely checking urinary albumin excretion, serum creatinine for calculation of estimated glomerular filtration rate (eGRF) values, to monitor kidney function, kidney damage and disease progression [1, 12, 13]. Serum creatinine may not correctly reflect kidney function in those patients with muscle wasting. The cystatin C-based equation for eGFR calculation might be more reliable in these patients; however, its utility in cystinosis needs validation. Healthcare professionals should bear in mind that closer monitoring may be required during periods of increased patients' vulnerability, for example immediately after diagnosis, with active Fanconi, during adolescence and with pre-dialysis treatment. All patients should have their cystine levels in WBCs monitored including those on dialysis and after kidney transplantation. Additional tests are advised according to individual patient needs and are summarized in Table 2.

6. The nervous system and neurocognitive aspects

Although there are different policies for monitoring the neurological impact of cystinosis in patients, we recommend the following routine neurocognitive assessments:

- Mini-Mental Status Examination (MMSE) or Montreal Cognitive Assessment (MoCA) to evaluate any reported problems with short-term memory, visual-motor coordination and signs of cognitive defect. The MoCA is a quick and easy to use cognitive screening tool with high sensitivity and specificity for detecting mild cognitive impairment, while MMSE is appropriate for patients showing more severe cognitive impairment [21].
- Brain magnetic resonance imaging (MRI) if any complaint of headache, symptoms of bradykinesia, stroke or potential cognitive deficit are reported by the patient.
- Appropriate referral to neurology colleagues as required.

Regular consultation with the neurology team is recommended in order to highlight and recommend where further neurological evaluation is required and follow up is maintained. However, we acknowledge that the frequency of the neurology assessment will vary from centre-to-centre and from country-to-country.

For more detailed information, please see Table 3.

7. Muscle involvement

Typically, the signs/symptoms of the onset of muscle involvement in cystinosis are distal muscle weakness and wasting in the upper and lower limbs. Swallowing difficulties and oral dysfunction tend to appear later. Patient follow-up for muscle involvement is exclusively clinical. During history-taking with each patient, we recommend assessing patient-reported difficulties with chewing, aspiration, dysphagia, excess of saliva, weight loss, mealtimes of long duration and respiratory symptoms including infection. Based on the reported history, we suggest specific tests such as: video-fluoroscopy of swallowing or fiber-optic endoscopic evaluation of swallowing.

As the nature of histological lesions are already well known in cystinosis (due to vacuolar myopathy), there is limited value in obtaining such histological information from the patient. We

Table 2. Recommendations for renal monitoring and management in specific patient populations

Patient population	Monitoring/management recommendations
Patients with Fanconi syndrome	• Use of supplements is recommended to control acidosis, chronic hypokalemia, hypophosphatemia and carnitine deficiency, if present • The use of indomethacin in adults is not recommended
Patients on dialysis	• Both dialysis modes are suitable depending on the medical and social situation of the patient • For patients on haemodialysis, tailoring the ultrafiltration and monitoring of potassium and phosphate levels by adapting supplementation accordingly is advised • Closely monitor electrolytes and acidosis, residual urine volume and other late complications of the disease • Make patients aware that transplantation may be their best treatment option • Cysteamine treatment should be continued in patients on dialysis to protect extra-renal organs o There is no evidence to support the need to adjust cysteamine dose in these patients
For patients after kidney transplantation	• Follow current guidance on post-transplant kidney function monitoring with specific attention to polyuria immediately post-transplantation • Begin cysteamine treatment as soon as oral medication can be administered o Implement strategies to promote patient adherence post-transplant

Table 3. Supplementary guidance for the nervous system

Specific area of interest	Recommendation
Central nervous system	• Clinical examination should be undertaken • Any history of headache investigated (as intracranial hypertension may be observed) • Regular ophthalmological examinations are needed (to exclude pseudotumor cerebri) • Presence of pyramidal or cerebellar syndrome, bradykinesia, and other focal features suggestive of stroke should be investigated • The MMSE should be used to evaluate potential cognitive defect • Brain MRI can be performed to look for brain atrophy, white matter signal anomalies, or ischaemic lesions; calcifications may be observed by tomodensitometry
Peripheral nervous system	• Use of a rating scale is recommended to evaluate and monitor signs and symptoms in chronic muscular disorders
Neurocognition	• The MMSE or MoCA (Montreal Cognitive Assessment) should be used for neurocognitive evaluation, particularly if there is some relevant patient complaint (for example, underperforming in school, visuo-spatial or behavior issues). Must include assessment of visual-spatial abilities, visual-motor coordination, and short-term memory evaluation
Further neurological evaluations	• Swallowing test • MMSE • Motor Function Measurement • 6 Minute-Walking-Test • Cranial MRI • ENMG

do not recommend performing muscle biopsy during routine patient follow-up.

Although different policies exist, when monitoring the impact of cystinosis on patients' muscles we recommend that electroneuromyography (ENMG) is used. For additional details on ENMG and a Test of Masticating and Swallowing Solids (TOMASS) [22], please see Table 4.

The frequency of assessments should be tailored to individual patient's need and clinical change. Frequent exercise should be encouraged with access to physiotherapy as required. Specific management for the effects of bone disease in patients with cystinosis has been previously outlined; it includes treatment with phosphate, bicarbonate/citrate and vitamin D replacement for rickets, and rhGH for short stature [14].

For supplementary data, see Table 3.

8. Ophthalmological considerations

We recommend that the ocular signs and complications of cystinosis are assessed by an experienced ophthalmologist. The frequency of ophthalmology examination should be tailored according to the needs of the patient and also based on the evaluation of clinical signs, typically 6 months to a year, but

Table 4. Supplementary data on ENMG and testing for swallowing problems

Specific area of interest	Recommendation
ENMG	• May be performed: o At baseline when signs of muscle weakness and wasting appear o Not as part of routine follow-up, but to differentiate muscle or peripheral nerve involvement
Swallowing problems	• May be best assessed by a swallowing test and video fluoroscopy • The Test of Masticating and Swallowing Solids (TOMASS) may be used [22] o Drink 100 mL of water; measure duration of drinking (choking present?) o A cracker (standardized; 5 cm^2) is offered, with the request: 'Please eat this as soon as you can' o After eating, the subject is asked to say their own name (assessment of voice) o Analysis and scoring: video recording, number of bites, chewing movements, swallowing movements, total duration of eating • Video fluoroscopy provides a moving image of swallowing in real time

Table 5. Supplementary data on ophthalmological considerations

Assessment	Recommendation
Ophthalmology assessment	• Minimum requirement: o Examination of the eyes with digital images from a slit lamp and fundus photography • Full ophthalmological examination: o Anterior and posterior segments, combined with complementary examinations ☐ Anterior-segment and/or posterior-segment optical coherence tomography (OCT) ☐ Visual field, if necessary
For the anterior segment	• Assessment should include: o Photophobia o Visual acuity test o Slit lamp examination for corneal depositions/neovascularization/keratopathy o Intraocular pressure (IOP)
For the posterior segment	• Despite photophobia symptoms, dilated fundoscopy is advised to investigate: o Crystals, particularly on the surface of the retina o Depigmentation o Pigment epithelial alterations o Affected vasculature

We note that although *in vivo* confocal microscopy are superior imaging techniques, it is not widely available outside of specialist centres. However, many ophthalmological centres are equipped with anterior-segment OCT to assess the extent of cornea crystal infiltration.

occasionally every 3 months [23]. We recommend that findings are documented with digital images as standard-of-care to monitor changes over time. For additional information on ophthalmology assessments, see Table 5.

We also advise that change in cornea assessments such as Gahl's score and photophobia score is indicative of patients' adherence with cysteamine eye-drops regimen and is a useful monitoring tool [24, 25]. Complaints related to cystinosis-associated ocular surface disease are frequent and can be improved by using artificial tears, anti-inflammatory agents or other local treatment related to the cornea complications due to the ocular cystinosis.

9. Cardio-respiratory considerations

In addition to routine pre-, post-transplant and dialysis cardiac care, patients with cystinosis should have an annual cardiology and respiratory review (whether symptomatic or asymptomatic) to determine which further investigations are required.

Optimal blood pressure management is required as many patients become hypertensive over time. As there is likely to be intervertebral muscle involvement in cystinosis, we recommend spirometry tests and specialist referral if dyspnea or obstructive lung disease is observed.

10. Endocrine aspects

We recommend regularly monitoring cystinosis patients for the following endocrine disorders: hypothyroidism, diabetes mellitus (especially in transplant patients) and hypogonadism.

We advise that annual laboratory tests for adults include thyroid function tests, fasting blood glucose and hemoglobin A1c (HbA_{1c}). Bone metabolism and sex hormone tests should be performed as clinically indicated. For supplementary data on monitoring/management of endocrine disorders, see Table 6.

11. Gastrointestinal and hepatological involvement

We recommend performing systemic liver function tests once a year unless new symptoms of hepatomegaly and/or hepatosplenomegaly are apparent and require referral. Since these complications are less common in adult cystinosis patients, we recommend that annual liver function tests (LFT), alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyltransferase (GGT), alkaline phosphatase (ALP), as well as lipase, are sufficient to monitor for liver and pancreas

Table 6. Supplementary recommendations and guidance for endocrine aspects

Endocrine disorder	Recommended monitoring/management
Hypothyroidism	• Thyroid function tests should be performed every 6 months from an early age using total thyroxine (FT3, T4) and thyroid-stimulating hormone (TSH) thyroid supplementation may be required
Diabetes mellitus	• Fasting blood glucose and hemoglobin A1c (HbA_{1c}) should be checked at every visit, ideally 3–6 monthly • May be necessary to alter immunosuppressive calcineurin inhibitor (CNI) regimens in transplant patients or to initiate insulin therapy
Hypogonadism	• Gonadal function tests in males should be performed annually (testosterone, Inhibin B, luteinizing hormone (LH), follicle stimulating hormone (FSH) • Testosterone replacement therapy may be used to restore secondary sexual characteristics in adolescent male patients, and for a limited time in some individuals to improve growth and final height (following expert guidance) • It is important to test regularly in boys in case testosterone replacement therapy is required when puberty is delayed. If appropriate, discussions on banking sperm may be considered • Patients should be given appropriate fertility counselling

dysfunction. If hepatomegaly or splenomegaly is apparent, we suggest using ultrasound together with LFTs in collaboration with a GI specialist.

It is worth noting that gastrointestinal side effects such as heart burn (acid reflux) can be caused by the treatments, e.g. cysteamine and potassium bicarbonate/citrate.

12. Dermatological considerations

We recommend annual skin examinations by a dermatologist in adult cystinosis patients, especially in those that have undergone a transplant. Skin examination can easily be performed in an out-patient visit. It is important to check regularly for skin lesions and striae (or bruising-like lesions) that can indicate cysteamine toxicity and requires prompt clinical evaluation [26]. All patients should be advised on the use of high-protection sunscreen.

13. Dental care

We recommend rigorous dental hygiene and regular dental check-ups in cystinosis patients to monitor for dental complications, such as enamel defects and caries, which can occur frequently due to the disease-related acidosis, rickets and impact of associated CKD on bones, as well as the large doses of potassium, citrate and bicarbonate supplements required by patients [27].

14. Quality of life and psychological well-being

Patients with cystinosis require a multi-faceted psychological and psychosocial support strategy. This should be coordinated through the identified clinical care coordinator, such as the adult nephrologist.

Some patients benefit from patient support groups, but others may prefer online forums, particularly if they need to travel long distances to specialist centres. The patient's family and wider support network should also be involved where possible.

We recommend the following psychological support is offered to adult patients with cystinosis, to improve adherence to treatment and quality of life [28]:

- A multidisciplinary, multiprofessional team approach to management, where all members are familiar with key aspects of the disease.
- An identified clinical care coordinator, e.g. adult nephrologist, or specialist in metabolic disease.
- Involvement of the patient's family, with provision of education and psychological support to them.
- Specific psychological support to cope with all aspects of the disease (numerous medications, early complications, long-term risks, psychosocial integration, anxiety, depression, burn-out, stigmatization, late-onset systemic abnormalities, work, partnership, insurances, legal issues, long-term disabilities).
- Use of validated screening tests to monitor patient's psychological well-being.
- Improved access to information.
- Access to social services support.
- Access to occupational therapy.
- Access to patient advocacy groups and/or online forums.

For supplementary data on validated screening assessments of psychological well-being, see Table 7.

15. Diet and lifestyle

Reduced appetite and weight loss are common problems encountered by patients with cystinosis. As a result, dietary restriction is unnecessary unless the patient has either diabetes mellitus, CKD or ESKD where relevant guidance should be followed. Diet and lifestyle are also especially important in transplanted patients, including regular physical activity.

We recommend emphasizing the importance of a balanced diet with normal for age and physical activity calories intake and avoiding dehydration to the patient at each consultation. It is important to have a good rapport and honest discussion with patients about how diet and lifestyle impact on their long-term outcomes.

If a problem is highlighted or suspected, patients should be encouraged to provide a dietary history at every meeting and their diet monitored with laboratory tests. Common targets should be defined, and the patient's efforts should be acknowledged at these visits.

We advise that individual dietary issues be treated in collaboration with a specialist dietitian, and personalized support is provided to patients via a nutritional support team on an individual basis as required.

Table 7. Supplementary recommendations and guidance for monitoring psychological well-being

Area of interest	Things to monitor and available resource
Validated screening tests	• Motivational interviewing [29, 30] • Screening for wellbeing; depression; anxiety [31–33] • Screening for disease-specific quality of life [34] • Screening for generic quality of life [35]
Psychosocial aspects that can have a negative impact on adherence and quality of life (QoL) [36, 37]	• High prevalence of depression and anxiety • Stigmatization due to short stature and halitosis—consequence: social anxiety and reduced social inclusion • Difficulties in solving typical developmental tasks of young adults (leaving parent's home, autonomy, financial independence, forming partnerships)
Additional resources used to support patients	• Education on practical aspects of therapy in everyday life (e.g. how to communicate about the disease, side effects of medication, reminders for medication, autonomy from parents, university, professional life, legal rights, how to make informed decisions about their care) • Structured transition programme [38] • Regular screening for low QoL, reduced well-being. [Patient Health Questionnaire (PHQ); Hospital Anxiety and Depression Score (HADS) or World Health Organisation-5 Wellbeing Index (WHO-5)] [31–33] o A disease-specific questionnaire (for cystinosis) has not yet been developed • Psychological support on how to cope with disease-specific distress, anxiety/depression, dependency on assistance, ideas on social and professional integration • Sharing experiences on websites, chat groups for patients o Not every person with cystinosis wants to be part of this community • Patient empowerment with patient-centered communication (motivational interviewing); possible as web-delivered intervention [39] • Written patient information and resources on https://cystinosis.org/ • The European cystinosis network at http://cystinosis-europe.eu can direct patients to information within their own countries

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

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